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ARTICLE TYPE

Design, characterization and application of a novel mono-layer pin-microvalve for microfluidic devices

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Valves are one of the key components in microfluidic devices to control the fluid flow. In this paper we introduce a novel manual pin-valve which can operate in both analogue (partially close) and digital (on/off) states. We also demonstrate implementation of this pin-valve in a hydrodynamic flow focusing (HFF) device.

Introduction

Microfluidics is playing a vital role in the rapidly growing fields of biomedical research such as genomics [1], proteomics [2], cellular and molecular biology [3,4], and the drug screening [5]. In the late 90's, Whitesides et al. introduced the soft lithography technique to enable rapid production of inexpensive and disposable platforms mostly in poly dimethylsiloxane (PDMS) [6]. In the last decade, researchers were urged to envisage new ways to control fluid flow to meet the specific requirements of biological applications [7]. An important component of control systems are valves. Hence, novel technologies emerged from soft lithography technique to provide microfluidic microvalves, broadly known as elastomeric microvalves.

Elastomeric valves can be categorized into two main classes based on their design: membrane microvalves and pinch microvalves. Membrane microvalves rely on a thin membrane to deform and block the flow channel. On the other hand, pinch microvalves rely on compressing the bulk polymer (such as PDMS) to pinch the flow micro-channel. These valves are relatively inexpensive to make and thus can be disposable.

Quake et al. introduced a normally open pneumatic membrane microvalve in which an extra control layer is required to transfer the pneumatic control to the valve [8]. Such microvalves need a peripheral source of energy to maintain the actuated valve state. Mathies et al. introduced an alternative pneumatic membrane microvalve which is similar to Quake valve, but it is normally closed. [9] In this valve, the flow micro-channel is divided into two parts, separated by a wall which is capped by a membrane. The elastomeric membrane is retracted from contact with the separation wall using a pneumatic control to facilitate flow. However, the production yield is reduced due to the possibility of undesired permanent bonding of the membrane to valve seat.

Another type of membrane microvalve are phase-change valves, which often utilise solids which melt when heated and re-solidify when cooled to restrict and release the fluid. Several phase-change microvalves have been reported such as paraffin actuated valves [10], hydrogel valves [11], electrowetting on dielectric (EWOD)-based [12], thermo-pneumatic actuated valves [13], and also polymer microvalves [14]. The phase change valves suffer from inherent slow speed of actuation.

In general, membrane microvalves require a peripheral source of energy, such as pressure or vacuum pumps for the pneumatic valves of Quake and Mathies or externally powered and controlled heaters for the phase change valves, to maintain the actuated state. The requirement to interface such valved chips to complex external active valve control systems can introduce complexity and limit the scale of integration. The complex interfaces can hinder portability and render prolonged experiments, with durations on the scale of days or even weeks, somewhat impractical.

Another main class of microvalves is the pinch valve. A variety of pinch valves has been reported, this includes active valves such as solenoid valves [15], and brail pin valves [16–18], or passive torque-actuated valves such as screw valves [19] and glass bead based valves [20]. Solenoid valves are relatively expensive and also the number of the solenoids on the chip is significantly restricted by the size of the solenoids. Moreover, Brail pin valves and solenoid valves both need an active source of energy to maintain their close state.

On the other hand, passive torque actuated valves do not need any additional source to maintain their state, since they are fully manual. However, the distance between the valves is limited by the size of the screw head [19] or the glass beads [20]. Also the valves must be configured individually which becomes time consuming and can introduce compounding human error as the number of the valves increases.

In this paper, we describe fabrication, and characterization of a novel pinch microvalve for microfluidic devices. We utilize micro milled PMMA pins to actuate the valves, and hence it is called pin-valve. We also demonstrate that the valve can be precisely controlled at partially closed states (analogue mode) as well as on/off states (digital mode). Then, we demonstrate implementation of pin-valves in our recently published hydrodynamic flow focusing (HFF) device [21], which allows the stable control of input channels resistance to vary fluid ratios on a single deign chip.

One of the advantages of our pin-valve over preceding methods is that it can be operated for a long time without any

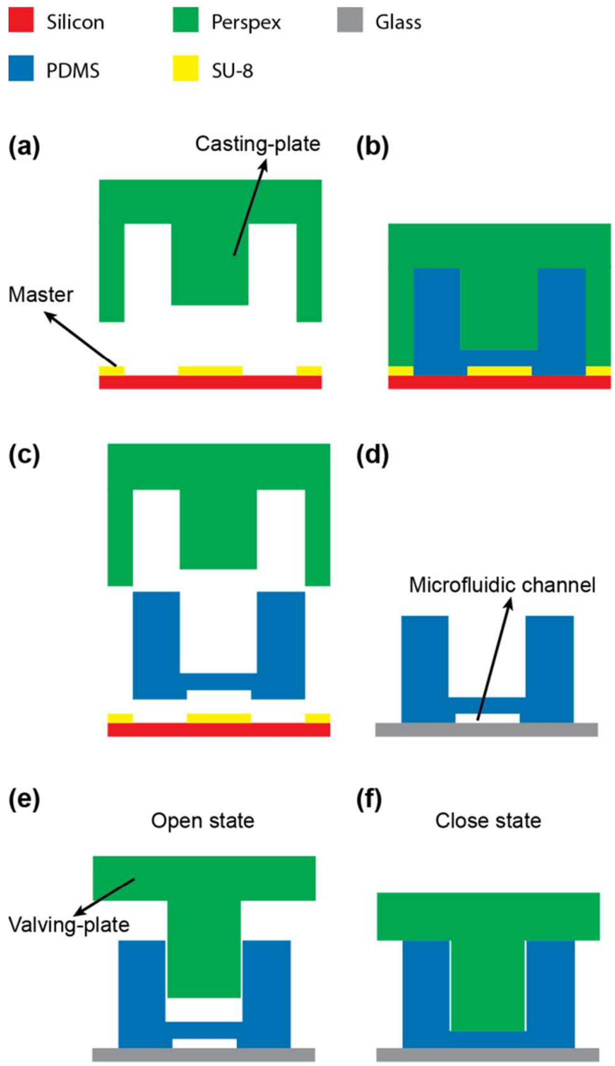

Figure 1 Pin-valve fabrication process: (a) Aligning the PMMA casting-plate on the silicon master before pouring PDMS, while casting-pin is shorter than the rest of the structures on the casting-plate to create a gap for making PDMS membrane. (b) Injecting PDMS between the master and the casting-plate and then curing the PDMS. (c) Releasing PDMS chip from the master and the casting-plate. (d) Placing the PDMS chip on a glass substrate. (e) and (f) Pin microvalve operation using valving-plate. The valving-plate contains pins which are longer and narrower than the casting pins.

peripheral source of energy in contrast to pneumatic valves which need bulky and complex pressure sources and electronic control. Additionally, our valve is addressable individually as well as in the groups. Moreover, the footprint of this novel valve can be smaller than the screw valves.

Fabrication Method

Figure 1 demonstrates the fabrication steps of our pin-valve. Figure 1 (a) represents the microfabricated master and the micro milled casting plate which were used to cast the PDMS chip.
To create the master, a silicon wafer was first spin-coated with the SU-8 2050 photoresist (Micro Chem. Corp, USA) at a thickness of 100 µm. Then, the remaining solvents were removed via soft baking and the sample was exposed to UV-light through a transparency mask. Subsequently, a post exposure bake and then developing process were applied to realize the SU-8 pattern on the silicon wafer.

A 12 mm thick poly methyl methacrylate (PMMA) sheet was micro milled using a 3-axis CNC machine (Isel CPM 3020, Germany) to create the casting-plate. The plate was patterned with two sets of pins: alignment-pins with an approximate diameter of 2 mm and casting-pins with a diameter of 0.9 mm. It should be noted that such structure can be also be fabricated using commercial 3D printers with a resolution of 100 µm.
The casting-plate was precisely placed on the master using the alignment-pins in order to position the casting-pins on desired locations of the SU-8 master. Then, PDMS (mixing ratio of 10:1 by weight for base to curing agent) was poured on the master to fill the space between the master and the casting-plate as shown in Figure 1 (b). This is analogous to injection molding technology. The height of the alignment-pins dictates the final thickness of the chip, which is taken as 6 mm in our design. The height of casting-pins was set to be 100 µm shorter than the alignment-pins such that a PDMS membrane with a thickness of 100 µm was created at intended valve's positions, hence the gap between the casting-pins and the SU-8 patterns on the master determined the thickness of the PDMS membrane on the valve.

After curing the PDMS, the chip was separated from the master and casting-plate respectively, and placed on a glass substrate as shown in Figure 1 (c) and (d).

A PMMA valving-plate, which contains valving-pins, was micro milled using a 12 mm thick PMMA sheet. These pins were 50 µm smaller in diameter, and 200 µm longer than casting-pins, so that they can reach the bottom of the channel.

The pin-valve operation in principle relies on compressing the bulk PDMS as well as the valve membrane. Figure 1 (e) and (f) shows the principle of pin-valve operation. The diameter of the valve chamber must be 200 µm smaller than the diameter of the valving-pin, but can be wider or narrower than the flow channel.

Results

Characterization

A Y-channel device with an integrated pin-valve into one of the micro-channels, (Figure 2 a), was used for characterization and validation of the proposed pin-valve.

Micro-channels were fabricated with a width of 100 µm and a height of 100 µm. The two inlets of the micro-channels were injected with blue and red water-based dyes using a syringe pump which was set to provide a flow rate of 10 µl/min. The valved micro-channel was injected with blue dye and the other with red dye. Two joining micro-channels had similar hydraulic resistance, so that when the valve was open, fluid from each micro-channel occupied half of the outlet micro-channel. To control the valve a valving-plate (containing only one pin) was placed on the top of the valve which was actuated using a screw. By actuating the valve, the pin and subsequently the membrane were pushed down, which in turn precisely increased the hydrodynamic resistance of the micro-channel, eventually stopping the flow.

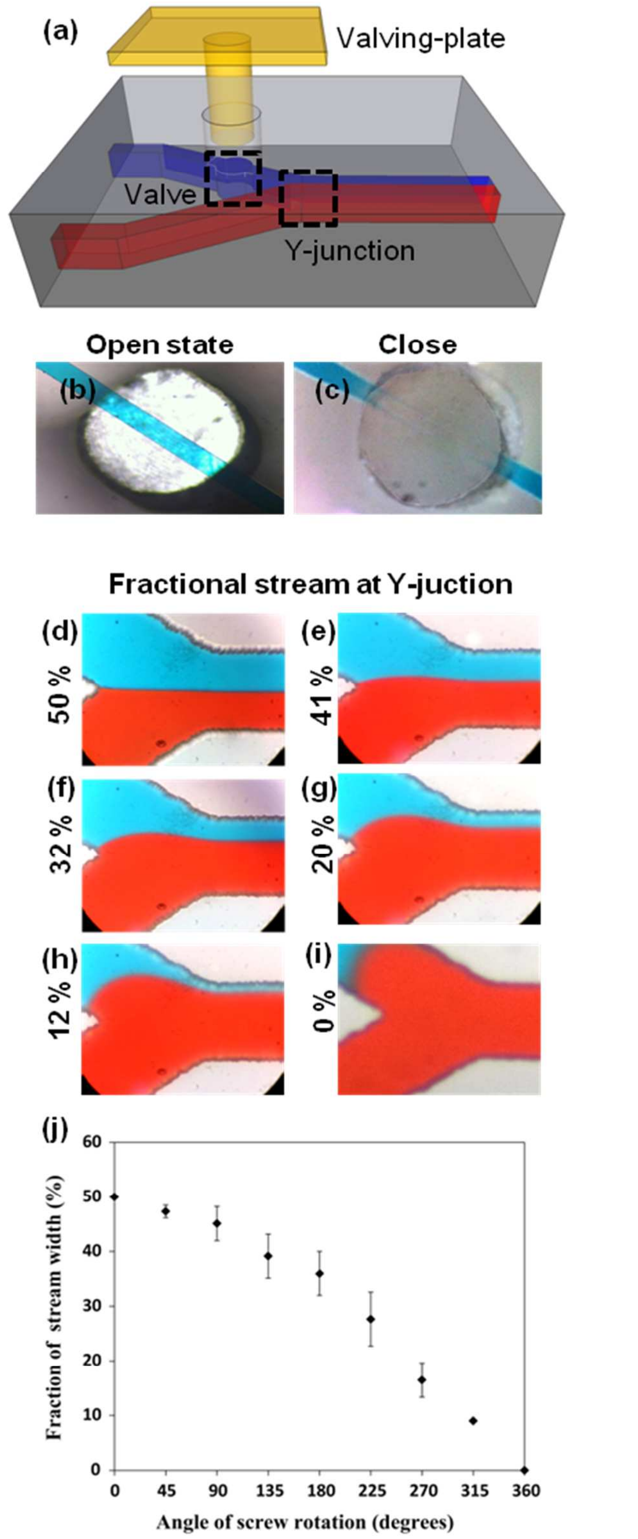

Figure 2 Pin-valve characterizations with a Y-channel device. (a) Schematic of the device with one pin-valve above one micro-channel. (b) Closed state of pin-valve (c) open state of the pin-valve after more than fifty times operation cycle. (d)-(i) Images of stream width based on the turning angle of screw (0, 90, 180, 270, 315 and 360 degrees clockwise). (j) behaviour of pin-valve by measuring the width of the blue stream in a Y-shaped microfluidic device. Reproducibility was tested by comparing the behaviour of the valve over 3 repeated operation cycles.

The partially closed state of the valve was characterized with the controlled pressing of the pin. The experiments were repeated 3 times to evaluate the consistency of the acquired result at each stage. Next, the valve was opened and closed sequentially for 50 times to evaluate the robustness of the valve when actively reconfigured. Finally, the input flow rate was increased from 1 µl/min up to 500 µl/min in increments of 50 µl/min with duration of 15 minutes for each step to determine the maximum operational flow rate for the valve.

Figure 2 (a) illustrates a Y-junction with an integrated pin-valve and valving-plate. Figures 2 (b) and (c) show the open and closed state of pin-valve, respectively. Figure 2 (d)-(i) show the optical microscopy images of the Y-junction.

The zero degree rotation of the screw corresponds to the fully open state of the valve in which half of outlet micro-channel was occupied with blue dye (50%), and 360 degree of rotation corresponds to the closed state of the valve in which the outlet channel was not contained any blue dye (0%). Figure 2 (e)-(h) present the partially closed states of the valve in which the fraction of blue dye from the outlet channel was 41%, 32%, 20%, 12%, respectively.

Figure 2 (j) plots the fraction of the outlet channel stream versus the rotation of the screw as a measurement of the pressure applied on the membrane. The error bars in Figure 2 (j) present the result of 3 repetitions of the experiment at each stage. There is an excellent agreement between the results of 3 repetitions.

We did not observe any failure or leakage during sustainability tests over 50 cycle of operation. Moreover, the valve endured the high flow rate of 500 µl/min.

The micro milled area of the PMMA casting-pins was smoothened by a second round of milling, improving the transparency of the cast PDMS, as shown in Figure 2 (b) and (c).

The footprint of our pin-valve is a circle with a diameter of 1 mm which is smaller than the screw valves (3.5 mm × 3.5 mm) and solenoid vales (10 mm × 10 mm) reported by Whiteside group [15], which allows a higher density of the valves on a single chip.

Hydrodynamic flow focusing (HFF) device using a single pump

Hydrodynamic focusing is a useful microfluidic technique that generates several independent tuneable flow streams in the same channel. Flow focussing devices control the width of each flow by adjusting the relative pressure of each stream introduced to the junction. This can be done directly using independent, positive pressure at the inlet of each stream. We have recently demonstrated that the relative pressure can also be configured by controlling the hydraulic resistance of the feeder channels when operated in a negative pressure configuration using a single pump at the outlet [21]. Each chip in our previous demonstration was of a fixed design, providing one particular stream width ratio. It would be advantageous to realise a similar chip but where the stream width ratio could be reconfigured.

If an asymmetric stream width ratio is desired, then asymmetric resistances are required on each of the feeder channels. However, this will also result in asymmetric drainage on each of the reservoirs and thus an imbalance in hydrostatic pressure will accumulate, perturbing the stream width ratio. Our previously published solution [21] was to adjust the foot print area

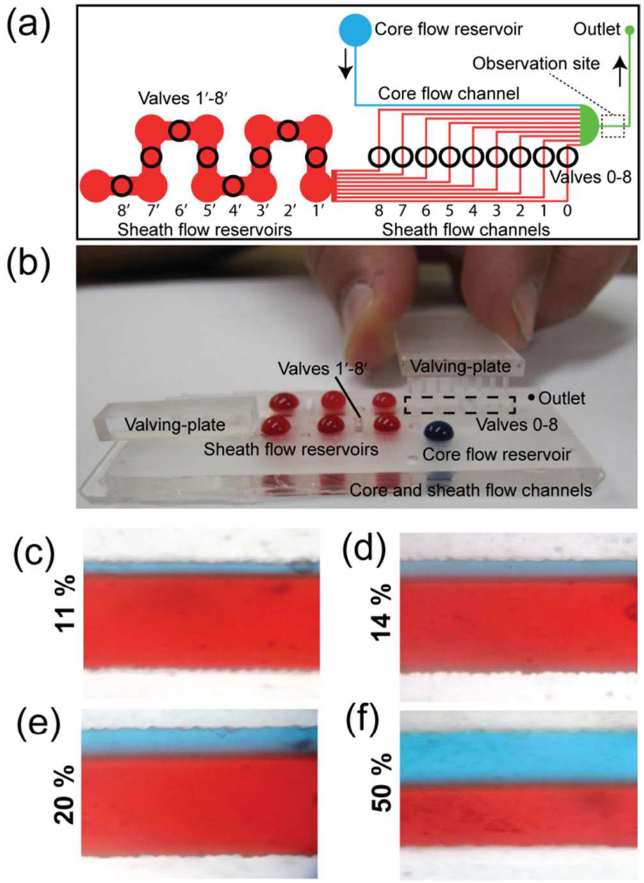

Figure 3 Hydrodynamic Flow Focusing (HFF) devices. (a) Illustration of the HFF system. (b) HFF System including two valving-pin, right: the valving-pin plate to configure hydraulic resistance, left: the valving-pin to set the right number of reservoirs in the circuit. (c)-(f) fraction variations of the blue color in output channel which are 11%, 14%, 20% and 50% for 1, 3, 5 and 8 valves are closed respectively.

of the reservoirs in inverse proportion to the feeder channel resistance so that the head height of the fluid was equal for the reservoirs of each of the streams throughout the experiment.

Hence, to achieve a reconfigurable and stable flow focussing device, it will be necessary to adjust both the resistance of the channels between the reservoirs and the junction and also the foot print area of the reservoirs. We propose that pin-valves could be used for both of these functions.

Figure 3 (a) presents a modified hydrodynamic flow focusing device. There are two streams indicated with blue and red. The blue stream is drawn from a simple reservoir and is connected to the junction using a simple channel of fixed resistance. The red stream is fed by a network of reservoirs and channels such that can be controlled by valves to enable its pressure to be varied. The red reservoir consists of nine wells, of identical volume to the blue reservoir, connected together in series by micro-channels at their base. Each of the micro-channels connecting the reservoirs had negligible resistance and could be opened or closed using a pin-valve. The network connecting the series of reservoirs to the junction for the red stream consisted of nine micro-channels arranged in parallel. Each of these nine channels was of the same length and cross-section as the channel feeding the blue stream and thus should have the same resistance. Each channel could be actuated with a pin-valve and thus the resistance of the network could be adjusted from that of a single channel (equal to the blue stream) down to 1/9 of the resistance. To ensure stable operation, it was ensured that the number of series reservoirs feeding the channels was number of open parallel channels and hence the drain rate was always the same for both blue and red streams.

The pin-valves in HFF device were operated in on/off mode only using a two valving-plate: one for all channel valves and another one for reservoirs valve. A distinct channel valving-plate is required for each of the considered configurations. Figure 3 (b) presents the HFF device and also the valving-plates.

To demonstrate the configurable hydrodynamic flow focusing, the series connected reservoirs were filled with red dye and the isolated reservoir was filled with blue dye. Fluid was withdrawn from the outlet using a syringe pump at a flow rate of 20 µl/min. Figure 3 (c)-(f) shows the junction between the two fluids with 8, 5, 3, and 1 open parallel channels, and an equal number of connected reservoirs on the red stream, respectively. It can be seen in Figure 3 (c)-(f) that the blue fluid occupies 11 µm (11%), 14 µm (14%), 20 µm (20%) and 50 µm (50%) of the 100 µm output micro-channel, respectively.

Conclusions

We have introduced pin-valve arrays as a new and convenient approach for valving complex microfluidic systems. The pin- simultaneously configuring numerous valves in either on/off mode or analogue (partially close) mode, which can be independently set for each micro-channel of the array. The system does not require external power sources to maintain its state and can be reconfigured from one state to another by simply replacing the valving-plate. The valves themselves have proven repeatable and reliable and can valve flow rates of 500 µl/min and remains close with no visible leak. Arrays of pin-valves have been successfully integrated in a microfluidic chip and a proof-of-concept reconfigurable flow focussing system has been demonstrated. Using this technique, an array of pin-valves can be operated using a single pin-plate. This means that increasing the number of valves will not increase the complexity of the actuation procedure. Although we have demonstrated the manual operation of the pin-valves, they can be readily automated using implementing a computer-controlled actuator.

The simple and inexpensive fabrication process and ease of use render the pin-valves good candidates for integration into micro total analysis system (µTAS). Pin-valves are in particular an excellent option for lab-on-a-chip systems in biological application with prolonged experiments, such as those involving cell culturing, since pin-valves do not need any peripheral equipment to operate as opposed to existing microvalve options such as pneumatic valves, solenoid valves and brail valves. For example, the fully self-contained pin-valve system could be easily transferred from an incubator to microscopy analysis station and the valving state could be easily reconfigured. Experimental exploration of the use of this system in such a microbiological context is currently underway.

Notes and references

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