Teflon films for chemically-inert microfluidic valves and pumps†‡

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We present a simple method for fabricating chemically-inert Teflon microfluidic valves and pumps in glass microfluidic devices. These structures are modeled after monolithic membrane valves and pumps that utilize a featureless polydimethylsiloxane (PDMS) membrane bonded between two etched glass wafers. The limited chemical compatibility of PDMS has necessitated research into alternative materials for microfluidic devices. Previous work has shown that spin-coated amorphous fluoropolymers and Teflon-fluoropolymer laminates can be fabricated and substituted for PDMS in monolithic membrane valves and pumps for space flight applications. However, the complex process for fabricating these spin-coated Teflon films and laminates may preclude their use in many research and manufacturing contexts. As an alternative, we show that commercially-available fluorinated ethylene-propylene (FEP) Teflon films can be used to fabricate chemically-inert monolithic membrane valves and pumps in glass microfluidic devices. The FEP Teflon valves and pumps presented here are simple to fabricate, function similarly to their PDMS counterparts, maintain their performance over extended use, and are resistant to virtually all chemicals. These structures should facilitate lab-on-a-chip research involving a vast array of chemistries that are incompatible with native PDMS microfluidic devices.

1. Introduction

Like transistors in electronic microprocessors, microfluidic valves and pumps are the fundamental elements of logic and control in many lab-on-a-chip devices.[1] Flexible elastomers make good candidates for the moving parts in valves and pumps, and elastomers like polydimethylsiloxane (PDMS) have found widespread use in a variety of normally-open[2] and normally-closed[3–5] microfluidic valves. Unfortunately, the limited chemical compatibility of PDMS has complicated its use in many microfluidic applications. Many chemicals commonly used in organic synthesis readily swell PDMS devices or dissolve PDMS oligomers from the elastomer.[6] Small hydrophobic molecules readily partition into and out of bulk PDMS, complicating the determination of their on-chip concentration.[7] Some reusable glass microfluidic devices must be equipped with removable, disposable valves because the PDMS valves would be destroyed by the harsh acid used to clean the device before reuse.[8,9] For these reasons, a large variety of interesting and useful chemistries may be unsuitable for use in native PDMS devices.

Various strategies for mitigating the problems associated with PDMS have been introduced. A variety of surface treatments for PDMS have been proposed.[10] These treatments are mostly aimed at reducing unwanted adsorption of analytes onto the PDMS surface or functionalizing the surface with chemical groups, not improving the resistance of the bulk PDMS to solvents or harsh chemicals. Recently, Rolland *et al.* presented a photocurable crosslinked perfluoropolyether (PFPE) that can be used in place of PDMS to form soft-lithography devices containing valves and pumps.[11] This remarkable fluorinated elastomer has already been used in applications as diverse as synthesizing DNA oligonucleotides[12] and casting nanoscale replicas of viruses.[13] However, the chemical inertness of a fluoropolymer is ultimately a function of the degree to which it is fluorinated, with the most inert fluorocarbons (like polytetrafluoroethylene or PTFE Teflon) comprised entirely of carbon and fluorine.[14] Unfluorinated organic moieties in PFPE that participate in polymerization also render the final elastomer more susceptible to chemical attack: chloroform, pyridine, 96% sulfuric acid, and trichloroethylene all cause discoloration or spots on the PFPE elastomer surface and swell bulk PFPE between 5.2% and 10.3% after seven days.[15] These are common chemicals that have essentially no detectable effect on fully-fluorinated fluorocarbons like PTFE.[14] So while PFPE is a versatile material that offers significantly better chemical compatibility than PDMS, the "holy grail" of elastomers that combines the moldable nature and ease of use of PDMS with the chemical resistance of PTFE remains elusive.

An alternative approach to making chemically-inert microfluidic valves and pumps involves using *existing non-elastomeric* fluorocarbons similar to PTFE Teflon. Unlike PDMS or PFPE, these materials cannot be easily molded or cast with channel features, so valves and pumps using these materials will probably need to utilize featureless sheets or films of the material. Previously-demonstrated monolithic membrane valves

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† The HTML version of this article has been enhanced with colour images.

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and pumps utilize featureless, commercially-available PDMS membranes sandwiched between two etched glass wafers.[3] Since the valve membrane is not molded or cast with features, many different materials can be substituted for PDMS in these valves and pumps. Recently, Willis *et al.* showed that spin-coated amorphous fluoropolymers and PTFE-fluoropolymer laminates could be used in place of PDMS in monolithic membrane valves and pumps.[16] The resulting glass–Teflon–glass structures have a number of advantages over glass–PDMS–glass monolithic membrane valves and pumps, including vastly improved chemical inertness, a wider range of operating temperatures, and faster actuation rates. However, the fluoropolymer films and laminates used by Willis *et al.* require complex fabrication (spin-coating multiple layers of amorphous fluoropolymers, bonding commercial Teflon sheets between these layers, dissolving supporting glass wafers in hydrofluoric acid, and depositing chromium or fluorocarbon adhesion promoters on the etched glass fluidic and pneumatic wafers) before the films and laminates can be bonded between the etched glass wafers to form a completed microfluidic device. The complexity of this fabrication process may limit its usefulness in many research and manufacturing contexts.

In this work, we present a simple alternative method for fabricating Teflon monolithic membrane valves and pumps in glass microfluidic devices. We have found that inexpensive, commercially-available fluorinated ethylene-propylene (FEP) Teflon films can be bonded between etched glass wafers to form chemically-inert monolithic membrane valves and pumps. Both PTFE and FEP are comprised entirely of carbon and fluorine and are similarly inert. But while PTFE is opaque and must be cut or skived to make rough thin sheets, FEP is transparent and available as a smooth, uniform thin film. Chemical compatibility data from nearly 50 years of use as a commercial product show that FEP is resistant to virtually all chemicals except "molten alkali metals, gaseous fluorine, and certain complex halogenated compounds such as chlorine trifluoride at elevated temperatures and pressures".[17] The resulting glass–FEP–glass devices are optically transparent and suitable for imaging or fluorescence applications (Fig. 1). The FEP Teflon valves permit unimpeded (0.9 μL s^{-1}) flow while open and negligible (< 250 pL s^{-1}) leakage while closed against 14 kPa fluid pressure. The FEP pumps can precisely meter nanoliter-scale volumes at up to microliter/second rates. The pumps also show excellent long-term durability with < 4% change in pumping rate after 13 days of continuous operation. By combining ease of fabrication with extreme chemical inertness, these Teflon monolithic membrane valves and pumps enable research involving a vast array of chemistries that are incompatible with native PDMS microfluidic devices.

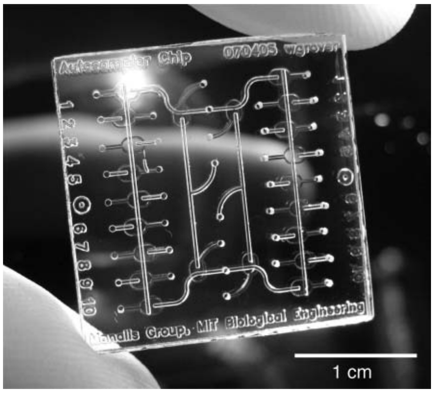

Fig. 1 Photograph of an Autosampler Chip containing 22 FEP Teflon monolithic membrane valves. The Autosampler Chip can deliver extremely caustic piranha solution (concentrated sulfuric acid and hydrogen peroxide) to clean an off-chip sensor without causing any detectable damage to the chip or its valves.[23]

2. Materials and methods

2.1 Overview of valve and pump operation

Monolithic membrane valves[3] are formed where an etched displacement chamber in a glass pneumatic wafer is oriented across a flexible membrane from a channel discontinuity in a glass fluidic wafer (Fig. 2). When a pneumatic pressure higher than atmospheric pressure is applied to the displacement chamber *via* the pneumatic channel, the FEP film is pressed against the gap between the fluid channels and the valve is sealed shut. When vacuum (pressure lower than atmospheric pressure) is applied to the displacement chamber, the FEP film is pulled

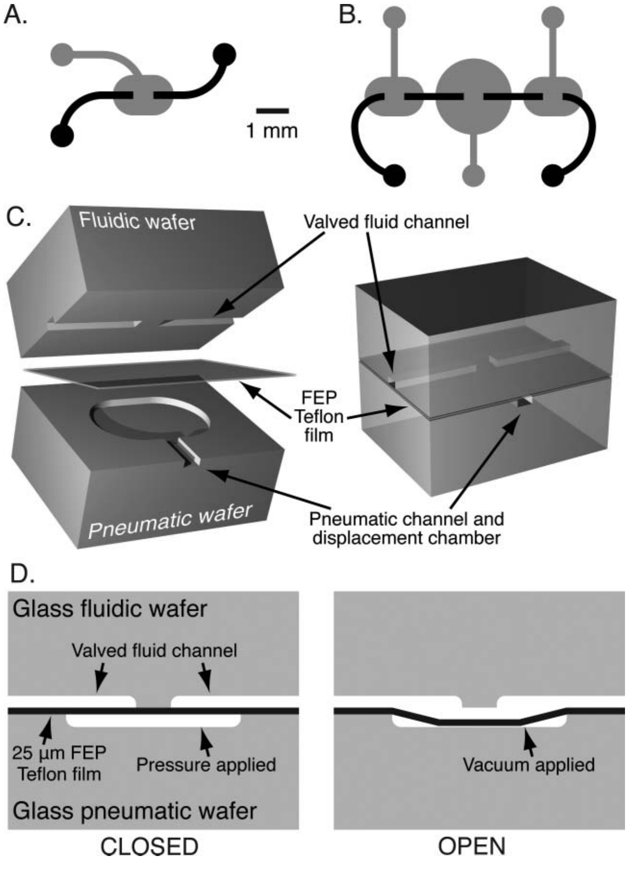

Fig. 2 Mask designs of a monolithic membrane valve (A) and pump (B); fluidic features are black, pneumatic features are gray, and small circles indicate the locations of drilled fluidic or pneumatic access holes. (C) Exploded and assembled illustrations of a single FEP valve. In the cross-sectional view of a single valve (D), the FEP film seals against the gap in the fluid channel when the valve is closed. Applying vacuum to the displacement chamber pulls the film away from the fluidic wafer and opens the valve.

away from the fluidic wafer and fluid can flow across the gap, thereby opening the valve.

Three monolithic membrane valves connected in series form a diaphragm pump (Fig. 2).[3] The pump is actuated by opening and closing the valves according to the six-step cycle photographed in Fig. 3. The volume pumped per cycle is ultimately determined by the volume pushed out of the middle (diaphragm) valve while closing in Step 5.

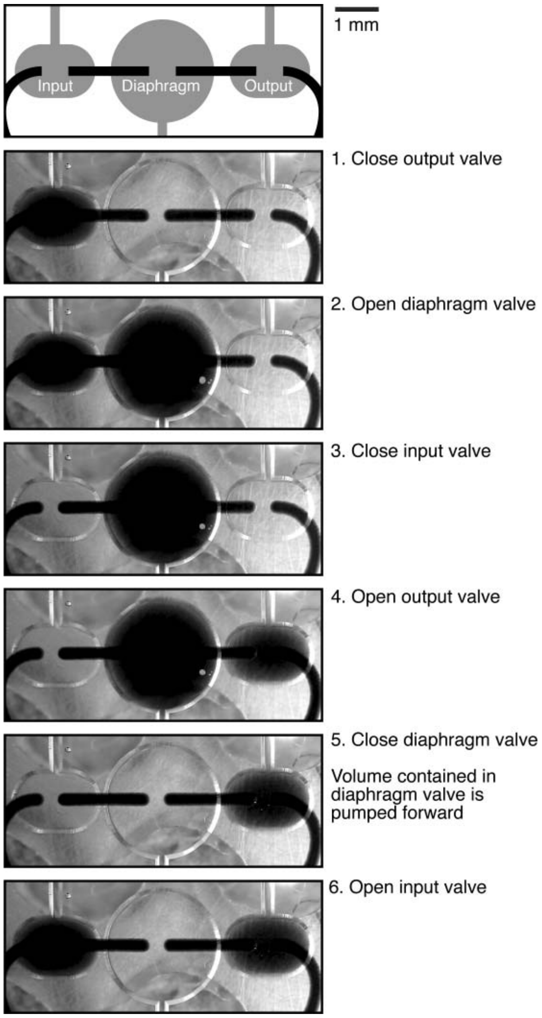

Fig. 3 Photographs of dye in a 340 nL FEP Teflon pump at each of the six steps in a single pump cycle. At the optimal actuation rate for this pump, this cycle repeats every 90 ms and pumps 1.1 µL s^{-1}.

2.2 Device fabrication

Commercial Borofloat borosilicate glass photomask blanks (Telic Company, Valencia, CA) are used as substrates for device fabrication. These 1.1 mm thick, 100 mm square glass plates come from the manufacturer pre-coated with 120 nm chrome and 530 nm AZ 1500 photoresist. Fluidic and pneumatic features are exposed in the photoresist using an ultraviolet lamp and a high-resolution transparency mask (Pageworks, Cambridge, MA). Exposed regions of photoresist are then removed by developing the plate in 0.5% w/v sodium hydroxide solution for 10 s, and exposed chrome is removed by immersing the plate in chromium mask etchant (Transene, Danvers, MA) for 1 min. After applying a self-adhesive vinyl sheet to protect the backside of the plate, the exposed regions of glass are etched to the desired depth in 49% hydrofluoric acid (~7 µm min^{-1}). Finally, the remaining photoresist and chrome are stripped in acetone and chromium etchant, respectively.

The resulting etched glass plate is diced into 16 separate pneumatic and fluidic layers (enough for eight assembled devices) using a carbide pencil "scribe and break" technique. In preparation for drilling, the glass pieces are bonded to plain glass backing plates on a 200 °C hot plate using pine rosin (Sigma, St. Louis, MO). The pieces are then drilled with fluidic and pneumatic access holes on a CNC mill using 400 µm diameter diamond-tipped drill bits (Amplex/Saint-Gobain Abrasives, Worcester, MA) in a process documented elsewhere.[18] After drilling, the pneumatic and fluidic layers are separated from the backing plates on the hot plate, cleaned of any residual glass debris using a 1% solution of Micro-90 detergent and a soft brush, and rinsed of residual pine rosin using acetone. Although not performed on the devices tested here, immersing the glass layers in piranha solution (sulfuric acid with hydrogen peroxide) for ten minutes, rinsing them in deionized water, and blowing them dry with nitrogen before bonding further strengthens the glass-FEP-glass bond and eliminates small bonding defects that were occasionally observed.

2.3 Device bonding

DuPont C-20 FEP Teflon film (25 µm thick; American Durafilm, Holliston, MA) comes from the manufacturer with a stable treatment that renders the film "cementable" (capable of bonding with conventional adhesives) but does not affect the chemical inertness of the FEP.[17] Details about the treatment are not available from DuPont, but corona treatment in solvent vapor is one reported treatment for fluoropolymer films.[19] X-ray photoelectron spectra reveal altered fluorine : carbon ratios and the slight presence of oxygen and nitrogen on the surface of the treated FEP film, elements that are essentially absent from untreated FEP film.§ The treatment appears to play a role in the strong thermal bond formed between the treated FEP film and glass, as both untreated FEP and atmospheric corona-treated FEP films yield poorer-quality glass bonds than the commercially-treated C-20 FEP. Also, as the bonds are performed at 90 °C (well below the 260–282 °C melting point of FEP[14]), it is unlikely that melting of the bulk FEP contributes to the glass–FEP bond.

Devices are assembled by first placing the glass pneumatic layer, etched features facing up, on a 16 mm thick borosilicate glass block (McMaster-Carr, Los Angeles, CA). A piece of C-20 FEP Teflon film is then placed across the pneumatic layer. The glass fluidic layer, etched features facing down, is then placed lightly on top of the FEP film. Since the FEP film does not stick to glass at ambient temperature under light pressure, the fluidic

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§ X-ray photoelectron spectroscopy revealed that the top few nanometers of a sample of untreated FEP film contains 65.3% fluorine, 34.6% carbon, 0.1% oxygen, and no detectable nitrogen (atomic percents). The surface of a sample of treated C-20 FEP film contains 63.2% fluorine, 32.5% carbon, 2.6% oxygen, and 1.7% nitrogen.

layer can be slid around to align its etched features to those on the pneumatic layer. After the layers are aligned, manually pressing the fluidic layer forms a weak glass–FEP–glass bond that maintains alignment during subsequent steps. A second 16 mm thick borosilicate glass block is then placed on top of the assembled device, and the entire stack is transferred into a small homemade press (details available as ESI‡). Screws on the press are tightened to apply approximately 7 MPa pressure to the bonding stack. The glass blocks serve to distribute the pressure evenly across the surface of the device during bonding. The press is then turned sideways and placed into an oven preheated to 90 °C. Orienting the bonding stack on its side during bonding keeps the FEP film from sagging into the etched displacement chamber of a valve (which can occur if the pneumatic wafer is oriented on the bottom) or sticking against the fluidic layer and sealing a valve shut (which can occur if the fluidic wafer is on the bottom). After two hours at 90 °C, the oven is turned off and cooled to room temperature over one hour. The bonded device is finally removed from the press and trimmed of excess FEP film using a razor blade. Alternately, shorter bonds at higher temperatures can also be used (*e.g.*, 1 h at 110 °C).

2.4 Valve and pump characterization

Each completed test chip is mounted between custom pneumatic and fluidic interfaces. The acrylic pneumatic interface contains 23 holes that align with the drilled pneumatic holes in the test chip. Laboratory tubing mounted in the pneumatic interface delivers actuation pressure (50 kPa) and vacuum (−70 kPa) from an array of computer-controlled solenoid valves (SMC, Indianapolis, IN) to the test chip. The PTFE Teflon fluidic interface contains 22 holes that align with the drilled fluidic holes in the test chip. FEP capillary tubing (800 µm od, 230 µm id; Upchurch, Oak Harbor, WA) inserted into the PTFE fluidic interface provides fluidic access to the test chip, and Simriz perfluoroelastomer O-rings (Size 001; Simrit, Plymouth, MI) seal between the PTFE fluidic interface and the test chip. After clamping the test chip between the pneumatic and fluidic interfaces using spring clamps (∼140 kPa pressure), the chip is ready for use.

Each of the ten valves in a valve test chip was tested by measuring the rate of fluid flow from a pressurized dye reservoir through the valve. The valves have identical 1.2 by 1.8 mm (post-etch) displacement chambers, 270 µm wide fluid channels, and 75 µm etch depths on both the fluidic and pneumatic layers. Fluid from the valve passes through a transparent, 200 µm ID FEP capillary mounted in the field of view of a Canon PowerShot A640 camera. Video of the fluid front advancing through the capillary was analyzed using ImageJ software (http://rsb.info.nih.gov/ij) to determine the volumetric flow rate. Using this procedure, the fluid flow rate through each open and closed valve was measured while varying the fluid pressure (the pressure applied to the upstream fluid reservoir).

Five different pump test chips were fabricated, each containing pumps with identical input and output valves (1.2 by 1.8 mm) and fluid channel widths (270 µm) but different diaphragm valve diameters (1.3, 1.5, 1.8, 2.0, and 2.3 mm). Using an isotropic etch model[3] and an etch depth of 75 µm, these diaphragm valve displacement chambers were calculated to contain 110, 160, 210, 270, and 340 nL. By connecting each of the six pumps on each test chip to a reservoir of fluid at atmospheric pressure and measuring the flow rate during actuation using a camera as described above, the volume pumped per actuation was measured for each of the five pump sizes. In addition, the pumping rate of a single pump was measured while varying the pump actuation rate. Finally, a single pump was operated continuously for 13 days to determine the effect of prolonged use on pump performance.

3. Results

Fig. 4 plots the mean rate of pressure-driven fluid flow through the FEP Teflon monolithic membrane valves being held open and closed by −70 and 50 kPa pneumatic pressure, respectively. Positive closing pressure is necessary because thermal bonding distorts the Teflon film slightly, introducing a small gap between the Teflon film and the fluidic channel. Applying a pneumatic closing pressure actively seals the film against the fluidic channel and closes the valve. The average flow rate through the open valves is high (0.9 µL s^{-1} at 14 kPa fluid pressure) and increases linearly with increased fluid pressure (reaching 6.4 µL s^{-1} at 76 kPa fluid pressure). This relationship is consistent with fluid flow through a valveless channel and confirms that the presence of the open valve in the channel has a negligible effect on the flow of fluid. In contrast, flow through the closed valves is negligible (< 250 pL s^{-1} at 14 kPa fluid pressure), and half of the valves actually have no detectable leakage at fluid pressures up to 48 kPa. At fluid pressures above the pneumatic valve closing pressure (50 kPa) the valves begin to leak: at 76 kPa fluid pressure the average flow rate through the "closed" valves (620 nL s^{-1}) is about a tenth of the average flow rate through the open valves at the same pressure.

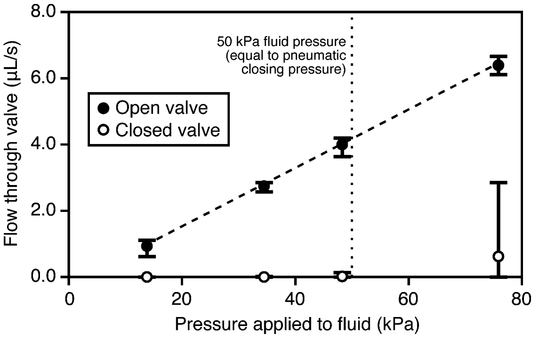

Fig. 4 Mean flow through ten open and closed FEP Teflon valves as a function of upstream pressure applied to the fluid. Flow through the open valve increases linearly with pressure, while flow through the closed valve is negligible at pressures below the pneumatic pressure used to hold the valve closed (50 kPa). Error bars show the range of individual flow rates for the ten valves measured.

The volume of fluid pumped per cycle by differently-sized FEP Teflon monolithic membrane pumps is shown in Fig. 5. To ensure that the diaphragm valves fill and empty completely with each pump cycle, each of the six steps in the cycle is given an excessively-long 500 ms to complete, for a total of 3 s per cycle. As expected, pumps with larger diaphragm valves pump more fluid per cycle. However, while similarly-sized

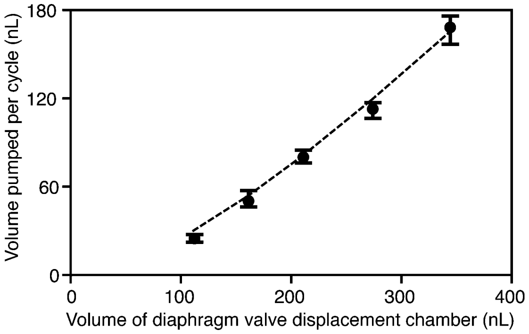

Fig. 5 Mean volume pumped per cycle by FEP Teflon pumps with diaphragm valves of five different volumes. The dashed line shows volumes predicted by modeling the volume inside the open diaphragm valve as a frustum of a cone (see text). Error bars show the range of individual pumping rates for the six pumps of each size measured.

PDMS monolithic membrane pumps pump about 82% of the volume of the diaphragm valve forward with each actuation,[3] the Teflon monolithic membrane pumps tested here pump between 22% (for the smallest pump) and 49% (for the largest) of the diaphragm valve volume per cycle. This suggests that the thicker PDMS membrane deflects further and contains more fluid in an open valve than the thinner FEP membrane. This observation is supported by a mathematical model for the maximum linear deflection w_0 of a uniformly-loaded circular membrane,[20]

$$w_0 = 0.662a\sqrt[3]{\frac{qa}{Eh}}$$

where a is the radius of the membrane (650 μm for the smallest pump tested), q is the applied load (70 kPa), E is Young's modulus for the membrane material (~750 kPa for PDMS[21] and 480 MPa for FEP[17]), and h is the membrane thickness (254 μm for PDMS and 25.4 μm for FEP). The calculated displacement for a PDMS membrane in the smallest pump is 267 μm, or 3.6 times greater than the 75 μm depth of the displacement chamber. Thus, the deflection of the thicker but more-elastic PDMS membrane is limited primarily by the size of the deflection chamber, so the membrane fills ~82% of the chamber when the valve is open and more fluid is pumped per actuation. In contrast, the calculated displacement for the FEP membrane in the smallest pump is 66.7 μm, slightly less than the 75 μm depth of the displacement chamber. Thus, the deflection of the FEP membrane is limited primarily by the lower elasticity of FEP, so the membrane fills only 22% of the chamber and less fluid is pumped per actuation.

Although Teflon monolithic membrane pumps deliver less fluid per actuation than their PDMS counterparts, it remains possible to design Teflon monolithic membrane pumps for pumping specific volumes. A simple model for the volume filled by fluid in an open valve is the volume V_f of a frustum of a cone,

$$V_f = \frac{\pi d}{12}\left(D_1^2 + D_1D_2 + D_2^2\right)$$

where d is the etch depth of the pneumatic layer, D_1 is the diameter of the displacement chamber, and D_2 is the diameter of the region of contact between the FEP film and the etched bottom of the displacement chamber, estimated at $D_2 = D_1 - 1.36$ mm. This crude model provides reasonable predictions of the volume pumped per cycle for the pumps used in this study (dashed line in Fig. 5) and could be used to design thin-film monolithic membrane pumps for pumping known volumes.

Fig. 6 explores the performance of a Teflon monolithic membrane pump operated at high speeds. The pump used has a diaphragm valve displacement chamber volume of 340 nL and pumps 160 nL cycle^{-1} for excessively-long 3 s cycles (Fig. 5). Cycle times as short as 360 ms (60 ms step^{-1}) still provide enough time to completely fill and empty the diaphragm valve during each cycle (open circles in Fig. 6). At cycle times shorter than 360 ms, the volume pumped per cycle drops off quickly, indicating that the diaphragm valve cannot fill or empty completely at such fast actuation rates. However, the volume pumped per unit *time* continues to increase as the pump is actuated even faster, reaching a maximum of 1.1 μL s^{-1} at 90 ms cycle^{-1} (15 ms step^{-1} or 11 cycles s^{-1}; closed circles in Fig. 6). Thus, for the pump tested, the fastest possible flow rate is attained at such a fast actuation rate that only 61% of the pump's 160 nL capacity is pumped per cycle. Pumps actuated at such high speeds may be less reliable for metering known volumes of fluid, but they may nonetheless be useful for fast filling or rinsing operations that do not require precise knowledge of volumes.

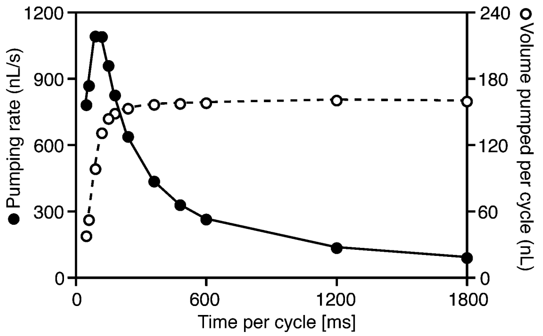

Fig. 6 Pumping rate and volume pumped per cycle as a function of actuation time for a 340 nL FEP Teflon diaphragm pump.

Finally, to test the long-term performance of the FEP Teflon pumps, a single 340 nL pump (160 nL cycle^{-1} at 3 s cycle^{-1}) was operated continuously for 13 days while periodically measuring the volume pumped per cycle. Fig. 7 shows that after 13 days and 374 000 actuations, the volume pumped per cycle changes less than 4% from the original value.

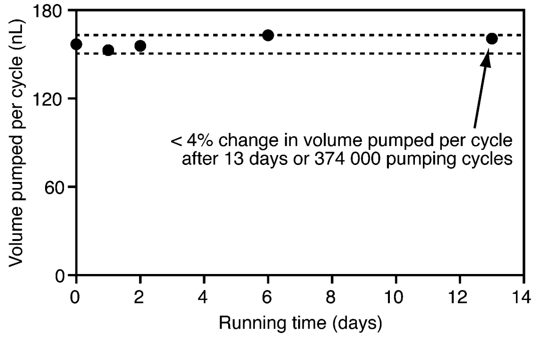

Fig. 7 Volume pumped per cycle by a 340 nL FEP diaphragm pump after 0, 1, 2, 6, and 13 days of continuous pumping. The dashed lines show the region of ± 4% change from the original value.

4. Discussion and conclusions

We have developed a simple method for fabricating glass microfluidic devices containing chemically-inert Teflon valves and pumps. These structures are modeled after previously-demonstrated monolithic membrane valves that utilize commercial PDMS membranes[3] or spin-coated amorphous fluoropolymers and PTFE–fluoropolymer laminates.[16] By using commercial FEP Teflon film in these structures, valved microfluidic devices can be created that combine ease of fabrication with maximum chemical resistance. The Teflon monolithic membrane valves and pumps previously demonstrated by Willis *et al.* were developed for space flight applications and hence satisfy a much more rigorous set of requirements than the FEP valves and pumps presented here. However, for terrestrial applications that require nanoliter- to microliter-scale manipulations of harsh chemicals and solvents, the FEP Teflon valves and pumps presented here offer a simple alternative method for fabricating chemically-inert microfluidics.

FEP Teflon monolithic membrane valves and pumps perform as well as their PDMS counterparts.[3] A fluid pressure of 14 kPa drives ~0.9 μL s^{-1} through valves held open by −70 kPa vacuum and less than 250 pL s^{-1} through valves held closed by 50 kPa pressure. Significant leakage through the closed valves is observed only when the pressure applied to the fluid exceeds the pneumatic pressure holding the valve closed. Also, while previously-demonstrated PTFE Teflon valves could not be closed with pneumatic pressures above 40 kPa without introducing air bubbles in the fluidic channel,[16] FEP Teflon valves can be closed with at least 50 kPa pressure without forming bubbles. The FEP pumps tested pump a predictable fraction of their diaphragm valve displacement chamber volume with each cycle, making on-chip metering of known volumes possible. The pumps show excellent long-term durability with < 4% change in the volume pumped per cycle after 13 days of continuous operation. Finally, the use of pre-coated glass photomask plates as device substrates[22] greatly expedites and simplifies fabrication by eliminating all deposition and spinning steps usually involved in preparing glass substrates for photolithography.

We have also used these Teflon monolithic membrane valves in the Autosampler Chip shown in Fig. 1, a microfluidic device that replaces and extends upon the functionality of a traditional bench-top autosampler instrument.[23] The Autosampler Chip automates biological measurements by routing samples, reagents, and cleaning solutions to and from a sensor, in this case a Suspended Microchannel Resonator or SMR mass sensor.[24,25] Preliminary experiments show that the FEP Teflon valves in the Autosampler Chip are capable of delivering piranha solution (concentrated sulfuric acid with hydrogen peroxide) to the SMR to strip bound layers from the silica surface of the sensor and reset it to a like-new state. While concentrated sulfuric acid dissolves PDMS,[6] exposure to piranha appears to have no detectable effect on the appearance or operation of the FEP valves in the Autosampler Chip.[23] We expect that this will be the first of many applications that will leverage the extreme chemical inertness of the microfluidic valves and pumps presented here.

Acknowledgements

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