

A Literature Survey on Pin Configuration and Performance of Some Restricted Sized Digital Microfluidic Biochip

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Abstract – In recent times, microfluidics is expected to lead to sensor systems for high throughput biochemical analysis. One of the most advanced technologies to build a biochip is based on microfluidics where micro / nanoliter droplets are controlled or manipulated to perform proposed biochemical operations on a miniature lab, called lab-on-a-chip (LOC). Compared to conventional laboratory procedures, which are cumbersome and expensive, miniaturized biochips offer the advantages of higher sensitivity, lower cost due to smaller sample and reagent volumes, system integration, and less human mistake. One critical problem for biochip synthesis is the pin configuration and area minimization. In this paper we analysis some algorithms for pin configuration and area minimization technique relating to digital microfluidic system.

Keywords – Lab-on-a-chip, Cross contamination, Design automation, Sample, Reagent, Pin constrained design, Algorithm.

I. INTRODUCTION

Biochip facilitates the convergence of electronics with life sciences through the precise control over nanoliter droplets of bio-chemical samples and reagents by using integrated circuit (IC) technology. Bio-chemical fluids are represented in the form of tiny droplets and they integrate on-chip various bioassay operations such as sample preparation, routing, mixing, detection, etc. In comparison to conventional laboratory measures, which are time consuming, expensive and erroneous due to manual involvement, biochip offers the advantages of higher sensitivity and lower cost due to smaller amount of sample and reagent and less likelihood of human error. In case of diagnosis to get a fast and appropriate result, biochip is much more reliable than the so called laboratory procedures. If we think of a particular diagnosis on a blood or serum sample, it needs to be collected from human body (whose volume is not less than some ml), it has to be preserved and then mixing with proper reagent (which is very much time consuming), and then detection is performed.

The mixing procedure is sometimes physical and sometimes it needs chemical reaction(s) as well. Again sedimentation is somehow required in some cases. To avoid the manual procedures and to perform all the operations, the importance of biochip reveals as lab-on-chip integrating all the operations within a chip using a very small amount of sample. Correspondingly the expense for the particular task gets reduced due to the reduced volume of reagent(s) used. So this technological jump facilitates in terms of time, space, and cost too.

Droplet based digital microfluidics are technologies that provide fluid-handling capability on a chip. It leads to the automation of laboratory procedures; that is why it is known as 'Lab-on-a-Chip' (LOC) [1-5]. In biochemistry and biomedical sciences, microfluidic biochip has of much importance that is realized at the level of microelectronic arrays of electrodes (or cells). These devices operate on microliter or nanoliter volume of biological samples, which are routed throughout the chip using electrowetting in a 'digital' manner under clock control on a 2D array of electrodes [3, 4, 10]. These electrodes in a DMFB combine electronics with biology and integrate various bioassay operations from sample preparation to detection. The foremost objective is to minimize the time required to get the result(s) of the assay using micro- and nano-level samples and reagents, where the perfectness of the results we obtain is greatly increased.

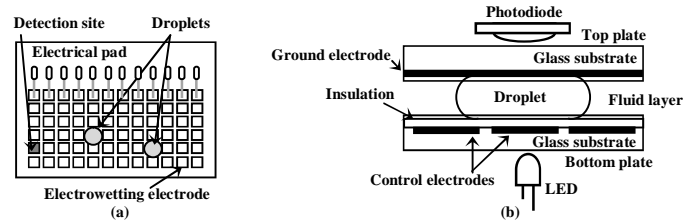


Fig. 1. (a) Top view of a microfluidic array with two droplets and a detection site. (b) A side view of digital microfluidic platform (of a cell) with a conductive glass plate present in a detection site.

Fig. 1(a) shows a typical $n \times n$ 2D array of microfluidic biochip holding two droplets and one detection site. Fig. 1(b) shows a side view of the biochip. It represents a typical detection site as well, where a mixed droplet can be detected optically and generates some desired results. When the LED glows and light passes through the electrode and also through the mixed droplet, the photoelectric diode measures the intensity of this light and draws some voltage against this intensity [22]. This voltage of the photoelectric diode helps to predict a set of desired outcomes of the parameters present in the sample we like to test.

II. PRELIMINARIES AND INHERENT CONSTRAINTS

A. Preliminaries

In this section, we briefly define some of the basic terms associated to the problem of DMFB. We know that in such a chip droplets are dispensed from outside of the array. So, there are several sources of droplets, either for sample, or for reagent, or for washing the chip.

Droplet creation [5, 11]: Droplet formation is a process of creating droplet of a desired size from a source (of larger volume) of the element (sample or reagent or wash droplet) we like to dispose into the array perpendicularly by activation and deactivation of adjacent electrodes. It is an additional task of creating a droplet that is performed outside the array for a minimum of three clock pulses. In general droplet sources are outside the periphery of the chip. By activating three consecutive electrodes adjacent to the source the fluid is extended throughout the three electrodes. Then the two consecutive electrodes are deactivated while the third one remains activated. As a consequence, fluid (sample or reagent) is separated on the third electrode in the form of a droplet of desired size, i.e., to be handled by a single electrode.

Routing path [3, 4, 6]: This is the passageway that a droplet uses for its movement following adjacent cells of an array through a synchronized activation and deactivation of the electrodes considering a predefined schedule. This path may route from a source to a mixer, then from a mixer to a detection site, and then from there to a sink. Such a path is usually measured by the number of cells belonging from a port / module to another port / module.

Mixer and mixing operation [13, 16, 20, 21]: This is a module in an array where the most important task of mixing happens. Here different sample(s) and reagent(s) come from their respective sources and are mixed for detection. This mixing operation takes the maximum amount of time needed for an assay. So, it dominates other operations in an assay in terms of time required. Mixing is sometimes physical reaction and sometimes chemical reaction. There is a variety of mixing procedures including diffusion of two droplets to be mixed. After mixing of two (or more) droplets, a mixed droplet may be routed in a different pattern of movement like unidirectional or zigzag way of rotation, etc. Accordingly, mixer size also vary like 1×2 , 1×3 , 1×4 , 2×2 , 2×3 , 2×4 [5, 20, 21], and so on. Fig. 2 shows all types of mixer size and mixing techniques that are available. A mixer can also be used for splitting of a droplet or dilute a sample droplet. A typical mixer takes ~ 1000 clock cycles (or more). Mixing completion time depends on the size of a mixer and the number of droplets to be mixed along with their viscosity.

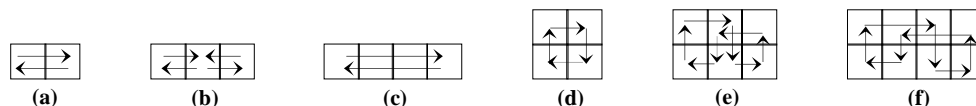


Fig. 2. (a) A 1×2 mixer with to-and-fro movement of mixed droplet. (b) A 1×3 mixer with merging-and-splitting of droplets. (c) A 1×4 mixer with to-and-fro movement of mixed droplet. (d) A 2×2 mixer with rotational movement of mixed droplet. (e) A 2×3 mixer with zigzag way of movement of mixed droplet. (f) A 2×4 mixer with zigzag way of movement of mixed droplet.

Detection site [22]: Detection site is a small module usually formed by a single cell in the array that helps to detect the parameters present in a sample to be detected. Generally it is done on mixed droplets, but it may be required to detect a sample or reagent before mixing as well. As optical detection is done in such a site, the electrodes used in that cell are transparent and light of a LED can pass through it, and a photodiode placed on the top can measure the intensity of the light that can detect anomalies, if any in the sample. Usually, the number of detection sites is not many (as it is a costly module) and their locations are also tentatively fixed.

Assay [1-7]: An assay is a whole operation that includes creation of droplets, their mixing, and detection of a sample's condition (either regular or irregular; if irregular, then how much and in which direction, etc.). Routing is also done to communicate between different modules. We usually deploy an array of electrodes that are activated and deactivated in a preferred synchronized fashion, and all subsequent steps of an assay are tracked to meet the objective(s) affirmed by the assay. In general, an assay is specified through the sequence graph in the high level synthesis approach.

B. Constraints in Performing Bioassay Operations

A bioassay operation involves a number of tasks like routing of droplets, mixing of droplets, detecting some parameters present in a sample, and many others. Obviously, some problem related constraints are there; some of which are fluidic constraint, electrode constraint, time constraint, and area constraint, as briefly discussed below.

Fluidic constraint: At the time of droplet routing, in static condition, at least one cell is supposed to be kept in between two electrodes containing two droplets to prevent unintended mixing. During movement of droplets following a particular direction, we may observe that at least a gap to two electrodes is must to avoid unwanted mixing. Hence, static and dynamic fluidic constraints are introduced [3, 16], as these are necessary for a pair of droplets for their minimum separation on a bioassay. Without loss of generality, we refer to two given droplets such as D_i and D_j . Now let us assume that a 2D microfluidic array is presented as (X,Y) , and let $X_i(t)$ and $Y_i(t)$ denote the location of D_i at time t . We must ensure that either $|X_i(t) - X_j(t)| \geq 2$ or $|Y_i(t) - Y_j(t)| \geq 2$ for these two droplets. To select the admissible locations of the droplets at the next time slot $t+1$, fluidic constraint rules [3] need to be satisfied as follows.

Rule #1: $|X_i(t+1) - X_j(t+1)| \geq 2$ or $|Y_i(t+1) - Y_j(t+1)| \geq 2$, i.e., their new locations are not adjacent to each other.

Rule #2: $|X_i(t+1) - X_j(t)| \geq 2$ or $|Y_i(t+1) - Y_j(t)| \geq 2$, i.e., the activated cell for droplet D_i cannot be adjacent to D_j . Otherwise, there is more than one activated neighbouring cells for D_j , which may lead to mischievous fluidic operation.

Rule #3: $|X_i(t) - X_j(t+1)| \geq 2$ or $|Y_i(t) - Y_j(t+1)| \geq 2$.

Note that Rule #1 can be considered as the static fluidic constraint, whereas Rule #2 and Rule #3 are dynamic fluidic constraints.

Electrode constraint [3, 4]: In case of pin constrained design, more than one electrodes are controlled by a single pin. This may introduce unwanted effect of voltage on some electrode, and as a result this electrode may activate a droplet staying in an adjacent electrode inadvertently. Hence the droplets may not move following a given schedule. This imposes several constraints during routing. If we can make proper voltage assignment over the pins, truthful movement of droplets can be guaranteed.

Timing constraint [3, 4]: Timing constraint in droplet routing is given by an upper bound on droplet transportation time. It is defined to have the proper synchronization among all the bioassay operations held in different modules. All the operations are pre-scheduled and the result should be out within some specified time limit. So, there is an upper bound on time for each individual operation, which is referred to as the timing constraint.

Area constraint [3, 4]: We want to perform all the bioassays in a minimum chip area in view of all the above-mentioned constraints. All kinds of assignments include droplet transportation from the source of droplet to the mixing region and also to the detection site. A mixing region is supposed to be located in a proper position for utilization of total array area. So a design must support how efficiently a chip of some fixed area can be utilized. Though we are supposed to satisfy all the constraints in isolation, maintaining all the constraints for some bioassay may introduce the problem of cross contamination.

Cross contamination problem [3, 4]: Cross contamination occurs when the residue of one droplet transfers to another droplet with undesirable consequences, such as misleading assay outcomes, i.e., incorrect diagnosis. The

problem of cross contamination may also occur when a common path is shared by two distinct droplets by fulfilling their timing constraint.

Sequencing graph [3, 4]: The vertices represent the assay operations (dispensing, mixing, detection, etc.) and the edges represent their mutual dependencies. This method allows user to describe bioassay at a high level of abstraction and it automatically maps behavioral description to the underlying microfluidic array.

III. AN EXTENSIVE SURVEY ON PIN CONFIGURATION

A. Pin Configuration of an Array Area

The digital microfluidic biochip (DMFB), which is known as lab-on-a-chip, is being tried to have a massive parallelism in bio-assay analysis. It requires concurrent droplet movements on a fixed size chip, i.e., concurrent movement of droplets are performed by the predetermined and proper sequence of activation and deactivation of electrodes under the control of some external control pins. So, the pin configuration must be so chosen that we can achieve the best performance in droplet transportation, which is also uncomplicated at the same time.

At the beginning of this century, the digital microfluidics is being tried to have massive parallelism in bioassay analysis. This parallelism consequently requires concurrent bioassay operations, i.e., concurrent movement of multiple droplets throughout the biochip and/or mixing of two or more reagents and samples in different regions of a bioassay in parallel. Droplets are moved by proper sequence of activation and deactivation of electrodes which are controlled by some external control pins. So the pins must be so preferred that we can achieve pipelining in droplet routing [9]. In this context, a true parallelism has been introduced in the present article. Now we survey to the point how droplets are moved to their destination and tasks are performed accordingly.

1. Direct Addressing Pin Configuration [3, 4, 15, 17]

To move a droplet, activation and deactivation of appropriate electrodes are required. So, every electrode must be controlled by some control pin to provide the necessary actuation voltage. The easiest procedure to assign pins to electrodes is to allot individual control pins. So, the number of pins required for an $n \times n$ array is n^2 ; a model array is shown in Fig. 3(a). A method of partitioning based on array may greatly reduce pin number as stated below.

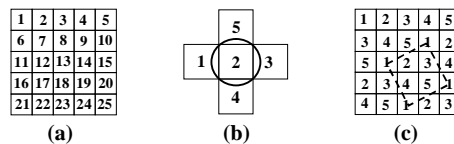


Fig. 3. (a) 25 pins are needed to cover all electrodes of a 5×5 array by direct addressing method. (b) Pin number 2 is a droplet holder that has four direct neighbour pins 1, 3, 4, and 5. (c) A 5×5 array is covered by five pins using *Connect-5* algorithm.

2. Array based Partitioning [3, 4, 9, 12, 19]

An array based partitioning is simple and efficient in respect of the number of distinct voltages we are supposed to provide as input. The chip is divided into some partitions depending on the activities performed there and an optimum number of pins are used to assign the electrodes of the partition. These partitions can be repeated anywhere on a chip to reduce the total number of control pins in the chip. If array based partitioning is done using *Connect-5* algorithm [4, 15], then we may find that any pin has four distinct immediate adjacent neighbours; see in Fig. 3(b). Thus, we obtain an array of any size by assigning only five pins as shown in Fig. 3(c). Though only five pins are sufficient to assign all the electrodes on an array of any size, only a single droplet can safely be allowed to move in such a vast area on a biochip.

Through the use of *Connect-5* algorithm, electrodes in an array of any size can be assigned to pins. Now, if there is more than one droplets to move to different directions, electrode interference may occur. By electrode interference, we mean that some of the electrodes in the array become activated due to the sharing of a set of five pins by all the electrodes and it results in undesired movement, mixing, splitting of the droplets, or resulting in stuck droplet and thus the performance of the whole chip degrades. In Fig. 4(a), there are two droplets each on pin 1 and tends to move to pin 3. As a result pin 3 is activated simultaneously deactivating pin 1 and both the droplets move to their destined position safely as shown in Fig. 4(b). On the other hand, in Fig. 4(c), the droplets are on pin 3 and D_1 is to move rightward on pin 4 whereas D_2 is to move upward on pin 1. So, pins 1 and 4 are activated simultaneously

deactivating pin 3. It results in stuck droplets at the junction of pins 1 and 4, as both of them are activated at a time as shown in Fig. 4(d). This type of unwanted circumstance is known as electrode interference. As a remedy of this problem the concept of cross referencing is introduced.

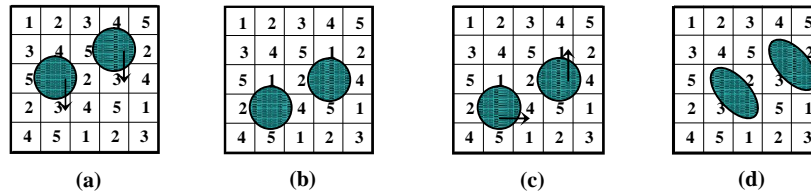


Fig. 4. (a) Both the droplets are on same pin and both of them intend to move to the same pin. (b) Safe movement is possible to pin 3. (c) Both the droplets are on same pin, but tend to move to different directions. (d) Both the droplets stuck between the two diagonally activated electrodes.

3. Cross Referencing [3, 4, 8, 18]

As a remedy to the problem of using $O(n^2)$ number of distinct pins for an $m \times n$ array of electrodes, where $m = O(n)$, array based partitioning method is greatly competent. But electrode constraint is again a hazard to this newly introduced method. Hence a pin constrained design technique is introduced, namely cross referencing [4, 9, 18], where only $m+n$ number of control pins are required to assign to all the electrodes in an $m \times n$ array. In this case, the electrode to be actuated is defined by the row and column number whose intersection contains a next-active (droplet holding) electrode. A next-active electrode is certainly such an adjacent electrode of an electrode that currently holds a droplet.

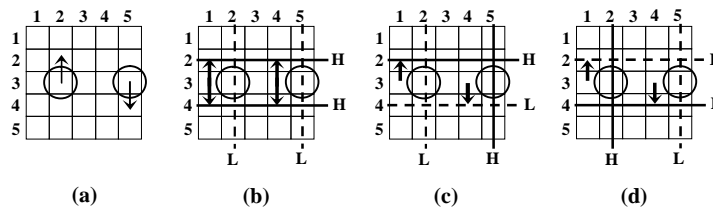


Fig. 5. (a) Two droplets are moving from their respective cells to the cells pointed by arrows. (b) Droplet movement will be in trouble due to electrode interference, as both rows 2 and 4 have been made HIGH. (c) Desired movement as wanted in Figure 4(a) is possible if row 2 and column 5 are made HIGH whereas row 4 and column 2 are made LOW. (d) An alternative solution, as desired in Figure 4(a), is obtained when row 4 and column 2 are made HIGH whereas row 2 and column 5 are made low.

A method named after *cross referencing* [4, 9, 18] has been introduced to directly decide the voltage to be applied (HIGH or LOW) at the row and column combination for proper movement of a droplet. Instead of many advantages of this pin assignment technique, there are some disadvantages too. When we activate a row and a column for moving a droplet using HIGH-LOW or LOW-HIGH combination, then some unwanted cells might also be activated that may allow unwanted movement of droplet. The following example of a part of scheduling shows this problem. To authorize only wanted movements, electrode constraints have been introduced accordingly.

HIGH-LOW combinations applied to rows and columns of an array of size 5×5 have been explained in Fig. 5. Say there are two droplets at cells (3,2) and (3,5) as shown in Fig. 5(a), and we like to move them to cells (2,2) and (4,5), respectively. A droplet movement is possible only when a LOW-HIGH or a HIGH-LOW combination is applied for an electrode in a row-column intersection. Hence if columns 2 and 5 are made LOW and rows 2 and 4 are made HIGH, then we may find that two desired LOW-HIGH combinations are obtained at cells (2,2) and (4,5) whereas two unwanted combinations are formed at cells (4,2) and (2,5) that confuse the droplets for their desired movements. So, these HIGH-LOW combinations of rows and columns, as shown in Fig. 5(b) are not allowable combinations.

On the other hand, there are at least two such desired HIGH-LOW combinations of rows and columns, as shown in Figs.5(c) and 5(d) each of which helps in allowing desired movements of the said droplets. So, for the desired movement of the distinct droplets in Fig. 5(b), rows and columns may be activated and deactivated as shown either in Fig. 5(c) or in Fig. 5(d) to get the desired solution. Incidentally, for a large array with a number of droplets, it has been proved that the problem of satisfying electrode constraints towards a desired solution is an NP-hard problem [3, 9, 23]. Though this is a voltage efficient technique, as a single row and a single column are made either LOW or

HIGH, in general for a big array with many droplets, we cannot develop a polynomial time algorithm that expectantly may solve each and every instance of the problem under consideration.

4. Broadcasting [3, 4, 14]

In broadcasting, control pins are assigned to electrodes taking into account the movement of droplets which is predefined in terms of scheduling of a complete assay, i.e., the activation-deactivation sequence of electrodes. It is stored in a microcontroller in digital term and the electrodes used to route a droplet is assigned to a control pin maintaining that activation-deactivation sequence. Thus for a specific bioassay it reduces the number of pins significantly and hence no electrode interference occurs. In case of pin constrained design, more than one electrodes are controlled by a single pin. It is voltage efficient, but there is a deficiency that if more than one droplets are to move we have to maintain electrode constraints as well. In this paper, we have adopted the notion of broadcasting to develop a pin configuration of a restricted sized chip for a set of parallel bioassay operations.

IV. A 15×15 ARRAY AND ITS WORKING PRINCIPLE

A. An Existing Bioassay

A digital microfluidic biochip of size 15×15 is shown in Fig. 6, where two operations are performed separately on two samples and two reagents [3, 4, 7]. A shared mixer is used, where a first sample (say S₁) and a first reagent (say R₁) are routed from their respective sources to the mixer and after a desired level of mixing, the mixed droplet is then routed to detection site 1 for necessary finding(s). After completion of this phase, a second sample (say S₂) and a second reagent (say R₂), in a similar manner from their respective origins, route to the mixer for their mixing and then the mixed droplet goes to detection site 2 for necessary outcome(s). So, there should be a delay in between the two operations as the array contains a common mixer, some paths below and above the mixer are common to different reagents and mixed droplets to respective detection sites. Now it is very important that such regions and paths are required to be washed in between every alternative mixing process; otherwise, unwanted contamination of residual samples, reagents, and mixed droplets might cause for erroneous results.

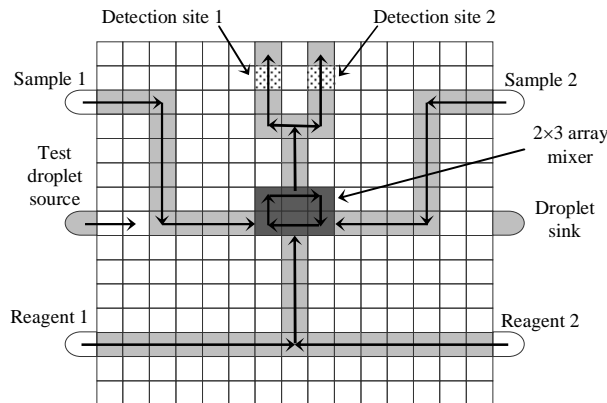


Fig. 6. A 15×15 array layout of droplet routing containing two sources of samples (Sample 1 and Sample 2) and two sources of reagents (Reagent 1 and Reagent 2) with one 2×3 mixer and two detection sites. Direction of arrows shows the movement of droplets along the paths.

					5	1	8	9							
	8	9	10	6	3	1	6	7	4	5	1	2			
S ₁	6	7	8	9	1	2	9	10	2	3	4	5		S ₂	
	9	10	6	7			25	21	22		5	1	2	3	
	8	9	10				23	24	25		3	4	5		
	6	7	8		20	16	17	18	19		1	2	3		
	9	10	6	7	18	19	20	16	17	3	4	5	1		
	7	8	9	10	16	17	18	19	20	1	2	3	4		
	10	6	7	8	19	20	16	17	18	4	5	1	2		
							13	14	15						
							11	12	13						
	3	4	5	1	2	3	14	15	11	7	8	9	10	6	7
R ₁	1	2	3	4	5	1	12	13	14	10	6	7	8	9	10
	4	5	1	2	3	4	15	11	12	8	9	10	6	7	8

Fig. 7. Pin assignment of the array using Connect-5 algorithm that covers all the distinct partitions and uses not more than 25 pins. Here for the movement of a droplet along a path, the adjacent cells are used as guard cells in most of the regions. Hence for a mixer of size 2×3 , an array of size 4×5 is deployed for its realization. Different colours (or shades) show the different partitions of the array for pin assignment.

Though there are two detection sites, as the mixing is done in sequential order the chip is underutilized. If we use only one shared mixer, as in this case of existing bioassay, washing of the mixing region as well as the paths below and above the mixer etc. is to be performed as a transitional task before each consecutive assay. So, in this case the mixing operation is sequential in nature, where an inter-operational break for washing is necessary.

To achieve the aforementioned assay operations, the *Connect-5* algorithm is used as pin assignment [3, 4, 15]. Hence, there are at least five independent partitions for desired movement of droplets obeying all necessary tasks as sought by the said assay, and as an optimized result 25 control pins are required [4, 5, 15], as shown in Fig. 7. Furthermore, based on a new requirement, say S_2 and R_1 are to be mixed first, and then S_1 and R_2 are to be mixed in another instance of time (from their respective sources, as shown in Fig. 6). Here also the process is exactly similar (as only one mixer is there in the array) to the earlier process of mixing.

An analogous situation occurs when S_1 and R_2 are taken care of for their mixing. Needless to mention that, an immediate washing is necessary between different pairs of successive mixing. Thus, using two samples and two reagents, six different combinations of mixing are possible (like S_1-R_1 , S_1-R_2 , S_2-R_1 , S_2-R_2 , $S_1-R_1-R_2$, and $S_2-R_1-R_2$) for their relevant detections in different instances of time, and all of them can be performed on the given array with appropriate scheduling providing desired stall and necessary washing in between [7, 15].

V. A MODIFICATION OVER THE 15×15 ARRAY

A modification of the array (in Fig. 7) introduced in the previous section has been proposed by Hwang *et al.* [2, 14], where the array size is reduced to 10×10 , the number of partitions is reduced to four, and the mixer size is 2×2 (instead of 2×3), as shown in Fig. 8(a). Though this modification reduces the number of pins required but yet the mixing or detection is sequential in nature as the number of mixers is not increased. In Fig. 8(b), we may observe that the mixing region of the array is the junction of four partitions (taking only one cell from each of the partitions), so several droplets (as necessary) can move to this region for mixing. Here the droplets do not suffer by the limitations of *Connect-5* algorithm; rather, the pin number is also reduced by 20% (as only four instead of five modules are present in this modification in comparison to the earlier array).

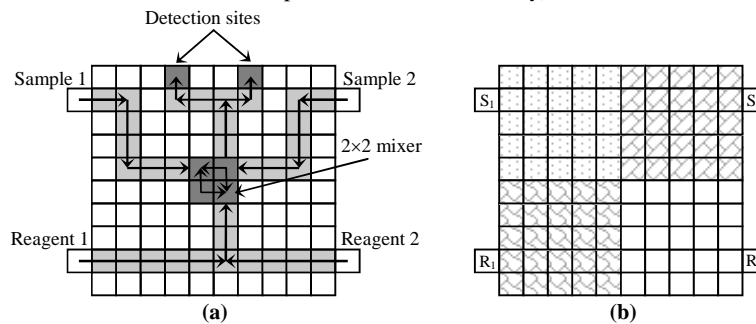


Fig. 8. (a) Layout and droplet routes of the 10×10 array chip with a 2×2 mixer. (b) Partitions along with pin configuration of the 10×10 array that requires 20 pins only. Here the 2×2 mixer resides at the middle of the array comprising pins 3, 10, 12, and 19, taking one cell from each of the partitions.

VI. COMPARISON BETWEEN TWO ARRAYS

In this section, we compare the two biochips, both are in existing article [3, 4, 14], based on their structural and functional characteristics. The primary differences are whether the bioassay operations are performed sequentially or in parallel, what are the sizes of mixers used, utilization of cells in the array, number of tasks carried out, number of assignments executed, and so on. These are included in Table I and thus explained in brief as follows.

We may note that the foremost biochip is very much under-utilized as herein 33.78% cells are idle [3, 4] and the later one claims that it fails to use 20.44% cells [2, 14]. Hence in the first array, we require 25 pins (see Fig. 7), whereas in the second case we need 20 pins only (see Fig. 8).

Table I. A table of comparison that assesses two existing arrays from their pattern and practical viewpoint, where m , d , w , and (w) are the number of clock pulses applied for mixing, detection, inter-assay washing, and intra-assay washing, respectively.

Array structure	15×15 (Fig. 7) [3, 4]	10×10 (Fig. 8) [2, 14]
Mode of operation	Sequential	Sequential
# of tasks	Six	Five
# of mixers	One	One
Mixer size	2×3	2×2
Pin count	25	20
# of active cells	58	48
# of guard cells	91	46
# of unused cells	76	6
Wash droplets	No	No
# of clock pulses (for two assays)	$2 \times (12 + 19 + m + d) + w$	$2 \times (8 + 5 + m + d) + w$

In the design of 15×15 biochip (see Fig. 7), a separate set of five pins has been introduced for the mixer to ensure a required level of mixing in isolation. Here, an intra-assay washing could be performed by dispensing wash droplets from the source of sample (or reagent), when the mixed droplet leaves the mixer and ready for detection and the next assay uses the same sample (or reagent). Evidently, if a new pair of sample and reagent is required to mix in the next assay, inter-assay washing is carried out as a mandatory task in between the subsequent assay operations.

VI. CONCLUSION

In this paper we have considered a restricted sized biochip with array capacity of 15×15 cells. In existing literature, such an array is used only for one bioassay operation at a time as there is only one mixer of size 2×3. This chip is underutilized and subsequently a 10×10 array is introduced with one mixer of size 2×2, where the assay operation is again executed in sequential form. Here in certain cases, only inter-assay washing is sufficient while doing successive multiple bioassay operations and in these cases if we introduce intra-assay washing, we may reduce the inter-assay washing time too before starting a new assay operation. If we could change the pin configuration so brilliantly, often the crossing of two different droplets could be avoided, and hence the problem of cross contamination is eventually resolved in order to achieve a novel design; additional cost and time for routing wash droplets could also be discarded. However, our next target is to design a more productive restricted sized array that requires even fewer pins, if possible, in realizing an utmost useful biochip. In practical systems, even if there are a very large number of individual droplets, there may have only a few droplets with some distinctive variation. The algorithms presented here do not take full advantage of this fact, even though it is believed that this could lead to a substantial decrease in the search space. Finally, extending the software to handle other common operations in DMFS, such as splitting-and-merging of droplets, could be an important direction of future research.

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