Exact Routing for Micro-Electrode-Dot-Array Digital Microfluidic Biochips

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Outline

- Motivation and background
- MEDA biochips
- Routing Problem & SMT Formulation
- Experimental Results
- Conclusions & Outlook

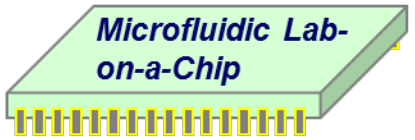
Motivation

Higher throughput, minimal human intervention, smaller sample/reagent consumption, higher sensitivity, increased productivity

CLINICAL DIAGNOSTIC APPLICATION

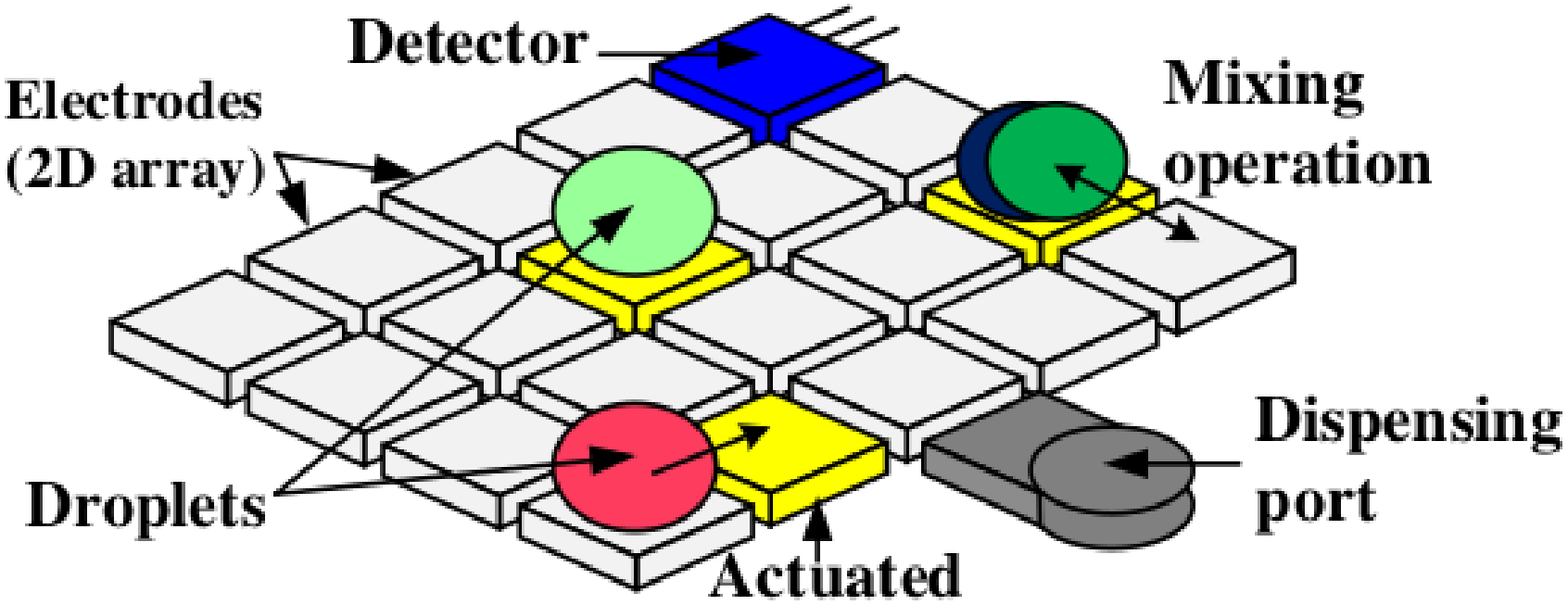
Conventional Biochemical Analyzer

Lab-on-a-chip for CLINICAL DIAGNOSTICS

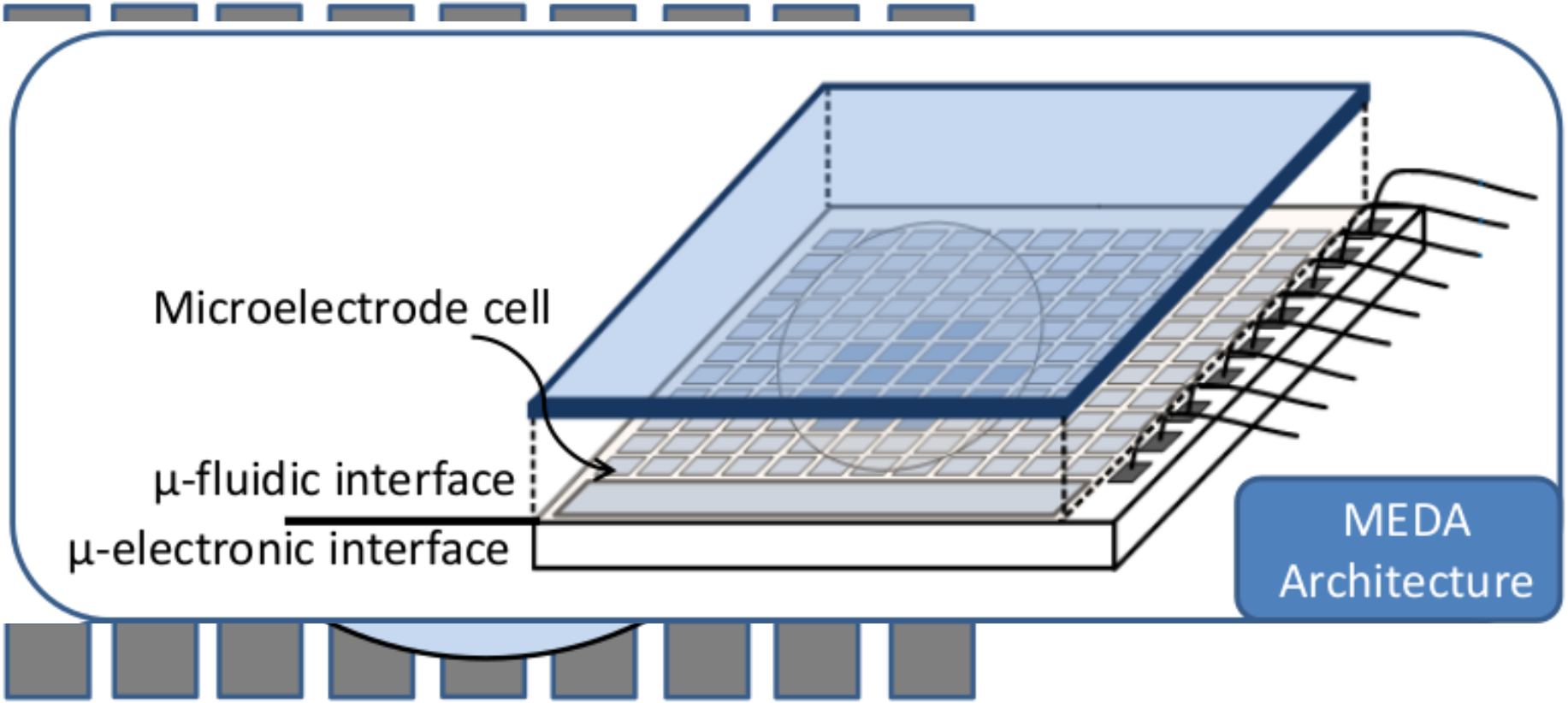


20nl sample

Conventional DMFBs

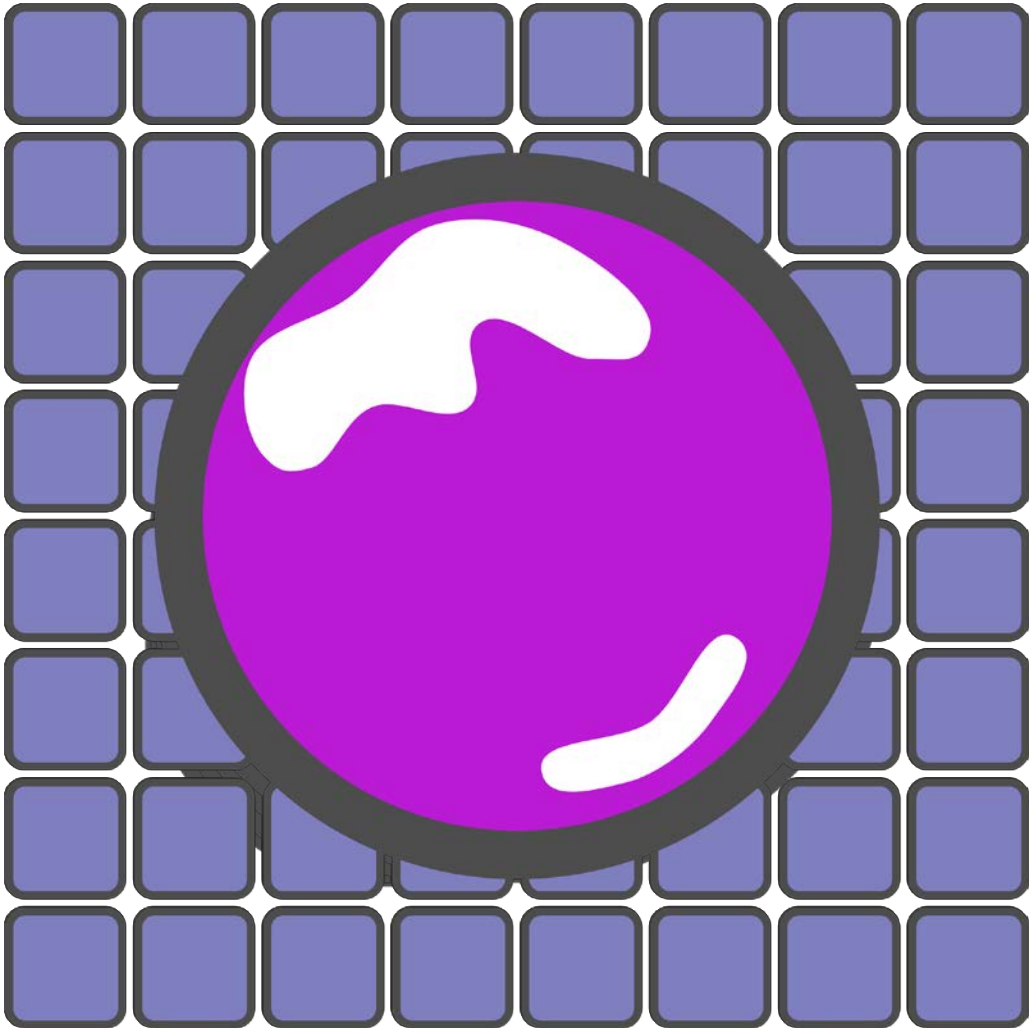


Micro-Electrode-Dot-Array

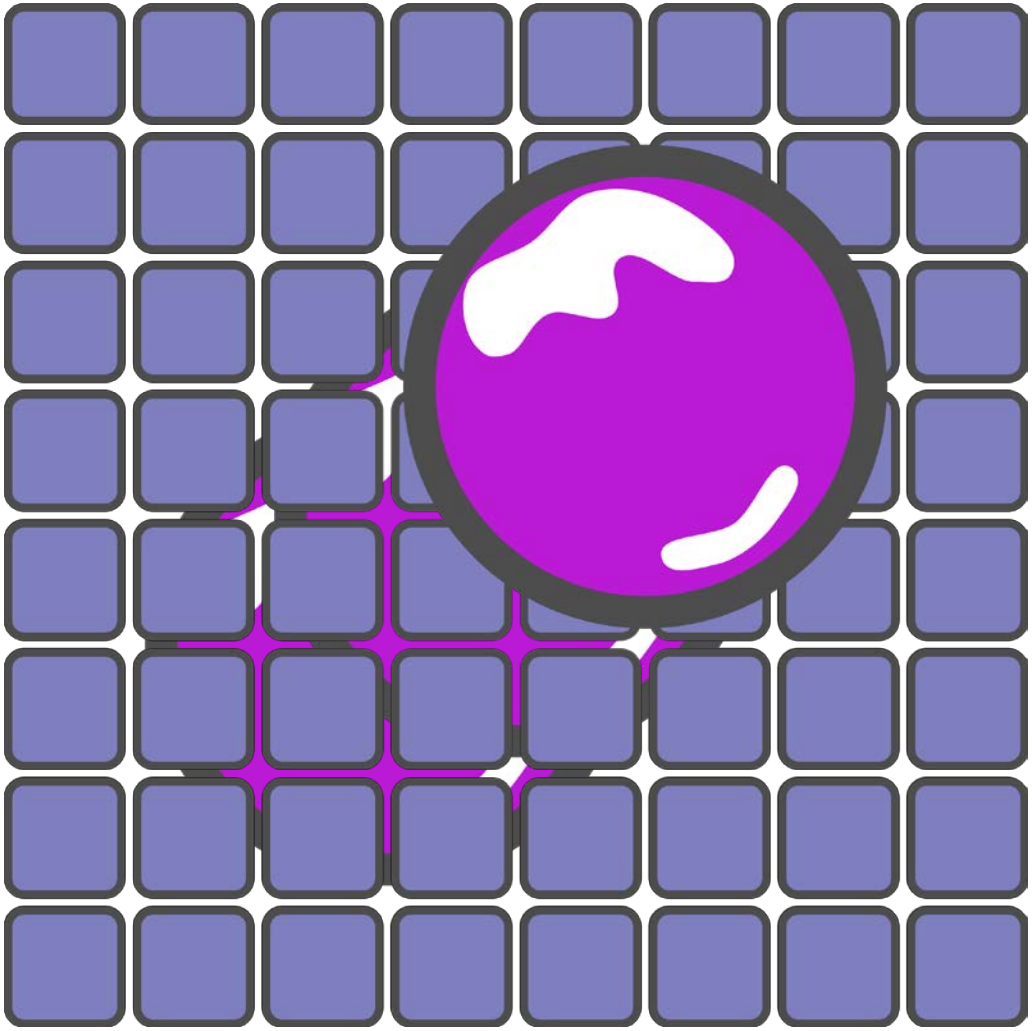


Images taken from: Li et al. *High-level synthesis for micro-electrode-dot-array digital microfluidic biochips*. DAC'16.

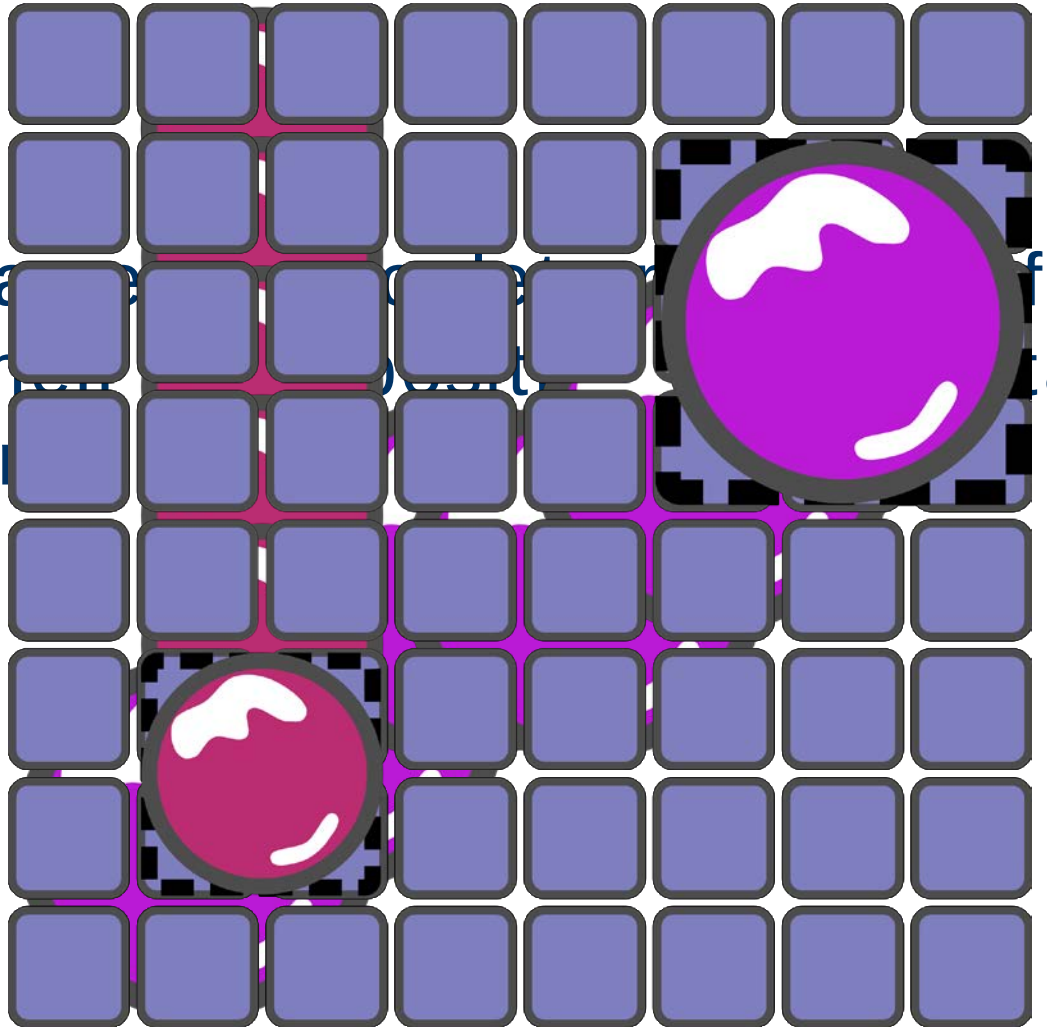
Shape Change of Droplets



Diagonal Movements



Droplet Routing



Given a [illegible] of them from th[illegible] target positio[illegible]

Complexity of Routing

Theorem 1 Routing on classical DMFBs is NP-complete.

Conjecture 1 Routing on MEDA DMFBs without diagonal movement is NP-complete.

Conjecture 2 Routing on MEDA DMFBs is NP-complete.

Proposed Approach

- Solving the routing problem is inherently difficult
- Our approach:
  - Model the problem at hand
  - Let a powerful solving engine produce a solution

Modelling of MEDA DMFBs

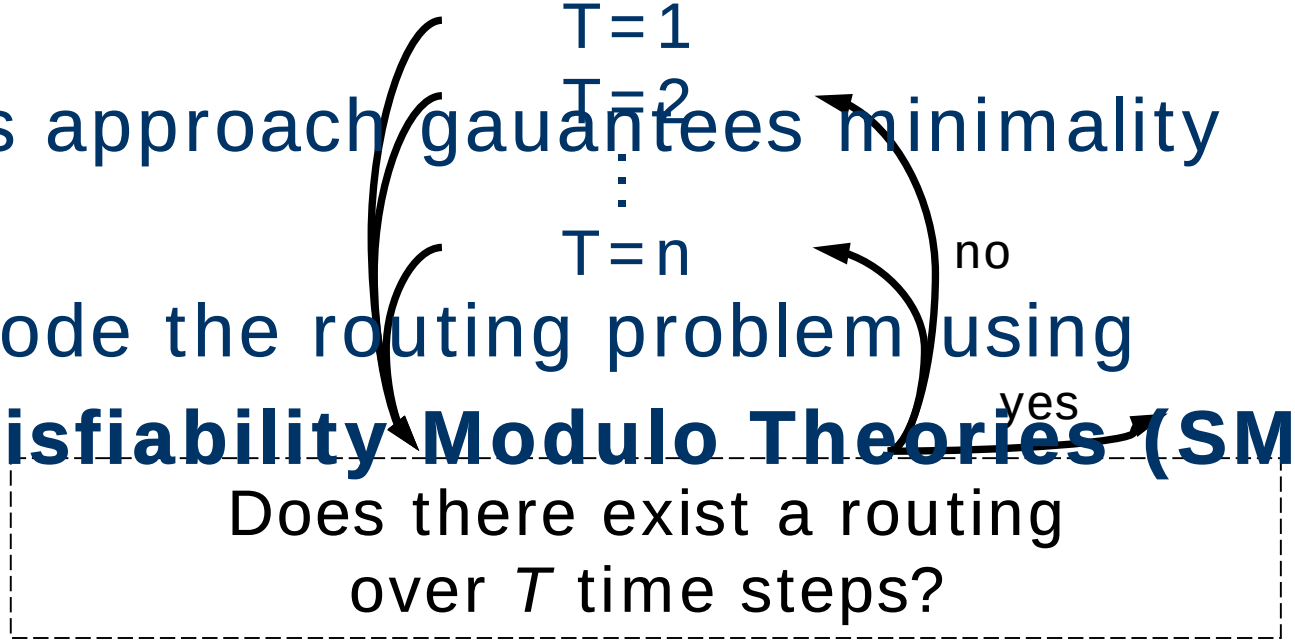
- The model automatically ensures correctness of the solution
- The solver can choose sophisticated computation methods to find the solution
- The model can easily be extended to respect further aspects – no new algorithm needs to be created

General Idea

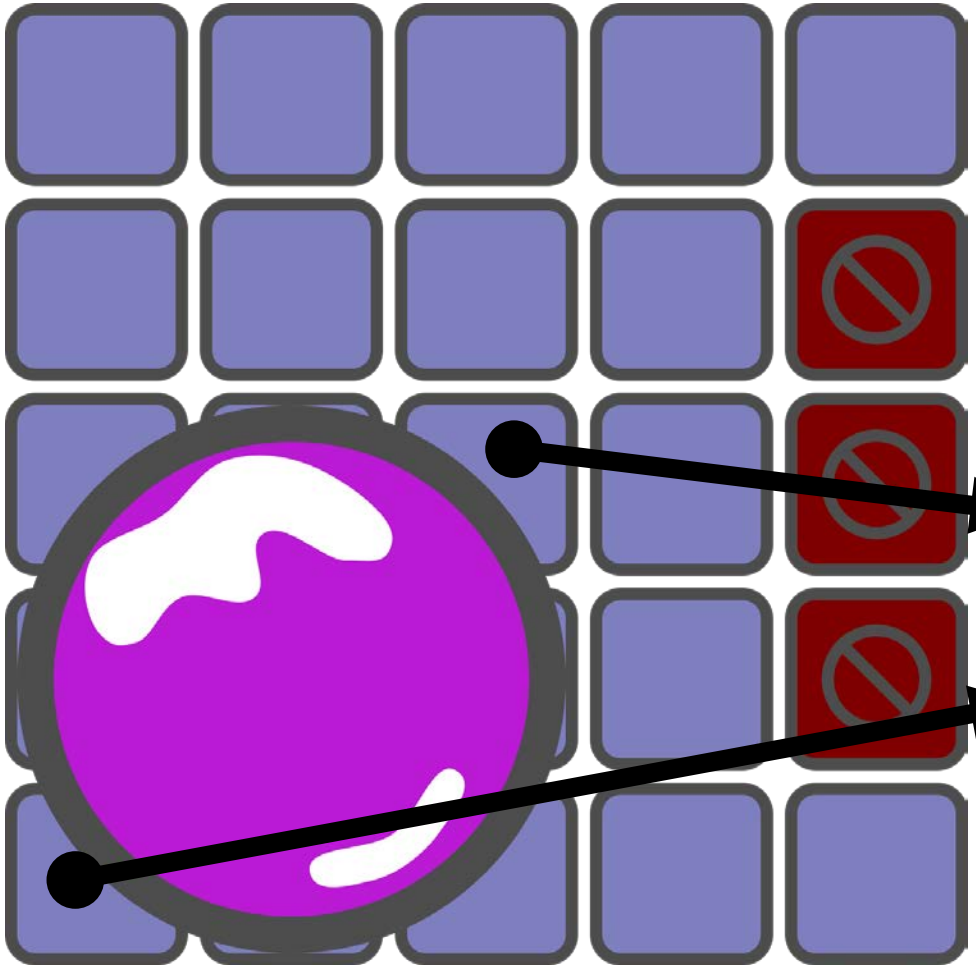
Routing problem formulated as sequence of **decision problems**

This approach guarantees minimality

Encode the routing problem using **Satisfiability Modulo Theories (SMT)**



SMT Encoding: Variables



Encoding for Droplets:

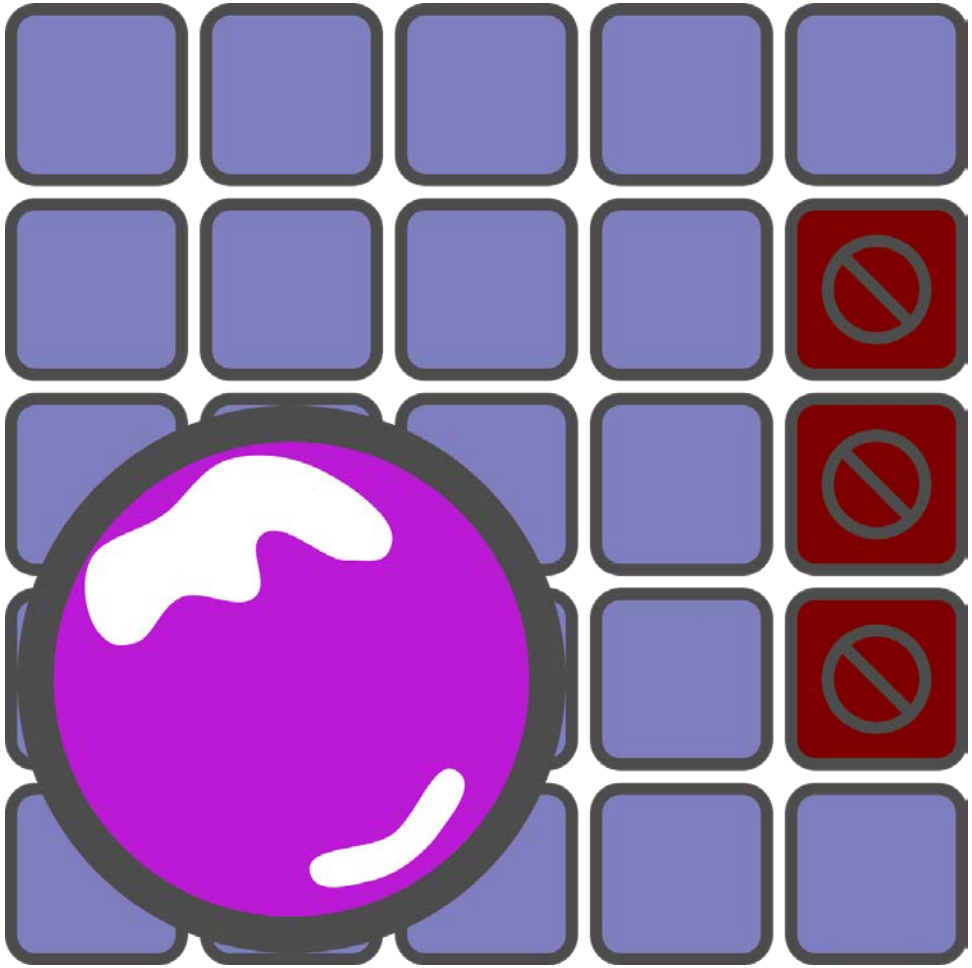
- model as rectangle
- store corners
- 4 int variables

$$\left(x_d^{\uparrow,t}, y_d^{\uparrow,t}\right)$$

$$\left(x_d^{\downarrow,t}, y_d^{\downarrow,t}\right)$$

$$p_d^t = \left(\left(x_d^{\downarrow,t}, y_d^{\downarrow,t}\right), \left(x_d^{\uparrow,t}, y_d^{\uparrow,t}\right)\right)$$

SMT Encoding: Constraints



Fix droplet on grid:

$$0 \leq x_d^{\uparrow,t}, x_d^{\downarrow,t} \leq W$$
$$0 \leq y_d^{\uparrow,t}, y_d^{\downarrow,t} \leq H$$

Prevent flipping:

$$x_d^{\uparrow,t} \geq x_d^{\downarrow,t} \wedge y_d^{\uparrow,t} \geq y_d^{\downarrow,t}$$

Source/Target config:

$$p_d^1 = p_d^* \wedge p_d^T = p_d^\dagger$$

Constraints (cont.)

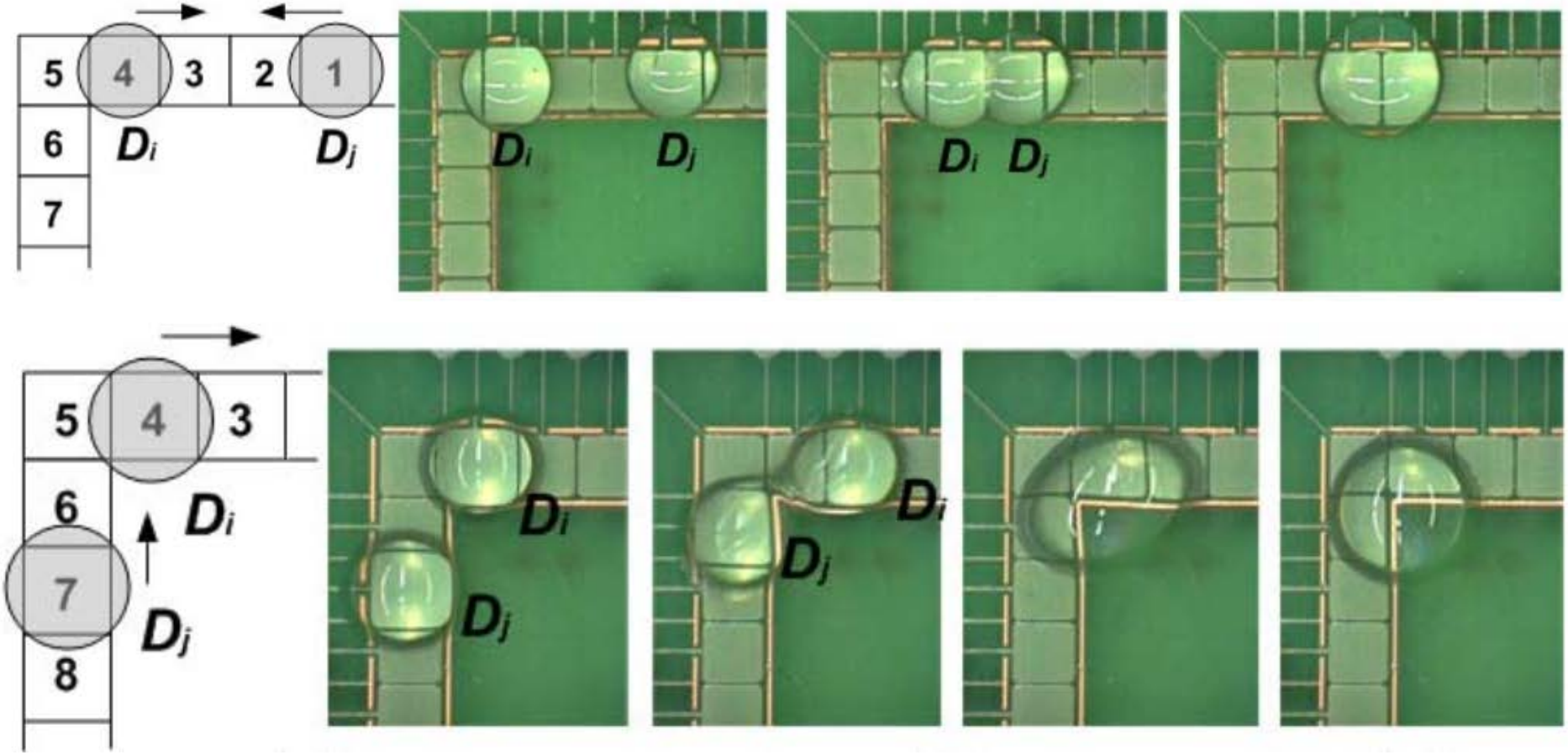
Droplet Movement

$$\left|x_d^{\uparrow,t} - x_d^{\uparrow,t-1}\right| \leq 1 \wedge \left|x_d^{\downarrow,t} - x_d^{\downarrow,t-1}\right| \leq 1 \wedge$$
$$\left|y_d^{\uparrow,t} - y_d^{\uparrow,t-1}\right| \leq 1 \wedge \left|y_d^{\downarrow,t} - y_d^{\downarrow,t-1}\right| \leq 1$$

Droplet Shapes

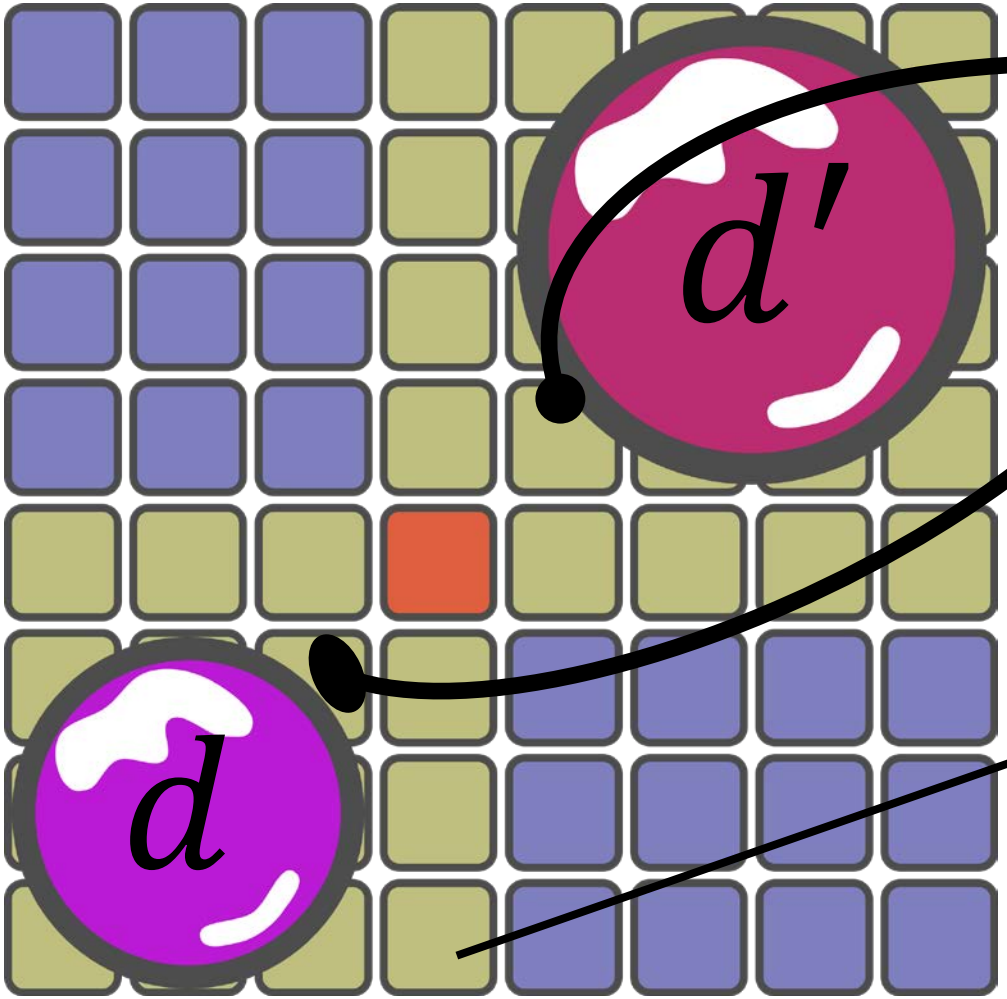
$$\bigvee_{(w,h)\in Shapes_d} x_d^{\downarrow,t} + w = x_d^{\uparrow,t} \wedge y_d^{\downarrow,t} + h = y_d^{\uparrow,t}$$

Fluidic Constraints



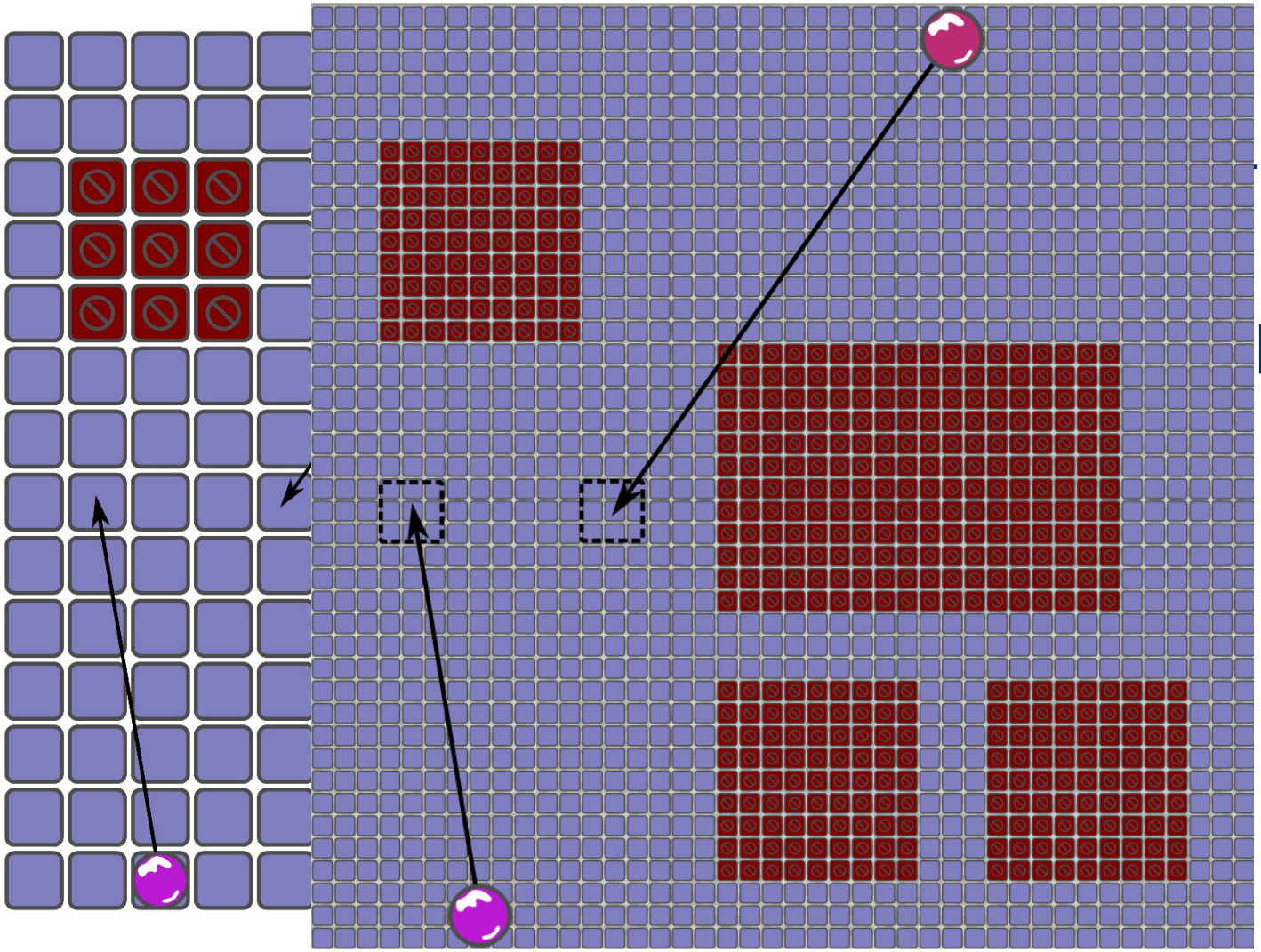
Images taken from: Su et al. *Droplet Routing in the Synthesis of Digital Microfluidic Biochips*. DATE'06.

Fluidic Constraints (cont.)



$$x_d^{\uparrow,t} + dist_f < x_{d'}^{\downarrow,t} \vee$$
$$y_d^{\uparrow,t} + dist_f < y_{d'}^{\downarrow,t} \vee$$
$$x_d^{\downarrow,t} - dist_f < x_{d'}^{\uparrow,t} \vee$$
$$y_d^{\downarrow,t} - dist_f < y_{d'}^{\uparrow,t}$$

Benchmarks



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pects

Influence of Droplet Shape

Name	Exact conventional DMFB [1]		Restricted shape		Unrestricted shape	
	max T	avg. T	max T	avg. T	max T	avg. T
in-vitro 1	18.00	11.20	18.00	11.67	18.00	11.67
in-vitro 2	16.00	10.07	16.00	9.64	16.00	9.64
protein 1	20.00	15.28	20.00	15.28	20.00	15.28
protein 2	20.00	9.53	20.00	9.49	18.67	9.44

Shape restriction (width,height):

(3,3), (3,4) (4,3) (4,4)

No diagonal movement

[1] Keszocze et al. *Exact Routing for Digital Microfluidic Biochips With Temporary Blockages*. ICCAD'14.

Influence of Diagonal Movement

Name	Exact conventional DMFB[1]		Unrestricted shape + diagonal movement	
	max T	avg. T	max T	avg. T
in-vitro 1	18.00	11.20	15.00	9.09
in-vitro 2	16.00	10.07	11.67	7.12
protein 1	20.00	15.28	17.67	12.47
protein 2	20.00	9.53	16.67	7.54

[1] Keszocze et al. *Exact Routing for Digital Microfluidic Biochips With Temporary Blockages*. ICCAD'14.

Comparison to previous Work

Name	Approximation [1]		Heuristic [2]		Proposed	
	max T	avg. T	max T	avg. T	max T	avg. T
in-vitro 1	12.33	8.20	15.33	9.55	15.00	9.09
in-vitro 2	10.67	6.33	11.33	7.29	11.67	7.12
protein 1	15.67	9.36	18.67	12.30	17.67	12.47
protein 2	12.33	5.25	16.67	7.84	16.67	7.54

[1] Li et al. *High-level synthesis for micro-electrode-dot-array digital microfluidic biochips*. DAC'16.
[2] Chen et al. *Droplet routing in high-level synthesis of configurable digital microfluidic biochips based on microelectrode dot array architecture*. BioChip Journal, 5(4), 2011

Conclusion Outlook

- Approach for exact routing for MEDA DMFBs, i.e. minimality is guaranteed
- Complexity handled through efficient solving engines
- Formal model for droplet movement and shape changing
- Parameterized
  - fluidic constraints
  - blockage distance

→ can easily be adjusted to new situations

Outlook

- Support for multiple droplet velocities (already implemented; not presented)
- There is a need for dedicated MEDA benchmarks
- Add support for non-rectangular shapes

Thank you for your attention!

Questions?