Portable Digital Microfluidics Platform with Active but Disposable Lab-On-Chip

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ABSTRACT

This paper reports successful development of a stand-alone microfluidics platform based on our electrowetting-on-dielectric (EWOD) droplet technologies. Four new major developments that empowered us to achieve the portable digital microfluidic system are presented: (1) time-multiplexed driving scheme that enables simultaneous driving of a large number of droplets; (2) electric sensing mechanism of droplet positions, opening the door for feedback control and Lab-On-Chip (LOC) performance monitoring; (3) fabrication of disposable and sealed LOC capable of full droplet manipulation; and (4) completion of stand-alone portable electronics board. Leaving the issue of biofluids manipulation to other reports, this paper will focus on the technology developments.

1. INTRODUCTION

We previously presented the development of digital microfluidics based on the EWOD principle [1]. Water droplets, immersed in oil [2] or even without such a restriction (i.e. in air) [3], can be manipulated by control of the wettability on a dielectric solid surface using electric potential. We subsequently achieved droplet-based microfulidic functions: a liquid can be transformed into droplets (i.e., digitized), and these droplets can be moved along a programmable path, divided into smaller droplets, and mixed with other droplets [4]. Mcirofluidics by electrowetting is very promising because the fabrication process is much simpler with no need to build moving micromechanical parts in the device [5].

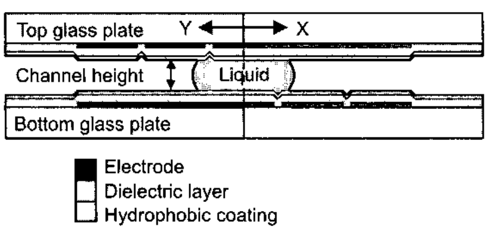


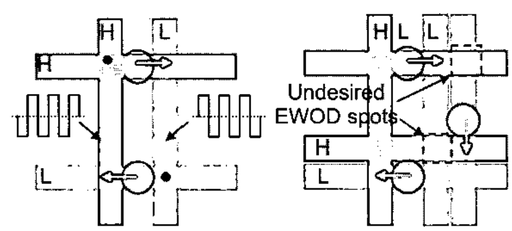
Figure 1. Cross section of a cross-reference EWOD device along the X and Y axes [1].

More recently we introduced a 2-D EWOD cross-reference grid to perform essential fluidic operations on full N×M grids for the first time [1]. As shown in Fig. 1, electrode rows are patterned on both top and bottom plates and placed orthogonally. This design frees one from the need of multi-layer processing of electrodes in direct-reference devices [6]. It also reduces the number of control electrodes from N×M to N+M. The fabrication and packaging of the device are dramatically simplified for the larger grid.

Our current cross-reference EWOD device was fabricated on a transparent ITO (Indium Tin Oxide) glass substrate for easy observation. After patterning ITO layer with desired electrode shape, PECVD silicon dioxide was deposited and patterned to expose part of electrode for electrical connection. A layer of Teflon® was then coated to make the surface hydrophobic.

2. TIME-MULTIPLEXED DRIVING SCHEME

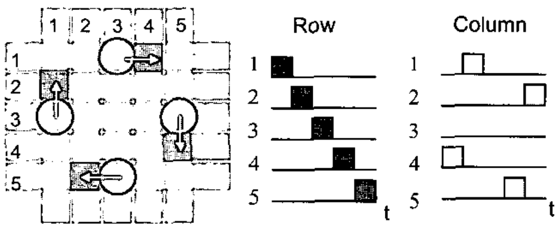
There is a particular driving problem for the cross-reference EWOD device to manipulate multi-droplets independently and simultaneously. Firstly, we show how we can drive two droplets and the problem for more droplets. By applying the driving signal with 180° phase difference, shown in Fig. 2, the cross positions between H (High) and L (Low) lines turn wetting and hold/attract droplets. We can avoid the undesired active cross points (or undesired EWOD spots) indicted with dots in Fig. 2(a) by just using one AC signal and ground by using these two out-of-phase potential differences across the plates. However, when adding a third droplet, as shown in Fig. 2(b), the undesired spots come out. Although, depending on the position of the droplets, the undesired spots are eventually evitable for more and more droplets and arbitrary moving paths. One potential solution for that is to generate more out-of-phase potential differences pairs (by various phase changes) to drive each droplet. Unfortunately driving circuit becomes much more complex if it needs as many potential pairs as the number of droplets.



(a) Solution for 2 droplets driving [1]. (b) Problem when adding a 3rd droplet.

Figure 2. Undesired EWOD spots limit the path of more than two droplets from being arbitrary.

A better and general solution is to use time multiplexing scheme, which divides the driving time instead of voltage phase, common in LCD displays. Fig. 3(a) shows the current and next positions of four droplets, compared with the case in Fig. 2(b). As can be seen in Fig. 3(b) and (c), the electrode rows are activated successively from 1 to 5. When a row is activated, the corresponding desired column (columns) is (are) activated simultaneously. After every scanning cycle, we can also repeat the whole scanning to increase the driving force. Here we define the time to scan one row as a scanning duration and the time to scan the entire device as a scanning period. The scanning period is decided by the scanning duration times the number of rows. In this scheme, undesired EWOD spots discussed before are no longer a problem. However the driving signals are now periodic instead of continuous AC signals. Experiments have been done to prove that the periodic AC signal can successfully fulfill EWOD driving. The equivalent driving force is proportional to the peak-to-peak driving voltage, the scanning duration, and the scanning period as well as the scanning repeat.



(a) Desired EWOD spots are marked. (b) Activation of rows. (c) Activation of columns.

Figure 3. *Time-multiplexing driving scheme.*

3. Droplet Position Sensing

Because of uncertainties, such as surface imperfection and degradation, the loading effect of the multiple droplets, variation of samples and reagents, and software/hardware glitches, it is quite useful to be able to sense the droplets position in real time. Analogous to the parity check in data communication, the position sensing will be instrumental in monitoring LOC operations so that the missed microfluidic protocol can be redone or redirected to other locations on the chip. Since an optical position sensing will require additional set-ups (e.g. CCD chip) and result in a relative long response time, we developed an electrical position sensing for better compatibility with chip fabrication and fast response.

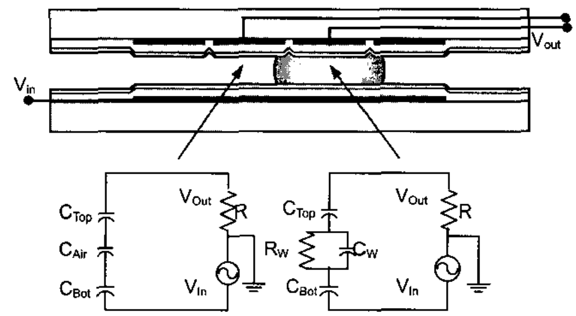
Fig. 4(a) shows the equivalent circuit of the EWOD configuration for the gap between top and bottom electrodes filled with air or droplet. The input signal is an AC waveform, small compared to the high driving voltage. Output signal is measured by the voltage across a resistor with a large resistance. Then the output detecting voltage amplitude can be predicted by the simple circuit analysis:

$$\left|\frac{V_{out}}{V_{in}}\right| = \frac{R}{\left|\frac{1}{i\varpi C_{ox}} + \frac{1}{i\varpi C_{air}} + R\right|}, \tag{1}$$

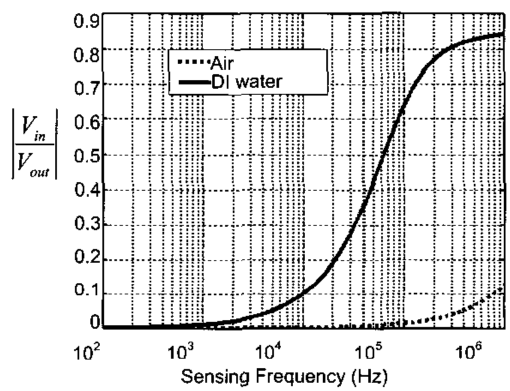
$$\left|\frac{V_{out}}{V_{in}}\right| = \frac{R}{\left|\frac{1}{i\varpi C_{ox}} + \frac{R_w}{i\varpi R_w C_w + 1} + R\right|}, \tag{2}$$

where: $C = \frac{\varepsilon_r \varepsilon_0 A}{d}$, $\varepsilon_0 = 8.854\times10^{-12} F/m$, ε_r is the dielectric constant, A is the area of the electrode, and d is the thickness of the dielectric film.

Because water has a very high dielectric constant (ε_r=78.4) compared with air (ε_r =1), the impedance between the top and bottom electrode would change significantly when an aqueous droplet replaces the air in the gap.



(a) Equivalent Circuit of EWOD Chip.



(b) Predicted output with or without droplet.

Figure 4. *Electrical position sensing by impedance measurement.*

Fig. 4(b) shows the theoretical voltage output over the sinusoidal AC input depending on its frequency for the 1.5 mm x 1.5 mm electrode pad and 1 mm gap. The EWOD device was fabricated with 2500 Å silicon dioxide and 2000 Å Teflon® on ITO glass. Experimental data were retrieved by FLUKE® 199C ScopeMeter Color with 200 MHz, 2.5 Gs/s bandwidth. The input signal is 1 kHz square wave (typical signal generated by Microchip®) with 20 V peak-to-peak voltage generated by HP 33120A, 15 MHz Function Generator and the detecting resistance is 1 MΩ. One droplet of DI water was placed between the top and bottom electrodes. The experimental results shown in Fig. 5 confirm the sensing scheme with noticeable signals.

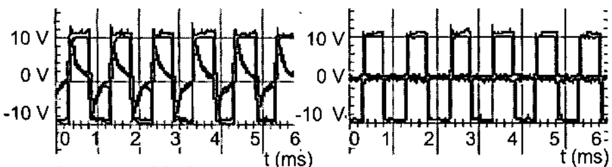


Figure 5. *Measured output signal and input signal for 1.5 mm × 1.5 mm electrode pad and 1 mm gap EWOD chip.*

By real-time collection of the electrical signals through Microchip®'s A/D port and comparison of the data with threshold value, which is set by user or system calibration, we can detect the presence of the droplet on position in 2-3 ms (2-3 periods for 1 kHz sensing signal). We then developed feedback driving scheme, which utilizes the position security, based on the time-multiplexed driving mode. Fig. 6 shows how we integrate the driving and sensing in the EWOD system. After one row scanning of driving (e.g., 70 V), the column driving voltage changes to sensing signal of 5 V, 1 kHz square waveform. At the same time, the detection circuit switches to electrode rows. The output signal is then collected by the Microchip®. The downloaded program on the Microchip® will decide whether to move on to the next row for scanning or to keep the same row for driving again, depending on the droplet movement. In this way, we can adjust the EWOD actuation force by changing the scanning duration dynamically to ensure droplet movement. Feedback control scheme for the droplet creation, cutting and mixing can also be developed in the same fashion.

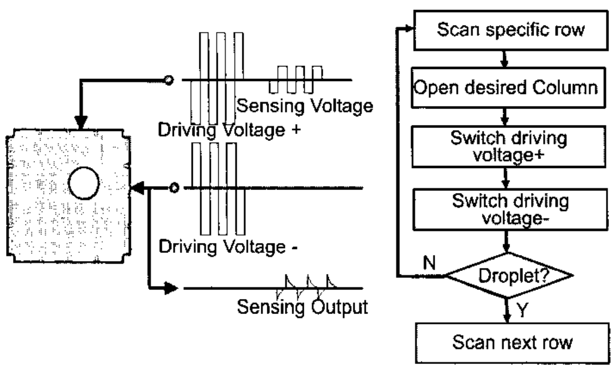


Figure 6. *Driving and feedback sensing scheme.*

4. DISPOSABLE LOC

We developed a disposable LOC insertion method, where the chip is placed into a reusable holder while establishing full electric connections with the PCB board without permanent wiring/bonding (Fig. 7). The challenge is to obtain a small enough gap (<100 μm) to enable droplet generation and cutting [4] without a complicated spacing scheme. We use anisotropic electrical conducting tape (~70 μm) to connect top and bottom electrode as well as defining the channel gap. All electrodes on the top plate are connected to the PCB board through vertical conducting elastomeric connector.

One set of fitting Pyrex® glass holders (top and bottom) was developed to fix the EWOD chips and clamp the electrical connector and tape. Six reservoirs and six drains are made inside the holders to help EWOD chips communicate with the outside world. The openings of the reservoirs/drains are opposite to the specific electrode lines (columns) in the bottom plate. Two extra electrode lines (rows) are fabricated at the edge of the top plate to help create and expel the droplets. During creation, after the edge row and column for specific reservoir are turn on, liquid in the reservoir would flow into the edge site. By quickly turning on the adjacent site and turning off the edge site, one droplet can be pulled from the reservoir. To expel the droplets to drain, we move the droplet to the edge site besides one drain, the droplet would joint into bulk liquid automatically. The walls of reservoirs are coated with Teflon® to make the surface hydrophobic and help create droplets.

We assemble the bottom holder to the PCB board, as well as the top and bottom holder together through screws. To minimize the evaporation and possible loss of liquids over time, the holders have O-rings around them: one O-ring between the top and bottom holder, two O-rings between the bottom and the PCB board. With such a level of sealing, one droplet (1.5 mm×1.5 mm×100 μm) in the gap would last over two days. Additional methods for sealing can be employed, if necessary, depending on the applications. The sealing also prevents the accidental liquid leakage from the reservoirs and drains.

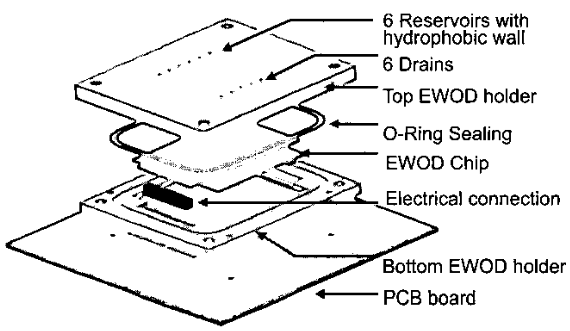
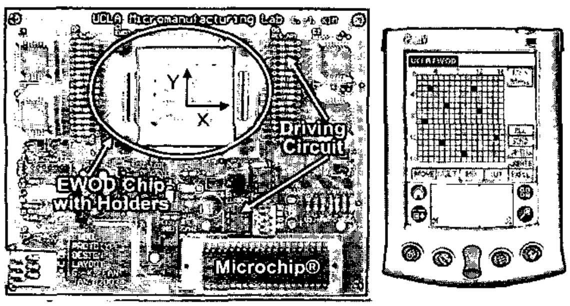


Figure 7. *Lab-on-chip (LOC) fabrication including sealing and packaging.*

5. PORTABLE SYSTEM

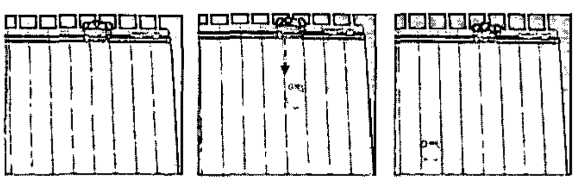
To facilitate the effective use of the EWOD device, we have developed a portable digital microfluidics platform with control circuits and a user interface, as shown in Fig. 8, which were conceptually introduced in [1]. The platform, currently built on a double-side printed circuit board (PCB) of 18 cm × 14 cm × 2.5 cm in size, is a complete system with batteries, droplet driving and sensing circuits, a microprocessor, an infrared user interface, and a 16×16 grid digital disposable lab-on-chip (LOC). The user interface is a Palm Vx PDA (Personal Digital Assistant), which adds portability to the system. Through this interface, user can wirelessly control droplets and program a user-defined microfluidics routine for a specific application. This gives the digital microfluidics platform the versatility needed for the general applications.



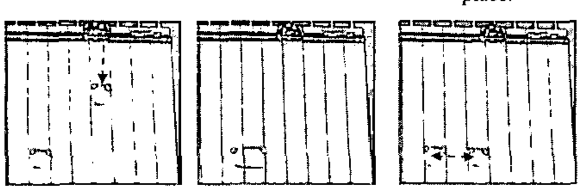
(a) EWOD System Board (b) User Interface

Figure 8. *Pictures of the portable platform and PDA user interface, shown in the same scale.*

With the system board complete with the user interface through a PDA to adjust driving parameters (scanning frequency, scanning duration, scanning repeat time, and driving voltage) and control droplet operation, we have succeeded to fulfill the four basic microfluidic functions (creation, moving, merging and cutting) [4] on the disposable LOC, as demonstrated in Fig. 9. The system performance depends on the driving parameters and the feedback control arithmetic, especially for the unstable processes during the creating and cutting droplets.



(a) Initial State. (b) Create one droplet. (c) Move to another place.



(d) Create another droplet. (e) Move and merge them into one. (d) Cut it into two droplets.

Figure 9. *Video clips of basic fluidic functions performed in the disposable EWOD chip operated on a portable system.*

6. CONCLUSIONS

A portable digital microfluidics platform with active but disposable lab-on-chip has been developed based on a cross-reference EWOD device with time-multiplexed driving scheme. The droplet driving, position sensing, and sealing packaging have been fulfilled to complete a microfluidics platform. The fine driving and feedback control of the system make the platform compatible with complex conditions. With the ability to handle some aqueous biomedical solution [7], we start to develop a few biomedical fluidic protocols and address important new issues.

ACKNOWLEDGEMENT

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