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Microfluidics

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Formation of Bubbles and Droplets in Parallel, Coupled Flow-Focusing Geometries

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This paper describes the mechanism of formation of bubbles of nitrogen in water containing Tween 20 as a surfactant, and of droplets of water in hexadecane containing Span 80 as a surfactant. The study of these microfluidic systems compares two or four flow-focusing generators coupled through shared inlets, supplying the continuous phase, and through a common outlet channel. The processes that form bubbles in neighboring generators interact for a wide range of flow parameters; the formation of bubbles alternates in time and space, and the bubbles assemble into complex patterns in the outlet channel. The dynamics of formation of bubbles in these systems are stable for long time (at least 10 min). For a certain range of flow parameters, the coupled flow-focusing generators exhibit two stable modes of operation for a single set of flow parameters. The dynamics of formation of droplets of water in hexadecane by the coupled flow-focusing generators are simpler – the adjacent generators produce only monodisperse droplets over the entire range of flow parameters that are explored. These observations suggest that the mechanism of interaction between coupled flow-focusing generators relies on the compressibility of the dispersed phase (e.g., the gas or liquid), and on variations in pressure at the flow-focusing orifices induced by the breakup of bubbles or droplets.

Keywords:
- coupling
- flow focusing
- lab-on-a-chip devices
- microfluidics
- synchronization

1. Introduction

Here we describe the breakup mechanism of bubbles of nitrogen in water, and of droplets of water in hexadecane, in systems of two or four hydrodynamically coupled flow-focusing generators. The coupling in these systems involves shared inlets supplying a continuous phase and a common outlet channel. We characterized the processes of formation of gas bubbles and liquid droplets in these coupled generators in terms of flow parameters (i.e., the pressure of gas and the rate of flow of liquid). The generators producing bubbles of nitrogen in water (with Tween 20 as a surfactant) showed the most complex and interesting behaviors. The formation of gas bubbles in adjacent generators interacted over a wide range of flow parameters, and the timing of the formation of bubbles in one generator depended on the timing in the neighboring generators. A coupled system of two generators stably generated different patterns of bubbles – monodisperse and bidisperse – over intervals of greater than 10 min (the longest

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time we continued to study a system for a given set of flow parameters). By contrast, there was little coupling in the formation of liquid droplets in these flow-focusing generators. Adjacent generators formed droplets in a seemingly independent fashion; each generator exhibited relatively simple dynamics, and formed only monodisperse droplets over the range of flow parameters that produced droplets. The difference in the complexity of the behaviors of bubble generators and droplet generators suggests that the mechanism of interaction between coupled generators involves the compressibility of the dispersed phase (i.e., gas or liquid), and thus on variations in pressure at the orifices induced by the break-up of the thread of gas or liquid.

1.1. Nonlinear Dynamics in Fluidic Systems

Fluidic systems exhibit complex dynamics. An important class of nonlinear dynamical behaviors includes the formation of bubbles and droplets.[1–4] Recent advances in the field of microfluidics have allowed the construction of microfluidic devices with an almost arbitrary range of designs. Multiphase flows of immiscible fluids in certain channel geometries result in emulsification of one phase into another immiscible phase. Among the many examples of emulsion-generating devices,[5–7] researchers have focused much attention – both experimentally and theoretically – on two broad classes of geometries, each operating via a different mechanism: the T-junction geometry[8–10] and the flow-focusing geometry.[11–14] The processes that form emulsions have received much attention, in part because these systems serve as convenient test beds for studying nonlinear dynamics; examples of such dynamics include bifurcation, and chaotic and oscillatory behaviors.[15]

The process of the formation of bubbles and droplets in a single flow-focusing generator is well characterized, and we consider a single flow-focusing generator as a module. We have continued to study the formation of bubbles and droplets in the flow-focusing geometry by investigating the interaction between several coupled flow-focusing generators. We observed complex collective behaviors that arise from this interaction of gas bubbles, but not from interaction of liquid droplets.

1.2. Implication for Lab-on-Chip Systems

For chemists and biologists, the multiphase systems that involve bubbles and droplets are becoming an increasingly important part of the microfluidic/lab-on-chip toolset. Current applications include the synthesis of particles,[16,17] crystallization of proteins,[18,19] transport and mixing of fluids,[20–22] encapsulation of fluids and gases,[23,24] and conduct of chemical reactions.[25–27] As these droplet-based lab-on-chip systems become more complex, for an increased range of applications, precise spatiotemporal control over the bubbles and droplets in channels becomes more important.[28]

Placing multiple bubble/droplet generators in lab-on-chip systems offers two major advantages: i) the ability to deliver multiple elements, contained in either bubbles or droplets, and ii) a throughput that is higher than a single device can generate. In the first kind of problem, when droplets are used to deliver multiple reagents or analytes in a lab-on-chip format, it is often essential to coordinate (or control) the generation and flow of these droplets. For example, Hung et al. demonstrated the fusion of two droplets containing reagents for the synthesis of nanoparticles.[29] In this scheme, the timing of generation of the droplets was crucial. The behavior of one droplet generator must be coordinated with the behavior of the other generator on the same chip – that is, the processes of droplet formation in the two generators must be synchronized – for two droplets containing different reagents to meet at the same location and to coalesce for chemical reaction. In the second kind of problem, while the use of microfluidic systems reduces the consumption of reagents or analytes, there are tradeoffs; the amount of product that these systems can generate in a given period of time is smaller than in a conventional, macroscopic device. To compensate for this shortcoming, multiple devices might, in principle, be placed in parallel to increase throughput. While multiple disjoint generators of bubbles or droplets would suffice for this purpose, each discrete generator would require a set of separate inlets for reagents. Placement of these generators in close proximity to one another on the same chip has the potential to cause problems. A recent paper by Nisisako and Torii showed that it is possible to form monodisperse droplets in a highly parallel geometry of coupled flow-focusing or T-shaped droplet generators.[30] However, it is not clear what the effective range of rates of flow is for which the behavior of the system remains controllable. The formation of bubbles and droplets by the neighboring generators could interact,[31] and their coupling would make the independent control of each generator difficult. We wished to design parallelized yet independent generators that share the same inlets and outlets for fluids.

In the work described in this paper, we studied the influence of the geometry of the devices, the nature of fluids, and the flow parameters on the dependence and independence of the parallelized flow-focusing generators of one particular geometry. We found that the formation of bubbles of gas in the coupled generators was strongly dependent on the interaction between adjacent generators, while the formation of droplets of liquid remained largely independent. The results suggest the possibility of constructing a system with multiple generators of droplets sharing the same inlet and outlet with high throughput, and with a high degree of control over the formation of droplets. The following section describes our approach to this control, in particular, the dependence and independence of the operation of the flow-focusing units on the change in the geometry of the channels and on the nature of fluids (i.e., gas or liquid).

2. Experimental Design

2.1. Coupling and Design of the System

A single flow-focusing generator produces bubbles and droplets in a well-defined oscillatory cycle. Several research groups have studied the effect of coupling in multiple microfluidic droplet generators arranged in parallel. For example, Raven and Marmottant[32] and later Sullivan and Stone[33] studied the coupling between the process of formation of bubbles and droplets and the resistance of the outlet channel in which the bubbles or droplets flowed. The authors showed that this coupling can introduce non-decaying fluctuations of the size of the bubbles or droplets formed and of the volume fraction of the dispersed phase, even at constant feeding of the microfluidic device. Barbier et al.[34] studied the dynamics of two T-junctions connected in parallel, and observed strong coupling – manifested both in irregular and in regular behaviors – between the formation processes at each of the two junctions, and between the process of formation and the hydrodynamic resistance added by the droplets flowing in the parallel section. Li et al.[35] studied a device comprised of four flow-focusing units connected in parallel and observed formation of monodisperse droplets. Still, the outstanding problem of coupling between bubble/droplet generators that are positioned in close proximity (as to maximize their number on a single chip) has not been tackled so far. In this study, we modified the geometry of a standard flow-focusing generator in order to couple the formation of bubbles/droplets in two or more generators. The generators shared common inlets for the continuous phase and a common outlet channel; neighboring generators communicated with one another via this fluidic link.

Figure 1a illustrates the geometry of a single flow-focusing generator; we supplied the dispersed phase through the middle channel, and the continuous phase through the channels on both sides. The three streams met in a single narrow channel (i.e., in a flow-focusing orifice), at which the streams of continuous phase pinched off the dispersed phase to form bubbles or droplets. The objective of this work was to investigate the behavior of several connected, or coupled, flow-focusing generators. Figure 1b and c illustrates schematically the design of the devices that were used in these experiments. Every system of coupled generators consisted of two or four flow-focusing generators arranged in parallel. In all devices, every two adjacent generators shared one of the inlets of the continuous phase, and all of the generators shared a common outlet channel. As the continuous phase in a shared inlet could flow into either of the neighboring generators, we observed interaction of the dynamics of the formation of bubbles in the adjacent generators.

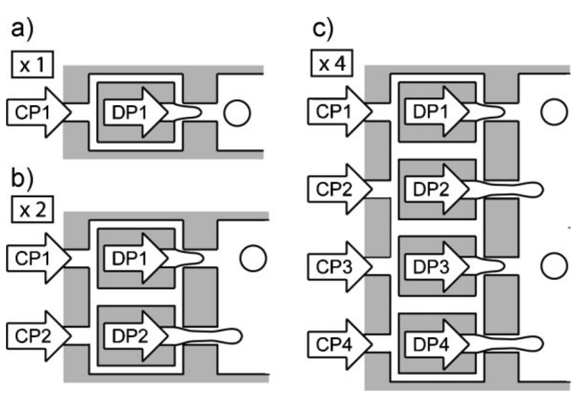

Figure 1. Schematic illustration of the systems of flow-focusing generators that we studied: a) a single flow-focusing generator; b, c) coupled flow-focusing generators. A coupled flow-focusing generator consisted of several (here, two or four) single flow-focusing generators in which the inlets of continuous phase of the two adjacent generators fused into one channel. In our experiments, the continuous phase (CP) was liquid (water or hexadecane); syringes mounted on independent digital syringe pumps supplied the continuous phase to the generators. The dispersed phase (DP) was either nitrogen gas supplied from a single tank of compressed gas, or water supplied by independent digital syringe pumps. All generators in a system shared a common outlet channel.

2.2. Choice of the Fluids

To study of formation of gas bubbles in liquid, we used nitrogen gas as the dispersed phase and an aqueous solution of a surfactant (Tween 20, 2% w/w) as the continuous phase. We had previously studied the formation of bubbles using this set of fluids in regular flow-focusing geometry.[13] The use of Tween 20 as a surfactant prevented the coalescence of bubbles, and facilitated wetting of the walls of the channels by the continuous aqueous phase (other surfactants, such as sodium dodecyl sulfate, produce a similar effect). Independent syringes controlled by digital syringe pumps delivered water to the system; we split the flow of nitrogen from a single pressurized tank into two or four streams, and delivered nitrogen to each of the dispersed phase inlets. In the study of the formation of droplets of water in hexadecane, deionized water was the dispersed phase, and hexadecane with a surfactant (Span 80, 2% w/w) was the continuous phase. Both fluids came from independent syringes controlled by digital syringe pumps.

In our previous study of a system composed of two or three independent flow-focusing generators that shared a common outlet channel, we observed that the formation of bubbles and droplets in the neighboring generators interacted.[31] In that study, the interaction between bubble generators was more prominent than between droplet generators. We hypothesized that this observation could be explained by the difference in compressibility of the dispersed phase. In the current study, we tested this hypothesis by investigating the formation of gas bubbles and of liquid droplets in the same systems of coupled flow-focusing generators. The following sections discuss the differences in the mechanism of formation of gas bubbles and liquid droplets in the coupled flow-focusing generators.

3. Results and Discussion

3.1. Nomenclature and Description of Parameters

Throughout this paper, the figures in square brackets denote a set of flow parameters – a descriptor of the form [p_d (psi), Q_c (mL h^{-1})] denotes the value of the pressure of nitrogen and the rate of flow of water, applied to each individual bubble generator; a descriptor of the form [Q_d (mL h^{-1}), Q_c (mL h^{-1})] denotes the rate of flow of water and the rate of flow of hexadecane, applied to each individual droplet generator. Unless specified otherwise, the subscript d denotes the dispersed phase, and the subscript c denotes the continuous phase.

3.2. Formation of Bubbles

We first studied the formation of bubbles in coupled flow-focusing generators. Strong interaction between the flow-focusing units resulted in bifurcation and the formation of complex patterns in systems that generated gas bubbles in water. The following section describes the formation of bubbles in single and coupled flow-focusing generators, and discusses the origin of the complexity in the coupled systems.

3.2.1. One-Orifice System

First, we studied the behavior of a single flow-focusing generator (Fig. 1a: one-orifice system). The dimensions of the inlet, the outlet, and of the flow-focusing region of the single generator were the same as those for each of the generators in the two- and four-generator systems that were investigated later. The single flow-focusing generator showed simple dynamics. Upon a stepwise increase in pressure of nitrogen gas, we observed only two types of behavior. At low pressure, the system generated monodisperse bubbles stably. In this regime, the size of bubbles increased monotonically as the pressure increased. At high pressure, the system developed co-laminar flow of gas and liquid. Figure 2a shows the responses of the system to increase in the applied pressure of nitrogen gas.

3.2.2. Two-Orifice System

In two coupled generators (Fig. 1b: two-orifice system), the formation of bubbles in the two generators influenced one another, and this dynamic interaction resulted in the emergence of complex behaviors. As we increased the applied pressure of nitrogen stepwise with the rate of flow of water held constant, the two-orifice system displayed a progression through a series of four distinct behaviors: i) disordered, polydisperse; ii) ordered, multi-disperse; iii) ordered, mono-disperse; and iv) no breakup, co-laminar.

i) Disordered, polydisperse. Each generator generated bubbles at apparently random intervals, and produced polydisperse bubbles. The period of formation of bubbles was neither constant in each orifice nor identical between two orifices (Fig. 2a; $\times$2, [0.85, 1.0] and [2.98, 1.0]). The system never reached a stable cycle that lasted for a prolonged period of time. One thread occasionally retracted outside of the observation window, and the other thread remained in the front, producing a burst of bubbles.
ii) Ordered, multidisperse. In this regime, the generation of bubbles alternated between two orifices. While the system always reached stable dynamics for any given values of pressure and flow, we could not predict the dynamics or the patterns of bubbles it would form. Each orifice generated either monodisperse or bidisperse bubbles (Fig. 2a; $\times$2, [4.34, 1.0]). The micrograph and the plot provided in Figure 2b correspond to the formation of bidisperse bubbles. While the pressure applied to each of the generators remained the same, the sizes of bubbles generated by the two coupled generators were not identical; one orifice could generate bubbles larger than the other (Fig. 3). In addition, one particular set of flow parameters sometimes showed two different modes of operation, and an external perturbation could switch the system between these two modes (we describe this phenomenon in more detail in this section below, and in the caption of Fig. 3).
iii) Ordered, monodisperse. In this regime, both orifices produced monodisperse bubbles. Unlike regime (ii), the sizes of bubbles generated by each of the orifices were, within the resolution of our measurements, indistinguishable, and the two orifices generated bubbles in alternation. We observed this regime at high gas pressure (Fig. 2a; $\times$2, [7.29, 1.0]); the outlet channel was packed with bubbles. We had observed previously that the ordered lattices that form at high volume fractions of gas in the outlet channel guided (and stabilized) the process of bubble formation,[36] and we speculate that the high volume fraction of bubbles in the outlet channel stabilized the oscillation of the pressure between the two orifices.
iv) Co-laminar. At the highest bound of the range of pressures we examined in this study, the thread of gas did not break up in either of the orifices, and penetrated into the outlet channel (Fig. 2a; $\times$2, [7.83, 1.0]). The system formed co-laminar flows of nitrogen and water. This mode of operation is similar to jetting, in that the gaseous thread does not exhibit large instabilities, and all the fluctuations of its diameter are transferred downstream.

Figure 2b shows optical micrographs representative of these four different behaviors (we describe the stability of the dynamic responses further in this section). In the plots, the pulses indicate the presence of the thread of gas in an orifice — the wider the width of the pulse, the larger the size of the bubble being generated. In (ii), the ordered, multidisperse and (iii), the ordered, monodisperse regimes the occupancy of orifice 1 and orifice 2 by the gas thread alternates strictly periodically.

As a single flow-focusing generator exhibited only simple behavior, we concluded that the complexity of the dynamic behavior of the system of two coupled generators (i.e., instability, bifurcation of the sizes of bubbles, and multi-stability of the system) emerges solely from the fluidic coupling of the two generators. We hypothesize that the interaction between the two adjacent generators resulted from the fluctuation of pressure at each orifice during formation of a bubble, and from the dependence of the dynamics of formation of a bubble on the pressure in the neighboring orifice; we describe later the mechanism for the interaction between the formations of bubbles in adjacent generators.

3.2.3. Four-Orifice System

Finally, we examined the behavior of a system of four coupled generators (Fig. 1c: four-orifice system). There were two distinct sets of generators: the two middle generators were equivalent, and the two outermost generators were also equivalent, because of the symmetry of the system. The formation of bubbles in the middle generators took place under a slightly different set of conditions than in the outermost generators — the sidewalls of the outlet channel

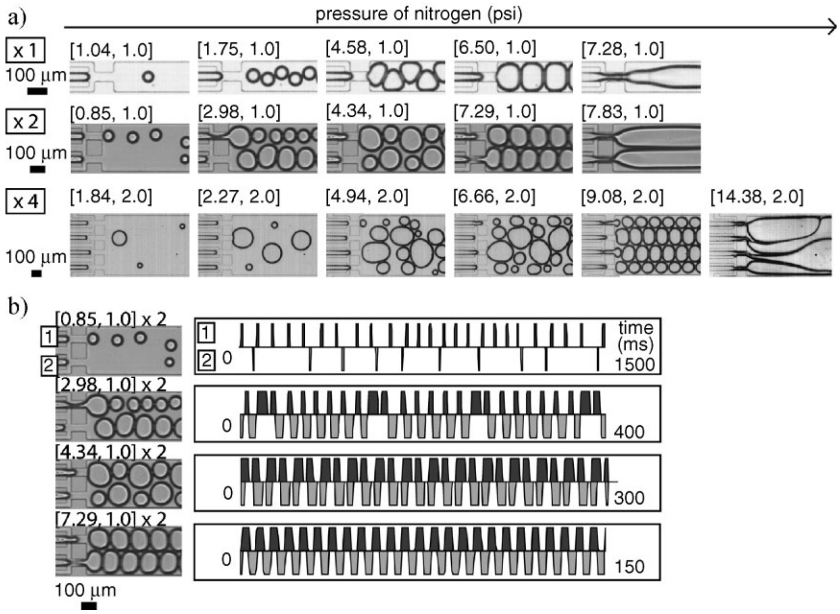

Figure 2. Optical micrographs of nitrogen bubbles in water that formed in the system of coupled flow-focusing generators. a) Optical micrographs showing representative behaviors of one-, two-, and four-orifice systems. The micrographs show the transition of the pattern of break-up upon a stepwise increase in the pressure of nitrogen, with the rate of flow of water held constant (the direction of flow is from left to right). The one-orifice system displayed only simple dynamics by generating monodisperse bubbles for a wide range of flow parameters (both p and Q), while two- and four-orifice systems displayed complex dynamic responses. b) Characteristic behavior of a two-orifice system, and plots representing the timing of bubble formation. The pulses in the graphs correspond to the occupancy of the orifice by the gas thread (top for the top orifice, and bottom for the bottom orifice). The width of each pulse corresponds to the size of the bubble being generated; for example, the plot for the flow parameters [4.34, 1.0] shows that bubbles of two different sizes were generated in each orifice.

provided confinement (increased the fluidic resistance) experienced by the output of the outmost generators. As the fluidic resistance of the outlet channel influences the generation of bubbles,[32] we speculate that it is because of the lower effective fluidic resistance in the outlet channel that the middle generators produced larger bubbles than the outer generators, when the system reached a stable oscillatory mode.

The four-orifice system demonstrated dynamic responses similar to those of the two-orifice system (Fig. 2a; $\times$4). At low flow rates, each orifice generated polydisperse bubbles with non-uniform periodicity. While the two middle generators produced bubbles regularly, the threads of gas in the two side generators either did not advance beyond the orifices, or generated small bubbles and remained far back in the gas inlet channels. The formation of bubbles was aperiodic, and appeared independent. As the pressure of gas increased, the system started to operate more stably—although the behavior of the system was not predictable, each generator produced monodisperse or multidisperse bubbles, and the breakup of the thread of gas in the neighboring generators alternated. Over time, the formation of bidisperse bubbles in the inner and outer generators led to stable generation of four different sizes of bubbles (Fig. 2a; $\times$4, [6.66, 2.0]). Further increase in pressure resulted in the formation of monodisperse bubbles; the two middle generators and the two outer generators produced monodisperse bubbles of different sizes. Finally, an additional increase in pressure resulted in the formation of co-laminar flows in all four generators.

In these ordered regimes, the system showed two types of regularity—regularities in time and in space. The configuration of the generators provided regularity in space. Firstly, the sizes of the bubbles formed in the middle orifices (orifices 2 and 3) were indistinguishable, as was the case in the outer orifices (orifices 1 and 4). The size of bubbles reflected the effective resistance of the outlet channel experienced by output from each of the generators, and equivalent generators produced bubbles of indistinguishable size. Second, the generation of bubbles in the neighboring generators exhibited temporal regularities. The formations of bubbles in every other orifice (orifices 1 and 3, and orifices 2 and 4) were in phase. Due to these spatiotemporal regularities, the system generated highly regular patterns of bubbles in the outlet channel.

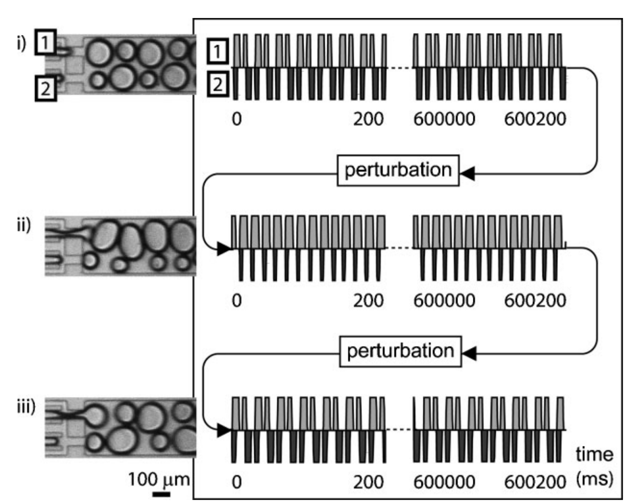

Figure 3. Bistability of bubble formation. Pulses in the graphs indicate the occupancy of each orifice by the thread of gas. After each 10 min period, we vented the pressure of nitrogen, and reapplied the same pressure (indicated as "perturbation"). The flow parameters remained the same before and after venting. The two distinct modes of operation were stable for at least 10 min. The flow parameters were [4.34, 1.0].

3.3. Multiple Stable States of a Gas–Liquid System

Interestingly, we observed that the two-orifice system could operate in multiple metastable oscillatory cycles under a single set of the flow parameters (Fig. 3). We observed these multistable modes of the two-orifice system in (ii), the ordered, multidisperse regime described in Figure 2. Under a single set of flow parameters, the system exhibited two stable modes, and an external perturbation switched the mode of operation of the system.

We set the parameters of flow for the system to [4.34, 1.0]. At $t = 0$, both orifices started to operate in a mode that generated bidisperse bubbles in each orifice; the system repeated the same cycle for 10 min. At $t = 10$ min, we vented the pressure applied to the system, and reapplied the same pressure to the inlets of gas. We observed that both orifices generated monodisperse bubbles in alternation, and the system repeated the same cycle for 10 min. We introduced the same perturbation again, and the system went back to the original mode that generated bidisperse bubbles. The system remained stable for another 10 min.

We found that the same system was stable against minor perturbations such as vibrations on the bench-top, or movements of the stage of the microscope. These observations suggest that it is possible to design a complex system of generators that has multiple stable modes of operation, and that could be switched among them, with stability sufficient to allow for the operation of the system in the same mode, in the absence of strong perturbations, for long time.

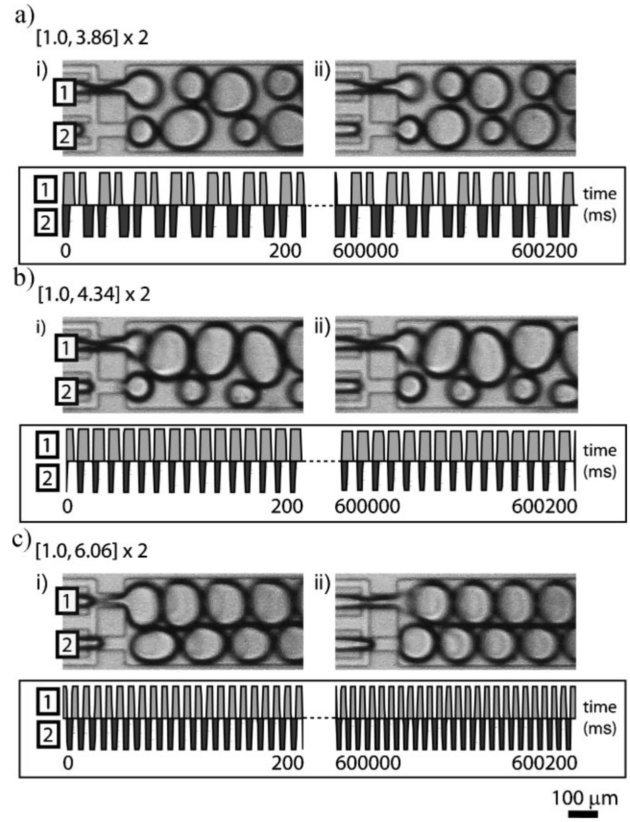

Figure 4. Stability of the formation of bubbles in the two-orifice system. The optical micrographs show the orifice and outlet channel with the flow parameters of: a) [1.0, 3.86], b) [1.0, 4.34], and c) [1.0, 6.06]. The micrographs correspond to the images at the time i) $t = 0$ ms, and ii) $t = 10$ min, respectively. The time $t = 0$ corresponds to the time the system started forming bubbles stably after we set the parameters of flows. The plots show the periodicity of the formation of bubbles in each orifice. The presence of pulses indicates the occupation of the orifices by gas, and the absence of pulses indicates the occupation of orifice by water.

3.4. Stability of the Gas–Liquid System

The pressure feedback loop between the two adjacent generators was stable for at least 10 min (>30 000 cycles). We stopped observation after 10 min. The diagram in Figure 4 shows the relative timing of the formation of bubbles in the two-orifice system. Figure 4a and b shows examples of the dynamics of breakup in regime (ii), the ordered, multidisperse regime. Figure 4c shows the same for regime (iii), the ordered, monodisperse regime. In both regimes, the dynamics were stable over the period of time for which we ran the experiments (10 min). We note that the frequency of the formation of bubbles drifted slightly over time; for example, the frequency of the formation of bubbles in the example of Figure 4c was 110 (Hz, or bubbles per second) at $t = 0$, and 125 Hz at $t = 10$ min. Each generator continued to form monodisperse bubbles and the relative timing of breakup of the thread of gas did not change over time.

We believe that the pressure feedback loop that coupled two generators made the system resistant to small perturbations. Vibrations on the bench-top, and small movements of the stage of the microscope, provide minor perturbations to the system. Such perturbations are likely to occur during extended operation of a device, and may well affect the dynamics of bubble formation in a single, isolated generator. For example, a gentle tapping on the needle of the syringe feeding the continuous phase often changes the mode of operation of a single flow-focusing generator. In a system of two coupled generators, however, the dynamics of bubble formation in each of the two generators was more stable against such small perturbations, and we attribute this increased robustness to the feedback between the generators.

3.5. The Mechanism of the Interaction Between Two Generators

The images in Figure 5 illustrate the breakup of bubbles in the two-orifice system. The pressure of gas applied to the two orifices was the same; we split the flow of nitrogen gas to the inlets from the same pressurized nitrogen tank. The breakup of the thread of gas is asymmetric in this geometry, because the fluidic resistance of the middle, or fused, channel for the continuous phase is different from that of the side channels. In addition, generation of bubbles in one generator alters the fluidic resistance for the path on which the generator resides, and changes the speed of continuous phase flowing from the middle channel to each orifice of the generator.

At the beginning of the cycle, when the thread of gas in one of the orifices (bottom orifice, Fig. 5a and d) advanced forward, the thread of gas in the other orifice entered the orifice and remained in position (top orifice, Fig. 5a and d). The tip of the thread of gas in the bottom orifice retracted behind the orifice immediately following the formation of the bubble (Fig. 5d, bottom orifice), while the tip of the thread of

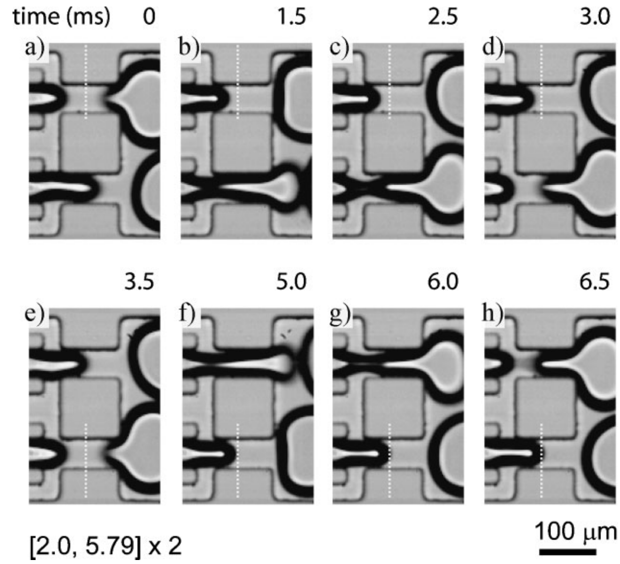

Figure 5. Mechanism of alternating formation of bubbles in the two-orifice system. We added the white dashed lines on the micrographs to aid tracking of the position of the threads of gas relative to the orifices.

gas in the top orifice remained roughly in place within the orifice (Fig. 5d, top orifice). Because the thread of gas retracted outside of the bottom orifice, the fraction of flow of liquid supplied from the middle (shared) inlet into the bottom orifice increased – that is, the fluidic resistance of the bottom orifice decreased. Simultaneously, the pressure exerted by the liquid from the middle inlet on the thread of gas in the top orifice decreased, as was evident from the change in curvature of the gas thread in the top orifice (Fig. 5e). The exit of the back end of the newly formed bubble from the bottom orifice decreased the fluidic resistance of the orifice, and thus released the pressure in the orifice and upstream of it. The evolution of the thread of gas in the top orifice proceeded through a sequence of steps (Fig. 5e–h, top), similarly to the sequence completed by the bottom orifice (Fig. 5a–d, bottom) in the beginning of the cycle.

Our current study describes the effects of coupling in systems of flow-focusing generators that shared common inlets for the continuous phase, but had independent inlets for the dispersed phase. We believe that if generators shared common inlets of the dispersed phase and had independent inlets for the continuous phase instead, the effects of coupling would be less prominent. As we have already discussed in the section describing the mechanism of coupling, the interaction between two adjacent generators stems from the dynamic switching of the patterns of flow from the coupled (middle) inlet of the continuous phase. In fact, we have observed that it is possible to couple the dynamics of multiple flow-focusing generators via inlets of the continuous phase only, without any additional coupling through the outlet channels. We therefore believe that the fluidic link between the inlets of the continuous phase is the key to hydrodynamic coupling in our current geometry.

In summary, the feedback loop between the two generators allowed them to generate bubbles in alteration. The fluctuation of pressure, followed by the fluctuation of the fraction of flow in the adjacent orifices, provided the means for neighboring generators to communicate with one another.

3.5.1. Holding the Thread of Gas Upstream of the Orifice

We previously postulated[10,37] and showed[38] that at low values of the capillary number, the process of formation of a droplet or a bubble is associated with large fluctuations of pressure in the continuous fluid upstream of the orifice or T-junction. As the bubble or droplet that is just forming penetrates the orifice (or the main channel in the T-junction device), it blocks the cross-section of the orifice (or main channel) and increases the resistance to flow of the continuous fluid through the orifice (or the main channel). As a consequence, the pressure upstream of the orifice (or of the junction) increases up to a value larger than the pressure in the inner thread. This imbalance of the pressure squeezes the inner thread, and leads to breakup. In the system of coupled, neighboring, flow-focusing geometries, the rise of the pressure upstream of one orifice is transmitted to the other orifice, and causes the thread of gas in the neighboring orifice to stay upstream of its orifice while a bubble is generated in the first orifice. After this bubble breaks off in one orifice, the pressure upstream of the same orifice is released and the neighboring system starts to form a bubble. The situation reverses, and the system operates in alteration (or out-of-phase).

3.5.2. Holding the Thread of Gas Within the Orifice

We previously showed[37] that the size (volume) of bubbles produced in the flow-focusing geometry is proportional to the pressure applied to the stream of gas, and inversely proportional to the viscosity of the continuous fluid (liquid). This relationship reflects the fact that when the thread of gas penetrates the orifice, it blocks the cross section of the orifice and effectively stops the outflow of liquid through it. As a consequence, when the bubble inflates in the outlet channel, it pushes out the bubble to the outlet channel, and the rate of flow of gas into the growing bubble, to a good approximation, equals the rate of flow in the whole outlet channel. Thus, the flow in the outlet channel is not constant, but rather pulsatory; as bubbles are produced, the contents of the outlet channel are pushed out in pulses. Further, the pressure immediately downstream of the orifice fluctuates from a low value at the instants when a bubble has just been released and the formation of the subsequent bubble has barely started (e.g., the thread has just began to advance into the orifice), to high values when the bubble inflates and pushes the bubbles already occupying the outlet channel forward. The high value is larger than the pressure head calculated for the average flow through the outlet channel, and the low value could be close to the ambient pressure (i.e., the pressure at the exit of the outlet channel).

In a system of coupled bubble generators, it is possible that, as a bubble is inflated in one of the orifices, the pressure immediately downstream of the orifices rises to the large value associated with the resistance to flow in the outlet channel. The pressure applied to each of the streams of gas is equal, yet the Laplace pressure that opposes either the growth of a bubble or the advancement of a thread of gas is different for each of the orifices; the growing bubble has lower curvature and thus lower Laplace pressure, while the thread of gas in the orifice has a larger curvature and experiences a larger Laplace "back" pressure. As a result, while a bubble grows from one of the orifices, the thread in the second orifice stays in place, without advancing forward. This mechanism coincides with the process depicted in Figure 5.

3.6. Formation of Droplets

In a previous study of systems of multiple flow-focusing generators, we observed similar effects of coupling that resulted in strong interactions among the neighboring flow-focusing units; in that study, the effect of coupling was more prominent in the formation of gas bubbles than in the formation of liquid droplets.[31] We hypothesized that the compressibility of the dispersed phase (i.e., bubbles) is the critical attribute that led to the complex dynamic response of the system. To verify our hypothesis, we studied the generation of gas bubbles and liquid droplets in the same systems of coupled flow-focusing generators; we indeed observed only simple dynamics with liquid droplets.

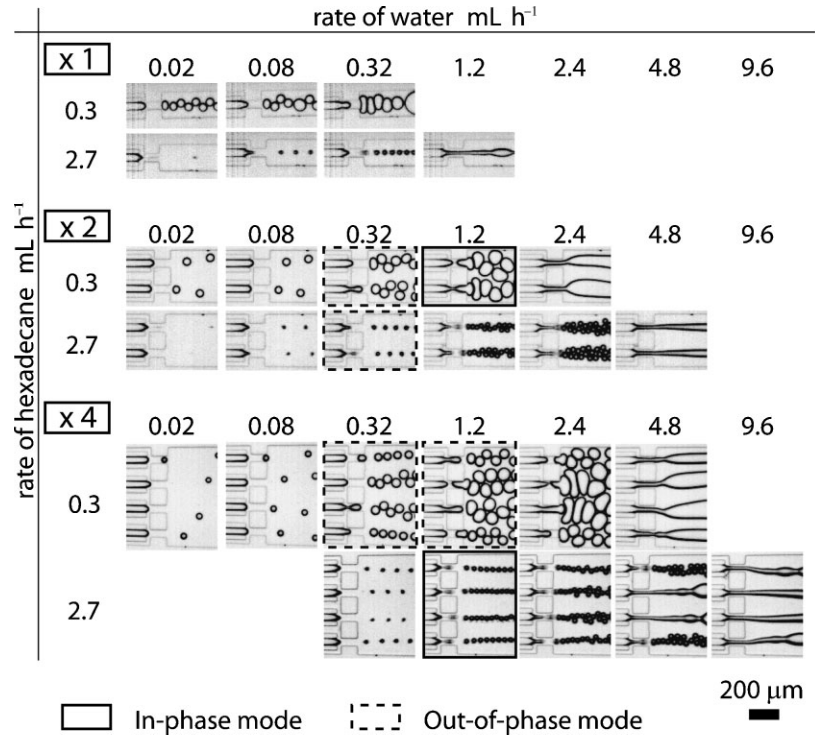

Figure 6. Optical micrographs showing the formation of droplets of water in hexadecane (with Span 80, 3% w/w) in coupled flow-focusing generators. For the entire range of rates of flows that allowed the formation of droplets, the size of droplets simply increased in response to the increase in the rate of flow of water (i.e., from left to right). Micrographs marked with solid rectangles represent the in-phase mode of operation of the generators, and those marked with dashed rectangles represent the out-of-phase mode of operation of the generators.

3.6.1. One-, Two-, and Four-Orifice Systems Involving Two Liquid Phases

We studied the formation of droplets in systems of flow-focusing generators comprising one, two, or four coupled generators, for four values of the rate of flow of the continuous phase (hexadecane with Span 80, 2% by weight) per orifice ($Q_c = 0.1$, 0.3, 0.9, and 2.7 mL h^{-1}). For each series of experiments (i.e., for each Q_c), we adjusted the rate of flow of the dispersed phase (Q_d) from the minimum value at which the formation of droplets was possible, to a value at which the stream of water ceased to break-up in the orifice; above the threshold value of Q_d, the streams of water and of hexadecane formed co-laminar flows in the outlet channel and did not produce droplets. We observed that, for a given value of Q_c, the threshold value of Q_d was higher for a multi-orifice device than for a one-orifice device. For example, for $Q_c = 0.3$ mL h^{-1}, the threshold value of Q_d was around 0.32 mL h^{-1} for a one-orifice system, 1.2 mL h^{-1} for a two-orifice system, and 2.4 mL h^{-1} for a four-orifice system. We discuss the reasons for these differences as well as the functional ranges of the flow parameter at the end of this section.

The one-orifice system generated monodisperse aqueous droplets ranging from approximately 50 μm to several hundreds of micrometers in diameter. The sizes of droplets formed in the single-orifice system increased monotonically with the increase in Q_d, and decreased with the increase in Q_c. The behavior of the two-orifice system was similar to that of the single-orifice system for the same values of the rates of flow per single orifice. The droplets were monodisperse and followed the same dependence on Q_d and Q_c as did the single-orifice system. There was no noticeable difference in the sizes of droplets generated by the two orifices. We did observe signatures of weak hydrodynamic coupling between the two orifices; this coupling manifested itself in locking of the dynamics into in-phase and out-of-phase behaviors. In the in-phase mode, the two orifices formed droplets simultaneously (Fig. 6; ×2, [1.2, 0.3]). In the out-of-phase mode, the two orifices formed droplets alternatively (Fig. 6; ×2, [0.32, 0.3]). These effects were, however, weak, in the sense that the system often switched between the two modes and also operated without noticeable coordination between the orifices. These fluctuations did not affect the sizes of droplets.

As with the system that formed bubbles, the four-orifice systems were different from the two-orifice systems in that the inner orifices and the outer orifices were not equivalent. The inner orifices produced larger droplets than the outer orifices. There were important similarities in the operation of the two- and four-orifice systems; the droplets produced in the four-orifice system were monodisperse within the two equivalent groups (inner and outer orifices). They also followed a similar dependence of the size of droplets on the rates of flow that was observed for the one-orifice and two-orifice systems.

As with the two-orifice system, we observed weak interactions between the orifices. Since there were four orifices, we observed more modes of synchronized formation of droplets. The different modes interchanged under ostensibly constant conditions of flow. Most often, we observed in-phase and out-of-phase modes of operation. In the in-phase mode, all orifices formed bubbles simultaneously (Fig. 6; ×4, [1.2, 2.7]). In the out-of-phase mode, the first and third orifice formed drops simultaneously, followed by the formation of droplets in the second and fourth orifice, followed by a repetition of this cycle (Fig. 6; ×4, [1.2, 0.3]). As with the two-orifice system, this weak coupling between the dynamics of different orifices did not noticeably affect the sizes of droplets that were generated.

3.6.2. Route to Coupling

Because all of the microfluidic devices used in this study were made of highly elastic poly(dimethyl siloxane) (PDMS), and because we used plastic syringes and tubing to supply the fluids of the continuous and the dispersed phases, we cannot exclude the possibility that the elasticity of these materials has played a role in the dynamics of coupling. We know from our previous observations that the use of glass syringes and the fabrication of the microfluidic chips from polycarbonate (a material less elastic than PDMS), shorten the time needed for the system to reach stationary behavior following a change of the rates of flow of the phases into the system. This observation suggests that the elasticity of the materials influences the system. Nevertheless, since we observe dramatically different behaviors for the gas–liquid (strong coupling) and the liquid–liquid (weak coupling) systems of the same experimental setup (plastic syringes, poly(ethylene terephthalate) (PET) tubing, and microfluidic devices made of PDMS), we believe that the elasticity of these materials has a secondary effect on the dynamics of bubble/droplet production by coupled flow-focusing generators.

Overall, while the liquid–liquid system did show dynamics that were in-phase and out-of-phase, the generation of droplets in different orifices was largely independent. This observation suggests that it is possible to design parallel systems of droplet generators with orifices placed in close proximity of one another (and even with a fluidic linkage of common inlets and outlets) without inducing complex higher-order behaviors[39] that arise from interactions between neighboring flow-focusing units.

3.7. Functional Ranges of the Coupled Devices

For both gas–liquid and liquid–liquid systems, we observed that, for fixed rates of flow, the multi-orifice systems could generate bubbles and droplets over wider ranges of flow parameters than the corresponding single-orifice systems. We note that the upper limit of the rate of flow of the dispersed phase, be it gas or liquid, was higher for coupled systems. Because in coupled-generator systems the inlets of the continuous phase were shared by the generators, one orifice could temporarily "borrow" the flow of continuous phase from the neighboring orifices. As a result, these systems could hold a higher pressure or a higher rate of flow of the dispersed phase than an isolated flow-focusing generator, without exceeding the threshold for the co-laminar flow regime.

We also speculate that the fluctuations of pressure associated with the process of break up in one of the orifices and transmitted to the neighboring orifice might induce instabilities in an otherwise stable thread of the dispersed phase. This postulate is supported by the empirical (although not systematic) observation that a single device operating at high rates of flow, in which we observe co-laminar flow and no breakup, when subject to small perturbations (such as gentle tapping on the feeding tubes) switches to the mode in which the thread breaks. Further, our observations suggest that the transition from breaking mode to non-breaking mode upon the increase in the rate of flow of the dispersed phase is associated with hysteresis. Consequently, when we increase the rate of flow of the dispersed phase, as the system continues to form bubbles (or droplets), the fluctuations of pressure in the orifice may help sustain the breakup mode. A system of coupled generators can therefore increase the throughput of the device not only via parallelization but also by increasing the range of rates of flow for which the system forms bubbles (or droplets).

4. Conclusions

The formation of bubbles in systems of several flow-focusing generators coupled through the inlets of continuous fluid and a common outlet demonstrated a variety of complex dynamics. With gas at low pressures, each generator produced monodisperse or bidisperse bubbles, and the sizes of bubbles that formed in different generators varied. At high pressures, all equivalent generators of a system produced monodisperse bubbles. For a wide range of pressures, the timing of breakup of bubbles in neighboring generators alternated. In contrast, the formation of droplets in the same systems of coupled flow-focusing generators showed little variation. Each generator produced only monodisperse droplets over the entire range of rates of flow of liquids capable of generating droplets. Our observations suggest that the difference in the dynamics between formation of bubbles and droplets originated from the compressibility of the dispersed fluids (e.g., nitrogen gas vs. water).

4.1. Parallelization of Flow-focusing Units and Applications in Lab-on-Chip Devices

The fluidic couplings that our designs provided did not influence the formation of droplets in the system. We infer that we can construct systems involving a number of flow-focusing generators that are linked, either through inlets or outlets, without considering the occurrence of unexpected dynamics that would result in unstable formation of droplets. Placement of multiple units in proximity is relevant to the design and construction of lab-on-chip systems, and can offer convenient means of constructing a microfluidic device with high throughput. In contrast, we observed strong coupling between the dynamics of bubble formation in several linked flow-focusing generators of bubbles. This work demonstrated that fluidic coupling can coordinate the dynamics of two oscillatory units through fluctuation in pressure. As the motion of bubbles and droplets in networks of microfluidic channels has been previously used for performing logical[40] and reversible[41] operations, the results of this study may be relevant to the design of microfluidic devices that process information.

4.2. Pattern Formation in a Dissipative System

The geometry of the coupled generators guaranteed that the neighboring generators produced bubbles alternately. As a consequence, the bubbles packed in the outlet channel in "staggered" patterns. Appropriate designs of these systems would allow for control of both temporal and spatial regularities in the structures of bubbles in the outlet channel, and make the formation of intriguing and ordered patterns possible.

4.3. Modular Approach to Create Complex, Emergent Behaviors

The placement of multiple flow-focusing generators in proximity resulted in unexpected behaviors of bubbles – bidispersity, bistability, alternate formation of bubbles, and formation of complex patterns. These dynamic behaviors arose from the interaction between single units; a single flow-focusing generator produced only monodisperse bubbles with regular periodicity in the regime of flow we explored in this paper. This demonstration is an example of the synthesis of a complex system created by the combination of multiple, well-characterized simple units. The collective behaviors of the entire system cannot be attributed solely to the individual units; it is the interaction among each unit that leads to complexity. This type of "synthetic" approach to the construction of complex systems has two characteristics useful for our studies: i) we can address the relevant parameters of individual units by changing experimentally tractable variables in each unit; and ii) we can address the interaction among individual units by changing the ways in which the unit interacts, and may provide an alternative approach (in contrast to the reductionist approach) to the way we understand and design complex systems.

5. Experimental Section

Device: We prepared the microfluidic channels using soft lithography.[42] The height of the devices was 36 μm. To study the formation of gas bubbles, we sealed PDMS molds against glass slides (Corning). To prevent the wetting of the inner surface of the device by the nitrogen gas, we filled the channel with aqueous solution of Tween 20 (2.0% w/w) immediately after sealing; this procedure allowed the surface of the channels to remain hydrophilic. To study the formation of aqueous droplets, we sealed the system of channel in PDMS against a flat PDMS slab. The device was baked at 150 °C overnight to ensure the hydrophobic character of the surface.

Formation of gas bubbles: The continuous phase was an aqueous solution (Millipore, deionized) of Tween 20 (Polysorbate 80, 2.0% w/w, Aldrich). The dispersed phase was nitrogen (ultrapure, Airgas).

Formation of aqueous droplets: The continuous phase was hexadecane (Sigma–Aldrich) containing Span 80 (Sorbitian monooleate, 3.0% w/w, Aldrich), and the dispersed phase was water (Millipore, deionized).

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

Imaging and image analysis: We used an upright microscope (Leica DMRX), a set of still- (Nicon Digital Camera DXM 1200), and fast-video (Phantom V7) cameras to visualize and record movies of the dynamics of the system. We used Adobe Illustrator C3 and Adobe Photoshop C3 to measure the size of bubbles and droplets, and to prepare the figures. Home-made software analyzed the fast-video movies to generate plots showing the timing of formation of bubbles.

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