A Field-Programmable Pin-Constrained Digital Microfluidic Biochip

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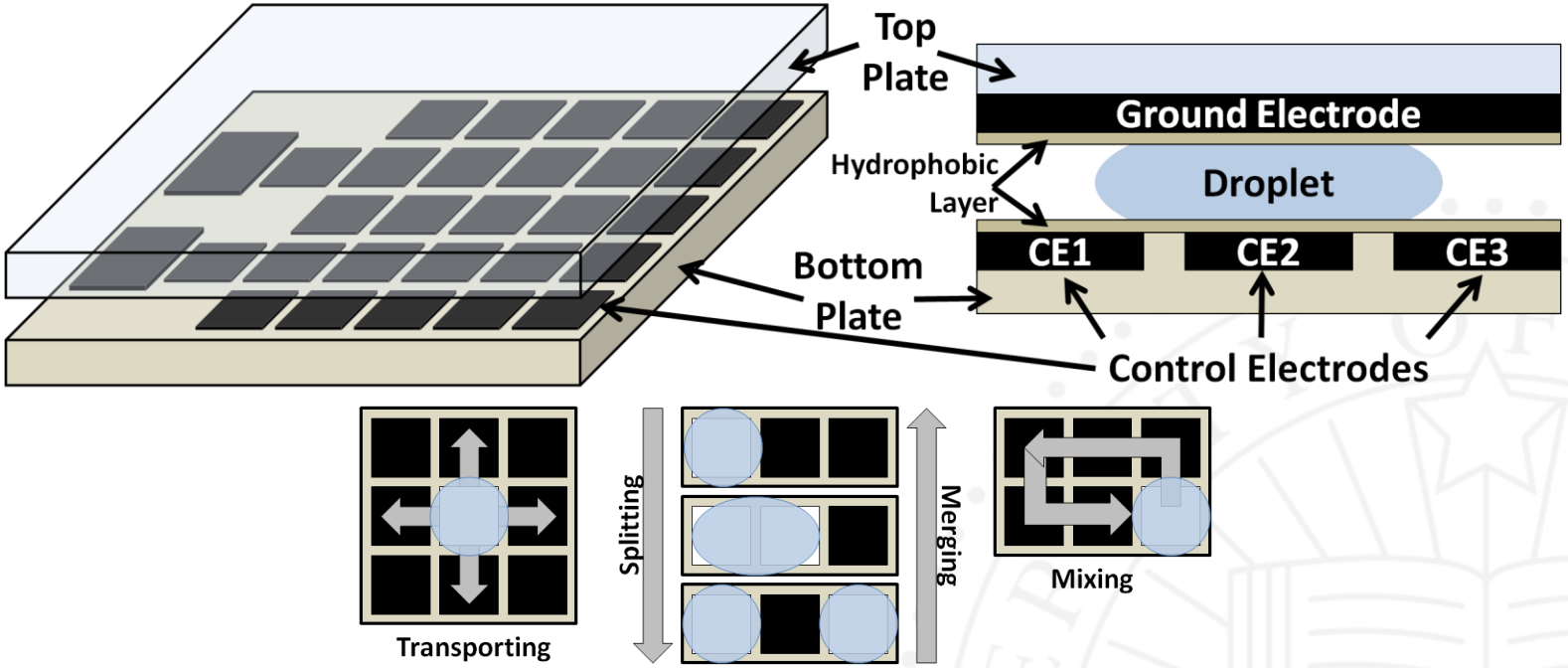
Digital Microfluidic Technology

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:

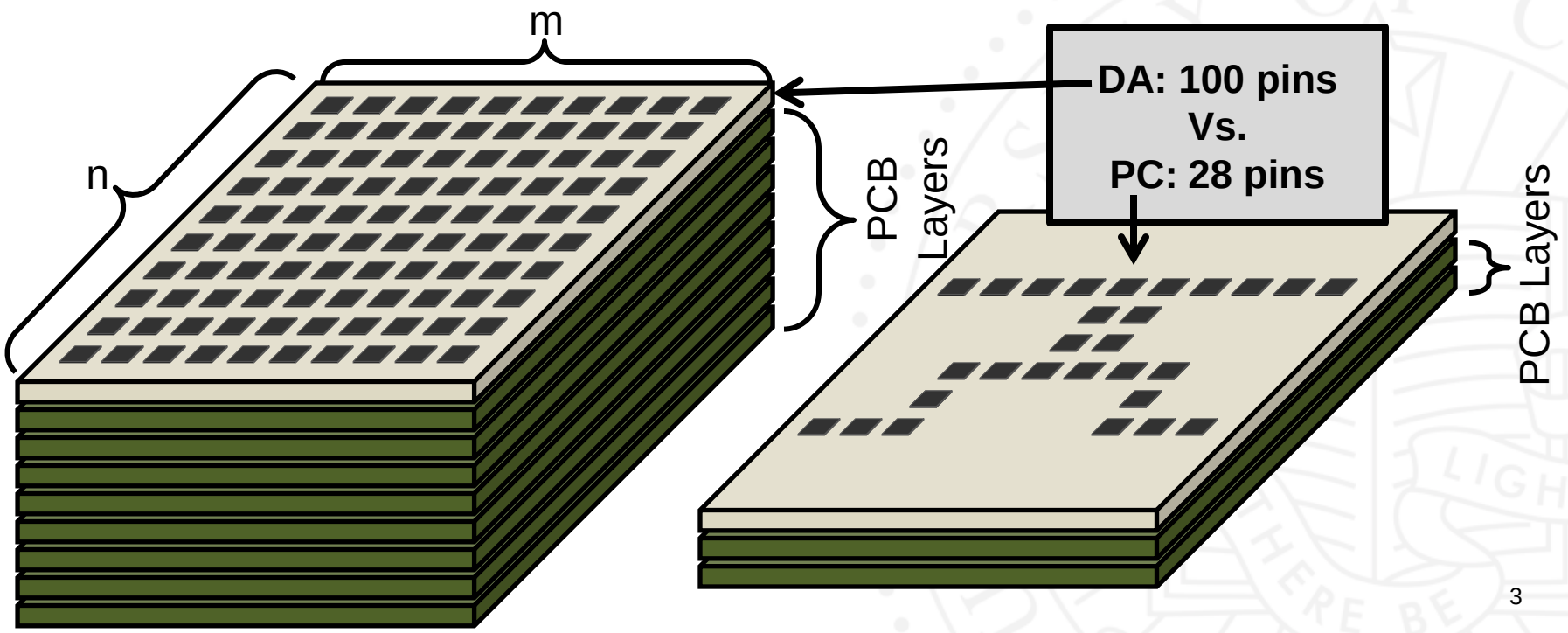
- Clinical pathology
- Point of care diagnostics
- Drug discovery
- Proteomics, DNA, PCR, etc.
- Real-time detection of biochemical terror attacks

Key advantages:

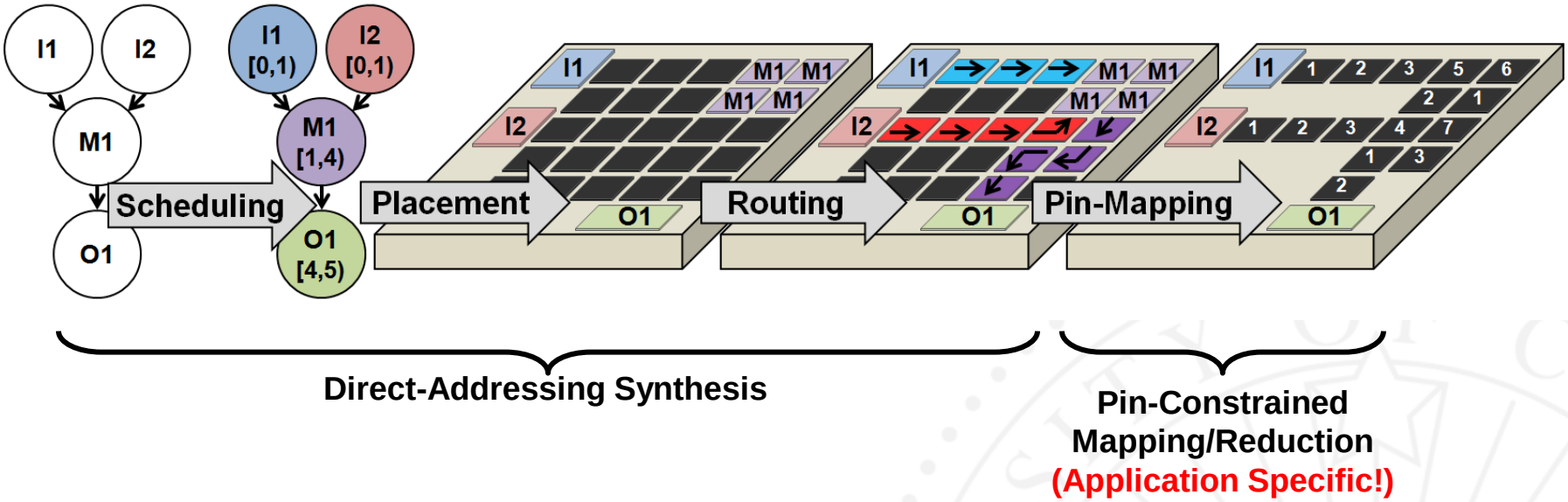
- Reduced cost
- Reduced reagent and sample sizes
- Increased throughput and efficiency
- Increased sensitivity and accuracy
- Automation and miniaturization

Goal

- **Goal:** DMFBs that are BOTH inexpensive & general-purpose
  - Affordable & accessible to poor/remote communities
  - Encourage broader and more-general use of microfluidics
- **Problem:**
  - Direct-addressing wire-routing is expensive ($m \times n$ wires)
  - Pin-constrained devices are application specific ($< m \times n$ wires)



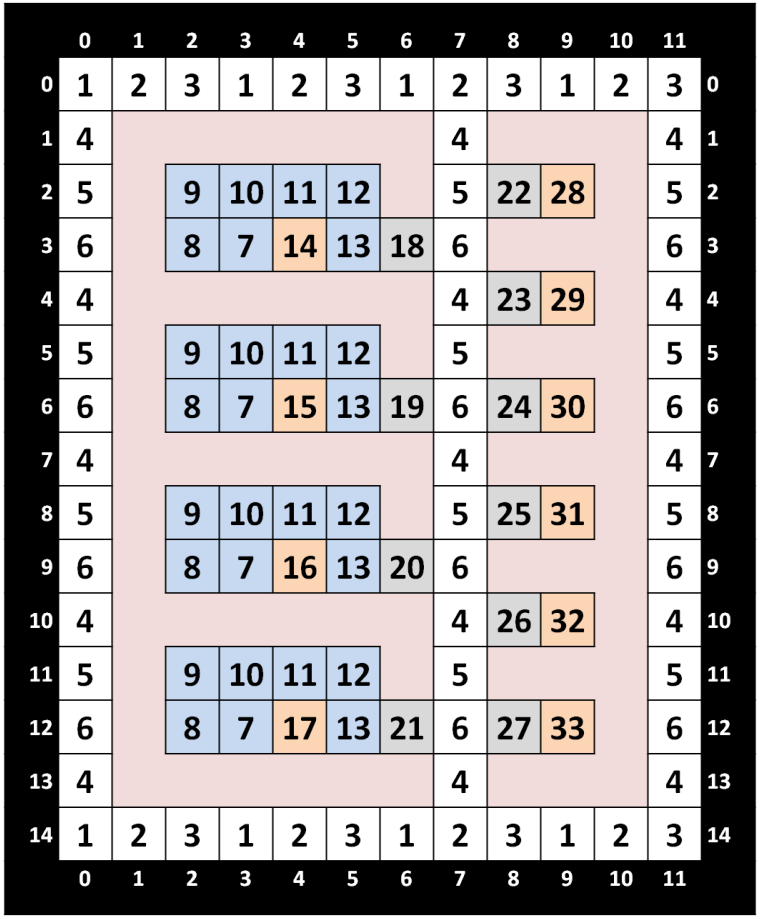
Pin-Constrained Synthesis



Typically, synthesis is first performed as on a direct-addressing DMFB (where electrodes are individually addressable); then, once a deterministic electrode-activation sequence is obtained, pin-constrained algorithms are used to tie groups of electrodes together to common external pins.

The Solution

- **Solution:** Field-programmable, pin-constrained (FPPC) DMFB
  - Generally and field-programmable (programmable after purchase)
  - Reduced pin-count (PCB layers) from direct-addressing DMFBs



ELECTRODE LEGEND

1-6	Routing (S)
7-13	Mixing (S)
14-17	Mixer Hold (I)
18-21	Mixer I/O (I)
22-27	Split-Store-Det. (SSD) I/O (I)
28-33	Split-Store-Det. (SSD) Hold (I)
	Interference Region (not actual electrode)

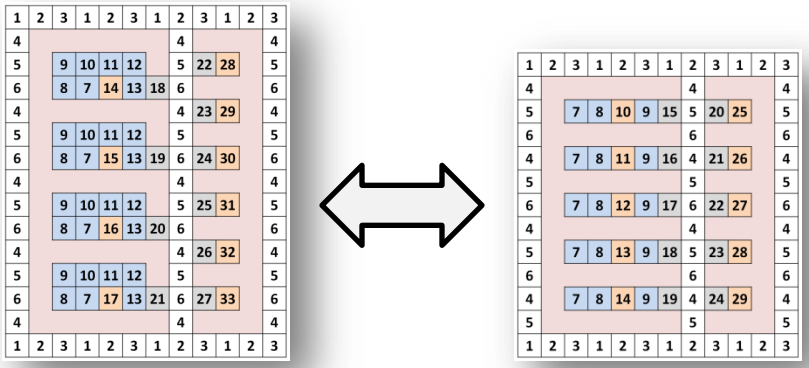
* S = Shared Pin, I = Independent Pin

	DMFB Type	
	DA	FPPC
Dimensions	12w × 15h	
# Electrodes	180	111
# Unique Pins	180	33

FPPC DMFB Features

- **Resizing without changing synthesis methods**
  - **DMFB Elongation**

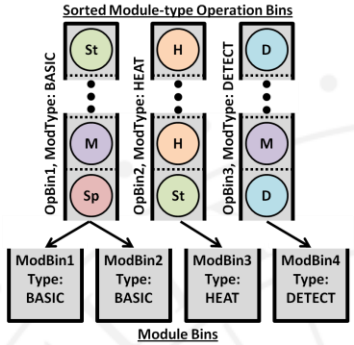
  - **Module-Size Variation**

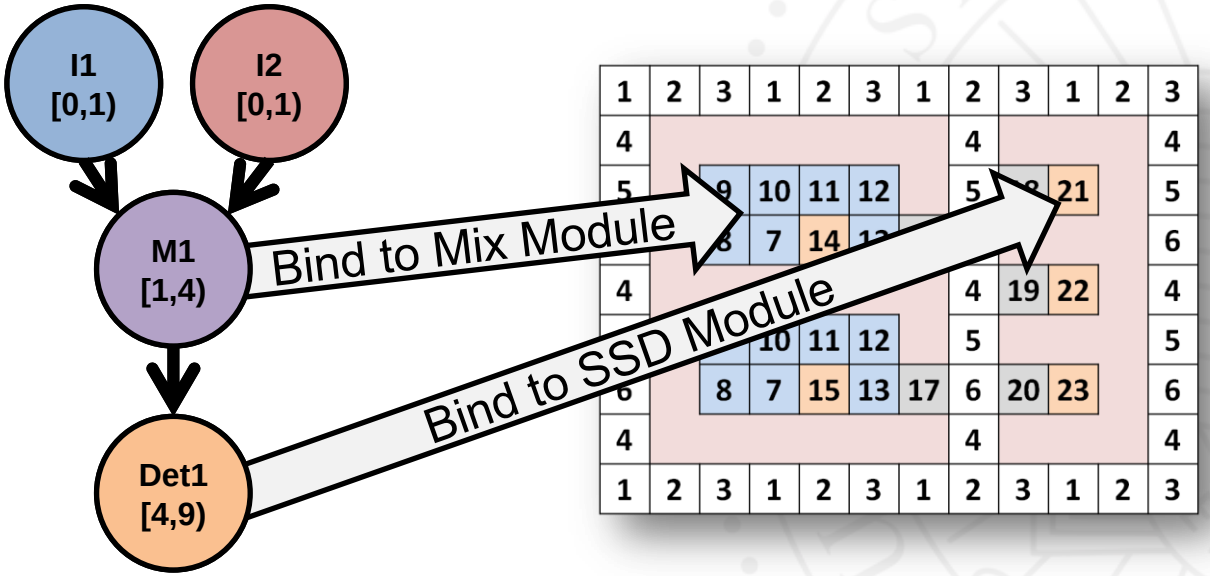


Allows users to buy off-the-shelf DMFBs with enough resources to run their assay.

FPPC DMFB Synthesis

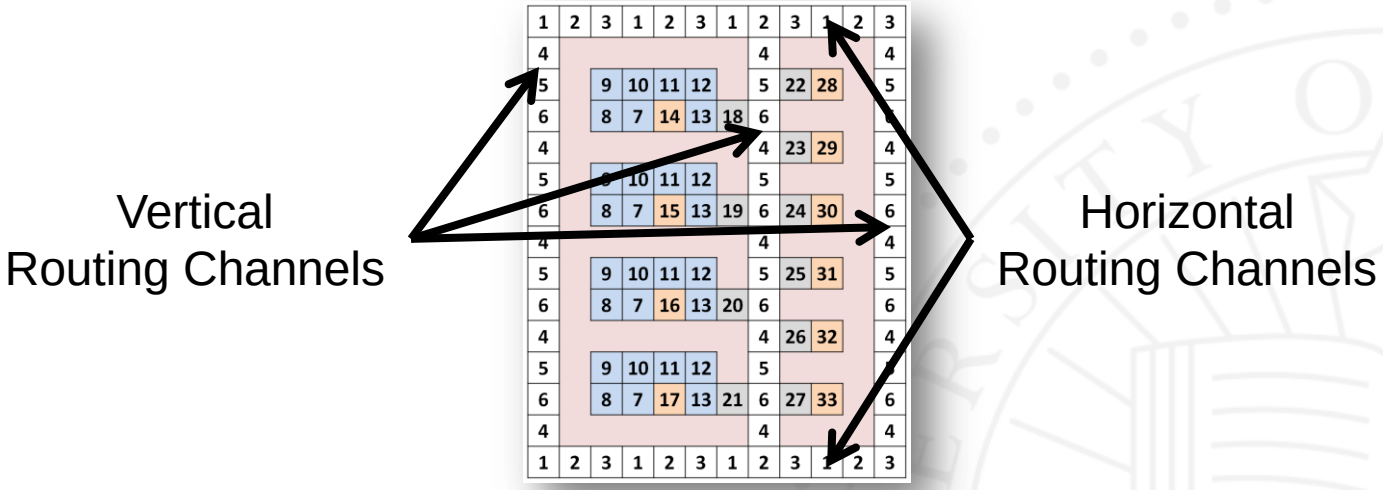
- **Complete Synthesis**
  - **List Scheduling onto discrete resources**
    - **e.g. 4 mixers, 4 split/store/detect modules**
  - **Simple, fast left-edge binding**



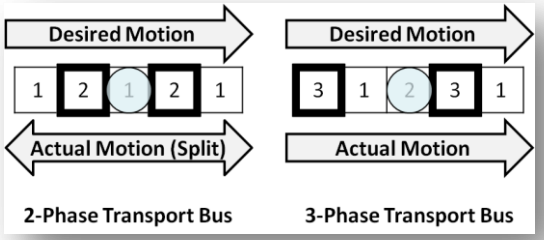


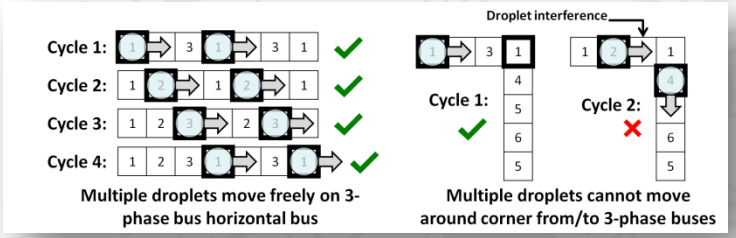
FPPC DMFB Droplet Routing

- **Complete Synthesis (cont'd)**
  - **Sequential router (I/O→Module, Module→Module, Module→I/O)**
    - **Routing cycles << operation time-steps**
    - **Horizontal/vertical routing channels**



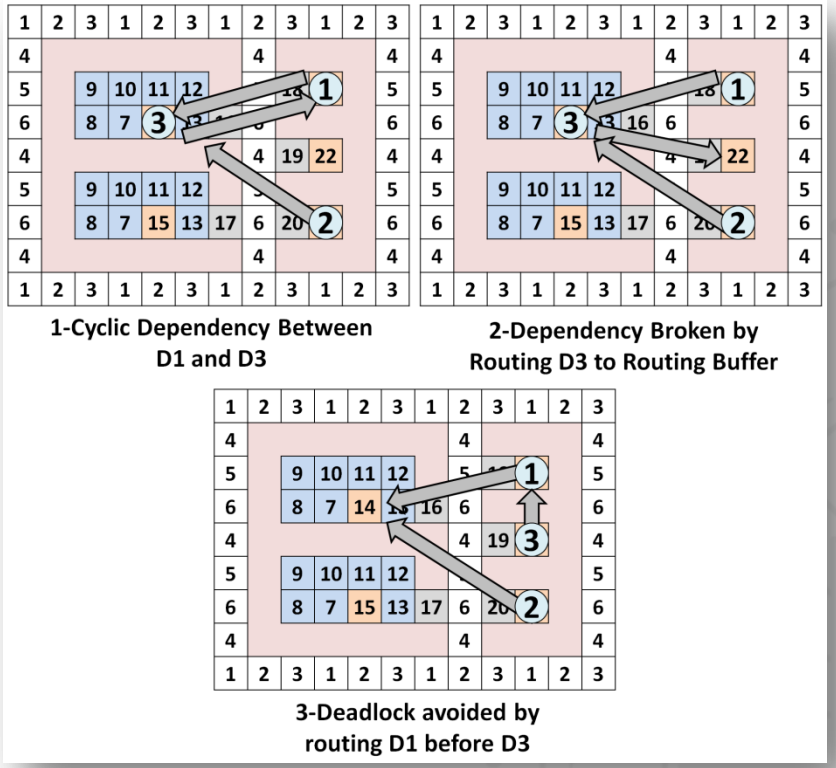
  - **3-pins per channel**





FPPC DMFB Deadlock Resolution

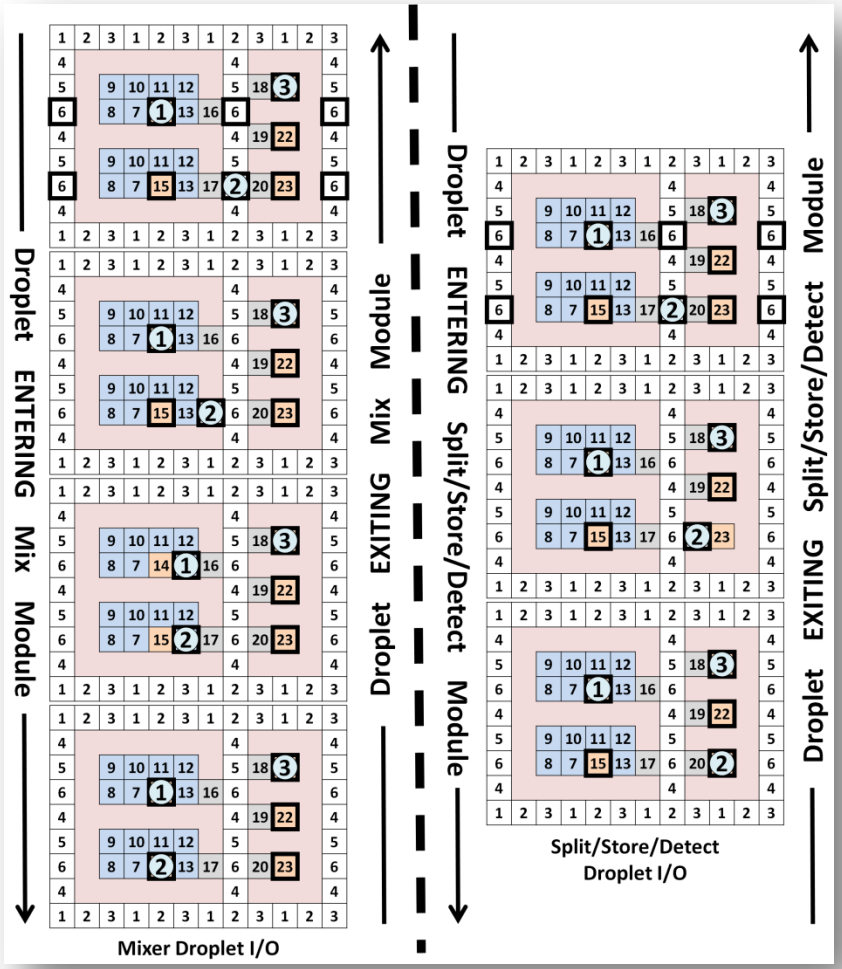
- **Well-defined deadlock-resolution policies**
  - **At least 1 SSD module left free for deadlock resolution**

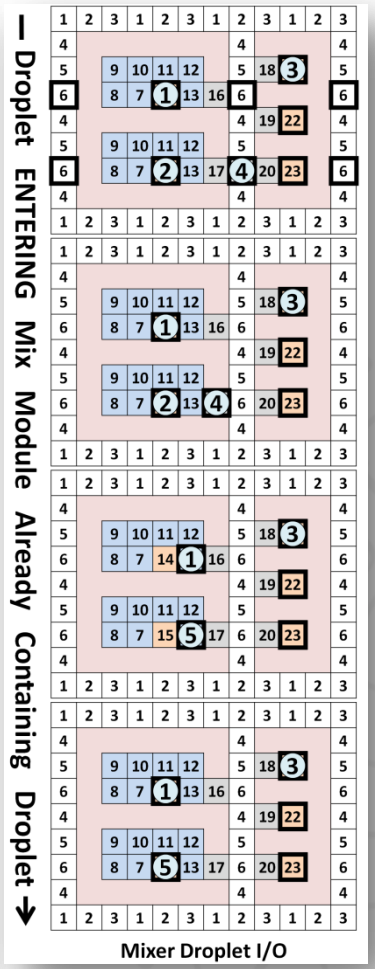


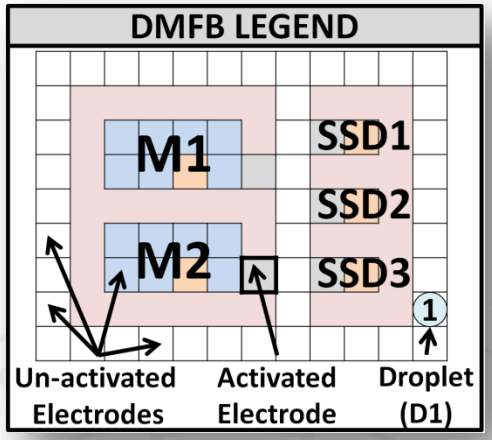
Cyclic routing dependencies can be broken by first routing a droplet in the cycle to the routing buffer module (one of the SSD modules). Arrows indicate that the droplet at the tail end is about to travel to the module at the head end.

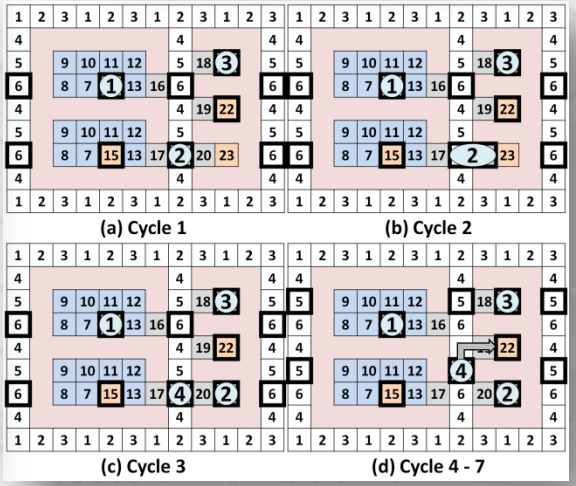
FPPC DMFB Module I/O

- **Well-defined module I/O**









Experimental Results

FPPC DMFB vs. Direct-Addressing DMFB

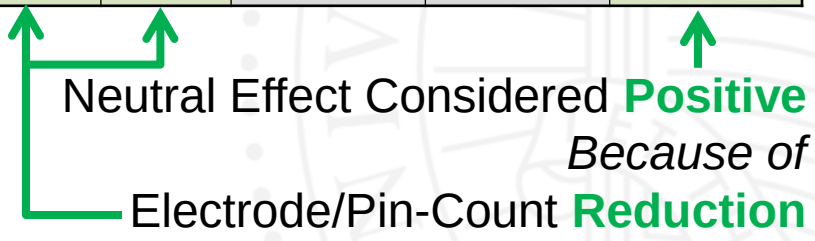
Direct-Addressing DMFB (DA) vs. Field-Programmable Pin-Constrained DMFB (FP)												
Benchmarks	Array Dim.		# Electrodes Used		# Pins		Routing Time (s)		Operations Time (s)		Total Time (s)	
	DA	FP	DA	FP	DA	FP	DA	FP	DA	FP	DA	FP
PCR	15x19	12x21	285	153	285	43	0.7	2.1	11	11	11.7	13.1
In-Vitro 1	15x19	12x21	285	153	285	43	0.7	2.6	14	14	14.7	16.6
In-Vitro 2	15x19	12x21	285	153	285	43	1.2	3.8	18	18	19.2	21.8
In-Vitro 3	15x19	12x21	285	153	285	43	1.9	6.2	22	18	23.9	24.2
In-Vitro 4	15x19	12x21	285	153	285	43	1.8	8.8	24	19	25.8	27.8
In-Vitro 5	15x19	12x21	285	153	285	43	2.9	11.6	32	25	34.9	36.6
Protein Split 1	15x19	12x21	285	153	285	43	1.8	2.9	71	71	72.8	73.9
Protein Split 2	15x19	12x21	285	153	285	43	6.2	6.1	106	106	112.2	112.1
Protein Split 3	15x19	12x21	285	153	285	43	13.9	13.5	176	176	189.9	189.5
Protein Split 4	15x19	12x21	285	153	285	43	32.9	29.3	316	316	348.9	345.3
Protein Split 5	15x19	12x25	285	177	285	49	63.6	61.4	670	596	733.6	657.4
Protein Split 6	15x25	12x29	375	203	375	55	161.2	127.4	1156	1156	1317.2	1283.4
Protein Split 7	15x25	12x31	375	239	375	63	290.3	260.6	2353	2276	2643.3	2536.6
Avg. Normalized Improvement: (> 1 is improvement)			**1.82**		**6.53**		**0.68**		**1.07**		**0.98**	

Negative Impact on Routing
Offset by
Positive Impact on Operation Time
Yields
Neutral Effect on Overall Assay Time

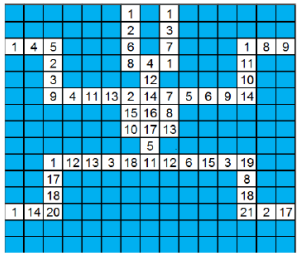
Experimental Results (Cont'd)

FPPC DMFB vs. Direct-Addressing DMFB

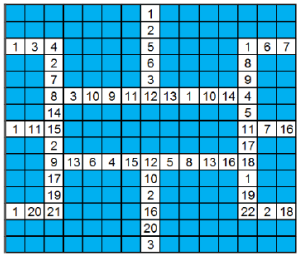
Direct-Addressing DMFB (DA) vs. Field-Programmable Pin-Constrained DMFB (FP)												
Benchmarks	Array Dim.		# Electrodes Used		# Pins		Routing Time (s)		Operations Time (s)		Total Time (s)	
	DA	FP	DA	FP	DA	FP	DA	FP	DA	FP	DA	FP
PCR	15x19	12x21	285	153	285	43	0.7	2.1	11	11	11.7	13.1
In-Vitro 1	15x19	12x21	285	153	285	43	0.7	2.6	14	14	14.7	16.6
In-Vitro 2	15x19	12x21	285	153	285	43	1.2	3.8	18	18	19.2	21.8
In-Vitro 3	15x19	12x21	285	153	285	43	1.9	6.2	22	18	23.9	24.2
In-Vitro 4	15x19	12x21	285	153	285	43	1.8	8.8	24	19	25.8	27.8
In-Vitro 5	15x19	12x21	285	153	285	43	2.9	11.6	32	25	34.9	36.6
Protein Split 1	15x19	12x21	285	153	285	43	1.8	2.9	71	71	72.8	73.9
Protein Split 2	15x19	12x21	285	153	285	43	6.2	6.1	106	106	112.2	112.1
Protein Split 3	15x19	12x21	285	153	285	43	13.9	13.5	176	176	189.9	189.5
Protein Split 4	15x19	12x21	285	153	285	43	32.9	29.3	316	316	348.9	345.3
Protein Split 5	15x19	12x25	285	177	285	49	63.6	61.4	670	596	733.6	657.4
Protein Split 6	15x25	12x29	375	203	375	55	161.2	127.4	1156	1156	1317.2	1283.4
Protein Split 7	15x25	12x31	375	239	375	63	290.3	260.6	2353	2276	2643.3	2536.6
Avg. Normalized Improvement: (> 1 is improvement)			**1.82**		**6.53**		**0.68**		**1.07**		**0.98**	



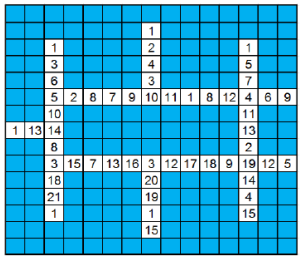
Pin-Constrained Comparison



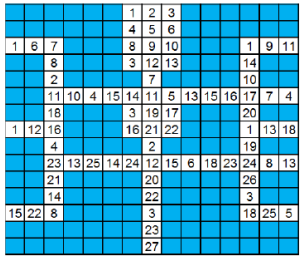
Multiplexed Immunoassay DMFB



PCR Assay DMFB



Protein Dilution Assay DMFB



Multi-Functional DMFB

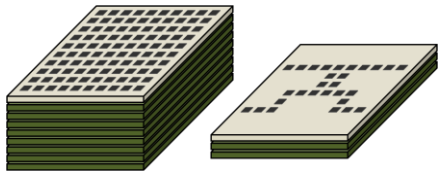
Xu's Pin-Constrained Results vs. Luo's Pin-Constrained Results						
Benchmark	Array Dim.	# Electrodes Used	# Pins		Total Time (s)	
			Xu	Luo	Xu	Luo
PCR	15x15	62	14	22	20	30
In-Vitro 1	15x15	59	25	21	73	90
Protein Split 3	15x15	54	26	20	150	170
Multi-Function	15x15	81	37	27	150	170

Total Assay Times for Increasing FPPC Array Size						
Array Dim.	#Module (Mix/SSD)	# Electrodes Used	# Pins	Total Time(s)		
				PCR	In-Vitro 1	Protein Split 3
12x9	2/3	62	23	18.59	19.00	-
12x12	3/4	89	27	15.89	17.26	-
12x15	4/6	111	33	12.88	16.56	-
12x18	5/7	133	39	13.00	16.60	189.65
12x21	6/9	153	43	13.08	16.60	189.53

- **Pin-usage for FPPC design on par with optimized PC DMFBs**
- **FPPC can perform general assays vs. optimized PC DMFB's 3 specific assays**

Conclusion

- New DMFB design
  - Pin-constrained design → Inexpensive
  - Field-programmable → Execute general assays

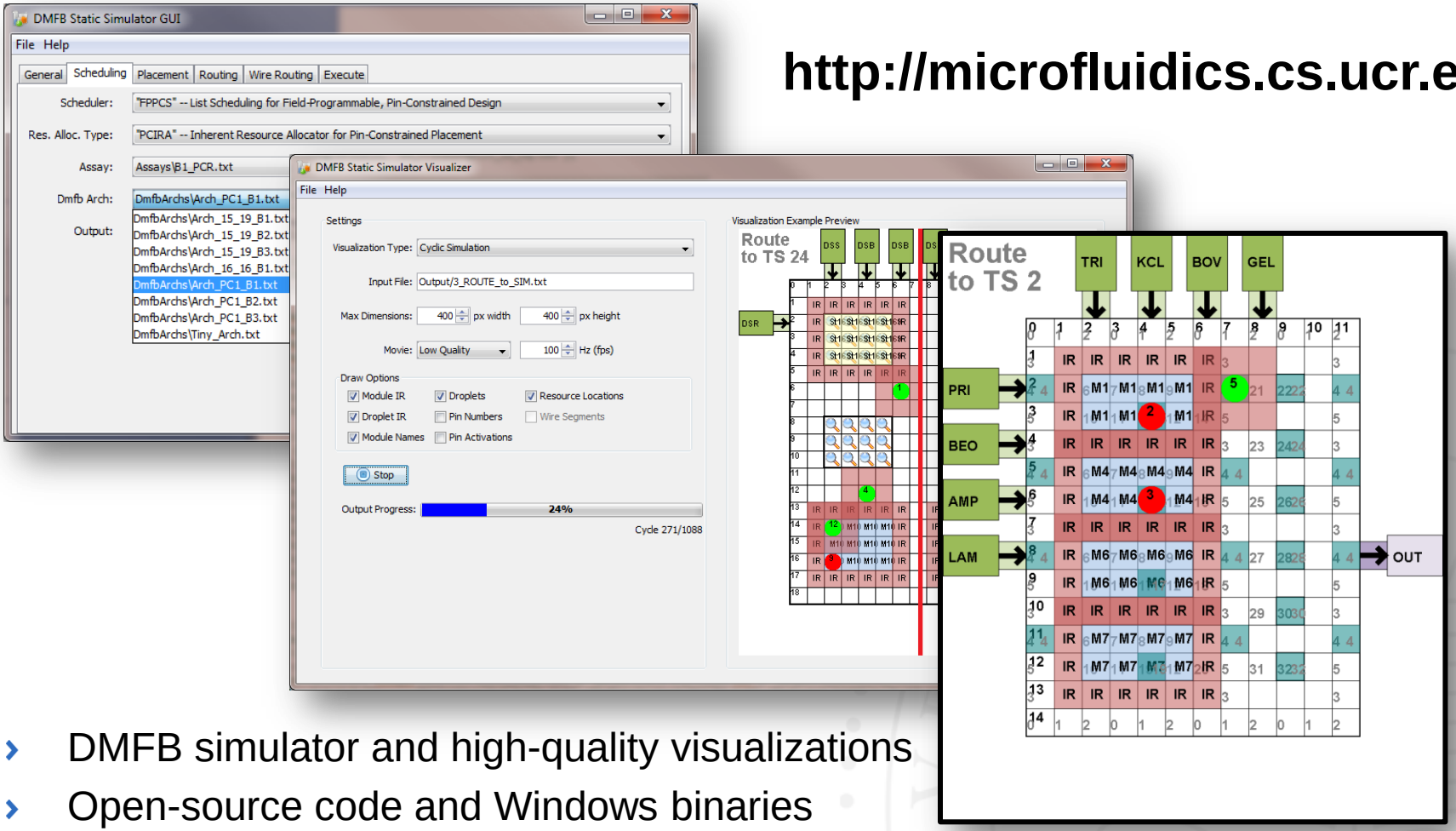


- Can buy an inexpensive, off-the-shelf device and run desired assay
  - Design facilitates different DMFB and module sizes

- Best of both worlds
  - Similar assay times and **flexibility** to recent direct-addressing DMFBs
  - Similar pin-counts to recent pin-constrained designs

Download the Framework

http://microfluidics.cs.ucr.edu



- DMFB simulator and high-quality visualizations
- Open-source code and Windows binaries
- Includes a number of synthesis methods including source code for DAC 2013
- Great for research implementations, teaching (project course work), high-quality graphics (for papers and presentations) and more…