

Fast Online Synthesis of Generally Programmable **Digital Microfluidic Biochips Dan Grissom and Philip Brisk** University of California, Riverside (UCR)

Digital Microfluidic Technology

Digital Microfluidic Biochips (DMFBs) are an emerging "lab-on-a-chip (LoC)" technology that perform biochemical reactions by operating on fluidic droplets on the scale of nano-liters.

Applications:

- Clinical pathology
- Point of care diagnostics
- Drug discovery
- Proteomics, DNA, PCR, etc.

Key advantages:

- Reduced cost
- Reduced reagent and sample sizes
- Increased throughput and efficiency
- Increased sensitivity and accuracy

Fast Synthesis

Scheduling : List Scheduling

-Greedy constructive algorithm -Non-iterative

-Limit number of droplets to prevent scheduling deadlock -Resource availability based on knowledge of placer/binder -Storage/module limited to number of I/O cells (2 in this case)

| | | | | | | | 1 | 1 | | | | | |
|----|----|-------|----|----|-----|--|-----|--------|------|-------------------------|----|--|----|
| 1 | IR | IR | IR | IR | IR | | IR | IR | IR | IR | IR | | 1 |
| 2 | IR | | | | IR | | IR | | | | IR | | 2 |
| 3 | IR | Sp \ |) | Sp |)IR | | IF(| D 1 |)) (| | IR | | 3 |
| 4 | IR | | | | IR | | IR | K | | $\overline{\mathbf{A}}$ | IR | | 4 |
| 5 | IR | IR | IR | IR | IR | | IR | | IR | | IR | | 5 |
| 6 | | | | | | | | | | | | | 6 |
| 7 | IR | IR | IR | IR | IR | | IR | | IR | | IR | | 7 |
| 8 | IR | | | | IR | | IR | | Q | | IR | | 8 |
| 9 | IR | Sp Sp |) | Sp |)IR | | IF(| Sp |))((| Sp | R | | 9 |
| 10 | IR | | | | IR | | IR | R | | R | IR | | 10 |
| 11 | IR | IR | IR | IR | IR | | IR | IR | IR | IR | IR | | 11 |
| 12 | | | | | | | | | | | | | 12 |

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
|----|----|-------|----------------|---------|-----|---|-------------------|---------|-----|---------|-----|----|
| 1 | IR | IR | IR | IR | IR | | IR | IR | IR | IR | IR | |
| 2 | IR | | | | IR | | IR | | | | IR | |
| 3 | IR | Sp \ | $\overline{)}$ | Sp 2 | IR | | IF <mark>(</mark> | D 1 |) (| Sp | IR | |
| 4 | IR | | | | IR | | IR | X | | | IR | |
| 5 | IR | IR | IR | IR | IR | | IR | | IR | IR | IR | |
| 6 | | | | | | | | X | | | | |
| 7 | IR | IR | IR | IR | IR | | IR | | IR | IR | IR | |
| 8 | IR | | | | IR | | IR | | Q | | IR | |
| 9 | IF | Sp Sp |) (| Sp |)IR | | IF <mark>(</mark> | Sp 5 | | Sp 6 |)IR | |
| 10 | IR | | | | IR | | IR | R | Q | Q | IR | |
| 11 | IR | IR | IR | IR | IR | | IR | IR | IR | IR | IR | |
| 12 | | | | | | | | | | | | |



Microfluidic Synthesis



If we limit the number of droplets and leave an empty spot (left), we can help prevent scheduling deadlock (right)

Placement: Module Binding

-Fixed binding instead of free placement -Greedy left-edge algorithm -Non-iterative

-Modules placed at fixed locations -Space left between modules guarantees a route



Routing: Simplified Maze Router (Roy)

Route to TS 35

-Based on Roy's Soukup Maze Router -Routes generated from source to destination in one pass

-Routes are compacted after computation

-Stalls added to beginning or middle of routes

Module Topology & Synchronization



Area Usage

Good

Best

Offline Assay Compilation

Performance

-Modules arranged regularly -Operations limited to chambers -Space left between modules for sufficient routing

clear path to its destination

Good

Best

Online Assay Interpretation

Area Usage

Performance

-Routes deadlock free because of fixed placer -Module spacing guarantees valid path -Module I/O cells prevent droplet deadlock

| ľ | | \triangleleft | \triangleleft | 4 | \triangleleft | | ·'- | 12 | \triangleleft | \triangleleft | \sim | ~ | | |
|----|----|--------------------|-----------------|------------------|-----------------|-------|-------|-----------------|-----------------|-----------------|---------------|---------------|-----|--|
| 10 | | Ś | Q | 9_ 6 | Q | | 15_ | 13 | Ś | Q | Q | Q | | |
| 11 | | | | 9_ 5 | | | 15_ | 14 | | | 11_ | 7 | | |
| 12 | | 11_ | 171_ | 18 <u>81 4</u> | 1151_ | 1141_ | 115_ | 181_ | m_ | 101_9 | 911_1 | B | | |
| 13 | IR | 1ík_ | ¹⁹ R | 9 _⊒ 3 | IR | IR | 15_ | 16 _R | IR | IR | IR | IR | IR | |
| 14 | IR | 1 <mark>₩</mark> 2 | 21612 | 20 <u>52</u> : | 21612 | 瞴 | 1155_ | 17 _R | M1 | 0 1 1 | 0 1 91 | 0 1 91 | 01R | |
| 15 | IR | 1612 | 8 9 M2 | 9 _M 1 | 0M2 | 0IR | | IR | M1 | 0 1 1 | 0 1 91 | 0 1 1 | 01R | |
| 16 | IR | M2 | 0M2 | 9 <u>_0</u> | 0M2 | 0IR | | IR | M1 | 0 1 1 | 0 1 91 | 0 1 91 | 01R | |
| 17 | IR | IR | IR | IR | IR | IR | | IR | IR | IR | IR | IR | IR | |
| 18 | | | | | | | | | | | | | | |

Evaluation of Synthesis Flow

-Performed comparison against classic offline synthesis flow -Performed experiments on Intel i7 and low-powered Atom processor

-List scheduling produces comparable schedules in much less time than long-running iterative algorithms

-Fixed placement/binding takes more space, but finds solutions much quicker

-Routing is a quick process on

| Genetic Scheduling vs. List Scheduling | | | | | | | | | | | |
|--|---------|--------------|-----------|-----------------|-----------|-----------|--|--|--|--|--|
| Davidaria | G | enetic Schec | luling | List Scheduling | | | | | | | |
| вепсптагк | i7 (ms) | Atom (ms) | Sched (s) | i7 (ms) | Atom (ms) | Sched (s) | | | | | |
| PCR | 395 | 2,621 | 12 | 1 | 1 | 12 | | | | | |
| InVitro_1 | 665 | 4,475 | 15 | 0 | 2 | 15 | | | | | |
| InVitro_2 | 1,293 | 8,122 | 17 | 0 | 5 | 19 | | | | | |
| InVitro_3 | 1,990 | 13,156 | 19 | 1 | 13 | 23 | | | | | |
| InVitro_4 | 3,541 | 22,376 | 23 | 1 | 17 | 26 | | | | | |
| InVitro_5 | 5,744 | 39,410 | 31 | 2 | 27 | 35 | | | | | |
| Protein | 3,297 | 22,334 | 110 | 3 | 14 | 116 | | | | | |

| | Placement vs. Binding | | | | | | | | | | | | | |
|--------------------|-----------------------|--------------|-------------|---------------|-----------|-------------|--|--|--|--|--|--|--|--|
|) a m ala ma a ula | Simula | ated Anneali | ing Placer | Module Binder | | | | | | | | | | |
| Senchmark | i7 (ms) | Atom (ms) | %Cells Used | i7 (ms) | Atom (ms) | %Cells Used | | | | | | | | |
| PCR | 16 | 200 | 16 | 0 | 0 | 20 | | | | | | | | |
| nVitro_1 | 621 | 12,843 | 16 | 0 | 0 | 24 | | | | | | | | |
| nVitro_2 | 105,138 | 141,177 | 21 | 0 | 0 | 28 | | | | | | | | |
| nVitro_3 | 72,311 | 506,767 | 29 | 0 | 0 | 36 | | | | | | | | |
| nVitro_4 | 19,789 | 3,317,571 | 32 | 0 | 0 | 45 | | | | | | | | |
| nVitro_5 | 74,899 | 1,399,936 | 36 | 0 | 0 | 48 | | | | | | | | |
| Protein | 4,867,220 | 79,531,695 | 29 | 0 | 4 | 46 | | | | | | | | |
| | | | | | | | | | | | | | | |

| | | | Simplified Roy R | Routing | 5 | | | | |
|-----------|---------|--------------|--------------------|--------------------------------------|-----------|------------------|--|--|--|
| | GA Sc | heduling - S | A Placement Flow | List Scheduling - Module Binding Flo | | | | | |
| Benchmark | ;7 (ma) | Atom (ma) | # Routing Cycles / | ;7 (ma) | Atom (ma) | # Routing Cycles | | | |
| | 17 (ms) | Atom (ms) | # Sub-problems | 17 (ms) | Atom (ms) | # Sub-problems | | | |



Input/output cells on modules of different sizes



both flows; is guaranteed with our online synthesis flow

| PCR | 0 | 2 | 78 / 4 | 0 | 6 | 56 / 4 |
|-----------|---|----|-----------|---|----|----------|
| InVitro_1 | 0 | 2 | 135 / 9 | 0 | 3 | 111/9 |
| InVitro_2 | 0 | 4 | 180 / 11 | 0 | 7 | 167 / 12 |
| InVitro_3 | 0 | 10 | 207 / 15 | 0 | 12 | 209 / 16 |
| InVitro_4 | 0 | 7 | 234 / 15 | 1 | 19 | 299 / 19 |
| InVitro_5 | 1 | 9 | 342 / 22 | 1 | 26 | 351/24 |
| Protein | 5 | 32 | 1212 / 71 | 3 | 76 | 638 / 45 |

| | GA Scł | nedulin | g - SA I | Placement | t - Simp | . Roy I | Routing | List Scheduling - Module Binding - Simp. Roy Routing | | | | | | | | | | |
|-------------------|-----------|--------------|----------|-----------|----------|---------|---------------|--|----------|-------------|-----------|--------|--------|---------------|--|--|--|--|
| | | Offline Flow | | | | | | | | Online Flow | | | | | | | | |
| -Our flow much | Denehmenk | Sche | dule | Placement | Rou | ting | Total | Donohmorik | Schedule | | Placement | Rou | ting | Total | | | | |
| more feasible for | вепсптагк | AT (s) | CT (s) | CT (s) | AT (s) | CT (s) | (AT + CT) (s) | вепсптагк | AT (s) | CT (s) | CT (s) | AT (s) | CT (s) | (AT + CT) (s) | | | | |
| | PCR | 12 | 3 | 0 | 1 | 0 | 16 | PCR | 12 | 0 | 0 | 0 | 0 | 12 | | | | |
| online synthesis | InVitro_1 | 15 | 4 | 13 | 1 | 0 | 34 | InVitro_1 | 15 | 0 | 0 | 0 | 0 | 15 | | | | |
| hacause of fast | InVitro_2 | 17 | 8 | 141 | 2 | 0 | 168 | InVitro_2 | 19 | 0 | 0 | 0 | 0 | 19 | | | | |
| because of last | InVitro_3 | 19 | 13 | 507 | 2 | 0 | 541 | InVitro_3 | 23 | 0 | 0 | 0 | 0 | 23 | | | | |
| algorithms | InVitro_4 | 23 | 22 | 3,318 | 2 | 0 | 3,365 | InVitro_4 | 26 | 0 | 0 | 0 | 0 | 26 | | | | |
| U | InVitro_5 | 31 | 39 | 1,400 | 3 | 0 | 1,474 | InVitro_5 | 35 | 0 | 0 | 0 | 0 | 35 | | | | |
| | Protein | 110 | 22 | 79,532 | 12 | 0 | 79,676 | Protein | 116 | 0 | 0 | 1 | 0 | 117 | | | | |

Contact

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