Synthesis of Digital Microfluidic Biochips with Reconfigurable Operation Execution

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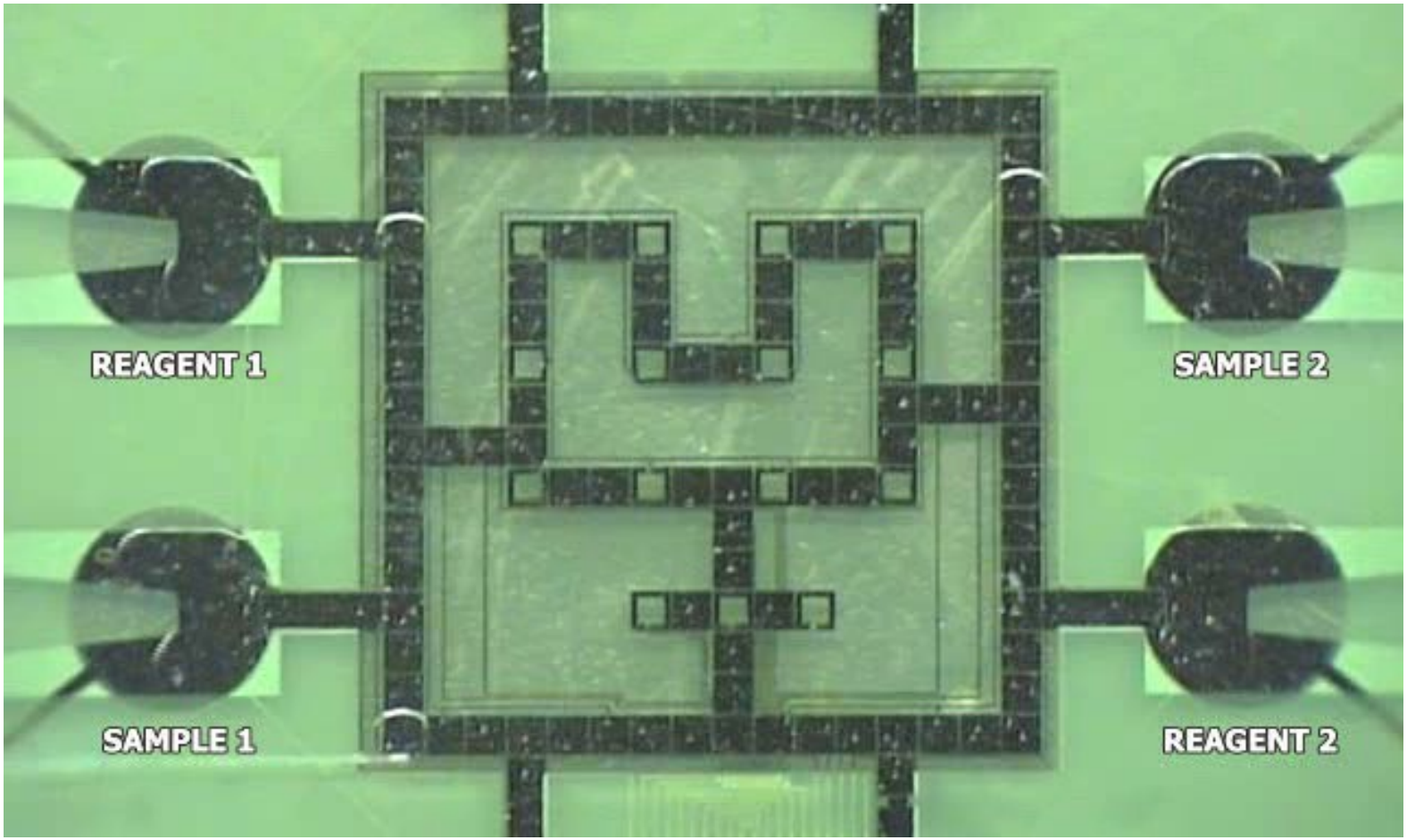
www.dreamstime.com

Digital Microfluidic Biochip



Duke University

Applications

- Sampling and real time testing of air/water for biochemical toxins
- Food testing
- DNA analysis and sequencing
- Clinical diagnosis
- Point of care devices
- Drug development

Advantages & Challenges

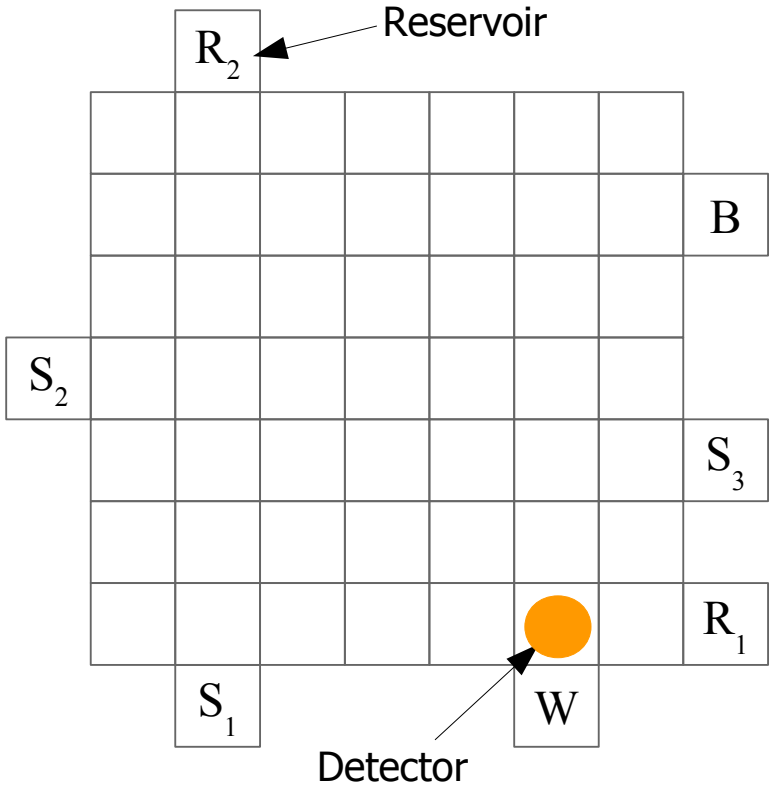
- Advantages:
  - High throughput (reduced sample / reagent consumption)
  - Space (miniaturization)
  - Time (parallelism)
  - Automation (minimal human intervention)
- Challenges:
  - Design complexity
  - Radically different design and test methods required
  - Integration with microelectronic components in future SoCs

Outline

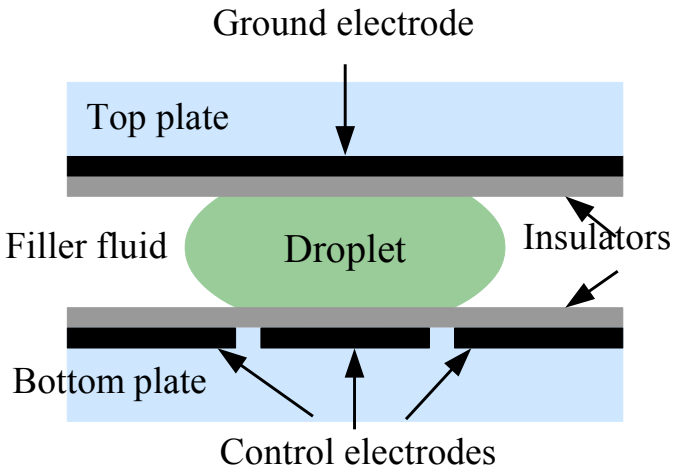
- Motivation
- Architecture
- Operation Execution
- Contribution I
  - Module-Based Synthesis with Dynamic Virtual Devices
- Contribution II
  - Routing-Based Synthesis
- Contribution III
  - Droplet-Aware Module-Based Synthesis
- Conclusions & Future Directions

Architecture and Working Principles

Biochip architecture

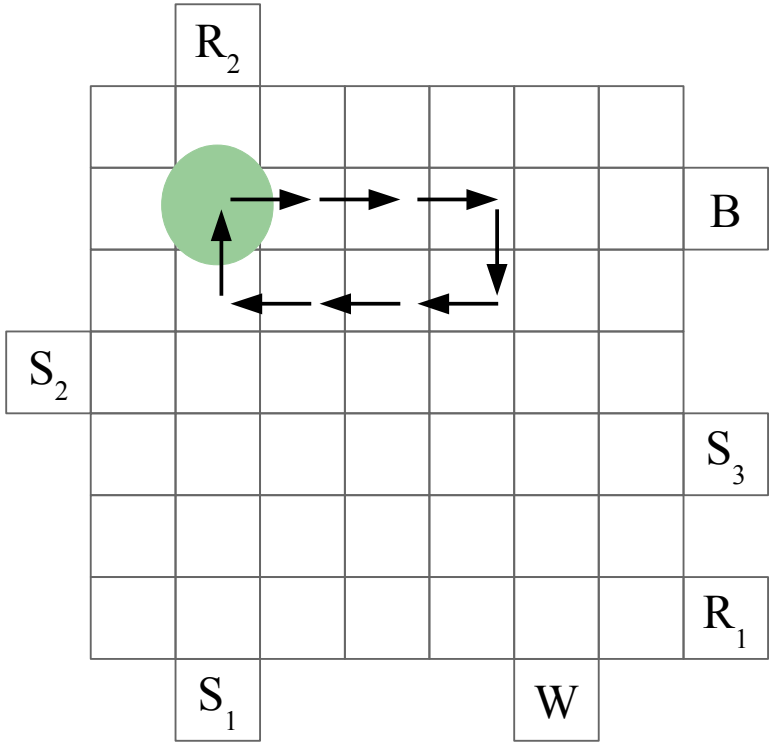


Cell architecture



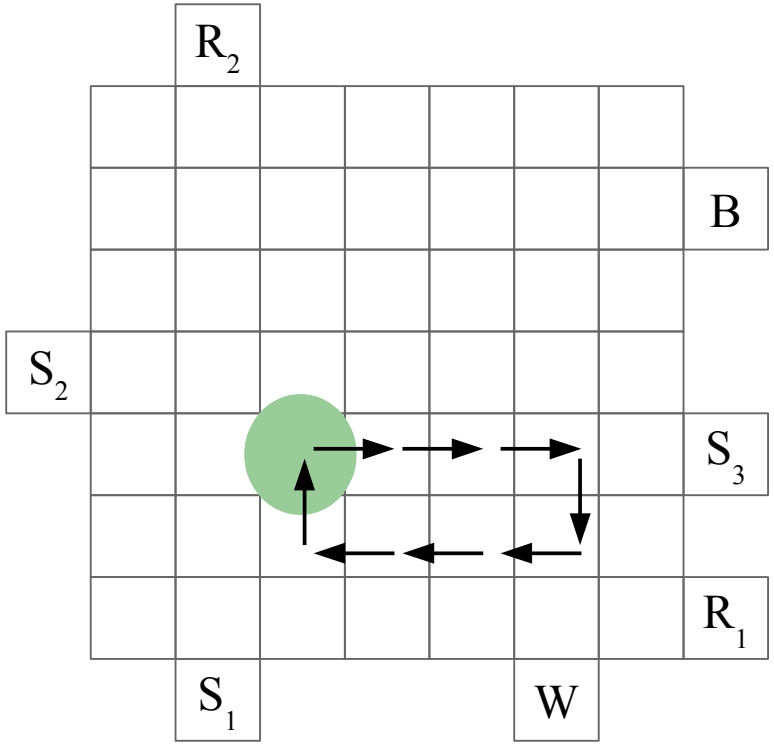
- Electrowetting-on-dielectric

Microfluidic Operations



- Dispensing
- Detection
- Splitting/Merging
- Storage
- Mixing/Dilution

Reconfigurability



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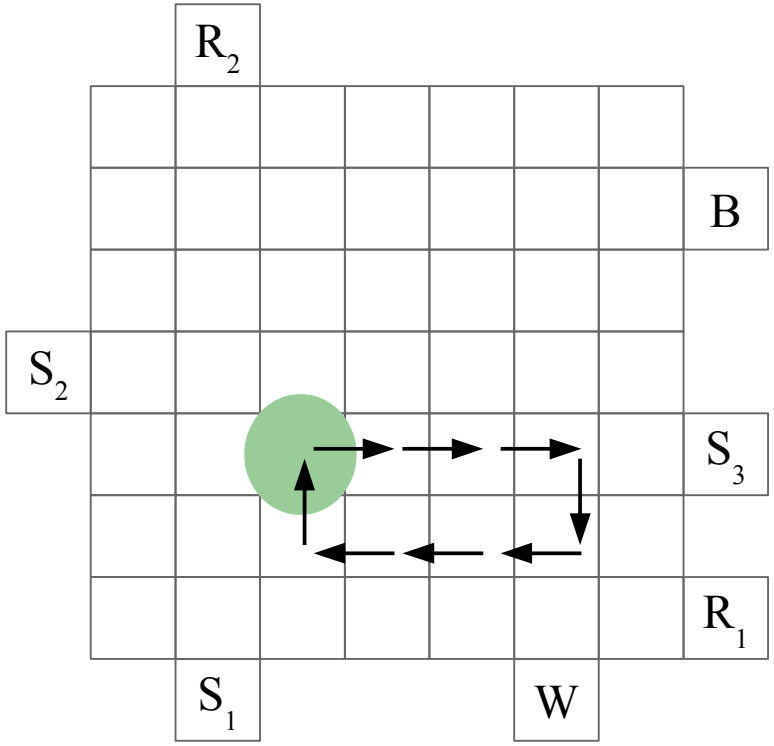
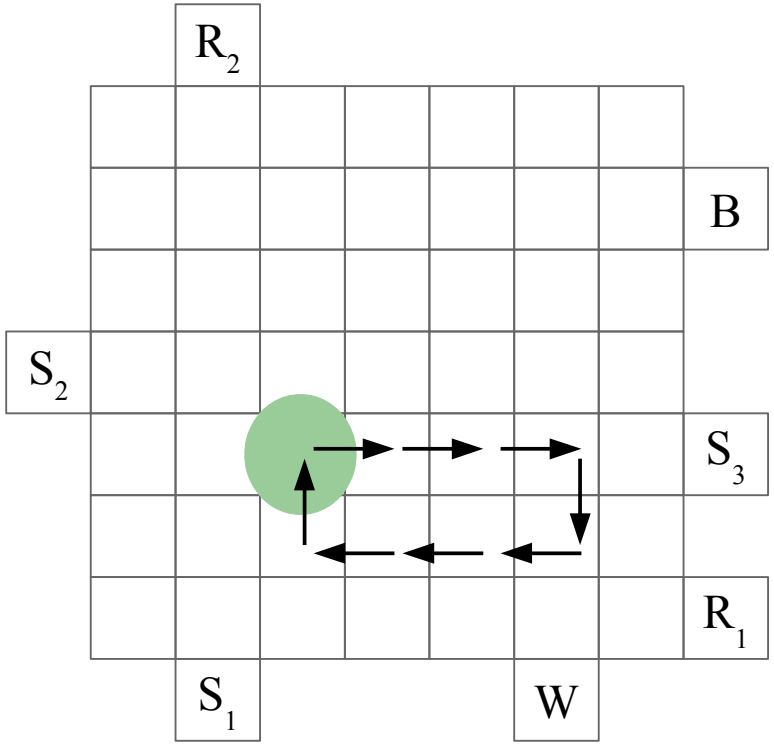


Non-reconfigurable

- Dispensing
- Detection
- Splitting/Merging
- Storage
- Mixing/Dilution

Reconfigurability



Non-reconfigurable

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- Detection

Reconfigurable

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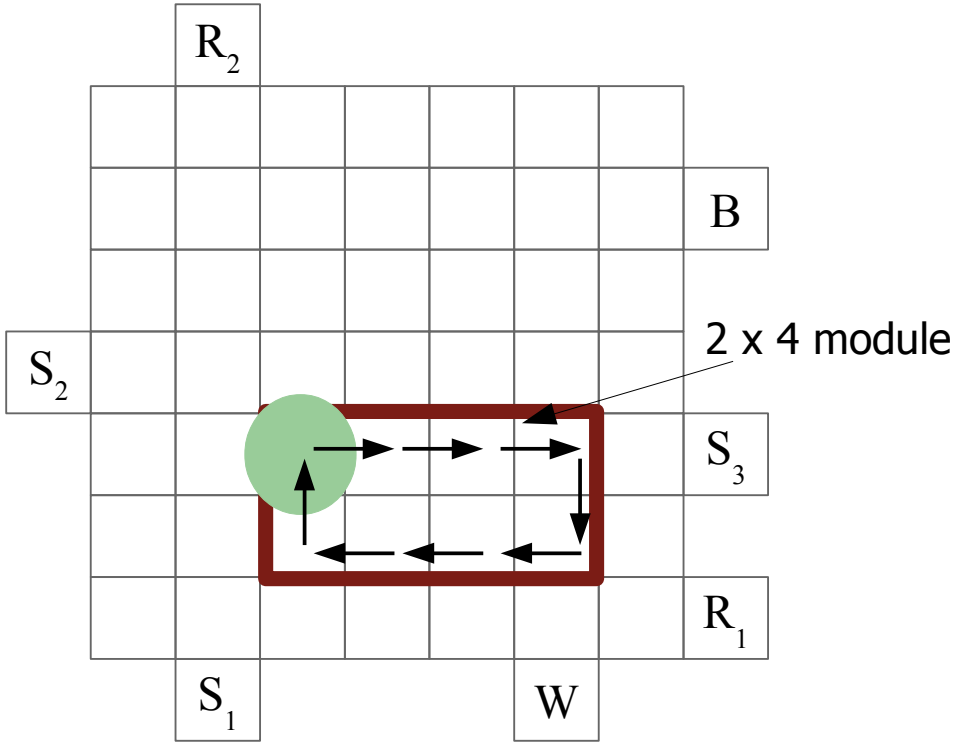
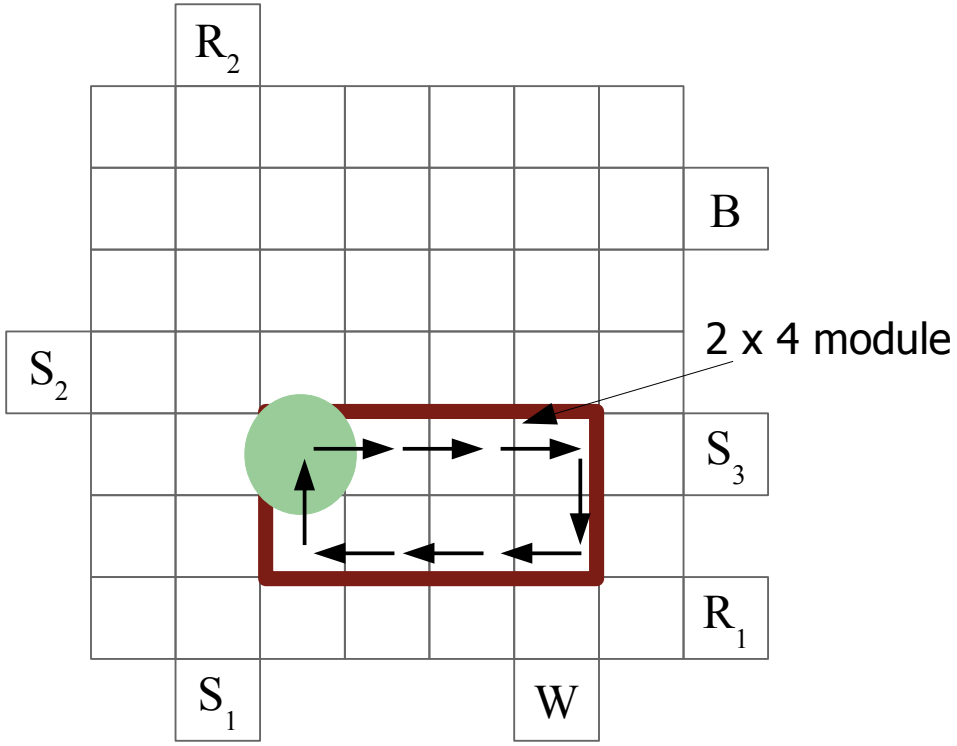
- Storage
- Mixing/Dilution

Module-Based Operation Execution



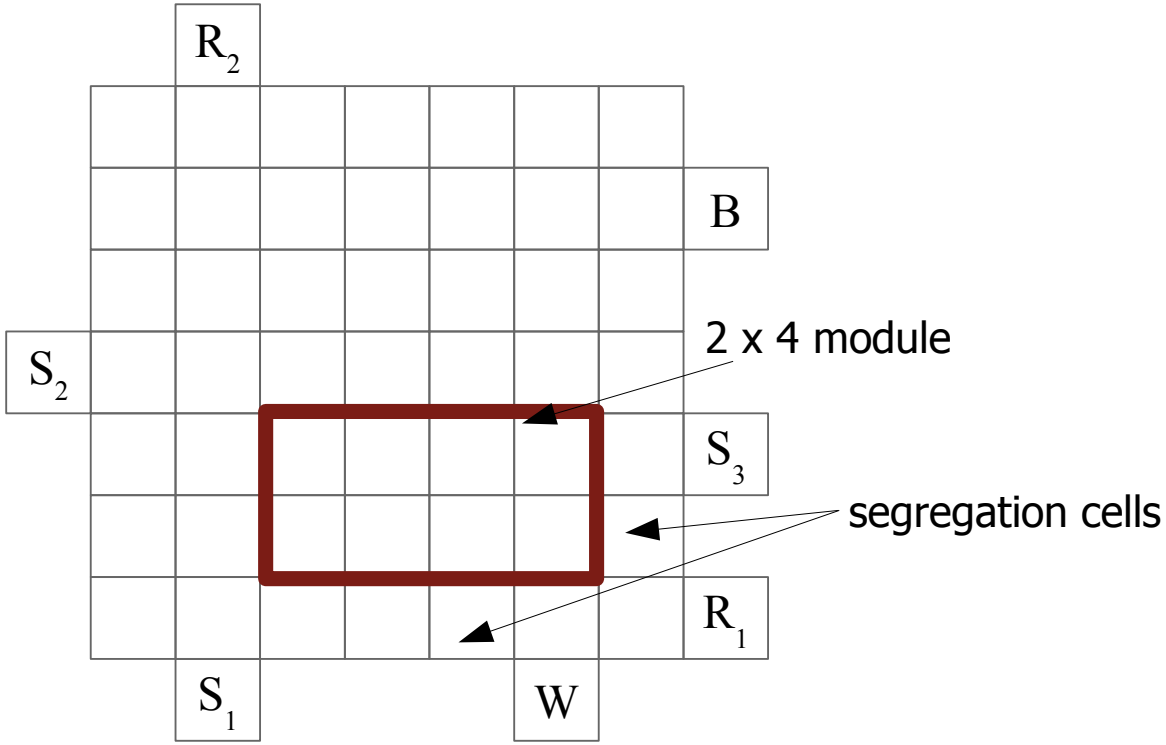
Module-Based Operation Execution



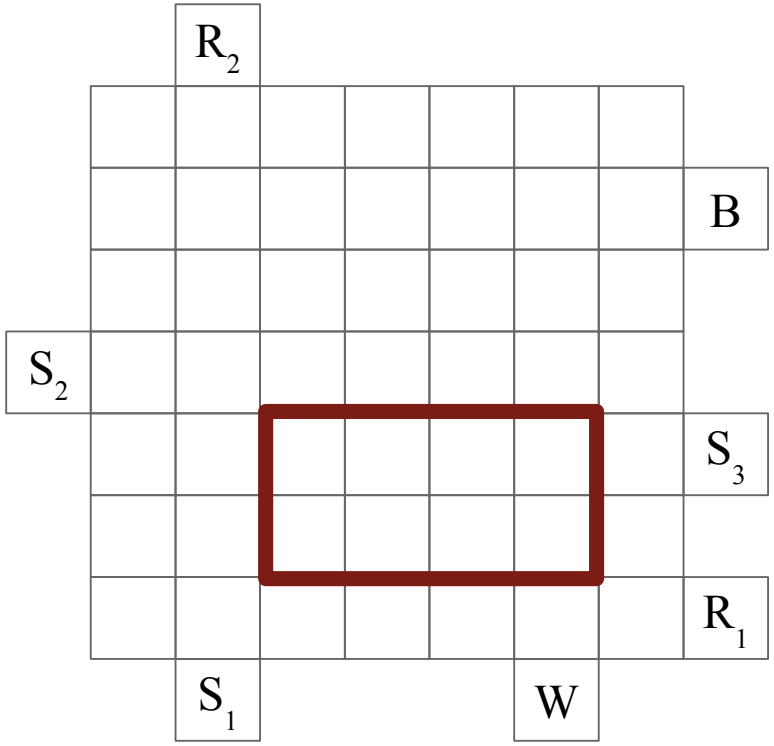
Operation	Area (cells)	Time (s)
Mix	2 x 4	3
Mix	2 x 2	4
Dilution	2 x 4	4
Dilution	2 x 2	5

Module library

Module-Based Operation Execution



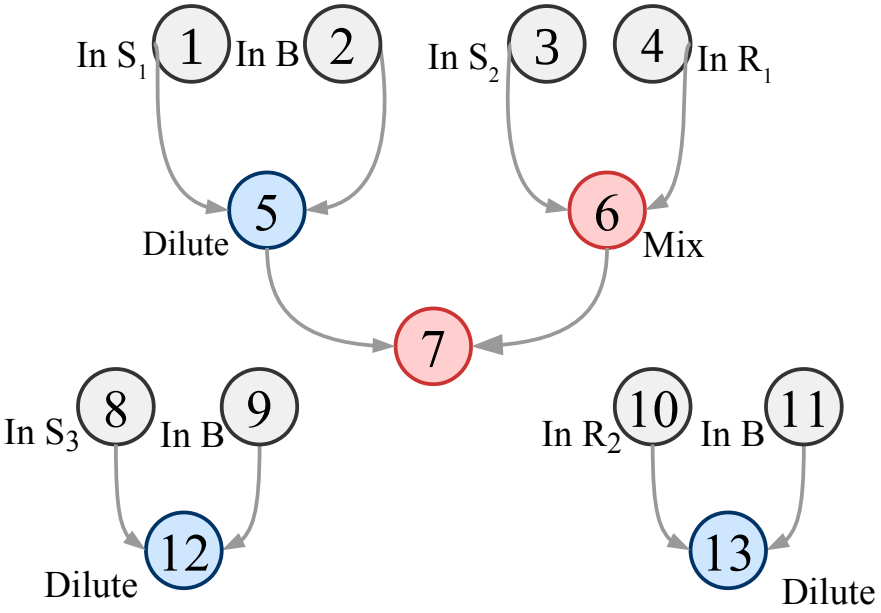
Module-Based Operation Execution



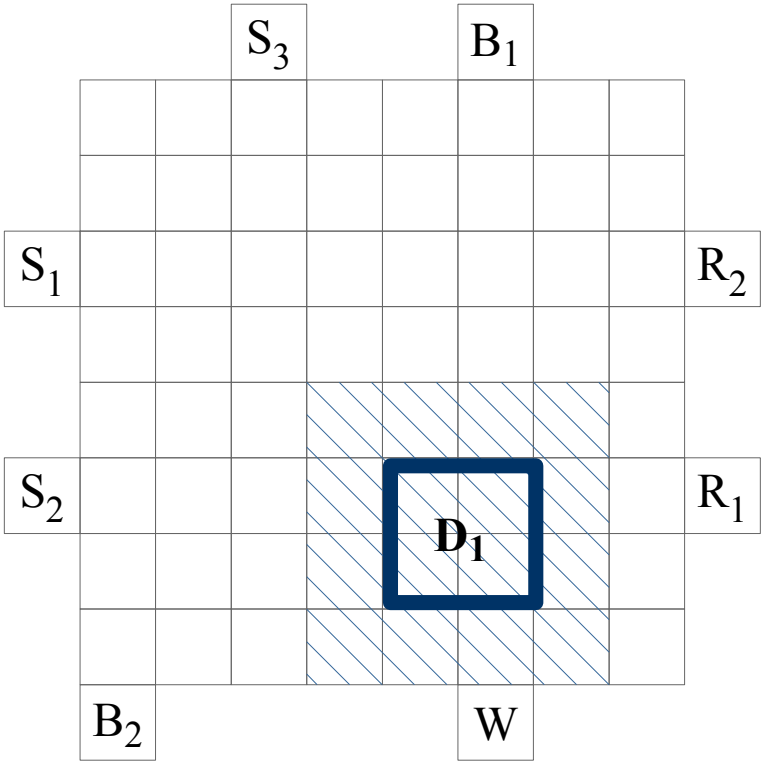
- Operations confined to rectangular, fixed modules
- Positions of droplets inside modules ignored
- Segregation cells

Module-Based Synthesis with Dynamic Virtual Modules

Example



Application graph



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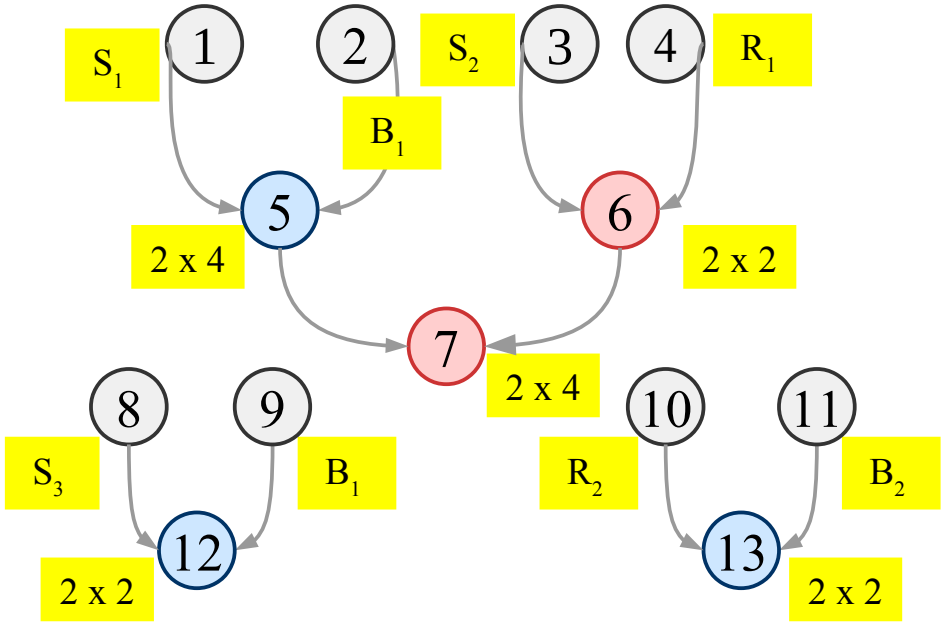
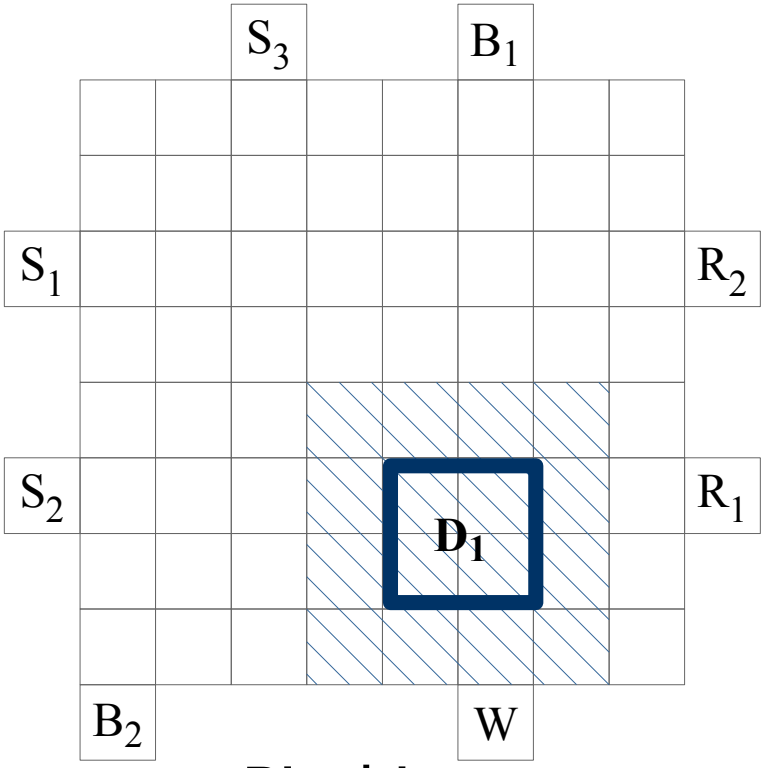
Example

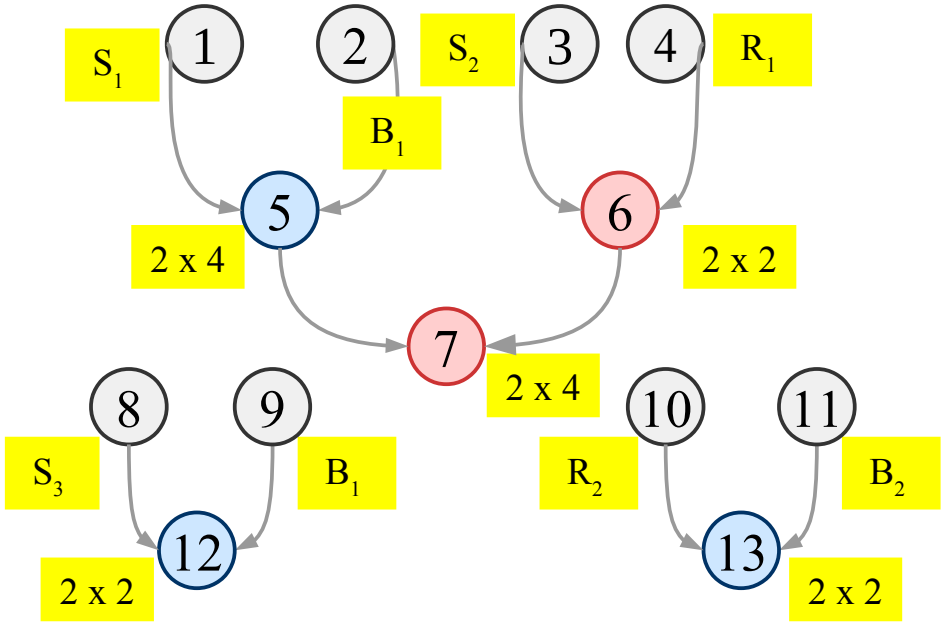


Application graph



Biochip

Example



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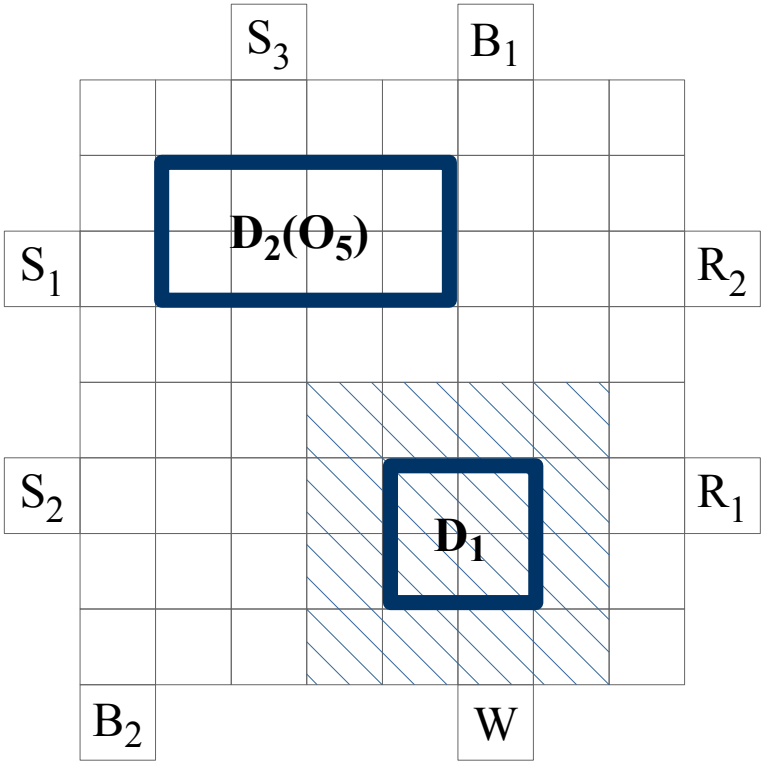

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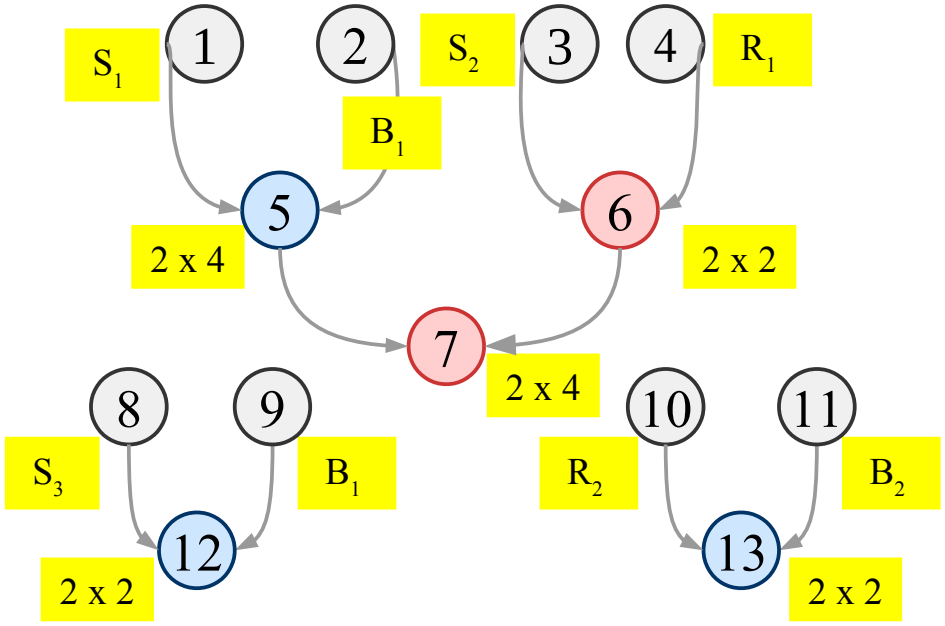

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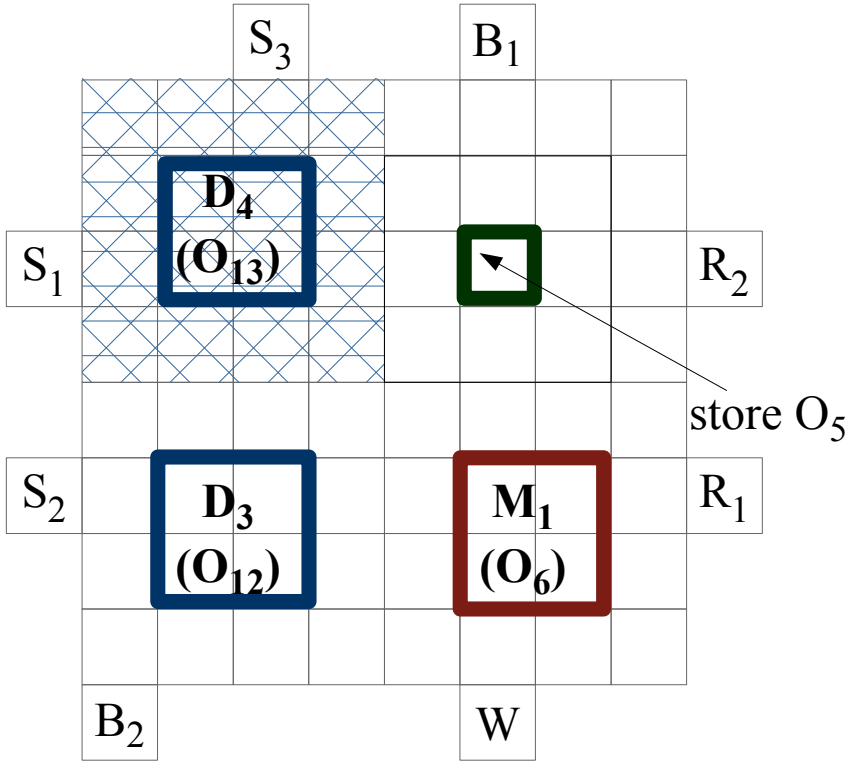

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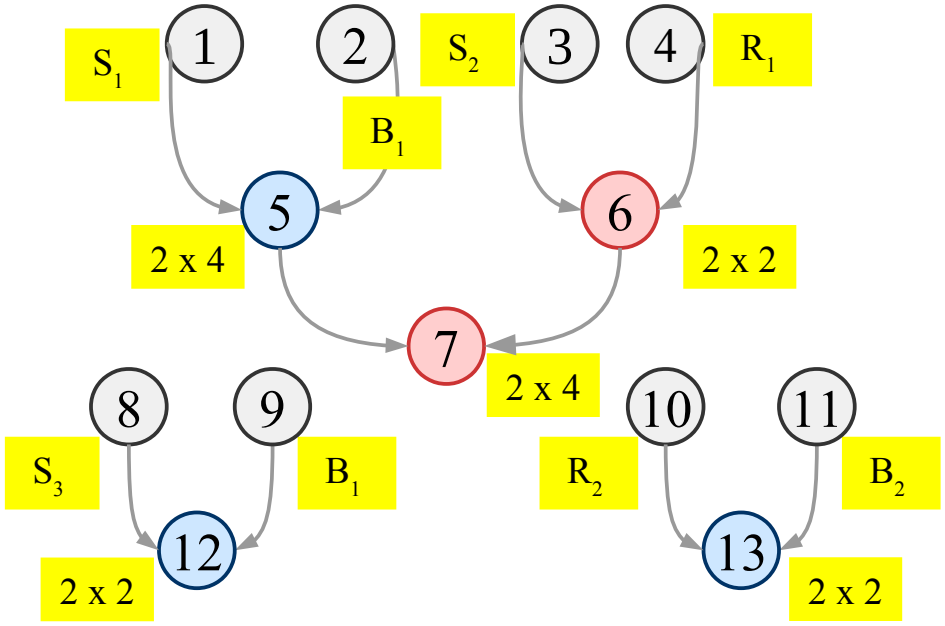
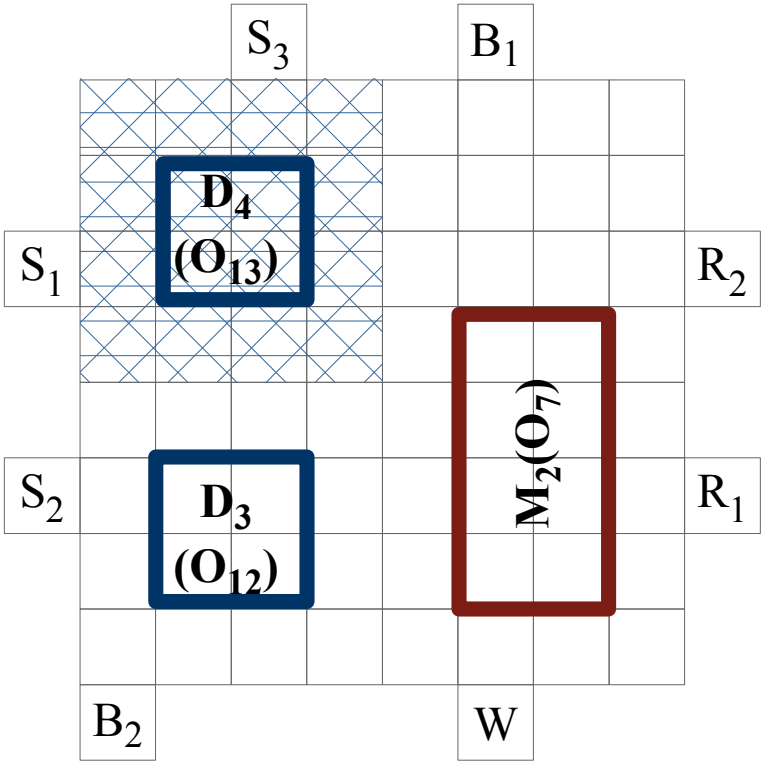
Example



Application graph



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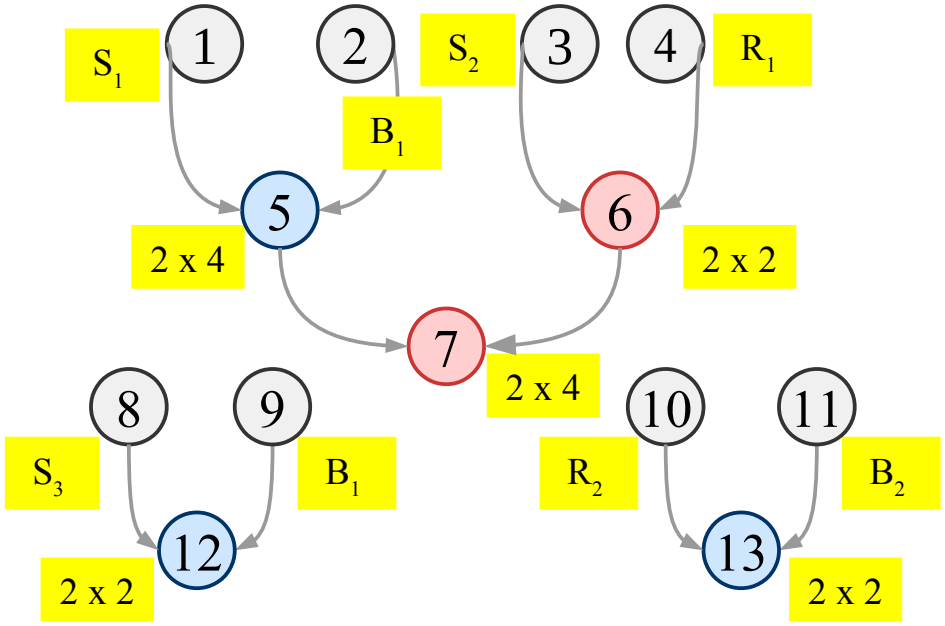
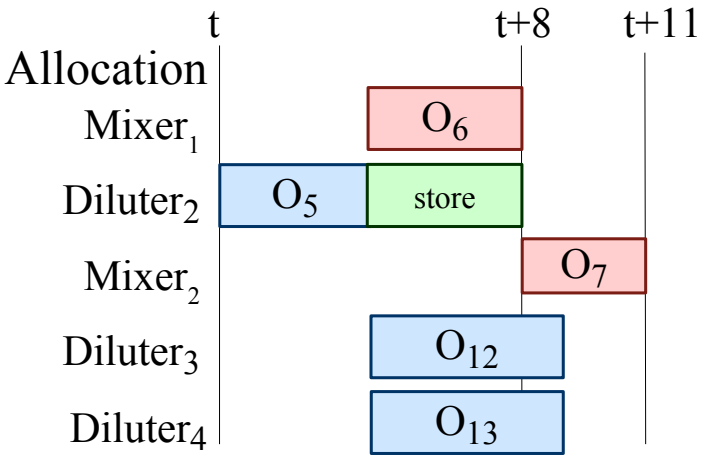
Example

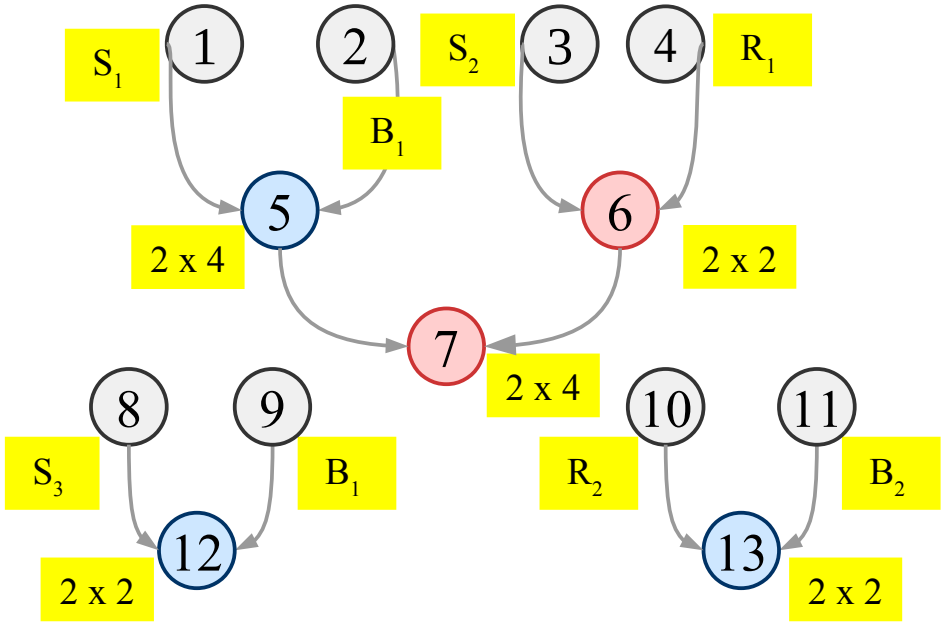


Application graph

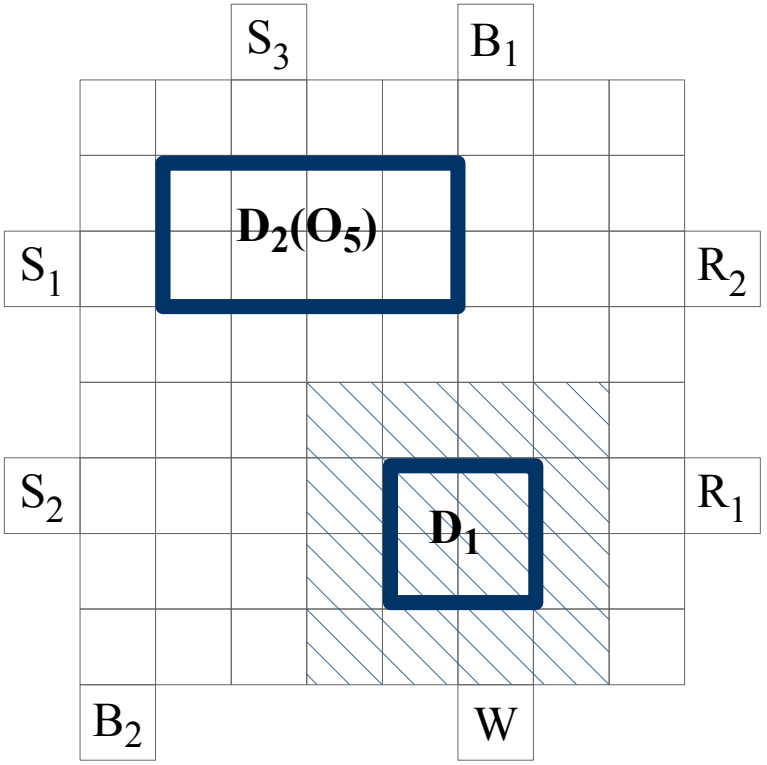


Schedule

Example



Application graph



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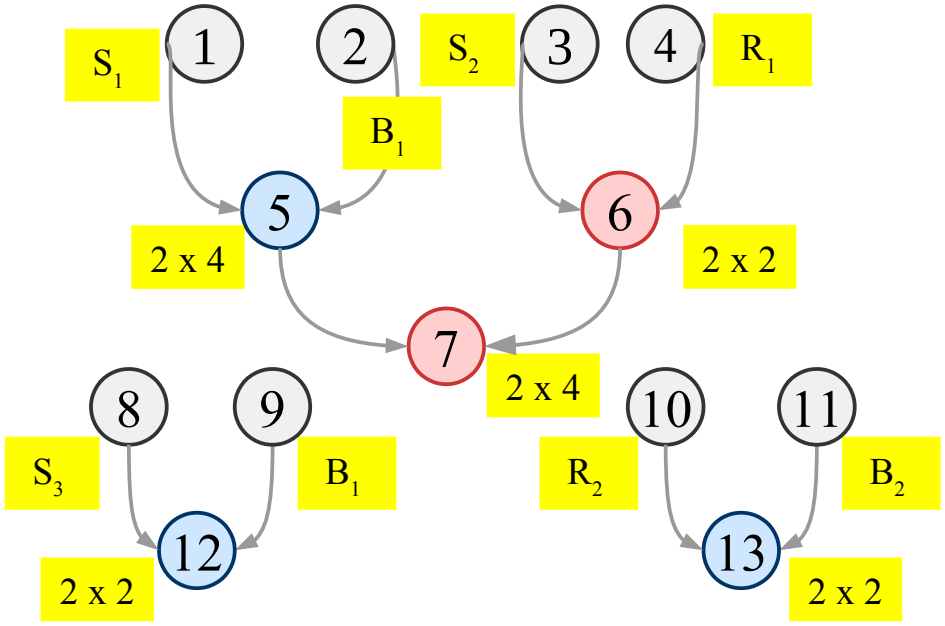
Example



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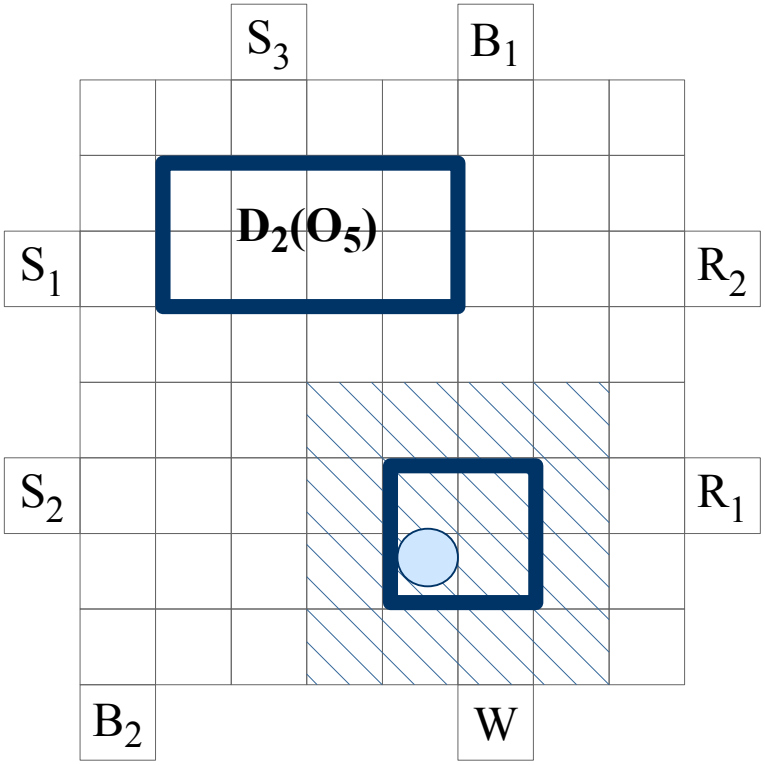

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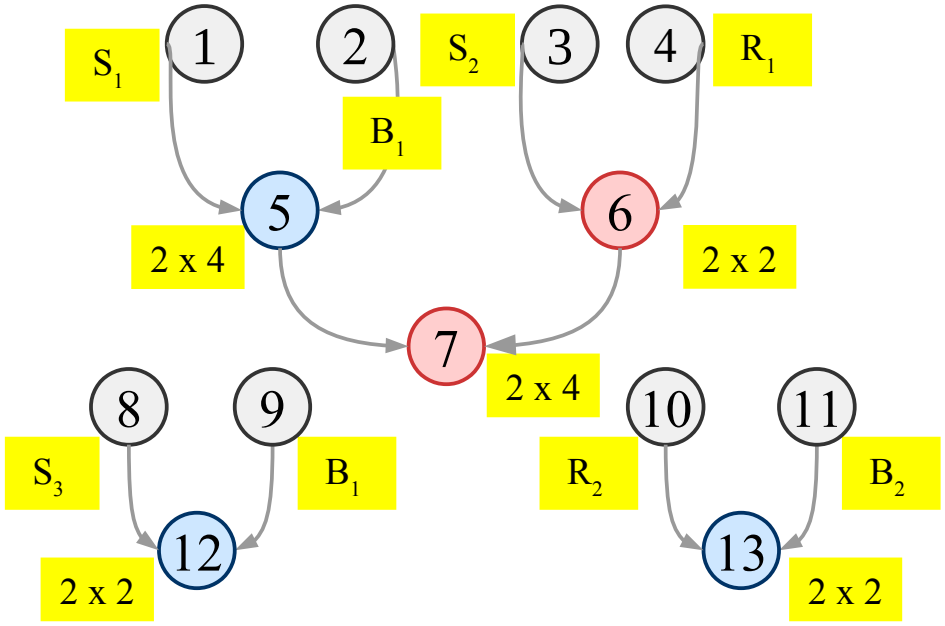

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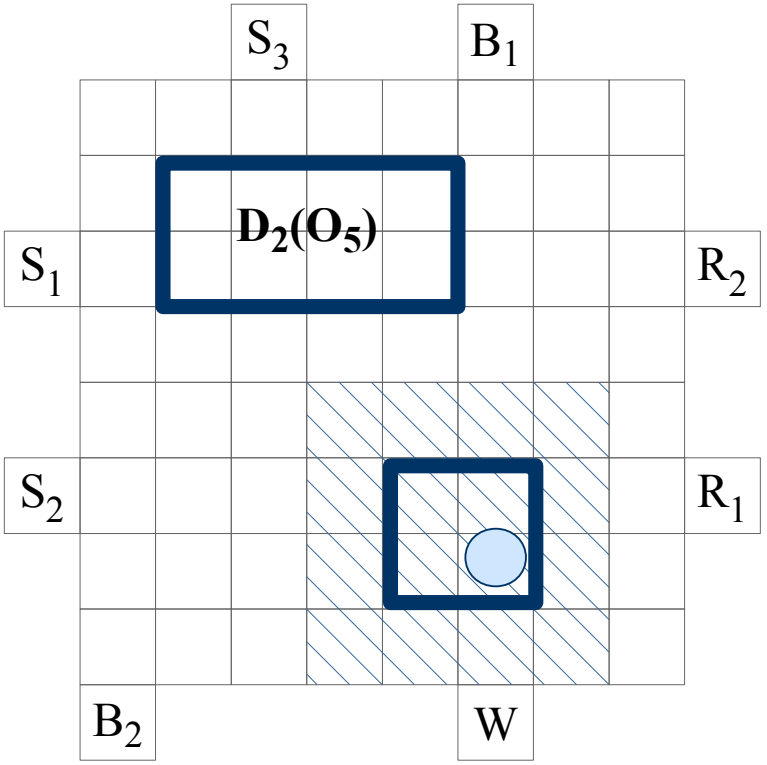

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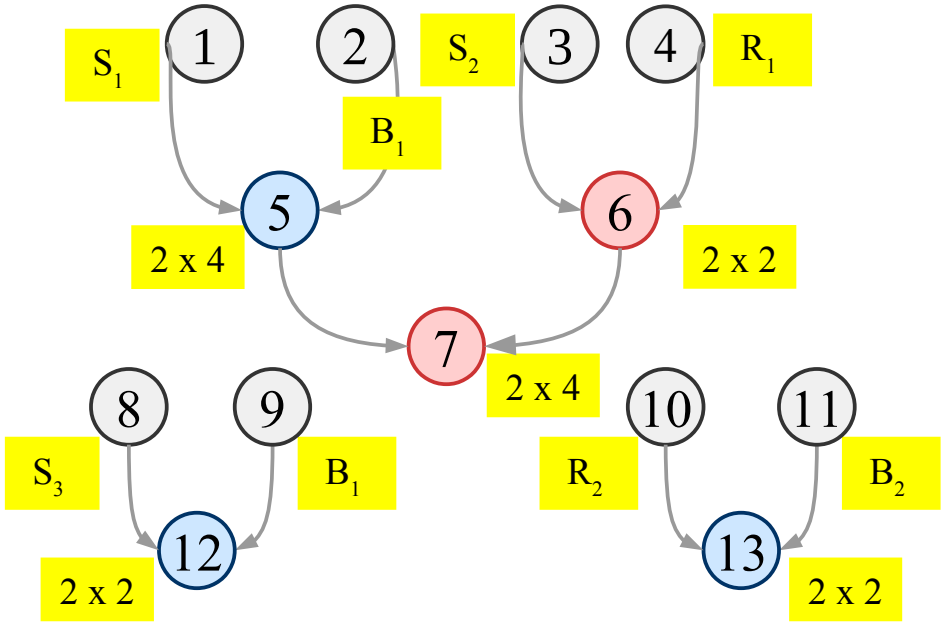

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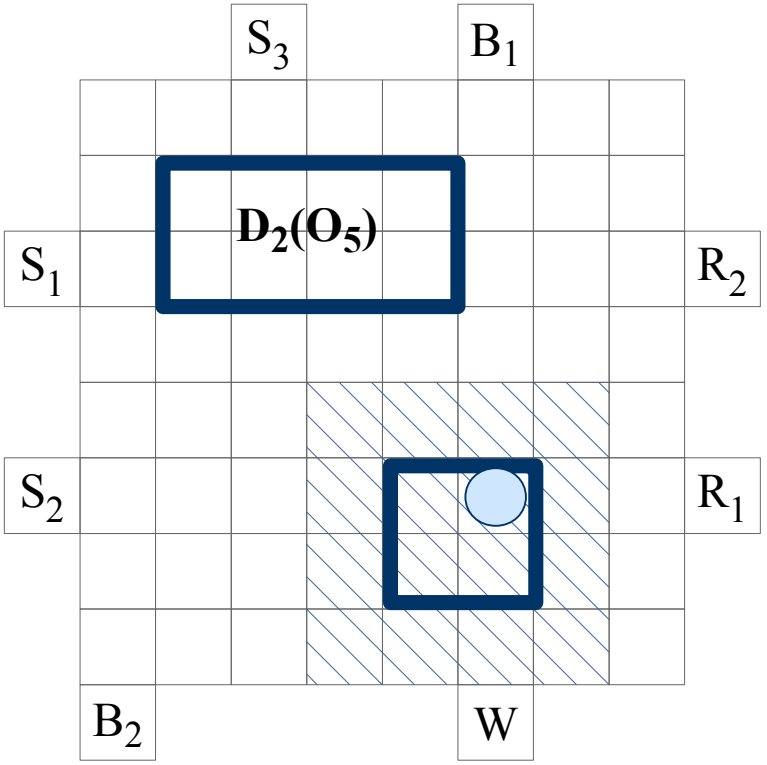

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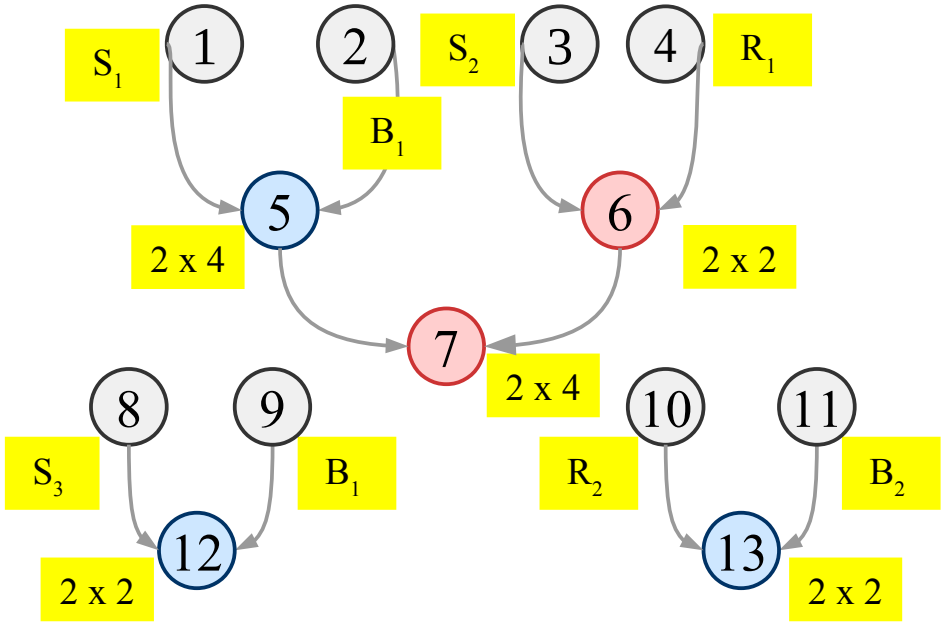
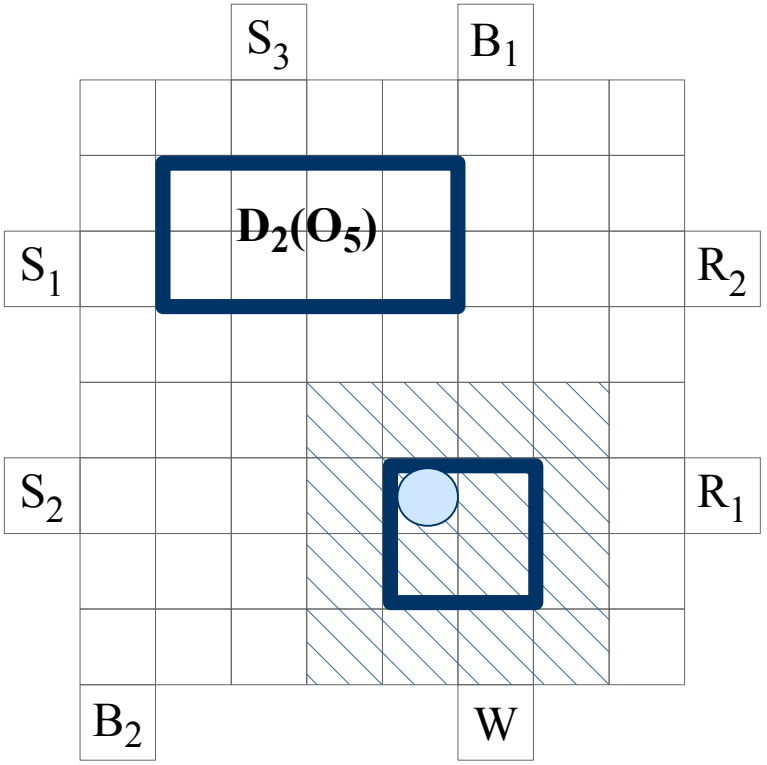
Example



Application graph



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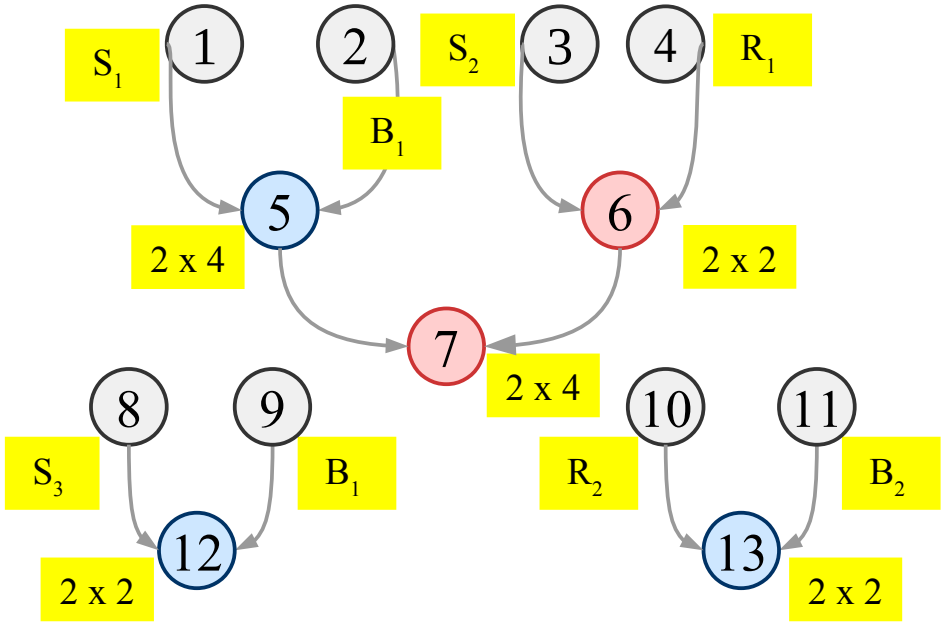
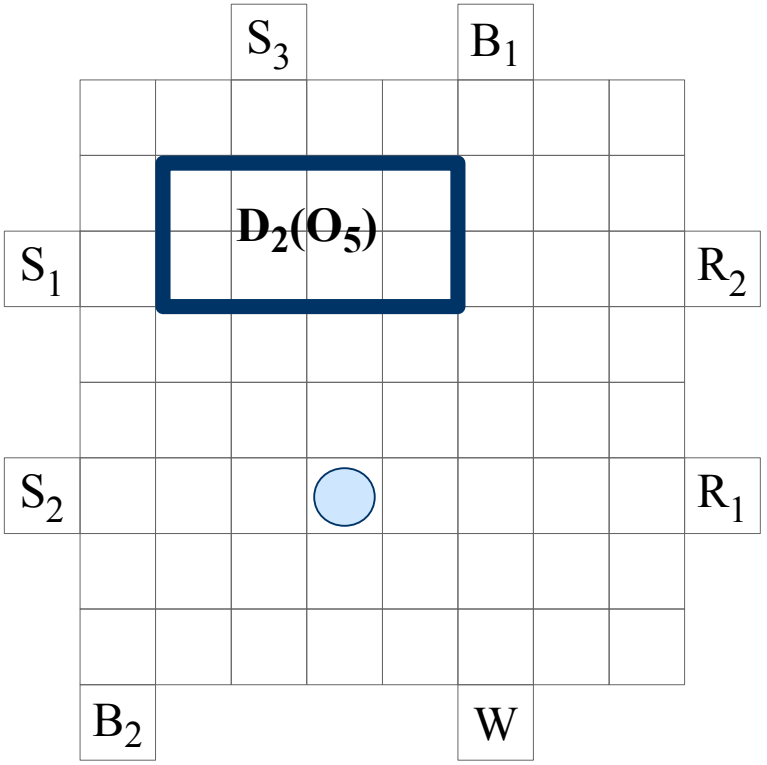


Application graph



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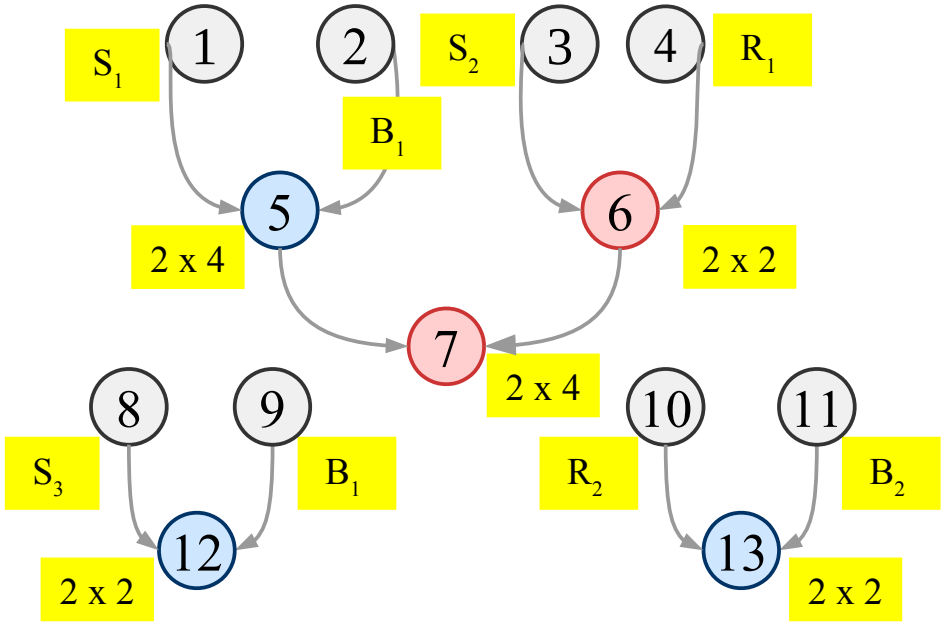

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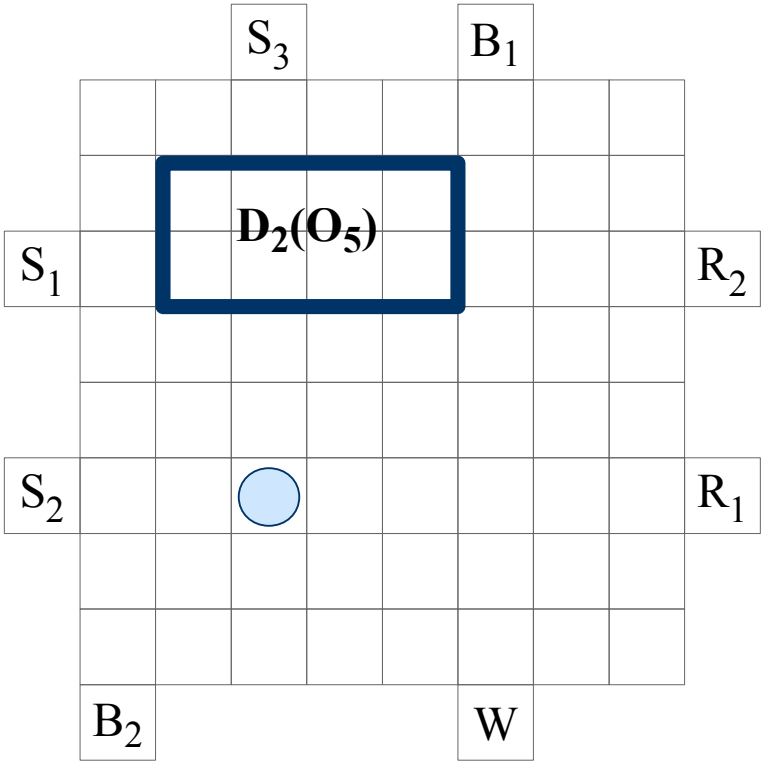

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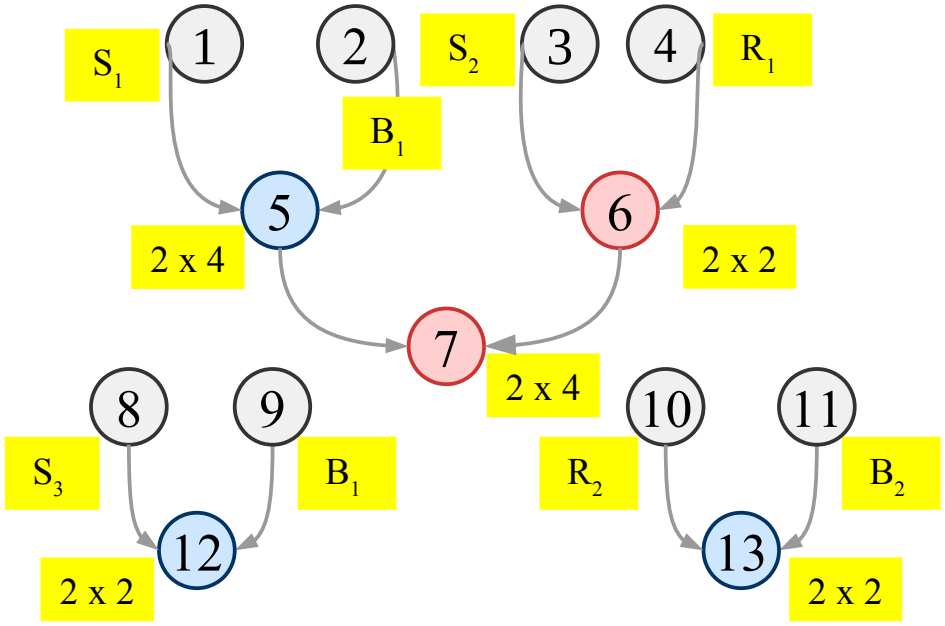

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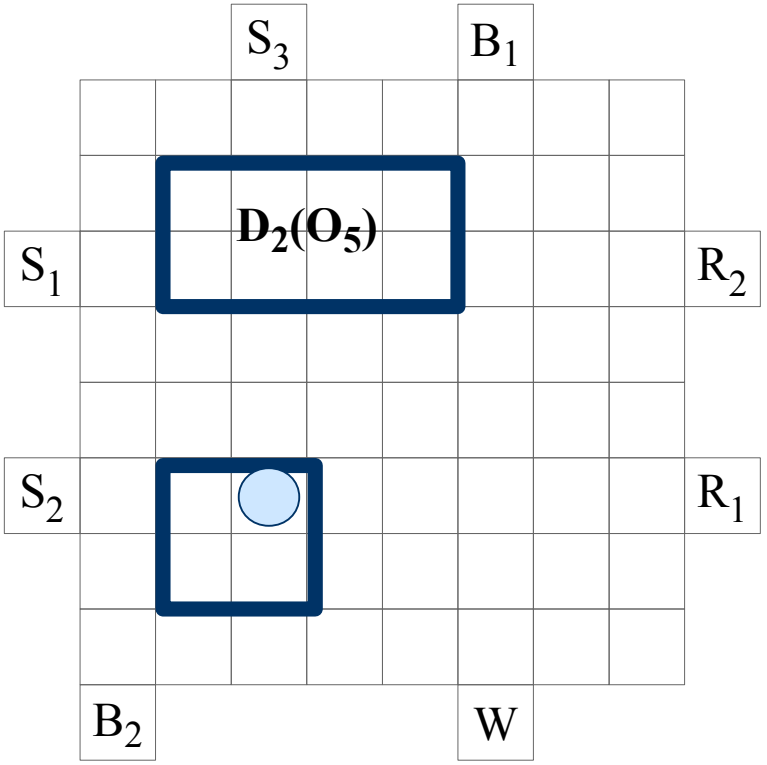

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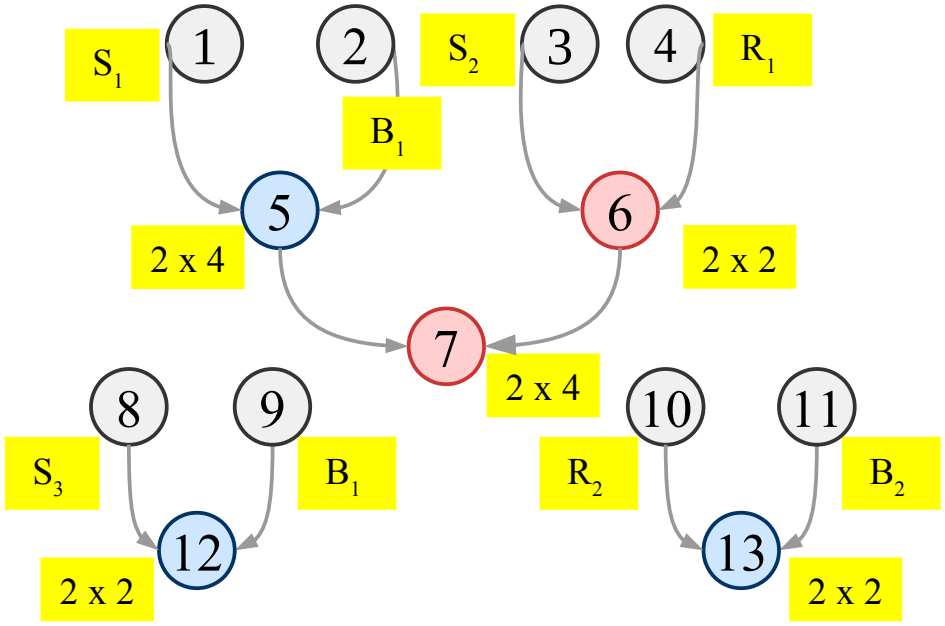

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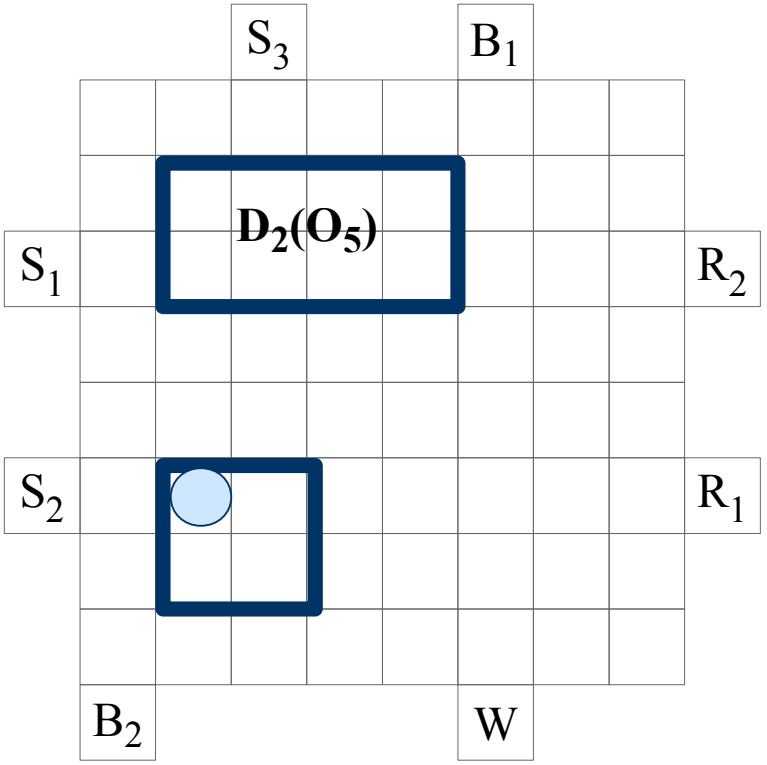

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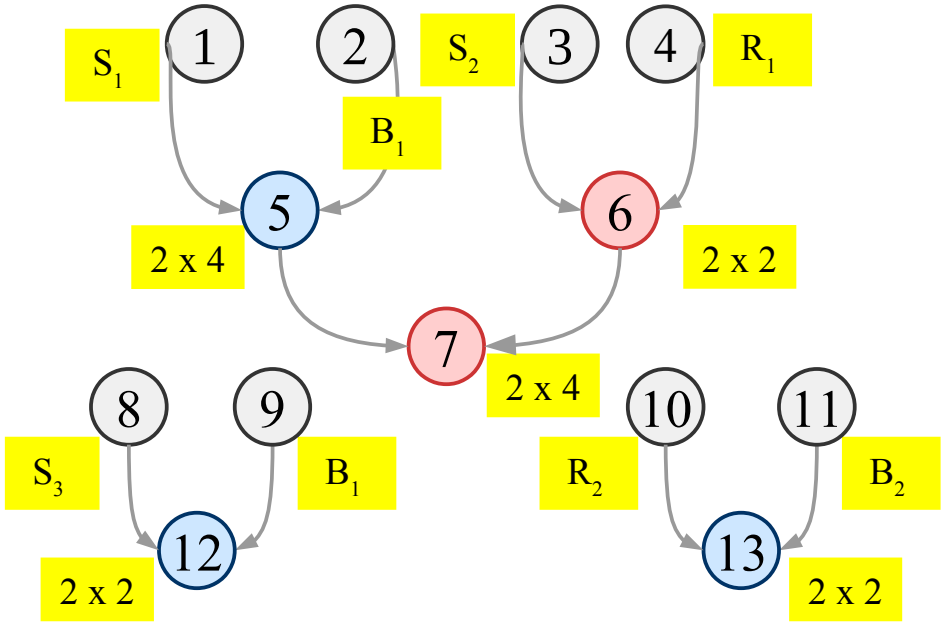
Example



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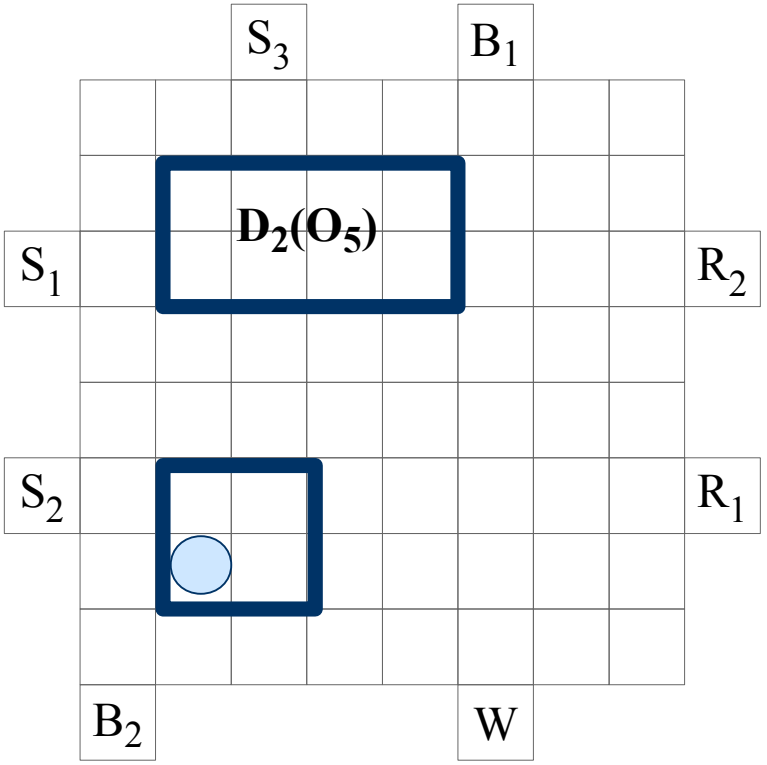

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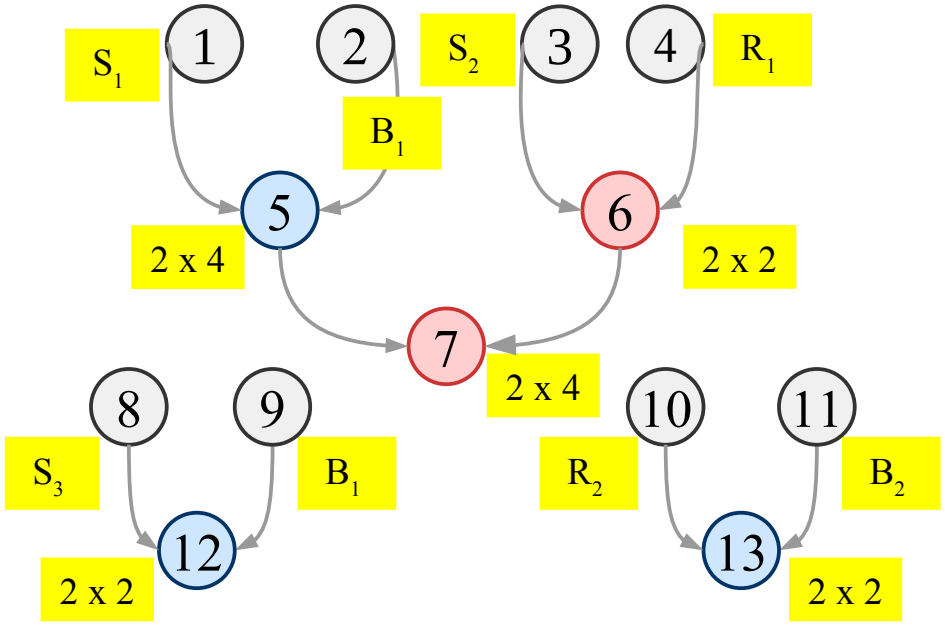
Example



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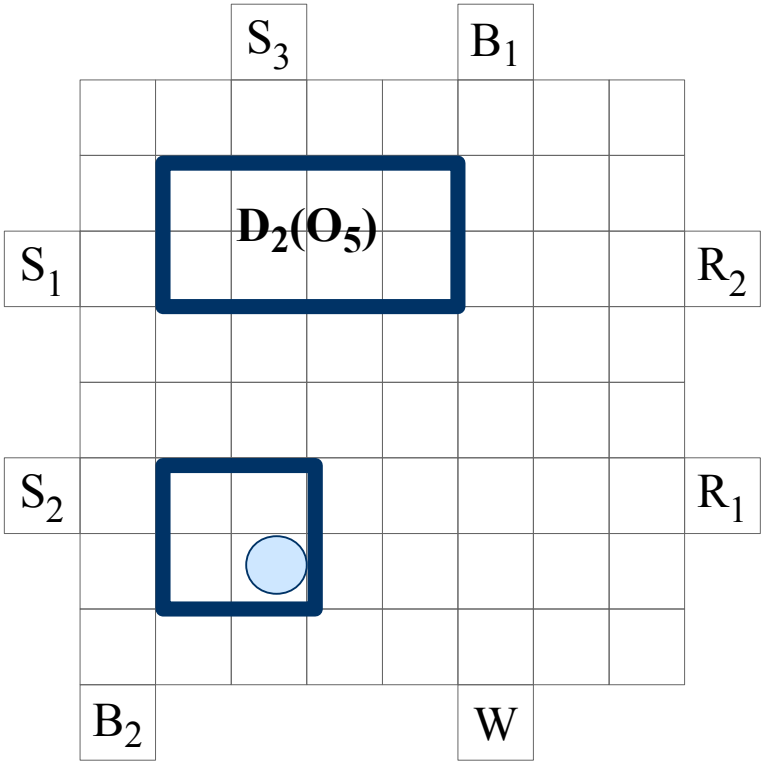

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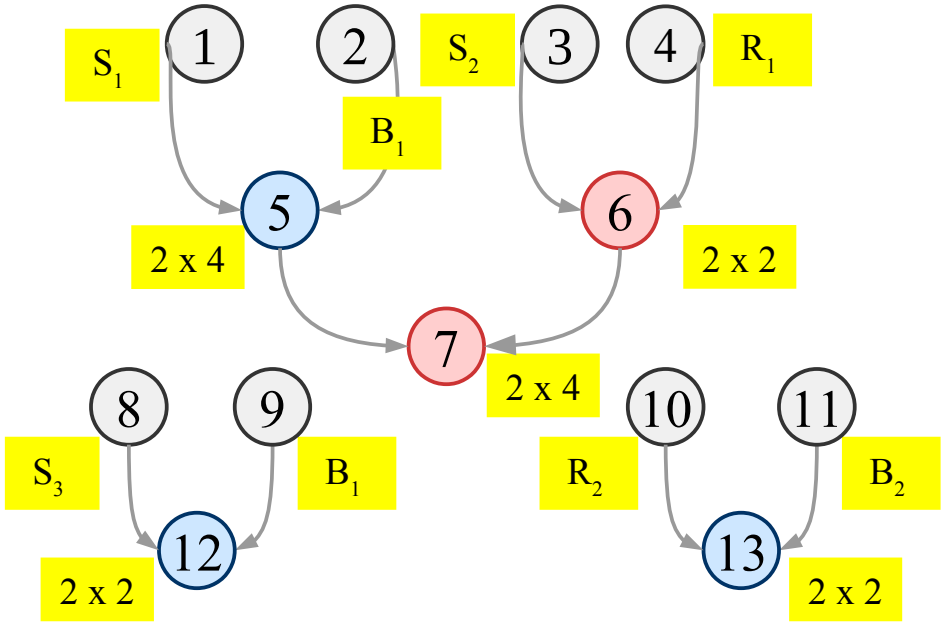
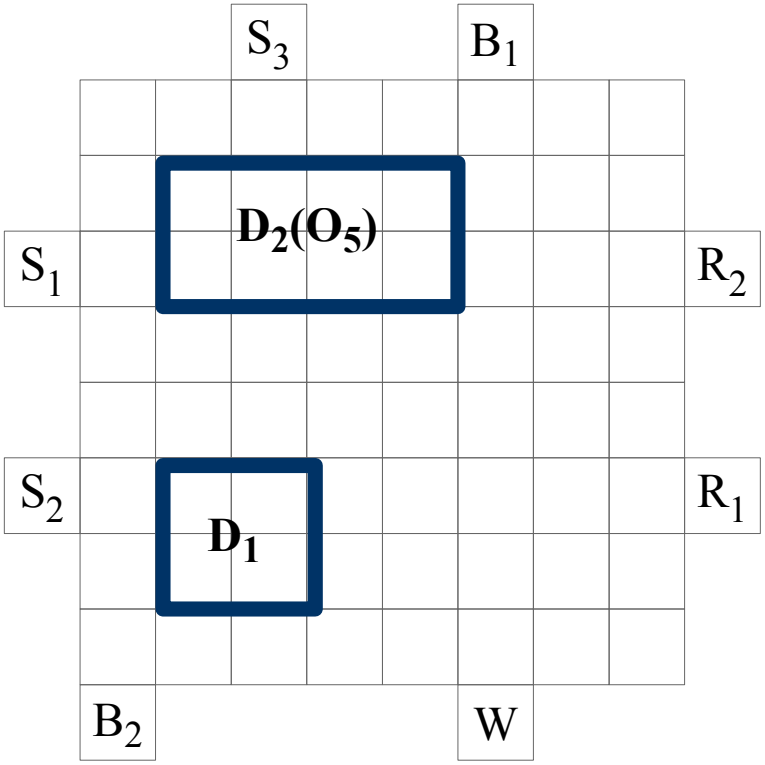


Application graph



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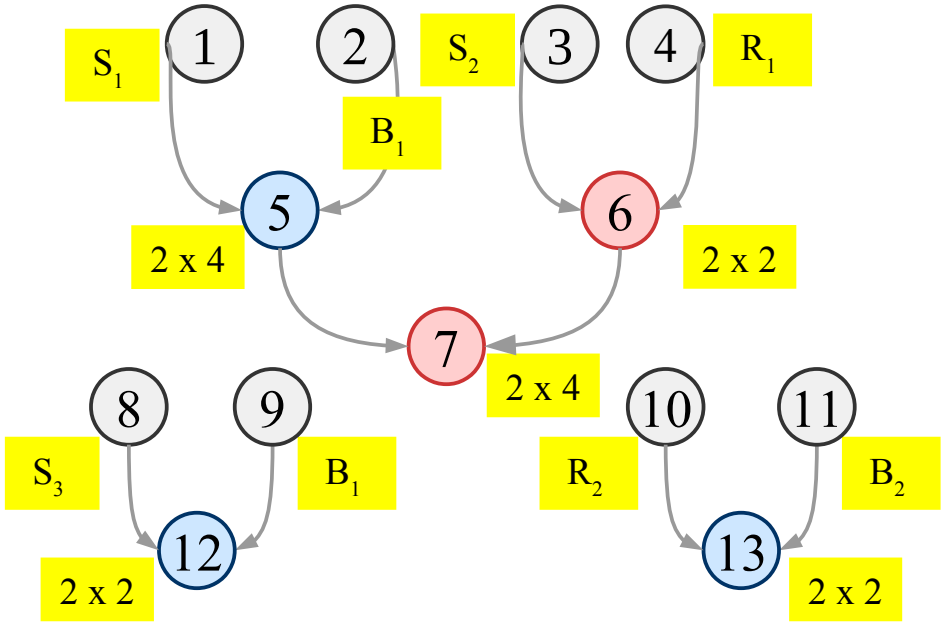
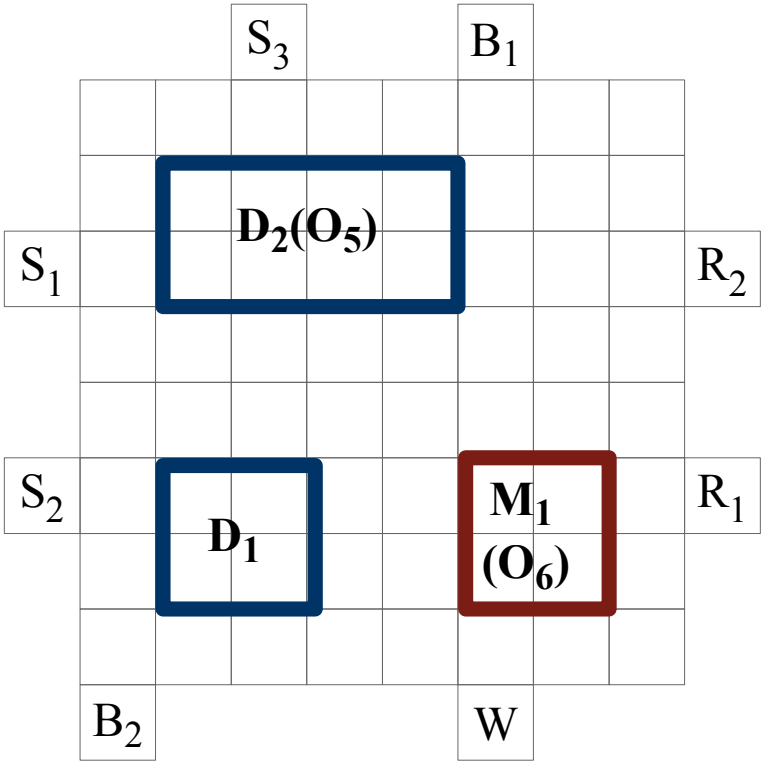
Example



Application graph



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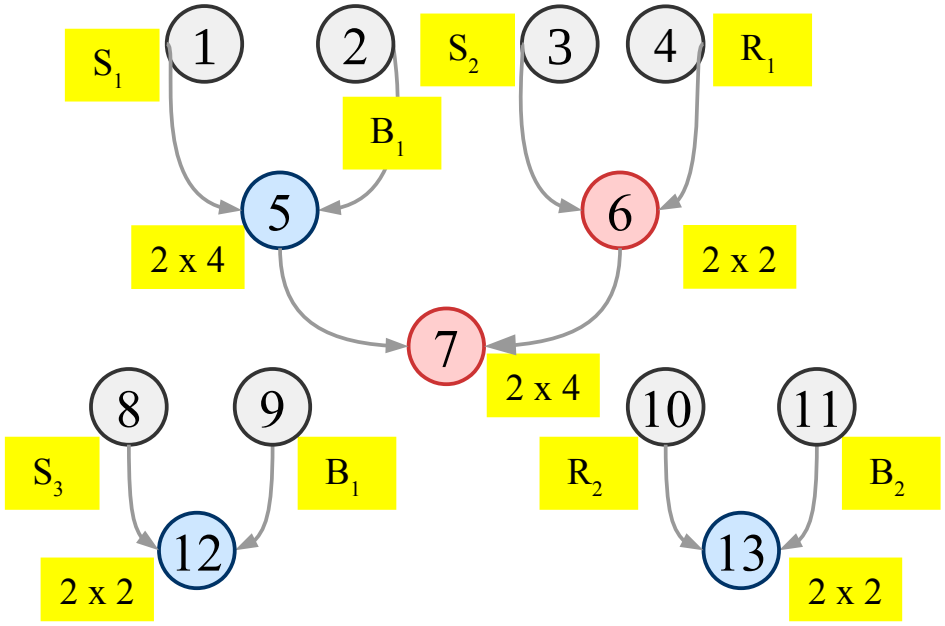
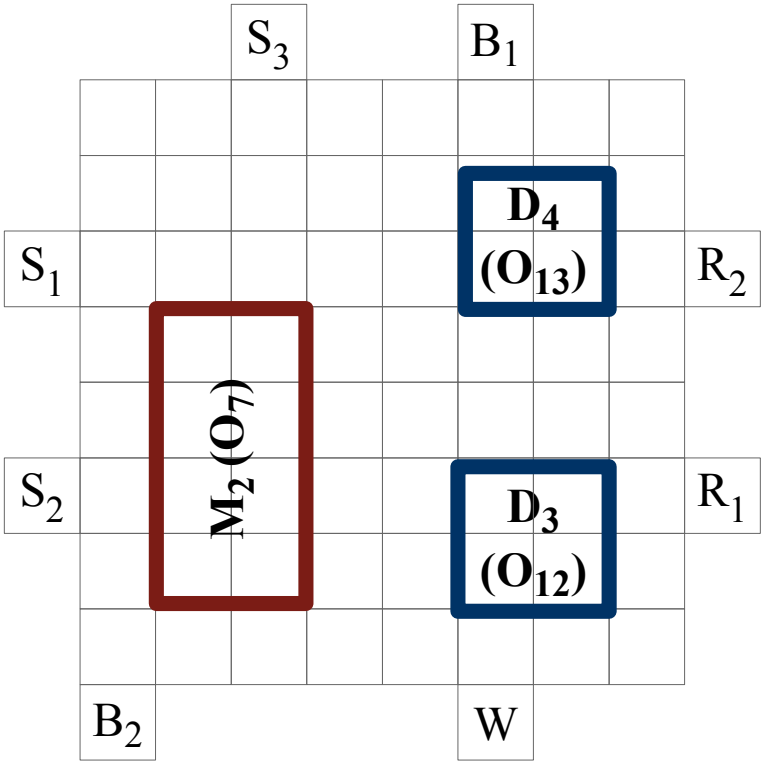
Example



Application graph



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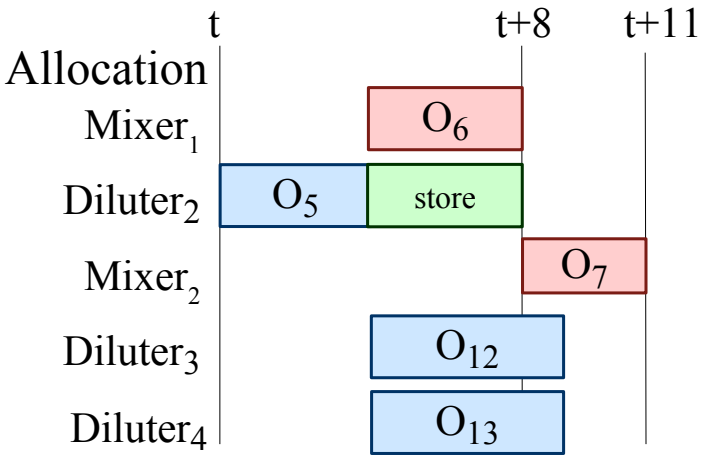
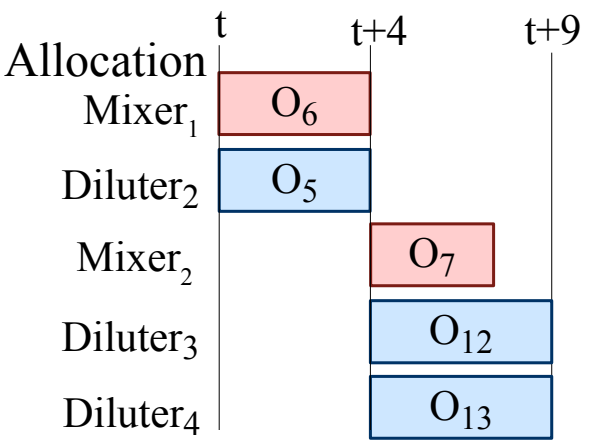
Example



Schedule – operation execution with fixed virtual modules

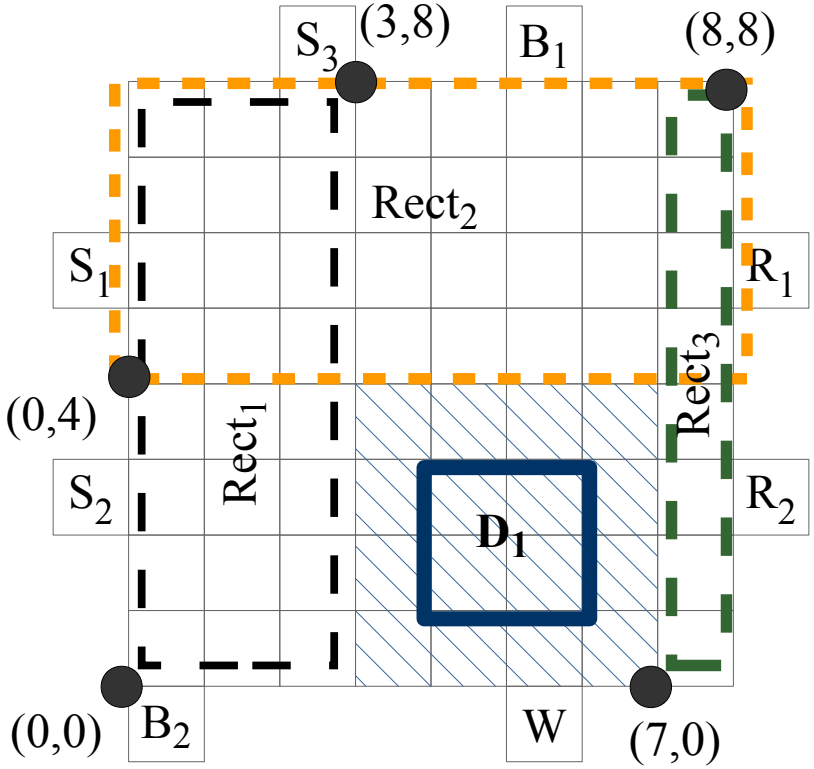


Schedule – operation execution with dynamic virtual modules

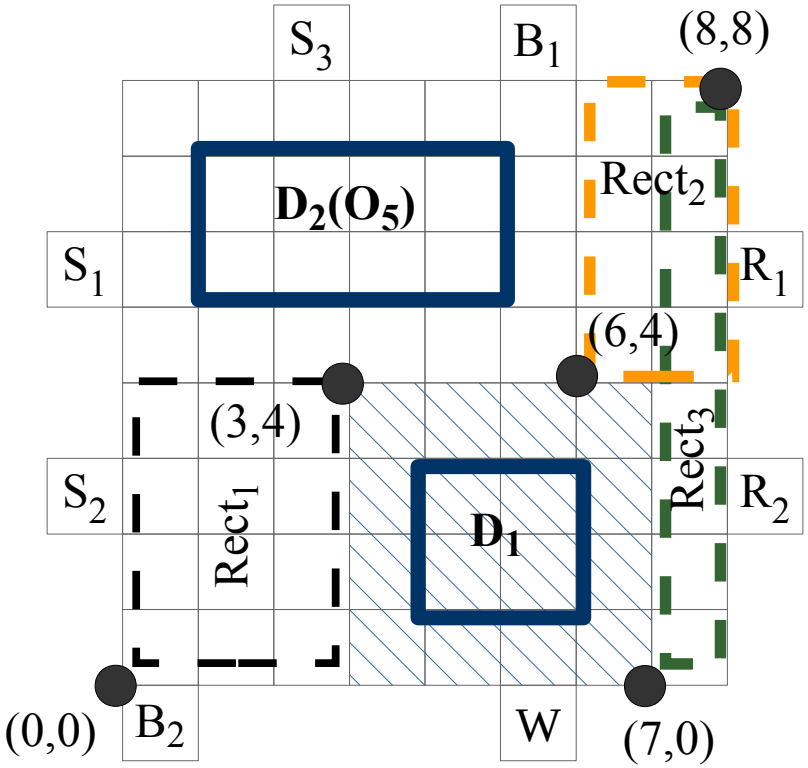
Solution

- Binding of modules to operations — **Tabu Search**
- Schedule of the operations — **List Scheduling**
  - Placement of modules performed inside scheduling
- Placement of the modules — **Maximal Empty Rectangles**
  - Free space manager based on [Bazargan et al. 2000] that divides free space on the chip into overlapping rectangles

Dynamic Placement Algorithm



Dynamic Placement Algorithm



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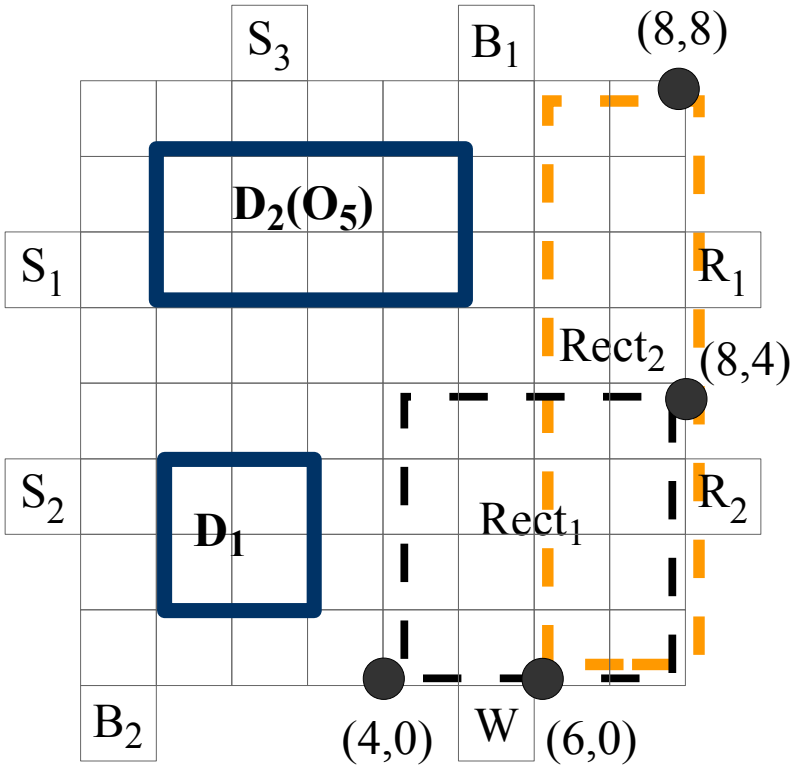


Experimental Evaluation

- Tabu Search-based algorithm implemented in Java
- Benchmarks
  - Real-life applications
    - Colorimetric protein assay
    - In-vitro diagnosis
    - Polymerase chain reaction – mixing stage
  - Synthetic benchmarks
    - 10 TGFF-generated benchmarks with 10 to 100 operations

- Comparison between:
  - Module-based synthesis with fixed modules (MBS)
  - T-Tree [Yuh et al. 2007]
  - Module-based synthesis with dynamic modules (DMBS)

Experimental Evaluation

Best-, average schedule length and standard deviation out of 50 runs for MBS

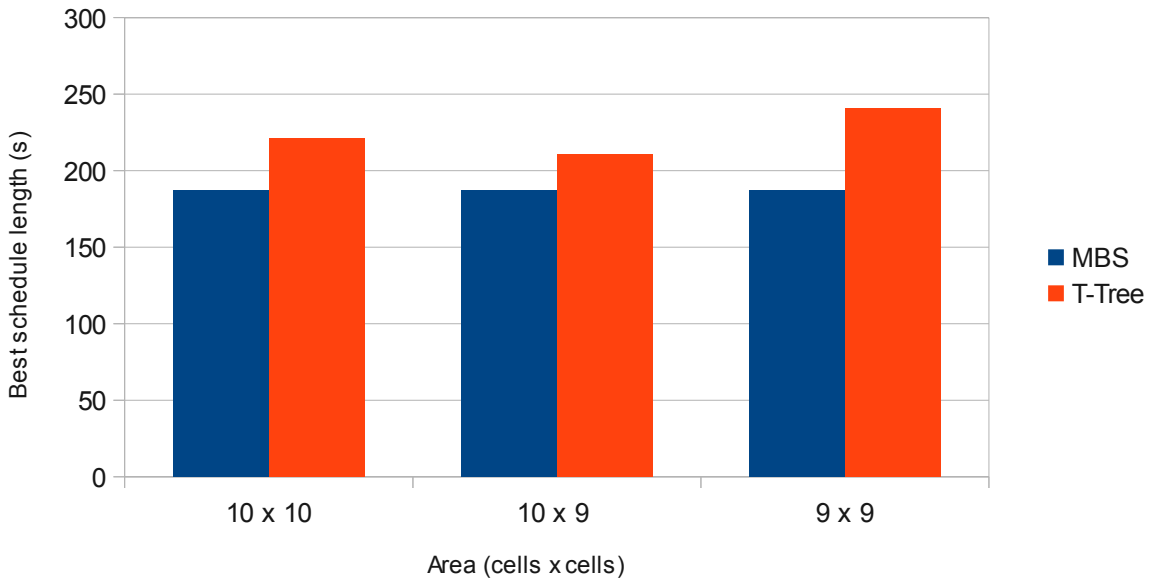
Colorimetric protein assay

Area	Time limit (min)	Best (s)	Average (s)	Standard dev. (%)
13 x 13	60	182	189.99	2.90
	10	182	192.00	3.64
	1	191	199.20	4.70
12 x 12	60	182	190.86	3.20
	10	185	197.73	6.50
	1	193	212.62	10.97
11 x 12	60	184	192.50	3.78
	10	194	211.72	14.37
	1	226	252.19	15.76

Experimental Evaluation

Best schedule length out of 50 runs for MBS vs. T-Tree

Colorimetric protein assay

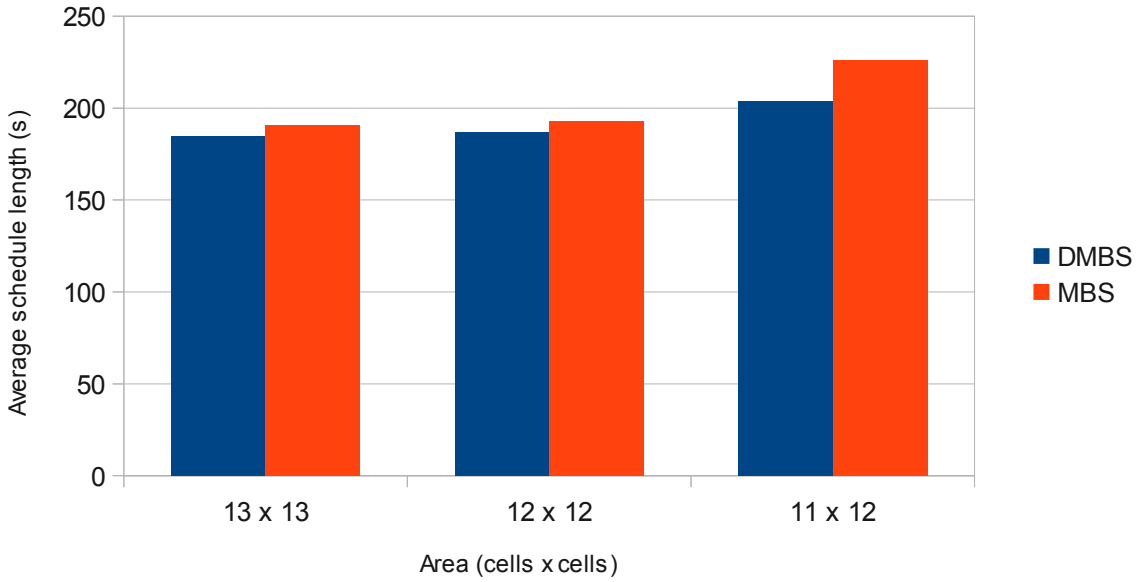


22.91 % improvement for 9 x 9

Experimental Evaluation

Average schedule length out of 50 runs for DMBS vs. MBS

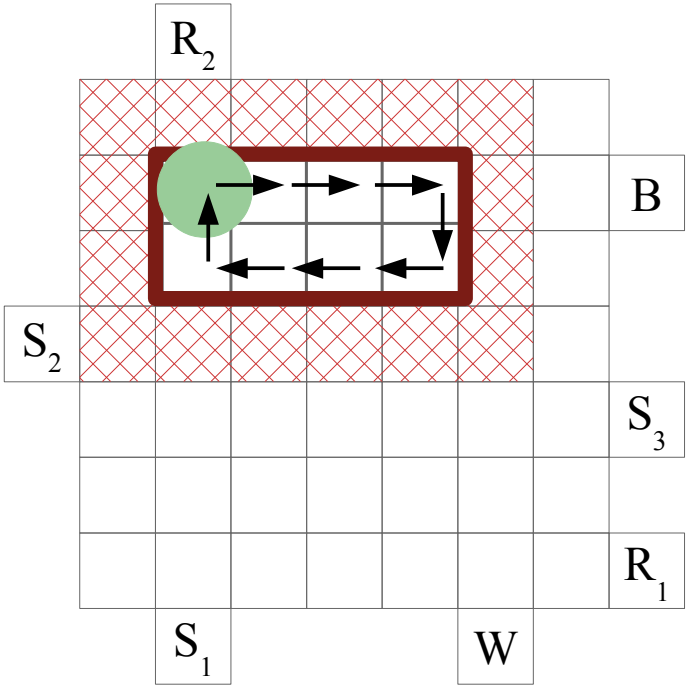
Colorimetric protein assay

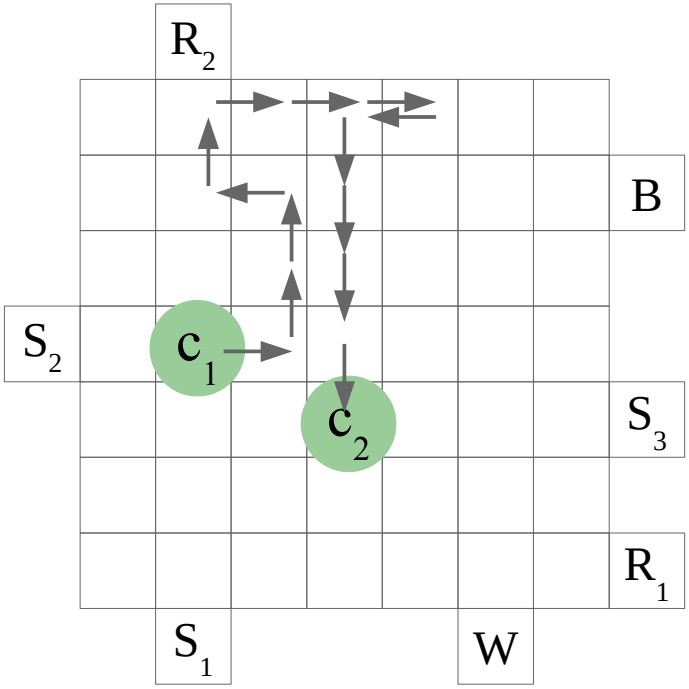


7.68 % improvement for 11 x 12

Routing-Based Operation Execution

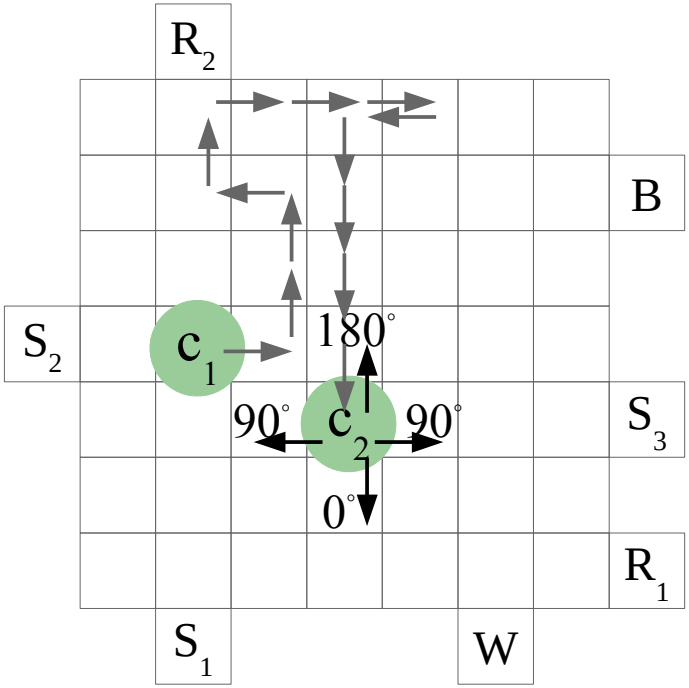
Module-Based vs. Routing-Based Operation Execution



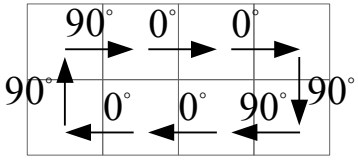


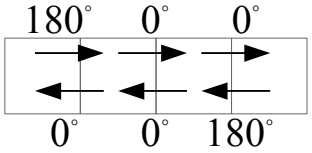
Operation Execution Characterization

p^{90}, p^{180}, p^{0} ?

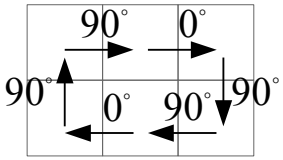


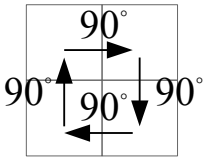
Operation Execution Characterization





p^{90}, p^{180}, p^{0}





Type	Area (cells)	Time (s)
Mix/Dlt	2 x 4	2.9
Mix/Dlt	1 x 4	4.6
Mix/Dlt	2 x 3	6.1
Mix/Dlt	2 x 2	9.9
Input	-	2
Detect	1 x 1	30

Electrode pitch size = 1.5 mm, gap spacing = 0.3 mm, average velocity rate = 20 cm/s.

Operation Execution Characterization

$p^{90} = 0.1\ \%$

$p^{180} = -0.5\ \%$

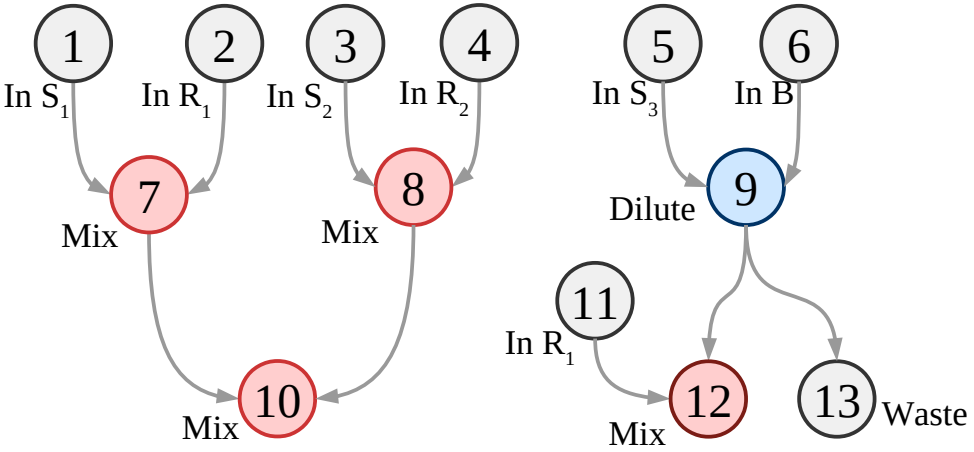
$p^{0}_{1} = 0.29\ \%$

$p^{0}_{2} = 0.58\ \%$

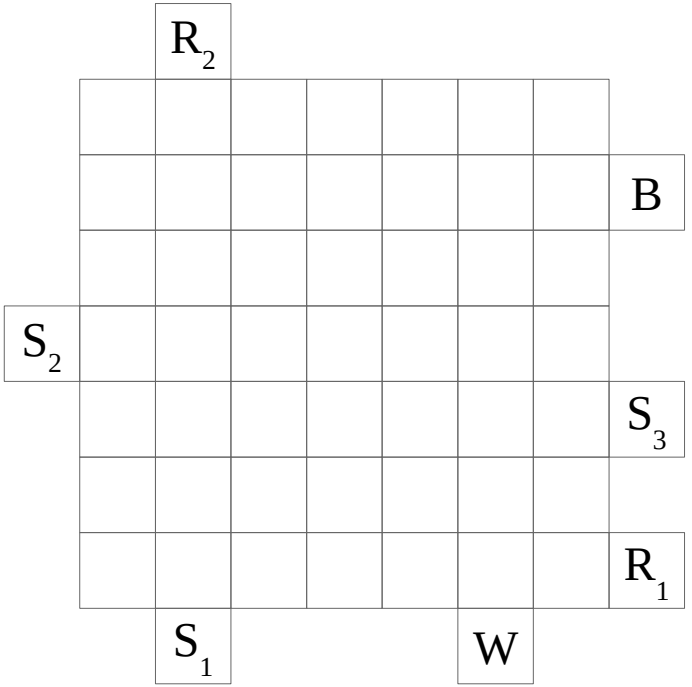
Type	Area (cells)	Time (s)
Mix/Dlt	2 x 4	2.9
Mix/Dlt	1 x 4	4.6
Mix/Dlt	2 x 3	6.1
Mix/Dlt	2 x 2	9.9
Input	-	2
Detect	1 x 1	30

Electrode pitch size = 1.5 mm, gap spacing = 0.3 mm, average velocity rate = 20 cm/s.

Example

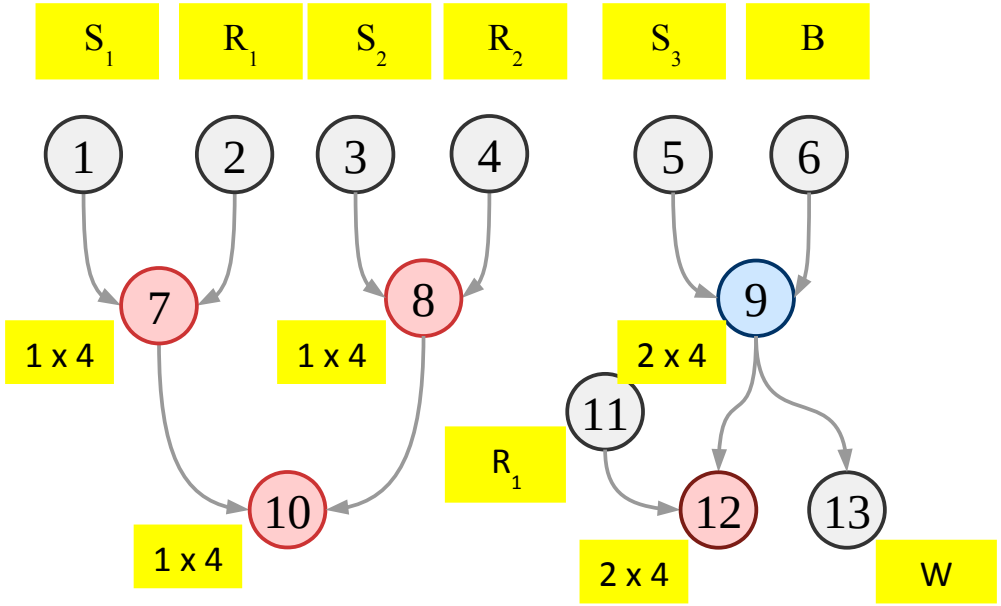


Application graph

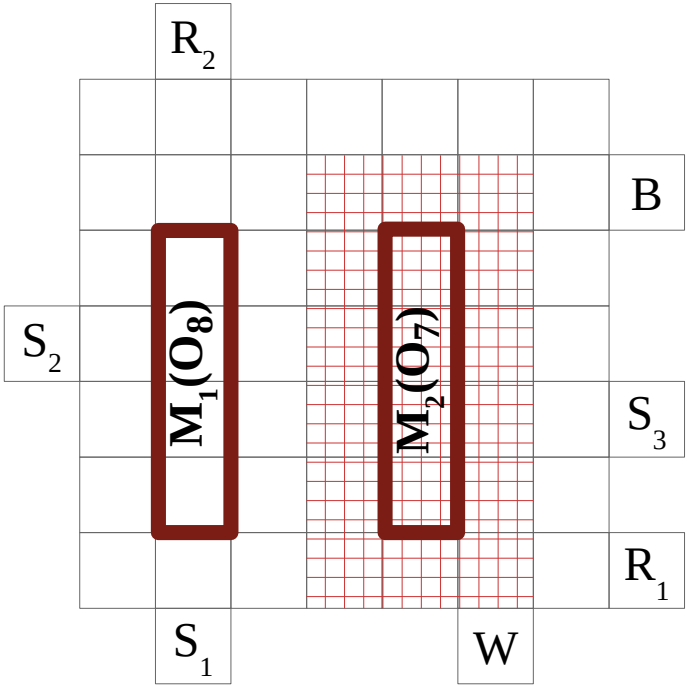


Biochip

Example

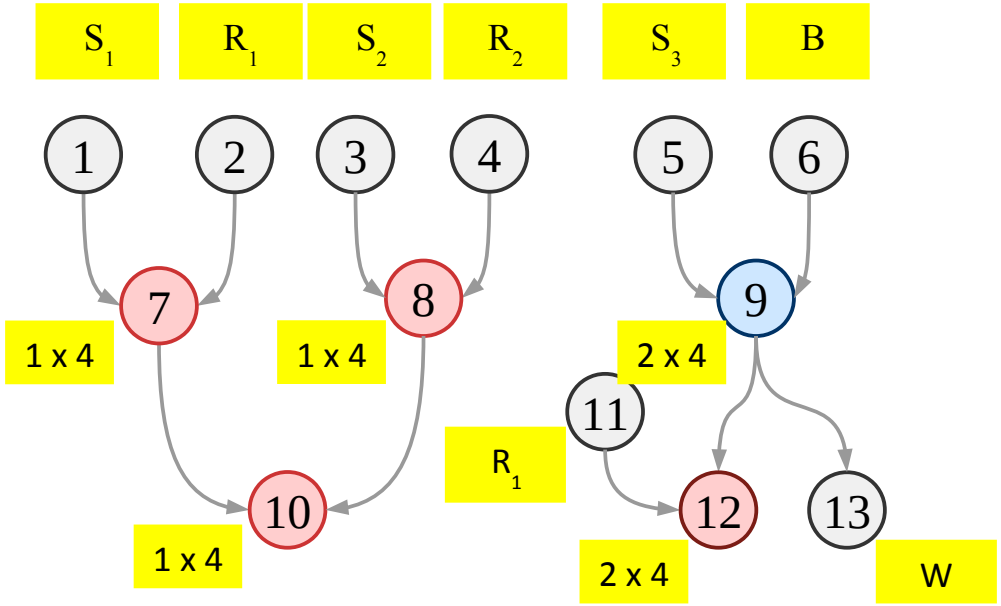


Application graph

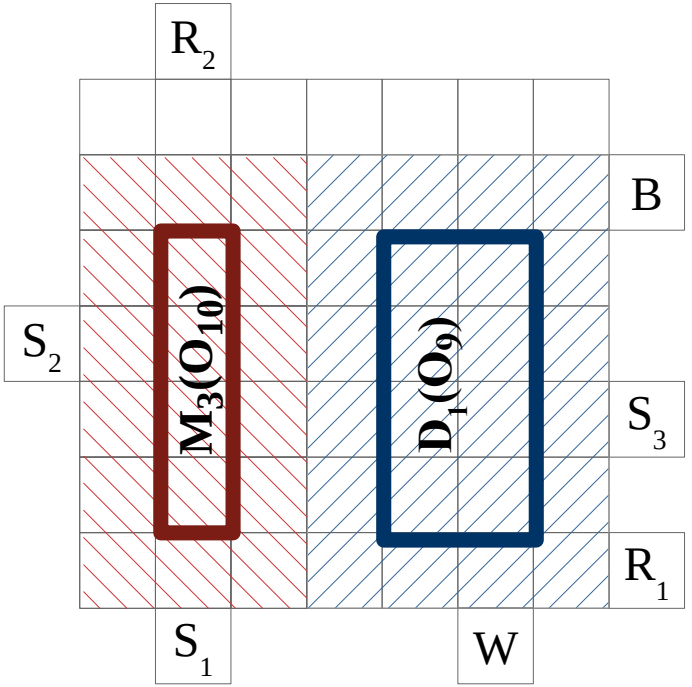


t = 2.04 s

Example

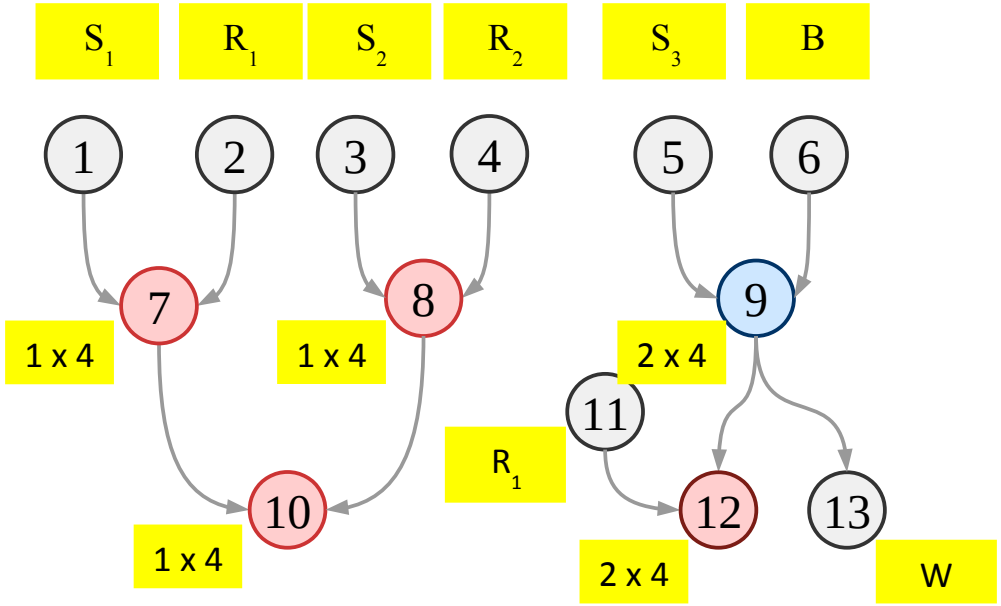


Application graph

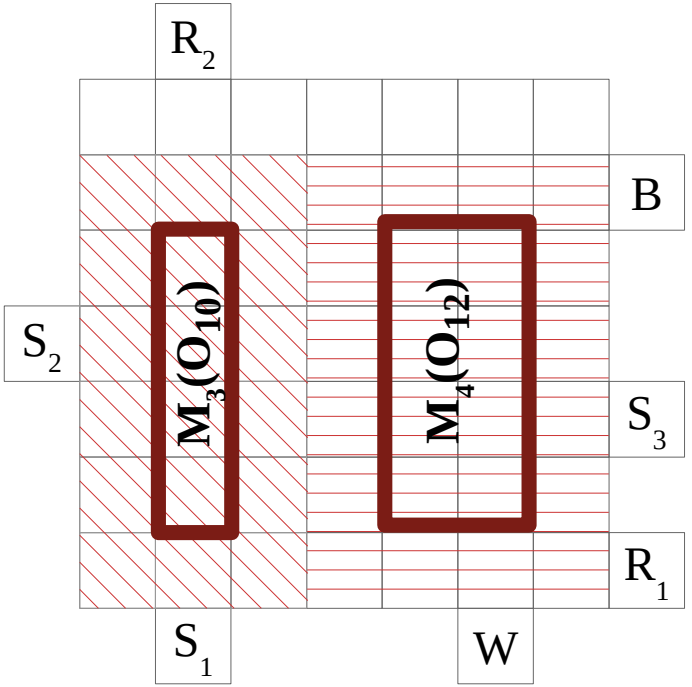


t = 6.67 s

Example

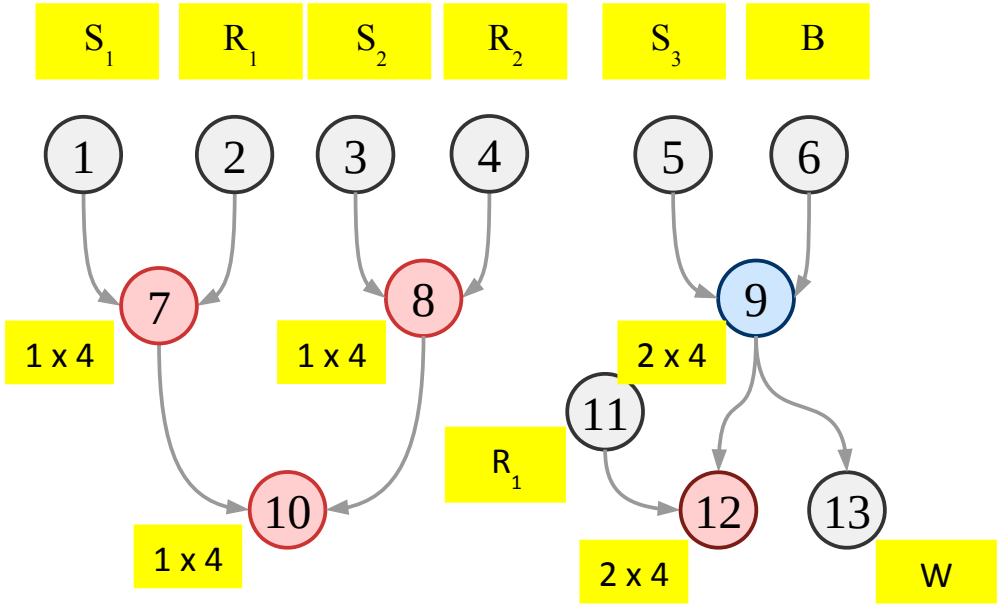


Application graph

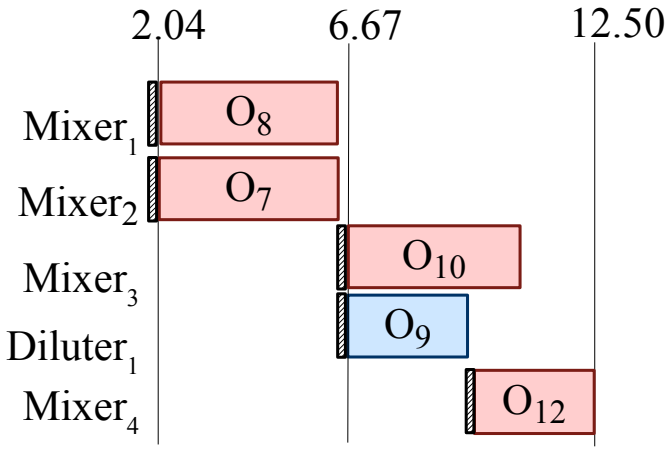


t = 9.5 s

Example

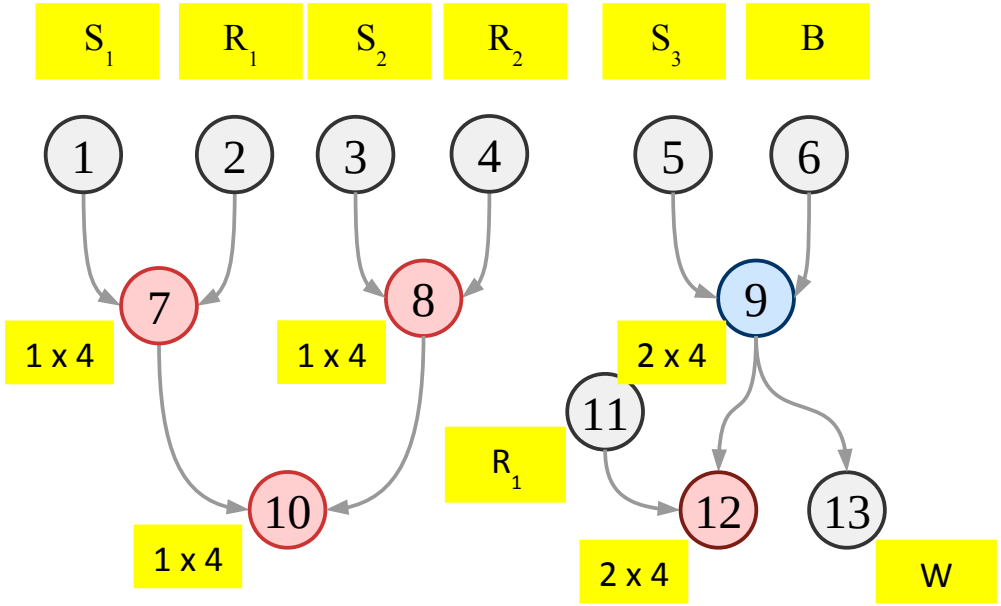


Application graph

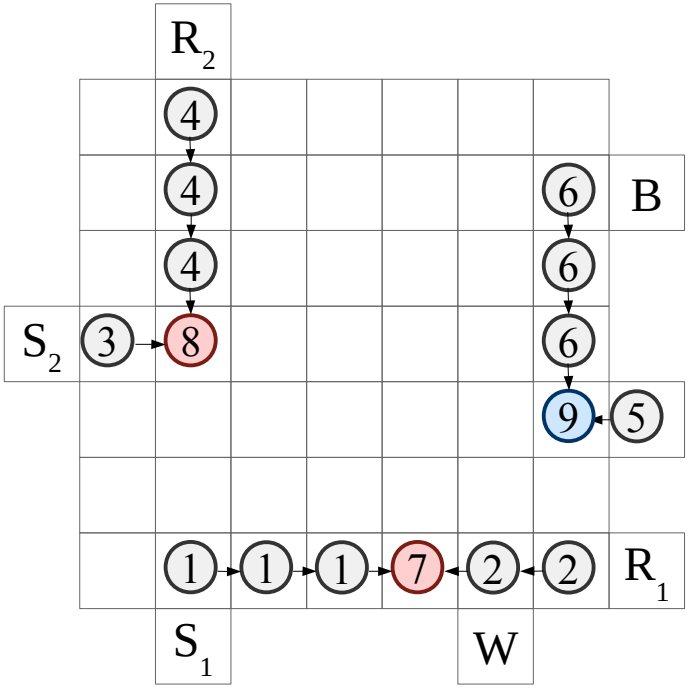


Schedule

Example

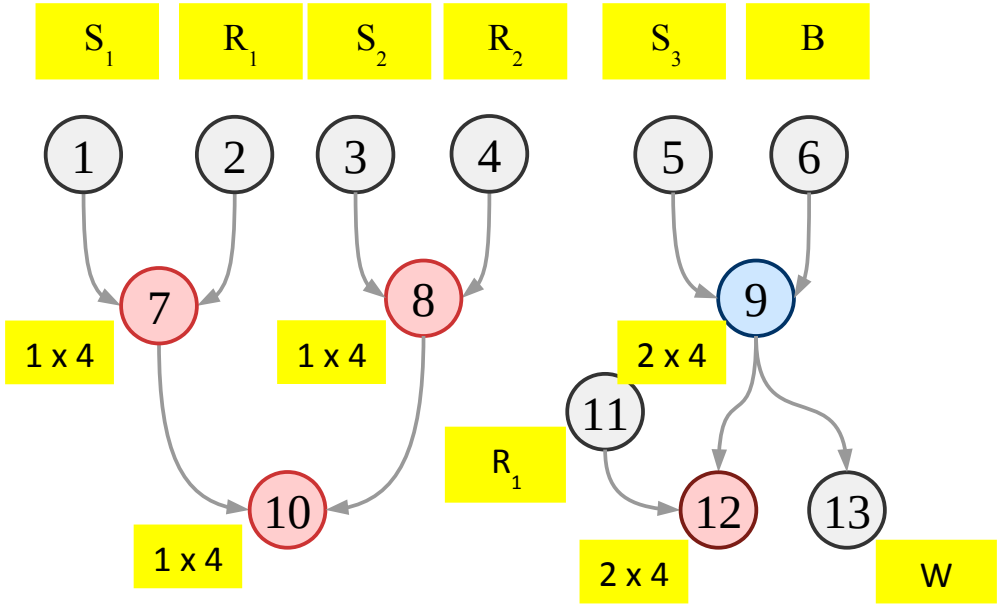


Application graph

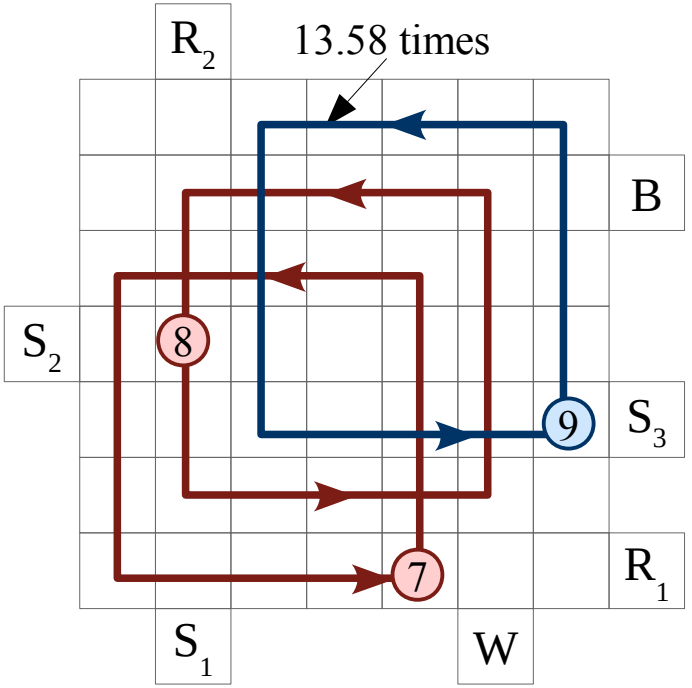


t = 2.03 s

Example

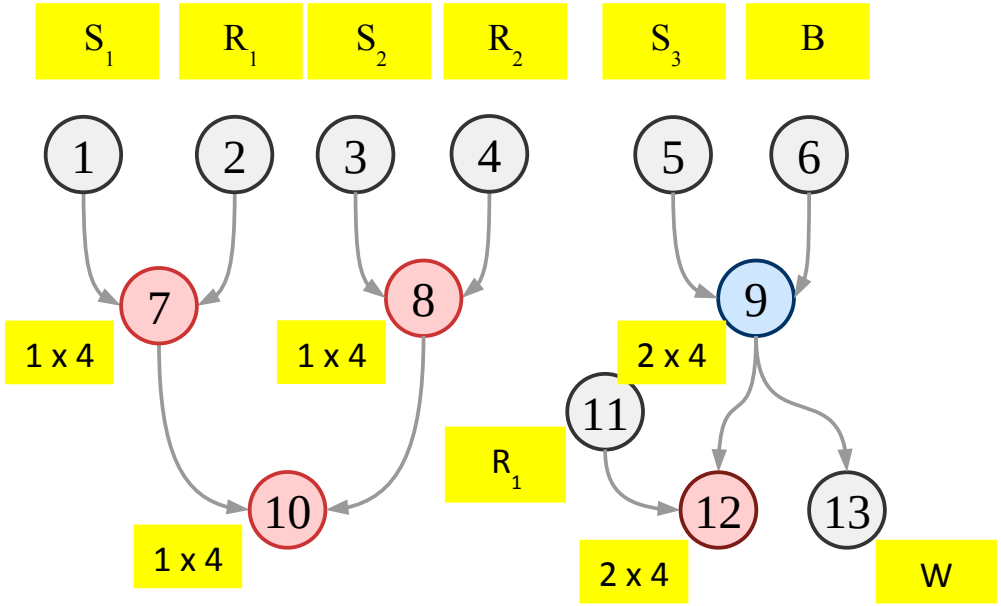


Application graph

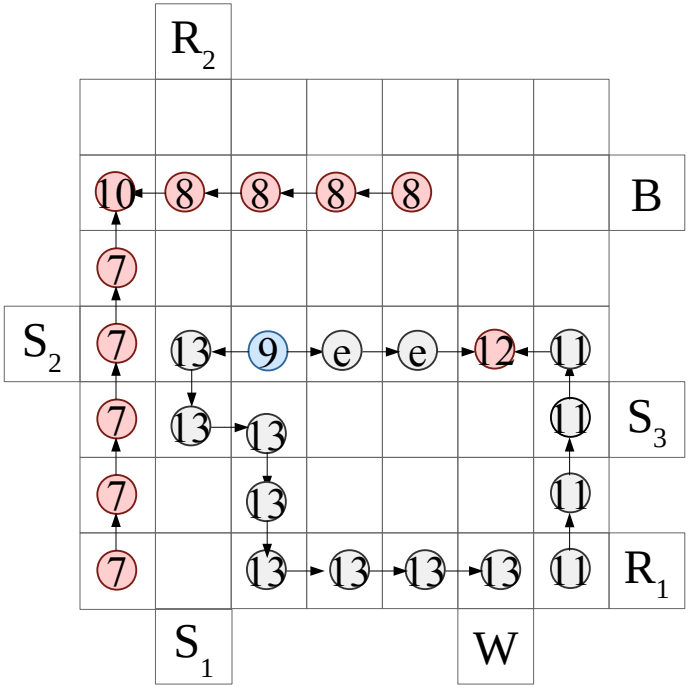


t = 4.20 s

Example

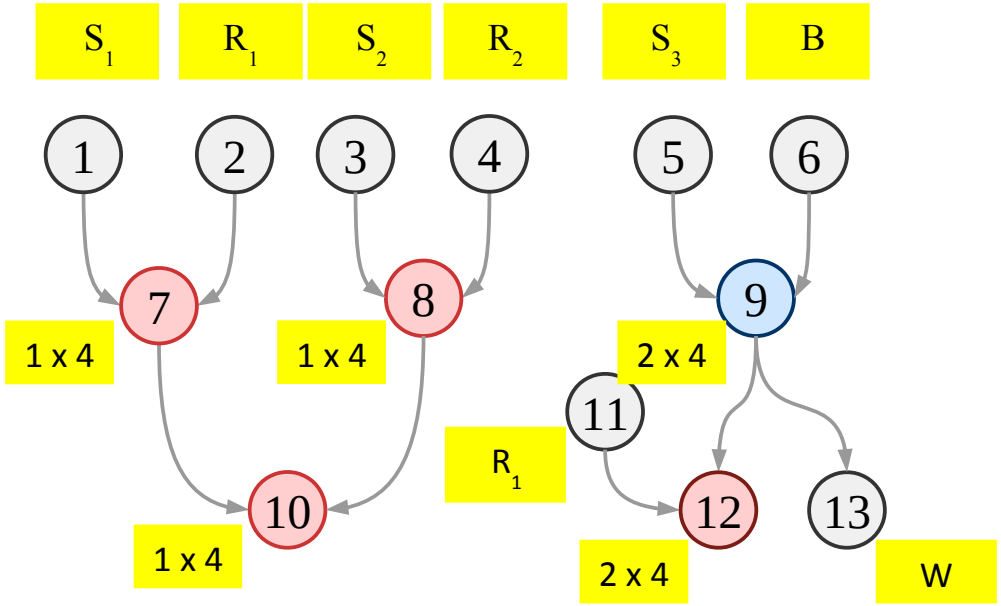


Application graph

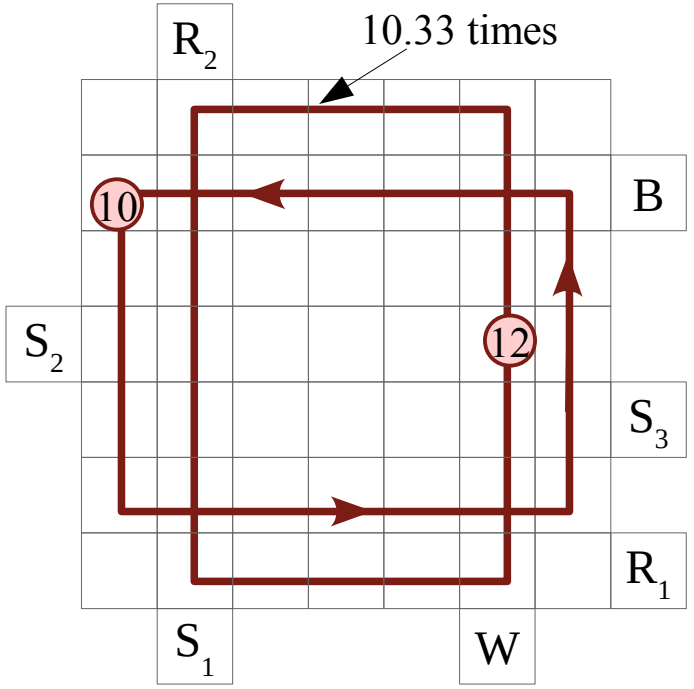


t = 4.28 s

Example

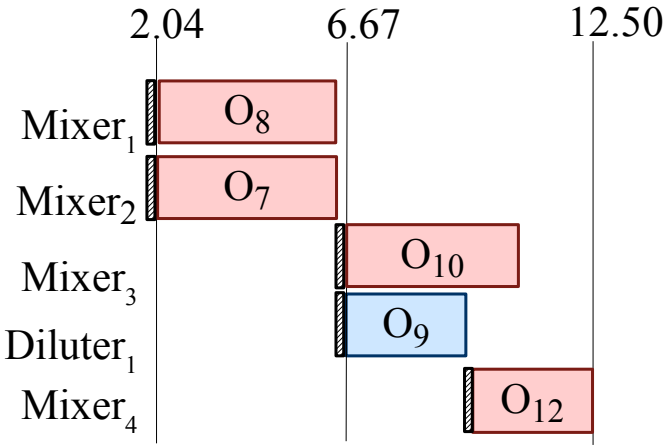


Application graph

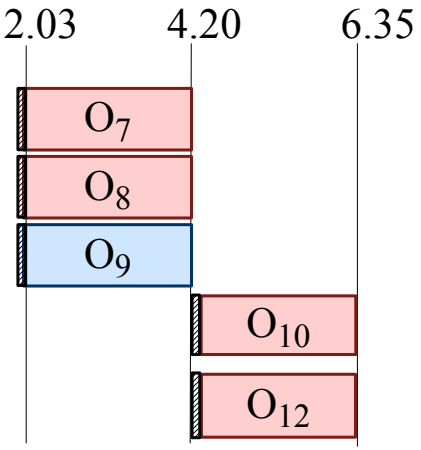


t = 6.34 s

Example

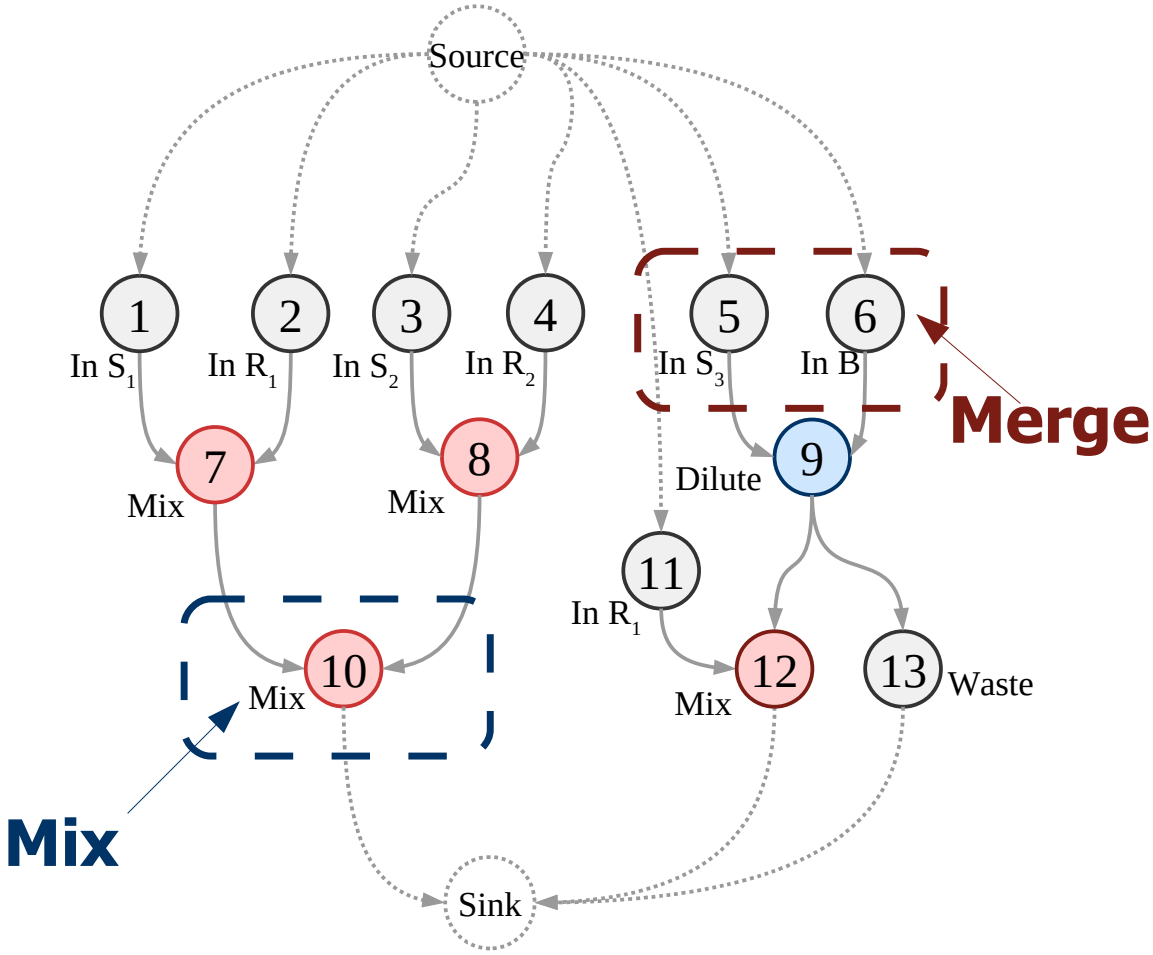


Schedule – module-based operation execution

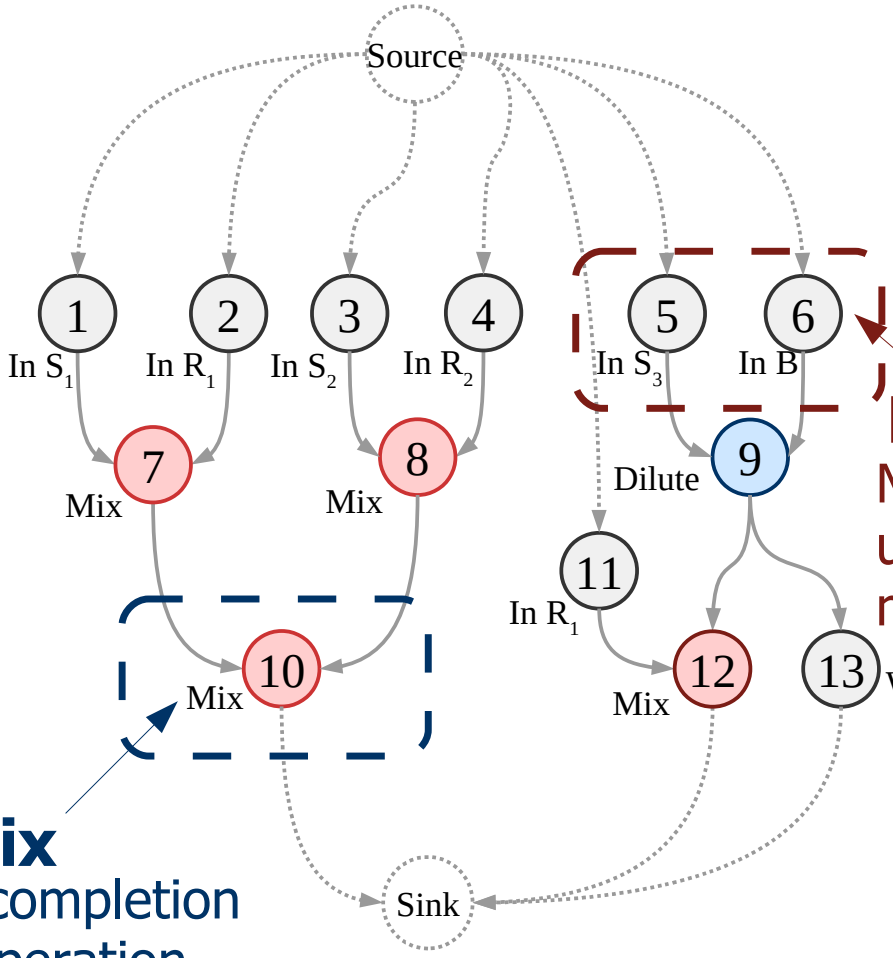


Schedule – routing-based operation execution

Solution


Source
1
In S1
2
In R1
3
In S2
4
In R2
5
In S3
6
In B
Merge
7
Mix
8
Mix
9
Dilute
11
In R1
10
Mix
12
Mix
13
Waste
Mix
Sink

Solution

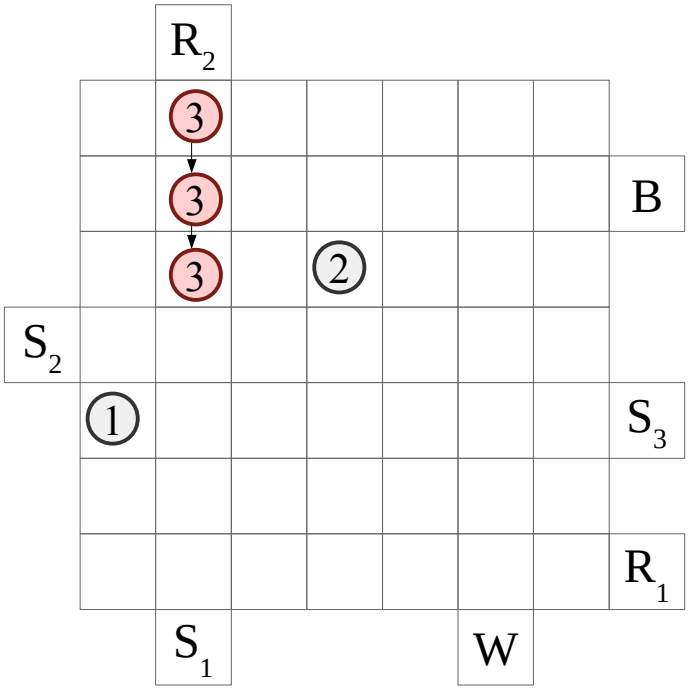


Merge
Minimize the time until the droplets meet

Mix
Minimize the completion time for the operation

Solution

- Greedy Randomized Adaptive Search Procedure (GRASP)



Solution

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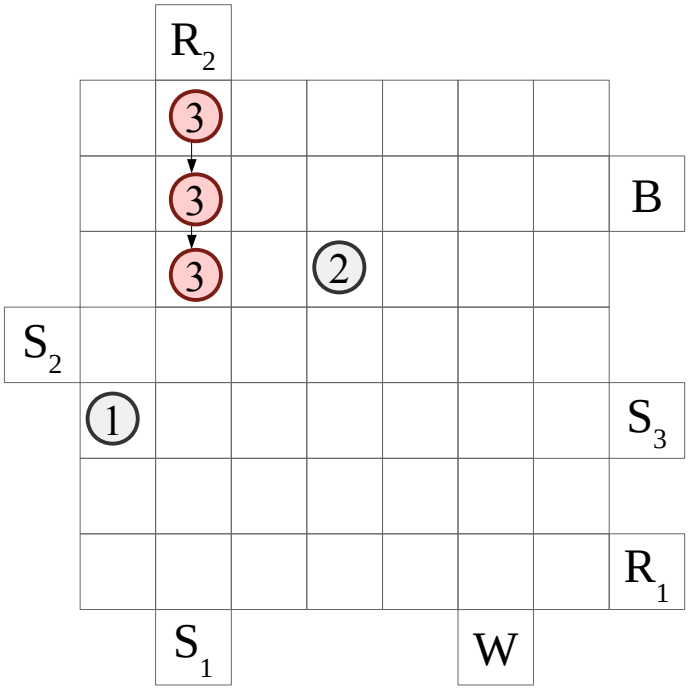
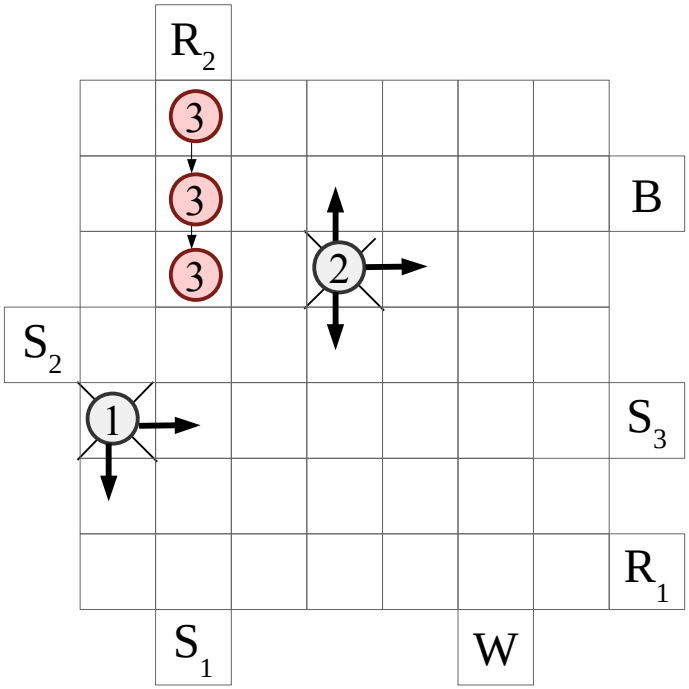


- For each droplet:
  - Determine possible moves
  - Evaluate each move
    - Merge: minimize Manhattan distance
    - Mix: maximize operation execution
  - Make a list of the best N moves
  - Perform a random move from N

Solution

- Greedy Randomized Adaptive Search Procedure (GRASP)



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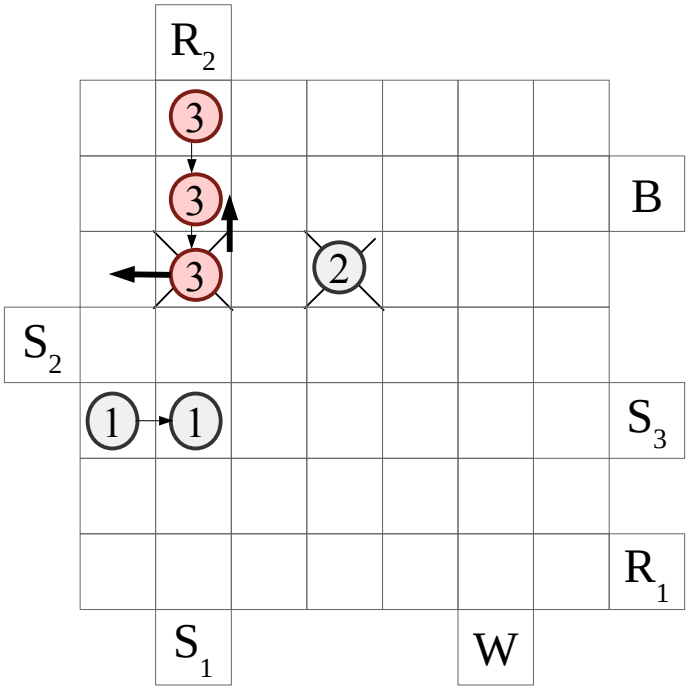

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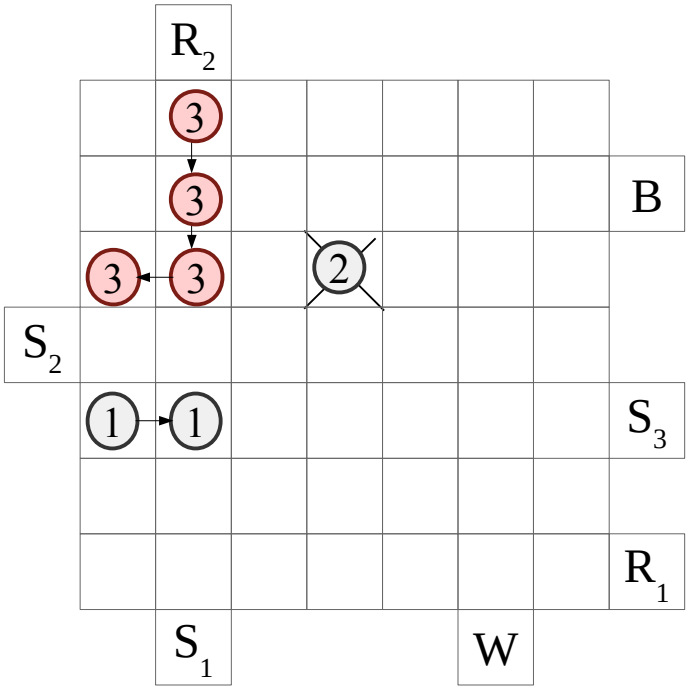

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  - Evaluate each move
    - Merge: minimize Manhattan distance
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  - Make a list of the best N moves
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Experimental Evaluation

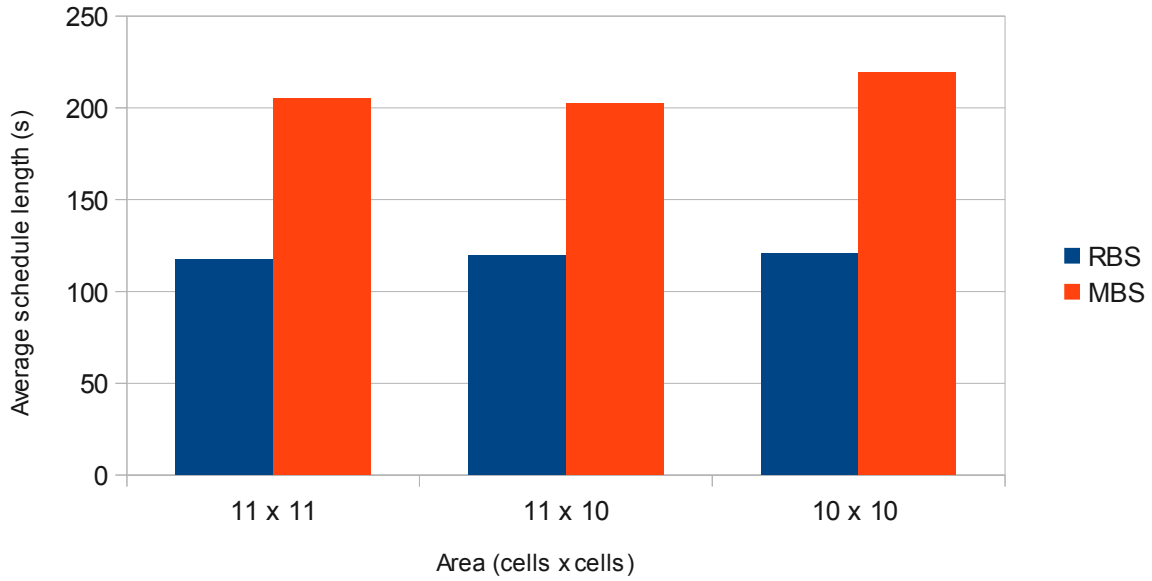
- GRASP-based algorithm implemented in Java
- Benchmarks
  - Real-life applications
    - Colorimetric protein assay
  - Synthetic benchmarks
    - 10 TGFF-generated benchmarks with 10 to 100 operations

- Comparison between:
  - Routing-based synthesis (RBS)
  - Module-based synthesis with fixed modules (MBS)

Experimental Evaluation

Average schedule length out of 50 runs for RBS vs. MBS

Colorimetric protein assay



44.95 % improvement for 10 x 10

Routing-Based Operation Execution - Conclusions

- Improved completion time compared to module-based synthesis
- Challenge: contamination

Routing-Based Operation Execution - Conclusions

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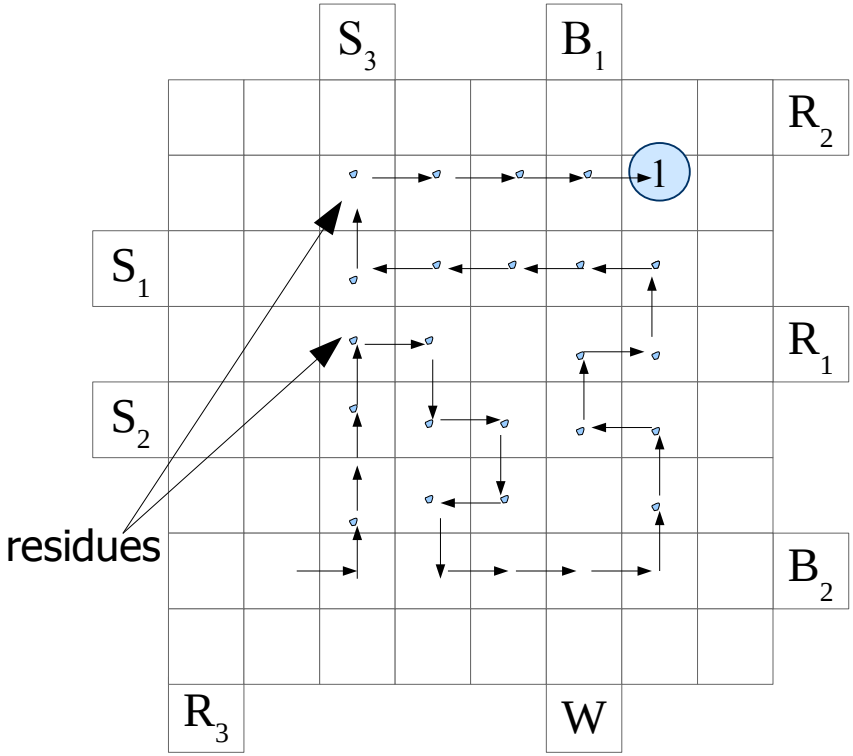

Routing-Based Operation Execution - Conclusions

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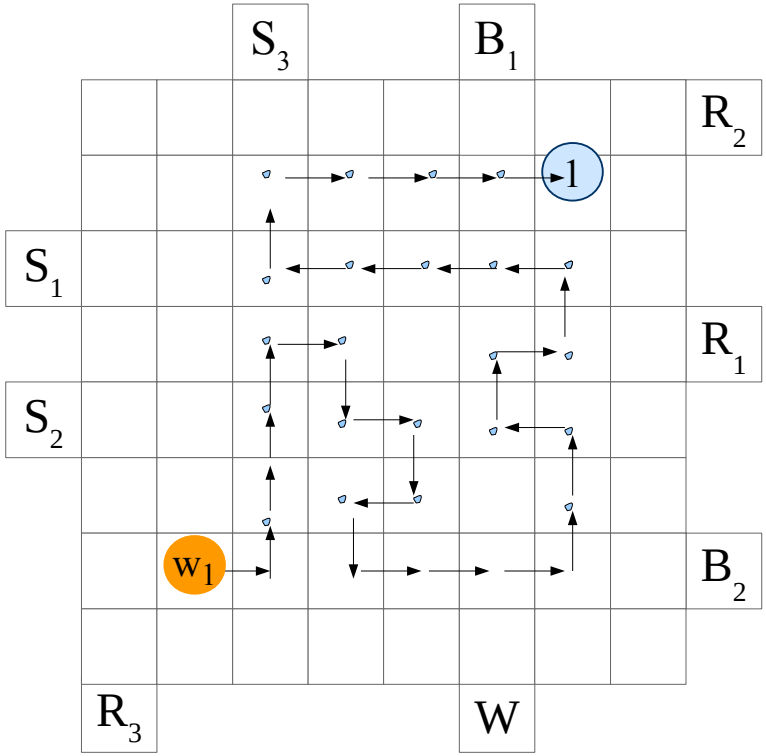

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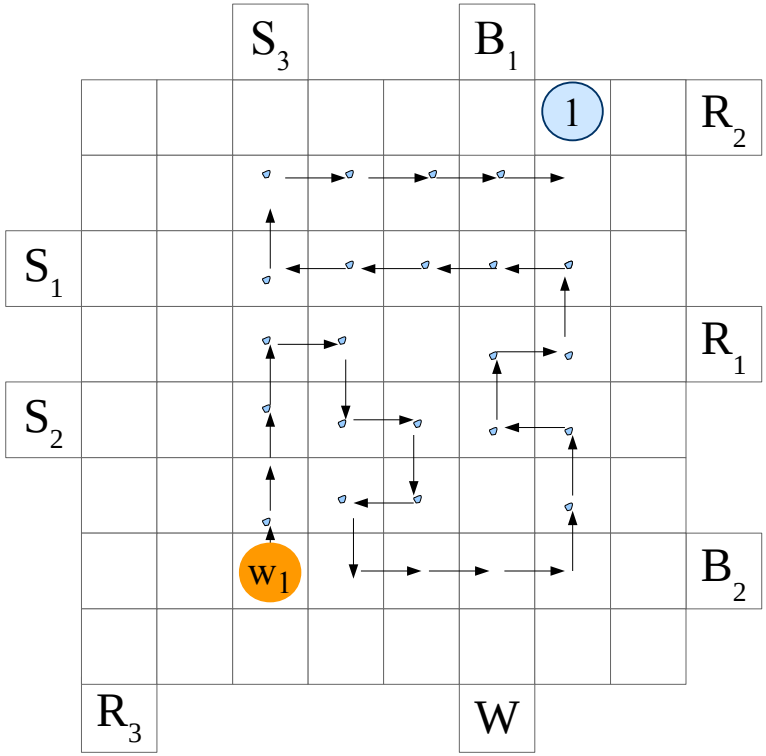

Routing-Based Operation Execution - Conclusions

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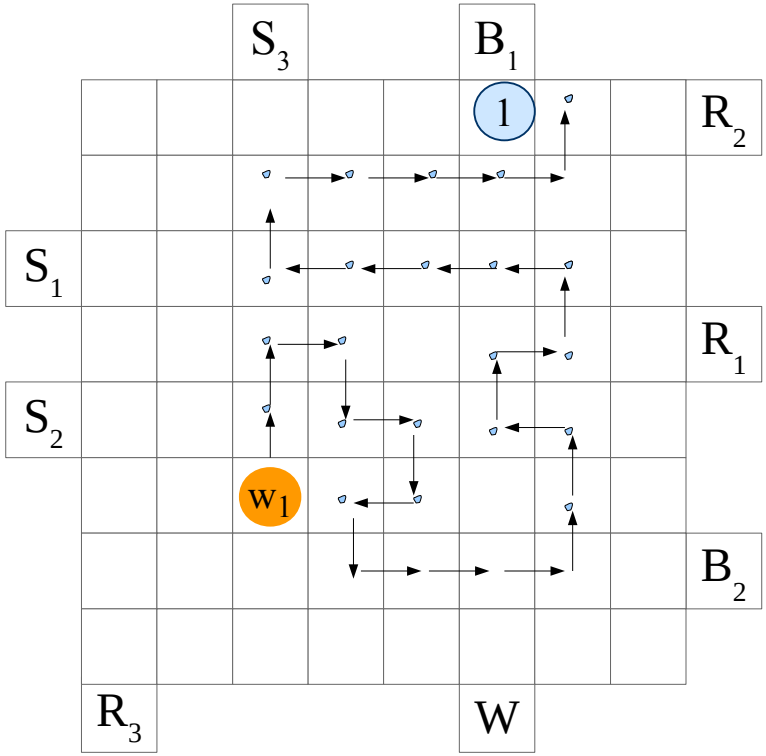

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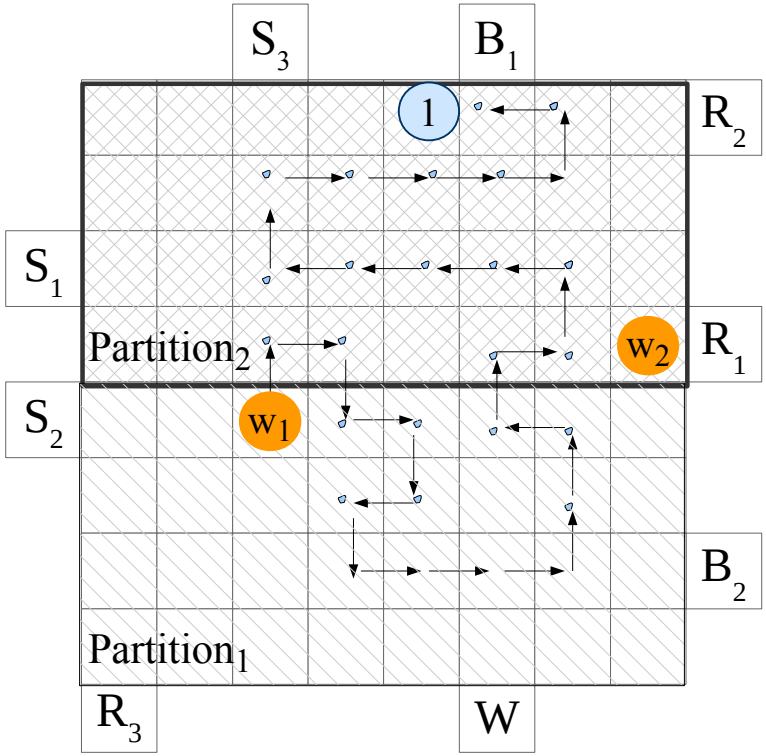
- Challenge: contamination



Routing-Based Operation Execution - Conclusions

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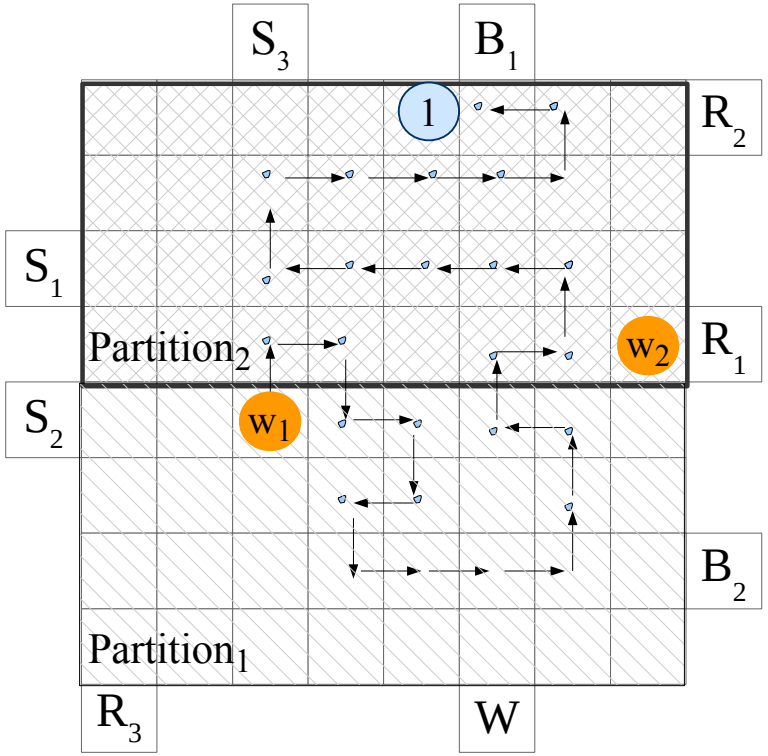

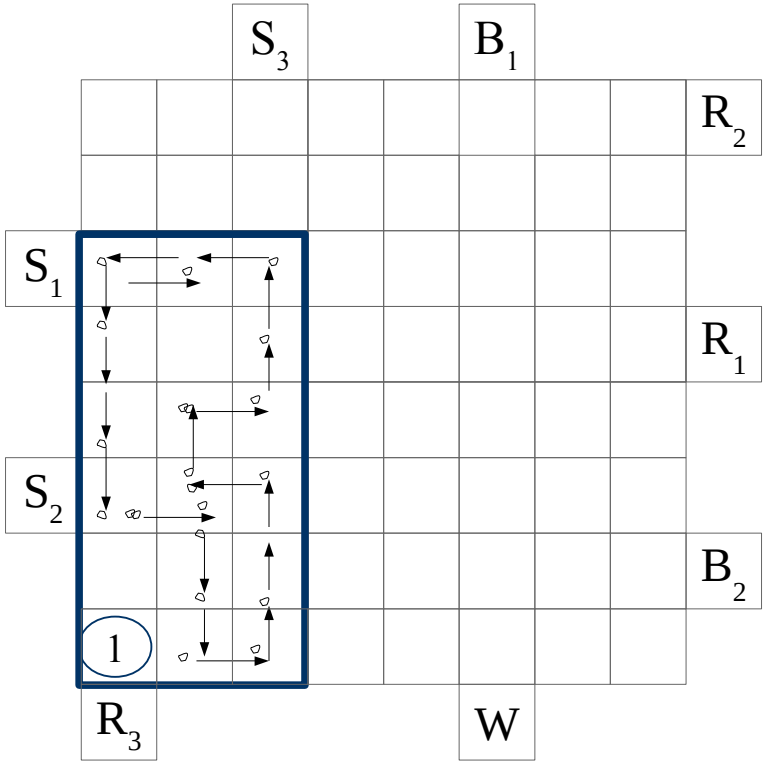

Routing-Based Operation Execution - Conclusions

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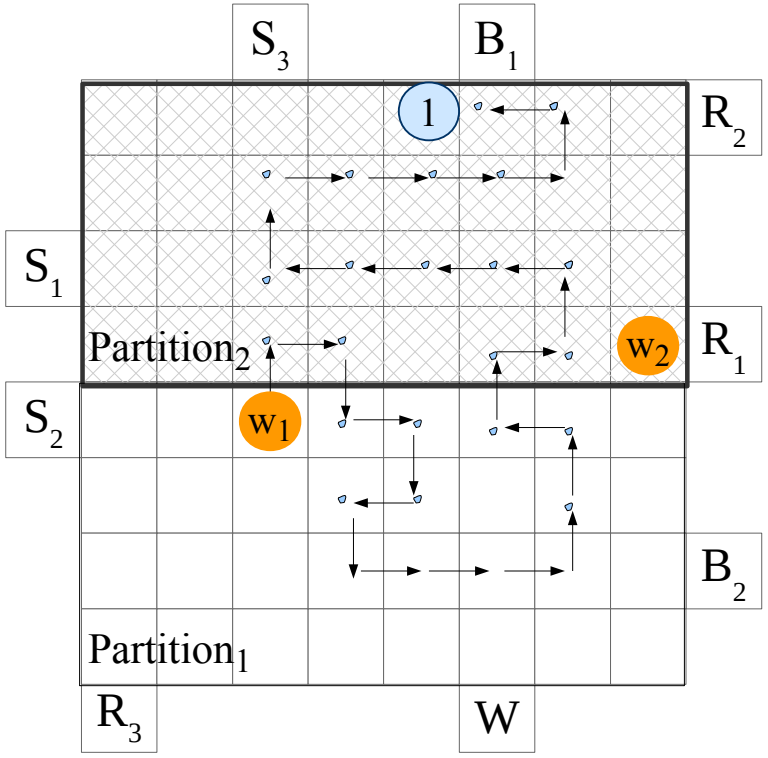
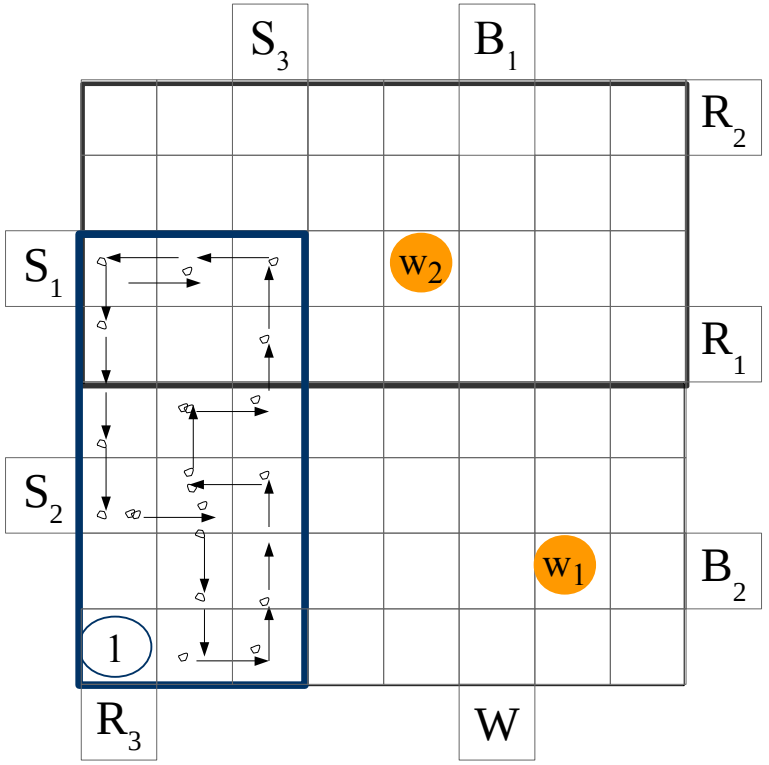
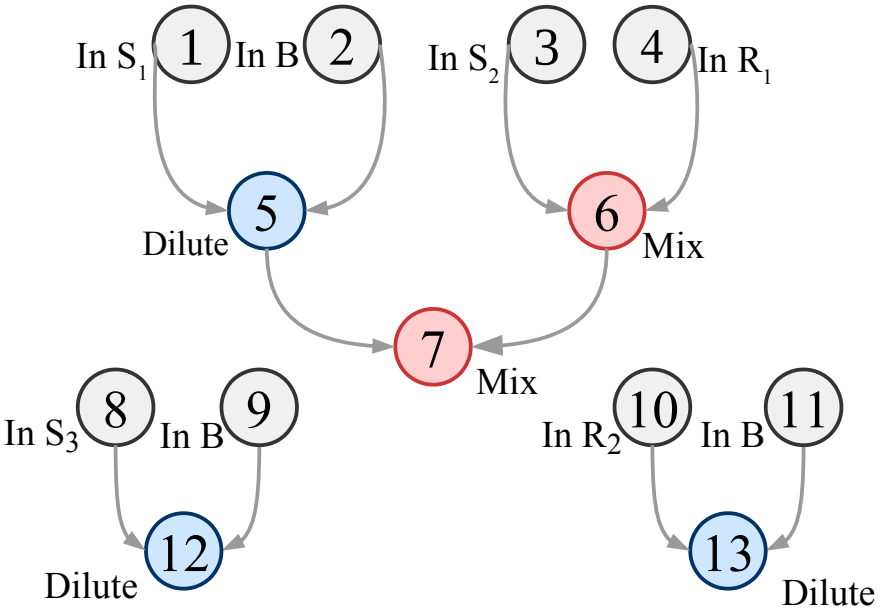


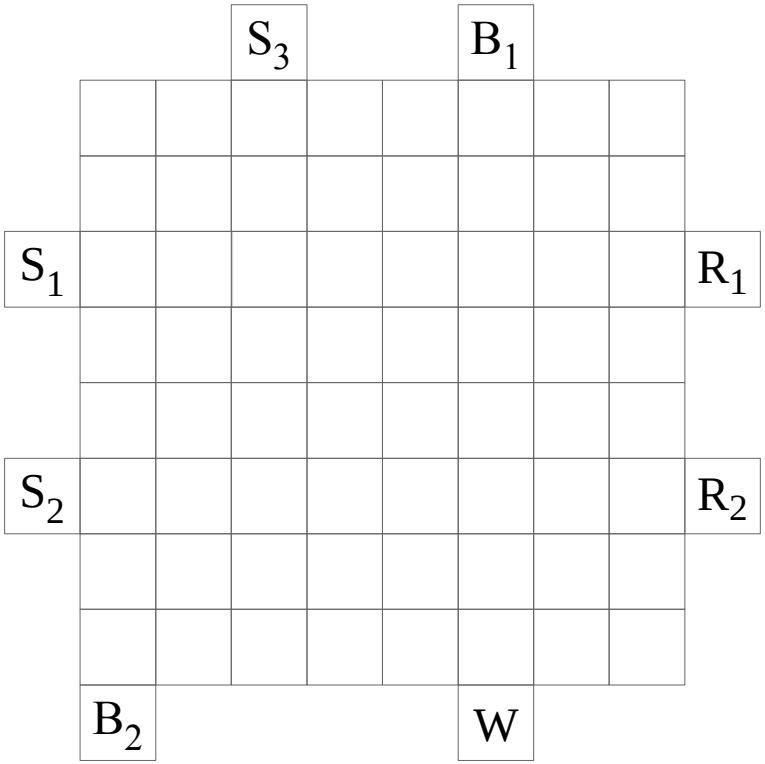


Droplet-Aware Operation Execution without Contamination

Example

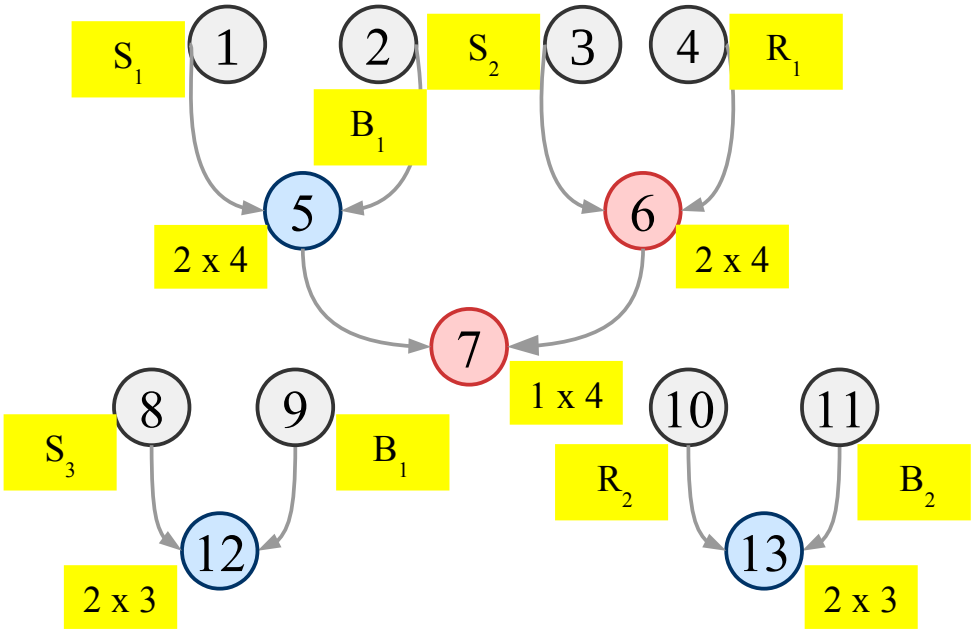


Application graph

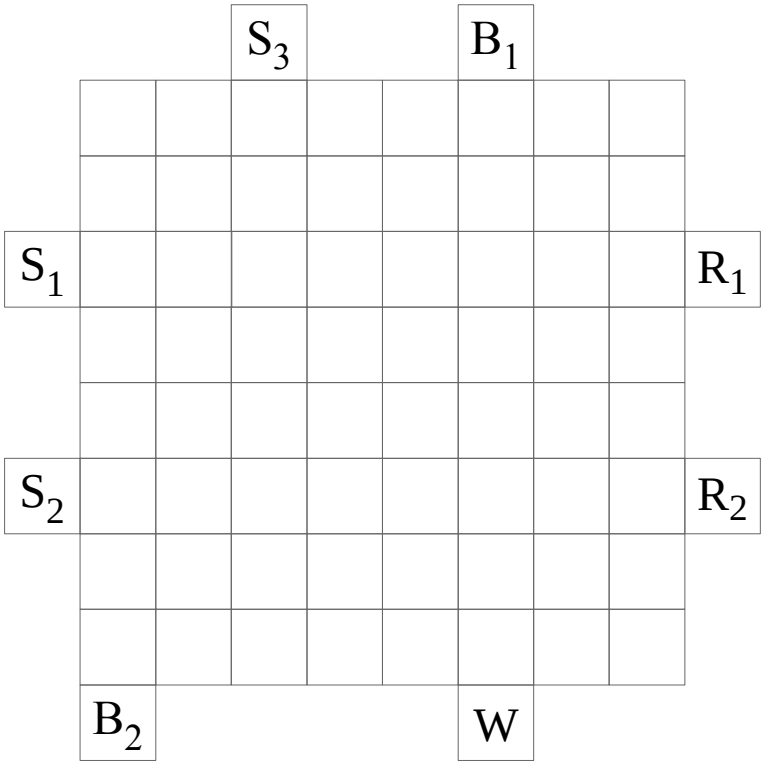


Biochip

Example

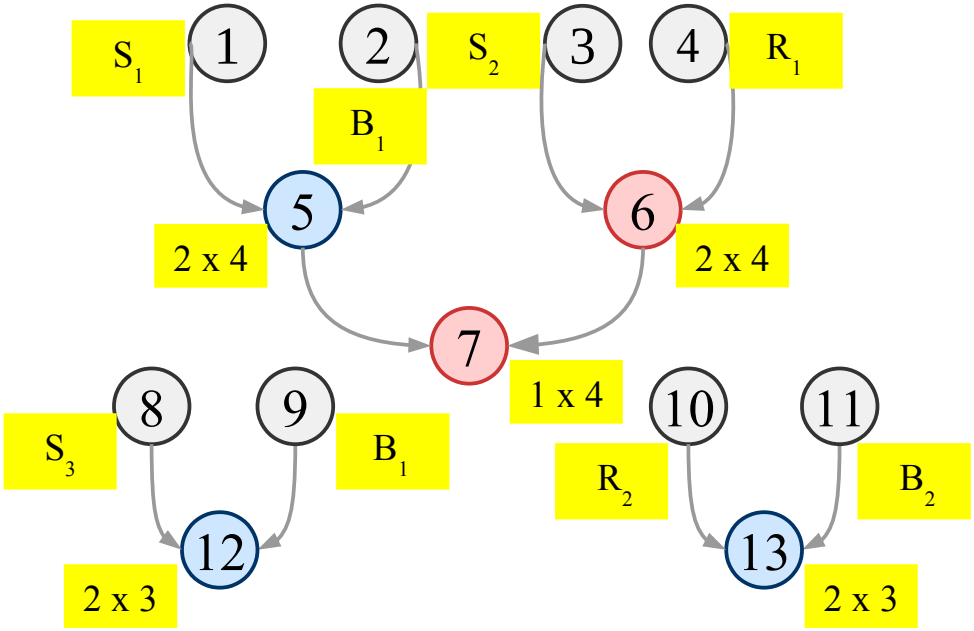


Application graph

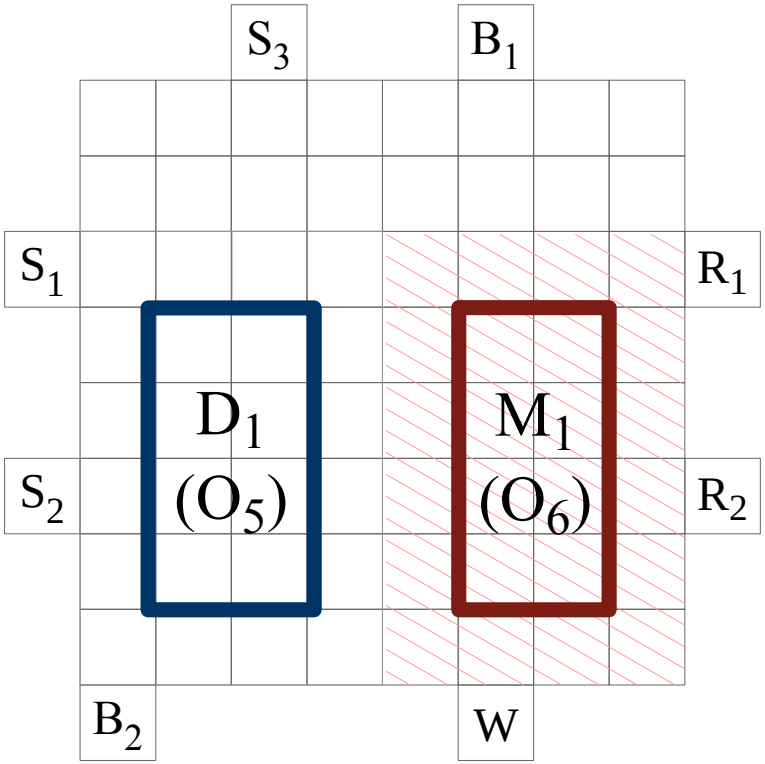


Biochip

Example

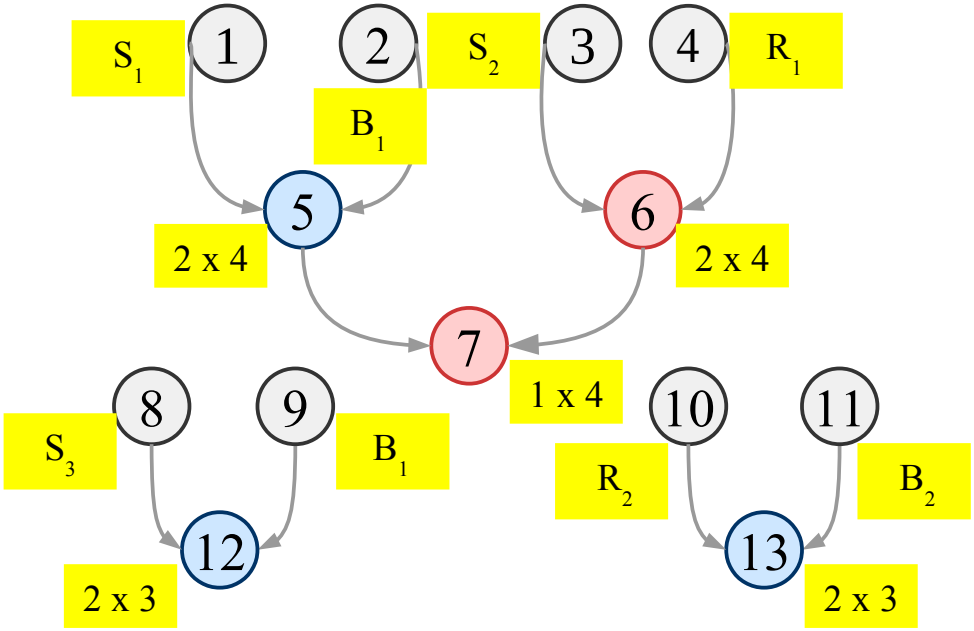


Application graph

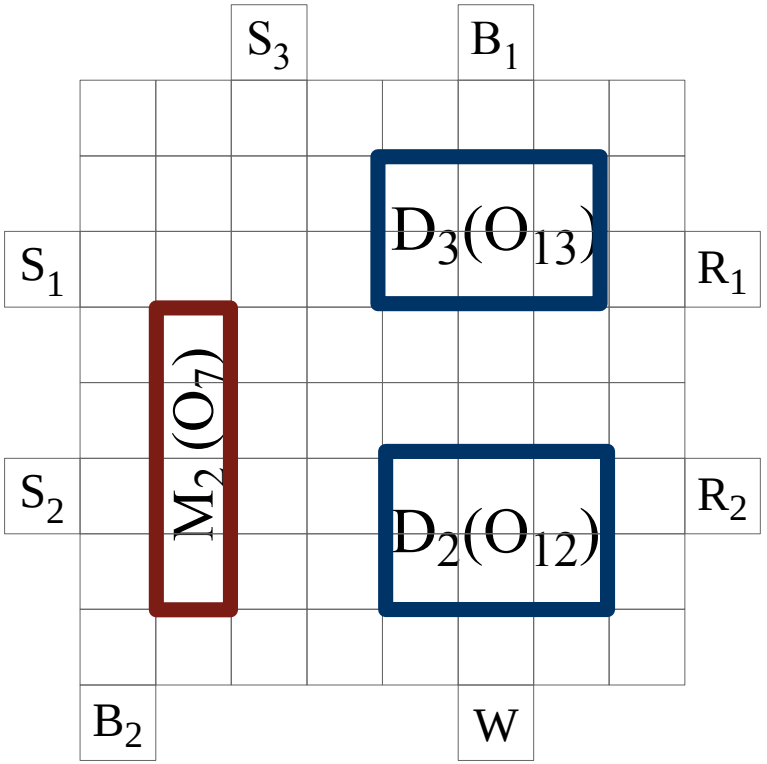


t = 2 s

Example

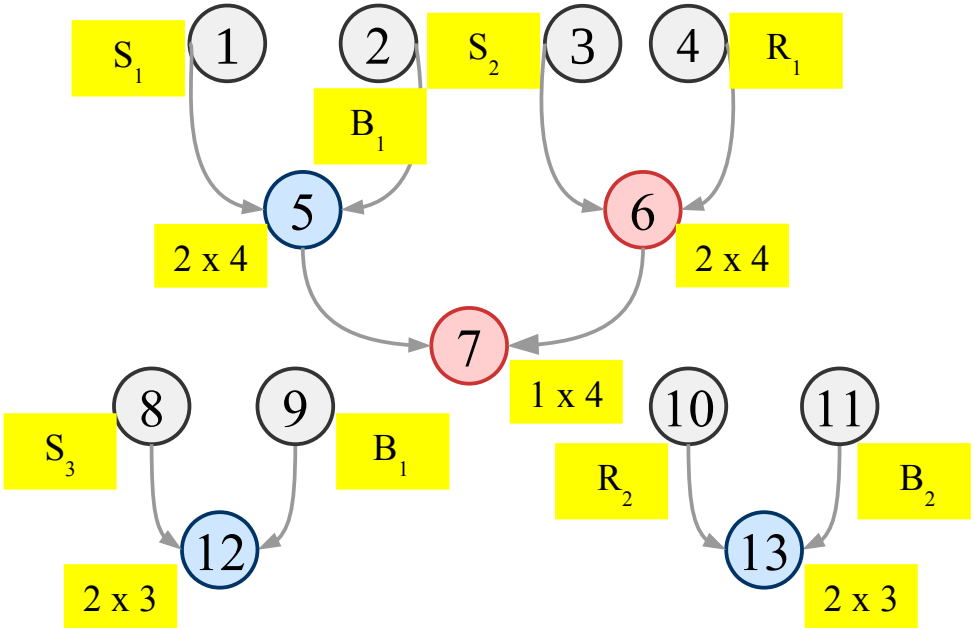


Application graph

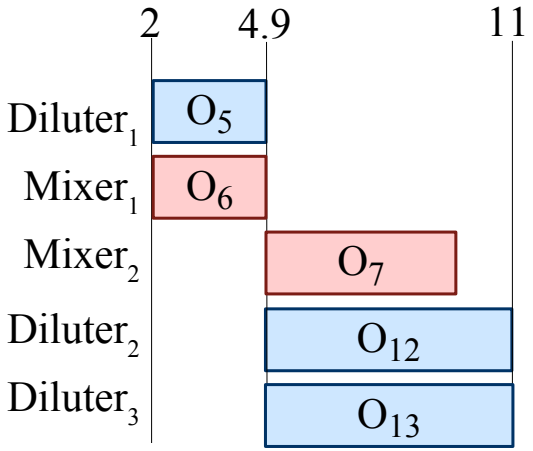


t = 4.9 s

Example

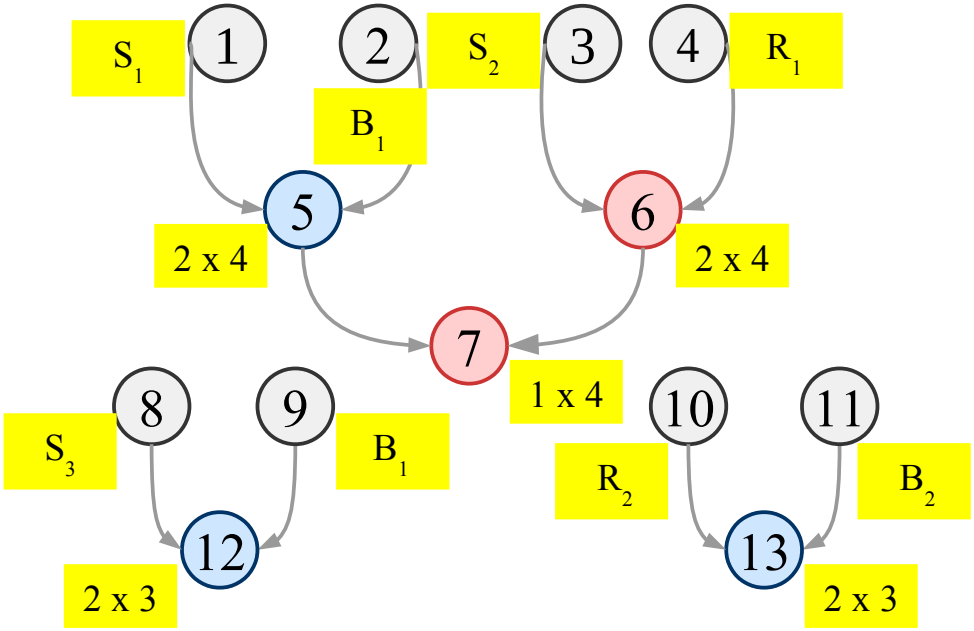


Application graph

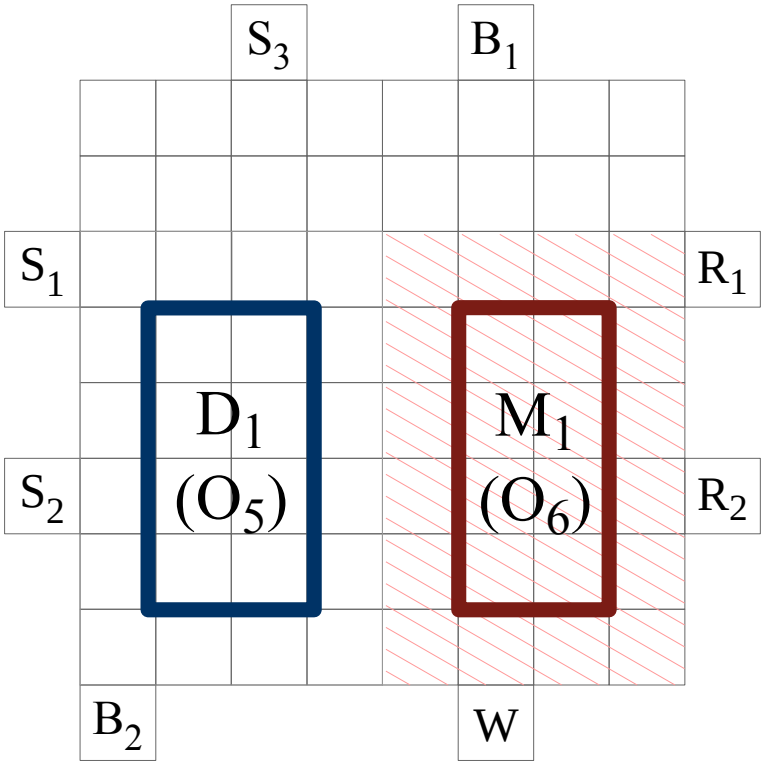


Schedule

Example

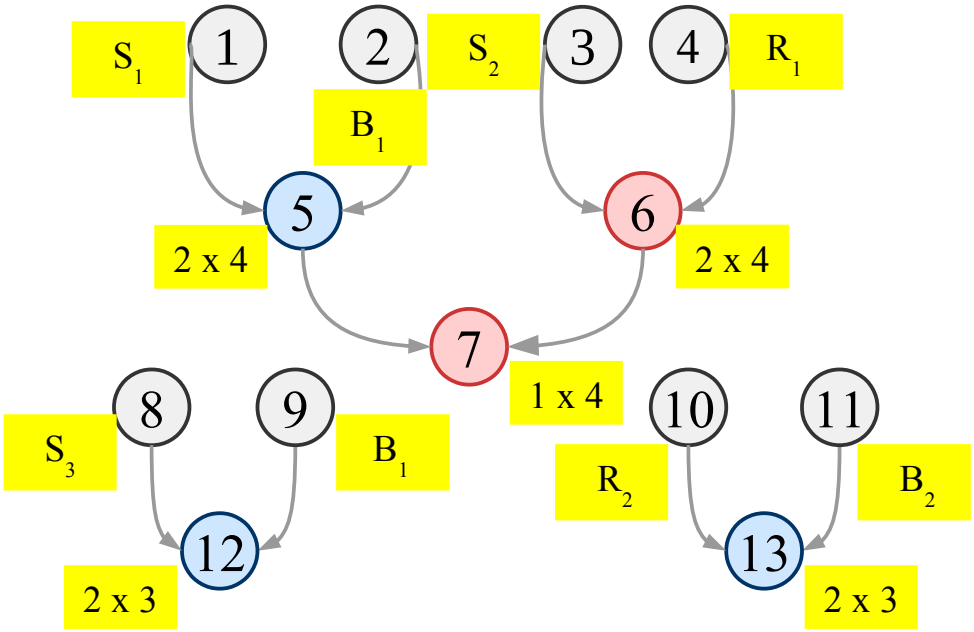


Application graph

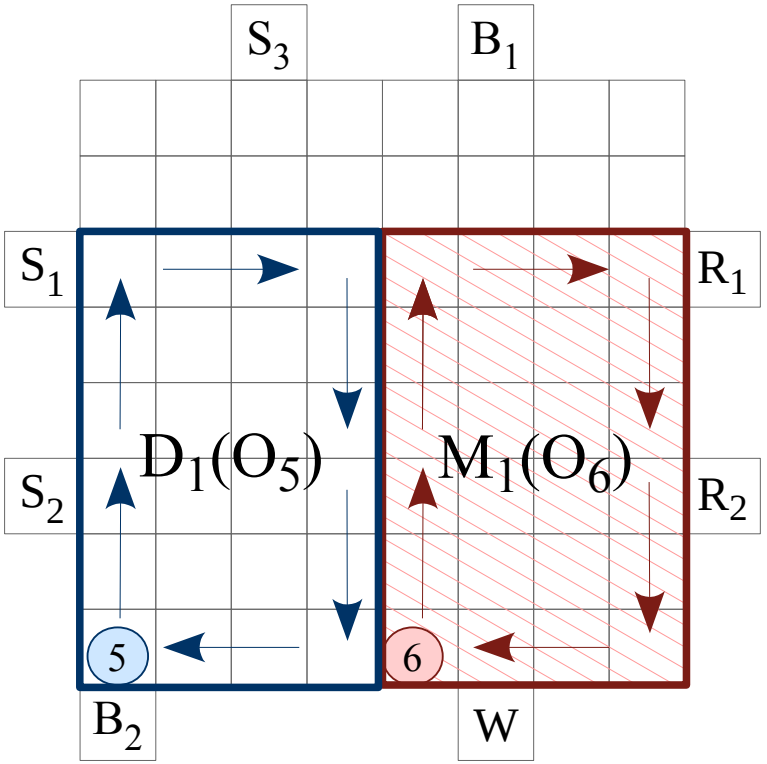


t = 2 s

Example

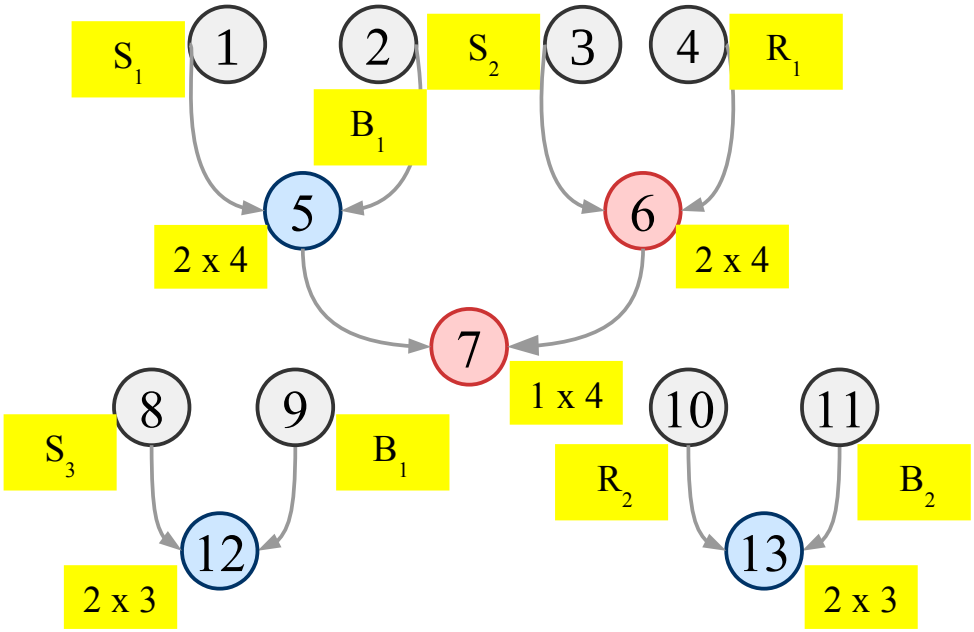


Application graph

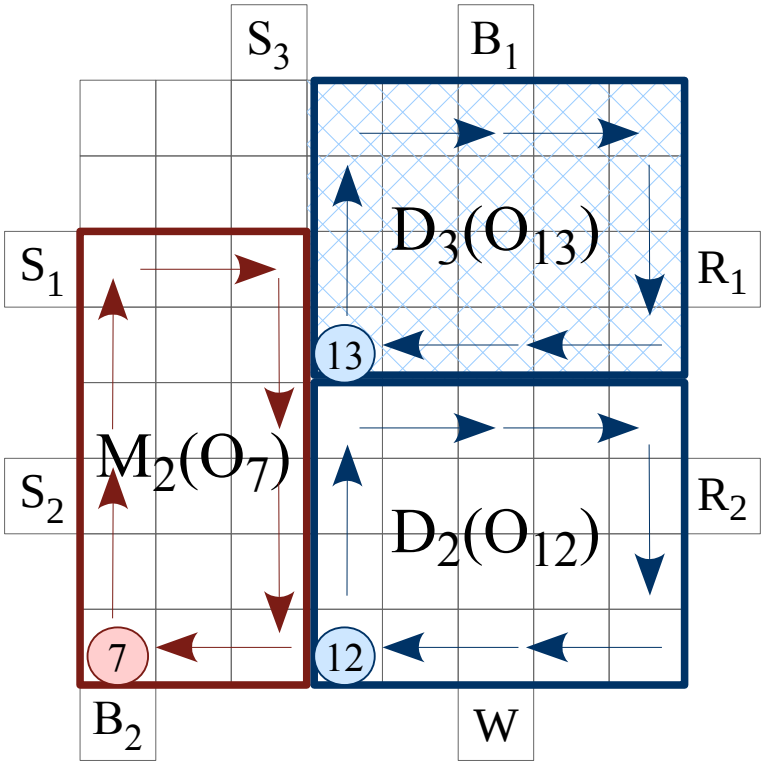


t = 2 s

Example

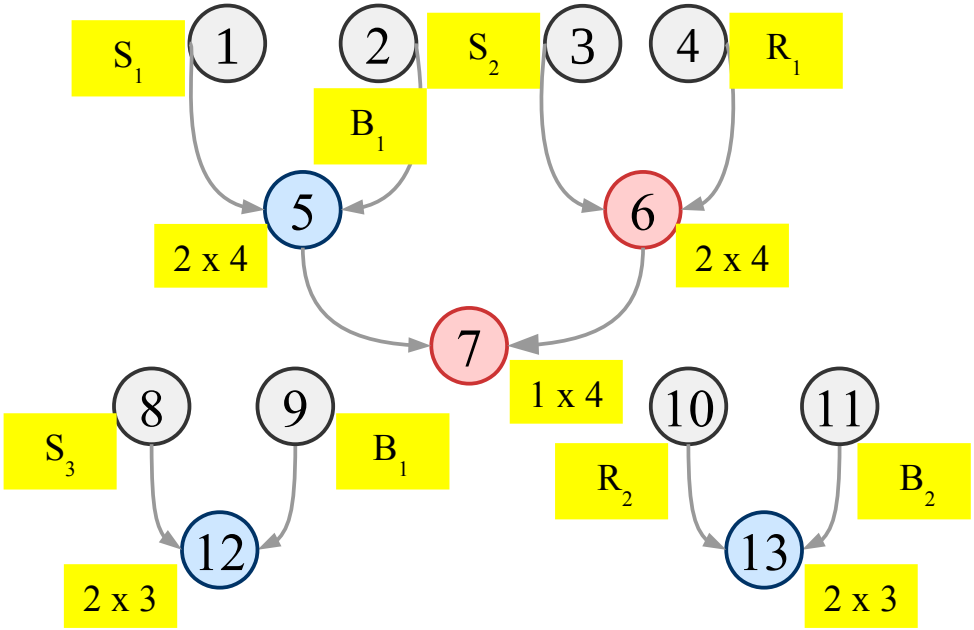


Application graph

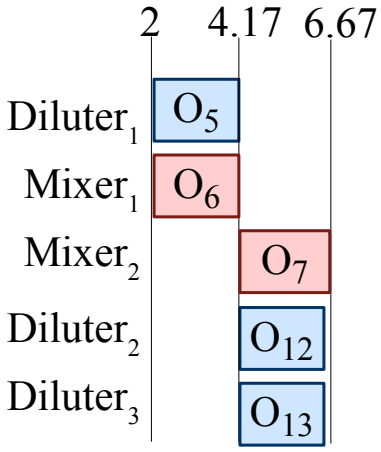


t = 4.17 s

Example

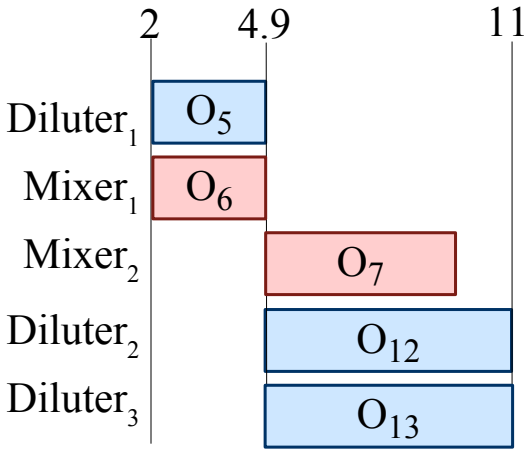


Application graph

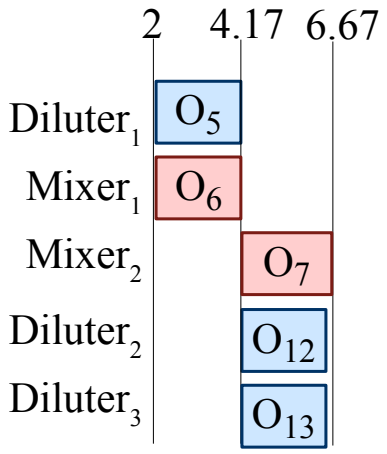


Schedule

Example



Schedule – module-based operation execution

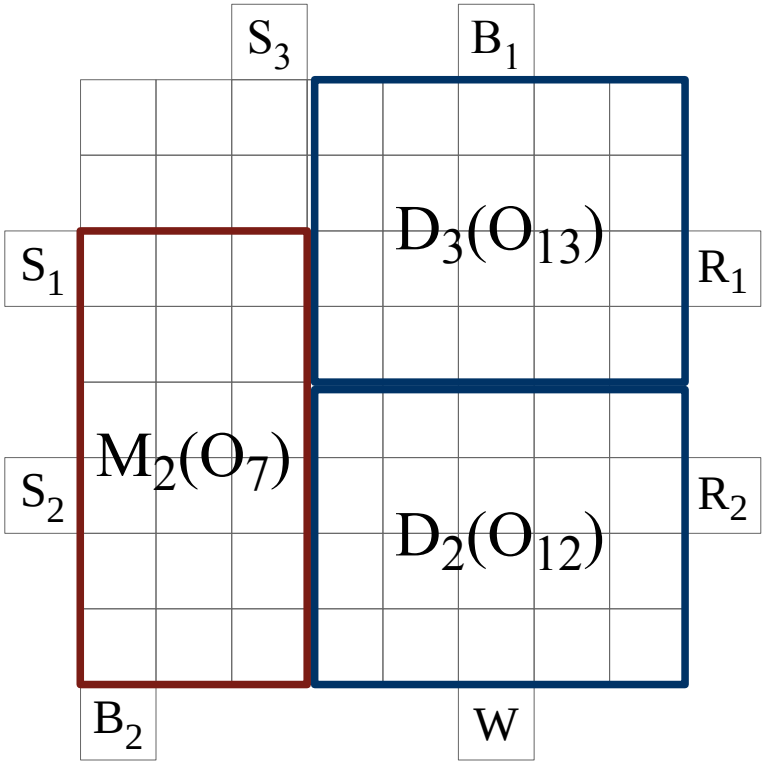


Schedule – droplet-aware operation execution

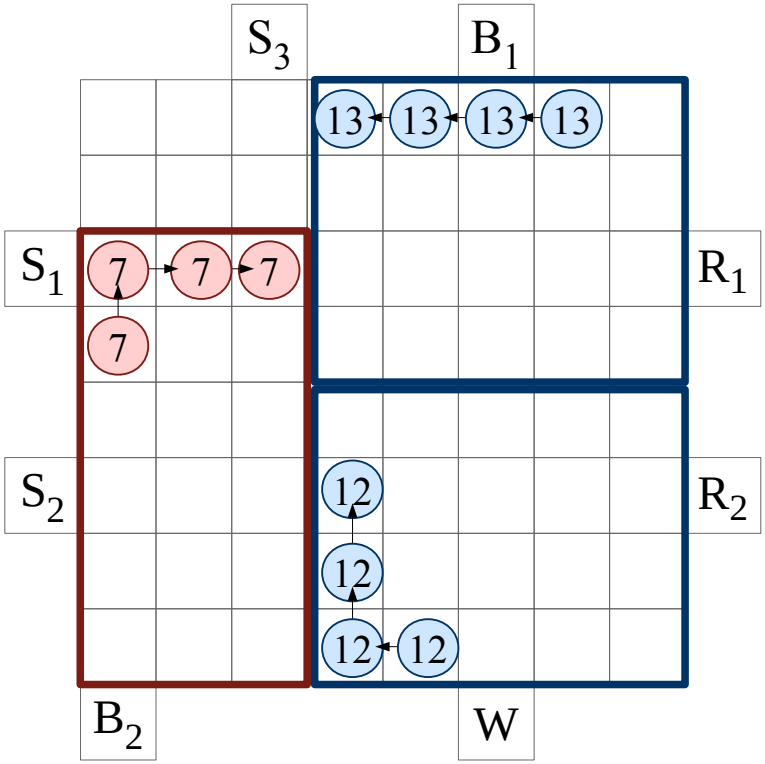
Solution

- Location of modules determined using Tabu Search
- Greedy movement of droplets inside modules
- Routing of droplets between modules and between modules and I/O ports determined using GRASP

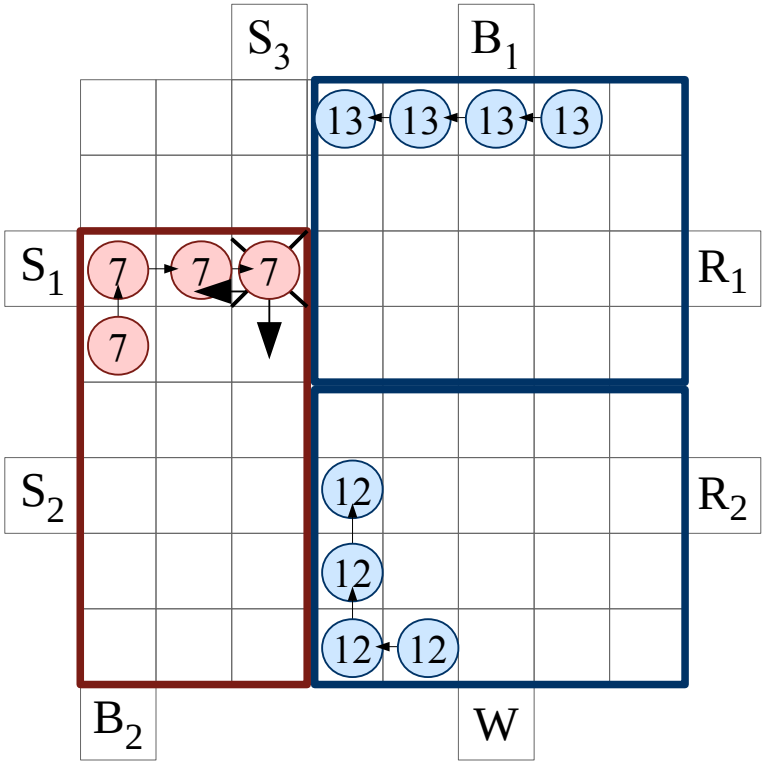
Droplet-Aware Operation Execution



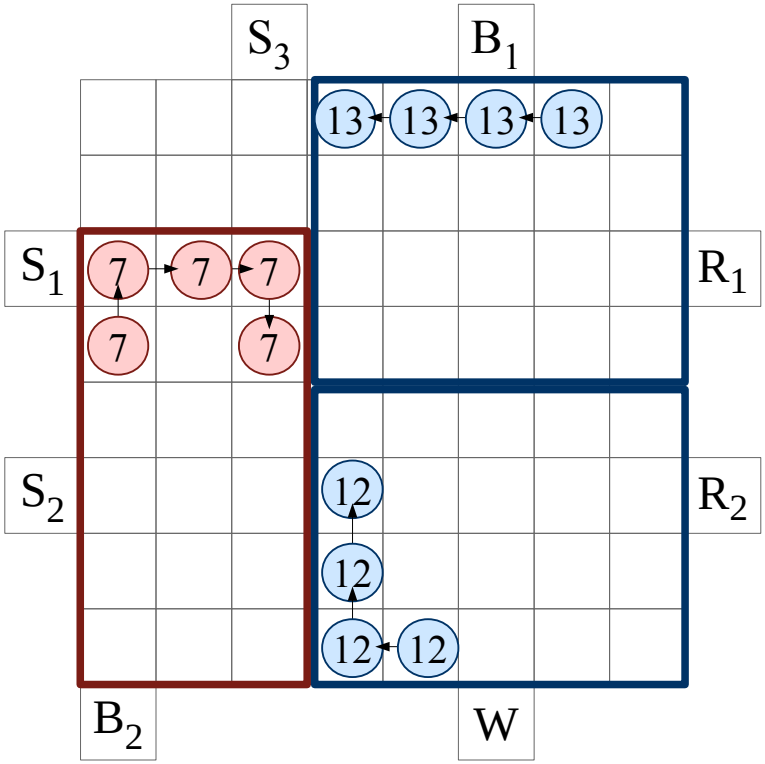
Droplet-Aware Operation Execution



Droplet-Aware Operation Execution



Droplet-Aware Operation Execution



Experimental Evaluation

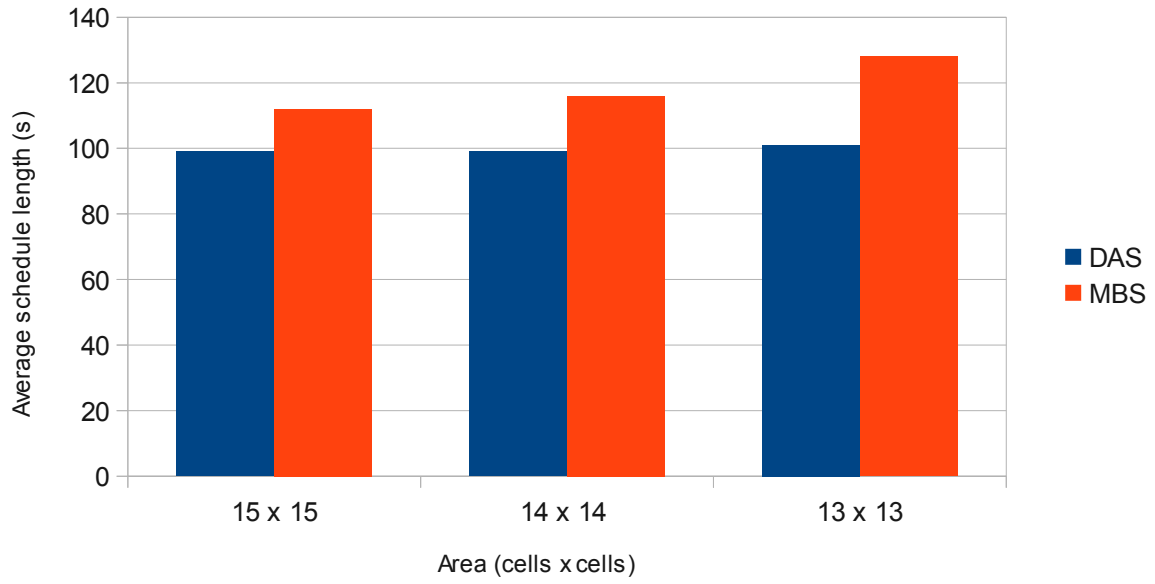
- Algorithm implemented in Java
- Benchmarks
  - Real-life applications
    - In-vitro diagnosis
    - Colorimetric protein assay
  - Synthetic benchmarks
    - 3 TGFF-generated benchmarks with 20, 40, 60 operations

- Comparison between:
  - Droplet-aware module-based synthesis (DAS)
  - Module-based synthesis (MBS)

Experimental Evaluation

Average schedule length out of 50 runs for DAS vs. MBS

Colorimetric protein assay



21.55 % improvement for 13 x 13

Experimental Evaluation

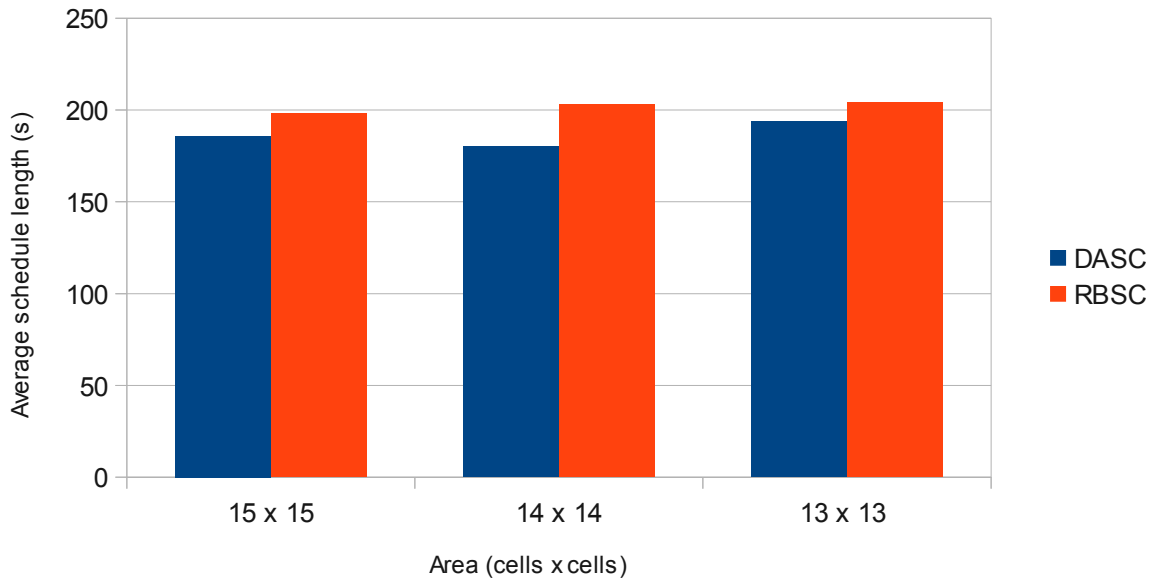
- Algorithm implemented in Java
- Benchmarks
  - Real-life applications
    - Colorimetric protein assay
  - Synthetic benchmarks
    - 3 TGFF-generated benchmarks with 20, 40, 60 operations

- Comparison between:
  - Droplet-aware module-based synthesis (DASC)
  - Routing-based synthesis (RBSC)
    with contamination avoidance

Experimental Evaluation

Average schedule length out of 50 runs for DASC vs. RBSC

Colorimetric protein assay



11.19 % improvement for 14 x 14

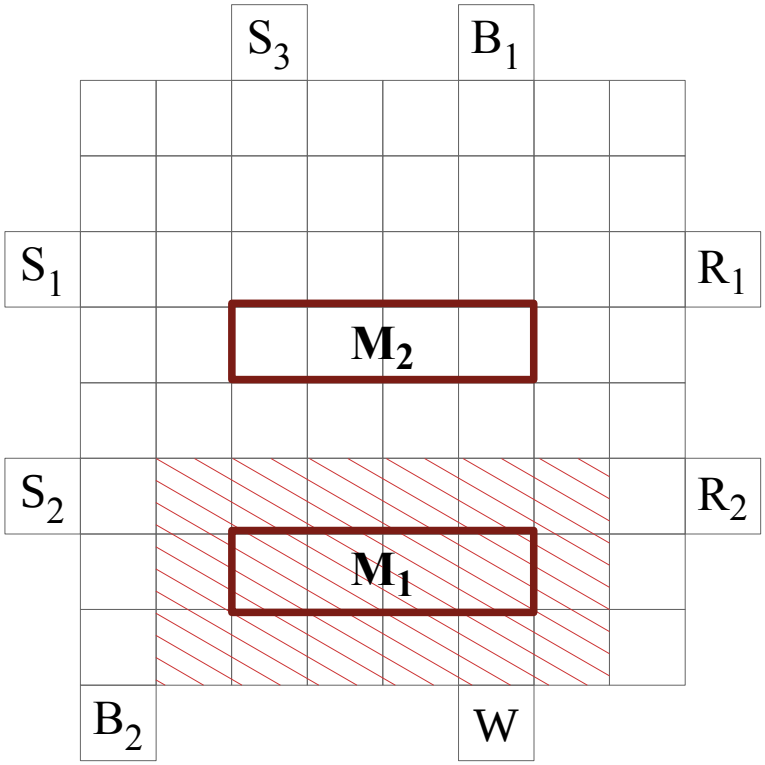
Contributions

- Tabu Search-based algorithm for the module-based synthesis with fixed devices [CASES09]
- Module-based synthesis with virtual devices [CASES09]
- Module-based synthesis with non-rectangular virtual devices [DAEM10]
- Analytical method for operation execution characterization [CASES10]
- Routing-based synthesis [CASES10] + contamination [DAEM, submitted]
- Droplet-aware module based synthesis [JETC, submitted]
- ILP formulation for the synthesis of digital biochips [VLSI-SoC08]

Conclusions

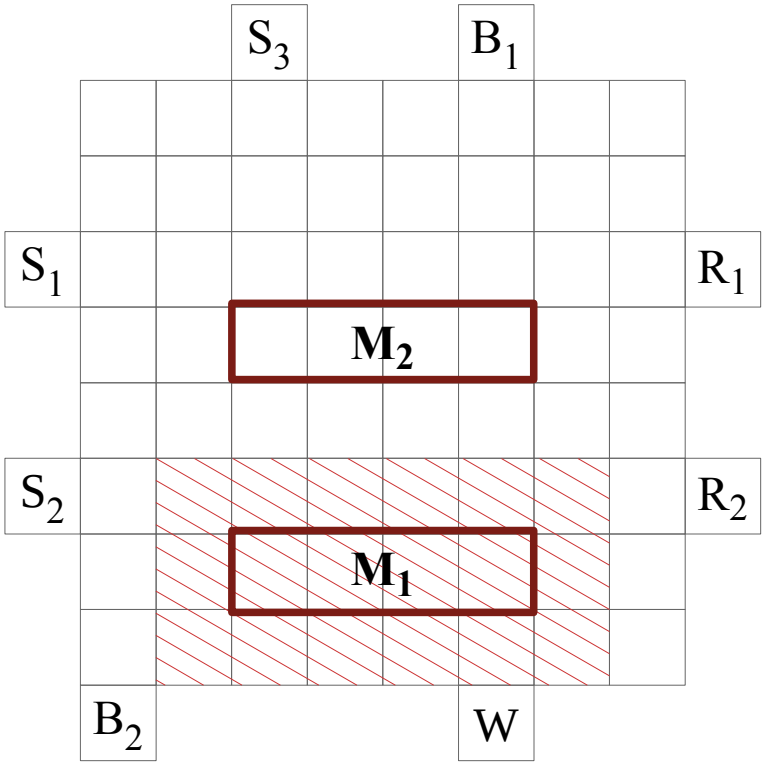
- Proposed several synthesis techniques for DMBs
- Considered the reconfigurability characteristic of DMBs
- Shown that by considering reconfigurability during operation execution improvements in the completion time of applications can be obtained

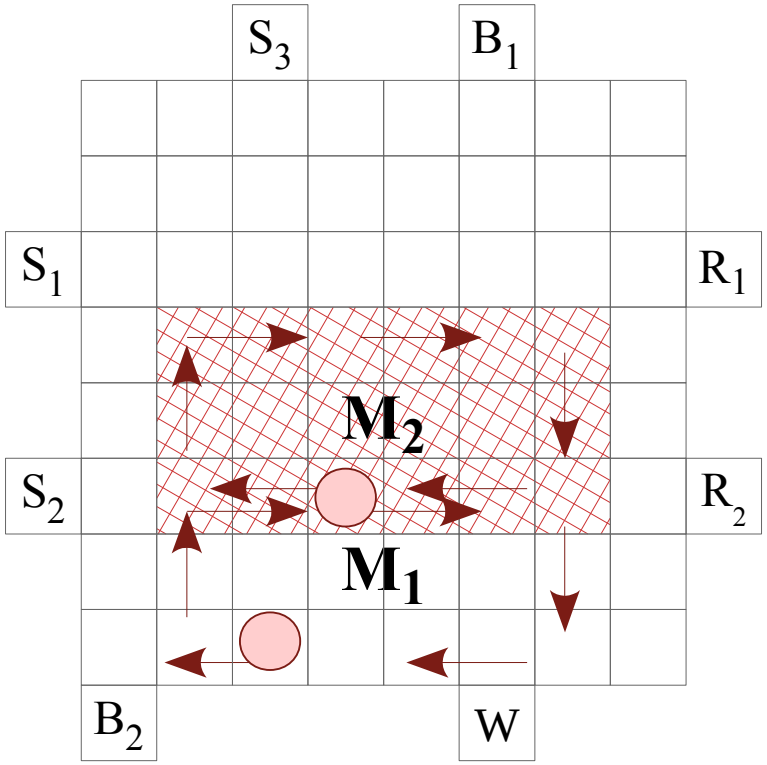
Future Directions



Future Directions

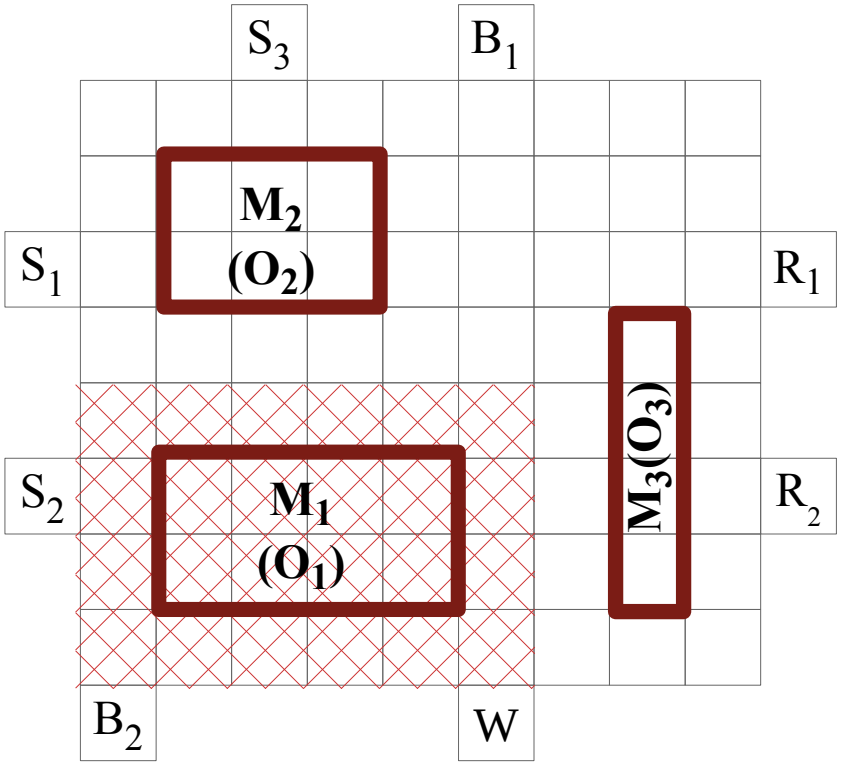
Module-Based Synthesis with Overlapping Devices

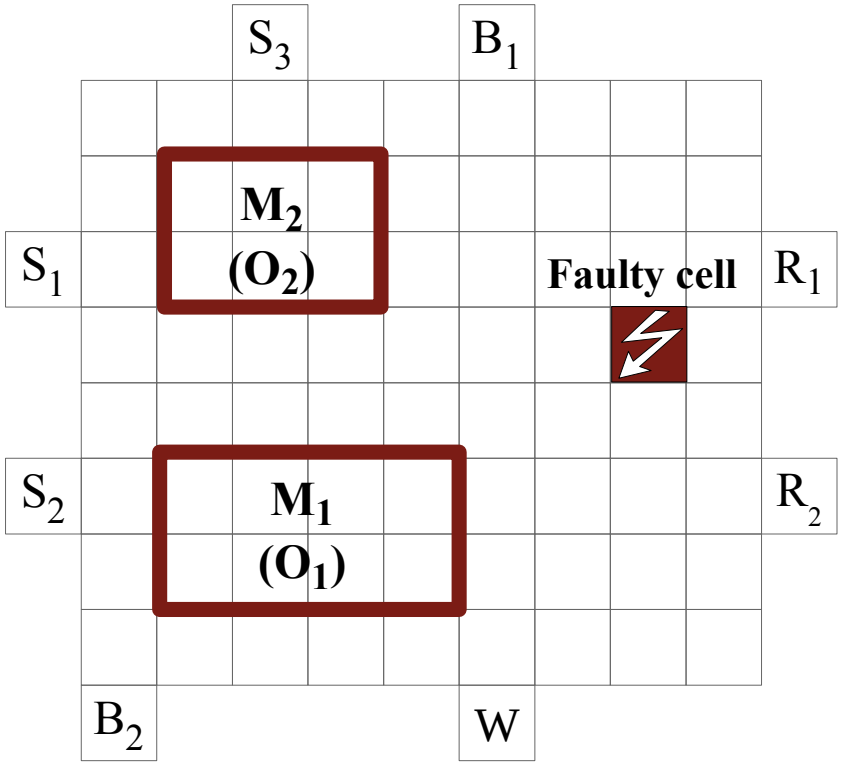




Future Directions

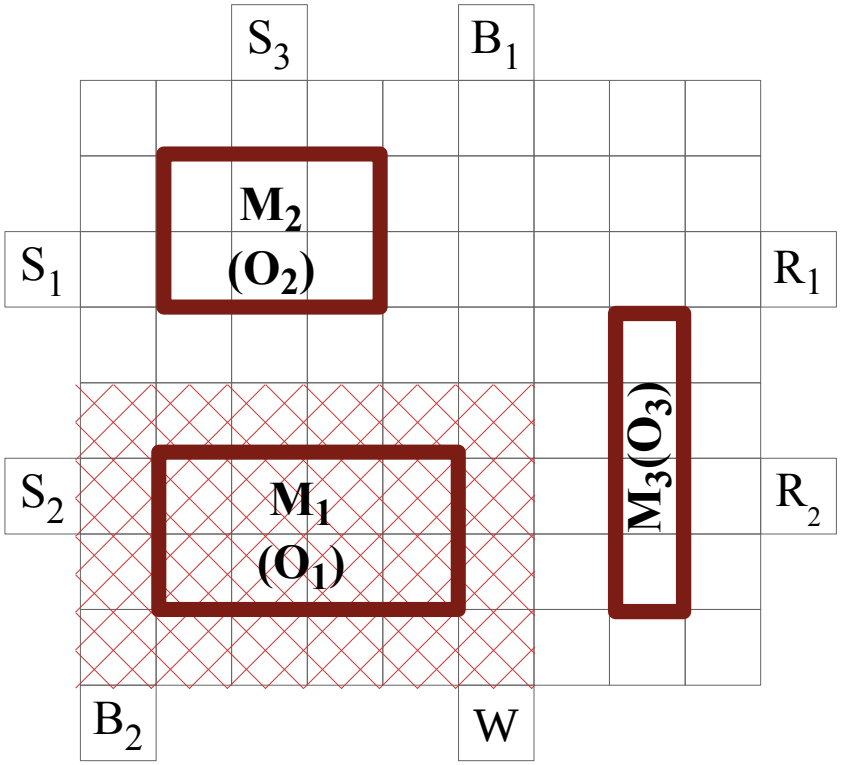
Fault-Tolerant Module-Based Synthesis

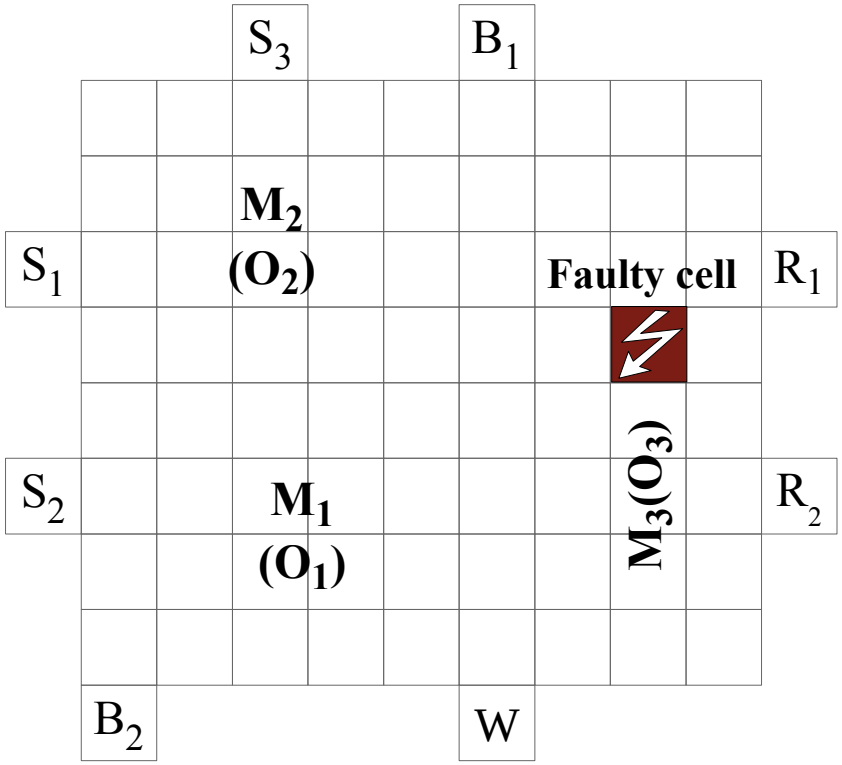




Future Directions

Fault-Tolerant Module-Based Synthesis

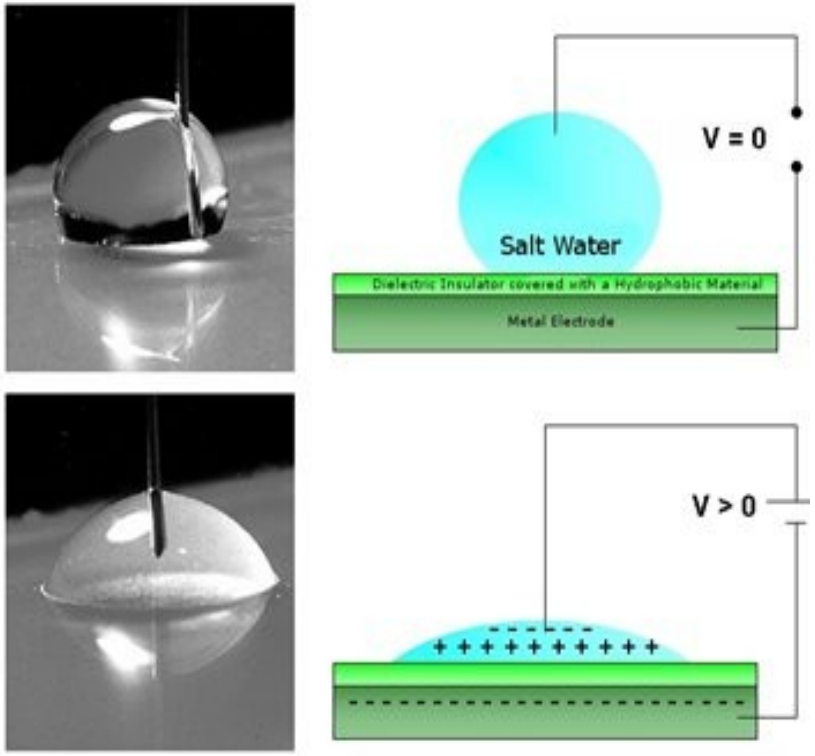




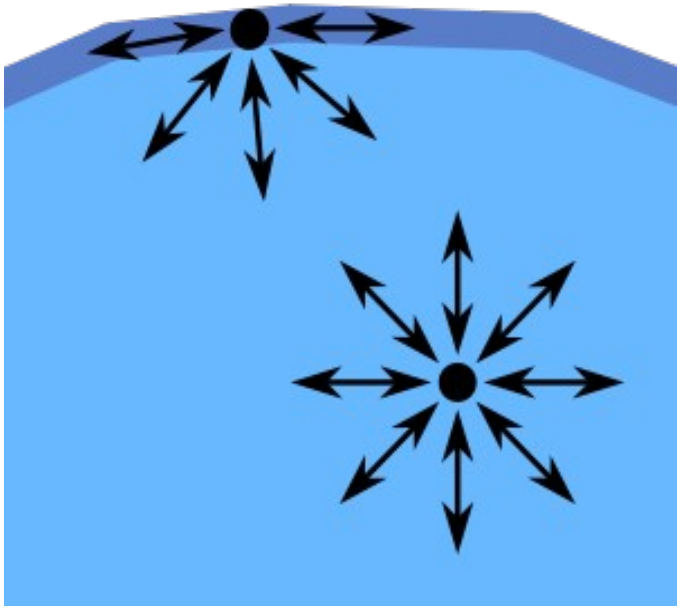

Questions

Back-up slides

Electrowetting

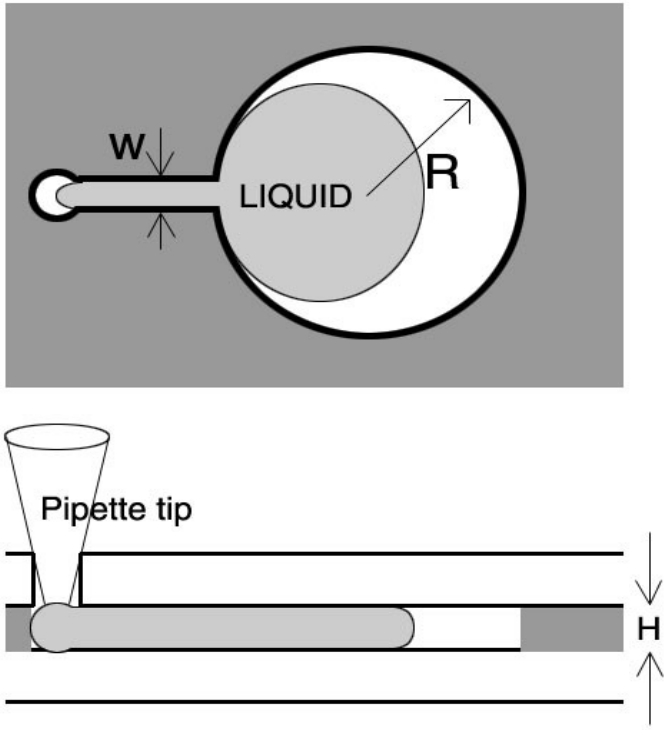


Surface Tension

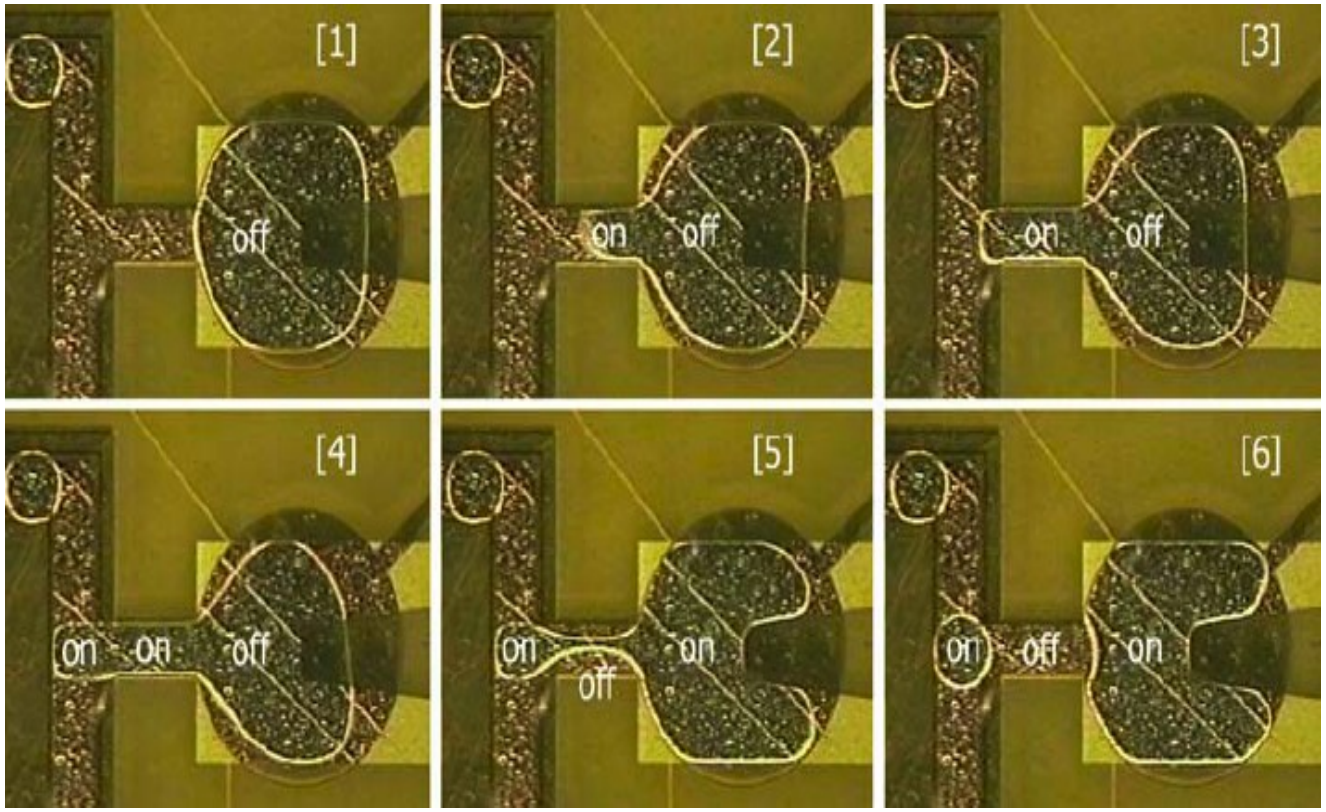


Imbalance of forces between molecules at an interface (gas/liquid, liquid/liquid, gas/solid, liquid/solid)

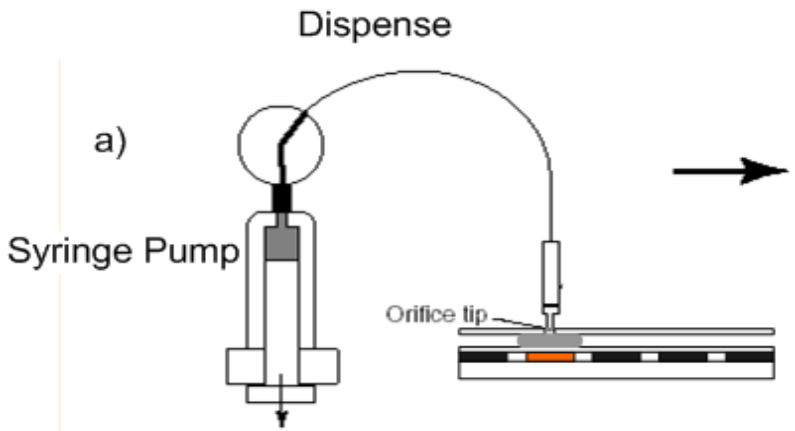
Dispensing

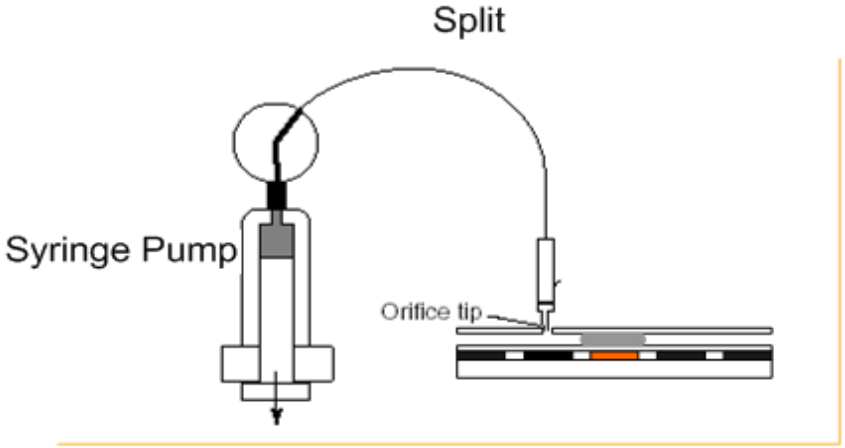


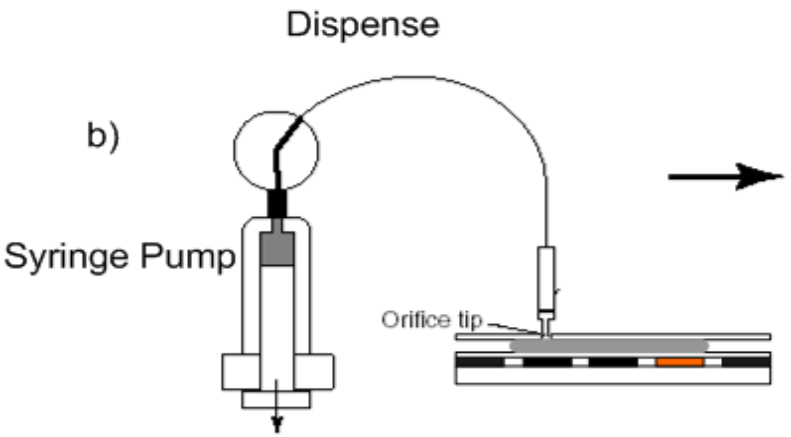
Dispensing

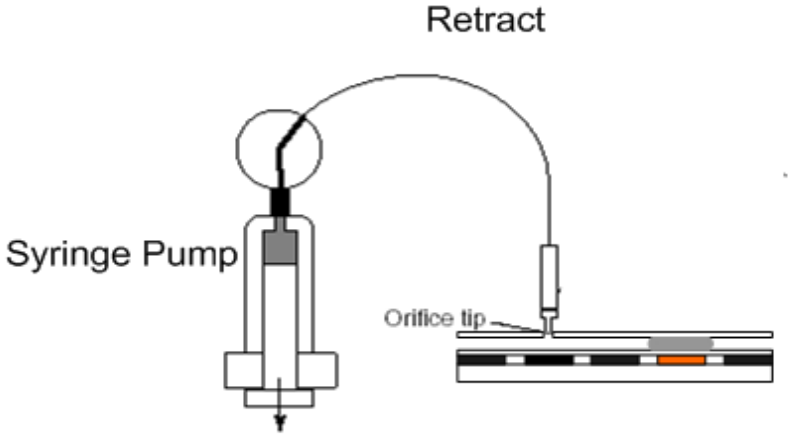


Dispensing


Dispense
a)
Syringe Pump
Orifice tip

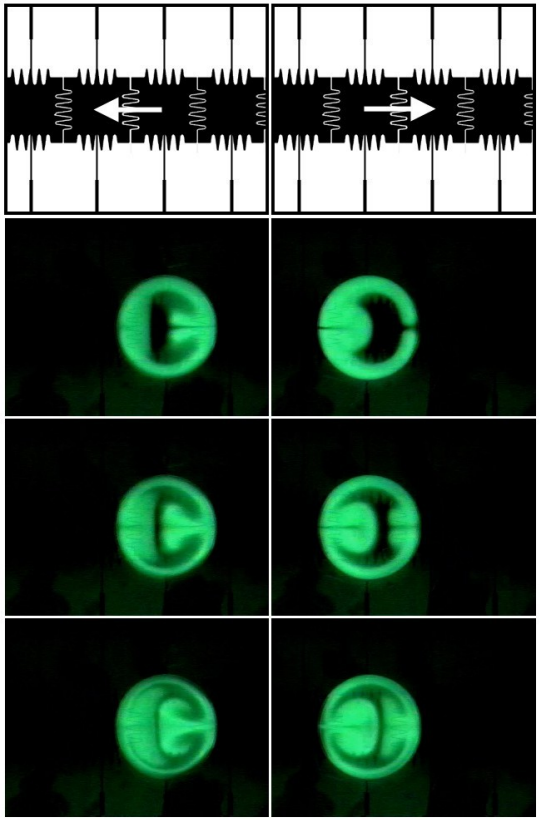

Split
Syringe Pump
Orifice tip

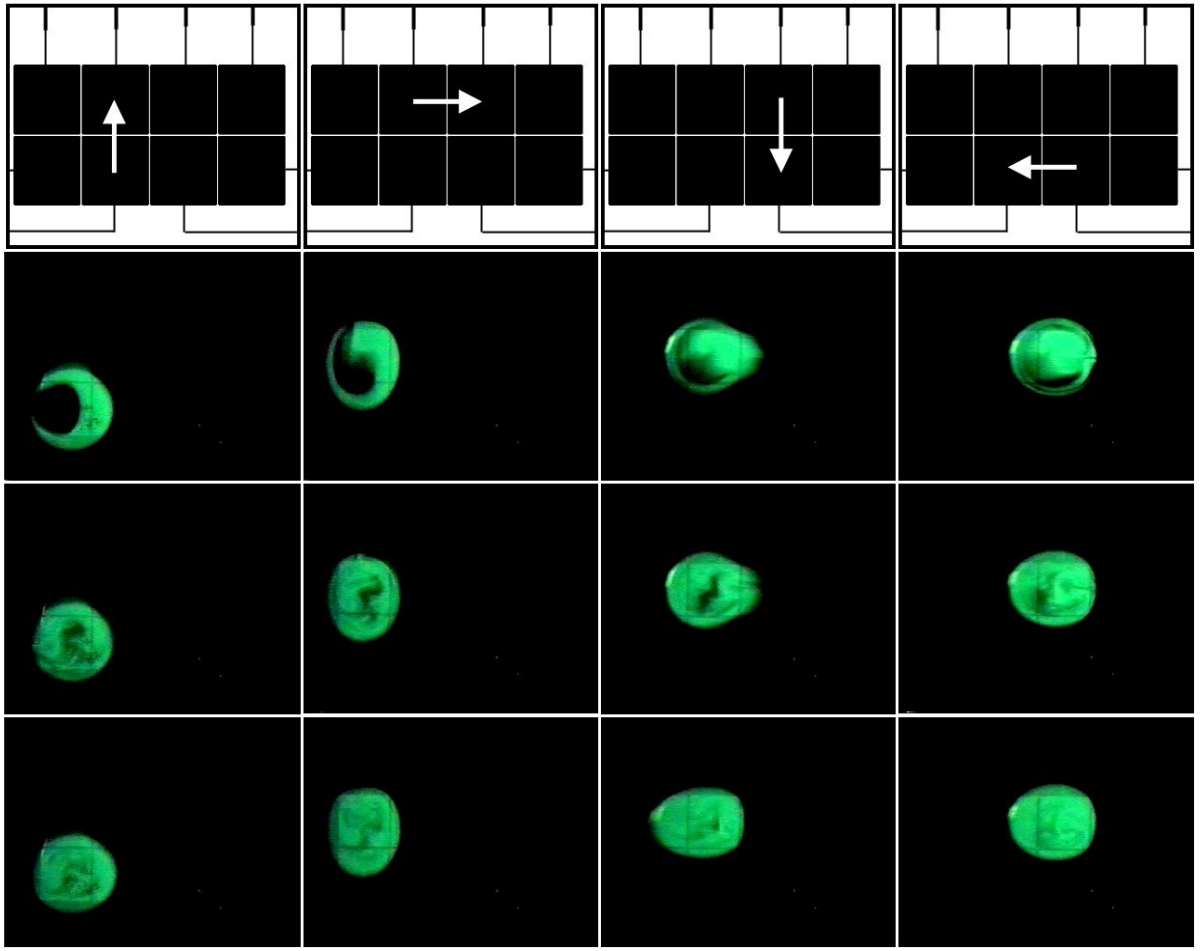

Dispense
b)
Syringe Pump
Orifice tip


Retract
Syringe Pump
Orifice tip

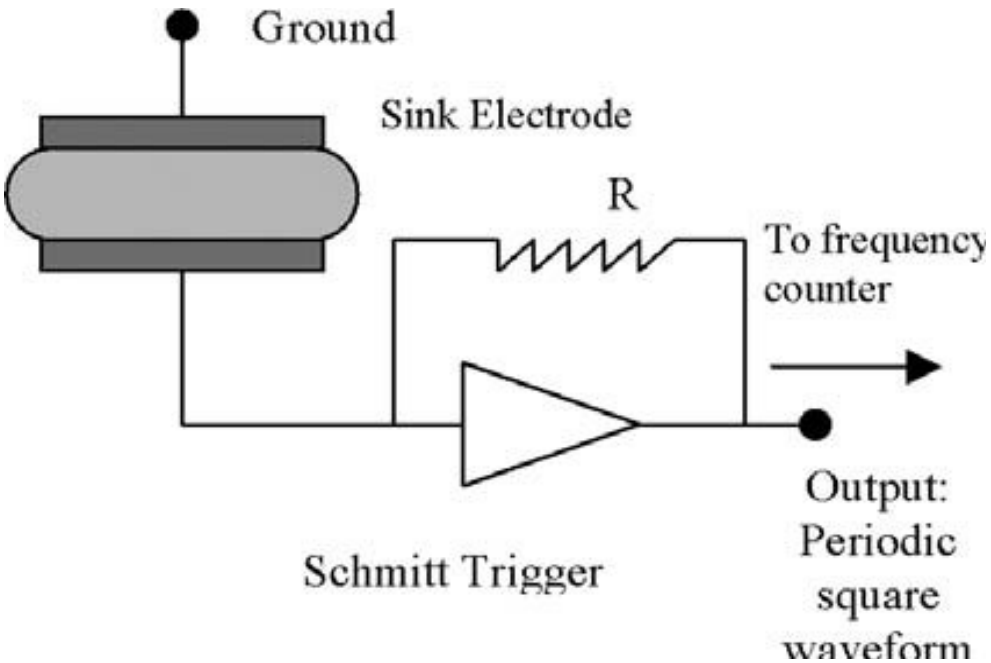
Splitting

Mixing

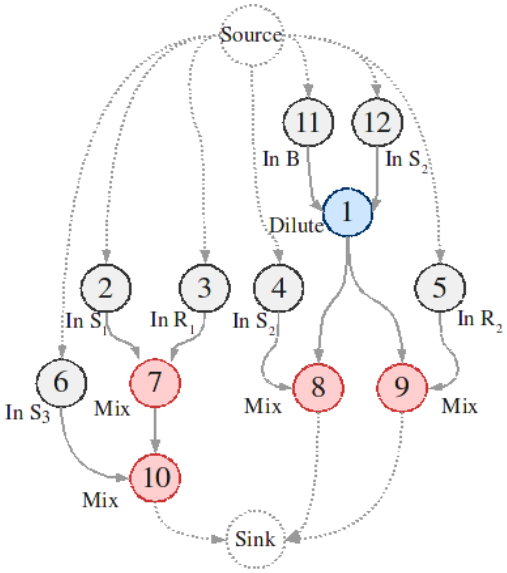




Capacitive sensor

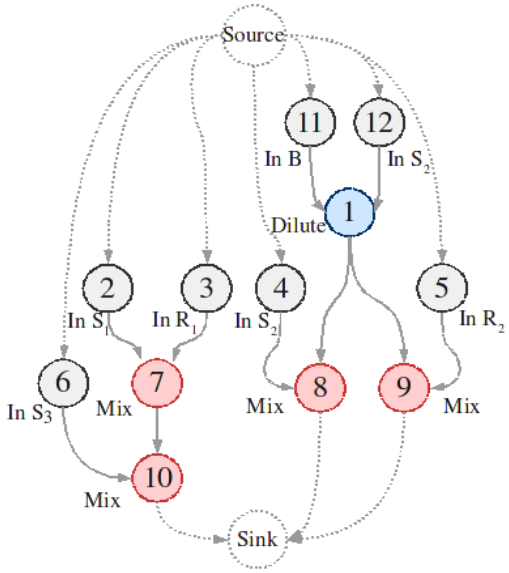


Design Tasks



Operation	Area(cells)	Time(s)
Mix	2 x 2	10
Mix	1 x 3	5
Dilute	1 x 3	8
Dilute	2 x 5	3

Design Tasks



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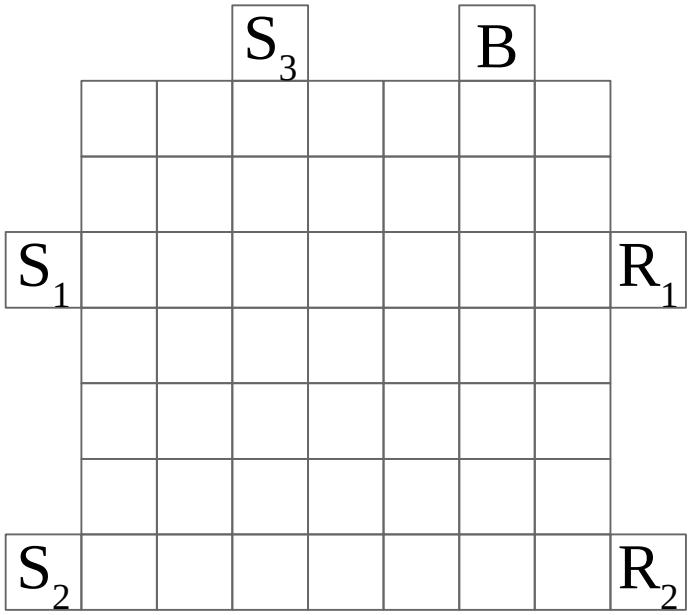
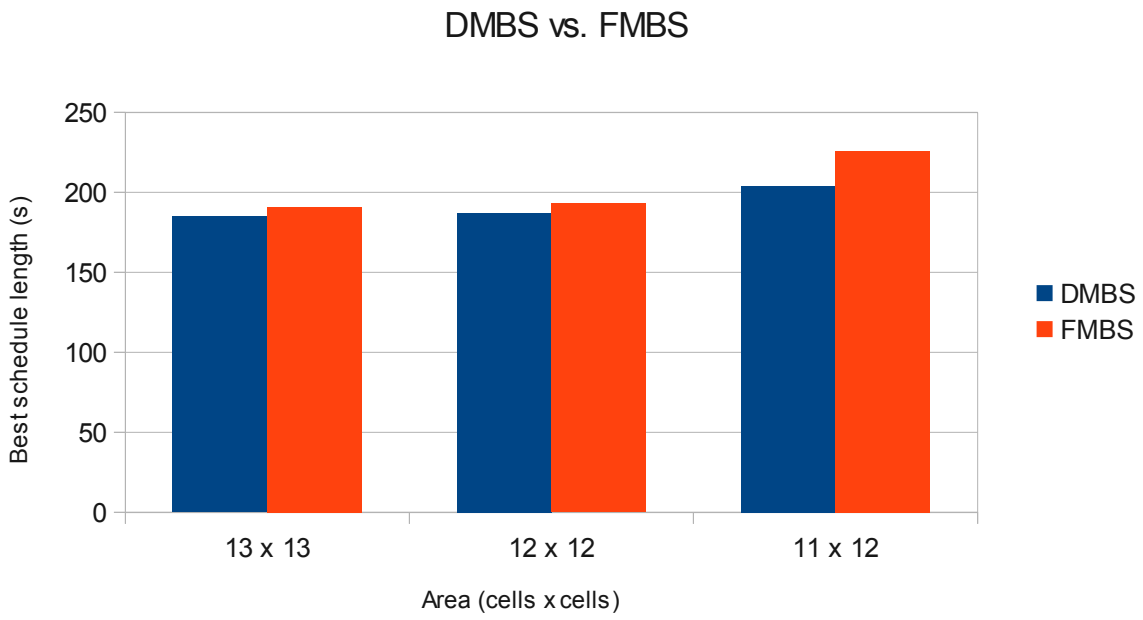


Experimental Evaluation

Quality of the solution compared to classical operation execution
Best out of 50

Colorimetric protein assay

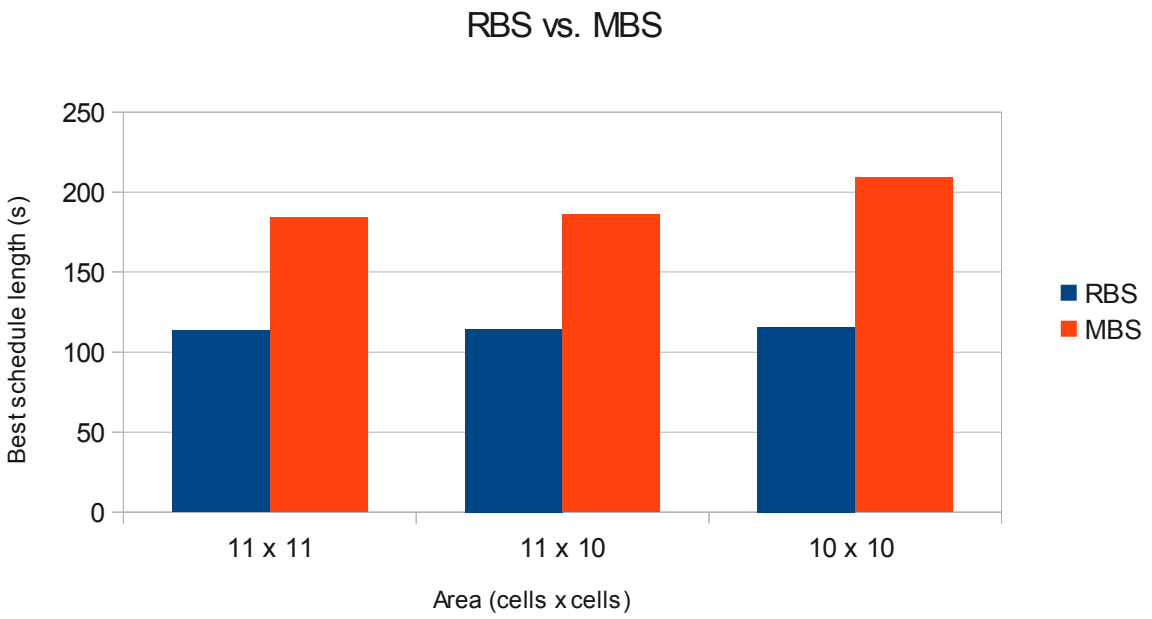


9.73% improvement for 11 x 12

Experimental Evaluation

Quality of the solution compared to classical operation execution
Best out of 50

Colorimetric protein assay

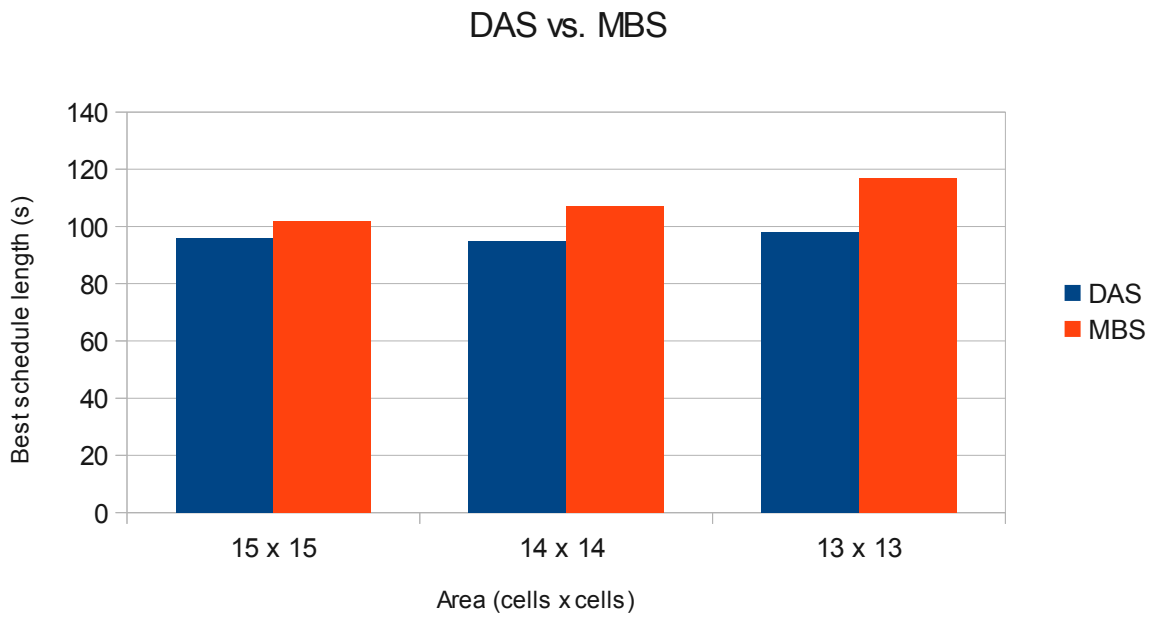


44.63% improvement for 10 x 10

Experimental Evaluation

Quality of the solution compared to classical operation execution
Best out of 50

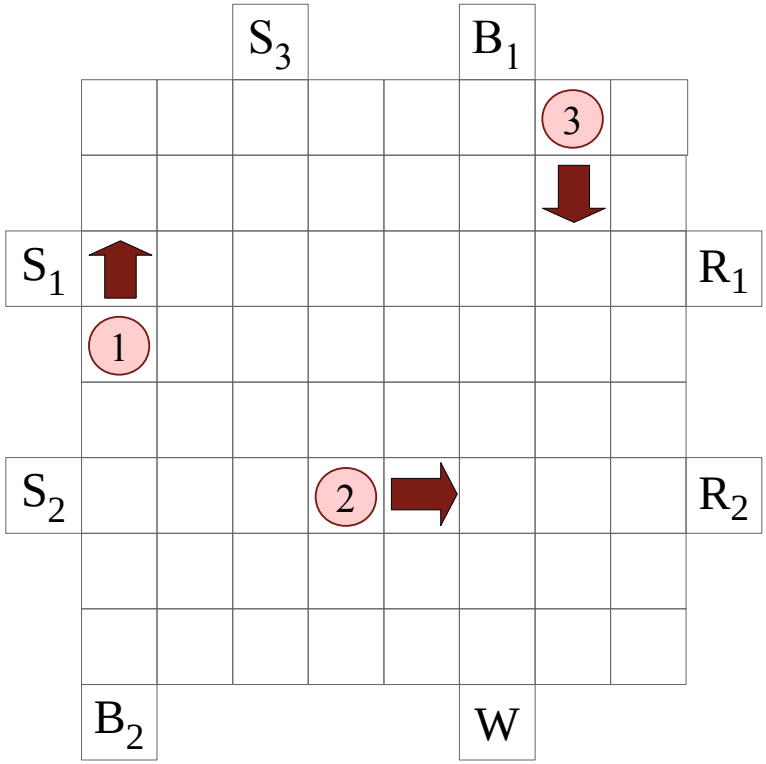
Colorimetric protein assay



15.76% improvement for 13 x 13

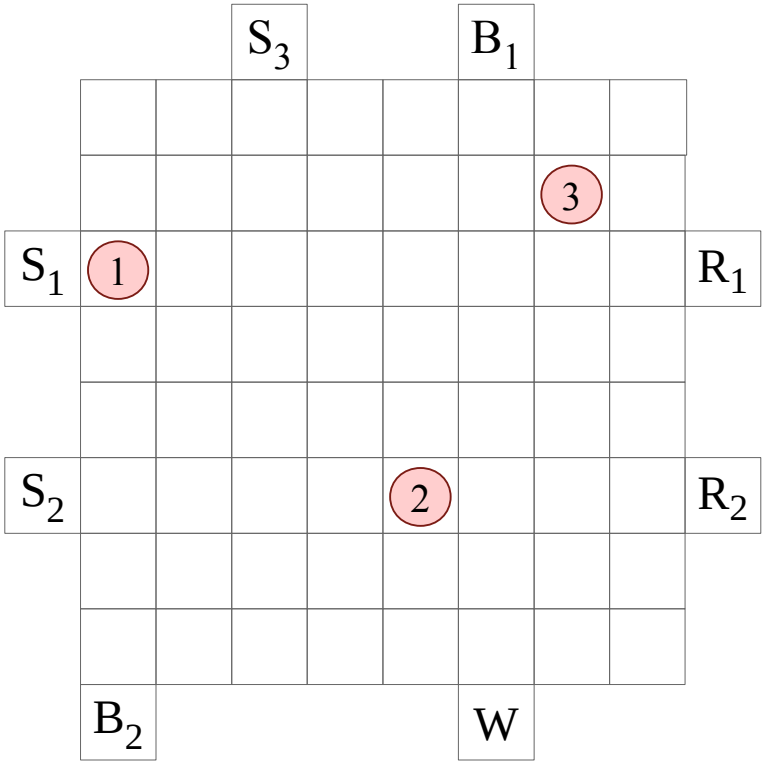
Future Directions

Pin-Constrained Routing-Based Synthesis



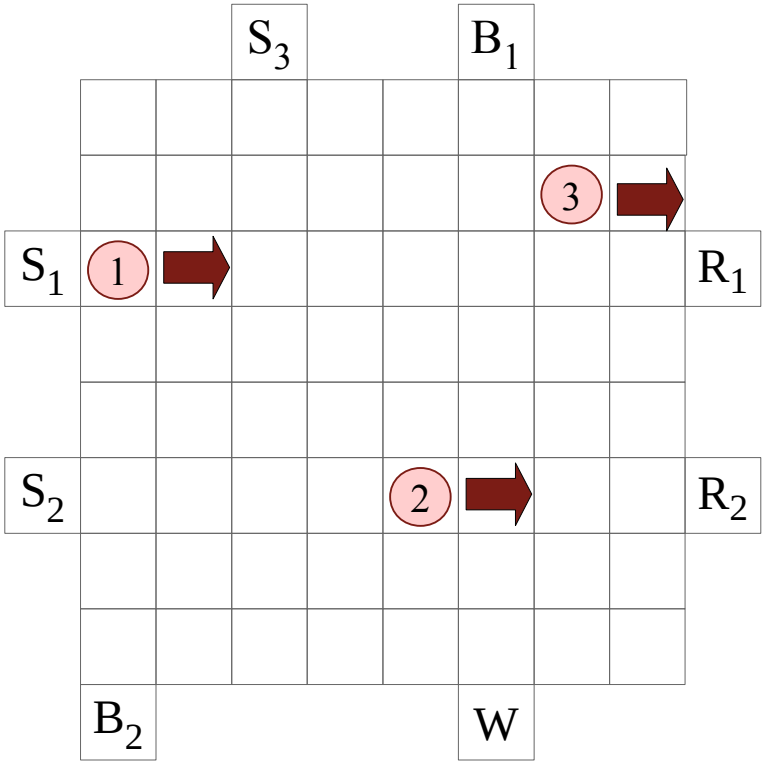
Future Directions

Pin-Constrained Routing-Based Synthesis

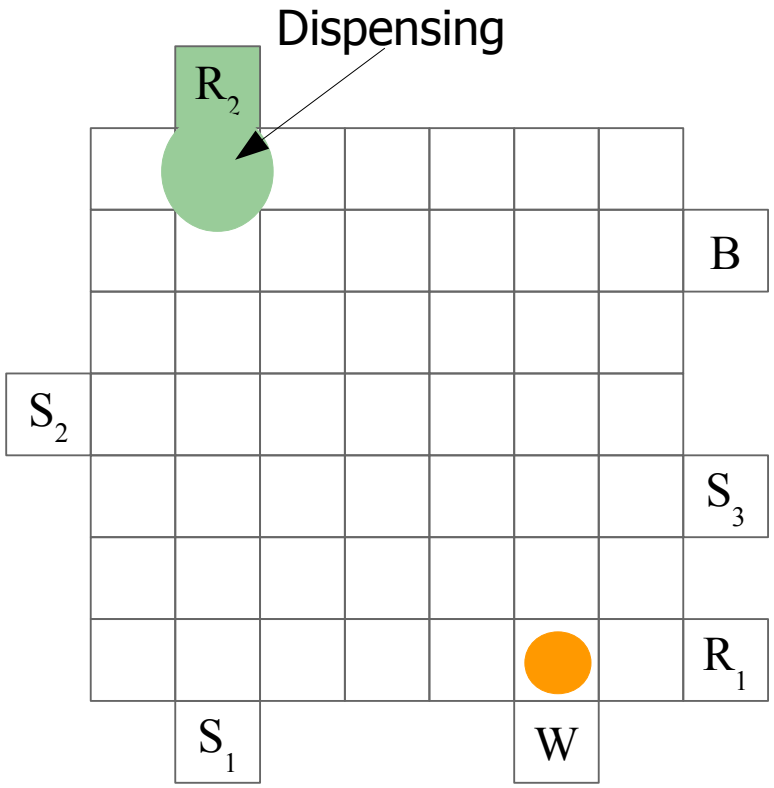


Future Directions

Pin-Constrained Routing-Based Synthesis

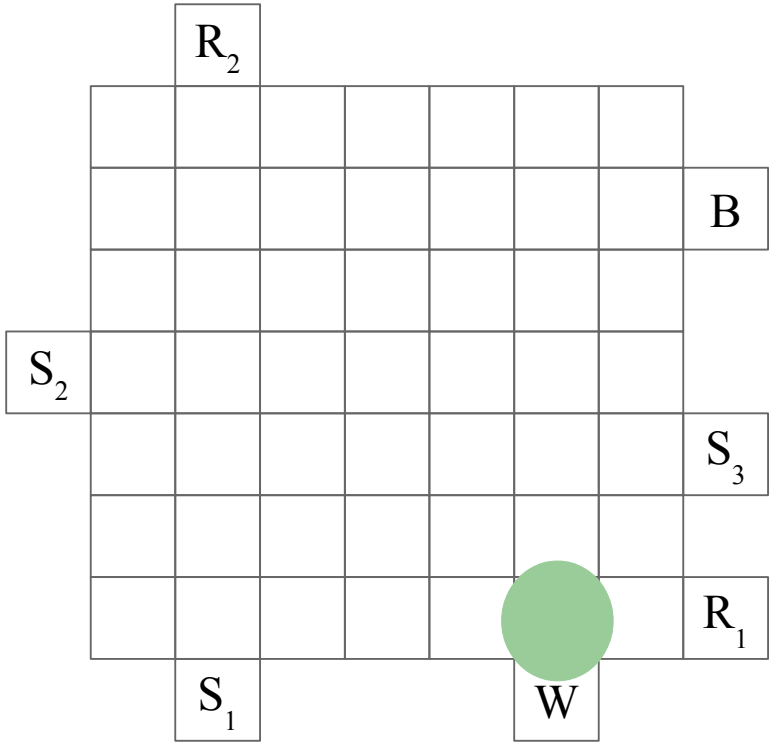


Microfluidic Operations



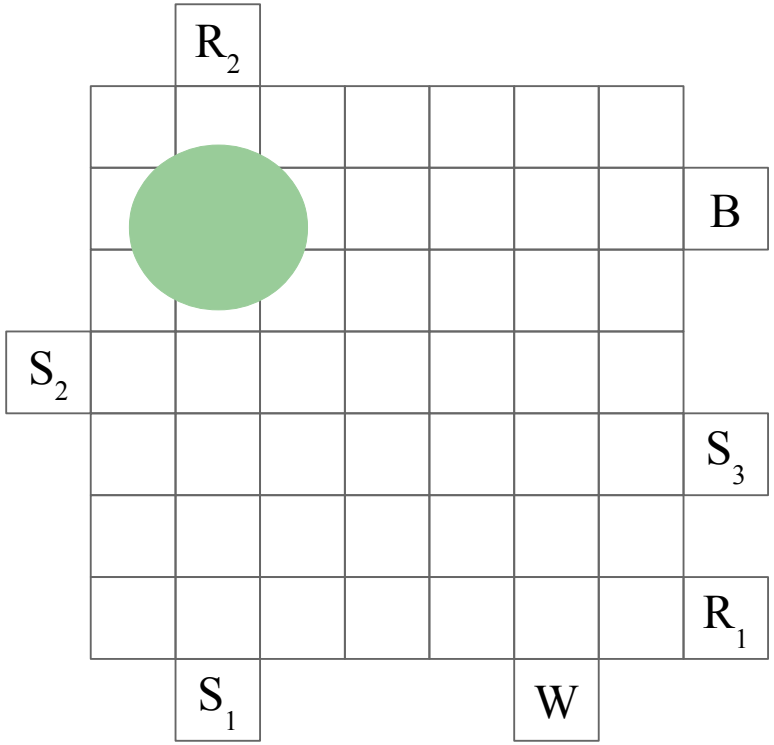
- Dispensing

Microfluidic Operations



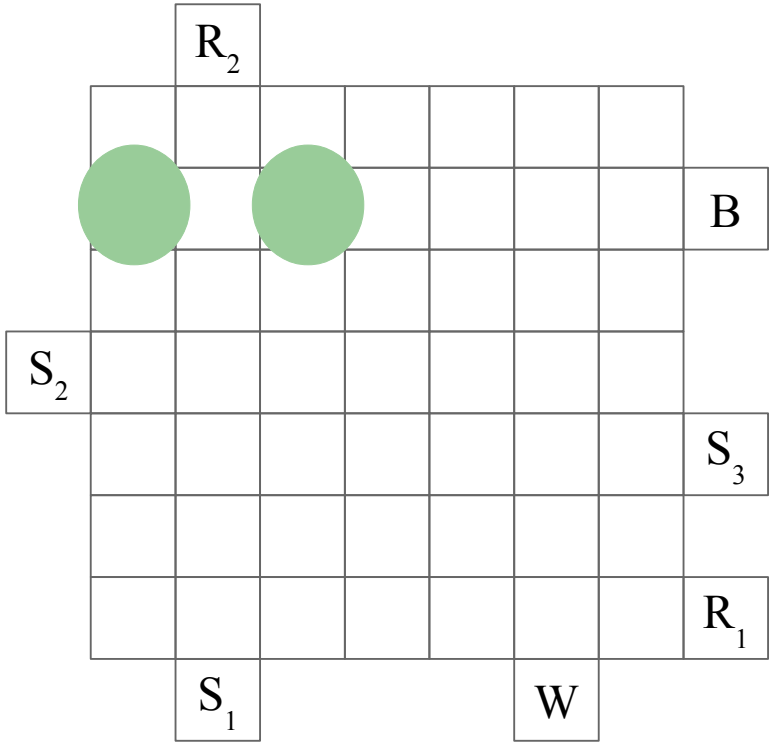
- Dispensing
- Detection

Microfluidic Operations



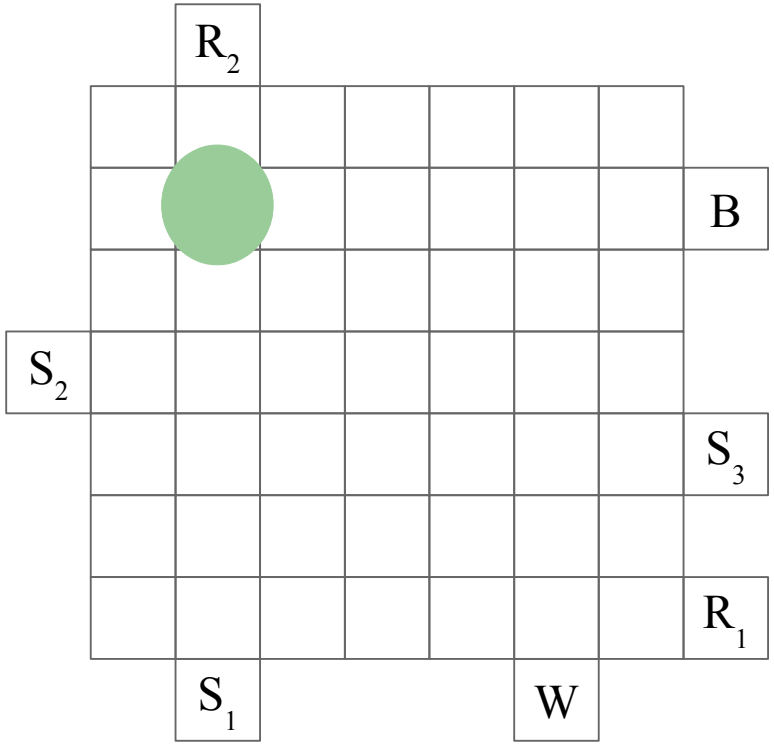
- Dispensing
- Detection
- Splitting/Merging

Microfluidic Operations



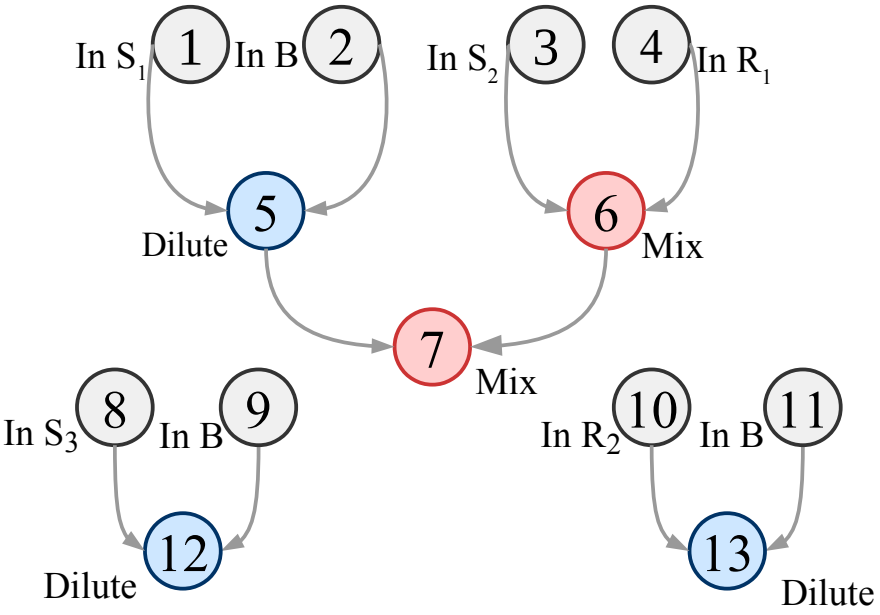
- Dispensing
- Detection
- Splitting/Merging

Microfluidic Operations



- Dispensing
- Detection
- Splitting/Merging
- Storage

Motivational Example (for the first contrib)

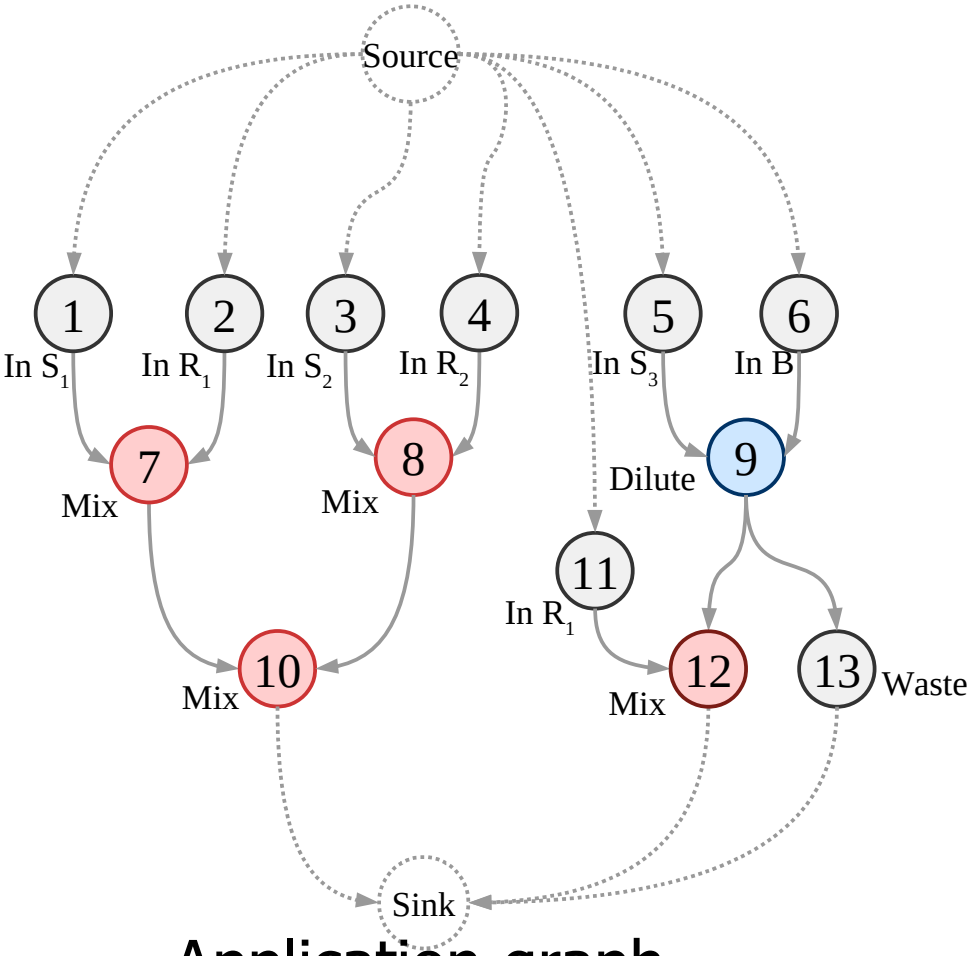


Application graph

Operation	Area(cells)	Time(s)
Mix	2 x 4	3
Mix	2 x 2	4
Dilution	2 x 4	4
Dilution	2 x 2	5
Dispense	-	2

Module library

Motivational Example(for the 2nd contrib)

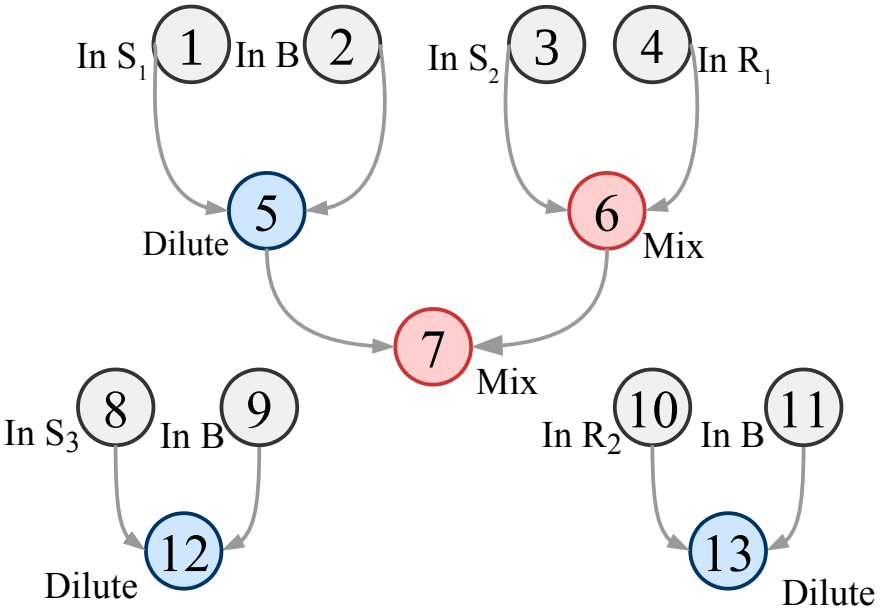


Application graph

Type	Area (cells)	Time (s)
Mix/Dlt	2 x 4	2.9
Mix/Dlt	1 x 4	4.6
Mix/Dlt	2 x 3	6.1
Mix/Dlt	2 x 2	9.9
Input	-	2
Detect	1 x 1	30

Module library

Example(for the 3rd contrib)



Application graph

Type	Area (cells)	Time (s)
Mix/Dlt	2 x 4	2.9
Mix/Dlt	1 x 4	4.6
Mix/Dlt	2 x 3	6.1
Mix/Dlt	2 x 2	9.9
Input	-	2
Detect	1 x 1	30

Module library