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Synthesis of Composite Emulsions and Complex Foams with the use of Microfluidic Flow-Focusing Devices

*Michinao Hashimoto, Piotr Garstecki, and George M. Whitesides**

Dedicated to our friend and colleague David Reinhoudt, on the occasion of his 65th birthday.

A method is described for the formation of stable, composite aqueous emulsions of 1) combinations of distinct families of bubbles of nitrogen, 2) combinations of distinct families of droplets of an organic fluid (either perfluoro(methyl)decalin or hexadecane), and 3) combinations of bubbles and droplets. A system of two or three microfluidic flow-focusing units is coupled to a single outlet channel. The composite emulsions can be precisely tuned, both in their composition and in the number fraction of components—either bubbles or droplets—of different types. The use of microfluidic technology, with closely coupled flow-focusing units, guarantees that the emulsions are mixed locally at a controlled local stoichiometry. The emulsions self-assemble in a nonequilibrium process to form a wide variety of highly organized periodic lattices.

Keywords:
- bubbles
- droplets
- flow focusing
- microfluidics
- self-assembly

1. Introduction

Microfluidics offers convenient methods for the preparation of monodisperse dispersions of gas in liquid,[1–6] and of liquid in liquid.[4,7–10] The popular geometries used for controlled formation of bubbles and droplets in microfluidic channels include the T-junction[4,6,7,9] and flow focusing.[1,2,8] Other methods exist, including breakup in a microterrace geometry,[11] in diverging channels,[12] and across a plate with arrays of channels.[13] Most of these methods make it possible to form dispersions characterized by narrow size distributions, to control the mean size of the bubbles and droplets, and to tune the volume fraction of the disperse phase. Bubbles and droplets on microfluidic chips find a growing number of uses, including chemical and biological assays inside droplets,[14,15] encapsulating cells,[16–18]and chemical synthesis of nanoparticles[19–21] and nonspherical particles.[22–24]

1.1. Microfluidic Methods for the Formation of Emulsions

Microfluidic systems offer an ability to engineer flow that is also useful in the formation of complex and composite emulsions. Torii and co-workers reported the use of two consecutive T-junctions for the formation of double emulsions (drops within drops).[25] Weitz and co-workers have also demonstrated the use of an axisymmetric device for the formation of complex emulsions.[26] Less attention has been paid to the formation of emulsions that contain more than one kind of the disperse elements of fluid (here we call such emulsions "composite"). Ismagilov and co-workers used a T-junction device to generate bubbles separating aqueous droplets and showed the usefulness of this technique in analytical applications.[27]

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1.2. Generation of Periodic Arrays of Droplets and Bubbles in Microfluidic Devices

Microfluidic systems that generate bubbles or droplets often allow for dynamic self-organization of the bubbles and droplets into flowing, highly ordered lattices.[1,2,5,28–32] Curiously, in spite of the fact that these structures are formed in an open—that is, dissipative—system, in an out-of-equilibrium process, the structure of the lattices can be understood by, or can at least be related to, the interfacial energy of the bubbles. For volume fractions of the disperse phase not exceeding 0.91 (maximum coverage of a plane by monodisperse disks), the bubbles and droplets form either rhombic or hexagonal assemblies, and there is a unique relation between the volume of the bubbles, the volume fraction of the disperse phase, and the structure of the periodic lattice.[2,30] This observation can be related to the preservation of the smallest possible deformation of the area-minimizing spherical shape (or discoid when bubbles and droplets are squeezed between the top and bottom walls of the outlet channel) of the bubbles and droplets. For volume fractions approaching unity, with the volume of each monodisperse bubble held constant, there is more than one possible ordered arrangement.[33] In a model system that we analyzed previously, all of the experimentally observed structures could be related to one of many local minima of the interfacial energy of a quasi-two-dimensional (2D) foam.[34]

1.3. Dynamic Templating and External Control over the Patterns

Although some elements of the mechanisms of formation of the ordered lattices are known,[5,33,35] the out-of-equilibrium process of self-organization in the confinement of a microfluidic channel is not completely understood. The structure of the periodic lattices can be controlled (or changed) by changing the resistance of the outlet channel, or, equivalently, by changing the pressure applied to the system[5] or the total rate of flow of fluids through the device.[33] The ability to control (or at least "affect" in a pronounced way) the process of self-assembly, by changing a small number of parameters that drive the system, lies at the core of the interest in dynamic self-assembly.[36,37] Interesting processes are those that generate structures in dissipative systems, and allow for alteration of the characteristics of these structures by tuning the external forces that drive the system. Here, we present an example of such a system and show that it is possible to engineer the structure of the composite lattices of bubbles and/or droplets.

2. Experimental Design

The system of a number of flow-focusing (FF) units combined into a single device can produce multiple distinct families of droplets or bubbles, with each family consisting of a large number of identical (monodisperse) components (i.e., bubbles and droplets). The system allows for extensive external control over the size and the size distribution of these components. We use these characteristics of our system to introduce complexity into the process of dynamic self-assembly of bubbles and droplets into regular lattices in microfluidic channels. Remarkably, over a wide range of parameters, these emulsions form highly ordered and stable lattices rather than random assemblies. These characteristics provide the basis for a simple experimental system that displays a perplexingly rich dynamic behavior manifested in the formation of a wide range of regular, but surprisingly complex, lattices of bubbles and droplets. Tuning the parameters that can be controlled externally—the rates of flow of all the fluids—results in changes in the number and volume fractions of each of the constituents of the composite foam and, as a consequence, in a change of the structure, symmetry, and morphology of the heterogeneous periodic lattices.

2.1. Design of the Device

We used multiple FF generators, fabricated in polydimethylsiloxane (PDMS) by conventional procedures,[38] connected to a single outlet channel to form the composite structure of bubbles and droplets. Figure 1 illustrates the geometry of the device used to form the composite emulsions and lattices. We placed independent FF generators in parallel, which fed into the end of a common channel. Each of the FF units can independently form distinct families of bubbles or droplets; the parameters of flow of each generator are individually addressable. Remarkably, the different FF generators interact; the performance of each FF generator is influenced by the others.

2.2. Choice of the Fluids

To prepare a composite lattice in the channel, we need to choose a set of fluids with the following properties: 1) the emulsions of disperse phases must be stable against coalescence, 2) the continuous phase must wet the walls of the channels, and 3) the continuous phase cannot swell PDMS.[39,40] Due to the low aspect ratio (height to width) of the outlet channel, the composite lattices that we prepared are quasi 2D; they comprise bubbles and droplets that are squeezed into discoid shapes, and the swelling of the continuous phase to PDMS causes the height of the channel to be nonuniform.[22]

To meet these three requirements, we chose aqueous solution of surfactants (SDS or Tween 20) as the continuous phase. The purpose of using surfactants is 1) to prevent coalescence between bubbles and droplets and 2) to facilitate wetting of the aqueous continuous phase to the inner wall of the channel. The use of surfactants makes it possible for both gas bubbles and oil droplets to form and coexist in the same flow. At the concentrations that we used (that is, above their critical micelle concentration), both Tween 20 (1% w/w) and SDS (2% w/w) worked equally well to generate lattices with stable structures.

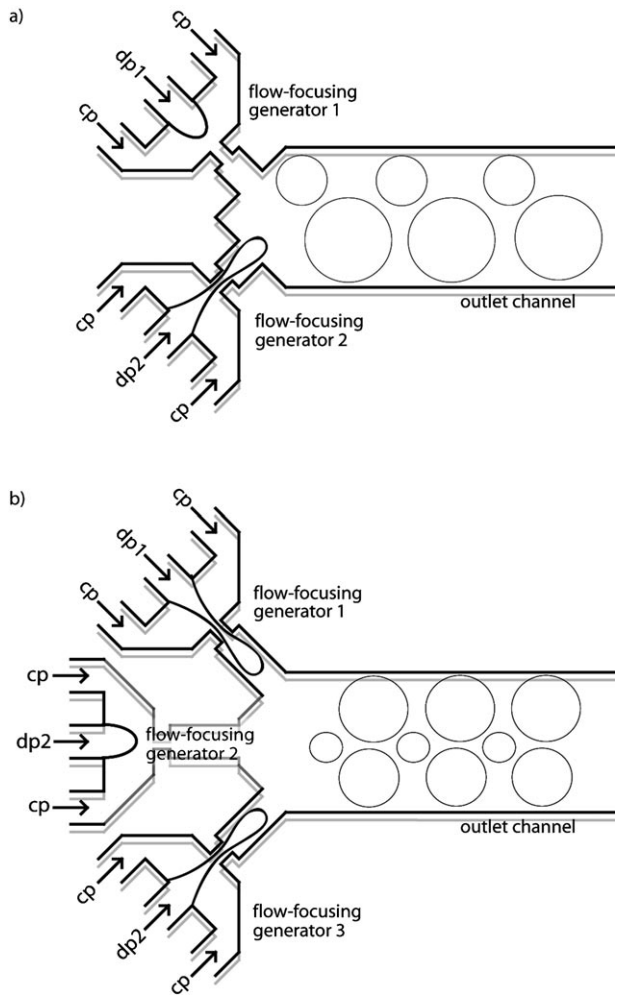

Figure 1. Schematic illustrations of multiple FF generators connected to a single outlet channel. a) Two FF generators placed in parallel and b) three FF generators placed in parallel. The abbreviations cp and dp denote the inlets of continuous and disperse phases, respectively. The arrows indicate the direction of the flow of each phase.

The aqueous phase also does not swell PDMS.[40] We kept the inner walls of the PDMS channel hydrophilic by introducing the continuous phase to the channel immediately after the preparation of the channel.[38] For the disperse phases we chose nitrogen, PFMD, and hexadecane, although other gases and organic fluids should also give analogous results.

2.3. Delivery of the Fluids

We used digital syringe pumps to deliver the liquid (e.g., water, hexadecane, and PFMD) to the device; the pump supplied liquids to the system at *a constant volumetric rate of flow*. We used a pressure-regulating valve connected to a pressurized gas tank (e.g., nitrogen) to deliver the gas to the device at *constant pressure*. The volumetric rate of flow of gas could be estimated as the product of the volume of the bubbles and the frequency of their generation. (Here, both parameters can be established by image analysis.) We did not characterize the volumetric rate of flow of gas, however, since in this work we were primarily interested in the qualitative characteristics of the behavior of the system. In the following, we describe the formation of composite lattice structures comprising either gas bubbles or liquid droplets, or both coexisting in the same continuous phase.

3. Results and Discussion

3.1. Convention

Throughout this article, the figures in parentheses, (Q_c (mL h^{-1}), p_d (psi)), denote the rate of flow of the continuous phase and applied pressure of the *gaseous* disperse phase (i.e., nitrogen), respectively. The figures in brackets, [Q_c (mL h^{-1}), Q_d (mL h^{-1})], denote the rates of flow of the continuous phase and the *liquid* disperse phase (i.e., PFMD or hexadecane), respectively.

3.2. Composite Lattice of Gas Bubbles

We first investigated the formation of multimodal emulsions of nitrogen in an aqueous solution of surfactant (SDS; 2% w/w). We used two FF units coupled to a single outlet channel, and inferred that these two units interacted from the synchronization of their generation of bubbles. When a bubble was forming in one generator, the resistance of the outlet channel increased,[41,42] and the speed of the advance of the gas thread in the other generator simultaneously decreased, because the speed of the pressure-driven flow is inversely proportional to the fluidic resistance. The pinch-off of the thread of the gas in one channel, in turn, accelerated the advance of the gas in the other channel. As a result, the gas threads in the two neighboring generators broke up in alternation. We have previously described a system of five FF elements coupled in series and fed from a common source of the continuous fluid; the system produced very long, stable, and repeating series of bubbles of different sizes.[43] The system that we study here is simpler than the previous one[43] in that it contains a smaller number of FF units which are independently addressable (fed) with the fluids; the system is also simpler in the observed dynamics. Similarly to the multi-orifice system,[43] the behaviors that we describe here are reproducible and stable over wide ranges of the rates of flow of the various phases.

As the resistance of the outlet channel depends on the structure of the foam that occupies (flows in) it, after changing the rates of inflow of the fluids into the device we had to allow the system to stabilize for intervals of time ranging from seconds to minutes. After this time, the system settled in a defined cycle of generation of bubbles. We thus obtained stable lattice structures that did not change with time (Figure 2). In this system, however, even a slight change in the flow parameters (e.g., 5% increase in the applied pressure) in *one* generator completely altered the behaviors of

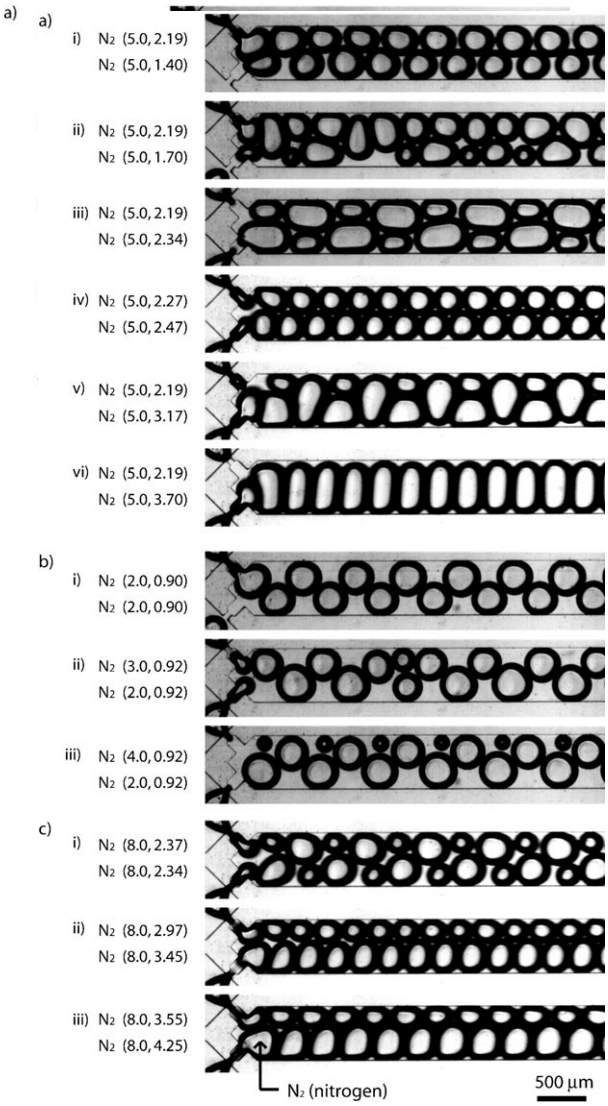

Figure 2. Optical micrographs of the self-assembled structures of nitrogen bubbles. a) Variation of the applied pressure of the nitrogen. The pressure applied to the bottom generator was varied, while the pressure applied to the top generator was held constant. The rate of the continuous phase was held constant for both generators. i) Only the top generator produced bubbles. ii) Both generators produced polydisperse bubbles. iii) Both generators produced bidisperse bubbles—large and small—in alternation. iv) Both generators produced monodisperse bubbles. v) The top generator produced monodisperse bubbles and the bottom generator produced bidisperse bubbles. vi) Only the bottom generator produced bubbles. b) Variation of the rate of flow of the continuous phase; the pressure applied to the system was fixed, and the rate of flow of water applied to the top generator was varied. i) The system produced monodisperse bubbles in both generators, and formed a stable structure of the composite lattice. ii) Both generators produced mostly ($\approx$80%) monodisperse bubbles. The top generator occasionally produced different sizes of bubbles, and stable structures of the composite emulsions were not obtained. iii) The top generator produced bidisperse bubbles and the bottom generator produced monodisperse bubbles. An ordered, composite lattice of bubbles was formed. c) Ordered structure of bubbles at high rates of flow of the continuous phase (8.0 mL h^{-1}). Both monodisperse and bidisperse stable lattice structures were accomplished. In (ii) and (iii), the relative sizes of bubbles are controlled.

both generators. It is thus more difficult to predict the size and dispersity of bubbles forming in a system of coupled FF generators than in a single FF unit.[1,2,31,44] In a single FF generator, we expect simple transitions from the monodisperse regime to the bidisperse regime, in response to the increase in the rate of flow.[2,45] In the coupled arrangement, the system is stable in either the monodisperse or bidisperse regime, but it is difficult to generalize the trend of the behavior. For example, an increase in the applied pressure in one generator, with all other parameters held constant, resulted in an unexpected transition of the pattern of the breakup in the generator. Figure 2a ii–vi shows this transition of breakup patterns. The bottom generator produced bubbles of varying size—changing from polydisperse to bidisperse to monodisperse to bidisperse to monodisperse—as the applied pressure to the bottom generator was increased stepwise. The fluctuation of the resistance in the outlet channel affects the size and dispersity of bubbles that are formed in both FF generators; since the formation of bubbles in each generator is strongly coupled, we cannot predict the behavior of one generator separately.

We do not presently have a "theory" of these coupled systems—the dynamics of two coupled generators are too complex to predict. We still found that at a high rate of flow of the continuous phase (8.0 mL h^{-1}; Figure 2c), the systems allowed independent control over the size of the bubbles. This observation is perhaps explained by the fact that the increase of the pressure drop in the outlet channel, due to the high rate of flow of the continuous phase (since we need to apply higher pressure to the system to sustain the imposed rate of flow), moderates the relative fluctuation of the pressures in the generators that results from the formation of individual bubbles. As a result, the formation of bubbles in one generator is less dependent on the other generator, and individual controls over the size of bubbles are allowed.

The structure of the foam in the outlet channel depended sensitively on the flow parameters. Although it was possible to obtain stable periodic assemblies for many combinations of flow parameters, the structure of the lattice in the outlet channel could also be disordered. Figure 3 displays a series of time-resolved images of the dynamic self-assembly of composite lattices. In this example, the structure of the lattice alternates between ordered and disordered states. The size of a bubble produced in one generator closely influences the size of the immediately subsequent bubble produced in the other generator. If one generator produces a slightly larger bubble than the preceding one, the next bubble produced is smaller than the preceding bubbles. The disproportion of the size of the bubbles increased as more bubbles formed subsequently (Figure 3d–j), and the system displayed irregular dynamics. After a certain interval of time (here, $\approx$1.5 s), the system locked back to the original periodic dynamics, with each generator producing monodisperse bubbles (Figure 3m and n). The system continued to switch between the simply periodic and irregular dynamics.

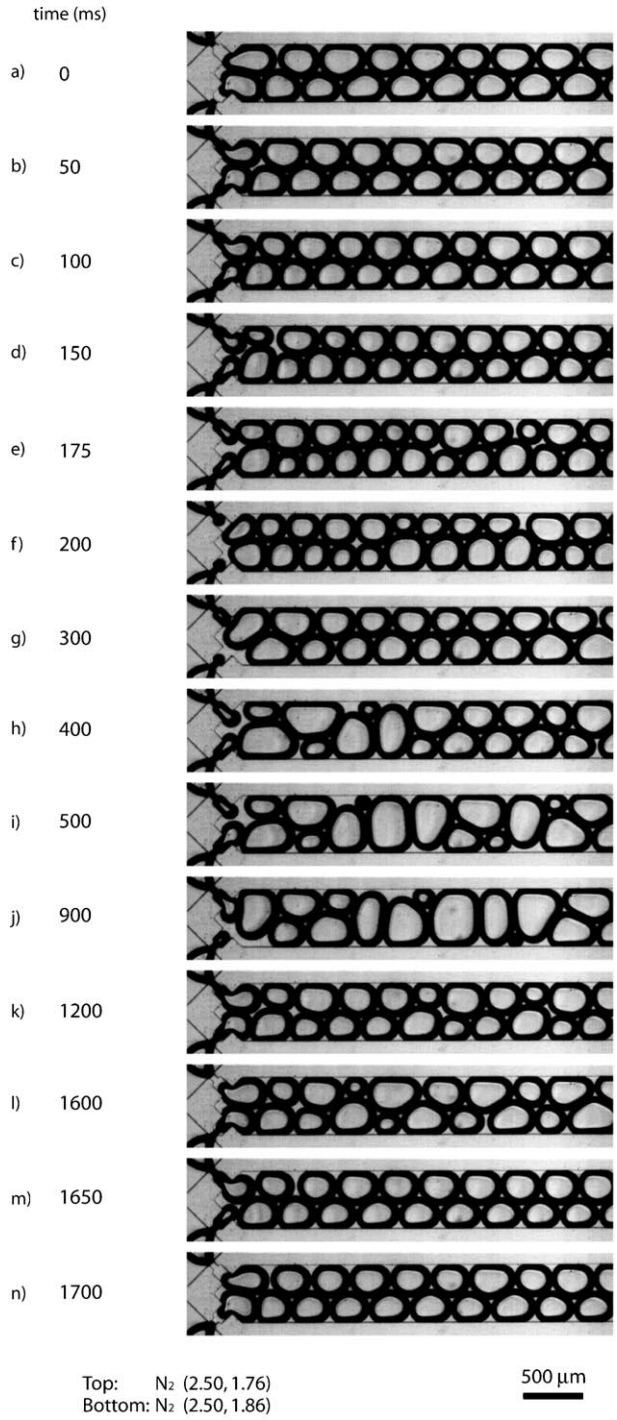

Figure 3. Time-resolved optical images displaying the transition from the ordered to the disordered structure of a self-assembled lattice of bubbles. a–c) Ordered, self-assembled lattice of bubbles. d) The bottom generator produced a larger bubble than the preceding monodisperse bubbles. This larger bubble caused the top generator to produce a smaller bubble. e–j) The fluctuation of the size of the bubbles formed in each generator gradually increased, and the disproportion in the size of bubbles formed in each generator became prominent. Both generators produced polydisperse bubbles, and the bubbles in the outlet channel formed disordered structures. k, l) The formation of the bubbles in the two generators started to stabilize again—each generator produced relatively similar sizes of bubbles in alternation. m, n) The system regained a steady state in which the generators produced monodisperse bubbles to form an ordered structure in the outlet channel.

3.3 Composite Lattice of Liquid Droplets

We also investigated the formation of liquid droplets in the same system comprising two FF units coupled to a single outlet channel. We used PFMD for the disperse phase and an aqueous solution of SDS (2% w/w) for the continuous phase. Droplets of PFMD were stable against coalescence in the presence of this surfactant.

When forming liquid droplets, we used digital syringe pumps to deliver the disperse fluid to the system; we set the *volumetric rates* of flow delivered to the system constant. In contrast to the formation of gas bubbles, where we set the *pressure* of applied gas constant, we observed that the two FF units interacted less than in the gas–liquid system. The rate of pressure-driven flow depends on the fluctuation of fluidic resistance in the device, while the rate of volumetric flow stays nearly constant for a set value. Since the neighboring unit causes the fluctuation of the resistance, the two FF units influence each other more significantly for pressure-driven flows than for volumetric flows. The strength of the interaction also plausibly reflects the fact that liquids are much less compressible than gases. As a consequence, we were able to exert precise, independent control over the operation of each of the two units, and tune the size and frequency of the formation of the droplets with greater predictability.

We created composite lattices made up of two different sizes of droplets. To control the size of the droplets, the rate of flow of the disperse phase was changed. The size of the droplets varied continuously and monotonically in response to the rate of flow of the disperse phase (Figure 4 a–f). As we increased the rates of flow of the continuous phases, the volume of each droplet became lower than that at lower rates of flow of the continuous phases. The span of the outlet channel held three rows of droplets, and we observed that the droplets assembled into a hexagonal lattice with periodic defects (Figure 4 g and h). Again, the relative sizes of the droplets were tuned by the rate of flow of the disperse phase.

The same system also permitted the control of the stoichiometry of droplets formed in each generator. The frequency of the formation of the droplets is controlled by the rate of flow of the continuous phase. We obtained stable composite lattices, in which the ratio of the frequencies of formation of the droplets (n:1; $n=1$–4) was controlled by changing the rates of flow in each of the two generators (Figure 5 a–d). The increase in the rate of flow of the continuous phase (water), with the rate of flow of the disperse phase (PFMD) held constant, resulted in two simultaneous changes: 1) an increase in the frequency of the breakup of the droplets, and 2) a decrease in the size of the droplets. (For the sets of flow rates we examined, the families of droplets formed in each generator stayed monodisperse.) The change in the size of the droplets can be, to some extent, compensated by the change in the rate of flow of the disperse phase. These controls over the size and frequency of the droplets permitted formation of stable, ordered lattice structures consisting of two sizes of droplets with defined stoichiometry.

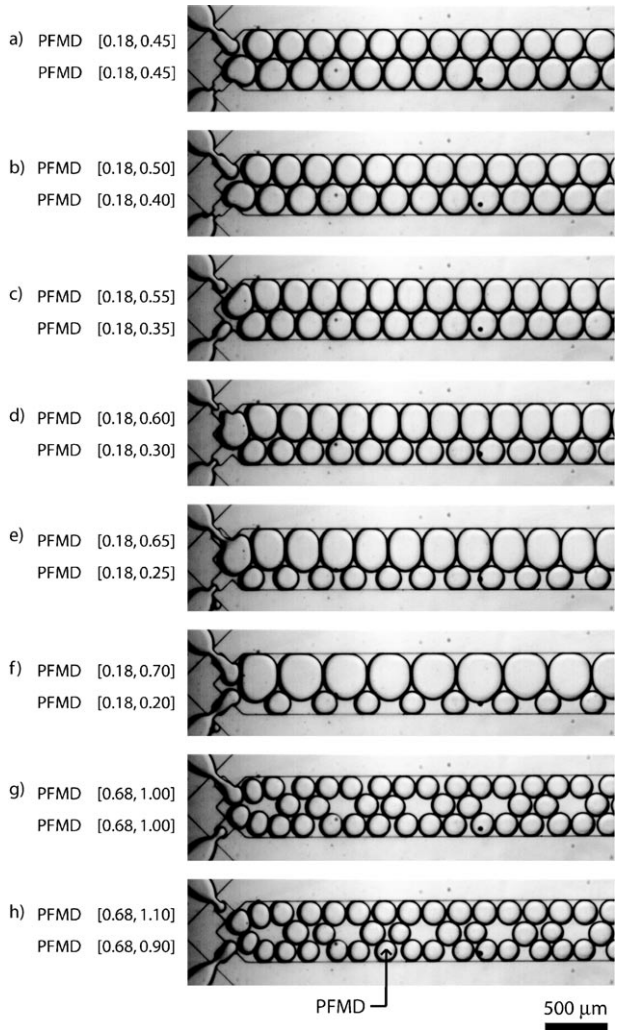

Figure 4. Optical micrographs of stable lattices of PFMD droplets. The size of droplets formed in each generator was controlled by tuning the rates of flow in each of the two FF units. a–f) The rate of flow of PFMD of the top generator was increased (with a 0.05 mL h^{-1} increment, starting from 0.45 mL h^{-1}), and the rate of flow of PFMD of the bottom generator was decreased (with a 0.05 mL h^{-1} decrement, starting from 0.45 mL h^{-1}). The flow rate of water was held constant (0.18 mL h^{-1}). The size of the droplets sensitively responded to the change in the rate of flow of PFMD. The series of micrographs shows the stepwise change in the size of the droplets. g, h) The images show another example of the response of the size of droplets to the rate of flow of PFMD. The rate of flow of water was held at 0.68 mL h^{-1}, a value higher than that in the example shown in (a–f). The system generated smaller droplets, which packed into a hexagonal pattern with periodically missing droplets (i.e., every third droplet in the middle row).

3.4. Mixed Composite Lattice of Gas Bubbles and Liquid Droplets

As disperse nitrogen gas, fluorocarbon liquid, and hydrocarbon liquid are stable against coalescence in an aqueous solution of surfactants, we were able to generate composite lattices of bubbles and droplets coexisting in the same continuous phase. Here, we demonstrate the formation of a mixed lattice of nitrogen gas bubbles and PFMD droplets.

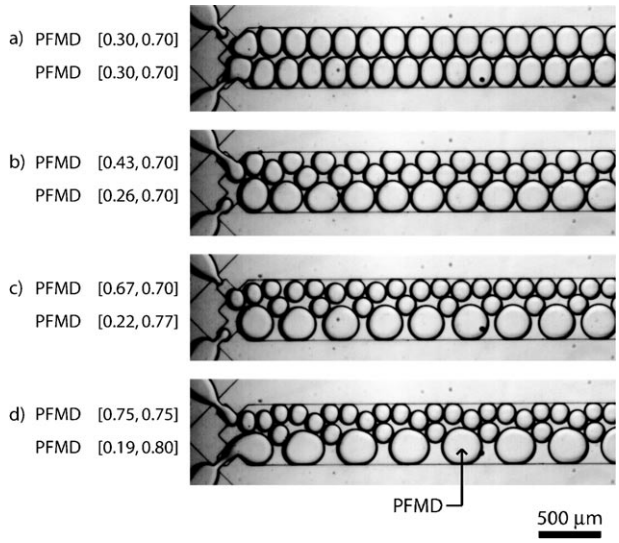

Figure 5. Optical micrographs of stable lattices of PFMD droplets. The control over the stoichiometry of the droplets produced in each generator by changing the frequency of the formation of droplets is demonstrated. The rate of flow of PFMD was kept nearly constant ($\approx$0.70 mL h^{-1}) and the rate of flow of water was varied. The higher the rate of flow of water, the higher the frequency of formation of the droplets in each generator. The ratio of the frequencies of formation of droplets (top generator to bottom generator) is: a) 1:1, b) 2:1, c) 3:1, and d) 4:1.

Figure 6 displays composite lattices consisting of bubbles and droplets, with an aqueous solution of SDS (2% w/w) as the continuous phase, and PFMD and nitrogen gas as the disperse phases. The formation of the bubbles synchronized spontaneously with the formation of droplets: when a droplet of PFMD was forming in the FF orifice, the thread of gas in the neighboring orifice "waited" upstream, and advanced into its orifice only after the droplet of PFMD had detached and moved into the outlet channel. In contrast to the system in which both generators formed liquid droplets, the formation of gas bubbles is strongly coupled with the formation of liquid droplets. We demonstrated some control (although not yet fully characterized) over the number ratio of the bubbles and droplets in the outlet channel (Figure 6a–d). At high pressures of applied gas ($p > 1.0$ psi), the bubbles and droplets filled the outlet channel at a high fraction of coverage of the channel floor (greater than 0.91), and the projections of the bubbles and droplets onto the floor of the channel became distorted into noncircular shapes (Figure 6e–g). Unlike the system of gas bubbles with high volume fraction (close to 1) that we described in a previous paper,[33] the operation of the system was stable over time.

3.5. Systems Composed of Three Flow-Focusing Generators

The simultaneous use of three generators (Figure 1b) made it possible to increase the variety of composite lattices that can be generated. As we could control the flow parameters of each of the three generators independently, we

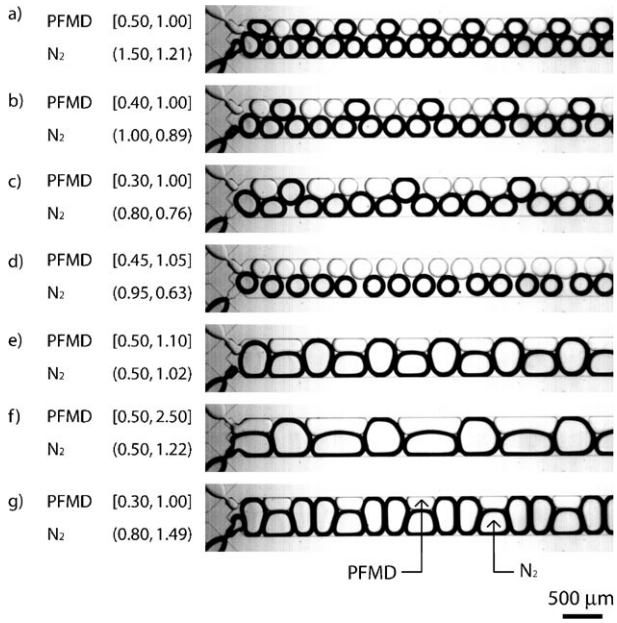

Figure 6. Optical micrographs of stable, periodic composite foams consisting of nitrogen bubbles and PFMD droplets. a–d) Variation in the stoichiometric ratio of PFMD droplets and nitrogen bubbles. e–g) Stable, ordered pattern of noncircular mixed foam (with the volume fraction greater than 0.91). Note that the bubbles of nitrogen appear to have darker rims than the droplets of PFMD, due to the large difference in the index of refraction between nitrogen and water.

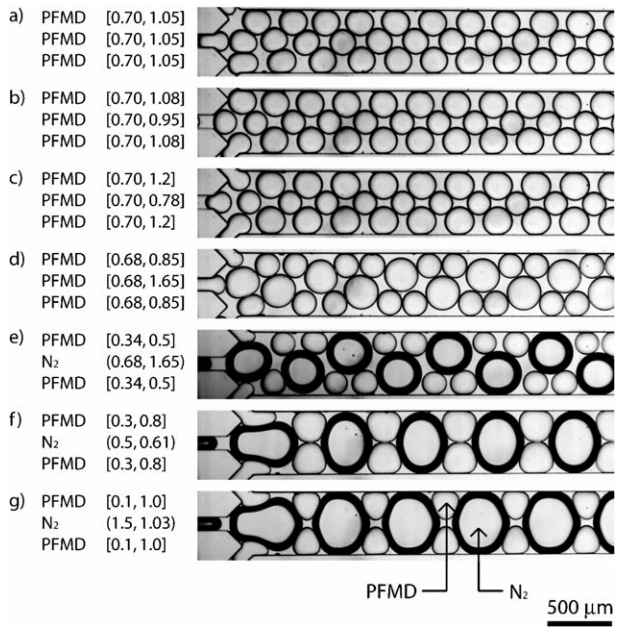

Figure 7. Optical micrographs of composite lattices formed in the channel connected with three generators. a–d) Composite lattices of PFMD droplets. Similarly to the system of two FF generators, the ratio of flow parameters in each generator influences the relative sizes of the PFMD droplets formed in each generator. e–g) Composite lattices of PFMD droplets and nitrogen bubbles. The bubbles spatially separated the PFMD droplets in the outlet channel.

were able to address the size and composition of each of the building blocks of the composite emulsion. Figure 7 displays examples of lattices that formed in a channel connected to three FF generators. The timing of the breakup of the gas or liquid at neighboring generators—that is, generators 1 and 2, and generators 2 and 3—are again, to a certain degree, synchronized.

The same system also permitted the formation of complex, composite lattices comprising three different components. We generated stable lattices by changing the size and stoichiometry of the three elements (Figure 8 and Figure 9). The examples in Figure 8 show composite lattice structures consisting of nitrogen bubbles, PFMD droplets, and hexadecane droplets. Although the system still needs to be fully characterized, it operated somewhat similarly to the system of two FF generators. For example, we obtained a mixture of PFMD droplets, nitrogen bubbles, and hexadecane droplets with a stoichiometric ratio of 1:1:1 (Figure 8c). An increase in the rate of flow of water in generator 2 (for nitrogen bubbles) doubled the frequency of the formation of bubbles; we obtained a combination mixture of the same emulsions, with a stoichiometric ratio of 1:2:1 (Figure 8d). Finally, an increase in the rate of flow of hexadecane in generator 3 resulted in an increase in the size of the hexadecane droplets, with the stoichiometric ratio of the emulsions remaining unchanged (Figure 8e). This demonstration makes it clear that sensible choice of the flow parameters permits control over relatively complex structures that are generated in the outlet channel.

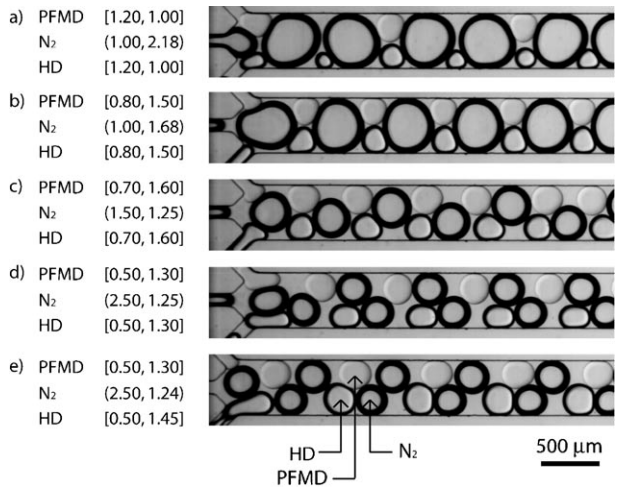

Figure 8. Optical micrographs of composite lattices formed in the system of three FF generators. The generation of stable lattices consisting of three different elements is demonstrated. a–e) Composite lattices consisting of PFMD droplets, nitrogen gas bubbles, and hexadecane droplets. The parameters of the flow in each generator influenced the size and stoichiometry of each element in the composite lattice structure obtained. The ratios of the number of droplets and bubbles are a) 1:2:2, b, c) 1:1:1, and d, e) 1:2:1 for PFMD droplets/nitrogen bubbles/hexadecane droplets, respectively. These three elements mixed locally at the entrance of the outlet channel to form a stable lattice structure.

small

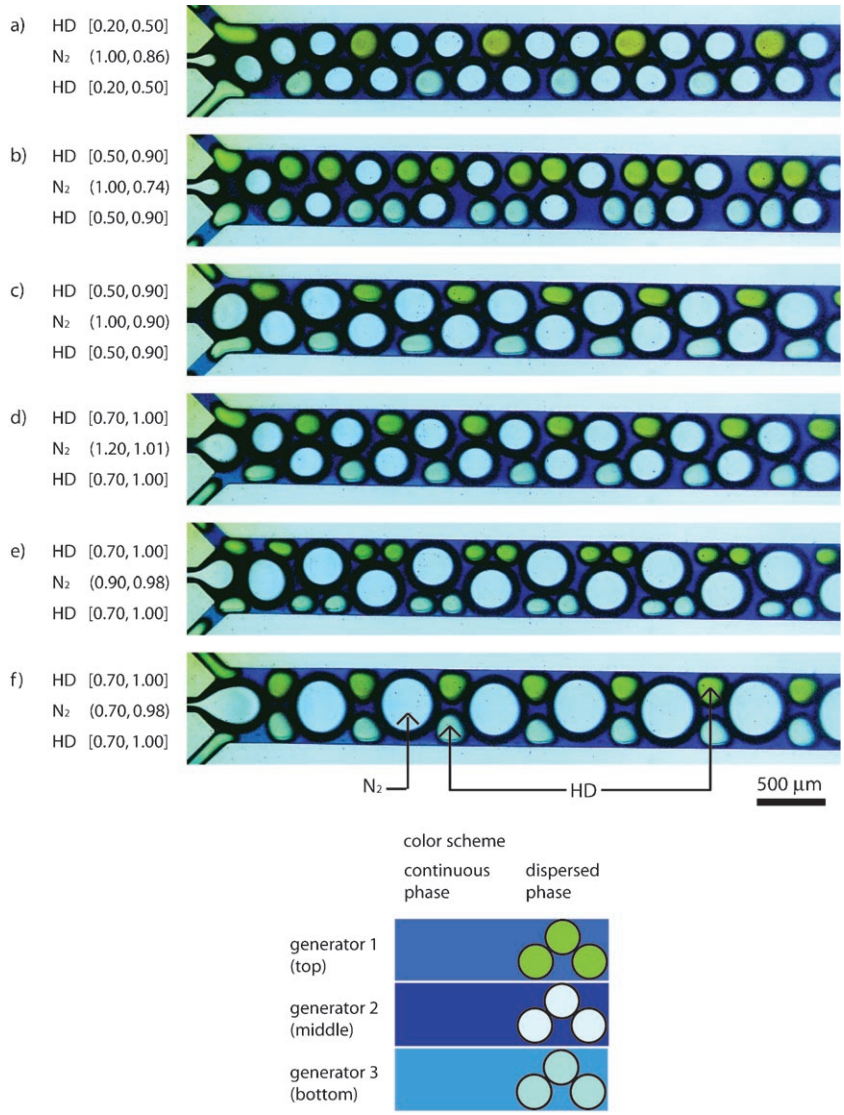

Figure 9. Optical micrographs of composite lattices formed in the system of three FF generators. The fluids used in each generator are colored with different dyes: generator 1 (blue, orange), generator 2 (purple, transparent), and generator 3 (green, yellow), where the colors in parentheses denote the colors of the continuous and disperse phases, respectively. Note that the colors of the fluids did not appear in the images as they appeared in the actual solutions that were prepared. a–f) Self-assembled, composite lattice structures obtained at different sets of flow parameters. The scheme of colors displays the average colors of each continuous phase and disperse phase, extracted from the original digital images.

Figure 9 displays the lattice structure generated in the same system using a set of colored fluids, which made it possible to visualize the flow of the continuous and disperse phases from each generator separately. The images indicate that the neighboring continuous phases are mixed locally as they flow downstream; the continuous phase shows progressively more uniform color when looking in the downstream direction. As mixing of co-laminar streams using bubbles has been demonstrated previously,[46] this observation suggests that the continuous phases of the composite lattices of emulsions—initially coming from different inlets—are mixed along the flow and eventually become homogeneous in the outlet channel.

4. Conclusions

We have demonstrated that the systems of multiple, coupled FF devices described here can generate composite emulsions containing bubbles or droplets of distinct sizes, compositions, and stoichiometry. These emulsions self-assemble into highly regular lattices in the outlet channel. The structure of the lattices can be controlled by changing the external parameters of flow.

4.1. Generation of Structures

The variety of the structures of emulsions that we obtained shows that microfluidic platforms combined with the FF generators offer convenient technologies for the design and generation of composite emulsions; all the important characteristics of the composite emulsions can be controlled. The system we used herein allows the design of emulsions containing droplets of different chemical composition and physicochemical properties, and mixes them locally at defined volume (or number) fractions. The choice of fluids used in our experiments was dictated by experimental feasibility. The use of other sets of fluids should be possible as long as the right surface chemistries of the microfluidic channels are taken into account. The flexibility in the type of emulsions that can be used, in addition to the control over the structures that can be created, offers new capabilities to arrange the positioning of multiple components in microfluidic platforms. In this work we have only studied the formation of quasi 2D (single layer of bubbles/droplets) lattices. It is possible that the processes described here could be extended to the formation of 3D heterogeneous and periodic lattices, perhaps by methods similar to those used in the self-assembly of monodisperse droplets into regular 3D lattices.[32,47]

4.2. Stability of the Lattice Structure

To obtain stable lattice structures reproducibly and predictively, the system needs to meet two criteria: 1) each generator must form monodisperse bubbles/droplets, and 2) bubbles/droplets must occupy a sufficiently high volume fraction to pack in the outlet channel.

As regards the monodispersity in the coupled system, for the formation of gas bubbles, the size of bubbles is strongly influenced by the state of the other generator and of the outlet channel (i.e., fluctuation of fluidic resistance). It is difficult to obtain monodisperse bubbles for an extended period of time, and consequently it is difficult to obtain stable lattice structures consisting only of bubbles. We discussed this strong interaction of the formation of gas bubbles in relation to Figure 3. For the formation of liquid droplets, each FF generator produces monodisperse droplets for a wide range of flow parameters. The size and the frequency of formation of droplets in each generator are individually addressable. The frequency of formation of bubbles/droplets can be controlled primarily by the flow rate of the continuous phase, and we can obtain stoichiometric ratios of the bubbles and droplets.

In addition to the monodispersity of the bubbles/droplets, a stable periodic pattern of the lattice also requires that bubbles/droplets "pack" in the outlet channel; the stability depends critically on the volume fraction of bubbles/droplets in this channel. At high volume fractions the periodic patterns are stable. At lower volume fractions (below the minimum threshold for contact between bubbles and droplets) the lattices are not stable—the system often switches to disordered arrangements of bubbles/droplets. The size of individual bubbles/droplets can be controlled primarily by the applied pressure of gas and the rate of flow of the disperse phase.

4.3. Coupling

We observed that placing the FF units in close proximity results in a coupling of their dynamics. Such coupling is of fundamental relevance in the problem of parallelization of the formation of bubbles and droplets on microfluidic chips. Interactions between the individual units can lead to high-order dynamic behaviors and to irregular dynamics, and might preclude formation of monodisperse emulsions. Here we show that coupling of the dynamics of the individual units can also be advantageous in stabilizing the modes of operation of the device, in which bubbles and droplets of a well-defined dispersity are emitted from each unit alternately to form composite emulsions and ordered lattices. Although we have not explored the coupling of the formation of bubbles in adjacent FF generators in detail here, we note that higher volume fractions of bubbles/droplets seem to increase the strength of interaction between the nozzles. Also, we observe that a gas–gas system (i.e., a system in which the disperse phase in both nozzles is a gas) shows more pronounced coupling of the dynamics of the individual orifices than do liquid–liquid systems. More research is required to understand how the physical properties of the fluids (e.g., interfacial tension, viscosity contrast) influence the strength of the interaction between neighboring orifices.

The alternating generation of droplets/bubbles by two or more FF nozzles lies at the core of the formation of periodic composite lattices. We suspect that this behavior results from negative feedback between the increased resistance to flow introduced by a bubble/droplet being generated from one orifice and the advance of the tip of the fluid in the neighboring generator. As there is now a growing understanding of microfluidic systems in which the dynamics of flow depend strongly on moving "resistors" (that is, bubbles or droplets),[5,46,48–52] it is possible that more complex protocols for the formation of repeating sequences of heterogeneous droplets/bubbles can be designed and executed, thus leading to more complex periodic lattices. Controlled fabrication of ordered, dissipative structure is of great interest in the study of complexity, and sequences of droplets of different compositions may also find applications in advanced lab-on-a-chip devices.

To the best of our knowledge, there is no existing theory for coupled FF devices. The operation of single FF devices is described both quantitatively and qualitatively in a number of reports.[1–3,5,8,10,26,29,33,34,44,45,53] We can refer to the work on rate-of-flow-controlled breakup in FF devices—the speed of breakup of bubbles is proportional to the inflow of the continuous phase into the orifice.[2,3] The same principle still holds, at least qualitatively, in the coupled system, as we demonstrated control over the stoichiometry of composite lattice structures.

The interplay between the blockage of one orifice by a gaseous thread and the rate of breakup in a neighboring orifice was also discussed previously.[43] Qualitatively, the mechanism behind the interaction between the neighboring orifices is that "blockage" of one orifice by the immiscible thread (during the process of formation of a bubble/droplet) increases the pressure in the continuous phase in both neighboring orifices. The increase in the pressure acts to squeeze the thread that is already in one of the orifices, and also acts to either prevent the entering of the thread into the second orifice, or—if that orifice is already occupied by the immiscible thread—speed up the breakup in both orifices. Both the entrance of the thread into the orifices and the breakup of the threads that are already in the orifices affect in turn the rate of formation of the bubbles/droplets; this effect closes the feedback loop between breakup and entering of the thread. In our current system, the feedback between the neighboring orifices results in alternating generations of bubbles/droplets, and this alternating generation, in turn, allows bubbles/droplets to self-assemble into stable, packed structures.

4.4 Dynamic Self-Organization

The microfluidic emulsion generator that we have demonstrated is an experimentally tractable system for the study of dynamic self-organization of bubbles and droplets into regular lattices. We can control the structure of these latti-

ces—their morphology and composition—by changing the rates of inflow of the fluids into the microfluidic system. These structures are new and exotic. It would be difficult, or impossible, to form these heterogeneous structures in an equilibrium process. Fortunately, even without a complete understanding of the mechanics of formation of the regular assemblies, it is possible to engineer complex periodic structures comprising heterogeneous elements.[54] Where such periodic arrangements of bubbles or droplets of distinct characteristics (be it size, shape, or chemical composition) will find a use remains to be seen, but possibilities include materials science (composite tapes), food and cosmetic formulations, composite mixtures of drugs, reagents in lab-on-a-chip devices, and others.

5. Experimental Section

Devices: We prepared the microfluidic channels by soft lithography.[39] The height of each device was uniform, and ranged from 130 to 150 μm depending on the device. The width of the channel was 500 μm for all devices; the aspect ratio of the outlet channel was close to 1:4 (height to width). The PDMS mold was sealed with a glass slide (Corning).[38] To prevent the wetting of the disperse phase on the inner surface of the device, the channel was filled with the continuous phase immediately after sealing the device.

Fluids: The continuous phase was an aqueous solution (Millipore, deionized) of Tween 20 (Polysorbate 80, 0.1–10% w/w, Aldrich), or SDS (2–10% w/w, Sigma–Aldrich). For colored continuous phases, an aqueous solution (Millipore, deionized) of ink (50% v/v, Montblanc Blue, Montblanc Green, or Waterman Purple) was prepared and SDS (2% w/w) was added. The disperse phase was nitrogen (ultrapure, Airgas), PFMD (Alfa Aesar), or hexadecane (Sigma–Aldrich). For colored disperse phases, we prepared saturated solutions of methyl yellow (Yellow, Sigma) or CALCO oil orange 7078 (Orange, Cyanamid Co.). The solute (200 mg) was placed in hexadecane (10 mL) and the undissolved solute was isolated by filtration.

Microfluidics: Digitally controlled syringe pumps (Harvard Apparatus, model PhD2000) were used to deliver the liquid phase to the microfluidic device. A pressure-regulating valve connected to the gas cylinder controlled the applied pressure of nitrogen gas to the device. Polyethylene terephthalate (PET) tubing (Becton, Dickinson and Company) connected the device to the source of the fluid (both gas and liquid).

Imaging: An upright microscope (Leica DMRX), a still camera (Nicon Digital Camera DXM 1200), and a fast-video camera (Phantom V7) were used to visualize and record movies of the system. Adobe Photoshop C2 and Illustrator C2 were used for image analysis and preparation of the figures.

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[1] A. M. Ganan-Calvo, J. M. Gordillo, *Phys. Rev. Lett.* **2001**, *87*, 274 501.
[2] P. Garstecki, I. Gitlin, W. DiLuzio, G. M. Whitesides, E. Kumacheva, H. A. Stone, *Appl. Phys. Lett.* **2004**, *85*, 2649.
[3] P. Garstecki, H. A. Stone, G. M. Whitesides, *Phys. Rev. Lett.* **2005**, *94*, 164 501.
[4] P. Garstecki, M. J. Fuerstman, H. A. Stone, G. M. Whitesides, *Lab Chip* **2006**, *6*, 437.
[5] J. P. Raven, P. Marmottant, F. Graner, *Eur. Phys. J. B* **2006**, *51*, 137.
[6] P. Guillot, A. Colin, *Phys. Rev. E* **2005**, *72*, 066301.
[7] T. Thorsen, R. W. Roberts, F. H. Arnold, S. R. Quake, *Phys. Rev. Lett.* **2001**, *86*, 4163.
[8] S. L. Anna, N. Bontoux, H. A. Stone, *Appl. Phys. Lett.* **2003**, *82*, 364.
[9] J. D. Tice, H. Song, A. D. Lyon, R. F. Ismagilov, *Langmuir* **2003**, *19*, 9127.
[10] Q. Y. Xu, M. Nakajima, *Appl. Phys. Lett.* **2004**, *85*, 3726.
[11] S. Sugiura, M. Nakajima, S. Iwamoto, M. Seki, *Langmuir* **2001**, *17*, 5562.
[12] D. R. Link, S. L. Anna, D. A. Weitz, H. A. Stone, *Phys. Rev. Lett.* **2004**, *92*, 054 503.
[13] T. Kawakatsu, Y. Kikuchi, M. Nakajima, *J. Am. Oil Chem. Soc.* **1997**, *74*, 317.
[14] H. Song, R. F. Ismagilov, *J. Am. Chem. Soc.* **2003**, *125*, 14 613.
[15] B. Zheng, J. D. Tice, L. S. Roach, R. F. Ismagilov, *Angew. Chem.* **2004**, *116*, 2562; *Angew. Chem. Int. Ed.* **2004**, *43*, 2508.
[16] S. Sugiura, T. Oda, Y. Izumida, Y. Aoyagi, M. Satake, A. Ochiai, N. Ohkohchi, M. Nakajima, *Biomaterials* **2005**, *26*, 3327.
[17] M. Y. He, J. S. Edgar, G. D. M. Jeffries, R. M. Lorenz, J. P. Shelby, D. T. Chiu, *Anal. Chem.* **2005**, *77*, 1539.
[18] Y. C. Tan, K. Hettiarachchi, M. Siu, Y. P. Pan, *J. Am. Chem. Soc.* **2006**, *128*, 5656.
[19] S. A. Khan, A. Gunther, M. A. Schmidt, K. F. Jensen, *Langmuir* **2004**, *20*, 8604.
[20] I. Shestopalov, J. D. Tice, R. F. Ismagilov, *Lab Chip* **2004**, *4*, 316.
[21] L. H. Hung, K. M. Choi, W. Y. Tseng, Y. C. Tan, K. J. Shea, A. P. Lee, *Lab Chip* **2006**, *6*, 174.
[22] S. Q. Xu, Z. H. Nie, M. Seo, P. Lewis, E. Kumacheva, H. A. Stone, P. Garstecki, D. B. Weibel, I. Gitlin, G. M. Whitesides, *Angew. Chem.* **2005**, *117*, 734; *Angew. Chem. Int. Ed.* **2005**, *44*, 724.
[23] W. J. Jeong, J. Y. Kim, J. Choo, E. K. Lee, C. S. Han, D. J. Beebe, G. H. Seong, S. H. Lee, *Langmuir* **2005**, *21*, 3738.
[24] D. Dendukuri, D. C. Pregibon, J. Collins, T. A. Hatton, P. S. Doyle, *Nat. Mater.* **2006**, *5*, 365.
[25] S. Okushima, T. Nisisako, T. Torii, T. Higuchi, *Langmuir* **2004**, *20*, 9905.
[26] A. S. Utada, E. Lorenceau, D. R. Link, P. D. Kaplan, H. A. Stone, D. A. Weitz, *Science* **2005**, *308*, 537.
[27] B. Zheng, R. F. Ismagilov, *Angew. Chem.* **2005**, *117*, 2576; *Angew. Chem. Int. Ed.* **2005**, *44*, 2520.
[28] L. Bragg, J. F. Nye, *Proc. R. Soc. London Ser. A* **1947**, *190*, 474.
[29] M. Seo, Z. H. Nie, S. Q. Xu, P. C. Lewis, E. Kumacheva, *Langmuir* **2005**, *21*, 4773.
[30] M. Hashimoto, B. Mayers, P. Garstecki, G. M. Whitesides, *Small* **2006**, *2*, 1292.

[31] E. Lorenceau, Y. Y. C. Sang, R. Hohler, S. Cohen-Addad, *Phys. Fluids* **2006**, *18*, 097 103.
[32] A. van der Net, W. Drenckhan, I. Weaire, S. Hutzler, *Soft Matter* **2006**, *2*, 129.
[33] P. Garstecki, G. M. Whitesides, *Phys. Rev. Lett.* **2006**, *97*, 024 503.
[34] P. Garstecki, G. M. Whitesides, *Phys. Rev. E* **2006**, *73*, 031 603.
[35] S. Hutzler, D. Weaire, F. Elias, E. Janiaud, *Philos. Mag. Lett.* **2002**, *82*, 297.
[36] B. A. Grzybowski, H. A. Stone, G. M. Whitesides, *Nature* **2000**, *405*, 1033.
[37] M. Fialkowski, K. J. M. Bishop, R. Klajn, S. K. Smoukov, C. J. Campbell, B. A. Grzybowski, *J. Phys. Chem. B* **2006**, *110*, 2482.
[38] D. C. Duffy, J. C. McDonald, O. J. A. Schueller, G. M. Whitesides, *Anal. Chem.* **1998**, *70*, 4974.
[39] Y. N. Xia, G. M. Whitesides, *Annu. Rev. Mater. Sci.* **1998**, *28*, 153.
[40] J. N. Lee, C. Park, G. M. Whitesides, *Anal. Chem.* **2003**, *75*, 6544.
[41] H. Wong, C. J. Radke, S. Morris, *J. Fluid Mech.* **1995**, *292*, 71.
[42] H. Wong, C. J. Radke, S. Morris, *J. Fluid Mech.* **1995**, *292*, 95.
[43] P. Garstecki, M. J. Fuerstman, G. M. Whitesides, *Nat. Phys.* **2005**, *1*, 168.
[44] A. M. Ganan-Calvo, *Phys. Rev. E* **2004**, *69*, 066 301.
[45] P. Garstecki, M. J. Fuerstman, G. M. Whitesides, *Phys. Rev. Lett.* **2005**, *94*, 234 502.
[46] P. Garstecki, M. A. Fischbach, G. M. Whitesides, *Appl. Phys. Lett.* **2005**, *86*, 244 108.
[47] C. Priest, S. Herminghaus, R. Seemann, *Appl. Phys. Lett.* **2006**, *88*, 024 106.
[48] D. N. Adamson, D. Mustafi, J. X. J. Zhang, B. Zheng, R. F. Ismagilov, *Lab Chip* **2006**, *6*, 1178.
[49] G. Cristobal, J. P. Benoit, M. Joanicot, A. Ajdari, *Appl. Phys. Lett.* **2006**, *89*, 034 104.
[50] M. J. Fuerstman, P. Garstecki, G. M. Whitesides, *Science* **2007**, *315*, 828.
[51] M. Prakash, N. Gershenfeld, *Science* **2007**, *315*, 832.
[52] L. F. Cheow, L. Yobas, D. L. Kwong, *Appl. Phys. Lett.* **2007**, *90*, 054 107.
[53] J. P. Raven, P. Marmottant, *Phys. Rev. Lett.* **2006**, *97*, 154 501.
[54] M. Seo, C. Paquet, Z. Nie, S. Xu, E. Kumacheva, *Soft Matter*, **2007**, *3*, 986.

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