Mechatronic Systems in Digital Microfluidics

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Abstract: A mechatronic system to drive and control a digital microfluidics (DMF) microchip is developed and demonstrated. It features two key functionalities for digital microfluidics: (1) the application of different driving forces/frequencies through integrated electronic circuitry, and (2) the capability of programming a series of DMF actuations on electrodes for automation with a friendly graphical user interface (GUI). Integration of a real-time monitoring system can expand system functionality to achieve a fully closed-loop control for practical applications. This article provides a guideline for the construction of a mechatronic system for DMF, which thus allows the utilization of a DMF microchip to automate biological laboratory procedures.

Keywords: Automation; electrowetting; mechatronics; robotics; LabVIEW

Introduction

Digital microfluidics (DMF), which focuses on the manipulation of tiny discrete liquids, or droplets, has recently attracted increasing interest for diverse applications [1-8]. It presents a new approach to handle liquids in miniaturized systems to reduce sample and reagent consumption. The liquid droplets in DMF are usually controlled as discrete droplets on an array of independent electrodes. The fluids can be manipulated as individual droplets by applying a series of signals to these electrodes. The droplets can be created from the reservoir, mixed with others and split into multiple droplets. Operations are carried out using simple mechanisms to control the electrodes. DMF does not require the use of pumps or valves. Multiple droplets can be controlled simultaneously and droplet operations can be programmed without changing the device design [9]. The re-programmability and easy controllability permits DMF with a high degree of flexibility, making it suitable for applications requiring complex, multistep protocols [10, 11]. A variety of reactions can be performed on a single DMF microchip to generate a variety of different products [12, 13]. Liquid reagent volume can be precisely controlled in the range of 100 ~ 1500 nL. No current is present, thus minimizing the production of heat and electrochemical reactions.

To use DMF technology in personalized medicine and point-of-care applications, full laboratory procedures must be conducted on a single DMF device. More importantly, the control circuitry and power source used to drive the DMF microchip must be suitably robust for use in the field. Most such devices currently integrate various laboratory instruments, including function generators, power amplifiers, data acquisition systems and other electronic components. This raises the need for a mechatronic system which can provide the required actuation signals to the corresponding electrodes for the programmed sequences to drive the DMF device.

This article proposes such a mechatronic system to drive and control a DMF microchip and discusses its design guidelines. The system requires two key functionalities for DMF: (1) the application of different driving forces/frequencies through integrated electronic circuitry, and (2) capability of programming a series of DMF actuations on electrodes for automation with a friendly graphical user interface (GUI). Integration of a real-time monitoring system can expand system functionality to achieve a fully closed-loop control for
practical applications. This article provides a guideline for the construction of a mechatronic system for DMF, which thus allows the utilization of a DMF microchip to automate biological laboratory procedures.

**DMF configuration**

Figure 1 illustrates a typical configuration of a DMF device, where discrete droplets are manipulated between two glass plates (gap=60μm). The top plate is a blank ITO glass covered by a hydrophobic layer (e.g., Teflon), while the bottom plate consists of an array of patterned electrodes coated with a dielectric layer and a hydrophobic layer.

![Figure 1. Basic configuration of a DMF device. A liquid droplet is driven to the right as an electrical potential is applied to the electrodes in the top and bottom plates.](image)

**DMF Microchip**

Figure 2(a) illustrates the generalized fabrication procedures of a DMF microchip. Photolithography is used to define the electrode patterns using an ITO glass. A dielectric layer is then coated to insulate the working fluids from the electrodes. A negative photoresist - SU-8 – with a thickness of about 1.5 μm is used. This layer can allow for a stronger electric field and permit a more significant electromwetting effect or a larger pressure difference to drive the droplet before incurring electrical breakdown or current leakage [14]. The chip is then coated with a thin film of a hydrophobic material (e.g. Teflon). In this study, the thickness of the Teflon layer is about 55 nm; this layer facilitates smaller contact angle hysteresis, thus allowing working fluids to move easily. The top glass contains an unpatterned ITO as a common ground electrode. The hydrophobic material (Teflon in this case), is dispensed. A spacer (e.g. photoresist tape) is used to define the gap between the bottom and top plates. A DMF device can be obtained as shown in Fig. 2(b).

**System Architecture of DMF Actuation**

To move droplets on DMF devices, one must apply the correct actuation signals on the corresponding electrodes. For instance, four fundamental operations

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(i.e. transportation, division, merging, mixing) are conducted in an air-filled environment using an electrical potential range of 25~100 V [15-17], though lower voltages can be used if the droplet is driven in silicone oil. Therefore, an electrical circuit capable of providing the device electrodes with a series of voltages from 25V to hundreds volts is required.

Figure 3. (a) System architecture to drive and control a DMF microchip. (b) Typical laboratory setup to drive a DMF system.

Figures 3(a) and (b) exemplifies the experimental setup, which is commonly used in research laboratories, for a DMF device to drive droplets. Voltage signals are initially generated by a function generator and being sent to an amplifier, which transfer converts small signals to larger signals which are then and transmitted to the DMF device. A connector, which facilitates easy attachment to and removal of the DMF microchip from the wirings of the actuation signals from the function generator.

Mechatronic Implementation and Design Considerations

Connector

A connector is used to temporarily connect a DMF device to the wiring terminal of a circuit for rapid tests, inspections or evaluations, facilitating easy attachment to and removal from the DMF control circuitry. One possible approach is to use a PogoPin type, as seen in [18] Another possible design is to have a connector like a paper clip, or to use a spring probe as a simple mechanical device to create an electrical connection between the DMF microchip and the wirings from the power source. Figure 4 shows an example. The spring can connect the DMF microchip and the connector with wirings. Pinching the connector opens the prongs (Fig. 4(c)), while releasing the connector allows the spring to pull the shut so that the connector holds the DMF device tightly (Fig. 4(d)). Each pin would contact one single electrode of the microchip.

Figure 4. (a) A DMF microchip and a connector were assembled together. (b) The connector can function as a clip. (c) The prongs in the connector open up, when the connector is pinched. (d) When the connector is released, the connector holds the DMF device tightly.

Electronics: Relay

To control individual droplets, the actuation signals must be applied to every electrode independently. This can be achieved by the use of a relay. A relay is a switch which can be operated at a low-power signal by electromagnetic, mechanical, solid-state or optical mechanisms, with appropriate electrical isolation between the control and actuation circuits.

In our system, the relay can be controlled by signals from a computer, a microcontroller unit (MCU), or an In/Output (I/O) interface card. Figure 5 illustrates such a generalized circuit scheme with relays to switch the actuations for a DMF microchip.

Figure 5. Circuit scheme with relay circuitry to control the actuations on a DMF microchip
In addition, as the requirement for DMF actuation is different from common applications of the relay on a commercial frequency at 50 or 60Hz with standard voltages of 6, 12, 24, 48, 100, and 200V, an appropriate relay must be carefully selected for DMF actuation, which may include:

1. Type of contacts – relays usually have two types: normally-open or normally-closed. A “normally-open” relay is used to minimize the power required to turn on the relays when controlling multiple electrodes on a DMF microchip at the same time.

2. Voltage rating of contacts and isolation between coil contacts: Because the DMF actuation may require AC actuations up to hundreds volts at 1kHz to MHz, the relay needs to be synchronized with the AC load, which can drastically shorten device lifetimes.

Control Interface

To simplify the multiple electronic components, a mechatronic system was integrated as shown in Fig. 6. A power source was used to provide the actuation signals to the DMF microchips with hundreds of voltages at 1~2MHz. Control signals could be programmed by users from a PC through USB and I/O interfaces, as well as sent to the relays to switch the actuation signals. The I/O interfaces could be either a data-acquisition (DAQ) card or a microcontroller (e.g. Arduino, Raspberry Pi, Freescale Freedom Broad, or ARM-based controller) at a much lower cost. Signal conditioning might be required if such microcontrollers are used.

Electronics Integration

The actuation voltage setup shown in Fig. 3 requires a variety of instruments, including a function generator, a power amplifier, and I/O cards. For commercialization or point-of-care applications, this setup needs to be integrated with proper electronics for portability at moderate cost.

The electronics therefore should provide the functionalities of the function generator and power amplifier. Considering the voltage requirement of DMF actuation, a voltage output of 0~400 Volts at DC or 1Hz~2MHz is needed for most common liquid applications on a DMF device.

Various solutions exist using a waveform generator with or without microcontroller chips. These approaches can produce high quality sine, square and triangle waveforms with high stability and accuracy. The output waveforms can be both amplitude- and frequency-modulated. Coarse frequency adjustment is accomplished using switches to produce the desired frequency ranges between 1Hz and 2MHz. The output amplitudes can be between 0 and 3 V with 5 V DC input.

To further boost the signal amplitudes for DMF actuation, a high voltage power amplifier is needed. For instance, a 400~500 V power operational amplifier that can have output voltages of ±200~250 V on dual supplies and a high frequency of power bandwidth can be employed. The output currents can go up to 200 mA. In practice, current limit resistors must be connected and additional external protection is recommended for safety and input protection. Figure 7 shows a prototype built based on the abovementioned guidelines.

Software

LabVIEW

LabVIEW is one of the most popular graphical programming languages and used extensively in industrial and academic environments. LabVIEW 2011 is used here as a simple interface to program the desired manipulation of the electrode to control the droplet movement. Controlling the actuation potential on the electrodes of the DMF microchip is straightforward. Figure 9 shows the panel containing the controlling bottoms in a layout similar to the electrode layout in the DMF microchip. A graphic user interface (GUI) provides an intuitive and easily reprogrammable interface.
Graphic User Interface (GUI)

Figure 9 shows a screenshot of the developed GUI, featuring three panels. The central panel is the control panel, allowing users to activate and deactivate electrodes on the DMF device by clicking the corresponding buttons. On the left, a smaller GUI screen allows users to select manual or automatic operating modes for respectively applying the electrical potentials step by step or based on programmed sequences. In addition, the users can determine the switch time of each electrical signal. At the bottom, a scheduling panel contains an array of the circles representing the electrodes to be actuated, allowing users to program the electrode actuation in a sequence.

Results

Actuation Voltages and Waveforms

To compare the characteristics of our mechatronic systems in Fig. 7 to those of the instrument shown in Fig. 3, the output waveforms from these two instruments were compared in Fig. 10. The mechatronic system contains a built-in waveform generator, amplifier, and relay circuits, and can be easily connected to the DMF device through a clip connector and controlled by PC via a USB cord. These actuation signals from the mechatronic system are shown as Channel 1, while Channel 2 shows the signals from the commercial instruments in Fig. 3. Different waveforms in the sine and square waves at 1kHz ~ 10kHz from 120 ~360 Vpp, respectively, were provided through relays. The signals from our mechatronic systems were supplied to a DMF device through a clip connector and successfully drove the water droplets. The droplet behaviors actuated with the signals from Channel 1 and Channel 2 in changes to the contact angle, while their respective speeds were almost identical without noticeable differences at constant actuation voltages and frequency, which validated the feasibility and applicability of the mechatronic system for a DMF microchip.

Conclusion

DMF has become increasingly popular in Lab-on-a-Chip applications, driving the need for mechatronic systems to drive and control different droplets on a DMF device. We discuss the design considerations such a system for DMF devices and demonstrated the system’s ability to measure instantaneous drop velocity and to control the applied electrostatic force. We believe that these combined features will be useful to end-users developing new assays or characterizing and optimizing device designs and controls.
Reference


