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Design and Fabrication of Integrated Passive Valves and Pumps for Flexible Polymer 3-Dimensional Microfluidic Systems

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Abstract. **This paper describes the fabrication of flexible, polymeric 3-dimensional microfluidic systems with integrated check valves (flap and diaphragm valves) and a pump by stacking patterned poly(dimethylsiloxane) (PDMS) layers containing microchannels and vias. We describe this procedure for fabricating, manipulating, and bonding of PDMS membranes and bas-relief plates into multilayer microfluidic devices. The fabrication and demonstration of integrated check valves and a pump in a prototype polymer 3-dimensional microfluidic system is a step toward practical realization of all-polymer, flexible, low-cost, disposable microfluidic devices for biochemical applications.**

Key Words. microfluidics, valves, PDMS

1. Introduction

Recent developments in microfluidic systems have been motivated in large part by the possibility of fabricating compact, integrated devices for genomic analysis, diagnosis, sensing, and other analytical functions (Manz et al., 1990, 1993, 1997; Harrison et al., 1993; Kopp et al., 1998; Kopp et al., 1997; Jacobson et al., 1998; Hadd et al., 1997; Simpson et al., 1998; Woolley and Mathies, 1995; Woolley et al., 1998). These systems are based on microfluidic components such as pumps, valves, and mixers; most have been fabricated in silicon, glass, and other materials adapted from the semiconductor industry (Kovacs, 1998; Elwenspoek et al., 1994; Gass et al., 1993; Gravesen et al., 1993; Schomburg et al., 1993; Shoji and Esachi, 1994; Verpoorte et al., 1994). Although a number of microfluidic devices have been demonstrated in these materials with impressive functionality, they are intrinsically expensive and mechanically fragile: these systems are also susceptible to malfunction when used with fluids containing suspend particles (e.g., blood) (Duffy et al., 1999). Inexpensive, rugged devices that can handle cells or fluids containing particles would facilitate microchemical analysis.

Several methods for controlling flow of liquids in microfluidic channels have been reported. Of these electroosmotic flow (EOF) has received the most attention. EOF has several features that make it an attractive option for miniaturized systems; it is, however, sensitive to the physicochemical properties of fluids being pumped—ionic strength, pH, and ionic composition—and to the presence of charged macromolecules in the fluid. Electroosmotic flow is also unable to pump liquids at high flow rates in wider channels—a capability that is needed for some microfluidic applications, e.g., sample preparation. Miniaturization of mechanical components for liquid handling—especially pumps and valves—have been technically problematic, and have spurred the development of microfabricated CE systems using EOF.

Microfluidic systems would benefit from the availability of new components, fabrication methods, and materials for appropriate pumps, valves, and mixing elements to manipulate fluids. Polymers are an attractive class of material for fabricating microfluidic systems. Our work has focused on elastomeric polymers for a number of reasons, including the fact that they suggest new approaches to pumps and valves. Microvalves based on flexible materials have been described (Elwenspoek et al., 1998; Young et al., 1999); these, however, were a small component of large, rigid Si-based devices.

We have developed a method for rapidly prototyping microfluidic systems in polydimethylsiloxane (PDMS) as an alternative to Si- and glass-based systems. We have demonstrated a micro-capillary electrophoresis (μCE) system (Duffy et al., 1998; McDonald et al., 2000). We and others have demonstrated substantially more sophisticated devices fabricated in PDMS (Anderson et al., 2000; Chiu et al., 2000; Jo and Beebe, 1999; Jo et al., 2000). The advantages of PDMS-based microfluidic systems are: (a) fabrication is straightforward, and patterned layers can be stacked to make multi-level channel structures, (b) rapid prototyping makes optimization of designs rapid, and (c) the PDMS-based microfluidic devices have the potential to be produced at low cost.

This paper describes the design and fabrication of new components—specifically passive valves and pumps—for microfluidic devices fabricated entirely using PDMS. These microvalves and pumps have small footprints, and low costs; they are simple to fabricate. The procedure for their fabrication includes, aligning, stacking, and bonding patterned membranes of PDMS to form interconnected 3-dimensional microchannels. We have demonstrated these fabrication techniques by constructing two related but distinct kinds of check valves (flap and diaphragm), and a pump that uses these valves.

2. Experimental

Rapid prototyping method was used for the design and fabrication of the microvalves and pumps. First, high-resolution transparencies were produced from a CAD file containing the design of microchannels and valves. These transparencies were used as masks in transferring the pattern into negative photoresist by conventional photolithography, yielding a master with positive relief of microchannels.

The microvalves were made from two molded PDMS bas-relief plates and a membrane. The parts were fabricated separately and later assembled to complete the device. Figure 1 shows the diagram of the fabrication steps. First, the PDMS bas-relief plate was fabricated by replica molding against the master (step a) using previously published procedures (Duffy et al., 1998; Xia and Whitesides, 1998).

Thin PDMS membrane was fabricated (step b) by casting and curing the PDMS prepolymer between a master and a Teflon sheet (1 mm thick Teflon FEP, DuPont, DE). Modest pressure (1 lb/in^2) was applied to the Teflon/PDMS/master sandwich while curing to squeeze out excess PDMS prepolymer. The PDMS membranes were 25–100 μm thick, as thick as the negative resist (SU-8, MicroChem, MA) used in making the master. Master with photoresist posts, as shown in the figure, was used to obtain PDMS membranes with through-holes. Prior to use, the Teflon sheet was molded against a flat Si wafer surface at 300°C ($T_g = 270$°C) to obtain a smooth surface.

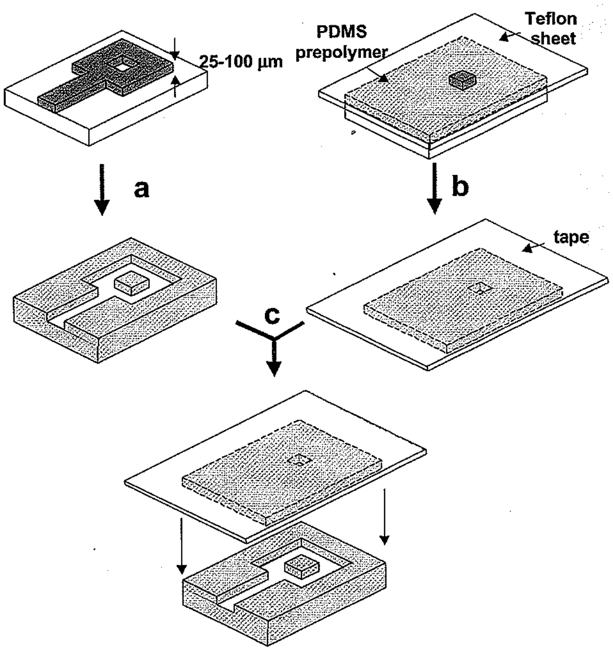

Fig. 1. *Schematic describing the process used for fabricating valves: (a) The bas-relief plate was made by replica molding against a master consisting of photolithographically patterned negative photoresist on a silicon wafer. (b) The PDMS membrane was fabricated by curing the prepolymer between a Teflon plate and the Si master while applying modest pressure; the membrane was then lifted from the Si master using an adhesive tape. (c) The individual pieces were aligned and bonded to form the final device.*

After curing, the Teflon sheet was removed to leave behind the PDMS membrane attached to the master. A pressure sensitive adhesive (PSA, Furon M803 adhesive tape with silicone adhesive on polyester backing, Furon, CT) was applied on the PDMS membrane. Due to stronger adhesion between PSA to PDMS than compared to that of PDMS to master, it was possible to transfer the membrane from the master to the PSA by peeling the tape away from master. The membrane, once transferred onto a PSA tape, could be handled without distortion. The PSA tape could be removed by applying appropriate solvents (acetone or ethanol) after manipulation.

The PSA/PDMS membrane was placed in an aligner and bonded with PDMS bas-relief plate to form the lower part of the valve (step c). The aligner was constructed from a set of *x*–*y*–*z* micrometer stages mounted on a translation post. The patterned PDMS membranes (supported on tape or master) and bas-relief plates were placed on the top and bottom micrometer stages and aligned using a stereo microscope. Irreversible bonding of the PDMS pieces was achieved by surface modification by oxygen plasma treatment as described previously (Duffy et al., 1998). After alignment, the assembly containing the aligner and the PDMS pieces were placed in oxygen plasma (Harrick, PA) for 30 seconds (60 W, 200 mTorr). The PDMS pieces were brought into contact immediately after they were removed from the plasma generator. Complete, functional valves were fabricated by repeating step c with another bas-relief plate that form the top channel.

3. *Results and Discussion*

The integrated microvalves were fabricated by assembling two prefabricated PDMS bas-relief plates and a membrane. Figure 2a shows the PDMS pieces that make up a diaphragm valve. The top and bottom bas-relief plates contained the network of microchannels and the top and bottom pieces for the valves. Figure 2b illustrates the principle of operation of the diaphragm check valve which takes advantage of the relatively easy deflection of the thin (25–100 µm) PDMS membrane with slight difference in pressure. The valve was designed such that the membrane could deflect in one direction to allow flow; flow in the opposite direction is inhibited by the presence of a barrier that blocks the deflection of the membrane. A micrograph of the diaphragm valve is shown in Figure 2c.

Figure 3 shows the PDMS structures used to fabricate a flap valve, and a micrograph of a functional valve. It operates in a manner similar to that of the diaphragm valve in that the flap, instead of a diaphragm, can be deformed in only one direction. Figure 3b illustrates the detailed working of the valve.

The diaphragm valves were tested for long-term operation using an external three-way electromechanical valve (Lee Valve, Westbrook, CT) connected to a pressurized air source (functionality of the valves were tested with liquids before and after long-term testing with pressurized air). The inlet of the PDMS microvalve was connected to the electromechanical valve which pressurized and vented the valve at ~ 10 Hz. The outlet of the valve was submerged in a water bath and the generation of a bubble with each opening and closing were monitored. The PDMS diaphragm valves were tested continuously for 10^5 openings and closings. The valves did not show any marked deterioration and were fully functional when tested with fluids (water).

Both the diaphragm and flap valves were still fully functional when tested after storing them for six months in the open laboratory. Only the valves that had dried solids around the membrane that could not be removed were not functional. The ones with particle/deposit that were washed and cleaned functioned without any problems.

Unlike the Si-based microvalves that are difficult to miniaturize due to limitations in materials properties, we believe that the PDMS microvalves can be miniaturized further to approximately 100 µm using present fabrication procedure (with slight change in valve characteristics). Some of the factors that will limit miniaturization of the valves below 100 µm are: (a) differential shrinkage of the membranes compared to the PDMS plates and (b) accuracy in alignment of plates to membranes (we can align to ± 10 µm routinely; but new techniques are needed beyond that point).

An integrated pressure-drive pump was fabricated using the process described earlier for the microvalves, Figure 4. The pump consists of a reservoir that is connected to two sets of check valves which open in opposite directions. Figure 4a shows the pump before it

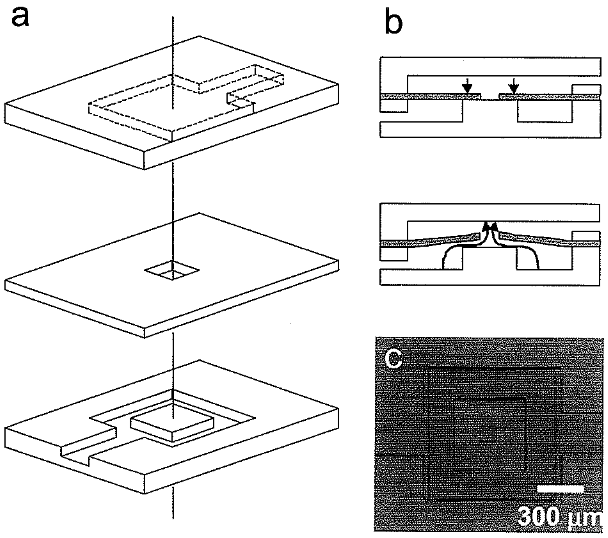

Fig. 2. Illustration of PDMS diaphragm valve: (a) Simplified representation of the passive diaphragm valve. The valve was fabricated by stacking and bonding two pieces of PDMS base-relief plates with a PDMS membrane: (a) Operational principle of the diaphragm valve. (c) Optical micrograph of the diaphragm valve.

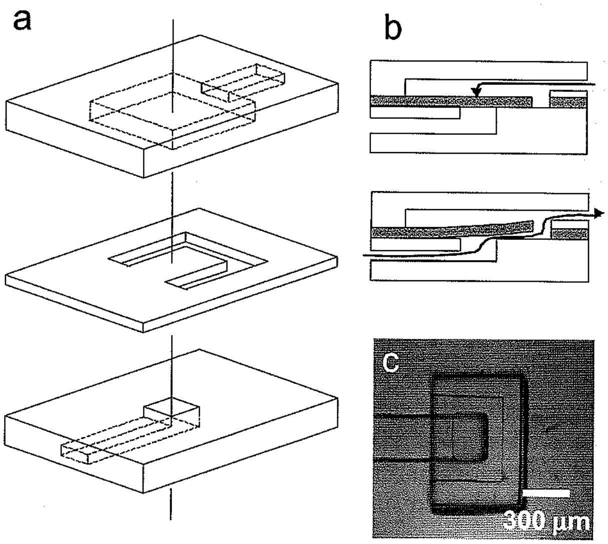

Fig. 3. Illustration of PDMS flap valve: (a) Simplified representation of the passive flap valve. The valve was fabricated by stacking and bonding two pieces of PDMS base-relief plates with a PDMS membrane. (b) Operational principle of the flap valve. (c) Optical micrograph of the flap valve.

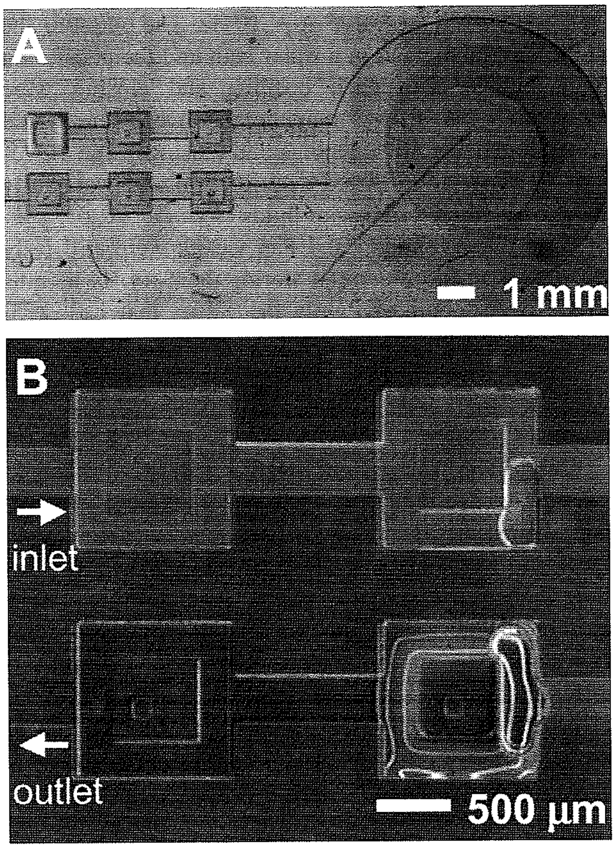

Fig. 4. *Optical micrograph of an integrated pump with a series of diaphragm microvalves. Photograph taken (a) before filling the pump with fluorescein and (b) while the fluorescein was being pumped.*

was filled with liquid (fluorescein). The reservoir on the right side of the picture is the elastomeric diaphragm that was actuated by finger pressure to pump the liquid. The series of three valves on the top microfluidic channel were designed such that they open toward the reservoir (inlet valves). Meanwhile, the valves on the bottom channel were designed to open away from the reservoir (outlet valves).

Actuation of the reservoir by applying a pressure result in the decrease in reservoir chamber volume (pump mode), forcing the fluid out through the outlet valves. When the pressure was released, due to the elastomeric nature of PDMS, the membrane returned to the original position (supply mode) thereby increasing the reservoir chamber volume back to original level and drawing the fluid into the reservoir through the inlet valves.

The size of the reservoir can be varied to change the pumping speed. Furthermore, valve design parameters such as flap/diaphragm size, thickness of the PDMS membrane, and others can be changed to adjust both the valves' and pump's operating characteristics.

4. Conclusions

The procedures described here make the fabrication of flap and diaphragm valves in PDMS straightforward. An integrated pressure-driven pump is fabricated by connecting the elastomeric diaphragm with a series of check valves. The valves and pump were functional after long-term storage (6 months) and repeated uses (10^5 openings and closings). Although flapper valves have been demonstrated in Si-based microfluidic systems, the high modulus of Si makes the miniaturization of these valves ($\sim 1\,\mathrm{mm} \times 1\,\mathrm{mm}$) difficult. In contrast, the elastomeric nature of PDMS make further miniaturization of valves ($\sim 100\,\mu\mathrm{m} \times 100\,\mu\mathrm{m}$) possible. The PDMS microvalves and pump described here can be used in pressure-driven microfluidic applications where electroosmotic pumping is not feasible. The PDMS-based microfluidic system is a low-cost technology with simple fabrication that can be used in manufacturing polymeric microfluidic devices for disposable diagnostic and drug screening applications.

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