Chapter

Prototyping and Production of Polymeric Microfluidic Chip

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Abstract

Microfluidic chips have found many advanced applications in the areas of life science, analytical chemistry, agro-food analysis, and environmental detection. This chapter focuses on investigating the commonly used manufacturing technologies and process chain for the prototyping and mass production of microfluidic chips. The rapid prototyping technologies comprising of PDMS casting, micro machining, and 3D-printing are firstly detailed with some important research findings. Scaling up the production process chain for microfluidic chips are discussed and summarized with the perspectives of tooling technology, replication, and bonding technologies, where the primary working mechanism, technical advantages and limitations of each process method are presented. Finally, conclusions and future perspectives are given. Overall, this chapter demonstrates how to select the processing materials and methods to meet practical requirements for microfluidic chip batch production. It can provide significant guidance for end-user of microfluidic chip applications.

Keywords: microfluidic chips, micro structure, mold insert, replication, microinjection molding, bonding

1. Introduction

On the basis of channels with dimensions of tens to hundreds of micrometers, microfluidics principally deals with the processing and manipulation of tiny amounts (normally from 10^{-9} to 10^{-18} liters) of fluids [1]. Although early microfluidic devices relied mainly on silicon and glass, the use of polymer materials has become increasingly common, which is largely attributed to its relatively low cost, admirable replication accuracy, optical transparency, biocompatibility, chemical stability, and good electrical insulation. Integrating with other apparatuses such as detectors and purifiers, polymeric microfluidics contains micro components, which principally includes microchannels [2, 3], microvalves [4–6], micropumps [7], micromixers [3, 8]. In fact, the elementary surface structures, which generally include channels, wells, chambers, and protruding arrays in microscale and submicro scale, are crucial for the functionalities of the entire microfluidic systems. The cross-sectional shape is normally square, and the aspect ratio is commonly less than two with a surface roughness being smaller than 50 nm.

For mass production of a microstructured plastic part for microfluidic applications, an appropriate tooling technology with the capability of enabling the

fabrication of multi-scale features and controllable surface quality is required, because the feature size and quality of microinjection molded microfluidic chip is highly related to the characteristics and quality of corresponding micro mold insert [9–12]. The essence of replication is the reproduction of microfluidic structures from the master to the substrate materials. In terms of the replication of surface structures using polymer materials, techniques such as injection molding [13, 14] (including microinjection molding, variotherm-assisted injection molding, and injection compression molding), embossing [15, 16] (hot embossing, UV embossing, roll-to-roll embossing), nanoimprinting [17] and 3D printing [18] are commonly applied. Among all the replication processes, injection molding and hot embossing are more viable for industrial production, due to their advantages of relatively low cost and suitability for different materials and product design. Injection molding can be particularly efficient for mass production.

After microinjection molding of microfluidic devices, sealing is required to achieve enclosed microchannels [19]. Some important parameters should be taken into consideration before selecting bonding methods. Bond strength should be one of the most important parameters. In some applications, the interfacial bond energy is expected to be as high as the cohesive strength of the substrate, while in other applications the weak and reversible bonds between the cover and the substrate are required. Another parameter should be the solubility of thermoplastic and solvent. The interfaces used for bonding should be compatible with some solvent so that they can be dissolved and bonded together, meanwhile, the microchannels should not be subjected to the deformation in the bonding process [19]. Other parameters include the surface roughness, optical properties as well as material compatibility. In general, bonding methods can be either indirect or direct. In the indirect bonding process, an intermediate adhesive layer is used to bond two substrates together [20]. The interfaces applied with adhesive will have different properties than the bulk substrate. In terms of direct bonding, no other material is added between the interfaces, and the surface of the substrates can be mated directly [21]. After bonding, the interfaces and bulk material have homogenous properties.

This chapter will overview these prototyping and mass production technologies and process chains for manufacturing of polymer microfluidic chips.

2. Rapid prototyping of microfluidic chips

In recent years, microfluidic devices find many advanced applications in chemical analysis [22], polymerase chain reaction (PCR) [23], biological analysis [24], and chemical synthesis [25]. Main rapid prototyping methods of fabricating microfluidic chips include PDMS casting, micromachining, and 3D printing, etc.

2.1 PDMS casting

PDMS casting is also named soft lithography. The polydimethylsiloxane (PDMS) is a kind of silicon-based organic polymer material that has been widely used in microfluidic devices by rapid prototyping [26]. PDMS casting fabrication process is typically divided into the following steps (see **Figure 1**): molds developing, PDMS casting, curing and releasing, bonding, and integration [14]. A master mold needs to be prepared firstly, where SU-8 epoxy resin usually is applied as the mold material [27]. The standard PDMS compositions are composed of silicon elastomer base and the curing reagent in a ratio of 10:1. The uncured PDMS is poured into the mold, followed by curing at 70–80 °C for an hour. After releasing PDMS from the mold, PDMS microfluidic chips can be obtained [28]. The post-process of PDMS

Figure 1.
Process steps of PDMS casting.

casting usually includes bonding and integration. Bonding can reduce the hydrophobicity of the PDMS chip to encapsulate its microchannel. To enhance the bonding strength of chips with other materials, adjusting bonding process parameters and surface modification by using oxygen plasma to form O-Si-O covalent bonds at the interface of PDMS microfluidic channels are commonly used [29]. Finally, some microsensors, microheaters and microfluidic pumps are integrated onto microfluidic chip for diversified performance [18]. **Figure 2** shows the practical microfluidic chip fabrication approaches by the PDMS casting process.

Although PDMS casting is a rapid prototyping process for disposable microfluidic chip fabrication, it is a complex process with many drawbacks. The microfluidic chip fabricated by PDMS casting has insufficient mechanical strength, non-conductivity, and non-magneticity. Also, under high temperature, high voltage, and pressure conditions, it is not easy to integrate other precision components on the microfluidic chip [19].

2.2 Micro machining

The microfluidic chip fabricated by micro machining, such as femtosecond laser or endmill, has relatively high accuracy and can be used repeatedly [20]. Combing with computer numerical control (CNC), micro machining can rapidly and accurately construct devices at several microns scale [21]. However, microchannels obtained from micro milling are too rough to use as a microfluidic chip, especially for the machining of polymer materials [22]. However, compared with micro milling, laser micro machining with improved accuracy can perform the direct writing ablation of polymers such as PMMA, PC, etc. Direct-write laser machining with UV and CO_2 assistance can realize microstructuring in polymer materials.

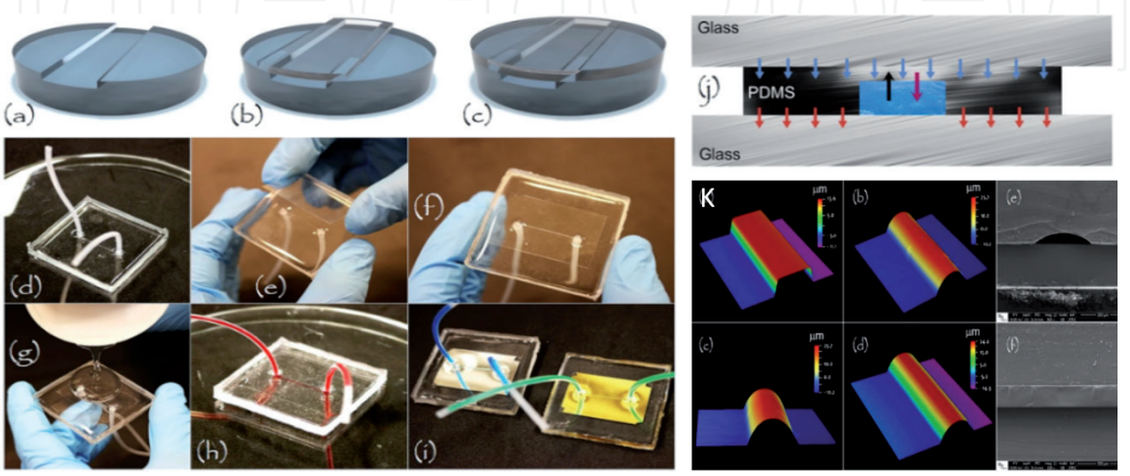

Figure 2.
PDMS casted microfluidic chip: PDMS substrate with microchannels (a); enclosing of microchannel (b, e, f); PDMS molding(g); PDMS curing (c, h); substrate integration to fluid pump (d); SWB was applied for prototyping PDMS (I; forces in reversible bonded microdevice (j), mold characterization and cross-section (k) [30].

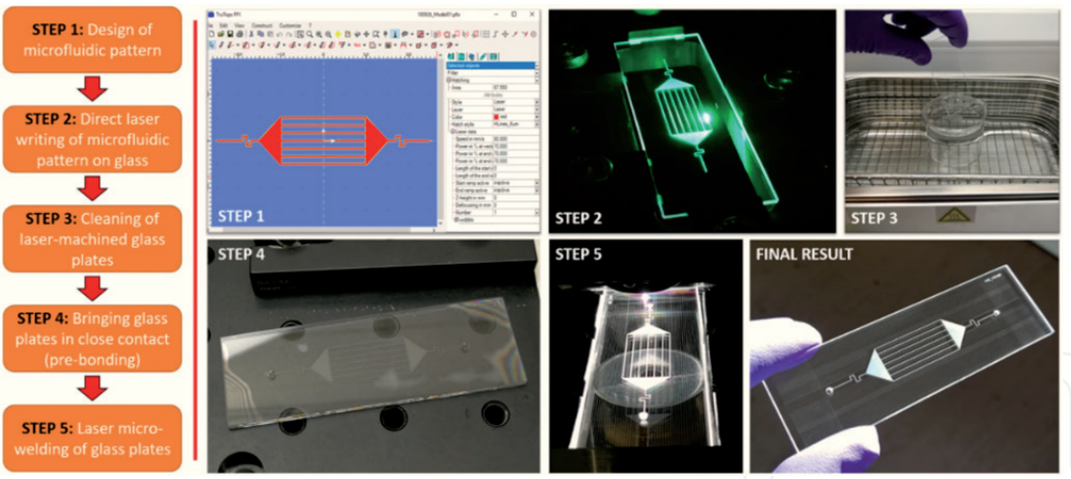

Figure 3.
Direct-write laser machining for microfluidic chip [31].

For laser micro machining, when the laser beam is moving above the workpiece space, the heated spots will gather to form various patterns. Through the reflection in the light path and the focusing effect of the focusing lens, the laser is finally focused on the workpiece, where the temperature of the focal point increases rapidly. After the polymer material melts and decomposes, scratches will be left on the surface of the polymer, where the microchannels are formed [24]. The scanning speed is programmed and controlled by a computer. **Figure 3** shows the specific process methods of laser micro machining and machined glass microfluidic chip.

2.3 3D-printing

3D-printing is different from traditional manufacturing techniques. It achieves the fabrication of materials utilizing additive manufacturing (AM). Under computer-aided control, it can construct the 3D structure layer by layer. The most common 3D printing technologies used in the manufacture of microfluidic devices are stereo-lithography (SL), multi-jet modeling (MJM), and fused deposition modeling (FDM). SL utilizes selective light exposure to photopolymerize precursor to construct object layer by layer [27]. For MJM, it works by using an inkjet head to spray curable liquid photopolymers into a tray, and photopolymerization will happen on each layer when exposed quickly to UV light. FDM uses a motor-driven nozzle head to print heated thermoplastic material in three dimensions. **Figure 4** demonstrates the 3d-printing devices and printed polymer microfluidic chips. A thin resin layer as printed material is solidified via laser beam for the fabrication of 3D-chip that features the channel layer and bottom layer of 500 μm and intersects at 45° and 20°. The printing resolution is 50 μm in line width. After the printing process, the chip needs to be washed using isopropanol (IPA) and deionized (DI) water in the micropump platform.

3. Scaling up production of microfluidic chips

In general, to achieve batch production of polymer microfluidic chips, a high-quality mold insert is indispensable for precision replication of micro structure using microinjection molding. In this case, developing a reliable tooling technology for mold insert fabrication is important. Besides, after microinjection molding of polymeric chips, the bonding process for sealing microchannels of chips determines the final functionality of microfluidic chips. Therefore, each process step is significantly important.

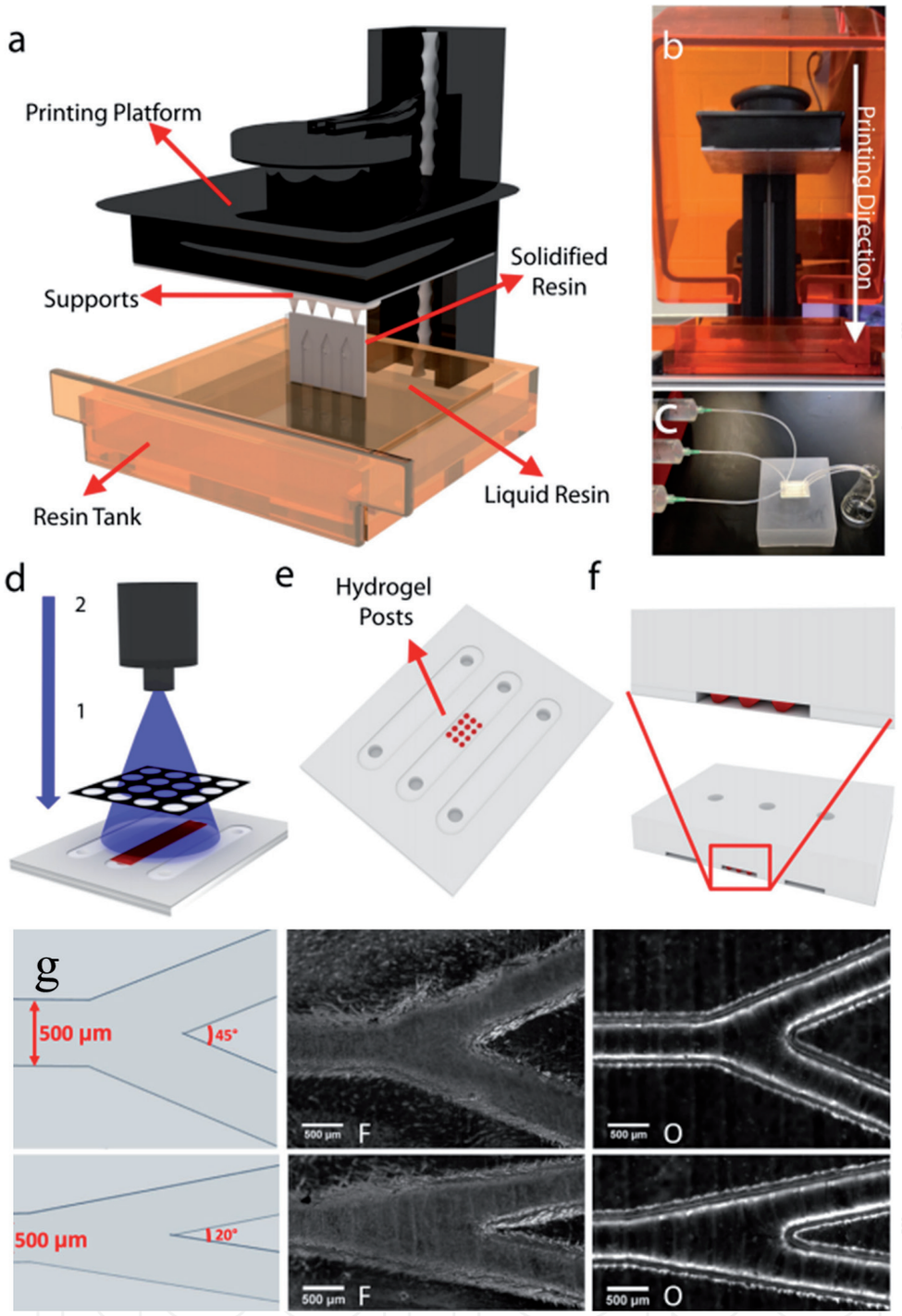

Figure 4.
3D printed polymer microfluidic chip: (a)schematic of SLA process; (b) printing platform configuration; (c) channel washing; (d) application of hydrogel; (e) remaining hydrogel remove; (f) cross-section of the 3D chip; (g) 500 µm raised structures intersecting at a 45° and 45° [32]. Copyright (2016) with permission from IOP publishing, LTD.

3.1 Tooling technology

There are a variety of manufacturing technologies available to fabricate micro mold inserts, such as ultraprecision micro milling, micro-electrical discharge machining (μEDM), electrochemical machining (ECM), silicon wet etching, deep reactive ion etching, laser machining, and LIGA-based processes (LIGA, UV-LIGA). **Table 1** shows a comparison among the mold insert manufacturing technologies according to the achievable feature size, surface roughness, aspect ratio, and machinable materials.

Technology	Feature size (μm)	Surface roughness (μm)	Aspect ratio	Material
Micro milling	25 ~ 100	0.2 ~ 5	10	Brass, COC, steel
μEDM	10 ~ 25	0.05 ~ 1	50 ~ 100	Conductive materials
ECM	10	0.02	NA	Conductive materials
Laser machining	1 ~ 5	0.4 ~ 1	<50	Any
X-ray lithography	0.5	0.02	100	Photoresist
UV lithography	0.7 ~ 1.5	NA	22	Photoresist
Deep reactive ion etching	2	NA	10 ~ 20	Silicon
Electroforming	0.3	<10	<10	Copper/nickel/alloy

Table 1.
Comparison between various manufacturing techniques for the fabrication of microstructured mold insert [33].

The selection of mold insert fabrication technology is based on the geometrical complexity, desirable feature size, aspect ratio, surface roughness, and processing cost. Micro milling or EDM generally is used for fabricating micro structure with feature sizes larger than 50 μm with a tolerance of several micrometers. However, it is difficult to achieve a low surface roughness and some sharp corners processing. **Figure 5** shows the microfluidic mold insert fabricated by micro milling and die-sinking EDM process. LIGA, silicon wet etching, and deep reactive ion etching have excellent advantages for sub-micron fabrication [34]. ECM is suitable for structuring 3D features with less sub-surface damage and higher dimensional precision at the nanometric range [35]. The selection of mold insert materials is also critical. When the production yield is less important and the mold insert lifetime is not critical, silicon wafer mold insert fabricated from deep reactive ion etching is favorable to the precision replication of plastic microchip with optical surface finishing [36]. However, in most instances, a long-life metal mold insert having high wear resistance and hardness is desirable for the mass production of microinjection molded microfluidic chips. For example, stainless steel mold insert can be against the feature being worn or surface quality degradation under up to tens of thousands of microinjection molding cycles. In this case, ultraprecision machining, LIGA process, laser machining, and μEDM can be more viable. Also, the LIGA process and μEDM can fabricate the micro structure with a high aspect

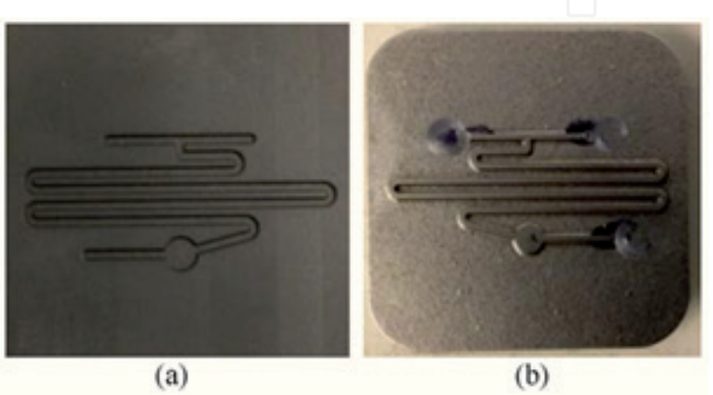

Figure 5.
Micro milling and die-sinking EDM fabricated mold insert: graphite electrode (a) and stainless tools (b) [33]. Copyright (2015) with permission from IOP publishing, LTD.

ratio and tight tolerance [37, 38]. **Figure 6** shows the dry-etched silicon wafer mold, UV lithographic photoresist mold, and electroformed nickel mold, which were fabricated by the author' team. In the following sections, the main manufacturing technologies for mold insert fabrication are detailed.

3.1.1 LIGA

LIGA technique comprising of lithography, electroforming, and molding is a multi-step replication process to generate micro structure with the desired patterns [39]. It has been a promising technology for industrial-scale commercialization [40, 41]. The typical process methods follow the consequential steps below: 1) the photoresist (AZ or epoxy resin SU-8) is firstly evenly coated on the silicon wafer substrate along with the subsequent baking process; 2) a pre-prepared photomask with the desired patterns is placed on the top surface of the photoresist at a good alignment manner for further irradiation exposure; 3) the exposed areas is removed/remained chemically using developer (depending on the type of photoresist), where the patterns are transferred to silicon wafer from mask and the dimensional accuracy of patterns can be controlled by lithography parameters (exposure time and exposure dose); 4) seed layers of adhesive layer (Ti/Cr) and conductive layer (Au/Ni) are sputtered onto the structured photoresist surface for metallization; 5) the following step is electroforming for fabricating a microstructured mold insert, where the metallized patterns on silicon wafer serve as a cathode for nickel deposition; after electroforming, a electroformed replica is relived via silicon chemically etching and photoresist is chemically removed; the final replica can be used as a mold insert; 6) such an electroformed mold insert can be used as a master for replication of microfluidic chips by microinjection molding process [42]. **Figure 7** details the specific process steps of mold insert fabrication in various microstructuring technologies assisted by electroforming.

Due to costly x-ray synchrotron for X-ray lithography, the LIGA process is not commonly used in the industrial field. As an alternative, UV lithography has been a favorable technology to prepare master for electroforming [37, 43]. As a result, UV-LIGA has been an acceptable process to fabricate the mold insert with the

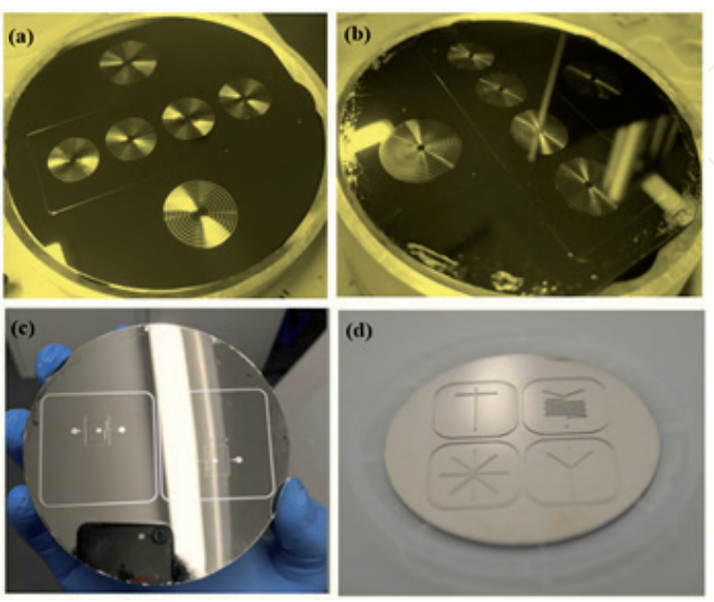

Figure 6.
(a) Dry etched silicon wafer; (b) UV lithographic photoresist master; (c) and (d) electroformed nickel mold insert. Copyright (2020) with permission from IOP publishing, LTD.

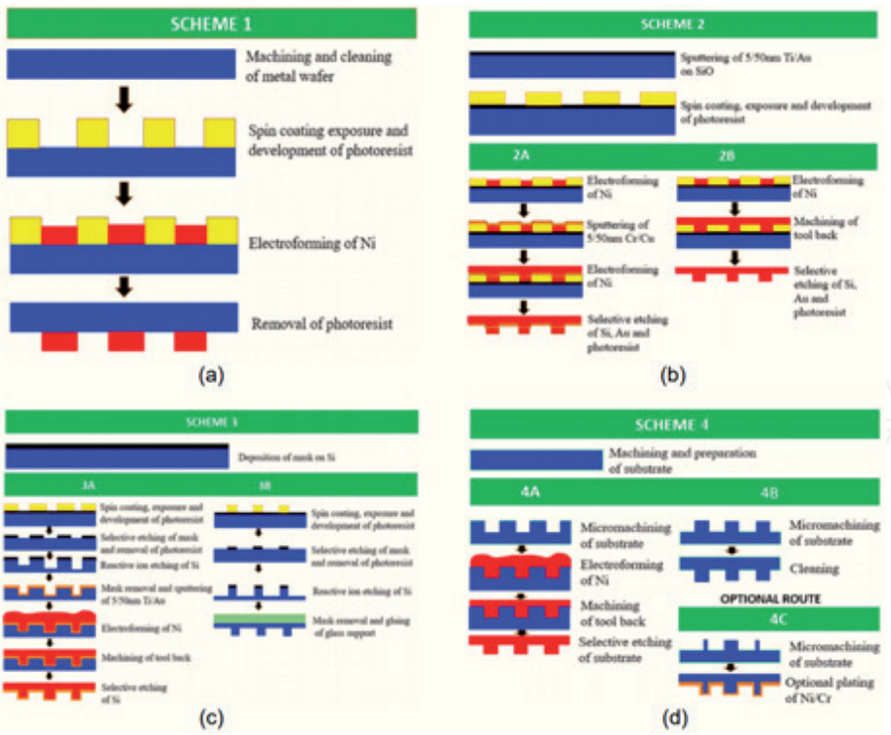

Figure 7.
Basic schemes of manufacturing of mold insert.: (a) metal substrate, lithography, and electroforming; (b) a silicon substrate, lithography, and electroforming; (c) deep reactive ion etching of silicon (d) micro-machining of non-silicon substrates [9]. Copyright (2020) with permission from IOP publishing, LTD.

feature size of several micrometers to hundreds of micrometers, although the reachable aspect ratio of this technique is limited in the range of ~20 [34]. Considering the specific microfluidic applications, UV-LIGA is sufficient to fabricate the desired micro structures. Additionally, some LIGA-like processes, such as EUV-LIGA, EBL-LIGA, IB-LIGA, are also developed towards nanoscale micro structuring [44]. However, these LIGA-like techniques still have some shortcomings for mold insert fabrication. First, the mold materials usually are nickel and nickel alloy, the tool steel is not included due to the restriction from the electroforming process. Besides, the integration of draft angle onto mold insert is not easy, but it is critical for demoulding of the polymeric part from mold insert to reduce the potential demoulding deformation and damages of micro structures [45]. The research shows that the draft angle can be achieved by properly adjusting the UV/X-rays exposure dose.

3.1.2 Laser machining

The fabrication of a metallic mold insert is generally time consuming and expensive. Laser machining seems to be more competitive than other mechanical machining techniques. It allows the rapid fabrication of micro structure with a feature size of several micrometers at an aspect ratio of ~10 [46]. However, due to the limitation of spot size, making high precision micro mold insert with tight tolerance by direct laser micromachining is challenging. The minimum spot size is usually half wavelength of the light utilized [47]. In this context, the laser LIGA technology combining laser ablation and electroforming process is developed to produce precision mold insert with 3D structures, where laser ablation is applied to form polymer stencil for subsequent metallic replication by electroforming to fabricate nickel micro mold insert. **Figure 8** shows the microstructure metal mold insert and polymer mold insert fabricated by laser machining and laser ablation, respectively.

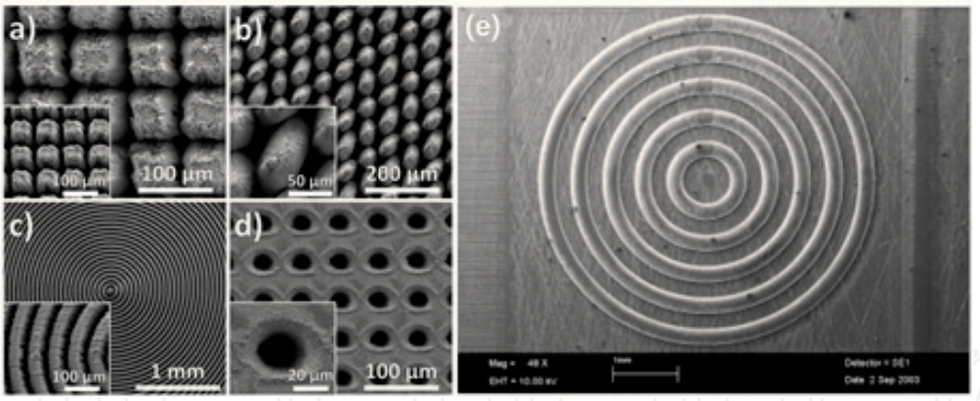

Figure 8.
(a-d) Micropatterns on metal mold insert fabricated by laser machining [48]; (e) Polymer mold insert fabricated by laser ablation [49]. Copyright (2004) with permission from Royal Society of Chemistry.

Of course, when micro mold insert with 3D structures is used for microinjection molding of the microfluidic chip, the use of conventional methods often brings challenges to microstructure demoulding.

3.1.3 Micro electrical discharge machining (μEDM)

The μEDM technology is a non-conventional electrochemical processing method. The mold insert is fabricated based on the material removal mechanism with the erosive effect of the electrical discharges that happen between electrode and workpiece. The electrode and workpiece are placed with a small enough gap so that the voltage–current system can efficiently ionize the dielectric. The shape and dimension of the processed workpiece are determined by the electrode pattern. Micro mold insert with the feature size of ~20 μm can be machined by μEDM technology but the forming accuracy and surface roughness are not able to be guaranteed. **Figure 9** demonstrates

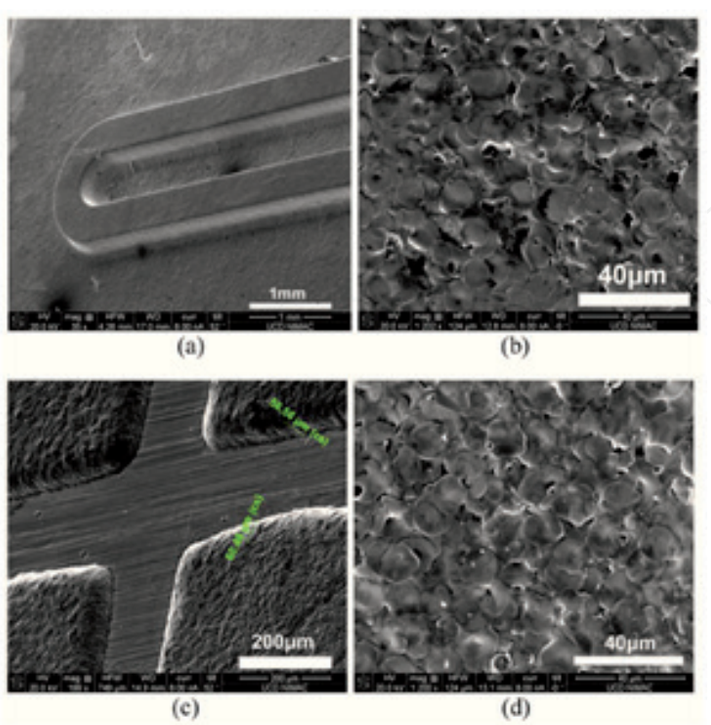

Figure 9.
Stainless steel mold insert fabricated by μEDM technology: graphite electrode with better geometry definition on micro-patterns (a); copper electrode with non-uniform edge finish (c); the crater size of both electrodes ((c) and (d)) [33]. Copyright (2015) with permission from IOP publishing, LTD.

the stainless steel mold insert machined by μEDM. With the assistance of other technologies, the surface finishing issues can be solved, such as ultrasonic-assisted μEDM. Overall, μEDM is a competitive technology, which has non-contact mechanical force, heat, and stress generation for machining the mold insert for microfluidic applications.

3.2 Micro injection molding of microfluidic structures

Micro injection molding is an important process to transfer patterns from mold to the surface of microfluidic patterns. Thanks to fast solidification and relatively high viscosity, filling of polymer melts into tiny micro patterned mold is challenging. Upon micro pattern is formed, separation of patterns from mold is problematic due to the distortion or damage of plastic micro structure from friction and adhesion between polymers. Here a brief introduction of these issues is presented by using a microfluidic chip as an example and a simulation strategy for microfluidic structure optimization is introduced.

3.2.1 Structures filling mechanism for micro injection molding

Figure 10(a) illustrates a fast prototyping mold for the injection molding of a flow cytometer chip, which has an area of 26.12 mm × 26.12 mm and a thickness of 1.05 mm [50]. **Figure 10(b)** shows surface structures that are used to fabricate inverted channels, all of which are 250 μm wide and 150 μm deep for the parts that had rectangular cross-sectional areas. The horizontal channel works as a fluidic channel, in which biological particles, such as cells, are focused by sheath flow from side inlets. Meanwhile, an optical fiber is integrated into the microfluidic chip using tilted channels. One channel is used for a fiber laser excitation beam and the other two are allocated for detection of forwarding scattering and side/fluorescence scattering by fibers. In order to minimize light intensity reduction of the excitation

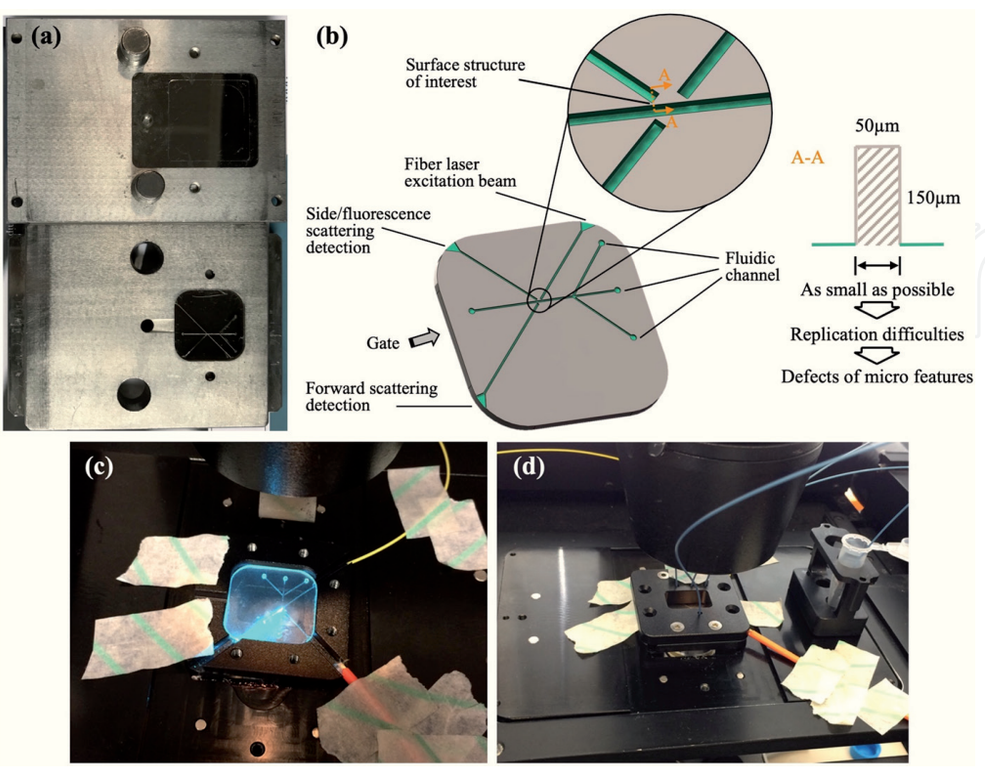

Figure 10.
Flow cytometer chip: (a) cassette mold, (b) three-dimensional model of surface structures on the chip, (c) actual chip assembly, (d) connection with tubing [55].

laser and to decrease potential scattering when the laser beam passes through plastic material, the distance between the fluidic channel and optical fiber channels has to be as small as possible. This requirement necessitates surface structures as shown in the upper image in **Figure 10(b)**. The protruding structures demonstrate a gradual aspect ratio, and the highest ones are at the places between the edge and the fluid channel, which have an aspect ratio of 3:1 nominally; it is these that were mainly investigated. **Figure 10(c)** shows the actual microfluidic chip (after bonding), which is assembled into a designed chip holder and connected with samples and PBS (Phosphate-buffered saline) sheath flow using PTFE (Polytetrafluoroethylene) tubing (**Figure 10(d)**).

In theory, the surface structures should fill more easily under such a layout because the gate was parallel to the feature of interest and the centre fluid channel [51]. However, replication of micro/nanoscale surface structures is challenging due to their high surface to volume ratios, especially for high aspect ratio features. Fast heat transfer rates mean that the polymer melts are inclined to solidify before the cavities are fully filled. For example, experimental results show that the cross-sectional area of the surface structure emphasized in **Figure 10(b)** only reaches up to 70.67% of the criterion. Combined with microscopy, process monitoring, and morphology, A combined melt flow and creep deformation model is proposed to explain the complex filling behavior of the surface structure. As shown in **Figure 11**, the overall replication is ordinarily composed of two parts: melt flow during the injection stage and creep deformation during the packing stage. Melt flow is related to injection velocity and pressure, while the extent of creep deformation is linked to mold temperature, packing pressure, packing time, etc. Based on this, increasing shot size to improve the replication quality of surface structures is proposed, and the replication is significantly improved and sufficient to satisfy the practical requirements of a microfluidic flow cytometer chip.

3.2.2 Process simulation and validation

In order to better understand the connection between product quality and process parameters, process simulation of injection molding has developed over several decades. Simulation in the early stages of part and mold design is relatively cost-efficient and offers the capability to evaluate various design options, such as runner design and gate designs. However, microscale effects, such as altering heat transfer coefficient (HTC), wall slip behavior, mold surface roughness, venting operations, which tend to be ignored in conventional injection molding simulation, should be considered in the simulation of microinjection molding effectively [52–54]. Another important concern is that most studies only used nominal machine processes, but they do not include the actual machine dynamics, which is important for microinjection molding of surface structures because microscale surface structures are much sensitive to process variation. As a result, simulation results are more or less unconvincing and cannot be adapted for real-world applications, and the simulation inaccuracy needs to be addressed.

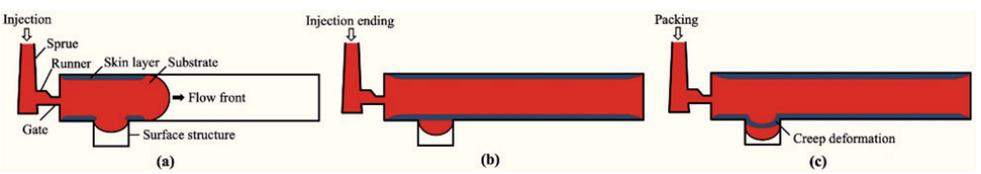

Figure 11.
Filling mechanism of surface structure on a substrate: (a) the injection stage, (b) the end of the injection stage, (c) the packing stage [50]. Copyright (2018) with permission from IOP publishing, LTD.

Based on an experimental study on the filling behavior of microfluidic surface structures (**Figures 10(b)** and **11(a)**), the real responses of the injection molding machine are acquired and adopted in the process settings of the simulation with the help of process monitoring [55]. In addition, the effect of microscale sensitive parameters on the replication of surface structures using simulation is systematically studied and validated by flow front profile, cross-sectional profile, and replication of the structures. Consequently, the combination including a relatively higher heat transfer coefficient (30,000 W/(m2·K)) of the injection stage, standard atmospheric pressure (0.1 MPa) as the initial air pressure of venting, 0.7 as the friction coefficient for wall slip and a freezing temperature of 20 degrees above the glass transition temperature is selected. In terms of the flow cytometer surface structures, replication defects in experiments (circled in **Figure 12(a)**) are successfully predicted after the optimization as the blue parts shown in **Figure 12(c)**. Besides, the insufficient replication of the droplet cylinders (the areas in white in **Figure 12(c)**) is also predicted after the selected parameters are applied.

3.3 Bonding techniques for microfluidic devices

The bonding methods for microfluidics comprises adhesive bonding, thermal fusion bonding, UV assisted thermal bonding, and solvent bonding. Following each section is introduced based on recent research findings with the mechanism, applicable materials, and process parameters of each bonding method. Finally, the challenges and relevant solutions for different bonding techniques are given.

3.3.1 Adhesive bonding

Adhesive bonding is a simple manner to seal microfluidic devices, compared to other bonding techniques. By applying the liquid adhesive onto the surface of the chips, the solvent composition starts to evaporate till two parts are bonded. Besides, some adhesives with epoxy or acrylate compositions need to be cured under UV light irradiation or upon heating. After mixing with the photo-initiator or catalyzing agent, polymerization or crosslink reaction can occur in the adhesive system [56], where the adhesive is cured and microfluidic devices are bonded.

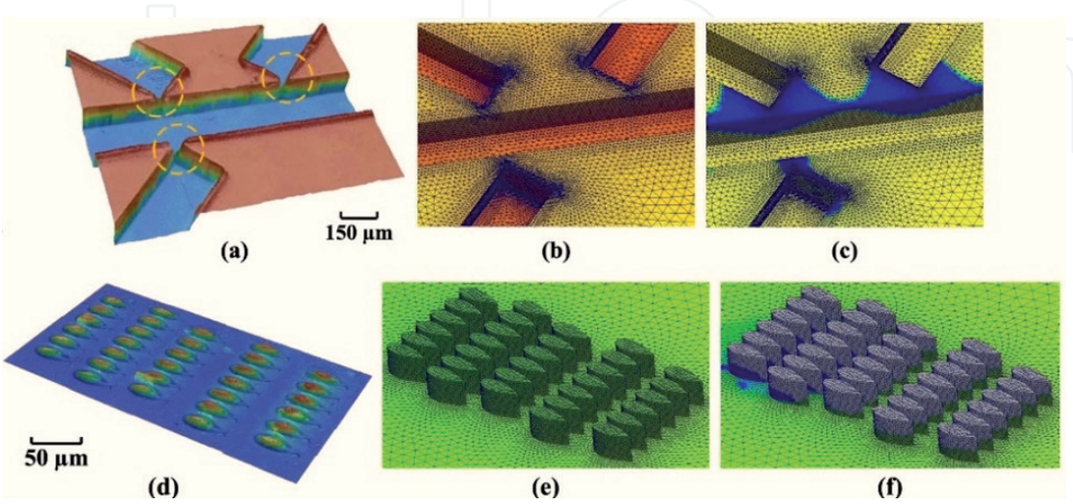

Figure 12.
Optimization and validation: (a) experimental result, (b) simulation result with default settings, and (c) simulation results (after the cycle including the packing and cooling stage) with optimized parameters for the replication of flow cytometer structures; (d) experimental result, (e) simulation result with default settings, and (f) simulation results (after the injection stage) with optimized parameters for the replication of microfluidic droplet cylinders [55].

UV-curable adhesive as an intermediate layer has also been developed to assemble the disposable PMMA chips [57]. The substrate is firstly washed by ultrasonic cleaning equipment with deionized (DI) water and flushed with nitrogen before bonding. Then the adhesive is applied to the cover plate by spin coating (**Figure 13b**). After spin coating, the cover plate is assembled with the substrate, then silicone tubes are connected to the inlet and outlet ports of the chips. According to **Figure 13c**, the isopropanol is injected into the inlet ports and comes out from the outlet port through the silicone tubes in the flushing process. This process is aimed at flushing out the uncured adhesive that has been trapped inside the microchannels to prevent the channel clogging. In the last stage, the assembled chips are exposed to the UV light irradiation and the polymer chains in the adhesive system are crosslinked. **Figure 14** shows the bonding state of a microfluidic chip with time using adhesive bonding technology.

Although this method is useful for disposable devices, the storage time of adhesives at room temperature should be highlighted. Meanwhile, using isopropanol to flush out the uncured adhesive is a complicated procedure, as it might also wash out the adhesive at the edge of the microchannels, then the bonding effect will be reduced. In this way, the burst pressure should be conducted in case the edge of the channels is not fully bonded.

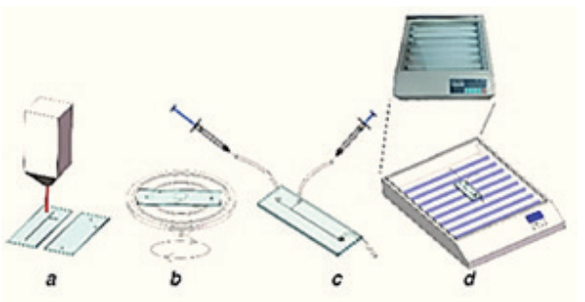

Figure 13.
Schematic diagram of the microchannel fabrication and bonding process: laser ablation for the fabrication of through holes on PMMA (a); spin coating of UV curable adhesive on cover plate (b); flushing out the un-crosslinked adhesives (c); UV exposure to induce the crosslinking of adhesives in the whole chip system [57].

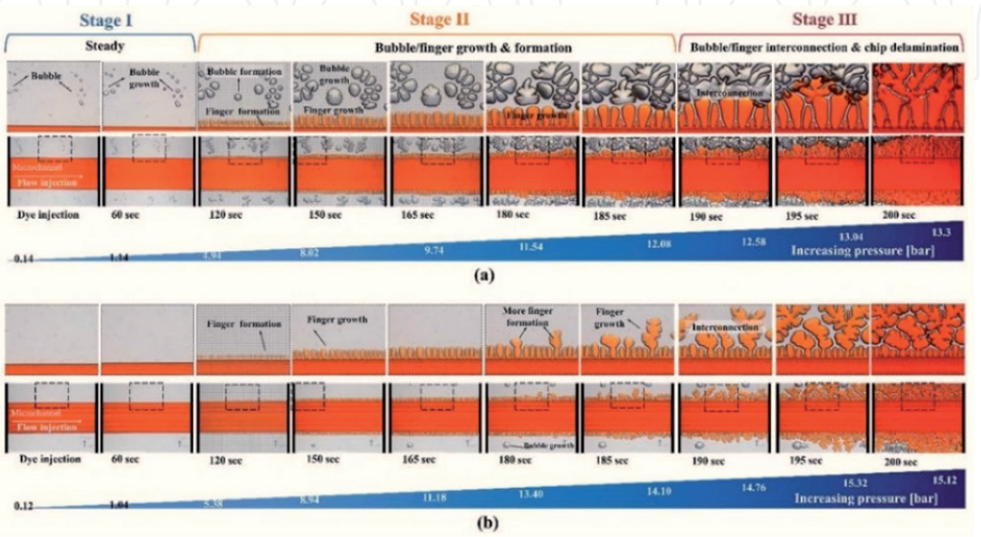

Figure 14.
The microfluidic chip bonding state with times [58].

3.3.2 Thermal fusion bonding

During the thermal fusion bonding process, the heating temperature is raised above the glass transition temperature (Tg) of the cover plate [19]. Meanwhile, a hold pressure is applied to enhance the mating contact forces between two surfaces. To achieve a strong bond, the heating temperature and the hold pressure should be high enough to ensure the complete diffusion of the polymer chains. In this case, the bond strength in the interface can be as high as the cohesive strength in the bulk material. According to **Figure 15**, the cover is first treated by O_2 plasma to make its surface more hydrophilic. In this case, the adhesion between the COC cover plate and PMMA substrate is greatly improved. During the thermal press process, heat and constant pressure are provided. Steel platen transfers both heat and pressure to the chips. Two rubber sheets are used to distribute the pressure evenly and two polyimide films are used for the anti-sticking purpose (**Figure 15**).

One critical problem of thermal bonding is that the temperature and the pressure cannot be too high, otherwise, the microchannels may collapse and their integrity cannot be well maintained. Therefore, the heating temperature, hold pressure, and hold time should be controlled and adjusted to achieve high bond strength and limit the channel deformation. The balance should be achieved among the heating temperature, hold time, and hold pressure. These parameters should be well adjusted to maintain the integrity of the channels.

3.3.3 UV assisted thermal bonding

The channel collapse is hard to avoid during thermal bonding, as the heating temperature is often higher than the Tg of material. Therefore, it is important to lower the heating temperature. In this case, the substrate or cover plate can be pre-treated by UV/Ozone to achieve bonding at low temperature. The pre-treated surface has higher energy due to oxidation. Therefore, the hydrophilicity and wettability are improved. As a result, the adhesion between the two surfaces is promoted.

Tsao et al. [60] compared the cross-section of the PMMA microchannels with and without UV/Ozone pre-treatment. As shown in **Figure 16(a)**, this chip treated by UV/Ozone had good bonding integrity. However, the untreated chips appeared obvious channel collapse as shown in **Figure 16(b)**. It is considered is because the treated chip had higher bond strength than the untreated chip (0.624 mJ/cm^2 compared to 0.003 mJ/cm^2).

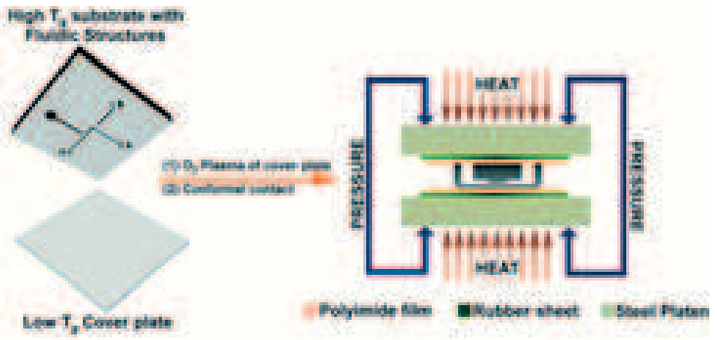

Figure 15.
Schematic of the protocol used for assembly of the hybrid-based fluidic devices and the thermal press instrument [59]. Copyright (2015) with permission from Royal Society of Chemistry.

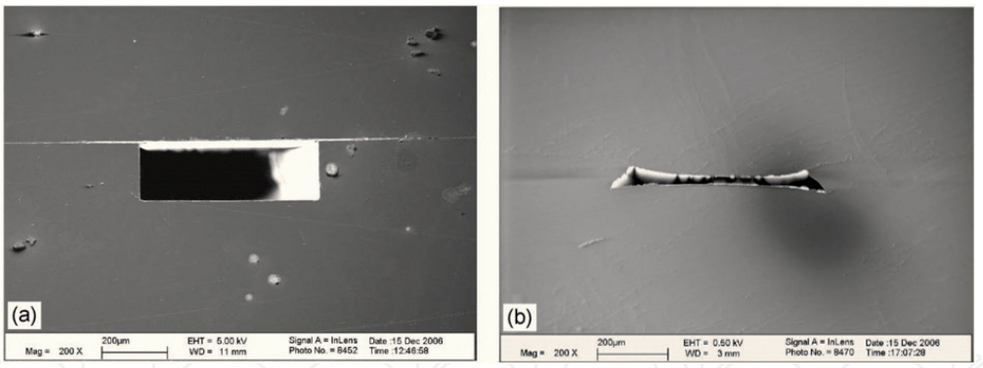

Figure 16.
SEM images of 500 mm wide, 180 mm deep PMMA microchannels: (a) thermal bonding of 24 min at 60°C, and (b) thermal bonding at 100°C [60]. Copyright (2007) with permission from Royal Society of Chemistry.

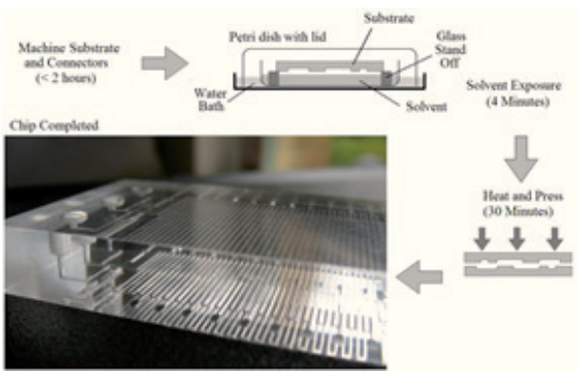

Figure 17.
Schematic of the bonding process. The PMMA chip shown has overall dimensions of 40[w] x 80[l] x 9.5 mm[h] [61].

3.3.4 Solvent bonding

Organic solvents can interact with polymer materials due to their similar solubility. Two polymer substrates are bonded together, which is called solvent bonding. This solubility can be determined by the Hildebrandt parameter (δ).

Ogilvie et al. [61] used chloroform vapor to bond the PMMA substrates. Two PMMA substrates were first exposed to chloroform vapor for 4 minutes. In this stage, the solvent was only 2–3 mm below the surface of the chip and both chips and solvent were covered by a glass lid to form a vapor exposure chamber (**Figure 17**). Then two substrates were bonded at 65 °C for 20 minutes, followed by the cooling process to room temperature in 10 minutes. All chips needed 12 hours of post-conditioning before use. The optical properties were well maintained after bonding and high bond strength was achieved. Solvent vapor is more controllable than traditional vapor bonding techniques such as dipping or soaking in the solvent. However, controlling the solvent concentration is necessary especially for solvent mixtures, as it will change during bonding.

4. Conclusions

In this chapter, the related manufacturing technologies for microfluidic chip fabrication are detailly described. Although rapid prototyping technologies for microfluidic chips, such as PDMS casting, micro machining, and 3D-printing, are well used in laboratory, the efficiency, machining accuracy and surface integrity of chips are still problematic for low-cost industrial batch production. Mass

production based on micro injection molding is important for the fabrication of plastic microfluidic chips, where multiple metal micro mold tool inserts can be used. The LIGA-like process with the characteristic of high precision replication, such as UV-LIGA, presents considerable advantages to fabricate industrial-grade mold tool inserts for the fabrication of plastic microfluidic chips. For future development direction of microfluidic chip fabrication, a hybrid tooling technology for multi-scale mold insert should be explored to combine feature from micrometer scale to nanometer scale; high aspect ratio microchannel replication is an important task, which is challenging micro injection molding; the rheological behaviors of polymer materials are worth studying in nanoscale for high-precision microinjection molding of polymeric parts. Functional precision components, such as microsensors, micropumps, and microelectrodes, should be integrated onto microfluidic chips along with the bonding process. Additionally, quality control of microfluidic chips should be highlighted, such as channel dimensions and consistency.

Acknowledgements

The authors gratefully acknowledge the support from the Science Foundation Ireland (SFI) (No. 15/RP/B3208), the National Science Foundation of China (61675149), and the '111'project by the State Administration of Foreign Experts Affairs and the Ministry of Education of China (No. B07014).

Conflict of interest

The authors declare no conflict of interest.

Notes/thanks/other declarations

Thanks Honggang Zhang, Haoyang Zhang, Tianyu Guan, and Xiangyu Wang for their original draft writing and Dr. Nan Zhang for his review & editing, and supervision.

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