

A New Low-Cost Microfluidics Device & Microscope

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Background

Microfluidics devices have previously been made as large, bulky instruments with a high price and high operating cost. Using such devices for single-cell analysis with droplet-based techniques allows for a high throughput and the ability to do further analyses that are not possible with non-single-cell devices. The focus of companies that produce these devices has primarily been increasing this throughput despite the devices' prices often being unreasonable for how much they will be used. This has inhibited droplet microfluidics techniques from being widely applied despite their benefits in areas such as high throughput cell profiling. In order to focus on decreasing the price of such beneficial devices, a droplet-based microfluidic control instrument was designed to replace the need of large, bulky machines costing researchers tens of thousands of dollars. Through the process of constructing the device, a low-cost microscope was also designed and developed to be used for any application of regular microscopes.

Materials & Methods

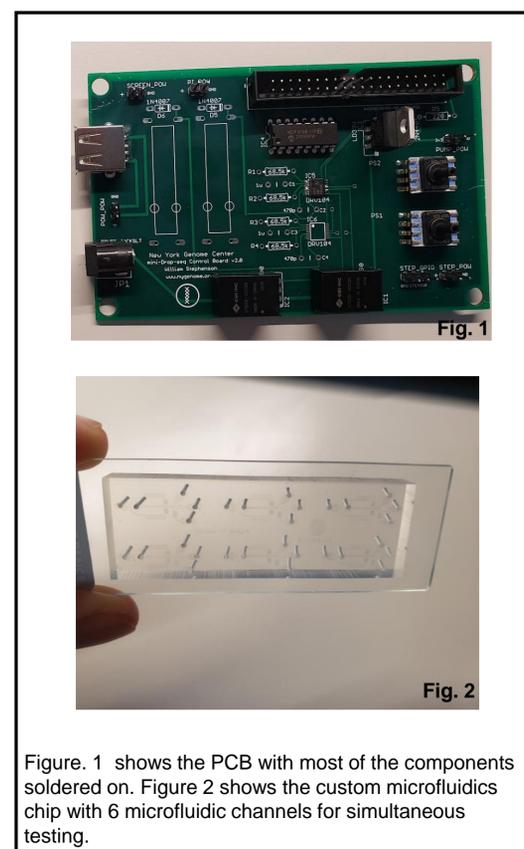
Materials:

- The user has access to a touchscreen on the microfluidics device to control a Raspberry Pi computer that has a program to control the air pumps and the microscope camera in the device.
- The devices also contains a custom printed circuit board (PCB), tubing and pressure gauges for pressure regulation and solution transfer, and vials to load the solutions into.
- A custom microfluidics chip is used to process and examine the droplets.
- The full bill of materials and access to the programs and designs are provided in the references¹.

Materials & Methods (continued)

Methods:

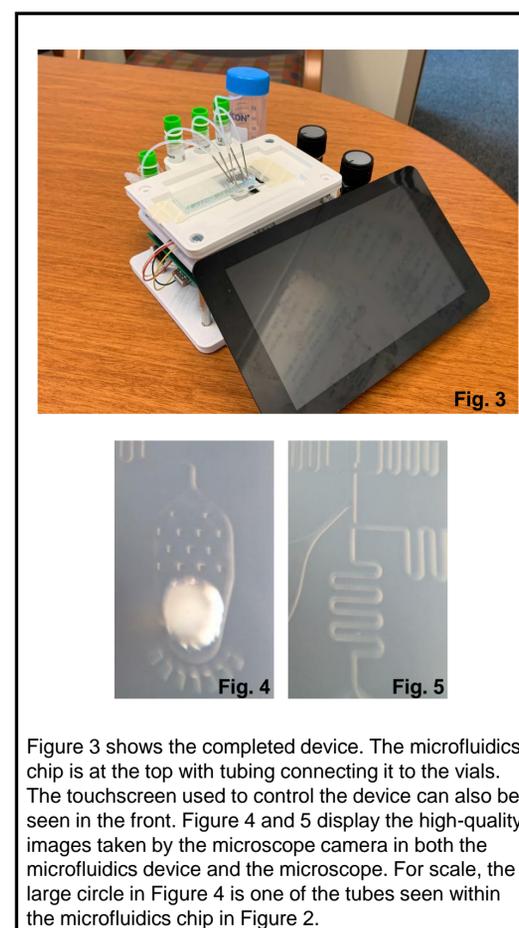
- The device was constructed by first soldering all the necessary components onto the PCB such as solenoid valves, pressure gauges, various wire connectors, etc.
- The tubing was then cut and connected to fit on the PCB and connect everything from the pressure gauges to the air pumps to the substance vials.
- The designs of the device's structure were then 3D printed and the tubing, PCB, camera, and other components were installed onto the device.
- The full step-by-step description of the build process is provided in the references¹.
- The microscope was designed, and its parts were also 3D printed. They were all put together through processes like that of the microfluidics device, but it only uses a Raspberry Pi, microscope camera, and touchscreen.



Results

The final microfluidics device creates a consistent sequence of aqueous droplets and oil droplets. The separation of single-cells into droplets allows for the analysis of how separate cells interact with certain substances in the aqueous solution as compared to the interactions of groups of cells. This would not be possible without droplet-techniques and microfluidics devices which are needed to separate each cell. The device controls the air pump and regulates the pressures in the solutions to create this consistent sequence of droplets. With the images and recordings taken from the microscope camera and saved onto the Raspberry Pi, the droplets' movements can be observed and cells or anything else within the droplets can be closely studied.

The final microscope based off the microfluidics device design takes high-quality pictures and recordings of anything the researcher would like to observe. The quality of this microscope's images and videos is comparable to that of a microscope that costs much more.



Discussion

Constructing this microfluidics device allows for a low-cost, high-throughput system to not only study single-cells but also study any other isolated biological components at a microscopic level. The applications of such a device cover a great range. For example, this device is useful for cell barcoding and RNA sequencing². In this purpose, the microfluidics device is able to use less reagents and other materials while maintaining the analysis of over 15,000 cells per hour². Such devices are made more unique by the fact that they are able to successfully capture and profile over 75% of the cells in the original sample². Microfluidics devices can also function beyond the main limitations of methods such as traditional flow cytometry and fluorescence-activated cell sorting because the cells can be compartmentalized separately³. Such separation allows researchers to analyze the proteins released or secreted from each cell³. This device can also use fluorescent analysis techniques as the device introduces beads coated with any substance having an affinity for the desired material in the cells³. Once these beads are introduced, the desired material collects onto the bead which creates a strong fluorescence to be detected by researchers.

Our lab's purpose with such a device is to sequence RNA from single-cells after they have been through gene knockout using CRISPR. With so many different applications for such microfluidics devices and microscopes as well, it is evident that their low-cost and analytical benefits will make them the best option for many experiments.

References

- 1) Stephenson, W., Donlin, L. T., Butler, A. *et al.* Single-cell RNA-seq of rheumatoid arthritis synovial tissue using low-cost microfluidic instrumentation. *Nature Communications* **9** (2018). <https://doi.org/10.1038/s41467-017-02659-x>
- 2) Zilionis, R., Nainys, J., Veres, A. *et al.* Single-cell barcoding and sequencing using droplet microfluidics. *Nat Protoc* **12**, 44–73 (2017). <https://doi.org/10.1038/nprot.2016.154>
- 3) Mazutis, L., Gilbert, J., Ung, W. *et al.* Single-cell analysis and sorting using droplet-based microfluidics. *Nat Protoc* **8**, 870–891 (2013). <https://doi.org/10.1038/nprot.2013.046>