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Preprogrammed capillarity to passively control system-level sequential and parallel microfluidic flows

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Abstract

In microfluidics, capillarity-driven solution flow is often beneficial, owing to its inherently spontaneous motion. However, it is commonly perceived that, in an integrated microfluidic system, the passive capillarity control alone can hardly achieve well-controlled sequential and parallel flow of multiple solutions. Despite this common notion, we hereby demonstrate system-level sequential and parallel microfluidic flow processing by fully passive capillarity-driven control. After manual loading of solutions with a pipette, a network of microfluidic channels passively regulates the flow timing of the multiple solution menisci in a sequential and synchronous manner. Also, use of auxiliary channels and preprogramming of inlet-well meniscus pressure and channel fluidic conductance allow for controlling the flow direction of multiple solutions in our microfluidic system. With those components orchestrated in a single device chip, we show preprogrammed flow control of 10 solutions. The demonstrated system-level flow control proves capillarity as a useful means even for sophisticated microfluidic processing without any actively controlled valves and pumps.

1. Introduction

High-throughput processing of biochemicals with microfluidic systems has shown great potential to facilitate assays, including protein crystallization,¹ enzymatic activity assay,² and immunoassays.³ Such assays using a microfluidic system typically require active control, which relies on external off-chip controllers including power supplies and syringe pumps.⁴⁻⁶ Importantly, a number of external off-chip controllers are necessary with the increasing number of active control for high throughput assays. Accordingly because of its complexity and cost, the active control poses a serious barrier against widespread use of

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microfluidic devices for non-technical users such as biochemists and clinicians. Thus, it is desirable to develop a method without any active external off-chip controllers, so called “purely passive” on-chip microfluidic control. With sequential and parallel assays enabled by such a microfluidic control method, microfluidic technology would be readily accessible to a larger group of users.

It is highly intriguing to utilize capillary motion of solutions for purely passive flow control in a microfluidic system. In contact with a solid surface, a liquid-gas meniscus yields a pressure gradient in the liquid phase (Laplace pressure). Notably, this pressure gradient drives the liquid’s spontaneous capillary motion. In microfluidics, the small sizes of channels and inlets give rise to large meniscus curvatures; the larger meniscus curvatures result in higher internal pressure gradients and could serve to generate the significant motion of microfluidic solutions without external power. However, when it comes to sophisticated capillarity-driven microfluidic assays that involved a large number of solutions, previous methods^{7,8} have largely relied on external electric fields.

Assays in a complex microfluidic system operated without active external off-chip controllers require fully passive preprogrammed control of the flow timing and flow direction for multiple solutions. The system-level operation further necessitates orchestrated multi-solution flow control for the entire microfluidic channel network. Thus, passive, yet sophisticated flow control solely depending on capillarity still remains nontrivial and readily perceived as a significant challenge. To date, quite a few researchers⁹⁻²¹ have demonstrated passive capillarity-based microfluidic flow operations. However, they applied these operations only for relatively simple channel architectures, with a small number of solutions. This limits the utility of the capillarity-based flow control approach in practical microfluidic assays.

Here, we demonstrate purely passive capillarity control for a microfluidic system with high complexity. How can we achieve that? The answer is successful system integration of capillarity-driven passive microfluidic components and well-preprogrammed orchestration of their operations. Our method involves *system-level* preprogrammed regulation of the *both* timing and direction of the capillary flow of multiple solutions. Once we load solutions using a pipette with predetermined time intervals, capillarity spontaneously controls the flow timing and direction of multiple solutions on a microfluidic chip in a fully passive manner. To achieve the process, we use passive microfluidic components, namely timing channels and synchronization channels, to control the meniscus motion timings in a channel (Figs. 1a and 1b). With the two components, we regulate the merging timings of solution menisci in a sequential and parallel manner. Then, we rely on a method that regulates the flow directions of merged solutions by appropriately setting meniscus pressures in inlet wells in conjunction with channel architectures (Figs. 1c and 1d). As a model system, we have constructed a microfluidic device consisting of a network of these components. Once 10 solutions are loaded using a pipette with predetermined time intervals, the device processes the solutions in a sequential and parallel manner without any active external controllers. Our study also develops a theoretical microfluidic circuit model and schemes such a system-level process based on the model’s prediction for the transport of a complex combination of multiple inlet-well meniscus flows.

2. Methods

2.1. Basic principle of capillarity-driven microfluidic flow control

We now explain how meniscus pressures in inlet wells and channels serve for controlling microfluidic flow. As shown in the step 1 of Fig. 1e, pipetting a solution to an inlet well forms two menisci: one at the inlet well and the other in a partially filled hydrophilic channel. Then, the relatively large meniscus curvature in the hydrophilic channel pulls down the solution to the channel. We use the condition of this meniscus within the channel to vary and synchronize the flow timing as explained later. Subsequently, in step 2 as we pipette another solution in the other inlet well, the original solution merges with it. As a result, the in-channel meniscus disappears. In step 3 the menisci at the two inlet well solely determine the motion of the solutions merged with each other. More specifically, the difference in the pressure between these two menisci in conjunction with the fluidic conductance along the channel determines the direction of the motion of the merged solutions. Our study expands this scheme for a more complex microfluidic system incorporating multiple inlet wells and channels by means of theoretical analysis using a sophisticated fluidic circuit model described below.

2.2. Theoretical modeling

To perform a fluidic circuit analysis for our system, we first modeled the meniscus-holding inlet wells as varying pressure sources and the channels as fluidic conductors (see Supplementary Fig. S1 for detailed derivation). Briefly, the pressure of well n ($P_{\text{well } n}$) is given by

$$P_{\text{well } n} = \frac{4\sigma h_n}{h_n^2 + r_n^2}, \quad (1)$$

where σ is the surface tension of a solution, and r_n and h_n are the radius of the well n and the convex meniscus height in the well (Fig. 1e), respectively.¹⁶ An end point of each fluidic conductor is defined as a node, and the pressure of node m ($P_{\text{n } m}$) is given by

$$P_{\text{n } m} = \frac{\sum_{i=1}^j c_i P_i}{\sum_{i=1}^j c_i}, \quad (2)$$

where P_i is either well or another node pressure and C_i is the fluidic conductance of channel i . The fluidic conductance is the inverse of fluidic resistance. The fluidic conductivity in the channel and the relative pressure difference between wells and nodes determine the rate of change of h_n as

$$\frac{dh_n}{dt} = \frac{2C_i (P_{\text{n } m} - P_{\text{well } n})}{\pi (r_n^2 + h_n^2)}, \quad (3)$$

These equations constitute simultaneous differential equations of the entire fluidic network. Numerically solving these equations for h_n , $P_{\text{n } m}$, and $P_{\text{well } n}$ by MATLAB programming

(Mathworks, Natick, MA) allowed us to predict the direction of the capillary motion of the solution between any two nodes of the network at a given instance of time. We used the model prediction in designing our microfluidic system.

2.3. Device fabrication

The device representing our microfluidic system consists of two layers; Fig. 1e shows its channel cross-section. The top layer containing microfluidic channels of 60 μm in height was fabricated in hydrophobic polydimethylsiloxane (PDMS) by soft lithography. We used a Cr photomask to make smooth and fine patterns, and $\sim 200\text{ }\mu\text{m}$ -thick PDMS was cured in 100 $^{\circ}\text{C}$ convection oven for 2 days. Then, the PDMS layer was punched to make 2 or 4 mm-diameter holes.

The bottom layer was made of hydrophilically surface-treated Si. For hydrophilic surface-treatment, SiO_2 (60 nm) was deposited on a Si wafer by low-pressure chemical vapor deposition (LPCVD). Then, a 400:1 (v/v) mixture of xylene and hexamethyldisilazane (HMDS) was spin-coated on the wafer and cured at 200 $^{\circ}\text{C}$ for 30 min for the hydrophilic surface treatment of the Si device bottom layer. After rinsing the wafer with deionized water, N_2 gas was used to blow out water and dry the silicon surface at 200 $^{\circ}\text{C}$ for 3 min. Finally, the wafer was cleaved to an appropriate size. Owing to the adhesiveness of PDMS, the two layers were reversibly bonded by mild pressure without plasma treatment, and experiments were performed right after the bonding.

2.4. Experimental conditions

To prevent air bubble formation during the solution dispensing process, we used a positive displacement pipette (Microman M10, Gilson). To minimize evaporation of the solutions during the experiment, we put the device in a petri dish partially filled with water and sealed it with a glass cover; the cover was opened only when we dispensed solutions. This method enabled us to prevent the evaporation of 1 μL droplet for two days. The working solution was 1% (w/v) bovine serum albumin (BSA) throughout our study presented in this paper, unless otherwise noted.

3. Results and discussion

3.1. Control of flow timing

Figure 2 shows that decreasing the channel width (or aspect ratio) changed the meniscus speed by 3 orders of magnitude from 116 $\mu\text{m}/\text{min}$ to 16 cm/min . This large meniscus-speed variation by the channel width provides an efficient means to regulate the flow timing. Here, we used a narrow channel to intentionally delay the meniscus motion by keeping its speed very low in the channel. The narrow channel acted as a passive valve for a designed amount of time, and we now call it a “timing channel.” We selected a 90 μm -wide channel as the timing channel in our device because the channels yielded a sufficiently low flow speed of $< 0.7\text{ mm min}^{-1}$ and showed consistent performance leading to the relatively small flow-timing variation with a standard deviation $< 12\%$ at each channel spot in Fig. 2c. The statistical variation was analyzed for each data point over 10 different devices, thus proving good device-to-device repeatability of the channel performance. In other cases, we used a

sufficiently large channel width ($>160\text{ }\mu\text{m}$) so that a solution's meniscus rapidly moves inside the channel. The wide channel operated as a spontaneous pump, which enabled the rapid filling of solutions in a complex channel network. Jointed together (Fig. 1a), the wide and the timing channel operated as a serially connected passive pump and valve. The hybrid structure combining these two types of channel enabled the sophisticated passive control of meniscus flow timing in a complex channel network. This allowed us to completely eliminate the use of any active pumps and valves from our device operation.

The remarkable variation of the meniscus flow speed by 3 orders of magnitude only with the 5-fold channel-width change is attributed to the heterogeneous internal wall surface of our channel. That is, the top and two side surfaces of the channel are hydrophobic while its bottom surface is hydrophilic. Now, we show that decreasing the hydraulic diameter (d) of the channel increases the effective dynamic contact angle (θ) of the heterogeneous surface, thereby providing the ability to widely change the meniscus flow speed. Our rectangular cross-section channel is $60\text{ }\mu\text{m}$ in height and varies its width between 70 to $360\text{ }\mu\text{m}$. This width variation translates into an only 1.6-fold variation of d . A distance (L) that a meniscus travels for a given time, which is equivalent to an average meniscus speed, is proportional to $d^2 \cos \theta$ according to Washburn equation.²² If d is assumed to experience a 1.6-fold increase while θ remains unchanged, Washburn equation predicts only a 2.6-fold increase in the value of L . Notably, this prediction is much less than the experimentally observed 3-order-of-magnitude variation of the meniscus flow speed. It suggests that θ should in fact increase with the decreasing d . In our case, because we use a rectangular cross-section channel and its height (h) is constant, the change of d translates into that of the channel width (w) or channel aspect ratio (w/h). That is, decreasing (or increasing) w/h makes the net channel surface property more hydrophobic (or hydrophilic). In this way, our simple heterogeneous channel structure yields the drastic meniscus-speed variation. Thus, it allows the channel to serve as either a timing channel or a passive pump depending on the value of w (or w/h) as described above.

To date, researchers have achieved meniscus speed control with such a wide range primarily by selectively coating the channel bottom surface with a hydrophilic film. This process yields local regions with a different degree of hydrophilicity along the channel.¹⁴ However, the approach makes the fabrication process more complex thus limiting its utility. Other studies^{11,12} showed that a droplet in an intermediate well between a target channel and an inlet well enabled flow timing control. But their approach required precise positioning of the droplet and its additional pipetting steps with an increasing number of timing steps. This made the droplet-dispensing process laborious. Another study¹⁸ demonstrated so called "paper microfluidics," where the researchers immersed multiple paper-legs of different length into a shared buffer-well, and used them to initiate and stop reagent flows. However, the buffer diluted the reagents and made their distribution spatially non-uniform in a detection zone. This degraded the fidelity and accuracy of the assay.

3.2. Synchronization of multiple meniscus motions

The flow timing across different solutions, however, can vary even within the same timing channel if the solutions have variations in their fluidic property (e.g. contact angle).

Regardless of the fluidic property variations, we established a method to consistently control the meniscus flow timing for our system. This method employed a common solution that triggers the motion of other solutions at a desired timing (trigger solution) and indirectly controlled the flow timing. The process of this control scheme is shown in the time sequence images of Fig. 3a.

Initially, the motion of the target solution was halted at the stop valve. This stop valve, formed by the abrupt expansion of the cross section at a channel,¹⁹ yielded a capillary-pressure barrier to temporarily stop the motion of the target solution. However, excessive wettability of the channel corner, resulted from the hydrophilic bottom layer, removes the capillary pressure barrier at the valve. This permits the target solution to pass the valve and to form an air bubble during the merging with another solution, thereby blocking the flow of the two solutions. To prevent the significant channel-corner wetting for a homogenous surface in a rectangular cross-section channel, previous studies^{23,24} show that the desirable contact angle is $> 45^\circ$. This similarly applies to our heterogeneous channel. Thus, we carefully selected the hydrophilicity of the device bottom layer; it allowed for realizing the stop-valve function with the valve structure, while maintaining the meniscus speed-control in the channels. Specifically, we adjusted the xylene-to-HMDS surface coating ratio during the device fabrication in Section 2.3, and obtained an appropriate degree of wettability for the bottom layer surface (See Fig. S2). Even under this condition, we still observed formation of a small air bubble at the lower corner of the channel as seen in Figs 3 and 4. This could be completely eliminated by adding an air vent to the channel corner. However, the bubble never blocked the solution motion throughout our experiment, causing no deleterious effect on the performance of our system. In addition, we never observed bubble formation in any other regions for the entire device chip.

Next, the trigger solution (1% BSA solution) passed through the timing channel and merged with the target solution. At the moment only the target solution (the yellow solution of Fig. 3a) moved towards the target channel while the motion of the trigger solution to the target channel was prevented. We schemed this selective motion by preprogramming the well pressures and the fluidic conductance of the channels. The middle panel of Fig. 3a depicts the channel connection having 4 inlet wells. Once the trigger solution in well 4 moved and merged with the target solution coming from well 3, the target solution moved to both the target and the timing channels. This is because the pressure of well 3 was higher than those of wells 4 and 1. As a result, the trigger solution did not move to the target channel and thus the target solution solely filled the target channel; detailed parameter values are shown in the circuit diagram of Fig. 3a. In this way, we indirectly controlled the target solution's flow timing by using the trigger solution. We eventually tested biochemical solutions with various contact angles (human plasmas, antibodies, and a buffer; see Fig. S3). We selected these solutions for our study as they are commonly used in immunoassays. Their flow timing to the target channel could be successfully controlled by the trigger solution.

This "indirect" control using the trigger solution is the basis of the function of the synchronization (Sync) channel, where the flow timings of multiple target solutions are synchronized. We achieved the synchronized stop-and-flow control for multiple solutions in parallel as shown in the time sequence images of Fig. 3b. The two yellow solutions represent

our target solutions pipetted in wells 3 and 4. They were two human plasmas having different contact angles (22 and 28°). As shown in the device schematic and the circuit diagram of Fig. 3b, the synchronization process was achieved by feeding the trigger solution from a single timing channel (ch6) into divided Sync channels (ch4) and by having it merge with the multiple target solutions in ch3 at the same time.

3.3. Prevention of flow crosstalk with auxiliary channels

After the step achieving the synchronized flow of the target solutions moving into the target channels, flow crosstalk could occur (Fig. 4a). Specifically, the two target solutions (yellow color) initially moved into the assigned target channels and merged with the pre-existing solution (dark blue color) in the channels. Then, the target solution did not fully fill the target channel on the right hand because the pre-existing solution also moved to the channel. This fluidic crosstalk results from pressure imbalance between the inlet wells, which is presumably caused by pipetting errors and/or the small variations of inlet diameters created upon the inlet-hole punching process.

Now, we theoretically show that even minor pressure difference between the wells causes flow crosstalk. The nominal dispensed volume of the target solutions of wells 3 and 4 (circuit diagram of Fig. 3b) was 1.4 μL each. We predict that this volume would yield 78 Pa pressure for each well. If assuming -0.05 and $+0.05$ μL variations from the nominal volume in wells 3 and 4, respectively, the initial well pressure difference between wells 3 and 4 would be 7 Pa. Similarly, the initial pressure of wells 1 and 2 might not be identical due to an error in the dispensed volume. Here, we assume that the pressure of well 2 was higher by up to 6 Pa than that of well 1 due to a sample volume error as high as 0.1 μL caused by the pipetting process. This condition would cause a local pressure imbalance between the wells (Fig. 4c). The location of local pressure nodes (n_1 , n_2 , and n_3) is shown in the circuit diagram of Fig. 3b. Regardless of the pressure difference between wells 1 and 2, the node pressure ratios are calculated to be $P_{n3}/P_{n2} > 1$ and $P_{n3}/P_{n1} < 1$. This allows us to explain why the pre-existing solution moved to the right-hand target channel (Arrow head of the bottom panel of Fig. 4a). Note that this fluidic motion could also happen in the left-hand target channel because a pipetting error occurs randomly.

To completely eliminate this problem, we added so called “auxiliary channels” (Fig. 4b). The target and the auxiliary channels were commonly connected to well 1 (Fig. 3b). This connection allowed the target solution to partially move to the auxiliary channel until all the well pressures equilibrated. Thus, as shown in the bottom panel of Fig. 4b, the stream of the target solution (arrow) flowing into the auxiliary channel yielded a flow barrier to the stream of the blue solution (arrow head). This prohibited the entry of the blue solution to the target channel. A previous study²⁶ used a trigger mechanism employing an electronic-diode like valve. But without achieving synchronized parallel flow of multiple solutions, the study only applied this mechanism for triggering one solution. The approach of this study possibly lacked the ability to control the flow direction for multiple solutions.

3.4. Control of sequential and parallel flows

Unlike other actively controlled microfluidic devices, our capillary-driven system passively controls the flow direction of merged solutions without any on-chip valves. Without orchestrating the operations of the on-chip passive components, flow crosstalk happens between merged solutions upon sequential flow processing. For example, a non-orchestrated operation causes flow crosstalk even with a simple 3-well system (see Fig. S4); A preceding solution unwantedly reflows into a detection channel while a subsequent target solution flows in. Therefore, an orchestrated component operation becomes very crucial especially when the passive components in Figs. 1a to 1d are integrated altogether in a common device platform.

We finally constructed a microfluidic device integrating all the passive components described above and demonstrated processing of 10 solutions in a sequential and parallel manner (Fig. 5a). To successfully achieve the flow direction control of the merged solutions, we carefully preprogrammed the fluidic conductance of the local channels in conjunction with the meniscus pressures at the inlet wells. Then, we orchestrated them with timing and synchronization units for flow-timing control (see Fig. S5 for the fluidic circuit diagram). Using the fluidic circuit model, we designed the device such that only the target solution would exclusively move to its assigned target channel at a predetermined time while keeping other solutions from entering the channel.

At the beginning of the flow processing, we sequentially pipetted each solution with a 1 min interval except for the last solution loaded with a 5 min interval; the pipetting sequence is noted as a number in the wells of Fig. 5a. In each step, the flow timing of each solution to the target channel was determined by both its preprogrammed delay time in the timing channel and the time interval between the pipetting steps. The number shown in Fig. 5a also identifies different wells and solutions. Wells 3a to 3d represent those having different sample solutions (solutions 3a to 3d). These solutions have different contact angles and thus we indirectly controlled and synchronized their flow timings with the trigger solution (solution 4). The other wells represent those having different reagent solutions that are sequentially provided to the target channels (red lines). The reagent solutions have similar contact angles and thus their flow timings were directly controlled with the timing channels. Fig. 5b shows the flow processing steps with colored dye solutions. Solutions 3a to 3d (Fig. 1e) were human plasmas and the other solutions were 1% BSA representing reagent solutions. In step 1, the meniscus of solution 1 introduced from well 1 sequentially moved to the target and the connection channels. Then in steps 2 to 5, when the solutions merged, they filled the target channels while moving to well 1 without any flow crosstalk.

Now, we can account for the flow direction of the solutions from the theoretically calculated time evolution of the inlet-well pressures (Fig. 5c). The pressure of well 1 (P_1) is predicted to increase in each step. Here, well 1 should work as a flow sink receiving solutions from the other wells, which causes its meniscus shape to be more convex. We see that this flow-sink function of well 1 resulted from the facts that P_1 gives the lowest value almost throughout all the steps (except step 3) and gradually increases due to its larger diameter than that of the other wells (4 vs 2 mm). In step 3, the initial pressure of well 4 is predicted to be the lowest,

thus preventing solution 4 (trigger solution) from entering the target channels. In each step, each target solution left the well for which the model shows a decreasing pressure, and then primarily moved to well 1. Note that, in step 4 (or step 5), the model predicts a slight decrease in the pressure of well 2 (or well 4) for some period; however, our experiment showed that the optimally designed channel fluidic conductance kept the solution in well 2 (or well 4) from even reaching the connection channels (Fig. 5a). To date, a theoretical analysis has been applied only for a very simple system consisting of two inlets and one channel^{13,16}. In contrast, we have successfully modeled the passive capillarity-driven system having the complex channel network that includes 10 multiple inlets. The modeling study has enabled us to achieve the orchestrated flow direction control for 10 solutions. The approach presented here could be readily extended for more complex capillarity control systems.

Conclusions

We have demonstrated the unprecedented capability to passively regulate the flow timing and flow direction of multiple solutions by exploiting capillarity in a complex microfluidic network. The original contributions of our work include: (1) system-level integration of passive capillarity-driven microfluidic components summarized in Fig. 1, (2) demonstration of sophisticated on-chip capillarity control in a preprogrammed manner, and (3) development of a theoretical model that well predicts the system performance and enables systematic design of a fully passive capillarity-driven microfluidic circuit on a single chip. Our approach only requires a manual pipetting process to dispense solutions. After loading the solutions to our device, capillarity alone enabled fully passive on-chip control of multiple reagents and samples in a sequential and parallel manner for the entire assay process. Thus, our scheme will open a new avenue in the sequential and parallel flow control of microfluidic devices without any reliance on bulky external controllers. The proposed passive fluidic control scheme would be widely used for biochemical assays and immunoassays where sequential and parallel flow processing is necessary.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Fig. 1.

Key functions and components for capillarity control. Target channels are marked in red lines. The white arrows show the flow direction and speed illustrated by their size. (a) Flow timing. A solution's meniscus moves faster in the wider channel. Then, the flow of the solution is delayed in the narrower timing channel. Thus, its flow timing at the entry to the target channel is regulated. (b) Synchronized flow timing of two solutions. The synchronization channel (Sync ch) triggers the simultaneous entry of the two solutions having different physical properties into their assigned target channels. (c) Flow blocking. The auxiliary channel prevents an unwanted solution (the one vertically moving up) from entering the target channel by forming a flow barrier. (d) Flow guiding. An appropriate combination of channel fluidic conductance and inlet-well meniscus pressure (i.e. well pressure) allows only an assigned solution to enter the target channel while preventing the other solutions' entry to the channel. This enables multiple solutions to move into a target channel in a preprogrammed sequence. (e) Device cross-section showing menisci in the channel and the inlet wells.

Fig. 2.

Flow-timing control. The working solution was 1% (w/v) BSA and the initial meniscus-pressure in the inlet-well was 100 Pa. (a) Photographs showing meniscus speed for varying channel width. The arrows indicate the meniscus position. (b) Meniscus speed as a function of channel width. The channel width changed the meniscus flow speed by 3 orders of magnitude; a narrow channel could delay flows, thereby operating as a timing channel, and a wide channel quickly moved the meniscus in a spontaneous way.

The inset shows the total time for the meniscus to pass through a 3 mm-long channel (flow time). Each error bar shows the standard deviation taken over at least 4 devices. (c) Time at which meniscus passes by local spots along 90 μm-wide channel.

The numbers shown in the inset represent the locations of the channel spots. The error bars represent the standard deviation taken over 10 devices.

Fig. 3.

Synchronized flow timing. (a) Indirect control of flow timing. A trigger solution (BSA, 1% w/v) passing through the timing channel initiated the flow of the tentatively stopped target solution. White arrows show the flow direction. In the device schematic, vent line is not included for simplicity and the numbers represent well numbers. In the fluidic circuit diagram, the fluidic conductance of channels 1 to 4 are 1.6×10^{-12} , 1.2×10^{-13} , 4.7×10^{-13} , and $1.9 \times 10^{-13} \text{ m}^5 \text{ N}^{-1} \text{ s}^{-1}$, respectively. The initial pressures of wells 1 to 4 are 20, 20, 78, and 5 Pa, respectively. The inlet diameters of well 1 and the other wells were 4 and 2 mm, respectively. (b) Synchronization of two target solutions' merging with the pre-existing solution in the target channels. Fluidic conductance of channels 1 to 4 is the same with (a), and those of ch 5 and 6 are 1.5×10^{-13} and $5 \times 10^{-13} \text{ m}^5 \text{ N}^{-1} \text{ s}^{-1}$, respectively. The initial pressures of wells 1 to 5 are 20, 20, 78, 78, and 5 Pa, respectively.

Fig. 4.

Prevention of flow crosstalk by auxiliary channels in Fig. 3b. (a and b) Photographs showing the flow of target solutions (a) without and (b) with auxiliary channels. The stream of the target solution (yellow arrow) into the auxiliary channel yielded a flow barrier to the pre-existing solution (blue arrow head), thus preventing it from entering the target channel. The unwanted flow of the pre-existing solution was induced by a pressure imbalance between wells. (c) Theoretical prediction of local pressure ratios. The location of local pressure nodes (n1, n2, and n3) is shown in Fig. 3b.

Fig. 5.

Passive control of sequential and parallel flows. (a) Schematic of a model system. The device incorporates the passive components in Figs. 1a to 1d. Section i shows an area including the target, Sync, and auxiliary channels. Section ii illustrates the device structure for the merging of solutions. All the numbered circles represent inlet wells 1-6. (b) Photographs showing sequential and parallel flow processing. Each panel represents section i or ii in (a), and the corresponding section is noted in the top left of each panel. Each white arrow shows the flow direction of the solution in each channel, and its size indicates the relative flow speed. (c) Theoretical time variation of well pressures in each step. The pressures of wells 1 to 6 are P_1 to P_6 , respectively. By integrating capillarity control components, we show fully passive on-chip regulation of the flow timing and direction of multiple solutions in a microfluidic device.