DOI 10.5162/EUROSENSORSXXXVI/PT6.188

CogniFlow: Integrated Modular System For Automated Droplet Microfluidic Bioanalysis

Rauno Jõemaa[1], Fariha Afrin[1], Nafisat Gyimah[1], Kanwal Ashraf[1], Kaiser Pärnamets[1], Lucas Giese[2], Mathieu Rocancourt[2], Tamás Pardy[1]
[1] Tallinn University of Technology, 5 Ehitajate tee, 19086 Tallinn, Estonia,
[2] ENSEA, 6 Av. Du Ponceau, 95000 Cergy, France

tamas.pardy@taltech.ee

Summary: Droplet microfluidics uses discrete, chemically isolated droplets to multiplex reactions in bioanalysis. Droplets also allow process control exceeding traditional means, as well as continuous flow microfluidics. Here we present the concept of CogniFlow, an integrated, modular droplet microfluidic instrumentation platform, which automates complete droplet generation, imaging and detection workflows. The platform is demonstrated in cell encapsulation and detection. It is our hope that CogniFlow can significantly lower the entry barrier to instrumenting existing droplet bioanalytical workflows.

Keywords: droplets, microfluidics, instrumentation, control, cognitronics

Introduction

Droplets allow excellent process control by chemically isolating pico- to nanoliter range reaction volumes (like tiny test tubes), allowing selection of samples from a pool of millions of non-specific targets, which would be nearly impossible with conventional tools (e.g. well-plate stations) [1], [2]. This has opened the way to novel applications in microfluidic bioanalysis and biotechnology [3]. However, biology teams desiring to automate their droplet-based workflows today primarily load functions onto highly complex microfluidic chips, and/or use combinations of general-purpose off-the-shelf instruments, resulting in highly complex, expensive systems, which are difficult to scale and replicate, take significant time to build and are not energy-efficient [4], [5]. In this poster, we propose a technology platform that can address these challenges and reduce development time and cost associated with instrumenting droplet bioanalytical and biotechnology applications. In our previous paper we presented the droplet generation module of the platform [6]. In this poster, we present the integrated system, including droplet imaging and detection.

Novelty

CogniFlow offers the following novelties:

Transferability: modules are compact and portable, can be swapped, but the system has its standards. System can be reconfigured (e.g. different filters, lenses and light sources, camera vs. photodiode etc.), but workflows are easily replicated between labs.

Scalability: Low cost (<1k€-2k€/module, using 3D printed parts, low-cost electronics and optics) and standardization ensure easy replication of results in different labs, as well as scaling up throughput. Despite the low cost, performance of thus-far demonstrated components has been on par with comparable systems [6].

Efficiency: modules have power consumption ~10-20W, enabling battery operation. Wireless communication via ECAL [7] further reduces device footprint and increases portability. Optimizations to flow control reduce reagent waste.

Total automation: CogniFlow has 3 main modules: 1. Droplet generation/encapsulation [6], 2. Droplet imaging and 3. Embedded object classification algorithm. These cover a complete droplet-based imaging or light intensity analysis workflow.

Demonstrations in literature meeting the majority of the aforementioned criteria are rare [1], [2].

System modules and results

Droplet generation [6]: the first demonstrated module of the platform generated droplets in 50-200 um range with 5-10% coefficient of variability at up to 1kdps (1000 droplets per second). We controlled pressure drop and droplet size in a piezoelectric pumping setup with rapid and precise controller response, but a simple and inexpensive setup. On the poster, we mention this module for the sake of completeness.

Droplet imaging: the second module of the system presented here for the first time is based on an affordable optical setup using a Basler

acA640-750uc and a cheap 20x magnification lens to achieve ~750 dps imaging rate [8]. The integrated system (Fig. 1) is built on the same framework as the first module, by swapping internal components. The footprint is 22 x 33 x 40 cm. Imaging system output with encapsulated cells is shown in Fig. 2.

Object detection *(Fig. 3):* a droplet segmentation and object classification algorithm based on YOLOv4 and TinyYOLOv4 is presented, which is capable of detecting single cells in droplets with 85% accuracy on an image stream of droplets in flow provided by our academic partners. The algorithm can run on an NVIDIA® Jetson Nano™ AI accelerator. The AI accelerator board fits on top of the electronics stack of the second module (Fig 1. left), and while it will double system power consumption, the total will still be well below what PD3.0+ compliant power bank can provide.

Between the two hardware and the one software module presented here, the following solutions are in common: both hardware modules rely on a Raspberry Pi 4 for control and communication. Wireless communication is implemented via ECAL, as presented in [6], however, for experiments, a wired Ethernet connection is also possible. Power electronics is the same between module 1 and 2, as is the mechanical frame, which consists of 3D printed parts and commonly used metal fasteners.

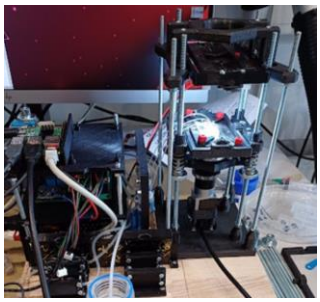

Figure 1: Integrated droplet imaging module of the CogniFlow platform. The mechanical frame and enclosure (not shown here) are shared between all platform modules, optics and electronics stages are changed according to the purpose.

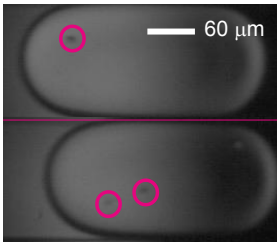

Figure 2: Droplets imaged with the droplet imaging module of CogniFlow using an affordable optical setup. Highlighted objects are algae cells encapsulated. Reagents used for droplet generation are described in [6].

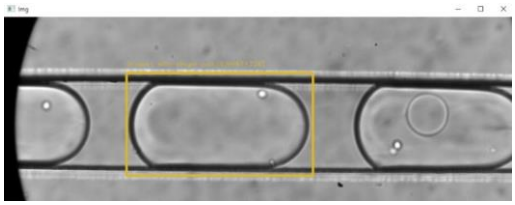

Figure 3: Object detection algorithm demonstration. Reference video of droplets with microbeads and cells encapsulated was kindly provided by University of Warsaw to test the algorithm on an independent dataset.

References

[1] C. Huang, Y. Jiang, Y. Li, and H. Zhang, 'Droplet Detection and Sorting System in Microfluidics: A Review', *Micromachines (Basel)*, vol. 14, no. 1, p. 103, Dec. 2022, doi: 10.3390/mi14010103.

[2] M. Gantz, S. Neun, E. J. Medcalf, L. D. van Vliet, and F. Hollfelder, 'Ultrahigh-Throughput Enzyme Engineering and Discovery in In Vitro Compartments', *Chem Rev*, vol. 123, no. 9, pp. 5571–5611, 2023, doi: 10.1021/acs.chemrev.2c00910.

[3] T. S. Kaminski, O. Scheler, and P. Garstecki, 'Droplet microfluidics for microbiology: techniques, applications and challenges', *Lab Chip*, vol. 16, no. 12, pp. 2168–2187, 2016, doi: 10.1039/C6LC00367B.

[4] Y. Zhou, Z. Yu, M. Wu, Y. Lan, C. Jia, and J. Zhao, 'Single-cell sorting using integrated pneumatic valve droplet microfluidic chip', *Talanta*, vol. 253, p. 124044, Feb. 2023, doi: 10.1016/J.TALANTA.2022.124044.

[5] Atrandi Biosciences, 'Styx | Atrandi Biosciences'. Accessed: Feb. 03, 2024. [Online]. Available: https://atrandi.com/styx

[6] R. Jõemaa *et al.*, 'CogniFlow-Drop: Integrated Modular System for Automated Generation of Droplets in Microfluidic Applications', *IEEE Access*, vol. 11, pp. 104905–104929, 2023, doi: 10.1109/ACCESS.2023.3316726.

[7] K. Ashraf, Y. Le Moullec, T. Pardy, and T. Rang, 'Design of Cyber Bio-analytical Physical Systems: Formal methods, architectures, and multi-system interaction strategies', *Microprocess Microsyst*, vol. 97, Mar. 2023, doi: 10.1016/J.MICPRO.2023.104780.

[8] K. Parnamets, A. Koel, T. Pardy, and T. Rang, 'Open Source Hardware Cost-Effective Imaging Sensors for High-Throughput Droplet Microfluidic Systems', *Proceedings of the 2022 26th International Conference Electronics, ELECTRONICS 2022*, 2022, doi: 10.1109/IEEECONF55059.2022.9810383.