# LUMPED ELEMENT SIMULATION OF A HIGHLY INTEGRATED BIOANALYTICAL CENTRIFUGAL PROCESSING UNIT ("BioCPU")

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## ABSTRACT

The centrifugal microfluidic platforms have evolved into a mature technology for a broad range of applications, for example in the life sciences, biomedical point-of-care diagnostics, and environmental monitoring. Whilst considerable progress has been made on functional elements of the Lab-on-a-Disc (LoaD) platform, the design of complex, highly integrated networks representing sample-to-answer automation of multi-step biochemical assays remains a significant challenge. This paper addresses a developed microfluidic simulation tool for the efficient layout, simulation and analysis of high-performance LoaD systems implemented by featuring a novel, "digital" flow control scheme.

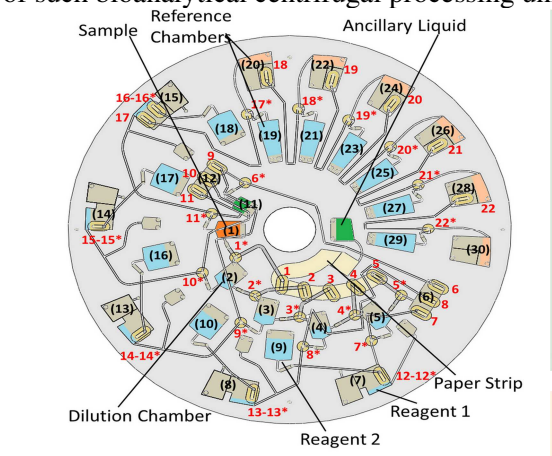
**KEYWORDS:** lumped-element simulation, centrifugal microfluidics, lab-on-a-disc, lab-on-a-chip

## INTRODUCTION

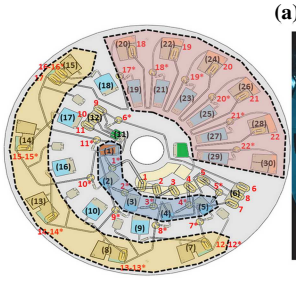
Over the recent years we have introduced centrifugal microfluidic systems featuring novel, "event-triggered" flow control [1, 2, 3] which, by virtue of its intrinsic, closed-loop process control as well as its robustness towards manufacturing tolerances, turns out to be well amenable to microfluidic large-scale integration (LSI). In addition, logical flow control operators such as AND and OR [1] have been introduced, thus enabling a modular system design akin to integrated circuits (ICs). Supported by this handshake-mode "digital" flow control and an internal clocking by film dissolution times and paper imbibition, we have implemented unprecedentedly complex microfluidic networks of more than 20 sequential or parallel laboratory unit operations (LUOs) for representing a variety of (bio-)analytical sample preparation and assay protocols. However, a mainly intuition-driven optimisation of these "microfluidic ICs" proves to be unmanageable towards higher levels of integration.

## EXPERIMENTAL

We present here a lumped-element simulation tool for significantly accelerating the development of such bioanalytical centrifugal processing units ("BioCPUs") with well predictable functionality [3].




(a)



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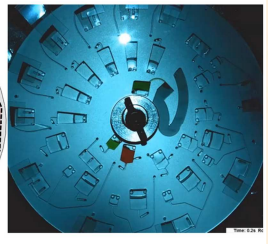

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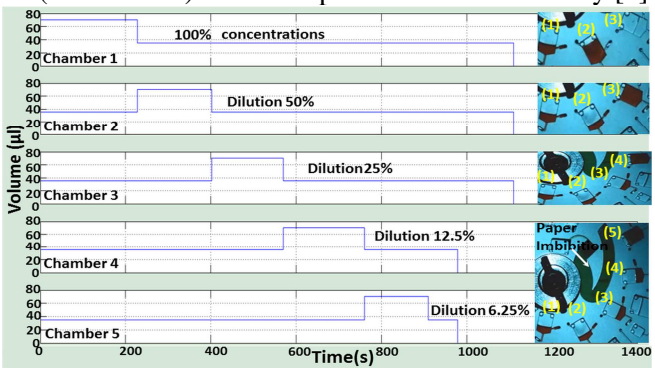
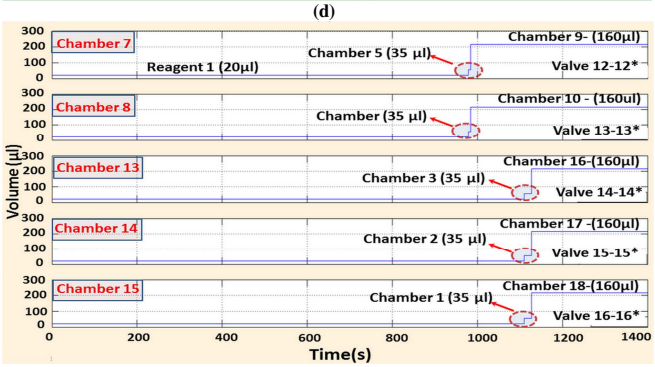



(d)




(e)

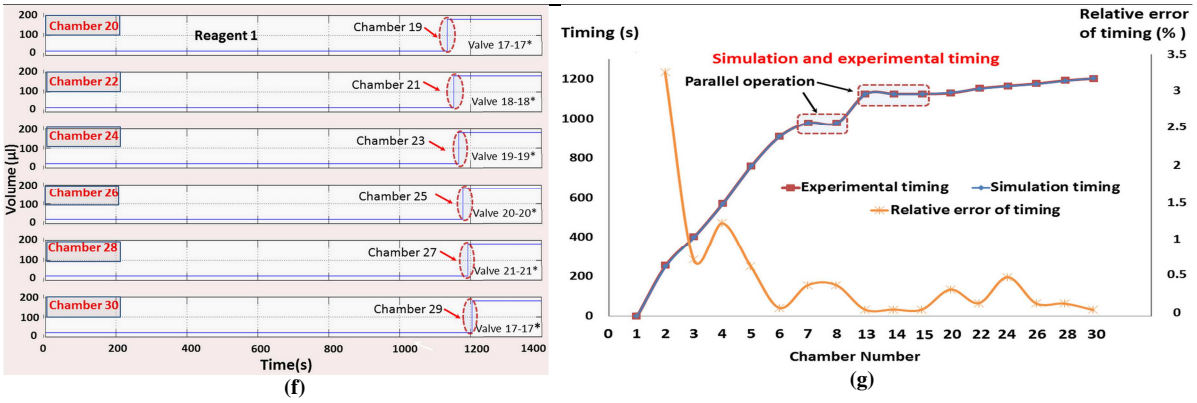



*Figure 1: (a) Pilot application with LoaD to be simulated for a multiplexed immunoassay panel composed of 22 event triggered valves and 30 chambers, (b) segmentation into three simulation batches and (c) photo of the disc at the start of the assay protocol [2], (d- f) illustration of dilution concentration and chamber filling timing diagram monitored in real-time through the lumped-element simulation, (g) comparison of Simulated vs Experimental timing of chamber fill operations.,*

Employing the lumped element method for simulation of centrifugal microfluidic platform [3]. On the analogy of electronics, low-dimensional descriptors such as pressure head ("voltage"), hydrodynamic resistance ("resistor") and flexible parts ("capacitance"), the fluid dynamics including flow rates and filling levels of the system are calculated as a function of the spin rate at discrete points, rather than over a full 3-dimensional lattice of the network [3].

As a pilot supplication, we simulate the multi-step / multi-reagent liquid handling for a multiplexed immunoassay [2]; this assay implements a 4-fold sample serial dilution (mixing / metering) followed by a branched cascade of 17 event-triggered valves with a total of 22 liquid handling steps along 30 chambers (subdivided in three simulation batches) during the experimentation period of 23 min (Fig. 1a-c).

## RESULTS AND DISCUSSION

In more detail, imbibition of ancillary liquid along a paper strip opens valve 1-1*, thus releasing 40 µl from chamber 1 to 2; this scenario reiterates until valve 5-5* gates a 4-folds dilution (Fig. 1d); next, liquid advances through chambers 7-30 (Fig. 1e & f). The simulation and experimentally observed timings prove to be in good agreement (Fig. 1g). The graph reveals that timing can be predicted at an accuracy in excess of 99% with a relative error of about 1%. The exceptionally large relative error in step 2 is attributed to delay in the start of the initial paper imbibition with the opening valve 1-1.

## SUMMARY & CONCLUSION

Our novel lumped-element tool can successfully simulate our digital microfluidic "BioCPU" representing the event-triggered liquid-handling automation of a multiplexed, multi-step / multi-reagent immunoassay panel. In the future, we will broaden our library of lumped elements to substantially extend the range of assay protocols; we will also incorporate design for manufacture (DfM) to our software tool.

## ACKNOWLEDGEMENTS

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