Lab on a Chip

Pneumatic valves in folded 2-D and 3-D fluidic devices made from plastic sheets and tapes

Journal:	*Lab on a Chip*
Manuscript ID:	LC-TIN-02-2014-000173.R1
Article Type:	Technical Innovation
Date Submitted by the Author:	12-Mar-2014
Complete List of Authors:	Cooksey, Gregory; National Institute of Standards and Technology, Biosystems and Biomaterials Division Atencia, Javier; National Institute of Standards and Technology, Biosystems and Biomaterials Division

Journal Name

Lab on a Chip

Dynamic Article Links ►

Cite this: DOI: 10.1039/c0xx00000x

www.rsc.org/xxxxxx

COMMUNICATION

Pneumatic valves in folded 2-D and 3-D fluidic devices made from plastic sheets and tapes

Gregory A. Cooksey,*[1] Javier Atencia[1,2]

Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX

DOI: 10.1039/b000000x

We present a rapid prototyping technique that expands elastomeric valving capabilities to devices made from thin materials such as plastic films and tapes. The time required from conception to full fabrication of functional devices is within a few hours. A key characteristic of this technology is that devices are thin (typically less than 0.5 mm in thickness), which allows for the fabrication of devices with many layers. This feature also permits folding of devices into 3D structures having fully functional valves. We illustrate this concept with the fabrication of a 25-mm-per-side cube whose walls contain microfluidic channels and valves. Control of liquid delivery through the faces of the cube is demonstrated with a chemotaxis experiment of *C. elegans* migrating within the enclosed volume of the cube as stimuli are delivered through the walls of the cube to the interior faces.

Elastomeric valves have been widely used to impart advanced functionality to microfluidic devices. In particular, microvalves can select and route fluids from multiple inputs, serve as pumps, control flow rates, trap cells or beads and more.[1] Despite the diverse functionality and degree of control now offered by microfluidics, barriers to the widespread use of these devices outside of engineering laboratories include the learning curve, time, and equipment involved in fabrication using photolithography. Generation of a silicon master from which elastomeric devices are cast (soft lithography) can take several days considering ordering a transparency mask and doing photolithography.[2] Despite this, poly(dimethylsiloxane) (PDMS) molding[3] has become ubiquitous in microfluidic applications in part because it provides the ability to incorporate elastic elements that can serve as mechanical valves.[4,5]

We and others[6-9] have developed technologies to create microfluidic devices from cut-out laminates and double-sided tapes. Not only are the materials from which these devices fabricated cheap to buy in a variety of types, but also the technologies to design and fabricate them are widely available and affordable (razor cutter, laser machines, etc.). Because this technology does not require clean room processes or generation of masters, turnaround times from conception to fully operational devices are approximately a few hours. These features make tape-based devices useful for rapid prototyping as well as flexibility in production and broad utilization. Here, we expand this technology to achieve active microfluidic systems containing integrated pneumatic valves and pumps.

We fabricate valves by sandwiching a thin PDMS membrane between two layers of material with cut-out channels (Fig. 1). One layer serves as fluidic layer and the other layer delivers pressure to PDMS membrane-covered valves. The concept is the same as the one introduced previously by Unger et al.[4] Here, however, the layers are made of double-sided tape and plastic laminates (Fig. 1B). To achieve self-alignment, layers are mirrored across a folding line on a single plastic laminate (Fig. 2A).

Tapes and plastics are cut on a plotter razor cutter (FC800, Graphtech) or laser machine (VLS2.30 VersaLASER, Universal Laser Systems). Channel heights of 130 µm are set by the tape thickness. For push-closed valve types,[4] we found it was important to create rounded channels within the fluidic layer in order to achieve complete closure when pressure was applied to the valve. Assembly involves removing the liner over the fluidic layer and pressing the tape against a substrate such as a glass slide. A small amount of PDMS (Sylgard® 184, 10:1 base:crosslinker, Dow Corning) diluted 1:1 by mass in solvent (*t*-butanol) is placed in the valving region of fluidic channels using a 25-guage microneedle (#75165A686, McMaster-Carr). Excess PDMS is spun or blown out of the channels with compressed air, leaving small amounts of PDMS in the corners of the channels. Upon curing at 70 °C for at least 1 h, the PDMS forms rounded edges against the substrate.

Alignment of the valves on the fluidic channels is facilitated by folding. A PDMS membrane (≈ 30-µm thick) is made by spinning PDMS onto polycarbonate discs (#1221T17, McMaster-Carr) at 314 rad/s (3000 rpm) for 30 s (Cee Model 100, Brewer Science, Inc.) and curing at 70 °C for 1 h. To fold the mirrored

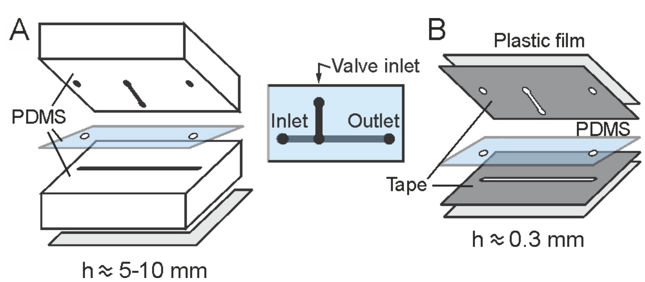

Fig. 1. (A) We present the fabrication of an elastomeric valve similar to Unger *et al.*[4], but by sandwiching a PDMS membrane between two layers of double-sided tape (B), the need for photolithography is removed and the thickness of devices is reduced by an order of magnitude.

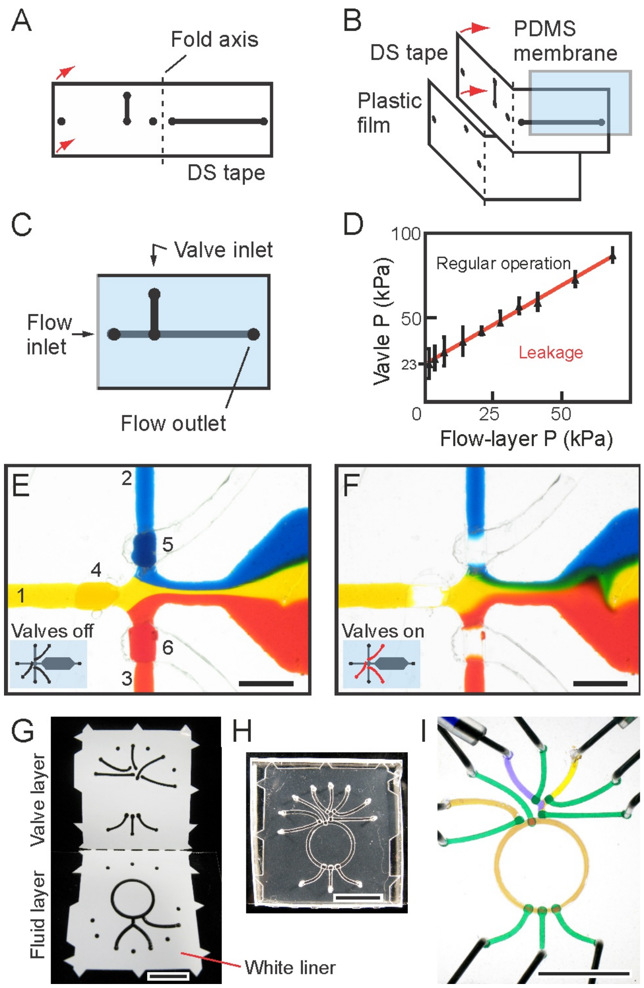

Fig. 2. (A) Cut-out laminates are designed with fluidic and valve layers mirrored across a folding axis such that alignment of the layers is achieved automatically. (B) Assembly of a functional laminate with embedded microvalves involves adhering a PDMS membrane onto the exposed double-sided tape of the valve layer followed by folding the closed fluidic layer on top. A plastic film forms the roof of the channels and contains the inlet ports. It can be attached before or after incorporating the membrane, but is necessary to complete the assembly of the thin device (C). (D) Complete closure of valves was found to occur at roughly 23 kPa (3.4 psi) above the pressure on the inlet fluids (data are means and standard deviations from triplicate devices). (E) Three independent valves (4, 5, 6) controlled fluid flow from 3 inlets (1, 2, 3), which contain food coloring to aid visualization. For example, the appropriate pressure at valve 4 closes inlet 1. When all valves were actuated, fluid flow through the chamber was stopped (F). (H) The assembled rotary mixer. (I) Mixer shown with yellow and blue food dye inputs after mixing around the ring. Valve channels are filled with green dye. Scale bars in E and F are 1 mm. Scale bars in G, H, and I are 10 mm.

layers around a PDMS membrane (Fig. 2B), the liner over the valve layer facing fluidic layer is removed and pressed into contact with the PDMS membrane and is then cut and peeled from the polycarbonate disc. The two halves of the device are then sealed around the PDMS membrane after removing the rest of the liner on the fluidic half of the device. The top of the device is closed with a plastic cover (#85585K102 127-µm thick polycarbonate, McMaster-Carr) containing ports for fluidic inlets (Fig. 2C), or, alternatively, a block of PDMS (with punched holes to match the inlets) that serves as a cover and facilitates connection of needles or tubing into the device.

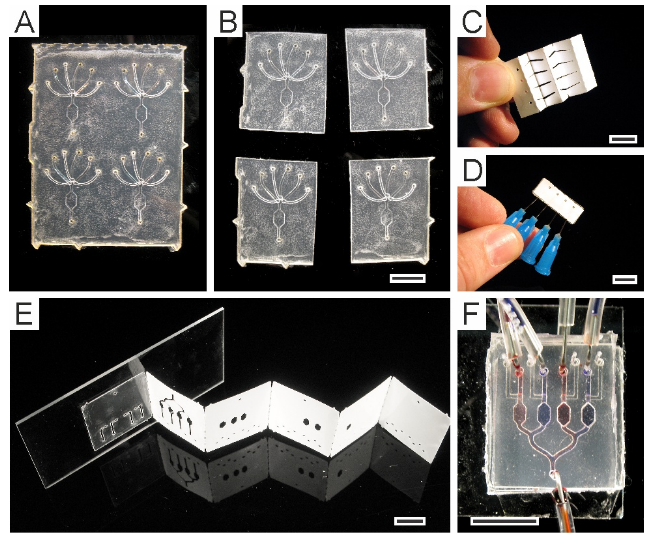

Fig. 3. (A) Multiple devices can be fabricated at once and cut apart after folding (B). (C) Incorporating multiple fold channels in a single layer can be used to create multilayer structures, such as an accordion-like structure of double-sided tape that folds around microneedles to form a connector that is ready to interface with devices (D). (E) A multilayer device having chambers whose heights are multiples of the film thickness can be laid out on a single layer of material. Chamber heights within the completed device (F) are 0.13 mm, 0.26 mm, 0.39 mm and 0.52 mm, respectively, from left to right. Scale bars are 10 mm.

The strength of the seal among layers depends on the materials and choice of adhesive.[10] We have found a double-coated silicone tape to be particularly effective (#96042, 3M™‡, 130 µm thickness) because it bonds strongly to the materials we have tested (PDMS, glass, polycarbonate, polyester, poly(methyl methacrylate)). Because this tape only comes with one liner, another liner (9015 FluoroSilicone Release Liner, Saint-Gobain Performance Plastics) was attached to the tape-exposed side to facilitate handling during device assembly. Tape thickness is a critical component in determining the minimum channel height that can be fabricated. To our knowledge, a transfer tape (3M^{TM} 91022, same adhesive as #96042) with thickness of 50 µm appears to be the thinnest material available that is capable of supporting valving with PDMS membranes. Devices as thin at 220-µm were fabricated using the transfer tape with 50-µm thickness polyester films as covers (#8567K24, McMaster-Carr).

The relationship between fluid pressure and valve pressure determine the condition for complete valve closure. Three devices were tested to determine the pressure needed to completely close the valves against applied fluid pressure (Fig. 2D). The results show the valve pressure needs to be ≈23.4 kPa (3.4 psi) higher than the fluidic pressure to completely close the valve. We found the devices could sustain pressures in excess of 140 kPa (20 psi) without leakage at any point in the tape-to-membrane or tape-to-cover bond; however, we typically operated devices well below 70 kPa (10 psi).

As demonstration of valve functionality, we show the use of 3 valves to control flow from 3 fluidic inputs (Figs. 2E, F). We also implemented a rotary mixer[11] with 3 inlets and one outlet controlled by 8 valves (Figs. 2G-I) to show that more complex functions could be realized.

The inherent alignment upon folding works well over large areas, which makes it straightforward to simultaneously fabricate multiple devices in parallel on a single substrate (Fig. 3A). Once assembled, devices can be separated into individual units (Fig. 3B).

A critical difference between this technology and tradition soft lithography is that finished devices are quite thin (≈300 µm compared to 5 mm), which makes it straightforward to extend the alignment method to multiple layers. We utilized this concept to fabricate an accordion-like structure that wraps around needles to create a fluidic connector manifold that can be attached to a device with the integrated tape (Fig. 3C, D). The number of layers needed to wrap around the device was selected to be slightly less than the diameter of the needle. In this case, we used 4 layers to wrap around 25-gauge needles (≈500-µm diameter). We also demonstrate a 6-layer chip, having microvalves in one layer control the flow into chambers whose heights are multiples of the tape thickness (Fig. 3B).

Because the layers are thin and flexible, like paper,[12,13] it is also possible to fold flat laminates into complex 3D shapes whose faces retain fluidic connectivity even around corners. As a demonstration, we designed a set of microfluidic channels into the faces of a cube. The device was fabricated from a single cut-out laminate (Figs. 4A, B) and folded into the shape of a cube. Overlapping adhesive tabs containing connection ports were incorporated into the design to facilitate connection of microchannels across separated faces and to seal the edges together (Fig. 4C).

The folded device forms a container – an enclosed environment that has fluids routed through the walls and can be designed to have fluids delivered to specific locations on the faces. We utilized this capability to study chemotaxis of nematodes. The interior of a cube was filled with an agar solution (0.2 % by weight agarose dissolved in M9 media) (Fig. 4D).

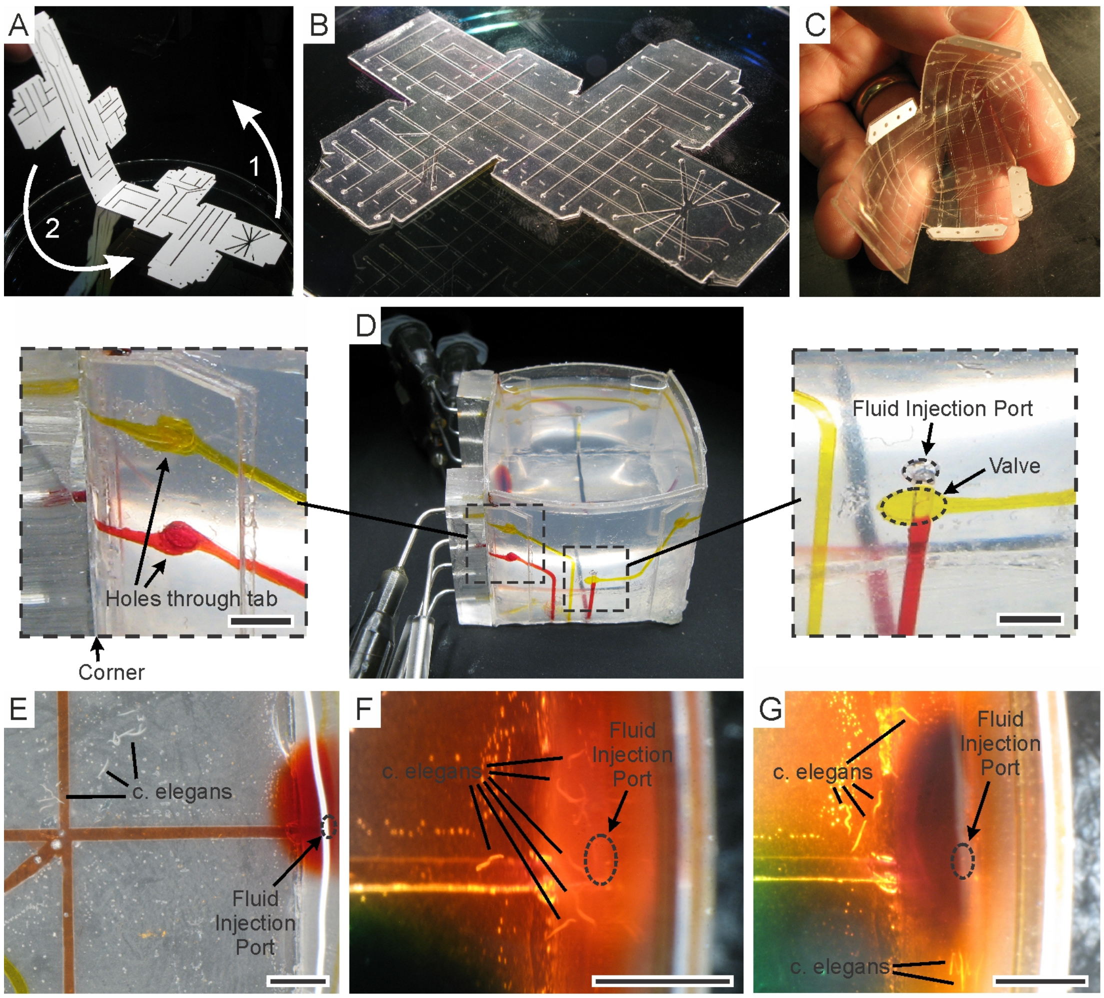

Fig. 4. Fabrication, loading, and operation of a 3D microfluidic cube. (A) Fluidic and pneumatic channels are laid out on faces of a cube and mirrored across a flat laminate. The valve layer was attached to a PDMS membrane spun cast on a PMMA wafer, (1) peeled off, and (2) folded over to sandwich the membrane between the valve and fluidic layers after the removing the back liner (B). The device was then folded into a cube (C) whose faces connect across adhesive tabs (shown with white liners still protecting the tape). The fluidic and pneumatic channels can switch between interior and exterior faces, though routing through the PDMS membrane and switching order across the tabs requires careful layout and poking through the membrane to establish connectivity. (D) The interior of a lidless microfluidic cube having one fluidic port on each interior face was filled with an agar solution and allowed to gel. Fluidic channels were filled with red food coloring and pneumatic channels were filled with yellow food coloring to demonstrate connectivity of channels around corners (left panel) and closure of valves controlling fluidic access to the interior face of the cube (right panel). (E) *C. elegans* were injected into the center of the agar; a bacterial food source containing red food coloring was injected in the right face of the cube. (F) After 2 h, the bacteria solution had diffused into the agar and attracted the nematodes. (G) Following injection of a high salt solution (darker red), the nematodes migrated away from the port. The sides of the cube are 25 mm and channels are 0.7-mm wide. Scale bars in D-G are 3 mm.

After gelation, a solution containing *C. elegans* was injected into the center of the agar with a needle (Fig. 4E). A solution containing *E. coli*, a food source for the nematodes plus red food coloring for visualization, was delivered to one face of the cube by opening the appropriate microvalves. After approximately 2 h, the worms had migrated from the center of the container to the face expressing *E. coli* (Fig. 4F). Subsequently the fluid was switched, using valves, to a saturated sodium chloride solution that repels the worms. After less than 1 h, the worms were observed to be moving away from the salt at the inlet (Fig. 4G).

The techniques that we describe to create multilayered and multidimensional devices have some limitations, including: (i) increased complexity of the designs requires longer fabrication time, due to the cutting time and necessity to remove the material that is cut away to form the channels, and (ii) solvents introduced to create the rounded channels may dissolve or deform some adhesives or plastics.

This technology affords the creation of microfluidic structures that are difficult – if not impossible – to fabricate with regular soft lithography, such as multilayer devices with integrated valves and folded devices with full valving functionality. Additionally, because materials are relatively cheap and there is no need of a clean room, photolithographic tools, or optical masks, and the time required from conception to completion is small (hours), we believe that this technique will lower the barrier to widespread design and use of microfluidic chips in non-engineering labs.

‡Disclaimer

Certain commercial products are identified in this report to adequately specify the experimental procedure. Such identification does not imply recommendation or endorsement by the National Institute of Standards and Technology, nor does it imply that the materials or equipment identified are necessarily the best available for the purpose.

Acknowledgements

We would like to thank Dr. Bryce Marquis for *C. elegans*.

Notes and references

* *gregory.cooksey@nist.gov; Tel: (+301) 975-5529*
[1] *Biosystems and Biomaterials Division, NIST, Gaithersburg, USA*
[2] *Department of Bioengineering, University of Maryland, College Park, Maryland 20742, USA*

1. A. K. Au, H. Lai, B. R. Utela, and A. Folch, *Micromachines*, 2011, **2**, 179-220.
2. Y. N. Xia and G. M. Whitesides, *Annu. Rev. Mater. Sci.*, 1998, **28**, 153-184.
3. D. C. Duffy, J. C. McDonald, O. J. A. Schueller and G. M. Whitesides, *Anal. Chem.*, 1998, **70**, 4974-4984.
4. M. A. Unger, H. P. Chou, T. Thorsen, A. Scherer and S. R. Quake, *Science*, 2000, **288**, 113-116.
5. K. Hosokawa and R. Maeda, *J. Micromech. Microeng.*, 2000, **10**, 415–420.
6. B. H. Weigl, R. Bardell, T. Schulte, F. Battrell, J. Hayenga, *Biomedical Microdevices,* 2001, **3**,267-274.
7. D. A. Bartholomeusz, R. W. Boutte and J. D. Andrade, *J. Microelectromech. Syst.*, 2005, **14**, 1364-1374.
8. P. K. Yuen and V. N. Goral, *Lab Chip*, 2010, **10**, 384-387.
9. J. Atencia, G. A. Cooksey and L. E. Locascio, *Lab Chip*, 2012, **12**, 309-316.
10. C. S. Thompson and A. R. Abate, *Lab Chip*, 2013, **13**, 632-635
11. H.-P. Chou, M. A. Unger, S. R. Quake, *Biomedical Microdevices*, 2001, **3**,232-330.
12. A. C. Siegel, S. T. Phillips, M. D. Dickey, N. Lu, Z. Suo, and G. M. Whitesides, *Adv. Funct. Mater.*, 2010, **20**, 28-35.
13. R. V. Martinez, C. A. Fish, X. Chen, G. M. Whitesides, *Adv. Funct. Mater.* 2012, **22**, 1376-1384.