

High-Order Multiple Emulsions Formed in Poly(dimethylsiloxane) Microfluidics**

A. R. Abate and D. A. Weitz*

Multiple emulsions are nested sets of drops.^[1,2] Drops of one kind of fluid are encapsulated inside drops of a second fluid, which themselves can be encapsulated inside drops of yet another fluid. Such “emulsions within emulsions” are very useful for many applications, including for the encapsulation of actives, such as nutrients, pesticides, drugs, and detergents, and as templates for the synthesis of colloids with structured interiors.^[3–5] Multiple emulsions are typically made in bulk using shear cells or porous membrane plates.^[6] To form the multiple emulsions, the drops from one emulsification are fed back into the apparatus with additional fluids and are emulsified again. Such methods can form large quantities of drops very rapidly; however, the individual drop formation is poorly controlled. This produces some double emulsions but they are exceedingly polydisperse.^[7] For higher-order multiple emulsions, such as triple emulsions or quadruple emulsions, the excessive polydispersity makes the methods impractical.

With glass microcapillary devices, monodisperse multiple emulsions can be formed with controlled structure, albeit in much smaller quantities.^[8,9] As opposed to bulk methods in which many drops are formed in parallel with little control, in microcapillary devices, drops are formed individually with a high degree of control. However, the glass devices are difficult to fabricate, requiring the hand alignment of separate microcapillary tubes. This is labor intensive and makes the devices difficult to scale up sequentially for producing higher-order multiple emulsions or in parallel for producing larger quantities. A superior method would combine the control of microfluidic drop formation with increased scalability.

In this paper, we present a simple system to form monodisperse high-order multiple emulsions. This method combines the control of microfluidic drop formation with the

scalability of lithographically fabricated devices.^[10] We use linear arrays of poly(dimethylsiloxane) (PDMS) drop makers with alternating wettability. The precision of the fabrication allows us to carefully engineer the channels to optimize drop formation; this allows us to produce monodisperse drops of a controlled size. The scalability of the fabrication is also critical because it allows us to add drop makers at will to specify the multiple emulsion order. To demonstrate this, we form a variety of multiple emulsions using our method: we begin with single emulsions and incrementally scale up to form quintuple emulsions. To quantify the monodispersity of the multiple emulsions we measure the diameter distributions of the inner drops and outer drop.

To form a water-in-oil single emulsion, we use a single drop maker with uniform hydrophobic wettability.^[11] For the drop formation junction, we use pinned-jet flow focusing (PJFF). PJFF is similar to flow focusing^[12] (FF) except that the central inlet is connected to a side inlet; thus, whereas with FF the inner phase flows into the drop formation junction through one inlet, with PJFF it flows into the junction through two inlets. This stabilizes drop formation, particularly at low flow rates, enabling production of monodisperse drops, as shown in Figure 1a.

To form a double emulsion, we require two drop makers functionalized to have opposite wettability.^[11,13–15] We concatenate a second drop maker onto the first drop maker and spatially pattern the wettability to make the first hydrophilic and the second hydrophobic. The first thus produces oil drops dispersed in water, which flow into the second where the wettability switches and additional oil is added; this encapsulates the oil drops in water drops producing oil/water/oil double emulsions, as shown in Figure 1b.

To form a triple emulsion, we scale up the device by adding a third drop maker, as shown in Figure 1c. However, with additional drop makers, synchronizing drop formation is more difficult: if the timing of even one drop maker in the array is off, the triple emulsion will not be formed, resulting in polydispersity. Therefore, to perfectly synchronize the devices, we hydrodynamically couple them using triggered drop formation. We design each nozzle such that it is slightly narrower than the incoming emulsion from the previous drop maker. This allows the incoming emulsion to obstruct the nozzle, perturbing flow, and triggering the formation of the outer drop. A single emulsion triggers the formation of a double emulsion in the second drop maker, which then triggers the formation of the triple emulsion in a third drop maker, as shown in Figure 1c. The triggered drop formation synchronizes the drop makers such

[*] Prof. D. A. Weitz, Dr. A. R. Abate
Department of Physics and
School of Engineering and Applied Science
Harvard University
Cambridge, MA 02138 (USA)
E-mail: weitz@seas.harvard.edu

[**] This work was supported by a Human Frontiers Grant (RGP0004/2005-C102), the NSF (DMR-0602684) and (DBI-0649865), and the Harvard MRSEC (DMR-0820484).

Supporting Information is available on the WWW under <http://www.small-journal.com> or from the author.

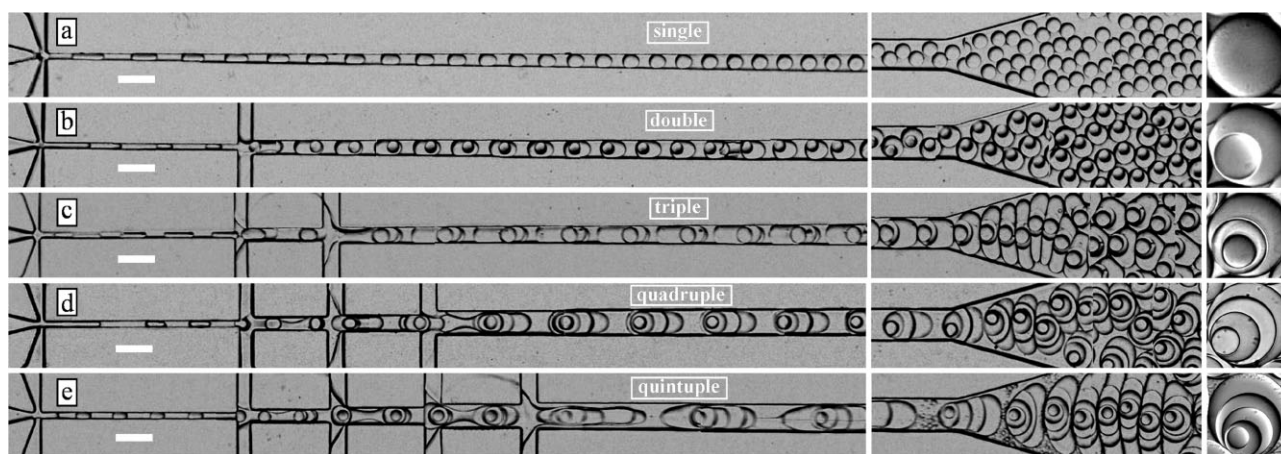


Figure 1. Drop maker arrays used to produce multiple emulsions with controlled order. Photomicrographs of a) single, b) double, c) triple, d) quadruple, and e) quintuple emulsion drop maker arrays. The multiple emulsions produced by the arrays are shown to the right. The scale bars denote 100 μm .

that the multiple emulsion formation is stable and periodic. It is so effective, in fact, that it can be extended to even longer arrays of drop makers, to produce even higher order multiple emulsions. To illustrate this, we synchronize an array of four drop makers to produce quadruple emulsions (Figure 1d) and even five drop makers to produce quintuple emulsions (Figure 1e). The scalability of the fabrication is thus crucial because it allows us to add drop makers as needed to specify the multiple emulsion order.

The precision of the fabrication is equally important because it allows us to carefully engineer the devices; this allows us to optimize drop formation, to produce the multiple emulsions monodispersely. When monodisperse drops are confined in a monolayer they pack hexagonally. We confine our drops in a monolayer by sandwiching them between two plates

that are 50 μm apart. The single emulsions pack hexagonally, as shown in Figure 2a. To quantify the monodispersity of the drops we measure their diameter distribution, as shown in Figure 2b. The diameter distribution is narrow, with coefficient of variation (CV) of 2%, or about 1 μm , our resolution limit. The double emulsions also pack hexagonally because they are also monodisperse (Figure 2c). For the double emulsions, we measure the diameter distributions of both the inner and the outer drops and plot them individually in Figure 2d. The distributions are narrow and have CV of 2%. Similarly, the triple, quadruple, and quintuple emulsions all pack hexagonally because all are monodisperse (Figure 2e, g, and i, respectively). Correspondingly, the diameter distributions for the outer drops and all of the nested inner drops are narrow, with CV of 2%, as shown in Figure 2f, h, and j.

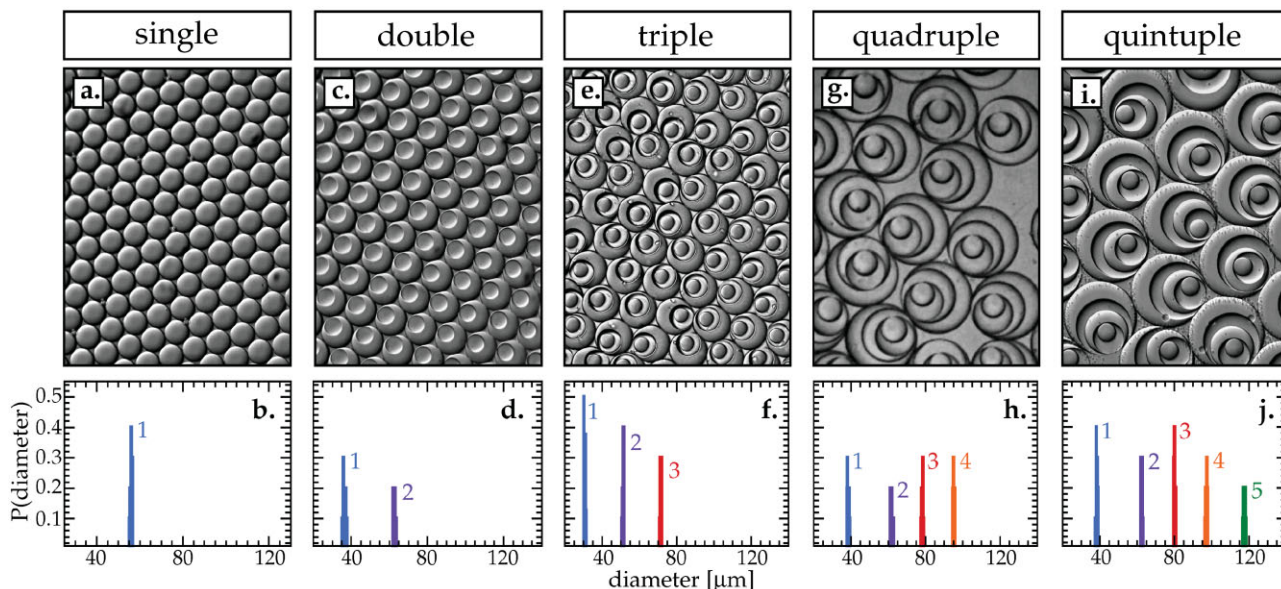


Figure 2. Photomicrographs of a) single, c) double, e) triple, g) quadruple, and i) quintuple emulsions. The emulsions pack hexagonally because they are confined in a monolayer and monodisperse. The diameter distributions are shown for the b) single, d) double, f) triple, h) quadruple, and j) quintuple emulsions; the distributions for the outer drops and each of the nested inner drops are plotted individually.

Lithographically fabricated devices with alternating wettability are optimal for forming multiple emulsions. They combine the precision and scalability necessary to form the emulsions with controlled morphology and with high monodispersity. The multiple emulsions should be useful for making materials with novel optical properties, for synthesizing particles with structured interiors, and as capsules for encapsulating actives.

Experimental Section

Preparation of devices: The devices are fabricated using soft-lithography in PDMS. [10] All devices are fabricated at a fixed channel height of 50 μm . The PDMS devices are bonded to a glass plate using oxygen-plasma treatment. To spatially control wettability, the devices are coated with a photoreactive sol-gel^[11] within 15 minutes after plasma bonding. The devices are filled with the photoreactive sol-gel mixture and heated with a hotplate set to 225 °C; this vaporizes the solvent in the mixture and deposits the coating. The coating makes the channels hydrophobic by default; to spatially pattern wettability, we graft patches of hydrophilic polyacrylic acid onto the interface using ultraviolet (UV) light-initiated polymerization. To accomplish this we fill the coated channels with the hydrophilic monomer solution and expose them to spatially patterned UV light. When exposed to light, the photoinitiator silanes embedded in the sol-gel release radicals that initiate polymerization of the acrylic acid monomers in solution. The resulting acrylic acid polymers are grafted to the sol-gel interface, tethered by covalent linkages with the photoinitiator silanes. This results in a dense covering of polyacrylic acid of the interface, making it very hydrophilic, suitable for forming oil-in-water emulsions.

Device operation: We form the multiple emulsions by injecting water and fluorocarbon oil with surfactants into the linear drop maker arrays. With the single emulsion device we form water-in-oil (W/O) single emulsions by injecting water into the first inlet and oil into the second inlet at 200 $\mu\text{L h}^{-1}$ and 400 $\mu\text{L h}^{-1}$, respectively. With the double-emulsion device we form O/W/O double emulsions by injecting the fluids into the first, second, and third inlets at 200, 400, and 600 $\mu\text{L h}^{-1}$, respectively. With the triple-emulsion device we form W/O/W/O quadruple emulsions by

injecting the fluids into the first, second, third, and fourth inlets at 200, 400, 600, and 800 $\mu\text{L h}^{-1}$, respectively. With the quadruple-emulsion device we form O/W/O/W/O quadruple emulsions by injecting the fluids into the first, second, third, fourth, and fifth inlets at 200, 400, 600, 800, and 1400 $\mu\text{L h}^{-1}$, respectively. With the quintuple-emulsion device we form W/O/W/O/W/O quintuple emulsions by injecting the fluids into the first, second, third, fourth, fifth and sixth inlets at 200, 400, 600, 800, 1400, and 2500 $\mu\text{L h}^{-1}$, respectively.

Keywords:

microfluidics · multiple emulsions · photoresponsive materials · sol-gel processes · wettability

- [1] W. Seifriz, *J. Phys. Chem.* **1925**, 29, 739–749.
- [2] A. T. Florence, D. Whitehill, *Int. J. Pharma.* **1982**, 11, 277–308.
- [3] A. Silva-Cunha, M. Chéron, J. L. Grossiord, F. Puisieux, M. Seiller, *Int. J. Pharma.* **1998**, 169, 33–44.
- [4] A. Edris, B. Bergnstahl, *Nahrung/Food* **2001**, 45, 133–137.
- [5] F. Cournarie, M.-P. Savelli, V. Rosilio, F. Bretez, C. Vauthier, J.-L. Grossiord, M. Seiller, *E. J. Pharma. Biopharma.* **2004**, 58, 477–482.
- [6] S. M. Joscelyne, G. Trägårdh, *J. Membrane Sci.* **2000**, 169, 107–117.
- [7] G. T. Vladislavljjevic, M. Shimizu, T. Nakashima, *J. Membrane Sci.* **2006**, 284, 373–383.
- [8] A. S. Utada, E. Lorenceau, D. R. Link, P. D. Kaplan, H. A. Stone, D. A. Weitz, *Science* **2005**, 308, 537–541.
- [9] L.-Y. Chu, A. S. Utada, R. K. Shah, J.-W. Kim, D. A. Weitz, *Angew. Chem. Int. Ed.* **2007**, 46, 8970–8974.
- [10] Y. Xia, G. M. Whitesides, *Ann. Rev. Mat. Sci.* **1998**, 28, 153–184.
- [11] A. R. Abate, A. T. Krummel, D. Lee, M. Marquez, C. Holtze, D. A. Weitz, *Lab Chip* **2008**, 8, 2157–2160.
- [12] S. L. Anna, N. Bontoux, H. A. Stone, *Appl. Phys. Lett.* **2003**, 82, 364–364.
- [13] T. Nisisako, S. Okushima, T. Torii, *Soft Matt.* **2005**, 1, 23–27.
- [14] M. Seo, C. Paquet, Z. Nie, S. Xu, E. Kumacheva, *Soft Matt.* **2007**, 3, 986–992.
- [15] N. Pannacci, H. Bruus, D. Bartolo, I. Etchart, T. Lockhart, Y. Hennequin, H. Willaime, P. Tabeling, *Phys. Rev. Lett.* **2008**, 101, 164502–4.

Received: April 2, 2009
Revised: May 18, 2009
Published online: