

LIQUID-IN-GAS DROPLET MICROFLUIDICS

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ABSTRACT

Here we demonstrate a novel concept of liquid-in-gas droplet microfluidics by using gas flow as the continuous phase for the production of liquid droplets. Within a specially configured co-flow microfluidic tubing device, a flow of liquid phase has been continuously dispersed into another outer stream of gas phase, producing discrete and monodisperse microdroplets. This process is robust and well-controlled, and supports various formation modes by systematically altering a variety of critical parameters, including water flow rate and gas pressure. Moreover, the resulting liquid droplets still remain intact during downstream transportation towards the outlet of the tubing, enabling them to be collected and stored for further study.

KEYWORDS

Droplet microfluidics, gas continuous phase, co-flow.

INTRODUCTION

The rapid development of biology, chemistry and nanotechnologies has urged an uprising quest on the manipulation of small volumes of liquids scaling from picoliters to nanoliters through well-controlled manners. Droplet microfluidics separates chemical and biological liquid samples into discrete, segmental volumes within geometrically confined microchannels, and has appeared as a powerful and versatile approach in response of such a growing demand. Since its debut in the 1990s it has aroused tremendous attentions across many multidisciplinary areas including analysis, synthesis, catalysis, diagnosis, reaction kinetics and even computing logics.[1-2] In a general scheme of droplet microfluidics, a flow of one stream, which is called as the dispersed phase (DP), is continuously dispersed into another flow of continuous phase (CP) to form a series of discrete, individual bubbles or droplets. Typical examples of droplet microfluidics include dispersing air stream into liquid flows to create microbubbles, and the dispersion of liquid flow into another liquid flow to form microdroplets (emulsion mechanism could be either Oil-in-Water or Water-in-Oil). [1-2] However, in each of these cases, the continuous phase has been limited to liquid phase only. While there have been significant impacts on the usage of gas as the continuous phase, to our knowledge it has not been fully explored yet.

The general characteristics of the proposed liquid-in-gas dispersion are expected to be as stable and monodisperse as possible, however, it should be noted that it is more restrictive than the liquid-in-liquid systems considering the more complicated dynamics during dispersion. From previous studies it has been well known that the dynamics of microfluidic mediated droplet production is controlled by the Rayleigh-Plateau instability interplayed by drag force exerted by the continuous phase and the interfacial forces. When the liquid outer stream is substituted by low viscosity gaseous flow, the possibility of breaking liquid DP flow into individual drops becomes questionable considering the much weaker drag force imposed by the gas flow running at a similar velocity. While large increase in the gas flow rate would also possibly ends up by destabilized droplet generation coupled small satellite droplets(similar to the asymmetric jetting mode in air spray) as the drag force significantly outcomes the liquid-gas interfacial stress, which is important to keep droplets intact. Consequently it is crucial to manipulate the gas flow in a moderate range that is sufficiently strong to drive droplet emission in steady state yet not break them into satellites. Moreover, it has been found that the droplet generation greatly depends on the substrate surface wetting properties, for example, aqueous droplets can only be produced on hydrophobic substrate supports [3].

Here, we demonstrate the production and transportation of discrete microscale liquid droplets inside a sealed microchannel using a gas flow as the continuous phase. To achieve this goal, a simple microfluidic tubing platform was realized using a co-flow droplet generator connected to a downstream channel. The sidewall of the microchannel was highly hydrophobic, ensuring successful aqueous droplet formation and transportation throughout the device. At the tip of droplet generator, a flow of liquid was continuously dispersed into a surrounding air flow, forming discrete and uniform water droplets (Figure 1). This process is robust and controllable, and could undergo various formation modes by altering a number of critical parameters. In this project, we have identified two distinctive modes of stable droplet production (“dripping without adhering” and “dripping with adhering” modes) by varying the gas pressure and liquid flow rate (Figure 2), and have studied their characteristic formation regimes with theoretical explanations.

EXPERIMENTAL

The co-flow microfluidic device employed in our experiments consisted of a 50 μm inner and 80 μm outer diameter glass capillary(VitroCom) within a 300 μm ID PTFE tubing(Cole-Palmer). The inner glass capillary was first connected to one end of a 5.0 cm length of 250 μm ID and 750 μm OD Tygon tubing (Cole Parmer). The other end of the Tygon tubing was inserted into a 10 μL plastic pipette tip with the end cut off. The open capillary end was positioned within the modified pipette top with a \sim 2 cm length outside the tip head. After inserting another Tygon tubing segment into the tail of the pipette for convenient introduction of the continuous phase, the tail was sealed with

epoxy. At the pipette tip, the glass capillary was inserted into the PTFE tubing, and the tip of the pipette was then sealed with PTFE tubing by Dow Corning 3140 silicone adhesive.

The flow of the liquid phase was controlled by a Harvard 2000 syringe pump. The air pressure of the gas continuous phase was generated using two bleach bottles at different vertical heights. Water was siphoned from one bleach container into another sealed bleach bottle, causing a rise in pressure of the lower bleach bottle as water flowed from the higher container. The sealed lower bleach bottle had a tube for the air to escape, and this air flow was connected to the Tygon tube on the end of the device to provide the gas continuous phase. The pressure generated was determined by the height difference between the water levels.

Microscopic monitoring of droplet production was achieved on a Nikon TE-2000S inverted fluorescence microscope, where 0.1% of sodium fluorescein dye was added into the water dispersed phase for better visualization.

RESULTS AND DISCUSSION

The co-flow microfluidic device was fabricated by simply assembling glass capillaries and plastic micro-tubing coaxially. The outer tubing has been chosen to be PTFE-based because of its naturally high hydrophobicity (contact angle of water is about 120°). Water DP flow does not adhere to the sidewall of PTFE tubing, allowing well-controlled droplet production and subsequent transportation towards the channel exit. Unlike previous open substrate systems, our droplet generator is configured in a geometrically confined environment, ensuring all the laminar flow characteristics for both the liquid DP and gas CP and ultimately contributing the success of stable droplet production. In addition, we also invented a simple and inexpensive apparatus to control gas CP pressure by placing two water bleach bottles at different heights. The pressure exerted by gas CP is directly proportional to the relative vertical position difference, which could be moderated conveniently into a suitable pressure range (0.5-3.0 psi) that helps droplet production.

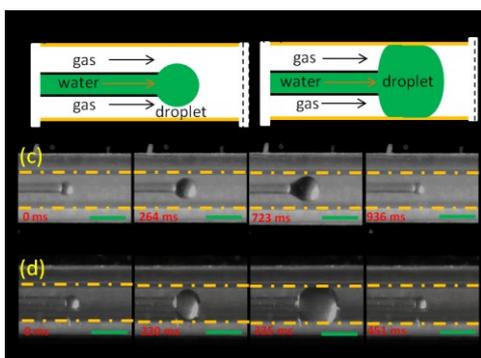


Figure 2. (a)&(b) Schematic illustrations of different droplet formation modes: (a) DwoA mode, (b) DwA mode; (c)&(d): Time evolution of the dynamic behaviors during (c) DwoA mode and (d) DwA mode. Scale bars of green in all the images are 300 μm .

Initially, surface tension dominates and anchors the small droplet at the tip, but as the droplet grows bigger and bigger, the drag force eventually becomes comparable. Once the net force acting on the droplet exceeds zero, Rayleigh-Plateau instability pinches the droplet off.

In order to obtain a better understanding on the liquid-in-gas droplet production, we have systematically varied a number of critical factors, including the DP flow rate and the pressure of gas CP, and studied the droplet formation behaviors at different regimes. We have observed two distinct modes when the DP flow rate is increased from its low end to high end, which we call as dripping without adhering (DwoA) mode and dripping with adhering (DwA) mode, respectively, as shown in Figure 2. In the DwoA mode, which occurs at low DP flow rates, droplets emerge from the inner tube and are emitted from the tube due to shear forces without first contacting the channel sidewall. In contrast, in the DwA mode, droplets grow rapidly to a size comparable to that of the microchannel before

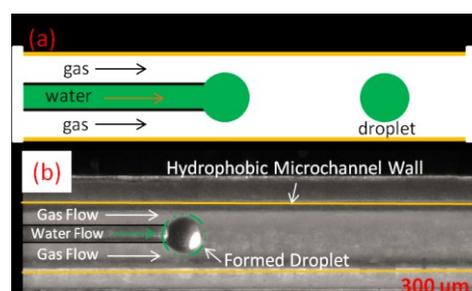


Figure 1. (a) Schematic Illustration of the coaxial co-flow droplet generator using gas CP; (b) Microscopic image showing the formation process of a droplet.

We first examined the possibility of success on controlled liquid-in-gas dispersion by inducing a water flow into the co-flow microfluidic system. The process of droplet production was directly monitored on a fluorescent microscope. As shown in Figure 1b, once the DP flow gets out of the capillary tip, a characteristic spherical profile has been developed as a result of the combined effect of minimized interfacial tension and surface hydrophobicity. Meanwhile, it also gets protruded forward by the outer gas CP stream with a thin thread neck at its tail. As the protrusion proceeds further, the thread neck gets stretched and becomes thinner and thinner. After a critical point, the neck thread becomes so thin that it cannot anchor the droplet at the capillary tip anymore, emitting a discrete droplet. Right after that, the neck thread retracts back to the capillary tip, repeating the same process to generate another droplet. It should be noted that this specific emission process is similar to the dripping mode founded in previous liquid-in-liquid systems.

The dynamic process can be explained by analyzing two competing forces that the droplet experiences during its growth: viscous drag forces exerted from the outer gas CP, which pulls it forwards and the surface tension of the liquid DP, which holds it at the capillary tip.

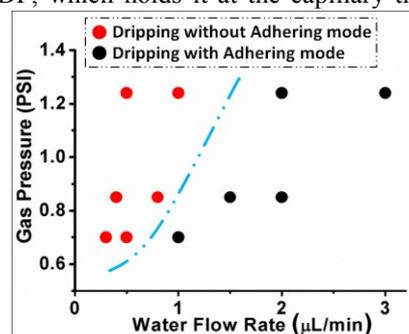


Figure 3. Phase diagram plot of different formation modes as a function of gas CP pressure and water DP flow rate.

pinching off due to high pressure gradient across the droplet induced by the continuous gas phase flow. Since the growth rate of droplet diameter is dependent upon the rate of mass supply into the drop, the Dwa mode usually happens at higher DP flow rates.

Dripping mode	Characteristic Behavior	Condition	Typical Regimes
Dripping without Adhering (DwoA)	Droplet emits without contacting channel sidewall	$T_{a,c} > T_{g,c}$	Low DP rate, moderate/higher CP pressure
Dripping with Adhering (DwA)	Droplet contacts channel sidewall before it emits	$T_{a,c} < T_{g,c}$	moderate DP rate, moderate/higher CP pressure

Table 1. Summary of characteristic behaviors and formation conditions for the two dripping modes, $T_{a,c}$ and $T_{g,c}$ refer to critical advection time and critical growth time, respectively.

The impact of DP flow rates on the two dripping modes can be further understood by isolating the droplet generation process into two independent, parallel sub-processes: a) droplet advection and b) droplet growth. During the droplet advection process, due to the dragging of gas CP, the tail thread of the droplet is stretched thinner and thinner, finally getting to a threshold state that it could no longer hold the droplet at the tip, ending up with droplet emission. The timescale span from the droplet initialization to droplet emission is defined as critical advection time: $T_{a,c}$. $T_{a,c}$ closely relates to the linear velocity of the gas CP flow and can be adjusted by varying the gas CP pressure. With regard to the sub-process of droplet growth, besides the axial process being pulled by the gas CP stream, the pendent droplet also grows laterally with an increasing diameter as a result of constant mass transfer of liquid from the inner capillary into the droplet. If the size of the droplet gets the chance to grow big enough, it would fully take up the entire space of the microchannel. The boundary of the droplet also would touch to the sidewall and transit into a cylindrical plug shape from the initial spherical geometry.[4] We define the time needed for full occupation of the microchannel as critical growth time, $T_{g,c}$ and it is largely related to the liquid DP flow rate. With the two time scale definitions, we then distinguish the two generation modes by simply comparing $T_{a,c}$ and $T_{g,c}$: the DwoA mode should happen at $T_{a,c} < T_{g,c}$, while the DwA mode should take place at $T_{a,c} > T_{g,c}$ (Table 1).

With the theory above, we can also explain the shifting of transition from DwoA mode to DwA mode on DP flow rate axis at different gas CP pressures (Figure 3). For example, at a higher gas pressure, the neck thread at the droplet tail would be thinned at a faster speed, resulting in a shorter $T_{a,c}$. On the other hand, the $T_{g,c}$ remains almost the same because of constant DP flow rate. Consequently, the corresponding transition point of the two modes would be delayed and shift towards higher flow rates of DP.

After droplet production, the controlled transport of produced droplets along the downstream microchannel has been successfully achieved as well. Droplets remain as discrete fluid volumes (Figure 4), that can be collected and stored in a downstream oil-filled reservoir with excellent monodispersity. It should be noted that the droplets remain intact during transport, with no satellite droplets adhering to the sidewall observed, demonstrating the robustness of the system. The integration of both droplet production and transportation enables the possibility to apply our system into various application circumstances.

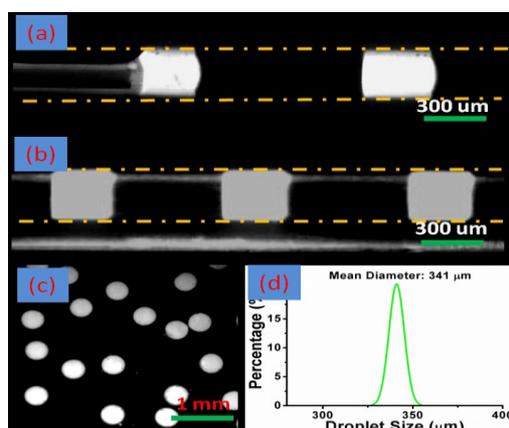


Figure 4. Microscopic images showing the integrated process of the droplet production, transportation and collection. (a) Droplet production at the upstream droplet generator; (b) Transportation of intact droplets along the downstream channel, which is 10 cm away from the droplet generator; (c) Droplet collected in a bottle reservoir filled with immiscible stabilizing oil phase; (d) size distribution chart of collected droplets by measuring a sample size of 100 droplets.

CONCLUSION

The presented liquid-in-gas droplet formation technique provides excellent control over both droplet production and transport. Compared to established liquid-in-liquid techniques, a key advantage of the liquid-in-gas method is that the resulting droplets are not contaminated by oil phases or surfactants, which is of critical importance for a variety of biological applications such as digital PCR, cell encapsulation and cell culturing.

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