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An Efficient Technique for Double Faults Detection and their Locations Identification in Digital Microfluidic Biochip

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Abstract: Progress of digital microfluidic biochip (DMFB) confronts for the defective and specious electrodes. Not only these hinder the routing of droplets but also the completion time of assay is influenced by those defective electrodes. As Microfluidic-based biochips are broadly used in the revolution of medical diagnosis, gigantic parallel DNA analysis, automatic drug discovery and real-time biomolecular recognition including numerous safety-critical applications, this biochip definitely responsible for appropriate and accurate result. Prior accepting it for perceptive purposes the microfluidic biochip must confirm its precision and robustness. In this article, an aspect of fast fault diagnosis appliance for perceiving double faults and recognizing the fault locations within the biochip is introduced. If the biochip is defect free then the proposed approach computes the traversal time as well. The suggested result outpoured that the propound technique is competent, efficacious as well as delineate signifying improvement over the surviving method. Furthermore this paper added expedient reconfiguration contrivance.

Keywords: Digital Microfluidic Biochips; Double Faults Detection; Fault Tolerance; Feasible Reconfiguration Level.

Introduction

Now-a-days the reinforcement of droplet-based biochip has gained rich attention from the researchers [1-5]. It is one of the most wondrous engineering dare in present decades [6]. This composite microsystem has come as an efficient alternative of the expensive and burdensome conventional laboratory equipment to facilitate the extremely perceptive task with better throughput compared to the conventional biochemical or biomedical laboratories with superior compassion, lower cost, less likelihood of human oversight and greater levels of system integrity [7-8]. Hence, it has been called as System-on-chip, Bio-MEMS or Lab-on-a-chip [9-12]. This device works as the nexus of areas like electro-mechanical, biomedical, biochemical, microelectronics etc. [12-15]. Discrete liquid (biochemical samples) droplets with picoliter or nanoliter volumes can be manipulated over a 2-dimensional grid of electrodes using the principle of electrowetting on dielectric (EWOD) or dielectrophoresis (DEP) [16-17]. Therefore many fluid handling operations like mixing, anticipation, dilution of samples, reagents and movement of droplets along the line of the electrodes can be carried through. The conventional biochip works on the principle of continuous liquid flow through the permanently fixed micropumps, microvalves, and microchannels on the basis of the principle of electrokinetics or electroosmosis [4-5, 15-17]. For proving subtle result and high throughput in almost every case the DMFB is enhancing many areas of biochemical, and biomedical applications. It offers exciting possibilities in wide areas, e.g. high-throughput DNA sequencing, point-of-care, medical diagnosis, enzymatic analysis, proteomic analysis, automated drug discovery, toxicity monitoring, air quality supervising, animal counting, food safety testing etc. [18]. As the biochips are being installed in such extremely sensitive places, every biochip must be reliable, precise and dependable.

TABLE 1 Different type of catastrophic faults and their models.

Category of Fault	*Fault Name*	*Cause of Fault*	*Fault Model*	*Fault Effect*
Catastrophic	Dielectric breakdown	Due to the use of high voltage levels, the dielectric can break creating a short between the droplet and electrodes.	A electrical short between the droplet and the electrode	The movement of the droplet resting on the corresponding electrode is affected.
	Insulator degradation	Ionization and slot discharge occur when the electrical field is high. These Ions can degrade the nearby insulating materials.	To irreversible charge concentration near the electrodes.	A consequence is that droplets often fragment and their motion is prevented.
	Short between two adjacent electrodes:	Electrical short occurs between two adjacent electrodes.	Electrical short between electrodes.	The droplet can no longer be transported.
	Irreversible charge concentration on an electrode	Electrode actuation for excessive duration.	Electrode-stuck-on	Unintentional droplet operations or stuck droplets
	Broken wire to control source	Abnormal metal layer deposition and etch variation during fabrication.	Electrode open	Failure to activate the electrode for droplet transportation.
	Grounding Failure.		Floating droplets (droplet are not anchored)	Failure of droplet transportation.
	Non-uniform dielectric layer	Coating failure	Dielectric islands (islands of Teflon coating)	Fragmentation of droplets and their motion is prevented
	Fluidic high-impedance between plates	Particle contamination	Fluidic open	A droplet cannot move across the obstacle
	Degradation of electrode	Retreated use of electrode.	Breakdown of electrode	Hinder in movement of droplet
	Sample residue on electrode surface	Protein adsorption during Bioassay	Resistive open at electrode contamination.	Droplet transportation is impeded.

Therefore prior adopting it for discriminating purposes we must be sure that the chip is fault free and robust. Hence testing and reconfiguration of the biochip are become obligatory before using it for any bioassay operation because the movement of the droplet as well as its overall performance can be suffered from different kinds of manufacturing malfunctions. The defects in biochip can be classified as catastrophic and parametric. The classification of different types of faults and the fault models were discussed in [19-22]. The detail portrayal about different types of faults and their types are discussed in Table 1 and Table 2 respectively.

There are miscellaneous prevailing means existed, those can sense single fault in a biochip. On the other hand, multiple fault detection is not an indicative of intelligence; as detection of multiple faults is very intricate grind [23]. After the reconfiguration of multiple faults some cells become totally unused as well as the costing of reconfiguration is fairly very high. Since these biochips are aiming for an extremely competitive and low-cost market sector, testing and diagnosis of the faults must be inexpensive and quick [24]. Beside these after reconfiguring so many faults, there remains a question about the actual strength of that biochip. In multiplexed in-vitro diagnostics on human physiological fluids and other point of care critical application the biochips are used, hence fault tolerance and feasible reconfiguration level are important issues in regards of preciseness and reliability of these devises. Hence, after considering all these aspects, a better option will be detecting, a number of faults; that are neither minimal (single) nor to high which violates the basic principle of evolving the biochip technology. In this paper, we are recommending a proficient and cost-effective double faults detection and location identification technique (one each in Internal and Boundary Traversal); furthermore the

TABLE 2 Different types of parametric faults and their models

Category of Fault	*Fault Name*	*Cause of Fault*	*Fault Model*	*Fault Effect*
Parametric	Geometrical parameter deviation:	Due to the variations in the process, there may exist deviations in the thickness of the insulator layer, the dimensions of the electrodes, and the gap between the lower and upper plates.	Deviation in insulator thickness, electrode length and height between parallel plates	These deviations may affect the accuracy of the fluidic handling operations
	Parasitic capacitance in the capacitive sensing circuit	Bad soldering	Oversensitive or insensitive capacitive sensing	False positive/negative in detection
	Unequal actuation voltages	Electrode electrostatic property variation in fabrication	Pressure gradient (net static pressure in some direction)	Unbalanced volumes of split droplets
	Irreversible charge concentration on the dispensing electrode	Electrode actuation for excessive duration	Dispensing-stuck-on (droplet is dispensed by not fully cut off from the reservoir)	No droplet can be dispensed from the reservoir
	Deformity of electrodes	Electrode shape variation in fabrication	No overlap between droplets to be mixed and centre electrode	Mixing failure.
	Change in viscosity of droplet and filler medium.	Unexpected biochemical reaction or changes in operational environment	Operation of biochemical reaction	Temperature variation.

possible reconfiguration technique of detected faults.

Micro-Electro-Mechanical Systems (MEMs) are a fairly fledgling arena compared to IC design and MEMS testing. It is in its embryonic stage till now. Nevertheless, as it consumes smaller amount of laboratory space and able to offer ultrasensitive detection very precisely at comparatively in much less cost, Bio-MEMs or DMFB becomes an exciting topic to the researchers.

A detail discussion about the application of digital microfluidic biochip in pharmacogenomics and other areas were described in [12, 18, 25-31]. An elaborating description of Chip-Level Design for Digital Microfluidic Biochips was found in [9]. A cost effective concurrent testing technique to increase the dependability of droplet based microfluidic biochip could be found in [32]. The fault tolerance analysis on the principle of Monte-Carlo simulations to distinguish the impact of parameter deviations on performance was clarified here. A defect-oriented testing and diagnosis technique for DMFB was presented in [33]. Here the test planning was formulated using the Euler circuit problem from the Graph Theory and binary partitioning method was applied to locate the fault area in the biochip.

An essential technique of functional testing of microfluidic device using parallel droplet trails in both on-line and off-line frameworks was emphasized in [34]. Effective fault modelling and fault simulation for continuous flow based biochip were referred in [35-36]. A very good technique to discover catastrophic fault was found in [37] and [33]. Concurrent testing methodology for identification of catastrophic defect and the problem of test planning and resource optimization had been discussed in [38]. An efficient integrated diagnosis technique to diagnose single and multiple defects of a biochip with high fault coverage but without flooding was expressed in [3]. Fault identification approaches in DMFB by using multiple droplets in parallel were proposed in [39-41]. Test planning in terms of graph partition and Hamiltonian path had been introduced in [42]. In [22], we got a defect oriented testing and diagnosis methodology. In that paper an experiment to evaluate the demonstration of electrode shorts at the fluidic behavioral level was introduced. Several methods to sense multiple faults and identification of their locations were represented in [43-44]. In [45], an online concurrent fault detection technique with natural bioassay operation was discussed. A fault detection technique that was based on capacitive sensor was described in [46]. We got the idea of parallel scan and built-in-self test and diagnosis technique from [47].

Discrete fundamental operations related to the biochip like droplet transportation, dispensing, mixing, splitting and capacitive sensing etc. were depicted in the paper [34]. A defect tolerance technique by using graceful degradation and dynamic reconfiguration were pointed out in [48]. An arduous double fault detection and diagnosis technique could be comprehended from [23].

The article is subdivided into five sections. Outside of introduction, Section 2 presents the proposed technique; in Section 3 we illustrate result and analysis along with a comparative study. Section 4 appraises the possible reconfiguration techniques and at the end conclusion is drawn in Section 5.

Proposed Technique

In this section our innovative idea for detecting double faults and locating those faulty positions within a microfluidic array is discoursed elaborately. Proper supervising of all the electrodes by applying control voltage of EWOD, are eventually responsible for movement of droplets within the microarray. It looks for, whither the chip is truthful or not. Dispensing from the source reservoir droplet naturally moves towards the sink reservoir. But if it is acquainted with any dispute in its way, the motion will cease at that faulty location.

Due to the electrode dispute the test droplet cannot complete the microarray traversal in the predefined route. As a result droplet deprives to reach to the sink. Our proposed approach traces the fault as well as the backtracking strategy identifies that fault location. This technique is also capable to count the traversal time for an errorless biochip. To make counting easier we are evaluating one edge movement as equivalent to one unit of time. For covering all the nodes and edges during scanning the proposed method follows two pathways; one of the strategies is Internal Electrode Traversal and the other is Boundary Electrode Traversal.

Internal Electrodes Traversal

The internal cells of a microfluidic biochip are selected for testing in this phase. By routing the test droplet from the source to the sink in some special movement patterns they are checked.

At first the test droplet which is dispensed from the droplet reservoir is placed on the source. Each traversal of droplet from the source to the sink is followed by special type of movement patterns RURU (Right-Up-Right-UP) and DLDL (Down-Left-Down-Left) continuously i.e., from start electrode, droplet first goes to right direction and then towards up direction again and again until it reaches to the boundary during the time of climbing, on the other hand during getting down it shifts one cell down and then to the left direction gradually as far as it touches the boundary line as shown in Figure 1.

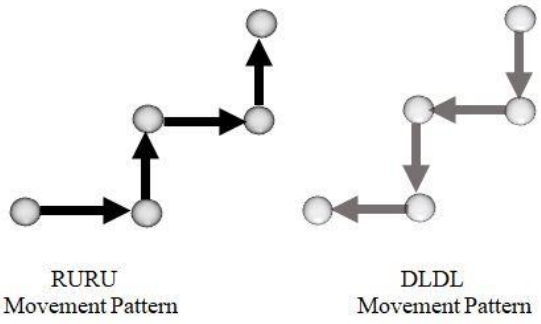

Figure 1. Test Droplet Movement Pattern

Based on the above mentioned routing strategy the test droplet traverses all the internal electrodes to reach the sink by initiating its journey from the source as shown in Figure 2.

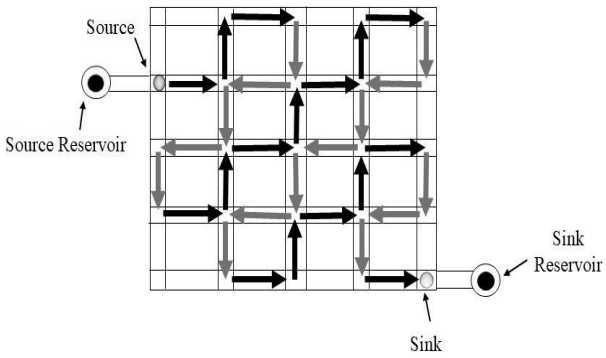

Figure 2. Internal Electrodes Traversal Path.

After being time out, correctness of the internal electrodes is checked by capacitive detection circuit. If droplet successfully reaches to the sink within specified time unit, it is considered that all the internal electrodes are intact. But if any of the cells has dispute, droplet cannot get into the sink. Then it becomes necessary to expose the fault and discover that error position. The backtracking procedure is responsible for identifying that error position.

If it is observed that the droplet does not complete its whole traversal procedure within predefined time period and does not reach to the sink reservoir after the completion of time. Then it is assumed that the chip is erroneous. To identify the fault position a control voltage is applied in the opposite direction of the original droplet movement. This procedure is depicted in Figure 3 and Figure 4 respectively. In course of traversal through the internal electrodes of microarray if the droplet ramble is cramped by any defective cell, it cannot move ahead. As

a consequence, movement ends in smoke which comes through the sink. It is deliberated that one edge movement of test droplet is coequal to one time unit. Now, if the droplet redirects to the source by backtracking strategy from a cell in its pathway in 11 units of time, it is foreseen that the fault location is situated at 11 units (edges) away from the source.

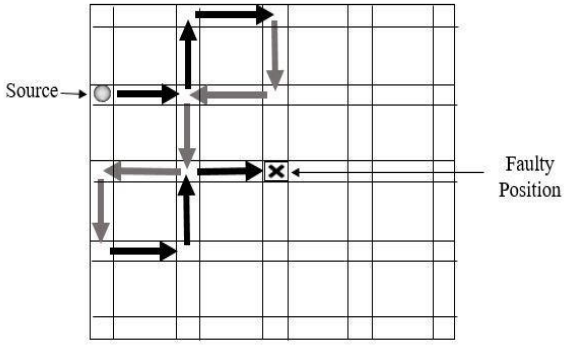

Figure 3. Traversal Path of Droplet upto Fault Location

Internal Electrodes Traversal Procedure:

Begin

1. Place the droplet at the source from the reservoir.
2. While it is doable to move further from the source.
3. Repeat step 4.
4. Apply RURU and DLDL movement patterns to move the droplet towards the sink.
5. If the droplet cannot travel the whole path to reach sink within particular time period.
6. Then backtracking process comes into play to roll back the test droplet to the source through same path and calculate the time.

End

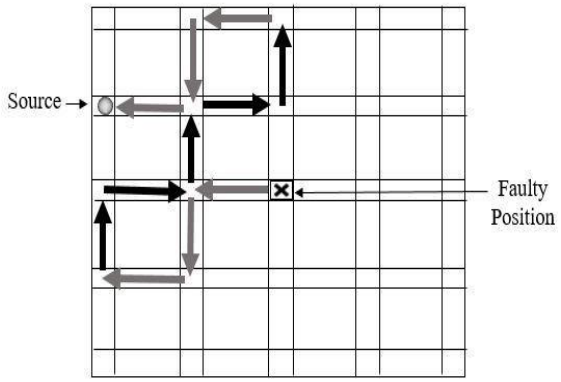

Figure 4. Backtracking Path of Droplet from Fault Location.

Boundary Electrodes Traversal

The boundary electrodes of a DMFB are tested in this phase. The test stimuli droplet moves through the boundary electrodes in anti-clock wise direction to cover all the nodes and edges along the boundary line which remain uncovered in internal cell traversal. Here, at first the test droplet is set at the starting location (i.e. the second row –first column in Figure 5) and after traversing all boundary electrodes the droplet reaches to the sink. Source and sink are identical in this case. While, traversing nodes and edges of the boundary electrode, the droplet routes from starting position (1, 0) and sequentially moves to (2, 0), (3, 0), (4, 0) ..... (0, 0) and finally to (1, 0) respectively.

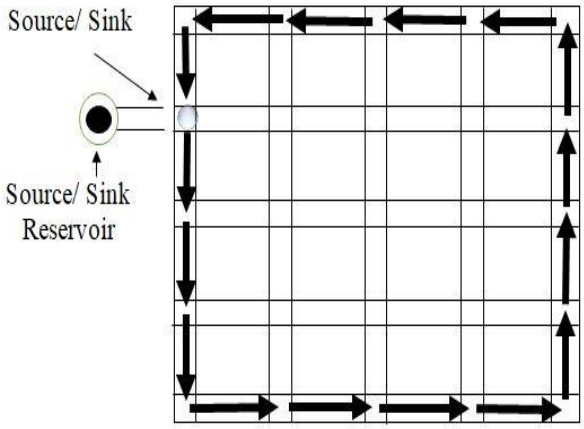

Figure 5. Path of Boundary Electrodes Traversal

We are also susceptible to perceive the fault in the boundary region by implementing backtracking procedure in a similar way as mentioned before. The two types of movement for boundary electrode traversal, forward and backtrack are exposed in Figure 6 and Figure 7.

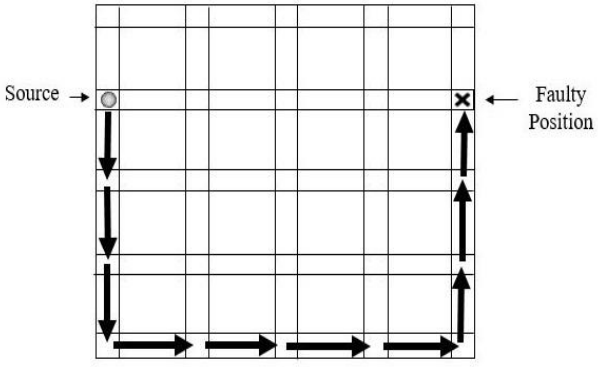

Figure 6. Boundary movement of droplet upto faulty location.

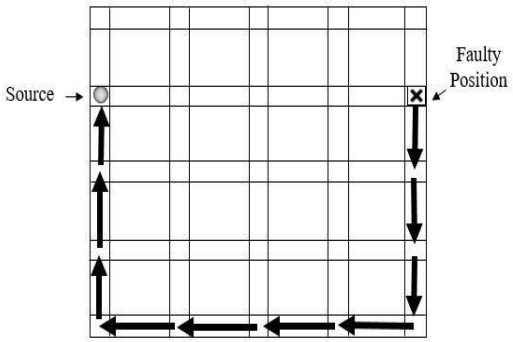

Figure 7. Backtracking along the boundary from faulty position.

The Boundary Electrodes Traversal Procedure

Begin

1. Place the droplet at the source from the reservoir.
2. While it is doable to move further at boundary wise.
3. Start routing from starting point and proceed along the boundary line in anti-clock wise direction towards sink.
4. If the droplet comes cramped somewhere and remain unable to complete the whole path within particular time period.
5. Backtracking procedure is applied to roll back the test droplet to the source through same path and calculate the time.
6. Otherwise stop traversing when it reaches at the sink (which is again source point).

End

The proposed capacitive sensing based technique can be useful to detect catastrophic as well as parametric fault. Catastrophic fault causes complete cessation of droplet's movement; hence the test droplet will never reach the sink and it is easily identifiable. Parametric fault degrades system performance and slow down the movement of the droplets. Naturally the test droplets will consume longer time than usual to reach the sink reservoir. It can be detected by timer and capacitive sensing circuit, attached to sink reservoir. Though the proposed technique can only identify the faulty locations in case of catastrophic defects.

Result and Analysis

We have implemented an effectual approach that can detect and locate double faults in a DMFB. Starting from the source to the sink, the test droplets are moving through the microarray to seek out the existence of any defect. If the droplet sticks somewhere and the further movement of the droplet is ceased, the technique not only analyses and locates that faulty cell but also adjusts the overall traversal time of the microarray, if the array is found to be fault free.

The droplet of boundary traversal, routes in anticlockwise direction to avoid merging and mixing of test droplet which traverses through the internal cells; where in we can traverse the internal electrodes and the boundary electrodes in parallel. The internal electrodes traversal time is always greater than the boundary traversal time. In this approach, the maximum time taken by any of these two traversal strategies is the proposed time; hence we can conclude that the internal cell traversal time is the proposed time. Taking one edge movement of test droplet is equivalent to one unit of time in consideration, we have calculated the proposed microarray traversal time.

For simulating with a huge number of microarray size and to collect the varieties of simulated results for analysis; we have recycled the aforesaid two procedures in our experimentation. Regarding the structure of the microarray as 2D matrices, the simulation is carried out in Turbo C++ environment. Broad analysis is done with a huge number of microarrays varying from 4×4 to 10×10 electrodes.

TABLE 3. The traversal time for an errorless microarray

Matrix Size	*Internal Traversal Time*	*Boundary Traversal Time*	*Proposed Time*
4×4	17	12	17
4×5	24	14	24
5×4	22	14	22
5×5	31	16	31
5×6	38	18	38
6×5	40	18	40
6×6	49	20	49
6×7	60	22	60
7×6	58	22	58
7×7	71	24	71
7×8	82	26	82
8×7	84	26	84
8×8	97	28	97
8×9	112	30	112
9×8	110	30	110
9×9	127	32	127
9×10	144	34	144
10×9	142	34	142
10×10	161	36	161

$$\% \text{ Improvement} = \frac{(\text{Existing Time} - \text{Proposed Time})}{\textit{Existing Time}} \times 100$$

TABLE 4. Comparison of proposed technique with existing technique [23, 39]

Matrix Size	Proposed	Existing [23, 39]	Improvement (%)
4×4	17	24	29.17
4×5	24	31	22.58
5×4	22	31	29.03
5×5	31	40	22.50
5×6	38	49	22.45
6×5	40	49	18.37
6×6	49	60	18.33
6×7	60	71	15.49
7×6	58	71	18.30
7×7	71	84	15.48
7×8	82	97	15.46
8×7	84	97	13.40
8×8	97	112	13.39
8×9	112	127	11.81
9×8	110	127	13.39
9×9	127	144	11.80
9×10	144	161	10.56
10×9	142	161	11.80
10×10	161	180	10.56

The details of simulated experimental results are encapsulated in Table 3. As in this proposed technique boundary traversal consumes lesser time than internal electrode traversal; we only concentrate on internal cells and edges traversal time. Internal traversal time, Boundary traversal time and Propose time are juxtaposed in Table 3.

Next we have presented the comparative studies of the proposed technique with [23, 39], [22, 33] and [43] in Table 4, 5 and 6 respectively. These 3 Tables clearly illustrate better completion time of droplet traversal than the techniques of [22, 23, 33, 39 and 43] in case of fault free biochip.

The proposed technique is also cost effective in terms of number of sources and sinks compared to a number of existing techniques like [22, 23, 24, 33, 39 etc.]. As these biochips are aiming for a particularly competitive and low-cost market sector, testing and diagnosis of the faults must be inexpensive and quick. By using only two open electrodes (for droplet source and sink) this technique also reduce the manufacturing and fabrication cost compared to others.

Reconfiguration Technique

If any cell can be found as defective (catastrophic fault); several techniques are applied to reconfigure that faulty cell [9, 49]; subsequently a defective biochip can be made usable. The three generally used techniques that have been applied for reconfiguration of a microfluidic biochip are mentioned below.

TABLE 5. Comparison of proposed with existing technique [22, 33]

Matrix Size	Proposed	Existing [22, 33]	Improvement (%)
4×4	17	29	41.38
4×5	24	38	36.84
5×4	22	37	40.54
5×5	31	47	34.04
5×6	38	58	34.48
6×6	49	70	30.00
6×5	40	58	31.03
6×7	60	83	27.71
7×5	47	67	29.85
7×6	58	83	30.12

Local Reconfiguration

The fault tolerance is possible at the module level using this technique [9, 21, and 49]. Here spare cells are added in each microfluidic module to reconfigure the faulty cell. Two spare rows of cells are added to a 2×4 micro-array as shown in Figure 8. The spare rows are highlighted in gray colour at the top and the bottom of the original microarray in the figure. If any primary cell is identified as damaged; then the spare cells are used to bypass that faulty cell. This technique is applied only to reconfigure the module and not altering the absolute settlement of the microarray; it is designated as local reconfiguration. As a module with faulty cell has to be found out, this procedure is very affable to implement comparatively any other reconfiguration technique. The technique can reconfigure faulty module without applying much effort. During operation of microfluidic biochip, online reconfiguration can be accomplished by this method.

Space redundancy is a disadvantage of this method as the size of the biochip is enlarged which may not be suitable for some applications like disposable carry-home glucose detectors.

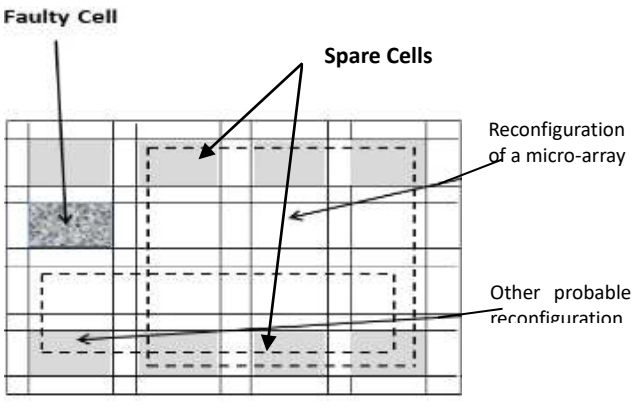

Figure 8. Local Reconfiguration.

Partial Reconfiguration

In contrast to the local reconfiguration technique which is only focusing to the local region of the module; in partial reconfiguration technique [9, 49-50]; reconfiguration is not only restrained to the local part of the microarray; it can be executed anywhere on the biochip while circumventing intersection with other dynamic modules. Defect/fault tolerance is considered at system level except integrating spare cells in particular solitary module. At this juncture, unexploited errorless cells are consumed to provide lodging or sufficient space for faulty module as shown in Figure 9. There is no need to elect any cell as spare. Therefore, the area size of the biochip preserve unlike the space-redundancy based method. To implement partial reconfiguration and the invention of new location for the module, a fast heuristic algorithm based on the notation of maximal-empty rectangles is used, as proposed in [51]. It is also applicable for self-motivated online reconfiguration throughout field operation of the DMFB.

TABLE 6. Comparison of proposed with existing technique [43]

Matrix Size	*Proposed*	*Existing [43]*	*Improvement (%)*
4×4	17	48	64.58
4×5	24	66	63.64
5×5	31	88	64.77
5×6	38	112	66.07
6×6	49	140	65.00
6×7	60	170	64.71
7×7	71	204	65.20
7×8	82	240	65.83
8×8	97	280	65.36
8×9	112	322	65.22

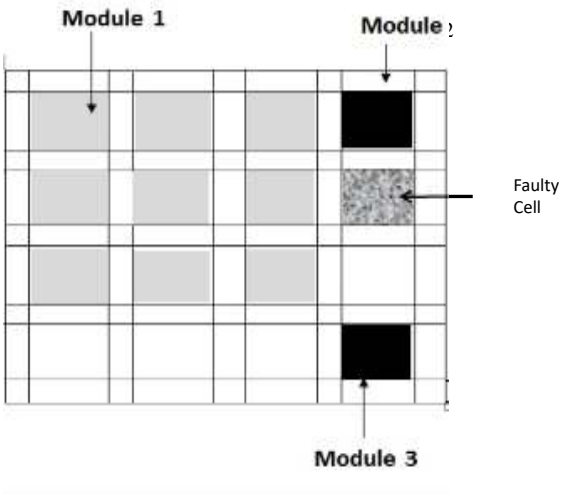

Figure 9. Partial Reconfiguration

Full Reconfiguration

During biochip corporal design, a defective cell can be taken into consideration as a superfluous restraint in this phenomenon. For achieving a new arrangement of microfluidic array a synthesis tool is used in order to bypass the defective cell. Instead of converging only on the flawed module, this technique also obliges the reconfiguration of unbroken modules. In spite of the existence of faulty cell, deduction of array area is possible using the synthesis tool. As full reconfiguration technique is much time consuming, costly and a lengthy procedure compare to any other reconfiguration technique; it is never chosen in an online reconfiguration. It always acts as an offline reconfiguration procedure. In spite of being costly and time taking, a strong benefit with this practice is that, more than one damaged cells can be remapped, consequently it is not mandatory to discard a faulty biochip [9, 49].

Conclusion

An effectual and novel, advanced double faults detection technique to identify and uncover double faults within a microfluidic biochip has been emphasized in this paper. We have first provided an overview on a number of frequently occurring faults and their types in DMFB. The causes of these defects related to fault models and observable errors have also been presented. Then we have tried to highlight emerging microfluidic platform after the reconfiguration of manufacturing defects. As biochips are worked on safety critical issues, these necessarily have some aspects like correctness, dependability, reliability etc. Next we have presented our proposed methodology for identifying the defect. The proposed approach is also able to pinpoint the error region by backtracking, test droplet; if any fault is detected. The simulated experimental result reveals that proposed technique achieved considerable improvement in completion time of fault free microarray traversal over the prevailing methods. We have also tried to investigate the possible reconfiguration of the faulty regions.

In spite of several advantages the proposed technique can only detects a single fault in a particular traversal (one each in Internal and Boundary Traversal). If there is a second fault in certain path, it cannot detect the later one.

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