COMPUTER VISION APPLIED TO MEMBRANE DISPLACEMENT TRAP ARRAYS FOR AUTOMATED DROPLET CONTROL AND MANIPULATION

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ABSTRACT

Computer vision and automation are applied to microfluidic membrane displacement trap (MDT) systems to demonstrate droplet control capabilities beyond that previously shown with manual operation. Repeatability is demonstrated by completing 475 trials of droplet capture in 2 hours, while gathering detailed positional and morphological measurements in real-time. Precision is demonstrated by metering droplets via electronically timed split captures, based on a model of MDT capture performance built from previously collected data. Lastly, ease of use is demonstrated by programming a simple bioanalytical assay with the aid of MDT array simulations.

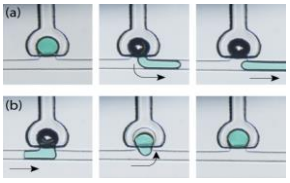

Figure 1. (a) Droplet release and (b) droplet capture in a single MDT

KEYWORDS: microwell, membrane displacement trap, multiplex, computer vision, machine vision, automation

INTRODUCTION

Membrane displacement traps (MDTs) are a powerful technology for sample discretization and droplet manipulation. They are simply fabricated 2D microwells whose volumes can be rapidly modified, as in pneumatic microvalves, by pressurizing an overlapping membrane [1]. Each MDT allows precise individual control over capture, splitting, metering, ejecting, and merging of discrete fluid volumes (Fig. 1).

The versatility of MDTs comes with a price; meticulous attention is required to perform these operations, which are governed externally by timing and actuation pressure. Automation is necessary to fully realize the applications of this technology, which range from characterizing MDT performance to conducting bioanalytical assays manipulating single cells.

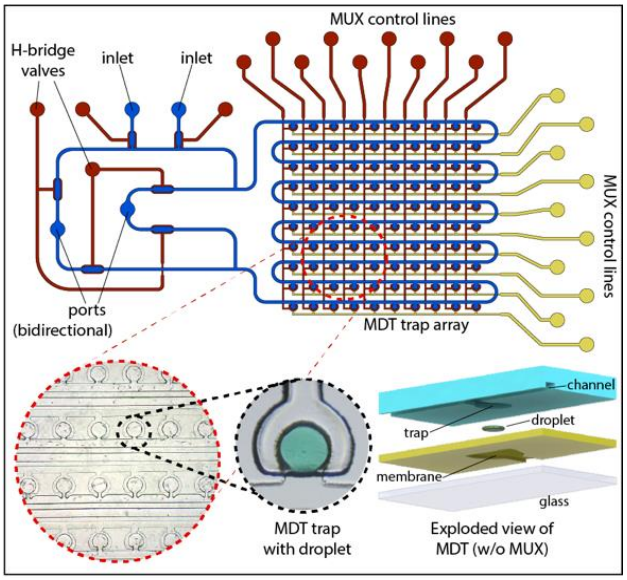

Figure 2. Multiplexed MDT array design with 100 microwells and bidirectional flow enabled by an on-chip fluidic H-bridge. Fabricated device views are shown inset, together with an exploded view of a single MDT revealing the simplicity of the device design.

EXPERIMENTAL

MDT devices were fabricated via soft lithography in two layers of polydimethylsiloxane (PDMS). In multiplexed devices, an additional layer of PDMS was added to form a second, opposing membrane in each microwell. Multiplexed MDTs eject their contents only when both membranes are pressurized (Fig. 2).

To achieve bidirectional controllable flow, an H-bridge valve topology was incorporated on-chip (Fig. 2). A constant pressure differential between ports causes fluid to flow through the MDT array, biased in a direction based on the state of two computer controlled valve pairs.

Computer vision and control was implemented in OpenCV-Python. Live video is processed in real-time to determine the size and position of droplets on screen. Pneumatic solenoid valves are actuated in response, operating the platform to follow an experiment.

The effect of MDT capture timing on satellite droplet formation was characterized by an automated experiment: A droplet was flowed down the channel until its trailing end was X horizontal distance from the center of a MDT. The MDT was actuated, and the areas of the captured droplet and satellites were recorded. This sequence was

repeated with X ranging from -150 to 100 pixels, for 475 trials. Droplets were dyed deionized water in light mineral oil, with 0.01% v/v Span-80 surfactant.

A computer simulation of an MDT array was developed to facilitate rapid testing and debugging of programmed experiments. To demonstrate use, an experiment was designed and programmed, reflecting operations currently desired for ongoing on-chip cell culture experiments. Red and yellow droplets representing immune cells and cancer tumor cells were sequentially perfused through a 56 trap array and captured in alternating microwells.

RESULTS AND DISCUSSION

MDT capture dynamics were characterized by measuring droplet and satellite size for 475 droplets captured at varying distances to MDT center. The fully automated experiment completed in 2 hours. Satellite size data shows a clear region where no satellites are formed because the droplet is fully captured. Adjacent are two tightly correlated regions where satellite size varies with distance from MDT center. Finally, outer regions indicate no capture occurred.

A subsequent experiment validated this data by using automated timing to capture droplets such that they formed an equally sized satellite. This represents another mechanism for metering droplets with MDTs, albeit one impractical without electronic timing.

The simulated biological assay filled all 56 wells in 8 minutes and 30 seconds. Not all wells were entirely filled, indicating potential for unwanted satellite droplets to form in a real MDT device. The time to program and debug the experiment was slightly under an hour.

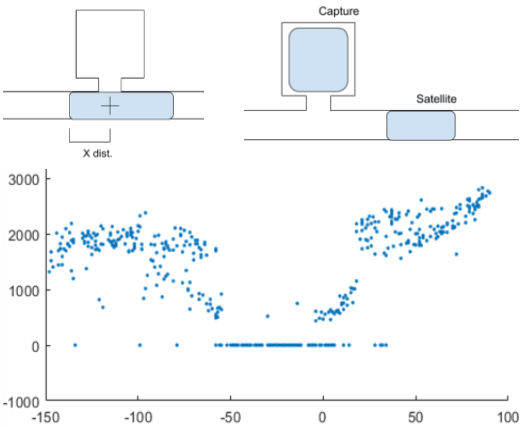

Figure 3: Plot of resultant satellite droplet area (pixels^2) vs X distance, n=475. Note tightly correlated region where satellite size is a fraction of the whole droplet proportional to X.

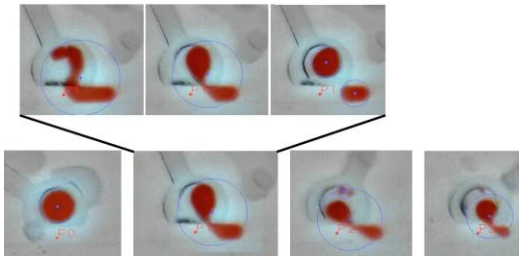

Figure 4. Timed droplet capture to meter an equally sized satellite droplet as the captured volume. Repeated in 3 consecutive MDTs with

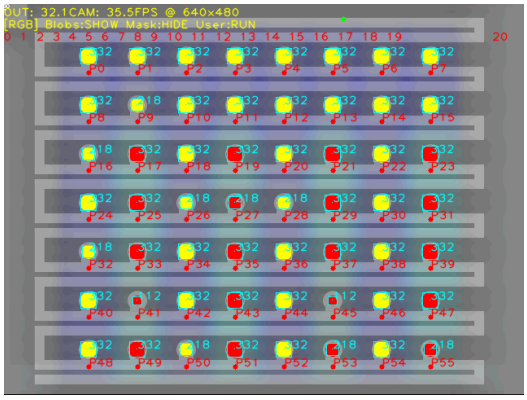

Figure 5. Simulated cell seeding experiment. Inconsistencies in capture size are more prominent in the last few rows.

CONCLUSION

Computer vision software was used to automate experiments on real and simulated MDT array platforms. Tasks such as repeating experimental sequences, gathering detailed measurements in real-time, and performing dynamic operations with precise timing were demonstrated. In verifying modeled MDT capture performance, an elegant new method of metering was discovered by timing captures to produce satellites of predictable size. MDT device simulations were shown to enable rapid development of an automated bioanalytical assay. These results confirm the value of computer automation in enabling MDT platforms to perform complex droplet microfluidic experiments.

ACKNOWLEDGEMENTS

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REFERENCES

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CONTACT

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