Negative Pressure Induced Droplet Generation in a Microfluidic Flow-Focusing Device

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Supporting Information

ABSTRACT: We introduce an effective method to actively induce droplet generation using negative pressure. Droplets can be generated on demand using a series of periodic negative pressure pulses. Fluidic network models were developed using the analogy to electric networks to relate the pressure conditions for different flow regimes. Experimental results show that the droplet volume is correlated to the pressure ratio with a power law of 1.3. Using a pulsed negative pressure at the outlet, we are able to produce droplets in demand and with a volume proportional to the pulse width.

Active droplet generation (ADG) in microfluidics provides an additional degree of freedom in manipulating both the size and the formation frequency of microdroplets. This additional control is extremely desirable for intricate operations which rely on the precise control of both parameters. For example, droplets in microfluidics are often used as a microreactor for various chemical and biological applications. After droplet generation, encapsulated droplets with chemical or biological contents are often detected, sorted and used for different analytical purposes. The encapsulation of biological materials in droplets also requires droplets to be of a suitable size for subsequent sorting using fluorescence-activated droplet sorting (FADS). The formation of slugs or satellite droplets may result in errors or unwanted noise. ADG induces external energy into the fluidic system such as magnetic fields, electric fields, acoustic, thermocapillary, or pneumatic actuation. Among the above concepts, pneumatic actuation is the most accessible as it only requires the use of pressurized air. Sophisticated labyrinth of networks and channel manipulation have been demonstrated using the Quake’s valve. These pneumatic actuation methods often rely on flow perturbation, geometry tuning or flow manipulation to control the size of the droplets. In introducing perturbation, a microvalve is integrated to form a multilayered device. If the valve is pressurized, perturbations are induced to control the size of the droplets formed. Flow manipulation involves similar valves which disrupts the fluid flows. In geometry tuning, the microchannels are often deformed to manipulate the flow parameters.

To date, pneumatic actuation reported in the literature are often complex in fabrication as they require the alignment of microvalves at the precise location. On the other hand, geometry tuning, which does not require alignments, may not be suitable for prolonged operation. Hence, we see an immediate need to address this technology gap. To the best of our knowledge, the direct use of a negative pressure to control droplet sizes has not been demonstrated.

In this work, we demonstrate the generation of mono-dispersed droplets by inducing a negative pressure at the outlet. This concept can be implemented easily through the use of a single pressure controller. We first balanced the water pressure and oil pressure, to obtain a stable interface. A negative pressure introduced at the outlet induces droplet formation. Increasing the magnitude of the negative pressure increases the size of the droplets generated. Applying the negative pressure offers several distinct advantages. For example, droplets can be produced on demand using the analogy to electric networks to relate the pressure conditions.
a series of periodic pulses. Negative pressure also enables droplet collection without inconsistencies due to droplet coalescence at the exit. Explicitly, when droplets enter the tubing, a disparity between the size of the microchannel and tubing often reduces the speed of the droplets and result in collisions or unintended merging. A constant negative pressure at the outlet allows droplets to flow consistently into the tubing/collection tube. In comparison to the use of syringe pumps, pressure driven flow generates highly monodispersed droplets due to the absence of pulsation effects induced by the stepper motors. We envisage that this simple technological innovation may be useful for many microfluidic analytical applications.

■ EXPERIMENTAL SECTION

A microfluidic flow focusing device was fabricated in polydimethylsiloxane (PDMS, Dow Corning) using standard photo and soft lithography techniques. The microchannels were treated with Aquapel (PPG Industries, U.S.A.) to render the surface hydrophobic. The channel height is about 28 um. The critical channel widths are illustrated in Figure 1b. A pressure controller (Elveflow, OB1MK3) was connected to the microfluidic device to induce both positive and negative pressures, Figure 1a. The positive pressure balances the fluid interface at a converging channel, Figure 1b. A negative pressure at the outlet induces droplet generation. All the pressures used unless otherwise stated are relative to the atmospheric pressure, \( P_{\text{ATM}} \). The microfluidic device is then mounted on an inverted microscope (Nikon Ti-E, Japan) and imaged with a high speed camera (Miro 3, Vision Research) at a frame rate of 200 fps. Mineral oil (M5904 with 0.5 wt % SPAN80, Sigma-Aldrich) and DI water were used as the continuous phase and dispersed phase, respectively. The equilibrium interfacial tension between the fluids is about 6.2 mN/m (Sinterface, PAT1). The dynamic viscosities of both oil and water are 23.8 mPa.s and 1 mPa.s respectively (TA Instruments, DHR-2). We measured different droplet parameters such as droplet area and speed using the automated droplet measurement (ADM) software. The droplet is assumed to have a cylindrical shape instead of a discoid as the error is negligible (Supporting Information, Figure-S2). Therefore, the droplet volume can be estimated as the product of the droplet area and the channel height.

■ RESULTS AND DISCUSSION

We first vary both \( P_O \) and \( P_W \) to generate the forward flow regime chart. The chart does not include the backflow regimes when \( P_O \) is a lot smaller than \( P_{\text{inlet}} \), or when \( P_W \) is a lot smaller than \( P_O \). Three distinct forward flow behaviors were observed at different \( P_W \) and \( P_O \) values in Figure 2. When \( P_O \) is slightly smaller than \( P_{\text{inlet}} \) we observed a parallel flow regime. When \( P_O \) is significantly higher than \( P_W \), a stable interface is formed at the junction. Droplets are generated between these two flow regimes.

In order to derive the relationships of both \( P_O \) and \( P_W \) in each regime, we modeled the fluidic flow paths for each regime using an electric circuit analogy, Figure 1d–f. The Hagen–Poiseuille’s law can be simplified to give the flow–pressure relation as

\[
Q_{O/W} = \frac{\Delta P}{R_{\text{total}}}
\]

where \( \Delta P \) is the pressure difference between the inlet and outlet. \( Q \) is the volumetric flow rates of either oil or water and \( R_{\text{total}} \) is the total hydraulic resistance in the flow path. For closed rectangular channels, the fluidic resistance for each section is given as

\[
R_i = 12\mu \frac{L_i}{W_i H_i^3 (1 - 0.63 \frac{H_i}{W_i})}
\]

where \( L_i \), \( W_i \), and \( H_i \) are the channel length, width, and heights of each section and \( \mu \) is the viscosity of the fluid. Details of the
specific measurements for each section can be found in (Supporting Information, Table-S1). When a stable interface is formed at the junction, the $R_{\text{total}}$ from Figure 1d can be expressed as

$$R_{\text{total}} = R_1 + (R_2 || R_3) + R_3$$  \hspace{1cm} (3)$$

where $R_{1-3}$ are the respective resistances at each section (Figure 1d). The values of $R_1$, $R_2$, and $R_3$ are approximately 0.9 × 10^{-14}$ kg·m^{-4}·s^{-1}, 10 × 10^{-14}$ kg·m^{-4}·s^{-1}, and 6 × 10^{-14}$ kg·m^{-4}·s^{-1}, respectively. Hence, eq 1 can be simplified as

$$Q_O = \frac{P_O}{(R_1 + \frac{R_2}{2} + R_3)}$$  \hspace{1cm} (4)$$

where $P_O$ is the imposed pressure at the inlet and $Q_O$ is the volumetric flow rate of the oil.

For the dispersed phase channel, the channel abruptly converges to a small orifice. As a result, the interface between the water and the oil has a high curvature. This creates a pressure difference, which is the Laplace pressure:

$$P_L = \gamma \left( \frac{1}{r_w} + \frac{1}{r_h} \right)$$  \hspace{1cm} (5)$$

where $\gamma$ is the interfacial tension between the oil and water, $r_w$ and $r_h$ are the radii of curvatures due to the wall and channel height. $P_L$ can be calculated by obtaining $r_w$ and $r_h$ through examining the recorded videos with a customized MATLAB program. We obtained a value of approximately 6.36 mbar for the Laplace pressure (Supporting Information, Figure-S3), which agrees well with literature.22,23 The wettability of the fluids with the PDMS wall and the corresponding contact angles may affect the droplet generation. However, this is currently beyond the scope of this technical note. Readers may refer to Tan et al.18 for more details on wettability and contact angle of the PDMS surface. When the forces are balanced, a static equilibrium is achieved and the water remains stationary and can be related as

$$P_w = P_L + P_J$$  \hspace{1cm} (6)$$

where $P_J$ is the pressure at the junction and $P_w$ is the imposed water pressure. $P_J$ can be obtained using a simple voltage divider rule (Figure 1d) and can be expressed as

$$P_J = \frac{P_O R_3}{R_1 + \frac{R_2}{2} + R_3}$$  \hspace{1cm} (7)$$

In order to express $P_O$ as a function of $P_w$, eq 4 is fitted into eq 7 and subsequently put into the governing eq 6, giving the final expression as

$$P_O = (P_w - P_J) \left( \frac{R_1 + \frac{R_2}{2} + R_3}{R_3} \right)$$  \hspace{1cm} (8)$$

A comparison between the proposed model plotted using eq 8 and experimental values show an excellent agreement. A slight divergence at higher pressures values is within expectation. This may be due to an expansion of PDMS24 at high pressure values which results in a change in the fluidic resistance. In the model, the fluidic resistances are assumed to be constant at different imposed pressures.

For the case of parallel flow, we adopt a similar electric circuit analogy. However, as the flows are separated, two electric circuits were used to mimic the flow paths (Figure 1e,f) of both oil and water. For the flow of both oil and water, the Hagen–Poiseuille’s law can be expressed

$$P_O = Q_O \left( R_1 + \frac{R_2 + R_4}{2} \right)$$  \hspace{1cm} (9)$$

$$P_W = Q_W (R_3 + R_6)$$  \hspace{1cm} (10)$$

where $R_4$ is the resistance due to the oil flow and $R_6$ is resistance due to the water. The values for $R_1$ and $R_3$ are the same as in the previous case and $R_4$ is about 0.04 × 10^{-14}$ kg·m^{-4}·s^{-1}. $R_1$ and $R_3$ are obtained based on eq 2 using the measurement of their respective fluid stream widths (Supporting Information, Figure-S4). For the parallel flow, as our channel is relatively flat, the fluidic resistance estimated with eq 2 is mainly determined by the channel height or the parabolic velocity profile along the height.21 Therefore, the influence of the boundary conditions of the channel width and the flat velocity profile along the width direction are not significant. This allows us to use eq 2 as an estimate for the fluidic resistance of each fluid stream. The pressures across each fluid stream along the channel are similar25 and hence can be expressed as (Supporting Information, Figure-S5),

$$\frac{Q_O}{2} R_4 = Q_W R_6$$  \hspace{1cm} (11)$$

$$\frac{Q_O}{Q_W} = \frac{2 R_6}{R_4}$$  \hspace{1cm} (12)$$

The relationship between both $P_W$ and $P_O$ is obtained from dividing eq 9 with eq 10 and then substituting eq 12 and simplified as

$$P_O = P_W \left( \frac{2 R_6 (R_1 + \frac{R_2 + R_4}{2})}{R_4 (R_3 + R_6)} \right)$$  \hspace{1cm} (13)$$

The green dashed line in Figure 2 depicts the relationship of $P_O$ and $P_W$ using eq 13. Here, our model effectively shows the relationship between $P_W$ and $P_O$. The slight difference may be due to experimental uncertainties in measurements. The good agreement shows that the assumption made for the boundary effects in width direction is valid. In comparison with the previous model for the stable interface, this model is more accurate as less pressure is buildup within the channels. This reduces the deformation of the PDMS which correspondingly results in the higher accuracy. Albeit this, both our models for the stable interface and parallel flow are able to provide simplified and accurate approximations for the effects of $P_O$ and $P_W$.

In the second part of our investigation, negative pressures were applied at the outlet to induce droplet formation. Five sets of $P_W$ and $P_O$ values (for a stable interface) were tested by varying $P_N$ in regular intervals of −100 mbar. Before $P_N$ was introduced, a stable interface was first achieved. When negative pressures were applied, the stable interface collapse due to the imbalance of pressure. The static equilibrium condition is broken as $P_L$ reduces, which results in the generation of droplets as shown in the Supporting Information, Video-S6. In brief, the droplet volume $V$ increased as $(P_W + P_N)$ increased for each pressure configuration. Increasing the initial $P_W$ value increases the change in droplet volume as $(P_W + P_N)$ increases. The slopes for each pressure configuration increases from 0.64 to

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1.44 when \( P_W \) increases from 100 to 500 mbar. Figure 3 shows the variation of droplet volume with the imposed pressures.

![Figure 3](image)

**Figure 3.** Variation of droplet volume with the imposed pressures. The inset shows that the experimental data collapsed to a power law of 1.3 when plotted using \( \frac{P_W + P_N}{R_0} \). \( P_W \) is in the unit of mbar.

In the final part of our investigation, we demonstrate the production of droplets on demand (Supporting Information, Video-S7). We fixed both \( P_O \) and \( P_W \) at about 107 and 50 mbar, respectively, to achieve the stable interface. A total of 10 consecutive square pulses at intervals of \( \Delta t = 0.02-0.05 \) s were applied to generate 10 droplets. The magnitude of the pulses was fixed at \( P_N = -120 \) mbar. Experimental results depict an almost linear increase in \( V \) as \( \Delta t \) increases, Figure 4a. This result is expected as a higher pulse duration allows more fluids to flow before breakup is induced. However, the complex interaction between \( P_O, P_W, P_N, \) and \( \Delta t \) is currently beyond the scope of this technical note.

We then examined the droplet breakup process using a customized MATLAB program. The program extracts the pressure values at the fixed time interval of \( \Delta t = 0.03 \) s. The values were extracted directly from the pressure controller (Figure 4b), which reflects the corresponding pressure conditions during the given time interval. In Figure 4b, the negative pressure was activated at \( t = 0.100 \) s and deactivated at \( t = 0.13 \) s. A close examination between the experimental videos and pressure profile depicts several interesting postulations. First, a sharp slope is observed during the start and end of the time period. This suggests a coupling between the droplet formation process and imposed pressure signal. Second, as the liquid finger fills up the orifice, this results in a slight increase in the pressure (Figure 4b, \( t = 0.123 \) s). At this stage, the flow of fluids are restricted and result in a pressure built up at the upstream. Subsequently, as the controller returned \( P_N \) back to 0 mbar, the abrupt change results in pressure fluctuations which is a consequence of the liquid neck thinning and breakup to form a droplet. We postulate that the pressure fluctuations induce instabilities, which enhances the droplet breakup process. A detailed investigation on this is also beyond the scope of this manuscript.

![Figure 4](image)

**Figure 4.** (a) Droplet volume, \( V \), at different pulse duration, \( \Delta t \). The pulse profile is shown in the inset. \( \Delta t \) is defined as the amount of time the negative pressure is turned on, within one period for a total of ten periods in one cycle. Insets shows images of droplets captured when \( P_W = 50 \) mbar, \( P_O = 107-111 \) mbar, \( P_N = -120 \) mbar. Scale bars show a dimension of 100 \( \mu \)m. (b) Measured pressure profile when \( \Delta t = 0.03 \) s, starting at \( t = 0.1 \) s and ends at \( t = 0.13 \) s.

### CONCLUSIONS

We introduced a simple and effective method to actively control the size of droplets generated in a microfluidic flow focusing device, where a negative pressure was induced to control the droplet generation and the production of droplet on demand. We proposed network models using electric circuit analogy to derive the relationship between both the pressure on the water phase, \( P_W \), and the pressure on the oil phase, \( P_O \), at different flow conditions. Both models fit well with the experimental results, with the stable interface model deviating at higher pressures as a result of PDMS deformation. We also derived the relationship between \( P_O, P_W, P_N \) and the volume of droplets generated. The experimental results show that the droplet volume can be related by using a power law of

\[
V \propto \frac{P_W + P_N}{R_0}^{1.3}
\]

Droplets can also be formed on demand by using a series of periodic square pulses. Increasing the time period increases the volume of the droplets. Extraction of the pressure values from the controller indicates a coupling between the droplet formation process and induced waveform. Pressure fluctuations can be seen during the droplet formation process.
**ASSOCIATED CONTENT**

**Supporting Information**
The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.analchem.6b05053.

- Video-S6: video of vacuum effect on droplet volume (AVI).
- Video-S7: video of droplet on demand (AVI).

**Table-S1**: measurement specifications for calculation of resistances. Figure-S2: comparison of droplet volume calculation method. Figure-S3: calculation of laplace pressure at stable interface. Figure-S4: calculation of resistances $R_0$ and $R_e$. Figure-S5: relationship for $Q_D$ and $Q_W$ in parallel flow (PDF).

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**Notes**
The authors declare no competing financial interest.

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