Digital Microfluidic Droplet Adapter for Interconnection of Biochips

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Abstract: As Digital Microfluidic Biochips (DMFBs) become more and more popular, large-scale integration of DMFB microarrays is desirable. Multiple DMFBs with different electrode size from various manufacturers may need to be integrated into a single chip. However, the incompatibility of electrode size poses a problem for the integration of multiple DMFBs. In this paper, a droplet size adapter to convert microfluidic droplets into different sizes is reported. In this way, the droplets coming out from one DMFB can be input to another DMFB to continue the processing. The function of the proposed adapter is verified with COMSOL simulation. COMSOL Multiphase Flow Model, Laminar Two-Phase Flow (tpf) and Level Set method are used in the simulation. The adapter allows bi-directional size conversion of microfluidic droplets. Reverse conversion can be achieved by simply reversing the voltage sequence. The proposed adapter can be used for the integration of multiple DMFBs with different electrode sizes.

Keywords: Digital microfluidic biochips (DMFB), droplet size adapter, COMSOL simulation, DMFB integration, Lab-on-a-chip (LoC).

1. Introduction

Digital Microfluidic Biochips (DMFBs) handling discrete microfluidic droplets have been used in DNA analysis, micro drug delivery, biomolecular recognition and other applications [1]. Compared to the traditional continuous flow microfluidic devices (also called "analog microfluidic biochips"), DMFBs have the advantages of significantly reduced sample size, low energy consumption, high throughput, as well as being reconfigurable and scalable in its architecture. The design automation [2], scheduling [3], fault model and testing [4], fault tolerance and reconfiguration [5] of DMFBs have been reported by many researchers. It is believed that DMFB technology will follow the similar trends as VLSI (Very Large Scale Integration) technology. Large scale integration of DMFBs with thousands and even millions of electrodes may eventually become possible. This would enable high-throughput handling of large amount of microfluidic droplets for more complex functionalities. Many concepts and algorithms in VLSI field such as scan-test [6], built-in self-test [7] have been transplanted into DMFBs. Currently DMFBs are still very small scale with tens of electrodes. Most DMFBs are individual components for customized applications. With the progress in microfabrication technology, DMFBs may eventually be fabricated in large scale with hundreds and thousands of electrodes. Board level integration of DMFBs from different manufacturers may become necessary. This allows DMFBs to grow significantly in its complexity so that more advanced functions can be achieved.

Up to now, very few research works about system integration of DMFBs are reported. In [8], the architecture for the integration of multiple DMFBs was proposed. It focused on the control and integration circuit design for coordinating the signals from multiple individual DMFBs to perform decision based testing. That is, each individual DMFB communicates with the control and integration circuits, but the DMFBs are not directly connected to each other to share the microfluidic droplets. For system integration of DMFBs, it may be necessary to connect multiple DMFBs into a single System-on-Biochip (SoB), so that the droplets coming out from one DMFB can be fed to the next DMFB for continuous processing. Since different DMFBs may have different electrode size, the droplet size incompatibility poses a problem for sharing the droplets among different DMFBs. Furthermore, inside one DMFB chip, electrodes with different size may be incorporated depending on the needs. In order to overcome this electrode/droplet size incompatibility issue, a microfluidic size adapter which can quickly convert the droplet into different size is needed. This allows DMFBs with different electrode size to be integrated together so that more complex functionalities can be achieved. In this paper, a DMFB size adapter to quickly convert droplet between different sizes is proposed. The size adapter is bi-directional and reverse size conversion is enabled by just reversing the voltage sequence. COMSOL simulation is used to verify the function of the size adapter. The size adapter allows DMFBs with different electrode sizes to be directly connected together, so that they can be integrated into a larger scale system.

2. Microfluidic Droplet Size Adapter Design

The proposed digital microfluidic droplet size adapter for interconnecting DMFB chips is shown in Figure 1. It includes input port, droplet size converter, T-shape droplet splitter, and several output ports. The droplet size converter consists of a large electrode with a small electrode embedded inside of it.

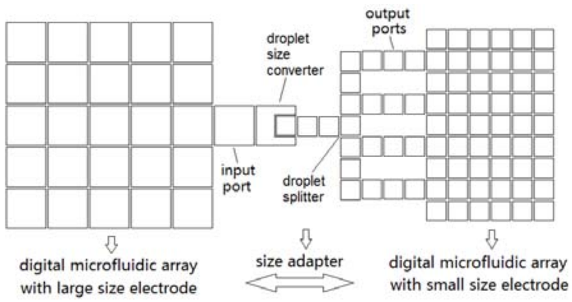


Figure 1. Design of microfluid droplet size adapter for interconnect of biochips

The working principle of the droplet size adapter is explained as below. When a large droplet comes to the input port of the size adapter from the left DMFB, it is driven to move to the size converter electrode first. A voltage pulse sequence will be applied to the small electrodes in its right side so that a small size droplet is dispensed out of the big droplet. The smaller size droplet is then further split into two equal-size halves by the T-shape splitter. After that, the process is repeated so that another small size droplet is dispensed from the remained part of the original big droplet and split into two smaller droplets. The obtained four equal-sized small droplets will then be driven along the horizontal arms to the right-size DMFB with smaller electrode size to continue the processing. The designed microfluidic size adapter is bi-directional. When it is used in the reverse direction, it can also convert smaller size droplets into larger size droplet. That is, two smaller size droplets from the DMFB in the left side will be merged together and driven into the droplet size converter. After that, another two smaller size droplets can be merged and driven into the droplet size converter to further merge into an even larger droplet. It is then driven to move into the DMFB in the left size for processing. This allows DMFBs with different electrode size to communicate directly with each other so that droplets can be shared in between.

In order to verify the function of the microfluidic droplet size adapter, a 3D COMSOL model is developed, as shown in Figure 2. The behavior of microfluidics is very complex. COMSOL simulation [9] is used to verify the function of the microfluidic size adapter and understand its working mechanism. The simulation results further guide us in the optimization of the design parameters of the device.

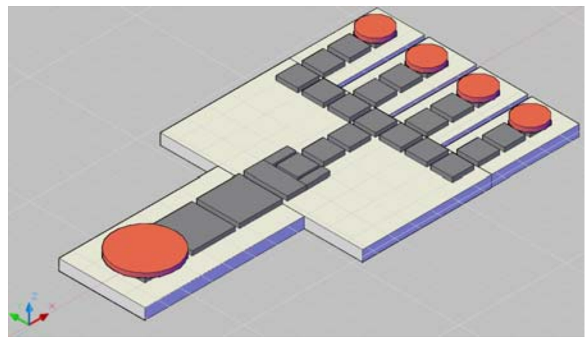


Figure 2. COMSOL model of the microfluidic droplet size adapter

Most DMFBs utilizes Electrowetting-on-dielectric (EWOD) for the actuation of droplets. As shown in Figure 3, a microfluidic electrolytic droplet is sandwiched between top and bottom glass plates with buried control electrodes [1]. The top common electrode plate is grounded, while the bottom embedded electrodes are individually addressable. A thin insulation layer (with thickness *t*) is coated on the bottom plate so that no current will be conducted through the droplet. Surfaces of both top and bottom plates are treated to be hydrophobic for smooth droplet actuation. The contact angle of the droplet will be reduced (hence the wettability is improved) by applying a voltage between its bottom plate and the top ground plate. By applying a voltage pulse to the electrode right next to the droplet, electrowetting causes the droplet to be deformed and eventually driven to move to the next electrode. The theory about how the electrode controls the actuation of droplet is still not well understood due to the complexity of microfluidic behavior. But Lippmann-Young equation can be used to predict the change of contact angle of droplet [10]. Assume θ_0 is the initial contact angle of the droplet, θ_V is the contact angle when voltage V is applied,

$$\cos\theta_V = \cos\theta_0 + \frac{\varepsilon_r \varepsilon_0 V^2}{2t\gamma_{lg}} \tag{1}$$

where, ε_r is the permittivity of the insulator layer, ε_0 is the dielectric constant of the vacuum, V is the voltage, t is the thickness of insulator layer, γ_{lg} is the surface tension between liquid and gas interface.

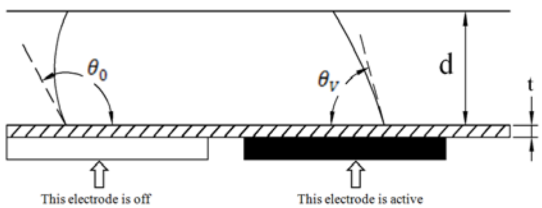


Figure 3. cross-section of the change of contact angle of droplet when voltage is applied [10]

Due to the contact angle difference at both ends of the droplet, a net force will act on the droplet and drive it to move. The equation of droplet's driving force f_m can be calculated as [11]

$$f_m = \gamma_{lg} (\cos \theta_V - \cos \theta_0) \quad (2)$$

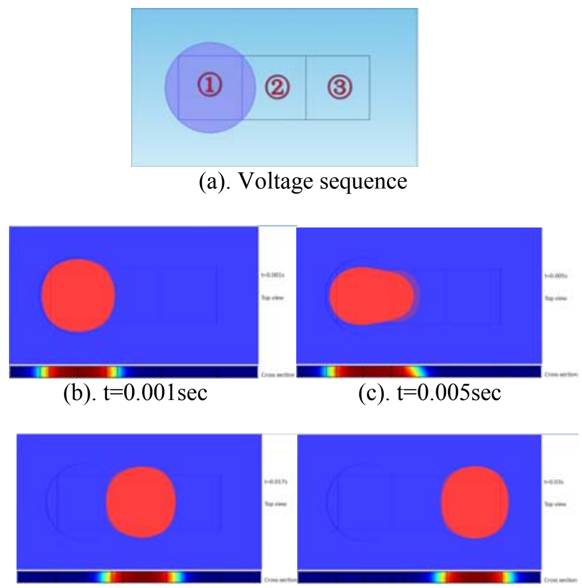
When the electrode is active, the contact angle will decrease according to the Lippmann-Young equation. That is, $\theta_V < \theta_0$, so the $f_m > 0$, the droplet will be driven to move forward. Electrowetting-on-dielectric (EWOD) actuation can manipulate microfluidic droplets to move, split, merge and perform other movements. The above theory is also used to analzye the movement of the microfluid inside the droplet size adapter.

3. Use of COMSOL Multiphysics

In this research, we used COMSOL Multiphysics to verify the function of the designed droplet adapter. Before simulating the microfluidic behavior inside the droplet adapter, we first started with the simulation of three basic droplet actuation behavior: moving, mixing and splitting of droplets. During COMSOL simulation, we used the Multiphase Flow model, Laminar Two-Phase Flow (tpf) model, as well as Level Set method.

3.1. COMSOL Simulation – Droplet Moving

The COMSOL simulation result of moving a single droplet with electrowetting-on-dielectric (EWOD) actuation is shown in Figure 4. The voltage sequence applied to electrodes to drive the droplet to move is shown in Figure 4(a). The squares are the electrodes, and the circled numbers show the order of voltage applied. The droplet is initially on the left electrode. The three electrodes are then activated consecutively with a voltage pulse of 85V. That is, the driving voltage pulse is first applied to electrode #1, and then to electrode #2, and then to electrode #3. The size of the droplet is slightly larger than the electrode so that it has a small overlap with the next electrode. This allows the droplet to be easily dragged to the next electrode when activated. Figure 4 (b), (c), (d), (e) show the COMSOL simulation results of the droplet (top view and cross-sectional view) at time t=0.001sec, 0.005sec, 0.017sec and 0.03sec respectively. From the simulation results, we can clearly see that the droplet is first dragged to cross the boundary between electrode #1 and #2, and eventually totally moved to electrode #2. The same procedure will occur again when the droplet is moved from electrode #2 to electrode #3. The complete droplet is moved without any residue. The movement of the droplet exactly follows the pattern of the applied voltage sequence.



(a). Voltage sequence

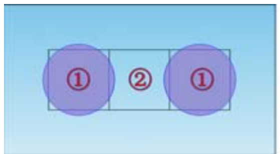
(b). t=0.001sec (c). t=0.005sec

(d). t=0.017sec (e). t=0.03sec

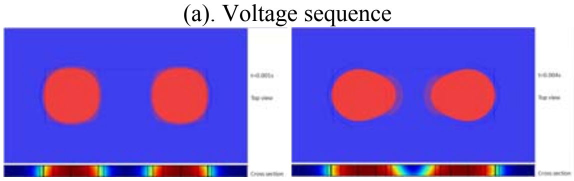
Figure 4. COMSOL simulation of droplet moving

3.2. COMSOL Simulation – Droplet Mixing

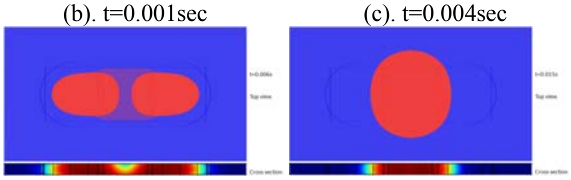
Droplet mixing can be achieved by moving two droplets toward each other. The COMSOL simulation results of droplet mixing is shown in Figure 5. In Figure 5(a), the applied voltage sequence is marked as numbers inside the electrodes. Two droplets are initially located in both side electrodes (marked with #1). After 0.002sec, both side electrodes are deactivated, and the central electrode is activated immediately at the same time. Both droplets will then move toward each other and collide at electrode #2 in the middle and merge into a larger droplet. Figures 5(b), (c), (d), (e) show the COMSOL simulation results of the microfluidic droplet (both the top view and cross-sectional view) at t=0.001sec, 0.004sec, 0.006sec and 0.015sec, respectively. Microfluidic droplets are laminar flow and their mixing can be challenging. By driving two droplets to collide with each other, the introduced disturbance helps the mixing process and eventually two droplets merged into a large droplet.



(a). Voltage sequence



(b). t=0.001sec (c). t=0.004sec

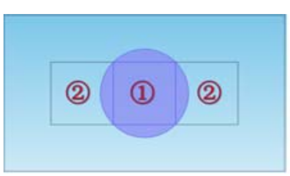


(d). t=0.006sec (e). t=0.015sec

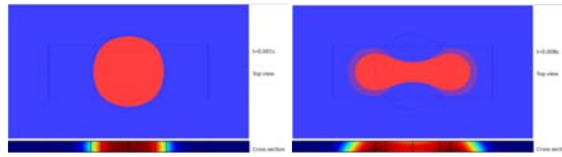
Figure 5. COMSOL simulation of droplet mixing

3.3. COMSOL Simulation - Droplet Splitting

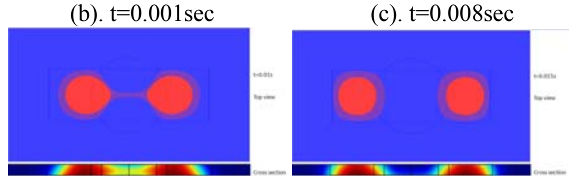
The voltage sequence to split a microfluidic droplet is shown in Figure 6(a). To split a microfluidic droplet, the droplet is first located in the middle of three neighboring electrodes (marked as #1). After that, the central electrode is deactivated, and both side electrodes are activated at the same time (marked as #2). The EWOD actuation will drag the droplet from both sides. The COMSOL simulation of the droplet (both top view and cross-sectional view) at time t=0.001sec, 0.008sec, 0.01sec and 0.015sec are shown in Figures 6(b), (c), (d), (e) respectively. Due to the dragging from both ends, the droplet narrows down in the middle, and eventually splits into two smaller droplets.



(a). Voltage sequence



(b). t=0.001sec (c). t=0.008sec



(d). t=0.01sec (e). t=0.015sec

Figure 6. COMSOL simulation of droplet splitting

4. COMSOL Simulation Results and Discussion

Based on the understanding in COMSOL simulation of droplet moving/merging/splitting, we designed and simulated the microfluidic droplet size adapter, as shown in Figure 7. Due to the complexity of microfluidic behavior, it takes excessive time to complete one round of COMSOL simulation. To simplify the simulation, we only simulated the microfluidic behavior in the size adapter, and the complete DMFBs in both sides are not included in the model. As shown in Figure 7, the microfluidic size adapter consists of three parts. The left part is the input port of the size adapter. It consists of three large size (2mm×2mm) electrodes connected in series. The right part is the output lines of the size adapter. It consists of four parallel lines of smaller size (1mm×1mm) electrodes. In the middle part, it consists of a size converter (a large electrode with enclosed small electrode) connected to a T-shape splitter (with nine 1mm×1mm small electrodes) to further split the droplet coming out from the size converter. The proposed design is actually a 4:1 size adapter. However, such design can be adjusted to any other size ratio as well. This microfluidic size adapter can change the size of droplet pass through it, so that the droplet coming from one DMFB can continue to be processed in another DMFB with different electrode size. The design parameters of the size adapter and the material properties used in COMSOL simulation are listed in Table 1 and 2 separately.

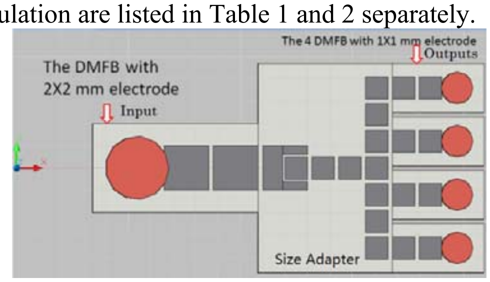


Figure 7. Top-view of microfluidic droplet size adapter design

Table 1. Design parameters for COMSOL simulation

Design Parameters	Values
Size of large electrode	2mm×2mm
Size of small electrode	1mm×1mm
Droplet height D	0.15mm
Actuation voltage V	85V
Initial contact angle θ_0	125°
Contact angle θ_V with voltage applied	45°
Insulation layer thickness t	1μm
Liquid-gas interfacial tension γ_{lg}	50×10^{-3}N/m

Table 2. Material properties used in COMSOL simulation

Material Property	Microfluid (CP)	Silicone Oil (DP)
Density (kg/m^3)	1000	1000
Dynamic viscosity (mPa· s)	1.5	8

4.1.Forward size conversion of the 4:1 size adapter

The applied voltage sequence for forward size conversion of the 4:1 size adapter is shown in Figure 8. The order of the applied voltage pulses are clearly listed in each electrodes as circled numbers. It requires totally 12 consecutive stages of voltage pulses to complete the size conversion process. Starting from electrode marked with number "1", a pulse voltage will be applied to electrodes consecutively stage by stage, till the final stage of "12". As a result, a large droplet coming from left size electrode will be split into four equal-size small droplets coming out from four parallel output ports.

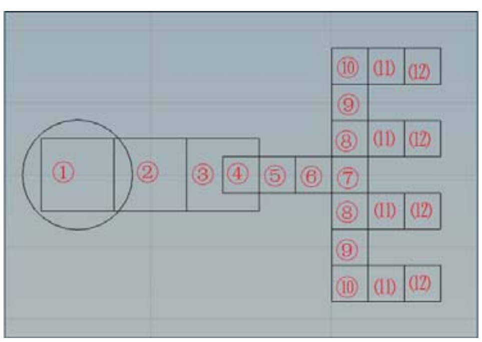
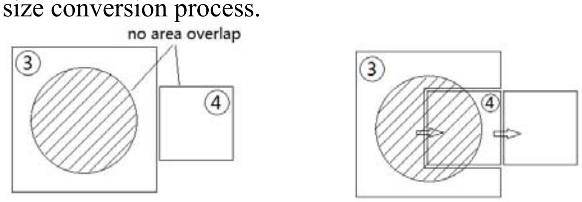


Figure 8. Voltage sequence for microfluidic size adapter

The key part of this size adapter is the size converter electrode: a large size electrode (marked with number "3" in Figure 8) with embedded small size electrode (marked with number "4") along its right side. This size converter electrode actually implements the size conversion process. The reason for this special design is explained as below. As shown in Figure 9(a), if the size converter does not have enclosed smaller electrode, after the first small droplet is separated out, the volume of the remaining droplet shrinks and it recesses back to the center of the electrode. As a result, it loses area overlap with its neighboring electrode, and the next electrode would not be able to drag it out. Thus the remained droplet will be trapped in the big electrode and the size conversion process cannot continue. However, if a smaller electrode is enclosed inside of the larger electrode, as shown in Figure 9(b), the recessed droplet can still have area overlap with the enclosed small electrode. Thus it can still drag the remaining droplet out and continue the size conversion process.

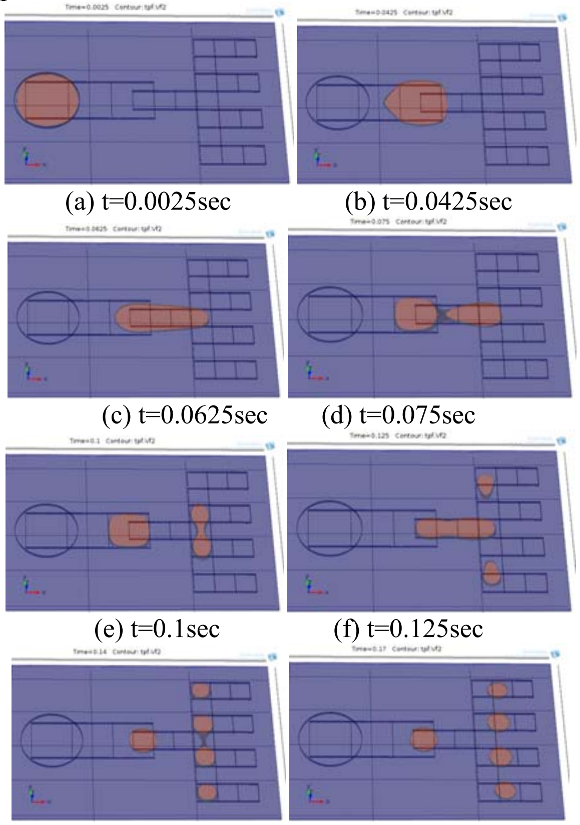


(a). without enclosed electrode (b). with enclosed electrode

Figure 9. Size converter with/without enclosed small electrode

The size converter electrode is the key part for the microfluidic size adapter. Its enclosed structure couples input electrode into the output electrode for droplet size conversion. Theoretically, once we design the enclosed electrodes with one electrode matching the size of input droplet, and the other enclosed electrode matching the size of output droplet, any droplet size conversion can be achieved. T-splitter can be used to further reduce the size of output droplets.

The COMSOL simulation results for the complete size conversion sequence of the microfluidic size adapter is shown in Figure 10. In Figure 10(a), the red circle shows the original droplet coming out from previous DMFB with large electrode size resides on the input electrode. The electrode under it is active to lock the droplet on top of it. At time t=0.0425sec, the droplet is driven to move to the size converter electrode (Figure 10(b)). In Figures 10(c)(d), part of the microfluid is separated out from the original droplet by the size converter electrode and becomes a new smaller droplet. In Figure 10(e), the separated droplet is further split into two smaller parts by the T-shape splitter while the remained droplet is hold inside the size converter. In Figure 10(f)(g), another small droplet is separated from the remained droplet in size converter, and it again is split into two smaller parts by the T-shape splitter. There is still a portion of the original droplet remained inside the size converter after four smaller droplets are converted out of it. In Figure 10(h), after four smaller droplets are converted from the original droplet, they are driven to move along the parallel output ports toward the next DMFB chip with the same small electrode size. The simulation results clearly shows the detailed procedure of how the microfluidic droplet is converted from large size into small size through the 4:1 microfluidic size adapter. It helps us better understand the microfluid behavior in the size adapter, and guide us in finding the optimized design parameters of the device.



(a) t=0.0025sec (b) t=0.0425sec

(c) t=0.0625sec (d) t=0.075sec

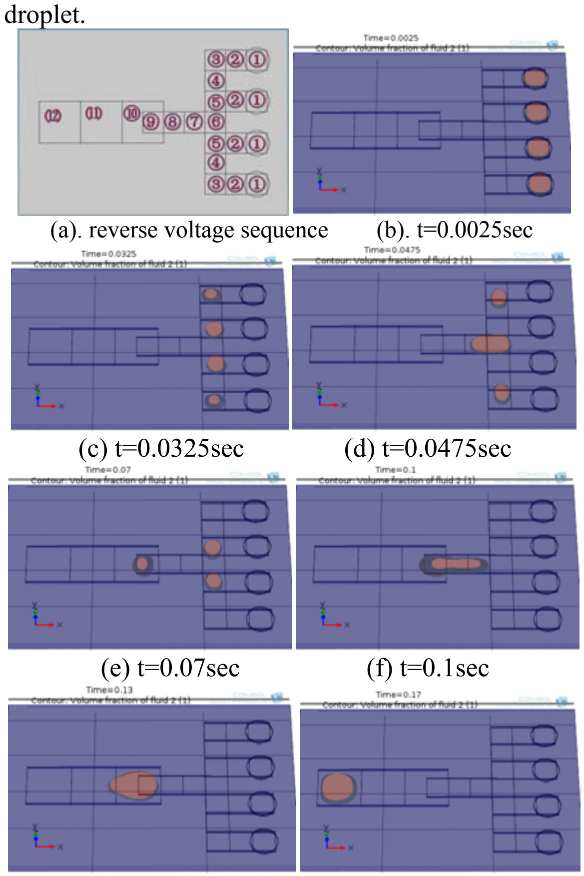
(e) t=0.1sec (f) t=0.125sec

(g) t=0.14sec (h) t=0.17sec

Figure 10. COMSOL simulation result of microfluidic size adapter

4.2. Reverse size conversion of the 4:1 size adapter

The proposed microfluidic size adapter is bi-directional. When the voltage pulses are applied in the reverse sequence, it can also convert the droplet size in the opposite direction. For the proposed 4:1 size adapter, the voltage sequence for the reverse size conversion is shown in Figure 11(a). The COMSOL simulation results for the detailed reverse size conversion process is listed in Figures 11(b)-(h). We can see that by applying the voltage sequence in the reverse order, four small size droplets can be merged back into a larger size droplet, and output to the DMFB with larger size electrodes for further processing. That is, it works as a 1:4 size converter which can combine four smaller droplets into a larger droplet.



(a). reverse voltage sequence (b). t=0.0025sec

(c) t=0.0325sec (d) t=0.0475sec

(e) t=0.07sec (f) t=0.1sec

(g) t=0.13sec (h) t=0.17sec

Figure 11. COMSOL simulation results for reverse size conversion of microflulidic size adapter

The above COMSOL simulation has verified the correct function of the designed microflulidic size adapter. It also helps us to understand the microfluidic behavior inside the size adapter, and guide us in device design optimization. In the size adapter design, the input/output electrode sizes are well defined. However, the droplet volume is designed to be slightly larger than the electrode size, so it still has some variation. Furthermore, the droplets after splitting may not have exactly equal volume. Although this is acceptable for DMFB operation, it is interesting if we can use COMSOL simulation to monitor the volume change of microfluildic droplets after size conversion, and see whether they can be precisely controlled.

In this research, a 4:1 size adapter is used as an example to demonstrate the concept. However, adapters with other size conversion ratio can be designed in a similar way by setting the size of enclosed electrodes in the size converter and the following splitter. Theoretically, any m:n droplet size converter can be achieved once we set the size of two enclosed electrodes in the size converter to match those of the input/output electrodes respectively. Such size adapter allows multiple DMFBs to be integrated together and share the microfluidic droplets in between. It is an important component for large scale integration of DMFBs.

5. Conclusion and Future Work

In this research, the design and simulation of a microfluidic droplet size adapter used to connect multiple DMFB boards with different electrode sizes is reported. The proposed droplet adapter can convert droplet into different sizes, so that the digital droplets can be passed between multiple DMFB boards with different electrode size. This facilitates the system integration of multiple DMFBs with different electrode sizes. A 4:1 size adapter is used as an example in this paper, and the conversion is bi-directional. That is, large droplet can be converted into small droplets, and small droplets can also be merged back into large droplet by reversing the voltage sequence. COMSOL simulation is used to verify the correct function of the adapter and guide the design optimization.

In the future, we will design and simulate microfluidic size adapter with other arbitrary size conversion ratio (i.e. any m:n ratio). We plan to design a "smart" size adapter which can automatically identify the size of input/output electrodes, and convert the size of input droplet to fit that of the output droplet. Such "universal" size adapter offers more flexibility in interconnecting DMFBs with different electrode sizes, and promote the DMFB system integration.

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