Scheduling and Routing Algorithm for Digital Microfluidic Ring Layouts with Bus-phase Addressing

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What is Digital Microfluidics

•Discrete droplets of nanoliter volumes can be manipulated in a “digital” manner under clock control on a two-dimensional array of electrodes.

•An especially promising technology platform is based on the principle of electrowetting-on-dielectric.

•The chemical analysis is performed by repeatedly moving, mixing, and splitting droplets on the electrodes.

Lab-on-a-chip (LOC)

- It is a device that integrates one or more laboratory functions into a single chip.

- The size of the chip can be from few millimeters to few centimeters.

- LOCs can handle extremely small fluids of volume down to Picoliters

Bus Phase Addressing

- **In this paper, the author presents an algorithm for coordinating droplet movement in batch mode with bus-phase addressing.**
- **In bus phase systems, each electrode is not individually addressable, instead a set of electrodes are all controlled by the same signal.**

Bus Phase Addressing-Working

- The presented algorithm allows
  - ❖ multiple independent reactions, each with two reactants and one product.
  - ❖ chain reactions with multiple stages, where each stage produces reactants for the next stage, to take place simultaneously on the chip.
- Merits: Hardware design of electrodes are simplified in chip fabrication.
- Demerits: It increases the complexity of routing droplets.

RING LAYOUT WITH BUS-PHASE ADDRESSING

Reservoir:

All sources from which reactants are introduced into the DMFS and all sinks to which waste and product droplets are sent, are classified as reservoirs. Each reservoir has a storage area and a neck. A droplet leaves or enters the storage area via the neck.

Outer ring:

It is a planar ring of electrodes with a fixed number of phases allotted to its electrodes in acyclic order.

Inner ring:

It is a planar ring of electrodes that allows reactions to proceed to completion.

RING LAYOUT WITH BUS-PHASE ADDRESSING

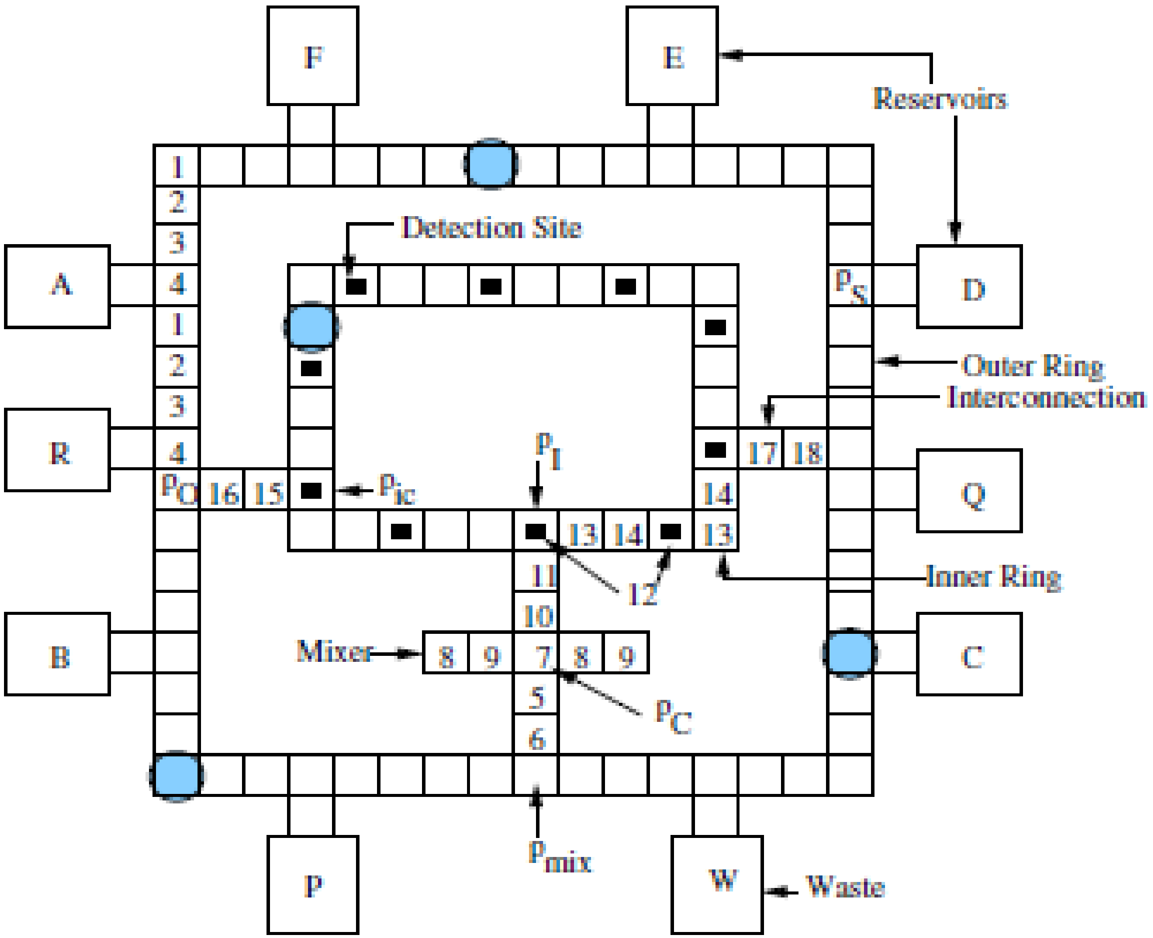
Mixer:

Any kind of mixing and splitting of droplets happens in the mixer. Mixing refers to the physical merging of two droplets that are supposed to react with each other and splitting refers to the formation of two product droplets from the merged droplet.

Interconnection:

It connects the outer ring and the inner ring and allows transport between them.

Chip Layout Diagram



Problem Statement

- **Goal**: Given a ring layout with bus-phase addressing, and a set of reactions, schedule and route the droplets so as to complete the chemical analysis, with all timing constraints on mixing, reacting, and sensing satisfied.
- **Input**: Number of electrodes in the rings, locations of mixer, inner ring, interconnections and reservoirs, reagents stored in each reservoir, electrode phase assignments, reactions to be carried out, and mixing, reaction, and sensing times.
- **Output**: Electrode activation schedule to coordinate droplet routing and to sense results of reactions.

Independent & Chain Reactions

An example set of independent reactions is:

$A + B \rightarrow P \;\; ; C + D \rightarrow Q \;\; ; \;\; E + F \rightarrow R$

An example of a chain reaction is:

$A + B \rightarrow C \;\; ; C + D \rightarrow E \;\; ; E + F \rightarrow G$

C, E are intermediate products and G is the final product.

We will call a pair of droplets of types that are supposed to react with each other a *compatible pair of droplets.*

Assumptions

- The mixer is used only for physical mixing of droplets. It can be entered from both the rings for chain reactions but only from the outer ring for independent reactions.
- Any new droplet formed in the mixer that is neither a final product nor an intermediate product is labeled a waste droplet. Such droplets exit only to the outer ring from the mixer and are directed to the waste outlet.
- The inner ring is used for completion of chemical reaction and for sensing of droplets. It can be entered only from the mixer.
- In both the rings, droplets move in the anticlockwise direction only.

Overview

1) Introduce the droplets into the system from sources.
2) Merge compatible pairs of droplets in the mixer. Move the merged droplet multiple times in the mixer for the input mixing time, t_{mix}, to ensure uniformity in composition inside the droplet.
3) Split the mixed droplet to form two regular-sized product droplets. Send one of them to the inner ring for completion of the chemical reaction and the other to the waste outlet.
4) Retain the product droplet in the inner ring for the prescribed reaction time, t_{react}, to allow the chemical reaction to complete.
5) For any sensing requirements, sense the product droplet for the input sensing time, t_{sense}.
6) Send final products to their respective sinks.

Algorithms

Droplet injection from sources

1)if *P_{S-2} is empty when P_{S-2} is activated then*

2)Activate neck electrode and turn off source electrodes simultaneously when *P_{S-2} turns on.*

3)Switch off neck electrode when *P_S turns on so that* one droplet is introduced into the outer ring.

4) Activate source electrodes again.

5)else Go to step 1.

Algorithms

<u>Movement of split droplets out of mixer(a)</u>

1. Split the merged droplet.
2. while *the mixer is not empty do*
3. if P_{I-2} *is empty when it is activated then*
4. Activate phase 11 when P_{I-1} *is activated so* that one of the split droplets moves toward the inner ring.
5. Activate phase 7 in the next clock cycle so that the other droplet reaches P_C.
6. Activate phase 10 and switch off phase 11 when phase *j is activated so that the first droplet* enters the inner ring while the second one moves toward it.
7. end
8. end

System Deadlock

- It means the system gets stuck in a particular state, preventing any further progress of the biochemical analysis.
- The number of droplets that can cause a deadlock is observed by the fact that the droplets can leave the system only through the outer ring.
- If the outer ring is filled to its capacity but has no waste or final product droplets
- If the mixer has at least one waste droplet that cannot exit to the outer ring, the system reaches a deadlock as none of the droplets from the outer ring can leave the system or enter the mixer.

Deadlock

- A deadlock can also occur if both the split droplets must go to the inner ring.
    - ❖if both the rings are filled to their capacity.
    - ❖the outer ring has no waste or final product.
- The outer ring has four phases, every fourth electrode will have a droplet on it.
- Since the Inner ring has three phases, every third electrode will have a droplet on it.

Result

- We define *completion time of the analysis as the number of* clock cycles.
- The state when all reactions have been completed and all product droplets on the array have been sent to the respective sinks or waste outlet,
- No droplet should be left on array.
- For chain reactions, the algorithm has been optimized by defining a stage with each reaction, i.e., the stage at which each reaction in the chain occurs is given as an input.

Challenges

- Automating continuous mode reactions.
- Optimum input rate and placement of components need to be identified to avoid congestion and deadlocks.
- Finding an optimum schedule to minimize completion time
- Generalizing the algorithm to control arbitrary layouts pose very interesting challenges.

Conclusion

- What is Digital Microfluidics
- Lab-on-a-chip (LOC)
- Bus Phase Addressing and its working
- Ring Layout
- Problem Statement and assumptions to solve it
- Sample Algorithms
- Deadlock
- Challenges faced
- Result