MACRO VALVE AND PERISTALTIC PUMP WITH CLEANROOM-FREE FABRICATION FOR MULTIPLEXED ORGAN-ON-CHIP APPLICATIONS

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ABSTRACT

Integrated microfluidic valves enable automated control in microfluidic systems as they can be applied for mixing, pumping, and compartmentalisation purposes. However, many organ-on-chip systems require channel dimensions in the range of hundreds of micrometres while the typical fabrication process for normally open micro valves requires a reflow photoresist which is not capable of achieving these dimensions. Here we show a mechanical macro valve, fabricated cleanroom-free by micromilling, closing and bridging a 400 µm high, 1000 µm wide channel. Furthermore, we use the valves to create an inlet switch and a peristaltic pump with a pumping rate of 2 µL/min.

KEYWORDS: Macro valve, PDMS integrated valve, cleanroom-free fabrication, micromilling, peristaltic pump

INTRODUCTION

Multiplexed organ-on-chip systems are currently a popular approach to increase the throughput of organ-on-chip research. However, automated, high-throughput systems of typical organ-on-chips have not been demonstrated yet [1]. Integrated microfluidic valves provide a tool for automated control in microfluidic systems as they can be applied for mixing, pumping, and multiplexing purposes. Fabrication of pneumatically actuated valves in poly(dimethylsiloxane) (PDMS) devices is common for channel heights up to tens of micrometres [2]. However, this approach relies on photoresist reflow to achieve rounded channels required for full sealing of the valve. This fabrication method has limitations for heights needed in organoid and organ-on-chip systems, which are up to hundreds of micrometres. Micromilling has great potential to solve this problem as it provides an approach which enables fast and low-cost organ-on-chip mould fabrication with complex 3D geometries containing these channels. A micromilled macro valve, closing a 360 µm high and wide channel has already been reported [3], however this fabrication method gives a negative mould requiring an extra PDMS to PDMS casting soft-lithography step. In addition, the dimensions are limited by the availability of cone-shaped milling tools.

Here, we show that it is possible to directly mill the positive mould facilitating the soft lithography process. We show a mechanical valve, fabricated cleanroom-free by micromilling, closing and bridging a 400 µm high, 1000 µm wide microfluidic channel. Furthermore, we expand the application of the macro valve to create an inlet switch and a peristaltic pump. Using this fabrication method, the valve can be easily integrated in multiplexed organ-on-chips to enable automated control of cell culture conditions.

EXPERIMENTAL

Two poly(methylmethacrylate) (PMMA) moulds were designed in 3D-CAD software (SOLIDWORKS®), a 200 µm high control layer and a 400 µm high, 1000 µm wide half rounded flow layer. The inlets and outlets are on a grid corresponding to the ISO Workshop Agreement 23:2016 standards [4]. The moulds were fabricated by micromilling in PMMA (Datron Neo). The final devices consist of three layers, two PDMS layers (control layer and flow layer) and one glass layer. The protocol for further fabrication of the valve is similar as shown in [2].

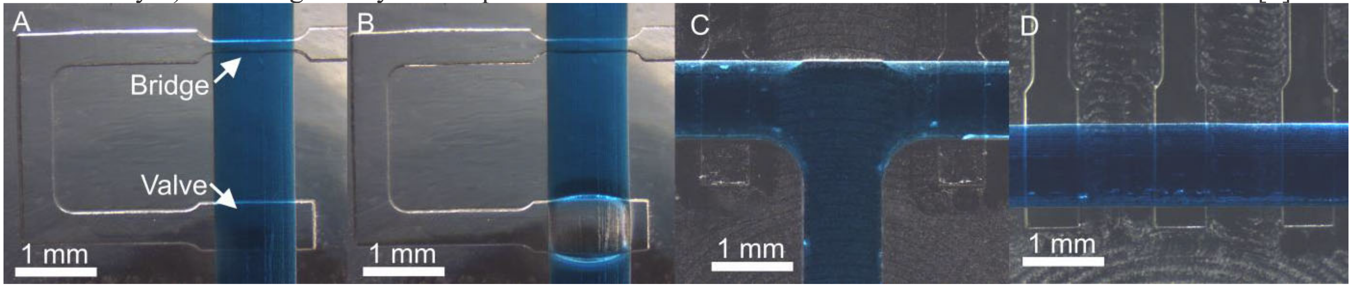

Figure 1: Fabricated PDMS structures. A) Open valve with bridge, B) Closed valve with bridge, C) Inlet switch, D) Peristaltic pump. Half round flow channels contain blue food colouring, control channels contain water.

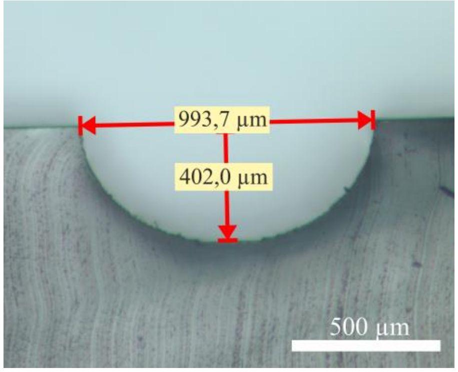

Figure 2: Cross section of PDMS cast of microfluidic flow layer.

RESULTS AND DISCUSSION

A valve with bridge, inlet switch, and peristaltic pump were fabricated (Fig.1). A cross section of PDMS cast of the half rounded flow layer is shown in Fig 2. The closing behaviour of the valve was examined by applying different pressures to flow and control layer (Fig.3). By applying more than 900 mbar to the control line, the valve can be closed for all four input pressures. A closed valve was examined for any potential leakage with a flow sensor more sensitive in the low flow rate regime (Fig.4a). The pumping rate of the peristaltic pump was examined by actuation of the valves with a '120°' phase pattern at different frequencies (Fig.4b). Initial results achieve a pumping rate of 2 µL/min, which makes it a promising, fully integrable tool for automated organ-on-chip system.

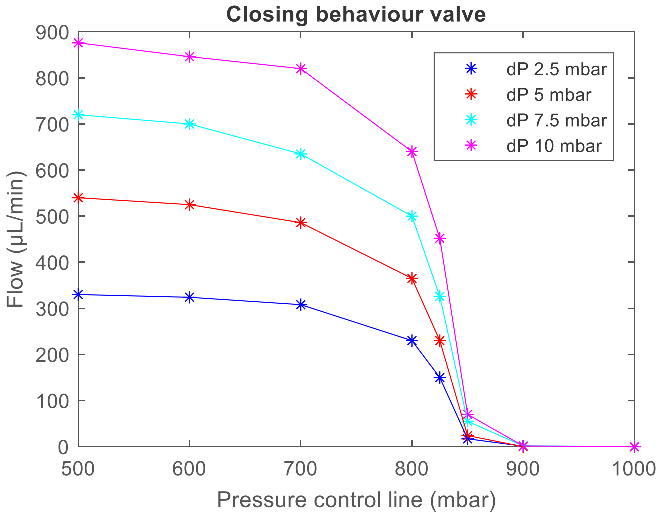

Figure 3: Closing pressure of macro valve. Line for visual guidance. dP = differential pressure between inlet and outlet pressure.

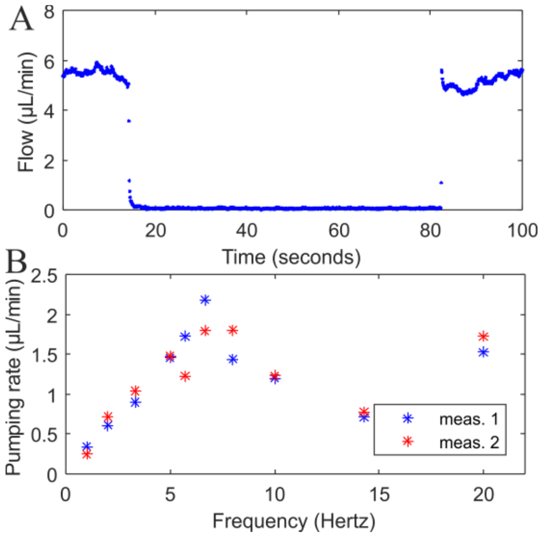

Figure 4: A) Closure of valve by applying 1000 mbar to the control line. B) Pumping rate of peristaltic pump at different frequencies of actuation ('120°' phase pattern).

CONCLUSION

We presented a macro valve fabricated without photo-lithography, which is able to close and bridge a 400 µm high, 1000 µm wide microfluidic channel. We used this macro valve as a tool to fabricate an inlet switch and a peristaltic pump with a pumping rate up to 2 µL/min. These tools can easily be integrated in (multiplexed) organ-on-chips. The valves can enable automated control of cell culture conditions and the possibility for a peristaltic flow in organ-on-chips with channel dimensions of hundreds of micrometres.

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