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Performances of Microfluidic Mixing Regulated using Active Pressure Controller

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***Abstract*— Microfluidics studies how fluid dynamic changes at the microscale level. Interest in microfluidic technologies has been driven by associated developments in bio-related fields such as cell biology, genomics, drug delivery, high-throughput screening and diagnostics, as well as a recognized need to perform fast and efficient experiments on small-sample volumes. Fluid behaviour in the microfluidic channel depends on channel geometry, complexity, and presence of external force (passive or active). Rapid and uniform mixing are fundamental principles on which effective design and development of micro-mixer relies on. In this paper COMSOL Multiphysics simulation software was used to investigate the flow characteristics within Y shaped microfluidic channel model for different pressure signals (sin, ramp, step), their periods (1 and 1.5 s) and amplitudes (10 mbar, 50 mbar and 100 mbar). Results were compared with experimentally gained data obtained using commercial flow control system. The results confirm that the best mixing performance was achieved with step signal shape, on shorter periods, and with the higher pressure.**

***Index Terms*—microfluidics, fluids, active mixer, biomedicine, COMSOL Multiphysics.**

I. INTRODUCTION

Microfluidics represents cutting-edge combination of science and technology, which roots date back to the 1950s, when the microfluidic was used for the realization of inject printer head. It is based on control and manipulation of fluids at a microliter scale. Thanks to related advantages such as reduced sample volume, scalability, laminar flow (therefore predictable fluid behaviour), short time analysis and low-cost fabrication, microfluidics is becoming one of the fastest growing area of science [1]. These major advances made possible for microfluidics to be incorporated and applied in other fields such as tissue engineering, biosensors, medical diagnostics, ecology monitoring, etc. The “organ-on-a-chip” technology, which represents cellularized constructs integrated in microfluidics platform, faithfully imitates physiological, and pathological conditions of complex tissues, thus revolutionizing existing approaches to drug screening and toxicology studies [2]. More than often, this remarkable studies are followed with extensive and thorough computerized simulations in order to verify and test in vitro models [3]. The computational analysis and simulations are also performed alongside microfluidic experiment, in order to get more reliable insight in chip performance [4].

A microfluidic chip consists of set of micro-channels etched or moulded into different material (glass, silicon, ceramics, or polymers) and fabricated using different fabrication technologies such as photolithography, soft-lithography, PDMS (polydimethylsiloxane), LTCC (Low Temperature Co-fired Ceramics), laser micromachining or xurography [5-7]. The selection of the appropriate materials and technologies depend on the concrete application, chip complexity, applied detection principle, operating temperature, biocompatibility and many other factors.

The new generation of microfluidic chips are composed of network of micro-channels, chambers, and reagent storages connected together in order to achieve the desired features (mix, pump, sort, or somehow otherwise process the fluid) and can be integrated with other components such as micro-pumps, valves, electronics or optics. This system of micro-channels and components realized inside the microfluidic chip can be connected to the outside by inputs and outputs pierced through the chip that serves as an interface between the macro- and micro-world [8]. In that manner, different fluids can be injected and removed from the microfluidic chip through tubing, syringe adapters or even simple holes in the chip with external active systems (pressure controller, syringe or peristaltic pump) or with passive hydrostatic pressure.

New microfluidic platforms appear every day as a toolbox for the development of new testing kits and solutions, most commonly in combination with other technology such as PCB (Printed Circuit Board), LTCC, cellulose paper, glass, etc. The complexity of the chips and features of the systems depend on the application-specific requirements that can vary from very simple devices to complex lab-on-chip platforms [1]. The special attention in paid on the development of novel materials for chip fabrication and development of low-cost, disposable microfluidic chip for rapid in-field testing.

The aim of this study was to investigate mixing performance of low-cost microfluidic chip controlled with external active system. The standard Y geometry shaped microfluidic channel was used in order to test effects of different pressures and their nature (signal shapes and period) on percentage of the fluids mixing. Results obtained in COMSOL Multiphysics modelling software are compared with experimentally obtained results. In this paper, we use a novel hybrid technology concept that can be easily used for the rapid fabrication of low-cost microfluidic chips [5]. The proposed fabrication process combines Polyvinyl Chloride (PVC) foils and green tapes, and relies on the cost-effective xurography technique and laser micromachining process. The experimental results confirm that the best mixing performance was achieved with step signal. Potential biomedical applications in area of drug delivery and personal treatment are further discussed.

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II. MATERIALS AND METHODS

A. *Materials*

For the fabrication of the proposed microfluidic chips PVC foil—A4 hot lamination foil (MBL® 80MIC, Serbia) with the thickness of 80 µm was used. The middle chip layer has been realized using Ceram Tape GC (CERAMTEC GmbH®, Germany) and Heraeus CT800 (Heraeus Electronics LTCC Materials, Germany) green tapes.

Distillate water was the selected fluid. Water and water based food dye colorant (Aroma 1990®, Belgrade, Serbia) were mixed with ratio 5:1. All experiments were recorded with Digital Microscope.

B. *Equipment*

Plotter cutter (CE6000-60 PLUS®, Graphtec America, Inc., Irvine, CA, USA) with the 45° cutting blade (CB09U) and the cutting mat (12” Silhouette Cameo Cutting Mat, Sacramento, USA) were used for carving inlets, outlets and edges of PVC layers for microfluidic chips. Ceram Tapes GC and Heraeus CT800 tapes were cut out with laser (Rofin-Sinar Power Line D-100, Germany). Bondage between PVC and green tapes are performed through lamination with A4 card laminator (FG320, Minoan Binding Laminating, Serbia).

Profiler Huwitz Panasis with bioimaging software for 3D profile of microfluidic channels was used for profiler analysis and measurement of the channel width.

Microfluidic flow control system ElveflowOB1 [9] was used to set different pressures, periods of relaxation and shapes of pressure signal. In this experiment, three signal shapes were used: sine, ramp and step. Pressures were set to pressure amplitudes of 10 mbar, 50 mbar, and 100 mbar, while periods of pumping were set to 1 s and 1.5 s.

C. *Methods*

COMSOL Multiphysics® software was used for initial simulations of microfluidic active mixers and testing of their performances. Experimental testing has been performed on the fabricated chips using microfluidic set-up that consists of ElveflowOB1 microfluidic flow control system, PTFE tubing, fittings, holder, connections and digital microscope. Mixing efficiency in the channel was detected optically using digital camera, and mixing rates were determined using image processing algorithm developed in Matlab.

III. CHIP FABRICATION

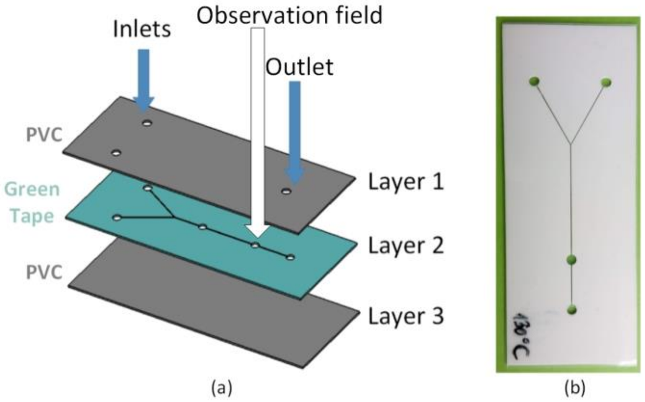


Fig. 1. Microfluidic chips fabricated using proposed hybrid technology (a) 3D model of the microfluidic chip, (b) Fabricated chip with Y-mixer.

The proposed microfluidic chip consists of three layers, as shown in Fig. 1. Top and bottom layers were realized using PVC foils, while the green tape was used for the middle layer. Fabrication of the chip was realized through of several steps. In the first step, laser cutting of the middle chip layer in the green tape, as for standard preparation of layers for LTCC technology was performed. Exact laser parameters used for microfluidic chip fabrication were: current 28 mA, frequency 10 kHz, and cutting speed of 15 mm/s. Plotter cutting of PVC layers, as for standard xurography technique, was used for cutting the inlets and outlet of the microfluidic channels. In the final step, lamination of the cut layers as for standard xurography technique (laminated first: Layer 1 and 2, and then Layer 3) has been accomplished at the temperature of 130 °C. Fig. 1b shows photographs of the fabricated Y-mixer microfluidic chip. In all designed chips, the width of the microfluidic channels has been set to 200 µm, while the inlet and outlet holes, and observation field have been manufactured with the diameter of 2 mm.

In the process of the fabrication, dimensions slightly changes due to imperfection of laser cutting and lamination processes. Therefore, we fabricated 10 microfluidic chips, five using Ceram Tape GS and five using Hereaus CT800 as a middle layer. Profiler Huwitz Panasis was used for the characterization of the microfluidic channel widths. The width of the channel was measured at eight different points. Fig. 2 shows the measured channel and standard deviation of the channel width. It can be seen that the measured width of channels realized in Ceram Tape GC is smaller than predefined value, while relatively good agreement is obtained for Hereaus CT800 tape. The variation of the channel width in the worst case was below 15%. For experimental testing we used the chip with width of 150 µm and with a minimal deviation of 5% (chip marked as #1GC).

IV. COMSOL MULTIPHYSICS SIMULATIONS

COMSOL Multiphysics® software was used for simulation and testing of the proposed microfluidic mixer. COMSOL Multiphysics® software uses finite element method for numerical solving of different equations dictated by physical laws. In microfluidic simulations, fundamental equation used for the description of fluid motion in micro channels is Navier-Stokes equation [10]. Multiphysics simulation software was used to investigate the flow characteristics within Y shaped channel for different input pressure signals (sin, ramp, step), their periods (1 and 1.5 s) and amplitudes (10 mbar, 50 mbar and 100 mbar). Three different signal shapes were used for inlet pressure in simulations: sine, step and ramp. In Fig. 3 used signal shapes with period of 1 s are shown.

For visualization of the mixing process, different colours of fluids were used, representing the concentration of fluids. The concentration of one liquid was set to 500 mol/m^3 and concentration of the other one was set to zero. Fig. 4 represents the part of the micro channel in two specific cases.

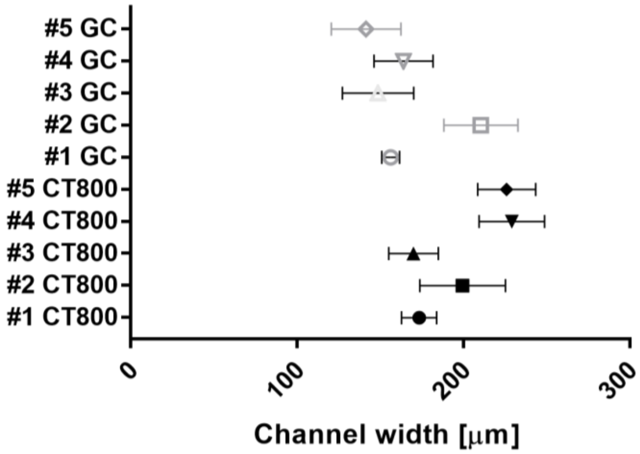


Fig. 2 The measured channel width and its standard deviation for 10 fabricated chips.

Fig. 4a shows simulation results for constant pressure flows of 50 mbar at both inlets, while Fig. 4b shows simulation results for sine shaped pressure signals at both inlets. It can be seen that liquids mix only in their contact region, which is the property of laminar flow. Fig. 4b represents mixing of liquids with sine shaped pressure signal on both inlets with amplitude of 50 mbar. Mixing in this case covers almost the whole channel and it can be seen that mixing of liquids is significantly better.

Fig. 5 shows the average value of concentration along the observation zone for the different signal shapes and pressures during 10 s. Results presented in Fig. 5 are simulation results with 1 s signal period. As it was expected, the better mixing of two fluids can be achieved for higher pressure values. Therefore, for 100 mbar pressure, mixing is achieved after 2 s, for 50 mbar after 4 s and for 10 mbar 10 s is not enough to achieve proper mixing of two fluids. Fig. 5 also shows that step signal gives the best mixing results in term of response time and mixing concentration.

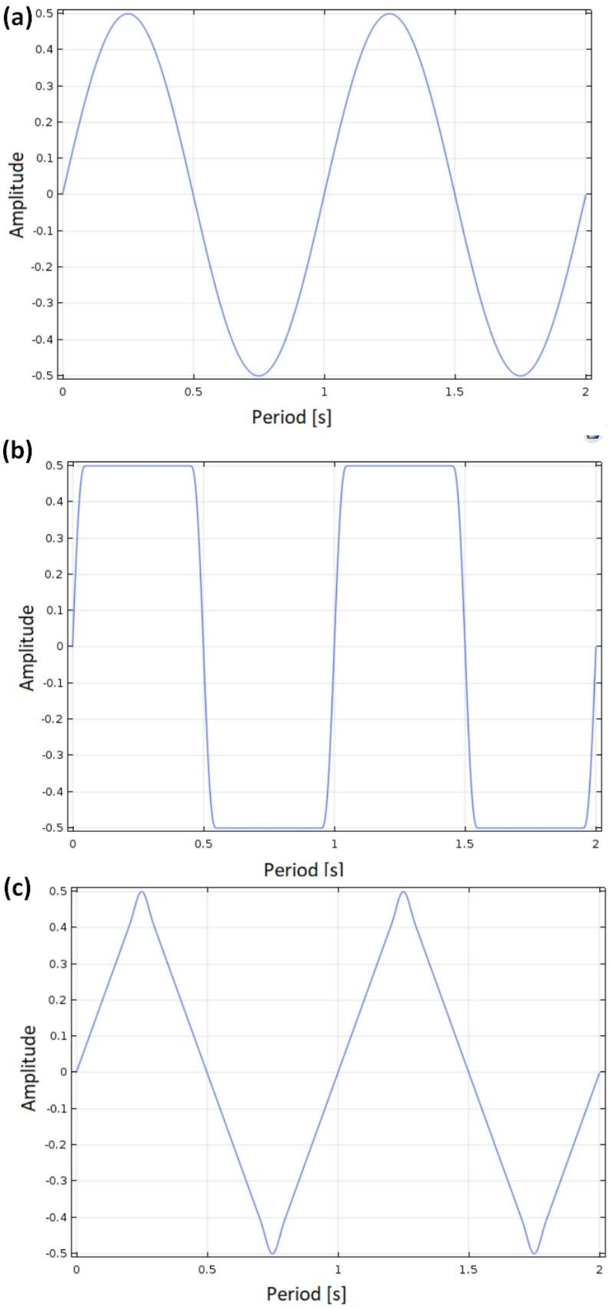


Fig. 3. Pressure signal at inlet of the chip: (a) Sine, (b) step, and (c) ramp.

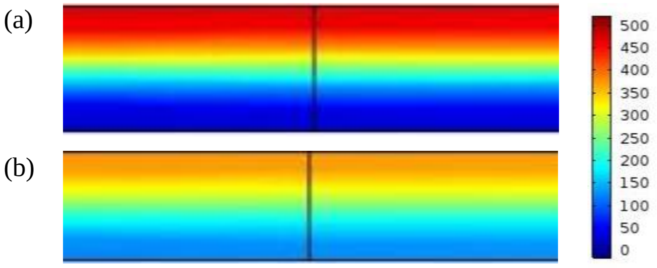


Fig. 4. Mixing of liquid for: (a) Constant pressure flows at inlets of mixer, and (b) Sine shaped pressure signal at inlets.

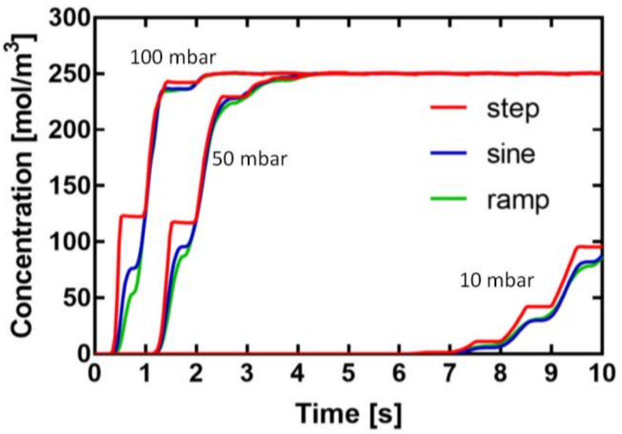


Fig. 5. Average value of concentration along the observation zone. Simulation results for step, sine and ramp signal shapes at pressures of 10, 50 and 100 mbar.

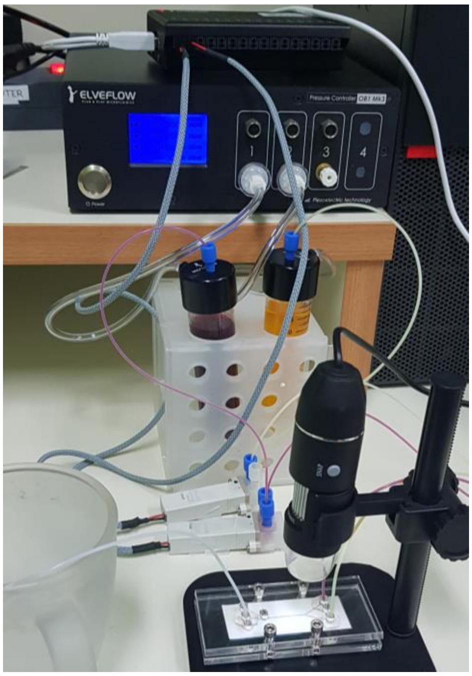


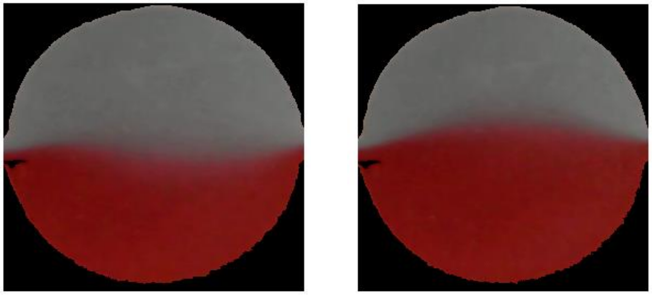
Fig. 6. Experimental set-up

V. Experimental Results

In order to verify simulation results, experimental testing has been performed on the fabricated chips. Set-up for conducting the experiment, shown in Fig. 6, consists of microfluidic flow control system ElveflowOB1, PTFE tubing, fittings, holder, connections and digital microscope.

Mixing in the channel was detected visually using digital camera and mixing rates were determined in Matlab. For every flow pressure signal, amplitude, and period, 12 independent photographs during one period of signal were recorded. Photographs had high resolution of 3648 x 2736 dpi. Two examples of the recorded photos are shown in Fig 7. All pictures are further processed in Matlab in order to determine mixing efficiency.

Matlab software was used to isolate the observation field, and isolate the pure red and green color in the image. Because of the equal flows at both inlets we assume that there is the equal amount of non-mixed red and yellow liquid. In the following step R, G and B components were determined in order to isolate pixels in the observation field, Fig. 9. Based on that for non-isolating, i.e. non-mixed liquids, pixels were classified and counted. The code is written to count the total number of pixels of the observation field, to take away the number of pure yellow/red, and to calculate the mixing efficiency. These results are presented as heat maps for the different amplitude and periods, after first period of signal. In Fig 9. heatmap of results is shown in percentage for different pressure, amplitude and period recorded after period of first impulse. As it was expected, better mixing is performed on shorter periods of pulsation, and higher pressures.



(a) (b)

Fig. 7. Photographs of the observation field after stimulation with: (a) sin, and (b) step signal with amplitude of 50 mbar within the period of 1 s.

(a) (b)

Fig.8. Isolated pixels of unmixed fluid based on 3 colour channels.

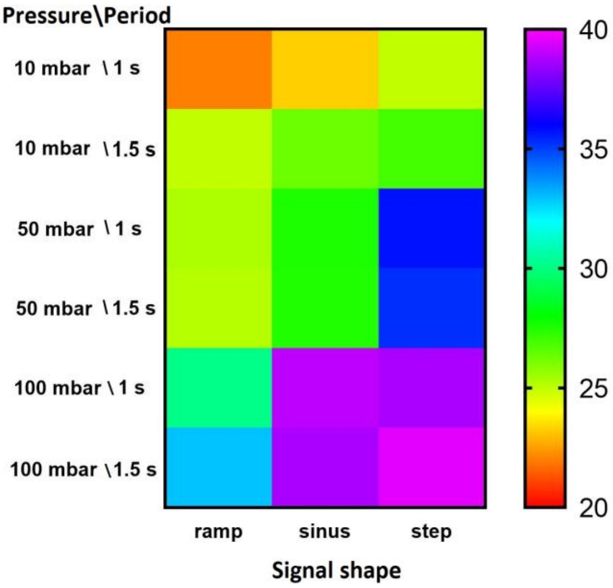


Fig. 9. Results of the mixing for different pressures, amplitude and period recorded after period of the first impulse.

The best mixing occurs for the stimulation with the step signal shape, because of the nature of signal itself, although mixing with sine and ramp signals give almost the same results. With the change of the shape of the signals and their period at the inlets of the microfludic chips the efficiency of the mixing can be increased for more than 30%.

VI. Conclusion

In this paper, we use novel technology concept for rapid fabrication of robust microfluidic mixer. The proposed fabrication process combines PVC foils and green tapes, and relies on the cost-effective xurographic technique and laser micromachining process. The comprehensive study of mixing performances on Y-shape microfluidic channel have been performed. Characteristics of mixing performances of Y shaped channel for different pressure signals (sin, ramp, step), their periods and amplitudes have been investigated using simulation and experimentally verified. Obtained results shows that the shape of signal at the inlets of active mixer, their amplitude and period can influence the mixing performances and can improve mixing efficiency.

The impact of the signal shape is demonstrated on a Y-mixer, but the same effect can also be applied to complex fluid mixing systems. Therefore, the proposed concept can be implemented in complex microfluidic mixing systems for applications in all types of lab-on-chip analysis where rapid mixing of two or more liquids is required.

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