Analysis and Extraction of Parametric Variation Effects on Microelectrofluidics-Based Biochips

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ABSTRACT

Microfluidic biochips require continued online test to ensure their functionality, performance, and reliability in the presence of runtime parametric variation and system wear-out. Previous techniques locate catastrophic defects which guide subsequent droplet scheduling and routing procedures. However, a significant number of defects on a microfluidic biochip are parametric variations, taking them as catastrophic defects leads to incorrectly identified defect locations, which compromises droplet scheduling and routing. This paper presents the first characterization method for continuous droplet movement after passing a faulty cell on a microfluidic biochip in the presence of parametric variations, and the first microfluidic biochip parametric variation extraction method locating the critical cells which originate unrecoverable droplet speed loss. The proposed techniques provide better characterization of parametric variations in droplet movement, and enable performance optimization in droplet scheduling and routing on a microfluidic biochip.

I. INTRODUCTION

Microfluidic biochips, also known as lab-on-a-chip or bio-MEMS, are miniaturized integrated micromechanical (MEMS) or microfluidic (MEFS) systems, which automate highly repetitive procedures including sample preparation, fluid transportation, mixing, reaction, separation, and analysis in clinical diagnostics, DNA sequencing, and other procedures in molecular biology.

The first generation of microfluidic biochips are based on continuous fluid flow through permanently etched micro-pumps, micro-valves, and micro-channels. The latest microfluidic biochips are based on moving discrete unit-volume droplets on a two-dimensional array of unit cells, e.g., by electrical actuation. Such “digital” microfluidic biochips are highly scalable and flexible, which enables large scale integration based on nanoscale devices, with defect tolerance provided by reconfigurability (of droplet transportation) [3].

In an electrowetting actuation based digital microfluidic system, droplets containing biomedical samples and the filler medium such as silicon oil are sandwiched between two parallel glass plates (Fig. 1 top). The bottom plate contains an array of individually controllable electrodes, the top plate is coated with a grounded electrode. The hydrophobic dielectric insulator is added to the plates to decrease wettability of the surfaces and increase capacitance between a droplet and a plate. A control voltage is applied to an electrode adjacent to the droplet, while the electrode under the droplet is deactivated (Fig. 1 bottom). The electrical field induced reduction in surface energy causes the droplet to locally spread out. The resulting change in contact angles sets up a pressure gradient which drives the droplet toward the actuated electrode. A droplet can achieve a speed of 20cm/s under a control voltage between 0 and 90V [5, 13].

Such complex integrated systems need a complete set of design and test automation tools [3], including every counterpart of a CAD toolset for a microelectronic system, such as device level simulation [1], cell library construction [12], and system-level simulation, synthesis at multiple levels [2, 7], scheduling [6], placement, routing [4], and parasitic parameter extraction. Functionality, performance, and reliability [11] need to be verified by simulation, validation and testing. Testing [9, 10] needs to be performed not only after fabrication, but also repeatedly during operation, because such microfluidic biochips resemble analog circuits, in that their performance are sensitive to the environmental variations and deteriorate during their lifetime. More often than the catastrophic defects, parametric
variations occur after fabrication or develop during their lifetime, for example, degradation of insulator thickness, and increase of viscosity of the filler fluid, and result in performance degradation [2, 9].

Electrowetting actuated microfluidic flow has its unique characteristics. It is not a continuous flow, in that after moving to a new cell a droplet usually waits for the control voltage to be applied to the next cell. This waiting time provides tolerance for parametric variations and provides recovering mechanism under parametric variations as is presented in this paper. Such uniqueness demands new test methods for electrowetting actuated microfluidic biochips.

Previous publications have presented a straightforward method to locate faulty cells with catastrophic defects [9], while study of parametric variation effect, characterization and extraction of parametric variations have been largely left open. Existing techniques are only able to extract the minimum allowable droplet speed for each droplet path [9].

The contributions of this paper are as follow.

1. The observation that a significant number of defects are parametric variations, taking them as catastrophic defects as in previous publications leads to incorrectly identified defect locations. E.g., a droplet is able to continue to move forward after passing a faulty cell of parametric variations, on the contrary of the claims in the previous publications [8, 9].

2. The first characterization method of continued droplet movement beyond a faulty cell of parametric variations by droplet speed loss, droplet lag distance, droplet grace distance, and maximum reliable control voltage speed.

3. The first parametric variation extraction method which locates critical cells which originate un-recoverable droplet speed loss. The located critical cells help to guide performance optimization in droplet scheduling and routing.

The rest of the paper is organized as follows. Section II introduces microfluidic biochip background, Section III presents the simulation-based droplet movement analysis, Section IV presents the proposed parametric variation test method, Section V gives experimental results, before Section VI concludes this paper.

II. BACKGROUND

A. Microfluid Droplet Motion Model

In a EWOD (electrowetting on dielectric) system, a droplet is actuated by applying a voltage to an electrode which is adjacent to a droplet, which reduces the interfacial energy on one side of a droplet. The resultant contact angle change leads to a pressure gradient, which enables droplet movement for reduced surface energy [1].

The hydrodynamics on a microfluidic biochip is governed by the Navier-Stokes equation and the continuity equation, which are given as follows for incompressible Newton fluid of constant temperature [13].

\[
\rho \left( \frac{\partial V}{\partial t} + V \cdot \nabla V \right) = -\nabla P + \mu \nabla^2 V + f
\]

\[
\nabla \cdot V = 0
\]  

(1)

where \( V \) is the fluid velocity, \( \rho \) is the density of the fluid, \( \frac{\partial V}{\partial t} \) gives acceleration, \( V \cdot \nabla V \) gives convective acceleration, \( -\nabla P \) is the pressure gradient, \( \mu \nabla^2 V \) gives viscosity, \( f \) is the other external force applied to the fluid.

The Navier-Stokes equation and the continuity equation are not easy to solve. The following empirical equation is more practical in depicting electrowetting actuated droplet movement [5, 9].

\[
\frac{\varepsilon_0 \varepsilon_R V^2}{2d} = B \left( \frac{\mu_0 U}{\gamma_{LM}} \right)^{0.3} \gamma_{LM} + \left( \frac{mL}{h} + s \right) \mu B + \zeta U
\]

(2)

where \( V \) is the applied control voltage, \( U \) droplet speed, \( \varepsilon_0 \) the permittivity in free space, \( \varepsilon_R \) the permittivity in fluid, \( d \) dielectric thickness, \( F_T \) threshold, \( \mu_0 \) fluid viscosity, \( \mu \) medium viscosity, \( \gamma_{LM} \) interfacial tension, \( L \) cell length, \( h \) droplet height, \( \zeta \) friction, and \( B, m, \) and \( s \) are coefficients.

The resultant droplet speed \( U \) is the average for a droplet to move between two adjacent electrodes. If the control voltage moves slower than this droplet speed \( U \), the droplet waits for the control voltage to be applied to the next cell. If the control voltage moves faster than the droplet speed, \( L \) becomes increasing large, leading to droplet deceleration and eventual complete stop of droplet movement.

B. Defects on a Microfluidic Biochip

A microfluidic biochip is a composite microsystem, e.g., a microelectromechanical (MEMS) or microelectrofluidic (MEFS) system, wherein defects can be categorized as catastrophic and parametric, e.g., as in a microelectrical system. Catastrophic defects on a microfluidic biochip bring a droplet to a complete stop and result in malfunction of the system, while parametric variations decelerate a droplet and lead to system performance degradation (which in severe cases accumulates and leads to a complete droplet stop hence system malfunction). Such defects include: (1) dielectric breakdown, i.e., a short circuit forms between a droplet and the underlying electrode, which prevents further transportation of the droplet, (2) open circuit of an electrode, which prevents a droplet to move to a cell, (3) short circuit between two electrodes, which prevents a droplet to move between two electrodes, (4) control voltage variation, (5) dielectric thickness variation, and (6) particle contamination, fluid viscosity, interfacial tension and friction variations. Catastrophic defects and parametric variations do not have a clear partition. For example, open circuit and short circuit of electrodes have been taken as catastrophic defects, while this paper presents that such defects do not always bring a droplet into an immediate complete stop. Particle contamination can also be either catastrophic or parametric, e.g., a particle could slow down or fragment a droplet, depending on the particle size.

C. Previous Testing Methods

It is relatively easy to locate catastrophic defects on a microfluidic biochip, for example, by moving an array of droplets across the chip, and collecting the droplets at the end of the rows(columns). Not receiving a droplet indicates the presence of catastrophic defect in the row(column) (Fig. 2) [9].
If multiple catastrophic defects are present, the grid formed by the faulty rows and columns confines the catastrophic defects. Avoiding the grid guarantees a catastrophic defect-free chip.

Parametric variations are detected by adjusting the duration time of the control voltage applied to each cell on the biochip [9]. For example, for a droplet to move continuously, it needs to reach an adjacent cell before the control voltage is applied to the adjacent cell. Otherwise, the droplet lags behind the control voltage, which could further slow down the droplet, and may bring the droplet to a complete stop. Consequently, adjusting the duration time of the control voltage applied to each cell on the biochip finds the minimum droplet speed in a path, e.g., the largest control voltage duration time which carries a droplet across the biochip gives the minimum droplet speed [9].

This method has several limitations. (1) The speed of a droplet is a function of the control voltage duration time. A droplet accelerates under a fast-paced control voltage and decelerates under parametric variation. Consequently, the minimum droplet speed detected by adjusting the control voltage duration time could well differ from the minimum droplet speed for a specific control voltage duration time. (2) Further, any parametric fault thus found is not located at specific cells, but in a droplet path. The number of possible droplet paths on a biochip prohibits exhaustive test of all paths.

This paper presents improvement of this parametric variation test method in two aspects: (1) a more accurate modeling of droplet movement with respect to control voltage speed, and (2) a test method which locates critical parametric variation cells.

### D. Notations

We take the following notations for the rest of this paper.

- $L$ = unit cell dimension on a microfluidic biochip
- $V$ = control voltage
- $T$ = control voltage duration time
- $U_c = L/T$ = control voltage speed
- $D_{\text{lag}}$ = droplet lag distance
- $U$ = average droplet speed
- $k$ = droplet speed loss
- $x$ = droplet location

### III. Droplet Motion Simulation and Observations

In this section, we analyze droplet movement based on droplet motion simulation results. Algorithm 1 gives the implemented droplet movement simulator. Table I gives the parameters in the simulation [9].

#### Algorithm 1: Droplet Motion Simulation

**Input:** Control voltage $V$, control voltage speed $U_c$  
**Output:** Droplet location $x$ and speed $U$

1. $D_{\text{lag}} = 0$
2. For each cell $i = 1$ to $n$ in droplet path
3.  
4.  
5.  
6.  
7.  

#### A. Droplet Does Not Necessarily Stop at a Faulty Cell

Previous publications have presented that a droplet stops at a cell of catastrophic defect, e.g., a droplet cannot cross a cell if the underlying electrode is shorted with an adjacent electrode. It has been pointed out that a droplet is able to cross such a cell of short circuit if the droplet moves in a direction perpendicular...
to the two cells of short circuit, although the droplet movement will be off the straight line [8].

However, the simulation results show that a droplet is able to continue to move forward albeit at a lower speed after passing a faulty cell of parametric variations, and even cross two shorted electrodes, (e.g., as is shown in Fig. 3) depending on the control voltage and the control voltage speed.

B. Droplet Movement Beyond a Faulty Cell

This leads us to further study droplet movement on a biochip in details. To characterize droplet movement on a biochip, we define the following terms.

**Definition 1** Droplet speed loss $k = 1 - U/V_c$ is the relative difference between the droplet speed and the control voltage speed at a cell.

$k$ indicates not only droplet speed but also droplet location.

**Definition 2** Droplet lag distance $D_{lag} = (1 + k)L$ is the distance between a droplet and the cell to which the control voltage is currently applied.

If parametric variations at a cell result in a $k \times$ droplet speed loss, subsequently at the next cell the droplet has a distance of $(1 + k)L$ to cross, and the droplet speed is given by $U(k, V)$. Table II gives simulation results for speed $U(k, V)$ of a droplet to start with a $k \times$ speed loss under control voltage $V_c$.

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**Definition 3** Maximum reliable control voltage speed $U^*(k)$ is the maximum control voltage speed under which a droplet would recover from a $k \times$ speed loss.

The total distance that a droplet crosses after passing a faulty cell is characterized by **droplet grace distance**.

### Table II

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### Table III

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**Definition 4** Droplet grace distance $D_{grace}(k, V_c, U_e)$ is the distance which a droplet crosses before coming to a complete stop after passing a faulty cell with droplet speed loss $k$, control voltage $V_c$, and control voltage speed $U_e$.

Table III gives droplet grace distance $D_{grace}$ for a variety of droplet speed loss $k$, control voltage $V_c$, and control voltage speed $U_e$. Obviously, a catastrophic defect leads to zero grace distance for a droplet.

**C. Critical Cells of Parametric Variations**

For a given control voltage $V$ of speed $U_c$, if the droplet speed after a loss of $k$ is higher than control voltage speed $U(k, V) \geq U_c$, the droplet will recover from this speed loss. If the collective effect of parametric variations at multiple cells decelerates the droplet to a speed below the control voltage speed $U(k, V) < U_c$, the droplet will not recover its speed loss, and will continue to decelerate before reaching the end of a droplet path.

This provides us a concise characterization for parametric variations. Unlike catastrophic defects, parametric variations are distributed at multiple cells while their effects are accumulated in a droplet path. In this paper, instead of extracting parametric variations for each cell, parametric variations on a microfluidic biochip are captured by critical cells.

**Definition 5** A critical cell $C_c(U_c, P)$ in a droplet path $P$ under control voltage speed $U_c$ is the last cell of parametric variations in a droplet path $P$, at which the droplet speed is lower than the control voltage speed $U(k, V) < U_c$.

The location of a critical cell can be back-traced from the final droplet location. This gives precise critical cell location assuming inexistent or negligible parametric variations after a droplet passes a critical cell. In other cases, where considerable parametric variations exist in the downstream of a critical cell, back-tracing may not give the exact critical cell location. In any case, locating the critical cells provides better characterization of the parametric variations on a microfluidic biochip.

### IV. Parametric Variation Extraction

Now we locate critical cells of parametric variations. Note that we cannot trace back to the critical cell simply by the droplet stop location, because different speed losses at different locations could lead to the same droplet stop location. To locate a critical cell with a droplet speed loss $k$, we can apply two different control voltages $V_1$ and $V_2$, and match the distance
between the two droplet stop locations $\Delta D$ with the difference between the grace distances $D_{\text{grace}}(k, V_1)$ and $D_{\text{grace}}(k, V_2)$.

Algorithm 2 gives a complete procedure to locate critical cells. We first move a droplet in a row under the required control voltage $V_1$ at speed $U_e = U(0, V_1)$. If the droplet is not received at the end of the row, we apply control voltage along all columns at a very slow pace, such that the droplet is received at the end of a column $x_1$. This clears the droplet from the faulty row and gives the location of the droplet under control voltage $V_1$ at speed $U_e = U(0, V_1)$. To locate a critical cell, we move a droplet in the same row by applying a lower control voltage $V_2 < V_1$. The droplet will stop again before reaching the end of the row and we apply control voltage at a very slow speed to collect the droplet at the end of a column $x_2$. Based on Table III (Fig. 4), we are able to locate a critical cell in the row, i.e., find the droplet grace distance $D_{\text{grace}}$ and the droplet speed loss $k$ in the critical cell.

Locating critical cells provides hints for droplet transportation speed on the microfluidic biochip. E.g., droplet movement in the path segment between the critical cell and the final droplet stop location subjects to little parametric variation and performance degradation, while droplet movement in the path segment before the critical cell subjects to significant parametric variation and performance degradation. These path segments can be assigned to different weights or distances to help performance optimization in droplet scheduling and routing.

### Algorithm 2: Parametric Variation Extraction

| Input: | Control voltages $V_1, V_2$ of speeds $U_{e_1}, U_{e_2}$ |
| Output: | Critical cells $C_{c_i}$ of parametric variations |
| 1. For each row |
| 2. Apply control voltage $V_1$ and receive droplet at the end of row |
| 3. If droplet not received |
| 4. Apply low frequency control voltage $V_1$ along all columns |
| 5. Receive droplet at end of column $x_1$ |
| 6. Apply control voltage $V_2 < V_1$ along the row |
| 7. Apply low frequency control voltage $V_1$ along all columns |
| 8. Receive droplet at end of column $x_2$ |
| 9. Trace back to a critical cell $C_{c_i}$ at $(x_i, y_i)$ |

The following experiments verify the proposed parametric variation extraction method and further study the effect of distributed parametric variations.

### V. Experiments

The proposed critical cell location algorithm is verified as follows. For an open circuit defect of an electrode, the droplet lags behind 2L distance when the control voltage is applied to the next cell. If no other significant parametric variation present beyond this open circuit defect, the droplet stops 20.94(17.34) distance away from the defect under a 30V(90V) control voltage, giving a distance between droplet stop locations of $\Delta D = 3.60$. For a short circuit between two adjacent electrodes, the droplet lags behind 1.5L distance when the control voltage is applied to the next cell. Assuming no significant parametric variations beyond this short circuit defect, the droplet stops 24.60(20.71) distance away from the defect under a 30V(90V) control voltage, giving a distance between droplet stop locations of $\Delta D = 3.89$. Finding $k$ for $D_{\text{grace}}(k, V_1, U_e) - D_{\text{grace}}(k, V_2, U_e) = \Delta D$ (checking Table III and Fig. 4) gives both droplet grace distances and the critical cell location.

### B. Effect of Distributed Parametric Variations

To study the combined effect of more evenly distributed multiple parametric variations, simulation is performed as follows. Parametric variations are randomly assigned to a $n \times n$ array of cells on a microelectrofluidic biochip, where the parametric variations include control voltage $V$, dielectric thickness $d$, droplet height $h$, and fluid viscosity $\zeta$, which are assumedly in independent Gaussian distributions, e.g., with $\sigma/\mu = 10\%$. The mean values of the parameters are taken the same as in Table I.
Table IV shows the means and the standard deviations of droplet speed as a result of control voltage $V$, dielectric thickness $d$, cell dimension $L$, or friction $\zeta$ variation. We observe that variation of control voltage has the most significant effect on droplet speed, dielectric thickness has the second most significant effect on droplet speed, while other parametric variations, such as cell dimension, friction, etc., do not have significant effect on droplet speed.

Table V shows the means and the standard deviations of droplet grace distance as a result of control voltage $V$, dielectric thickness $d$, cell dimension $L$, or friction $\zeta$ variation. 100% correlated parametric variations are assumed for each cell; less tightly correlated parametric variations lead to less significant droplet grace distance variations. The means of the droplet grace distance increases in the presence of parametric variation (compared with Table ), because positive parametric variations help a droplet to recover from speed loss. Again we observe that the control voltage and the dielectric thickness are dominant parametric variations.

VI. Conclusion

This paper presents analysis results and test methods for droplet transportation on a microfluidic biochip in the presence of parametric variations. Previous techniques locate catastrophic defects which guide subsequent droplet scheduling and routing procedures. However, a significant number of defects on a microfluidic biochip are parametric variations, taking them as catastrophic defects as in previous publications leads to incorrectly identified defect locations, which compromises subsequent droplet scheduling and routing procedures. The contributions of this paper includes the first characterization method for continuous droplet movement beyond a faulty cell by droplet speed loss, lag distance, and grace distance, as well as the first parametric variation extraction method to locate the critical cells which originate un-recoverable droplet speed loss. The extracted critical cells provide better characterization of droplet transportation (giving speeds at differential droplet path segments), and enable performance optimization in droplet scheduling and routing.

REFERENCES


