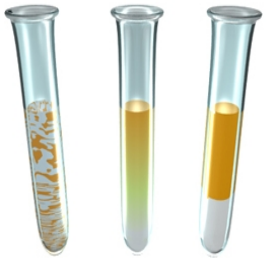
Online Synthesis for Error Recovery in Digital Microfluidic Biochips with Operation Variability

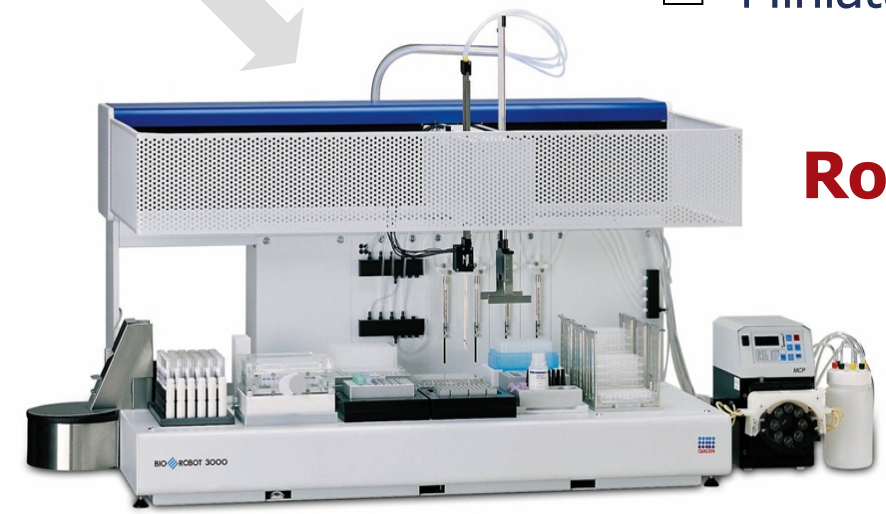
Mirela Alistar, Paul Pop, Jan Madsen
Technical University of Denmark, Lyngby

Biochips



Test tubes

- ☐ Automation
- ☐ Integration
- ☐ Miniaturization

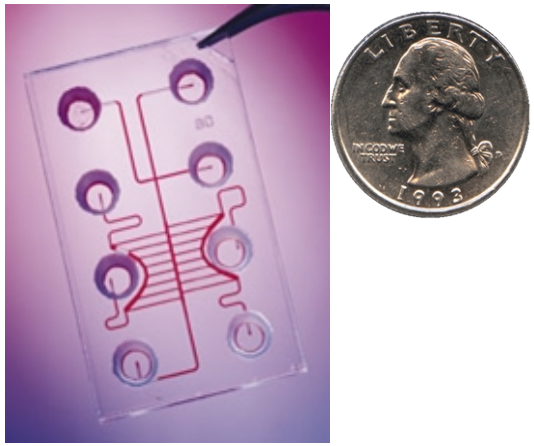


Robotics

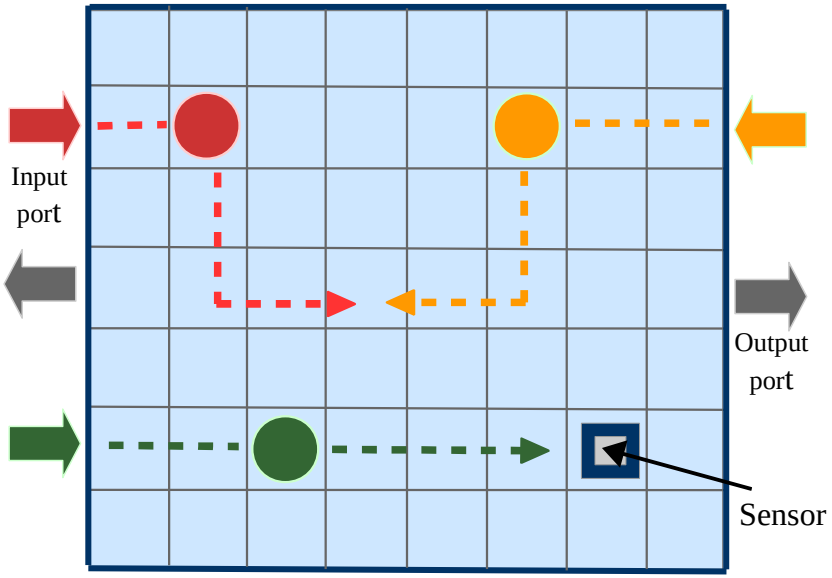
- ☑ Automation
- ☑ Integration
- ☐ Miniaturization

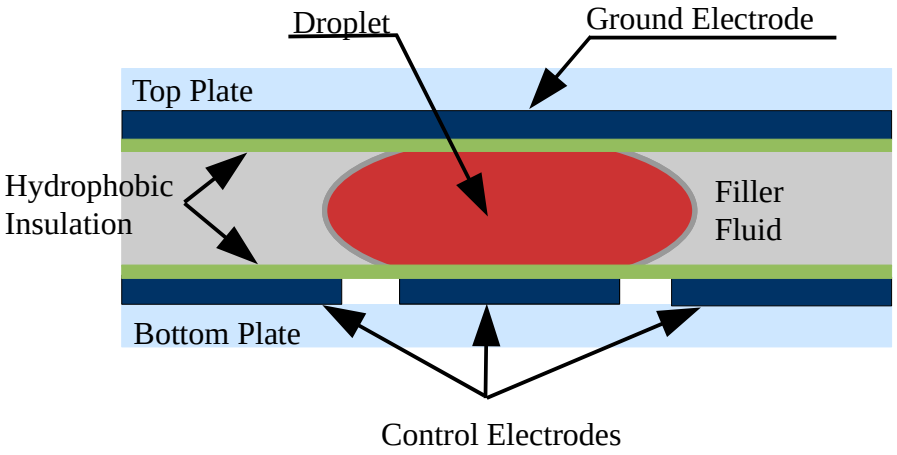
Microfluidics

- ☑ Automation
- ☑ Integration
- ☑ Miniaturization

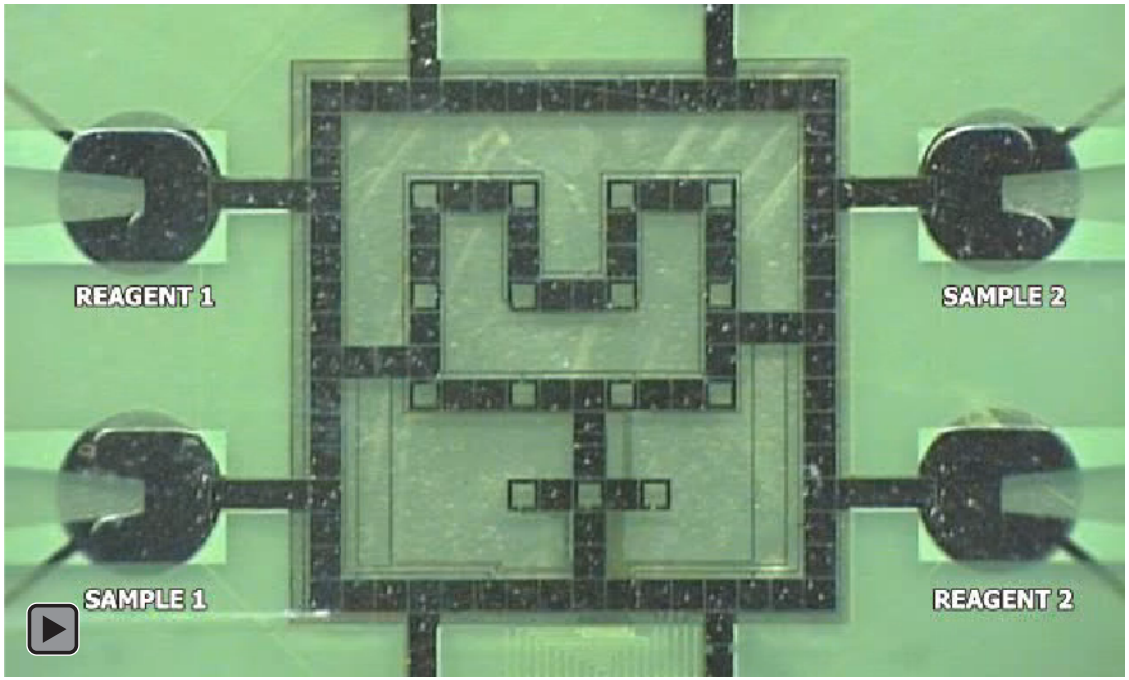


Biochip Architecture



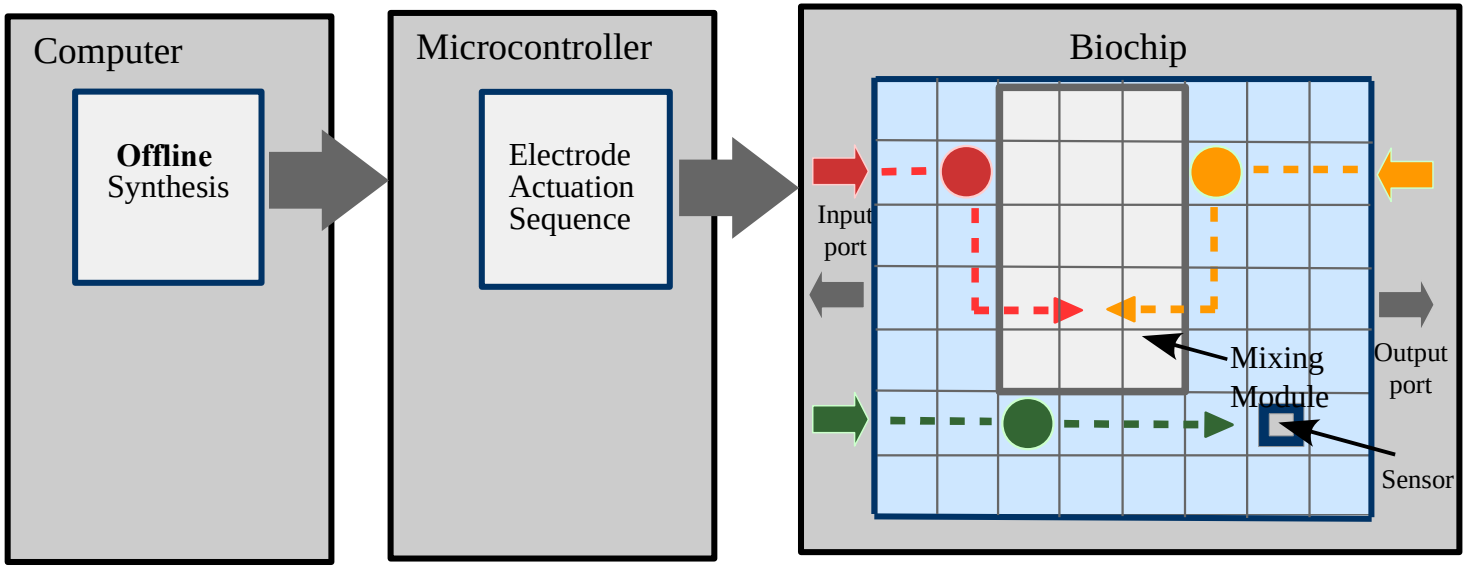


Biochip Architecture

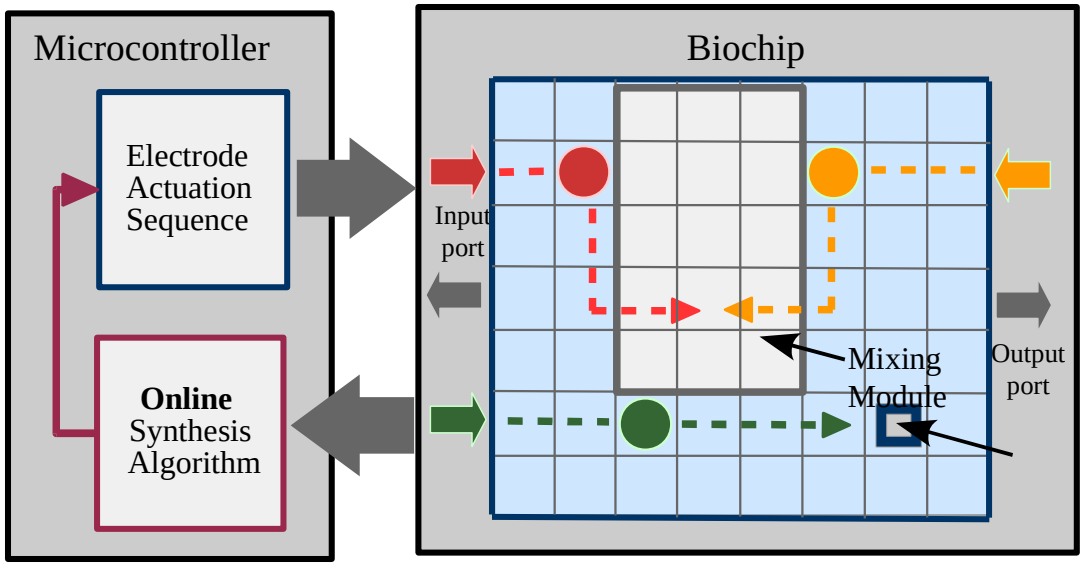


Video source: Duke University

Offline Synthesis Flow



Online Synthesis Flow

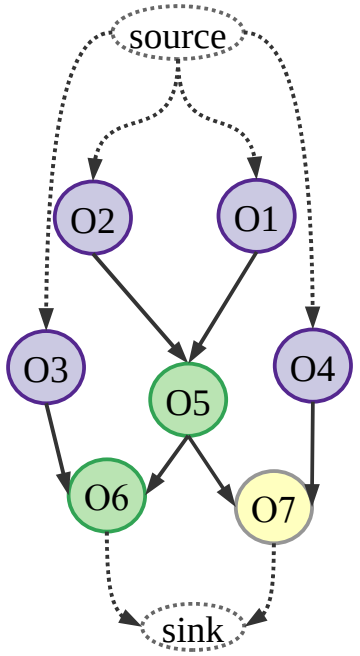


Synthesis: Main design tasks

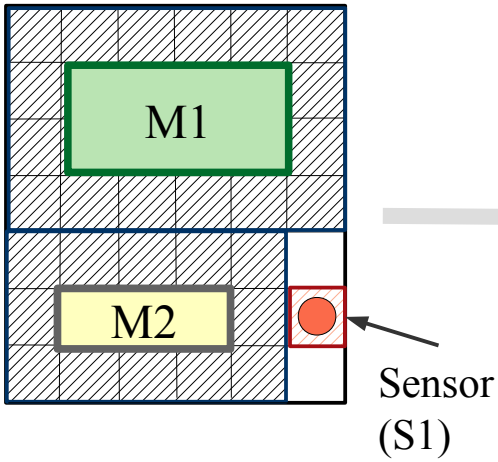
Allocation

Operation	Area	Time (s)
Mix	2x5	2
Mix	2x4	3
Mix	1x3	5
Mix	3x3	7
Mix	2x2	10
Detection	1x1	30

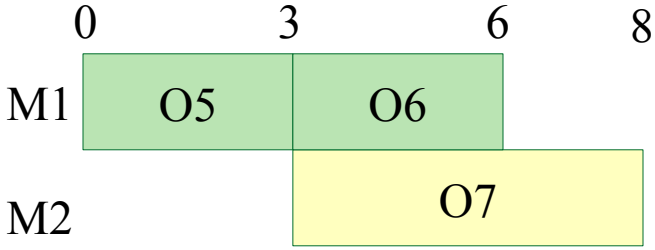
Binding



Placement

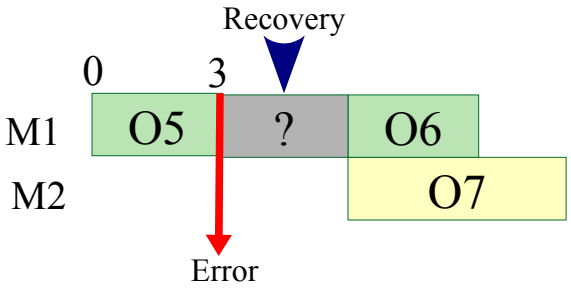


Scheduling



Motivation: Fault

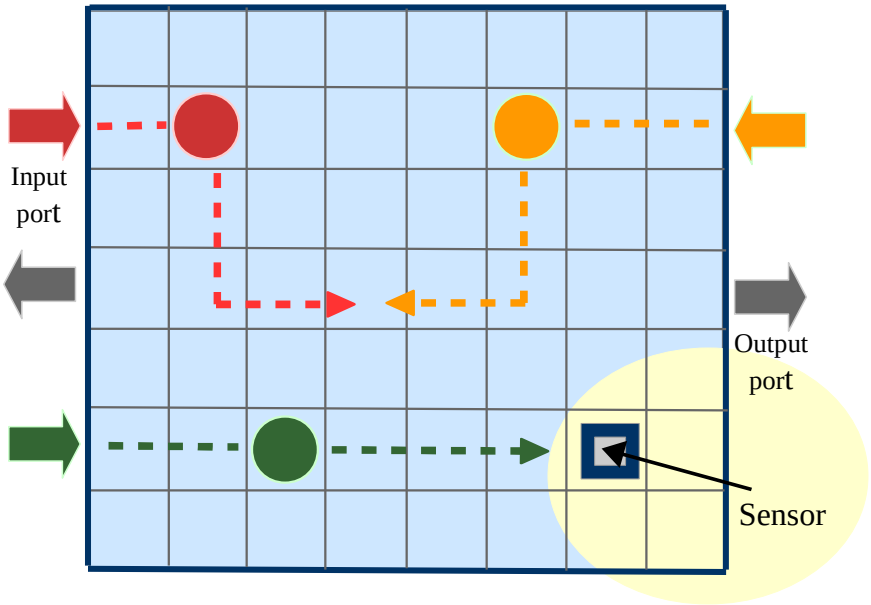
- Types of faults
  - Permanent
    - T. Xu, K. Chakrabarty, "*Functional testing of microfluidic biochips*", 2007
    - E. Maftei, P. Pop, "*Droplet-aware Module-Based Synthesis for Fault-Tolerant Digital Microfluidic Biochips*", 2012

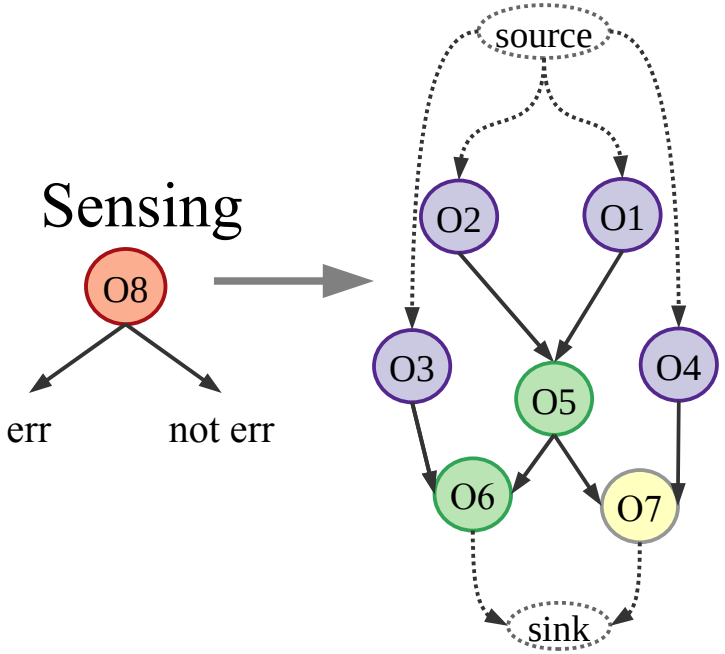


- Parametric
  - Malfunctioning during runtime
  - Faulty operations, ex: unbalanced split
  - High sensitivity to volume variations
    - +- 2% precision for microdialysis
    - +- 10% precision for drug discovery

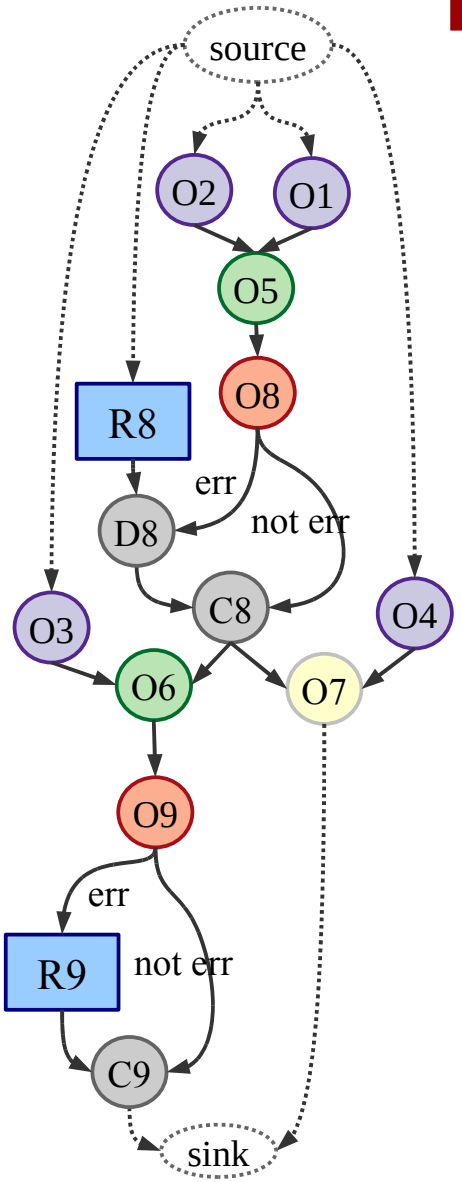
  - Zhao, K. Chakrabarty, "Integrated Control-Path Design and Error Recovery in the Synthesis of Digital Microfluidic Lab-on-Chip"

Error Detection



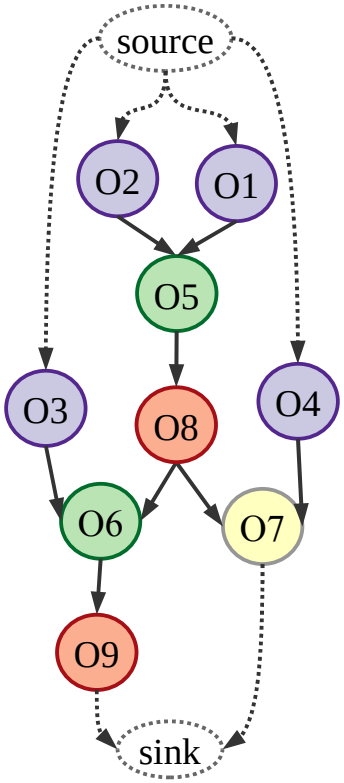


Fault-tolerant Application Model



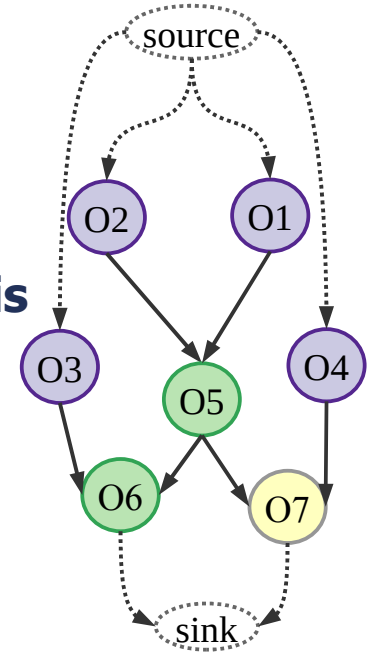
(c) $\mathcal{G}$

Recovery



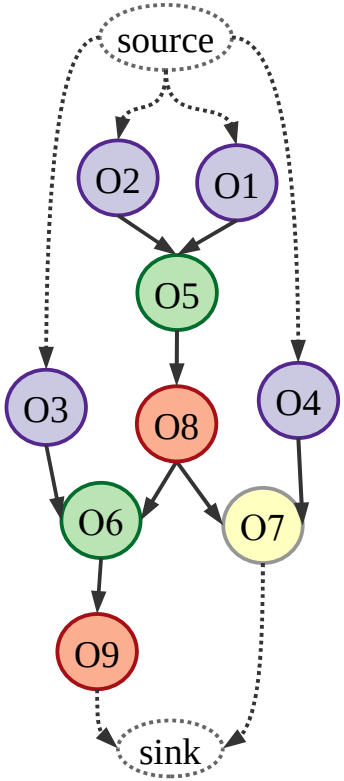
(b) $\mathcal{G}^{+}$

Error Analysis



(a) $\mathcal{G}^{0}(\mathcal{V},\mathcal{E})$

Error Analysis



$$E_{Ds} = E_{Dlt} = E_{Slt} = 8\% \quad E_{Mix} = 10\% \quad E_{Thr} = 15\%$$

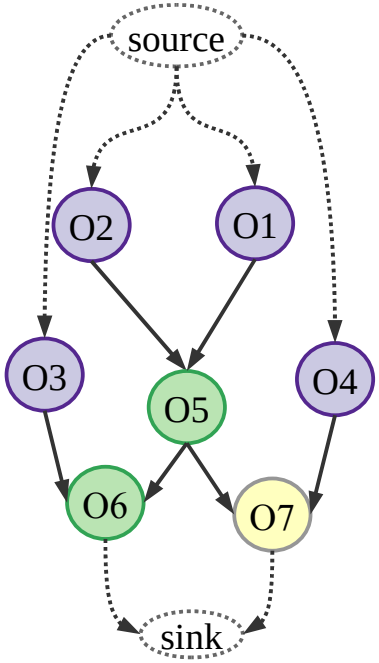
i) $\epsilon_{Ds} = E_{Ds}$

ii) $\epsilon_{Trans} = \sqrt{I^2 + E_{Trans}^2}$

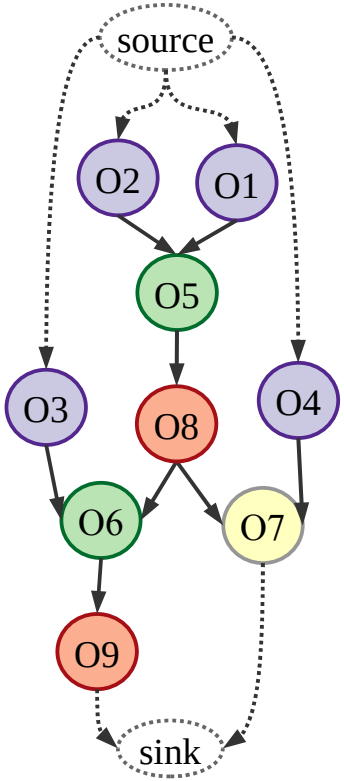
iii) $\epsilon_{Slt} = \sqrt{I^2 + (2\,E_{Slt})^2}$

iv) $\epsilon_{Mix} = \sqrt{(0.5\,I_1)^2 + (0.5\,I_2)^2 + E_{Mix}^2}$

v) $\epsilon_{Dlt} = \sqrt{(0.5\,I_1)^2 + (0.5\,I_2)^2 + (2\,E_{Dlt})^2}$



Error Analysis



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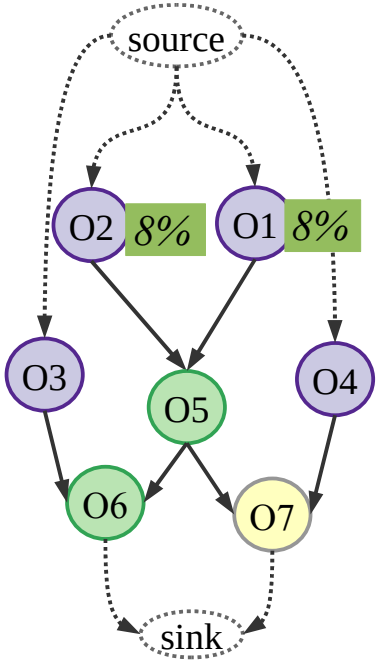
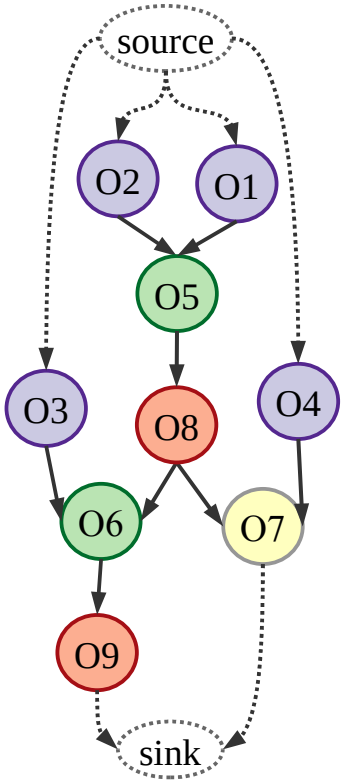


Error Analysis



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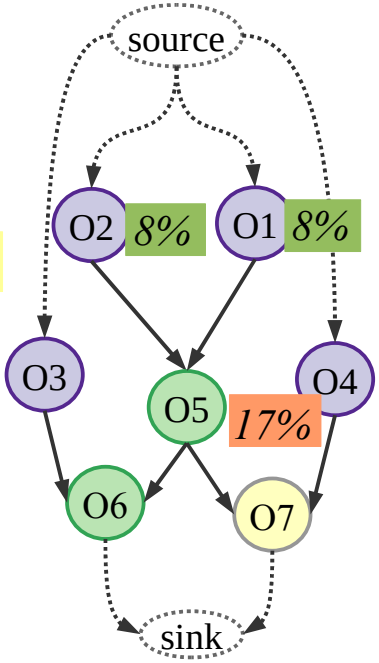

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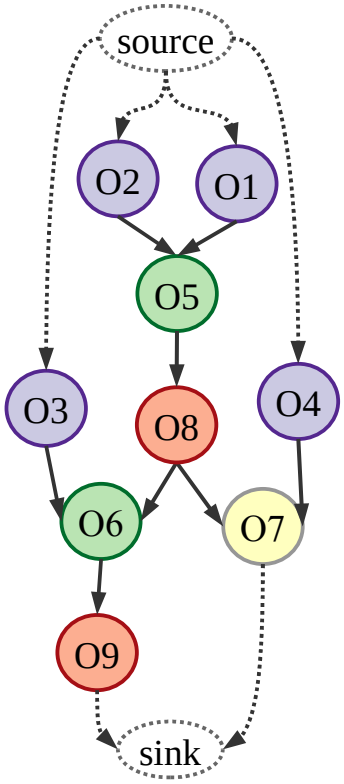

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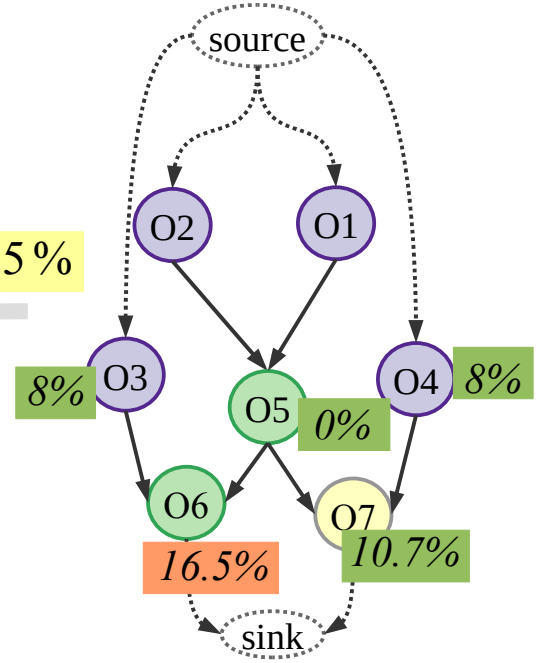
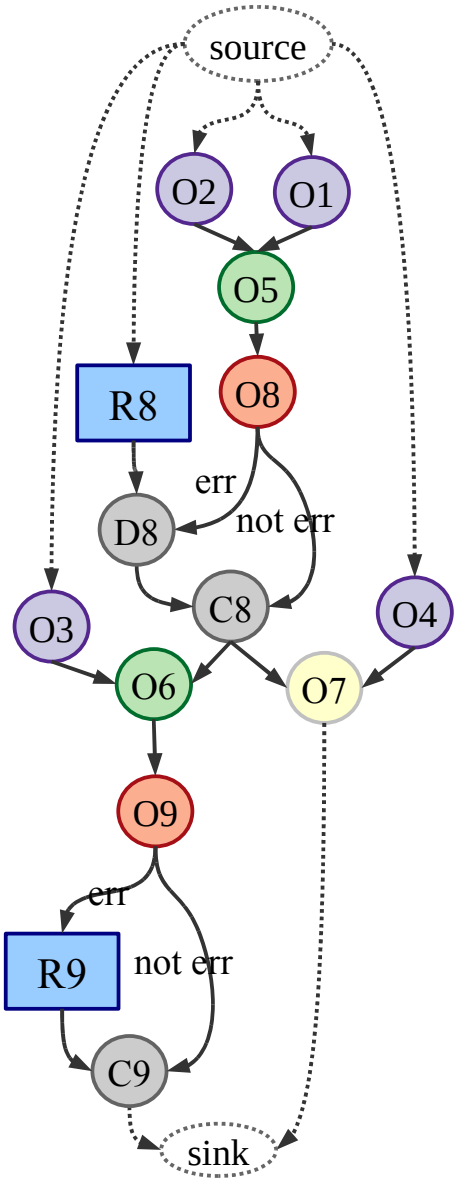
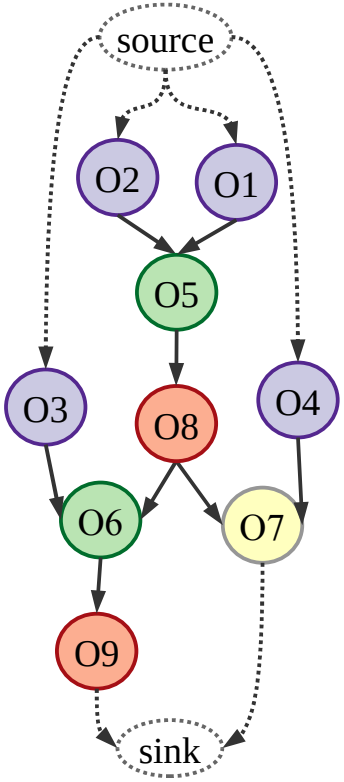


Recovery

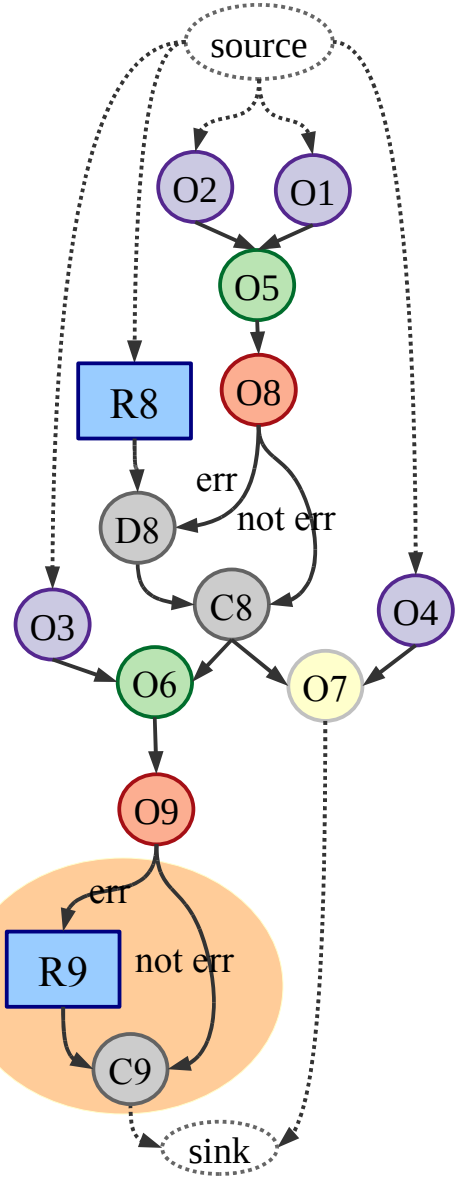


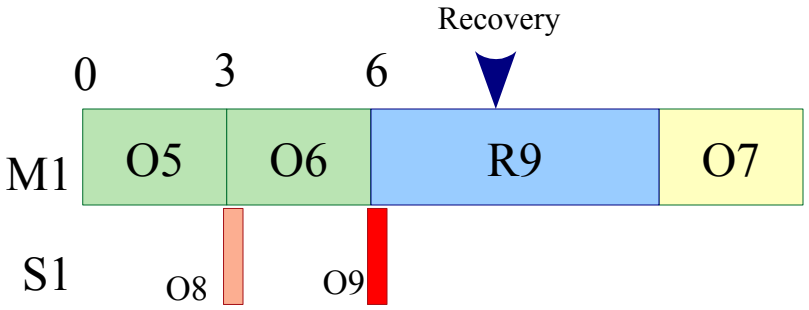
Recovery

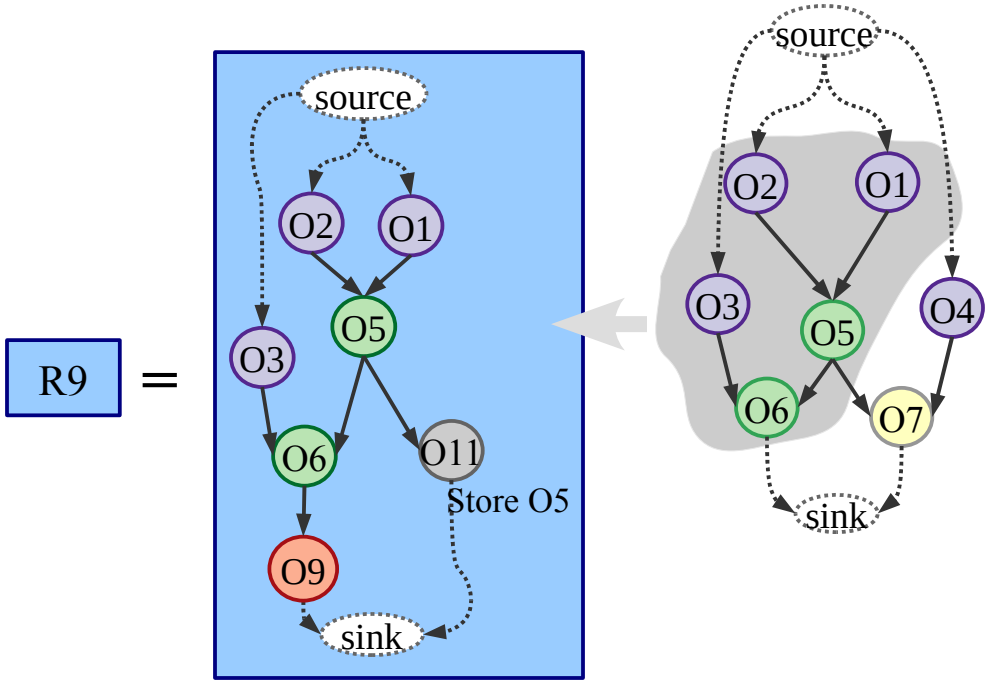
R8 R9



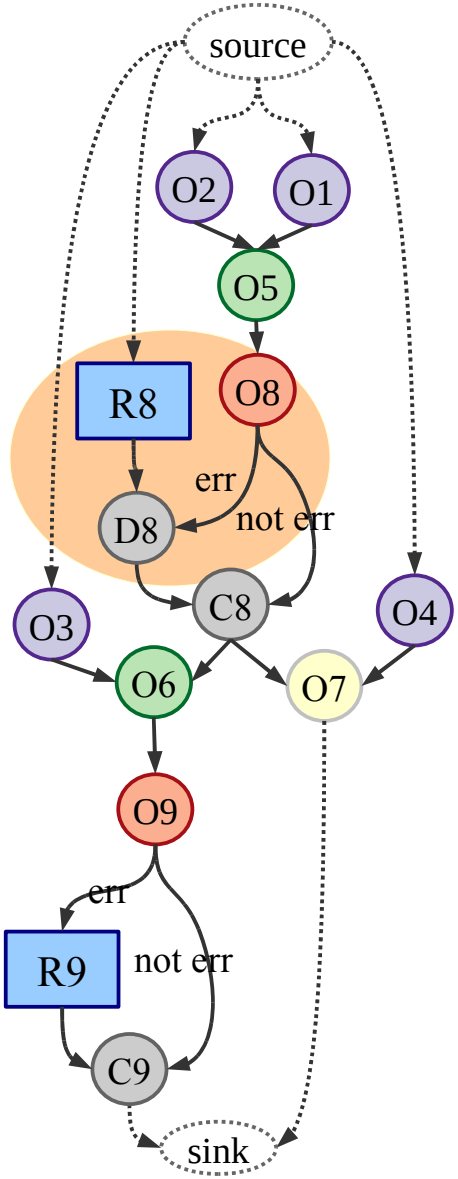
Time redundancy

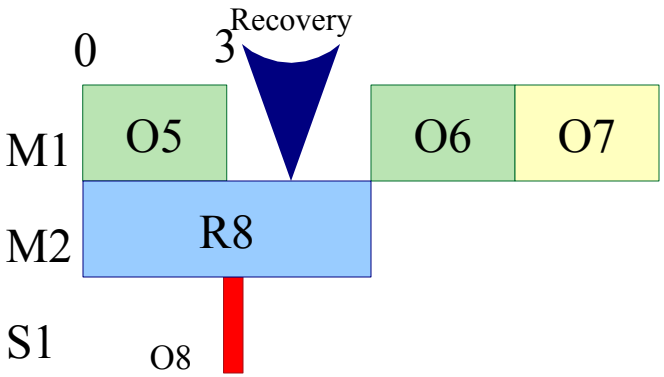


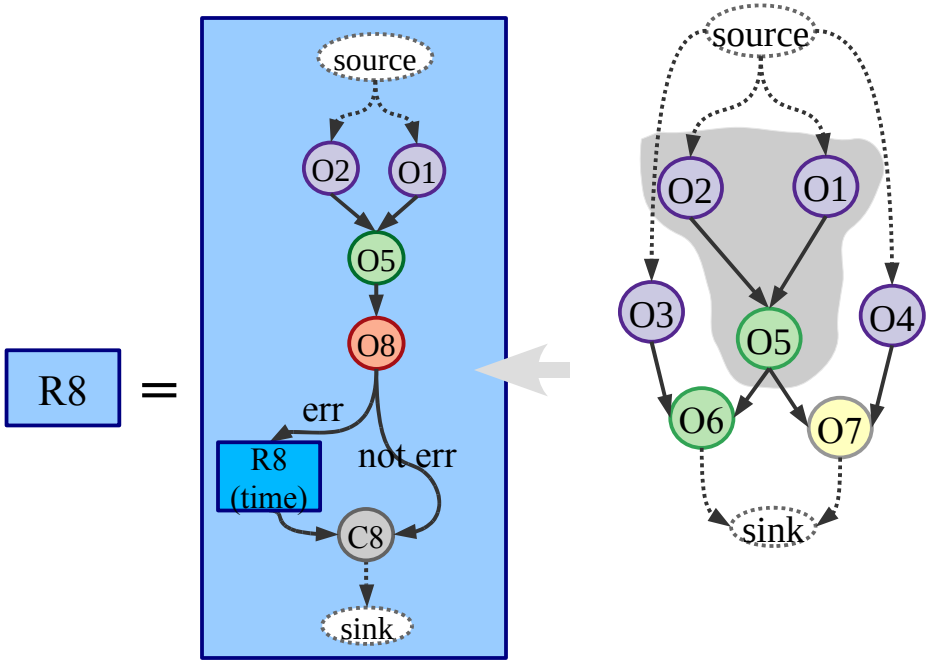




Space redundancy





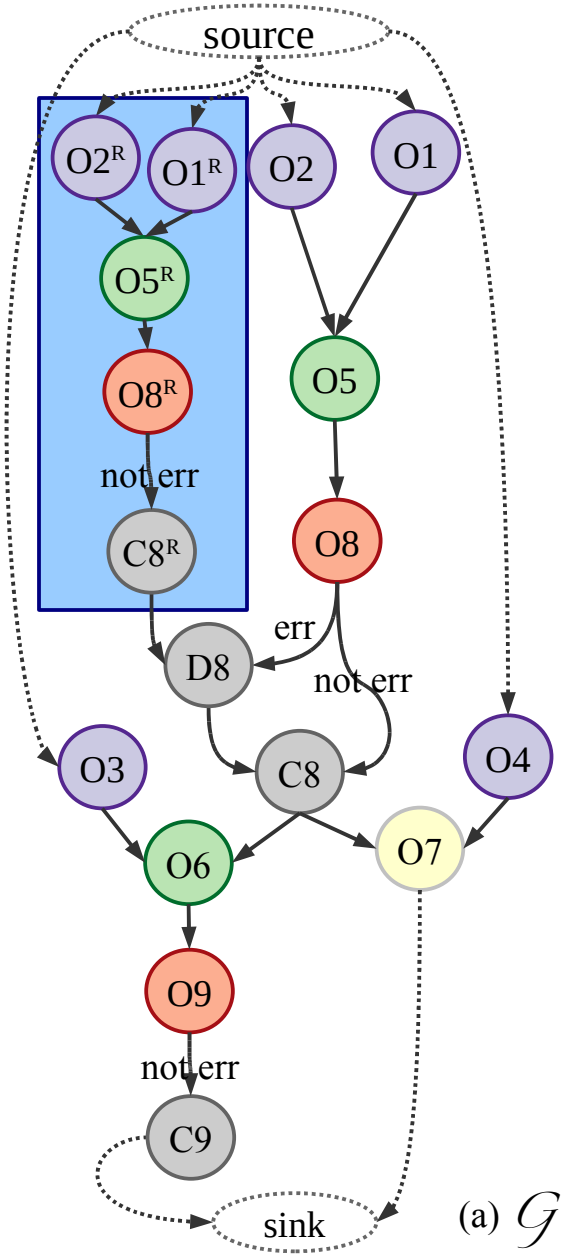


Problem Formulation

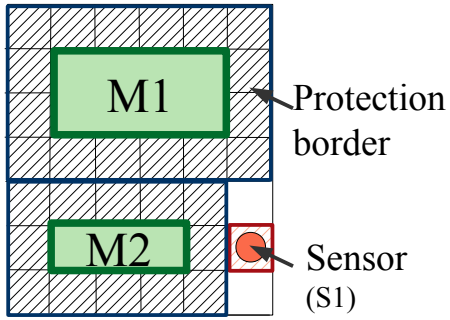
- Given
  - **Fault model**
    - Intrinsic error limits
    - Error threshold
    - Recovery subgraphs
  - Biochip architecture
  - Application Graph
  - Module library

- Determine
  - Online Fault-tolerant implementation
    - Minimized worst-case completion time

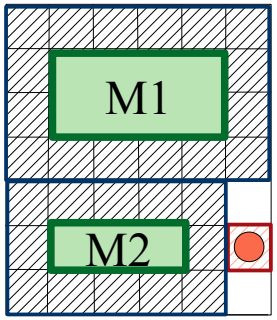
Offline Synthesis



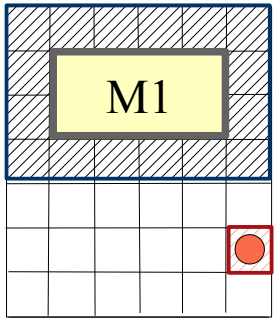
(a) $\mathcal{G}$



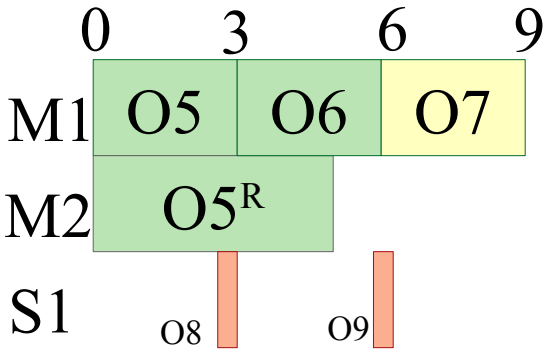
(b)Placement at t=0



(c) t=3

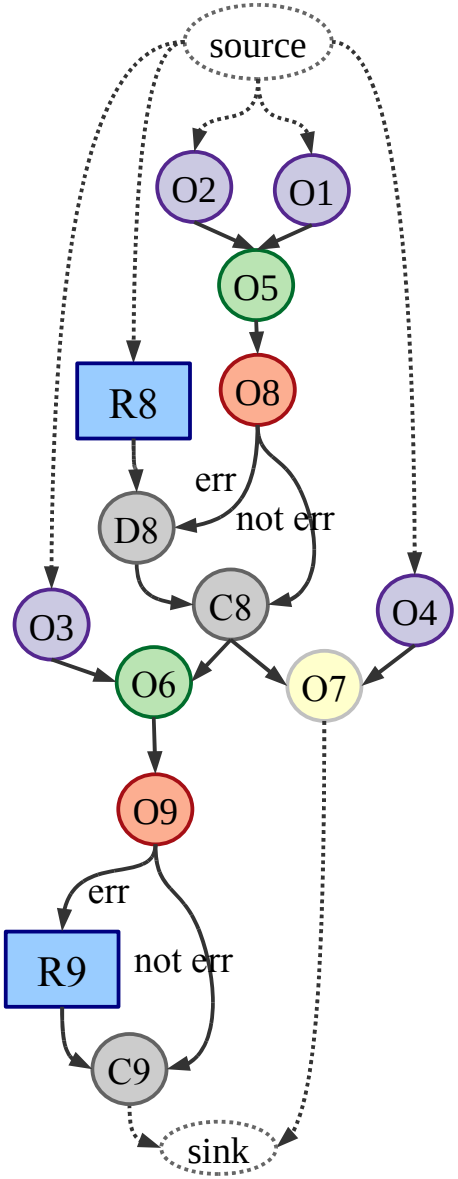


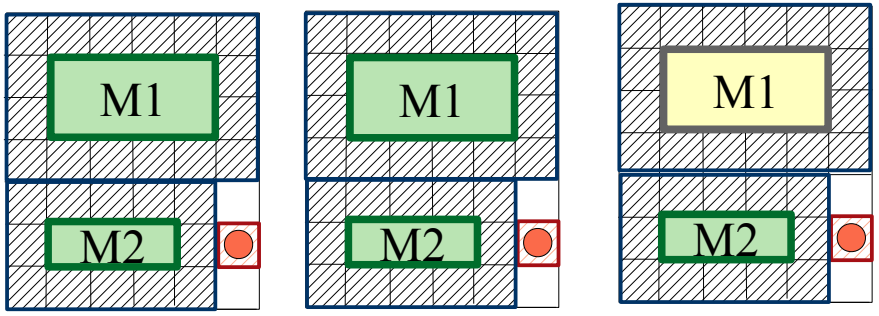
(d) t=6



(e) Schedule

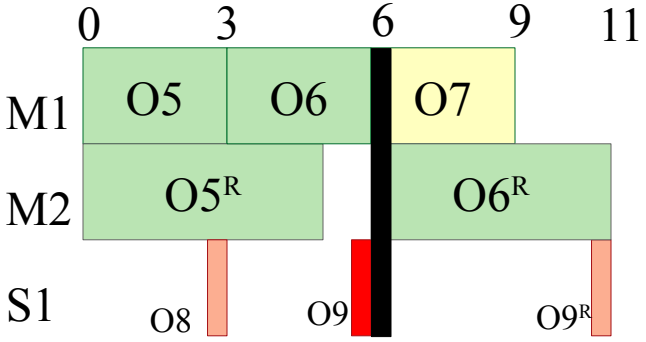
Online Synthesis (ONS)





(ii)Placement at t=0 (iii) t=3 (iv) t=6

Error on O_9

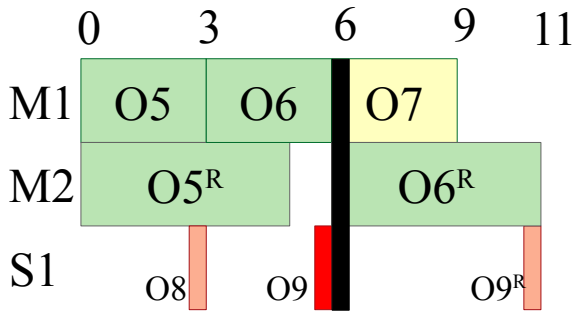


(i)Schedule

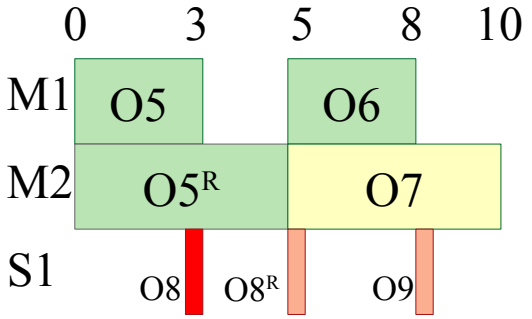
ONS vs FTS

ONS [us]

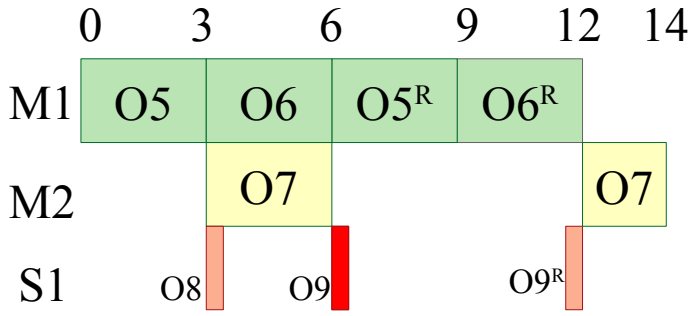
Time



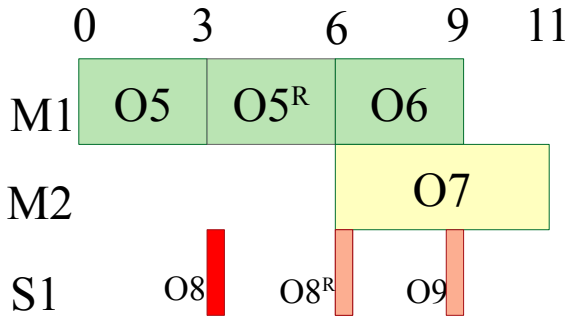
Space



FTS [Zhao*]



Error on O_9



Error on O_8

* Zhao "Integrated Control-Path Design and Error Recovery in Synthesis of Digital Microfluidic Lab-on-Chip"

Experimental results

App.	Area	E_{thr} (%)	Sensing Ops.	Space Subgr.	Time Subgr.	TS(G^0) (s)	FTS (s)	ONS (s)
PCR	7x7	9	7	1	6	12	min 14 max 17 avg 14.92	min 12 max 14 avg 13.85
IVD	7x7	10	9	1	8	15	min 14 max 17 avg 14.92	min 15 max 19 avg 16.44
CPA	10x10	15	39	1	38	36	min 14 max 17 avg 14.92	min 38 max 43 avg 39.34

Average overhead added by ONS (%) is 15.4 (PCR), 9.6 (IVD), 13.38 (CPA)

Conclusions

- Biochemical Applications are **sensitive to faults**
  - Parametric faults can result in operation variability
- Fault-tolerant application model
  - Detection : SENSING
  - Recovery: Time- and Space-Redundant Subgraphs
- Online Synthesis
  - Fast: List Scheduling-based
  - Exploits the biochip configuration

Backup Slides

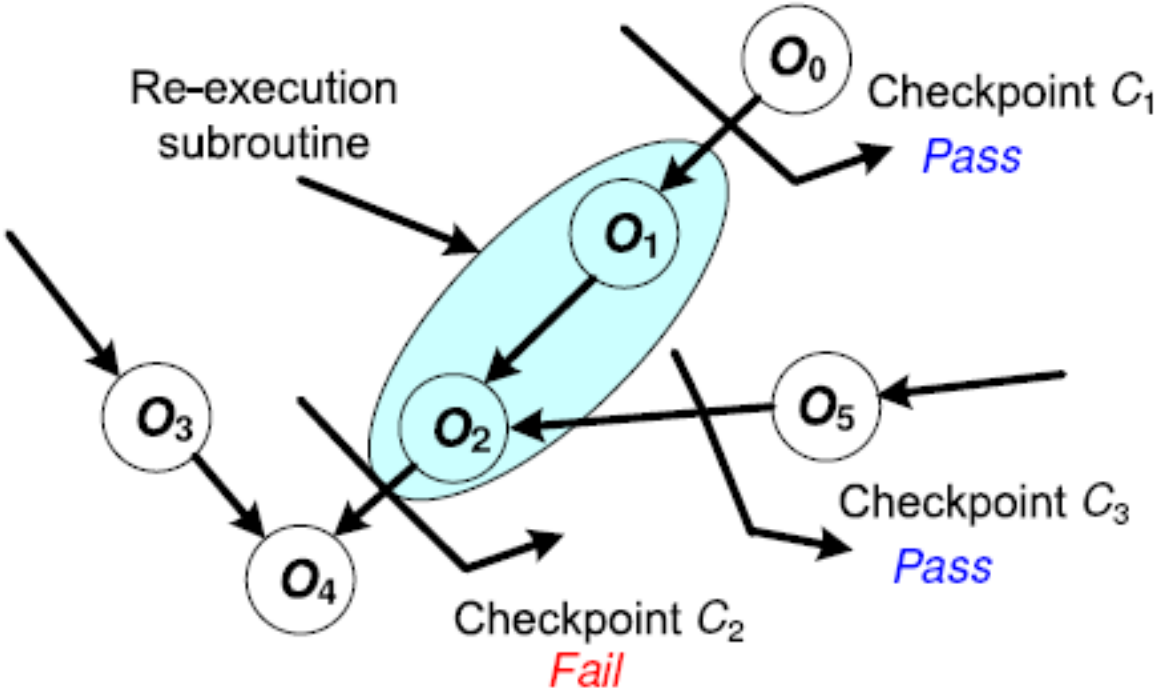
Related Work

Y. Zhao, T. Xu and K. Chakrabarty,
"***Control-path design and error recovery in digital microfluidic lab-on-chip***",
accepted for publication in
ACM Journal on Emerging Technologies in Computing Systems, 2010

Pictures taken from Krish Chakrabarty, Duke University

Control-Path Design

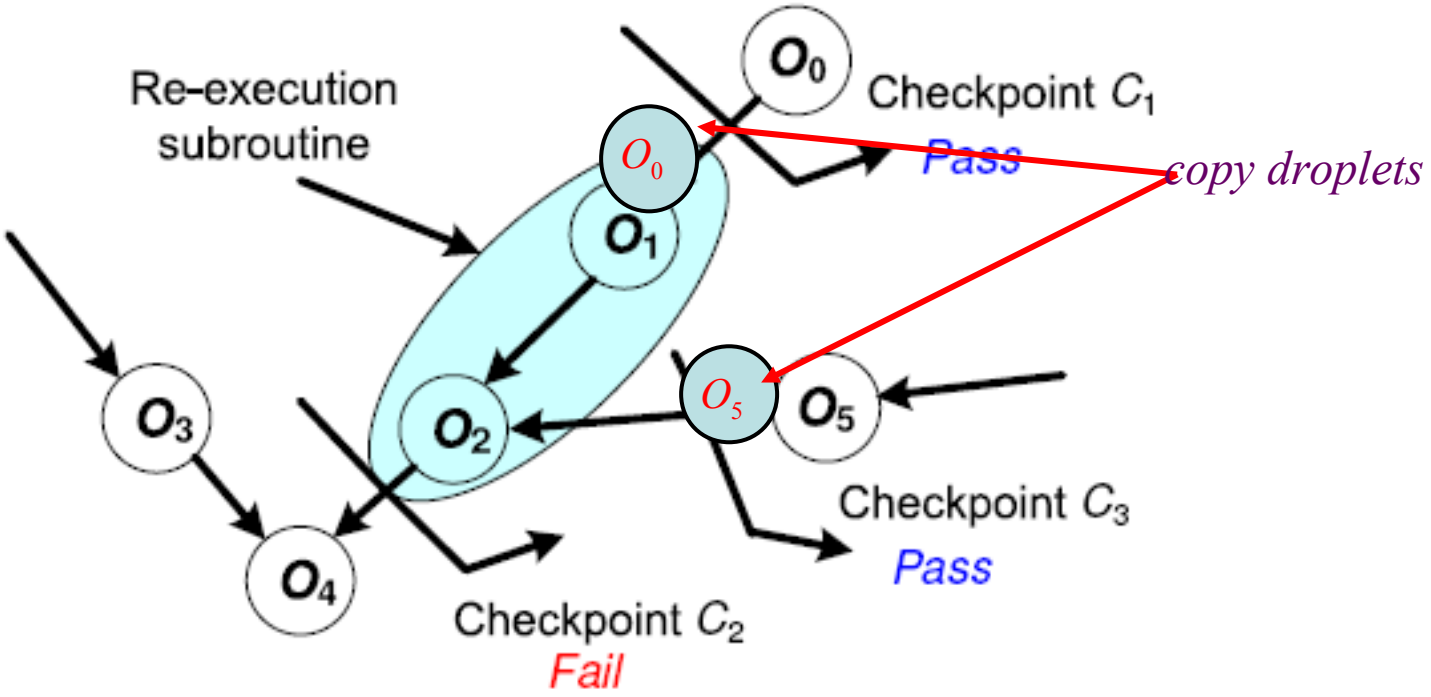
- Add *checkpoints* to monitor outcomes of fluidic operations
  - **Checkpoint**: storage of the intermediate product droplet
- Assign each checkpoint a *re-execution subroutine*
  - **Subroutine**: fluidic operations between checkpoints



Figures taken from Krish Chakrabarty, Duke University

Control-Path Design

- Extra **copy droplets** needed
- **Checkpoints**: where ?
- Costs:
  - Time
  - Area



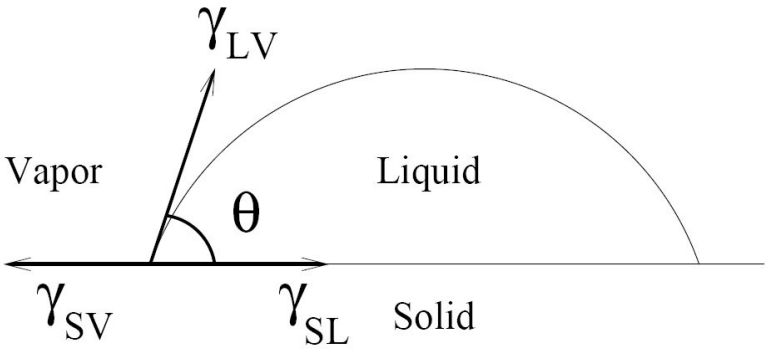
Figures taken from Krish Chakrabarty, Duke University

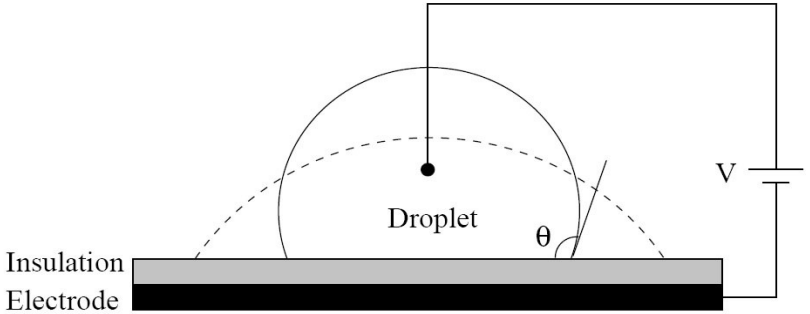
And the droplet moves!

- Electrowetting on dielectric principle (EWOD)
  - Electrical modulation of the solid-liquid interfacial tension

Young equation

$$\gamma_{LV}\cos(\theta) = \gamma_{SV} - \gamma_{SL}$$

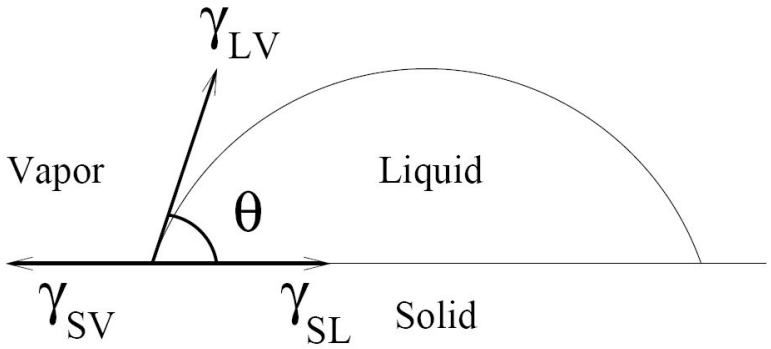




Figures taken from Krish Chakrabarty, Duke University

Electrowetting: Physical Principles (I)

- Motion of droplets is based on the differences between contact angles in the advancing and receding lines of a droplet.
- When a droplet rests on a non-wetting solid surface, the forces acting at the solid-liquid-vapor interface equilibrate and result in a contact angle θ between the droplet and solid, as described by Young's equation,



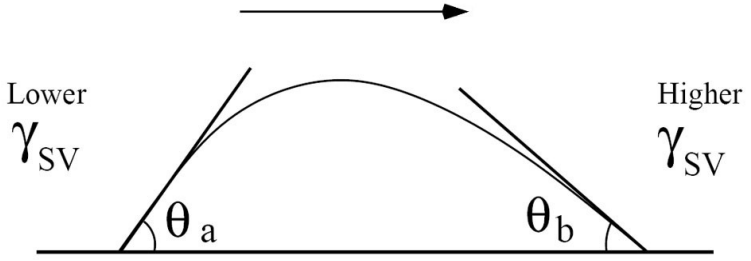
$$\gamma_{LV}\cos(\theta) = \gamma_{SV} - \gamma_{SL}$$

γ_{LV}, γ_{SV} and γ_{SL} are the liquid-vapor, solid-vapor and solid-liquid surface energies

Slide taken from Krish Chakrabarty, Duke University

Electrowetting: Physical Principles (II)

- When an imbalance in these surface energies occurs (as in the case of a droplet resting on a surface with a gradient surface energy), a net force is induced
  - Initiate droplet motion
- Imbalance can be induced by chemical, thermal, or electrostatic means
  - In the case of thermally-induced droplet motion, a surface tension gradient can be induced by differentially heating the ends of a droplet, since the surface tension of a liquid decreases with temperature.

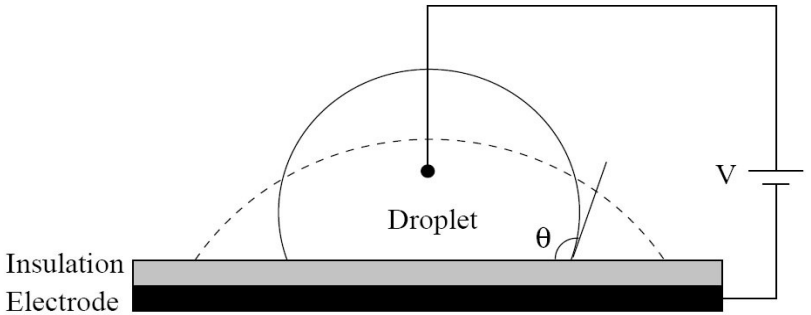


Electrowetting: Physical Principles (III)

- Electrowetting-based actuation of droplets: electrical fields used to induce surface tension gradients.
  - Electrowetting effect ⇒the surface energy can be directly modified by the application of an electric field
- Consider a droplet resting on a electrode separated by a hydrophobic insulator
  - A potential is applied between the droplet and the electrode, resulting in a capacitive energy *E* stored in the insulator. The resulting energy is:

$$E = \frac{\varepsilon_0 \varepsilon_r A}{2d} V^2$$

$$\Rightarrow \gamma_{SL}(V) = \gamma_{SL}(0) - \frac{\varepsilon_0 \varepsilon_r A}{2d} V^2$$



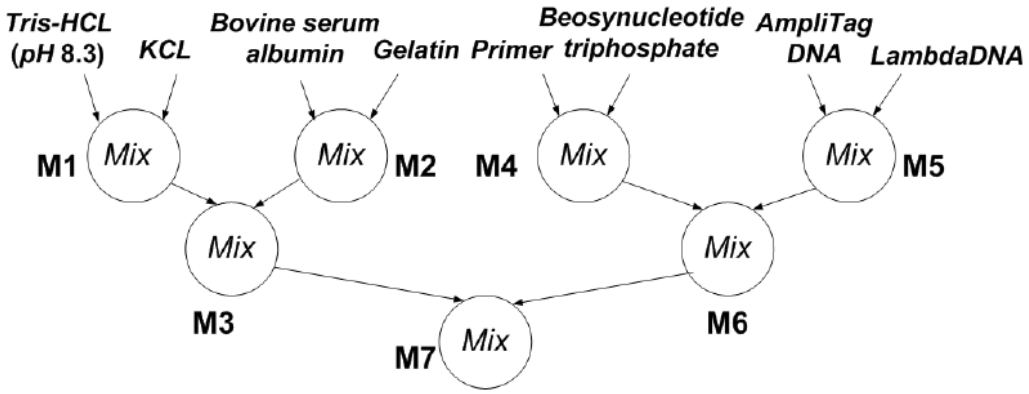
Contact angle change:

$$\cos\theta(V) = \cos\theta(0) - \frac{\varepsilon_0 \varepsilon_r A}{2d\gamma_{LV}} V^2$$

Reference: P. Y. Paik, V. K. Pamula and K. Chakrabarty,
"Adaptive Cooling of Integrated Circuits using Digital Microfluidics", Artech House, Norwood, MA, 2007.

Benchmarks: PCR

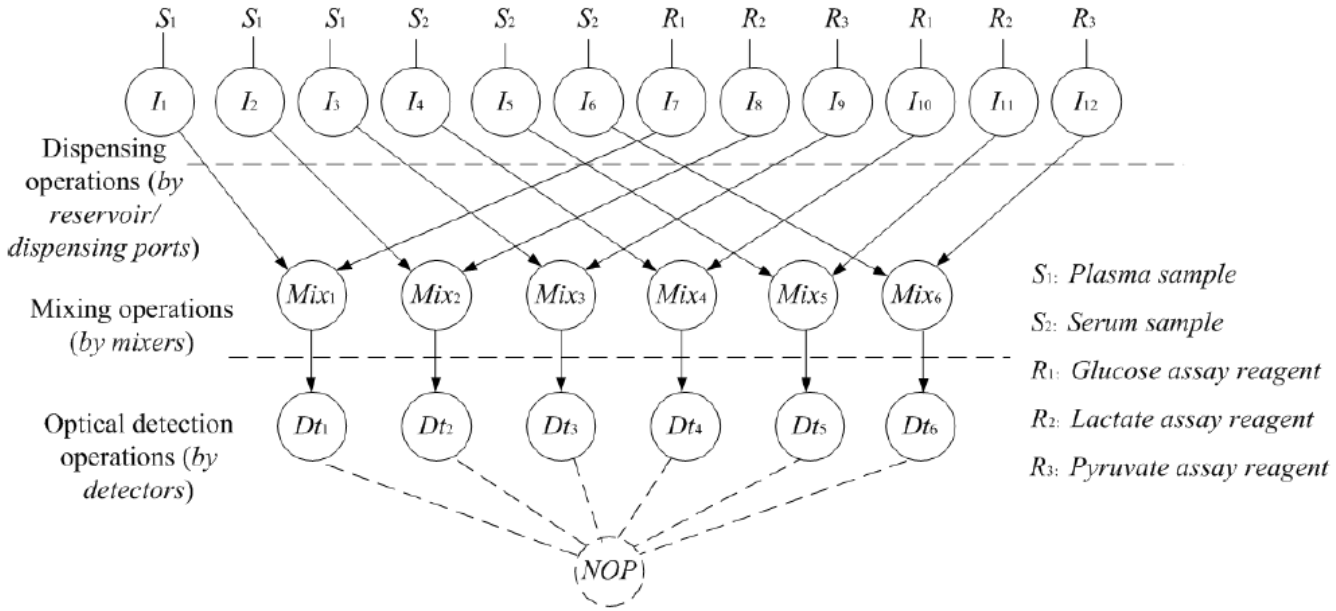
- Mixing stage for Polymerase Chain Reaction
- Electrode pitch: 1.5 mm, Gap height: 600 μm



Operation	Hardware*	Module	Mixing time
mixing	2x2 electrode array	4x4 cells	10s
	4-electrode linear array	3x6 cells	5s
	2x3 electrode array	4x5 cells	6s
	2x4 electrode array	4x6 cells	3s

Benchmarks: IVD

- Multiplexed in-vitro diagnosis
- Electrode pitch: 1.5 mm, Gap height: 600 μm



Benchmarks: CPA

- Colorimetric Protein Assay
- Electrode pitch: 1.5 mm, Gap height: 600 µm

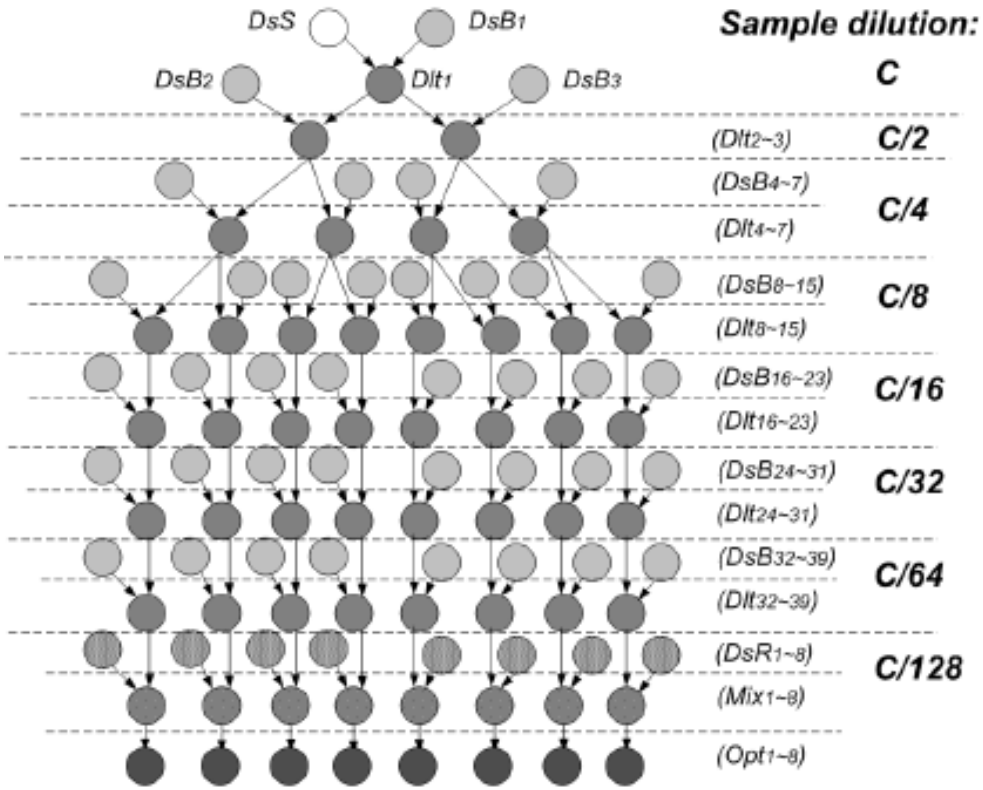


Figure 3-2. Sequencing graph for a protein assay.