Surfactant-free, UV-curable core–shell microcapsules in a hydrophilic PDMS microfluidic device

Cite as: AIP Advances 10, 065101 (2020); https://doi.org/10.1063/5.0004736
Submitted: 13 February 2020 . Accepted: 03 May 2020 . Published Online: 02 June 2020

Adrian J. T. Teo, Fariba Malekpour-galogahi, Kamalalayam Rajan Sreejith, Takayuki Takei, and Nam-Trung Nguyen

COLLECTIONS

Paper published as part of the special topic on Chemical Physics, Energy, Fluids and Plasmas, Materials Science and Mathematical Physics

This paper was selected as Featured

Sign up for topic alerts
New articles delivered to your inbox
Surfactant-free, UV-curable core–shell microcapsules in a hydrophilic PDMS microfluidic device

Cite as: AIP Advances 10, 065101 (2020); doi: 10.1063/5.0004736
Submitted: 13 February 2020 • Accepted: 3 May 2020 • Published Online: 2 June 2020

Adrian J. T. Teo,1 Fariba Malekpour-galogahi,1 Kamalalayam Rajan Sreejith,1 Takayuki Takei,2 and Nam-Trung Nguyen1,a)1,a)

AFFILIATIONS
1 Queensland Micro- and Nanotechnology Centre, Griffith University, 170 Kessels Road, 4111 Queensland, Australia
2 Department of Chemical Engineering, Graduate School of Science and Engineering, Kagoshima University, 1-21-40 Korimoto, Kagoshima 890-0065, Japan

a)Author to whom correspondence should be addressed: nam-trung.nguyen@griffith.edu.au

ABSTRACT
We demonstrate a method to create surfactant-free core–shell microcapsules in a hydrophilic polydimethylsiloxane microfluidic device. An ultraviolet light curable polymer was used to encapsulate an oil core. These microcapsules ensure contamination-free compartmentation of the core material without any surfactant, while maintaining the monodispersed generation at a rate of 100 microcapsules per second. The device fabrication process is greatly simplified without the alignment of microchannels and hydrophobic/hydrophilic surface treatment. After drying, physically shaking the collection chamber can crack the capsule to release the liquid core material. Such solid microcapsules with a liquid core are ideal for the storage and delivery of oil-based materials in skincare products or reagents for biochemical assays.

© 2020 Author(s). All article content, except where otherwise noted, is licensed under a Creative Commons Attribution (CC BY) license (http://creativecommons.org/licenses/by/4.0/). https://doi.org/10.1063/5.0004736

I. INTRODUCTION
Core–shell microcapsules play a significant role in research and commercial products. These microcapsules serve as miniature containers for the storage and delivery of substances. The current production methods include emulsion-based, liquid marble-based, and microfluidic approaches. Emulsion-based methods generate double emulsions through homogenization or ultrasonification of two liquid phases. Surfactants are accordingly needed to ensure interfacial stability by reducing interfacial tension between the different liquid layers. However, surfactants may affect chemical processes, such as enzymatic activities in the droplet. This makes them unsuitable for certain enzyme-related research. Liquid marbles, a liquid droplet coated with hydrophobic powder, are also constrained by their relatively large size. On the contrary, smaller microcapsules can be obtained through electro-spraying with a strong electric field. These methods, however, require the use of additional equipment for electric field generation. Microfluidics has been a viable option for generating microcapsules. However, the challenges for this approach are with the breaking and misalignment of glass capillary devices and dual hydrophobic/hydrophilic surface treatment of polydimethylsiloxane (PDMS) devices. The dual surface treatment is required for the complete wetting of the microchannels to ensure a steady and reliable liquid flow within each microchannel. The applied treatment accordingly depends on the interfacial tension of the bulk liquid flowing through each microchannel. In general, hydrophobic treatment is employed when oil-based liquids are used to wet the microchannel. Hydrophilic treatment is used for the water-based counterpart. Reducing the amount of surface treatments in a microfluidic device significantly simplifies the fabrication process of the devices. Furthermore, the shell material of the existing solutions has been often limited to alginate, a salt of alginic acid and sodium or calcium. Addressing all these bottlenecks, we present here a method for generating surfactant-free, ultraviolet (UV) light curable core–shell microcapsules in a fully hydrophilic PDMS microfluidic device.
II. MATERIALS AND METHODS

The polydimethylsiloxane (PDMS) device was fabricated using standard photo and soft lithography methods. Flow focusing configuration was used for all junctions in the device design. After air plasma treatment, the patterned PDMS substrate was bonded to a glass slide. The microchannels with a height of \( H = 100 \mu \text{m} \) were immediately flooded with deionized (DI) water to maintain the pristine hydrophilicity. The device was placed on an inverted microscope (Eclipse Ti, Nikon Instruments) with a camera (Phantom Miro3, Vision Research) for real-time image acquisition and video recording. The camera was connected to a computer, which was also used for controlling the flow rates of the syringe pumps (neMESYS, Centoni GmbH). All captured videos were analyzed using the automated droplet measurement (ADM) software to obtain the respective droplet areas. Similarly, other variables like droplet separation distance, major axis length, and frequencies were also obtained. The major axis length refers to the longest droplet dimension that is used for calculating the droplet area in the ADM software.

We used (1) for the core droplets as they retain the spherical shape after formation. Equation (2) was accordingly used for core–shell droplets as the droplet is squeezed into a discoid shape by the channel walls with \( D_{\text{EQ}} > H \). In the following, the "droplet size" is referred to as the droplet area.

As the core liquid, we used HFE7500 fluorinated oil (Novec, 3M) with a viscosity of \( \mu_{\text{CO}} = 1.31 \text{ mPa s} \), a surface tension of \( \sigma_{\text{CO}} = 15.52 \text{ mN/m} \), and a density of \( \rho_{\text{CO}} = 1.63 \text{ g/ml} \). The shell polymer (\( \mu_{\text{SH}} = 42 \text{ mPa s} \), \( \sigma_{\text{SH}} = 32.5 \text{ mN/m} \), and \( \rho_{\text{SH}} = 1.07 \text{ g/ml} \)) was prepared by mixing 0.05 g camphorquinone (Merck), 0.06 g ethyl-4(dimethylamino)benzoate (Merck), and 10 g of trimethylolpropane trimethacrylate (TMPTMA, Merck) using a magnetic stirrer at 600 rpm for 30 min. The second and third junctions were supplied with 50% glycerol solution (Chemsupply, \( \mu_{\text{CN}} = 6 \text{ mPa s} \), \( \sigma_{\text{CN}} = 67 \text{ mN/m} \), and \( \rho_{\text{CN}} = 1.12 \text{ g/ml} \)) into the side channels.

III. RESULTS AND DISCUSSION

We first optimized the flow rates used for the liquids to achieve consistent generation of thin shell droplets. Due to the high viscosity of the polymer, adjusting the shell flow rate resulted in a slow response time of approximately 30 min. Therefore, we fixed the shell flow rate at \( Q_{\text{SH}} = 150 \mu\text{l/hr} \), which allowed us to produce core–shell droplets of around \( 10^{4} \mu\text{m}^{3} \). This flow rate also enables us to accommodate the subsequent high flow rates of the spacer liquid at the third junction, which was adjusted up to \( 2000 \mu\text{l/hr} \). We proceeded to experimentally optimize the formation process by increasing the flow rates of the core liquid (oil) and the suspension liquid (glycerol solution).

Figure 2(a) shows the typical results of the formation process upon adjusting \( Q_{\text{CR}} \), where the glycerol flow rates at the

![Diagram](image_url)
Correspondingly, the generation frequency of the core droplets \( f_1 \) is increased from 73 drops/s to 130 drops/s. The correlation between the core droplet area remained unchanged at around 4000 \( \mu m^2 \). The frequency and the droplet volume is increased from 400 \( \mu l/h \) to 1200 \( \mu l/h \). Fixing \( Q_{CN} \) at 40 \( \mu l/h \) led to consistent core size and separation distance as shown in Figs. 3(a) and 3(b). Increasing \( Q_{CN} \) decreased the size of the core–shell droplet as given in Fig. 3(a). This simultaneously increases \( f_2 \) according to (4). However, the core droplet generation frequency \( f_1 \) only slightly increased from 75 drops/s at 400 \( \mu l/h \) to 83 drops/s at 1200 \( \mu l/h \) [inset of Fig. 3(b)]. We also observed that the major axis length of the droplet is much less than the core separation distance. This proved that the generation frequency played a greater role than the major axis length in the consistent production of core–shell droplets. The microscope images of the outlets at different flow rates are given in Fig. 3(c).

At the third junction, the glycerol flow rate \( Q_{SP} \) has a negligible influence on the droplet size and the generation frequency. This behavior can be explained by the difference between the upstream and downstream pressures at the junctions. The expansion chamber downstream has a lower fluidic resistance than the upstream microchannel. Thus, the spacer liquid only flows downstream, increasing the separation between the core–shell droplets. This effectively prevents accidental coalescence of the core–shell droplets before collection.

We subsequently optimized the oil and glycerol flow rates to achieve thin–shell microcapsules [Figs. 4(a)–4(d)]. The optimized flow rates were \( Q_{CR} = 100 \mu l/h \), \( Q_{SH} = 150 \mu l/h \), \( Q_{CN} = 800 \mu l/h \), and \( Q_{SP} = 1600 \mu l/h \). These values lead to a core area of 4700 \( \mu m^2 \) and a total microcapsule area of 9500 \( \mu m^2 \). The optimized generation frequencies were approximately \( f_1 \approx f_2 \approx 100 \) drops/s. The core–shell droplets were guided into a collection chamber [Fig. 4(a)] and exposed to ultraviolet (UV) light at 36 W for 5 min [Fig. 4(b)]. Individual droplets formed solidified microcapsules due to the UV-curing process of the TMPTMA polymer. Subsequently, the collection chamber was dried overnight on a hotplate at 90 °C. The dimensions of the droplets after drying as observed under the microscope [Fig. 4(c)]. This effectively prevents accidental coalescence of the core–shell droplets before collection.

Another application for microcapsules would be polymerase chain reaction (PCR). Each microcapsule can serve a single microreactor, eliminating the need for well plates. This reduces

\[
Q_{CN} = f_1 V_S. \quad (3)
\]

With \( Q_{CN} = 400 \mu l/h \) at the second junction, the generation frequency of the droplets \( f_2 \) increased from approximately 75 drops/s to 90 drops/s. This was also accurately reflected through a modification of (3) into

\[
Q_{CR} + Q_{SH} = f_2 V_D. \quad (4)
\]

Evaluating the frequencies in the inset of Fig. 2(b) revealed that consistent core–shell formation occurs when \( f_1 \approx f_2 \). When \( f_1 > f_2 \), irregular splitting of core droplets was observed. This causes the inconsistent formation of core–shell droplets [Fig. 2(c)], as the core droplets were too closely packed after the first junction [insets of Fig. 2(a)]. Further investigation also revealed that the separation distance between cores needs to be greater than the major axis length of the core–shell droplet for consistent formation [Fig. 2(b)].
The need for plastic consumables in laboratories, while lowering experimental costs by using less reagents. As PCR mixtures are predominantly water-based, we hypothesize that replacing the hydrophilic surface treatment with hydrophobic surface treatment using Aquapel\textsuperscript{12} would enable the stable production of water-based core–shell microcapsules.

We demonstrate a simplified production method of core–shell microcapsules in a PDMS microfluidic device. Our method provides multiple advantages over the existing state-of-the-art approaches with no surfactant, no additional equipment, and no dual surface treatment. In addition, the biocompatible shell polymer\textsuperscript{23} makes our microcapsules suitable for applications, such as polymerase chain reaction (PCR).\textsuperscript{22} The solid shells hermetically isolate the core liquid, reducing contamination and evaporation. This feature makes the microcapsules reported here a highly practical and extremely attractive option for the storage and delivery of pharmaceutical products. Our current proof-of-concept experiments can produce 100 microcapsules per second at low flow rates, which is predicted to increase with higher flow rates. We are also able to easily obtain the core liquid from the microcapsules by manually shaking the chamber by hand.

**ACKNOWLEDGMENTS**

N.-T.N. acknowledges financial support from the Australian Research Council, Project No. DP180100055. The devices were fabricated in the Queensland Microtechnology Facility, part of the Queensland node at Griffith University of the Australian National Fabrication Facility, a company established under the National Collaborative Research Infrastructure Strategy to provide nanofabrication and microfabrication facilities for Australia’s researchers.

**DATA AVAILABILITY**

The data that support the findings of this study are available within the article.
REFERENCES

1. D. Lensen, K. van Breukelen, D. M. Vriezema, and J. C. van Hest, “Preparation of biodegradable liquid core PLLA microcapsules and hollow PLLA microcapsules using microfluidics,” Macromol. Biosci. 10, 475–480 (2010).

2. G. T. Vladisavljević, R. Al Nuumani, and S. A. Nabavi, “Microfluidic production of multiple emulsions,” Micromachines 8, 75 (2017).

3. D. Lensen, D. M. Vriezema, and J. C. M. van Hest, Macromol. Biosci. 8(11), 991–1005 (2008).

4. N. Garti, “Double emulsions—Scope, limitations and new achievements,” Colloids Surf., A 123-124, 233–246 (1997), frontiers in Colloid Chemistry an International Festschrift to Professor Stig E. Friberg.

5. K. R. Sreejith, L. Gorgannezhad, J. Jin, C. H. Ooi, H. Stratton, D. V. Dao, and N.-T. Nguyen, “Liquid marbles as biochemical reactors for the polymerase chain reaction,” Lab Chip 19, 3220–3227 (2019).

6. Y. Zhao, Z. Xu, H. Niu, X. Wang, and T. Lin, “Magnetic liquid marbles: Toward “lab in a droplet,”” Adv. Funct. Mater. 25, 437–444 (2015).

7. S. A. Nabavi, G. T. Vladisavljević, S. Gu, and E. E. Ekanem, “Double emulsion production in glass capillary microfluidic device: Parametric investigation of droplet generation behaviour,” Chem. Eng. Sci. 130, 183–196 (2015).

8. L.-Y. Chu, A. S. Utada, R. K. Shah, J.-W. Kim, and D. A. Weitz, “Controllable monodisperse multiple emulsions,” Angew. Chem., Int. Ed. 46, 8970–8974 (2007).

9. T. F. Tadros, Surfaceactants in Agrochemicals (Marcel Dekker, 1994), p. 54.

10. Y. Liu, S.-Y. Jung, and C. P. Collier, “Shear-driven redistribution of surfactant affects enzyme activity in well-mixed femtoliter droplets,” Anal. Chem. 81, 4922–4928 (2009).

11. H. Wang, Z. Zhao, Y. Liu, C. Shao, F. Bian, and Y. Zhao, “Biomimetic enzyme cascade reaction system in microfluidic electrospray microcapsules,” Sci. Adv. 4, eaat2816 (2018).

12. A. J. T. Teo, S. H. Tan, and N.-T. Nguyen, “On-demand droplet merging with an AC electric field for multiple-volume droplet generation,” Anal. Chem. 92, 1147–1153 (2020).

13. Y. Song, Y. Jeong, T. Kwon, D. Lee, D. Y. Oh, T.-J. Park, J. Kim, J. Kim, and S. Kwon, “Liquid-capped encoded microcapsules for multiplex assays,” Lab Chip 17, 429–437 (2017).

14. C.-X. Zhao, D. Chen, Y. Hui, D. A. Weitz, and A. P. Middledberg, “Controlled generation of ultrathin-shell double emulsions and studies on their stability,” ChemPhysChem 18, 1393–1399 (2017).

15. J. Wang, A. J. T. Teo, S. H. Tan, G. M. Evans, N.-T. Nguyen, and A. V. Nguyen, “Influence of interfacial gas enrichment on controlled coalescence of oil droplets in water in microfluidics,” Langmuir 35, 3615–3623 (2019).

16. J. Courte, R. Renault, A. Jan, J.-L. Viovy, J.-M. Peyrin, and C. Villard, “Reconstruction of directed neuronal networks in a microfluidic device with asymmetric microchannels,” Methods in Cell Biology (Elsevier, 2018), Vol. 148, pp. 71–95.

17. Z. Z. Chong, S. B. Tor, A. M. Gañán-Calvo, Z. J. Chong, N. H. Loh, N.-T. Nguyen, and S. H. Tan, “Automated droplet measurement (ADM): An enhanced video processing software for rapid droplet measurements,” Micromini. Nanofluidd. 20, 66 (2016).

18. A. J. Teo, K.-H. H. Li, N.-T. Nguyen, W. Guo, N. Heere, H.-D. Xi, C.-W. Tsao, W. Li, and S. H. Tan, “Negative pressure induced droplet generation in a microfluidic flow-focusing device,” Anal. Chem. 89, 4387–4391 (2017).

19. M. H. Rausch, L. Kretschmer, S. Will, A. Leipertz, and A. P. Fröba, “Density, surface tension, and kinematic viscosity of hydrofluoroethers HFE-7000, HFE-7100, HFE-7200, HFE-7300, and HFE-7500,” J. Chem. Eng. Data 60, 3759–3765 (2015).

20. T. Takei, Y. Yamasaki, Y. Yuji, S. Sakoguchi, Y. Ohzuno, G. Hayase, and M. Yoshida, “Millimeter-sized capsules prepared using liquid marbles: Encapsulation of ingredients with high efficiency and preparation of spherical core-shell capsules with highly uniform shell thickness using centrifugal force,” J. Colloid Interface Sci. 536, 414–423 (2019).

21. S. Gregory, “Physical properties of glycerine,” Glycerine (Routledge, 2018), pp. 113–156.

22. K. R. Sreejith, L. Gorgannezhad, J. Jin, C. H. Ooi, T. Takei, G. Hayase, H. Stratton, K. Lamb, M. Shiddiky, D. V. Dao, and N.-T. Nguyen, “Core-shell beads made by composite liquid marble technology as a versatile microreactor for polymerase chain reaction,” Micromachines 11, 242 (2020).

23. K. H. Vining, J. C. Scherba, A. M. Bever, M. R. Alexander, A. D. Celiz, and D. J. Mooney, “Synthetic light-curable polymeric materials provide a supportive niche for dental pulp stem cells,” Adv. Mater. 30, 1704486 (2018).