

## Review of Polymer Microfluidic Device Manufacturing Using Laser Technology

Safa N. Salman<sup>\*1a</sup>, Fatema H. Rajab<sup>1b</sup> and Ahmed A. Issa<sup>2</sup>

### Abstract

Authors affiliations:

1\*) Department of Laser and Optoelectronics Engineering, College of Engineering, Al-Nahrain University, Baghdad, Iraq. a) <u>safa.aljabery8@gmail.com,</u> b)<u>fatema.h.rajab@nahrainuniv.edu.i</u> q

2) Mechatronics and Medical Devices Engineering Department, Faculty of Engineering and Information Technology, Al Azhar University-Gaza, Palestine a.issa@alazhar.edu.ps

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### 1. Introduction

Working with tiny quantities of samples, reagents, and solvents has several advantages, such as enhanced environmental protection resulting from the simplicity of managing small fluid volumes and the reduced generation of hazardous waste. Moreover, it enhances personal safety in environments where the bulk of chemical fluids utilized in analytical research are flammable and have the potential to cause injury or damage. Therefore, employing small quantities of liquid will reduce the likelihood of sustaining injuries. Reduced microfluidic devices allow the creation of completely self-governing point-of-care devices and analytical systems used in the field. Smaller microfluidic systems have the ability to identify single molecules by reducing the background signal. Reducing consumption of samples, solvents, and reagents is a cost-effective measure that can lead to savings on purchases and trash disposal [1, 2].

Microfabrication methods integrated into semiconductors facilitated the advancement of microfluidics. These approaches provided essential methods for constructing microfluidic circuits and included many operations, such as expansion, sampling, and separation. Microfluidic devices play a crucial role in integrating sub-units for various

This paper provides a comprehensive overview of microfluidic device (MFD) manufacturing processes. The review starts with an introduction elucidating the significance and advantages of MFDs. Subsequently, a brief description of the materials employed in MFD fabrication is presented. The manufacturing process used to create MFDs is then thoroughly examined, with a focus on the application of laser technology.

Keywords: CO<sub>2</sub>, PMMA, MFD

الخلاصة:

تقدم هذه المقالة نظرة شاملة لعمليات تصنيع أجمزة الموائع الدقيقة .(MFD) تبدأ المراجعة بمقدمة توضح أهمية ومزايا .MFD ، يتم تقديم وصف موجز عن المواد المستخدمة في تصنيع .MFD يتم بعد ذلك فحص عملية التصنيع المستخدمة لإنشاء MFDs بدقة، مع التركيز على تطبيق تكنولوجيا الليزر.

functions such as mixing, cooling, heating, separating, detecting, signal processing, and chemical processes. The proven capability of microfluidic devices to do intricate chemical analysis has clear implications in several disciplines. MFD decreases the cost of biomedical research efforts by compensating for the expenditure of expensive procedures such as measurements for proteomics, metabolomics, or genomics [1, 3, 4].

MFD may be obtained in many designs, including straight channel, Y channel, T-channel, cross-junction, etc., depending on their geometry. All of these designs have been fabricated utilizing various techniques, like lithography, etc.. Various materials, including glass, polymer, and silicon, have been used for making MFDs, depending on the specific application [1, 5, 6]. In this paper, commonly used manufacturing techniques focused on using laser technology in MFD are reviewed.

# 2. Common Materials for Microfluidic Devices

Microfluidic devices are manufactured from various materials, including silicon, glass, metals, polymers, and ceramics [7,8,9]. These various materials have both benefits and limitations depending on their

NJES is an open access Journal with ISSN 2521-9154 and eISSN 2521-9162 This work is licensed under a <u>Creative Commons Attribution-NonCommercial 4.0 International License</u> intended use [10]. Metals are cost-effective, easy to machine, and widely accessible. They resist ultimate heat, corrosive chemicals and pressure, making them suitable for various applications. Aluminium, copper, and iron are commonly employed metals for microfluidic devices, which are typically alloyed with other metals to optimize their chemical resistances [9]-[11]. Moreover, tiny electronic devices such as microchips can be manufactured using lowtemperature ceramic, which makes them ideal due to its unique chemical composition on their surfaces, withstanding corrosive conditions, and remaining stable even at high temperatures [12,9]. While ceramics offer advantages, they have some drawbacks in terms of maintaining dimensions stability, controlling porosity (empty spaces), and preventing brittleness. These challenges produce difficulties when integrating ceramics into complex miniature systems [9]. Silicon is a popular option for manufacturing microfluidic devices because of its numerous availability, chemical compatibility, and capacity to resist high temperatures. However, it has several limitations, such as the low transparency in silicon, making it unsuitable for optical detection in visible and ultraviolet ranges, and the difficulty in incorporating active components like valves and pumps into the silicon platform. Silicon's usage is limited by its high cost nature [7,12].

Glass exhibits thermal stability [13], electrical insulation [13], biocompatibility [7,12], chemical inertness [12], rigidity [13], and facilitates straightforward surface functionalization [7,13]. Glassprovide based microreactors the necessary characteristics to effectively conduct chemical reactions under demanding circumstances, such as elevated temperatures, increased pressures, and corrosive solvents [14]. In comparison to silicon, glass offers superior optical transparency [12], the potential for incorporating active components [7,12], and a more affordable cost [7,13]. Glass is also the conventional material used by chemists and biologists for the manufacture of most laboratory equipment [9]. The compatibility of glass with biological substances makes it valuable for biochemical studies [12]. Although glass is inexpensive, its manufacturing into chips is costly due to the need for time-consuming labour and preparation in cleanrooms, as shown in references [13].

Compared to silicon and glass, polymers are increasingly used in microfluidic device manufacture due to their adaptability and cost-effectiveness [9], [14]. Polymers-based microreactors are suited for applications at room temperature or higher temperatures, reaching up to 200 °C [10], and enable visual observation of the progression of the reaction, which is particularly crucial in nano-crystallization processes [14]. The predominant polymers used in the manufacturing of microfluidic devices include polydimethylsiloxane (PDMS), polymethylmethacrylate (PMMA), fluoropolymers, cyclo-olefin polymers and copolymers (COPs/COCs), and Theolen polymers (TEs). Figure 1 illustrates the many uses of silicon, glass, and polymers.





Figure (1): Examples of applications of silicon, glass and polymers.

# 3. Common Fabrication Methods of Microfluidic Devices

To create microfluidic devices, two or more layers are usually bonded together after the required (such microstructure as microchannels or microchambers) has been embedded on one of the surfaces of the layers. The microstructure can be sealed or bonded using mechanical, solvent-assisted, adhesive, or thermal techniques. The most widely used fabrication processes include hot embossing, injection moulding, laser ablation, lithography, etching, soft lithography, precision micromachining, and micro milling to create microchannels and other microfeatures [15]. Another technique that can be used to quickly prototype centrifugal microfluidic platforms is thermoforming with polymeric films or foils [16]. Soft lithography or replica moulding, including the creation of a rigid master, pouring a liquid polymer into the mould, curing it with heat, and then removing the polymer, is a widely used technique for creating biomedical microfluidic devices [7,17].

Photolithography, shown in Figure 2, is a technique that imprints designs onto light-sensitive substances like photoresists by selectively illuminating a photomask with UV light. High-quality photomasks are produced on transparent substrates like glass or polymer. Microchannels are formed by integrating photolithography and etching techniques on silicon and glass substrates [18]. Wet etching creates nanochannels by submerging the sample in a chemical etchant, while dry etching uses reactive ion etching to create deep and narrow channels [19].

Hot embossing is a widely used method in microfabrication for producing microfluidic devices and it involves shaping by heat and pressure the thermoplastics after melting it, as seen in Figure 3. Optimal vacuum and precise temperature distribution are essential factors for achieving effective replication. This technique maintains the optical characteristics of the substrate by accurately duplicating even nano-sized features without causing any internal strain. Optical detection in microfluidic systems is highly reliant on this factor. Micro-thermoforming is a process where a thin polymer layer is pressed against a master structure, **NJES** 27(1)38-45, 2024 Salman et al.



similar to hot embossing. Replication precision is comparatively lower than that of hot embossing. This technique is used to thermoform a centrifugal microfluidic disc for the purpose of creating a realtime polymerase chain reaction (PCR) genotyping test [20].

Figure 4 illustrates the process of injection molding, which is a commonly used industrial technique for producing microchannels utilizing polymers. This process involves the heating of polymer pellets, which are then placed into a chamber containing a duplicate master. Injection molding is a very suitable method for creating intricate structures due to its ability to provide accurate and uniform outcomes across several dimensions [21]. Precision micromachining is used to precisely abrade the surface of the substrate, facilitating the prototype of microfluidic devices. This affordable devices within a short timeframe (few minutes) and does not need a cleanroom facility [7,22].



Figure (2): Photolithography process



Figure (3): Hot embossing process.



Figure (4): Injection molding process

### 4. Review of Laser Micromachining of Polymer Materials for MFD Manufacturing

There are a few limitations attached to the standard techniques for creating microfluidic devices, such as the multi-step process, high cost, and limited size of the fabrication features [23, 24]

Laser material processing, on the other hand, has been around for approximately 60 years and is a significant part of the contemporary manufacturing sector and economy [25]. Compared to traditional methods, laser processing provides fast, accurate, and non-contact options, along with the added advantage of flexibility in terms of materials, designs, and features that can be created. Its easy-to-use interface makes it a perfect tool for swiftly prototyping intricate as well as simple designs. Laser processing can also be used to add extra features to microfluidic devices, like placing microelectrodes inside thin metal films or creating microchannels with complementary functions[26, 27, 28, 29].

Laser systems are now more reasonably priced, which makes them a desirable option for creating microfluidic channels in materials like glass and polymers. Applications in precision engineering and industry frequently use laser processing. Comparing laser micromachining to other methods, such as lithography, reveals several advantages. These benefits include the ability to create complete 3D microstructures in a single step without the need for clean-room facilities or the mask or mold preparation process, as well as a faster fabrication time [26, 27, 28, 29]. It has been demonstrated that material processing is influenced by the specific thermo-physical and optical characteristics of the workpiece, the processing regime, the laser parameters, and the optical performance of the laser beam. Consequently, machining process optimization should be the focus of efforts [30]. UV lasers and other short-wavelength lasers have high photon energies that can break most polymer bonds. This leads to ablative photodecomposition, a "cold" chemical process that reduces substrate heat damage. On the other hand, longer wavelengths mostly cause thermal reactions, such as the material melting, and evaporating. Thus, during laser processing, the laser wavelength is crucial in minimizing the heat-affected zone (HAZ) [24]. Regarding pulsed lasers, the ablated microchannel quality and the mechanisms of laser-material interaction are significantly influenced by the duration of each pulse. The duration of the laser pulse directly controls the rate of material removal, which has an impact on the overall efficiency and precision of the ablation process [24]. Diode, excimer, fiber lasers, CO<sub>2</sub>, and Nd:YAG are the most often used lasers in MFD manufacturing.

Yiqiang Fan et al. [31] investigated the impact of utilizing  $CO_2$  laser machining of plastic paper coated with wax and showed this method resulted in a better surface quality and smoother channel compared with that achieved without wax cover.

S. Prakash and S. Kumar have published several works related to the micromachining of polymer targets for MDF manufacturing. They used a CO<sub>2</sub> laser to create a microchannel on PMMA for microfluidic



applications. They investigated how the width, depth, and softened zone of the microchannel were affected by the laser power, scanning speed, depth of focus, processing environment, and using a Cu mask during processing. They found that increasing scanning speed had the opposite effect of increasing power, which resulted in a decrease in the microchannel's width, depth, and softening zone. Accurate output widths with little impact from deposited energy were obtained through mask-assisted processing [32, 33, 34]

A. Sen et al. examined the impact of fiber lasers on the creation of microchannels on PMMA substrates and how various process parameters (wavelength of 1064 nm, scan speed of 10 to 300 mm/s, pulse frequency of 50 to 90 kHz, average power of 5.0 to 15.0 W, and number of passes of 1 to 5) affected the depth and width of the heat-affected zone and the microchannel width. The work's findings showed that when scanning speed increases, the width of the fine channels decreases, depth also follows a similar path, and the width of the (HAZ) increases correspondingly. Additionally, it was noted that while the depth and width of the heat-affected zone increased, the microchannel's width decreased as the pulse frequency increased. In addition to increasing the microchannel's depth and width, the number of passes also improved its characteristics [35].

A 10.6  $\mu$ m CO<sub>2</sub> laser with a maximum power output of 80 W, a scanning speed of up to 500 mm/s, a 60 mm focal length, and a 60  $\mu$ m spot diameter on COC polymer were used to create an MFD by J. Cai et al.[36]. The profile of the ablated microchannel was similar to a Gaussian curve. The smallest achievable width and depth for the microchannels are approximately 223  $\mu$ m and 132  $\mu$ m, respectively. Variations in the microchannels' width and depth were observed under different laser power and scan speeds.

Carlos Matellan et al. [37] investigated the use of different power (10%-80% of  $P_{max}$ ) and DF (3-40mm) CO<sub>2</sub> lasers (10.6µm wavelength, 30 W  $P_{max}$ ) for the rapid and inexpensive prototyping and assembly of PMMA microfluidic devices. They succeeded in creating channels with widths between 250µm and 0.25 mm and depths between 20µm and 300µm. They stated that there was a linear relationship between laser power and the aspect ratio, depth, and channel width. The results showed narrow and deep cross-section channels when the laser configuration was used within the focus area (DF). Conversely, a disorganized arrangement led to a low aspect ratio, and shallow semi-circular channels.

Hubeatir K et al.[38] explored the effects of the Taguchi method in conjunction with a  $CO_2$  laser to deepen the engraving of PMMA by applying a range of laser engraving processes (power, scanning speed, line overlapping, spot size) and they demonstrated how process parameters affect the interaction between engraving depth and surface roughness. Their results suggested that the surface roughness and depth were proportional to the laser power, while the engraving depth decreased with increasing scanning speed.

The reconfigurable acrylic-tape hybrid microfluidics were developed and manufactured by Yundong Ren et al. [39] utilizing a direct and efficient CO<sub>2</sub> laser manufacturing method. This study demonstrated how the geometrical design and processing parameters affect the capillary flow velocity. A crucial parameter that was examined was the microfluidic device's length and its correlation with the Reynolds number. They recommended that using acrylic tape is a promising tool for this application. They also mentioned the usage of inexpensive acrylic film microfluidic devices because of their numerous applications, particularly in the clinical and medical domains.

Kexin Gao et al. [40] created a polymer MFD on PMMA material coated in Kraft tape to improve laser absorption. They used a 1.6 W and 5 mm/s diode laser. The authors used (2–7) W of power and (1–20) mm/s of speed to analyze the width and depth of microchannel changes as a function of power and speed before MFD manufacturing. They contrasted their findings with those obtained with a CO<sub>2</sub> laser. They discovered that a diode laser was used to create the Vshaped channel, and a CO<sub>2</sub> laser was used to create the U-shaped channel.

Mahdee Samae et al. [41] produced a paper-based Y-shaped micromixer with a straight and zigzag arrangement between two PVC layers in the same year. While the xerography technique was used to cut 1mm wide inlet and outlet holes on the top PVC layer, the laser was used to cut a 300µm-wide channel on three different types of paper. To lessen the hydrophobicity of the paper layer and preserve good adhesion during the lamination bonding process, the paper layer was submerged in melted paraffin wax for fifteen minutes following the laser cutting process. They claimed that the zigzag pattern improved mixing efficiency and that the kind of paper had an impact on mixing properties.

Using xerography and laser micromachining, Sanja P. Kojic et al. [42] created a Y-shaped, straight, and zigzag design on a Ceram Tape layer sandwiched between two PVC foil layers in 2019. While the PVC layer's inlet and outlet holes were cut using the xerography technique, the Ceram Tape layer's Y-shaped (straight and zigzag) models and holes were cut using a laser. The diameter of the inlet and outlet holes was 2 mm, and the MFD channel width was 200µm. In the study, an A4 laminator was used to laminate materials using the thermal press bonding technique. They stated that the low-cost, repeatable, and reproducible lab-onchip MFD device manufacturing process can benefit from this manufacturing process.

A. Sen and colleagues [43] investigated the parametric effects of fibre laser micro-machining for PMMA microchannel generation. The laser that was used had the following specifications: Its wavelength was 1064 nm; its scan speed ranged from 10 to 30 mm/s; its pulse frequency varied from 50 to 90 kHz; its laser power ranged from 5 to 15 W; and it was used for one to five passes. According to their report, the number of passes on both width and depth had a greater impact than the remaining parameters.

Ismail Bilican et al. [44] engraved microchannels on PS and PMMA to serve as the foundation for a microfluidic device chip using a  $CO_2$  laser (10.6  $\mu$ m) in the same year. A 30W power laser was used, with a speed of 2.25 mm/s in the vertical direction and 27.1 mm/s in the horizontal direction. Defocusing the laser



beam at various separations (9, 3, 6, and 0 mm) affected the PS and PMMA materials. Overall, they found that PMMA performs better than PS because it doesn't contain any impurities, which prevents bubbles from forming inside the channels.

Additionally, in 2020, A. Farahinia et al. [45] conducted a numerical analysis to investigate the effects of various cross-sections and input angles on the microfluidic mixer's mixing performance and concluded that, at low velocities, a Y-shaped microchannel performed better at mixing than a T-shaped configuration.

Also in 2020, Xingjian Hu et al.[46] created a multilayer polyimide MFD using a novel fabrication technique based on the idea of additive manufacturing using UV laser. They manufactured MFD's complex three-dimensional (3D) microchannels with properties of high bonding strength, scalable cross-sectional geometries, good reagent mixing performance, a high surface-to-volume ratio, and exceptional durability. An ultraviolet (UV) laser was used to ablate the film's microchannels. the microchannel edge shape, which can range from a trapezoid to a rectangle, is controlled by the impact of the UV laser on the channel width. The outcomes of an organic synthesis experiment and a computational fluid dynamics simulation of 3D microchannel structures showed that the device has excellent reagent mixing efficiency.

Konari, P. R. et al. studied the analysis of laser micromachining of microchannels in common microfluidic substrates (PMMA, PDMS, and glass) using CO<sub>2</sub> laser in 2021 and found that among the materials, PMMA channels were the deepest and PDMS channels the widest [47].

Also in 2021, Imarn H et al.[48] studied the effect of  $CO_2$  laser parameters on the micro-engraving of PMMA material. They reported that engraving speed affected significantly the engraving roughness and depth while the laser power had a significant effect on the engraving time.

Again in 2021, Choi l et al.[49] examined the effects of green picosecond laser machining of thermoset and thermoplastic carbon fiber reinforced polymers. The study's lens focal length was 170 mm, and its settings were 515 nm, 200W, 800KHz, 1 ps, and 6 m/s. They established that machining with a green picosecond laser is superior due to its negligible thermal effect with narrow HAZ and small taper angle.

A. Bonament et al. [50] proposed a 2D analytical model for the prediction of concentration profiles at a passive mixer's outlet in 2022. They investigated the impact of the channel's length as well as its shape (Y and line). They stated that promising outcomes in terms of mixing velocity, pressure, and concentration can be obtained with the suggested model.

S. Gucluer and O. Guler [51] recently proposed a quick and easy MFD fabrication technique for separating bacteria-sized microparticles from cells in 2023 using a  $CO_2$  and PMMA substrate and they showed that very basic techniques can be used to create disposable, inexpensive microfluidic devices that are capable of effectively separating bacteria and cells. The prior research on laser micromachining of polymers is listed in Table 1.

Table 1: Laser Micromachining of polymer				
Author	year	Polymer	laser	Reference
Yiqiang Fan et al.	2013	PMMA	CO <sub>2</sub>	[31]
S. Prakash and S. Kumar	2015	PMMA	$\rm CO_2$	[32]
A. Sen et al.	2016	PMMA	Fiber	[35]
S. Prakash and S. Kumar	2016	PMMA	$\rm CO_2$	[33]
J. Cai et al.	2017	COC	CO <sub>2</sub>	[36]
S. Prakash and S. Kumar	2017	PMMA	$CO_2$	[34]
Carlos Matellan et al.	2018	PMMA	$CO_2$	[37]
Hubeatir K et al.	2018	PMMA	CO2	[38]
Yundong Ren et al.	2019	PDMS	$\rm CO_2$	[39]
Kexin Gao et al.	2019	РММА	Diode and CO <sub>2</sub>	[40]
Mahdee Samae et al.	2019	PVC	$\rm CO_2$	[41]
Sanja P. Kojic et al.	2019	PVC	$\rm CO_2$	[42]
A. Sen et al.	2020	PMMA	Fiber	[43]
Ismail Bilican et al.	2020	PMMA and PS	CO <sub>2</sub>	[44]
A. Farahinia et al.	2020	Modelling of mixing efficiency using COMSOL		[45]
Xingjian Hu et al.	2020	polymer	UV	[46]
Konari, P. R et al.	2021	PMMA and PDMS	$CO_2$	[47]
Imran H et al.	2021	PMMA	CO <sub>2</sub>	[48]
Choi l et al.	2021	CFRP	ps	[49]
A. Bonament et al.	2022	Modelling of mixing efficiency using COMSOL		[50]
S. Gucluer and O. Guler	2023	PMMA	$CO_2$	[51]

By the end of this section, it is clear that a range of lasers were used for machining polymer materials and manufacturing MFDs, and the CO2 laser was the most widely used. This might be related to the high adsorption of CO<sub>2</sub> laser radiation by polymer materials.

#### 5. Conclusions

It can be concluded that MFDs provide various benefits that are useful in several applications, like biomedical, drug delivery, sensors, energy savings, and optoelectronics. MFDs have been produced using a variety of methods, like lithography, hot embossing, and laser. Laser is comparable due to its advantages of fast process and environmentally clean processing method. Several lasers, including CO2, UV, diode, and ps lasers, have been used for the processing of polymers and MFD manufacturing. Each laser has advantages and disadvantages, and the choice of lasers and processing parameters is based on the materials being used and the desired MFD properties. It is reported that microchannel ablation using UV or short pulses lasers provided a low thermal effect, while the thermal processing mechanism was recognized by CO<sub>2</sub> laser interaction with polymer. It has been possible to process glass, polymers, and ceramics using CO<sub>2</sub> lasers.



For polymer MFD, the CO<sub>2</sub> laser was the most widely parameters affect the used. Laser channel characteristics and dimensions. Deep theoretical analysis is required to understand the effect of laser parameters on microchannel fabrication on polymer substrates.

#### 6. References:

- [1] S. Solanki, C. M. Pandey, R. K. Gupta, and B. D. Malhotra, "Emerging trends in microfluidics based devices," Biotechnol J, vol. 15, no. 5, p. 1900279, 2020.
- [2] A. K. Yetisen, M. S. Akram, and C. R. Lowe, "based microfluidic point-of-care diagnostic devices," Lab Chip, vol. 13, no. 12, pp. 2210-2251, 2013.
- [3] W. K. Tomazelli Coltro, C. Cheng, E. Carrilho, and D. P. de Jesus, "Recent advances in low-cost microfluidic platforms for diagnostic applications," Electrophoresis, vol. 35, no. 16, pp. 2309-2324, 2014.
- [4] J. P. Lafleur, A. Jönsson, S. Senkbeil, and J. P. Kutter, "Recent advances in lab-on-a-chip for biosensing applications," Biosens Bioelectron, vol. 76, pp. 213–233, 2016.
- [5] L. Lin and C.-K. Chung, "PDMS microfabrication and design for microfluidics and sustainable energy application," Micromachines (Basel), vol. 12, no. 11, p. 1350, 2021.
- [6] A. W. Martinez, S. T. Phillips, and G. M. Whitesides, "Devices (uPADs)-are a new platform designed for ASSURED," Anal. Chem, vol. 82, pp. 3-10, 2010.
- [7] A.-G. Niculescu, C. Chircov, A. C. Bîrcă, and A. M. Grumezescu, "Fabrication and applications of microfluidic devices: A review," Int J Mol Sci, vol. 22, no. 4, p. 2011, 2021.
- [8] J. Hwang, Y. H. Cho, M. S. Park, and B. H. Kim, "Microchannel fabrication on glass materials for microfluidic devices," International Journal of Precision Engineering and Manufacturing, vol. 20, pp. 479-495, 2019.
- [9] A. Singh, C. K. Malek, and S. K. Kulkarni, "Development in microreactor technology for nanoparticle synthesis," Int J Nanosci, vol. 9, no. 01n02, pp. 93–112, 2010.
- [10] Y. Song, J. Hormes, and C. S. S. R. Kumar, "Microfluidic synthesis of nanomaterials," small, vol. 4, no. 6, pp. 698-711, 2008.
- [11] M. James, R. A. Revia, Z. Stephen, and M. Zhang, "Microfluidic synthesis of iron oxide nanoparticles," Nanomaterials, vol. 10, no. 11, p. 2113, 2020.
- [12] J. B. Nielsen, R. L. Hanson, H. M. Almughamsi, C. Pang, T. R. Fish, and A. T. Woolley, "Microfluidics: innovations in materials and their fabrication and functionalization," Anal Chem, vol. 92, no. 1, pp. 150-168, 2019.
- [13] J. P. Martins, G. Torrieri, and H. A. Santos, "The importance of microfluidics for the preparation of nanoparticles as advanced drug delivery systems," Expert Opin Drug Deliv, vol. 15, no. 5, pp. 469-479, 2018.

- [14] V. Sebastián Cabeza, "Advances in microfluidics-New applications in biology, energy, and materials sciences. Chap 17: High and Efficient Production of Nanomaterials by Microfluidic Reactor Approaches," IntechOpen, 2016.
- [15] A. Ben Azouz, S. Murphy, S. Karazi, M. Vázquez, and D. Brabazon, "Fast fabrication process of microfluidic devices based on cyclic olefin copolymer," *Materials and Manufacturing Processes*, vol. 29, no. 2, pp. 93–99, 2014.
- [16] M. Vázquez, D. Brabazon, F. Shang, J. O. Omamogho, J. D. Glennon, and B. Paull, "Centrifugally-driven sample extraction, preconcentration and purification in microfluidic compact discs," *TrAC Trends in Analytical Chemistry*, vol. 30, no. 10, pp. 1575–1586, 2011.
- [17] V. Faustino, S. O. Catarino, R. Lima, and G. Minas, "Biomedical microfluidic devices by using low-cost fabrication techniques: A review," J *Biomech*, vol. 49, no. 11, pp. 2280–2292, 2016.
- [18] X. Yuan and R. D. Oleschuk, "Advances in microchip liquid chromatography," *Anal. Chem*, vol. 90, no. 1, pp. 283–301, 2018.
- [19] D.-K. Lee, J. Y. Kwon, and Y. H. Cho, "Fabrication of microfluidic channels with various cross-sectional shapes using anisotropic etching of Si and self-alignment," *Applied Physics A*, vol. 125, pp. 1–7, 2019.
- [20] M. Focke *et al.*, "Microstructuring of polymer films for sensitive genotyping by real-time PCR on a centrifugal microfluidic platform," *Lab Chip*, vol. 10, no. 19, pp. 2519–2526, 2010.
- [21] B. S. Lee *et al.*, "A fully automated immunoassay from whole blood on a disc," *Lab Chip*, vol. 9, no. 11, pp. 1548–1555, 2009.
- [22] M. Islam, R. Natu, and R. Martinez-Duarte, "A study on the limits and advantages of using a desktop cutter plotter to fabricate microfluidic networks," *Microfluid Nanofluidics*, vol. 19, pp. 973– 985, 2015.
- [23] R. R. Gattass and E. Mazur, "Femtosecond laser micromachining in transparent materials," *Nat Photonics*, vol. 2, no. 4, pp. 219–225, 2008.
- [24] C. G. K. Malek, "Laser processing for biomicrofluidics applications (part I)," *Anal. Bioanal. Chem.*, vol. 385, no. 8, pp. 1351–1361, 2006.
- [25] M. Sparkes and W. M. Steen, "Light' industry: an overview of the impact of lasers on manufacturing," *Advances in Laser Materials Processing*, pp. 1–22, 2018.
- [26] C. G. Khan Malek, "Laser processing for biomicrofluidics applications (part II)," *Anal Bioanal Chem*, vol. 385, pp. 1362–1369, 2006.
- [27] C. G. Khan Malek, "Laser processing for biomicrofluidics applications (part I)," *Anal Bioanal Chem*, vol. 385, pp. 1351–1361, 2006.
- [28] J. Choi and C. Schwarz, "Advances in femtosecond laser processing of optical material for device applications," *Int J Appl Glass Sci*, vol. 11, no. 3, pp. 480–490, 2020.
- [29] H. Wang, Y. Zhang, W. Wang, H. Ding, and H. Sun, "On-chip laser processing for the development of multifunctional microfluidic chips



(Laser Photonics Rev. 11 (2)/2017)," Laser Photon Rev, vol. 11, no. 2, p. 1770022, 2017.

- [30] J. Schille, Investigation of micromachining using a high repetition rate femtosecond fibre laser. The University of Manchester (United Kingdom), 2013.
- [31] Yiqiang Fan Huawei Li Ying Yi Ian G. Foulds, "Laser micromachined wax-covered plastic paper as both sputter deposition shadow masks and deep-ultraviolet patterning masks for polymethylmethacrylate-based microfluidic systems," 2013.
- [32] S. Prakash and S. Kumar, "Fabrication of microchannels on transparent PMMA using CO 2 Laser (10.6 μm) for microfluidic applications: An experimental investigation," *International Journal of Precision Engineering and Manufacturing*, vol. 16, pp. 361–366, 2015.
- [33] S. Prakash and S. Kumar, "CO2 laser microchanneling process: effects of compound parameters and pulse overlapping," in *IOP Conference Series: Materials Science and Engineering*, IOP Publishing, 2016, p. 012018.
- [34] S. Prakash and S. Kumar, "Fabrication of rectangular cross-sectional microchannels on PMMA with a CO2 laser and underwater fabricated copper mask," *Opt Laser Technol*, vol. 94, pp. 180–192, 2017.
- [35] A. Sen, B. Doloi, and ·B. Bhattacharyya, "Fibre Laser Microchanneling of Polymethyl Methacrylate (PMMA)," vol. 0, pp. 1–16, 2016.
- [36] J. Cai *et al.*, "Rapid prototyping of cyclic olefin copolymer based microfluidic system with CO 2 laser ablation," *Microsystem Technologies*, vol. 23, pp. 5063–5069, 2017.
- [37] C. Matellan and A. E. del Río Hernández, "Cost-effective rapid prototyping and assembly of poly (methyl methacrylate) microfluidic devices," *Sci Rep*, vol. 8, no. 1, p. 6971, 2018.
- [38] K. A. Hubeatir, M. M. Al-Kafaji, and H. J. Omran, "Deep engraving process of PMMA using CO2 laser complemented by Taguchi method," in *IOP Conference Series: Materials Science and Engineering*, IOP Publishing, 2018, p. 012068.
- [39] Yundong Ren, Subhrodeep Ray, and Yuxiang Liu, "Reconfgurable Acrylic-tape Hybrid Microfuidics," 2019.
- [40] Kexin Gao, Jingji Liu, Yiqiang Fan, and Yajun Zhang, "Ultra-low-cost fabrication of polymerbased microfluidic devices with diode laser ablation," 2019.
- [41] Mahdee Samae Pawarit Ritmetee Somyot Chirasatitsin Sanja Kojić Tijana Kojić Jovana Jevremov Goran Stojanović Hani Al Salami, "Precise Manufacturing and Performance Validation of Paper-Based Passive Microfuidic Micromixers," 2019.
- [42] G. M. S. and V. R., Sanja P. Kojic, "Novel Cost-Effective Microfluidic Chip Based on Hybrid Fabrication and Its Comprehensive Characterization," 2019.
- [43] A. Sen, B. Doloi, and B. Bhattacharyya, "Parametric infuences of fber laser micro-machining for the generation of micro-channels on PMMA," Jul. 2020.



- [44] I. Bilican and M. T. Guler, "Assessment of PMMA and polystyrene based microfluidic chips fabricated using CO2 laser machining," *Appl Surf Sci*, vol. 534, p. 147642, 2020.
- [45] A. Farahinia and W. J. Zhang, "Numerical analysis of a microfluidic mixer and the effects of different cross-sections and various input angles on its mixing performance," *Journal of the Brazilian Society of Mechanical Sciences and Engineering*, vol. 42, pp. 1–18, 2020.
- [46] X. Hu, F. Yang, M. Guo, J. Pei, H. Zhao, and Y. Wang, "Fabrication of polyimide microfluidic devices by laser ablation based additive manufacturing," *Microsystem Technologies*, vol. 26, pp. 1573–1583, 2020.
- [47] P. R. Konari, Y.-D. Clayton, M. B. Vaughan, M. Khandaker, and M. R. Hossan, "Experimental analysis of laser micromachining of microchannels in common microfluidic substrates," *Micromachines* (*Basel*), vol. 12, no. 2, p. 138, 2021.

- [48] H. J. Imran, K. A. Hubeatir, and M. M. Al-Khafaji, "CO2 laser micro-engraving of PMMA complemented by Taguchi and ANOVA methods," in *Journal of Physics: Conference Series*, IOP Publishing, 2021, p. 012062.
- [49] I. Choi, S.-J. Lee, D. Shin, and J. Suh, "Green picosecond laser machining of thermoset and thermoplastic carbon fiber reinforced polymers," *Micromachines (Basel)*, vol. 12, no. 2, p. 205, 2021.
- [50] A. Bonament, A. Prel, J.-M. Sallese, C. Lallement, and M. Madec, "Analytic modelling of passive microfluidic mixers," *Mathematical Biosciences and Engineering*, vol. 19, no. 4, pp. 3892– 3908, 2022.
- [51] S. Gucluer and O. Guler, "A Low-Cost Laser-Prototyped Microfluidic Device for Separating Cells and Bacteria," *Applied Sciences*, vol. 13, no. 13, p. 7938, 2023.