Feedback-driven Assay Interpretation Using Digital Microfluidic Biochips

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Objective

- Miniaturized, automated programmable (bio-)chemistry

Outline

• Digital Microfluidic Biochip (DMFB) Technology
• Static DMFB Compilation
• Dynamic DMFB Interpretation
• Experiments
• Conclusion
Electrowetting on Dielectric (E WoD)

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

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

4th Full Integration #4
Individual Moving using AM driving
“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
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

Two droplets brought together and merged.

State 1 → State 2 → State 3 → State 4 → ...

- 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

1: Detect an error in state k

2: Dynamic Recompilation

3: Dynamically update the state machine and resume execution
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Virtual Architecture

• 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

- **Placer:** Simulated Annealing

- **Router:** Adaptation of Soukup’s Algorithm from VLSI routing
  P. Roy et al., GLS-VLSI (2010) 441-446
Assay Execution Time

- Static Compiler
- Interpreter

Minor performance loss in a few cases
Computation Time

Experiments performed on a single-threaded Intel Atom™ Processor

- **Static Compiler**
- **Interpreter**
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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