Supporting Information for Lab on a Chip

Controlled stimulation-burst targeted release by smart decentered core-shell microcapsules in gravity and magnetic field

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Materials and Microfluidc device.

N-Isopropylacrylamide monomer (NIPAm, Kohjin, 97%,0.452g), Pluronic F127 (Sigma Aldrich, 0.04 g), N,N -methylenebisacrylamide (MBA) crosslinker (Sigma Aldrich,0.0308 g), and ammonium persulfate (APS, Sigma Aldrich,0.024g) dissolved in deionized water (4 ml),which was used as the middle fluid. Magnetic iron oxide nanoparticles (1.0 wt.‰) were dispersed in the above aqueous solution with 1.0 wt.‰ TX-100(99%, &K Chemical) surfactant to stabilize the dispersion of the iron oxide nanoparticles. Thus the middle phase were obtained, then put the middle phase in ultrasound for 30 minutes to disperse the magnetic nanoparticles evenly. Soybean oil with 5% (w/v) polyglycerol polyricinoleate (PGPR 90, Danisco) and 0.1% (w/v) Sudan Red as active substance, and soybean oil with 5% (w/v) PGPR 90 were used as the inner and outer fluids, respectively. 2,2,-Dimethoxy-2-phenylacetophenone (99%, Sigma Aldrich, 2.0 wt.%) was added in middle phase as photoinitiator. Thus, the material for preparing O/W/O double emulsions are prepared.

As shown in FigS1, the microfluidic device was a 400 mm $\times 25$ mm $\times 37$ mm polymetyl methacrylate (PMMA) chip using an end mill. Two cross junctions are approximately 1.50 mm wide $\times 1.50$ mm high. The inner phase fluids are introduced trough the micro-needle with innerdiameter of 160 µm and outer-diameter of 300 µm. There are two micro capillaries which are used as middle and outer fluids channels. The capillary channel for middle phase has 1.05 mm innerdiameter and 1.5 mm outer-diameter whose end is tapered using a micropipette puller (P-97, SUTTER Co. Ltd., USA) for the injection of the middle phase fluid. The diameter of the tapered orifice is approximately 340 µm. The first tapered capillary is inserted into a second capillary for the outer phase. The outer diameter of the capillaries are 1.5 mm which match the inner diameter of the cross junction to maintain the coaxality. The second capillary is not tapered with 1.05 mm inner-diameter and 1.5 mm outer-diameter. And the microcapillary of middle fluid was dipped in 30.0 wt.% NaOH aqueous solution for 5 hours to modify the surface more hydrophilic. Four PTFE pipes are inserted into sides of the chip channel for carrying middle and outer phase fluids. And we used thermal bonding method to bond the PMMA chip, and used adhesive glue to seal the glass capillaries from leakage. Thus our microfluidic device could ensure the coaxial ability and no leakage. Three micro-syringe pumps (LSP01-1B, Baoding Longer Precision Pump Co. Ltd) are used to pump the four-phase system into the microfluidic device respectively.



Fig. S1 Microfluidic device composing of two coaxial micro capillary. The inner flow is red, the middle flow is yellow and the outer flow is blue. A single emulsion (O/W) is prepared in the first stage, thus a red droplet which is inner core is synthesized, then the outer flow encapsulates the middle flow with inner core, thus the core-shell double emulsion (O/W/O) is synthesized.

Synthesis of Monodispersed Core-shell double emulsions.

Firstly, we dissolved Nipam polymer, Pluronic F127 surfactant, crosslingker MBA and initiator APS with stirring for 30 minutes in deionized water. Then we dispersed iron dioxide nanoparticles into the aqueous solution and added TX-100 as stabilizer. After 30 minutes ultrasound treatment, aqueous solution with monodispersed magnetic nanoparticles was prepared as middle phase. Soybean oil with 8.0 wt.% PGPR and 2.0 wt.% photoinitiator was prepared as outer phase, while soybean oil with PGPR and 2.0 wt.% Sudan Red as dye and active substance was used as inner oil phase. Inner oil phase flowing through the first stage micro capillary was sheared by middle aqueous phase flow, forming an oil droplet, and then they flow through the second stage micro capillary sheared by outer oil phase flow, forming core-shell double emulsions. The surface hydrophilic modification of the micro capillary of middle fluid is to ensure that there is enough middle water phase separated between the inner oil phase and the outer oil phase for these two oil phase are totally immiscible. The typical magnitude order of inner, middle and outer flows rates are 1 µL min⁻¹,10 µL min⁻¹, and 100 µL min⁻¹, respectively. The core sizes change from 100µm to 400µm, while the shell size change from 700 µm to 1000 µm. During the experiments, Reynold and Capillary numbers are relatively small. The calculation of Reynold number and Capillary number was:

$$Re = \frac{\rho v d}{\mu}$$
$$Ca = \frac{\mu v}{\sigma}$$

We put the density, the flow rates and the cross area of the channels, the inner diameter of the channels and the viscosity of the middle and outer phases and the interfacial tension into the above

equation. For encapsulation of the inner phase, the Reynold Numbers were in the range of $0.1 \sim 0.6$, and the Capillary Numbers were in the range of $1.0 \times 10^{-4} \sim 8.0 \times 10^{-4}$ for the middle phase flow; For encapsulation of the middle phase, he Reynold Numbers were in the range of $1 \sim 6$, and the Capillary Numbers in the range of $2.0 \times 10^{-3} \sim 10.0 \times 10^{-3}$ for the outer phase flow.

In microfluidic device, when flow mechanism is dripping, the formed droplets could be controlled in small size distribution with high monodispersity. The two stage droplet formation mechanism are dripping (the synthesis process of the emulsions could be found in movie S1) thus the monodispersed core-shell double emulsions was prepared. Fig. S2(a) to Fig. S2(f) represent the core-shell emulsion with different size of inner cores and outer shells. From these pictures, we could see that the emulsions were monodispersed. We also collected >100 double emulsions, and measured their size, then calculate the size distribution. The coefficient of variation (CV) was less than 5%.

Furthermore, we also measured the relationship of the size of the inner core to the different flow rates. The results are shown in Fig. S3. Fig. S3(a) shows the relationship of the inner cores size to the inner flow rates. Fig. S3(b) shows the relationship of the inner cores size to the middle flow rates. Fig. S3(c) shows the relationship of the inner cores size to the outer flow rates. From these data, we found that the size of inner cores increased with the inner flow rates, decreased with the outer flow rates and had little relationship with the outer phase. So the inner core sizes were only related to the inner and middle flow rates. Then we developed a semiempirical model to predict the inner cores size. The deduction process were as follows:

$$\frac{d_i}{D_i} = k(\frac{Q_i}{Q_m})^{\alpha} (\text{Ca})^{\beta}$$

Herein d_i represented the inner core size, D_i represented the inner diameter of the inner flow channel, Q_i represented the inner flow rates, Q_m represented the middle flow rates, and Ca represented the capillary number.

And,
$$Ca = \frac{u\mu}{\sigma}$$
, $u = \frac{Q_m}{A}$

Herein μ , σ are physical properties which don't change during the process, and A is the area of capillary channel for middle phase, thus the first formula could be induced as:

$$\frac{d_i}{D_i} = k Q_i^{\alpha} Q_m^{\beta - \alpha}$$

So according to the Fig. S3(a) and Fig. S3(b), we could obtain the α and β , and then we draw the relationship of $\frac{d_i}{D_i}$ to $Q_i^{\alpha} Q_m^{\beta-\alpha}$, so obtained the relationship shown in Fig. S3(d). From Fig. S3(d), we could predict the inner core size according to the inner and middle flow rates.



Fig. S2 The different size and number of inner cores



Fig. S3 The relationship of inner and middle droplets' diameter with the flow rate

After the preparation of double emulsions, we examined the solidification time of NIPAm emulsion under UV-light to choose the best UV light exposure time to prepare transparent and solid microcapsules. Transparent microcapsules are useful in later release observation through microscope. Fig. S4 shows the microphotographs of microcapsules under different time of UV exposure. To balance the transparency and the strength, we choose to solidify our emulsions under around 100s UV exposure.



Fig. S4 The relationship of solidification level with exposure time to UV-light