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<td>As Published</td>
<td><a href="http://dx.doi.org/10.1103/PhysRevE.86.026301">http://dx.doi.org/10.1103/PhysRevE.86.026301</a></td>
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<tr>
<td>Publisher</td>
<td>American Physical Society</td>
</tr>
<tr>
<td>Version</td>
<td>Final published version</td>
</tr>
<tr>
<td>Accessed</td>
<td>Wed Jan 23 19:56:29 EST 2019</td>
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<tr>
<td>Citable Link</td>
<td><a href="http://hdl.handle.net/1721.1/74169">http://hdl.handle.net/1721.1/74169</a></td>
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Bubble-induced damping in displacement-driven microfluidic flows

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(Received 2 January 2012; revised manuscript received 25 June 2012; published 1 August 2012)

Bubble damping in displacement-driven microfluidic flows was theoretically and experimentally investigated for a Y-channel microfluidic network. The system was found to exhibit linear behavior for typical microfluidic flow conditions. The bubbles induced a low-pass filter behavior with a characteristic cutoff frequency that scaled proportionally with flow rate and inversely with bubble volume and exhibited a minimum with respect to the relative resistances of the connecting channels. A theoretical model based on the electrical circuit analogy was able to predict experimentally observed damping of fluctuations with excellent agreement. Finally, a flowmeter with high resolution (0.01 μL/min) was demonstrated as an application of the bubble-aided stabilization. This study may aid in the design of many other bubble-stabilized microfluidic systems.

DOI: 10.1103/PhysRevE.86.026301 PACS number(s): 47.61.Fg, 47.55.D–

I. INTRODUCTION

Microfluidics refers to control and manipulation of fluids in submillimeter geometries, which has found diverse applications in life sciences [1], energy [2], environment [3], and defense [4]. Provision of stable flows with defined flow rates is often essential for proper functioning of microfluidic devices. Typically, such flows are achieved using syringe pumps that displace fluid at a set volumetric flow rate. However, step motor-based syringe pumps often generate undesirable pulsatile flows, especially at low flow rates, which can disrupt proper functioning of the devices. A number of undesirable pulsatile flows, especially at low flow rates, which have been proposed to provide stabilized flow rates in microfluidic devices, using nonlinear viscosity of effective ways have been proposed to provide stabilized flow rates in microfluidic devices, using nonlinear viscosity of polymers [5], flexible membranes [6], and electrostatic [7] and magnetic actuators [8], which may involve complicated designs or fabrication processes. Introduction of bubbles into the system offers a simple, yet effective, method to create a fluidic capacitance to decrease the effect of these fluctuations. The effect of radial vibration of air bubbles to damp external pressure waves was theoretically explored in detail by previous studies [9–11]. Pravda et al. [12] achieved 2 orders of magnitude improvement in accuracy of electrochemical detection in microdialysis by introduction of air bubbles in syringes associated with high-resistance microchannels. Very recently, Kang and Yang [13] employed a similar approach and experimentally showed the effects of various parameters such as bubble volume, input frequency, resistance of channels, and other factors on amplitude of output signal with respect to periodic input signal. Although the general effects of these parameters on flow rate amplitude fluctuations were studied and a lumped parameter model was proposed, key dimensionless parameters governing the system were not derived. In addition, although low-pass filter behavior was identified, the functional dependence on the major system parameters was not developed. In the present study, we develop and experimentally validate a theoretical framework to predict the damping characteristics of microfluidic flows driven by syringe pumps with bubbles.

The device used for studying bubble-induced damping is a microfluidic flow comparator comprising a Y-shaped microchannel where two fluid streams converge to form an interface whose position in the channel directly relates to the ratio of the two flow rates. Such devices can measure one flow rate if the other is known, and they are useful for quantifying small or rapidly changing flow rates [14–16]. Figure 1(a) shows a schematic of a Y channel fabricated in poly(dimethylsiloxane) (PDMS) with an approximately 200 μm × 20 μm channel cross section, where deionized water and fluorescent dye are supplied by two syringes driven by pumps. When water and fluorescent dye streams were pumped at 0.2 μL/min, fluctuations in the interface position were observed. However, the amplitude of the fluctuations was significantly reduced when air bubbles were introduced in each syringe [Figs. 1(b) and 1(c)]. We investigate mathematically and experimentally the effect of air bubbles introduced in the driving syringes on microchannel flow rate fluctuations and identify characteristic nondimensional parameters to determine the reduction in the amplitude of the fluctuations and time scales of damping.

II. MODELING AND FORMULATION

To understand the effect of bubbles on the reduction of fluctuations, we constructed a simple mathematical model using the electrical circuit analogy [Fig. 2(a)]. \( Q_1 \) and \( Q_2 \) are the instantaneous flow rates in each channel branch, and \( Q_{s,1} \) and \( Q_{s,2} \) are instantaneous input flow rates from syringe pumps. These instantaneous flow rates fluctuate around the nominal mean flow rates \( Q_{1,0} = \langle Q_{s,1} \rangle \) and \( Q_{2,0} = \langle Q_{s,2} \rangle \). All the microchannel sections were modeled as resistive elements as their capacitance was negligible compared to that of the bubbles. The resistance and capacitance of the rigid PTFE tubing (300 μm ID, 760 μm OD) connecting the syringes to the device were estimated to be negligible. The air bubbles were assumed to be isothermal due to the small thermal time scale (∼0.01 s) estimated based on the syringe inner diameter.

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FIG. 1. (Color online) (a) Schematic diagram of experimental setup. Fluids are introduced with flow rates of $Q_1$ and $Q_2$ into a Y-shaped flow comparator and form two distinct streams showing setup. Fluids are introduced with flow rates of $Q_1$ and $Q_2$. (b) Instantaneous snapshots of the flow streams when $Q_1 = Q_2 = 0.2 \mu L/min$ without air bubbles in syringes (top) and with air bubbles of 5 $\mu L$ (bottom). (c) Time traces of interface position normalized by the channel width for two different bubble volumes; 0.0 corresponds to the lower wall and 1.0 corresponds to the upper wall of the channel.

($\sim$1 mm). With these assumptions, the rate of volume change of bubbles can be expressed as follows:

$$\dot{V}_1 = Q_1 - Q_{s,1}, \quad \dot{V}_2 = Q_2 - Q_{s,2}, \quad (1)$$

where $V_1$ and $V_2$ are (time-dependent) air bubble volumes. The overdot indicates time derivatives ($=d/dt$). Neglecting the effects of surface tension, the ideal gas law for isothermal condition is given as

$$P_1 V_1 = P_0 V_{1,0}, \quad P_2 V_2 = P_0 V_{2,0}, \quad (2)$$

where $P_0$ is the initial pressure of bubbles, i.e., 1 atm, and $V_{1,0}$ and $V_{2,0}$ are the initial volumes of bubbles 1 and 2 under pressure $P_0$, respectively. The relations between flow rates and pressure drop can be expressed by the definition of hydraulic resistances $R_1$, $R_2$, and $R_3$ of each channel section:

$$Q_1 = \frac{P_1 - P_1}{R_1}, \quad Q_2 = \frac{P_2 - P_1}{R_2}, \quad Q_1 + Q_2 = \frac{P_1 - P_0}{R_3}, \quad (3)$$

where $P_j$ indicates the pressure at the Y-channel junction. Equation (3) can be rearranged, and then the following relations are obtained:

$$P_1 = P_0 + (R_1 + R_3)Q_1 + R_3Q_2, \quad P_2 = P_0 + R_3Q_1 + (R_2 + R_3)Q_2. \quad (4)$$

Differentiation of $V_1$ and $V_2$ with respect to time $t$ and combining with Eq. (2) leads to the following relations:

$$\dot{V}_1 = Q_1 - Q_{s,1} = \frac{d}{dt} \left( \frac{P_0 V_{1,0}}{P_1} \right) = -\frac{P_0 V_{1,0}}{P_1^2} dP_1 \frac{dP_1}{dt},$$

$$\dot{V}_2 = Q_2 - Q_{s,2} = \frac{d}{dt} \left( \frac{P_0 V_{2,0}}{P_2} \right) = -\frac{P_0 V_{2,0}}{P_2^2} dP_2 \frac{dP_2}{dt}. \quad (5)$$

Substitution of Eq. (4) into the above relation results in the following expressions:

$$Q_1 - Q_{s,1} = -\frac{V_{1,0}}{P_0} \left[ 1 + \frac{(R_1 + R_3)}{P_1} Q_1 + \frac{R_3}{P_1} Q_2 \right]^2 \times [(R_1 + R_3)Q_1 + R_3Q_2],$$

$$Q_2 - Q_{s,2} = -\frac{V_{2,0}}{P_0} \left[ 1 + \frac{R_3}{P_1} Q_1 + \frac{(R_1 + R_3)}{P_1} Q_2 \right]^2 \times [R_3Q_1 + (R_2 + R_3)Q_2]. \quad (6)$$

If we define

$$\delta_1(t) \equiv \frac{Q_1(t) - Q_{1,0}}{Q_{1,0}}, \quad \delta_2(t) \equiv \frac{Q_2(t) - Q_{2,0}}{Q_{2,0}},$$

$$q_1(t) \equiv \frac{Q_{s,1}(t) - Q_{1,0}}{Q_{1,0}}, \quad q_2(t) \equiv \frac{Q_{s,2}(t) - Q_{2,0}}{Q_{2,0}},$$

further rearrangement yields the following equations:

$$\begin{bmatrix} \delta_1 \delta_2 \end{bmatrix} = A \begin{bmatrix} -\delta_1 + q_1 \\ -\delta_2 + q_2 \end{bmatrix} + \text{NL} \quad (7)$$

where $A$ and the nonlinear terms NL are

$$A = \left( \frac{P_0}{V_{1,0}R_3} \right) \frac{1}{(R_1^* + 1)(R_2^* + 1) - 1} \times \left[ \begin{bmatrix} (R_2^* + 1)D_1^2 - (Q_{2,0}/Q_{1,0})(V_{1,0}/V_{2,0})D_2^2 \\ -(Q_{1,0}/Q_{2,0})D_1^2 - (R_1^* + 1)(V_{1,0}/V_{2,0})D_2^2 \end{bmatrix} \right],$$

$$\text{NL} = A \left[ \begin{bmatrix} (1 + (R_1^* + 1)Q_{2,0}/Q_{1,0}Q_{1,0}^* / R_1^* K)^2 - 1 \\ (1 + (R_1^* + 1)Q_{2,0}/Q_{1,0}Q_{1,0}^* / R_1^* K)^2 - 1 \end{bmatrix} \right],$$

where

$$D_1 = 1 + [R_1^* + 1 + (Q_{2,0}/Q_{1,0})]K, \quad D_2 = 1 + [1 + (R_1^* + 1)(Q_{2,0}/Q_{1,0})]K, \quad (8)$$

$R_1^*$ and $R_2^*$ are channel resistances (pressure drop per unit flow rate) normalized by $R_1$. $K = Q_{1,0}R_3/P_0$ is the normalized pressure drop along the channel. In the present experiments, $K$ ranged $O(0.001-0.1)$. $R_1^*$, $R_2^*$, $Q_{2,0}/Q_{1,0}$, and $K$ are the four independent dimensionless groups that define the system. However, the damping effect of the bubbles is strongly influenced by the pressure on the bubbles. We have therefore defined two dependent dimensionless groups, $D_1$ and $D_2$, to account for the pressure on each bubble under operating conditions. These dependent dimensionless groups are expressed as a function of the independent dimensionless groups, $R_1^*$, $R_2^*$, $Q_{2,0}/Q_{1,0}$, and $K$, as shown in Eq. (9). $D_1$ and $D_2$ thus
represent the normalized baseline pressures of the bubbles in channels 1 and 2, respectively, due to the pressure drop from the exit of channel 3 up to the bubbles. The actual pressures $P_1$ and $P_2$ on bubbles 1 and 2, respectively, fluctuate around the baseline pressures $P_0D_1$ and $P_0D_2$.

**III. CHARACTERISTICS OF BUBBLE-INDUCED DAMPING**

The bubble acts as a nonlinear spring where the stiffness $k = P_0V_0/V^2 - 1/V^2 \sim P^2$ (see the Appendix). Since the channel geometries and the mean flow rates are predetermined, this

\[
\frac{\lambda_{1,2}}{\omega_0} = \frac{\left( R_1^* + 1 \right) D_2 \frac{\lambda_{1,2}}{\omega_0} + \left( R_2^* + 1 \right) D_1^2 \pm \sqrt{\left( R_1^* + 1 \right) D_2 \frac{\lambda_{1,2}}{\omega_0} - \left( R_2^* + 1 \right) D_1^2 + \frac{4\omega_0^2 D_1^2 D_2^2}{\lambda_{1,2}}}}{2[\left( R_1^* + 1\right)(R_2^* + 1) - 1]},
\]

where $\omega_0$ is a characteristic frequency defined as $P_0/V_{1,0}R_3$. Diagonalization of $A$ leads to further simplified equations:

\[
\begin{pmatrix}
\delta_1^* \\
\delta_2^*
\end{pmatrix} = \begin{pmatrix}
\lambda_1 & 0 \\
0 & \lambda_2
\end{pmatrix} \begin{pmatrix}
-\epsilon_1^* + \tilde{q}_1^* \\
-\epsilon_2^* + \tilde{q}_2^*
\end{pmatrix},
\]

where $\left( \epsilon_i^* \right)^\dagger = X^{\dagger}\left( \tilde{q}_i^* \right)^\dagger$, $\left( \tilde{q}_i^* \right)^\dagger = X^{-1}\left( \tilde{q}_i^* \right)^\dagger$, and $X$ is the eigenvector matrix composed of eigenvectors $\tilde{x}_1$ and $\tilde{x}_2$. This is a first-order dynamic system, e.g., a low-pass filter, for $\epsilon_i^*$ with external sources $\tilde{q}_i^*$ ($i = 1, 2$). Writing $\tilde{q}_i^* = \sum_{n=0}^{\infty} \left( \tilde{a}_{1,i}e^{j\omega_n t} + \tilde{a}_{2,i}e^{-j\omega_n t} \right)$ and $\epsilon_i^* = \sum_{n=0}^{\infty} \left( \tilde{b}_{1,i}e^{j\omega_n t} + \tilde{b}_{2,i}e^{-j\omega_n t} \right)$, where $\tilde{a}_{1,i}$ and $\tilde{b}_{1,i}$ are complex conjugates of $a_{1,i}$ and $a_{2,i}$, and substituting these series into Eq. (12) reveals that the amplitude ratios $|b_{1,i}|/|a_{1,i}|$ are damped for inputs with frequencies above $\lambda_1$ and $\lambda_2$, respectively:

\[
\frac{|b_{1,i}|}{|a_{1,i}|} = \frac{1}{\lambda_1 + j/\omega_0} = \frac{1}{\omega_0\sqrt{1 + (\lambda_1/\omega_0)^2}},
\]

indicating $|b_{1,i}|/|a_{1,i}| \sim 1/\omega_0$ for $\omega_0 \gg \lambda_i$ while $|b_{1,i}|/|a_{1,i}| \approx 1/\lambda_i$ for $\omega_0 \ll \lambda_i$. These cutoff frequencies $\lambda_1$ and $\lambda_2$ reflect bubble compression effects represented by $D_1$ and $D_2$. For example, when $R_1^* = R_2^*$ and $Q_{2,0}/Q_{1,0} = 1$, then $D_1 = D_2 = D$, and the cutoff frequencies scale with $\omega_0D^2$ according to Eq. (11). More importantly, the cutoff frequency can be also obtained from an analogous system where a linear spring represents the bubble compression (see the Appendix), and therefore

\[
\omega_{\text{cutoff}} \approx \frac{k}{R} \approx \frac{P_0}{V_0R_3} \left( \frac{V_0}{V} \right)^2 \sim \begin{cases} \omega_0D^2 & \text{for } R_1^*(\sim R_2^*) \leq O(1) \\
\frac{\omega_0D^2}{R_3} & \text{for } R_1^*(\sim R_2^*) \gg O(1). \end{cases}
\]

Note that $R \sim (1 + R_1^*)R_3$. The cutoff frequency is characteristic of a system comprising a bubble and resistance external to the bubble, and the stiffness of the bubble is influenced by the pressure acting on the bubble. Consequently, the cutoff frequency depends on the parameters that affect the pressure of the bubble, i.e., $R_1^*$, $R_2^*$, $Q_{2,0}/Q_{1,0}$, $K$, and $D_1$, $D_2$. Considering the former case $[R_1^* (\sim R_2^*) \leq O(1)]$ for further discussion, $\omega_{\text{cutoff}} - \omega_0$ for small pressure drops in the channels (i.e., $D_1$, $D_2 \sim 1$). While $q_1^*$, $q_2^*$ may be arbitrary functions, the effects of a single input, i.e., $q_1^* = 0.1 \sin \omega t$ and $q_2^* = 0$ on the amplitude gain of $\delta_1^*$, $\delta_2^*$ and $\delta_1^*$, $\delta_2^*$, are depicted [Fig. 2(b)]. Here, the amplitude gain is defined as a ratio of the root-mean-square (rms) of output and input functions, i.e., $\|f_{\text{out}}\|/\|f_{\text{in}}\|$, where $\|f\|_{\text{rms}} = \sqrt{\frac{1}{T} \int_{0}^{T} f(t)^2 dt}$ for an arbitrary function $f(t)$. The amplitude gains of $\delta_1^*$, $\delta_2^*$ are reduced for input frequencies $\omega$ higher than the cutoff frequencies $\lambda_1$ and $\lambda_2$ (\sim $\omega_0D^2$). Since $\delta_1^*$ and $\delta_2^*$ are projected components of vector $\tilde{\delta} = (\delta_1^*, \delta_2^*)$ on eigenvectors $\tilde{x}_1$ and $\tilde{x}_2$, they do not scale directly with $\epsilon_1^*$, $\epsilon_2^*$ but monotonically decrease above the cutoff frequencies. The amplitude gains of $\delta_1^*$ for different $K$ values collapse on a single curve when the input frequency $\omega$ is normalized by $\omega_0D^2$ [Fig. 2(c)], which indicates the effect of bubble compression on the cutoff frequency [Eq. (14)].

For the results depicted in Figs. 2(b) and 3, the linear Eq. (10) was solved. Results in Figs. 2(c) and 2(d) were obtained by solving Eq. (7), whereas those in Fig. 4 were obtained by solving Eq. (6). When the nonlinear effects are small, we expect the scaling factor $\omega_0D^2$ to apply to results obtained from solving the nonlinear equation (7).

For different values of $R_1^*$ and $R_2^*$, Fig. 2(d) shows the cutoff frequencies $\omega_{\text{cutoff}}$, defined as the frequency at which the amplitude gain (\|\tilde{b}_i^*/\|\tilde{q}_i^*\|), after solving Eq. (7), is reduced to 50%, analogous to that of a conventional first-order low-pass filter. Since the nonlinear effect is negligible, we analyzed the linearized Eq. (10) to obtain insight into this behavior. When $R_1^*$ and $R_2^*$ are large, a large bubble stiffness is induced and $\omega_{\text{cutoff}}$ is higher. The cases for small $R_1^*$ and $R_2^*$ (<1) are quite interesting. Due to small pressure drop in channels 1 and
2 (small \(D_1\) and \(D_2\)), a small \(\omega_{\text{cutoff}}\) (~\(\omega_0 D^2\)) is expected. However, small \(R_1^*\) and \(R_2^*\) produce a large difference in eigenvalues [Eq. (11)]; i.e., the responses of \(\epsilon_1^*, \epsilon_2^*\) in the diagonalized system [Eq. (12)] are significantly different from each other. Since the fluctuations in flow rates, \(\delta_1^*, \delta_2^*\), are a linear combination of \(\epsilon_1^*, \epsilon_2^*\), i.e., \((X\delta) = X(\epsilon)\), where \(X\) is the eigenvector matrix, \(\delta_1^*, \delta_2^*\) may not have the same trend with respect to \(\omega\) as \(\epsilon_1^*, \epsilon_2^*\), which have cutoff frequencies \(\lambda_1\), \(\lambda_2\), respectively. Figure 3 shows the amplitude gain of \(\epsilon_1^*, \epsilon_2^*\), \(\delta_1^*, \delta_2^*\) as a response of \(q_1^* = 0.1 \sin \omega t, q_2^* = 0\) for various \(R_1^*\) and \(R_2^*\). For small \(R_1^*\) and \(R_2^*\), the reduction of \(\delta_1^*\) is delayed, and therefore the \(\omega_{\text{cutoff}}\) for \(\delta_1^*\) becomes larger than that at moderate values of \(R_1^*\) and \(R_2^*\) [Figs. 3(a) and 3(b)].

For moderate values of \(R_1^*\) and \(R_2^*\), the difference in \(\lambda_1\) and \(\lambda_2\) becomes small, and \(\omega_{\text{cutoff}}\) increases with \(R_1^*\) and \(R_2^*\), as shown in Fig. 2(d) as well as Figs. 3(b) and 3(c). It can be also noted that for \(R_1^* \sim R_2^* \gg O(1), \omega_{\text{cutoff}} \sim \omega_0 D^2 / R_1^* \sim \omega_0 R_1^*\) from Eq. (14), and therefore \(\omega_{\text{cutoff}}\) is proportional to \(R_1^*\) rather than to \(R_1^*^2\) (~\(D^2\)). When \(R_1^*\) is large, its effect dominates, and \(\omega_{\text{cutoff}}\) is almost independent of \(R_2^*\). Hence, there exists a minimum \(\omega_{\text{cutoff}}\) for a certain set of \(R_1^*\) and \(R_2^*\) [Fig. 2(d)].

Interestingly, the nonlinear effects were not significant even for very large amplitudes of input fluctuations \(q^*\), i.e., \(q^* \sim O(1)\). For input fluctuations with a low frequency \(\omega\), the bubble volume and stiffness do not change significantly, and the system is essentially linear. On the other hand, input fluctuations at high frequencies result in rapid changes in bubble stiffness, and this “noise” in stiffness tends to produce different responses in \(\delta_1^*, \delta_2^*\) compared to the linear case. However, due to a low-pass filter effect, the magnitudes of \(\delta_1^*, \delta_2^*\) become smaller with high \(\omega\), which damps the nonlinear effects. As a result, the difference in \(\delta_1^*, \delta_2^*\) from solving the nonlinear equation and the linearized one was again quite negligible. For \(\omega\) near cutoff frequency, where neither of the two effects is dominant, the mean values of \(\delta_1^*, \delta_2^*\) from the nonlinear equation were found to be slightly off-zero values (~0.1% of maximum amplitude), and the difference in rms values from both equations was small but noticeable (~3%).

IV. EXPERIMENTAL SETUP AND VERIFICATION

A Y-shaped microfluidic comparator with a 200 \(\mu\)m \(\times\) 20 \(\mu\)m channel cross section was fabricated by micromolding in PDMS (Dow Corning Sylgard 184 Elastomer kit). First, the mold was fabricated by lithography in the photoresist SU-8. Next, the PDMS base (part A) and the curing agent (part B) were mixed in a 4:1 mass ratio. This mass ratio was chosen to produce a rigid microchannel to reduce any effects from channel deformation during experiments. The mixture of parts A and B was poured on the mold and degassed and cured for 3 h in an oven with a temperature of 70 °C. After the PDMS channel part was separated from the mold, the PDMS and a glass slide were exposed to air plasma briefly, and they were bonded to form the PDMS microchannel. Before bonding, a profilometer was used to measure the height at three or four locations of each channel segment, and the averaged channel heights \(h\) are shown in Fig. 8 (see the Appendix) with
Amplitude gains of outputs $e_1^*$, $e_2^*$, $\delta_1^*$, $\delta_2^*$ for different $R_1^*$, $R_2^*$ for periodic input perturbations, $q_1^* = 0.1 \, \sin \omega t$, $q_2^* = 0$, from syringe pumps at different frequencies $\omega$ normalized by $\omega_0$, where $Q_{2,0}/Q_{1,0} = 1$, $V_{2,0}/V_{1,0} = 1.0$, $K (= Q_{1,0}R_1/P_0) = 0.5$ are assumed. Blue dashed lines indicate the corresponding $\omega_{\text{cutoff}}$ where the amplitude gain of $\delta_1^*$ is 0.5, corresponding to the definition of cutoff frequency of a conventional low-pass filter. The values of $\omega_{\text{cutoff}}/\omega_0$ are (a) 21.80, (b) 6.17, (c) 7.73, and (d) 24.48.

FIG. 3. (Color online) Amplitude gains of outputs $e_1^*$, $e_2^*$, $\delta_1^*$, $\delta_2^*$ for different $R_1^*$, $R_2^*$ for periodic input perturbations, $q_1^* = 0.1 \, \sin \omega t$, $q_2^* = 0$, from syringe pumps at different frequencies $\omega$ normalized by $\omega_0$, where $Q_{2,0}/Q_{1,0} = 1$, $V_{2,0}/V_{1,0} = 1.0$, $K (= Q_{1,0}R_1/P_0) = 0.5$ are assumed. Blue dashed lines indicate the corresponding $\omega_{\text{cutoff}}$ where the amplitude gain of $\delta_1^*$ is 0.5, corresponding to the definition of cutoff frequency of a conventional low-pass filter. The values of $\omega_{\text{cutoff}}/\omega_0$ are (a) 21.80, (b) 6.17, (c) 7.73, and (d) 24.48.

other dimensions, including the PTFE tubing (Cole Parmer, ID of 300 $\mu$m, OD of 760 $\mu$m). Note that the differences in channel heights were caused by the nonuniform height of the mold since spin-coating of the SU-8 photore sist does not result in perfectly uniform thickness. In the present study, dextran-conjugated tetramethyl rhodamine (Invitrogen, MW 70 000) at a concentration of 0.5 mg/mL was used as a fluorescent dye to visualize the interface with the deionized water stream. The high molecular weight dye was chosen to obtain a sharp interface due to its low diffusivity. However, the dye is easily adsorbed on the PDMS surface, which makes it difficult to accurately track the interface positions. To prevent dye adsorption, poly(perfluorobutenylvinylether) (CYTOP, Bellex International Corporation) was coated on the channel walls. Cytop (CTL-809M) and a solvent (CT-Solv. 180) were mixed in a mass ratio of 1:19. The mixed Cytop solution was then introduced into the microchannel under a pressure of 8 psi for 10 min, followed by flowing nitrogen into the channel for 1 h in an oven with a temperature of 85 °C to dry the solution. Two 50-$\mu$L syringes (Gastight 50-$\mu$L glass syringe, Hamilton) mounted on separate syringe pumps (PHD 2000 and PHD Ultra, Harvard Apparatus) delivered deionized water and the fluorescent dye to the Y channel. The Cytop coating rendered the microchannel surface hydrophobic. Thus, after the deionized water and fluorescence dye solution were introduced in the microchannel, the channel was pressurized by a nitrogen source with a pressure of 2–3 psi for about 5 min to remove any air bubbles in the channel. The channel was placed on a microscope (TE2000, Nikon) with a fluorescence filter. The fluorescence intensity profile in each photo frame was read in MATLAB, and the interface positions were identified as the steepest slope of the fluorescence intensity at a cross section 400 $\mu$m downstream of the junction [Fig. 1(a)]. Considering the small Reynolds number $[Re = U/D_h/\nu \sim O(0.1–1)]$, where $D_h$ is a hydraulic diameter), this distance is sufficiently long for the flow to be fully developed [17].

To experimentally verify the derived equations, a step input was applied to the microfluidic comparator by abruptly increasing the input flow rate of the fluorescent stream to 2.5 $\mu$L/min, with both streams initially flowing at 1 $\mu$L/min. The interface positions were tracked with time for bubbles with volumes of 2.5, and 10 $\mu$L introduced in the syringes. $R_1 = 0.14$, $R_2 = 0.20$, $R_3 = 0.25$ psi min/$\mu$L were calculated based on the channel geometries measured by a profiler, assuming rectangular channels with fully developed laminar flows [18]. $R_1$ and $R_2$ were different due to slight differences in geometry resulting from the fabrication process. For the simulation side, we assumed $q_1^* = q_2^* = 0$ in Eq. (7) for simplicity and directly solved Eq. (6) for $Q_1$ and $Q_2$ as responses of abrupt change
FIG. 4. (Color online) (a) Time traces of interface positions for three different volumes of air bubbles, i.e., 2, 5, and 10 μL. Solid lines indicate traces predicted from the model. The inset shows traces of interface positions based on nondimensionalized time $t_{\omega_0}$, where $\omega_0$ is given as $P_0/V_1 R_3$. (b) The rms values of the fluctuations of the interface positions from the average position for different bubble volumes and flow rate inputs. The squares, circles, and diamonds show rms values calculated from experiments for nominal flow rates of syringe pumps of 0.1, 0.2, and 0.5 μL/min, respectively; the black line with circles shows rms values predicted by the model based on inputs $Q_{1,0}$ and $Q_{2,0}$, which are obtained from recorded interface positions with zero bubble volume.

The step input induced an overshoot of the interface position; the interface then relaxed to a steady position corresponding to the flow rate ratio of two streams. The relaxation time increased with air bubble volume, given by $t_0 \sim 1/\omega_0 D^2 \sim 1/\omega_0 = V_1 R_3/P_0$ based on the values of $D_1$, $D_2$ (1.07 and 1.09, respectively). When time was normalized using $t_0$, all the experimental curves collapsed upon a single curve predicted by the model, indicating that Eqs. (6) and (7) accurately describe the system response [Fig. 4(a), inset].

We further investigated the effect of bubbles on the reduction of fluctuations by monitoring the rms fluctuation of the interface at different bubble volumes and the same nominal flow rate inputs. Three sets of 400 consecutive interface positions were obtained with a time interval of 0.3 s for bubble volumes of 0, 2, 5, and 10 μL and for three different nominal flow rates of 0.1, 0.2, and 0.5 μL/min from both syringe pumps. The observed fluctuations of the interface in the zero bubble volume case were used to estimate fluctuations in the flow rate inputs from the pumps ($Q_{1,0}$ and $Q_{2,0}$), which means that each set of interface positions at zero bubble volume served as an input for $Q_{1,0}$ and $Q_{2,0}$ to solve Eq. (6) and calculate the rms values for bubble volumes of 2, 5, and 10 μL. Since the interface position represents only the ratio of flow rates of the two streams, the sum of the flow rates of the two streams was assumed to be constant. The rms values were then calculated from the predicted interface positions by solving Eq. (6) and compared with the rms values calculated directly from the experimentally observed interface positions. As shown in Fig. 4(b), for all three different flow rates of

FIG. 5. (Color online) Correlation between $Q_1/Q_2$ and $W_1/W_2$. Squares, data points for $Q_{1,0} + Q_{2,0} = 2 \mu$L/min; inverted triangles, data points for fixed $Q_{2,0} = 0.25 \mu$L/min. $Q_1$ is varied from 0.25 to 0.29 μL/min with a step of 0.01 μL/min. (a) Correlation in the range of $Q_1/Q_2 = 0.3$–3.0. (b) Magnified view of circled part in (a). Bubble volume was 5 μL in both syringes. Error bars denote one standard deviation from $n = 3$ experiments on the same device.
syringe pumps, fluctuations of the interface were reduced upon introduction of bubbles, which was quantitatively predicted by the model. Larger bubbles more effectively damped the fluctuations, as expected from the lower cutoff frequency for larger bubble volumes [Eq. (14)]. Although the overshoot of the interface for a single step input was the same regardless of the bubble volume [Fig. 4(a)], larger air bubbles stabilize the interface more effectively for inputs composed of random fluctuations by cutting off the high-frequency components [Fig. 4(b)].

V. APPLICATION

Finally, we examined the effect of bubble stabilization on the performance of the comparator as a flow rate measurement device. To obtain the relationship between the performance of the comparator as a flow rate measurement (d) corresponding electrical circuit.

\[ \text{Fig. 4(b)}. \]

fluctuations by cutting off the high-frequency components of the bubble volume [Fig. 4(a)], larger air bubbles stabilize the interface for a single step input was the same regardless and \( W \).

\[ \text{Fig. 5}. \]

...the volume fluctuations of the bubbles is small relative to the bubble volume, which is expected for typical syringe pump flow fluctuations. Thus, flow rates on the order of 0.01 \( \mu \text{L}/\text{min} \) were resolved. Given a cutoff frequency of \( \sim 0.03 \text{ Hz} \), this device enables flow rates to be measured with \( \sim 0.01 \mu \text{L}/\text{min} \) resolution with \( \sim 100 \text{ s} \) per measurement. In the absence of bubbles, large fluctuations in the interface made it diffused and difficult to track, although, in principle, time-averaging of the interface position should yield similar resolution.

VI. GENERALIZATION TO ARBITRARY MICROFLUIDIC NETWORKS

The analysis for reduction of fluctuations in flow rates by air bubbles can be extended to more complex microfluidic systems comprising multiple flow-driving syringes with air bubbles. This generalization is valid when the amplitude of the volume fluctuations of the bubbles is small relative to the bubble volume, which is expected for typical syringe pump flow fluctuations.

A syringe with an air bubble connected to an external fluidic resistance can be represented by an electrical circuit equivalent comprising a current source with a resistor in series and a shunt capacitor, as shown in Figs. 6(a) and 6(b). The capacitor absorbs high-frequency components from the input current source (which is analogous to a syringe pump providing certain flow rate), and therefore a current of low-frequency components with a shifted phase flows through
the resistor. As shown in Fig. 6(a), if a current source provides an instantaneous current \( Q_s \), the voltage balance for the \( RC \) circuit is given by

\[
C \int (Q_s - Q) dt - QR = 0, \tag{15}
\]

where \( C \) is the capacitance of the capacitor and \( Q \) is the instantaneous current flowing through the resistor with resistance \( R \). Differentiating Eq. (15) with time \( t \) and defining nondimensional fluctuations \( \delta^* = \frac{Q - Q_0}{Q_0} \), \( q^* = \frac{Q - Q_0}{Q_0} \) (\( Q_0 \) is nominal mean current) as before yields

\[
\dot{\delta}^* + \frac{C}{R} \delta^* = \frac{C}{R} q^*. \tag{16}
\]

In comparison with the system of one syringe with an air bubble [Eq. (A4) in the Appendix], the equivalent capacitance is obtained as

\[
C = \frac{P_0 V_0}{V^2} = \frac{P^2}{P_0 V_0}. \tag{17}
\]

Here, \( P_0, V_0 \) represent the state of the bubble at atmospheric pressure, and \( P, V \) represent its (time-averaged) state under flow conditions. Due to the fact that the fluctuation characteristics are essentially linear, we can simply build up combinations of \( RC \) circuits for describing a system comprising multiple syringes and bubbles. The equivalent resistances and input currents in the circuits can be obtained via analogy with hydraulic resistance of channels and input flow rates from the pumps. Since \( P \) and \( V \) in Eq. (17) are time-averaged values, they can be extracted by solving for the steady-state potentials (or pressures, indicated by \( P_1 - P_4 \) in Fig. 6) in the circuit for constant driving currents (i.e., flow rates) without any capacitances (i.e., bubbles). Knowing the initial bubble volumes and pressures, Eq. (17) can then be used to calculate the bubble capacitances under conditions of flow that compress the bubbles and alter the capacitance [which are the same conditions of pressure as \( P_0 D_1 \) and \( P_0 D_2 \) from Eq. (9)]. Once the bubble capacitances are known, the entire system is cast in terms of an electrical circuit with capacitances, resistances, and current sources. The fluctuations are then obtained by solving the set of differential equations for each component [as in Eq. (16)] or simply using an electrical circuit solver such as PSPICE [19].

**VII. CONCLUSIONS**

In summary, bubbles introduced in syringes can significantly attenuate fluctuations in microfluidic flow rates. A simple model was developed to describe the response of the microfluidic device to step and random inputs, with excellent agreement with experiments. The bubbles act as low-pass filters, where the fluctuations in flow rates are reduced after a characteristic cutoff frequency. The cutoff frequency was analytically identified as a function of the bubble volume, flow rates, and channel resistance. While the cutoff frequency decreases with larger bubble volumes and smaller flow rates, a minimum cutoff frequency exists for a specific set of resistances of microfluidic devices. Based on this low-pass filter behavior, a high resolution (0.01 \( \mu \)L/min) of a flowmeter was demonstrated as one application. Finally, the approach was generalized to enable the fluctuations to be estimated for an arbitrary microfluidic circuit. These results may guide the introduction of bubbles as a simple technique to stabilize flows in a variety of microfluidic devices.

**ACKNOWLEDGMENTS**

The authors would like to thank the King Fahd University of Petroleum and Minerals, Dhahran, Saudi Arabia, for funding the research reported in this paper through the Center for Clean Water and Clean Energy at MIT and KFUPM under Project No. R10-CW-09. Devices were fabricated in the Microsystems Technology Laboratory at MIT. We thank Marco Cartas for helpful discussions.

**APPENDIX**

1. **Analogy between a linear spring and a bubble in a single channel**

For the case where a linear spring with stiffness \( k \) per unit cross section area delivers the force from a syringe pump to the flow (Fig. 7), the balance between forces from the spring and the flow resistance leads to the governing equation for \( Q \):

\[
k \int (Q_s - Q) dt = R Q. \tag{A1}
\]

Differentiating with respect to time \( t \), the following equation is obtained:

\[
\dot{Q} + \frac{k}{R} Q = \frac{k}{R} Q_s, \tag{A2}
\]

where a cutoff frequency \( \omega_{\text{cutoff}} \) for the response \( Q \) to the input \( (k/R)Q_s \) can be found to be \( k/R \).

If we define \( \delta^* = \frac{Q - Q_0}{Q_0}, q^* = \frac{Q - Q_0}{Q_0} \), where \( Q_0 \) is mean flow rate,

\[
\dot{\delta}^* + \frac{k}{R} \delta^* = \frac{k}{R} q^*. \tag{A3}
\]

**FIG. 7.** (Color online) (a) Electrical circuit based models for a single channel with spring of stiffness \( k \); (b) air bubble of volume \( V \). \( P \) is a pressure on the spring or bubble, \( P_0 \) is ambient pressure, \( Q_s \) is the input flow rate, and \( Q \) is the flow rate in the channel with hydraulic resistance \( R \).
while for a single channel with a bubble instead of the spring, the governing equation is given as
\[ \dot{\delta}^* + \frac{P_0 V_0}{V^2 R} \delta^* = \frac{P_0 V_0}{V^2 R} \beta^*, \]  
(A4)
where \( V_0 \) is the initial volume of the bubble. From this analogy, it can be seen that the equivalent stiffness of the bubble is obtained as \( k \sim \frac{P_0 V_0}{V^2 R} \) and \( \omega_{\text{cutoff}} \) is given as
\[ \omega_{\text{cutoff}} = \frac{k}{R} = \frac{P_0 V_0}{V^2 R}. \]  
(A5)

2. Device dimensions

The dimensions of the Y-shaped flow comparator made of PDMS are shown in Fig. 8.