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ARTICLE TYPE

Controllable geometry-mediated droplet fission using "off-the-shelf" capillary microfluidics device

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We describe "off-the-shelf" capillary microfluidic devices for droplet fission. The cheap and simple commercial capillary adapters are characterized by perfect sealing, easy assembling and convenient cleaning. Primary droplets, bigger than 65μm, without being plugs, can be split into uniform daughter droplets（15μm-170μm）to obtain smaller droplets and increase its content concentration. The relative size of daughter droplets can be easily controlled by adjusting the length of glass capillary tube.

Introduction

During the two decades, droplet-based microfluidics technology which is characterized by small volume of materials, rapid mixing and detection, easy manipulating and parallel processing, has received more and more attraction in biochemical applications such as protein crystallization[1, 2], cell encapsulation[3-5], drug delivery[6], tissues engineering[7, 8], polymerase chain reaction (PCR)[9-11], microreactors[12, 13] and so on. In most cases, we need precise control over the droplet size and smaller droplet means fewer consumptions and higher efficient for reaction. Polydimethylsiloxane (PDMS) chips have been proved to be successful for droplet generation[14-18]. However, droplet size is sometimes limited by the structure or the bonding pressure of PDMS chips. To obtain uniform smaller droplets, several researchers adopt droplet fission method to make the primary droplet split into daughter droplets[19, 20]. This method is a critical operation to effectively increase droplet throughout and add droplet content concentration. It is further divided into active fission and passive fission[21]. Electrowetting on dielectric (EWOD) is an effective way to actively control droplet fission[22, 23] while it costs much and needs additional external operation. Within a traditional PDMS microchannel of specific design[19, 24-27], a droplet can be passively broken into several small daughter droplets. However, these methods are not so flexible to alter the channel length to change flow resistance, unless another given shape microchip is fabricated.

Recently, Terray et al[28] , Benson et al [29] and Wu et al[30] have successfully used some "off-the-shelf" devices for microfluidic experiments. As demonstrated by Wu et al, this micro-cross can be assembled / disassembled easily, and endure a pressure of 4000 psi, far higher than the conventional PDMS chips. According to these, we work further to find a novel way for droplet fission. Here we use two micro-cross connecting directly with glass capillary tubes to perform as droplet generating and geometry-mediated breaking up devices. We can get two different uniform sizes of daughter droplet by either flexibly changing the length of capillary tubes at a constant flow rate or adjusting flow rate. Furthermore, unlike the droplet fission within PDMS channel, the primary droplets above do not need plugging regimes, meaning that this device is capable to split smaller droplets.

Materials and methods

Two "off-the-shelf" devices are used to build the whole system, one for flow-focusing droplet generator and another for droplet fission device. The micro-cross (135 $, IDEX Health& Science, P-777) contains several fluidic fitting parts as shown in Fig. 1(a) . The individual components can be disassembled for cleaning by alcohol or ultrasonic, drying by nitrogen, and reassembled. After inserting capillary glass tubes (1.6 $/m, OD360μm, ID250μm) into the micro-cross through the female nuts and ferrules, pushing firstly against the bottom ledge, fingers tighten securely, a simple capillary microfluidic device is done. We inject deionised water as dispersed phase and mineral oil with 2% (v/v) surfactant EM90 as continuous phase by syringe pump (ABI 140D Solvent Delivery System), and the observation is under the microscope (OL YMPUS SZX16). For the secondary device, we enclose one outlet (shown in Fig.1(c)) with glue to form a T-like junction and the two branching flow forces the primary droplet flowing and crashing the edge angle of the junction, thus droplet fission is achieved. During the fission process, flow resistance of two branching channel determines the relative size of two daughter droplets. As a consequence, we highlight that the relative size of daughter droplets can be conveniently controlled in this device just by adjusting the relative tube length of two outlets. Aiming to obtain some knowledge about how the flow rate and length of capillary tube affect droplet size, we firstly change the flow rate of both tubes with constant length, then observe and measure droplets carefully. After that we change the relative capillary tube length and repeat former experiments. Both micro-cross and glass capillary tubes are reusable for easily implementing the droplet fission.

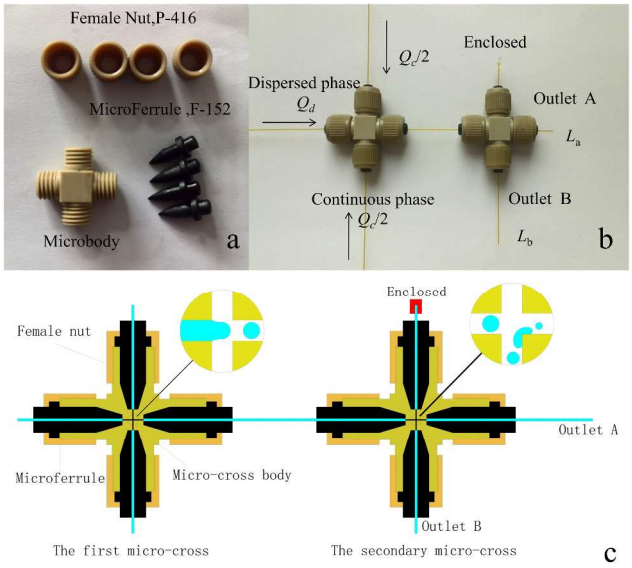

Fig. 1 (a) A whole micro-cross containing a micro-cross body, 4× female nuts (P-416) and 4× micro ferrules (F-152) (b) The droplet generation and fission device, one of the secondary micro-cross outlets is enclosed with glue. (c) Schematic of the whole fission device. A droplet is formed in the first micro-cross, and then flows into the secondary one, until it crashes the edge angle of the channel and breaks up into two daughter droplets.

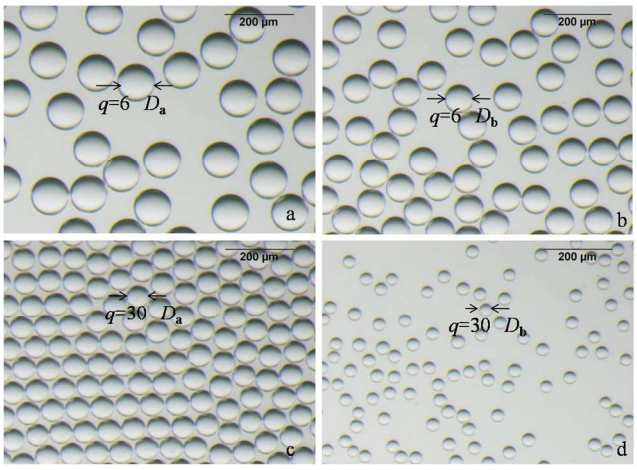

Fig. 2 The dispersed phase flow rate Q_d is 5μL/min, the length of capillary tubes are fixed at L_a=2 cm, L_b=4 cm; (a) flow rate ratio q=6, the mean diameter (D_a) of daughter droplet from Outlet A is 108μm, λ=2.08%. (b) q=6, the mean diameter (D_b)of daughter droplet from Outlet B is 82μm, λ=2.56%. (c) q=30, D_a = 64μm, λ=2.78%. (d) q=30,D_b= 38μm, λ=3.02%.

Results and discussion

Droplet formation and fission

We use the first micro-cross as an axisymmetric flow-focusing device to produce primary droplets with suitable size as required. As reported in many articles, the droplet diameter is inversely relevant to the flow rate ratio (q=Q_c/Q_d) in microfluidic system. Highly monodisperse emulsions can be produced as shown in Fig. 2, and the polydispersity index (λ) defined as the ratio between the standard deviation and the mean of droplet diameter, is less than 3.02%. This droplet fission device can get homogeneous daughter droplets as we expected.

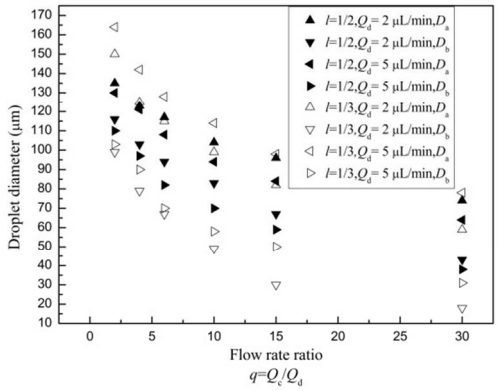

Fig. 3 Size of daughter droplets versus flow rate ratio. For l=1/2, the length of capillary tubes are L_a=2 cm, L_b=4 cm; for l=1/3, L_a=2 cm, L_b=6 cm.

We believe that the flow rate ratio q not only determines the size of the primary droplet but also affects the daughter droplets. Though droplet production has different mechanisms as a function of flow rate ratio[31] in T-junction, we often discuss the case of q>1 in flow focusing device. As shown in Fig. 3, we keep the capillary tube length L_a, L_b, and the dispersed phase flow rate Q_d fixed (L_a=2cm, L_b=4cm, Q_d=5μL/min), then increase the continuous phase flow rate Q_c. It is observed that both daughter droplets diameter decrease, the same as a single droplet generator. Changing dispersed flow rate as Q_d=2 μL/min, we can get the same conclusion. Comparing with the case of different relative capillary tube length l=1/2 and l=1/3 (l=L_a/L_b), we find the relative daughter droplet size becomes susceptible and we will give a further exploration between them in the following. Moreover, the production frequency can reach 6000 droplets/sec comparing with 3500 droplets/sec of PDMS chips[20, 24, 30, 32].

Relative size distribution and the mechanism

In this section, we will show the relationship between capillary tube relative length l and daughter droplet relative size d (D_a/D_b). Unlike traditional PDMS chips, here we cut the capillary tubes to be of different lengths and assemble them to micro-cross body to alter flow resistance. We change the flow rate and tube length, and then repeat a large amount of experiments as in the former section. In Fig. 4, we observe that the relative daughter droplet size is proportional to the flow rate ratio q when L_a<L_b and the tendency is opposite if L_a≥L_b. Furthermore, we try to obtain equal-sized daughter droplets and find the critical length ratio l. Finally, we ascertain l=0.8 and the combined polydispersity index is 4.15%. Moreover, the relative length of two armsides is negative correlation to the relative droplet size owing to that the longer tube means larger flow resistance resulting that smaller daughter droplet will be split. Link et al once made the droplet-splitting microfluidics analog of an electriccurrent-splitting device and mentioned that droplet volume ratio from the two armsides is inversely proportional of the ratio of arms length V_a/V_b≈L_b/L_a[24](ranging from 1:1 to 1:8.1). We fail to find the same conclusion by reason of that the splitting-device used by Link et al is T-shape like and the branching flow is symmetric in direction. Moreover, we have successfully made a droplet which is about 65 μm split into two daughters in spite that the feature

size of channel is 150 μm. It indicates that primary droplets here is not plugs sometimes, and the electriccurrent-splitting mechanism may not be a reasonable analogy in this case. A large number of experiments show that primary droplets without being plugs can be split into smaller uniform daughter droplets（15μm-170μm）in the droplet fission device by changing the flow rate of continuous and dispersed phase.

The most surprising and interesting phenomenon in all of our experiments lies in that $D_a<D_b$ when $L_a=L_b$. In presence of local

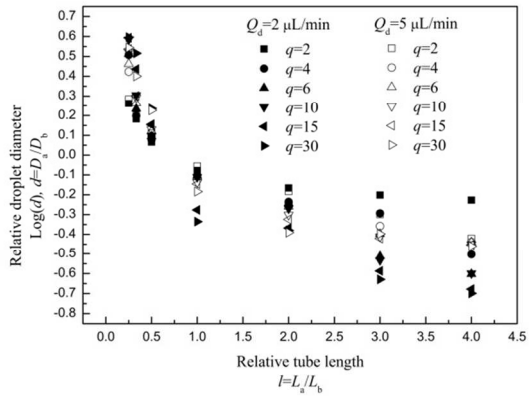

Fig. 4 Relative droplet size versus relative tube length. We respectively keep the dispersed flow rate Q_d=2 μL/min and 5 μL/min, adjust the continuous flow rate at a constant l, and then vary L_a, L_b to observe the dependence of it.

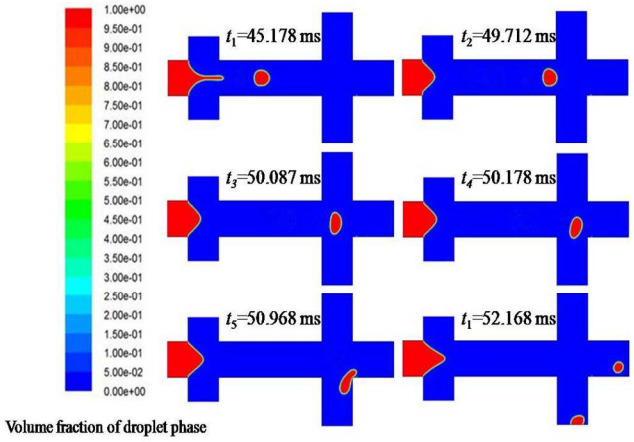

Fig. 5 Numerical simulation of the droplet splitting process. The calculational material properties are shown as follows: channel size is 150 μm, mineral oil dynamic viscosity η_c=0.02Pa•S, density ρ_c=840kg/m^3, continuous phase flow rate Q_c=60 μL/min; deionised water dynamic viscosity η_d=0.001Pa•S, density ρ_d=1000kg/m3, interfacial tension σ=0.015N/m, dispersed phase flow rate Q_d=2 μL/min.

knowledge, the relative flow resistance should be $R_a<R_b$ and the primary droplet should be inclined to flow through outlet A with the expected relative droplet size $D_a>D_b$ as reported by Fleury et al that higher resistance means smaller droplet[33]. Since the puzzling result is confirmed repeatedly in our observations, we make some numerical simulations by VOF method in Fluent to observe the detailed splitting process[34-36]. The simulation result in Fig. 5 validate again that $D_a<D_b$. We find the primary droplet deforms strongly by two branching elongation flow, and the trajectory of its centre do not go right against the edge angle, but a bit lower when the crash happens, leading to the result $D_a<D_b$. We believe this is caused cooperatively by asymmetric flowing and outer viscous drag in the junction, and the inner vorticity of the droplet may also play a role. However, the detailed mechanism still needs to be further explored.

Conclusion

As was described in this innovation, this device is capable to split primary droplet into homogeneous daughter droplets ranging from 15-170 μm with polydispersity index less than 3.02%. Comparing with conventional PDMS microchip for droplet fission, this reusable and reassemble microfluidic device containing adapters and capillary tubes is simple, high pressure resistance, quite cheap, durable, and easy to be cleaned. These characteristics make it possible for large-scale production. Varying either the flow rate or tube length, we can obtain diverse daughter droplets. Though these cross-junctions are generally used in biological research and application as assembly connectors, we develop them as a valuable choice for both droplet generation and droplet fission.

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Notes and references

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1. B. T. C. Lau, C. A. Baitz, X. P. Dong and C. L. Hansen, *J Am Chem Soc*, 2007, 129, 454-455.
2. B. Zheng, L. S. Roach and R. F. Ismagilov, *J Am Chem Soc*, 2003, 125, 11170-11171.
3. S. Koster, F. E. Angile, H. Duan, J. J. Agresti, A. Wintner, C. Schmitz, A. C. Rowat, C. A. Merten, D. Pisignano, A. D. Griffiths and D. A. Weitz, *Lab on a chip*, 2008, 8, 1110-1115.
4. J. F. Edd, D. Di Carlo, K. J. Humphry, S. Koster, D. Irimia, D. A. Weitz and M. Toner, *Lab on a chip*, 2008, 8, 1262-1264.
5. J. S. Fisher and A. P. Lee, *Roy Soc Ch*, 2005, 647-649.
6. C. X. Zhao, *Advanced drug delivery reviews*, 2013, 65, 1420-1446.
7. S. Moon, S. K. Hasan, Y. S. Song, F. Xu, H. O. Keles, F. Manzur, S. Mikkilineni, J. W. Hong, J. Nagatomi, E. Haeggstrom, A. Khademhosseini and U. Demirci, *Tissue Eng Part C-Me*, 2010, 16, 157-166.
8. S. Tasoglu and U. Demirci, *Trends Biotechnol*, 2013, 31, 10-19.
9. B. J. Hindson, K. D. Ness, D. A. Masquelier, P. Belgrader, N. J. Heredia, A. J. Makarewicz, I. J. Bright, M. Y. Lucero, A. L. Hiddessen, T. C. Legler, T. K. Kitano, M. R. Hodel, J. F. Petersen, P. W. Wyatt, E. R. Steenblock, P. H. Shah, L. J. Bousse, C. B. Troup, J. C. Mellen, D. K. Wittmann, N. G.

Erndt, T. H. Cauley, R. T. Koehler, A. P. So, S. Dube, K. A. Rose, L. Montesclaros, S. Wang, D. P. Stumbo, S. P. Hodges, S. Romine, F. P. Milanovich, H. E. White, J. F. Regan, G. A. Karlin-Neumann, C. M. Hindson, S. Saxonov and B. W. Colston, *Anal Chem*, 2011, 83, 8604-8610.

10. M. Nakano, J. Komatsu, S.-i. Matsuura, K. Takashima, S. Katsura and A. Mizuno, *Journal of Biotechnology*, 2003, 102, 117-124.
11. A. C. Hatch, J. S. Fisher, A. R. Tovar, A. T. Hsieh, R. Lin, S. L. Pentoney, D. L. Yang and A. P. Lee, *Lab on a chip*, 2011, 11, 3838-3845.
12. A. M. Nightingale, S. H. Krishnadasan, D. Berhanu, X. Niu, C. Drury, R. McIntyre, E. Valsami-Jones and J. C. deMello, *Lab on a chip*, 2011, 11, 1221-1227.
13. E. M. Chan, A. P. Alivisatos and R. A. Mathies, *J Am Chem Soc*, 2005, 127, 13854-13861.
14. S. L. Anna, N. Bontoux and H. A. Stone, *Applied Physics Letters*, 2003, 82, 364.
15. S. L. Anna and H. C. Mayer, *Physics of Fluids*, 2006, 18, 121512.
16. W. C. Jeong, J. M. Lim, J. H. Choi, J. H. Kim, Y. J. Lee, S. H. Kim, G. Lee, J. D. Kim, G. R. Yi and S. M. Yang, *Lab on a chip*, 2012, 12, 1446-1453.
17. T. D. Martz, D. Bardin, P. S. Sheeran, A. P. Lee and P. A. Dayton, *Small*, 2012, 8, 1876-1879.
18. E. Castro-Hernandez, W. van Hoeve, D. Lohse and J. M. Gordillo, *Lab on a chip*, 2011, 11, 2023-2029.
19. K. Kawai, M. Fujii, J. Uchikoshi, K. Arima, S. Shoji and M. Morita, *Current Applied Physics*, 2012, 12, S33-S37.
20. D. N. Adamson, D. Mustafi, J. X. Zhang, B. Zheng and R. F. Ismagilov, *Lab on a chip*, 2006, 6, 1178-1186.
21. S. Y. Teh, R. Lin, L. H. Hung and A. P. Lee, *Lab on a chip*, 2008, 8, 198-220.
22. W. C. Nelson and C. J. Kim, *J Microelectromech S*, 2011, 20, 1419-1427.
23. Y. Wang, Y. Zhao and S. K. Cho, *Journal of Micromechanics and Microengineering*, 2007, 17, 2148-2156.
24. D. Link, S. Anna, D. Weitz and H. Stone, *Physical Review Letters*, 2004, 92.
25. Y.-T. Chen, W.-C. Chang, W.-F. Fang, S.-C. Ting, D.-J. Yao and J.-T. Yang, *Microfluidics and Nanofluidics*, 2012, 13, 239-247.
26. Y.-J. Yang, X. Feng, N. Xu, D.-W. Pang and Z.-L. Zhang, *Applied Physics Letters*, 2013, 102, 123502.
27. M. Yamada, S. Doi, H. Maenaka, M. Yasuda and M. Seki, *Journal of colloid and interface science*, 2008, 321, 401-407.
28. W. Wang, R. Xie, X. J. Ju, T. Luo, L. Liu, D. A. Weitz and L. Y. Chu, *Lab on a chip*, 2011, 11, 1587-1592.
29. B. R. Benson, H. A. Stone and R. K. Prud'homme, *Lab on a chip*, 2013, 13, 4507-4511.
30. P. Wu, Y. Wang, Z. F. Luo, Y. T. Li, M. F. Li and L. Q. He, *Lab on a chip*, 2014, 14, 795-798.
31. V. Chokkalingam, S. Herminghaus and R. Seemann, *Applied Physics Letters*, 2008, 93, 254101.
32. T. Moritani, M. Yamada and M. Seki, *Microfluidics and Nanofluidics*, 2011, 11, 601-610.
33. J.-B. Fleury, O. Claussen, S. Herminghaus, M. Brinkmann and R. Seemann, *Applied Physics Letters*, 2011, 99, 244104.
34. M. Seo, C. Paquet, Z. Nie, S. Xu and E. Kumacheva, *Soft Matter*, 2007, 3, 986.
35. S.-H. Huang, W.-H. Tan, F.-G. Tseng and S. Takeuchi, *Journal of Micromechanics and Microengineering*, 2006, 16, 2336-2344.
36. T. Nisisako, S. Okushima and T. Torii, *Soft Matter*, 2005, 1, 23.