

# Latest Trends In 3D Printed Microfluidics

## Dernières tendances en matière de microfluidique imprimée en 3D

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**ABSTRACT.** Over the last decade, there has been a large interest in the use of 3D printing to manufacture microfluidic devices, since it has the ability to circumvent traditional fabrication techniques limitations. These include being unable to really make complex three-dimensional architectures, expensive and time-consuming processes to change device designs, and difficulty transitioning from prototyping to mass production. In this literature review, we will look at the current trends in 3D printed microfluidics, as well as recent advances and new developments in fabrication techniques, materials, and applications. Integration of 3D printing in microfluidics research has helped in the rapid prototyping of fluidic channels and structures with high complexity at an effective cost. Applications of 3D printed microfluidics are described in the areas of healthcare, diagnostics, chemical synthesis, and biotechnology. This paper also delineates the challenges and future prospects of 3D printed microfluidics, giving insight into potential research directions and technological developments.

**RÉSUMÉ.** Au cours de la dernière décennie, l'utilisation de l'impression 3D pour fabriquer des dispositifs microfluidiques a suscité un grand intérêt, car elle permet de contourner les limites des techniques de fabrication traditionnelles. Celles-ci comprennent l'impossibilité de réaliser des architectures tridimensionnelles complexes, des processus coûteux et longs pour modifier la conception des dispositifs, et la difficulté de passer du prototypage à la production de masse. Dans cette revue de la littérature, nous examinerons les tendances actuelles de la microfluidique imprimée en 3D, ainsi que les avancées récentes et les nouveaux développements en matière de techniques de fabrication, de matériaux et d'applications. L'intégration de l'impression 3D dans la recherche en microfluidique a permis le prototypage rapide de canaux et de structures fluidiques très complexes à un coût raisonnable. Les applications de la microfluidique imprimée en 3D sont décrites dans les domaines des soins de santé, du diagnostic, de la synthèse chimique et de la biotechnologie. Ce document décrit également les défis et les perspectives d'avenir de la microfluidique imprimée en 3D, en donnant un aperçu des orientations potentielles de la recherche et des développements technologiques.

**KEYWORDS.** Microfluidics, Micro-fabrication, 3D printing, Additive manufacturing, Fused deposition modeling (FDM), Stereolithography (SLA), Digital Light processing (DLP).

**MOTS-CLÉS.** Microfluidique, microfabrication, impression 3D, fabrication additive, modélisation par dépôt en fusion (FDM), stéréolithographie (SLA), traitement numérique de la lumière (DLP).

## 1. Introduction

Microfluidics is a technique for systematically manipulating and controlling fluids in micro-scaled channels. Since her first development in the 1970s, this technology has been explored by various industries for diverse applications. It has gradually integrated into many fields, including biology, physics, medicine, and analytical chemistry [WAN 20] [LEE 16]. Compared with traditional techniques, microfluidic techniques have many merits, such as low cost and a small footprint leading to portability, fast analysis speed, small sample consumption, and component integration [WAN 21].

A microfluidic chip, also known as lab-on-a-chip, is a set of micro-channels through which fluids flow, connected to achieve the desired features (Fig.1). This network of microchannels trapped in the microfluidic chip is linked to the outside by several holes of different dimensions (inputs and outputs) pierced through the chip. Through these pathways, fluids are injected into and evacuated from the device with some external active systems. Owing to their microscale dimensions, microfluidic devices are typically operated at low Reynolds numbers, and fluidically characterized by laminar flow behavior. Under laminar flow, mixing between adjacent parallel streams is minimal and diffusion is the only mechanism of mixing [LI 17]. While mixing based on diffusion could take days in conventional flask-based systems, the small distances within microfluidic channels enable complete mixing within seconds

or minutes, reducing volumes of samples and reagents, saving save costs on reagents, and producing less waste [TAR 14].

Microfluidic devices can be fabricated from a range of materials using different processes including soft lithography, paper microfluidics, micromachining, injection molding, and hydride paper-based open-channel microfluidics [REH 20]. In the last two decades, soft-lithography using polydimethylsiloxane (PDMS) micro-molding has been a widely used method as PDMS is biocompatible, cheap, and transparent (240nm-1100nm), has low autofluorescence, water-impermeable, and rapidly prototyped with high precision using simple procedures [BHA 16]. However, these processes can be time-consuming, imprecise, expensive, or challenging for design changes and they often require a dust-free (cleanroom) environment to ensure error-free devices. In addition, they show a lack of truly three-dimensional (3D) architecture and flexibility in device design. Recently, three-dimensional printing (3D Printing) or additive manufacturing (AM) has emerged as a potentially revolutionary technology in the field of microfluidics through its ability in overcoming the limitations of traditional techniques.

3D printing refers to a set of additive manufacturing techniques used for fabricating parts layer by layer directly from a computer-aided design (CAD) data file. This technology offers the benefit to produce complex parts with a shorter cycle time and lower cost compared to traditional manufacturing process [MOH 15]. The advantages of 3D printing rely on its simplicity, fast and efficient prototyping with no need for photomasks, photoresists, and clean room facilities [GAA 17] which require neither tooling nor assembly, produce minimal waste and minimize distribution costs. So, the ability to rapidly prototype a physical model in a few hours has already revolutionized the product design process by allowing designers to test designs before investing in tooling or fabrication processes [AU 16].

The three main additive manufacturing techniques employed for microfluidics are fused deposition modeling (FDM), stereolithography (SLA), and PolyJet/MultiJet Modeling (PJM/MJM) [BHA 16] [LIF 14] [MAC 17]. The use of FDM printers is becoming common for low precision microfluidics. FDM printers are affordable and readily available in the market with low or no technical expertise required from the user. The same is the case with SLA printers, being the best option if the resolution requirement is above 500  $\mu\text{m}$  and if the fluid used in the specific application is not constrained by cost or quantity [BEA 17]. On the other hand, printers like Polyjet modeling are costly and have issues like support material removal problems and limited optical characteristics. Therefore, we focus in this review only on extrusion-based printing and stereolithography-based printing.

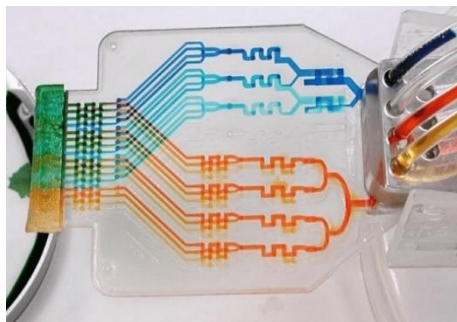
Among the latest trends in 3D printed microfluidics are techniques for multi-material printing, which enable the production of functional fluidic systems with different properties and functionalities [REV 21]. Another focus area is the integration of sensors and actuators into the 3D-printed microfluidic devices to actively monitor and control the fluidic processes in real time [LAS 21]. Another strong trend is the increased integration of microfluidics with other technologies, including nanotechnology and bioprinting, to create new functions and applications [ANU 24]. Ongoing interest in advanced materials that can help to improve the performance and function of 3D-printed microfluidic devices includes biocompatible and antibacterial materials [ANU 24].

Other very active directions in the field of microfluidics have been the application of combinations of machine learning with 3D printing [AMI 17]. By applying machine learning algorithms, researchers have optimized the design of 3D printed microfluidic devices for performance and functionality in specific applications.

Other important trend is the application of 3D printed microfluidics in the development of organ-on-a-chip systems [MIL 23]. These systems try to mimic the structure and function of human organs and offer a platform for drug testing and disease modeling. By using 3D printing in the creation of the organ-

on-a-chip devices, one can make complex microfluidic networks with enhanced performance and potential impact in pharmaceutical and biomedical applications [LI 23].

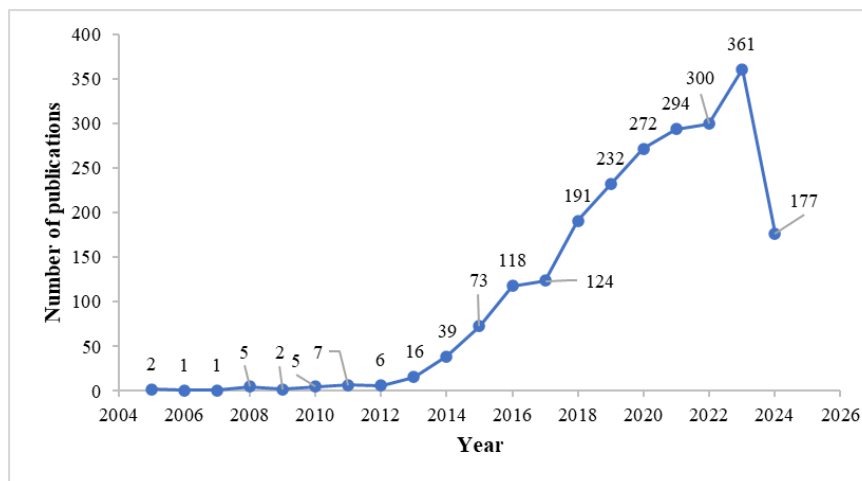
In this review, we will present the current trends in 3D printed microfluidics and highlight the applications to diverse fields, along with the recent advances in materials and methods for 3D printed microfluidics by the use of bio-compatible materials, and different printing techniques such as stereolithography, fused deposition modeling, and inkjet printing. We will also present the recent advances, challenges, and future prospects for 3D printed microfluidics.



**Figure 1.** *Microfluidic device.*

## 2. 3D printed microfluidics

This has been the subject of hundreds of investigations on the use of 3D printing in the fabrication of microfluidic devices, as reflected by the great number of publications and their citation rate over the last decade. The statistics were derived using a mixture of algorithms for machine learning and data analysis in identifying trends in research activity concerning 3D printed microfluidics. Figure 2 shows the number of publications and citations per year. It is seen that the number of publications per year increased considerably over the last decade, from 16 in 2013 to 361 in 2023.



**Figure 2.** *Number of publications on 3D printed microfluidics per year. (Scopus)*

### 2.1. Fused deposition modelling

Fused deposition modeling (FDM) is the most widely used 3D Printing technology, likely due to its cost-effectiveness in producing custom thermoplastic parts and prototypes, as well as the wide range of materials available [GYI 21]. Generally, in this technique, a heated thermoplastic material is melted into a liquid state in a liquefier head and then selectively deposited through a nozzle that traces the part's cross-sectional geometry to produce 3D parts directly from a CAD model in a layer-by-layer manner [MOH 15]. Microchannel fabrication with FDM has been a challenge because of several reasons: (1) the filaments laid down by the extrusion process cannot be arbitrarily joined at channel intersections; (2) the

lack of structural integrity between the layers results in weak seals; and (3) the size of the filaments extruded are larger than typical channels used in microfluidics [8]. To ensure the quality of 3D-printed microfluidic devices with the FDM technique and to improve the dimensional precision of microchannels, the process parameters must be determined for each application [MOH 15].

FDM can be used to prepare microchannels and to use the resulting structures as a verification system for modeling fluid flow in microchannels.

Jia Min Lee et al. designed a part with common microfluidic features such as channels, slopes, and circular holes. It was fabricated using inkjet printing and filament-based deposition. The results have shown that the resolution of poly-jet printing is superior in all axes to FDM. Poly-jet printed parts can be printed with nominal x and z dimensions of 500 and 100  $\mu\text{m}$  with observable features formed. The poly-jet printer produced better spatial accuracy in all three axes with an average deviation of 25.2  $\mu\text{m}$  across all measurement series, as compared to 67.8  $\mu\text{m}$  for FDM. The poly-jet printer produces smooth features with a surface roughness measurement of 0.47  $\mu\text{m}$  as opposed to FDM-printed parts of 42.97  $\mu\text{m}$  [LEE 16].

Gabriel Gaal et al. were able to 3D-print transparent and sealed PLA microchannels despite limitations in resolution imposed by the FDM technology. Important achievements included good transparency, the printing of microchannels without collapsed structures, use of a cheap and more accessible material (PLA) [GAA 17].

Niall P. Macdonald et al. found that, by reducing the distance between deposition passes, it was impossible to fabricate laminar flow chips with channels smaller than 500  $\mu\text{m}$  with FDM. Channels were consistently smaller than designed due to the spreading of the polymer as it is extruded. It was observed that the channel was difficult to visualize once multiple layers of polymer were deposited under the channel to form the chip base. This was due to the cross-hatch nature of the base and entrapment of air between the filament, due to incomplete fusing of the extruded polymer. Form FDM's low resolution particularly in the XY plane means that  $< 500 \mu\text{m}$  is an impossibility at this stage, the roughness (10.97  $\mu\text{m}$ ) does make the FDM well suited to fabricating low-cost micromixers [MAC 17].

Valentin Romanov et al. tested the ability to control and replicate channels of varying heights and widths using two different FDM 3D printers. They showed that the average channel width variation was 0.32% with a height variation of just 0.08% across all tested print channels. Measured channel dimensions closely matched designed specifications regardless of the printer. They found that transparency is a function of nozzle temperature, print speed, and cooling rate. The resolution of FDM-based 3D printers available commercially is still limited to 250  $\mu\text{m}$  – 300  $\mu\text{m}$  for repeatable fabrication of open microfluidic channels, without any supporting structures [ROM 18].

Muhammad Asif Ali Rehmani et al. demonstrated the possibility to fabricate the internal features of the microfluidic device using an FDM printer by optimizing the printer's parameters. They successfully printed the linear, curved, and spiral microchannels with a diameter of less than 0.5 mm where the path of the microchannel was along with the print layer. The printed results from the FDM printer show that the accuracy of the printer not only varies with the type of the printer but it also varies if the microchannels are along with the print layers or perpendicular to the print layers. All the microchannels with a diameter of 0.3 mm and less started to leak even at minimum flow rates. There is no leakage observed in linear and curved microchannels with a diameter of 0.4, 0.45, and 0.5 mm up to the flow rate of 40  $\mu\text{L}/\text{min}$ . [REH 20]

## 2.2. Stereolithography

Stereolithography (SL), was first described and patented by Hull in 1986. It is based on the photopolymerization of a liquid photopolymer by a UV laser or similar light source. The light source is either a single-point laser that illuminates every single voxel independently or a digital micromirror-

array device (DLP) that allows the curing of an entire layer simultaneously [WEI 19]. The prototype (model) is built by sequentially polymerizing layers (slices) created by the software in the SLA tool using a CAD file as its input. Initially, a platform is filled with the photopolymer to the thickness of the first layer (50-150  $\mu\text{m}$ ) and the laser is scanned across the surface to polymerize the layer. The platform is then lowered by a layer thickness, the polymer is dispensed and the laser beam polymerizes it again and the process is repeated until the entire model is built [LIF 14].

Anthony K. Au et al. showed that at the beginning of 2015, Ilios announced a printer with 25 mm XY resolution (6 mm Z layers) and capable of four-material prints, Old World Labs announced another printer with <1 mm XYZ resolution and Carbon3D announced a printer capable of printing in minutes instead of hours with 1 mm XYZ resolution. [AU 16]

Michael J. Beauchamp et al. have mentioned that SLA 3D printers have achieved approximately 100  $\mu\text{m}$  in fabricating microfluidic channels. In addition, SLA offers smooth channel surfaces which facilitate laminar flow. [BEA 17]

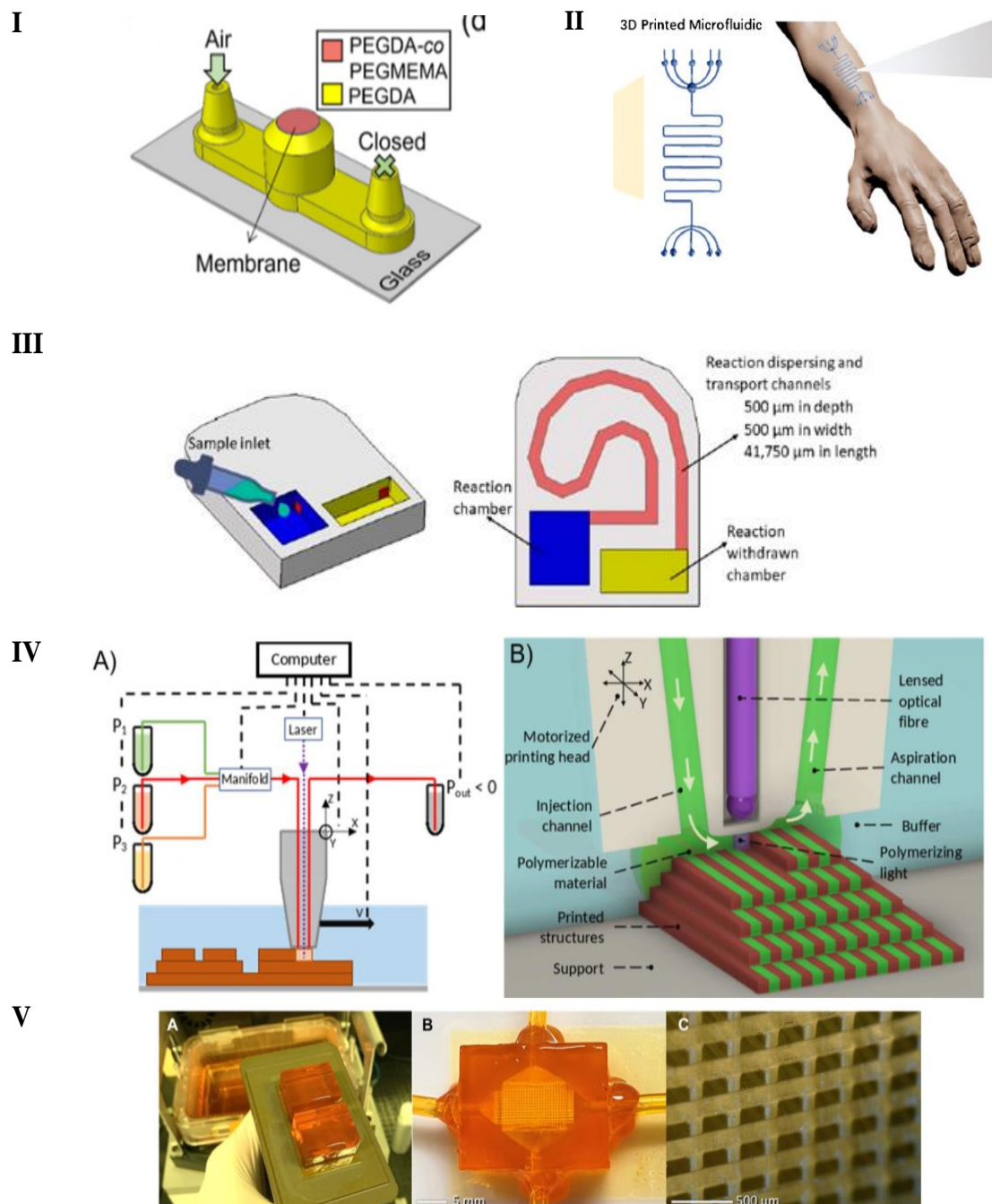
Michael J. Beauchamp et al. (2018) used a 3D printer with a nominally 385 nm light source and 7.6  $\mu\text{m}$  pixel size in the image plane and found that the minimum width ridge that could be successfully printed was 30  $\mu\text{m}$ , which was with an exposure time of 1500 ms. The results showed that to achieve a minimum trench width at full depth, there are three different possibilities: 500 ms exposure without compensation, 1000 ms exposure without compensation, or 1000 ms exposure with compensation. All three of these approaches produced a trench 100  $\mu\text{m}$  deep and about 20  $\mu\text{m}$  wide; however, the de-signed widths were all different (4, 5, and 6 pixels, respectively). [BEA 18]

Yongquan Li et al. designed some microfluidic devices with different channel widths/diameters and different shapes (cylindrical and rectangular), to investigate the surface roughness and structural accuracy of the 3D printed chips. It was observed that with an increase in the designed channel width, the geometric deviation decreased. The actual channel diameter of the cylindrical-shaped microfluidic chip was even smaller than the actual channel width of the rectangular-shaped microfluidic chips even though they were intended to have the same channel diameters and widths. The cylindrical channel was not perfectly cylindrical, as an obvious striation appeared in the images indicating surface roughness. [LI 23]

Brenda M. et al. developed an electrochemical microfluidic device for the creation of a low-cost reusable analytical microsystem, using a low-cost commercially accessible SLA printer. They achieved the fabrication of microfluidic channels of 100 x 200  $\mu\text{m}$  and created. [BRE 22]

### 3. Latest trends in 3D printed microfluidics

Besides the already discussed trends, a lot of emphasis has been placed on the development of materials for 3D printing microfluidics that are environmentally friendly and sustainable [SAR 24]. Researchers and industry experts are taking efforts to develop biodegradable polymers and recyclable materials for mitigating the environmental effect of the fabrication of microfluidic devices. Therefore, Fournié et al. developed a new microfluidics-assisted photopolymerization method for multi-material 3D printing (Fig.3 IV). They demonstrated that by controlling the flow rate ratio, printhead velocity, and gap distance between the printhead and substrate, they could achieve precise material confinement and prevent cross-contamination between different materials. This control allowed them to create complex 3D structures with high resolution, showcasing the effectiveness of their novel approach [FOU 23]. Ahmadianyazdi et al. introduced a new type of resin for 3D printing microfluidic devices, called PEGDA-co-PEGMEMA. The new resin retains the benefits of PEGDA, such as low viscosity and biocompatibility, while offering tunable elasticity. They successfully printed microfluidic actuators with a hybrid structure, combining a flexible PEGDA-co-PEGMEMA membrane within a rigid PEGDA housing (Fig.3.I). This was achieved using a "Print-Pause-Print" (3P-printing) method [AHM 23].



**Figure 3.** I) 3D CAD model of a pressurization chamber 3P-printed in PEGDA (yellow) to measure the deflection of a PEGDA-co-PEGMEMA membrane (red), illustrating the pneumatic inlet (green arrow) and the blocked outlet (green cross) [33]. II) Schematic illustration of the 3D printed microfluidic platform and the application of such platforms to skin for measuring multiple parameters and biomarkers from sweat [37]. III) Test device for *Streptococcus pyogenes* detection [36]. IV) 3D Illustration of the 3D-FlowPrint concept. (A) Planar schematics showing the setup of the instrument (B) Schematic of the opto-fluidic processes with a XZ cross-section of the head. V) 3D printed artificial lungs [35].

In addition, the idea of on-demand and customizable 3D printed microfluidic devices is gaining prominence. With the continuous advancement in 3D printing, much focus is now directed toward facilitating personalized solutions for particular applications [ECE 24]. Accordingly, Fleck et al. developed a 3D printed microfluidic artificial lungs, that are small enough to be implanted or used in portable devices. They created a proof-of-concept microfluidic device designed to mimic the gas exchange function of natural lungs (Fig 3.V). They used a biocompatible material called

polydimethylsiloxane and high-resolution 3D printing to fabricate the intricate network of microchannels within the device [35]. In another research, Uysal et al. created a rapid and accessible diagnostic tool for *Streptococcus pyogenes* using a 3D printed microfluidic device and the Loop Mediated Isothermal Amplification (LAMP) method (Fig 3. III). The device was designed to be an accessible and rapid diagnostic tool for bacterial DNA amplification [FLE 24].

Furthermore, automation and robotics integrated into the 3D printing process of microfluidics are an emerging trend. It will allow streamlining the workflow of fabrication and reducing the need for human intervention in the process so that the outcome becomes consistent with respect to quality and reproducibility of devices produced [ZHA 20]. For example, Ece et al. demonstrated a robotic 3D bioprinting system that could directly deposit cell-laden bioinks into complex microfluidic structures in an automated manner (Figure 3. II). This approach increased the efficiency and precision of fabricating multi-material microfluidic devices integrated with living cells [UYS 24].

## 4. Conclusion

There has been a surge in interest in employing 3D printing to create microfluidic devices, because of the convenience and the simplicity of the fabrication process. In this review, we showed that FDM and SLA are the main candidates for the accessibility of the 3D printed microfluidic devices even if they both still face some challenges including dimensional accuracy and printing resolution. Among other issues, SLA devices have limitations with biocompatibility and FDM with surface quality.

Advancements in 3D printed microfluidics cover a wide range of trends and applications, resulting in the convergence of 3D printing technology and microfluidics to produce ground-breaking solutions. As researchers, engineers, and practitioners continue to investigate and apply these trends, a new era of possibilities emerges, reshaping the landscapes of healthcare, biotechnology, and materials science with 3D printed microfluidics.

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