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UV picosecond laser processing for microfluidic applications

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Abstract. In recent years, the fields of nanomedicine and nanopharmaceuticals have seen extensive use of microfluidic technologies. A microfluidic system transports fluids through micrometer-sized channels usually generated by replication on silicones. However, using laser technology and glass material together reduces manufacturing time, while maintaining high accuracy, and has the greatest benefit of being flexible. In this frame, the work aims to evaluate the potential of an ultrafast laser source for rapid and precise prototyping of a glass micromixer device. The study involves scanning electron microscopy to analyze the morphology, and confocal microscopy to investigate the topography of the sample. In addition, the study investigates the main process strategy to gain optimization of the processing time. Finally, the functionality of the manufactured devices is assessed, through a mixing test of two fluids with different pH.

Introduction

Nanomedicine and nanopharmaceuticals are two fields where microfluidics has potential as an emerging technology. A microfluidic system can carry fluids through channels with a micrometer dimension and can translate the distinctive properties of nanomaterials into therapeutic products. Different materials, including silicon, glass, hydrogel, paper, and polymers, and different technologies can be used to create these devices.

While polydimethylsiloxane (PDMS) silicone is the most used material in laboratory research, due to its ease of production and excellent resolution, glass has advantages over PDMS for microfluidic applications which requires resistance to various chemical and organic solvents, and good thermal and mechanical stability. Particularly, the "replica molding" process involves curing PDMS through photolithography on a mold that creates a negative image of the circuit to be made. Afterward, a glass layer is plasma-bonded onto the PDMS to seal the circuit. This implies creating a mold for each specific circuit [1, 2]. So, thinking about the device process chain, producing micro-molds required for PDMS-based systems is a time-consuming process that affects development and prototyping.

For applications where a batch may consist of several hundred pieces and where prototyping is a crucial step, the use of glass in combination with laser capability can be particularly advantageous. Examples of these applications include the production of diagnostic kits or drug delivery systems, and the creation of micromixers for the precipitation of nanoparticles for active ingredients [3], respectively. Particularly, the variety of applications of a micromixer device range from the synthesis of several types of nanoparticles to cell separation and microfiltration, and others that are continuously expanding.

Ultrashort laser ablation is considered an ideal method for the rapid and precise prototyping of microdevices since only a minimal amount of material is removed during the process: several recent works have used this technology to engrave channels on glass in different ways [3–10].

Three different processes of 3D laser processing are proposed in [9], including laser ablation, laser reduction, and laser-induced surface nano-engineering. While the work [4] reviews the ultrafast laser-based process to fabricate nanofluidic systems, such as additive laser or subtractive laser, ablation or assisted etching. They present the challenges for issues concerning channel sizes and fluid dynamics, and some integrated solutions of micro/nano devices. These studies follow the approach of performing in-bulk processes, within the material volume, often assisted by chemical etching.

A more consolidated approach is to create the 2.5D structures on the surface of the glass and seal it with a silicon cover, to create a closed channel [8, 11]. By allowing the depth and width of each channel to vary, this approach offers a straightforward method to increase the precision of the generated geometries [12]. An aspect to consider is that the microchannel surface roughness can be altered by laser irradiation. Compared to longer laser pulse durations, the issue for ultrashort laser pulses is significantly reduced, and in some cases, may not require post-treatment. Ultrashort laser processing characterized by the removal of material without significant heat transmission to surrounding areas is also interesting for good quality microdrilling [8, 13], where the thermal load is critical for successful processing.

Therefore, in this work, the aim is to create a hybrid microfluidic mixer using laser ablation to create microchannels on glass, followed by plasma bonding of a silicone layer with punched holes for the device inlet and outlet. In addition, the possibility of laser drilling the holes directly in the glass will be demonstrated, keeping all conclusions about the functionality of the device valid. Once the channel geometry has been selected to allow mixing between the fluids fed into the system, the accuracy that the laser can achieve will be demonstrated. Then, the mixing efficiency of the device will be qualitatively evaluated by pH measurement of the outlet flow of two fluids with different inlet pH.

Materials and Methods

The material used in this study is a commercially available float glass of 76x26x1 mm. The same material was used in [12], where chemical and physical characteristics are given.

The geometry chosen for the micromixer is adapted from previous works [14–16]. It has a double “Y” shape with a pair of inlet branches, a pair of outlet branches, and a central main channel, as depicted in Figure 1 and Table 1. Each branch has an inlet or outlet seat, while holes replace the seats in the case of inlets and outlets drilled into the glass. Each pair of branches joins at opposite ends of the main channel in which the mixing unit, a series of grooves, is realized. These grooves, or so-called "herringbones", are asymmetrically V-shaped and are periodically reversed to form different cycles.

Table 1: Geometric parameters

Channel depth *H* [μm]	80
Grove depth *h* [μm]	30
Groove step *s* [μm]	90
Groove width *w* [μm]	45
Slope *Θ* [°]	60
Distance *d* [μm]	140
Number of grooves per cycle	5

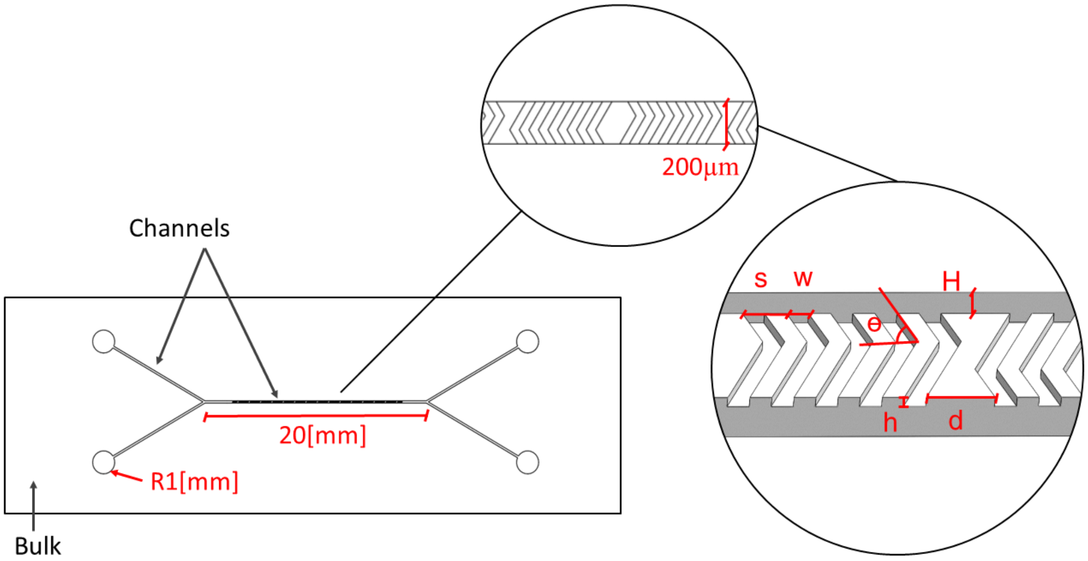

Figure 1: Perspective view of the device with detail on herringbones

This design exploits passive microfluidics by generating flow chaoticity over a wide range of Reynolds numbers to lead to mixing, see Figure 2. The geometry previously studied by Stroock et al. [16] was used as a starting point. The other dimensions were chosen taking into account the overall dimensions of the feeding accessories and the slide on which the system was derived [17].

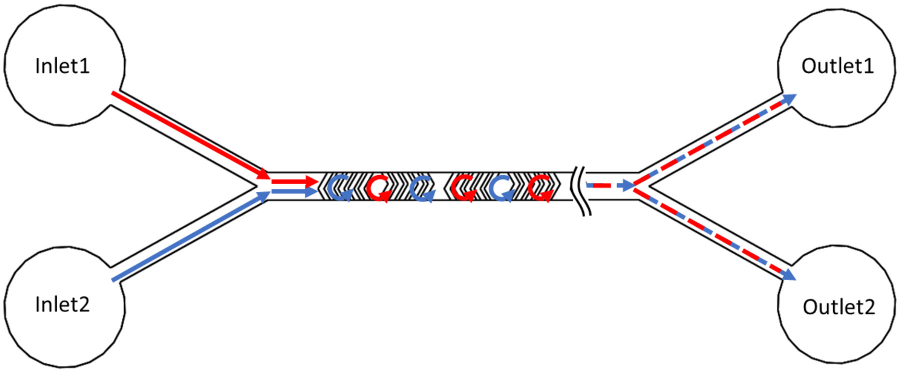

Figure 2: Fluid dynamics and mixing process

Channels have been etched onto a glass surface using a picosecond laser. The experimental set-up of the ultrafast laser system used consists of an EKSPLA Atlantic 50 laser source, emitting at the 355 nm wavelength, a Galvanometric scanner and a f-theta lens that focuses the beam to about 10 µm in diameter. The glass sample was processed by placing the ends on fixtures, suspending the lower surface in air during the ablation, to avoid back reflections.

The scan strategy was mainly a hatching of the geometry to be created. During the processing the galvanometer mirrors are kept in motion while working on laser emission, turning it on or off in creating the different geometries. In this way, micrometer-sized geometries can be processed with a scan speed of millimeters per second, reaching time resolutions of microseconds, removing the effects of accelerations, and optimizing the processing time. The laser parameters were chosen based on our previous work [11], optimizing them to achieve the accuracy and depths imposed by the device design. For the main channels the laser parameters chosen are 100 kHz of repetition rate, a pulse energy of 7 µJ, a scan strategy made of parallel longitudinal lines 3 µm spaced, and a scan speed of 300 mm/s to equally distribute the energy along and between the scanlines, all repeated for 11 passes. For the herringbones the same parameters were chosen, but with 6 passes.

The total process time is about 5 minutes: the seats are the largest and slowest feature to manufacture. In this context, the drilled holes can be made on the 1 mm thick glass using a 5 µm spaced spiral scanned at 2500 mm/s, 300 kHz and 16 µJ in about 1.5 minutes per drill. The automated procedure consists of slowly lowering the scan head while performing the spiral to change the focal height and achieve breakage. Furthermore, in this way, all the processing steps are made on a single glass slide.

Morphological analysis of the samples was obtained using the secondary electron detector (ETD) of a Scanning Electron Microscope (SEM) and then compared with the topography obtained from confocal microscopy. The confocal microscope setup used in this study was a Leica inverted research microscope with motorized XYZ, 40x HCX objective at Oil immersion, white laser light (WWL) set at a wavelength of 532nm.

After ablating the channels using the laser, the device was assembled by bonding the glass with a commercial silicone layer to seal the channels.

A pH qualitative test was performed to evaluate the mixing functionality. An RWD R462 double syringe pump was connected to the two inlets of the device through Tygon® hosing with a 1.6 mm internal diameter, as in Figure 3. One syringe was filled with acetic acid, the other with distilled water.

The pump flow rate was set for a flow in the main channel of the device with a Reynolds number equal to 10, to have a perfectly laminar flow in the channel [15]. The pH of the two outlets of the device was checked using litmus paper.

Figure 3: a) Feeding unit; syringe pump R462 RWD; b) Micromixer with detail on inlets and outlets.

Results and Discussion

Morphological analysis

Figure 4 shows SEM images of the main channel with its surface aspects. The topography looks chaotic and random. It is not easy to obtain a reliable measure of the areal parameters, but the resulting structures are at the micrometric and sub-micrometric scales, Figure 4– b).

Figure 5 shows a tilted image of the different details of the micromixer: a) the seat, b) the Y channel and the herringbones at two different magnifications, c) and d). Sharp edge delimiting the geometry, quasi-vertical sidewalls and the two-level depth are evidently achieved.

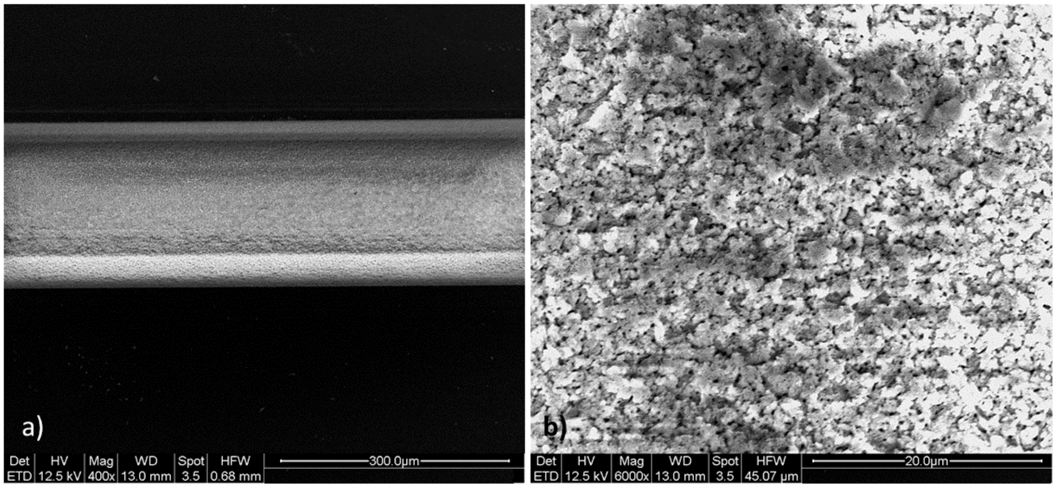

Figure 4: SEM images showing the microstructure of the channel obtained by laser ablation at two different magnifications, a) and b).

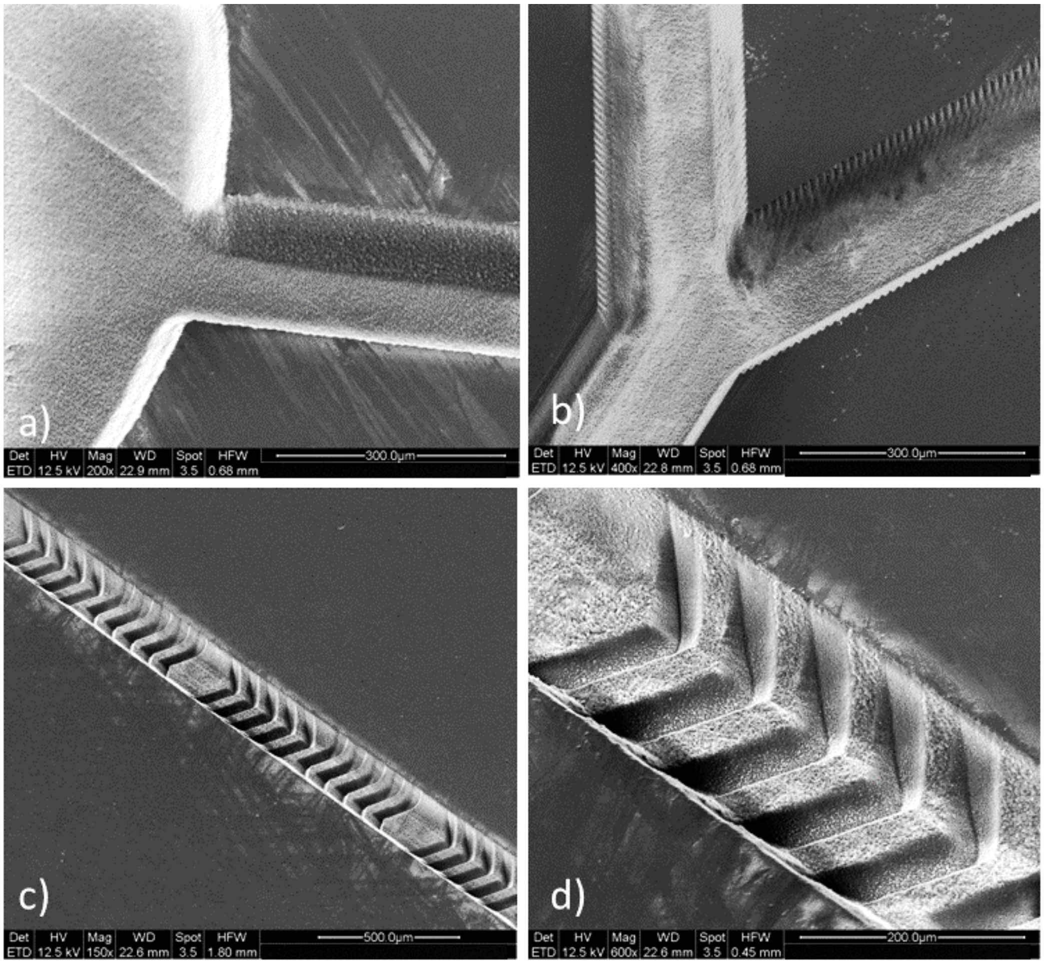

Figure 5: Tilted image of the different details of the micromixer: a) the seat, b) the Y channel and the herringbones at 2 different magnifications, c) and d).

The drilled seats, namely the holes alternative to the seats of Figure 5 - a), showed very good quality. The slight ellipticity in Figure 6-a) is probably due to the effects of linear polarization, beam ellipticity and astigmatism. It should be mentioned also that the scan strategy adopted for the holes was a spiral. The inlet flow port is gradual and smooth, Figure 6- b), with a weak conicity irrelevant to fluid entry and the device functionality.

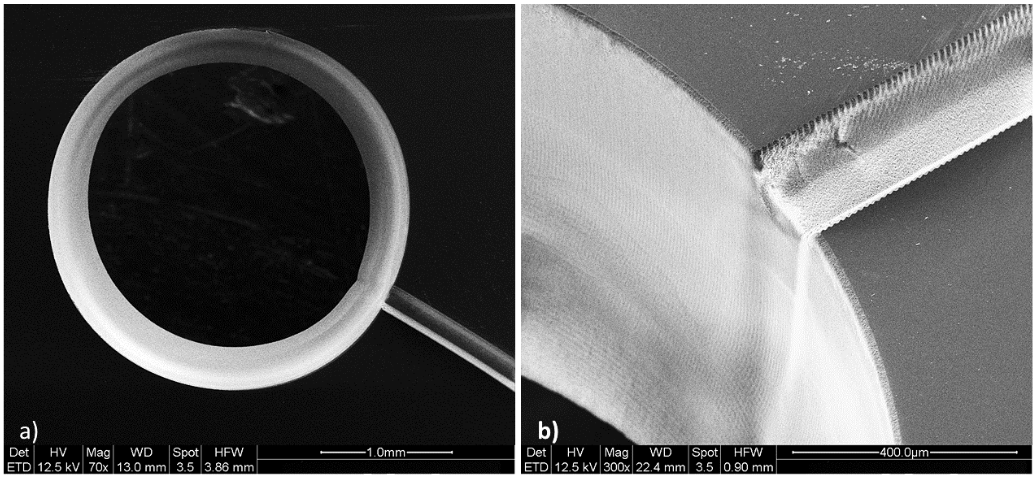

Figure 6: SEM images showing the quality of laser-drilled holes: a) frontal image b) focus on the fluid entry into the channel.

Topographic analysis

To evaluate the topography of the samples, images were acquired with a confocal microscope at different heights with a Z stack selection and a step size of 1 µm. The results can be seen in the 2D profiles with scale bars in Figure 7. The actual depth reached is about 80 µm for the main channel and 35 µm for the herringbone channel. The noise signals in Figure 7 may have been caused by artifacts generated by glass reflections, microscope data acquisition or data conversion software error. The inclination of the walls is constantly about 25°. It depends on reflections of oblique laser light at the vertical wall and plasma formation in the cavity. Consequently, the walls of the herringbones are almost V-shaped because of their narrow width.

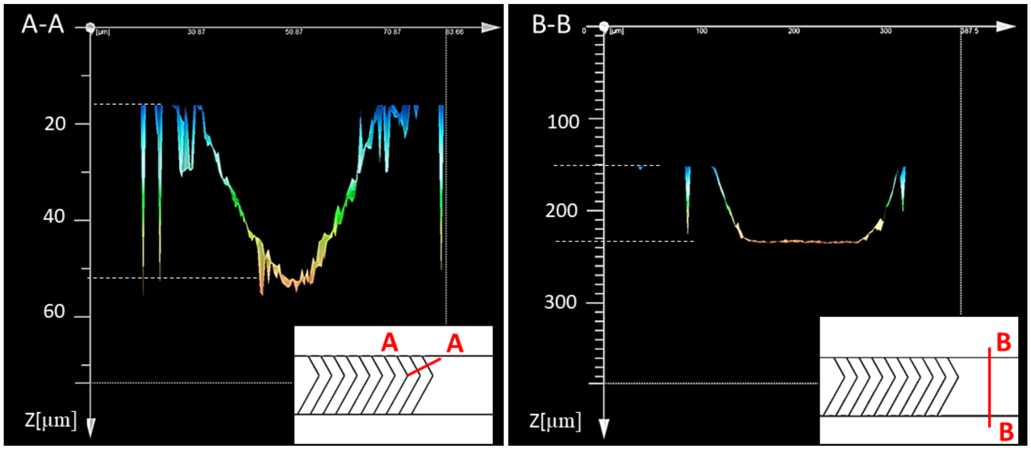

Figure 7: Cross-sectional profile reconstruction by confocal microscope of a single herringbone groove (A-A) and the section of the main channel (B-B).

Qualitative mixing test

The pH test results are reported in Figure 8, where “A” identifies the side of the micromixer branch where the acetic acid was introduced, “B” identifies the side of distilled water branch.

Comparing the colors obtained by dipping the litmus papers into the fluids at the outlets of the micromixer device without herringbone grooves, Figure 8– 1, and with herringbones grooves, Figure 8– 2, the pH test shows different results.

At the outlets of the device without grooves (1), the pH of the two fluids is easily distinguishable, the side “A” litmus paper has a deep red color that is associated with a pH ≅ 2, the side “B” litmus paper has a light orange corresponding to a pH ≅ 5. On the contrary, for the device with herringbones (2), the two litmus papers, “A” and “B”, have an intermediate color to the previous two, between the pH =3 and pH = 4, showing the successful mixing of the two flows.

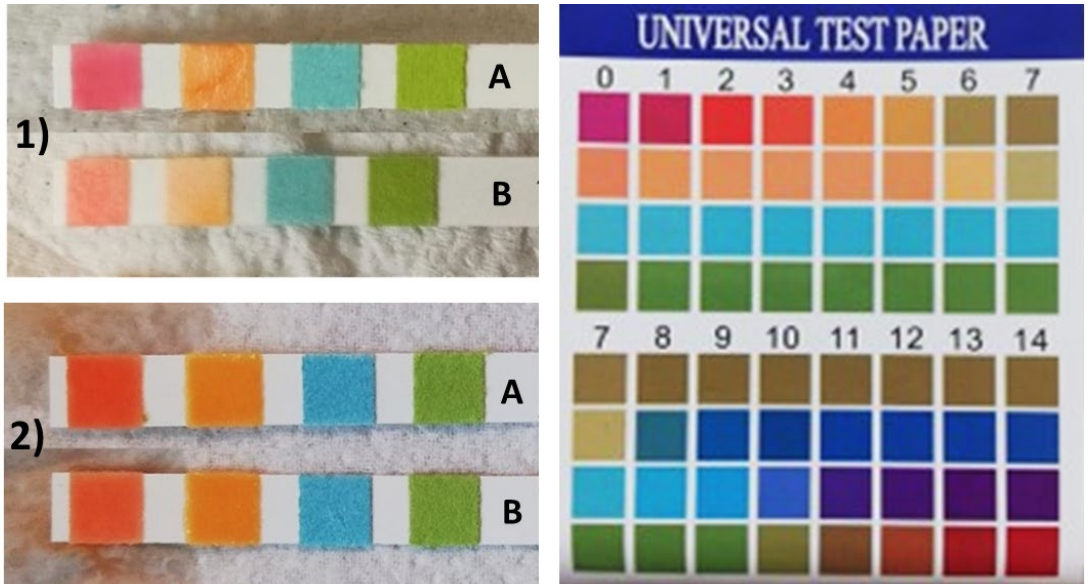

Figure 8: Litmus paper test where A = acid-side outlet channel and B=water-side outlet channel. Results at device outlets without (1) and with herringbones (2).

Conclusions

Ultrashort laser ablation offers a direct manufacturing approach for quick and accurate prototyping of glass microfluidic devices. The major advantages that this technology can offer are high accuracy, low manufacturing lead time and unprecedented flexibility. The beam can follow a wide variety of geometries easily generated by scanning software and modified as needed once functional tests have been performed, without previously creating a mold for each model, and that's a great advantage.

In this study, a complex channel geometry was selected to allow the mixing of two fluids, with dimensions ranging from millimeters to micrometers. Nevertheless, by choosing the optimal scanning parameters, the obtained geometry was faithful in shape. Certainly, with an appropriate set-up of laser processing parameters, i.e., the number of passes or the laser power, tight tolerance can be achieved.

Mixing between the two fluids has been shown to occur correctly, using a simple but effective qualitative test with litmus paper.

Additionally, the inlet and outlet holes, which are commonly made in the silicone layer, were laser drilled into the same glass slide on which the channels were made, resulting in excellent hole quality and a reduced device manufacturing time.

As a potential avenue for future work, it may be worthwhile to:

- seal the processed glass slide directly with another glass slide, i.e., by diffusion bonding, to obtain an entire glass device.
- quantitatively evaluate the mixing efficiency by introducing two different fluids of known composition into the device’s inlets and measuring the resulting composition of the fluids at the outlets; this would provide a more accurate assessment of the degree of mixing.

In this way, ultrafast laser technology can be a viable alternative to fabricate highly functional biochips integrated with almost arbitrary shapes.

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