RECENT DEVELOPMENTS IN MANUFACTURING MULTIPLE EMULSIONS USING MEMBRANE AND MICROFLUIDIC DEVICES

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1.1 Emulsification Processes and Equipments

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Keywords: membrane emulsification; microfluidics; microcapillary device; multiple emulsion; uniformly sized drops

Abstract

Membrane and microfluidic devices are new routes for controllable production of multiple emulsions with uniformly sized drops and accurate control of the internal drop structure. Membrane emulsification involves injecting single emulsion through a porous membrane into continuous phase in a stirred cell or cross-flow membrane module. In this work an alternative method to generate shear at the membrane surface was applied, based on the low frequency oscillation of the membrane at 10-90 Hz in a direction perpendicular to the flow of the injected phase. The advantage of oscillating membrane technique is that the risk of the drop breakage in the continuous phase is minimal, because the shear is generated only at the membrane surface. The oscillation signal was provided by an audio generator which fed a power amplifier driving the electro-mechanical oscillator on which the inlet manifold was mounted. The membrane was a microsieve-type membrane with regular pore spacing formed by Ni electroforming. At the constant maximal shear stress at the membrane surface the mean size of oil globules in W/O/W emulsions decreased with increasing the amplitude of oscillation. The most narrow drop size distribution with a span of 0.36 was obtained at 70 Hz and the peak amplitude of about 0.4 mm.

A disadvantage of membrane emulsification is that the internal drop structure cannot be accurately controlled. Microfluidic devices with co-axial glass microcapillaries developed in Weitz Lab have been found convenient for controllable generation of both core-shell drops and multiple emulsion drops with a controlled number of inner drops in the outer drop. In this work core-shell drops with a size between 50 and 150 μm have been produced at the production rate ranging from 1,000 to 10,000 drops/s. The shell thickness was accurately controlled by adjusting the ratio of the middle fluid flow rate to the inner fluid flow rate and the drop size decreased with increasing the outer fluid flow rate.

1. Introduction

A water-in-oil-in-water (W/O/W) emulsion consists of aqueous phase droplets dispersed within larger oil droplets, which are themselves dispersed in an aqueous continuous phase (1). W/O/W emulsions are traditionally prepared by a two-step emulsification process using two surfactants with high and low HLB value to stabilize the outer and inner water/oil interface, respectively. The first emulsification step is usually carried out under high-shear conditions to produce fine inner droplets, while in the second step low shear is applied to avoid release of the inner droplets from the oil phase. Mild hydrodynamic conditions usually result in polydisperse oil globules, while in the great majority of controlled release applications a high degree of drop size uniformity is required. In addition, using conventional emulsification methods it is hard to achieve accurate control over the internal structure of multiple emulsions. Therefore, new strategies are needed to achieve better control over drop size and morphology in multiple emulsions. In this work, novel methods for production of controllable multiple emulsions with high encapsulation efficiency and uniform drop size have been developed.

2. Experimental

2.1 Membrane emulsification

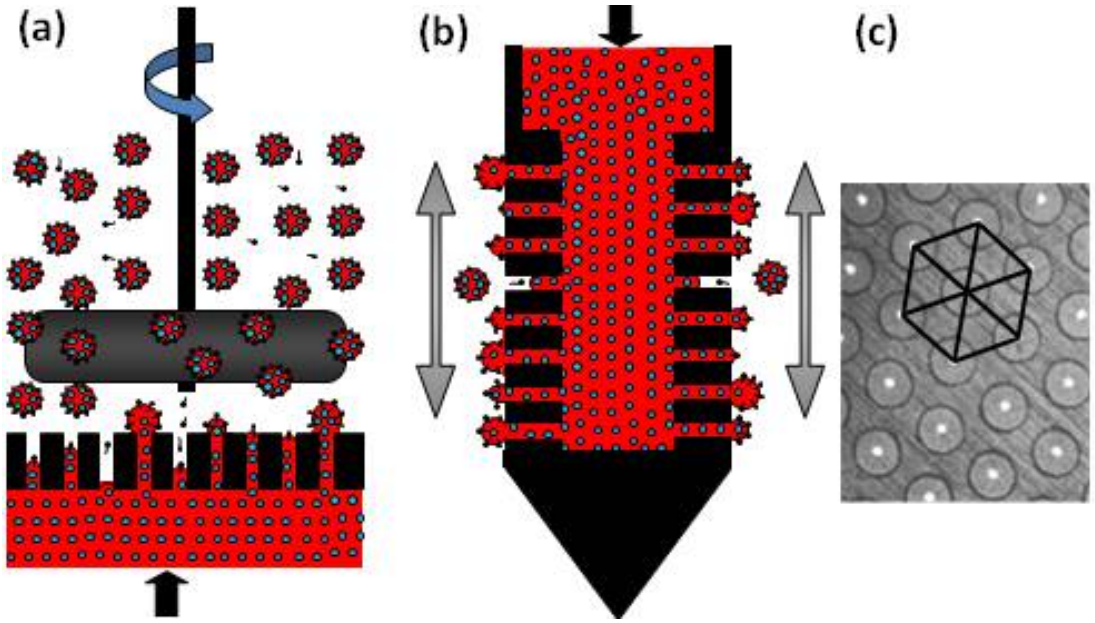

Fig.1. Schematic view of membrane emulsification systems based on stationary disc membrane in stirred cell (a) and oscillation candle membrane (b). A micrograph of the microsieve membrane used in both systems is shown in (c).

The oil phase in W/O/W emulsions was unrefined pumpkin seed oil or sunflower oil containing 10 wt% PGPR (polyglycerol polyricinoleate). The inner aqueous phase was 0.9 wt% NaCl solution and the continuous phase was 2 wt% Tween 20 (polyoxyethylene sorbitan monolaurate) dissolved in 0.9 wt% NaCl solution. Two different membrane emulsification systems were used for the second emulsification step (Fig. 1). A stirred cell where shear at the membrane surface is provided using a paddle stirrer attached above the disk membrane is illustrated in Fig. 1(a) (2). The disadvantage of such system is that it is not an industrial solution for generation of large amount of droplets but it is a quite suitable as laboratory technique. Oscillating membrane emulsification illustrated in Fig. 1(b) is a more promising approach for industrial application due to its inherent scalability (3). The membrane was in the form of a candle, with an external diameter of 15 mm and a working length of 57 mm. At the bottom end of the membrane, a stainless steel cap sealed off the membrane tube, and the cap had a pointed end to reduce turbulence during oscillation. The shear stress required for droplet detachment from the membrane surface can be controlled by adjusting the frequency, or the amplitude of oscillation. The oscillation signal was provided by an audio generator that fed a power amplifier driving the electro-mechanical oscillator fitted on the inlet manifold. Both systems were supplied by Micropore Technologies Ltd, Loughborough, UK. The dispersed phase was a water-in-oil (W/O) emulsion containing 30 vol% of aqueous phase prepared by Ultra-Turrax. The membrane used in both systems was a microsieve membrane fabricated by Ni electroforming. A regular hexagonal array of cylindrical pores with uniform pore spacing can be seen from Fig. 1(c).

2.2 Glass microcapillary device

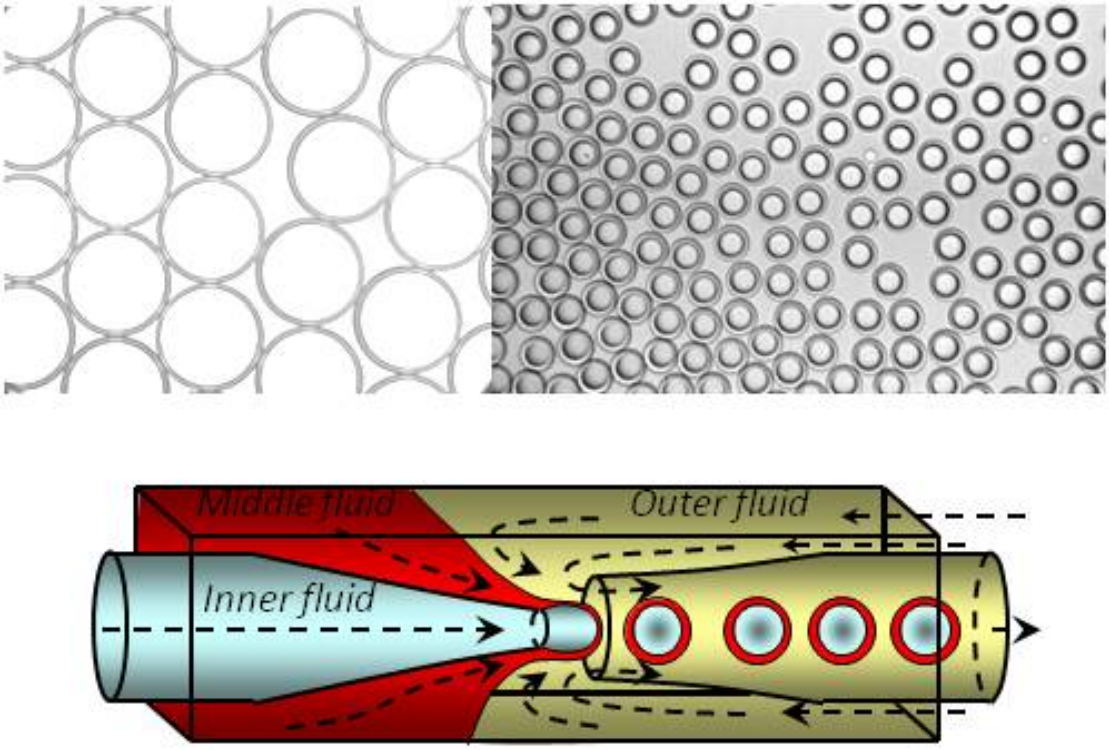

Fig.2. A microscopic picture of monodisperse core/shell drops with a core diameter of 62 µm and a shell thickness of 8 µm taken under different magnification and a schematic view of glass microcapillary device used in this work for generation of core/shell drops.

Microfluidic devices can be used to obtain uniform core/shell drops with accurate shell thickness (4) or larger uniform drops containing a controlled number of uniform inner drops (5). Core/shell drops have been used as templates for the production of functional vesicles such as liposomes, polymerosomes and colloidosomes (4) and core/shell particles, such as hollow hydrogel particles (6). In this work, core/shell drops with a controllable shell thickness were produced using microcapillary device shown in Fig. 2 (7). This device consists of two cylindrical glass capillaries with tapered ends inserted into a square capillary. The inner fluid (milli-q water) was pumped through the injection capillary tube while the middle fluid (2 wt.% Dow Corning 749 Fluid + 98 wt.% PDMS) was supplied through the pockets between the square capillary and the injection capillary tube. The continuous phase (2 wt. % poly(vinyl alcohol) + 40% glycerol) was delivered from the opposite side through the pockets between the square capillary and collection capillary tube. All three liquids were forced into tapered tip of the collection capillary, which resulted in the rupture of the coaxial jet followed by the formation of discrete core/shell drops.

3. Results and discussion

3.1 Membrane emulsification

The results obtained in stirred cell are presented in Fig. 3. As expected, the biggest droplets were obtained at the lowest value of the stirrer speed. The median drop size increased with increasing the transmembrane flux, which could be explained by an increase in the amount of oil phase flowed into a drop during the snap-off process. The most uniform droplets with a span value of 0.45-0.55 were obtained at moderate stirrer speeds of 600-1000 rpm corresponding to the average shear stress over the membrane surface of 3 to 8 Pa.

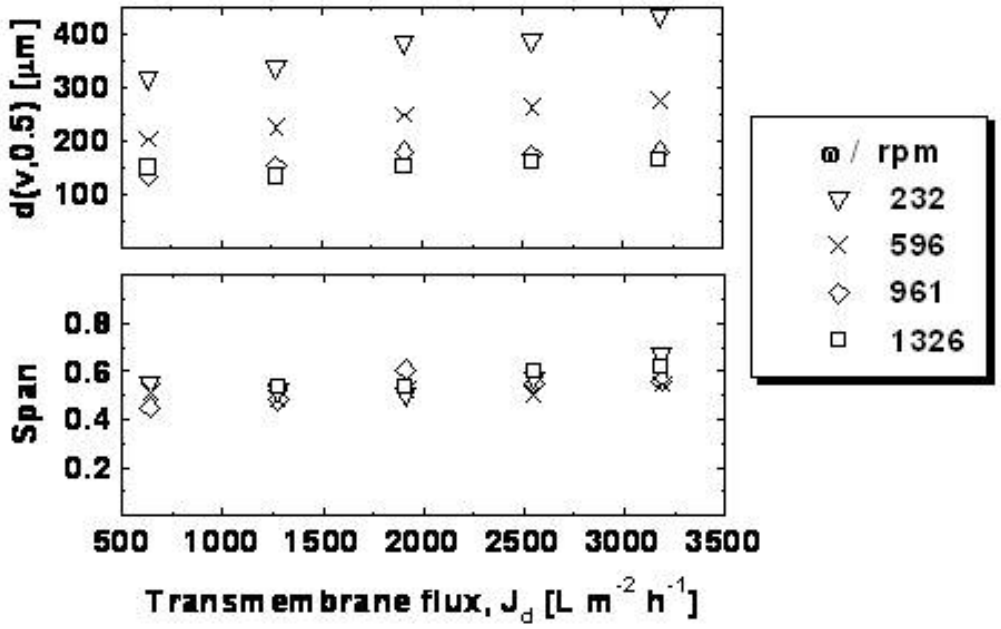

Fig.3. The effect of stirrer speed and dispersed phase flux on the median drop size and span of particle size distribution. Oil phase: unrefined pumpkin seed oil; membrane pore size: 19 µm; pore spacing: 140 µm.

Multiple emulsion drops obtained in oscillation membrane system are shown in Fig. 4. Low transmembrane flux of 30 $Lm^{-2}h^{-1}$ was maintained, in order to minimise any effect due to droplet push-off force. The shear stress at the membrane surface was a sine function of time ranging from zero to a maximal value alternatively in an upward and downward direction. The most uniform drops with a span of 0.36 have been obtained at the frequency of 70 Hz and the peak amplitude of 0.39 mm, corresponding to the peak shear stress of 3 Pa. At the constant peak shear stress, the drop size decreased with increasing the amplitude of oscillation.

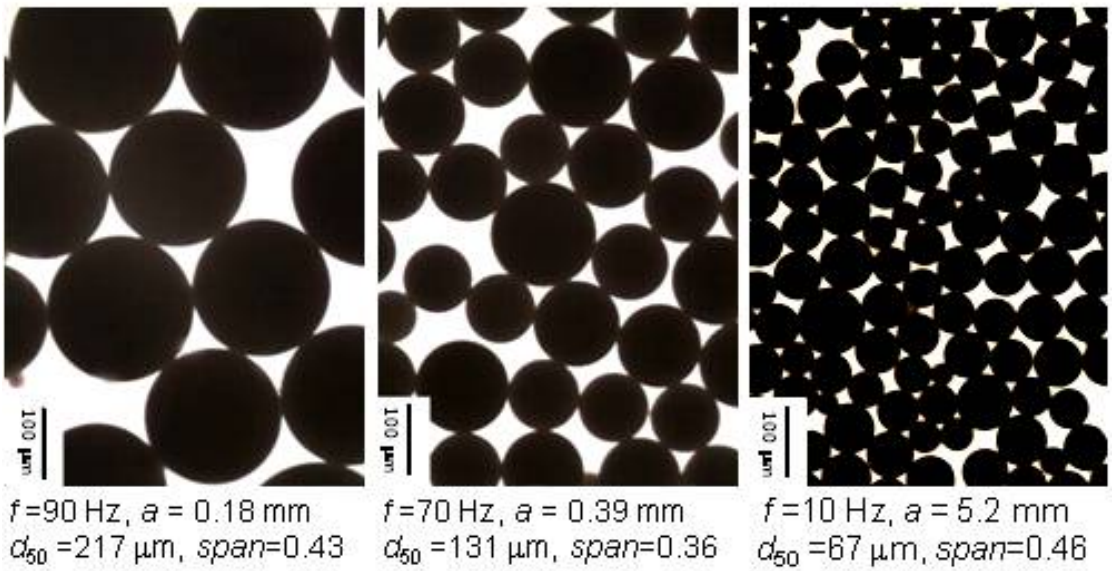

Fig. 4. Multiple emulsion drops produced using oscillating membrane. Oil phase: sunflower oil; membrane pore size: 10 µm; pore spacing: 180 µm.

3.2 Glass microcapillary device

As the outer liquid flow rate Q_o increases, the viscous drag force between the outer and middle phase increases and the drop size d_o decreases, resulting in the higher drop generation frequency, ν. It is illustrated in Fig. 5, showing that the drop generation frequency was nearly 10 kHz at the maximum value of Q_o of 45 ml/h. A mass balance for the drop generation process gives:

$$d_o = [6(Q_m+Q_i)/(\pi\nu)]^{1/3} \qquad \text{Eq. (1)}$$

where Q_m is the middle liquid flow rate. The drop diameters calculated from Eq. (1) were consistent with the experimental d_o values estimated from microscopic images, as shown in Fig. 5. The shell thickness δ is given by:

$$\delta = [3Q_i)/(4\pi\nu)]^{1/3}\{[1+(Q_m/Q_i)]^{1/3}-1\} \qquad \text{Eq. (2)}$$

Eq. (2) shows that the shell thickness should increase with increasing the Q_m/Q_i ratio, which is clear from the video recordings shown in Fig. 6. As anticipated from Eq. (2), the shell thickness at Q_m/Q_i =6 was significantly larger than that at Q_m/Q_i =0.25.

Core/shell drops shown in Figs. 2 and 6 can be used as templates for production of monodispersed particles with liquid cores and solid shells. They can be produced by evaporation of volatile solvent from the middle phase liquid containing a dissolved polymer. An alternative route could be based on gelation of gel-forming polymer dissolved in the middle phase liquid, triggered by diffusion of cross-linking agent from the outer liquid.

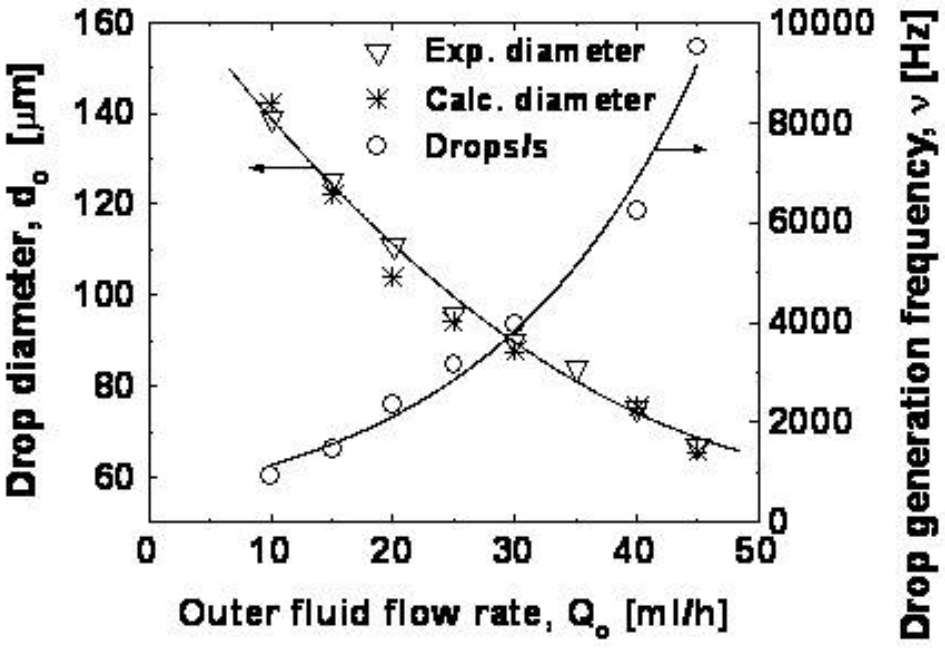

Fig.5. The effect of outer fluid flow rate on the drop diameter d_o and the drop generation frequency at Q_i = 4 ml/h and Q_m = 1 ml/h. The injection capillary orifice size: 44 μm; the collection capillary orifice size: 115 μm.

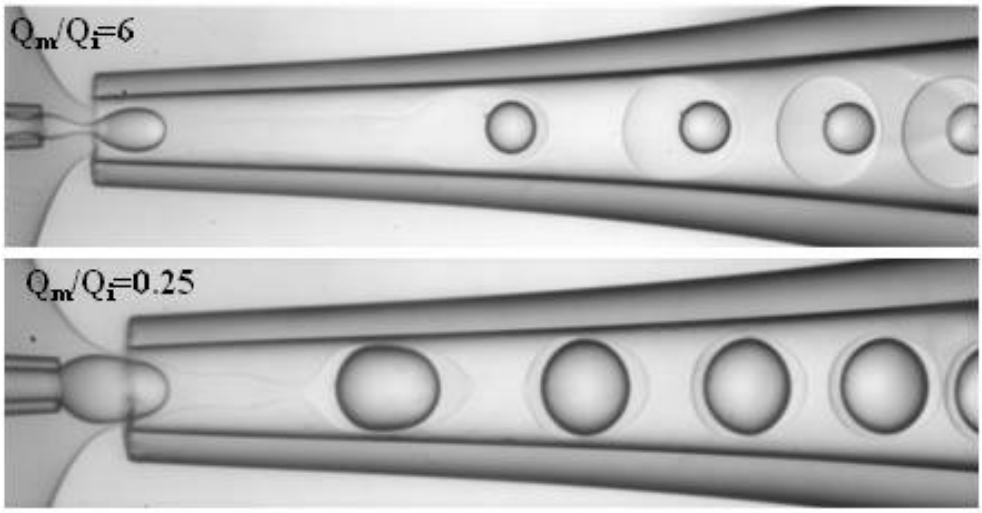

Fig. 6. Control over the shell thickness of core/shell droplets by adjusting the ratio of the middle fluid flow rate Q_m to the inner fluid flow rate Q_i at the constant outer liquid flow rate.

4. Conclusions

The formation of size controlled multiple emulsion drops using membrane oscillation parallel to the membrane surface with 10 to 90 Hz frequency has been described. The technique can be scaled by providing a larger membrane area in the membrane oscillation assembly. The advantages of using glass microcapillary devices for production of multiple emulsions are that the generated droplets are highly uniform in size and the internal drop structure can be accurately controlled. In this work the shell thickness ranged from less than 1 μm to several tens of μm and was tuned by controlling the ratio of the middle liquid flow rate to the inner liquid flow rate. The production rate was in the range from 1,000 to 10,000 drops per second and was controlled by controlling the flow rate of the continuous phase liquid.

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