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MODELING PHARMACOKINETICS AND MASS TRANSPORT IN LAB-ON-A-CHIP-SYSTEMS WITH SIMULATIONX

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INTRODUCTION

The development of complex 3d-tissue cultures and micro-fluidic systems is becoming more and more important for both tissue engineering and the replacement of animal testing used in the cosmetics and pharmaceutical industries [1]. The following tool presents a way to simulate mass transport, nutrient supply, pharmacokinetics and fluid flow in lab-on-a-chip systems which enable the developer to test and optimize different fluidic layouts.

SETUP

Modeling and measurements are based on a micro-fluidic platform which integrates pneumatically actuated peristaltic pumps, valves, liquid reservoirs and culture chambers [2]. Fig. 1 shows an exploded view of the device. The flow cell is cast in polydimethylsiloxane (PDMS) which is plasma bonded to a glass slide. A connection panel includes fluidic and pneumatic ports. Fluid flow was observed with micro-particle-image-velocimetry (µPIV) [3]. Furthermore oxygen saturation was measured with fluorescence life-time analysis [4]. The micro-fluidic network was modeled in Simulation-X. Several models for the pump, the valves and connecting channels as well as substance transport, permeation and consumption were developed. The simulation tool can also deal with non-Newtonian flow behavior, e.g. bloodstream in small vessels and oxygen transport by erythrocytes.

RESULTS

Fig. 2 shows the Simulation X model of the micro-fluidic network. Flow velocity was measured with µPIV in each channel for different pump speeds. Fig. 3 compares modeled to measured flow velocity in the lower channel. By applying pressure to the membranes, the flow can be controlled in each channel of the branched fluidic system.

[1] M. Baker: "A Living system on a chip", Nature, 471, 664-665, 2011.
[2] K. Schimek and M. Busek et al: "Integrating biological vasculature into a multi-organ-chip microsystem", Lab Chip, 13, 3588-3598, 2013.
[3] M. Busek et al: "Automated Micro-PIV measurement in Lab-on-a-Chip systems", Biomed Tech, 57 (Suppl. 1), 927-930, 2012.
[4] C. Winkelmann et al. "Hohlfaserbasiertes Lab-on-a-Chip Dual-Perfusions-System mit integrierter fluoreszenzbasierter Sauerstoff-überwachung." 11. Dresdner Sensor Symposium (2013): 283-288.

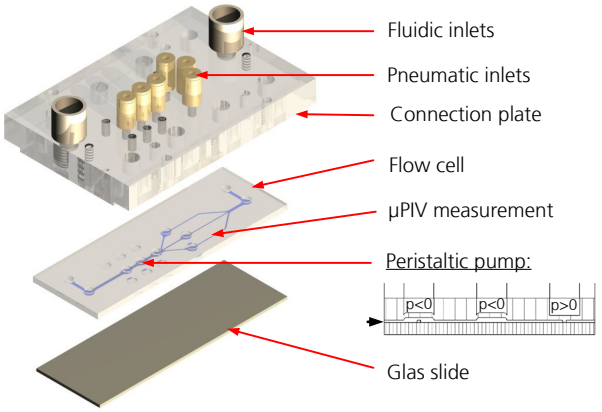

FIG. 1:
Exploded view of the micro-fluidic system.

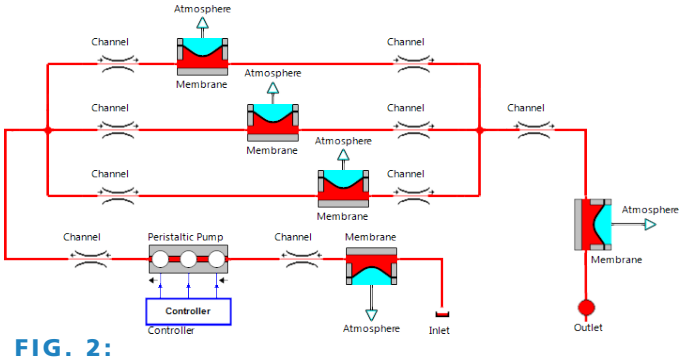

FIG. 2:
Simulation X model of the micro-fluidic system.

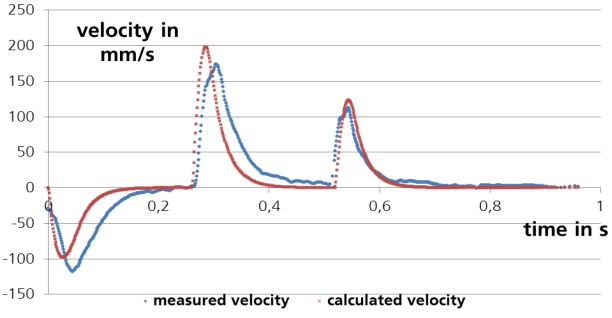

FIG. 3:
Simulated vs. measured velocity in lower channel.