Feedback-driven Assay Interpretation Using Digital Microfluidic Biochips

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National Science Foundation
Cyber-Physical Systems Virtual Organization (CPS-VO) PI Meeting
October 4, 2012

Objective

- Miniaturized, automated programmable (bio-)chemistry

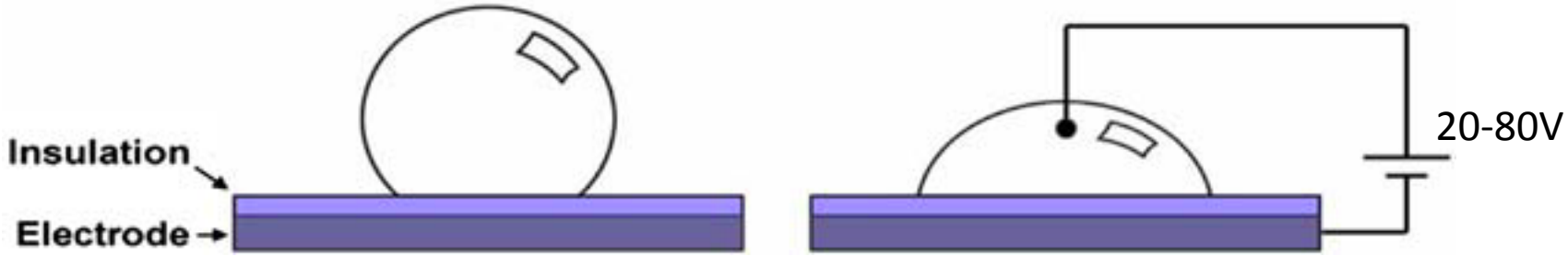
http://www.chemistry.umu.se/digitalAssets/4/4612_science_chemistry.gif

http://files.healthymagination.com/wp-content/uploads/2010/08/chip.jpg

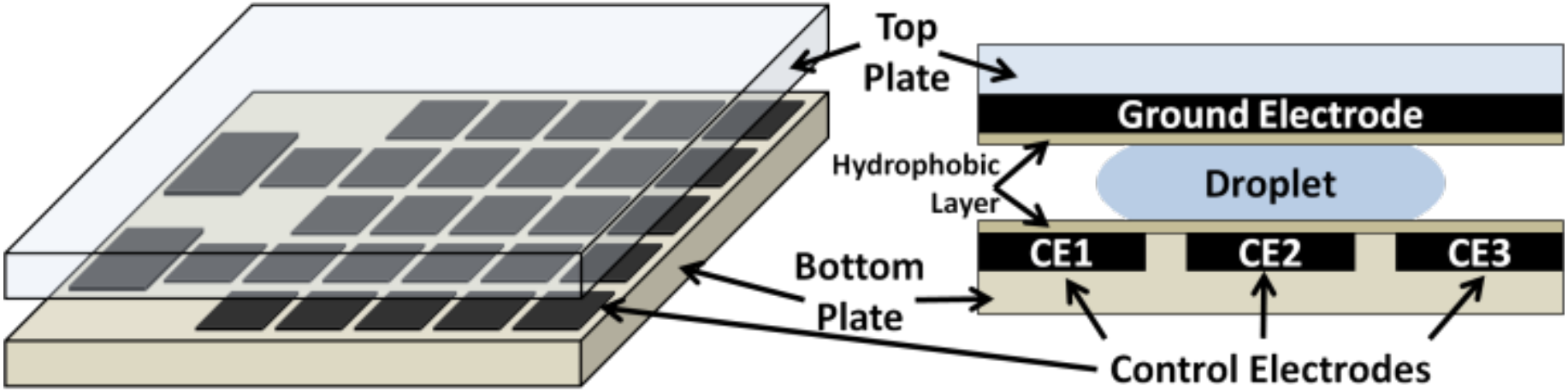
Outline

- Digital Microfluidic Biochip (DMFB) Technology
- Static DMFB Compilation
- Dynamic DMFB Interpretation
- Experiments
- Conclusion

Electrowetting on Dielectric (EWoD)

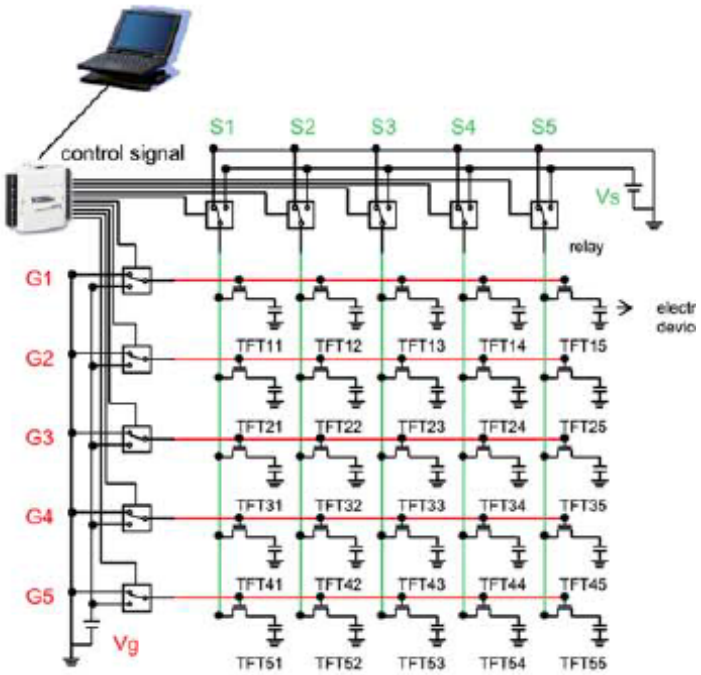


R.B. Fair, Microfluidics and Nanofluidics (2007) 3:245–281, Fig. 3

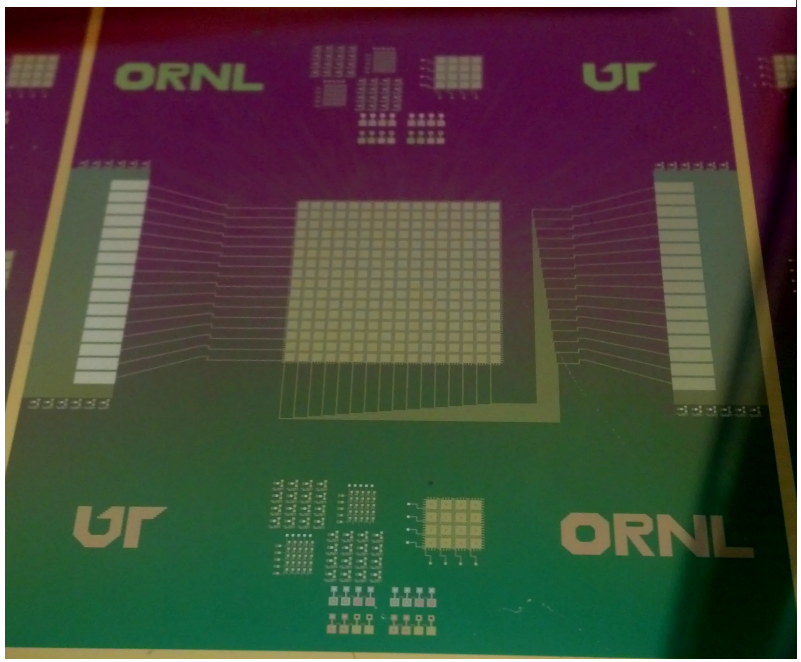


M.G. Pollack et al. Lab-on-a-Chip (2002) 2:96-101

Active Matrix Control



J.H. Noh et al., Lab-on-a-Chip (2012) 2:353-369, Fig. 1

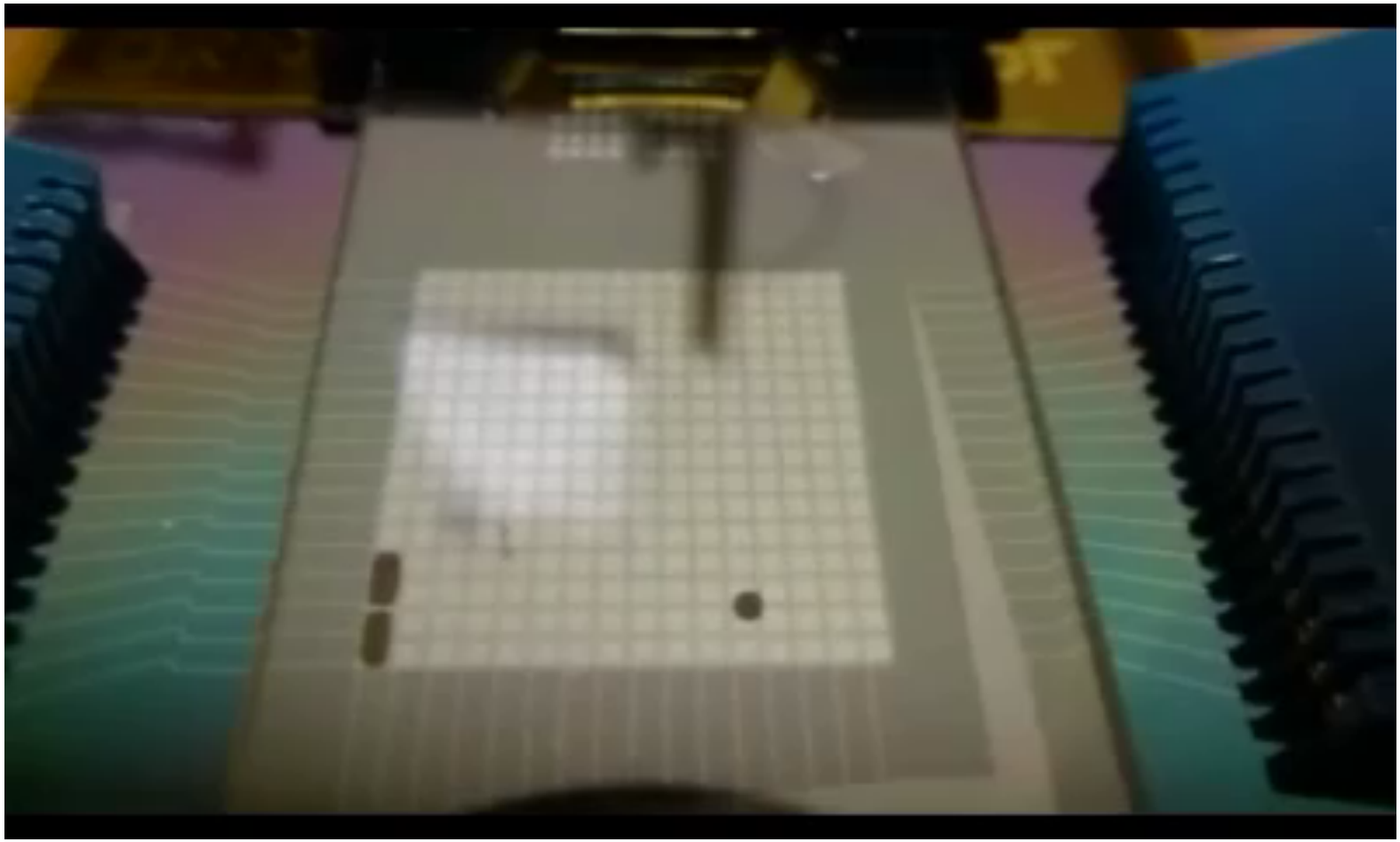


- M+N inputs independently control MxN electrodes
- 16x16 device fabricated and tested 2 weeks ago by Dr. Philip D. Rack's group at the University of Tennessee, Knoxville, and Oakridge National Laboratory

Active Matrix Addressing in Action

“Blob” Motion

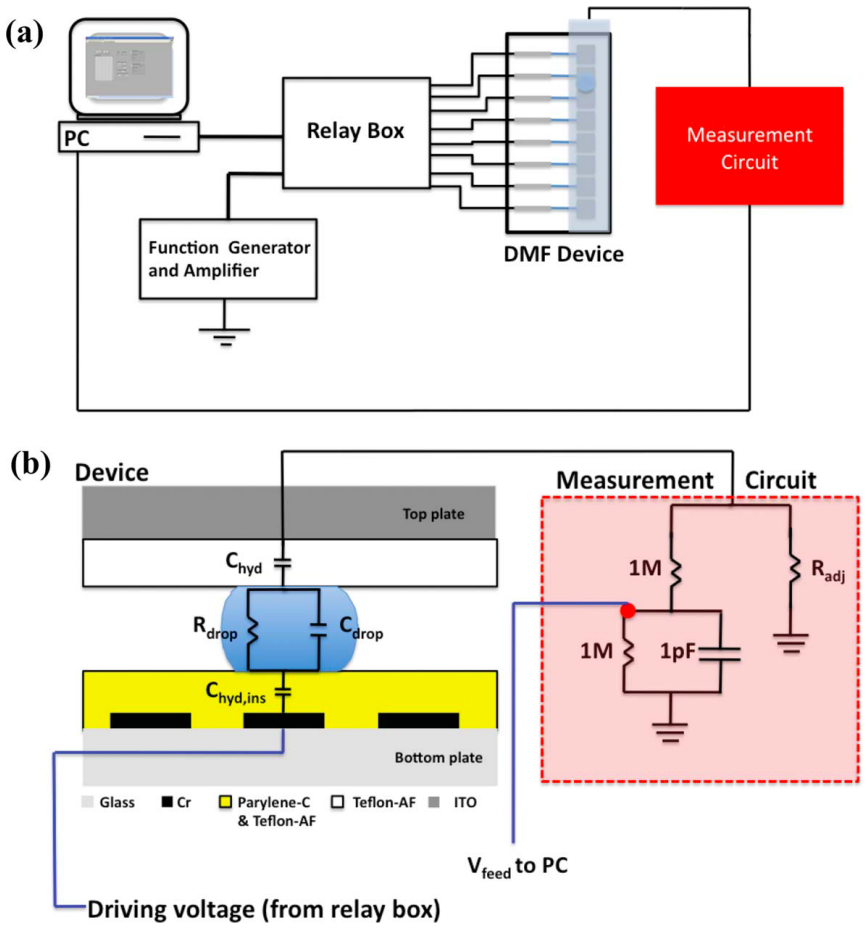
“Oblong Blob” Motion



CPS Challenges

DMFBs are "dumb"

- Microcontroller sends signals to electrodes
- Limited feedback from sensors
- Physical state of the system is unclear



S. C. C. Shih et al., Lab-on-a-Chip (2010) 11:535–540, Fig. 1

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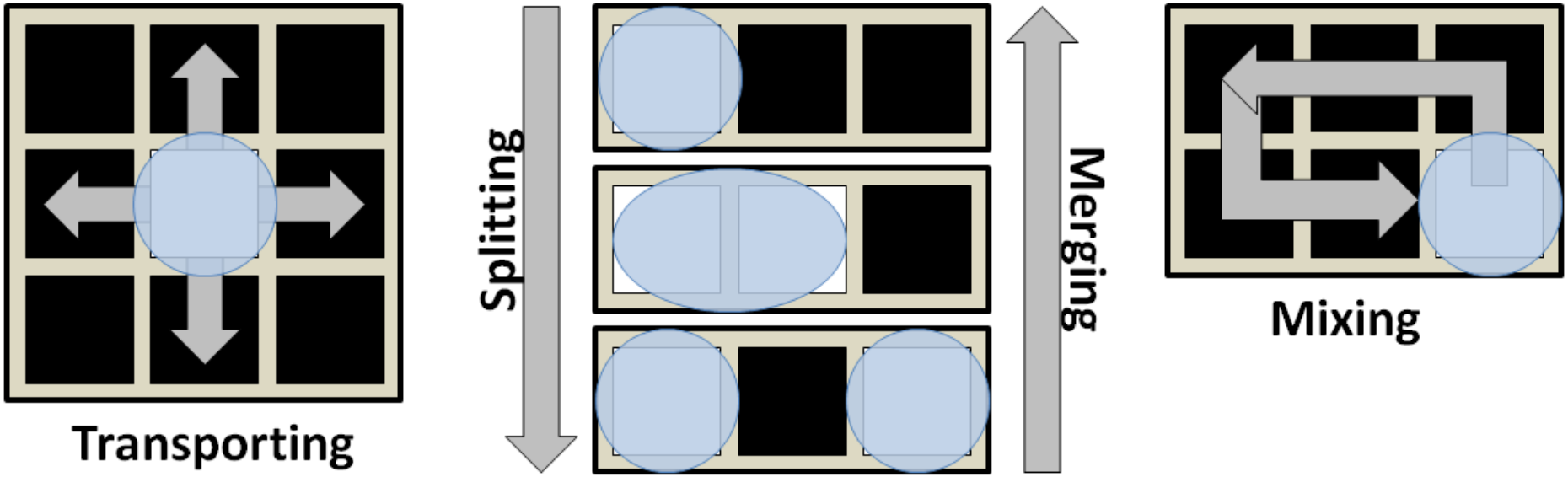
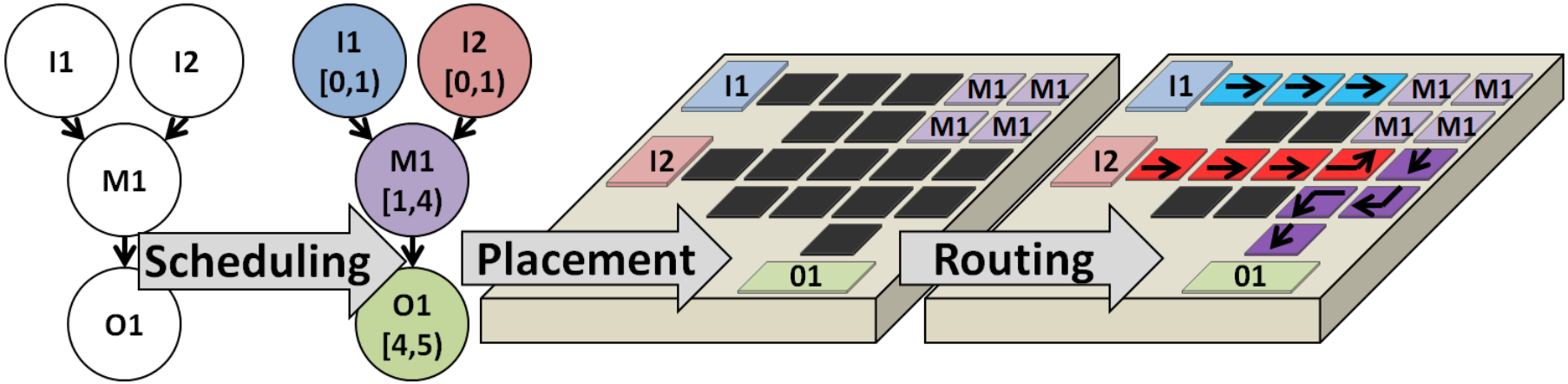
Fundamental Operations



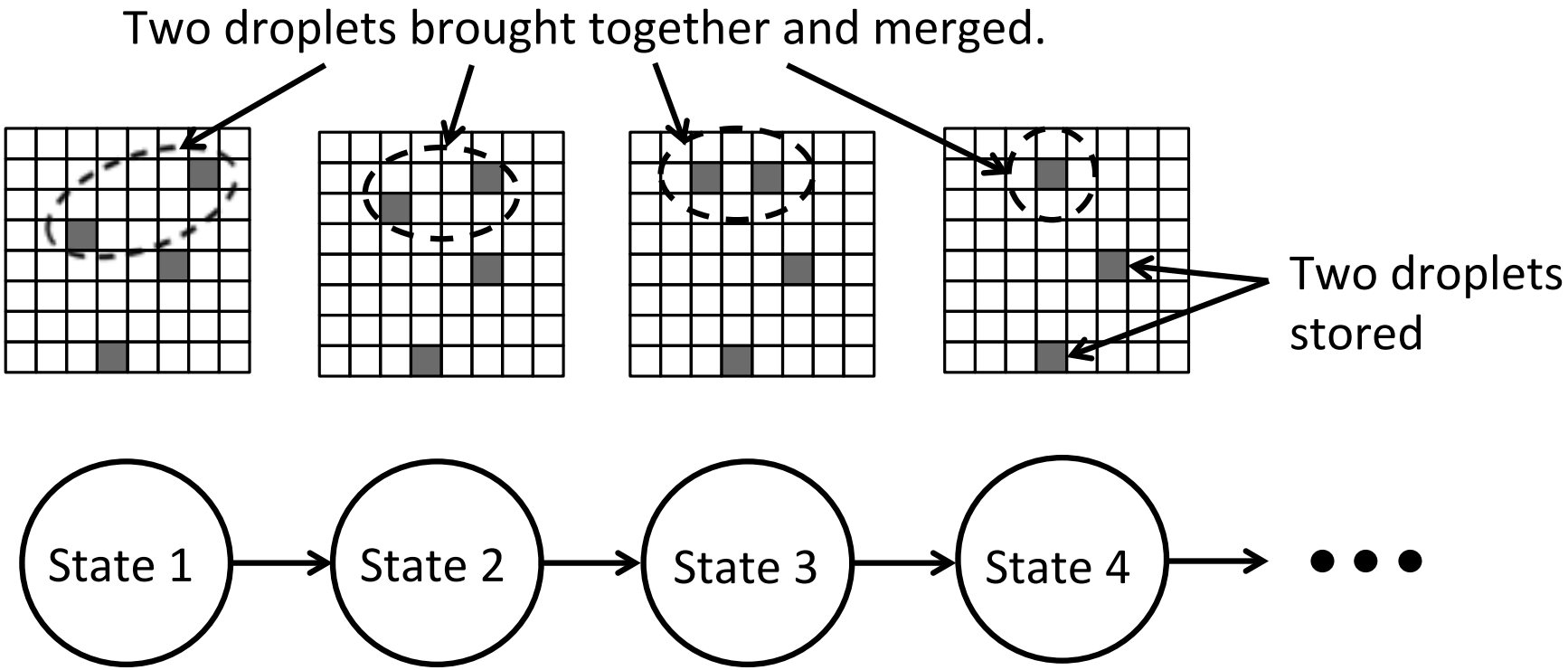
+ External components
  - Heaters, detectors, sensors, etc.
  - Placed at pre-specified locations on the DMFB
  - Route droplet(s) to the location

Static DFMB Compilation



1. Schedule assay operations and select module types (e.g., mixer dimensions)
2. Place assay operations on the DMFB
3. Route droplets to their destinations

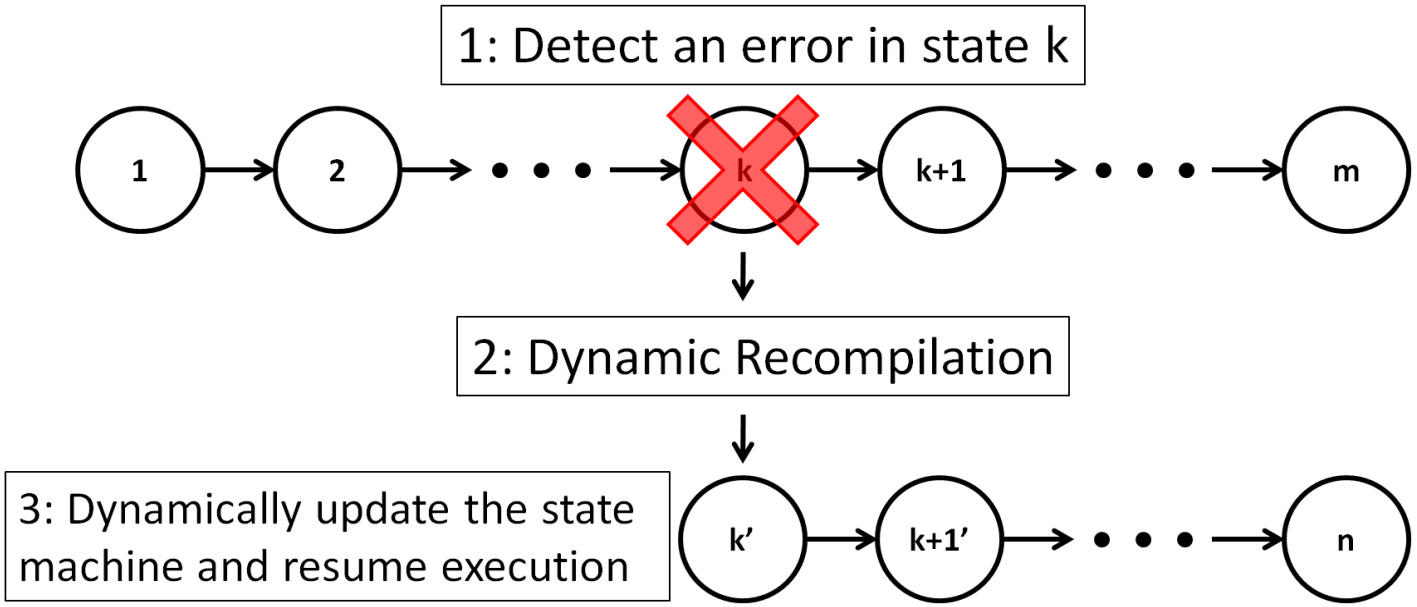
Linear State Machine Control Model



- Timed state transitions (e.g., wait 10ms)
- Feedback-driven transitions (e.g., by capacitive sensing)

Variability in the Linear Model

- Limitations
  - No control flow
  - Variable-latency operations
  - Error detection and recovery



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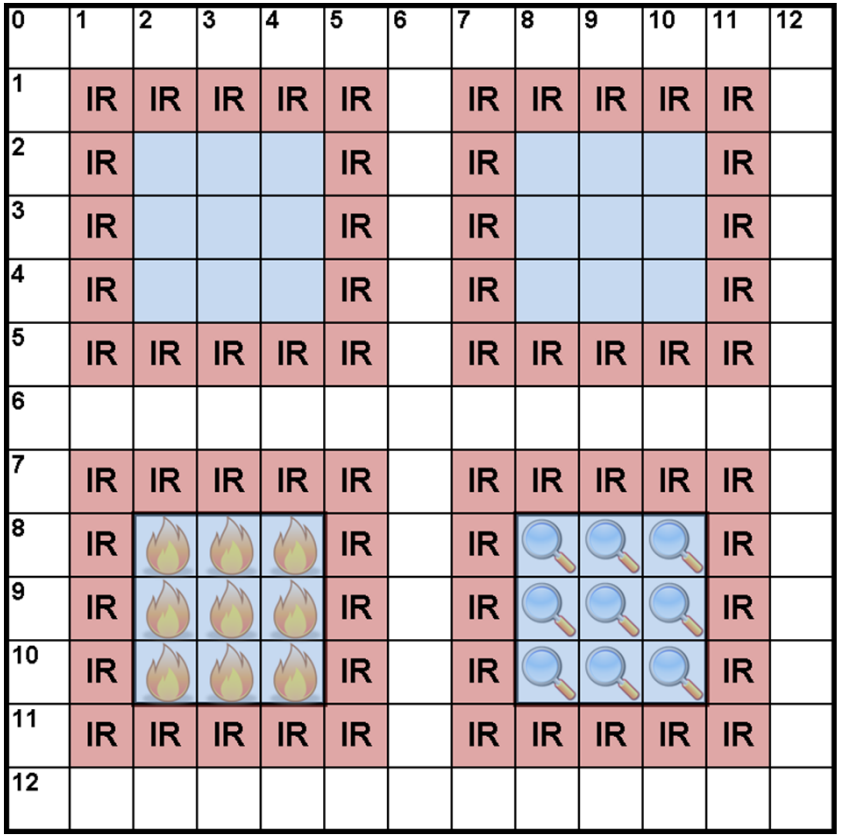
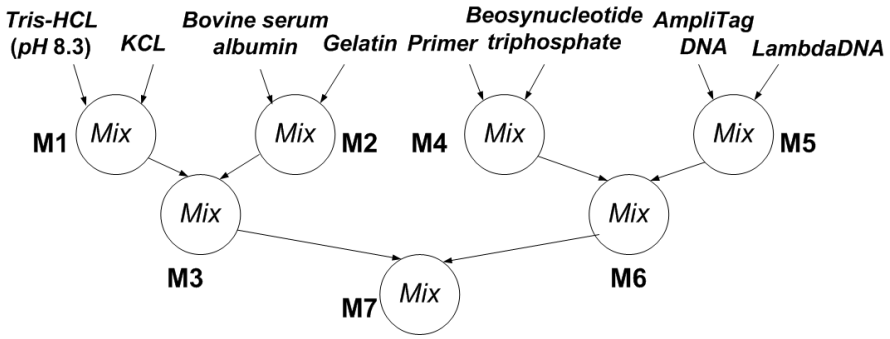
Virtual Architecture



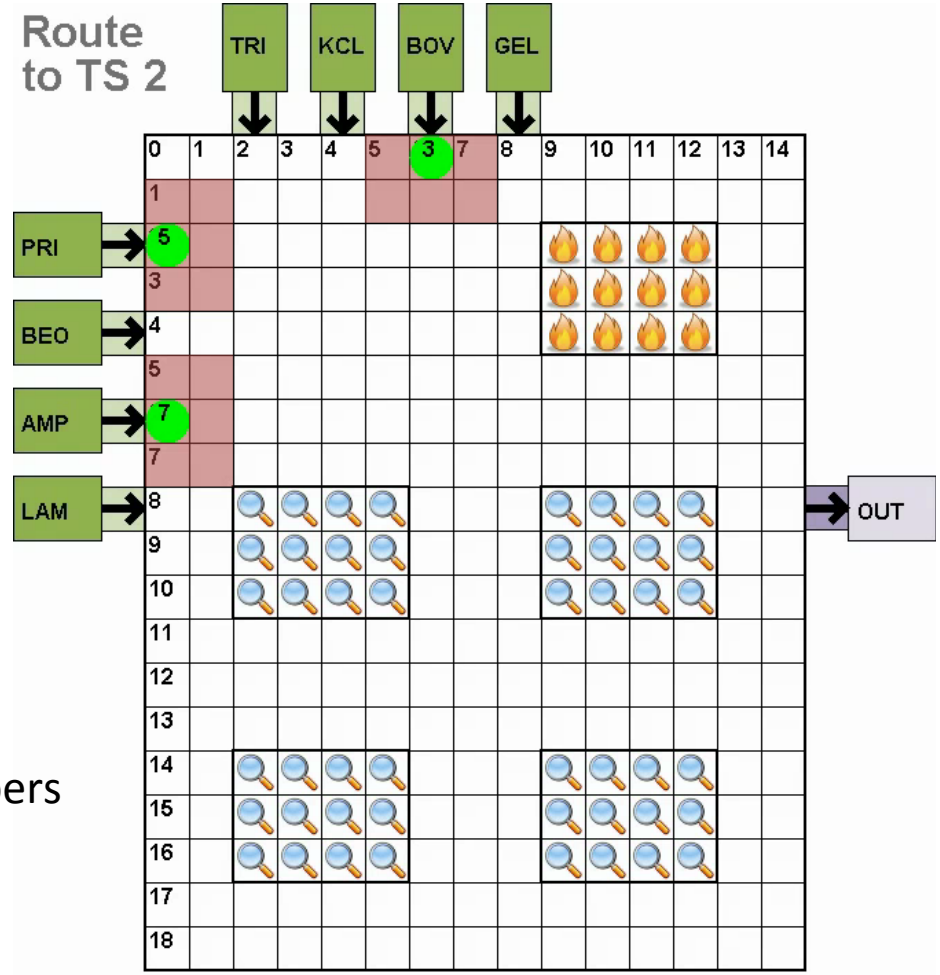
D. Grissom and P. Brisk, CODES-ISSS (2012)

- Dynamically execute the assay in an on-line fashion

Dynamic Interpretation



Polymerase Chair Reaction (PCR) Mixing Stage



Interpreter Overview

- Update the schedule on-the-fly
- Dynamically bind operations to work chambers
- 2D mesh layout simplifies routing
- Naturally scalable to larger active matrix arrays

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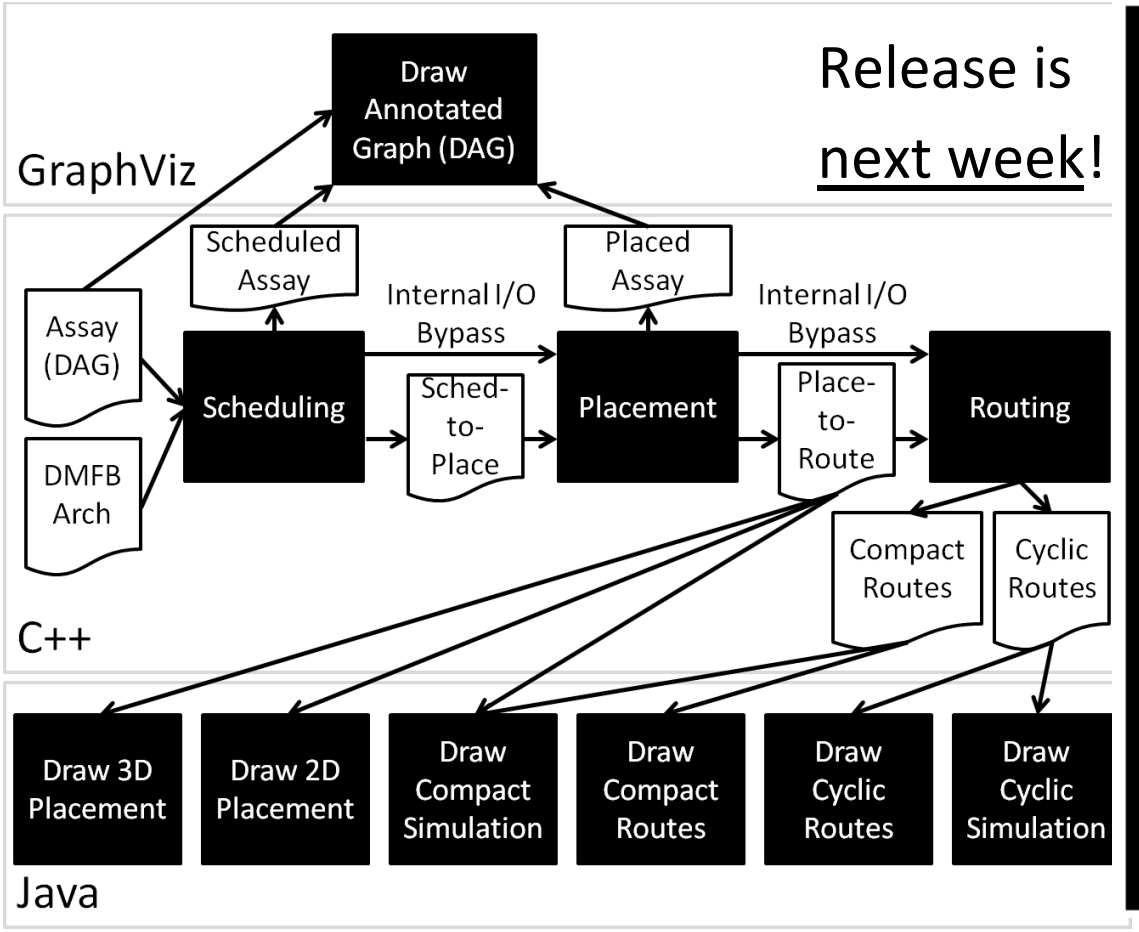
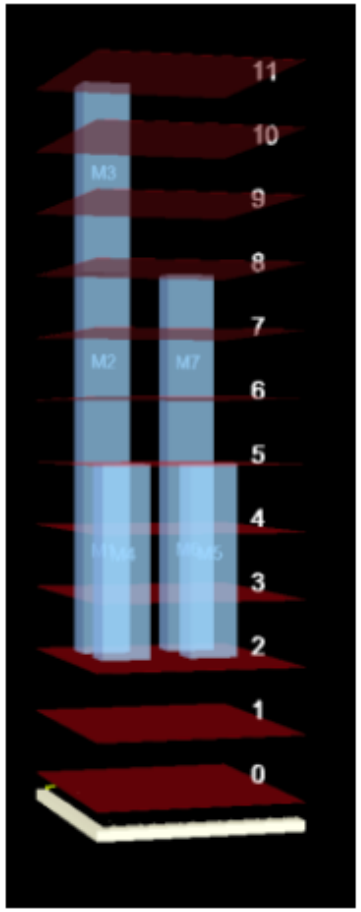
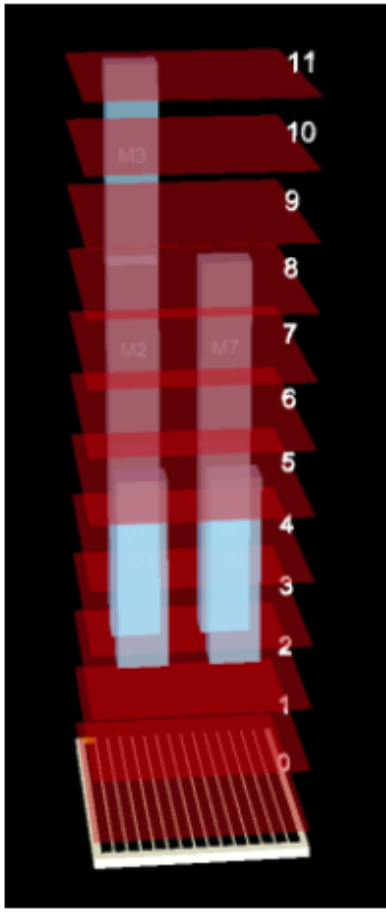
Open Source Synthesis Framework

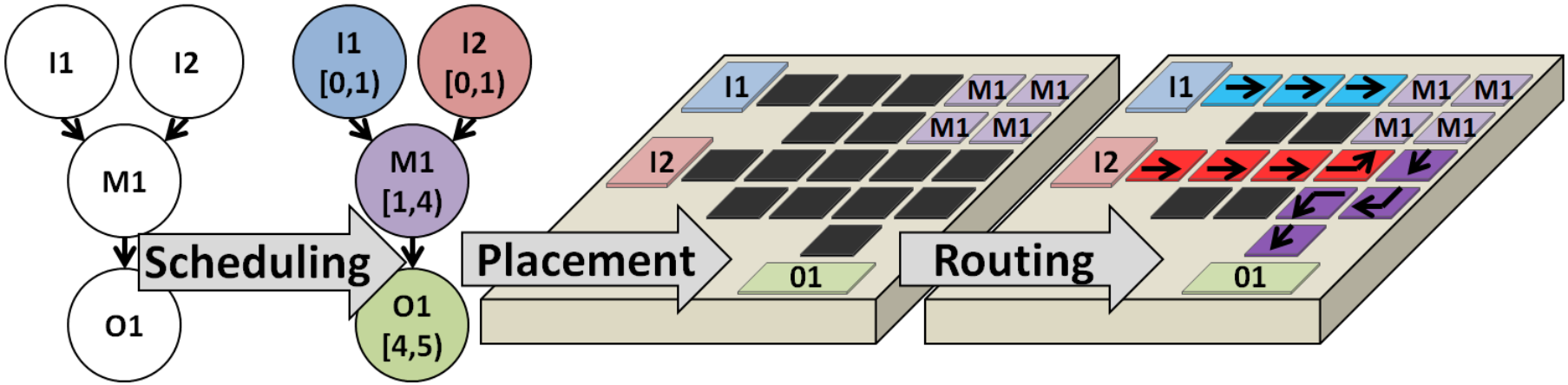






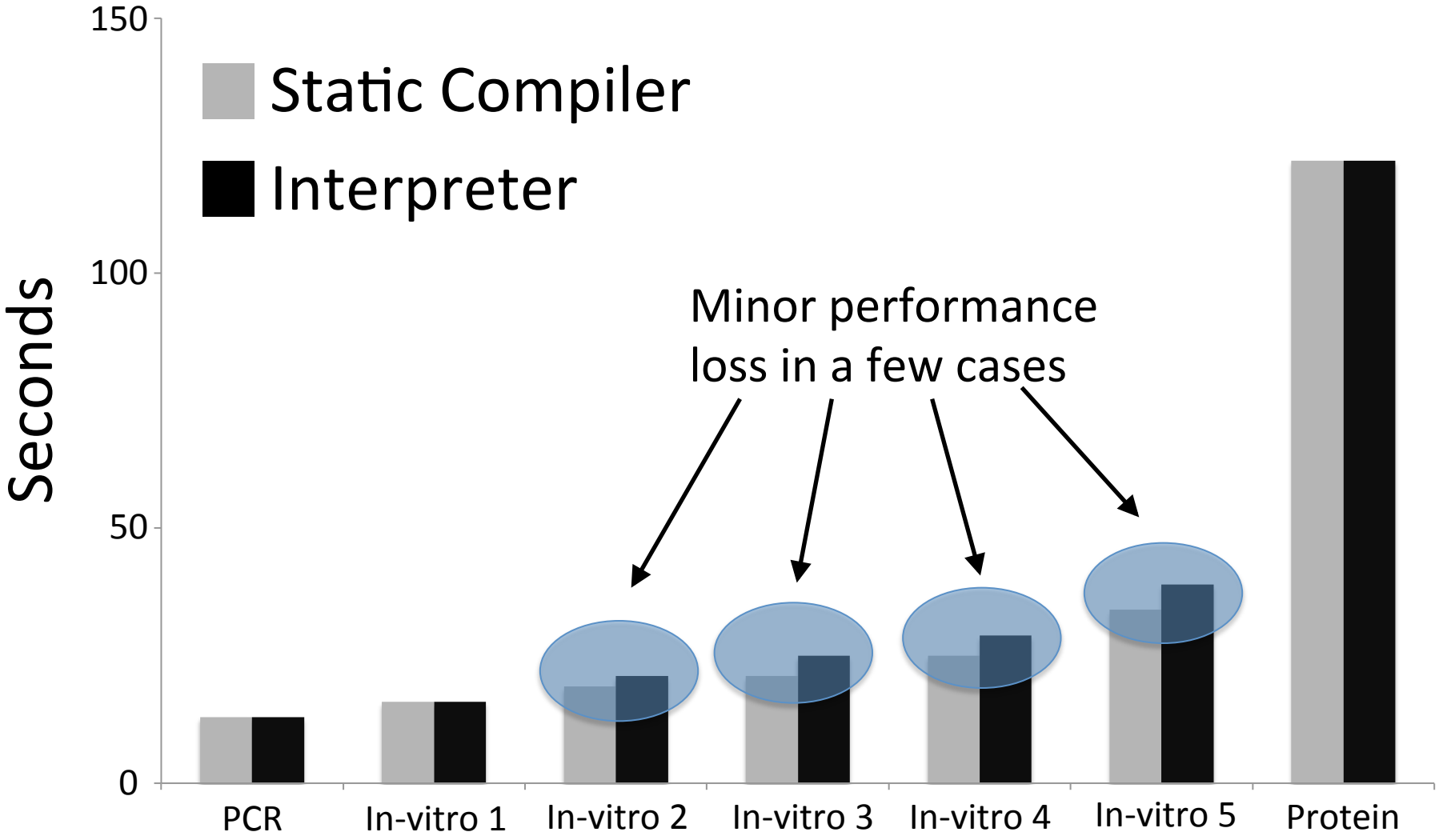
D. Grissom et al., VLSI-SoC (2012)

Compiler Implementation

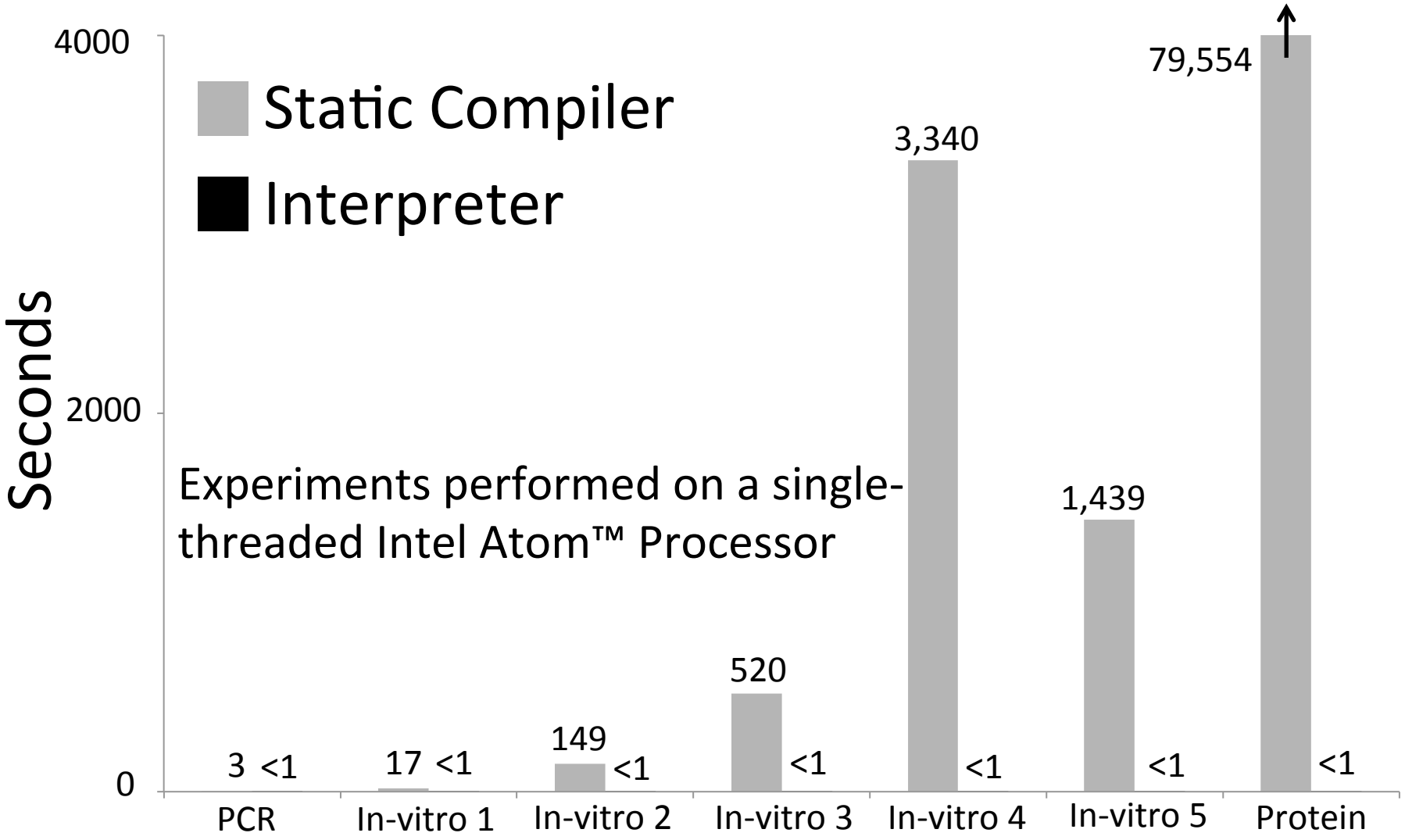


- Scheduler: Genetic Algorithm
  F. Su and K. Chakrabarty, ACM JETC (2008) 3(4): article #16
- Placer: Simulated Annealing
  F. Su and K. Chakrabarty, ACM TODAES (2006) 11(3):682-710
- Router: Adaptation of Soukup's Algorithm from VLSI routing
  P. Roy et al., GLS-VLSI (2010) 441-446

Assay Execution Time



Computation Time



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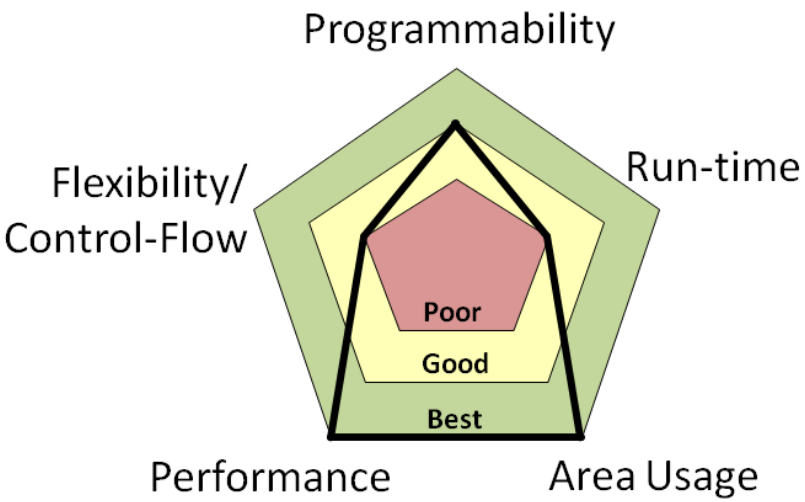
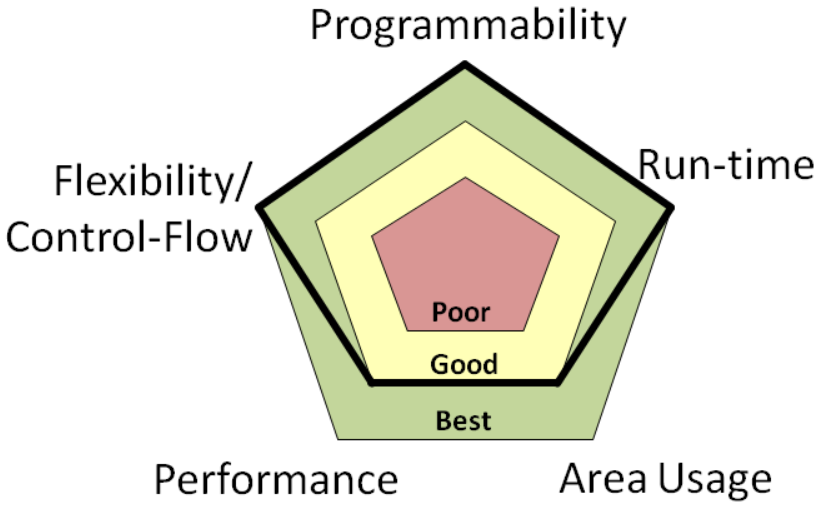
Conclusion for the CPS Community

- Assume high variability and uncertainty in physical processes
  - Take an online, rather than an offline, approach!

- Life does become easier if the "cyber" folks can influence the design of the physical part of the system



Offline Assay Compilation



Online Assay Interpretation