

Open-Source Incubation Ecosystem for Digital Microfluidics – Status and Roadmap

(Invited Paper)

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Abstract—Electrowetting-on-dielectric (EWOD) is a mechanism that allows physical handling of liquids with only electrical signals, such as digitizing a liquid into tiny droplets and manipulating them on a chip, thus enabling “digital microfluidics”. As an elegantly simple platform free of pumps or valves, EWOD digital microfluidics has been attracting high research interest in the past two decades and has recently been transitioned to a few commercial products in displays and biochemistry. However, the number of labs utilizing this technology is still small, due to the difficulty in translating design intent to manufactured devices. Accordingly, in this paper, we propose a cloud-based open-source EWOD cybermanufacturing ecosystem that enables an automatic translation from user requirements to manufactured digital microfluidics. The incubation cyber ecosystem is to be accessible to a wide range of end users, allowing researchers, entrepreneurs, students, and hobbyists alike to focus on their own ideas and applications without having to master the subtleties of EWOD engineering and manufacturing. This can be thought of as an “operating system” for EWOD community, similar to Windows and macOS for people with no computer hardware background. The proposed cyber ecosystem aims to ease the process of designing and eliminate the burden of fabricating EWOD chips so that the user pool is increased and more applications found for EWOD digital microfluidics.

I. INTRODUCTION

Electrowetting, especially in the form of electrowetting-on-dielectric (EWOD) [1], is a versatile actuation mechanism for microfluidics since it enables control over fluid shape and flow by electrical signals alone. As an elegantly simple platform technology, EWOD has attracted much attention during the past two decades for microfluidic applications including optical lens [2] and reflective display [3].

Particularly in the field of digital microfluidics, EWOD has been appreciated as a promising actuation mechanism to design microfluidic chips [4]. Such chips are capable of manipulating tiny nano/pico-liter sized discrete droplets automatically on a two dimensional electrode array, with various advantages such as high precision, high flexibility, and low power consumption.

Fig. 1(a) shows the schematic of an EWOD-driven digital microfluidic chip (henceforth referred to as EWOD chip).

Unlike traditional flow-based microfluidics, where fluid control is achieved by integrating a large number of dedicated components such as pumps and valves into the chip [5]–[10], EWOD chip is composed of a patterned electrode array, conduction wires, and electrical pads [11]. With these electrical components, time-varying actuation voltage can be applied to the electrodes through external control devices, thereby generating electrohydrodynamic force to drive the movement of droplets. Furthermore, since droplets on an EWOD chip can be manipulated in parallel, various applications such as point-of-care diagnosis [12] and drug discovery [13], can be integrated now into the same chip and automatically completed based on a pre-customized execution plan. Because of the advantages above, EWOD digital microfluidics has attracted high research interest among computer scientists over the past few years and a number of computer algorithms for the design automation of EWOD chips have been proposed [14]–[19].

Though impressive progress has been made in the research of EWOD digital microfluidics during the past decades, EWOD chips to handle arrays of liquid droplets did not see any commercialization until 2015 when Illumina announced a tabletop DNA library preparation system named NeoPrep [20]. Thereafter, several other companies have developed their own EWOD chips for specific applications [21], [22], but the processes have been painfully slow. The situation is similar in academic/industrial laboratories, as the burden to establish the technology discourages most non-engineers who can benefit from the use of EWOD chips. Fig. 1(b) illustrates how the EWOD digital microfluidics has failed to reach its full potential while identifying two bottlenecks: technical barrier and reliability issue.

Technical barrier is the most significant factor that prevents the development of EWOD community. Currently, almost every lab who works on the EWOD digital microfluidics makes everything themselves, from chip design and fabrication to control electronics and software, in addition to the application aspect, which most labs really want to focus on. Lacking any basic chassis or standard components to build the EWOD

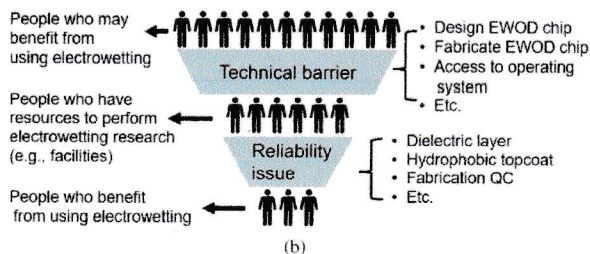
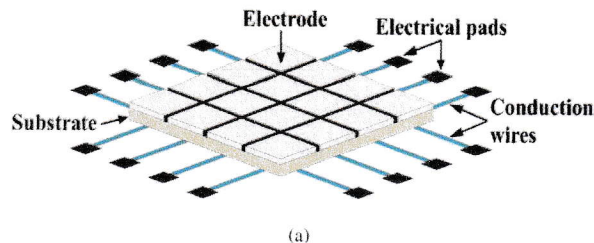


Fig. 1: (a) Schematic of an EWOD-driven digital microfluidic chip [4] and (b) technical barrier and reliability issue are two major bottlenecks that limit the development of EWOD microfluidic community.

system upon, the wide adoption of EWOD chips has been stifled by the following burdens:

- *Control system*: Since EWOD chips are operated by electric signals, an electronic system with multiple instruments such as a voltage source and a software controller is required to realize an accurate control of on-chip electrodes. Moreover, since most applications require to control plenty of electrodes (> 100) independently, making the control system very large and cumbersome. The need of this electronic controller is often a major deterrence to most of the non-engineering labs.
- *Chip fabrication*: The fabrication of EWOD chips is usually not straightforward due to the importance of material qualities as well as chip packaging, and it takes several months for a technician to learn the corresponding techniques with a professional training program. In a typical lab, one would spend most of the resources and time drawing the chip manually and fabricating it without standardized design rules.
- *Non-standardized design*: With each lab building their own EWOD chips for specific applications using different rules and conditions, there is no connectability or interoperability among these devices and systems, thereby inhibiting the synergistic development of the whole EWOD community.

Reliability is another issue that prevents the wide adoption of EWOD chips. The current leakage through dielectric layer (short-term failure) and the electric charging of hydrophobic topcoat (long-term degradation) are two major failure mechanisms that affect the lifetime of EWOD chips [1]. Moreover, the so-called electrowetting saturation [23], perhaps related to the failure mechanisms above, is a hotly debated issue with no conclusive explanation yet. The fundamental issues mentioned above are important to advance the development of EWOD chips, but in reality they are being managed by: choosing high-quality dielectric materials to increase the breakdown voltage, using AC voltage to alleviate the polarity issue, filling the EWOD chip with oil to make the droplet movements easier, etc. Other reliability-related issues include the size of and minimum gap between electrodes, the spacer thickness between the top and bottom plates, etc. These numerous variables indicate the difficulty of EWOD technology despite its apparent simplicity and explain why only a few labs

succeed in utilizing this technology.

The aforementioned bottleneck problems prevent many potential users/researchers from joining the EWOD community and thus slow down the commercialization process of EWOD technology. To overcome these problems and advance the development of the whole digital microfluidic community, in this paper, we propose a cloud-based open-source EWOD cyber-manufacturing ecosystem that enables an automatic translation from user requirements to manufactured digital microfluidics. With standardized chip fabrication and assembly process, by integrating computer-aided design (CAD) tools, foundry service, control systems, as well as online community for user interaction together, the cyber ecosystem allows users to focus on their own ideas and applications without worrying about the engineering and manufacturing technologies of EWOD.

The remainder of this paper is organized as follows. Section II presents the overall framework of the proposed cybermanufacturing system. Section III discusses the details of each module in the proposed system. Finally, the conclusions are drawn in Section IV.

II. FRAMEWORK OF THE PROPOSED EWOD CYBERMANUFACTURING SYSTEM

Inspired by how computer operating systems such as Windows flourished the PC industry, the EWOD cybermanufacturing system aims to boost the digital microfluidic community, by building an exclusive working system of EWOD chip design and fabrication, for people who know little about EWOD engineering and manufacturing.

The EWOD cyber ecosystem resides on a cloud server through which end users can be connected to various online resources. Fig. 2 shows its overall framework. To start with, end users (e.g., a biochemistry researcher) only need to provide an application specification indicating the corresponding experiment protocol/workflow. Polymerase chain reaction (PCR), for example, is a biochemical application used in molecular biology to make many copies of a specific DNA segment [24]. The protocol of this assay usually includes several steps such as reagent mixing, magnetic-bead-based clean up, cyclic heating, etc. [25]. Note that the application protocols can be uploaded to the cybermanufacturing system through a software

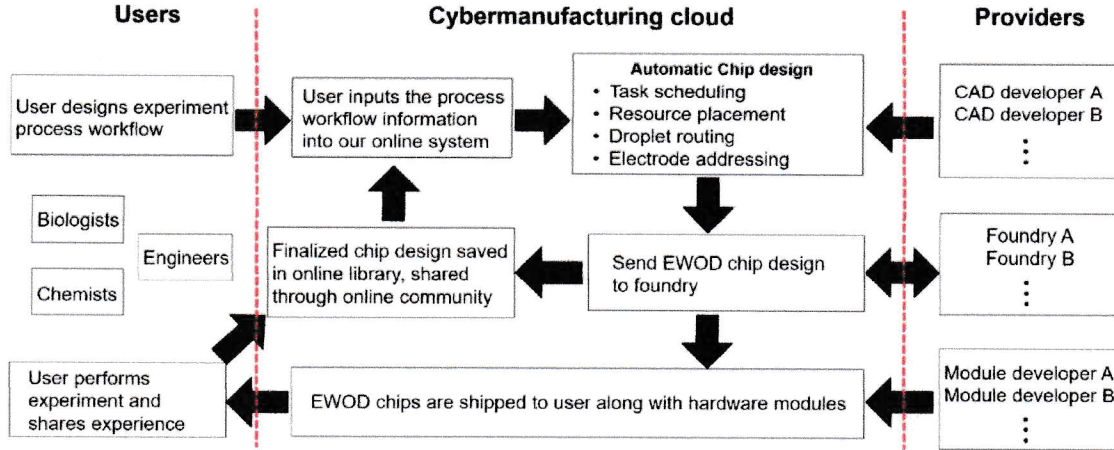


Fig. 2: The overall framework of the proposed EWOD cybermanufacturing system.

wizard that resides in cloud. Moreover, through this software wizard, experimental conditions such as reagent volume, reaction time, temperature, etc., can be adjusted by end users directly. After receiving the application protocols, an automatic EWOD chip design process will be started immediately on the cybermanufacturing system.

Once the chip design is completed, the resulting design files will be transferred to foundries for verification and fabrication, meanwhile the manufacturing status is updated online so that users can grasp the real-time status of their chip orders. Note that orders of all the end users share the same fabrication process with standardized design rules and materials in the proposed system. Furthermore, users can also purchase EWOD control systems and peripheral modules, such as heating element and magnetic actuator, based on their needs through the same cybermanufacturing system. The manufactured EWOD chips, control systems, together with peripheral modules will be shipped to end users once they are completed. In particular, the cybermanufacturing system will also include an online community with effective incentive mechanisms, through which users are encouraged to share their design files and to provide feedbacks after using the chip, thereby facilitating beginners in the field as well as users with similar interests to deal with their design requirements. Fig. 3 shows a potential example of the portal website of the proposed ecosystem.

III. DETAILS OF THE PROPOSED EWOD CYBERMANUFACTURING SYSTEM

In this section, the details of each module in the proposed system are discussed systematically, including automatic EWOD chip design, foundry service, EWOD operating system, as well as online community. These modules are coordinated and cooperated with each other and thus forming an "organic whole", so that users without EWOD technical background

can design and fabricate digital microfluidics for their own needs directly.

A. Automatic EWOD Chip Design

As discussed previously, after uploading the application protocol to the cybermanufacturing system, an automatic EWOD chip design process will be performed to generate an optimized chip architecture. As illustrated in Fig. 2, the design flow consists of the following steps: resource binding and scheduling, module placement, droplet routing, and electrode addressing.

1) *Resource binding and scheduling:* With the application protocol provided by end users, this step aims to find an efficient task scheduling scheme, so that each operation defined in the protocol such as reagent mixing and separating can be bound to specific device to execute, while the overall execution time of the application can be minimized. Moreover, the cybermanufacturing system also provides a component library for operation execution, including reservoirs/dispensing ports, optical detector, magnetic bead actuator, mixer, storage, etc. Note that several operations may be executed in parallel as long as there is no resource conflict among them. For example, the protocol of PCR usually contains many mixing operations [24], some of them can be executed simultaneously if the following conditions are satisfied: 1) the input samples/reagents of these operations are ready to use and 2) there are enough mixers in the component library that can be allocated to execute these operations. In the proposed cybermanufacturing system, existing CAD tools for resource binding and scheduling [26], [27] are adopted directly to generate an optimized solution.

2) *Module placement:* After generating the resource binding and scheduling scheme, placement stage assigns exact locations for the allocated devices on the EWOD chip [28], [29], while considering optimization goals such as chip area,

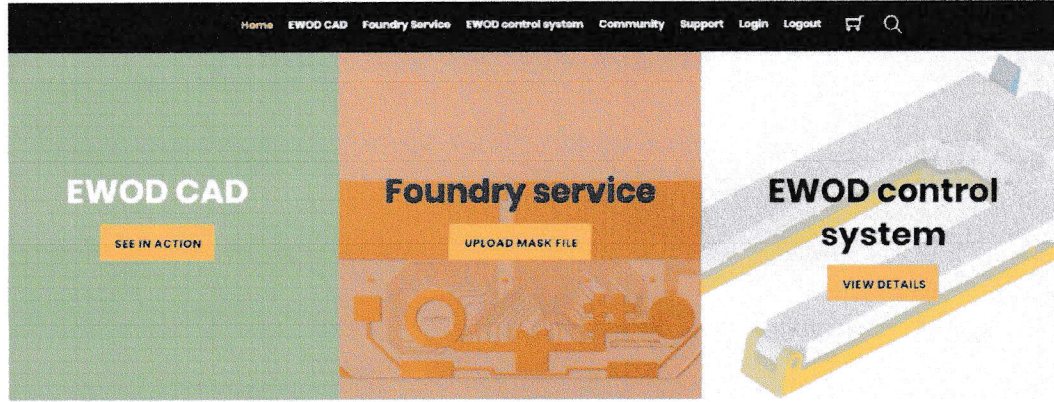


Fig. 3: An anticipated example of portal website of the cybermanufacturing system.

TABLE I: Comparison among EWOD chips made with different manufacturing techniques

Technique	Configurations	Property	Cost
glass	· air with cover plate · oil with cover plate · air with open device	transparent	high
PCB	· oil with cover plate · air with open device	opaque	medium
paper	· air with open device	opaque	low

droplet routability, fault tolerance, etc. Moreover, positions of electrodes are also determined in this step so that droplets can be routed efficiently on the chip surface. Note that electrodes may be time multiplexed for a multi-functional EWOD chip [30].

3) *Droplet routing*: With exact locations of allocated devices and electrodes, droplet routing constructs pathways on the EWOD chip so that reagents and samples can be transported between devices without any conflict, while obeying the previously generated scheduling scheme [31]. The major optimization goal of this step is to minimize the number of electrodes used in each pathway, so that the transportation latency can be minimized accordingly.

4) *Electrode addressing*: To correctly drive the electrodes, electrode addressing is introduced in this step, through which electrodes are assigned to control pins to identify input signals [4] (see Fig. 1(a)). Traditional EWOD chip design, however, relies on direct addressing [30], where each electrode is assigned to a dedicated control pin directly and independently. Though this method maximizes the flexibility of electrode controls, for large-scale electrode arrays, a large number of control pins can be introduced to the chip, leading to very complex electrical connections and high fabrication costs. Accordingly, in the proposed cybermanufacturing system, a pin-constrained design method, also referred to as *broadcast addressing*, is

adopted to achieve a low-cost electrode-addressing scheme [4]. In this method, to reduce the number of control pins used in the chip, electrodes that can be actuated in a compatible manner are connected to a single control pin. In other words, multiple electrodes are controlled by the same control signal and are thus driven simultaneously.

B. Foundry Service

After completing the chip design, a certain chip architecture with high execution efficiency and low total cost is generated. Then, users are able to download the corresponding design files, place an order, and make payment online. The design files as well as the order information will then be transferred to the foundry for manufacturing. Moreover, the ancillary modules used for chip control can also be ordered online by end users. Once the fabrication is completed, the chip entities as well as the corresponding ancillary modules will be shipped to the address specified by users. During this period, end users can log into the system to track the manufacturing, testing, and shipping status. In particular, the proposed cybermanufacturing system is expected to provide three distinctive foundry services assigned to different manufacturing facilities, including 1) the glass-based EWOD chip, 2) the printed circuit board (PCB)-based EWOD chip, and 3) the paper-based EWOD chip. The trade-offs among these manufacturing techniques are listed in Table I.

The glass-based EWOD chips are fabricated inside a clean-room and such chips take full advantage of the microfabrication facilities. The flatness of chip surface, the gap between electrodes ($< 10\mu\text{m}$), as well as the quality of the dielectric layer are the best among the three techniques. These advantages enable various droplet manipulations such as moving and mixing can be performed directly in air environment. In particular, since glass materials have the advantage of transparency, users can observe the on-going biochemical operations continuously when using a glass-based EWOD

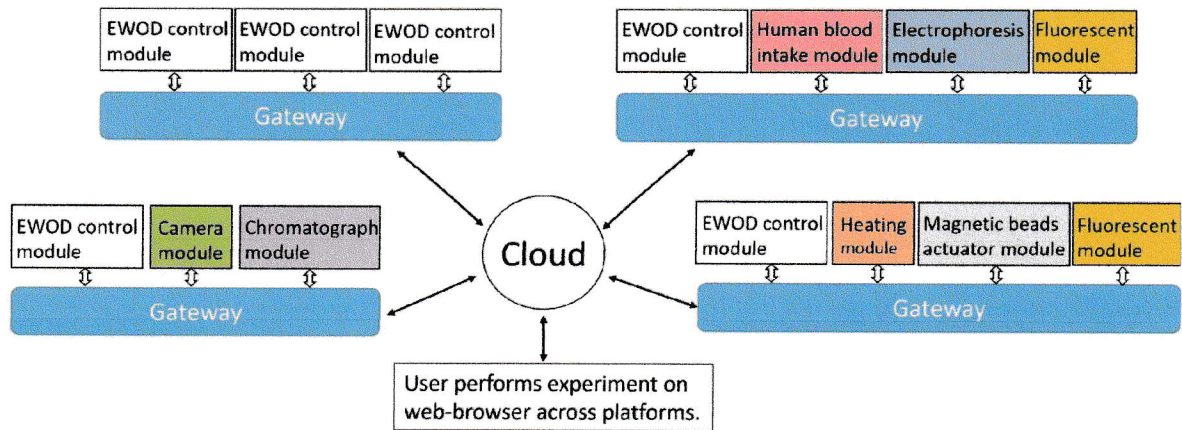


Fig. 4: Illustration of the hardware-software co-designed gateway.

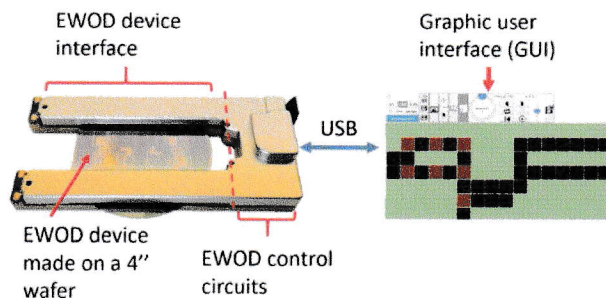


Fig. 5: An assembled digital microfluidic device, where the EWOD control circuits, the EWOD device interface, and the graphic user interface form an operating system essentially.

chip, thus grasping the overall execution procedure of applications. In comparison, PCB-based EWOD chips require oil environment to manipulate the movement of droplets, but the fabrication cost is lower than that of the glass-based EWOD chips. Moreover, paper-based EWOD chips have the lowest fabrication cost and the shortest manufacturing cycle, but the performance of such chips is usually inferior to the other two types of chips. It can be seen that the aforementioned manufacturing techniques each have their own advantages and shortcomings. Correspondingly, end users can select any one of them for chip fabrication according to their budgets and product requirements.

C. The EWOD Operating System

After receiving the fabricated EWOD chip and the corresponding ancillary modules, these components can be assembled to form a complete and ready-to-use digital microfluidic device. To coordinate the operation of these modules, as shown in Fig. 4, a hardware/software co-designed gateway is integrated into the proposed cybermanufacturing system,

through which multiple EWOD modules can be synchronized to work in a collaborative manner. Furthermore, gateway also allows end users to remotely control these modules at different locations through a graphic user interface (GUI) resided in cloud. The online GUI also enables users to save and share their operation sequence of the EWOD chip, so that other users who want to duplicate the experiment can order the same EWOD chip directly and replay the operation sequence automatically.

Fig. 5 shows an assembled digital microfluidic device, which includes an EWOD chip made on a 4" wafer, an EWOD control circuit, and an EWOD device interface. Moreover, through a USB cable, the EWOD control circuit is connected to an online GUI, essentially forming an EWOD operating system. This operating system provides end users with the following functions: 1) drive the operation of EWOD chips in different types, sizes, and application goals, 2) enter operating commands in a line-by-line manner, and 3) debug and perform stress test on any local region of the EWOD chip.

D. Online Community

As discussed in Section II, the proposed cybermanufacturing system will also establishes an online community for end users to share and discuss their experiments as well as EWOD chip experience. Incentive mechanisms such as discounts for orders and ranking of users' profile are adopted to encourage end users to share their design files and to provide feedbacks on their chips. In this way, other users can modify and combine existing experiment protocols and designs to create EWOD chips with more complex functions. Furthermore, users are also encouraged to ask/answer questions through an online forum, and senior users will be invited to give talks periodically in the online community.

IV. CONCLUSION

In this paper, we have proposed a cloud-based EWOD cybermanufacturing ecosystem to allow a wide range of users using digital microfluidics with little training. This cyber ecosystem integrates chip design, foundry service, operating system, and online community as an “organic whole”. Sitting in front a computer and performing mouse clicks, users can have their digital microfluidics designed, fabricated, and delivered. The EWOD cybermanufacturing system is proposed to serve as an accelerator in application exploration and new product development of digital microfluidics, thus advancing the development and progression of the whole microfluidic community.

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