Design and Fabrication of a Continuous Microfluidic Formulator

William J. Matloff[1,2], Kevin T. Seale[1,2], and John P. Wikswo[1,2,3]

***Short Abstract* — We are developing an automated microfluidic device that can deliver a continuous flow of arbitrary mixtures of up to 16 compounds. Through the use of a double-buffered configuration of mixers, accurate mixtures can be created while still producing a continuous output. Such a device will allow for multiple-input and multiple-output (MIMO) biological experiments that involve the constant perfusion of a dynamic chemical mixture.**

***Keywords* — Chemical formulation, microfluidics, automation, systems biology, systems identification**

I. Purpose

CHARACTERIZING complex biological systems may require experimental tools that allow for arbitrary, concurrent, and continuous chemical perturbations [1,2]. Many current microfluidic chemical signal generators, while useful, can only create chemical signals with a small number of chemicals [3,4]. In contrast, Hansen et al created a microfluidic formulator device using multilayer soft lithography to serially create and output arbitrary 5 nanoliter mixtures of a large number of different chemicals [5,6] However, in many biological experiments, it is necessary to have a continuous perfusion of mixed solution. To this end, we are developing a device based on that by Hansen et al that can continuously output arbitrary mixtures of a large number of chemicals. We believe that this could be a useful tool for systems biology, serving as the control knobs in multiple-input and multiple-output (MIMO) experiments.

II. Materials and Methods

The device used the multilayer soft lithography technique to form pneumatic valves that control fluid flow [5,6]. Two mixers serve as a double buffer to allow for the device to output and mix simultaneously, creating a continuous output flow. Device testing was completed using deionized water and food coloring. Metal ion solutions and Inductively Coupled Plasma Optical Emission Spectroscopy (ICP-OES) are used to measure the accuracy of the device.

Acknowledgements: This work was funded by VIIBRE and Searle Systems Biology and Bioengineering Undergraduate Research Experience (SYBBURE)

[1]Vanderbilt Institute for Integrative Biosystems and Education (VIIBRE). Email: william.j.matloff@vanderbilt.edu

[2]Department of Biomedical Engineering, Vanderbilt University

[3]Department of Physics, Molecular Physiology and Biophysics Vanderbilt University, Nashville, TN, USA

III. Results

The device and experimental setup is shown in Figure 1. Many different solutions can fill each mixer, as shown in 1d.

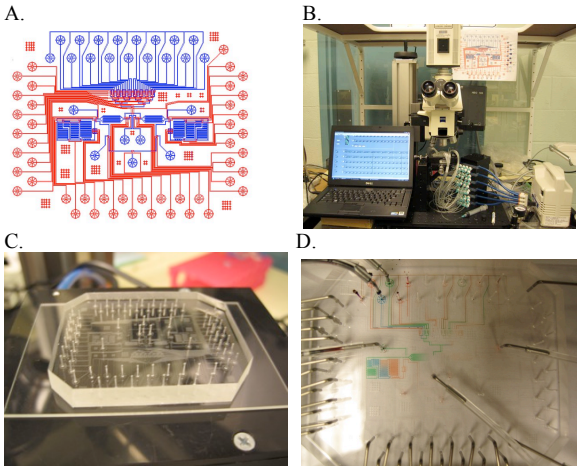

Figure 1: Design (a), experimental setup (b), fabrication (c), and testing (d) of the microformulator.

IV. Conclusion

A continuous microfluidic formulator may have important applications in biological systems identification. Its continuous nature allows it to serve as the input to chemostats and cell cultures, permitting a variety of complex, automated experiments.

References

[1] Miesenbock G. 2009. "The optogenetic catechism." Science 326:395–99.

[2] LeDuc, Philip R, William C. Messner, and John P. Wikswo. "How Do Control-Based Approaches Enter into Biology?" *Annual Review of Biomedical Engineering* 13.1 (2011): 369–396.

[3] Bennett, M. R, and J. Hasty. "Microfluidic devices for measuring gene network dynamics in single cells." *Nature Reviews Genetics* 10.9 (2009): 628–638.

[4] Jovic, A., B. Howell, and S. Takayama. "Timing is everything: using fluidics to understand the role of temporal dynamics in cellular systems." *Microfluidics and nanofluidics* 6.6 (2009): 717–729.

[5] Unger, Marc A et al. "Monolithic Microfabricated Valves and Pumps by Multilayer Soft Lithography." *Science* 288.5463 (2000): 113–116.

[6] Hansen, Carl L., Morten O. A. Sommer, and Stephen R. Quake. "Systematic Investigation of Protein Phase Behavior with a microfluidic Formulator." *Proc Natl Acad Sci USA* 101.40 (2004): 14431 –14436.