Connecting labs for higher level organ-on-chip systems: integration of a pH sensor and a blood vessel-on-chip on a standardized platform

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Introduction

Highly specialized development of chips for organ-on-chip (OoC) applications results in novel, cutting-edge technologies. However, these chips rarely leave the developers' labs due to specialized handling or incompatible interfacing with other chips. As a result, their impact on the OoC field is severely limited. Previously, we have shown that fluidic circuit boards (FCBs) with ISO-standardized interfacing can connect different chip modules to create a higher level system [1]. Here, we take the next step by moving from platforms designed and tested within a single lab to a platform which connects chips from three different developers from three different universities. Specifically, a blood vessel-on-chip (TU Eindhoven) is combined with a pH sensor (TU Delft) on an FCB (UTwente and Micronit) with the aim of performing online measurements of pH for monitoring cell metabolism. We show the fluidic connection of all chips and first proof-of-principle measurements using DI water, pH 4 buffer and cell culture medium incubated at different CO_2 levels.

Experimental procedure

The FCB fabrication was commercially outsourced to Micronit Microtechnologies. The pH sensor working principle and blood vessel-on-chip were previously reported in [2] and [3], respectively. The chips were made from hybrid materials and were mechanically clamped onto the FCB using bolts as reported in [1].

Results and Discussion

Fig.1 shows the FCB design and tests with blue food coloring which show that the platform was assembled leakage-free. First proof-of-concept measurements using the pH sensor show that a current change can be measured when switching from DI water to a pH 4 buffer solution in the assembled system. On another chip, two different media with different CO_2 levels (5% and 0.04%) were monitored by introducing the liquid by micropipette to the sensing area. Repeated testing shows a clear difference between the media, due to different CO_2 levels.

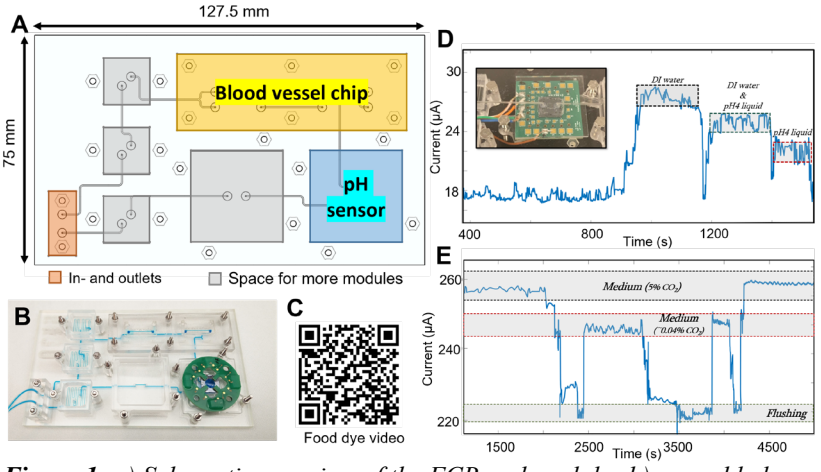

***Figure 1**: a) Schematic overview of the FCB and modules b) assembled platform filled with blue food coloring c) video of food dye flow d) current change in response to pH change in assembled platform and e) on a separate chip using medium incubated at 5% and 0.04% CO_2.*

Conclusion and Outlook

By using an ISO-standardized system, we were able to combine chips from different labs into a single system with a higher level purpose. In future, we will culture endothelial cells in the blood vessel-on-chip and monitor the pH drop in the cell medium in response to the cells' metabolism.

Acknowledgments

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[1] S. Dekker et al, *Microsyst Nanoeng* **4** 34 (2018); [2] H. Aydogmus et al., TRANSDUCERS (2021); [3] A. Pollet et al., *Micromachines* **11** 43 (2020).