Applied Physics Letters

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Citation: Appl. Phys. Lett. **101**, 234107 (2012); doi: 10.1063/1.4769985
View online: http://dx.doi.org/10.1063/1.4769985
View Table of Contents: http://apl.aip.org/resource/1/APPLAB/v101/i23
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APPLIED PHYSICS LETTERS **101**, 234107 (2012)

Analyzing threshold pressure limitations in microfluidic transistors for self-regulated microfluidic circuits

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(Received 11 October 2012; accepted 19 November 2012; published online 7 December 2012)

This paper reveals a critical limitation in the electro-hydraulic analogy between a microfluidic membrane-valve (μMV) and an electronic transistor. Unlike typical transistors that have similar on and off threshold voltages, in hydraulic μMVs, the threshold pressures for opening and closing are significantly different and can change, even for the same μMVs depending on overall circuit design and operation conditions. We explain, in particular, how the negative values of the closing threshold pressures significantly constrain operation of even simple hydraulic μMV circuits such as autonomously switching two-valve microfluidic oscillators. These understandings have significant implications in designing self-regulated microfluidic devices. [http://dx.doi.org/10.1063/1.4769985]

Electric circuit analogy is widely used in microfluidic circuit design and analysis. For example, electric resistors correspond to microfluidic channel resistances and capacitors to flexible membranes. The analogy is based on the similarity in equations between these circuit components. Since the theory and simulation methods of electric circuits are well-established, they greatly facilitate the design and analysis of various microfluidic circuits.[1]

Recently, analogy has been drawn between electronic transistors and microfluidic membrane-valves (μMV), which are used for self-regulated microfluidic circuits such as frequency-specific flow regulators,[2] digital logic circuits,[3–6] and oscillators.[7–9] Like an electronic circuit that operates itself with only a power source and thus minimize the use of its external controllers, the self-regulated microfluidic circuits have the potential to greatly reduce reliance on expensive and complex external controllers, which are barriers to broader use of microfluidic devices. A μMV is a crucial component that enables operation of self-regulated microfluidic devices through its on-off switching.

Similar to the electronic transistor, the μMV's on-off switching is determined by the relative difference between the source (P_S) minus gate pressure (P_G) versus the threshold pressure (Figure 1). As depicted in Figure 1(a), when P_S is sufficiently greater than P_G, the membrane of the μMV deflects down and the μMV is on (open). In other words, the μMV is on when $P_S - P_G$ is greater than opening threshold pressure ($P_{th\text{-}open}$). To turn off (close) the μMV, $P_S - P_G$ is less than closing threshold pressure ($P_{th\text{-}close}$). In typical silicon transistors,[10,11] the difference between on and off threshold voltage is negligible, thus providing a large parameter space for the design and operation of large-scale integrated circuits. Pneumatic μMVs also exhibit small differences between opening ($P_{th\text{-}open}$) and closing ($P_{th\text{-}close}$) threshold pressures.[5,12] However, in self-regulated microfluidic devices, the detailed characteristic of μMV's threshold pressure in the context of other microfluidic parameters such as fluidic resistor and inflow rate is largely unknown.

Here, we report that $P_{th\text{-}open}$ and $P_{th\text{-}close}$ are significantly different in *hydraulic* μMVs, where liquid directly passes through. We further analyze implications of this threshold pressure gap for fluidic circuit design using, as a model system, a constant flow-driven oscillator that functions like an

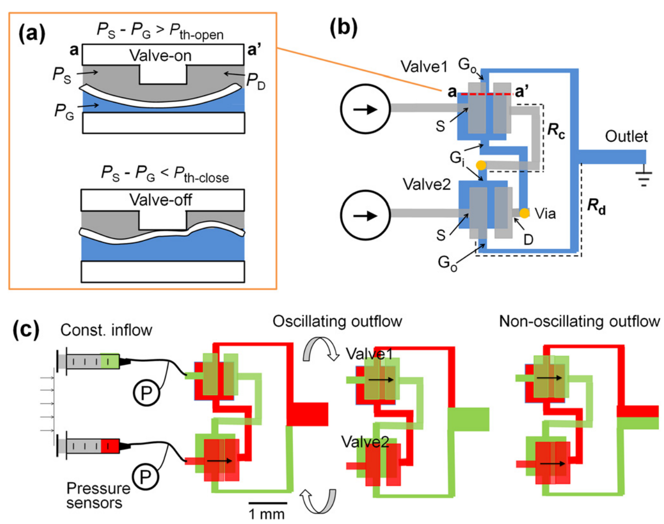

FIG. 1. Microfluidic oscillator with two membrane valves. (a) Cross-section of a microfluidic valve showing its on- and off-conditions. P_S, P_G, and P_D are pressures at the source (S), drain (D), and gate (G) terminals, respectively. $P_{th\text{-}open}$ and $P_{th\text{-}close}$ are opening and closing threshold pressures, respectively. (b) Schematic of the oscillator consisting of two microfluidic membrane valves. The valve has S, D, and inlet and outlet gate terminals (G_i and G_o). Gray and blue areas represent the bottom and top channels of the oscillator, respectively. R_c and R_d are connection and downstream resistance, respectively. (c) Schematic showing oscillating and non-oscillating outflows. The oscillating and non-oscillating outflows are determined by R_d/R_c and the inflow rate (Q_i). Constant Q_i is provided by a syringe pump (enhanced online) [URL: http://dx.doi.org/10.1063/1.4769985.1] [URL: http://dx.doi.org/10.1063/1.4769985.2].

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electronic DC to AC converter.[7,8] Then, we reveal the fundamental mechanisms of oscillation as well as the restrictions on operational circuit design parameters when using these hydraulic μMVs that exhibit negative $P_{\text{th-close}}$ and a dependency of $P_{\text{th-open}}$ on external parameters.

Experimental setups and device fabrication were explained in our previous study.[8] Briefly, each device consists of three layers of poly(dimethylsiloxane) (PDMS): top and bottom slabs for 75 μm-high channels and valves, and middle layer for thin membrane. A syringe pump was used to provide a constant inflow and two pressure sensors were connected at the inlets to measure source pressures. We used commercial software (PLECS, Plexim GmbH, Switzerland) for the numerical simulation of the microfluidic oscillator.[13]

In a hydraulic μMV, we observed that $P_{\text{th-open}}$ and $P_{\text{th-close}}$ are significantly different. For the initial valve-on state, the hydraulic μMV also requires a positive threshold pressure [i.e., $P_S - P_G > P_{\text{th-open}} > 0$, see Figure 1(a)]. Then, we could turn off the hydraulic μMV, only when P_S is $< P_G$. This result means additional P_G greater than its on-state is necessary and, in turn, $P_{\text{th-close}}$ has a negative value (i.e., $P_S - P_G < P_{\text{th-close}} < 0$); through repetitive experiments, we measured $P_{\text{th-close}}$ to be -1 ± 0.2 kPa in our system.[13] On the other hand, positive value of $P_{\text{th-open}}$ can be measured directly from the two P_S profiles of the oscillator's two μMVs under the condition that downstream resistance [R_d, defined in Figure 1(b)] is one order of magnitude higher than the connection resistance (R_c).[8]

The origin of the positive $P_{\text{th-open}}$ comes from the elastic force of the membrane and the adhesive force between the valve seat and its membrane, but that of negative $P_{\text{th-close}}$ is different. When a μMV is on and P_S is relatively close to P_G, the membrane of the μMV tends to restore its off-state owing to the membrane's elastic force. In a pneumatic μMV, its adhesive force can be easily recovered for the valve's off-state, because there is only air between the valve seat and the membrane. In a hydraulic μMV, even when its membrane approaches the valve seat, additional pressure is necessary to squeeze out liquid and to recover the valve's adhesive force, thus requiring a negative $P_{\text{th-close}}$.

Figure 2 explains how the two threshold conditions determine the μMV on- and off-states in the oscillator. The oscillator is an excellent system to study the effect of threshold pressures because its continued oscillation [Figure 1(c)] is possible only when hydraulic μMV can be turned off (close) each cycle, under conditions that satisfy the $P_{\text{th-close}}$ values. In the oscillator, two microfluidic valves are connected to each other through their drain and gate terminals [Figure 1(b)]. For example, valve 2's drain terminal (D) is sequentially connected to valve 1's gate inlet terminal (G_i), gate outlet terminal (G_o), and finally to the outlet of the device. For simplicity, the pressure profile of just valve 2 is shown in Figure 2. Here, P_S and P_G of valve 2 are noted as P_{S2} and P_{G2}, respectively. Initially, valve 2 is in the off-state and $P_{S2} - P_{G2}$ of valve 2 increases because P_{S2} accumulates through constant inflow and P_{G2} is constant. After $P_{S2} - P_{G2}$ reaches $P_{\text{th-open}}$, valve 2 turns on. Then, its high P_{S2} shuts off valve 1 through valve 1's gate terminal. Then, $P_{S2} - P_{G2}$ decreases as fluid flows out from the open valve 2 (the first gray region in Figure 2). Likewise, when valve 1 turns on,

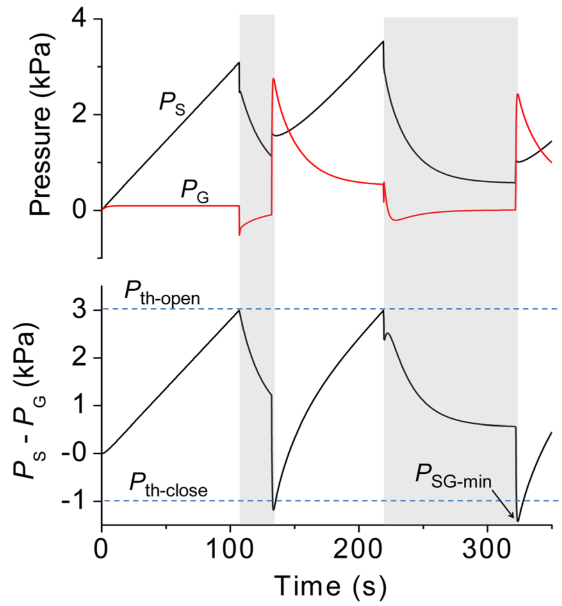

FIG. 2. Simulated source and gate pressure profiles of valve 2 at the onset of oscillation. Q_i is 2 μl/min. Gray region corresponds to valve 2-on state. At the bottom panel, $P_{\text{SG-min}}$ is a minimum value of $P_S - P_G$. If $P_{\text{SG-min}}$ is $> P_{\text{th-close}}$ at the moment of valve 1-on to valve 2 off, valve 2 stays on. As a result, both valves are on and oscillation stops.

P_{G2} of valve 2 jumps up, thereby making $P_{S2} - P_{G2} < P_{\text{th-close}}$ of valve 2. This causes valve 2 to turn off. In this way, owing to alternating on-off states of the two valves, oscillation continues.

Note that, for the oscillation, on-off state of the two valves is always opposite. If valve 2 is on but does not satisfy $P_{S2} - P_{G2} < P_{\text{th-close}} = -1$ kPa at the moment of valve 1 on, both valves are on and oscillation stops. This condition can be described as $P_{\text{SG-min}} > P_{\text{th-close}}$, where $P_{\text{SG-min}}$ is defined in Figure 2.

In the hydraulic μMV of microfluidic oscillators, we show how negative $P_{\text{th-close}}$ constrains operational ranges of the ratio of downstream to connection resistance (R_d/R_c); R_d and R_c are depicted in Figure 1(b). Under the constraints of negative $P_{\text{th-close}}$, oscillation occurs at $R_d/R_c = 7.5$ and 13.7 but not at $R_d/R_c = 0.3$ [Figure 3(a)]. For oscillation to be maintained, valve 2 must be turned off when valve 1 turns on. At the moment valve 1 turns on, the serially connected R_d and R_c work as a pressure divider;[13] the relation between P_S of valve 1 (P_{S1}) and P_G of valve 2 (P_{G2}) is

$$P_{G2} \approx P_{S1} r/(r+1), \tag{1}$$

where r is R_d/R_c. When this relationship is applied to valve 2's off-condition ($P_{S2} - P_{G2} < P_{\text{th-close}}$), this gives $P_{S2} - P_{S1} r/(r+1) < P_{\text{th-close}} < 0$. Because P_{S2} is $< P_{S1}$ at the moment valve 1 turns on, as long as R_d/R_c (i.e., r) is large enough valve 2's off-condition is satisfied and the outflow oscillation continues [inset of Figure 3(a)]. In contrast, in an equivalent electronic oscillator, oscillation is possible even at $R_d/R_c = 0.3$ because of positive $P_{\text{th-close}}$, thus allowing more flexibility in the range of fluidic resistances.

Interestingly, in addition to contributions from the intrinsic properties of the μMV such as membrane elasticity and adhesion, $P_{\text{th-open}}$ of the hydraulic μMV changes with different operating conditions such that the value increases

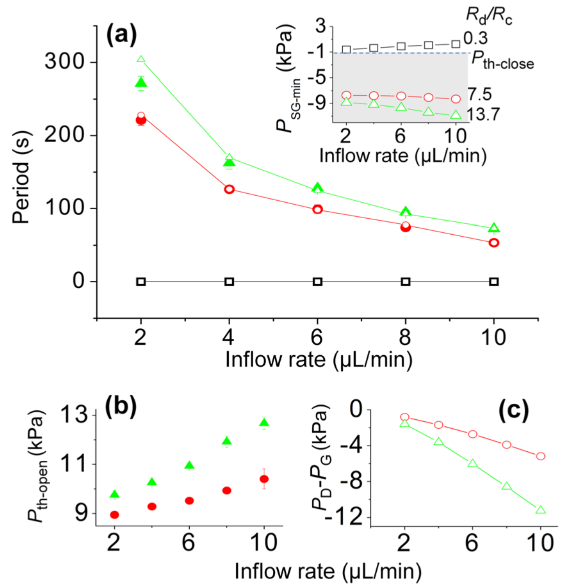

FIG. 3. Effect of $P_{th\text{-}close}$ on the operational range of the ratio of fluidic resistance [R_d/R_c, defined in Fig. 1(b)]. Filled and unfilled points are the experimental and simulation results, respectively. The color of the points corresponds to the R_d/R_c values shown in the inset of (a) and R_c is fixed as 1.46×10^{12} N·s/m^5. (a) Change of oscillation periods by R_d/R_c. There is no oscillation at the square points. When $P_{SG\text{-}min}$ (defined in the bottom panel of Fig. 2) is $< P_{th\text{-}close}$, outflow oscillation is available (gray region of the inset). (b) Corresponding opening threshold pressures, $P_{th\text{-}open}$. (c) Corresponding drain minus gate pressure just before the valve-on.

with increasing Q_i and R_d (we change R_d but fix R_c); see Figure 3(b). Compared to electronic transistors where threshold voltage is an intrinsic property, $P_{th\text{-}open}$'s dependency on external parameters (Q_i and R_d) makes design of μMV circuits more complex. This dependency can be explained by the drain minus gate pressure ($P_D - P_G$). If $P_D - P_G$ of the off-valve becomes more negative, as illustrated in the valve-off state of Figure 1(a), its membrane more tightly presses its seat at the drain side thereby increasing $P_{th\text{-}open}$. To explain how increasing R_d makes $P_D - P_G$ more negative [Figure 3(c)], we consider the state of valve 1 on and valve 2 off [see Figure 1(b) with valves 1 and 2 labeled]. P_D of valve 2 is close to the outlet pressure (≈0 kPa) because valve 2 is off and there is negligible flow between valve 2's drain and the outlet. On the other hand, P_G of valve 2 (P_{G2}) increases with increasing R_d at constant Q_i because P_{G2} follows Poiseuille's law at valve 1 on. Thus, $P_D - P_G$ of valve 2 becomes more negative at higher R_d [Figure 3(b)], thereby increasing $P_{th\text{-}open}$. In the same way, $P_{th\text{-}open}$ also increases with increasing Q_i because $P_D - P_G$ becomes more negative by Poiseuille's law. Despite the increasing $P_{th\text{-}open}$ by Q_i, the oscillation period ($\propto P_{th\text{-}open}/Q_i$, Ref. 8) decreases at higher Q_i [Figure 3(a)] because increment of $P_{th\text{-}open}$ is $\ll Q_i$. Specifically, as shown in Figure 3(b), $P_{th\text{-}open}$ changes from 9.8 to 12.7 kPa and from 8.9 to 10.4 kPa, whereas Q_i changes from 2 to 10 μl/min; this makes the increment of $P_{th\text{-}open}$ and Q_i as 30% and 16% for $P_{th\text{-}open}$ and 400% for Q_i.

Notably, negative $P_{th\text{-}close}$ also limits the operational range of Q_i. At a higher Q_i, outflow changes from oscillatory to non-oscillatory flow (Figure 4). The inset of Figure 4 shows how $P_{SG\text{-}min}$ changes with increasing Q_i; in the case of the equivalent electronic transistor having positive $P_{th\text{-}close}$, it is clear that the oscillator will have higher operational Q_i.

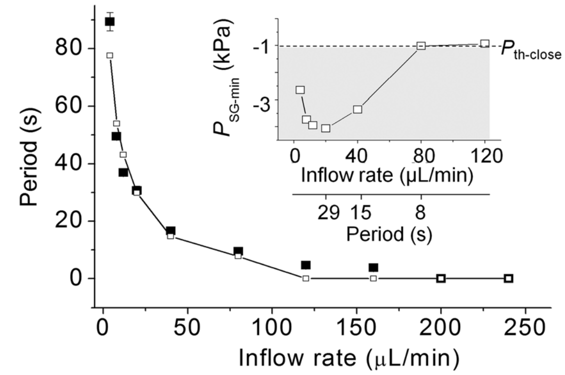

FIG. 4. Effect of $P_{th\text{-}close}$ on the operational range of the inflow rate. Filled and unfilled points are the experimental and simulation results, respectively. $R_d + R_c$ is 1.7×10^{13} N·s/m^5. Gray region ($P_{SG\text{-}min} < P_{th\text{-}close}$) of the inset is oscillation region.

Interestingly, $P_{SG\text{-}min}$ initially decreases; then it increases and finally becomes greater than $P_{th\text{-}close}$ (i.e., no oscillation). The initial decrease of $P_{SG\text{-}min}$ comes from increasing $P_{th\text{-}open}$ with increasing Q_i. This is because the switching-on valve's increased $P_{th\text{-}open}$ directly raise the switching-off valve's P_G and thus $P_{SG\text{-}min}$ of the switching-off valve decreases. However, as the switching becomes faster, the on-valve, which is to be switched off, cannot faithfully follow the change of $P_{th\text{-}open}$. To explain, we compare off- and on-valves' P_S: in the off-valve, the accumulation rate of P_S is proportional to Q_i, whereas in the on-valve, regardless of Q_i, the release of P_S follows characteristic time constant (τ) that is approximated as $(R_c + R_d)C_{tot}$; see Figure S3.[13] When the valve's on-to-off switching is faster than its τ, the on-valve's P_S discharges insufficiently, thereby raising $P_{SG\text{-}min}$. τ is calculated as 13 s for one on-valve and twofold of that τ for a two valve system. This approximated critical period (26 s) is in relatively good agreement with the base of $P_{SG\text{-}min}$ (inset of Figure 4) obtained from computational simulation. The on-off condition of valves and oscillation conditions are summarized in Table S1.[13]

In conclusion, we show that hydraulic membrane-valve have significantly different closing and opening threshold pressures and that the opening threshold pressure changes depending on circuit design parameters such as channel resistances and operation conditions such as flow rates. The negative closing threshold pressure constrains the values of resistors and flow rates that can be used to achieve oscillation. A comprehensive analysis of how the microfluidic resistors and inflow rates affect the oscillator circuit's ability to turn valves off clarifies the conditions under which oscillation can occur. This study provides a fundamental understanding and theoretical framework for a broad range of microfluidic valve-based devices.

This work was supported by the NIH (GM096040-01 and HL084370-05) and Institutional Program for Young Researcher Overseas Visits, Japan Society for the Promotion of Science (JSPS). Devices were partially fabricated in the Lurie Nanofabrication Facility, a member of the National Nanotechnology Infrastructure Network, which is supported by the National Science Foundation.

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[13]See supplementary material at http://dx.doi.org/10.1063/1.4769985 for details on close threshold pressure, the oscillator circuit models, and movies.