Dynamic Topology-Aware Flow Path Construction and Scheduling Optimization for Multilayered Continuous-Flow Microfluidic Biochips

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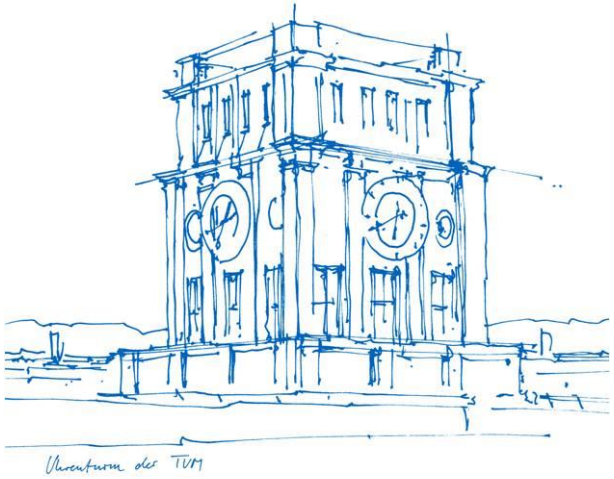


Outline

1. Multilayered Continuous-Flow Microfluidic Biochips
2. Challenges
   - Conflict
   - Dynamic Topological Change
3. Our Method
   - Problem Formulation
   - Quadratic Programming Model
4. Experimental Results

1. Multilayered Continuous-Flow Microfluidic Biochips

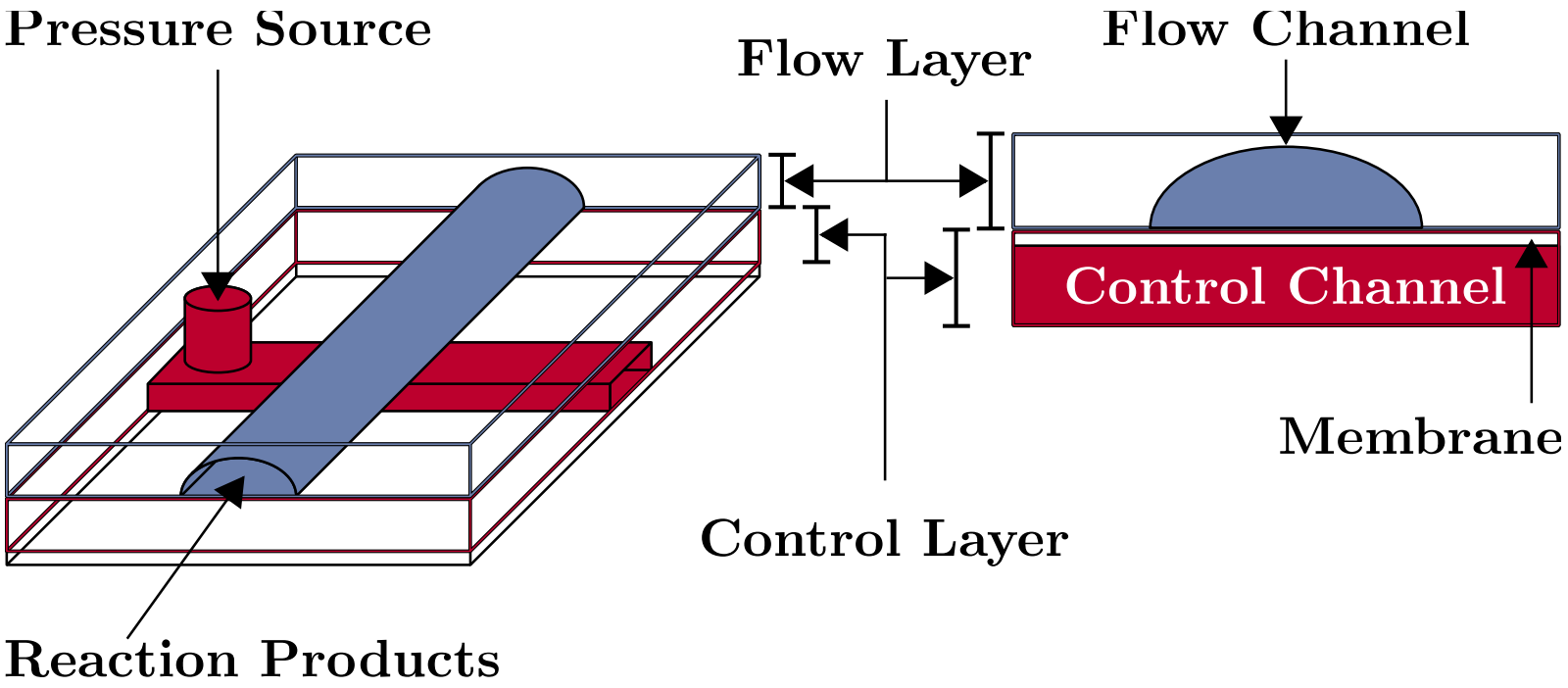


Fig. 1: Schematic of a multilayered continuous-flow microfluidic biochips.

2. Challenges — **Conflict**

- **Parallel-executed** operations
  - Contaminated reaction products
  - Unexpected channel blockages
- Limitations of existing methods
  - Identification[1]: fluids traverse common components.
    - $F_2 \nparallel F_3$: s_2, s_3
    - $F_1 \nparallel F_2$: s_1
    - $F_1 \parallel F_3$
  - Resolution: sequential execution

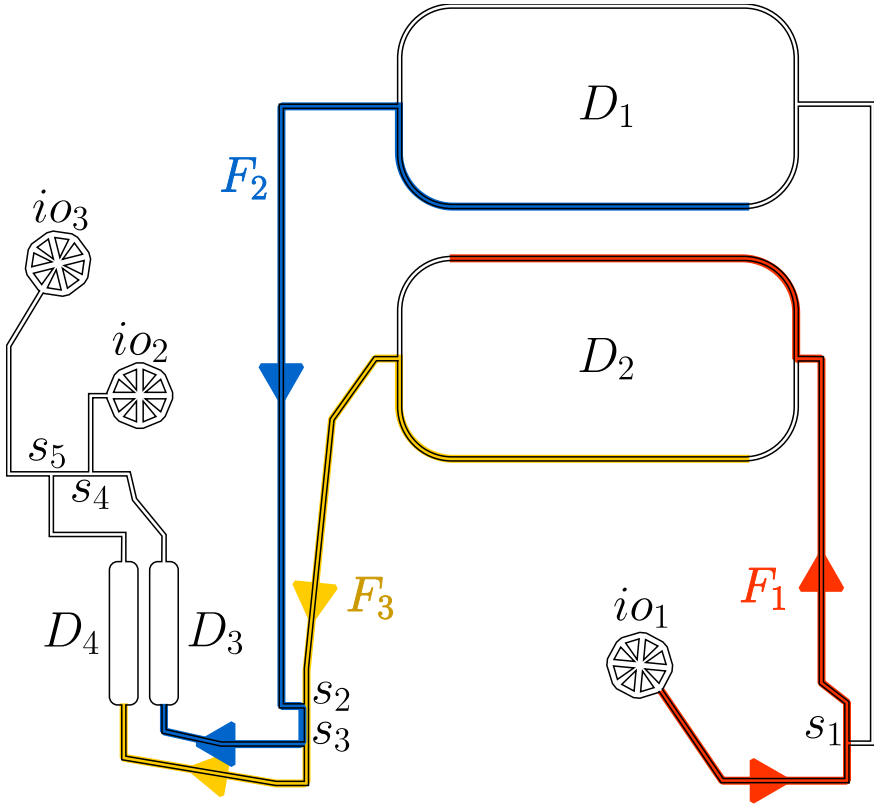


Fig. 2: A partial biochip synthesized using Columba 2.0[2].

source:
[1] Wajid Hassan Minhass, Paul Pop, and Jan Madsen. **System-level modeling and synthesis of flow-based microfluidic biochips,** CASES, 2011.
[2] Tsun-Ming Tseng et al. **Columba 2.0: A co-layout synthesis tool for continuous-flow microfluidic biochips**, IEEE TCAD, 2018.

2. Challenges — **Dynamic Topological Change**

- Hydraulic behavior
  - *Hagen-Poiseuille's law*[3]
  - *Ohm's law*
- Recall
  - $F_2 \nparallel F_3$: s_2, s_3
  - $F_1 \nparallel F_2$: s_1
  - $F_1 \parallel F_3$
- Equivalent fluid circuit:
  - $c(F_1, F_3)$
  - $c(F_1, F_2, F_3)$

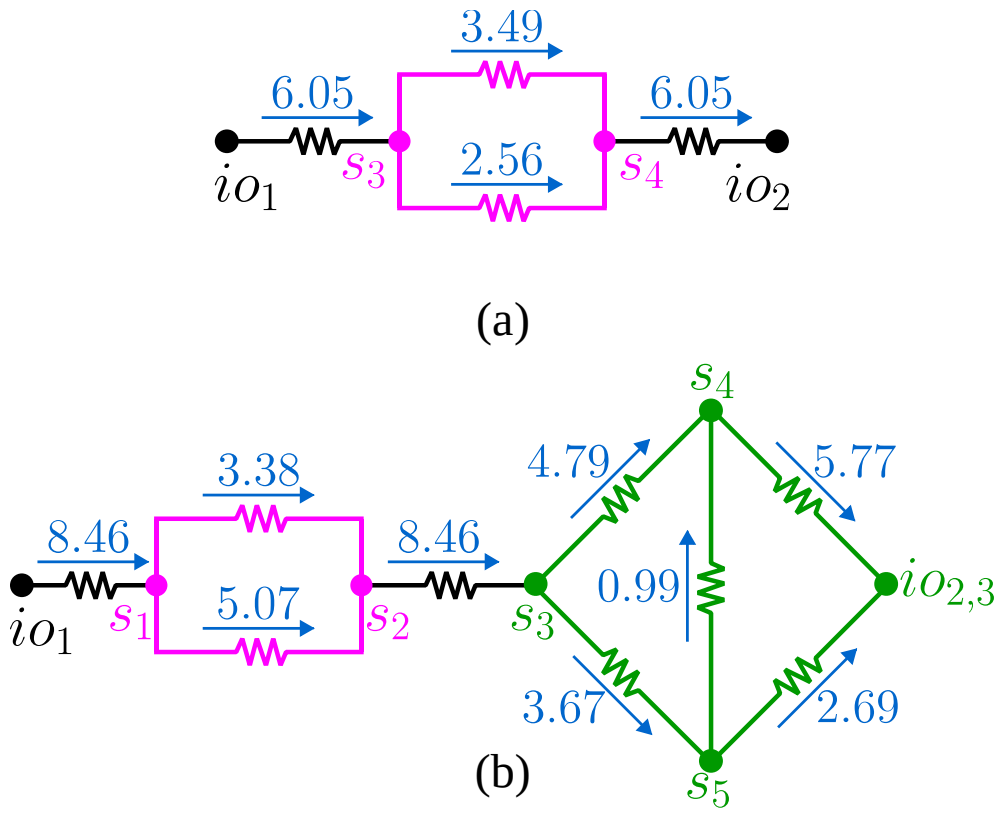
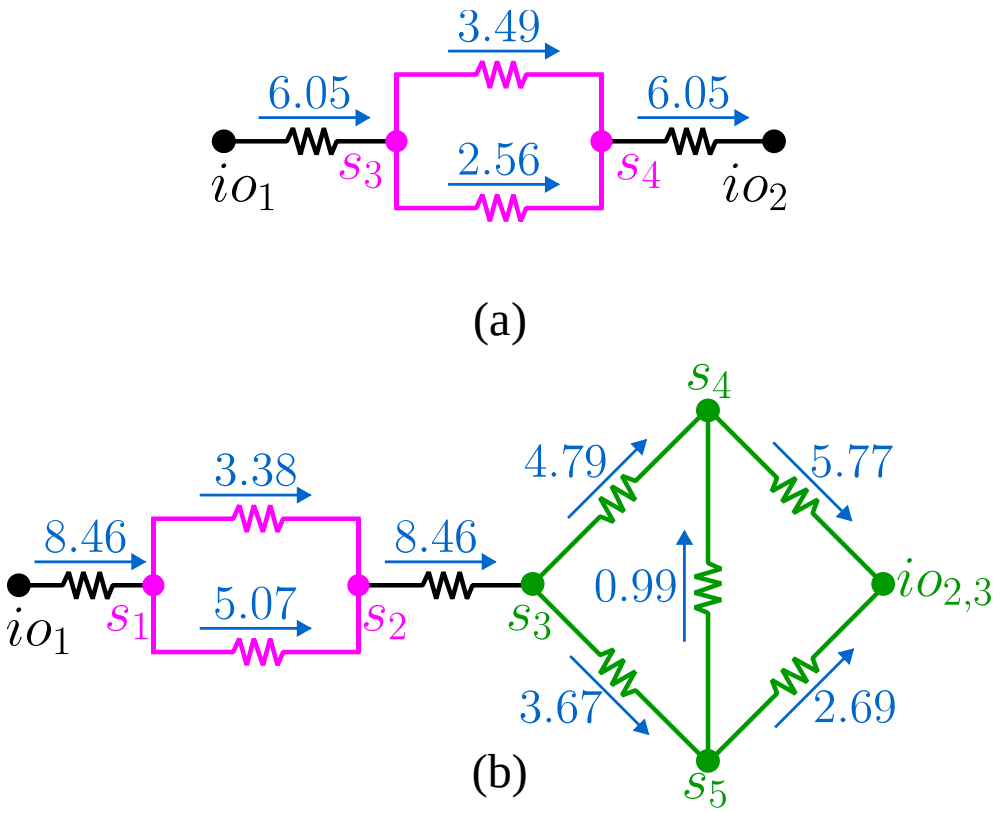


Fig. 3: Equivalent fluid circuits (a) $c(F_1, F_3)$ and (b) $c(F_1, F_2, F_3)$.

source:
[3] Kwang W. Oh, Kangsun Lee, Byungwook Ahn, and Edward P. Furlani. **Design of pressure-driven microfluidic networks using electric circuit analogy,** Lab Chip, 2012.

2. Challenges — **Dynamic Topological Change**

- Constant flow velocity
  - $10\,\mathrm{mm\,s^{-1}}$ [1,4]
- Non-serial connection
  - Parallel connection:
    $c(F_1, F_3)$
  - Bridge connection:
    $c(F_1, F_2, F_3)$



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- Non-serial connection
  - Parallel connection: $c(F_1, F_3)$
  - Bridge connection: $c(F_1, F_2, F_3)$
- **Parallel** vs. **Sequential**
  - 35% ⬇

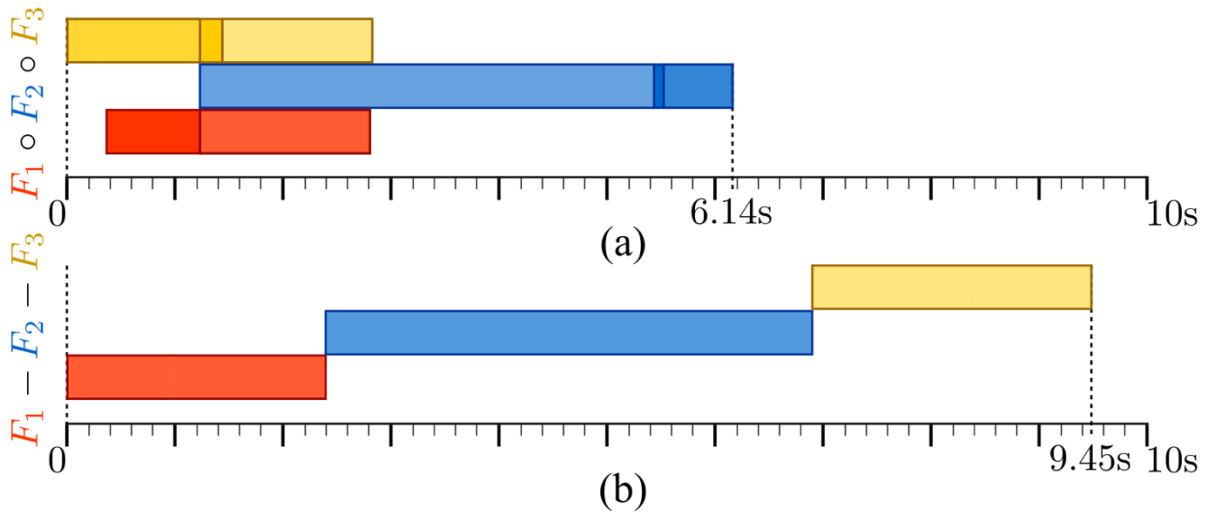

Fig. 4: Scheduling schemes for executions:(a) $F_1 \circ F_2 \circ F_3$ and (b) $F_1 - F_2 - F_3$.

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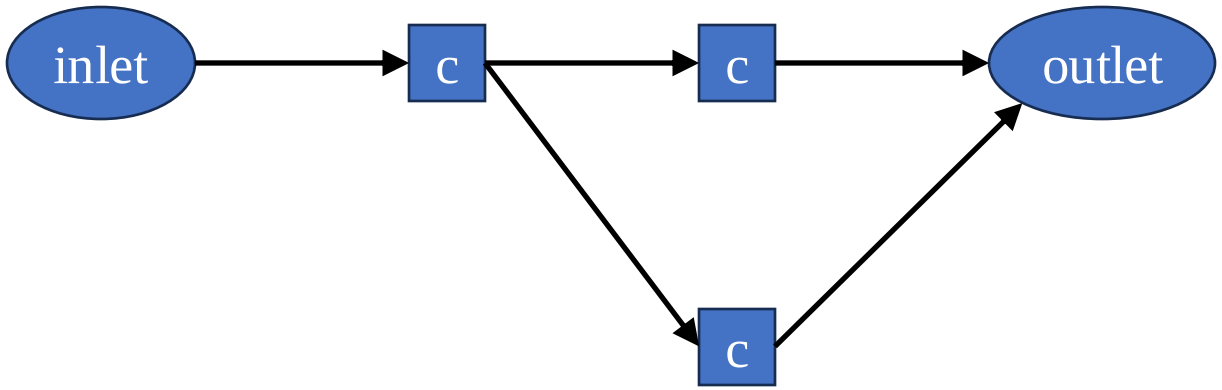
3. Our method — **Problem Formulation**

- Quadratic Programming (QP) Model
- Inputs:
  - Flow-layer structure: weighted graph $\mathcal{A}$
  - Bioassay with a binding function: sequencing graph[5]
- Outputs:
  - Optimized scheduling schemes
- Subject to:
  - Flow paths must be valid.
  - Parallel execution must not result in conflicts.
- Objective: **minimize bioassay completion time**

source:
[5] Krishnendu Chakrabarty and Jun Zeng. **Design automation for microfluidics-based biochips,** J. Emerg. Technol. Comput. Syst. 1(3), 2005.

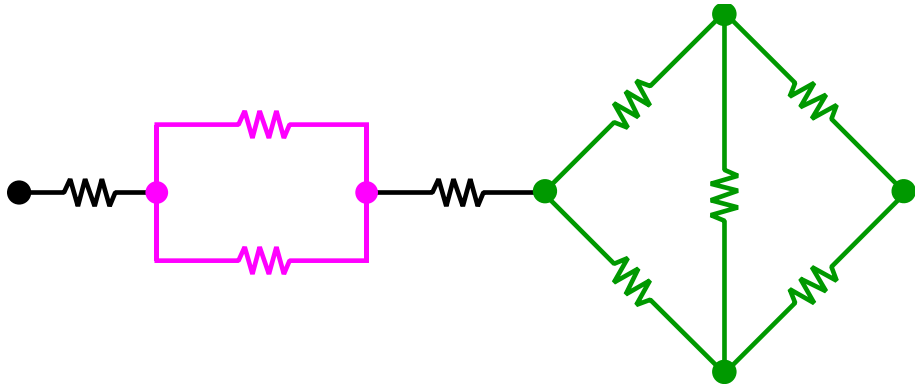
3. Our method — **Quadratic Programming Model**

- Flow path construction:
  - Each flow path must include an *inlet* and an *outlet*.
  - Each involved component must have at least
    - **incoming**: except at inlets
    - **outgoing**: except at outlets



3. Our method — **Quadratic Programming Model**

- Flow velocity calculation:
  - Assumption: flow velocity is uniform along each channel segment.
  - Flow velocity changes at time $t_i^n \equiv$ arrival time of fluids in F_i at component *n*.
  - Identify non-serial connections
    - Fluid module construction
    - *Hagen-Poiseuille's law*[3]



$$\text{velocity} \times \text{resistance} = \frac{\text{input pressure}}{\text{height} \times \text{width}}$$

  - Fluid transportation time $\text{velocity} \times \text{time} = \text{distance}$

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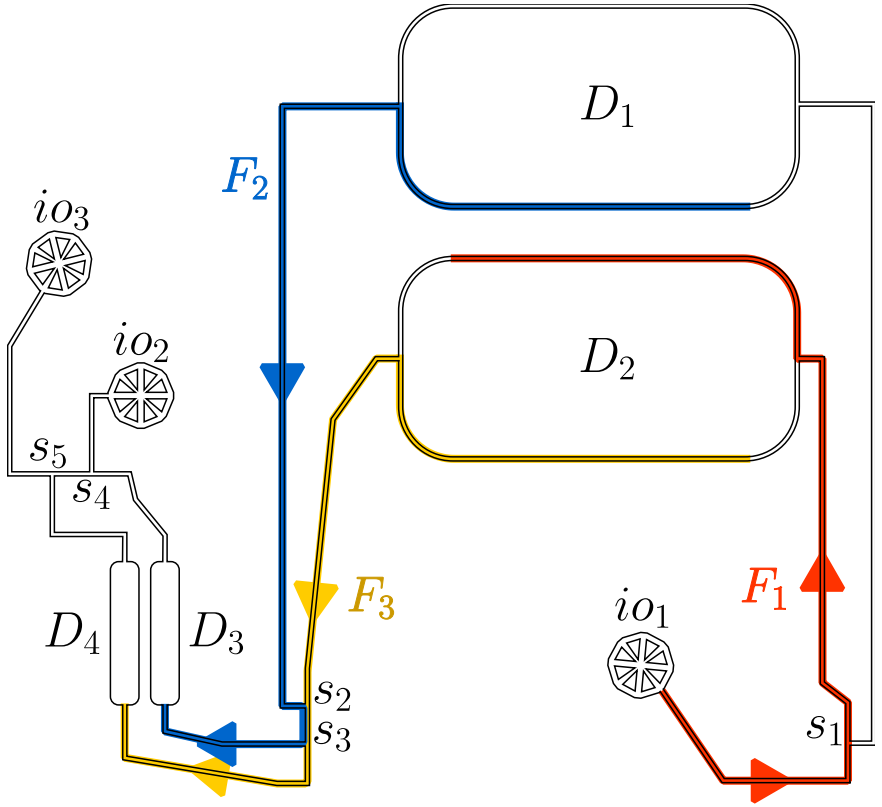
3. Our method — **Quadratic Programming Model**

- Conflict Identification:
  - *Complete*: $F_2 \nparallel F_3 : s_2, s_3$
  - *Partial*: $F_1 \nparallel F_2 : s_1$
  - *Operational*
- Conflict Resolution:
  - Fluids reach s_2, s_3 asynchronously.
  - Fluid reach s_1 first or allow F_2 to finish first.
  - Delay one operation until the other finishes.



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4. Experimental Results

Test Cases

Case	1	2	3	4
Transportations	4	6	8	9
Bio-operations	2	2	4	3
Flow Ports	4	5	5	5
Devices	2	3	4	3
Branches	2	3	9	3
Edges	7	10	21	9
Modules	51	1251	143	1242

Experimental Setup

- Input pressure: 100Pa
- Channel dimensions:
  - Height: 50μm
  - Width: 100μm
- Bio-operation: 2s
- VOM[6]: sequential execution

source:
[6] Mengchu Li, *et al.* **VOM: Flow-path validation and control-sequence optimization for multilayered continuous-flow microfluidic biochips,** IEEE/ACM ICCAD, 2019.

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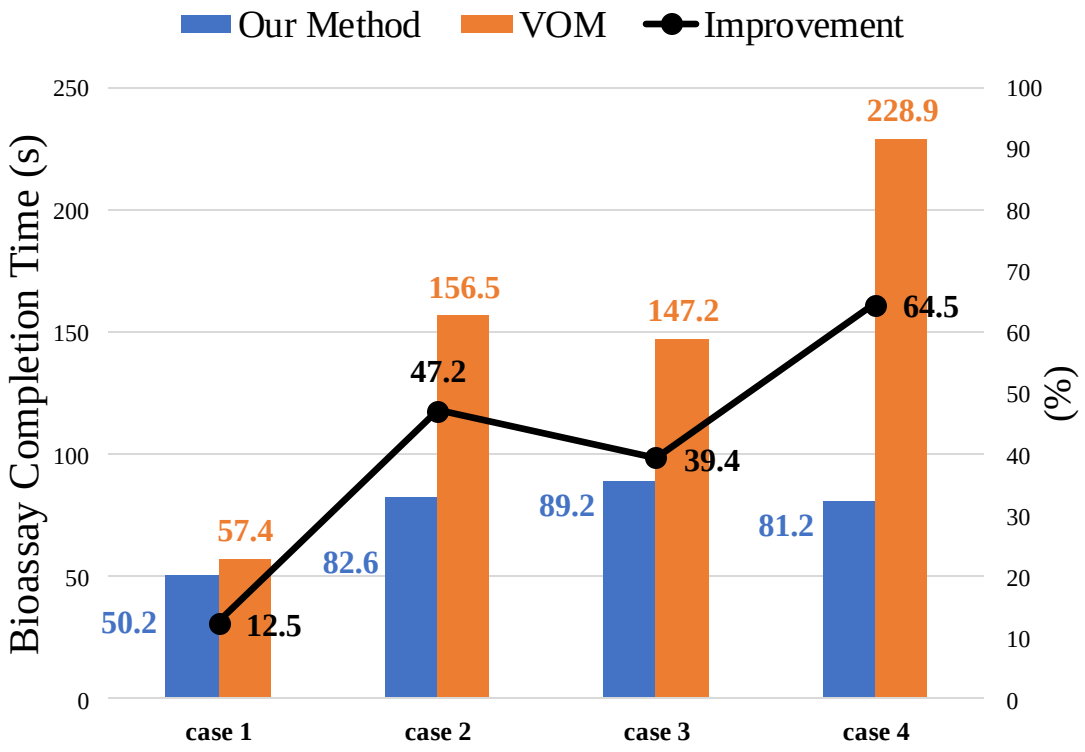
Comparison: 40.9%



4. Experimental Results — **Case 4**

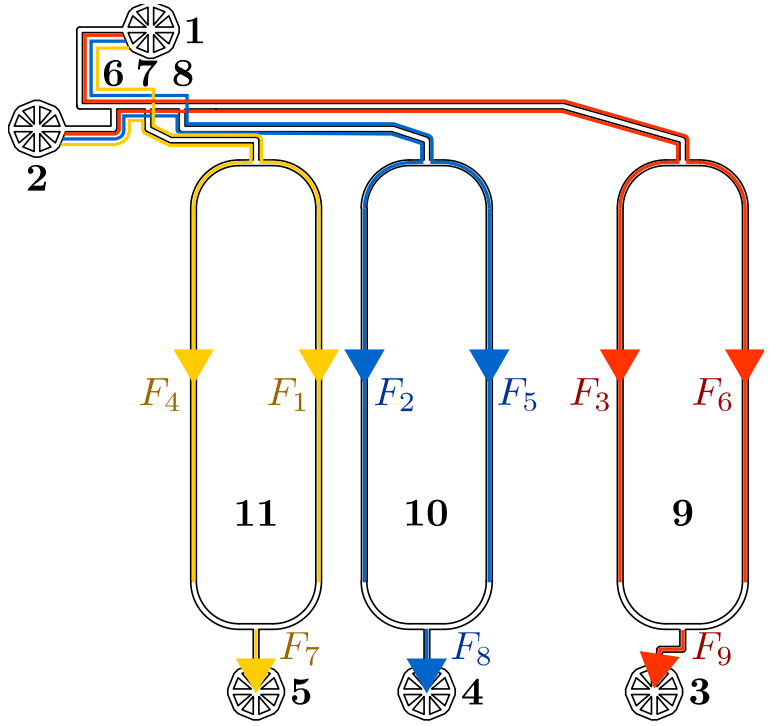


Fig. 5: Fluid transportation operations.

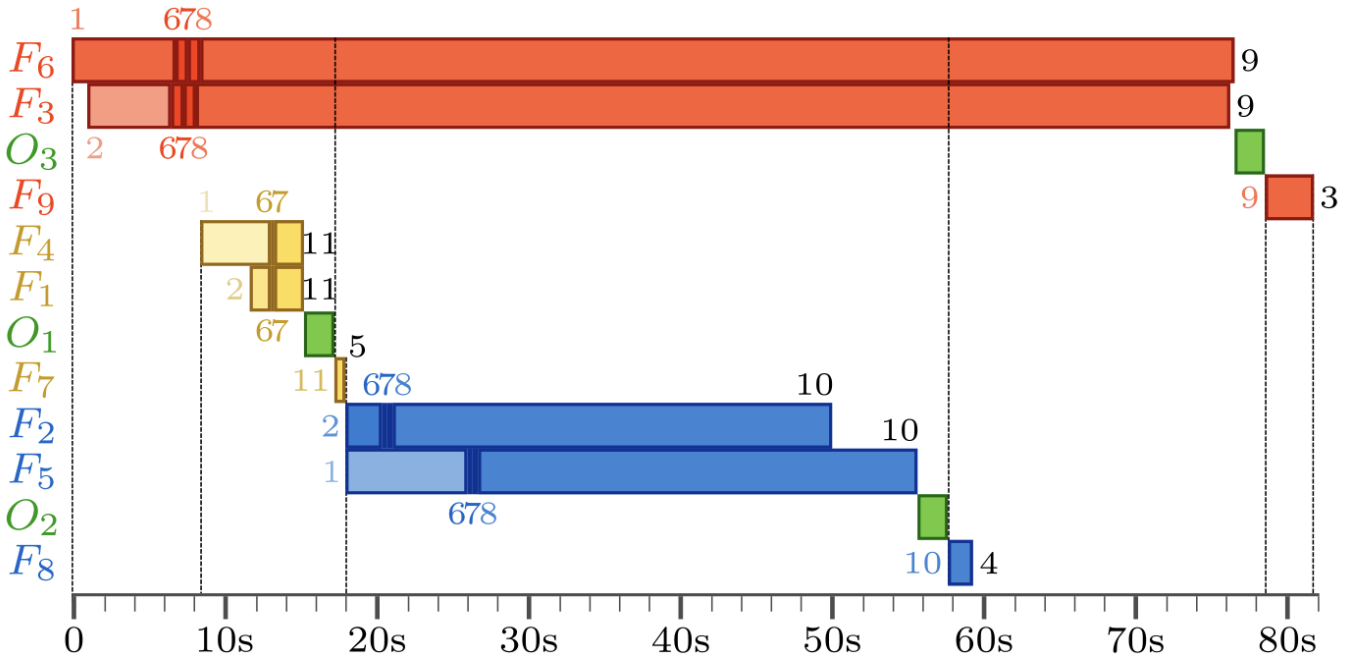


Fig. 6: Optimized scheduling scheme.

Thank you for your attention!