Rapid fabrication of microfluidic chips based on the simplest LED lithography

Article *in* Journal of Micromechanics and Microengineering · April 2015

DOI: 10.1088/0960-1317/25/5/055020

CITATIONS
10

READS
1,007

8 authors, including:

Ping Wu
University of Science and Technology of China
10 PUBLICATIONS **75** CITATIONS
SEE PROFILE

Zhaofeng Luo
University of Science and Technology of China
52 PUBLICATIONS **792** CITATIONS
SEE PROFILE

Yuxuan Ren
The University of Hong Kong
77 PUBLICATIONS **571** CITATIONS
SEE PROFILE

Rapid fabrication of microfluidic chips based on the simplest LED lithography

2015 J. Micromech. Microeng. 25 055020

(http://iopscience.iop.org/0960-1317/25/5/055020)

IOP Publishing Journal of Micromechanics and Microengineering
J. Micromech. Microeng. **25** (2015) 055020 (7pp) doi:10.1088/0960-1317/25/5/055020

Rapid fabrication of microfluidic chips based on the simplest LED lithography

Yue Li[1], Ping Wu[1], Zhaofeng Luo[2], Yuxuan Ren[3], Meixiang Liao[1], Lili Feng[1], Yuting Li[1] and Liqun He[1]

[1] Department of Thermal Science and Energy Engineering, University of Science and Technology of China, 96 Jinzhai Road, Hefei, Anhui, 230027, People's Republic of China
[2] School of Life Sciences, University of Science and Technology of China, 96 Jinzhai Road, Hefei, Anhui, 230027, People's Republic of China
[3] National Center for Protein Science Shanghai, Institute of Biochemistry and Cell Biology, Shanghai Institutes for Biological Sciences, CAS, Shanghai, 201210, People's Republic of China

E-mail: heliqun@ustc.edu.cn

Received 16 September 2014, revised 12 February 2015
Accepted for publication 25 February 2015
Published 17 April 2015

Abstract

Microfluidic chips are generally fabricated by a soft lithography method employing commercial lithography equipment. These heavy machines require a critical room environment and high lamp power, and the cost remains too high for most normal laboratories. Here we present a novel microfluidics fabrication method utilizing a portable ultraviolet (UV) LED as an alternative UV source for photolithography. With this approach, we can repeat several common microchannels as do these conventional commercial exposure machines, and both the verticality of the channel sidewall and lithography resolution are proved to be acceptable. Further microfluidics applications such as mixing, blood typing and microdroplet generation are implemented to validate the practicability of the chips. This simple but innovative method decreases the cost and requirement of chip fabrication dramatically and may be more popular with ordinary laboratories.

Keywords: microfluidic chips, ultraviolet LED, photolithography

S Online supplementary data available from stacks.iop.org/JMM/25/055020

(Some figures may appear in colour only in the online journal)

1. Introduction

Microfluidics is widely believed to be one of the keys to next-generation technology for biochemical analyses, including high-throughput protein or cell biochemical assays in laboratories or diagnostics of body fluid in clinical applications [1–5], which would reduce costs tremendously both in time consumption and amounts of chemicals due to the reduction in volume from milliliters to nanoliters or even picoliters for chemical reactions. To date, most microfluidic devices are fabricated through soft lithography [6] derived from the fabrication of integrated circuit boards based on lithography. Thanks to Whiteside's work, the flexible poly(dimethylsiloxane) (PDMS) was found to be a simple, low cost alternative to classical mold materials [7]. Though people have also been devoting themselves to developing other convenient and lower-cost methods for fabrication of microchips such as waxing dipping [8], glass-based chips [9, 10] and paper-based chips [11, 12], soft lithography, especially the replica molding method, is still the most popular method for rapid prototyping of microfluidic chips.

However, in many laboratories, such a flexible method remains too expensive to realize for the innovations of microfluidics. One of the most expensive pieces of equipment is the lithography machine, which supplies high-power, collimated ultraviolet (UV) light for projection on the photoresist (SU-8) to fabricate the SU-8 patterns. This high-precision machine always requires rigorous environmental conditions such as appropriate temperature, humidity and a high class of cleanliness, leading to additional increase of the cost. Recently,

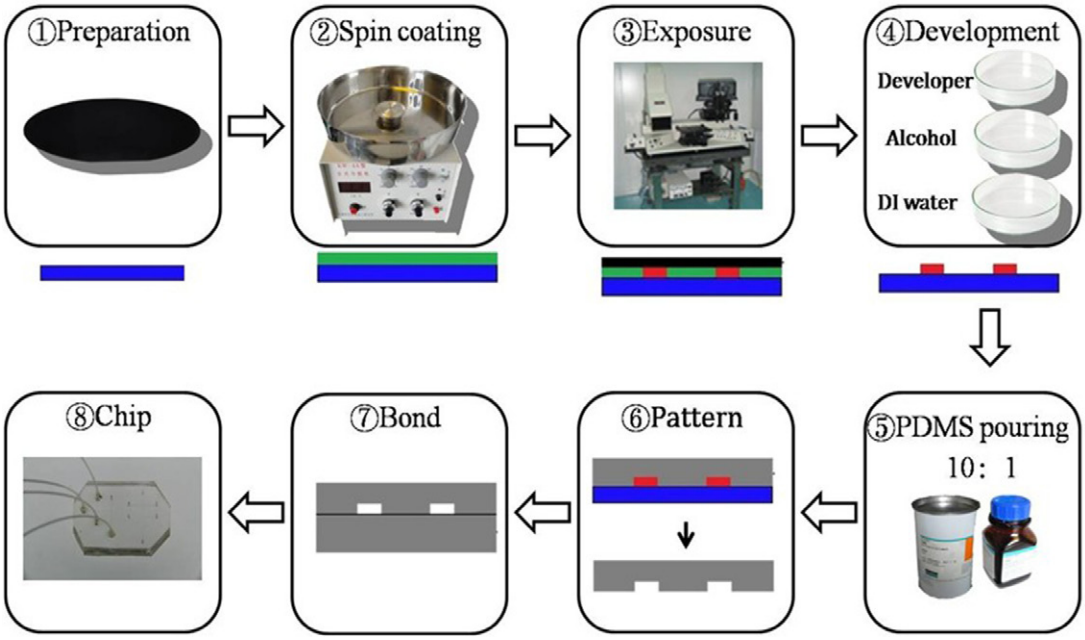

Figure 1. The process of fabrication: (1) silicon wafer pretreatment to maintain a clean and dry surface; (2) SU-8-2050 photoresist is coated onto a wafer with a thickness of 40 μm by spin coating at the speed of 5000 rpm for 60 s; (3) UV light is projected on the photoresist via a mask; (4) the unexposed portion of photoresist is dissolved in the developer, leaving behind a master of desired features; the alcohol washes out the developer and deionized (DI) water is adopted for the final washing; (5) a mixture of PDMS pre-polymer and its curing agent (10:1, w/w) is poured against the master; (6) after being cured at 90 °C for 1 h, the PDMS replica is peeled off and (7) bonded to a smooth surface (a second piece of PDMS or slide) after surface treatment in plasma cleaner (the bonding strength can bear a maximum pressure of 100 psi [18]), and then forms an integrated device; (8) connections of inlets and outlets to form a microfluidics device.

researchers have proposed many methods to reduce the costs of lithography, e.g. UV bulbs employed in the printed circuit board (PCB) industry [13], a grayscale maskless lithography system [14], ultraviolet nanoimprint lithography using nanospheres [15], a UV direct writing lithography system [16] and a UV-LED array with a rotary stage system [17]. However, in this paper, another lower-cost means of lithography is achieved with a portable light emitting diode (LED) to produce a collimated UV light source for photoetching. It has been reported that the UV-LED is suitable for the exposure of different photoresists. Using this handy LED device, we can fabricate qualified microfluidic chips more cheaply and simply without the demand of a high-level clean room, and more safely without the use of a high-voltage mercury lamp. Some common chips based on the novel method are demonstrated, and our two-year results of various on-chip biochemical applications indicate that the described method is suitable for PDMS microfluidics fabrication.

2. Materials and methods

2.1. Replica molding

Soft lithography is a diverse set of techniques using elastomeric materials for rapid prototyping, and replica molding is one of the most common methods. In essence, replica molding refers to a procedure employed to fabricate PDMS chips against relief structures made of photoresist on a silicon wafer. There are many advantages for using PDMS for replica molding, such as low cost, fast process, non-defect replication from SU-8 master, easy sealing and bonding to other substrates, suitability for biological and cellular applications and so on [7]. The detailed progress is shown in figure 1, and we note that the fabrication of the SU-8 patterned master involves traditional photolithography, which requires the most expensive equipment of all the steps due to the expensive machine maintenance and high environment requirement.

2.2. UV light source for photolithography

Many commercial lithographic machines are specifically designed for the microfabrication of micro devices, e.g. the MA6 (Karl Suss, Germany), LS30 (OAI, USA), URE-2000/25 (IOE, CAS, China). Recently, some highly precise lithography systems without the need of photomasks have also become commercially available for SU-8 exposure systems, e.g. SF-100 XCEL (IMP, USA). In the microelectronics industry, the epoxy-based SU-8 has been used as a high-contrast photoresist in photolithography for fabricating MEMS. The maximal absorption of SU-8 is in the UV range (350–400 nm), whereas most of the commercial lithographic machines with high-voltage mercury lamps provide light with a broad spectrum, including the so-called i line, g line and h line as well as visible and infrared light. The extra components in the spectra are not needed for etching, thus filters are needed in these machines to guarantee the required wavelengths. In order to avoid the effect of dust in the air on chips in the fabrication process, a clean room of class 100 000 is needed to keep the dust density, temperature and humidity in the air at controlled levels. The mercury arc lamps, which

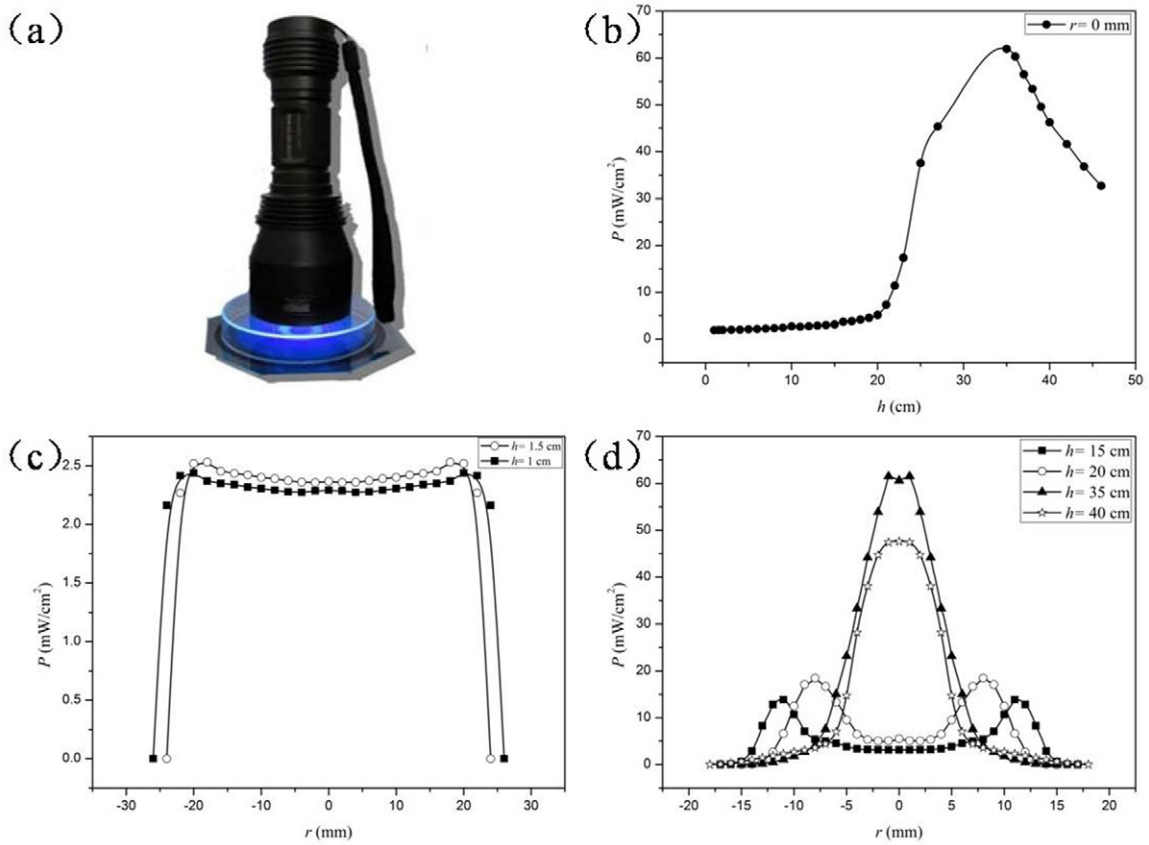

Figure 2. (*a*) The portable UV LED device (LUYOR-365). (*b*)–(*d*) The distribution of power density: (*b*) along the propagation direction of LED light; (*c*) along the transverse direction with the distance away from the light $h = 1$ and 1.5 cm; (*d*) along the radial direction of the light spot with distances $h = 15$, 20, 35 and 40 cm in sequence.

require high voltage to illuminate, are still potentially dangerous sources.

Here, we propose to replace the mercury arc lamp with an LED lamp (shown in figure 2(*a*)) to fabricate microfluidics channels. Unlike the mercury arc lamp, the LED can produce a monochromatic light with center wavelength at around 365 nm, highly efficient for SU-8 UV exposure. The uniformity of the LED light is evaluated through measurement of the power density with a photometer (LS126A, Linshang Technology, China). Figure 2(*b*) shows that the power density varies along the propagation direction. The density keeps nearly constant when the distance from the LED is below 20 cm, then the value increases dramatically with increasing distance; when the distance goes up to 35 cm, the power density starts to decrease. Further, the detector was placed at a distance of $h = 1$ cm and 1.5 cm; the measured power density profiles along the transverse direction are shown in figure 2(*c*). The transverse profile shows a flat top, which means that the illumination is uniform. Detailed analysis indicates that the uniformities are 0.8, 1.3 and 2.7% across the circle with radius 10, 15 and 20 mm for distance $h = 1.5$ cm, and 0.5% ($r = 10$ mm), 1% ($r = 15$ mm) and 2.2% ($r = 20$ mm) for distance $h = 1$ cm. Additionally, the uniformities are evaluated at different distances; as the distance increases to 20 cm, the size of the uniform area decreases to approximately 10 mm in diameter, and the flat-top disappears when the distances are more than 30 cm. Considering the uniformity and the range, we recommend the working distance for the lithography experiment as $h = 1$–1.5 cm. In addition, the parallelism of this UV LED has also been checked (shown in supplementary data).

The photomasks with the desired patterns are designed in CorelDRAW software and then printed on high-transparency photographic sheets. Before exposure, the mask is placed directly on the photoresist and the lamp is vertically fixed on the support. According to the scale, we can adjust the height between the support and platform to control the separation distance between the light source and the substrate. When the distance is set to be 1 cm, Si wafers with a layer (40 μm) of SU-8-2050 photoresist are exposed through the mask for 3 min to form a channel with the widths of 10–400 μm and height of 40 μm. Repeating the well reported patterns made by technical exposure machines, this portable LED UV light source really reduces both the complexity in the operation procedure and the requirement of conditions for fabricating microfluidics chips in laboratories.

3. Results and discussion

3.1. Chip structure

As a demonstration, we fabricated a series of microfluidics channels with various patterns using a previously described method. The verticality of the channel sidewall and the resolution of the lithography are the most important parameters qualifying the lithography. We can observe in figures 3(*a*),

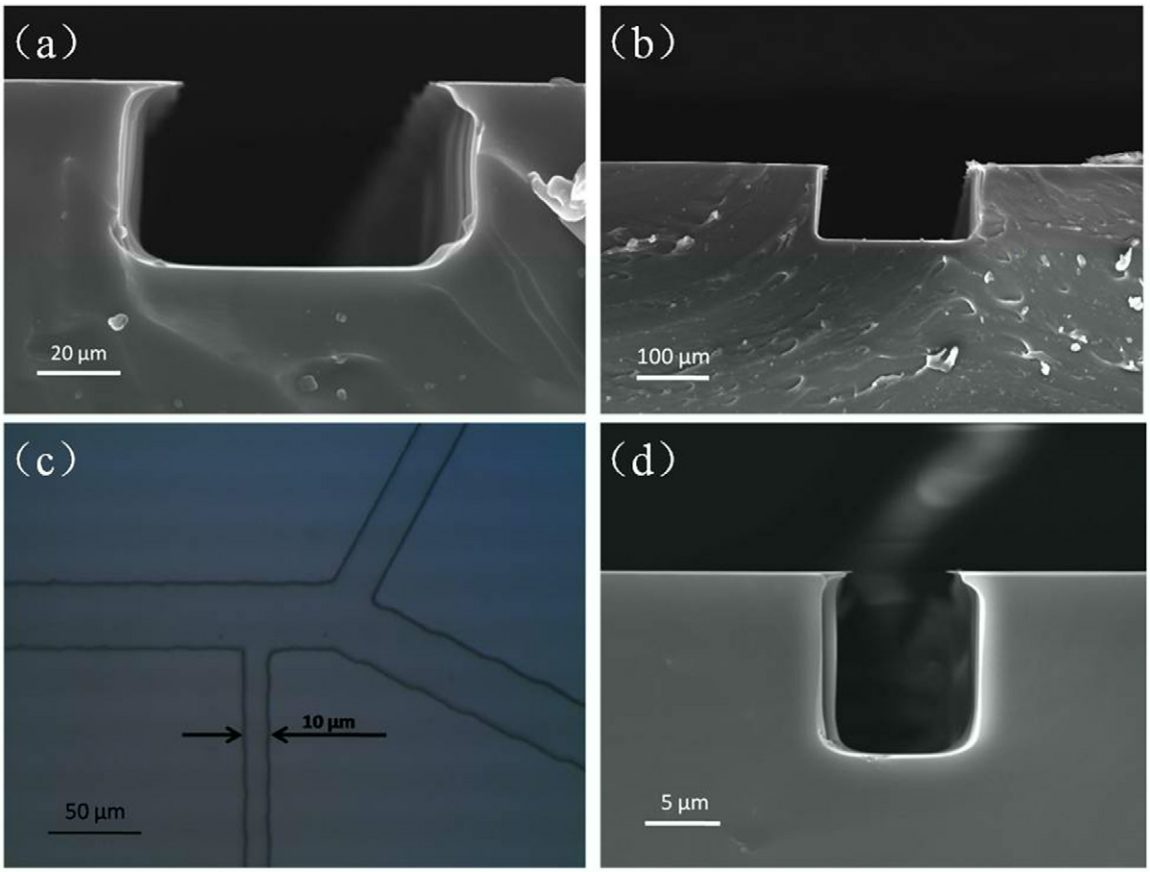

Figure 3. (*a*)–(*d*) The chips we have fabricated: (*a*) cross section of the PDMS channel 40 μm high and 80 μm wide under the scanning electron microscope (SEM); (*b*) the channel 100 μm high and 200 μm wide under the SEM; (*c*) the plane of PDMS with a 10 μm wide channel under the microscope; (*d*) the corresponding cross section of the 10 μm wide channel.

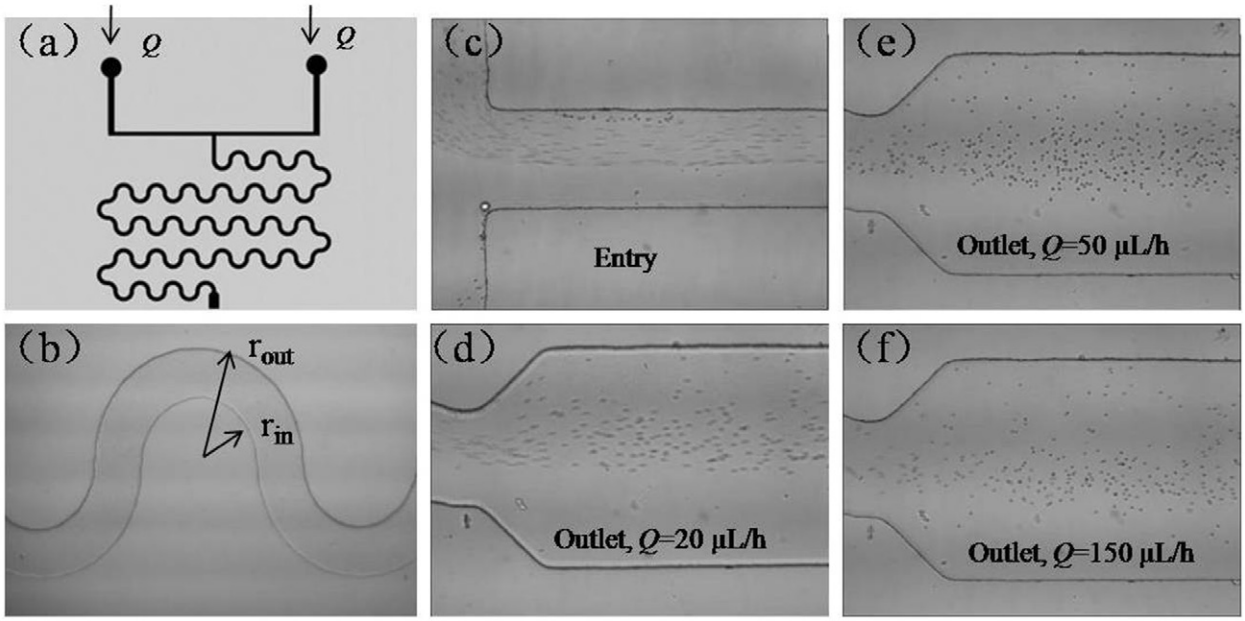

Figure 4. (*a*) Mixing by curved channels, Q denotes the inlet flow rate of RBC suspension and saline solution; (*b*) the width of the inlet and curving channel is 200 μm, the radius r_{in} = 200 μm, r_{out} = 400 μm; (*c*) stratified flow at the entry of the T-junction; (*d*)–(*f*) micrographs of the mixed cells at the outlet with different inlet flow rates.

(*b*) and (*d*) that the collimation of the channels is qualified in the cross section, and all the sidewalls of the cross section are almost perpendicular to the bottom surface, meaning that the parallelism of UV light generated by the LED is comparably suitable for lithography. Meanwhile, we find that the development time could directly affect the SU-8 mold

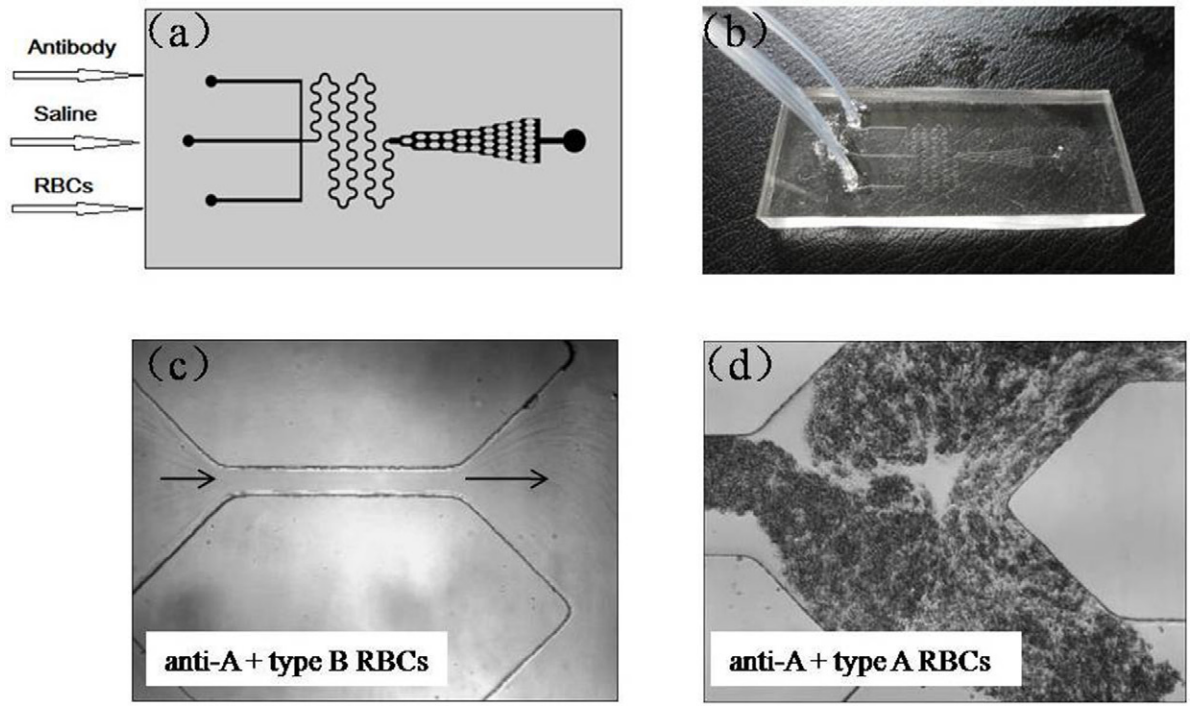

Figure 5. (*a*), (*b*) Microfluidic chip for blood typing; (*c*) no agglutination occurs when anti-A meets with type B RBCs; (*d*) strong agglutination to block the channel when anti-A meets with type A RBCs. The RBC suspension in the experiment is diluted by saline solution as 1:100 (v:v), and the flow rate of the antibody and RBCs is equal and maintained constant, $Q_{anti} = Q_{RBC} = 50\,\mu l\,h^{-1}$.

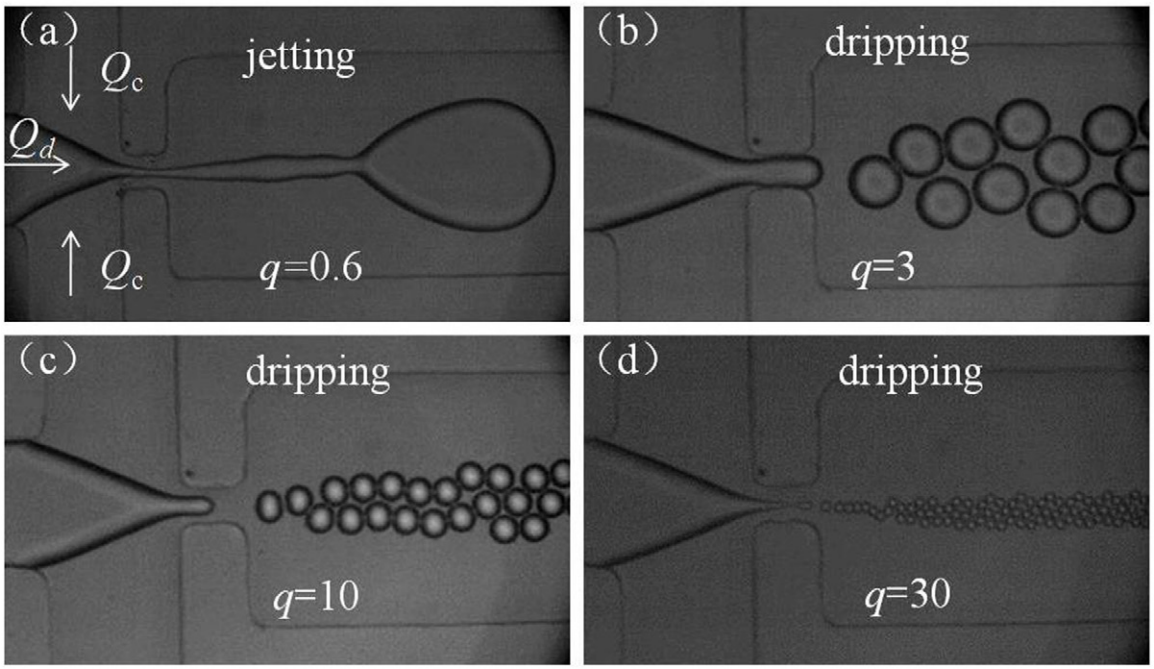

Figure 6. (*a*)–(*d*) Jetting and dripping regime within the flow-focusing microfluidics. The width of the orifice is 50 μm; Q_c and Q_d denote the flow rate of the continuous phase and dispersed phase, respectively. The flow rate ratio $q = Q_c/Q_d$ and Q_d is maintained constant ($Q_d = 50\,\mu l\,h^{-1}$).

and consequently brings about eaves on top of the replicated PDMS microchannel (shown in figures 3(*a*) and (*d*)). By carefully selecting the development time, we could fabricate the microchannel with a nearly perfect wall. Moreover, we measure the widths of different channels and the result shows that the minimum resolution of this process is 10 μm (figures 3(*c*) and (*d*)). It is of particular interest that the thickness of the SU-8-2050 coating here exceeds 100 μm, much higher than most common chips (5–30 μm), indicating that the LED could produce microfluidics with acceptable vertical sidewalls, especially for applications of thin microchannels. Under the condition of this great verticality of the channel sidewall,

our method is more advantageous than the latest UV bulbs employed in the PCB industry [13], which has the same resolution of 10 μm.

To validate the applicability of the fabricated microfluidic chips, we further conduct some experiments with them. Inlets/exits in these chips are connected by PE tubes (fine bore polythene tubing, Smiths Medical International, UK), and syringe pumps (New Era Pump Systems, USA) supply the power for liquid injection.

3.2. Mixing

The first experiment we conduct is the cell mixing through the curvature structure of the microfluidic channels. Reynolds number is extremely low when fluid flows within these microscale channels, and laminar flow leads to difficulty for turbulent mixing between multiple streams, so only slow diffusional mixing occurs. To obtain better mixing, active control such as an electrokinetic effector ultrasonic oscillator is employed [19, 20]. Alternatively, we design a curved channel to implement the fluid mixing as a passive method shown in figures 4(*a*) and (*b*). The channels feature a T-junction and a series of tiny curved structures. The fabrication technique is described in the previous section. Microfluidic channels with such structure promote the mixing between two liquids by producing the well known Dean vortices [21, 22]. We aim to mix a suspension of red blood cells (RBCs) and saline solution. The flow rates of two inlets are fine tuned and controlled to be identical. One can observe the stratified flow at the entry of the T-junction in figure 4(*c*), and cell mixing is achieved at the outlet as shown in figure 4(*d*). The Dean vortex effect is strengthened when increasing the flow rate of the entry side. Higher flow rate leads to better uniformity of the mixture.

3.3. Blood typing

Another validation is done with the ABO blood typing, an application of microfluidics that has received much attention owing to its rapid detection, and low reagent consumption [23–25]. Based on the mixing unit in figure 4(*a*), a simplified chip is designed to show the proof-of-concept on-chip blood typing method, as shown in figure 5. The saline performs as buffer liquid and is injected into the channel through the central inlet in advance to fulfill the surface wetting. The antibody and the RBCs are poured in at the same flow rate, and the curving channel is conducive to their mixture. Before the outlet we design some hexagonal obstacles to form a narrow porous gap (the gap size is about 20 μm), as seen in figure 3(*a*), aiming to observe the agglutination phenomenon between RBCs and antibody. Once the agglutination reaction exists during the mixing, the conglomeration will be obstructed to flow through the narrow gap, indicating the information of the RBC type. We can observe obviously the agglutination or non-agglutination in the chip when using different antibodies and blood. The conglomeration can be washed out with buffer to ensure the reusability of the chip.

3.4. Droplet generation

The last demonstration is the generation of droplets within a flow-focusing chip (shown in figure 6). Monodisperse droplets provide versatile means for biochemical analysis such as polymerase chain reaction (PCR) [26, 27], drug delivery [28] and microreactors [29, 30]. As illustrated, deionized water in droplet phase is injected through the central inlet, and mineral oil is a continuous liquid flowing from two lateral inlets. In the presence of the narrow orifice, the water is squeezed into a thread in the upstream of the orifice and ultimately breaks into droplets due to natural instability when the thread is sufficiently thin by shear stress from the viscous continuous fluid. The most famous dripping and jetting flow regime is also observed in our experiments as many researchers have reported [31–33], and the device here can produce homogeneous microdroplets ranging from 10 to 200 μm by controlling the flow rate ratio between continuous and dispersed fluid. The higher the flow rate ratio, the smaller the droplets that are generated.

Notes about using the LED device: (1) before exposing, make sure the lamp is vertically fixed on the support and the substrate is placed horizontally; (2) the pattern on the transparency mask should be put in the area of the light spot; (3) when the pattern exceeds the area of the light spot, separate the pattern into several parts with the opaque baffle, and then move the lamp horizontally to expose each part in sequence; (4) the photomask should be placed as tightly as possible against the photoresist to minimize the sidewall slope of the developed channels; (5) make sure the light battery is well charged; (6) the distance between the light source and substrate must be adjusted to the working distance (1–1.5 cm); (7) during exposure, do not touch the exposure equipment.

4. Conclusion

In summary, we propose that the LED can be used for microfluidics fabrication which is portable and cheap as compared with conventional lithography equipment. We validate the LED by replicating reported chips, and the resultant channels demonstrate that the LED source could produce chips similar to those produced by the expensive exposure machine. This method makes it possible for most laboratories to do research work on microfluidics without the need to go to a clean room. Additionally, the LED lamp can be directly purchased online, costing less than $750. Comparing with the light source of other low-cost lithography systems which need researchers to assemble and manufacture, this means is easier and quicker. Moreover, the photomasks (highly transparent photographic sheets) we used above cost only $1.5 per A4 sheet. With the minimum resolution of 10 μm and the good verticality of the channel sidewall, this process shows great promise for rapid prototyping of photoresist, and it provides a simple and low-cost way for many researchers to enter microfluidics research.

Acknowledgments

The authors would like to acknowledge the support from the NSFC (50876100) and the Grade A Technology Development Foundation of USTC (ZC9850340103). The authors also thank Dr Lei Gong for help on the LED beam characterization. We thank the Guangdong Provincial Key Laboratory on Functional Soft Condensed Matter, School of Materials and Energy, Guangdong Unversity of Technology.

References

[1] Edd J F, Di Carlo D, Humphry K J, Koster S, Irimia D, Weitz D A and Toner M 2008 Controlled encapsulation of single-cells into monodisperse picolitre drops *Lab Chip* **8** 1262–4

[2] Mazutis L, Gilbert J, Ung W L, Weitz D A, Griffiths A D and Heyman J A 2013 Single-cell analysis and sorting using droplet-based microfluidics *Nat. Protoc.* **8** 870–91

[3] Sia S K and Whitesides G M 2003 Microfluidic devices fabricated in poly(dimethylsiloxane) for biological studies *Electrophoresis* **24** 3563–76

[4] Sims C E and Allbritton N L 2007 Analysis of single mammalian cells on-chip *Lab Chip* **7** 423–40

[5] Verpoorte E 2002 Microfluidic chips for clinical and forensic analysis *Electrophoresis* **23** 677–712

[6] Xia Y N and Whitesides G M 1998 Soft lithography *Annu. Rev. Mater. Res.* **28** 153–84

[7] McDonald J C and Whitesides G M 2002 Poly(dimethylsiloxane) as a material for fabricating microfluidic devices *Accounts Chem. Res.* **35** 491–9

[8] Songjaroen T, Dungchai W, Chailapakul O and Laiwattanapaisal W 2011 Novel, simple and low-cost alternative method for fabrication of paper-based microfluidics by wax dipping *Talanta* **85** 2587–93

[9] Bu M Q, Melvin T, Ensell G J, Wilkinson J S and Evans A G R 2004 A new masking technology for deep glass etching and its microfluidic application *Sensors Actuators* A **115** 476–82

[10] Deng N N, Meng Z J, Xie R, Ju X J, Mou C L, Wang W and Chu L Y 2012 Simple and cheap microfluidic devices for the preparation of monodisperse emulsions *Lab Chip* **11** 3963–9

[11] Songjaroen T, Dungchai W, Chailapakul O, Henry C S and Laiwattanapaisal W 2012 Blood separation on microfluidic paper-based analytical devices *Lab Chip* **12** 3392–8

[12] Lu Y, Shi W W, Jiang L, Qin J H and Lin B C 2009 Rapid prototyping of paper-based microfluidics with wax for low-cost, portable bioassay *Electrophoresis* **30** 1497–500

[13] Pinto V, Sousa P, Cardoso V and Minas G 2014 Optimized SU-8 processing for low-cost microstructures fabrication without cleanroom facilities *Micromachines* **5** 738–55

[14] Aristizabal S L, Cirino G A, Montagnoli A N, Sobrinho A A, Rubert J B, Hospital M and Mansano R D 2013 Microlens array fabricated by a low-cost grayscale lithography maskless system *OPTICE* **52** 125101

[15] Jeong G H, Park J K, Lee K K, Jang J H, Lee C H, Kang H B, Yang C W and Suh S J 2010 Fabrication of low-cost mold and nanoimprint lithography using polystyrene nanosphere *Microelectron. Eng.* **87** 51–5

[16] Guijt R M and Breadmore M C 2008 Maskless photolithography using UV LEDs *Lab Chip* **8** 1402–4

[17] Suzuki S and Matsumoto Y 2008 Lithography with UV-LED array for curved surface structure *Microsyst. Technol.* **14** 1291–7

[18] Lee K S and Ram R J 2009 Plastic-PDMS bonding for high pressure hydrolytically stable active microfluidics *Lab Chip* **9** 1618–24

[19] Lynn N S, Henry C S and Dandy D S 2008 Microfluidic mixing via transverse electrokinetic effects in a planar microchannel *Microfluid. Nanofluidics* **5** 493–505

[20] Johansson L, Johansson S, Nikolajeff F and Thorslund S 2009 Effective mixing of laminar flows at a density interface by an integrated ultrasonic transducer *Lab Chip* **9** 297–304

[21] Sudarsan A P and Ugaz V M 2006 Multivortex micromixing *Proc. Natl Acad. Sci. USA* **103** 7228–33

[22] Jiang F, Drese K S, Hardt S, Kupper M and Schonfeld F 2004 Helical flows and chaotic mixing in curved micro channels *AICHE J.* **50** 2297–305

[23] Kim D S, Lee S H, Ahn C H, Lee J Y and Kwon T H 2006 Disposable integrated microfluidic biochip for blood typing by plastic microinjection moulding *Lab Chip* **6** 794–802

[24] Makulska S, Jakiela S and Garstecki P 2013 A micro-rheological method for determination of blood type *Lab Chip* **13** 2796–801

[25] Kline T R, Runyon M K, Pothiawala M and Ismagilov R F 2008 ABO, D blood typing and subtyping using plug-based microfluidics *Anal. Chem.* **80** 6190–7

[26] Zhu Z, Jenkins G, Zhang W H, Zhang M X, Guan Z C and Yang C Y J 2012 Single-molecule emulsion PCR in microfluidic droplets *Anal. Bioanal. Chem.* **403** 2127–43

[27] Nakano M, Komatsu J, Matsuura S, Takashima K, Katsura S and Mizuno A 2003 Single-molecule PCR using water-in-oil emulsion *J. Biotechnol.* **102** 117–24

[28] Tang K and Gomez A 1994 Generation by electrospray of monodisperse water droplets for targeted drug-delivery by inhalation *J. Aerosol Sci.* **25** 1237–49

[29] Shum H C, Bandyopadhyay A, Bose S and Weitz D A 2009 Double emulsion droplets as microreactors for synthesis of mesoporous hydroxyapatite *Chem. Mater.* **21** 5548–55

[30] Fidalgo L M, Whyte G, Ruotolo B T, Benesch J L P, Stengel F, Abell C, Robinson C V and Huck W T S 2009 Coupling microdroplet microreactors with mass spectrometry: reading the contents of single droplets *Angew. Chem. Int. Edn* **48** 3665–8

[31] Anna S L, Bontoux N and Stone H A 2003 Formation of dispersions using 'flow focusing' in microchannels *Appl. Phys. Lett.* **82** 364–6

[32] Utada A S, Fernandez-Nieves A, Stone H A and Weitz D A 2007 Dripping to jetting transitions in coflowing liquid streams *Phys. Rev. Lett.* **99** 10949

[33] Nunes J K, Tsai S S H, Wan J and Stone H A 2013 Dripping and jetting in microfluidic multiphase flows applied to particle and fibre synthesis *J. Phys. D: Appl. Phys.* **46** 114002