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# ADDITIVE MANUFACTURING OF MICROFLUIDIC LAB-ON-A-CHIP DEVICES

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## ABSTRACT

Additive manufacturing (AM) technologies, also known as 3D printing, which offer advantages such as design flexibility, short lead time and cost effectiveness compared to traditional production methods, are used in many different areas. With the exponentially increasing technological developments, complex structures at micron level can be produced and used in customized applications. One promising unique application of AM is Lab-on-a-chips (LOCs). These microfluidic devices can effectively be used in laboratory experiments carried out on a very small scale in biomedical, chemistry and clinical cases. Lab-on-chip systems, which are time-consuming, specialization-required, and expensive to produce with traditional 2D microfabrication technologies such as lithography and PDMS-glass bonding, have become easily producible with AM methods. Although there are many different AM methods can be used in 3D printing of microfluidics, Multi Jet Printing (MJP) method is frequently preferred because of its high sensitivity and dimensional accuracy. MJP AM technology is based on spraying photopolymer resins to a layer thickness of down to 16 µm, then curing with UV light. This paper critically reviews relevant methods and materials used for 3D printing of microfluidics, especially for the MJP based technologies. 3D-printed microfluidic chips with various microchannel structures were fabricated using a commercial material jet-based 3D printer (Objet 30 Prime – Stratasys). 3D printed samples were examined for surface roughness and dimensional accuracy by profilometer analysis. In addition to the model material used in the study, the curing wavelengths of various photopolymer resins were determined by spectrophotometer analysis. In line with the data obtained, the removal of the support structures stuck in the micro-channels and the improvement of the surface properties were discussed. The results show that the 3D printing of microfluidics is a promising area for often novel applications.

**Keywords:** Additive Manufacturing. 3D Printing. Lab on a Chip. Microfluidics.

## 1. INTRODUCTION

Since the early 1990s, researchers from different disciplines have been working on laboratories systems that can perform as traditional fully equipped laboratories analyzes but on the micro scale with improved features like a smaller volume, faster, portable and cost effective [1]. This new technology, called Micro Total/Integrated Analysis Systems (µBA) or Lab-On-a-Chip (LOC), has the potential to take place in our lives by breaking new ground in chemistry [2], biology [3] and medical field [4]. In this manner portable LOC systems used in many different applications such as glucose meters used by diabetes patients [5] or detection of carcinogenic substances, biological pollutants, toxic chemicals [6]. These portable tests, which can be performed without the need for user intervention, are based on the principle of membrane and capillary principle. While capillary motion can be defined as the movements that occur as a result of molecular interaction between the micro diameter cross section of solid surface. Thus, while the liquid passes through the micro channel, the particles in the fluid can be separated thanks to the membranes which are selective barrier allows some particle to pass through but stops others [7]. In addition, the analysis of samples can be done using valves, channels, reactors, detectors and pumps on a chip.

The working principle of LOC is based on the microfluidic principle. Micro channels provide laminar flow by decreasing Reynold number to below 1. Theoretical models and calculations can be precisely defined in these fluids that move steady state conditions [8]. The regularity of the flow in LOCs allows the control of interactions and molecular concentrations at the molecular level. Thus, LOCs can be used in different physical and chemical processes that are not possible to investigate in large devices. So, although LOC appears to be a scaled-down version of the laboratory system that performs the same task on a large scale, microfluidic system designs need to be reconstructed because the micro-sized fluid rheology differs significantly. When designing a LOC system case study must be clearly defined at the first stage. Then, the most suitable production technique which have ensure the minimum number of parts of the design, ease of production and cost should be chosen. The flow analysis of the system should be calculated by finite element analysis or theoretical methods and then the system must be optimized. The prototyped LOCs are then exposed to a series of tests, and the results are compared with analytical solutions [9].

The ability to use LOCs in the desired application and obtain the required microchannel network is directly related to the method of production as well as the material. Besides the production technique depends on the material, LOCs' material directly affects the flow regime as well as the device's performance, production cost, reliability and ease of use [10]. Inorganic, polymeric and composite materials are frequently used as LOC material [11]. Silicone and glass are known as the inorganic material firstly used in LOC applications. Silicone can be used in LOCs due to its moldability, high thermal conductivity and stable electroosmotic mobility [10]. However, due to the hard structure of silicon, it is not suitable for making active microfluidic components such as pumps and valves. In addition, silicon has a light-proof character at visible wavelengths of light. For this reason, the use of silicon in LOCs may cause problems in the external observation of moving liquids or in the analysis stage. With biocompatible, optically transparent and electrically insulating properties, glass is frequently used in LOC applications such as Capillary electrophoresis (CE), which is the electrokinetic separation method applied in sub-millimeter diameter capillaries and microfluidic channels [12]. However, similar to silicone, there are many limitations in glass applications in microfluidics due to its hardness and high production cost in consequence of the high temperature and pressure requirement during the manufacturing process [13].

Elastomers, another material used in LOCs, come to the forefront with their flexible behavior. PDMS (polydimethylsiloxane) is the most widely used elastomer material in LOCs with its easy manufacturability, flexibility, bonding capability and optical transparency properties [13]. In addition, unlike glass and silicon, it enables the production of elastic valves and pumps thanks to its low elastic module (350-450 kPa) [14]. PDMS, which is preferred in cell culture applications due to its gas permeability, can evacuate air that remains in the micro channels when the fluid initiates to fill into. However, bubbles may form during the passage of gas through the PDMS [11]. Another type of material that can be used in LOCs, Thermoplastic polymers are not suitable for cell cultures and microcomponent production, due to their low gas permeability and rigidity respectively, although they are suitable for microprocessing and show translucent properties [10].

Many different thermoplastic polymers can be used for LOCs production such as biocompatible, inert and rigid polystyrene [15], durable and transparent Polycarbonate [16], cheap and hydrophilic Poly-methyl methacrylate (PMMA) [17] or strong, resilient and elastomer Polyurethane [18] can be used in LOC production. In addition, paper, hydrogel and composite materials are used to make LOCs [11]. A comparison table regarding the materials and properties used in LOC production is given in Table 1.

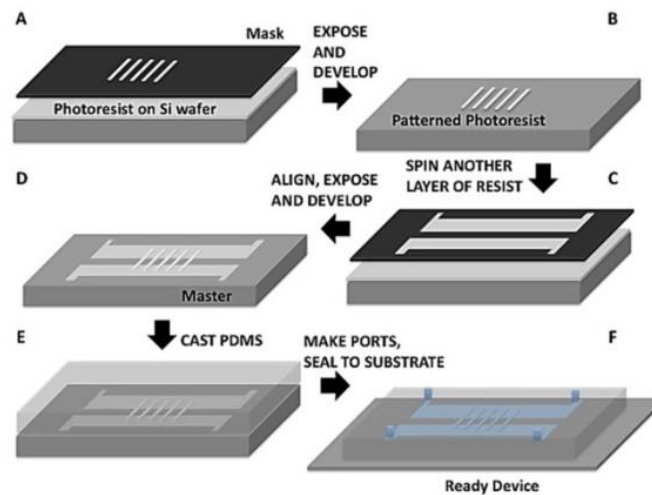
**Table 1.** Comparison of the properties of different LOC materials [11].

Property	Silicon/glass	Elastomer	Thermoplastics
Young's (tensile) modulus (GPa)	130-180 / 50-90	~0.0005	1.4-4.1
Fabrication method	photolithography	casting	thermomolding
Smallest channel dimension	<100 nm	<1 $\mu$ m	~100 nm
Channel profile	limited 3D	3D	3D
Thermostability	very high	medium	medium to high
Resistance to oxidizer	excellent	moderate	moderate to good
Solvent compatibility	very high	low	medium to high
Surface charge	very stable	not stable	stable
Permeability to oxygen (Barrer*)	<0.01	~500	0.05-5
Optical transparency	no/high	high	medium to high

\*Barrer is a non-SI unit of gas permeability mostly used in the membrane technology [19]. The permeability coefficient is defined as the flux of fluid passing through the unit membrane thickness under the influence of certain pressure.

## 2. CONVENTIONAL MANUFACTURING OF LAB ON A CHIPS

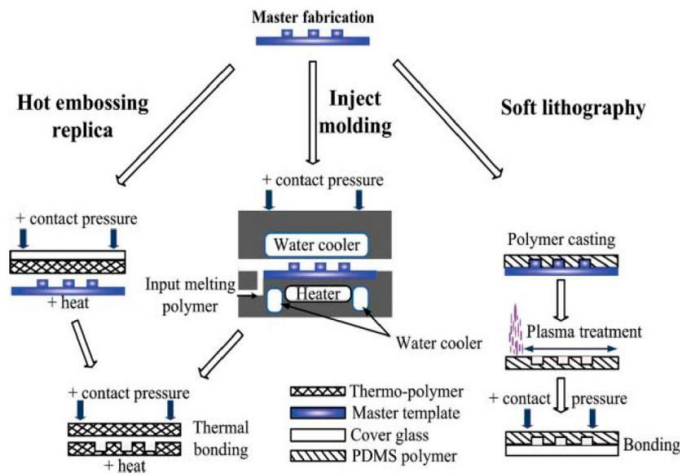
While producing LOCs with customized equipment and specification, many different methods can be used. In Laminate technique from these methods, independently cut layers are connected to each other to form channels and obtain microfluidic properties [20]. Soft lithography technique is based on the use of photolithography to produce molds on which a liquid polymer such as PDMS is poured and then hardened. Figure 1 shows the production stages of LOC produced from PDMS material using Soft-lithography method.



**Figure 1.** Soft-lithography process for fabrication of LOCs. In the process; The photoresist layer is placed on the wafer, and then the desired surfaces are obtained after the expose by using the photomask with unique patterns. PDMS is poured on the obtained mold and then cured. The device is cleaned and covered with a glass coverslip [21-22].

In the injection molding technique, the molten thermoplastic is injected into the space between the female and male molds, and after cooling removed from the mold. In another molding technique, in hot embossing, the thermoplastic film placed between the molds is heated and compressed so that casting mold is created. With this technique material stress can be reduced by providing a smaller flow distance of thermoplastic on the contrary of injection molding [23]. Hot embossing also has many production advantages, such as reducing shrinkage and thereby ensuring that precision parts are produced.

However, this technology also has different production limitations such as the limited availability of thermoplastics and the difficulty of manufacturing complex three-dimensional structures. Figure 2 shows LOC production methods based on the molding method. In addition to the molding and lamination method, LOCs can be produced with nanoscale lithographic methods (Nanoimprint lithography, Electron Beam and Extreme Ultraviolet) and non-lithographic (Anodic Aluminum Oxidation) micro production methods [20].



**Figure 2.** LOC production methods based on the molding method [24].

### 3. ADDITIVE MANUFACTURING OF LAB ON A CHIPS

Additive manufacturing, also known as 3D printing, can radically change manufacturing methods. Because even objects with complex geometry can be produced quickly and economically with 3D printers [25]. Additive manufacturing is a unique manufacturing method that solid parts can be produced directly by using computer aided design (CAD) model data. In this method, materials are printed layer by layer using sliced CAD data. Thus, final parts can be created more easily, quickly and cost efficient compared to traditional manufacturing methods [26-27]. Additive manufacturing techniques differ according to the type of materials and production methods. The most preferred of these techniques can be listed as follows; SLA (Stereolithography Apparatus) solidifies the photopolymer resin by curing [28], FDM (Fused deposition modeling) deposits the plastic filament in a semi-molten state [29], SLS (Selective Laser Sintering) sintering metal powders with laser [30]. Thus, rapid prototyping has been rapidly increasing in recent years in many fields such as aviation [31], automotive [32], medical [33] architecture [34], education [35] and fashion [36].

In recent years, micro-scale structures and microfluidic devices have become producible with the increase in printing quality and precision [37]. Complex microfluidic devices can be printed in one step with AM methods. In a different approach, AM methods are used to create a master mold that can be used for soft lithography. In both approaches, the use of 3D printing technology is feasible compared to complex, difficult and costly traditional LOC production methods [38-39]. Also, thanks to AM's design flexibility, changing design features is significantly easier compared to traditional methods. Thus, high performance LOCs can be produced by making improvements with iterative design processes. In addition, microfluidic technology, which has become more accessible by producing with AM methods, can accelerate innovations in various fields [40].

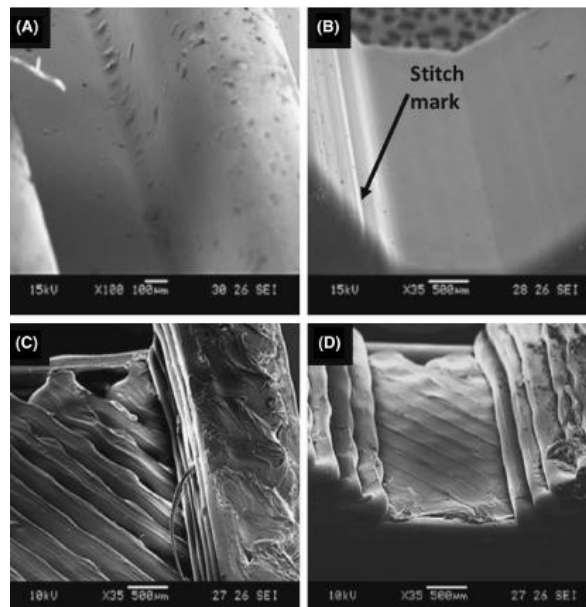
3D printed LOCs can be used in various applications from biosensors [41] such as soft artificial skin for hand motion detection [42] to chemical sensing [43]. Knowlton et al. have developed controllable 3D cell culture environments for long-term cell culture and growth [44]. LOCs can be used in some medical inspections that are difficult to treat for reasons such as the complexity of neurological system. Johnson et al. have developed a bio-inspired, customizable 3D printed chip to examine viral infection in the nervous system [45]. In another study Adamski et al. also used Inkjet 3D printed LOC for DNA analysis for the first time using the on-chip gel electrophoresis method [46]. Additive manufacturing of Lab-on-a-

Chip offers many advantages in field of biomedical, as well as some challenges [47-48]. For example, one of the biggest limitations of using 3D printed LOCs in biotechnology and medical applications is the biocompatibility, depending on the material [49]. Carve et al. have discussed methods to reduce material toxicity as well as factors affecting material biocompatibility, thus promoting its application in these research areas [50]. The another problem based on low optical transparency of LOCs polymers to allow in vitro imaging of samples [51]. The types of materials used are directly linked to printing techniques [52]. Process capabilities of the main 3D printing methods for using LOC production have given in Table 2.

**Table 2.** Process parameters of main AM methods used in LOC production [52].

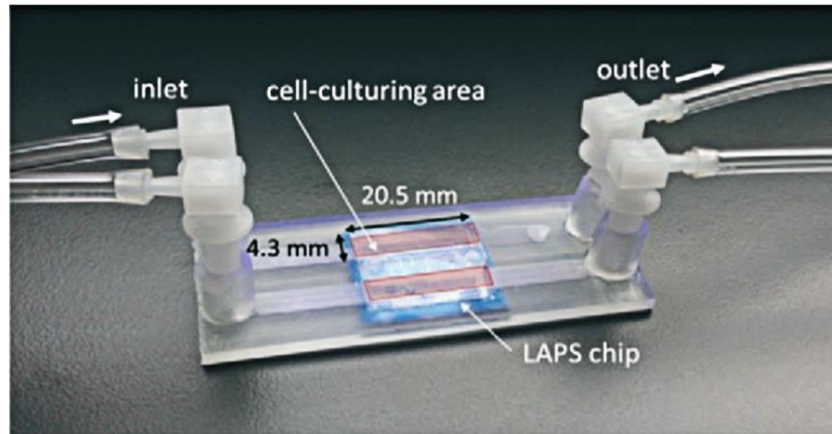
Process Parameter	Inkjet	SLA	FDM
<b>Material</b>	Rigid, elastomeric, translucent, opaque, ABS-like photopolymers	Rigid and clear polycarbonate, ABS-like resin semi-flexible resin	ABS, PLA, polycarbonate, semi-flexible or composite filaments
<b>Layer thickness (<math>\mu\text{m}</math>)</b>	16 (high resolution) 30 (low resolution)	50-100 (high resolution) 120-150 (standard resolution)	50 Max 200 Average
<b>Min feature size (<math>\mu\text{m}</math>)</b>	600 (high resolution)	250-380 (high resolution)	-
<b>Max build size (mm)</b>	500 x 400 x 200	600 x 700 x 500	600 x 700 x 500

The most commonly used method for the production of LOCs is the photopolymer-based Polyjet (also referred to as Multijet Printing (MJM)) method, which capable of producing precision models (up to 16  $\mu\text{m}$ ) [53]. Figure 3 shows the SEM images of the channel produced with Polyjet and FDM technology. As seen in the picture, stair steps are formed in low resolution FDM technology [54]. This situation adversely affects the flow regime. However, Bauer et al. has designed and produced an affordable FDM printed testing apparatus to detect malaria with a cost efficient [55]. Again, thanks to the pore structure obtained by the lithography-based ceramic manufacturing (LCM) method, LOC acts as a membrane with separating cell culture chambers at different levels, which imitates the typical configuration of transwell assays [56]. Furthermore, in a SLA-based printer, an LOC capable of detecting H<sub>2</sub>O<sub>2</sub> and glucose can be produced under \$1 [57]. Also by using AM techniques together with different methods such as femtosecond laser nanofabrication, precious and advanced hybrid LOCs can be achieved [58].



**Figure 3.** SEM images of printed channels. polyjet-printed on the top and FDM-printed channel on the bottom [54].

In addition to biomedical applications, many electronic applications from micro electromechanical systems (MEMS) for acoustofluidic applications [59] to piezoelectric polymer actuators [60] has been conducted using AM of LOCs. Sochol et al. have examined MJM 3D printed fluidic components including fluidic capacitors, fluidic diodes, and fluidic transistors. Afterwards, they have evaluated the potential of using these equipments on LOC via geometric modification of component parameters [61]. Su et al have produced fully inkjet printed LOCs for electrical and sensing applications. While horizontal resolution up to 5  $\mu\text{m}$  and printing precision up to 4.6  $\mu\text{m}$  / layer in vertical direction, SU-8 was used as the main and PMMA for support material and silver reinforced ink was used to print the electrodes [62]. Takenaga et al. have proposed a new microfluidic design for semiconductor based biosensors. The microfluidic produced by the 3D printer in a short time can be mounted on a light-addressed potentiometric sensor (LAPS) chip as shown in Figure 4 for propose of cell growth [63].



**Figure 4.** LAPS chip with attached microfluidic channels for culturing cells [48].

As mentioned above AM of LOCS can be used wide spreading field of applications such as electronic, biomedical [64], tissue, membrane [65], pump, valve [65], flow micro reactor [66]. So, it is predicted that this technique will prevent traditional methods thanks to its features such as fast, reliable and inexpensive [67].

LOC consists of several sections specialized for different processes. These process sections are divided into two as active and passive components. In active components fluid needs to be driven by the external forces, while in the passive components capillary effect or external actuation are used to manipulate the fluid flow [68]. The design, manufacture, and integration of microfluidic components of LOCs requires a considerable amount of effort and time [69]. Thanks to the ability to produce passive components with AM, LOCs with different functionality such as micro mixer [70], gradient generator [71] or reaction ware [72] can be produced. In addition, active microfluidic components such as membrane-based valves and pumps can be produced using AM methods [73].

#### 4. MATERIALS AND METHOD

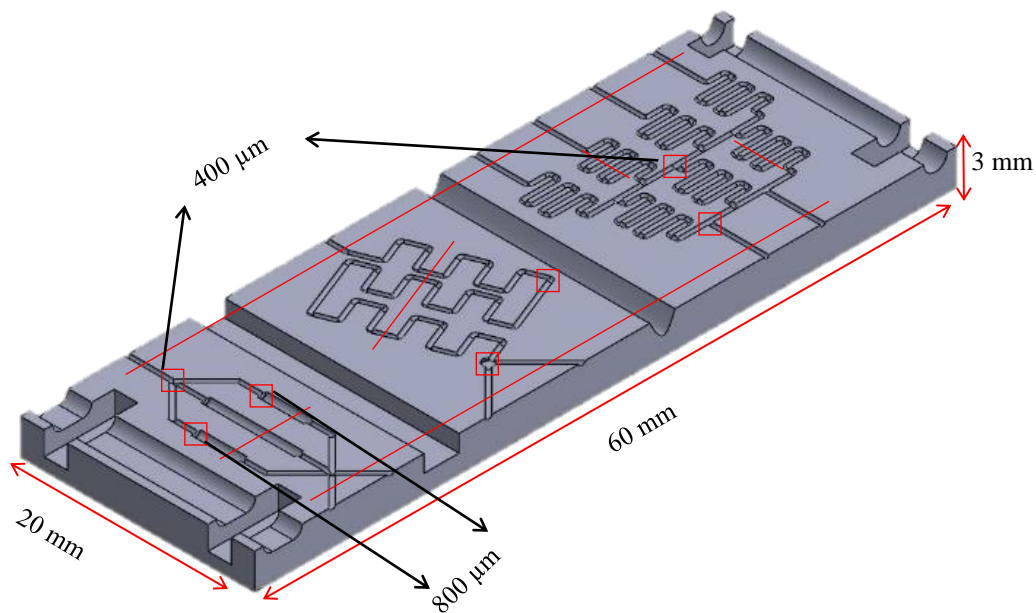
A case study was conducted 3D printing of microchannels effectively used in very small-scale laboratory experiments in biomedical, chemistry and clinical situations. Although there are many different Additive Manufacturing methods for 3D printing of microfluidic channels, the Multi Jet Printing (MJP) method, which is based on depositing photopolymer resins down to 16  $\mu\text{m}$  layer thickness, is often preferred due to its high precision and dimensional accuracy [74]. 3D printed microfluidic Lab-on-a-chip (LOC) of various designs using a commercial material jet based 3D printer Objet 30 Prime – Stratasys is shown in Figure 5. Vero White photopolymer resin was used as model material. Geometrically critical locations for microflow performance were evaluated from the dimensional accuracy perspective. It was also important to produce samples without support materials as post removal of supports from the small channels is extremely difficult if not impossible in many ways.



**Figure 5.** 3D printed microchannel samples.

#### 4.1. Sample Characterization

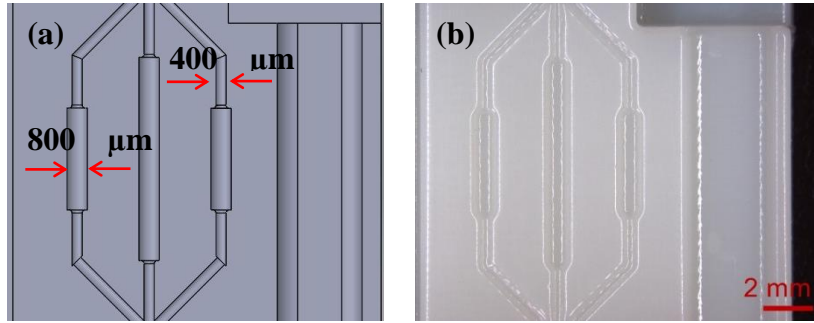
3D printed samples were compared with the 3D CAD models using various technics including optical scanner based reverse engineering, optical microscope, and 3D profilometer. Data obtained from the result of optical scanner based reverse engineering method was poor due to not enough reflected rays from microchannels features. However, it is suggested that gold plating can be applied to the sample surface to solve this problem. The critical points of the sample were marked in Figure 6 to be examined under the optical microscope, those points were detailed in the examinations and the channels were observed in general.



**Figure 6.** Multipurpose LOC design. Critical points highlighted in red.

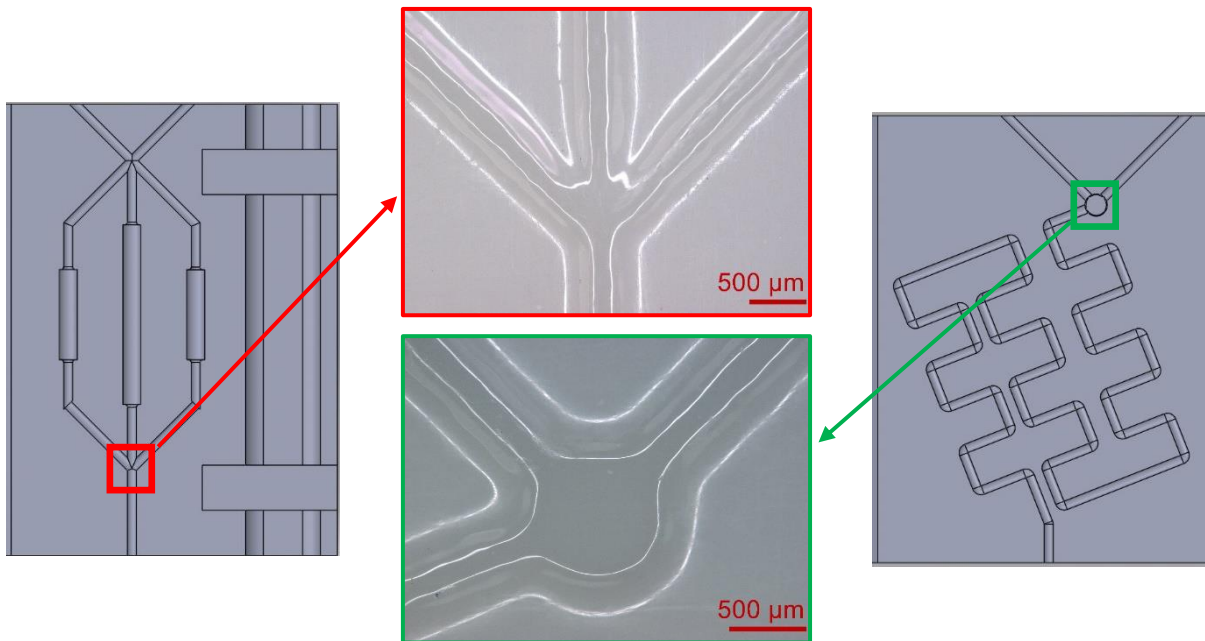
Figure 7 shows the CAD data of the structure containing microchannels in different diameters and the optical microscope image of the sample produced with Polyjet AM technology. It has been determined that geometries with sharp edges and sudden diametrical changes are produced as smooth transitions in 3D printing.





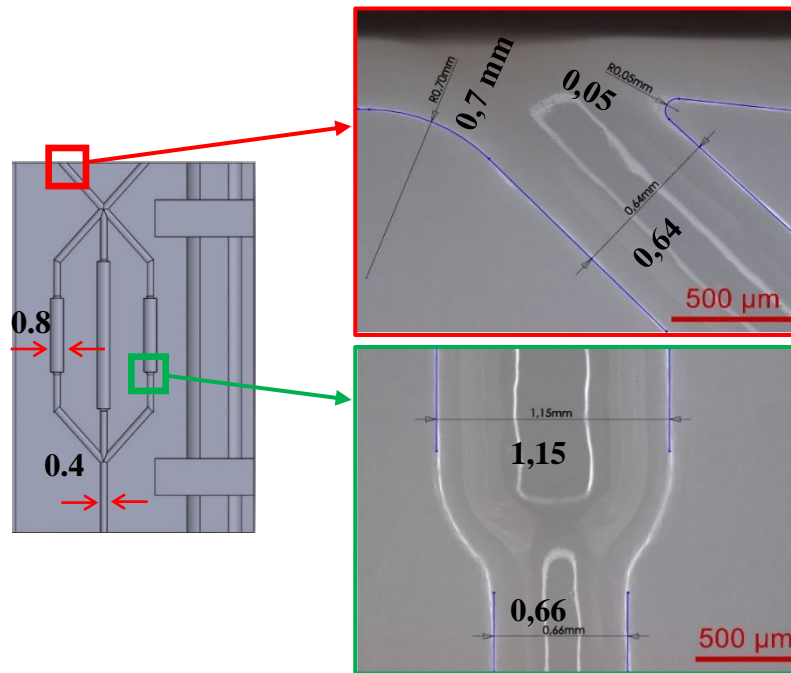
**Figure 7.** Microchannel structure in (a) CAD model and (b) 3D printed sample.

Figure 8 shows the junction points of the microchannels. Joints are of critical importance for micro channels. In order to ensure a flawless and homogeneous flow, the channels must come together in equal clearance. Moreover, by using structures such as the junction chamber, the homogeneity of the mixture can be achieved while eliminating the production-related errors.



**Figure 8.** Junction points of the microchannels. While the direct connection is seen on the left side, the right side has a junction chamber connection.

It was observed that there was a difference between the canal sizes obtained from the microscope images and those measured on the CAD model. The channel dimensions of the additively manufactured sample were found to be approximately 50% larger than the CAD model (Figure 9).

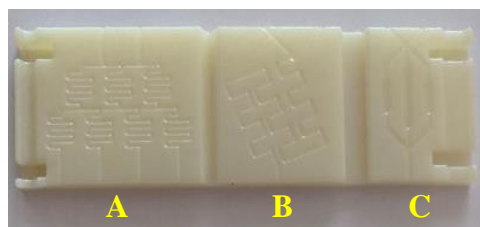


**Figure 9.** Comparison of additively manufactured LOC samples dimensional with CAD model measurements.

#### 4.2. 3D Profilometer Analysis

Another method used for the characterization of sample microfluidic channels 3D printed is 3D profilometer analysis [53]. In this study; Stylus Dektak 150 type profilometer device was used. Stylus profilometers use a probe to detect the surface, physically moving a probe along the surface in order to acquire the surface height. This is done with a feedback loop, in which the force between the tip and the sample surface is controlled while mechanically scanning across the surface. The 3D profilometer analysis application has many different analytical functions to measure surface texture and other parameters. Analytical functions are grouped according to applications as roughness, waviness, height and geometric parameters. The red Reference (R) cursor and green measurement (M) cursor in the result plots identify the section of the profile trace for leveling or performing analytical functions. It can be adjusted to average the data points within the bandwidth of each cursor. This is useful for average step height measurements. Among the parameters, ASH (Delta average step height); It is used to obtain step height measurement in applications where there is roughness or noise in the profile trace. Calculates the difference between two average height measurements. The ASH value is critical in determining the channel diameters of the printed sample microfluidic channels.

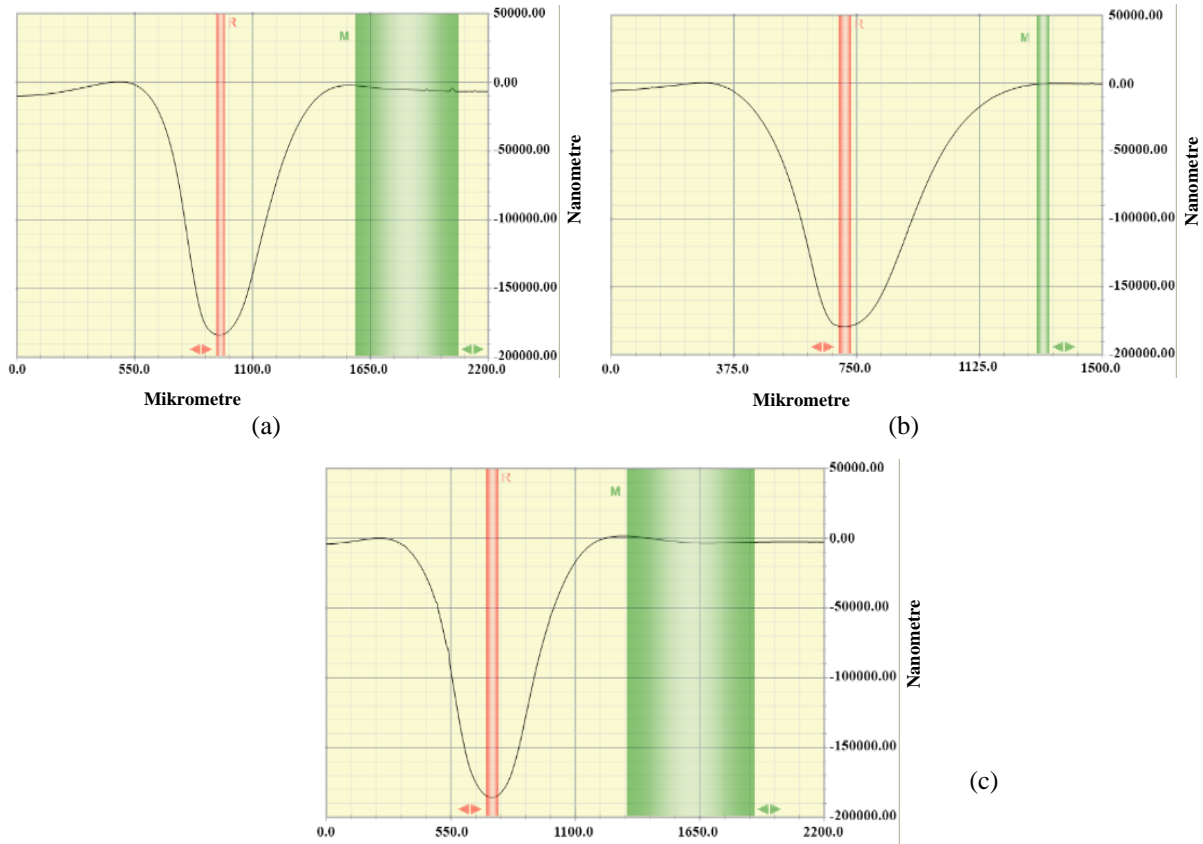
Random measurement lines were determined from the 3D printed microfluidic chip piece with different channel types (type A, type B and type C) shown in Figure 11, channels with the same diameters, and measurements were made using a probe 3D profilometer device. Obtained values were compared with the 3D CAD model.



**Figure 10.** Type A, B and C microchannels for which profilometer analysis was performed.

The cross-section profiles of the microfluidic channels designed in circular geometry are seen as valleys in the graphs (a), (b), (c) in Figure 11. This profile difference in the result graphs is due to the measurement time. During the application, the measurement time was chosen as 75 seconds, but it should be noted that the scanning accuracy may differ according to the measurement time. As the

measurement time increases, the scanning speed of the probe decreases, thus increasing the scanning sensitivity. Depending on this, the profile shapes obtained can also change. The valley views in the graphics can be converted into circular section profiles by increasing the measurement time.



**Figure 11.** (a) Profilometer measurement graphic of channel type A (b) Profilometer measurement graphic of channel type B (c) Profilometer measurement graphic of channel type C.

The analysis results of the chip whose 3D profilometer analysis measurement graphics are shown above and the measurement parameters used during the application are given in Table 3. According to the ASH values in the table; When the 0 line is based as the surface, the channel depths measured from the surface are approximately 178 μm for channels A and B, and approximately 183 μm for channel C. When compared with the CAD model, it is seen that the microfluidic channel diameters are designed as 400 μm, that is, the valley depths should be 200 μm. These differences between the measurements may be due to the measurement time during the application and the scanning sensitivity that changes accordingly.

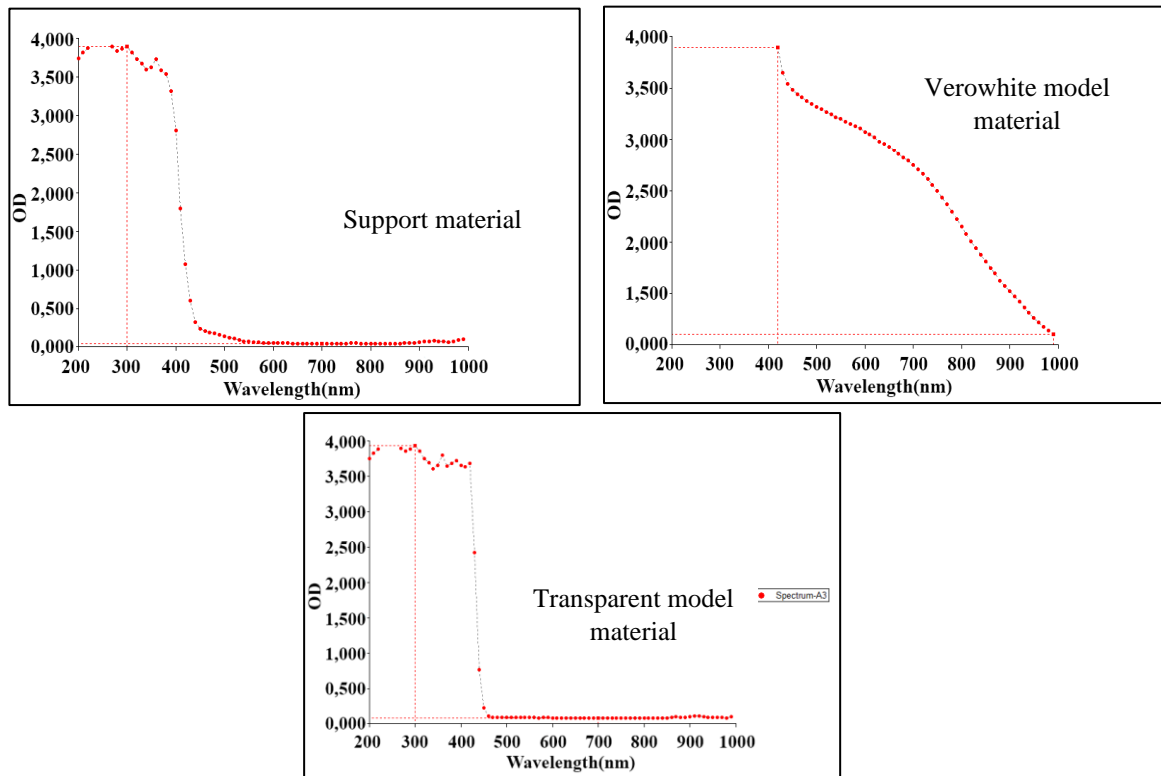
**Table 3.** 3D profilometer analysis measurement parameters and results of A, B and C microfluidic channels.

Scan Parameters		Analytical Results	Type A	Type B	Type C
<b>Scan Type</b>	Standard Scan	<b>ASH</b>	178486 nm	178607 nm	183075 nm
<b>Profile</b>	Hills & Valleys	<b>Ra</b>	10300.52 nm	28805.29 nm	27756.21 nm
<b>Duration</b>	75 sec	<b>Rq</b>	13352.88 nm	31813.83 nm	30624.13 nm
<b>Force</b>	5.0 mg	<b>Rv</b>	-53240.18 nm	-54076.38 nm	-55298.38 nm
<b>Lenght</b>	2200.0 um	<b>Rp</b>	15032.08 nm	42631.26 nm	42712.56 nm
<b>Location</b>	0.0 um, 0.0 um	<b>Rt</b>	68272.26 nm	96707.64 nm	98010.94 nm
<b>R. Cursor</b>	Pos: 974.9 um Width: 43.4 um	<b>Skew</b>	-1.37	-0.08	0.01
<b>M. Cursor</b>	Pos: 1582.9 um Width: 485.4 um	<b>RzDin</b>	22610.02 nm	49363.18 nm	48782.75 nm

### 4.3. Spectrophotometer Analysis

The photopolymer resin is cured with specific wavelength UV light. Dimensional accuracy can be achieved by determining the curing wavelength of the liquid resin that solidifies by curing [53]. Semi-solid or rapid hardening resin can cause poor surface properties and dimensional misalignment. In addition, the curing wavelength of the photopolymer resin that forms the support structures in the micro channels has been determined. These support structures, which are very difficult to remove from the micro channel when completely solidified, can be cured at the appropriate UV wavelength to remain in a loose state. In addition, in case of determining a wavelength in which the model material is permeable and the support structure is absorbent, it can be easier to remove the support structure with UV post-printing after printing. Spectrophotometer analysis was performed to determine the wavelengths of different photopolymer resins (support material, Verowhite and transparent material) used in Polyjet AM technologies. Spectral scanning was performed with a UV Spectrophotometer in the wavelength range of 200-999 nm. Test results for different materials are shown in Figure 12.

According to the test result, a peak was observed at 360 nm for support and transparent materials. A second peak is visible at 390 nm for the transparent material. This shows that the absorbent material is cured by absorbing light at the relevant wavelength. Since the solidified material in further wavelengths does not allow light to pass, no value is seen. Similarly, the Verowhite model material is opaque, so measurement could not be done by the device and no peak was observed. For the analysis of the solid samples produced, measurement with a refractometer is required. Alternatively, XRD and XRF analysis have been proposed.



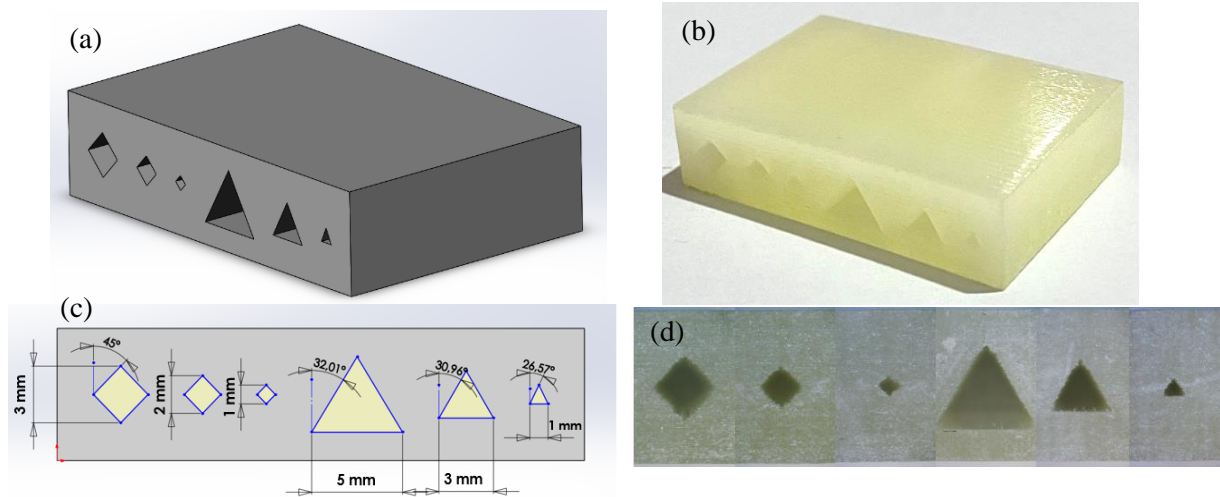
**Figure 12.** Spectrophotometer analysis results of photopolymer resins used in Polyjet AM methods.

### 4.4. Different Microfluidic Channel Geometries

Recently, microchannels with different cross-section geometries have been fabricated for both commercial and scientific applications. The examination of fluid flow in microchannels with different cross-sections, including circular, elliptical, rectangular, rhombic, triangular and hexagonal, is important in terms of velocity distribution and pressure drop of fully developed laminar flow [75]. A more linear and homogeneous flow can be achieved by choosing the appropriate one among the different channel geometries. In addition to its performance characteristics, microchannel geometry is also crucial for AM

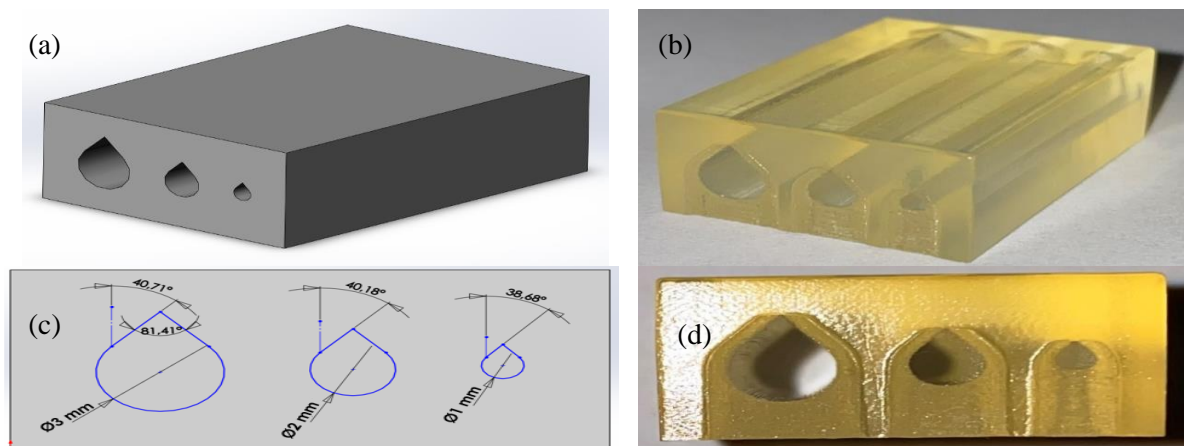
of chips. Since it is very difficult to remove the support structures from the microchannel, support-free microchannel structures should be performed.

Blocks with different channel geometries were printed to evaluate the printing characteristics and limitations of the printer and AM technique used. The samples were designed with all channel walls angles of 45 degrees or less, thus eliminating the need for a support structure. As employed in the study, some AM machines utilize a support structure for each overhang. In this case, microchannel profiles at different scales were used to observe the effect of channel size on the removal of supports and on surface and geometric properties. The images in Figure 13 and Figure 14 show sample channel prints have square, triangular and waterdrop profiles.



**Figure 13.** (a) CAD model of the sample with square and triangular channel geometries designed in different sizes (b) Image of 3D printed sample (c) Showing the channel dimensions and channel wall angles of the designed channels in the CAD model (d) Image of 3D printed channel profiles.

The dimensional accuracy of the microchannel decreases as the profile size gets smaller. In the MJP AM process, the resin is jetting through micro nozzles. Nozzle diameters determine the minimum feature size and part accuracy. In addition, the dimensional accuracy in sharp corners is considerably poor due to the circular cross-section nozzles. While support materials can be easily removed from 2 mm wide profiles, a long process and various chemical solutions are required for smaller microstructures. The water drop profile (Figure 14) is very effective in preventing turbulence thanks to its curve structure. It is also very suitable for providing unsupported structure in AM production methods [76].



**Figure 14.** (a) CAD model of the sample with waterdrop channel geometries designed in different sizes (b) Image of 3D printed sample (c) Showing the channel dimensions and channel wall angles of the designed channels in the CAD model (d) Image of 3D printed channel profiles.

## 5. CONCLUSION

With AM technology, LOCs can be produced quickly, cost effectively and without expertise compared to traditional methods. Despite all these advantages, it is important to consider the limitations of AM method in the production of LOCs. Considering the design criteria, possible obstacles encountered in the production of microchannels are explained by design for additive manufacturing (DfAM) approach. The surface roughness and dimensional deviations seen in the 3D printed samples were examined within this scope. Sharp edges should be avoided in the LOC design for AM. In addition, the design of microchannels should be scaled precisely to improve surface quality and ensure dimensional accuracy. Curing wavelengths of various photopolymer resins were determined by Spectrophotometer Analysis. Thus, surface properties can be improved by providing smooth and precise curing during printing. In addition, the appropriate wavelength can be determined to facilitate the evacuation of support structures stuck in micro channels. By using different microfluidic channel geometries, a linear and homogeneous flow can be achieved and the difficulty of removing support structures can be eliminated by producing microchannels that do not require support.

## REFERENCES

1. Ürkmez, B., "Lab on a Chip", <http://www.acikbilim.com/tag/lab-on-a-chip>, May 4, 2021.
2. Chow, A.W., "Lab-on-a-chip: Opportunities for chemical engineering" *AICHE Journal*, Vol. 48 Issue 8, Pages 1590-1595, 2002.
3. Gupta, K., Kim, D.H., Ellison, D., Smith, C., Kundu, A., Tuan, J. and Levchenko, A., "Lab-on-a-chip devices as an emerging platform for stem cell biology", *Lab on a Chip*, Vol. 10, Issue 16, Pages 2019-2031, 2010.
4. Li, G.P., Bachman, M. and Lee, A. U.S. Patent Application No. 10/763, 540, 2004.
5. Chin, C.D., Linder, V. and Sia, S. K., "Lab-on-a-chip devices for global health: Past studies and future opportunities", *Lab on a Chip*, Vol. 7, Issue 1, Pages 41-57, 2007.
6. Ríos, Á., Zougagh, M. and Avila, M., "Miniaturization through lab-on-a-chip: Utopia or reality for routine laboratories A review", *Analytica Chimica Acta*, Vol. 740, Pages 1-11, 2012.
7. Britannica, The Editors of Encyclopaedia, "Membrane", <https://www.britannica.com/science/membrane-biology>. Accessed, May 4, 2021.
8. Hansen, C.L., Skordalakes, E., Berger, J.M. and Quake, S.R., "A robust and scalable microfluidic metering method that allows protein crystal growth by free interface diffusion", *Proc. Natl. Acad. Sci. USA* 99, Pages 16531–16536, 2002.
9. Takayama, S., Ostuni, E., LeDuc, P., Naruse, K., Ingber, D.E. Whitesides, G.M., "Subcellular positioning of small molecules", *Nature*, Vol. 411, Issue 1016, 2001.
10. Ren, K., Zhou, J. and Wu, H., "Materials for microfluidic chip fabrication. *Accounts of chemical research*", Vol. 46, Issue 11, Pages 2396-2406, 2013.
11. elveflow.com, "Materials for microfluidic device fabrication: a review", May 4, 2021.
12. Kemp, G., "Capillary electrophoresis", [https://en.wikipedia.org/wiki/Capillary\\_electrophoresis](https://en.wikipedia.org/wiki/Capillary_electrophoresis), May 4, 2021.
13. Wu, W.I., Sask, K.N., Brash, J.L. and Selvaganapathy, P.R., "Polyurethane-based microfluidic devices for blood contacting applications", *Lab on a Chip*, Vol. 12, Issue 5, Pages 960-970, 2012.
14. Nge, P.N., Rogers, C.I. and Woolley, A. T., "Advances in microfluidic materials, functions, integration, and applications", *Chemical Reviews*, Vol. 113, Issue 4, Pages 2550-2583, 2013.
15. Grist, S.M., Oyunerdene, N., Flueckiger, J., Kim, J., Wong, P.C., Chrostowski, L. and Cheung, K. C., "Fabrication and laser patterning of polystyrene optical oxygen sensor films for lab-on-a-chip applications", *Analyst*, Vol. 139, Issue 22, Pages 5718-5727, 2014.

16. Ogończyk, D., Węgrzyn, J., Jankowski, P., Dąbrowski, B. and Garstecki, P., “Bonding of microfluidic devices fabricated in polycarbonate”, *Lab on a Chip*, Vol. 10, Issue 10, Pages 1324-1327, 2010.
17. Bilenberg, B., Nielsen, T., Clausen, B. and Kristensen, A., “PMMA to SU-8 bonding for polymer based lab-on-a-chip systems with integrated optics”, *Journal of Micromechanics and Microengineering*, Vol. 14, Issue 6, Page 814, 2004.
18. Testouri, A., Ranft, M., Honorez, C., Kaabeche, N., Ferbitz, J., Freidank, D. and Drenckhan, W., “Generation of crystalline polyurethane foams using millifluidic Lab-on-a-Chip technologies”, *Advanced Engineering Materials*, Vol. 15, Issue 11, Pages 1086-1098, 2013.
19. Stern, S.A., “Barrer”, <https://en.wikipedia.org/wiki/Barrer>, May 4, 2021.
20. Gale, B.K., Jafek, A.R., Lambert, C.J., Goenner, B.L., Moghimifam, H., Nze, U. C. and Kamarapu, S. K. A., “Review of current methods in microfluidic device fabrication and future commercialization prospects”, *Inventions*, Vol. 3, Issue 3, Page 60, 2018.
21. D Jadhav, A., Wei, L. and Shi, P., “Compartmentalized platforms for neuro-pharmacological research”, *Current Neuropharmacology*, Vol. 14, Issue 1, Pages 72-86, 2016.
22. Taylor A.M., Blurton-Jones M., Rhee S.W., Cribbs D.H., Cotman C.W., Jeon N.L., “A microfluidic culture platform for CNS axonal injury, regeneration and transport”, *Nat. Methods*, Vol. 2, Issue 8, Pages 599–605, 2005.
23. Hecke, M. and Schomburg, W.K., “Review on micro molding of thermoplastic polymers”, *J. Micromech. Microeng.*, Vol. 14, 2004.
24. Wu, J., Gu, M., “Microfluidic sensing: State of the art fabrication and detection techniques”, *J. Biomed. Opt.*, Vol. 16, Issue 8, 2011.
25. Chua, C.K., Leong, K.F., “3D Printing and Additive Manufacturing: Principles and Applications”, 5th ed., World Scientific, 2016.
26. Sood, A.K., Ohdar, R.K. and Mahapatra, S.S., “Parametric appraisal of mechanical property of fused deposition modelling processed parts”, *Mater Des.*, Vol. 31, Pages 287–295, 2010.
27. Zhong, W., Li, F., Zhang, Z., Song, L. and Li, Z., “Short fiber reinforced composites for fused deposition modeling”, *Mater Sci. Eng. A.*, Vol. 301, Pages 125–130, 2001.
28. West, A.P., Sambu, S.P. and Rosen, D.W., “A process planning method for improving build performance in stereolithography”, *Comput Aided Des*, Vol. 33, Issue 1, Pages 65-79, 2001.
29. Dudek, P., “FDM 3D printing technology in manufacturing composite elements”, *Arch Metall Mater*, Vol. 58, Issue 4, Pages 1415-1418, 2013.
30. Kruth, J.P., Wang, X., Laoui, T. and Froyen, L., “Lasers and materials in selective laser sintering”, *Assem Autom*, Vol. 23, Issue 4, Pages 357-371, 2003.
31. Wagner, S. M. and Walton, R.O., “Additive manufacturing’s impact and future in the aviation industry”, *Production Planning & Control*, Vol. 27, Issue 13, Pages 1124-1130, 2016.
32. Leal, R., Barreiros, F.M., Alves, L., Romeiro, F., Vasco, J.C., Santos, M., & Marto, C., “Additive manufacturing tooling for the automotive industry”, *The International Journal of Advanced Manufacturing Technology*, Vol. 92, Issues 5-8, Pages 1671-1676 2017.
33. van Eijnatten, M., van Dijk, R., Dobbe, J., Streekstra, G., Koivisto, J. and Wolff, J., “CT image segmentation methods for bone used in medical additive manufacturing”, *Medical Engineering & Physics*, Vol. 51, Pages 6-16, 2018.

34. Lim, S., Buswell, R. A., Le, T.T., Austin, S. A., Gibb, A. G. and Thorpe, T., "Developments in construction-scale additive manufacturing processes", *Automation in construction*, Vol.21, Pages 262-268, 2012.
35. Go, J. and Hart, A. J., "A framework for teaching the fundamentals of additive manufacturing and enabling rapid innovation", *Additive Manufacturing*, Vol. 10, Pages 76-87, 2016.
36. Gürcüm, B.H., Börklü, H.R., Sezer, K. and Eren, O., "Implementing 3D Printed Structures as the Newest Textile Form", *J. Fashion Technol. Textile Eng.* Issue 4, Page 19, 2018.
37. Kitson, P. J., Rosnes, M. H., Sans, V., Dragone, V. and Cronin, L., "Configurable 3D-Printed millifluidic and microfluidic 'lab on a chip' reactionware devices", *Lab on a Chip*, Vol. 12, Issue 18, Pages 3267-3271, 2012.
38. Lee, W., Kwon, D., Choi, W., Jung, G. Y., Au, A. K., Folch, A. and Jeon, S., "3D-printed microfluidic device for the detection of pathogenic bacteria using size-based separation in helical channel with trapezoid cross-section", *Scientific Reports*, Vol. 5, Issue 1, Pages 1-7, 2015.
39. Chan, H. N., Chen, Y., Shu, Y., Chen, Y., Tian, Q. and Wu, H., "Direct, one-step molding of 3D-printed structures for convenient fabrication of truly 3D PDMS microfluidic chips", *Microfluidics and Nanofluidics*, Vol. 19, Issue 1, Pages 9-18, 2015.
40. O'Neill, P. F., Ben Azouz, A., Vazquez, M., Liu, J., Marczak, S., Slouka, Z. and Brabazon, D., "Advances in three-dimensional rapid prototyping of microfluidic devices for biological applications", *Biomicrofluidics*, Vol. 8, Issue 5, 2014.
41. Li, J., Rossignol, F. and Macdonald, J., "Inkjet printing for biosensor fabrication: combining chemistry and technology for advanced manufacturing", *Lab on a Chip*, Vol. 15, Issue 12, Pages 2538-2558, 2015.
42. Chossat, J. B., Tao, Y., Duchaine, V. and Park, Y. L., "Wearable soft artificial skin for hand motion detection with embedded microfluidic strain sensing", *International conference on robotics and automation (ICRA)*, Pages 2568-2573, IEEE, 2015.
43. Comina, G., Suska, A. and Filippini, D., "3D printed disposable optics and lab-on-a-chip devices for chemical sensing with cell phones", In *Microfluidics, BioMEMS, and Medical Microsystems XV*, Vol. 10061, International Society for Optics and Photonics, 2017.
44. Knowlton, S., Yu, C. H., Ersoy, F., Emadi, S., Khademhosseini, A. and Tasoglu, S., "3D-printed microfluidic chips with patterned, cell-laden hydrogel constructs", *Biofabrication*, Vol. 8, Issue 2, 2016.
45. Johnson, B. N., Lancaster, K. Z., Hogue, I. B., Meng, F., Kong, Y. L., Enquist, L. W. and McAlpine, M. C., "3D printed nervous system on a chip", *Lab on a Chip*, Vol. 16, Issue 8, Pages 1393-1400, 2016.
46. Adamski, K., Kubicki, W., & Walczak, R., "3D printed electrophoretic lab-on-chip for DNA separation", *Procedia Engineering*, Vol. 168, Pages 1454-1457, 2016.
47. Zhu, F., Macdonald, N. P., Cooper, J. M., & Wlodkowic, D., "Additive manufacturing of lab-on-a-chip devices: promises and challenges", *International Society for Optics and Photonics*, Vol. 8923, 2013.
48. Waheed, S., Cabot, J. M., Macdonald, N. P., Lewis, T., Guijt, R. M., Paull, B. and Breadmore, M. C., "3D printed microfluidic devices: enablers and barriers", *Lab on a Chip*, Vol. 16, Issue 11, Pages 1993-2013, 2016.
49. Krujatz, F., Lode, A., Seidel, J., Bley, T., Gelinsky, M. and Steingroewer, J., "Additive Biotech Chances, challenges, and recent applications of additive manufacturing technologies in biotechnology", *New Biotechnology*, Vol. 39, Pages 222-231, 2017.
50. Carve, M., & Wlodkowic, D., "3D-printed chips: Compatibility of additive manufacturing photopolymeric substrata with biological applications", *Micromachines*, Vol. 9, Issue 2, Page 91, 2018.



51. Zhu, F., Macdonald, N. P., Skommer, J. and Wlodkowic, D., “Biological implications of lab-on-a-chip devices fabricated using multi-jet modelling and stereolithography processes” In *Bio-MEMS and Medical Microdevices II*, Vol. 9518, 2015.
52. Lifton, V. A., Lifton, G. and Simon, S., “Options for additive rapid prototyping methods (3D printing) in MEMS technology”, *Rapid Prototyping Journal*, 2014.
53. Walczak, R. and Adamski, K., “Inkjet 3D printing of microfluidic structures—on the selection of the printer towards printing your own microfluidic chips”, *Journal of Micromechanics and Microengineering*, Vol. 25, Issue 8, 2015.
54. Lee, J. M., Zhang, M. and Yeong, W. Y., “Characterization and evaluation of 3D printed microfluidic chip for cell processing”, *Microfluidics and Nanofluidics*, Vol. 20, Issue 1, Page 5, 2016.
55. Bauer, M. and Kulinsky, L., “Fabrication of a lab-on-chip device using material extrusion (3D printing) and demonstration via Malaria-Ab ELISA”, *Micromachines*, Vol. 9, Issue 1, Page 27, 2018.
56. Lantada, A. D., de Blas Romero, A., Schwentenwein, M., Jellinek, C., Homa, J. and García-Ruíz, J. P., “Monolithic 3D labs-and organs-on-chips obtained by lithography-based ceramic manufacture”, *The International Journal of Advanced Manufacturing Technology*, Vol. 93, Issues 9-12, Pages 3371-3381, 2017.
57. Comina, G., Suska, A. and Filippini, D., “Low cost lab-on-a-chip prototyping with a consumer grade 3D printer”, *Lab on a Chip*, Vol. 14, Issue 16, Pages 2978-2982, 2014.
58. Sima, F., Sugioka, K., Vázquez, R. M., Osellame, R., Kelemen, L. and Ormos, P., “Three-dimensional femtosecond laser processing for lab-on-a-chip applications”, *Nanophotonics*, Vol. 7, Issue 3, Pages 613-634, 2018.
59. Cesewski, E., Haring, A. P., Tong, Y., Singh, M., Thakur, R., Laheri, S. and Johnson, B. N., “Additive manufacturing of three-dimensional (3D) microfluidic-based microelectromechanical systems (MEMS) for acoustofluidic applications”, *Lab on a Chip*, Vol. 18, Issue 14, Pages 2087-2098, 2018.
60. Pabst, O., Perelaer, J., Beckert, E., Schubert, U. S., Eberhardt, R. and Tünnermann, A., “All inkjet-printed piezoelectric polymer actuators: Characterization and applications for micropumps in lab-on-a-chip systems”, *Organic Electronics*, Vol. 14, Issue 12, Pages 3423-3429, 2013.
61. Sochol, R. D., Sweet, E., Glick, C. C., Venkatesh, S., Avetisyan, A., Ekman, K. F. and Hanson, K., “3D printed microfluidic circuitry via multijet-based additive manufacturing”, *Lab on a Chip*, Vol. 16, Issue 4, Pages 668-678, 2016.
62. Su, W., Cook, B. S., Fang, Y. and Tentzeris, M. M., “Fully inkjet-printed microfluidics: a solution to low-cost rapid three-dimensional microfluidics fabrication with numerous electrical and sensing applications”, *Scientific Reports*, Vol. 6, 2016.
63. Takenaga, S., Schneider, B., Erbay, E., Biselli, M., Schnitzler, T., Schöning, M. J. and Wagner, T., “Fabrication of biocompatible lab-on-chip devices for biomedical applications by means of a 3D-printing process”, *Physica Status*, Vol. 212, Issue 6, Pages 1347-1352, 2015.
64. Femmer, T., Flack, I. and Wessling, M., “Additive manufacturing in fluid process engineering”, *Chemie Ingenieur Techn.*, Vol. 88, Issue 5, Pages 535-552, 2016.
65. Yazdi, A. A., Popma, A., Wong, W., Nguyen, T., Pan, Y. and Xu, J., “3D printing: an emerging tool for novel microfluidics and lab-on-a-chip applications”, *Microfluidics and Nanofluidics*, Vol. 20, Issue 3, Page 50, 2016.
66. Pranzo, D., Larizza, P., Filippini, D. and Percoco, G., “Extrusion-based 3D printing of microfluidic devices for chemical and biomedical applications: A topical review”, *Micromachines*, Vol. 9, Issue 8, Page 374, 2018.
67. Bhattacharjee, N., Urrios, A., Kang, S. and Folch, A., “The upcoming 3D-printing revolution in microfluidics”, *Lab on a Chip*, Vol. 16, Issue 10, Pages 1720-1742, 2016.

68. Amin, R., Knowlton, S., Hart, A., Yenilmez, B., Ghaderinezhad, F., Katebifar, S. and Tasoglu, S., "3D-printed microfluidic devices", *Biofabrication*, Vol. 8, Issue 2, 2016.
69. Temiz, Y., Lovchik, R. D., Kaigala, G. V. and Delamarche, E., "Lab-on-a-chip devices: How to close and plug the lab?", *Microelectronic Engineering*, Vol. 132, Pages 156-175, 2015.
70. Shallan, A. I., Smejkal, P., Corban, M., Guijt, R. M., & Breadmore, M. C., "Cost-effective three-dimensional printing of visibly transparent microchips within minutes", *Analytical Chemistry*, Vol. 86, Issue 6, Pages 3124-3130, 2014.
71. Lee, K. G., Park, K. J., Seok, S., Shin, S., Park, J. Y., Heo, Y. S. and Lee, T. J., "3D printed modules for integrated microfluidic devices", *Rsc Advances*, Vol. 4, Issue 62, Pages 32876-32880, 2014.
72. Symes, M. D., Kitson, P. J., Yan, J., Richmond, C. J., Cooper, G. J., Bowman, R. W. and Cronin, L., "Integrated 3D-printed reactionware for chemical synthesis and analysis", *Nature Chemistry*, Vol. 4, Issue 5, Pages 349-354, 2012.
73. Au, A. K., Bhattacharjee, N., Horowitz, L. F., Chang, T. C. and Folch, A., "3D-printed microfluidic automation", *Lab on a Chip*, Vol. 15, Issue 8, Pages 1934-1941, 2015.
74. Waldbaur, A., Rapp, H., Länge, K., & Rsp, B. E., "Let there be chip-towards rapid prototyping of microfluidic devices: one-step manufacturing processes", *Analytical Methods*, Vol. 3, Issue 12, 2011.
75. Tamayol, A., Bahrami, M., "Microchannels with noncircular cross section", *Fluids Engineering*, Vol. 132, Issue 11, 2010.
76. Guo, X., Zhou, J., Zhang, W., Du, Z., Liu, C., Liu, Y., "Self-supporting structure design in additive manufacturing through explicit topology optimization", *Computer Methods in Applied Mechanics and Engineering*, Vol. 323, Pages 27-63, 2017.