Independent Control of Drop Size and Velocity in Microfluidic Flow-Focusing Generators Using Variable Temperature and Flow Rate

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This paper describes a method to control the volume and the velocity of drops generated in a flow-focusing device dynamically and independently. This method involves simultaneous tuning of the temperature of the nozzle of the device and of the flow rate of the continuous phase; the method requires a continuous phase liquid that has a viscosity that varies steeply with temperature. Increasing the temperature of the flow-focusing nozzle from 0 to 80 °C increased the volume of the drops by almost 2 orders of magnitude. Tuning both the temperature and the flow rate controlled the drop volume and the drop velocity independently; this feature is not possible in a basic flow-focusing device. This paper also demonstrates a procedure for identifying the range of possible drop volumes and drop velocities for a given flow-focusing device and shows how to generate drops with a specified volume and velocity within this range. This method is easy to implement in on-chip applications where thermal management is already incorporated in the system, such as DNA amplification using the polymerase chain reaction and nanoparticle synthesis.

This paper describes a method to achieve independent control of the size and the velocity of drops generated in a microfluidic flow-focusing device,[1,2] by simultaneous tuning of the temperature of the nozzle of the device and of the flow rate of the continuous phase. Independent control of the drop size, and of its velocity inside the microfluidic device, is important for droplet-based microfluidic analytical applications, in which both the volume of the droplet (containing reagents and analytes, for example) and the duration of the characterization or reaction steps determine the efficiency and the overall throughput of the system.[3] The velocity of the drops is inversely proportional to the duration of the travel of the drops inside the device; velocity determines, therefore, the duration of the processing steps. Examples of applications include DNA detection and amplification using polymerase chain reaction (PCR),[4−7] nanoparticle synthesis,[8] the study of the kinetics of nucleation and growth of crystals in supersaturated aqueous solutions,[9] and the production of microbeads by polymerization.[10]

A common way to control the size of the drops dynamically in microfluidic drop generators is by applying different flow conditions during the operation of the device. A decrease in the rate of flow of the continuous phase typically increases the size of the droplets;[1,2] the velocity of the drops also decreases, however. Decoupling the drop size from the drop velocity requires a different way of controlling the drop size.

Recently Nguyen et al. varied the temperature of the nozzle of a flow-focusing device to control the drop size dynamically at fixed rates of flow.[11] In this note, we combined this temperature-based control with variation in flow rate to achieve dynamic and independent control of the volume and the velocity of the drops. We also maximized the range of the size of the drops generated at different temperatures through the choice of the liquids as the continuous phase. The volume of the droplets generated by changing the nozzle temperature of our microfluidic device varied by almost 2 orders of magnitude; this range of volumes achieved exceeds that reported by Nguyen et al.[11] by at least an order of magnitude. Since aqueous droplets are the most relevant for common laboratory-on-a-chip applications, we focus on using water as the disperse phase and different inert oils as the continuous phase.

EXPERIMENTAL DESIGN AND METHODS

Fabrication and Experimental Setup. We fabricated microfluidic flow-focusing drop generators in poly(dimethylsiloxane) (PDMS) using soft lithography.[12] The PDMS channel was sealed to a glass slide, which formed its bottom. The microfluidic device

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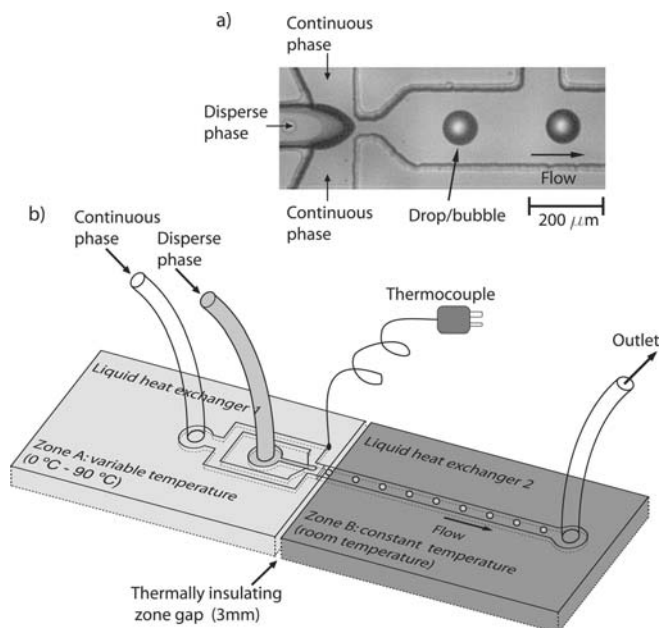
Figure 1. Experimental setup. (a) Top view of the microfluidic flow-focusing generator in operation. Drops of water were generated in a continuous phase of mineral oil. The rates of flow of water and mineral oil were 0.1 and 4.0 mL/h, respectively. The device also had a side channel that was kept plugged for the experiments described here. (b) The device was placed in contact with two copper liquid heat exchangers that made up the two constant-temperature zones, A and B. We used a thermocouple to measure the temperature of the nozzle.

had a flow-focusing nozzle connected to a straight channel (Figure 1a). The flow-focusing nozzle was 125 μm tall, 40 μm wide, and 70 μm long. The straight channel had a rectangular cross section, with a width of 200 μm, a height of 125 μm, and a length of approximately 50 mm. We placed the glass side of the device in direct contact with two heat exchangers (Figure 1b). The flow-focusing nozzle was placed above one of the heat exchangers (zone A), and the channel downstream sat above the other heat exchanger (zone B). Because of the low thermal conductivities of PDMS and glass, the nozzle had a temperature close to the one of zone A, while most of the channel had a temperature close to the one of zone B. We kept the temperature constant in zone B and changed the temperature of zone A to vary the volume of the drops.

We varied the temperature of zone A by running liquid from a basic constant-temperature bath (VWR International 1160S) through heat exchanger 1. Zone B was thermally insulated from zone A by a 3 mm gap filled with Teflon. Water, pumped in a closed circuit from a 20 L barrel at room temperature (20−25 °C), controlled the temperature of zone B. The large thermal mass of the barrel ensured the temperature stability of zone B. To measure temperature, we inserted the tip of a thin thermocouple (Omega Engineering, K-type, 0.25 mm wire diameter) through the PDMS slab near the nozzle until it touched the glass slide that formed the bottom of the microfluidic device. The tip of the thermocouple and the nozzle were both placed 4 mm away from the gap, inside zone A.

Our experiments consisted of generating droplets of water, or bubbles of nitrogen, in various liquids as the continuous phase. We pumped the liquids with syringe pumps (Harvard Apparatus

PHD2000) at constant flow rate and supplied nitrogen at constant pressure using a gas pressure regulator. A microscope imaged the device while a fast digital camera (Vision Research Phantom V7) recorded movies of the generation of droplets. We calculated the average volume of the drops by dividing the rate of flow of the disperse phase by the frequency of the generation of drops; the drop frequency was measured by counting of the number of droplets that were generated over a known period of time in the recorded movies. For bubbles, we measured their size by multiplying their digitized image size in pixels with the magnification factor of our imaging setup.

Choice of Liquids for a Large Dependence of the Volume of the Drops on Temperature. The size of drops formed in microfluidic devices scales inversely proportional to the capillary number (Ca) of the continuous phase:[13,14]

$$D(T) \propto \mathrm{Ca}^{-1} = \left(\frac{\eta_\mathrm{c}(T)u_\mathrm{c}}{\gamma_\mathrm{c}(T)}\right)^{-1} = \frac{\gamma_\mathrm{c}(T)}{\eta_\mathrm{c}(T)u_\mathrm{c}} \qquad (1)$$

where T is the temperature, D is the diameter of the drop or bubble, η_c is the dynamic viscosity of the continuous phase in mPa·s, u_c is the characteristic speed of the continuous phase in m/s, and γ_c is the interfacial surface tension between the continuous and the disperse phase in mN/m.

Both viscosity and surface tension decrease with temperature for most liquids. The key to achieving a large variation of drop volume with temperature is, therefore, to use liquids that have a much larger variation of only one of these properties. In previous work that investigated the effect of temperature on the drop size, the relative changes in viscosity and surface tension were comparable.[11] In this study we focused on liquids that have a very steep change in viscosity with temperature. For the liquids that we have used, viscosity decreased exponentially by a factor of 15−30 as the temperature increased from 0 to 80 °C. (See Figure S-1 in the Supporting Information for quantitative viscosity data.) We found that surface tensions had a much weaker, and approximately linear, dependence on temperature, changing by at most a factor of 1.5 over the same temperature range. (Figure S-2 in the Supporting Information section shows the temperature dependence of the surface tension for the liquids that we used.)

To find liquids suitable for efficient tuning of drop volume with temperature, we surveyed liquids that are commercially available based on the following criteria: (1) large variation of viscosity with temperature, (2) immiscibility with water, (3) compatibility with PDMS, (4) availability and low price, and (5) availability of viscosity−temperature calibration data. The liquids that we used as the continuous phase were (i) light mineral oil (Sigma-Aldrich, U.S. catalog part no. 330779), (ii) Dynalene SF (Dynalene Inc., trademarked bath fluid mixture made from alkylated aromatic hydrocarbon oils), (iii) perfluoroperhydrophenanthrene (PFP, Alfa Aesar U.S. catalog part no. L17370), and (iv) a mixture of 98% v/v perfluoroperhydrophenanthrene with 2% v/v perfluoroocta-nol (PFO, Sigma-Aldrich U.S. catalog part no. 370533). PFO is a PFP-soluble and water-insoluble surfactant. Mineral oil satisfies criteria 1, 2, 3, and 4, but the manufacturer did not specify its

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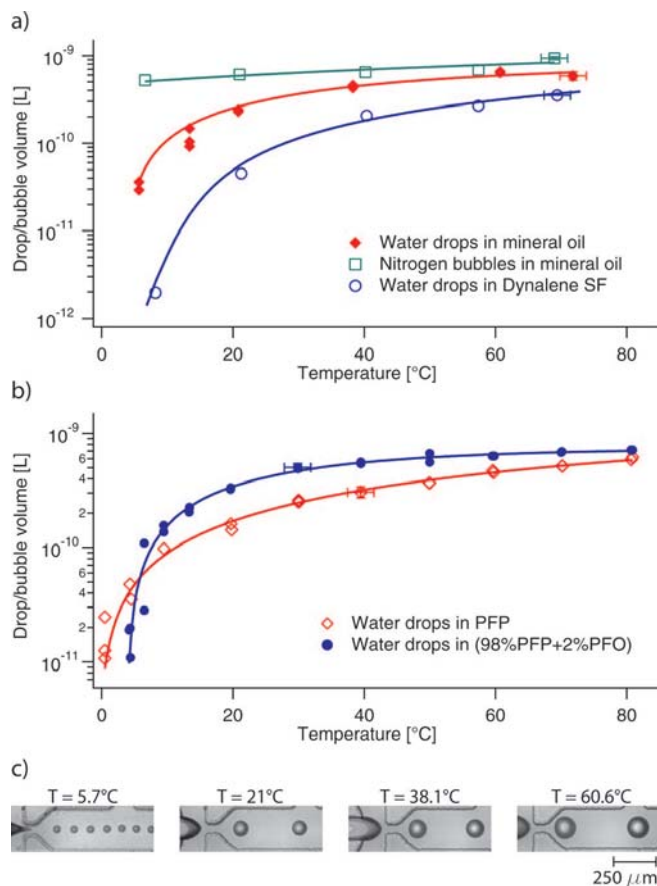
Figure 2. Variation of the drop volume with the temperature of the nozzle of the flow-focusing device. To generate drops of water we used light mineral oil, Dynalene SF, PFP, and a mixture of 98% v/v PFP with 2% PFO as the continuous phases. (a) Water drops in mineral oil (flow rate 4.1 mL/h) and Dynalene SF (5.3 mL/h), nitrogen bubbles in mineral oil (2 mL/h). (b) Water drops in PFP (7.2 mL/h) and in PFP−PFO mixture (2.1 mL/h). The error bars represent the accuracy of the measurement of temperature and volume; for clarity we show only one pair of error bars for each data set. The lines in the graphs are guides to the eye only. (c) Images of drops of water generated in mineral oil at a total rate of flow of 4.1 mL/h, at different temperatures.

viscosity. Constant-temperature bath fluids usually have their viscosity specified across their usable temperature range; the same applies to calibration oils for viscometers, but the bath fluids are significantly cheaper. Many perfluorinated hydrocarbon liquids, although expensive, are chemically inert and immiscible with water, PDMS, and many organic solvents; some have a large variation of viscosity with temperature.

RESULTS AND DISCUSSION

Variation of the Volume of the Drop with Temperature and Flow Rate. Figure 2 shows the variation of the volume of the drops and bubbles with the temperature of the flow-focusing nozzle. The volume of the drops and bubbles always increased as we raised the temperature. The volume of the drops increased by almost 2 orders of magnitude when we increased the temperature from 0 to 80 °C. The volume of the bubbles increased much less—approximately a factor of 2.0. We applied rates of flow such that the generation of water drops occurred in dripping or jetting regimes[14] only and that the drops generated were monodisperse. The sum of the rates of flow of water and of the disperse phase
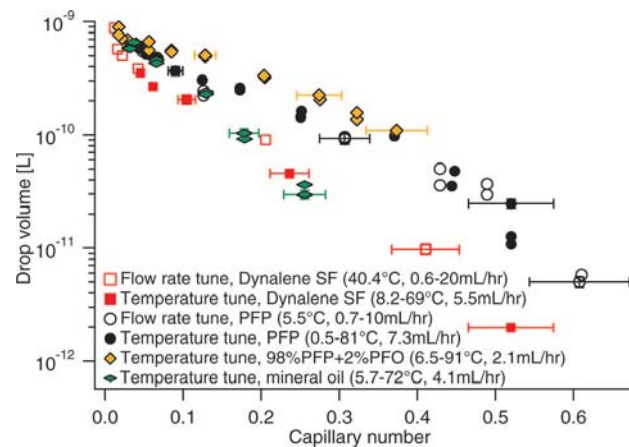
Figure 3. Comparison of the range of volumes of water drops generated by changing the temperature, or by changing the flow rate, in PFP and Dynalene SF. The range over which we can change the volume of the drops is similar for both methods. For a particular pair of liquids the capillary number is the only parameter that determines the size of the drops. Also shown here is the data on the temperature dependence of the volumes of drops of water in mineral oil and in a mixture of 98% PFP and 2% PFO. The error bars represent the accuracy of the measurement of the capillary number and of the drop volume; for clarity we show only a few error bars for each data set.

was constant for all temperatures. In the case of bubble generation the rate of flow of the continuous phase was constant, and we adjusted the pressure of the nitrogen gas to the minimum pressure at which the generation of bubbles was stable and monodisperse.

Figure 3 compares the tuning of the volume of the drop by changing the temperature with that by changing the flow rate. We plotted the drop volume against the capillary number for two types of scans: in one we changed the temperature while keeping the flow rate constant, and in the other we changed the rate of flow while keeping the temperature constant. For a fixed pair of liquids, changing the temperature or changing the rate of flow generates approximately the same range of volumes of the drops.

Independent Variation of Drop Volume and Drop Velocity Using Variable Temperatures and Flow Rates. Many basic microfluidics setups have the ability to change the rates of flow easily; for these setups, the most practical way to change the volume of a drop in a flow-focusing generator is to change the rate of flow of the continuous phase. The velocity of the drops increases at a higher rate of flow. The drop volume and the drop velocity are therefore dependent variables.

Figure 4 shows the correlation between the drop volume and velocity for a few nozzle temperatures. At room temperature, the possible volume−velocity combinations were restricted to a line in this graph. But if both the flow rate and the temperature are changed, new volume−velocity combinations become possible. The graph in Figure 4 is also a "map" of the operational range of a flow-focusing device. The points in the region between the lines for the highest and the lowest temperatures are accessible by operating the device at intermediate temperatures.

With the use of the volume−velocity map, the temperature and flow rate for a desired volume−velocity combination can be found by interpolating between the measured data. For example, assume that using the geometry of our microfluidic device we need 0.2 nL drops that travel at 100 mm/s through the device,
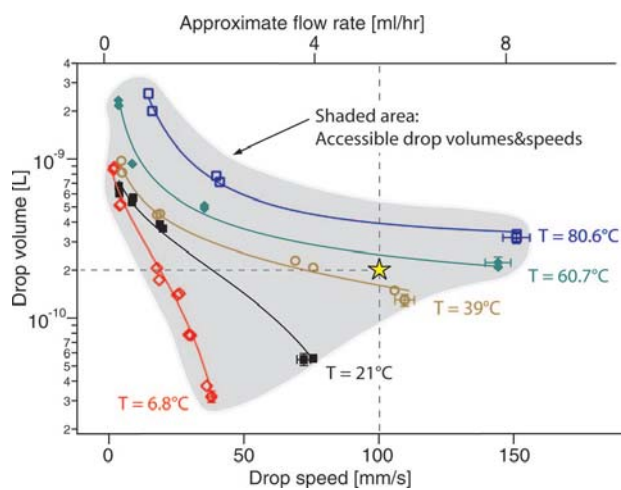
Figure 4. Independent tuning of the drop volume and drop velocity using simultaneous variation of temperature and flow rate. For the data in this graph, we generated drops of water in a mixture of 98% PFP and 2% PFO at different temperatures. The lines in the graph are guides to the eye and indicate how, at constant temperature, the volume of the drop depends on the velocity of the drop as the flow rate changes. The gray area indicates the volumes and velocities of the drop that can be achieved if both the temperature and the flow rate are changed simultaneously. The top axis shows the approximate flow rate of the continuous phase using the geometry of our microfluidic device. Because the drop velocity depends on both the flow rate and the drop size, the relation between drop velocity and flow rate deviates from a linear relationship.

represented by a star in the figure. Such a combination is impossible at room temperature, but using Figure 4, one can estimate that the temperature at which it *is* possible should be around 50 °C (by interpolation between the 39 and 60.7 °C curves) and the total flow rate should be around 5.7 mL/h (by interpolation of flow rates for data on 39 °C curve).

CONCLUSIONS

This note describes a method to control the volume and transit velocity of aqueous drops generated in a flow-focusing device dynamically and independently. Changing the temperature of the flow-focusing nozzle changes the volume of the drops because the viscosity of the continuous phase changes.[11] Here we optimized this method and showed that if the viscosity of the continuous phase has a steep dependence on temperature, the range of volumes of the drops generated is roughly the same as the range obtained by changing the rate of flow of the continuous phase. Simultaneous variations in the temperature of the nozzle and in the rate of flow of the continuous phase expand the range of drop volumes and drop velocities that can be achieved by the droplet generator. This note also describes a procedure for charting the range of operation (drop volume and drop velocity) of a flow-focusing generator and for finding the flow and temperature conditions for generation of drops with specified volume and velocity.

Independent control of volume and velocity of the drops is useful for many microfluidic applications that exploit the kinetics of chemical reactions. The increased degree of control over the

generation of drops also facilitates microfluidic design and testing, reducing the number of prototyping cycles.

The use of variable temperature during the generation of drops could affect the subsequent processing of the drops if the nozzle temperature causes chemical reactions inside the drops, or if it affects the stability of the drops against coalescence.[15] Localizing the temperature variations at the nozzle mitigates such problems, because it restricts the time and the distance over which such changes might occur. Accurate evaluation of the temperature of the drops as they move in a channel with variable temperature is a difficult fluid dynamics problem and is beyond the scope of this note. For our experiment and for flow rates of the continuous phase between 2 and 4 mL/h, we estimated that the drops traveled a distance on the order of 1 cm downstream of the beginning of zone B, or for approximately 0.5 s after generation, before their temperature was within 1 °C of room temperature. This fast thermal stabilization prevented temperature-induced drop coalescence because the drops were generated such that they were spaced apart from each other, and the drops remained spaced as they traveled the first few centimeters of the channel downstream of the flow-focusing nozzle.

The volume of the drops generated in a flow-focusing device can also be changed dynamically using electric fields[16] or microfluidic devices with variable nozzle geometry.[17] These methods could also be used to achieve independent control of the volume and velocity of the drops. Changing the volume by temperature variation has a practical advantage in applications that require temperature control, because thermal management is already incorporated in the system. In microfluidic devices that amplify DNA inside aqueous drops,[4−7] for example, thermal cycling is necessary for PCR; the thermal hardware used for cycling (heaters and coolers) could be adapted to vary the drop volume.

SUPPORTING INFORMATION AVAILABLE

Additional information as noted in text. This material is available free of charge via the Internet at http://pubs.acs.org.

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