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Rapid development of centrifugal microfluidic assay automation by network-simulation based fluidic design

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Introduction

The centrifugal microfluidic platform allows for automation of laboratory processes on the basis of scalable microfluidic unit operations. Recently, complex sample to answer systems[1] have been reported. Their integration makes accurate predictions of occurring fluid dynamic interactions mandatory during the design process. In this context, we present lumped network models for centrifugal microfluidics that yield the necessary simulation results in split-seconds to minutes. The simulation method is developed in close cooperation with in-house prototyping in order to provide an efficient idea-to-chip transfer (cf. Fig. 1). The design workflow comprises assay specification, simulation based fluidic layout, prototyping and experimental validation.

Methods & Workflow

Using the Simscape™ network simulation environment, we developed model blocks for unit operations capturing two-phase flow with pneumatic-, hydrostatic-, capillary- and euler-pressures, viscous dissipation and temperature effects.

The simulations calculate the network wide fluid flow which allows for the prediction of valving events and the layout of chamber and channel dimensions. Furthermore robustness against manufacturing tolerances is assessed and finally centrifugal protocols are derived (cf. Fig. 2).

Results

As a case study, the simulation based layout of a sample to answer disk[1] (cf. Fig. 3) is presented. For the release of elution buffer, channel dimensions were derived to ensure robust priming. To minimize losses during liquid transfer due to manufacturing tolerances, the optimal frequency protocol was calculated ensuring a transfer of > 95% liquid. The layout of the pre-amplification structure (cf. Fig. 2) is based on simulating the influence of geometries, the centrifugal protocol and temperature effects on the liquid volume provided for downstream analysis. Simulation predicts 88% pump efficiency of the applied centrifugo-dynamic inward pumping[2] unit operation. Experimental validation yields 85±5%

Conclusion & Outlook

The use of network simulation speeds up the design process, reduces the number of required prototype iterations and renders lab-on-a-chip systems more robust. Further model blocks will encompass filtering and reaction kinetics.

References

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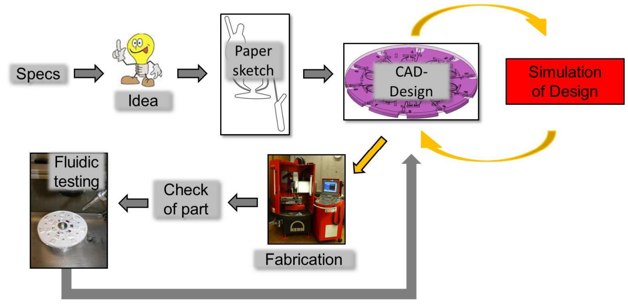

Figure1: Schematic of the centrifugal microfluidic design process.

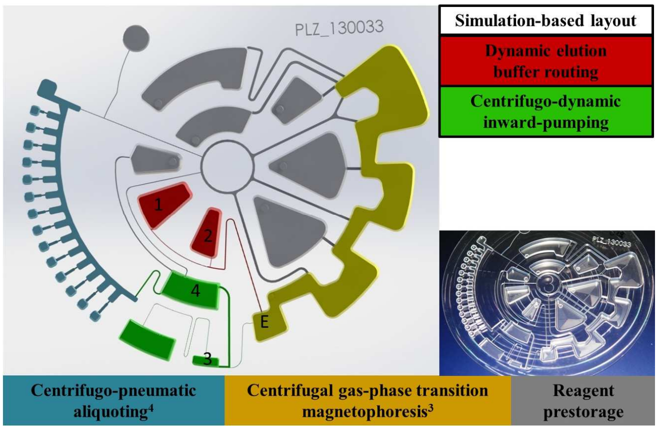

Figure 2: CAD-design of the sample to answer disk. Red and green structures are based on the lumped network simulation approach. Elution buffer starts to transfer from chamber (1) & (2) to the eluate chamber (E) by decelerating with -20 Hz/s from 52 Hz to 10 Hz. The transfer is completed by increasing the frequency to 25 Hz for 10 s. The centrifugo-dynamic inward-pumping structure pumps liquid from the pre-amplification chamber (3) to chamber (4). To achieve this, the rotation frequency is reduced from 60 Hz to 1 Hz within 3 s and held there for 10 s. The bottom right inset shows the thermoformed disk, manufactured in-house by the Lab-on-a-Chip Design & Foundry Service in scalable foil technology.

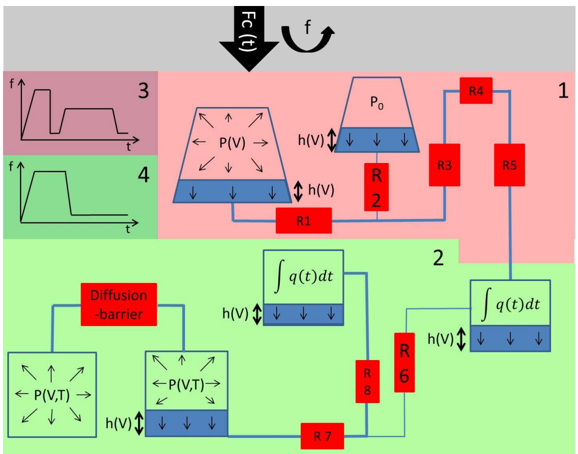

Figure 3: Equivalent lumped networks used. Part 1 shows the network model for dynamic elution buffer routing. Part 2 shows the model of the centrifugo-dynamic inward pumping. Parts 3 & 4 show qualitative centrifugal protocols to operate the respective networks. The network consists of channels with variable fluidic resistances, volume chambers and pneumatic pressure chambers with variable shapes.

Keywords: network-simulation, centrifugal microfluidics, sample to answer