# Pumping fluids in microfluidic systems using the elastic deformation of poly(dimethylsiloxane)†

**Douglas B. Weibel,*[ab] Adam C. Siegel,[b] Andrew Lee,[b] Alexander H. George[b] and George M. Whitesides*[b]**

***Received 24th September 2007, Accepted 2nd October 2007***
***First published as an Advance Article on the web 18th October 2007***
**DOI: 10.1039/b714664g**

This paper demonstrates a methodology for storing and pumping fluids that provide a useful capability for microfluidic devices. It uses microfluidic screw valves to isolate fluids in poly(dimethylsiloxane) (PDMS) microcompartments, in which the pressure of the liquid is stored in the elastic deformation of the walls and ceiling of the compartments. Fluids can be stored under pressure in these structures for months. When the valves are opened, the walls and ceiling push the fluid out of the compartments into microfluidic channels. The system has five useful characteristics: (i) it is made using soft lithographic techniques; (ii) it allows multiple reagents to be preloaded in devices and stored under pressure without any additional user intervention; (iii) it makes it possible to meter out fluids in devices, and to control rates of flow of fluids; (iv) it prevents the user from exposure to potentially toxic reagents; and (v) it is hand-operated and does not require additional equipment or resources.

## Introduction

This note describes a technique for storing and pumping fluids in microfluidic devices fabricated in poly(dimethylsiloxane) (PDMS) using microfluidic valves based on small machine screws embedded in a layer of polyurethane that is bonded to PDMS; we refer to these components as "TWIST" valves.[1] The method uses TWIST valves to create compartments in which fluids are stored under pressure. The pressure produced by overfilling compartments with fluid is stored in the elastic deformation of the walls and ceiling of the PDMS; opening, and adjusting the valves releases the fluid and controls its rate of flow into outlet microchannels. This technique takes advantage of the elastic modulus of PDMS (Young's modulus, 2.4 mPa; 360 psi).[2] It also takes advantage of three important characteristics of TWIST valves: (i) they can be used to keep channels closed indefinitely without any additional user intervention or source of pressure; (ii) they resist a back-pressure of $\geqslant$500 kPa ($\geqslant$73 psi) without failure; and (iii) they can be used to control the rate of flow of fluid through a microfluidic channel.

At present, there are few techniques for pumping reagents through microfluidic channels in devices that can be considered portable. Obeid *et al.* and Linder and co-workers described the use of plugs of liquid containing different reagents separated by air to introduce reagents into microfluidic channels using a pump;[3,4] a hand pump allows the devices to be used in the field.[4] Walker and Beebe, and Juncker *et al.* showed that capillary effects could be used to pump liquids passively through channels.[5,6] Moorthy *et al.* developed a thumb-actuated pump for microfluidic systems.[7] Several groups have designed portable fluidic systems with integrated power sources for pumping liquids using capillary electrophoresis.[8–11]

It would be useful to have a collection of different techniques for storing and pumping fluids in microfluidic devices that were designed to minimize the external equipment required for their operation. The successful integration of these techniques into devices would eliminate the need for external instrumentation—syringe pumps and power sources, or vacuum sources—and would accelerate the development of *portable* analytical and diagnostic tools for settings where access to equipment is limited.[12] We and others believe that simple, reliable, inexpensive analytical systems will find use in healthcare in developing countries, and in biomedical and environmental analysis performed by first responders, emergency medical personnel, and the military.[13]

The approach described in this technical note forms the basis for portable, disposable, microfluidic devices in which liquid reagents are preloaded into compartments, where they are stored under pressure and released later. The end-user can carry out all of the fluid-handling steps on devices preloaded with reagents by actuating the valves with a screwdriver or knife (or, depending on the form of the screw, with a fingernail); this characteristic eliminates the need for external pumps and makes it possible to fabricate portable, analytical systems that do not require electrical power for their operation.

## Materials and methods

### Device fabrication

We fabricated microfluidic devices in PDMS using soft lithography and rapid prototyping;[14,15] We used a ratio of

[a]*Department of Biochemistry, University of Wisconsin-Madison, 433 Babcock Drive, Madison, WI 53706, USA. E-mail: weibel@biochem.wisc.edu*
[b]*Department of Chemistry and Chemical Biology, Harvard University, 12 Oxford Street, Cambridge, MA 02138, USA. E-mail: gwhitesides@gmwgroup.harvard.edu*

† Electronic supplementary information (ESI) available: Characterization of pressurized microfluidic systems, liquid pumps, liquid–air–liquid pumps, non-specific adsorption of proteins on channel walls, Equation S1, Table S1, and Fig. S1–S9. See DOI: 10.1039/b714664g

 

10 : 1 of the base/curing agent for PDMS and cured the polymer for 3 h at 65 °C; the Young's modulus of this material after curing was 2.4 mPa. In this paper, all of the PDMS microfluidic channels and chambers had a rectangular or square cross-section; we varied the height, width (or diameter), and length of the structures as indicated. The technique we describe for storing and pumping fluids also works with compartments and channels that have a hemispherical cross-section.

Slabs of PDMS embossed with microfluidic channels were treated with an oxygen plasma and sealed irreversibly to glass slides. Before bonding, holes for inlets and outlets were punched in the slabs of PDMS with an autopsy needle (1 mm diameter). Polyethylene tubing (PE 60, I.D. 0.76 mm, O.D. 1.22 mm, Becton Dickinson) was inserted into the inlet and outlet holes.

### Valve fabrication

TWIST valves were fabricated using a procedure described previously.[1] Briefly, we bored a 3 mm diameter hole into the PDMS above a microfluidic channel with an autopsy needle; the depth of the hole was typically 2–3 mm. A smaller, concentric hole (1 mm wide, 1 mm deep) was bored into the PDMS inside the first hole using an autopsy needle (1 mm diameter) and a stainless steel machine screw (1.4 mm wide, 7 mm tall, 300 μm pitch) was pushed into the hole; the distance between the bottom of the screw and the top of the microfluidic channel was ~1 mm. We added a photocurable urethane (Norland optical adhesive, NOA 81) around the screw and cured the polymer with UV light. The polyurethane formed a stiff layer that retained an impression of the threads of the screw and formed a bond to the adjacent layer of PDMS. All of the valves described in this paper were made with stainless steel machine screws with the dimensions described above.

### Filling compartments with fluids

We inserted polyethylene tubing into the inlets of microfluidic channels connected to the compartments. The other end of the tubing was connected to a Hamilton Gastight syringe (100 μL) filled with liquid. The syringe was mounted on a digital syringe pump (Harvard Apparatus, model PhD2000) that was calibrated for dispensing volumes of fluid between 0.2–10 μL. With the valves on the inlet and outlet channels open, we began filling compartments with fluid *via* the inlet channel, typically at a rate of 4 μL of fluid $min^{-1}$; after approximately one volume of fluid was added, we closed the valve on the outlet channel and continued filling the compartment. When the desired volume of fluid was added, we turned the pump off, closed the valve on the inlet channel, removed the tubing from the channel, and stored the fluid under pressure in the compartment.

## Results and discussion

### Design and operation

We integrated TWIST valves into microfluidic channels that were connected to compartments in which reagents were stored. The compartments had an initial volume $V_C$—the volume of the empty compartment—and were filled with solutions of reagents using a syringe pump; the volume of the liquid, $V_L$, delivered to the compartment was determined by metering out the fluid using a syringe pump. When we 'overfilled' the compartments with fluid—that is, $V_L = \sim 20\ V_C$—the pressure of the liquid caused the volume of the compartment to expand. We blocked the inlet and outlet channels using the valves and stored the pressure of the fluid in the elastic deformation of the PDMS walls and ceiling of the compartments; when the valve on the outlet channel was opened, the elastic stress stored in the compartment pushed the liquid out through the channel (Fig. 1).

Fig. 2 shows the relationship between the excess volume of liquid introduced into a compartment ($V_L - V_C$) and the volume of fluid released. We measured this relationship in compartments with the following dimensions: A (21 μm tall, 5.2 mm diameter, volume of 0.44 μL), B (18.7 μm tall, 6.0 mm wide, volume of 0.51 μL), and C (10.9 μm tall, 7.3 mm tall, volume of 0.55 μL). The compartments were filled with water and the inlet and outlet valves closed for 5 s to check for leaks. The valve on the outlet microfluidic channel was opened and the volume of fluid released was measured. We observed that the relationship between the volume of excess fluid in the compartment and the volume of fluid released was approximately linear. More details on the design of these microfluidic systems can be found in the electronic supplementary information.†

When we repeated these experiments by storing the fluid in compartments for >10 min before releasing it into outlet microfluidic channels, we observed that a fraction of the total volume of fluid stored in the compartments was released. The excess pressure stored in the compartments was released before all of the fluid was pushed out of the compartment; we suspect that the non-reversible relaxation of the polymer chains in PDMS under strain is responsible for this behavior. To understand how the hysteresis of the polymer affects the ratio of the volume of fluid stored/released over time, we explored the relaxation of PDMS compartments in more detail.

### Hysteresis of PDMS compartments

We measured the relaxation of the polymer chains in PDMS by storing dimethylsulfoxide (DMSO) under pressure in compartment B (dimensions above) for different amounts of time, and then opened the valve on the outlet channel and determined the total volume of DMSO released (Fig. 3). DMSO was chosen for this particular experiment because of its low solubility in PDMS and its relatively high boiling point (189 °C), which reduces the amount of liquid lost to evaporation during the experiment.[16]

We used a syringe pump to fill 25 devices with 3.0 μL of DMSO; the fluid was isolated in the compartments by closing the valves on the inlet and outlet channels. After waiting for 0–400 min at 25 °C, we opened the valve on the outlet channel and measured the volume of liquid released from the compartment. We measured the volume of fluid released at eight different intervals of time in triplicate (one measurement per device). Fig. 3 shows a plot of the volume fraction of fluid

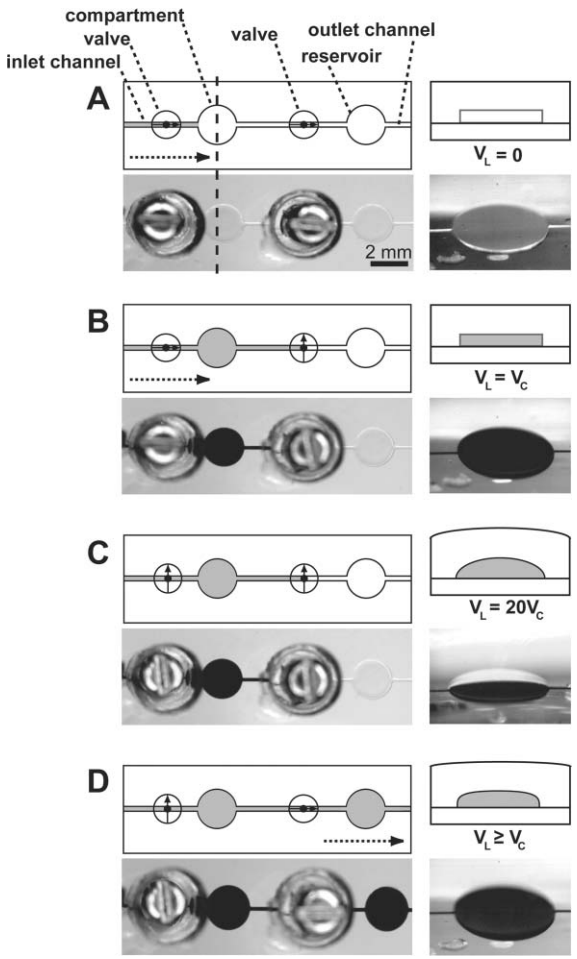


**Fig. 1** A schematic diagram illustrating the operation of compartments. Frames A–D illustrate how liquid is stored and released in a compartment; each frame shows a single microfluidic compartment with an inlet and outlet channel with integrated TWIST valves. The microfluidic channels (200 μm wide, 28 μm tall) and compartments (2 mm diameter, 28 μm tall, $V_C \approx 90$ nL) are embossed in PDMS and bonded to a glass slide. Each frame (A–D) contains four panels—in clockwise order starting from the upper left, they are: (i) a schematic diagram of the compartment; (ii) a cartoon depicting the compartment viewed from the side; (iii) an image of the compartment viewed from an oblique position; and (iv) an image of a compartment. (A) The valves on the inlet and outlet channel were open and fluid was pumped into the inlet channel; the dashed arrow shows the direction of the flow of fluid in the compartment. The dashed line shows the position where the cross-section is drawn; the cross-section of the empty compartment was rectangular. (B) The compartment was filled with one volume of liquid ($V_L = V_C$); the valve on the inlet channel remained open while the valve on the outlet channel was closed. (C) More liquid was pumped into the compartment ($V_L \approx 20\ V_C$) and the valve on the inlet channel was closed to store the liquid under pressure. The oblique view shows the deformation of the walls and ceiling of the compartment into a hemispherical shape (in this experiment, $V_L \approx 2$ μL). The light region is an artifact from the light source. (D) The valve on the outlet channel was opened and the pressure stored in the compartment pushed the liquid through the outlet channel; after 10 min, more than one equivalent of liquid remained in the compartment ($V_L \geq V_C$). The image on the bottom left was taken 2 s after opening the valve on the outlet channel; the dashed arrow shows the direction of flow.

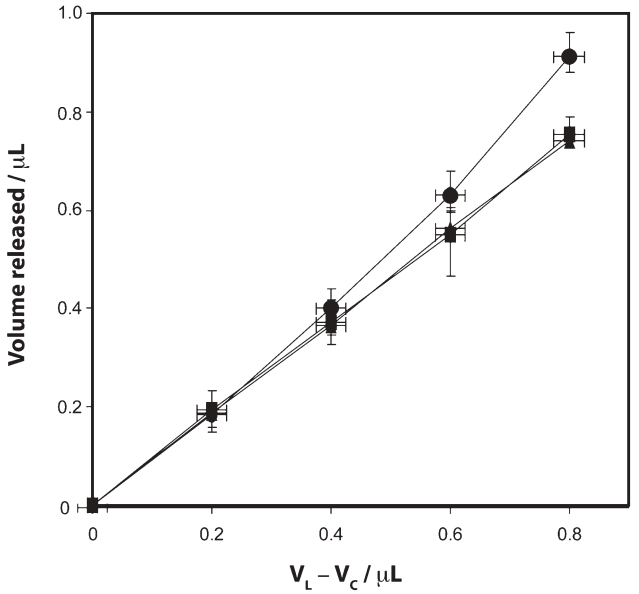


**Fig. 2** The relationship between the excess volume of fluid introduced into a compartment and the volume of fluid released. We filled three different compartments with water using a precision syringe, waited 5 s to check for failure, and released the fluid from the compartment by opening the valve on the outlet channel. We measured the volume released after 60 s. The compartments had the following volumes: A (●, 0.44 μL) B (▲, 0.51 μL) and C (■, 0.55 μL). Each data point represents the mean volume released based on five replica measurements with five separate devices; error bars represent minimum/maximum values of volume (*y*-axis) and the accuracy of the volume of the syringe (*x*-axis).

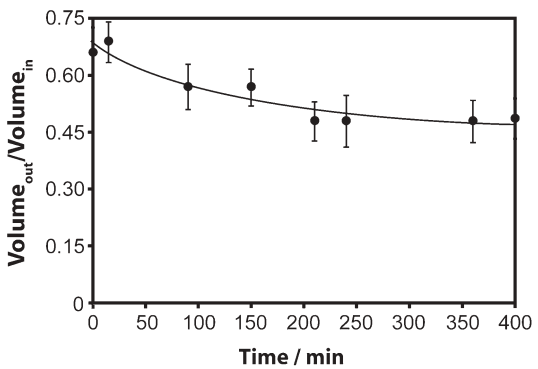


**Fig. 3** A plot of the volume fraction of fluid (volume out/volume in) released from compartments as a function of time. We measured the relaxation of the polymer chains in PDMS by storing DMSO (3.0 μL) under pressure in compartment B for different amounts of time, and then opened the valve on the outlet channel and determined the volume fraction of DMSO released. For each time point, we measured the volume fraction in triplicate using three separate devices, and averaged the volume of fluid released. The error bars represent the standard deviation from the mean of the values of the volume fraction for these measurements.

released over time (volume out/volume in). If PDMS were a perfectly elastic polymer, 2.5 μL of fluid (a volume fraction of 0.85) would be pushed out of the compartment. We observed that PDMS clearly exhibits a time-dependent hysteresis during the course of these experiments that limits the volume of fluid

that can be released from the compartment. Our understanding of the time dependent relaxation of PDMS under strain is still emerging.[17–19]

**Freezing compartments prevents the evaporation of solvents**

The evaporation of DMSO and other high boiling point solvents during experiments should be negligible and have little effect on the volume of fluid released. Evaporation will, however, be an issue for the long-term storage of devices in which compartments are filled with aqueous solutions of reagents, since water is lost by permeation through PDMS.

Assuming the radial diffusion of water through the slab of PDMS embossed with microfluidic channels, and a diffusion coefficient of water vapor through PDMS of $10^{-9}$ $m^2$ $s^{-1}$,[20] the root mean square distance traveled by water stored in compartments is approximately 4 mm $h^{-1}$. Since the slab of PDMS embossed with the channels is approximately 4–5 mm thick in these devices, evaporation is a potential problem for the long-term storage of aqueous solutions of reagents that are preloaded onto devices. To avoid this problem, we explored the freezing of devices after they were preloaded with reagents.

We filled compartments (volume, 0.5 μL) in microfluidic devices, described above, with 4 μL of black ink, and stored them at −20 °C for up to three months. We warmed the devices to 25 °C, opened the TWIST valve on the outlet channel, and measured the volume of fluid released from the compartments. After storing the devices for 93 days we found that 2 ± 0.5 μL of liquid was released; the total volume that can be released from compartments in these experiments is 3.5 μL. This experiment demonstrates that storing devices in a freezer reduces the evaporation of liquid from compartments and does not impede the mechanism of fluid storage and delivery described in this paper.

## Conclusions

This work demonstrates a method of storing and pumping fluids in microfluidic devices fabricated in PDMS using TWIST valves to isolate compartments that are filled with liquids under pressure. This method builds on our previous work fabricating disposable, portable microfluidic devices, and adds a new capability—namely, the ability to move fluids in microfluidic devices using the elastic strain stored in PDMS. This approach makes it possible to manipulate fluids in microfluidic systems without electrical power. This method requires minimal equipment—microfluidic compartments can be pre-filled using syringe pumps (or by hand)—and combines the concepts of preloading devices with reagents, with a method of delivering reagents to specific locations in a device that can be operated without bulky external instrumentation. In many of the experiments described in this note, the microfluidic devices were filled with fluids under pressure, and then carried (by hand, in a pocket, and so on) into other rooms in the lab where analyses took place. The components described in this paper will be useful for carrying out a variety of different bioanalytical applications, including those that we have reported previously.[1]

There are several characteristics of this technique that need to be improved. (1) The hysteresis of the PDMS prevents all of the available liquid in a compartment from being released. One approach to overcoming this problem is to reinforce the top of the slab of PDMS with a stiff layer of polymer or another material. (2) Water evaporates by permeation through the polymer walls and ceiling. We have demonstrated that freezing the devices preloaded with fluids prevents evaporation, but freezing may not be an option for portable devices used in the field. Coating the top layer of PDMS with another material may slow down the rate of evaporation. Alternatively, using solutions of reagents in DMSO or *N*,*N*-dimethylformamide may be an acceptable option in certain circumstances.[16] (3) The size of the valves prevents high-density arrays of compartments from being fabricated on the same device, and reduces the number of reactions or assays that can be performed. This characteristic is an intrinsic limitation of this technique. (4) Devices that incorporate these valves may be difficult to mass-produce. (5) Many different classes of molecules adsorb on the surface of PDMS non-specifically, which may complicate bioanalytical reactions and analyses in microfluidic systems fabricated in PDMS. The adsorption of solutes on PDMS is minimized when compartments are filled with aqueous reagents and kept frozen until they are operated (see supplementary Fig. S5†). If freezing is not an option, there are several ways to address this issue, by coating the walls of the PDMS channels with small molecules, proteins, or polymers.[21–26]

Microfluidics is still a technique predominantly used in the laboratory, not in the field. We believe that the technique described in this paper is a step toward developing portable analytical and diagnostic tools for settings where access to equipment is limited. It offers several improvements over existing techniques for manipulating fluids in portable devices: (i) ease of fabrication and use; (ii) low cost; (iii) storage of multiple reagents in one device with the ability to manipulate reagents—and control their rate of flow—independently; and (iv) integration of multiple fluids in a microfluidic device.

## Acknowledgements

This research was supported by the National Institutes of Health (ES16665) and DARPA, and used the MRSEC-shared facilities supported by the NSF under award No. DMR-0213805. A.C.S. acknowledges a graduate fellowship from the Howard Hughes Medical Institute.

## References

1 D. B. Weibel, M. Kruithof, S. Potenta, S. K. Sia, A. Lee and G. M. Whitesides, *Anal. Chem.*, 2005, **77**, 4726–4733.
2 J. C. McDonald and G. M. Whitesides, *Acc. Chem. Res.*, 2002, **35**, 491–499.
3 P. J. Obeid, T. K. Christopoulos, H. J. Crabtree and C. J. Backhouse, *Anal. Chem.*, 2003, **75**, 288–295.
4 V. Linder, S. K. Sia and G. M. Whitesides, *Anal. Chem.*, 2005, **77**, 64–71.
5 G. M. Walker and D. J. Beebe, *Lab Chip*, 2002, **2**, 131–134.
6 D. Juncker, H. Schmid, U. Drechsler, H. Wolf, M. Wolf, B. Michel, N. de Rooij and E. Delamarche, *Anal. Chem.*, 2002, **74**, 6139–6144.
7 J. Moorthy, G. A. Mensing, D. Kim, S. Moharty, D. T. Eddington, W. H. Tepp, E. A. Johnson and D. J. Beebe, *Electrophoresis*, 2004, **25**, 1705–1713.
8 R. Renzi, J. Stamps, B. A. Horn, S. Ferko, V. A. VanderNoot, J. A. A. West, R. Crocker, B. Wiedenman, D. Yee and J. A. Fruetel, *Anal. Chem.*, 2005, **77**, 435–441.

9 D. J. Jackson, J. F. Naber, T. J. Roussel, Jr., M. M. Crain, K. M. Walsh, R. S. Keynton and R. P. Baldwin, *Anal. Chem.*, 2003, **75**, 3643–3649.
10 R. Kappes, P. Schnierle and P. C. Hauser, *Anal. Chim. Acta*, 1999, **393**, 77–82.
11 T. Kappes, B. Galliker, M. A. Schwartz and P. C. Hauser, *TrAC, Trends Anal. Chem.*, 2001, **20**, 133–139.
12 S. K. Sia, V. Linder, B. A. Parviz, A. Siegel and G. M. Whitesides, *Angew. Chem., Int. Ed.*, 2004, **43**, 498–502.
13 C. D. Chin, V. Linder and S. K. Sia, *Lab Chip*, 2007, **7**, 41–57.
14 Y. Xia and G. M. Whitesides, *Angew. Chem., Int. Ed.*, 1998, **37**, 550–575.
15 D. C. Duffy, J. C. McDonald, O. J. A. Schueller and G. M. Whitesides, *Anal. Chem.*, 1998, **70**, 4974–4984.
16 J. N. Lee, C. Park and G. M. Whitesides, *Anal. Chem.*, 2003, **75**, 6544–6554.
17 B. Meissner, *Polymer*, 2000, **41**, 7827–7841.
18 T. Gervais, J. El-Ali, A. Günther and K. F. Jensen, *Lab Chip*, 2006, **6**, 500–507.
19 M. A. Unger, H.-P. Chou, T. Thorsen, A. Scherer and S. R. Quake, *Science*, 2000, **288**, 113–116.
20 W. Hellmich, J. Regtmeier, T. T. Duong, R. Ros, D. Anselmetti and A. Ros, *Langmuir*, 2005, **21**, 7551–7557.
21 B. Huang, H. Wu, K. Samuel and R. N. Zare, *Lab Chip*, 2005, **5**, 1005–1007.
22 D. Wu, B. Zhao, Z. Dai, J. Qin and B. Lin, *Lab Chip*, 2006, **6**, 942–947.
23 S. Hu, X. Ren, M. Bachman, C. E. Sims, G. P. Li and N. Allbritton, *Anal. Chem.*, 2002, **74**, 4117–4123.
24 J. M. Wu, Y. Chung, K. J. Belford, G. D. Smith, S. Takayama and J. Lahann, *Biomed. Microdev.*, 2006, **8**, 99–107.
25 S. Lee and J. Voeroes, *Langmuir*, 2005, **21**, 11957–11962.
26 D. Xiao, T. Van Le and M. J. Wirth, *Anal. Chem.*, 2004, **76**, 2055–2061.