IN SITU NANO 3D PRINTING OF A MICROFLUIDIC DIODE

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ABSTRACT

Microfluidic components capable of mimicking the functions of electronic circuit elements are critical to applications including soft robots [1] and biochemical fluids processing [2-4]. The emergence of state-of-the-art additive manufacturing or "three-dimensional (3D) printing" technologies has afforded a level of submicron-scale geometric versatility that is not possible using conventional microfabrication techniques. Here we leverage these capabilities to 3D print microfluidic diode structures *via* Direct Laser Writing (DLW) *in situ* within polydimethylsiloxane (PDMS)-on-glass microchannels for the first time. Experimental results revealed *Diodicities* (*Di's)* ranging from 3.0±1.9 to 2.0±0.6 for $0.05 < Re < 0.25$. These results suggest that the presented approach could be expanded upon to achieve the production of numerous additional nano3D printed microfluidic circuit components.

INTRODUCTION

Microfluidic Circuitry

The development of microfluidic circuitry components such as diodes, transistors, and capacitors that functionally mirror their electronic counterparts have enabled significant strides in autonomous fluidic processing applications [1-4]. The autonomy of such applications (*e.g.* soft robots, organ-on-a-chip systems, and biofluids processing platforms) is directly correlated with the inclusion of microfluidic circuitry components that reduce the need for active external flow control [5,6]. In the field of soft robotics, for example, a key focus has been the deviation from rigid power and control systems in exchange for soft microfluidic systems with integrated microfluidic logic schemes that improve the autonomy of the robot [1,7]. At present, microfluidic chips are typically constructed by means of conventional multilayer soft lithography protocols, which suffer from cost-, labor-, and time-intensive manufacturing processes [1-4]. To overcome these challenges, researchers have recently investigated *in situ* fabrication techniques to generate structures within single-layer microchannels; however, the processes used to do so are limited by their exclusive production of monolithic geometries [3, 8-11]. Consequently, alternative techniques are needed to further enhance microfluidic circuitry fabrication.

Direct Laser Writing (DLW)

Recently, researchers have proposed the use of 3D printing technologies as a promising alternative for the fabrication of micro/mesoscale fluidic circuit components utilizing technologies such as stereolithography and multijet/polyjet modeling to achieve resolutions on the order of 100 μm [12-15]. To reduce the size of 3D printed microfluidic circuits by several orders of magnitude, only one additive technology is capable: DLW. DLW is an extension of stereolithography in which multiphoton absorption is used to directly photocure (*i.e.* solidify) a liquid-phase photoreactive material at spatially-controlled locations. The technology uses a femtosecond-pulsed two-photon laser to print in a layer-by-layer manner, affording feature resolutions in the 100 nm range. Here, we utilize DLW to 3D print a microfluidic diode structure *in situ* within microchannels.

CONCEPT

Figure 1 provides a general conceptual overview of the function of the microfluidic diode. Figure 1a shows an illustration of the designed diode structure within a PDMS microchannel, and the image depicted in Figure 1b illustrates the functional portion of the structure, featuring a wall with an aperture behind a hemispherical plug atop a flexural member. A conceptual depiction of the response of the diode to forward and reverse flow conditions is shown in Figure 1c. Under forward flow conditions, the pressure increases across the diode in the direction of flow, thus forcing fluid through the aperture, bending the flexural member and hemispherical plug away from the aperture, and allowing fluid to pass through the channel (Fig. 1c – *left)*. Upon reversal of the flow polarity, the fluid forces the plug back into the aperture, thereby obstructing fluid flow in that direction (Fig. 1c – *right*).

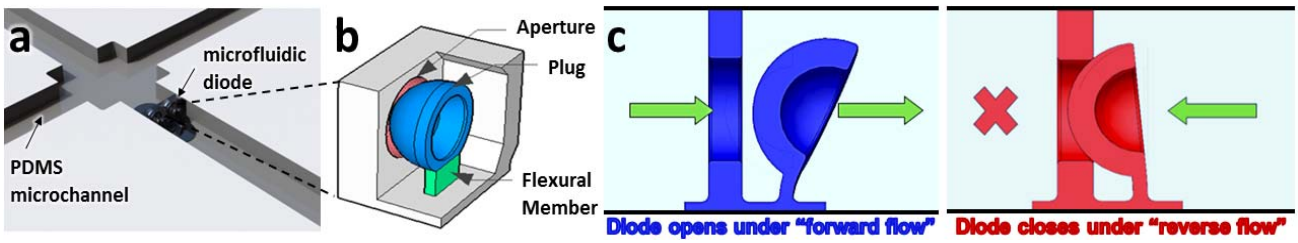

Figure 1: Conceptual illustrations of a nano3D printed microfluidic diode. (a) Illustration of the printed microfluidic diode structure within a PDMS microchannel. (b) Conceptual design of the functional portion of microfluidic diode structure, featuring a wall with an aperture and a hemispherical plug atop a flexural member in front of the wall. (c) Schematic overview of the response of the diode to flow conditions. Under forward flow, the diode will flex forward and permit flow. Under reverse flow, the diode will flex backward, plugging the aperture and restricting flow.

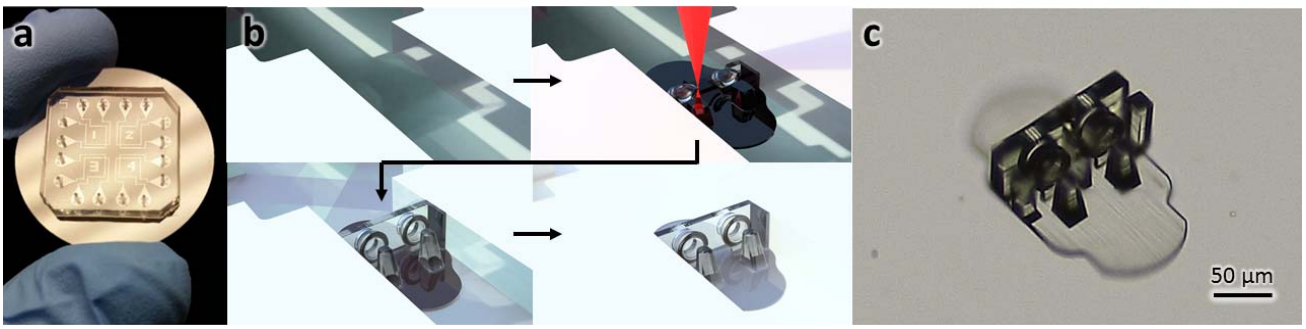

Figure 2: Conceptual schematic of the DLW printing process. The microfluidic platform shown in (a) was loaded with photoresist by establishing a negative pressure inside the microchannels with a vacuum, which drew photoresist into the channel passively by pressure differential. Then, the device was loaded into the 3D printer and the structure was fabricated layer-by-layer using a femtosecond pulsed laser (b, top). Photoresist developer was perfused through the channel and subsequently cleared, leaving the diode inside the microchannel (b, bottom). A 45° brightfield micrograph of the printed diode structure is depicted in (c). Scale bar = 50 µm

This process is repeatable and can be controlled by changing the flow polarity as desired.

The DLW process is schematically depicted in Figure 2. Like many other stereolithographic processes, DLW uses controlled beams of light to cure photoreactive materials into precisely defined structures. In this case, the "bath" of photoresist in the microchannel (Fig. 2b – *top left)* is photocured in spatially controlled locations in a layer-by-layer manner by a two-photon femtosecond-pulsed laser with nanoscale precision (Fig. 2b – *top right*). Upon completion of the print, the photoresist bath is eliminated by a developing solution that completes the curing of the structure (Fig. 2b – *bottom left*). After roughly 20 minutes, the developer is washed away, leaving the printed structure within the microchannels (Fig. 2b – *bottom right*).

MATERIALS AND METHODS

Here we present a new methodology that combines DLW with conventional single-layer soft lithography to fabricate microfluidic diode structures inside of sealed PDMS-on-glass microchannels. For the fabrication of the microfluidic diode channels shown in Figure 2a, a conventional single-layer soft lithography procedure was used. Photolithography of the negative photoresist SU-8 2100 was used to fabricate 50 µm tall x 120 µm wide microchannels on a 100mm silicon wafer. Following chemical development, a PDMS elastomer (Sylgard 184 10:1 base:curing agent) was cast over the fabricated design, de-gassed in a vacuum, and thermally cured at 100°C for 40 minutes. The cured PDMS was then peeled away from the substrate, and diced into individual units. To seal the microchannels, diced devices were bonded to borosilicate glass substrates using an oxygen plasma treatment with a power of 150 Watt at 1 Torr of pressure for 45 seconds.

Fabrication of proof-of-concept microfluidic diode components was accomplished using the Nanoscribe Professional GT DLW 3D printer to photopolymerize liquid-phase poly(ethylene glycol) diacrylate (PEGDA) with 3% of the solution composed of the photoinitiator Irgacure®. Initially, a vacuum loading technique was used to infuse the PEGDA solution into the microchannels by establishing a negative pressure with a vacuum pump. After removing the device from the vacuum chamber, a droplet was applied to the inlet of the channel and was drawn into channel via the pressure differential. A computer-aided design (CAD) of the diode structure was prepared for printing using the proprietary software DeScribe (Nanoscribe) and uploaded to a computer interfaced with the printer. Then the device was loaded into the Nanoscribe DLW 3D printer in conventional oil-immersion mode. This entailed passing a two-photon laser (laser power 50-56 mW, scan speed 2000-8000 µm/s) from a 63x objective lens through a layer of oil beneath the glass substrate, thus polymerizing photoresist on the top portion of the glass substrate. A Fluigent flow rate platform was used following DLW of the diode structure to perfuse a solution of isopropyl alcohol through the channel to develop the print and evacuate the remaining uncured PEGDA from the microchannels. This process left a fully developed microfluidic diode inside of the sealed microchannel. Subsequently, the performance of the diode under varying

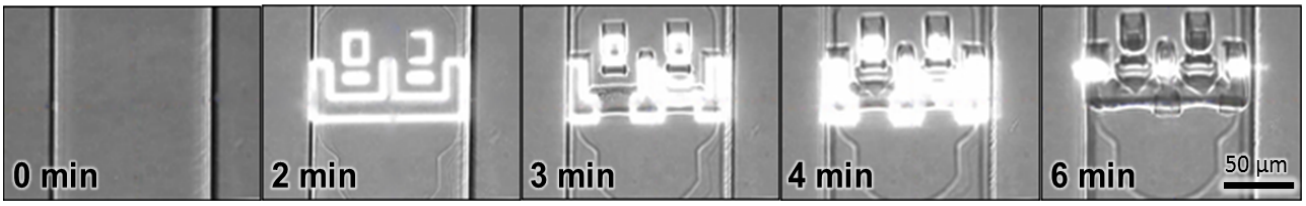

Figure 3: Brightfield micrograph frames collected from a video of the fabrication of the microfluidic diode structure. The images show the layer-by-layer, progressive nature of the fabrication process. The process was completed in under 10 minutes and was fully autonomous, requiring only an initial file input and placement of the substrate in the printer. Scale bar = 50 µm

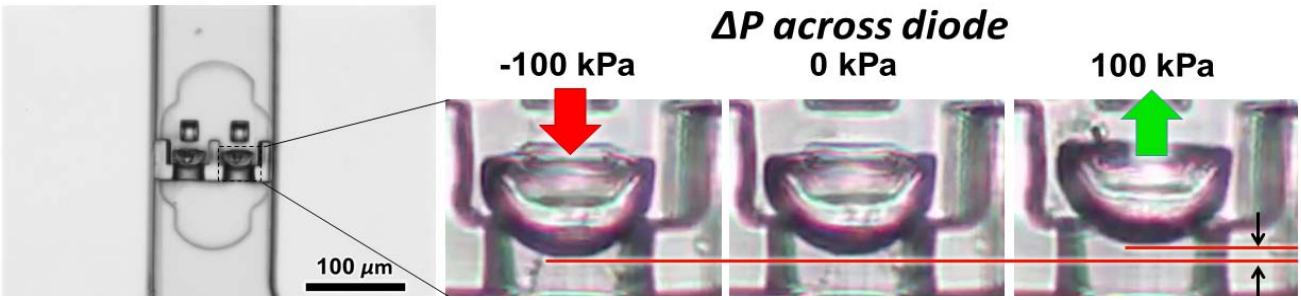

Figure 4: Experimental illustration of hemispherical diode flexure in response to applied pressure. The image on the left shows an overhead brightfield micrograph of the microfluidic diode structure after development (scale bar = 100 μm) and the images on the right depict a comparison of the physical response of an individual diode unit under -100 kPa,0 kPa, and 100 kPa pressure differences across the diode.

flow conditions, both positive and negative, was investigated with the Fluigent MAESFLO platform.

RESULTS AND DISCUSSION

DLW Print Results

Figure 2c depicts a 45° brightfield microscopy image of the printed structure and Figure 3 shows brightfield micrograph frames collected from a video of the printing process. These two figures suggest that the functional portion of the diode was fabricated with nano-scale fidelity to the predefined CAD structure. The process required only an input file and loading of the microfluidic substrate into the printer. The printing process was completed in under 10 minutes, with the top 10 μm of the device requiring roughly 40% of the total print time. The extension in printing time for the top portion of the device stems from the bottom-to-top printing process. As the structure increases in height, a greater laser dosage is required to maintain curing of the photoresist. Consequently, the speed at which the laser scanned across the print area was decreased and the power of the laser was increased to ensure curing in the top 10 μm of the device.

Experimental Flow Rectification Results

Experimental testing revealed distinct, repeatable differences in the behavior of the microfluidic diode component associated with changes in the flow polarity, shown in Fig. 4. In the presence of forward flow, the plug portion of the diode was forced forward, thus increasing the distance between the plug and the aperture and permitting a greater volume of fluid to pass through the channel (Fig 4 – *right*). Following a change in polarity, reverse flow forced the plug back into the aperture, thus minimizing the volume of fluid that was able to pass (Fig 4 – *left*). Quantification of measured forward and reverse flow rates is depicted in Figure 5. A comparison of flow rates in the forward and reverse directions over a range of applied pressures from 0-600 kPa revealed a repeatable average increase of 41% for the forward flow case (Fig. 5a). Quantification of *Di's* corresponding to the observed flow behavior ranged from 3.0±1.9 to 2.0±0.6 for $0.05 < Re < 0.25$ (Fig. 5b).

CONCLUSIONS

Microfluidic circuit components have enabled the development of autonomous fluid processing technologies at low *Re* [1,3,6,14]. Here we presented a process for the 3D printing-based fabrication of microfluidic diodes *in situ* within single-layer PDMS-on-glass microchannels *via* DLW. Experimental results determined *Di* values of 3.0±1.9 to 2.0±0.6 for $0.05 < Re < 0.25$. Although these results demonstrate flow rectification, these values are similar, if not low in comparison to other reported microfluidic diode *Di* performances. [3,16-18]. We presume that this performance was a direct result of the leakage of flow through and around the microfluidic diodes that was observed under reverse flow conditions. This is a

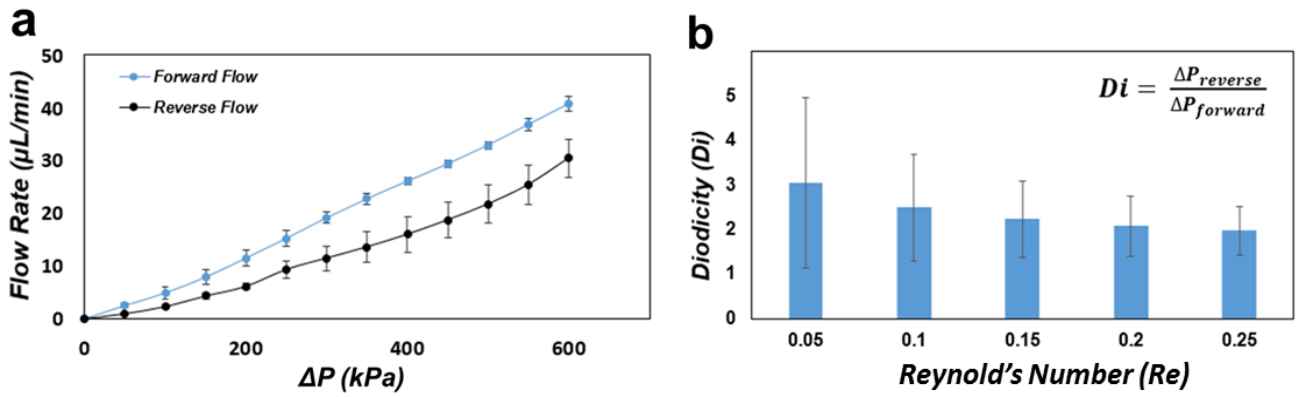

Figure 5: Experimental flow rectification results of the microfluidic diode. (a) Comparison of flow rates permitted by the microfluidic diode under increasing applied pressure conditions in the forward (top curve) and reverse (bottom curve) directions. (b) Quantified Di performance of the microfluidic diode structure at distinct, low (< 1) Re conditions, depicting a decrease in diode efficiency as fluid velocity increases.

consequence of the use of PDMS, a porous material that prevented the formation of a perfect seal between the wall portion of the microfluidic diode and the channel walls. Furthermore, the elasticity of the PDMS allowed the channels to expand upon application of pressure, thus increasing the volume of fluid that leaked around the diode and diminishing the function of the structure. We envision that the use of a sol-gel microchannel coating process [19] could reduce the elasticity of the channels while also allowing for a complete seal of the structure to the walls. Additionally, modifications of the PDMS composition to increase stiffness and/or decrease porosity could be explored to limit flow leakage around the diode and increase *Di* performance. Finally, apart from channel modification, placement of several microfluidic diodes in series, as others have investigated previously, would also be expected to aid in overall *Di* performance within the channel [3,18]. Nonetheless, these preliminary results represent a proof-of-concept demonstration of a functioning nano3D printed microfluidic circuit component, which could have important implications for microfluidic applications such as soft microrobots and lab-on-a-chip processors. Further studies will aim to optimize diode performance and fabricate other microfluidic circuitry components such as transistors and capacitors to potentially enable the development of sophisticated pressure-driven microfluidic logic systems mirroring circuitry in the electronic domain.

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REFERENCES

[1] M. Wehner, R. L. Truby, D. J. Fitzgerald, B.Mosadegh, G. M. Whitesides, J. A. Lewis, and R. J. Wood, "An integrated design and fabrication strategy for entirely soft, autonomous robots." *Nature*, vol. 536, pp. 451-455, 2016.

[2] J. Melin and S. R. Quake. "Microfluidic large-scale integration: the evolution of design rules for biological automation." *Annual Review of Biophysics and Biomolecular Structures,* vol. 36, pp.213-231, 2007.

[3] Sochol *et al*. "Single-layer 'domino' diodes via optofluidic lithography for ultra-low Reynolds number applications." in *Proceedings of the IEEE 26th International Conference on Micro Electro Mechanical Systems (MEMS 2013),* pp. 153-156.

[4] N. S. G. K. Devaraju and M. A. Unger. "Pressure driven digital logic in PDMS based microfluidic devices fabricated by multilayer soft lithography." *Lab on a Chip*, vol. 12, pp. 4809-4815, 2012.

[5] F. Zhu, J. Skommer, N. P. Macdonald, T. Friedrich, J.Kaslin, and D. Wlodkowic, "Three-dimensional printed millifluidic devices for zebrafish embryo tests." *Biomicrofluidics,* vol. 9, pp. 046502-1 – 046502-10, 2015.

[6] K. C. Bhargava, B. Thompson, D. Iqbal, and N.Malmstadt, "Predicting the behavior of microfluidic circuits made from discrete elements." *Scientific Reports,* vol. 5, pp. 15609, 2015

[7] D. Rus and M. T. Tolley, "Design, fabrication and control of soft robots." *Nature,* vol. 521, pp. 467-475, 2015.

[8] R. D. Sochol, C. C. Glick, A. Lu, M. Wah, T.Brubaker, K. Y. Lee, K. Iwai, L. P. Lee, and L. Lin, "Single-layer microfluidic 'spring' diodes via optofluidic lithography for ultra-low Reynolds number applications." in *2013 Transducers & Eurosensors XXVII: The 17th International Conference on Solid-State Sensors, Actuators and Microsystems,* pp. 2201-2203.

[9] S. Lin, W. Wang, X. Ju, R. Xie, and L. Chu, "A simple strategy for *in situ* fabrication of a smart hydrogel microvalve within microchannels for thermostatic control." *Lab on a Chip,* vol. 14, pp. 2626-2634, 2014.

[10] A. Caliò, J. Leng, J. Decock, L. De Stefano, and J. B.Salmon, "Microscopy assisted fabrication of a hydrogel-based microfluidic filter." *Journal of the European Optical Society,* vol. 10, pp. 15058, 2015.

[11] M. Kaynak, A. Ozcelik, N. Nama, A. Nourhani, P.E.Lammert, V. H. Crespi, and T. J. Huang, "Acoustofluidic actuation of *in situ* fabricated microrotors." *Lab on a Chip,* vol. 16, pp. 3532-3537, 2016.

[12] A. K. Au, N. Bhattacharjee, L. F. Horowitz, T.C.Chang, and A. Folch, "3D-printed microfluidic automation." *Lab on a Chip,* vol. 15, pp. 1934-1941, 2015.

[13] Sochol *et. al.* "3D printed microfluidic circuitry *via* multijet-based additive manufacturing." *Lab on a Chip,* vol. 16, pp. 668-678, 2016.

[14] K. C. Bhargava, B. Thompson, and N. Malmstadt, "Discrete elements for 3D microfluidics." *PNAS,* vol. 111, pp. 15013-15018, 2014.

[15] G. W. Bishop, J. E. Satterwhite-Warden, K.Kadimisetty, and J. F. Rusling, "3D-printed bioanalytical devices." *Nanotechnology,* vol. 27, pp. 284002, 2016.

[16] P. C. Sousa, F. T. Pinho, M. S. N. Oliveira, and M.A.Alves, "High performance microfluidic rectifiers for viscoelastic fluid flow." *RCS Advances,* vol. 2, pp. 920-929, 2012.

[17] J. E. Mates, T. M. Schutzius, J. Qin, D. E. Waldroup, and C. M. Megaridis, "The fluid diode: Tunable unidirectional flow through porous substrates." *ACS Applied Materials & Interfaces,* vol. 6, pp. 12837-12843, 2014.

[18] R. D. Sochol, A. Lu, J. Lei, K. Iwai, L. P. Lee, L.Lin, "Microfluidic bead-based diodes with targeted circular microchannels for low Reynolds number applications." *Lab on a Chip*, vol. 14, pp. 1585-1594, 2014.

[19] A. R. Abate, D. Lee, T. Do, C. Holtze, and D.A.Weitz, "Glass coating for PDMS microfluidic channels by sol-gel methods." *Lab on a Chip,* vol. 8, pp. 516-518, 2008.

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