Mapping biochemical applications onto microfluidic-based biochips

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Embedded Systems Engineering

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DTU Informatics
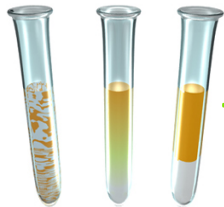Department of Informatics and Mathematical Modeling

Outline

- Motivation & relation to MPSoC

- Biochip architectures

- The mapping problem
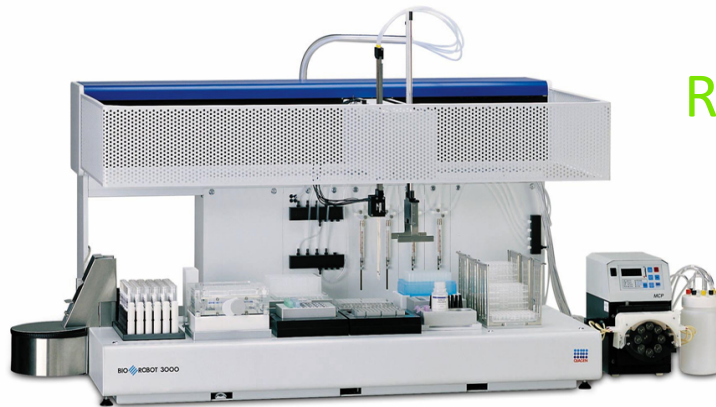
Motivation

- Biotech
  - DNA analysis
- Medicine
  - Clinical diagnosis
  - Therapeutics
- Ecology
  - Monitoring the quality of air/water/food
- Pharmacy
  - Screening
  - Synthesis of new drugs

Motivation

Test tubes

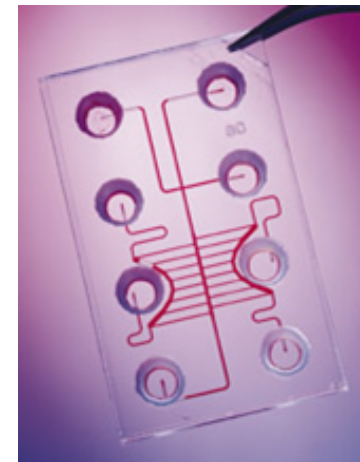☐ Automation
☐ Integration
☐ Miniaturization

Robotics

☑ Automation
☑ Integration
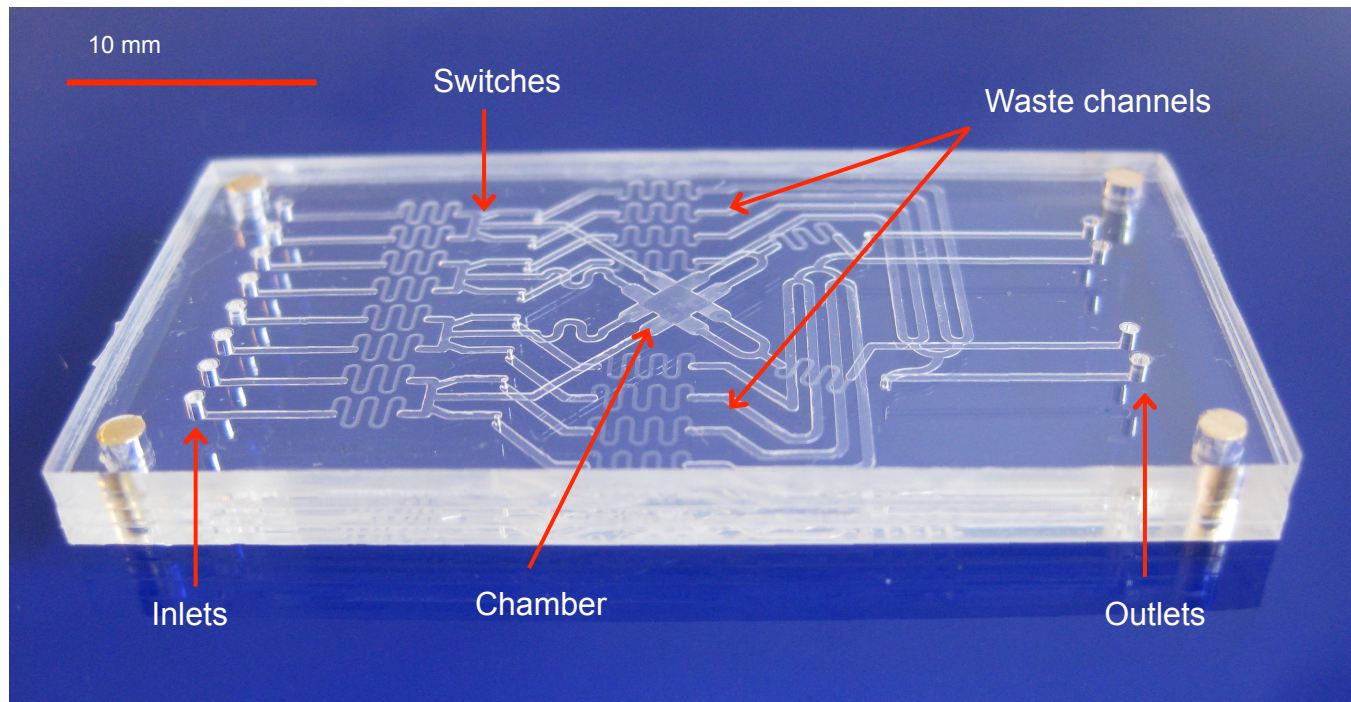☐ Miniaturization
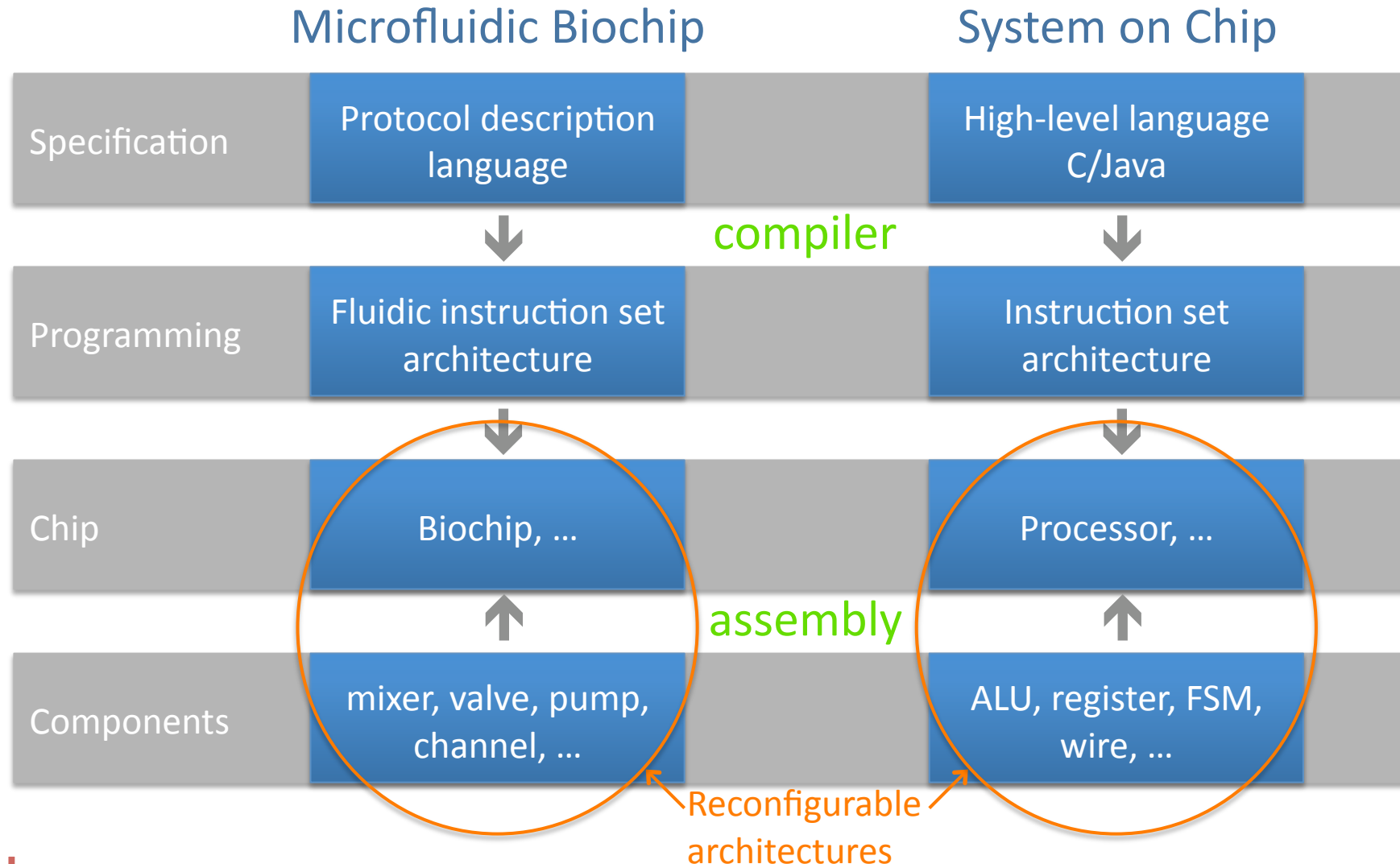
Microfluidics

☑ Automation
☑ Integration
☑ Miniaturization

Microfluidic biochip?
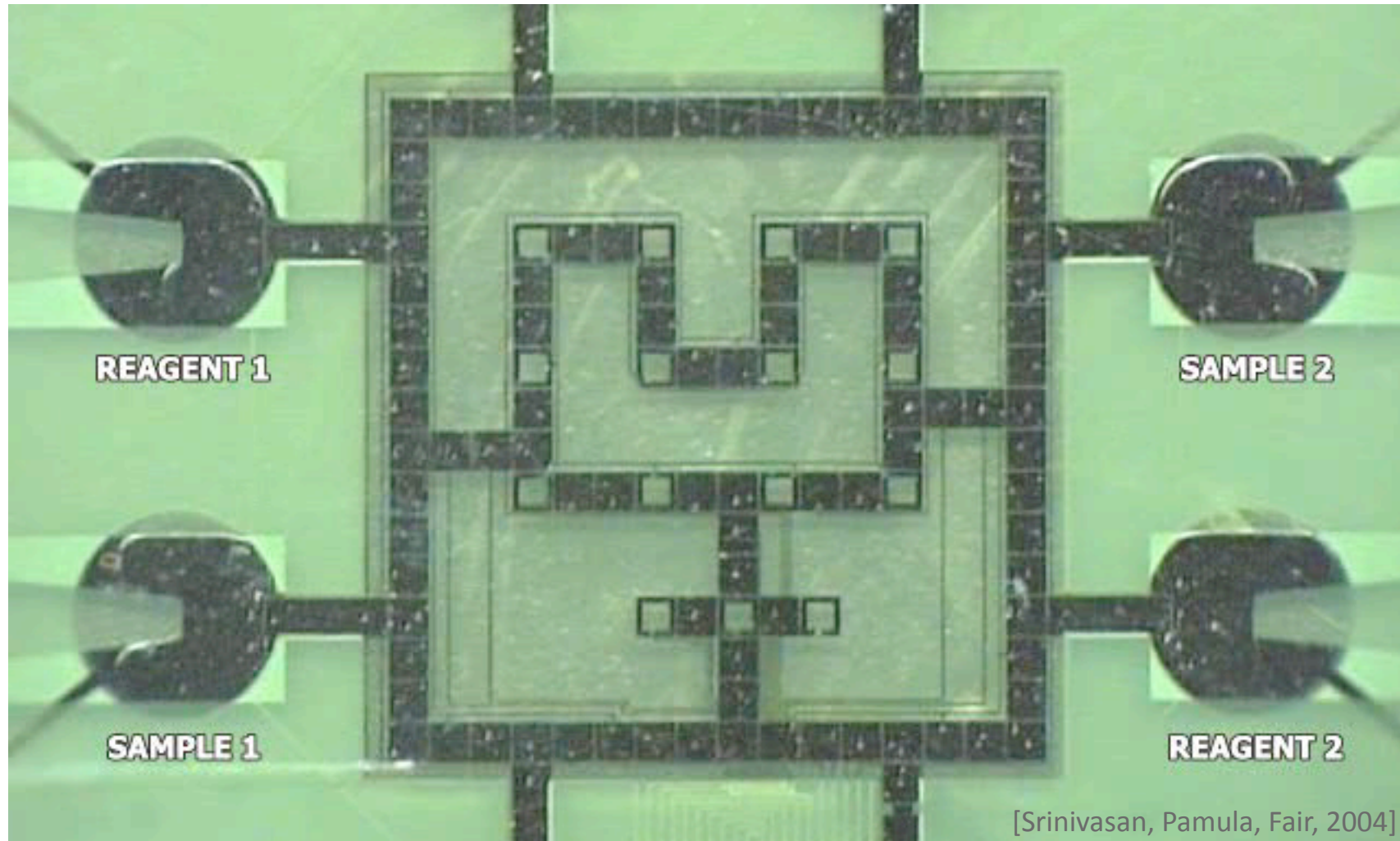
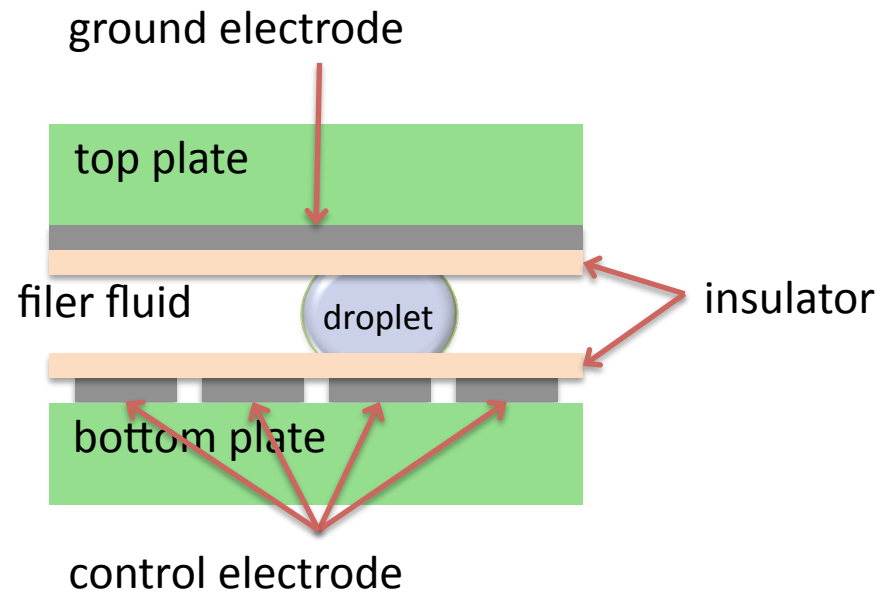- Manipulations of continuous liquid through fabricated micro-channels

Biochip design

	Microfluidic Biochip		System on Chip	
Specification	Protocol description language		High-level language C/Java	
	⬇	compiler	⬇	
Programming	Fluidic instruction set architecture		Instruction set architecture	
	⬇		⬇	
Chip	Biochip, …		Processor, …	
	⬆	assembly	⬆	
Components	mixer, valve, pump, channel, …		ALU, register, FSM, wire, …	

Reconfigurable architectures

Digital microfluidic biochip

[Srinivasan, Pamula, Fair, 2004]

Digital microfluidic biochip

ground electrode

top plate

filer fluid

droplet

insulator

bottom plate
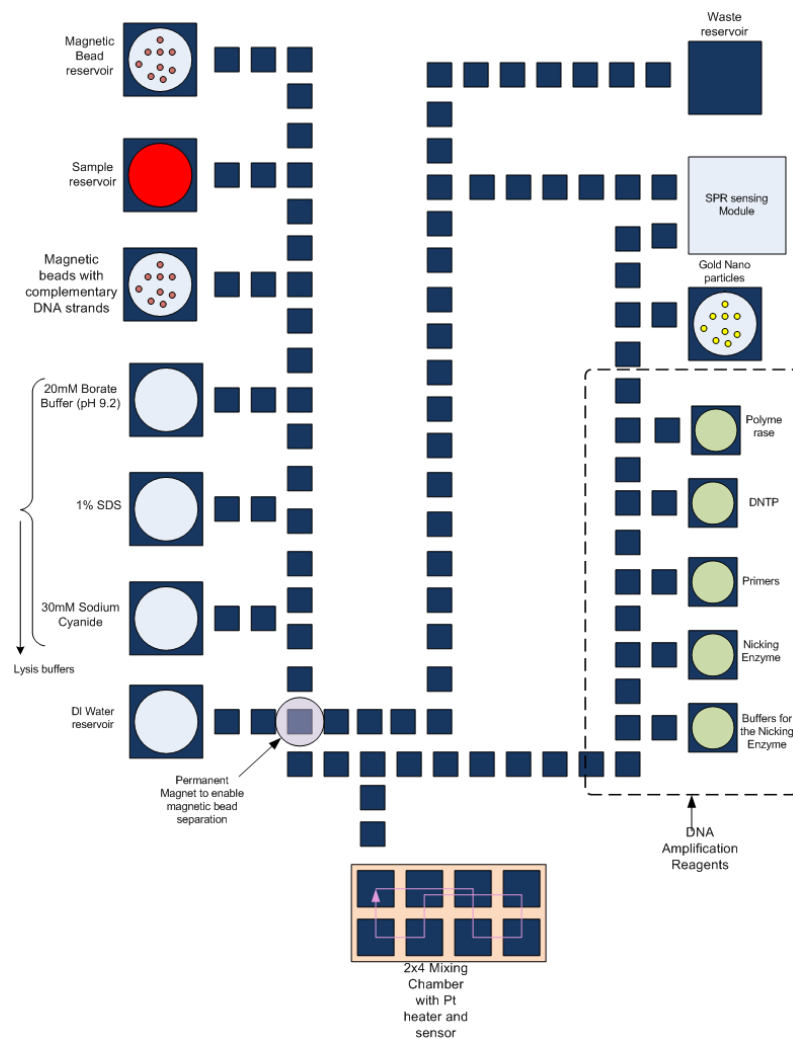
control electrode

Speed: 12-25 cm/s
Size of electrode: 0.15 cm
Cell-to-cell transport: ~0.01 s

Biochip architecture?

- **Application specific** architecture
  - Spatial and temporal assignment done at design-time

- **General purpose** architecture
  - Spatial assignment done at design-time
  - Temporal assignment done at run-time

- **Reconfigurable** architecture
  - Spatial and temporal assignment done at run-time

Application specific biochip

Magnetic Bead reservoir

Sample reservoir

Magnetic beads with complementary DNA strands

20mM Borate Buffer (pH 9.2)

1% SDS

30mM Sodium Cyanide

Lysis buffers

DI Water reservoir

Permanent Magnet to enable magnetic bead separation

2x4 Mixing Chamber with Pt heater and sensor

Waste reservoir

SPR sensing Module

Gold Nano particles

Polymerase

DNTP

Primers

Nicking Enzyme

Buffers for the Nicking Enzyme

DNA Amplification Reagents

- Biochip for malaria detection

- Operation:
  - Infected cell isolation
  - Cell Lysis
  - DNA extraction
  - DNA amplification using PCR
  - Optical detection using SPR

General purpose biochip
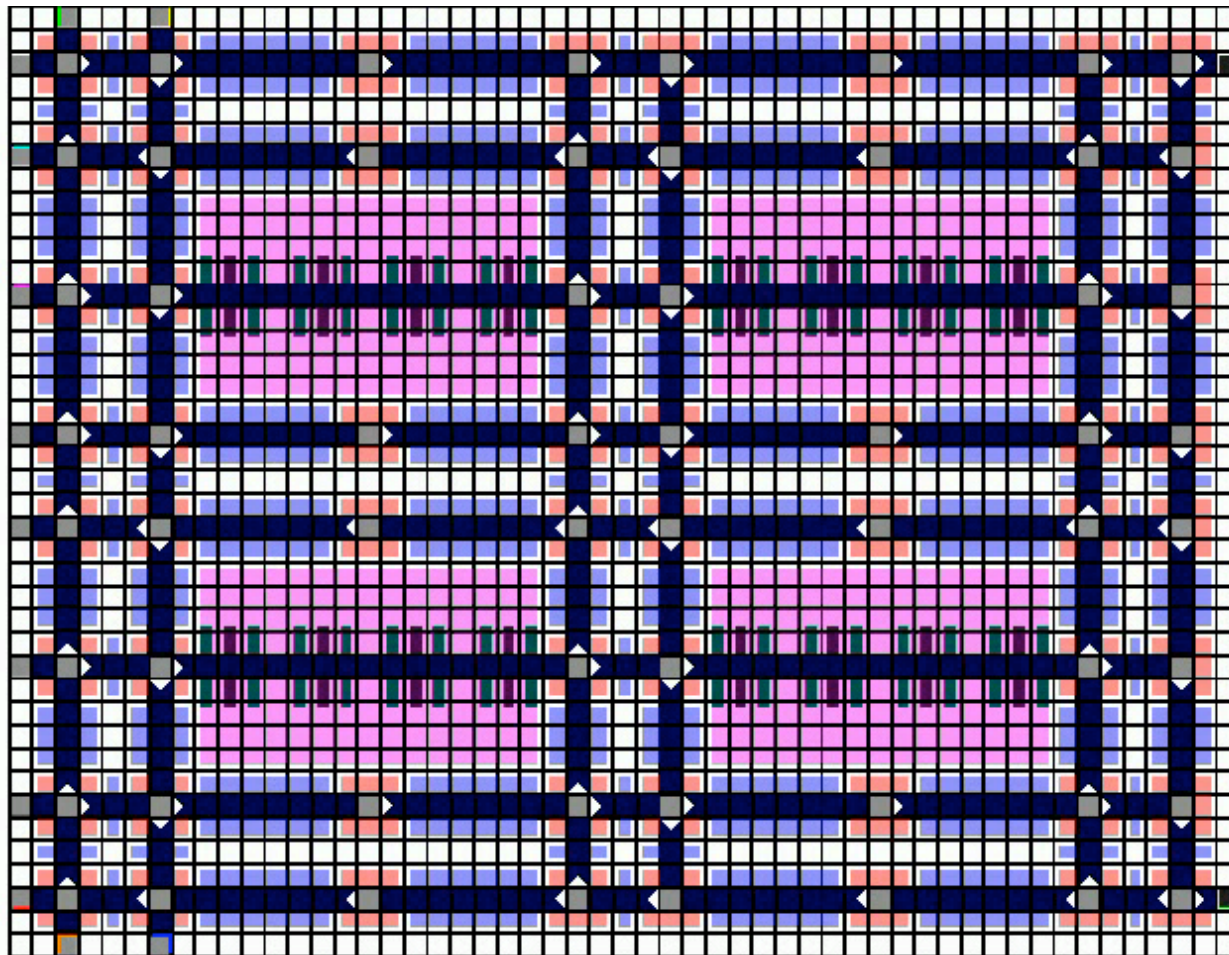
[Griffith, Akella, 2005]

Reconfigurable biochip

input port

output port

Photodiode
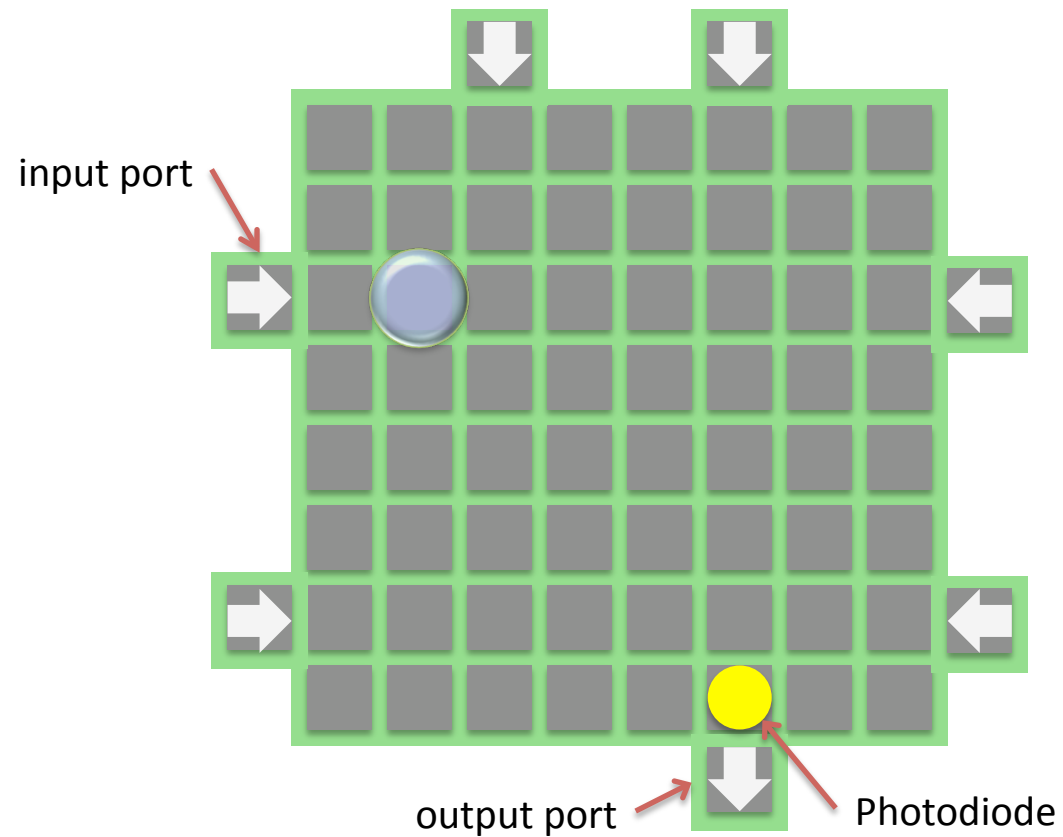
Biochemical operations

- Transport
- Merging
- Mixing
- Splitting
- Diluting
- Detection

- ...
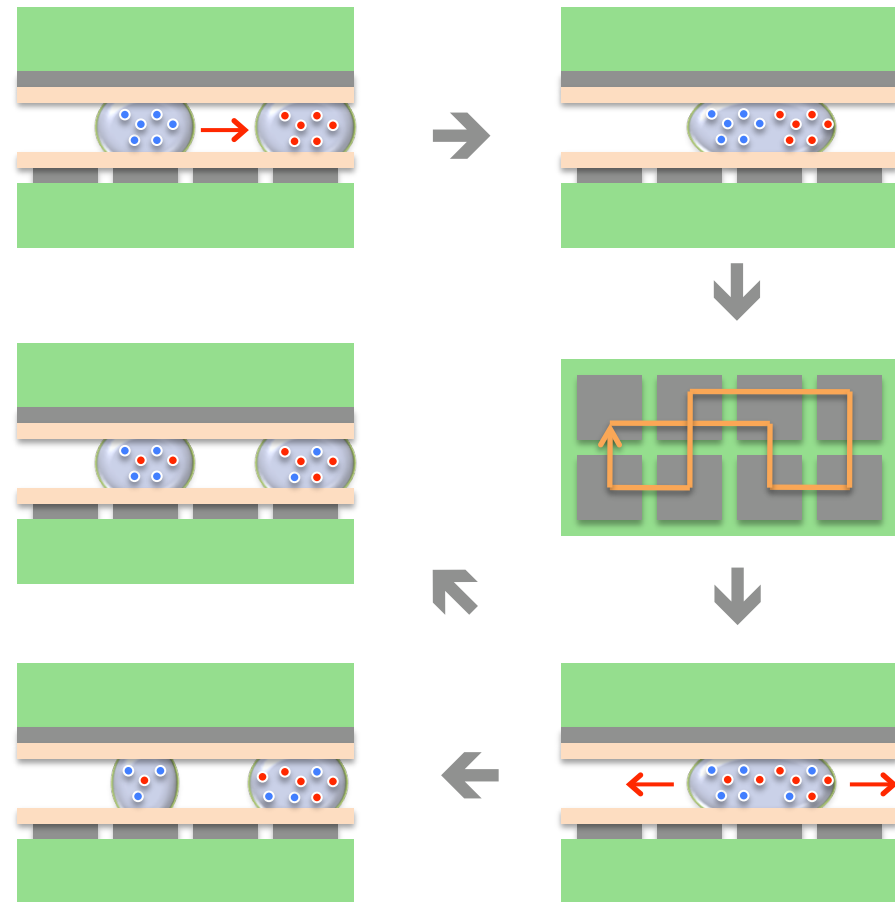
Biochemical application

application G
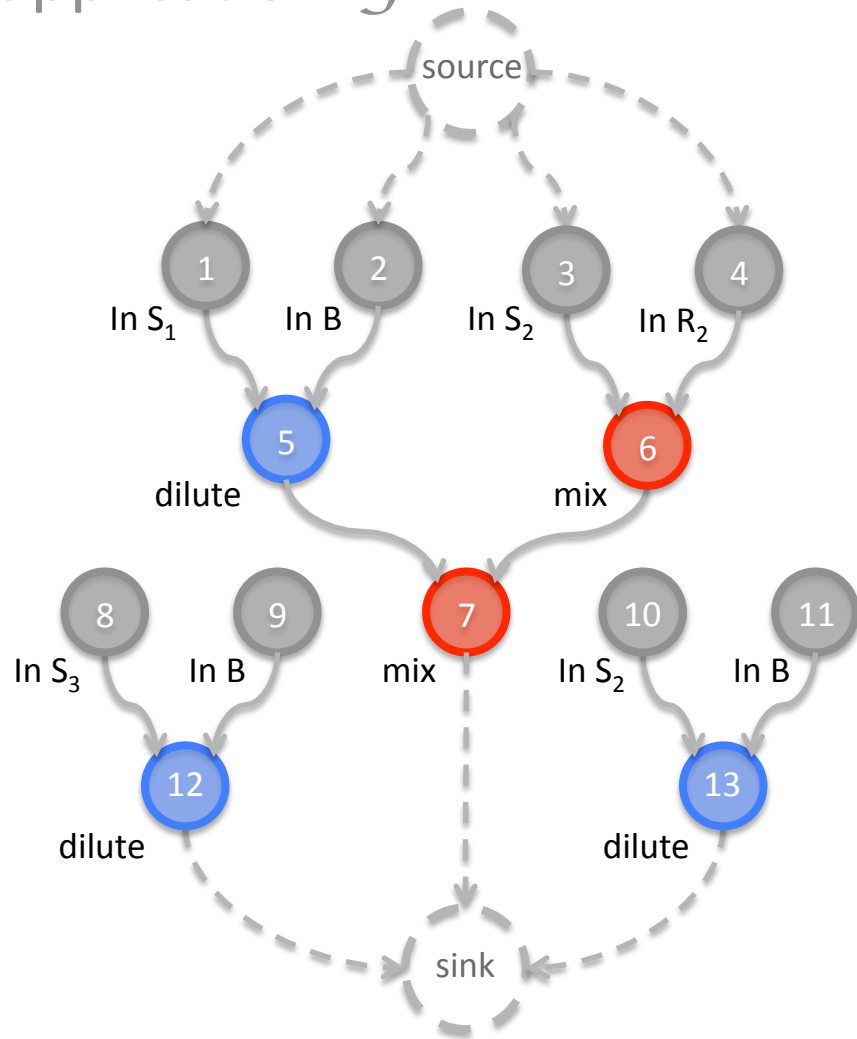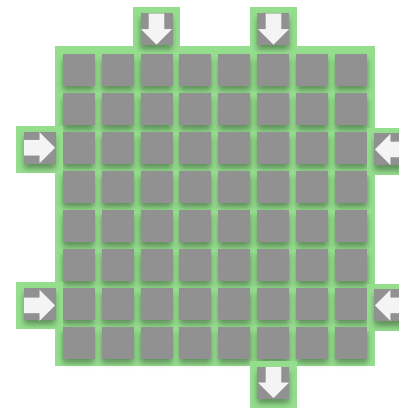

library L

module	Operation	Area (cells)	Time (sec)
M1	Mixing	2x4	3
M2	Mixing	2x2	4
D1	Dilution	2x4	4
D2	Dilution	2x2	5

array C

Mapping biochemical applications onto microfluidic biochips

- Allocation $\mathcal{A}$
  - Determine modules $\mathcal{M}_k$ from library $\mathcal{L}$
- Binding $\mathcal{B}$
  - Assign each operation O_i to a module $\mathcal{M}_k$
- Schedule $\mathcal{S}$
  - Determine start time t_i^{start} of each operation O_i
- Placement $\mathcal{P}$
  - Place modules on the $m \times n$ array
- Synthesis Ψ
  - Given $<\mathcal{G},\ \mathcal{C},\ \mathcal{L}>$, find $\Psi = <\mathcal{A},\mathcal{B},\mathcal{S},\mathcal{P}>$ which minimize the schedule length $\delta_{\mathcal{G}}$

Scheduling
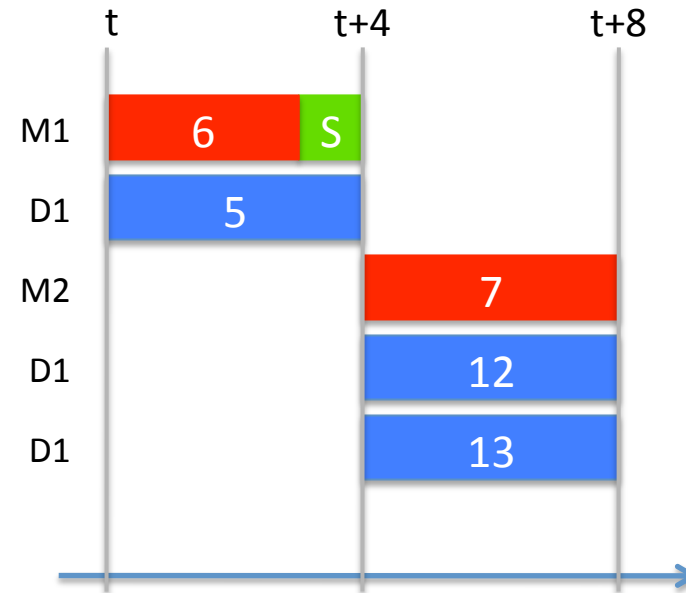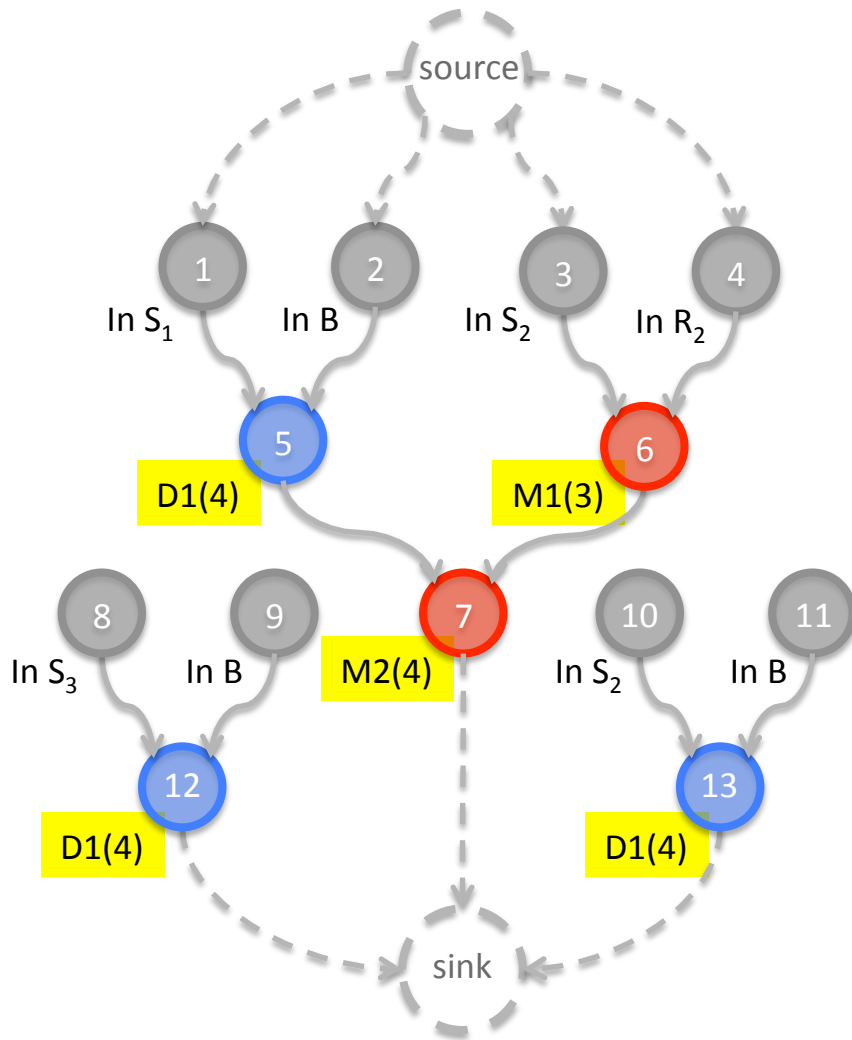
Scheduling
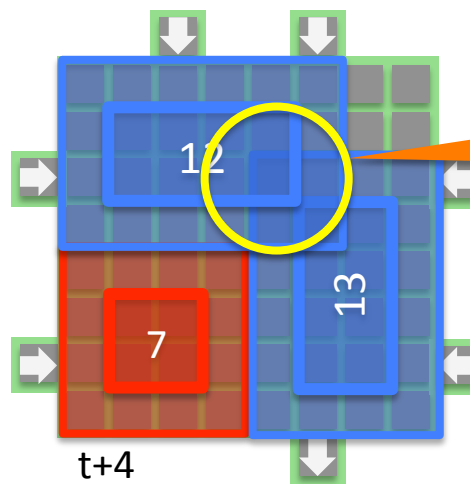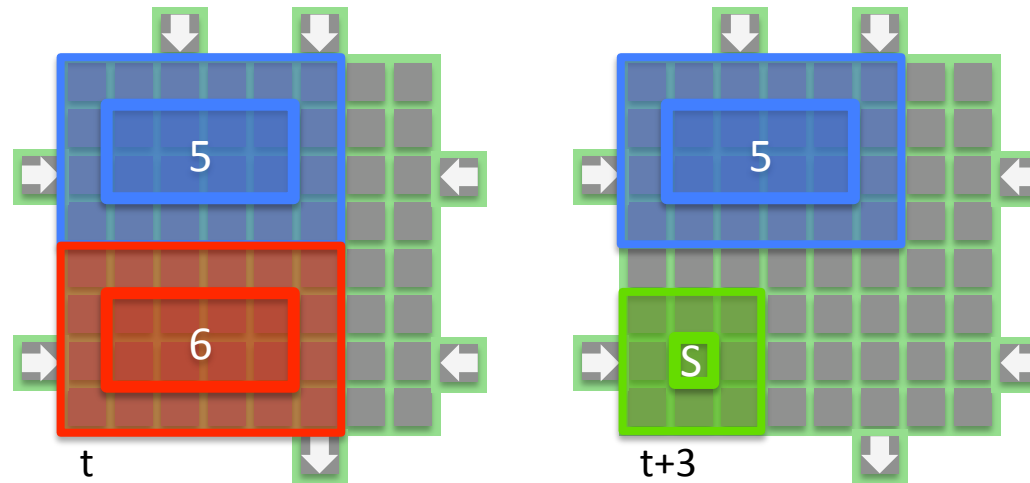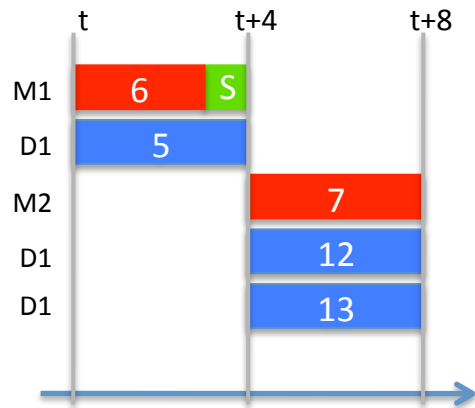
Overlapping modules
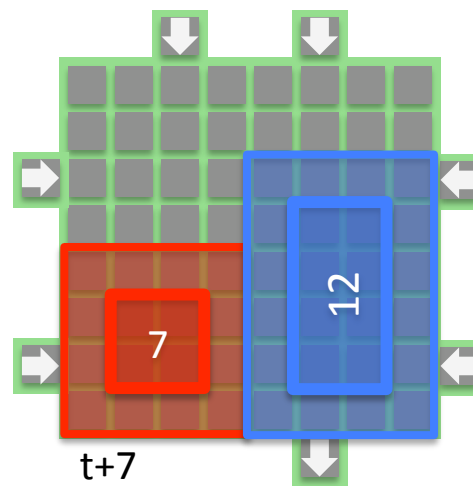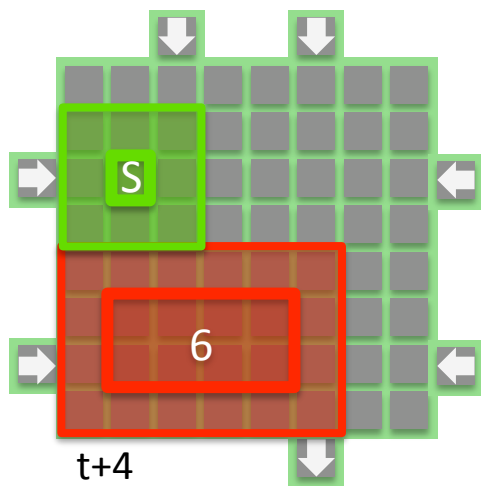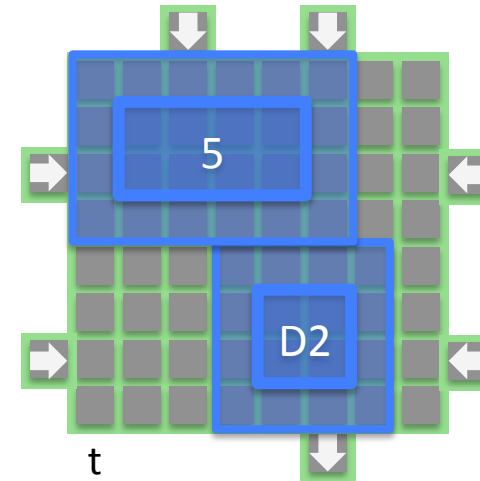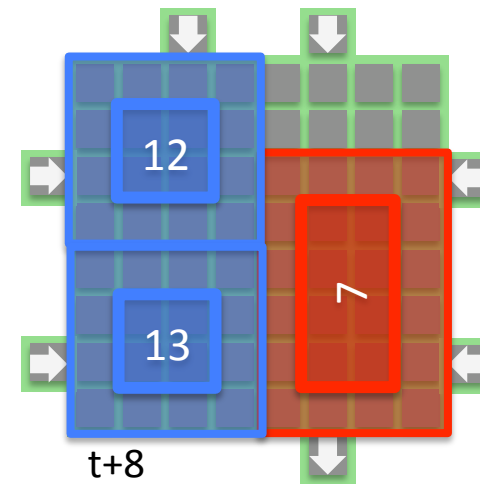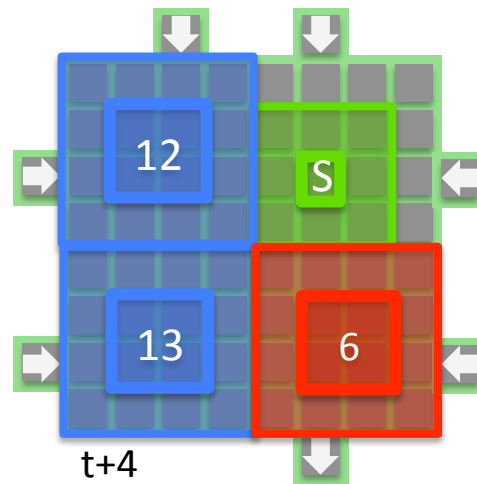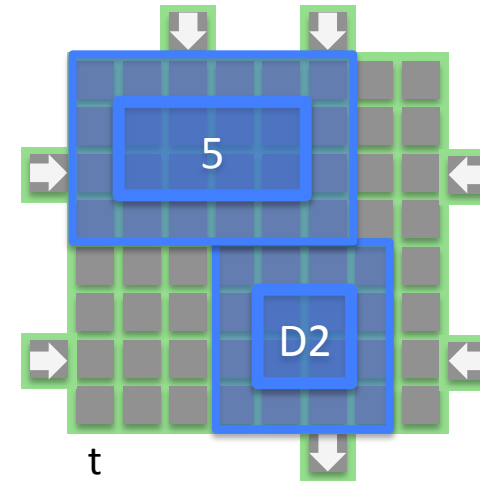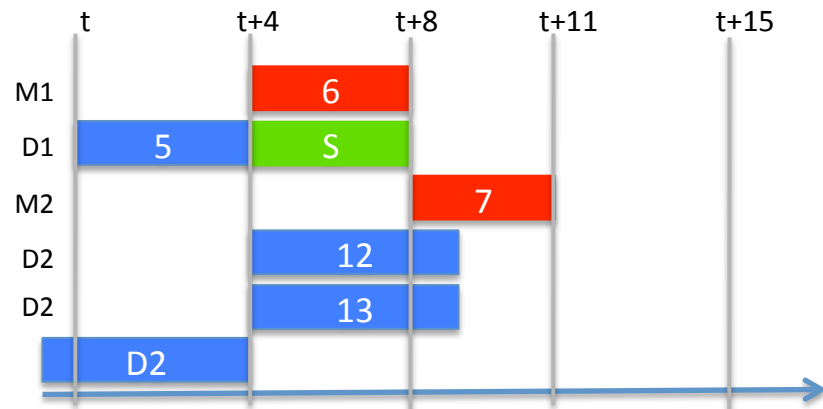
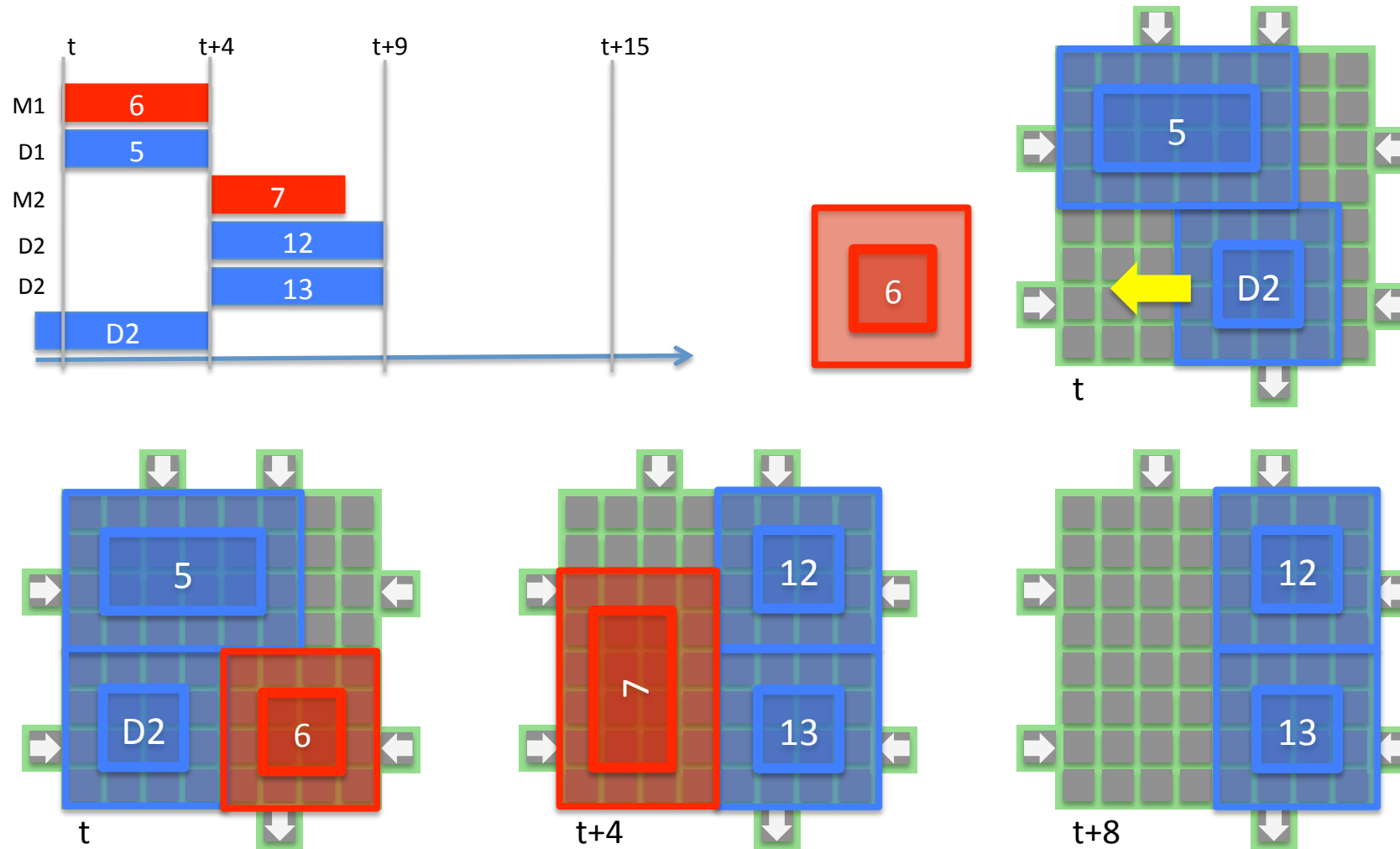Concurrent biochemical applications

Scheduling with placement
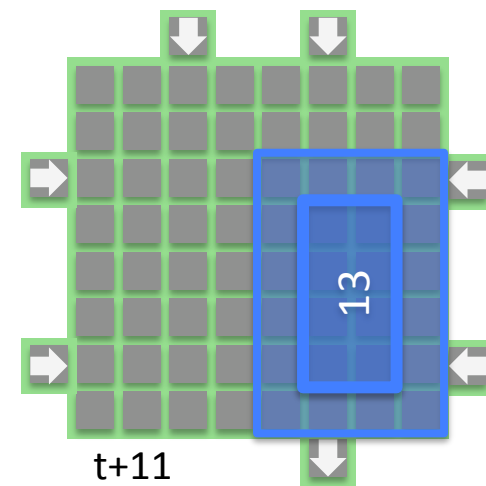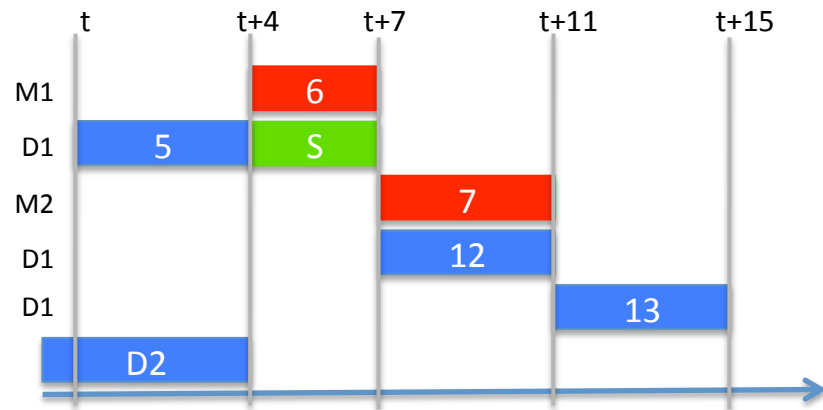
Scheduling with placement

Scheduling with dynamic placement

Summary

- Biochip architectures

- Synthesis of digital microfluidic biochips

- Run-time resource management leads to considerable better results

- Integration with MPSoC to allow online monitoring and feedback

- ➜ *Conditional biochemical operations*

Acknowledgements

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THANK YOU FOR YOUR ATTENTION