Hindawi
Advances in Polymer Technology
Volume 2020, Article ID 2460212, 7 pages
https://doi.org/10.1155/2020/2460212

Research Article

Design and Fabrication of a PDMS-Based Manual Micro-Valve System for Microfluidic Applications

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Received 21 May 2019; Revised 19 August 2019; Accepted 6 November 2019; Published 12 January 2020

Academic Editor: Szczepan Zapotoczny

In this study, a manual micro-valve system (dimension: $w \times h$: $1000 \times 50\,\mu$m with 8-integrated channel valves was designed for controlling up to 8 different flows of agents (including magnetic nanoparticle flow) injected into the mixture zone of the microfluidics. The working parts of the micro-valve and microfluidic channel were fabricated from Poly(dimethyl siloxane) materials. The aperture of each channel valve was manually manipulated by a screw and a support kit (made of Plexiglas® materials). This valve system was connected to a microfluidic device with two important modules: a multi-liquid mixing component and a micro-reactor (~5 μL of volume). The study on controlling liquid flows proved that this valve system was effective for the experiments on the flow mixing and delivering the reactants into the micro-reaction chamber in order. The results are the first step for the fabrication of liquid flow controllers in integrated microfluidic systems towards biological analysis applications.

1. Introduction

Recently, the micro/nanofluidic devices are interested in biomedical and chemical analyses. The micro/nanofluidics with very small channels (μm size) have advantages such as: reducing the consumption of agents; increasing sensitivity thanks to small volume (micro/nano litter) with large surface-to-volume ratio [1, 2]. In addition, the development of nanotechnology and micro/nano electromechanical system (MEMS, NEMS) helps to easily fabricate and integrate microelectronic components and functionalized modules. Therefore, the development tendency of microfluidic system is design and fabrication of a "Lab-on-a-chip" model by integrating with functionalized modules such as sample mixers, micro-reactors, sensors, etc. [3–5]. These chips are studied and applied in biomedical (e.g., DNA, cell, and PCR analysis) or chemical analyses [6, 7], and they will be power tools for many analysis processing. However, each biomedical or chemical analysis is used to carry out with many chemicals or biological agents (e.g., solvents, buffer solution, biological agents, nanoparticles, etc); these agents are often introduced into a reactor, sequentially. Regarding a microfluidic system, the add-on devices connecting to the microfluidic needs to be miniaturized, and all agents are injected into micro-channels by micro-pumps; the sequence of flow needs to be controlled by a micro-valve system [8, 9].

Typical studies [9–11] on microfluidics reported that it was easy to control the on/off chip flows based on a valve structure. There are several commercial valve systems, e.g., the MUX WIRE system from Elveflow® company or LINEUP™ Series from Fluigent® company. These valves systems are professional but quite expensive. In the literature, some models of "Lab-made" valves were designed for controlling liquid flows of microfluidic system in laboratories [12, 13]. These valves were proved to be effective for controlling the flows in the microfluidic systems, and they had reasonable fabrication cost for end-users in laboratories. In generally, the microfluidic valves are used in some types of control structures: operating mechanics, pneumatic, electro-kinetic, phase changes, or introduction of external force [13]. The microfluidic valves can be classified by two main types of valve states: the active valves and the passive valves depending on mechanical or non-mechanical moving parts [14].

The poly(dimethyl siloxane)—PDMS is one of the most popular materials for fabricating microfluidic systems and others components such as control valves or pumps in laboratories [14]. Concerning the "Lab-made" cheap valves, Zhang [12] reported the hydraulic valve design (using PDMS materials). This valve was integrated fully in microfluidics as an internal part, and it was controlled by adjusting the pressure in a displacement chamber on the pneumatic layer via a computer-regulated solenoid [12]. Elizabeth Hulme [15] designed and fabricated screw, pneumatic and solenoid valves embedding directly into microfluidic devices. These valve systems were generated easily by a replica molding process and a PDMS rapid prototyping technique due to a soft lithography process [15]. The direction unit for the screws of these valves was made of cured epoxy that was filled on top of the PDMS slap to fix the screws. However, these valves do not work stably due to the deformation of the microchannels when the valve was screwed, directly interfering with the channels [16, 17]. Brett [9] designed and fabricated a manually actuated pin valve for controlling the fluid flow (on/off) within microfluidic channels [9]. This valve consisted of a simple pushing pin (a polydimethylsiloxane tip) and was integrated inside an inlet that connected to the microchannel. However, it cannot be separate from the microfluidic system, so that such valves are not reusable.

In this study, a valve was designed and fabricated as an individual part of a microfluidic system for different applications that needs the flows to be controlled. Besides, a specific multi-valve switch also has been designed and fabricated to manipulate flows that injects from syringe pumps into a multi-inlet channel. This switch is very useful to stop the flow, in order to change the injected liquids in the channel and to control the multi-flows during the operation of the microfluidic system. Different to the single inlet case, this design avoids the tube plugging/un-plugging actions causing a certain mechanical force. It is very important because the flow inside the channel is very sensitive with this force due to the small volume of the channels. Moreover, it has absolute precision and rapid response time during the operation progress, similar to expensive commercial products (e.g., the valve systems of Elveflow® or Fluigent®).

2. Materials and Equipment

The 2-inch silicon wafers were from The Institute of Electronic Materials Technology (ITME)—France. Poly(dimethyl siloxane) (PDMS) was in the Sylgard 184 Silicone Elastomer Kit, purchased from Dow Corning Corporation. PTFE tubes (0.8 mm ID) were supplied by Cole—Parmer. The photoresist SU-8 3050 was from MicroChem Corp. Teflon layer was a CYTOP® product (AGC Chemicals Company). Other chemicals were obtained from Sigma Aldrich Inc.

The fabrication processes were carried out in a clean room of The Nano and Energy Center (NEC)—VNU, Vietnam with a system consisting of: The OAI Model 800E Mask Aligner system for lithography process; and a Pico plasma cleaner system (Diener electronic GmbH) for the plasma treatment; all thermal treatments or bonding processes were performed in a MEMMERT heating and drying oven, and hot plates.

3. Results and Discussion

3.1. Design and Fabrication of the PDMS Manual Micro-Valve System

3.1.1. Description of the Manual-Controlled Valve System. The working principle of the valve is based on the mechanical structure (in Plexiglas® materials) and flexible materials (PDMS) as described in Figure 1.

The valve system has a working part including a microchannel and a thin film made of the PDMS material (Figures 1(a) and 1(b)). The PDMS film was fabricated with 100 μm thickness and bonded on top of the channel by a plasma technique. The microchannel was fabricated with dimensions of $W \times D \times L$: $1 \times 0.05 \times 10$ mm in PDMS *via* a soft lithography technique. The mechanical structure for opening and closing the flow of the valve was combined with two components: a screw (~3 mm of diameter, with 0.5 mm of thread pitch) is guided thanks to a threaded hole in Plexiglas slab fixing with second slab; a PDMS piece (~2.5 mm) is smaller than the screw hole and freely moves in this hole. The PDMS piece helps the screw head not crack the PDMS film during the working process.

Concerning the valve as shown in Figure 1(d), there are two main structures including PDMS and Plexiglas® parts. The PDMS part contained channels part (relevant to the channel valves) and an intermediate PDMS slab that had several holes with diameter the same as that of the screws. They were located onto the top of each channel-valve position. The two mechanical structures were fabricated using Plexiglas® material, including: the first part was designed with threaded array holes (as described above); the second part was a bottom support that combined with the first part (as a clamp) to fix all structures of the valve system.

3.1.2. Fabrication of the Manual-Controlled Valve. Firstly, the channel valve (PDMS material) was prepared by using the SU-8 master mold in the clean room. The SU-8 master mold of the channel valves was fabricated on a silicon wafer by the soft lithography technique. A 50-μm thick layer of the photoresist SU-8 3050 was spin-coated in two steps onto the silicon wafer (2 inches). The first spin step was at 500 rpm speed for 5–10 s with an acceleration of 100 rpm/s; the second spin step was at 3000-rpm speed for 30 s with an acceleration of 300 rpm/s. After the spin coating, the photoresist layer was soft-baked on a hotplate at 95°C for 15 min (a). Then it was exposed in UV radiation (with a transparent mask) at 250 mJ/cm^2 of power (b). After that, it was taken for a post bake at 65°C for 1 min, and at 95°C for 5 min. The development process was achieved by a SU-8 developer solution for 5 min. Finally, the mold was rinsed with isopropanol and dried in a nitrogen flow (c).

Secondly, the PDMS valve channels were fabricated by replica molding and the PDMS rapid prototyping technique

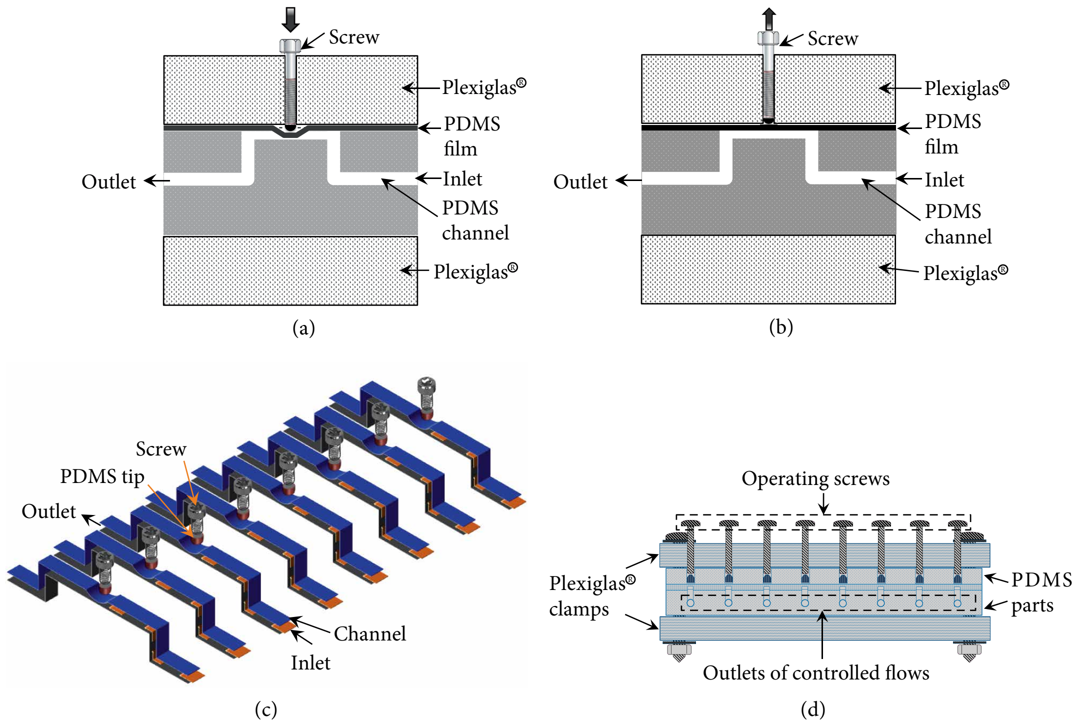

FIGURE 1: Design of the multi-valve system for controlling the inlet flows into microfluidic system. (a) and (b) The cross sections of valves switch (at one flow controlling); (c) and (d) the multi-flow controlling arrangement and construction.

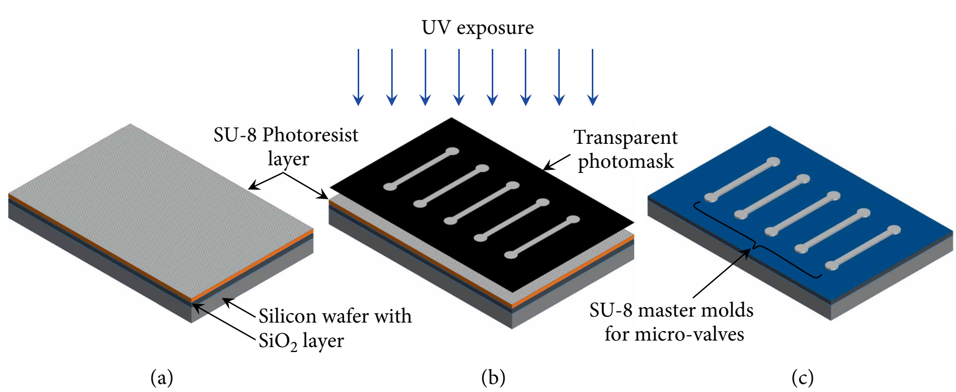

FIGURE 2: Fabrication of the SU-8 mold for valve channels. (a) Prepare a SU-8 photoresist layer on a 2-inch silicon wafer; (b) UV-exposure with a transparent mask; (c) a SU-8 master mold obtained after the final step.

[18]. The fabrication process was performed as follows: *Step 1.* The fresh PDMS was prepared by mixing uniformly two components: silicone elastomer base and curing agent at a ratio of 10 : 1 (wt./wt.). After mixing, the mixture was degassed in a vacuum chamber. Then, fresh PDMS was poured onto the mold (from Figure 2(c)), and cured at 90°C for 1 h or at 75°C for 2 h (Figure 3(a)); *Step 2.* The embossed channel was carefully released from the SU-8 mold (Figure 3(b)) and cut in a suitable shape; *Step 3.* Inlets and outlets of channels were drilled directly by PDMS tool kits (Figure 3(c)); In the last step (4), the valve channels were bonded to a 20-μm thick PDMS layer to close them. This PDMS layer was obtained by spin-coating the fresh PDMS (10 : 1 ratio) onto a silicon wafer with a certain 5 μm-thick of Teflon-coated layer (prepared by using the CYTOP® product (AGC Chemicals Company)) in order to easily peel off. Then, this PDMS layer was cured in an oven at 75°C for 1 h. The bond of PDMS valve channels to the PDMS layer was carried out by using oxygen plasma treatment in 1 min. The bonding step was taken by thermal treatment at 75°C for 1 hour. This bond was irreversible bonding.

3.1.3. Fabrication of Plexiglas® Clamps and Its Assemblage with the Valve System. Two clamps (Plexiglas® materials) of the valve were fabricated by the CNC (computerized numerical control) technique. The design of these clamps, with parameters of $W \times D \times L$: $3.5 \times 0.8 \times 7$ cm, is shown in Figure 4. One pair of clamps included a bottom support, Figure 4(b), and a top support that were used for operating

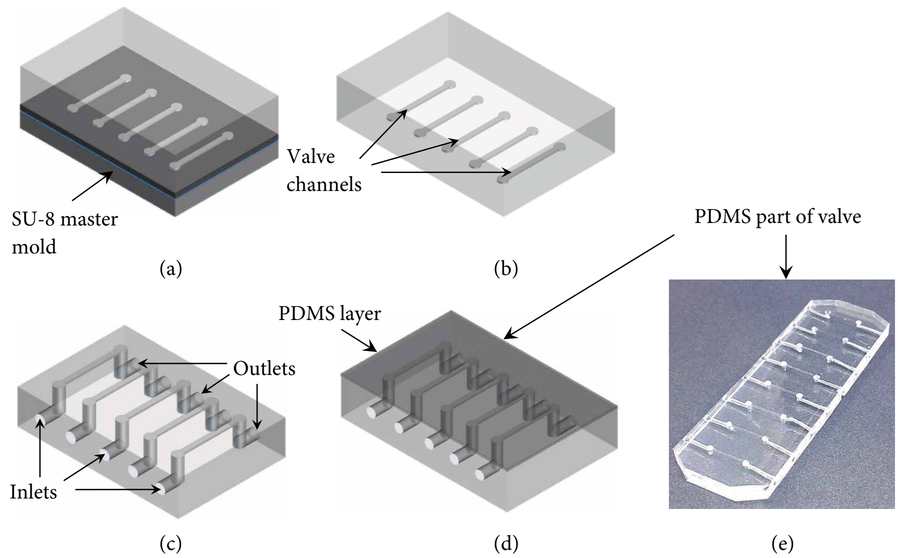

FIGURE 3: Fabrication of PDMS parts by rapid prototyping technique. (a) Pouring fresh PDMS on SU-8 mold; (b) Releasing PDMS channel from SU-8 mold after curing; (c) Making inlets and outlets of channel by PDMS tool kits; (d) Bonding a PDMS film on top of valve channel; (e) PDMS part of the valve.

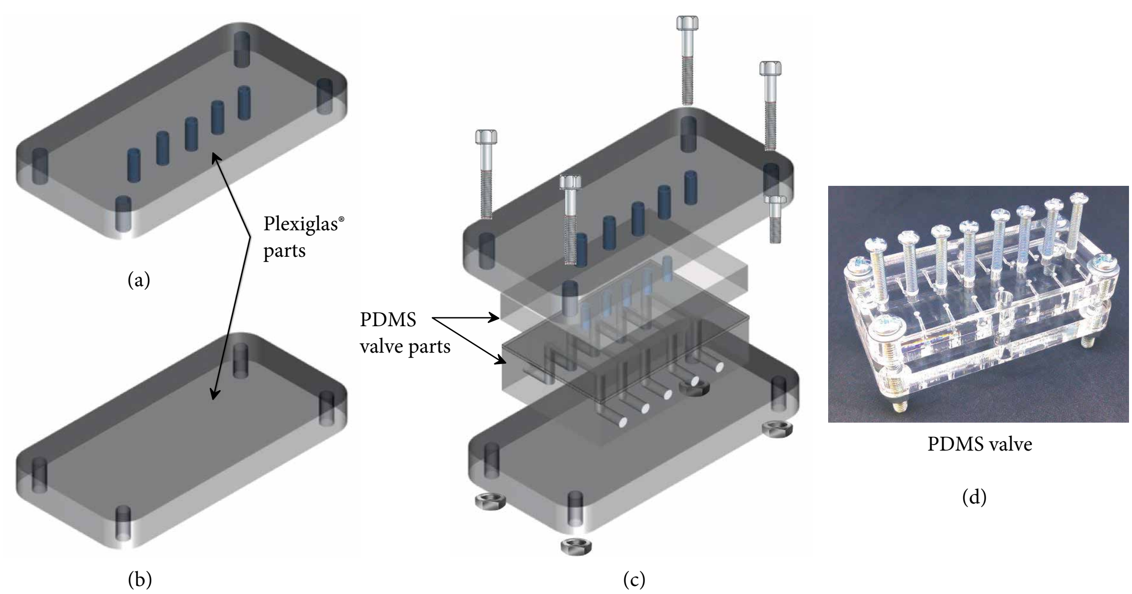

FIGURE 4: Description of the Plexiglas clamp design and the assemblage of the valve system. (a) and (b) Top and bottom support, respectively; (c) Assemblage of PDMS valve channels to Plexiglas clamps. (d) Final PDMS valve.

screws to generate a force on the PDMS layer Figure 4(a). The assemblage of the PDMS valve channels and clamp parts was shown in Figure 4(c). Four screws were used to fix the PDMS parts (including valve channels and PDMS support slap) by two clamps. These screws need to be fixed tightly enough to avoid blocking the channel valve.

3.2. Test of Controlling the Liquid Flow in the Microfluidic Device. The manual-controlled valve system was connected to a microfluidic system with multi-inlets for mixing purpose. The experimental setup for testing the liquid flows is shown in Figure 5.

The valve system was connected to micro-syringe pumps and microfluidics via PTFE tubes (0.8 mm ID). The valve was tested for the mixing process using three liquid flows (Figure 6): two solutions of methylene blue (1st and 3rd flow) and DI water (the 2nd flow at the middle). The microfluidics was designed with multi-inlets and outlets that can be used for performing ELISA (The Enzyme-Linked Immunosorbent Assay) experiments.

Firstly, the three syringe pumps were set at the maximum flow rate of 150 μL/min to inject the liquids into the microchannels through the multi-controlled valves. Secondly, the three flows were controlled by setting the level of releasing or closing screws in three different modes (Table 1).

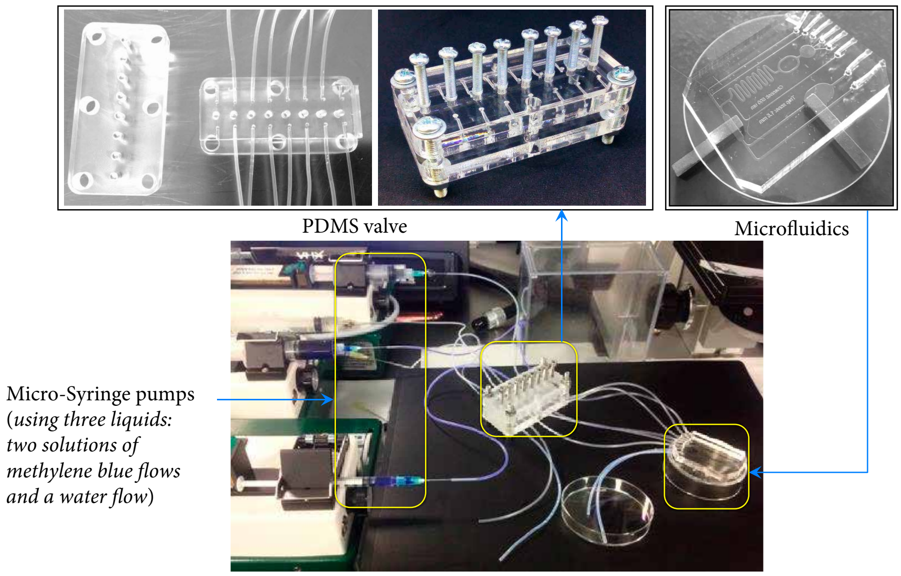

FIGURE 5: The experimental setup of multi-controlled valve connecting to microfluidic system and micro-syringe pumps.

TABLE 1: Data of operation modes in mixing process experiments.

Working mode	Flow 1 (Methylene blue) (μL/min)	Flow 2 (DI water) (μL/min)	Flow 3 (Methylene blue) (μL/min)
Mode 1	150	150	From 150 to 0
Mode 2	150	From 150 to 0	From 150 to 0
Mode 3	From 150 to 0	150	150

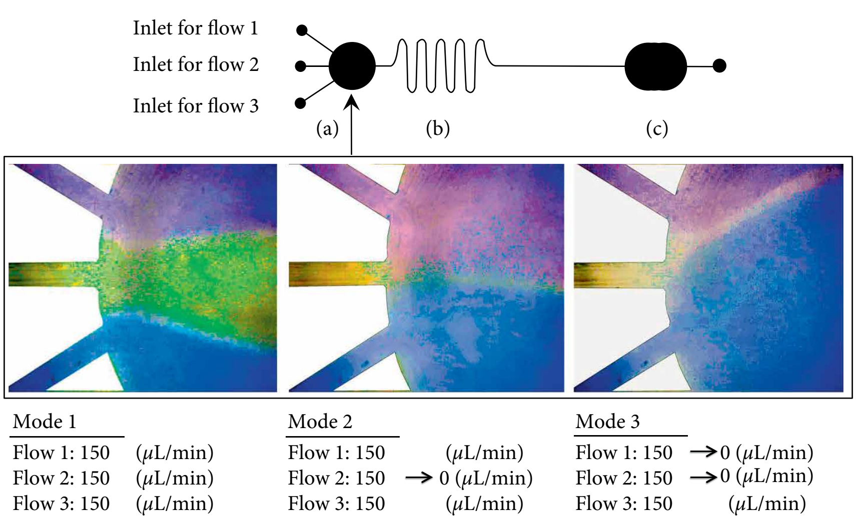

FIGURE 6: Test results of the mixing process of three liquid flows: two methylene blue solutions and DI water. Microfluidics: (a, b) the mixing module, and (c) the reservoir.

(i) *Mode 1:* three flows were opened at the maximum flow rate.

(ii) *Mode 2:* the 1st and 3rd flows (methylene blue solution) were opened at the maximum flow rate, the 2nd one (DI water) was reduced from 150 to 0 (μL/min).

(iii) *Mode 3:* the 1st and 2nd flows were reduced from 150 to 0 (μL/min); the 3rd one was opened at the maximum flow rate.

The results of controlling the fluid flows by the valve with the purpose of mixing the liquid in the microchannels are shown in Figure 6.

By using the valve, the process inside the channels could be controlled thanks to either the stop-flow mode or the continuous-flow mode. It is very effective to perform a complex analysis working with multi-liquid flows that needs to be controlled (e.g., ELISA immunoassay in microfluidic system). In

Table 2: Results of studying effect of screw operation on liquid volume at outlet of microfluidics.

Turn number of screw in closing trip, (n)	Flow rate (μL/min)	Liquid volume, V, (μL)	Percentage (%)
0	250	245	98
1/2	250	130	52
1	250	70	28
1 1/2	250	25	10
2	250	~0	0
3	250	~0	0

addition, the stability of the flow inside the channel was very sensitive with small actions such as plugging/un-plugging the tubes to replace liquids in each step of the experiment. Therefore, the control of the injected flows became easy and smooth by the multi-controlled valve system.

The stability and durability of the valve system were verified *via* several experiments of the mixing process in the microfluidic system. It was indicated that the valve system could work stably for hundreds of times of the opening/closing cycles. This valve achieved durable levels thanks to the stability and elasticity of the PDMS film. The responding time and stability of the liquid flows during the controlling process were proved to be in good control characteristics such as: the responding time was about 1-2 s; the liquid flow was controlled flexibly in open/close task or the flow rate adjustment task.

To study the operation of the valve in adjusting the flow rate of the liquid that was injected into the microfluidic system, we connected an outlet of the valve to an inlet of the microfluidic channel (width × height: 1000 × 50 μm). Then, a flow of DI water with the flow rate of 250 μL/min was injected into the channel through the channel valve by the micro-syringe pump. The opening/closing level of the valve was defined by twisting the screw with a screwdriver. The turn number of the screw (n) was corresponded to liquid volume (V) that flowed through the microfluidic channel. The liquid volume (V) was measured at the outlet of the microfluidic channel thanks to the micro-syringe (from KLOEHN Inc.) in 1 min. The results are shown in Table 2, which was obtained by averaging the data of 10–15 experiments. The average data were approximate values because the PDMS channel was flexible and/or the channel could be deformed by the force of screwing level.

As shown in Figure 7, when the screw was twisted to close the channel, the PDMS piece on top of the channel was turned down and pushed the PDMS layer to block the channel.

Although the microchannel was only 50 μm high, this channel was completely closed as the screw had to be twisted up to 2 turns corresponding to about 1 mm of distance of the screw moving down (because the thread pitch of this screw was 0.5 mm). The correlation of open/close state of the valve and the turn number of the screw was not regular because the PDMS structures (an elastic polymer) of the valve actuator (Figure 7) were deformed when there was a force that acted on the PDMS parts in the adjusting process of the screw.

As seen in Table 2, the valve was closed after two turns of the screw. When the microfluidic system needed to work at a certain flow rate, the micro-syringe pump should be fixed at that rate rather than adjusting the open/close level of the valve system. At this running mode, it is recommended that the valve system should work at full opening mode or full closing mode.

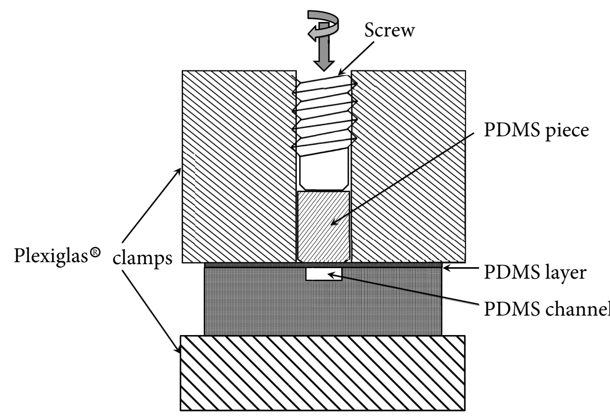

Figure 7: Actuator structure of the valve.

4. Conclusions

The "lab-made" manual micro-valve system was designed and fabricated successfully by the micro-fabrication technique. This valve consisted of two main components: Plexiglas® clamps and PDMS complex structures. The Plexiglas® clamps contained an array of screws for controlling the level of opening/closing flows. The PDMS component included an important PDMS film as the actuator part, and this film was fabricated easily in the step of closing valve channel. Significantly, the valve system was fabricated as a separated device, and easily connected to microfluidic system by tubes. The valves operated uniformly and performed reproducibly with repeated use in the mixing process experiments.

The valve system is compatible with multi modes of the operation, but it is recommended to use in fully opening/closing mode of the flow. The range of controlling the liquid flows depends on applications of the microfluidic system. It can be adjusted by changing the size of the channel valve. The valve system is also inexpensive because of the low costs of materials: Plexiglas clamps, general machine screw, PDMS, etc.

Data Availability

The data used to support the findings of this study are included within the article.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Acknowledgments

This research was financially supported by the Vietnam National Foundation for Science and Technology Development (NAFOSTED); code: 104.99-2018.357. The authors are grateful to Prof. Elisabeth Dufour-Gergam, and to other members of the "MicroSystems and NanoBiofluidics" Department, The Center for Nanosciences and Nanotechnologies (C2N), University Paris-Saclay in some experimental works.

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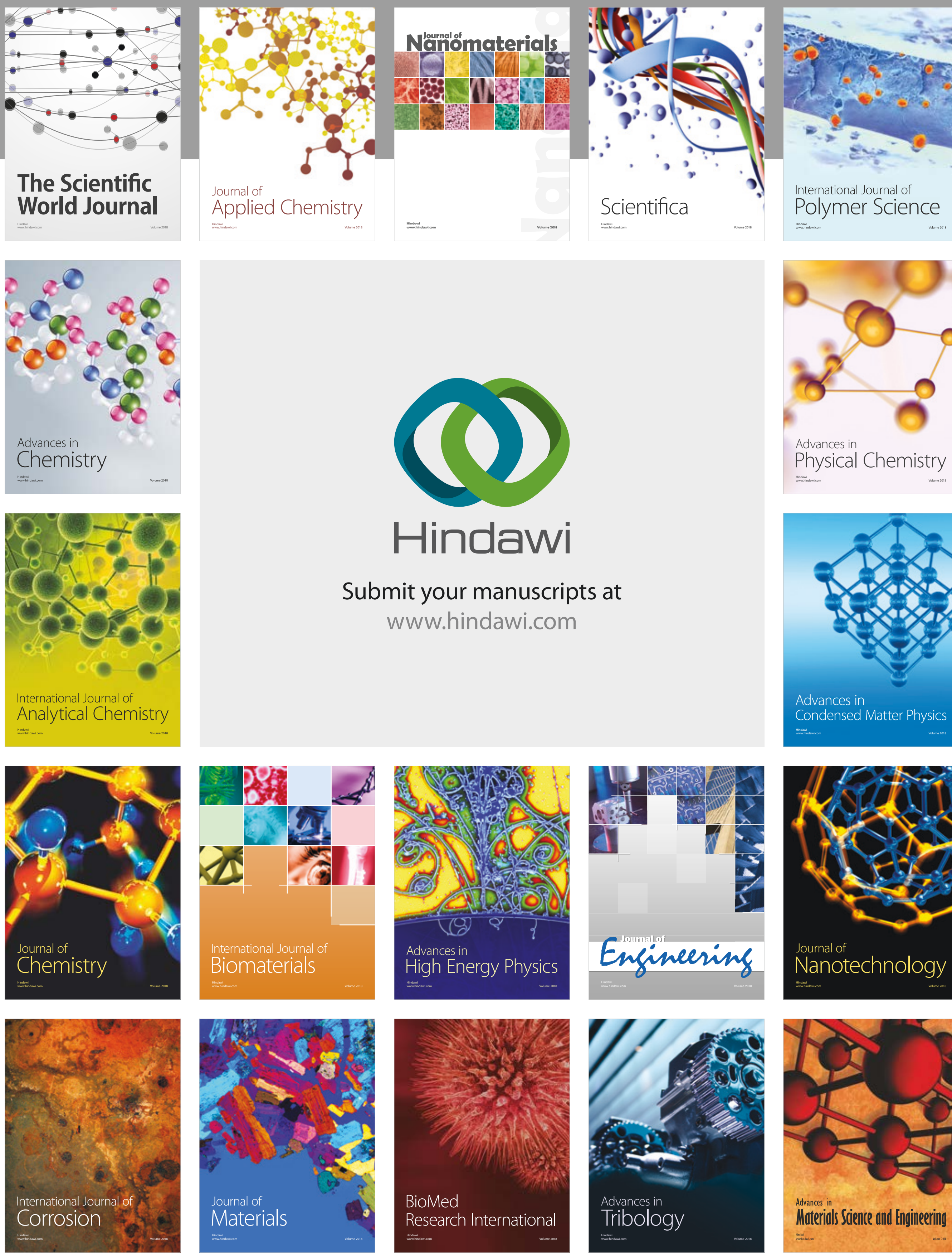
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