

Production of Quasi-monodisperse Emulsions with Large Droplets Using a Micromachined Device

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ABSTRACT: The development and operation of a modified method for the preparation of quasi-monodisperse (CV < 16%) emulsions are reported. The device uses a microfabricated-nozzle (MN) array, produced by micromachining technology, to achieve a higher rate of emulsification [76.8 m³/(m²·h)] than previously reported for microchannel (MC) emulsification methods. The dispersed phase is extruded into a continuous phase through the MN, and the emulsion droplets are formed by viscous drag force of the continuous phase. The droplet diameter decreased with an increase in the flow velocity and viscosity in the continuous phase, which was explained by the theoretical model. The range of droplet diameters produced (130 to 370 μm) was larger than in previously reported MC emulsification, membrane emulsification, and shear-rupturing methods.

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Emulsions have been widely used in various industries, including foods, cosmetics, and pharmaceuticals. Many of the most important properties of emulsion-based products (e.g., shelf life, appearance, texture, and flavor) are determined by the size of the droplets they contain (1). Emulsions are conventionally prepared by using colloid mills, rotor-stator systems, and high-pressure homogenizers. Emulsions produced by these methods are polydisperse and require high energy input (2).

Several methods have been developed for preparing quasi-monodisperse emulsions. Nakashima *et al.* (3) developed a membrane-emulsification process for producing monodisperse emulsions (CV of 10–20%). This technique is applicable to both oil-in-water (O/W) emulsions and water-in-oil (W/O) emulsions (4,5). The emulsion droplet size is controlled by the size of the membrane pore (3), the dispersed-phase flux, and the continuous-phase flux (6–11). The rate of emulsion formation is determined by the flux of the dispersed phase. In membrane emulsification, the maximum flux of the dispersed phase for an emulsion containing 25% volume fraction is 3.55

m³/(m²·h) (4). A different method has been proposed to produce quasi-monodisperse emulsions by shear rupturing in Couette flow (12–14). In this method, quasi-monodisperse emulsions are produced through droplet rupturing in viscoelastic fluids. The rate of emulsion production for this technique is 1 to 2 L/h for an emulsion containing 70 to 85% volume fraction of oil phase (14).

Recently, we proposed a novel method for making monodisperse emulsion droplets from a microfabricated channel (MC) array (15), i.e., MC emulsification. Emulsions with a CV of 5% (16) and droplet sizes of 3 to 100 μm (17,18) have been prepared successfully using this technique. As the driving force for droplet formation, MC emulsification exploits interfacial tension, the dominating force on a micrometer scale. During droplet formation, the distorted dispersed phase is spontaneously transformed into spherical droplets by interfacial tension (16). Droplet formation by spontaneous transformation at a high production rate is difficult, since in theory there is a higher limit for the flow rate of the dispersed phase (19). In using MC emulsification, the production rate for an emulsion containing a 25% volume fraction of oil phase is 0.4 to 4 mL/h. For scaling up, we recently proposed an array of microfabricated through-holes of uniform size (20). In through-type systems, in which 10,000 of the through-type MC were fabricated on a 1.0 × 10⁻⁴ m² plate, the droplet formation volume rate was 26 mL/h/MC plate for an emulsion containing a 25% volume fraction of oil phase. Further scaleup is required for the industrial application of these methods for preparing emulsions with a narrow size distribution.

In this study, we proposed a novel microfabricated-nozzle (MN) array system in which the droplet formation mechanism was different from MC emulsification. With this device, droplets were formed by the viscous drag force caused by continuous-phase flow, which enabled us to prepare quasi-monodisperse emulsions at high productivity rates.

EXPERIMENTAL PROCEDURES

Materials. Soybean oil was purchased from Wako Pure Chemical Industries (Osaka, Japan) and used for the dispersed oil phase. Sodium alginate was obtained from Kimica

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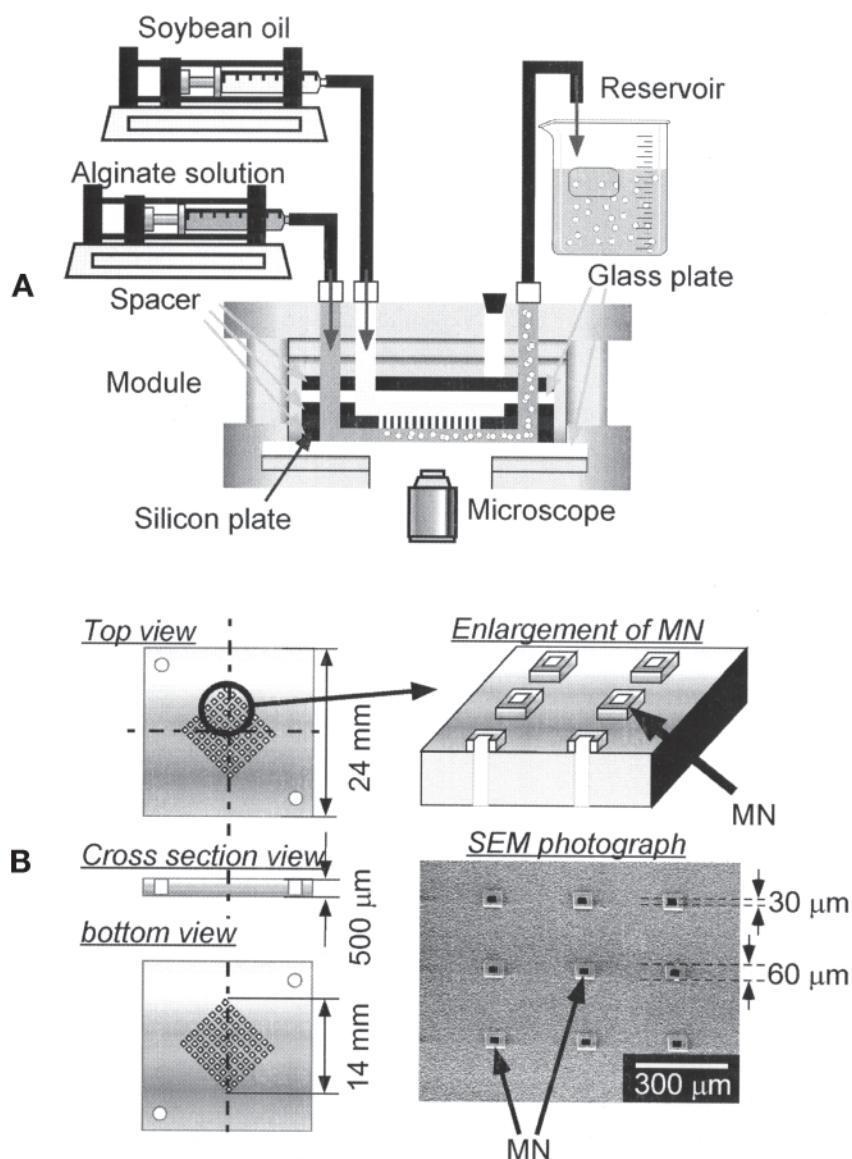


FIG. 1. (A) Schematics of experimental equipment; (B) silicon plate and scanning electron microscopy photograph of a microfabricated-nozzle array.

Corporation (Tokyo, Japan) and dissolved into the continuous water phase to control the viscosity. SDS was purchased from Wako Pure Chemical Industries and used as the surfactant for emulsification.

Measurements and analytical method. The interfacial tension was measured with a fully automatic interfacial tensiometer (PD-W; Kyowa Interface Science Co., Ltd., Saitama, Japan) using a pendant drop method. The viscosities of the continuous phases were measured with a Cannon-Fenske capillary viscometer (SO No. 50, 100 and 200; Shibata Scientific Technology Ltd., Tokyo, Japan). The densities were measured with Wadon-type pycnometers. Scanning electron microscopy photographs of the silicon plate were taken with a JSM-5600LC (JEOL Ltd., Tokyo, Japan). The optical microscope photographs of the prepared emulsions were taken with a DMIRM microscope (Leica Microsystems AG, Wetzlar, Germany) and

used to determine the average droplet diameter and CV (16). Winroof (Mitani Corporation, Fukui, Japan) software was used to analyze the captured pictures.

Emulsification. Figure 1A schematically illustrates the experimental equipment for the emulsification system. The laboratory-scale apparatus for preparing emulsions consists of a silicon MN array, a module, and syringe pumps supplying continuous and dispersed phases. The silicon plate on which MN are fabricated is attached to the module with rubber spacers. The flow channels for the dispersed and continuous phases are formed with rubber spacers. The emulsification behavior is observed through the glass plate using a microscope. The dispersed phase supplied from syringe pumps is extruded into the flow of the continuous phase through MN, and droplets are formed. The formed droplets are recovered by the continuous-phase flow.

Figure 1B schematically depicts the MN array fabricated on

TABLE 1
Viscosity and Interfacial Tension with Different Compositions of the Continuous Phase

Continuous phase		Viscosity (mPa·s)	Interfacial tension (mN/m)
Alginate concentration (%)	SDS concentration (%)		
0	1.0	0.9	5.9
0.1	1.0	1.8	5.8
0.5	1.0	9.3	4.8
1.0	1.0	32.5	3.9
1.5	1.0	77.3	3.7

the silicon plate. The MN are fabricated by photolithography and a two-step deep reactive ion etching process (19). The microfabricated nozzle is square and has internal dimensions of $30 \times 30 \mu\text{m}$, external dimensions of $60 \times 60 \mu\text{m}$, and a nozzle height of $15 \mu\text{m}$.

RESULTS AND DISCUSSION

Table 1 shows the viscosity of the continuous phase and the interfacial tension for each experimental formulation. The viscosity at the continuous phase increased significantly with increasing alginate concentration. The interfacial tension decreased with increasing alginate concentration in the continuous phase.

Figure 2 presents microscope photographs of the droplet formation process and prepared emulsions at different alginate concentrations. The flow rate of the dispersed phase was 5 mL/h , and the flow velocity of the continuous phase was 103 mm/s corresponding to a 1200 mL/h flow rate of the continuous phase. At 0 and 0.1% alginate concentrations, droplets were successfully formed from MN as shown in Figures 2A and 2B. The dispersed phase was sheared by the continuous-phase flow, and droplets were formed on the surface of the silicon plate. Although some droplets collided with each other, no coalescence was observed as a result of the presence of surfactant. The prepared emulsions at 0 and 0.1% alginate concentrations are shown in Figures 2C and 2D. The number-average diameters and CV of the emulsions

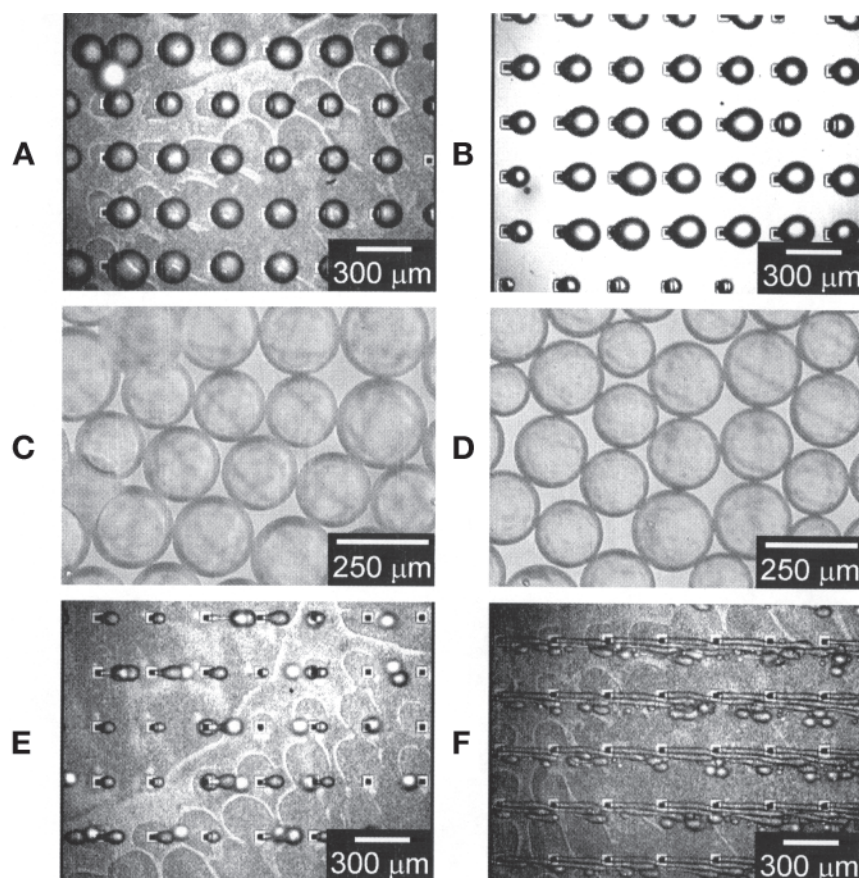


FIG. 2. Microscope photographs of the droplet formation process (A, B, E, F) and prepared emulsions (C, D) at different concentrations. Concentrations of alginate were 0 (A, C), 0.1 (B, D), 0.5 (E), and 1.0% (F).

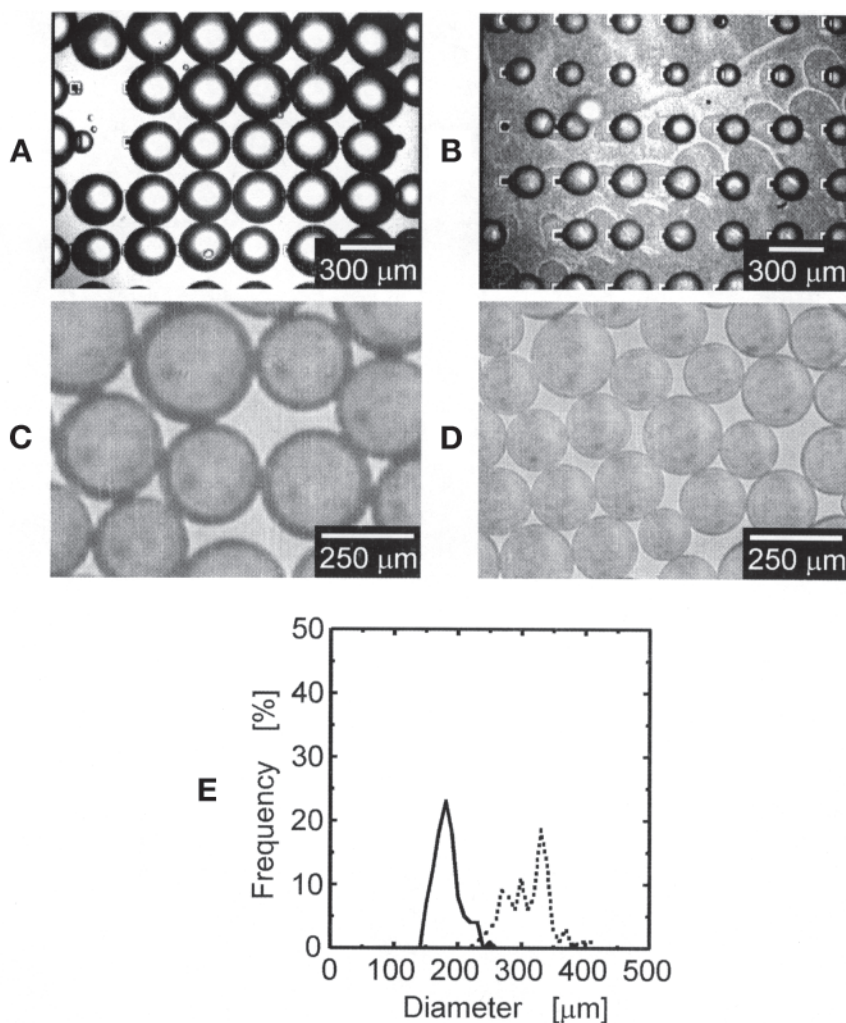


FIG. 3. Droplet formation behavior and emulsions prepared at different flow velocities of the continuous phase. (A, B) Microscope photographs of droplet formation behavior. (C, D) Microscope photographs of prepared emulsions. (E) Diameter distributions of droplets. Flow velocities of the continuous phase were 51.3 (A, C, dotted line in E) and 154 mm/s (B, D, solid line in E).

were 210 μm and 9.5% for 0% alginate concentration, and 186 μm and 11.3% for 0.1% alginate concentration. At 0.5% alginate concentration, the dispersed phase was extended slightly downstream of the continuous phase, as shown in Figure 2E. At 1.0% alginate concentration, the dispersed phase was extended downstream of the continuous phase over the next MN, as shown in Figure 2F. At 1.5% alginate concentration, the dispersed phase was extended downstream of the continuous phase in a similar manner. Under these conditions, the viscous force dominated the interfacial tension force.

During droplet formation, emulsion droplets are produced by the viscous drag force of the continuous phase, and the droplet diameter is determined by the balance of this against the interfacial tension. We investigated the effects of flow velocity of the continuous phase on the droplet formation process and on the emulsion produced. The alginate concentration in the continuous phase was 0% in both cases, and the flow rate of the dispersed phase was constant at 5 mL/h. Figures 3A and

3B show the droplet formation process at 51.3 and 154 mm/s flow velocity of the continuous phase (i.e., flow rates of 400 and 1200 mL/h). Figures 3C and 3D show the corresponding emulsions produced. The number-average diameters and CV of the emulsions were 310 μm and 11.4% at 51.3 mm/s, and 183 μm and 11.6% at 154 mm/s. Figure 3E shows the diameter distributions of emulsions for different flow velocities of the continuous phase. The droplet diameter decreased significantly with increasing continuous-phase flow.

Figure 4 shows the effects of flow velocity and viscosity of the continuous phase on the droplet diameter distribution. The flow rate of the dispersed phase was constant at 5 mL/h. The diameters of the prepared emulsions ranged from 130 to 370 μm, and the CV were less than 16%. The droplet diameter decreased with increasing flow velocity of the continuous phase. In addition, the droplet diameter slightly decreased as the viscosity of the continuous phase increased. In contrast, the CV was almost constant, independent of the continuous-phase flow velocity and viscosity.

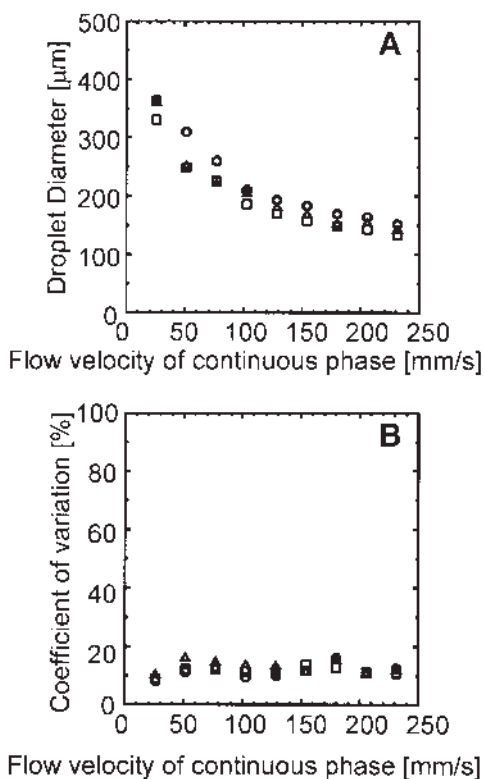


FIG. 4. Effects of flow velocity and viscosity of the continuous phase on droplet diameter (A) and on the CV (B). The continuous phase composition is SDS 1% (○), SDS + alginate 0.05% (△), and SDS 1% + alginate 0.1% (□).

The interfacial tension forces (F_i) working on the droplet are estimated by following equations (21):

$$F_i = \gamma \pi d \quad (1)$$

where d is the equivalent diameter of the nozzle and γ is the interfacial tension. Viscous drag forces (F_v) working on the droplet are estimated by the following equations (22):

$$F_v = \int_S \frac{1}{2} \rho V^2 f dS \quad (2)$$

where ρ is the density of fluid of the continuous phase, V is the flow velocity of the continuous phase, S is the droplet projection area perpendicular to the continuous phase, and f is the friction factor expressed by the following equation when the Reynolds number (Re) ranges from 2 to 500 (22):

$$f \approx \frac{18.5}{Re^{3/5}} \quad (3)$$

The Re is defined as follows:

$$Re = \frac{\rho VD}{\mu} \quad (4)$$

where D is the slit width between the silicon MN plate and the glass plate and μ is the viscosity of fluid of the continuous-phase. The droplet diameter is determined by the balance be-

tween F_i and F_v . Although it is difficult to determine F_v analytically, it is obvious that F_v increases with increasing flow velocity and viscosity of the continuous phase. Consequently, the droplet diameter decreases. These results are consistent with the experimental results shown in Figure 4. In this study, Re for the continuous phase flow ranged from 13.6 to 123, which means the continuous phase flow is laminar. A laminar flow provides a stable shearing force, which leads to stable droplet formation. In addition, the system leads to minimal energy input during emulsification compared with the conventional emulsification technique. The nozzle size d affects the F_i as shown in Equation 2, which indicates that the droplet diameter is controlled by the nozzle size.

The droplet diameter range of the present system (130 to 370 μm) is a larger range than MC emulsification (1 to 100 μm), membrane emulsification (1 to 50 μm) (6), the shear-rupturing method (0.3 to 10 μm) (14), and the spinning membrane method (0.1 to 6 μm) (23). Generally, droplet diameter is controlled by the MC structure in MC emulsification (24). Therefore, precise microfabrication of the MC plate is required to prepare different-sized droplets. In contrast, the present system enables us to control the droplet diameter by changing the flow velocity of the continuous phase without reproducing an expensive MN plate. The CV of the prepared emulsions was less than 16%, which was similar to those of membrane emulsification and the shear-rupturing methods. It was not as good as previously reported for MC emulsification. The present system utilizes viscous drag force as shearing force, which allows high productivity, whereas fluctuation of the continuous phase flow induces inhomogeneous droplet formation. It results in higher CV than MC emulsification.

Emulsion productivity was determined by the flow rate of the dispersed phase. In the present system, stable droplet formation with a CV less than 20% is possible up to a 180 mL/h dispersed phase flow rate, which corresponds to emulsion productivity of 720 mL/h for an emulsion of 25% volume fraction when the flow velocity of the continuous phase is 103 mm/s and the alginate concentration of the continuous phase is 0%. The emulsion productivity of the present system is much higher than for MC emulsification. The droplet formation in the present system is caused by shearing with laminar flow, which leads to higher productivity as compared to MC emulsification, in which droplets are formed by spontaneous transformation. The emulsion productivity is not so high compared with the membrane-emulsification and shear-rupturing methods. The present system has 104 active nozzles for droplet formation. The 104 nozzles occupy 2.4×3.9 mm on a 24×24 mm silicon plate. The productivity of alginate droplets from the unit area is $76.8 \text{ m}^3/(\text{m}^2 \cdot \text{h})$ for a 25% volume fraction. Compared with membrane emulsification, in which the maximum flux of dispersed phase was $3.55 \text{ m}^3/(\text{m}^2 \cdot \text{h})$ for the emulsion containing 25% volume fraction (4), the system we studied has the possibility of higher emulsion productivity. The module used in this study has a thin (500 μm) slit as the continuous-phase flow channel. This thin channel for the continuous phase leads to an effective utilization of viscous drag force by the continuous-phase flow, and it results in the high productivity

per unit area. Compared with the shear-rupturing method, a silicon chip with an MN array larger than 15 cm² enables us to achieve the same productivity level.

The monodisperse emulsions with large droplets prepared in this study are useful as precursors of microcapsules and microparticles because monodisperse microcapsules and microparticles with diameters of 10 to 300 μm are difficult to produce. They are expected to be applied in various industrial fields such as fine chemicals, cosmetics, and pharmaceuticals.

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