

Miniaturizing 3D Printed Microfluidics

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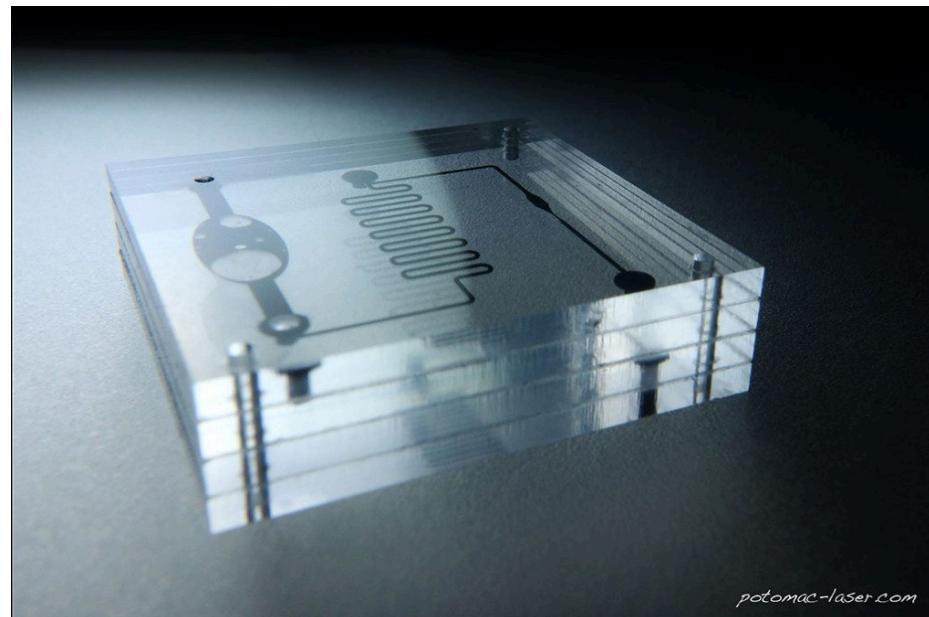
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Microfluidic Devices

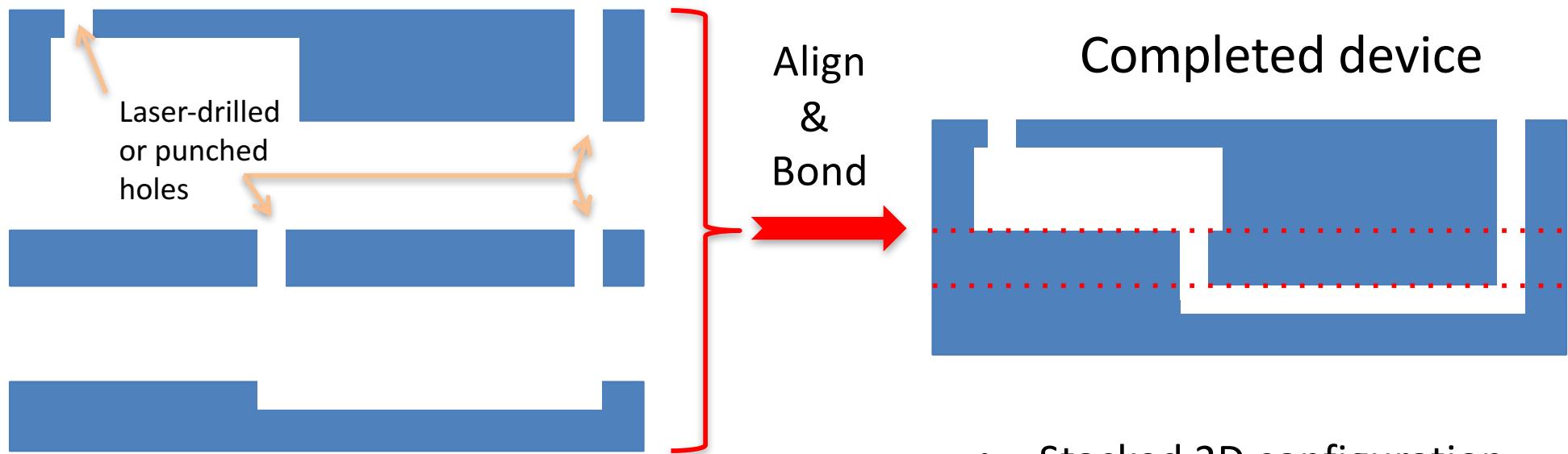
- Comprise interconnected hollow regions (voids) in bulk material



- Microfluidics → **micro**voids (<100 μm)

Traditional Microfluidic Device Fabrication

Individual layers



Layers:

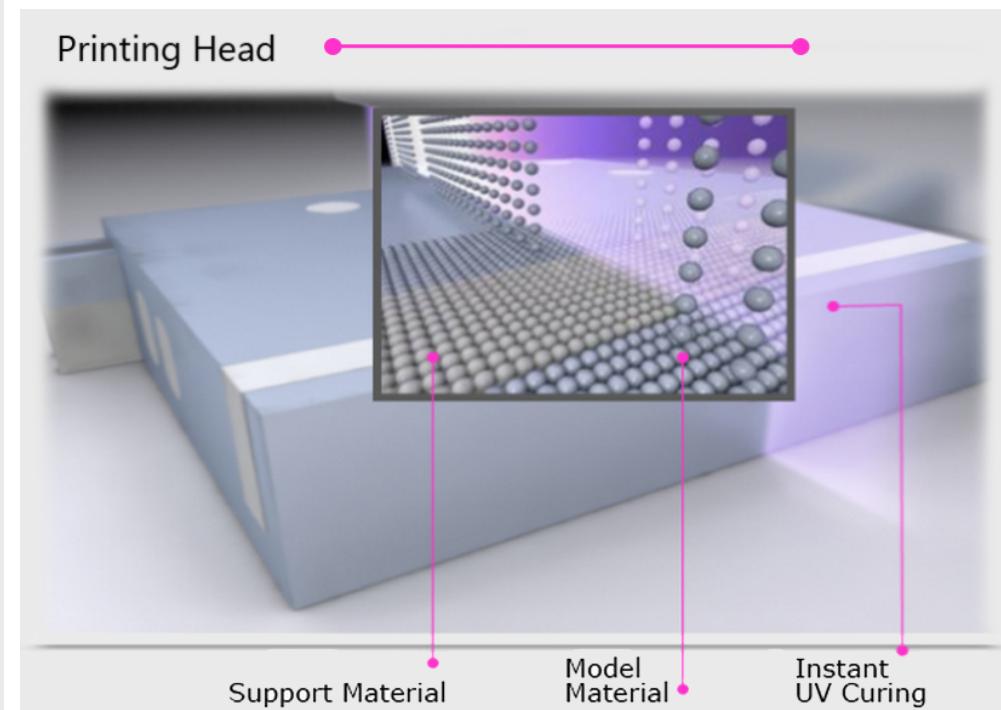
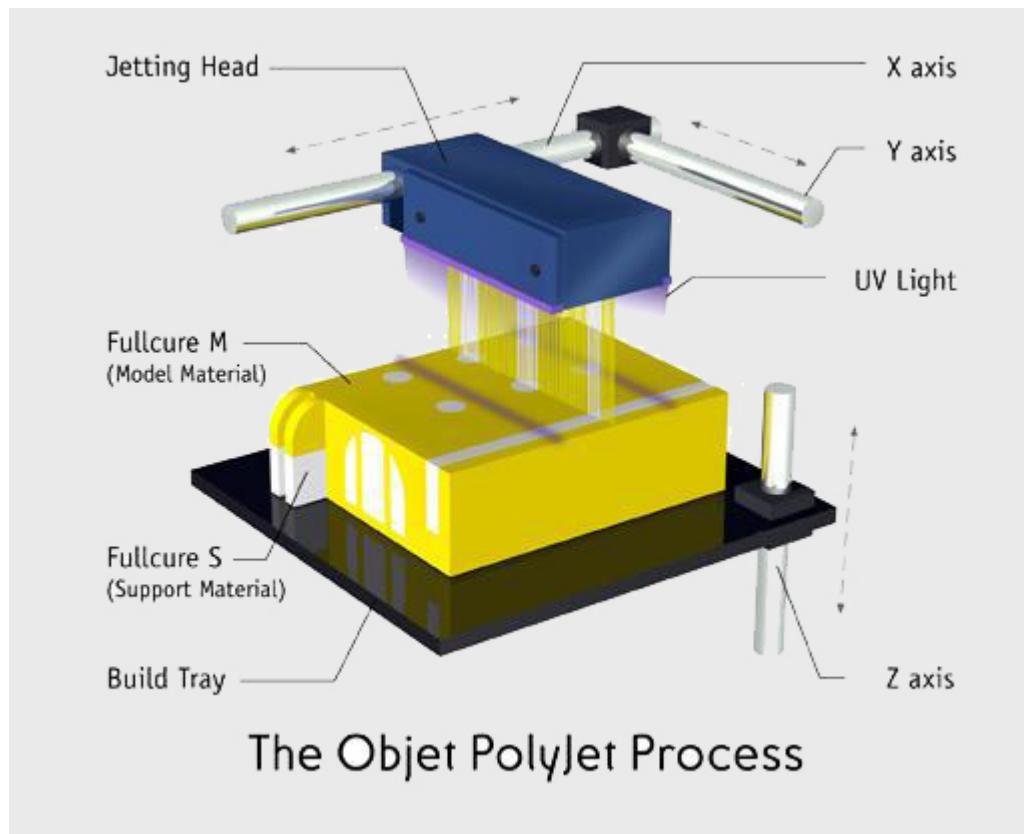
- Hot-embossed or injection molded plastics
 - External valves
- PDMS
 - Elastomeric
 - Integrated valves

- Stacked 2D configuration
- Few layers

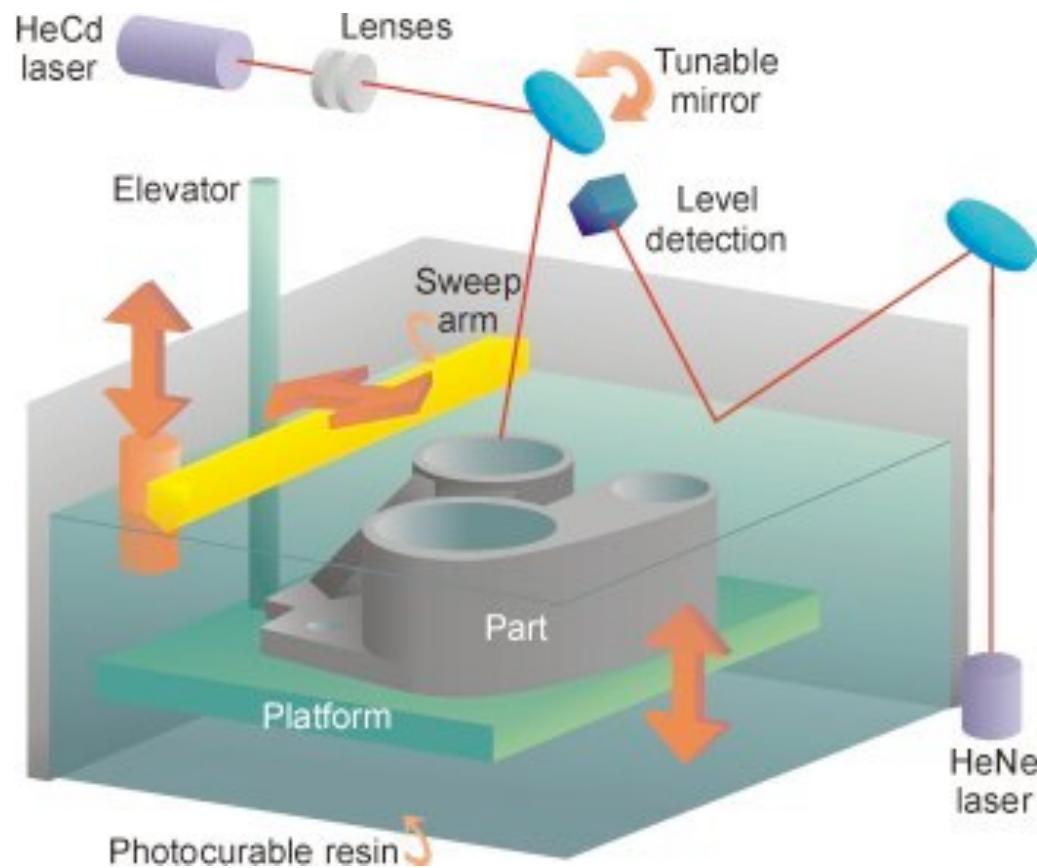
3D Printing

- Possible approaches:
 1. Existing commercial printers and materials
 2. Existing commercial printers + custom materials
 3. New tools + custom materials
- Microfluidics → **microvoids (<100 μm)**

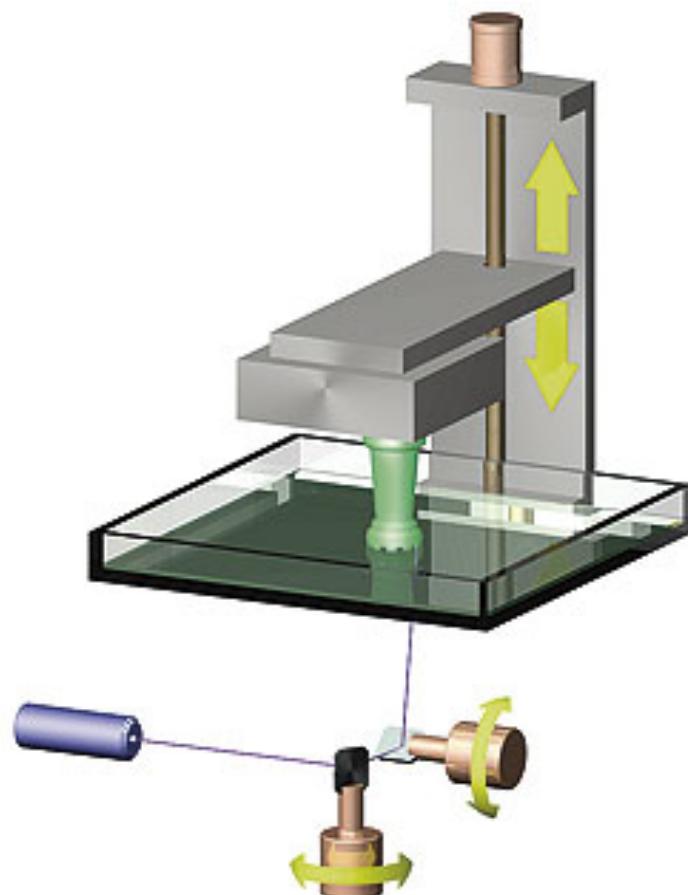
Inkjet – Polyjet - Multijet



Stereolithography: Scanned Laser—Top



Stereolithography: Scanned Laser—Bottom



Formlabs Form 2
\$3,500

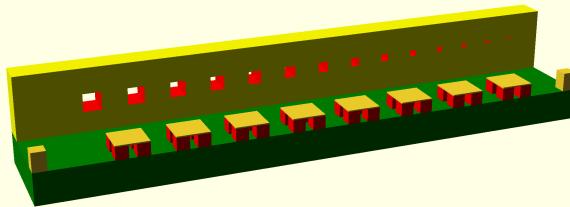


[http://www.meccanismocomplesso.org/en/
xfab-la-stampante-3d-laser-per-il-mercato-consumer/](http://www.meccanismocomplesso.org/en/xfab-la-stampante-3d-laser-per-il-mercato-consumer/)

Commercial 3D Printer Service Bureaus

- High-end 3D printers
- Commercial resins

Gong et al., RSC Adv. 5, 106621 (2015)



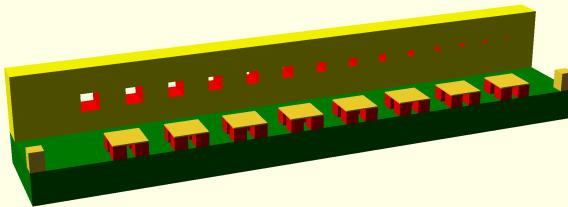
- Channels
 - 1.08 mm long
- Printer resolution
 - SLA—Scanned Laser:
 - 75 μm in x-y
 - 25 μm in z
 - Polyjet:
 - 42 μm in x-y
 - 16 μm in z

Channel size	Invent-A-Part	Stratasys Polyjet	Stratasys μHDSL	3D Systems Quickparts	Fineline
700 μm \times 700 μm					
650 μm \times 650 μm					
600 μm \times 600 μm					
550 μm \times 550 μm					
500 μm \times 500 μm					
450 μm \times 450 μm					
400 μm \times 400 μm					
350 μm \times 350 μm					
300 μm \times 300 μm					
250 μm \times 250 μm					

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650 μm \times 650 μm					

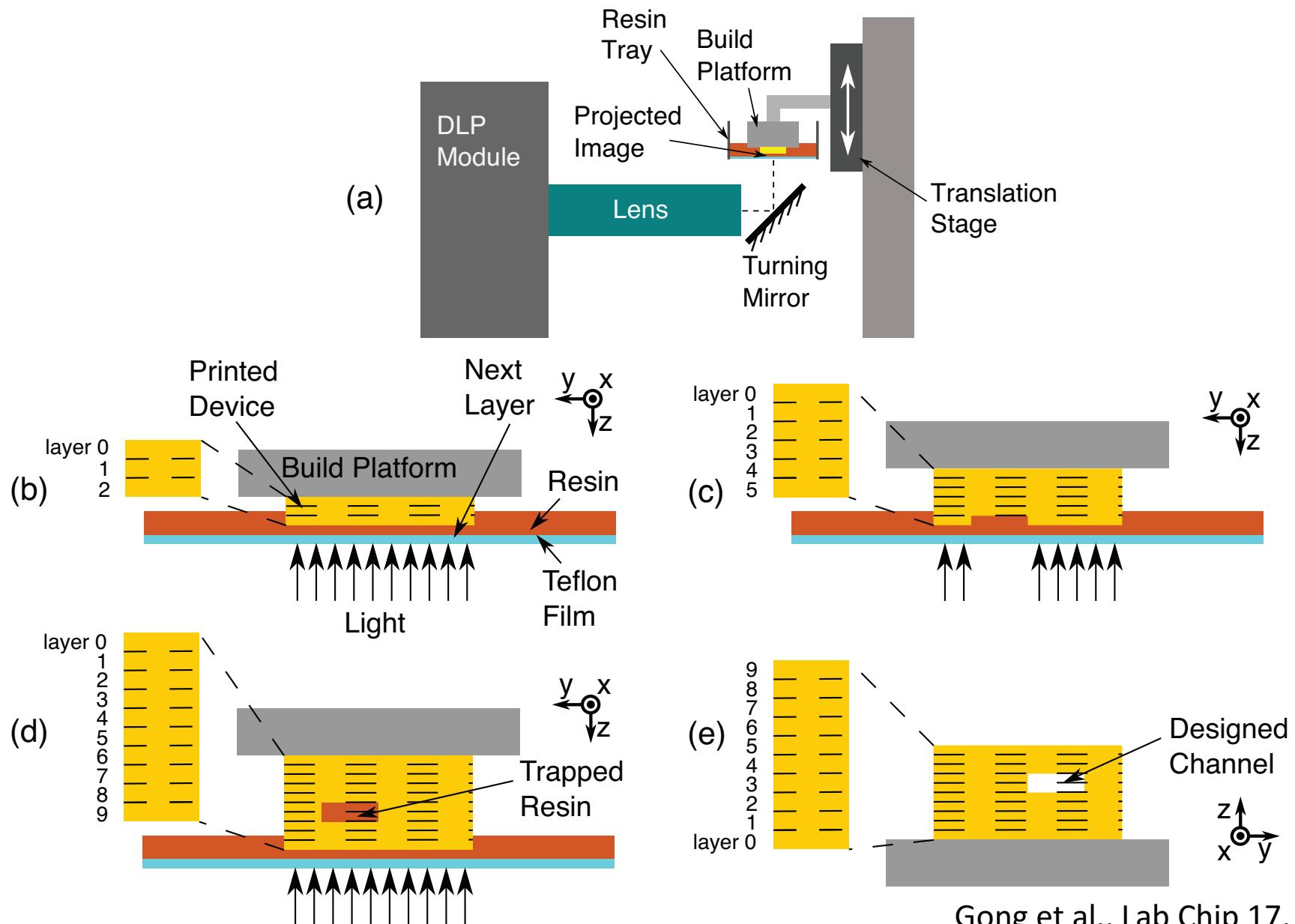
Manufacturer resolution specs



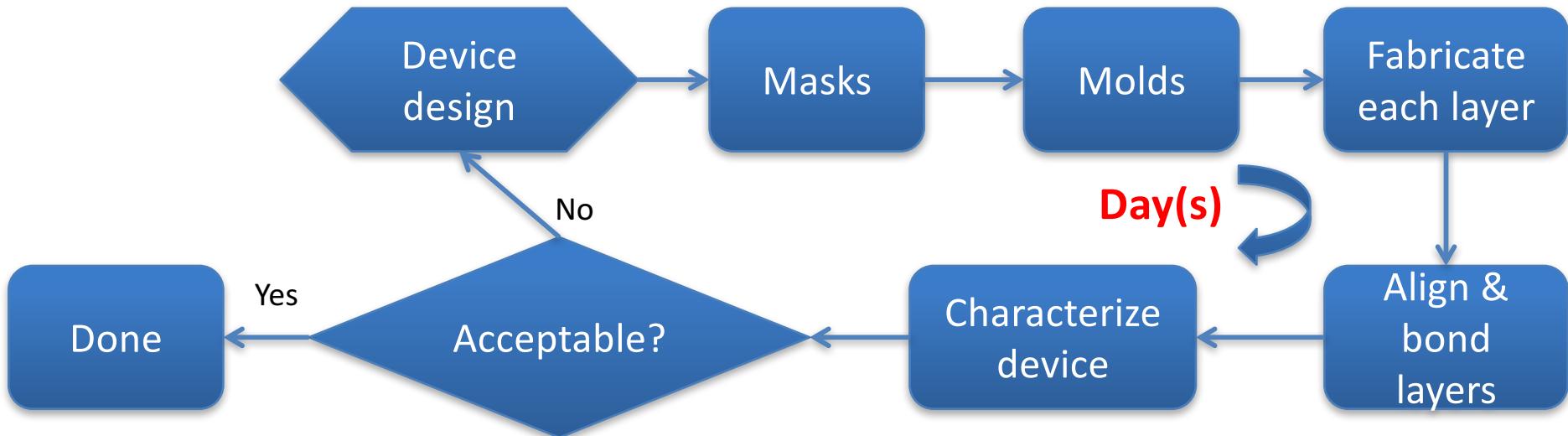
Achievable void size!

350 μm \times 350 μm					
300 μm \times 300 μm					
250 μm \times 250 μm					

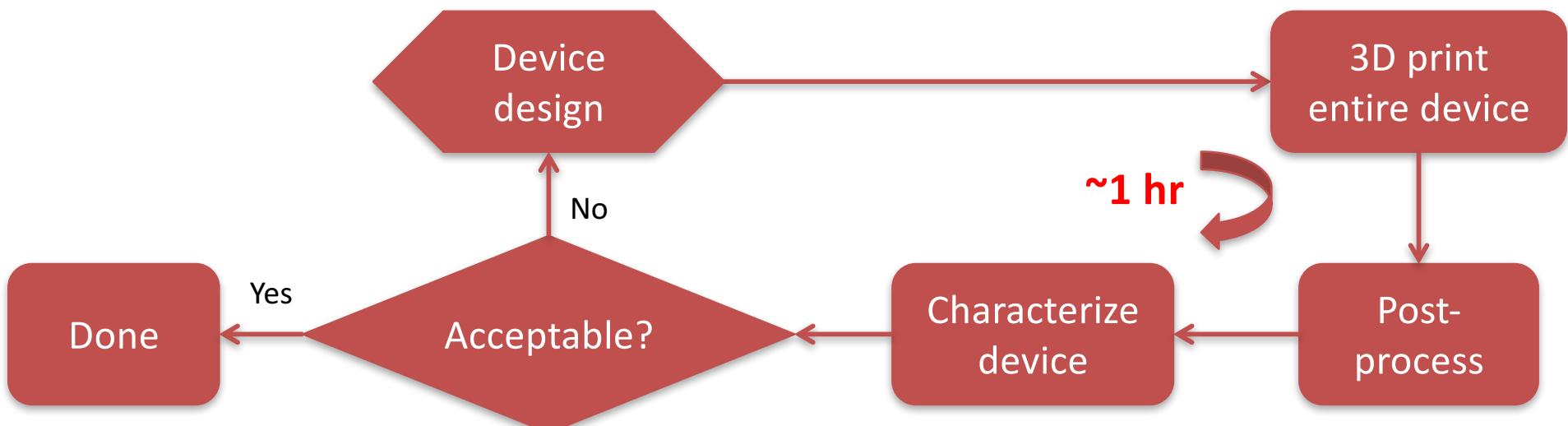
DLP-SLA 3D Printing for Microfluidic Devices



Process - Conventional



Process – 3D printer



Benefits

- True rapid prototyping
- Development process becomes:
 - Fail fast & often
 - Early & rapid empirical feedback drives progress
- Dramatic reduction in:
 - Opportunity cost to try new ideas
 - Barrier to entry
 - No cleanroom required
- Utilize full 3D volume
 - Size reduction
 - Parallel fabrication → path to manufacturing
 - Same tooling and materials for prototyping and manufacturing

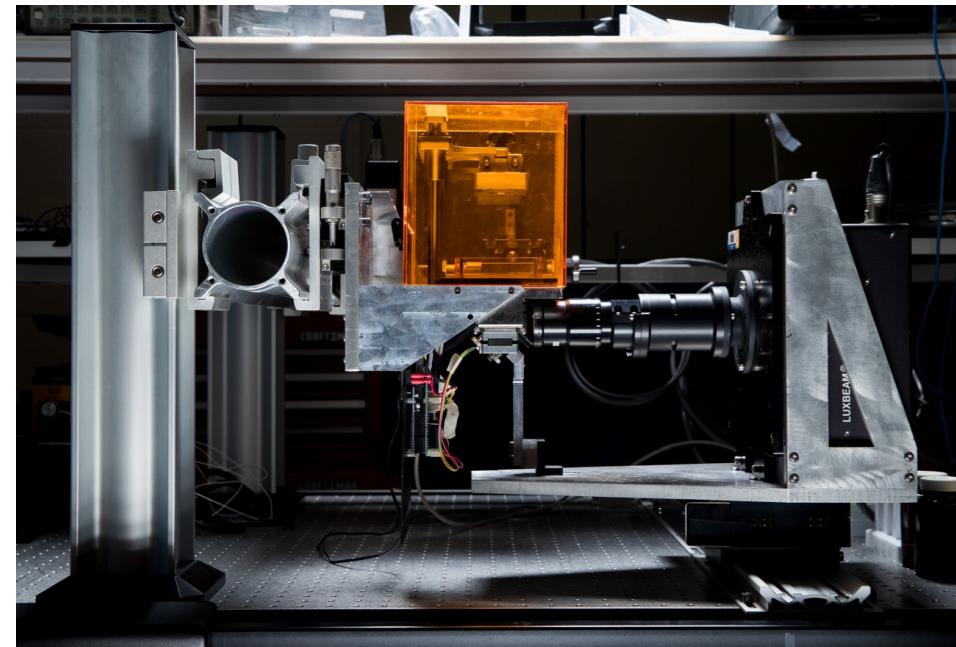
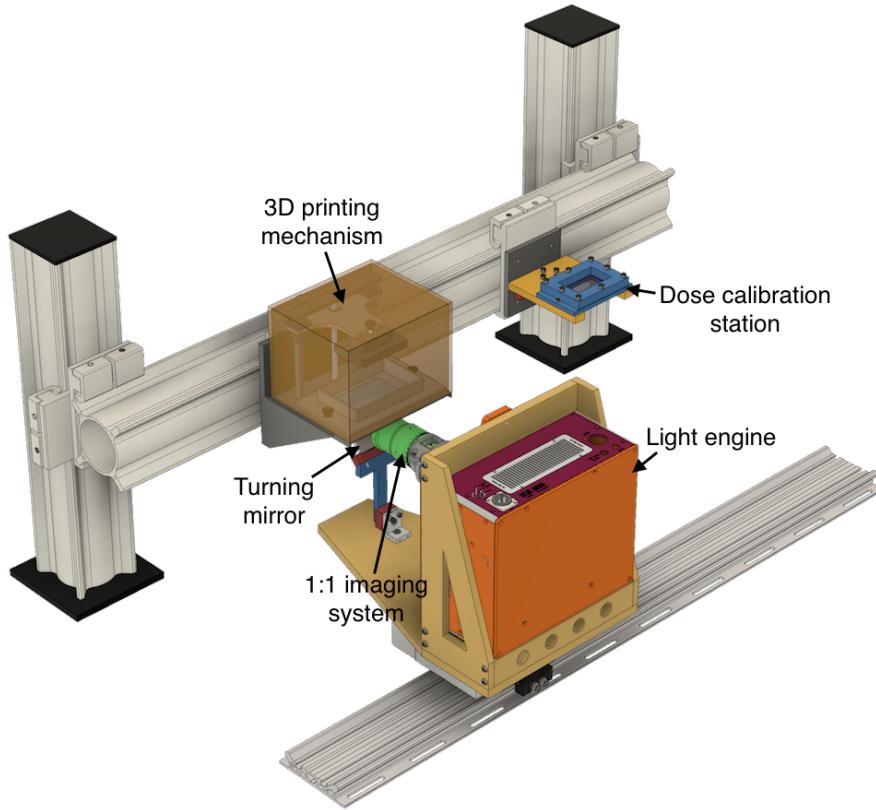
Barriers

- Feature sizes are in the millifluidic rather than microfluidic regime
 - Need features $\lesssim 100 \mu\text{m}$ or lose advantage of using small sample and reagent volumes ($\sim 1 \mu\text{L}$)
- Market pull
 - Dental, custom jewelry, audiology
- Commercial 3D printers
 - $\sim 50 \mu\text{m}$ x-y resolution
 - $\sim 50 \mu\text{m}$ z layer thickness
- Proprietary commercial resins
 - Viscosity (affects feature size)
 - Lack of tailorabile mechanical, optical, biocompatibility properties

Overview

- Focus on our work over the last year
- Custom 3D printer
 - High XY resolution: 7.6 μm
 - UV light source: 385 nm LED
- Custom low-cost resin development
- Small channels
 - 18 μm x 20 μm
- Valves and pumps
- Integrated mixer and pump with selectable mixing ratio
 - $\sim 6.3 \text{ mm}^3 = (1.85 \text{ mm})^3$

Custom DLP-SLA 3D Printer



Optical Engine - Visitech

- 2560 x 1600 pixels
- 7.6 μm pixel pitch
- 1:1 lens system
- 19.5 x 12.2 mm^2
- 385 nm LED

Mechanical System – Modified Solus

- Teflon film
- Tipping quartz window
- Typical build layer thickness:
5 – 10 μm

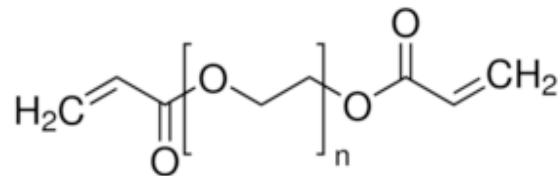
Software

- Custom in-house developed 3D printer control (Python)
- Open source 3D CAD
- Open source slicer

Custom Resin Formulation

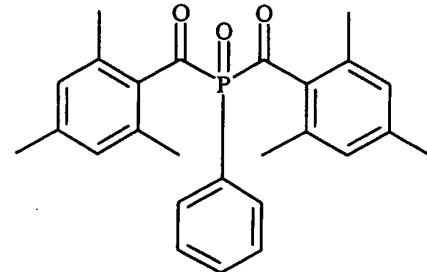
Monomer

Polyethylene glycol diacrylate (PEGDA)
258 Da, 57 cPs



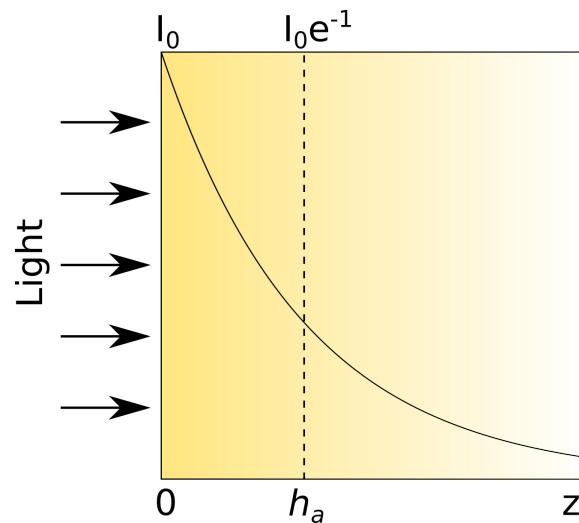
Photoinitiator

Irgacure 819

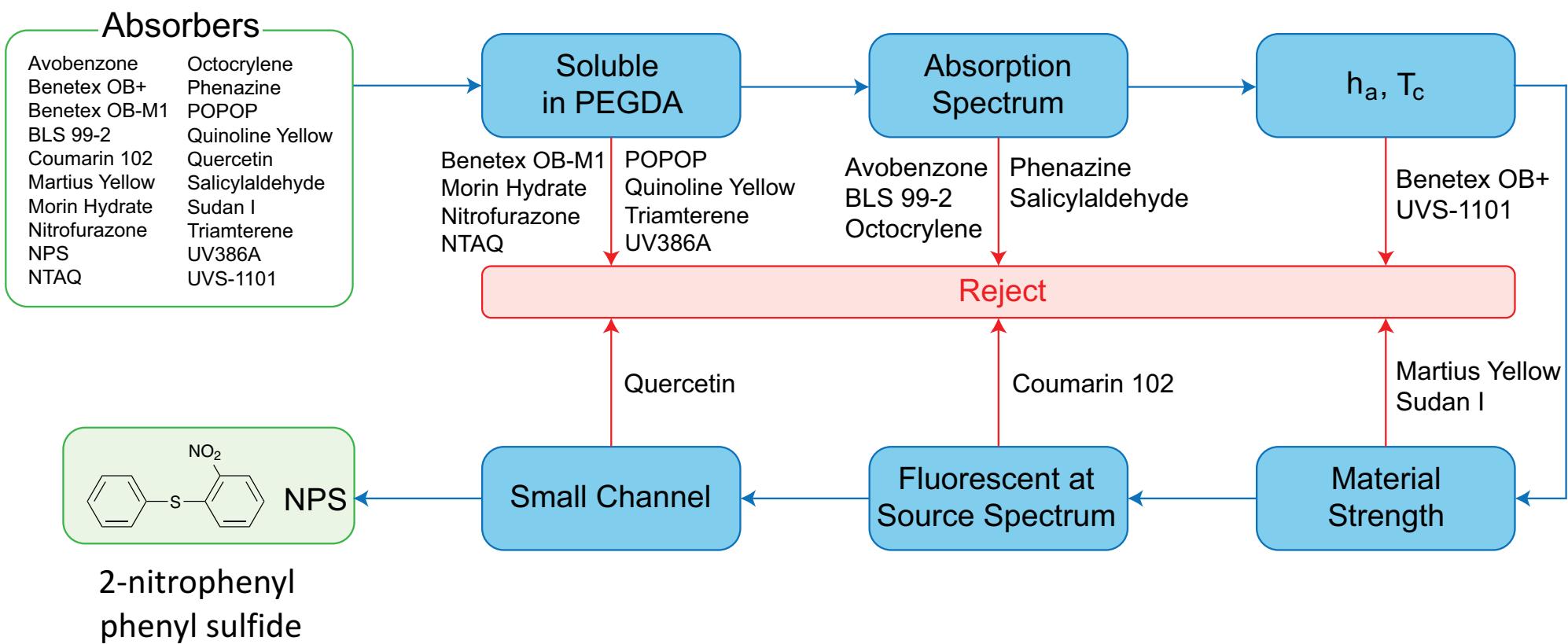


- Rogers et al., Anal. Chem. 83, 6418–6425 (2011)
- Rogers et al., Biomicrofluidics 9, 016501 (2015)
- Gong et al., RSC Advances, 5, pp. 105521 (2015)
- Gong et al., Lab on a Chip, 17, 2899 (2017)

UV Absorber



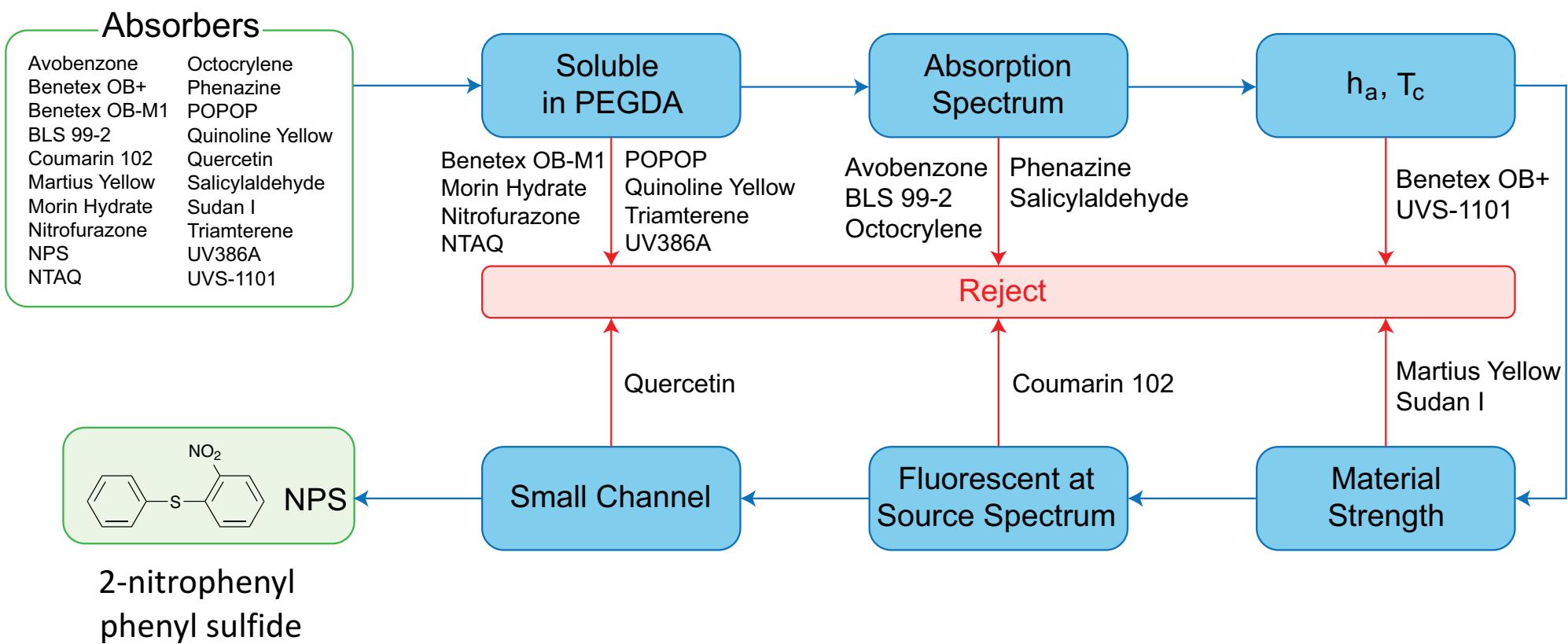
UV Absorber Selection Criteria



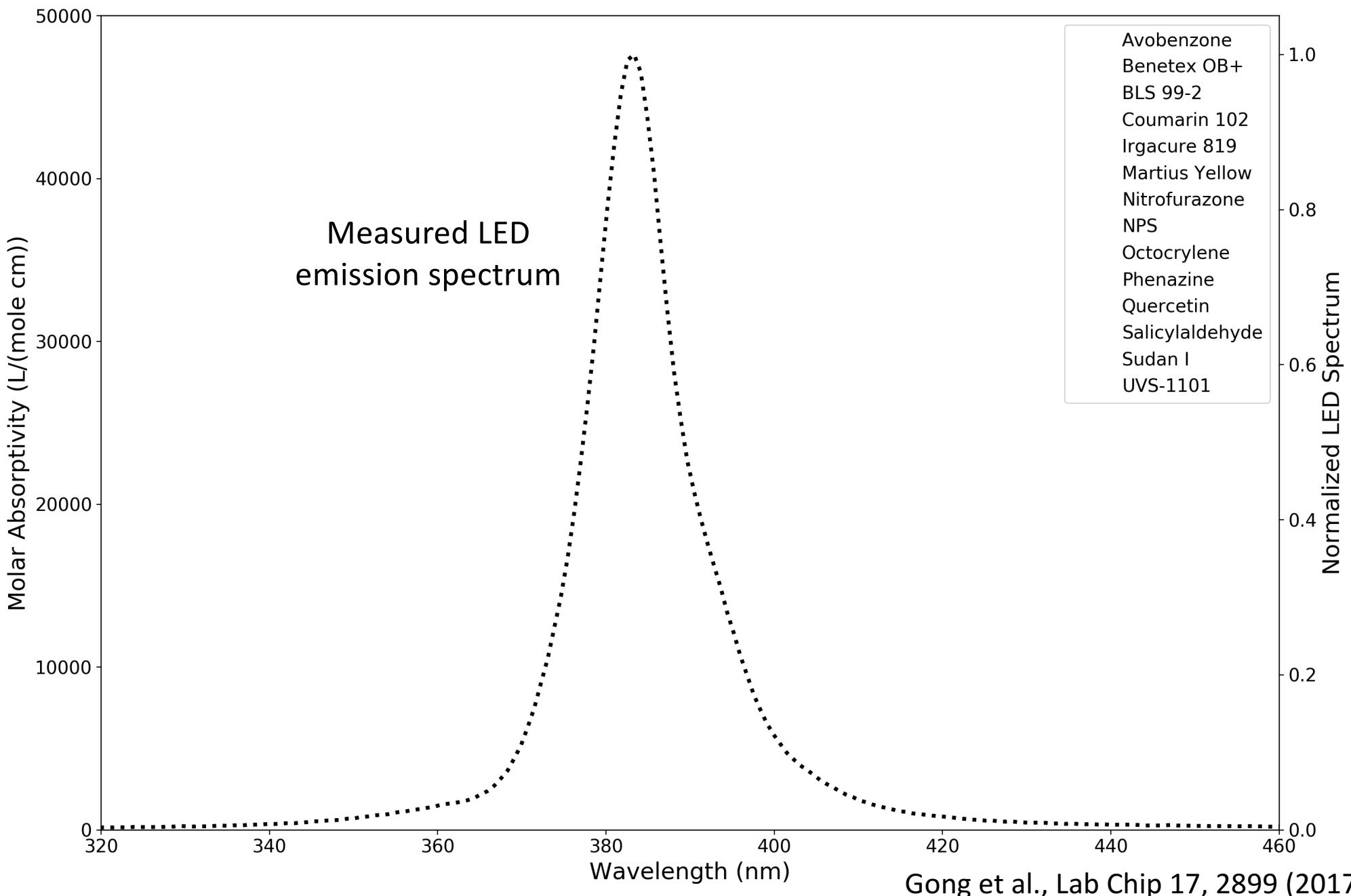
UV Absorber Solubility in PEGDA

Material	Solubility (%) (w/w)	Fluorescent (with 385 nm excitation)
Avobenzone	>5	
Benetex OB+	0.25	Yes
Benetex OB-M1	—	Yes
BLS 99-2	>5	
Coumarin 102	0.8	Yes
Irgacure 819	>5	
Martius Yellow	3	
Morin hydrate	—	
Nitrofurazone	0.07	
NPS	>5	
NTAQ	—	
Octocrylene	>5	
Phenazine	1.8	
POPOP	—	Yes
Quercetin	0.8	
Quinoline yellow	—	
Salicylaldehyde	>5	
Sudan I	2.7	
Triamterene	—	Yes
UV386A	—	
UVS-1101	0.5	Yes

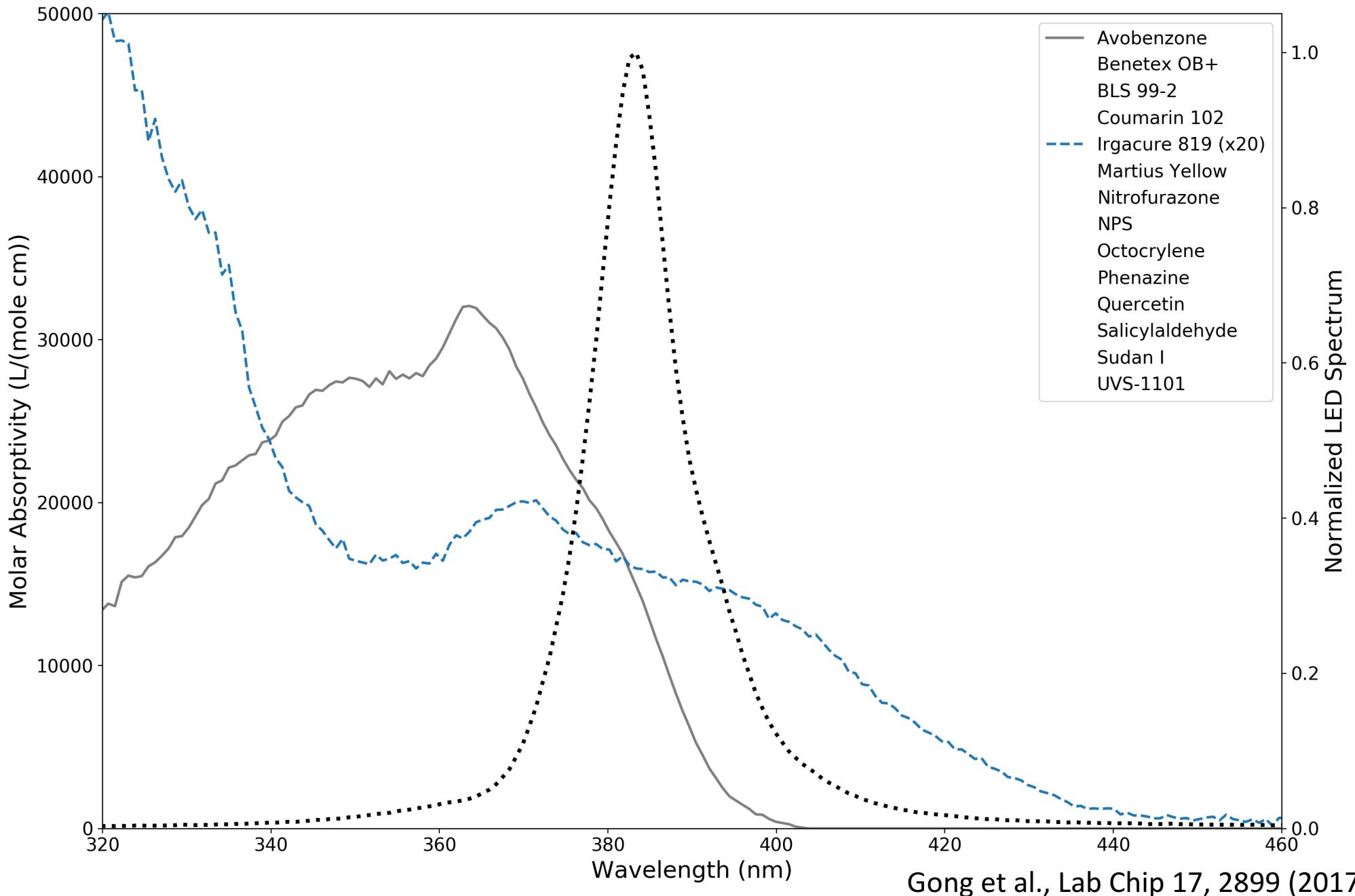
UV Absorber Selection Criteria



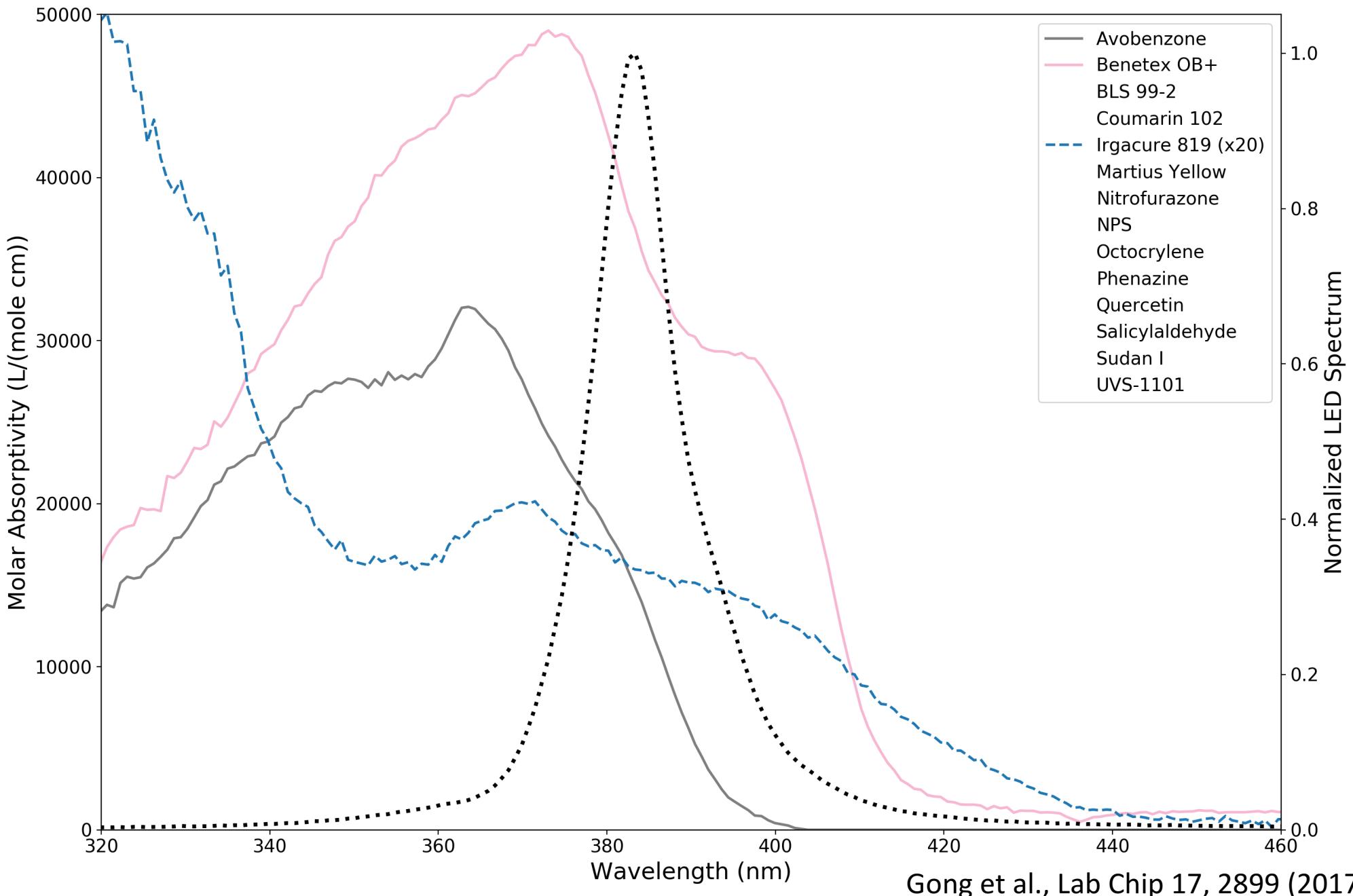
Absorption Spectra



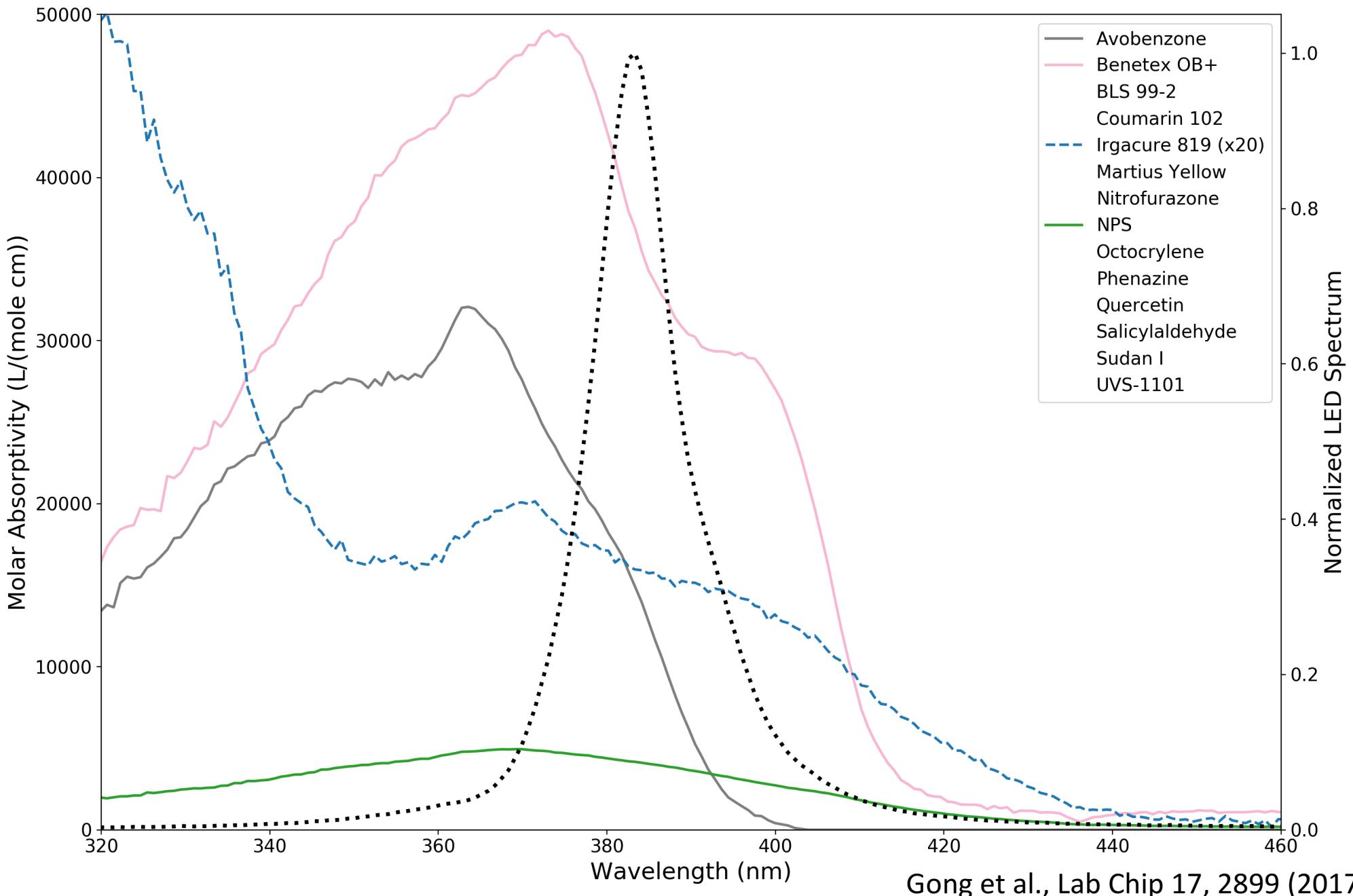
Absorption Spectra



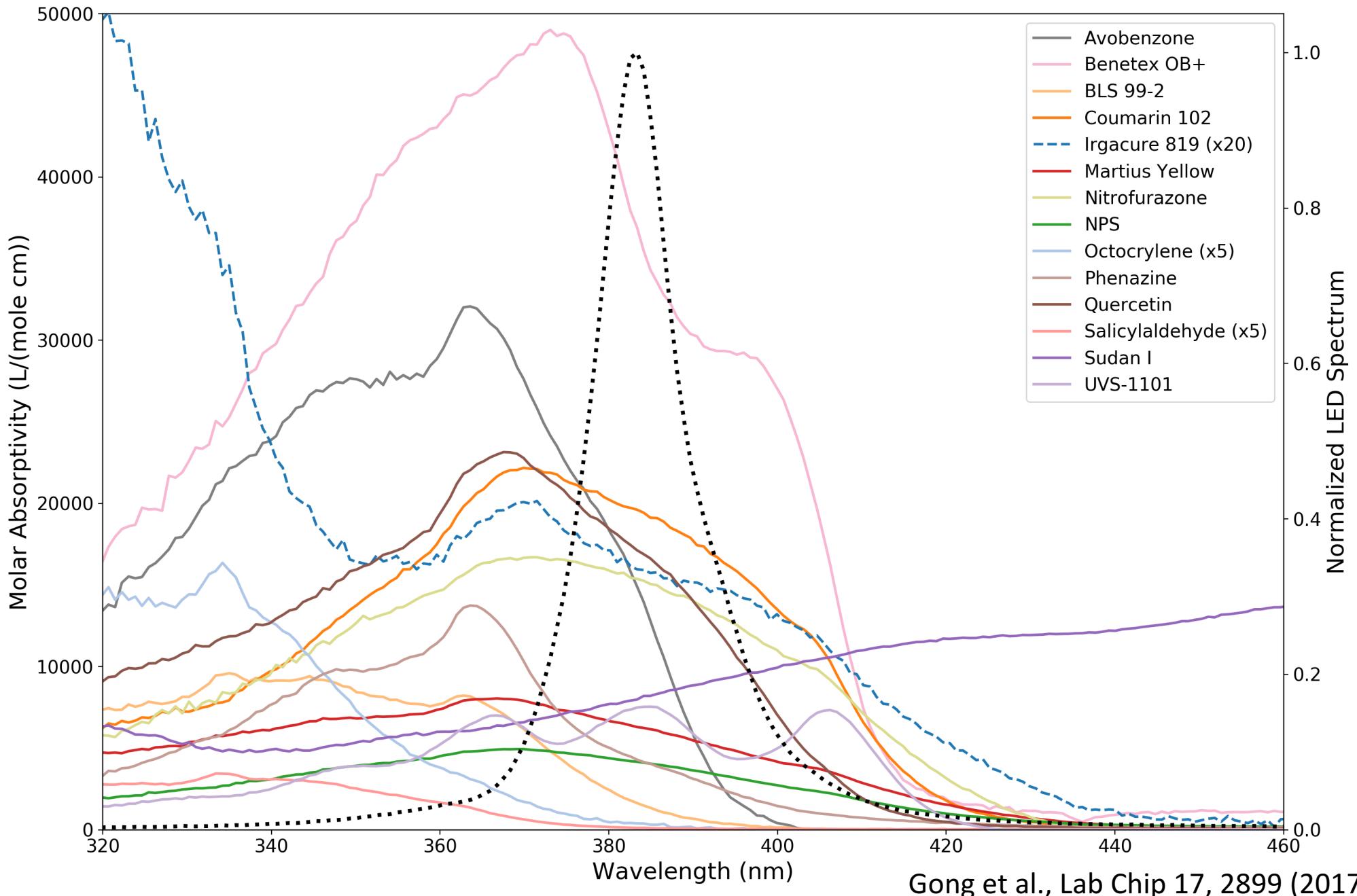
Absorption Spectra



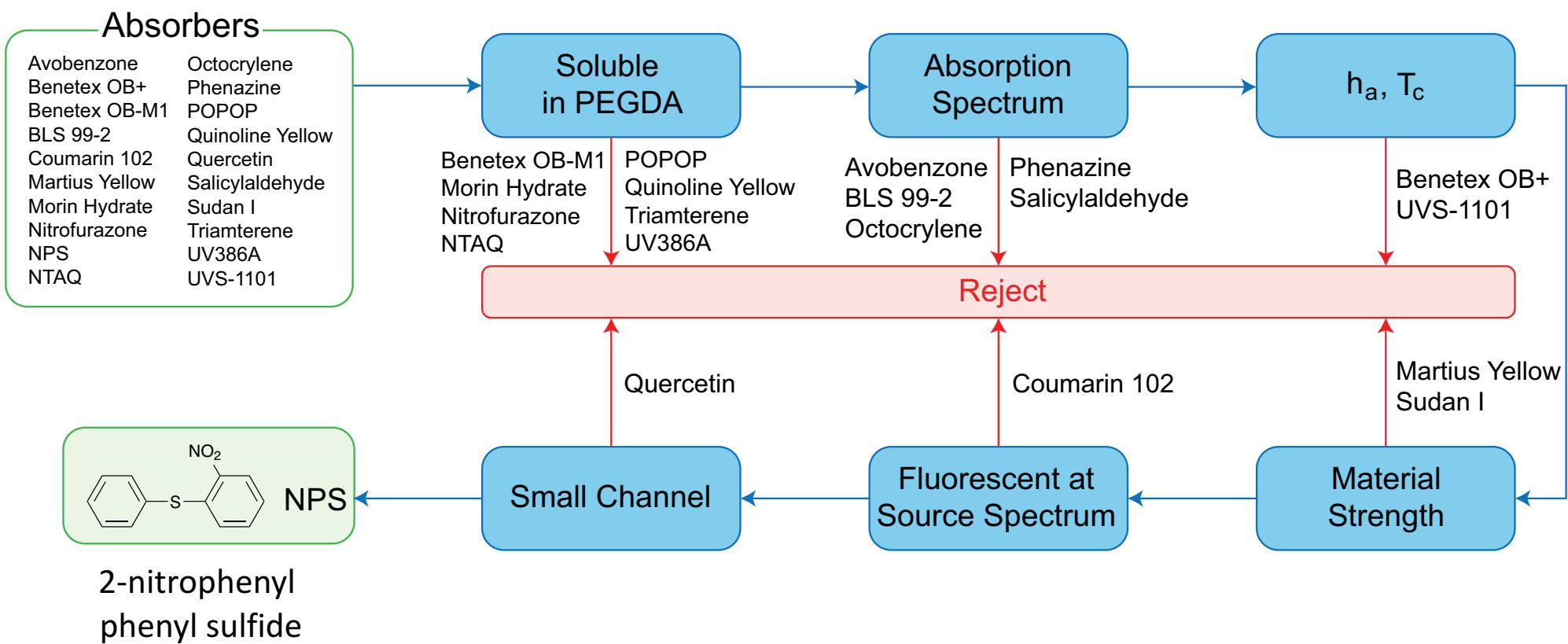
Absorption Spectra



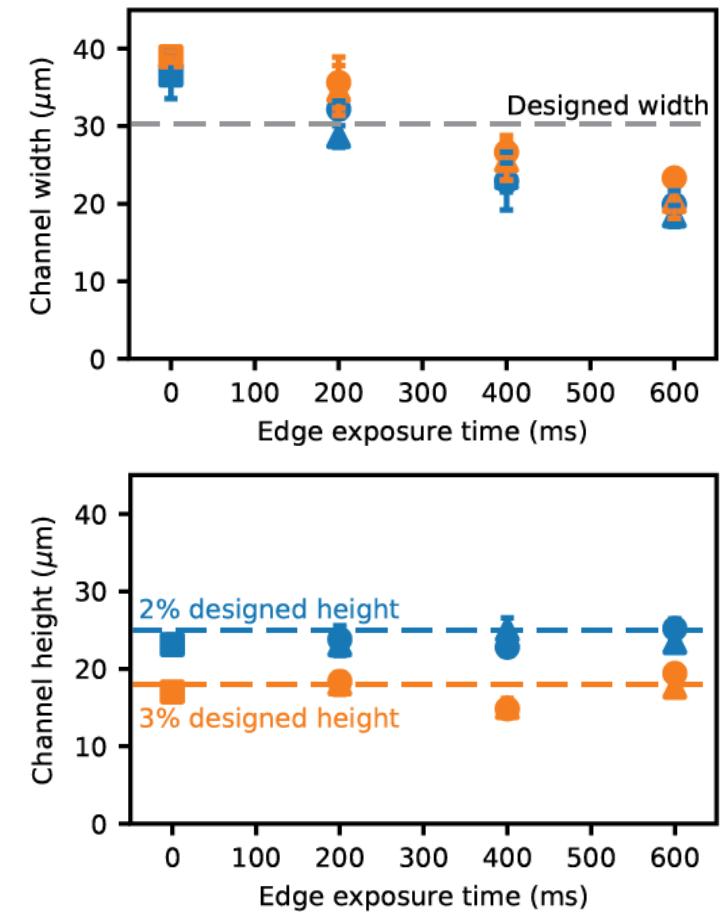
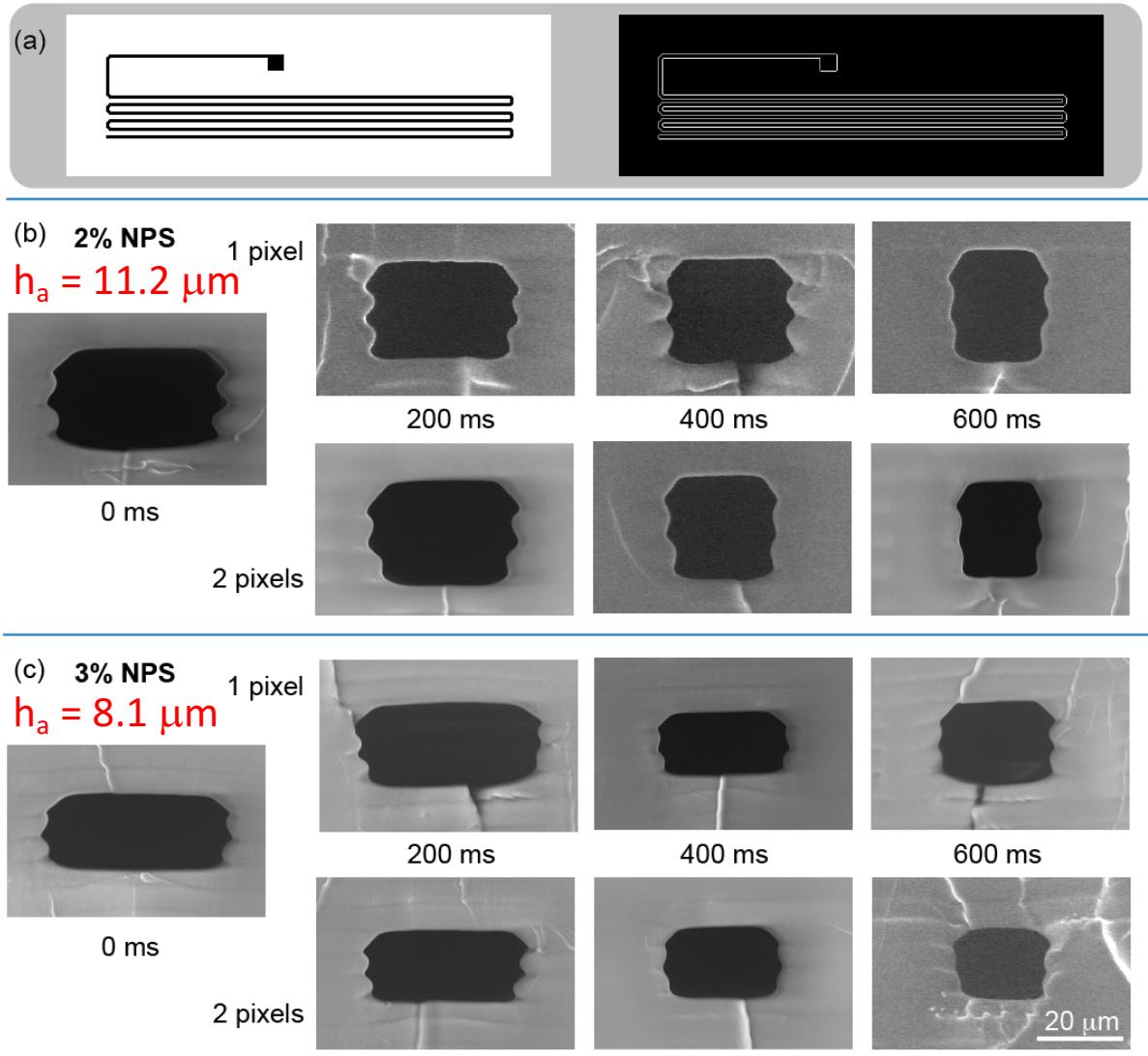
Absorption Spectra



UV Absorber Selection Criteria



Minimizing Channel Size



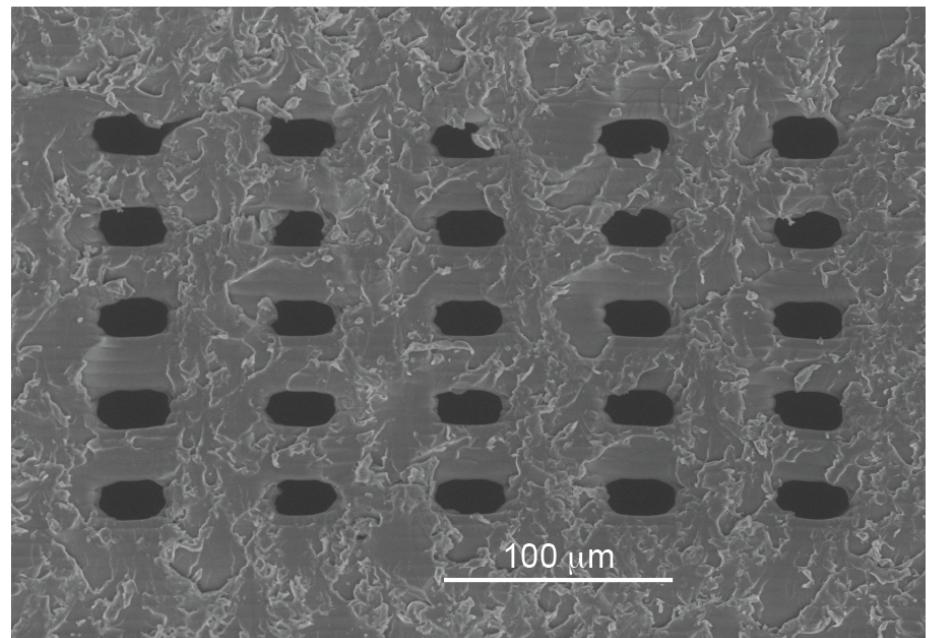
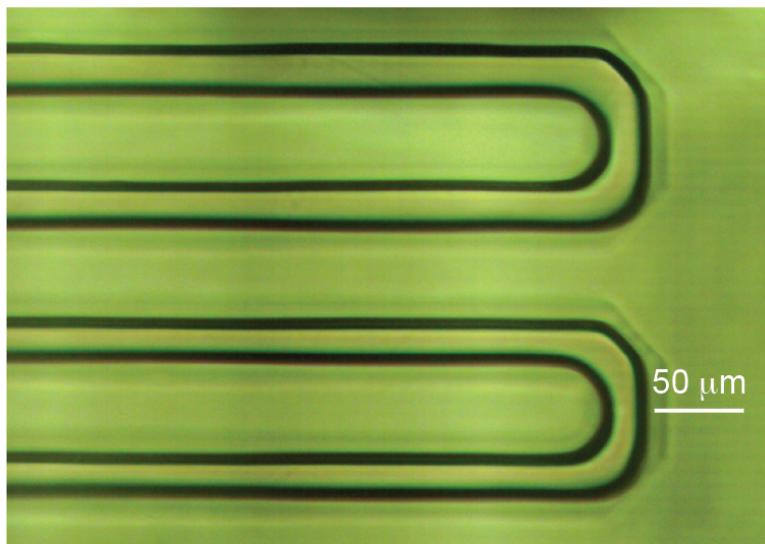
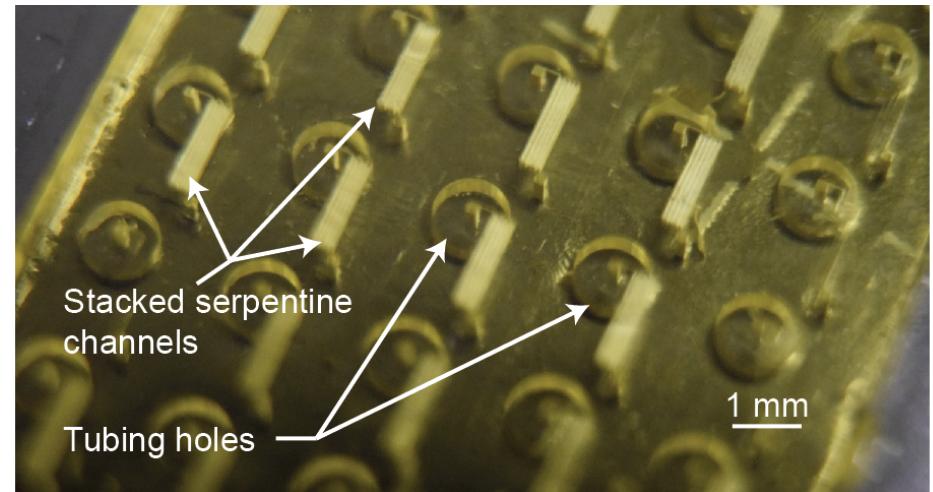
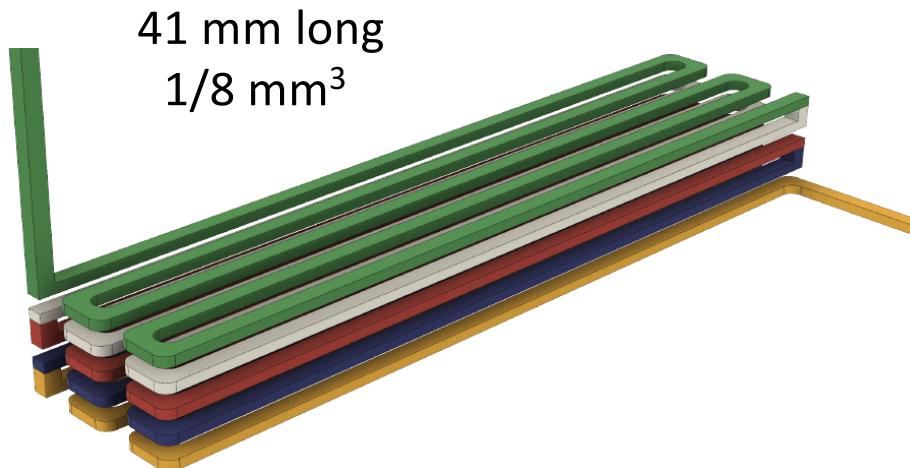
NPS	None	1 pixel	2 pixels
2%	■	●	▲
3%	□	○	△

Gong et al., Lab Chip 17, 2899 (2017)

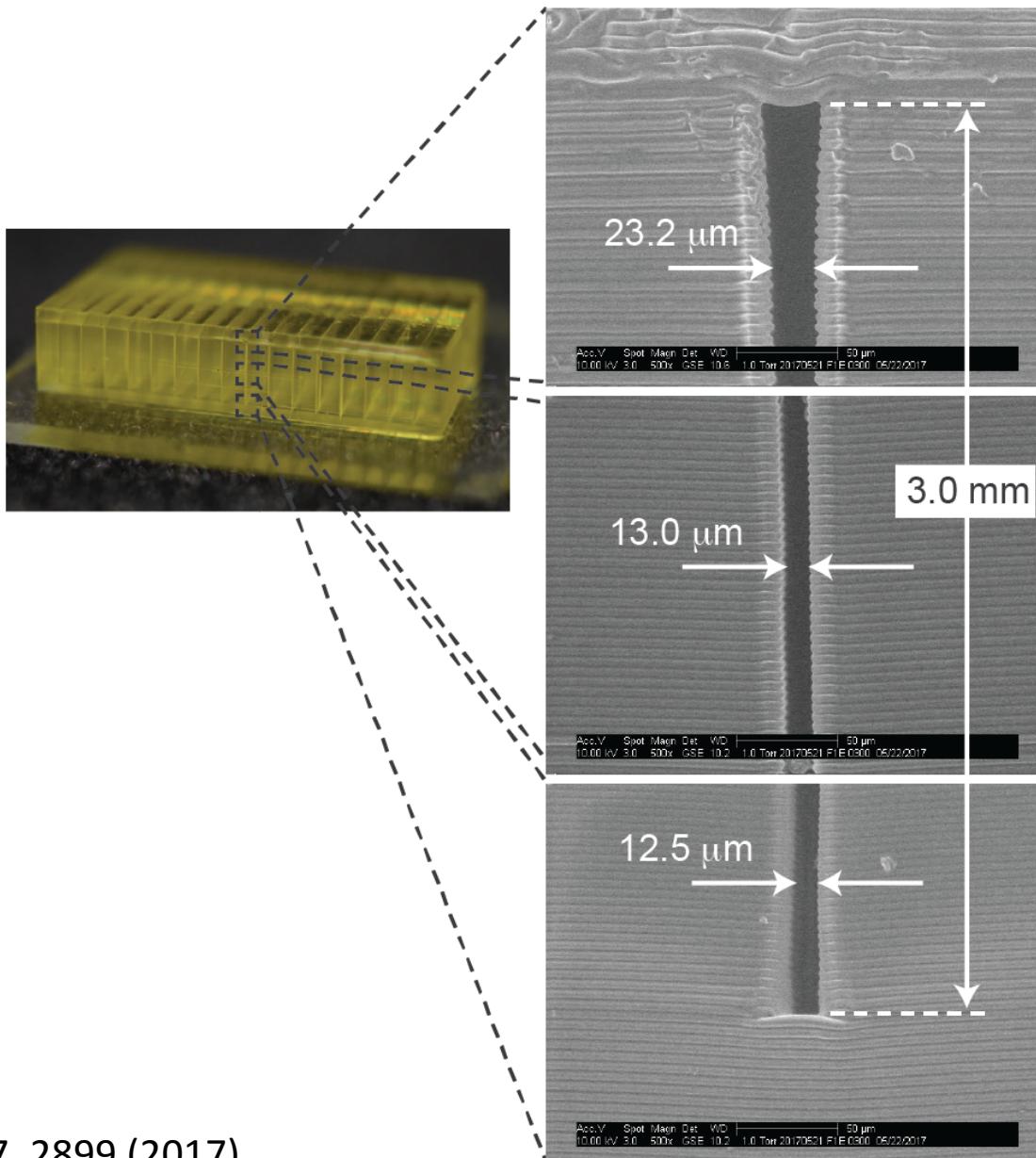
Channel Size

Property	Rule of Thumb	Controlling Parameters
Height (Z)	$L_{min} \approx 2.3h_a$	UV absorber concentration & spectral overlap
Layer Thickness	$z_l = L_{min}/3$ $\frac{z_l}{h_a} \approx 0.77$	Z stage resolution
Width (XY) (design 4 pixels)	No edge exposure: 5 – 6 pixels With edge exposure: 2.5 – 3 pixels	XY image resolution

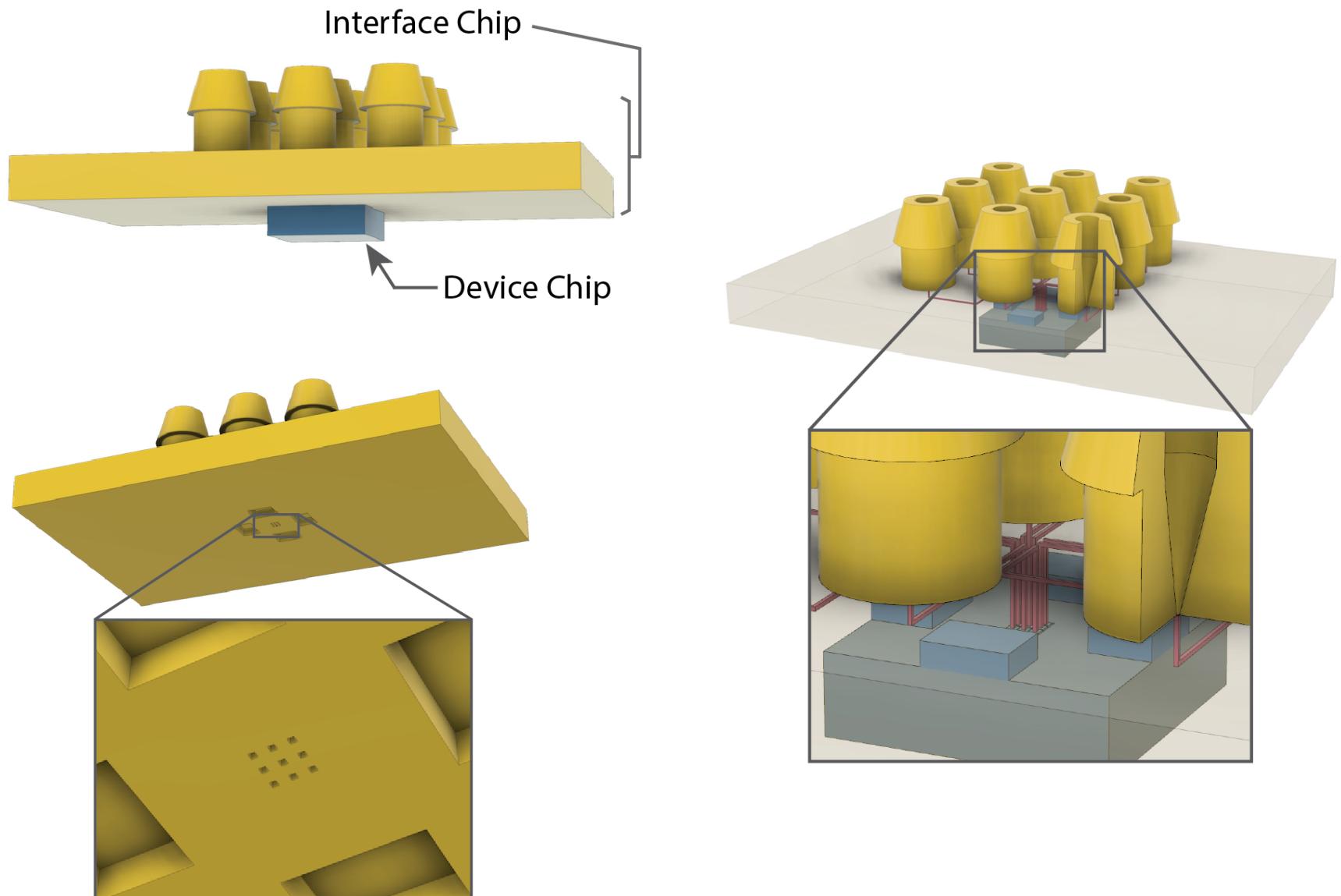
3D Serpentine Channels



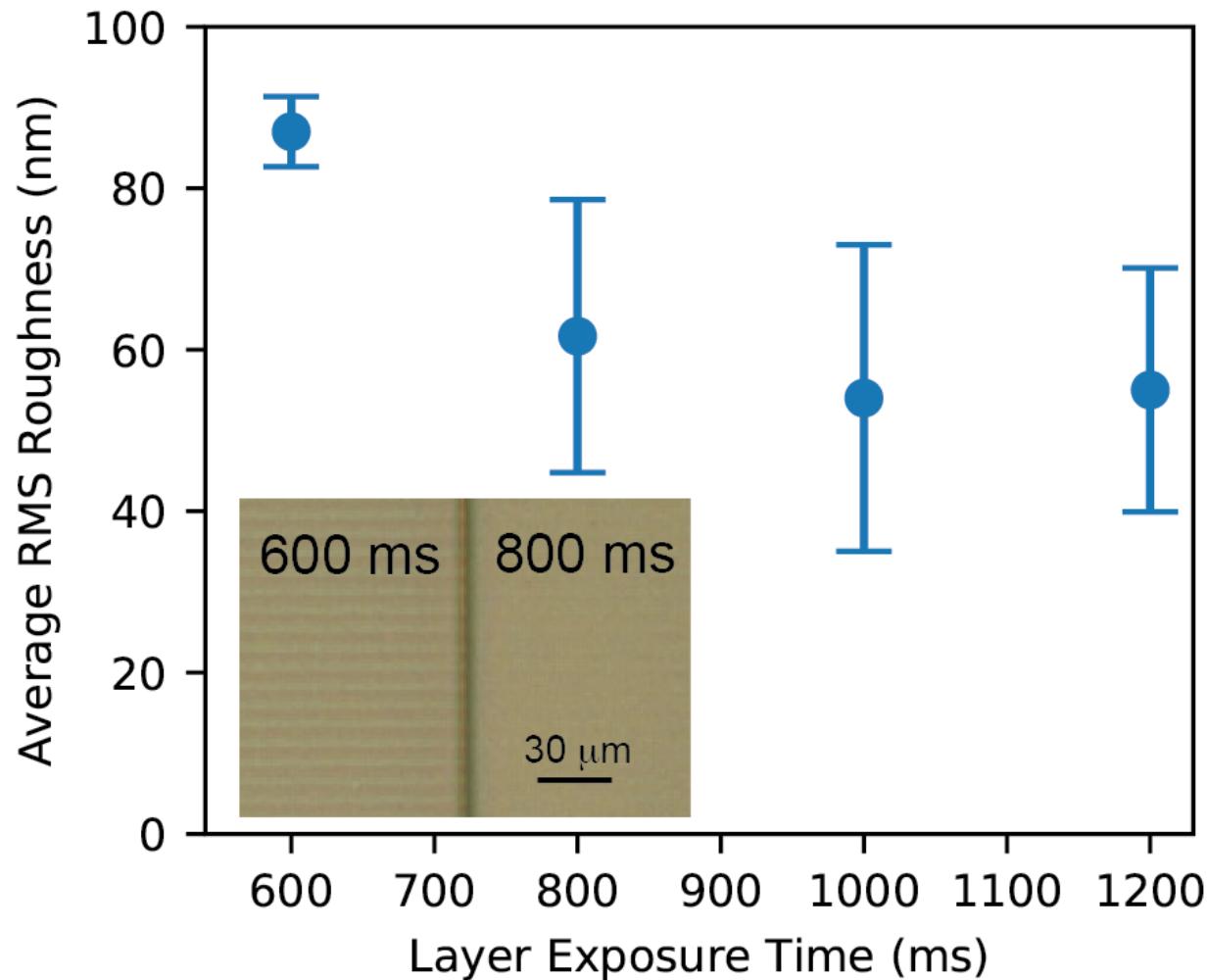
High Aspect Ratio Channels



Delegate Chip-to-World Interconnects to Separate Interconnect Chip

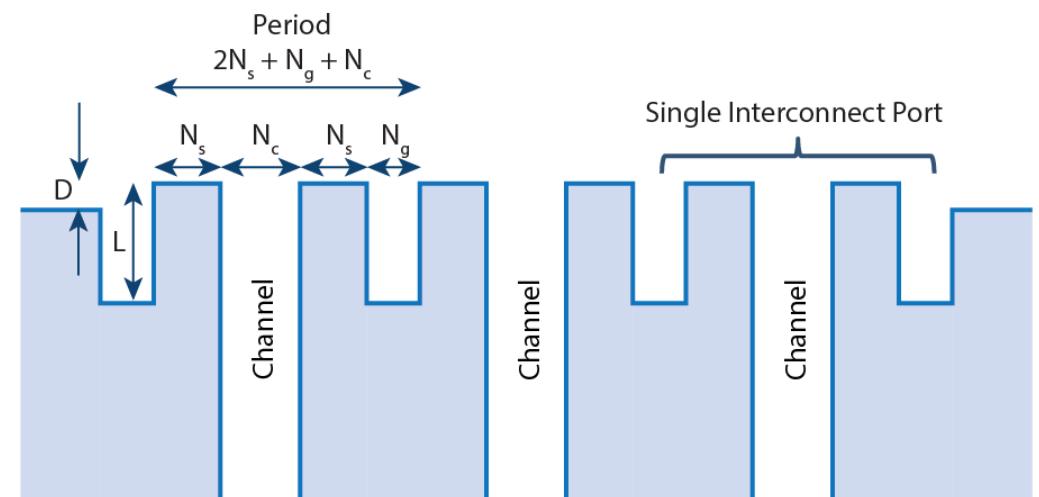
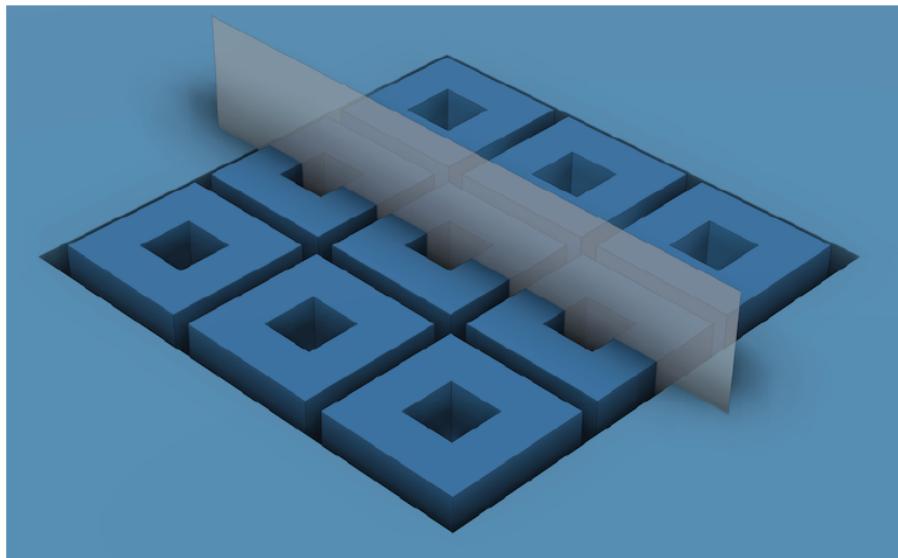


Surface Roughness



Interconnect Concept

Use 3D printed material itself as micogasket

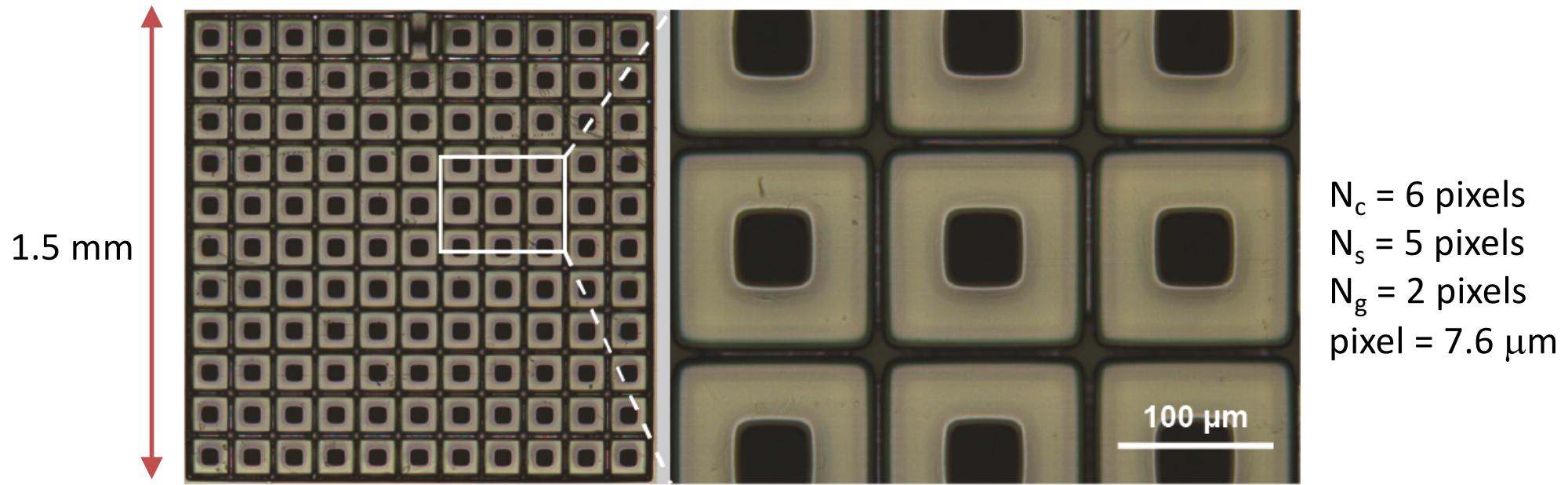


- $D = 10 \mu\text{m} = 1 \text{ layer}$
- Young's modulus $\sim 8 \text{ Mpa}$
- 3D print micogasket as part of device
- No additional materials or structures needed

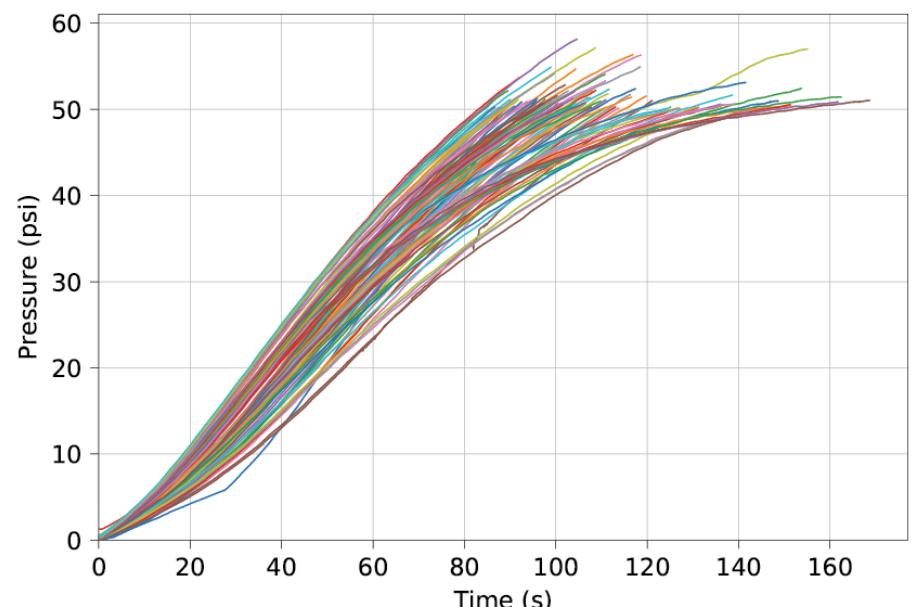
Interconnect Operation



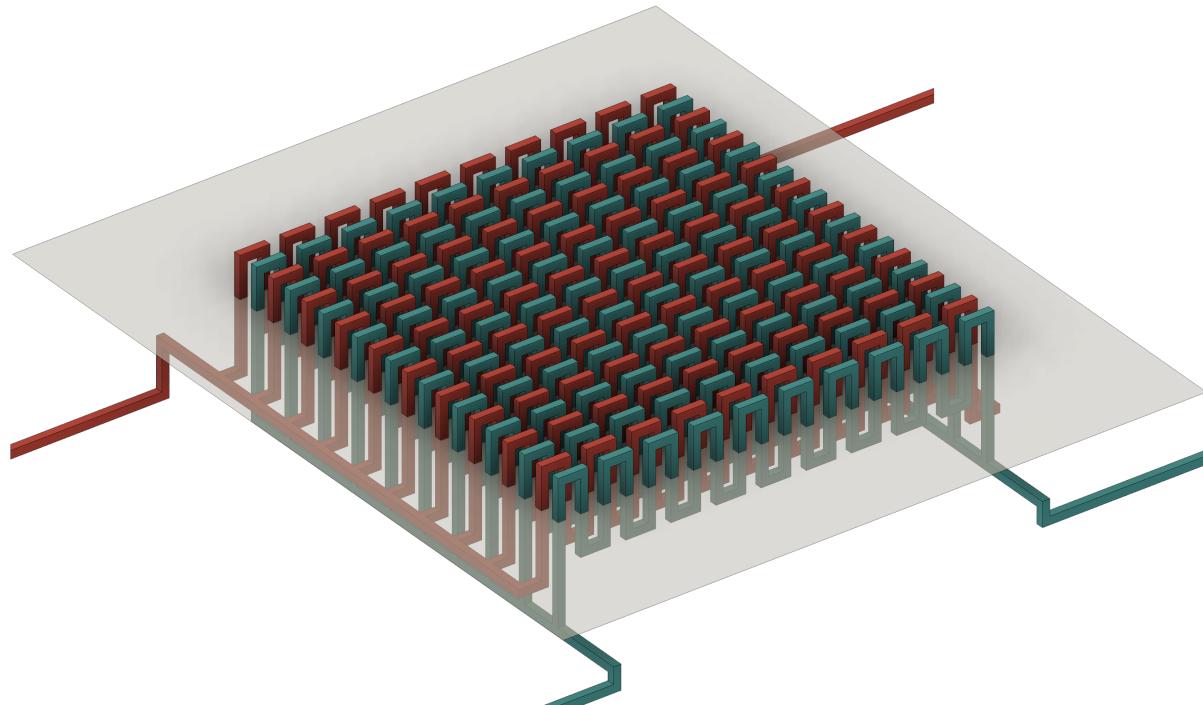
121 Interconnects



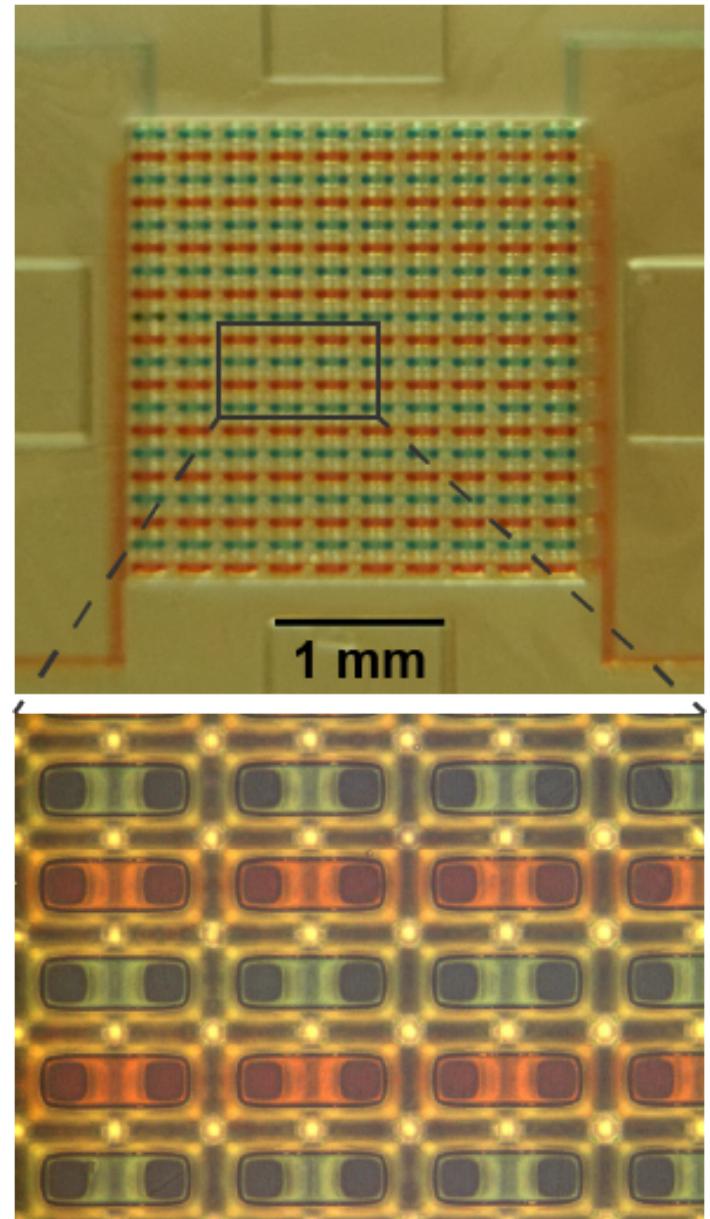
- 11 x 11 array
- 137 μm period
- 53 interconnects/ mm^2
- Reusable - 100 repeated pressure tests



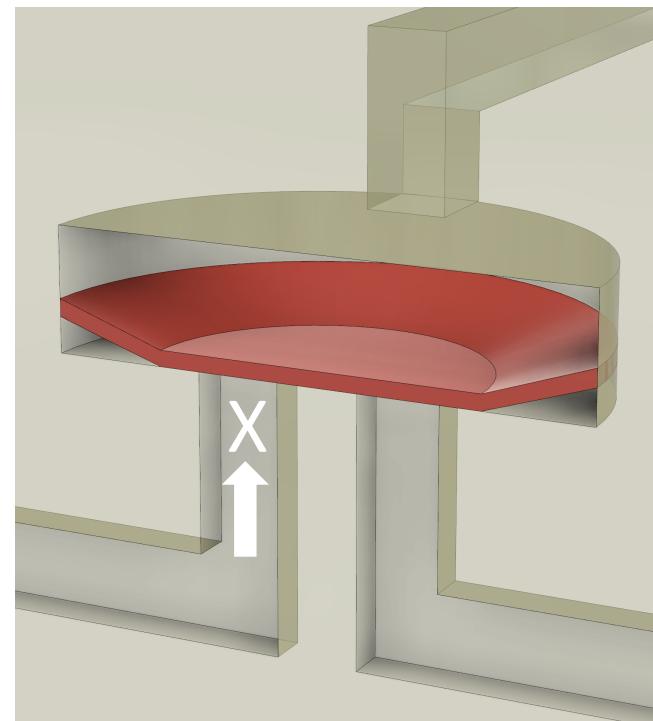
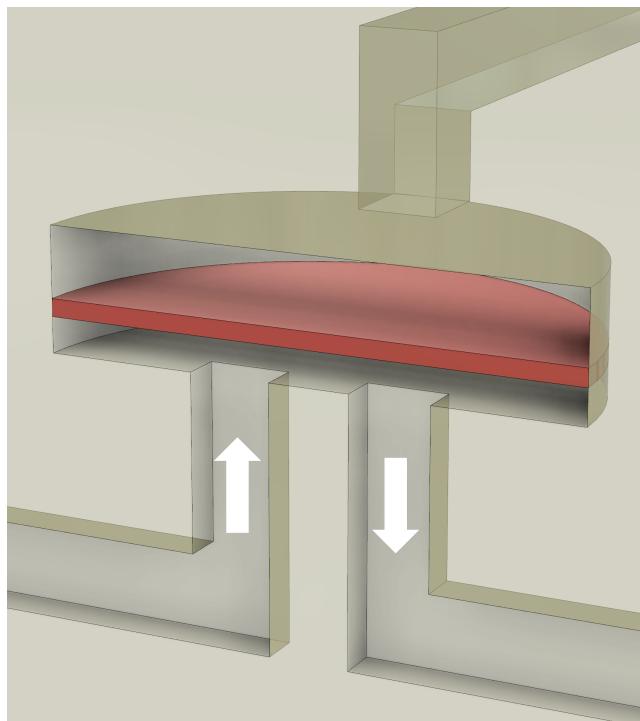
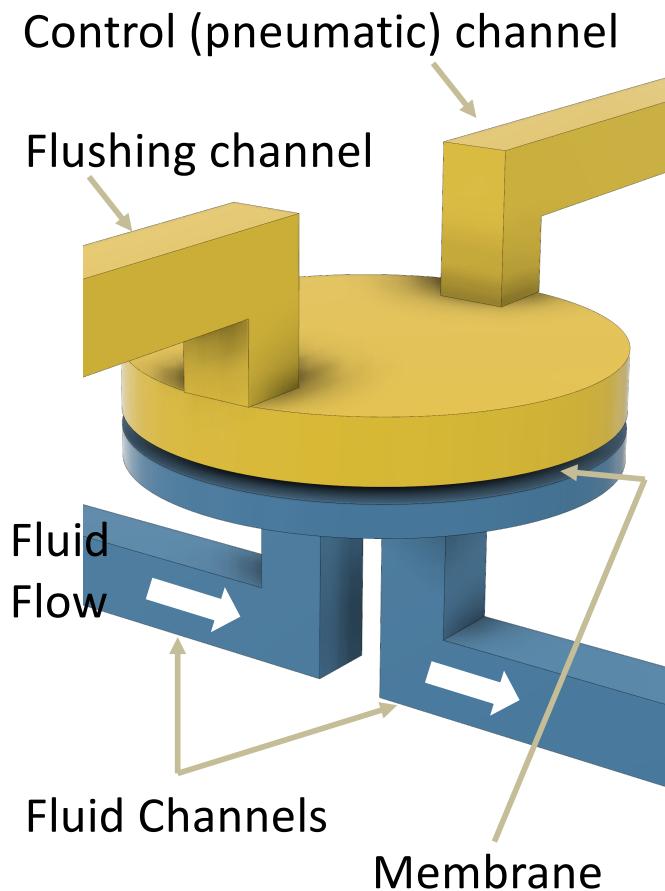
400 Interconnects



- 20 x 20 array
- 137 μm period
- 53 interconnects/ mm^2

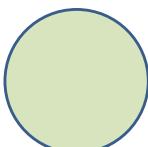
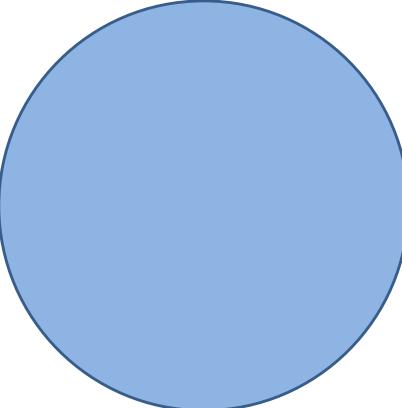
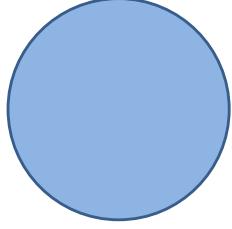


3D Printed Membrane Valve

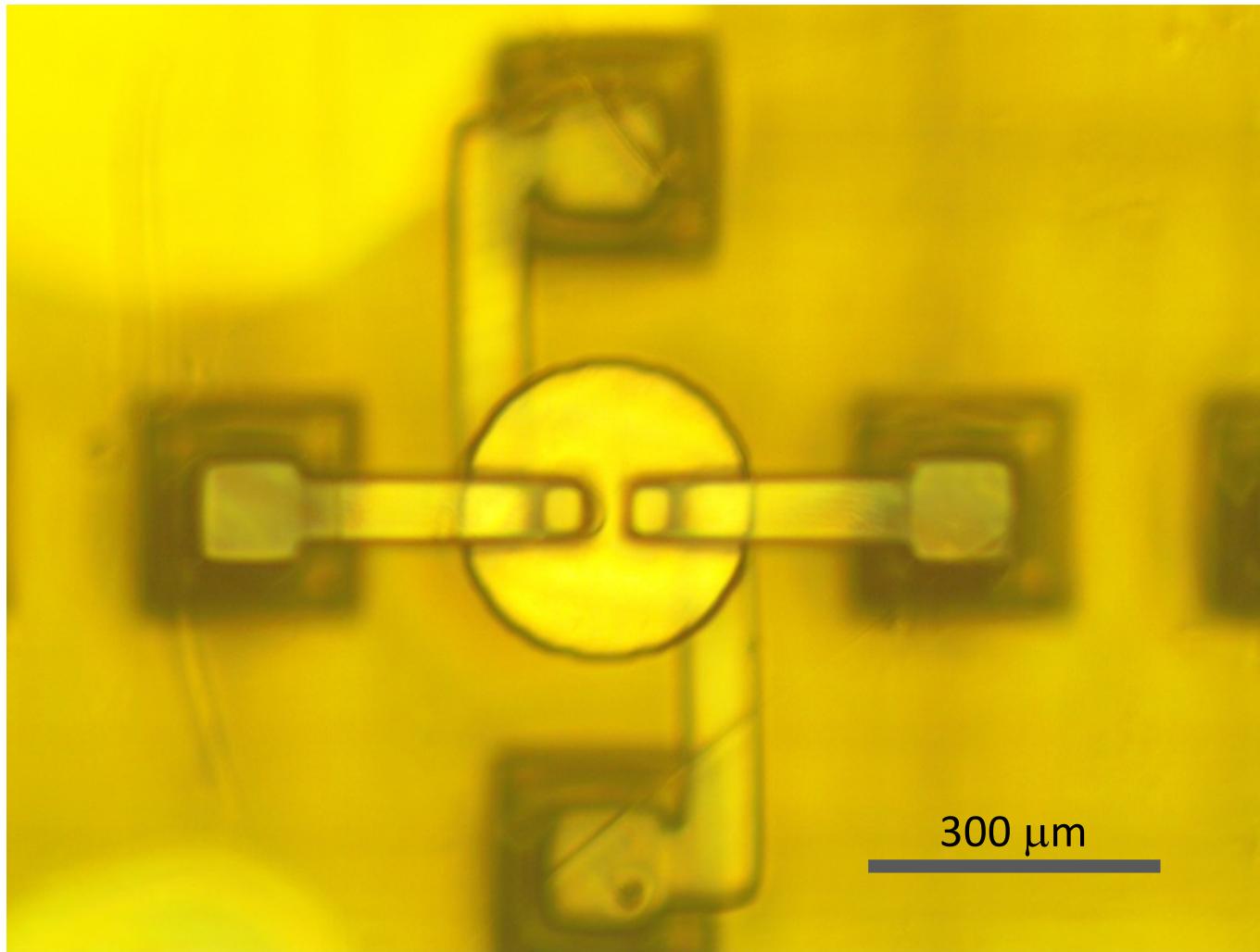


C. Rogers et al., Biomicrofluidics, 9, 016501 (2015)
H. Gong et al., Lab Chip 16, 2450 (2016)

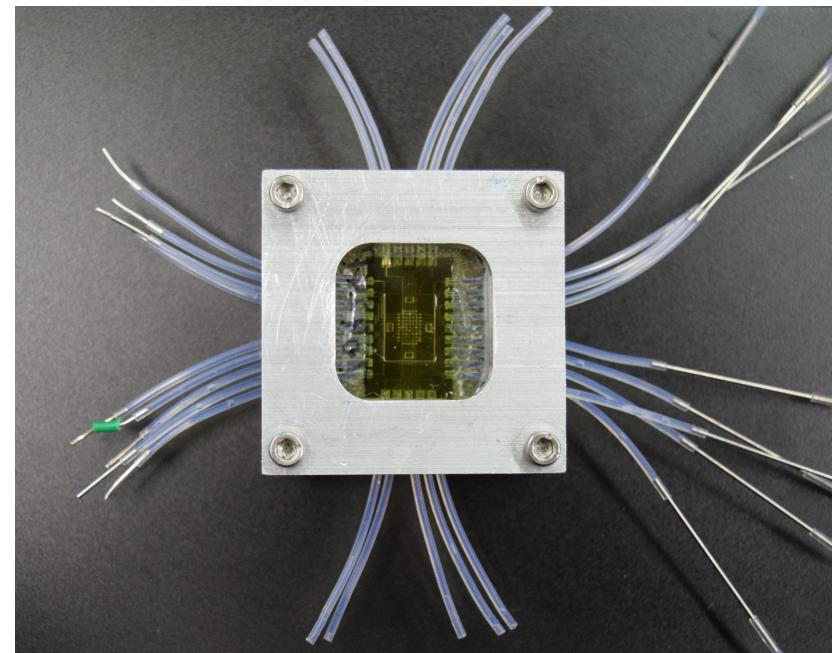
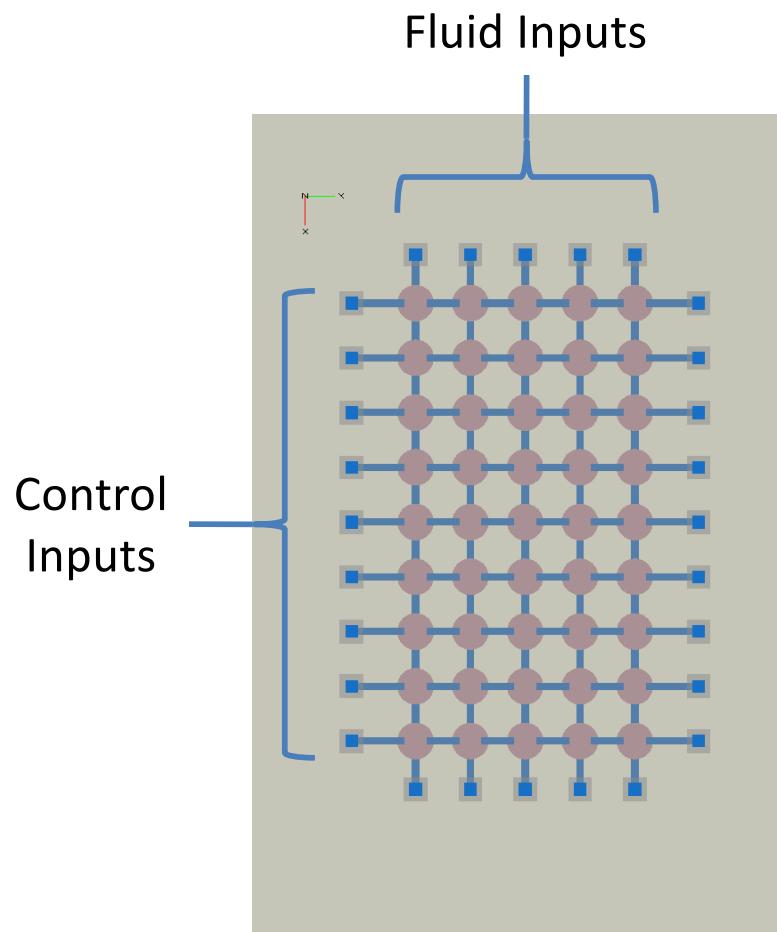
Valve Size

Fabrication	Relative Size	Diameter	# Actuations	Reference
Cleanroom PEGDA resin		700 μm	115,000	Sens. & Act. B 191, 438 (2014)
B9 Creator Custom Sudan I resin		2 mm	800	Biomicrofluidics 9, 016501 (2015)
Asiga Custom Sudan I resin		1.08 mm	1,000,000	Lab Chip 16, 2450 (2016)
Custom 3D printer Custom NPS resin		300 μm	1,000,000	This work

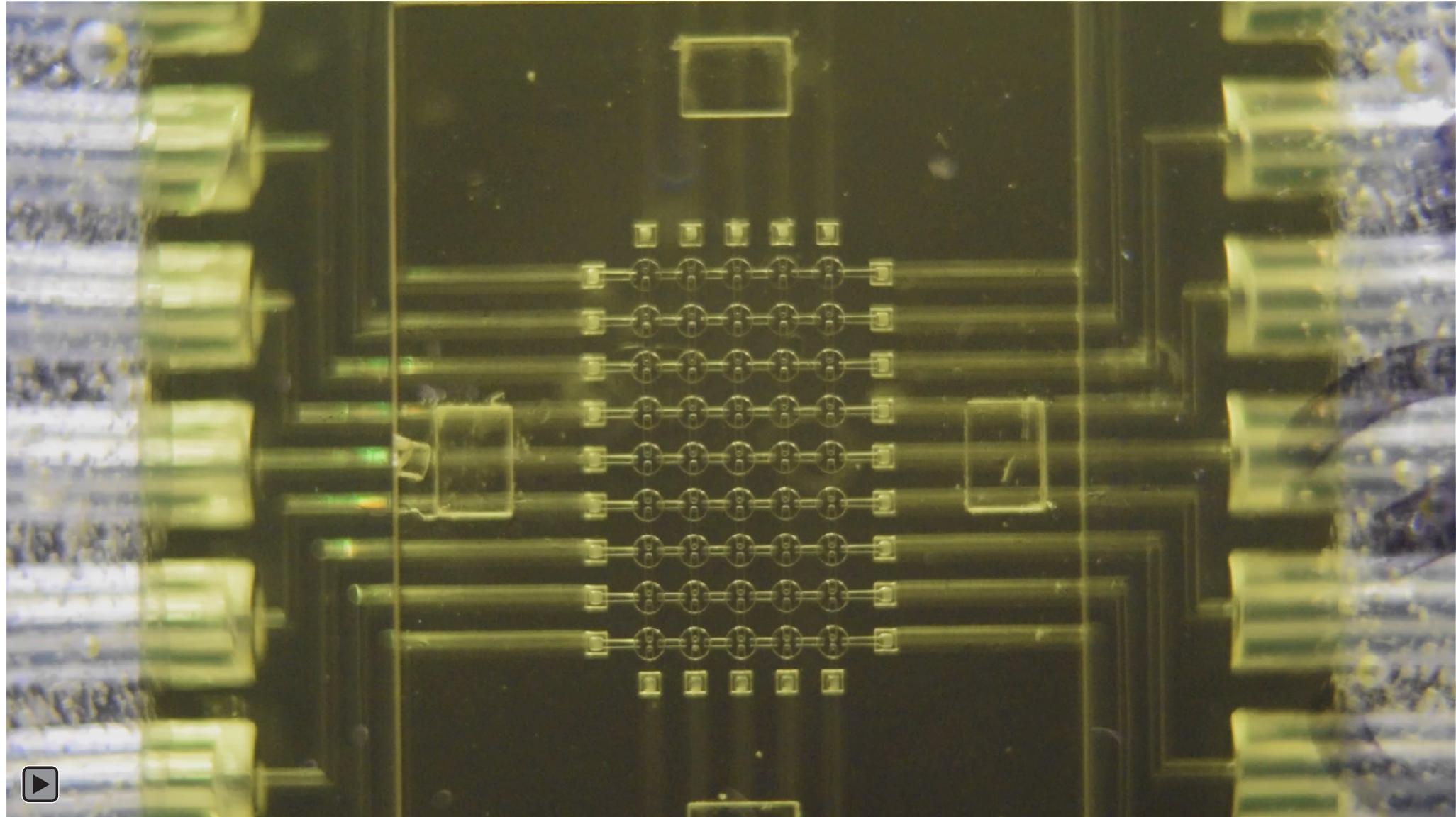
3D Printed Valve



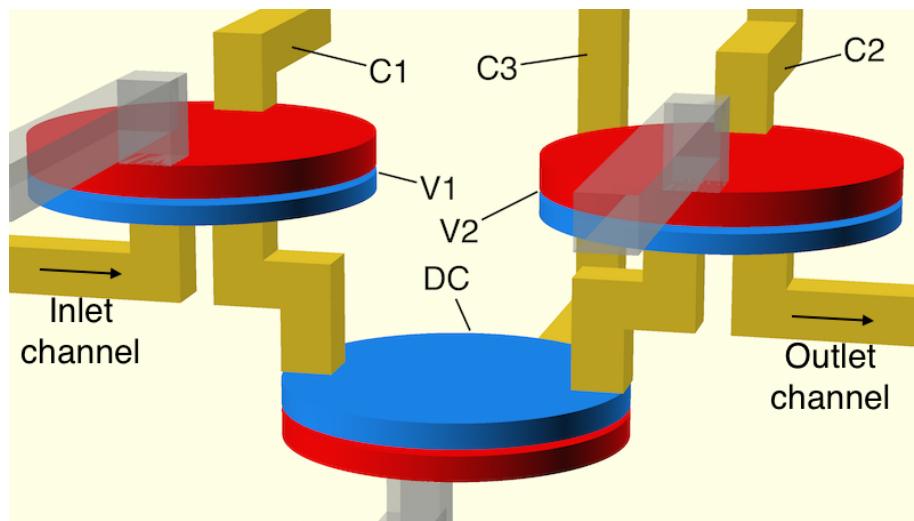
45 Valve Test Array



50 ms Scrolling Valve Actuation



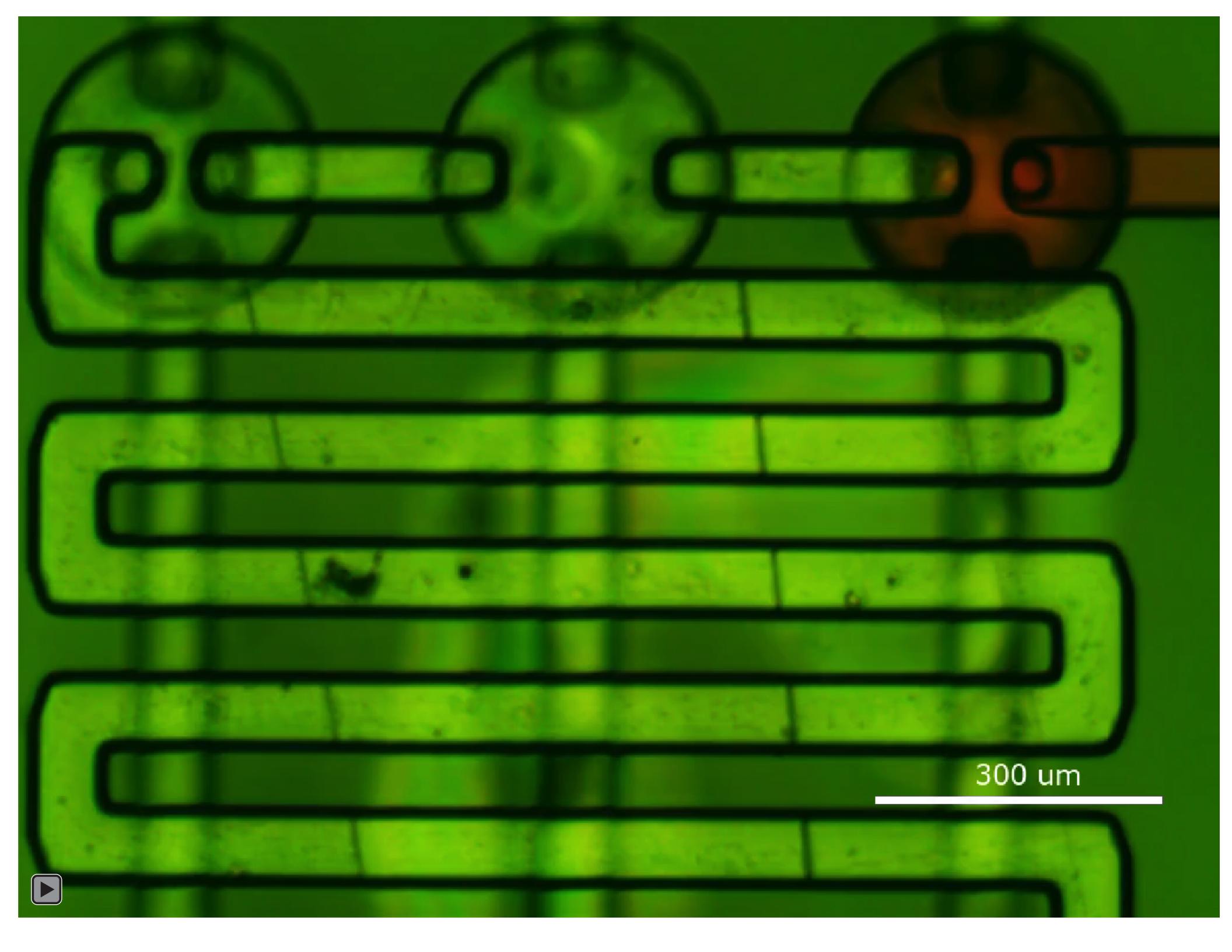
3D Printed Pump



H. Gong, A.T. Woolley, G.P. Nordin,
Lab Chip, 16, 2450 (2016)

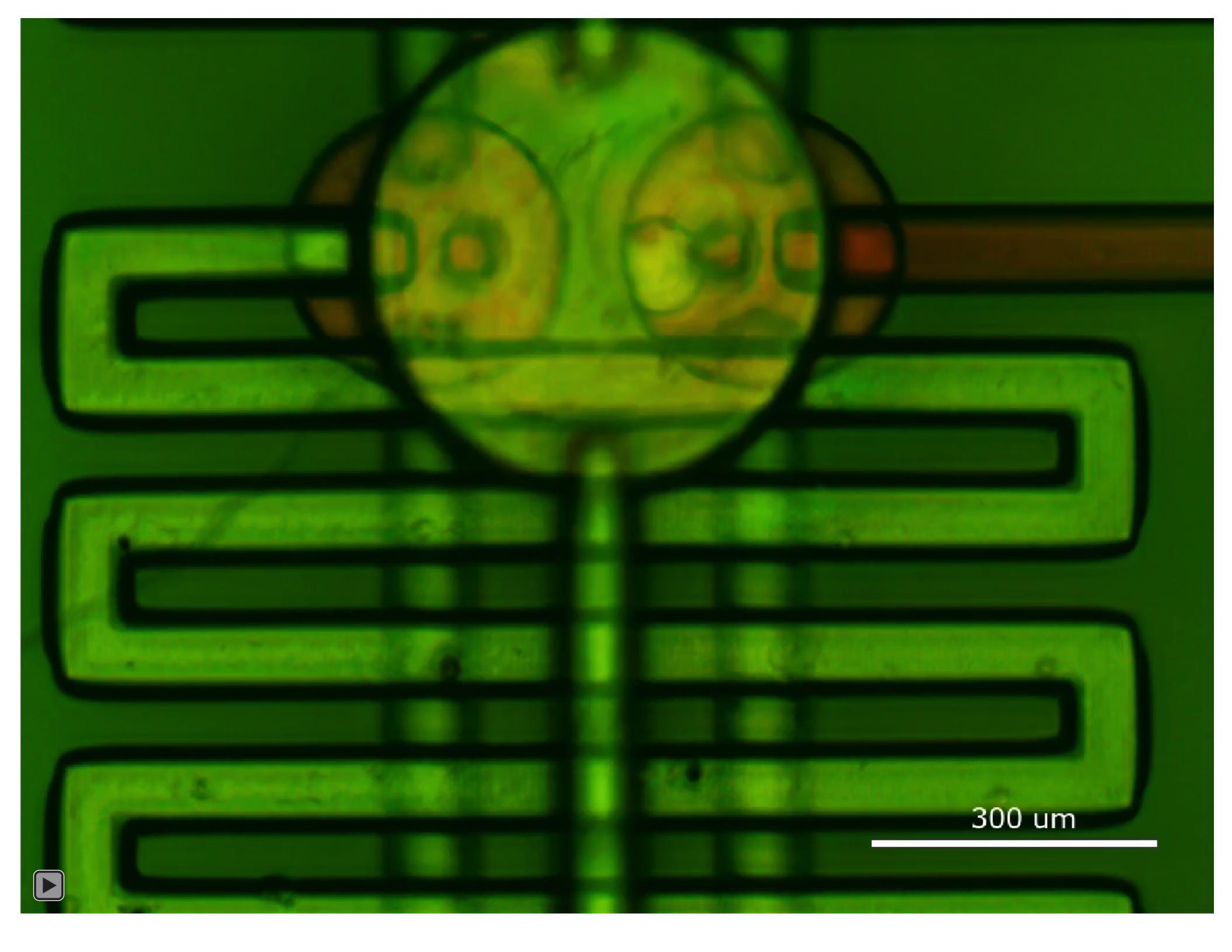
Table 1 Pump timing logic. Red: actuated (pressure applied; valves closed); green: not actuated (valves open)

	t_0	t_1	t_2	t_3	t_4
V1	●	●	●	●	●
DC	●	●	●	●	●
V2	●	●	●	●	●



300 μ m



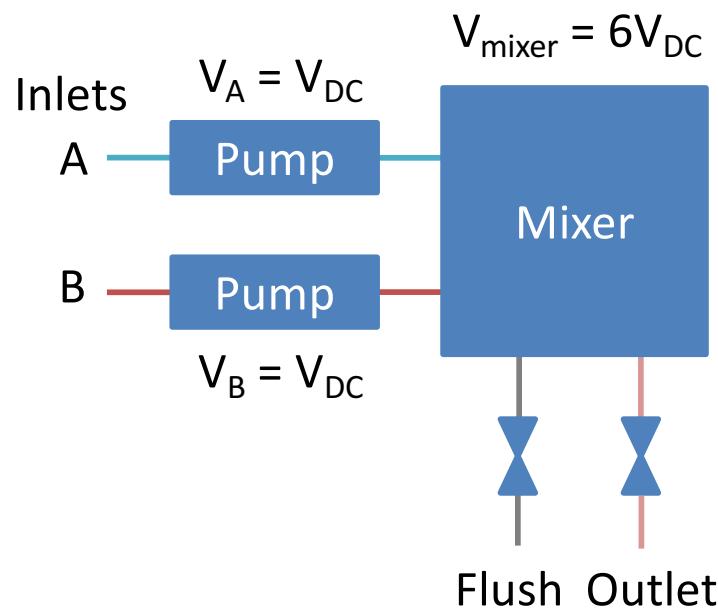


300 μ m

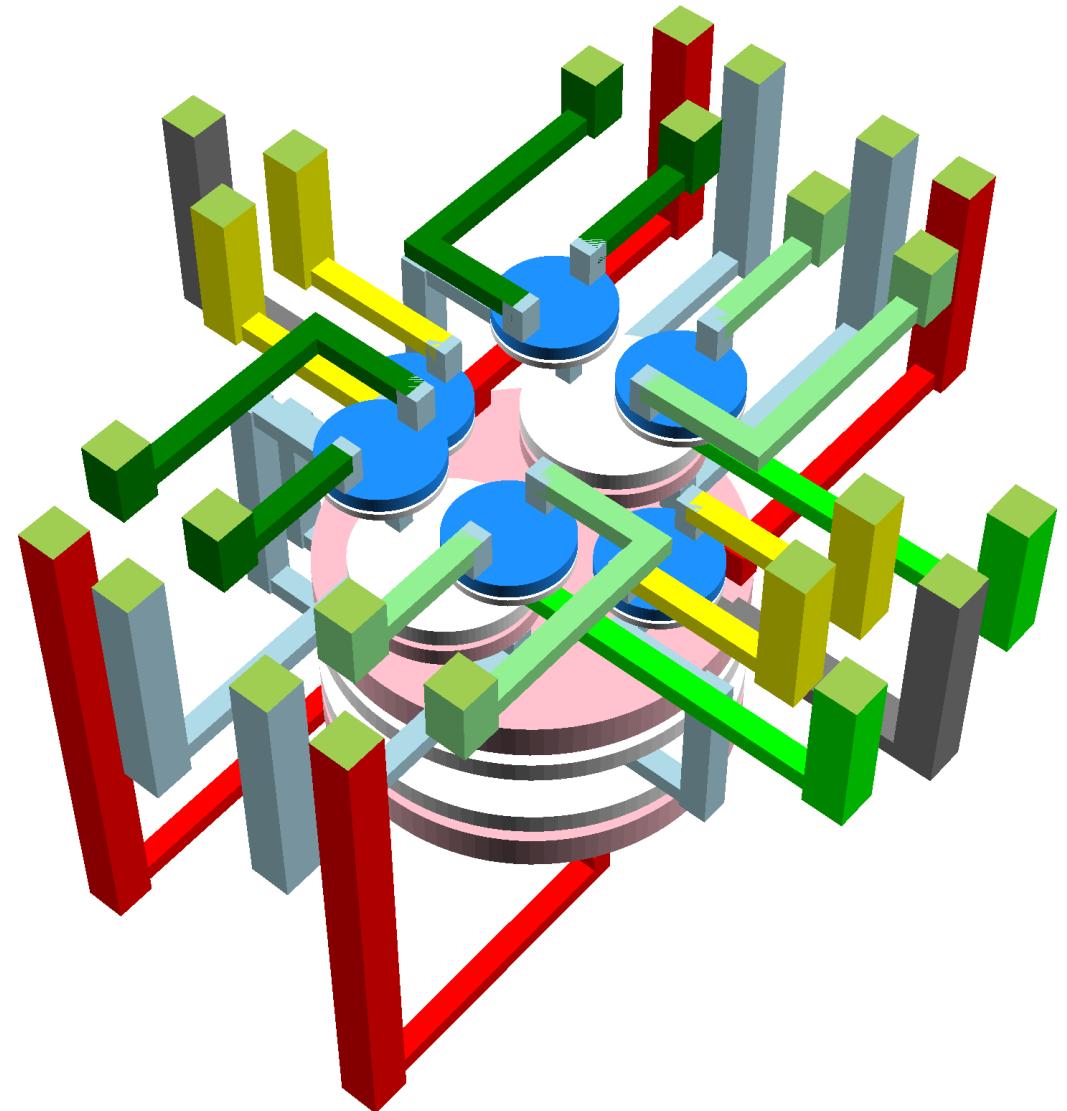
This fluorescence micrograph shows a green microfluidic device. The device features a central circular area with two smaller circular regions containing bright yellow/orange spots. This central assembly is connected to a network of rectangular channels. A vertical channel on the left has a T-junction at the top. A horizontal channel on the right has a T-junction at its midpoint. Below these, there are four parallel horizontal channels. A scale bar in the bottom right corner indicates a length of 300 micrometers.

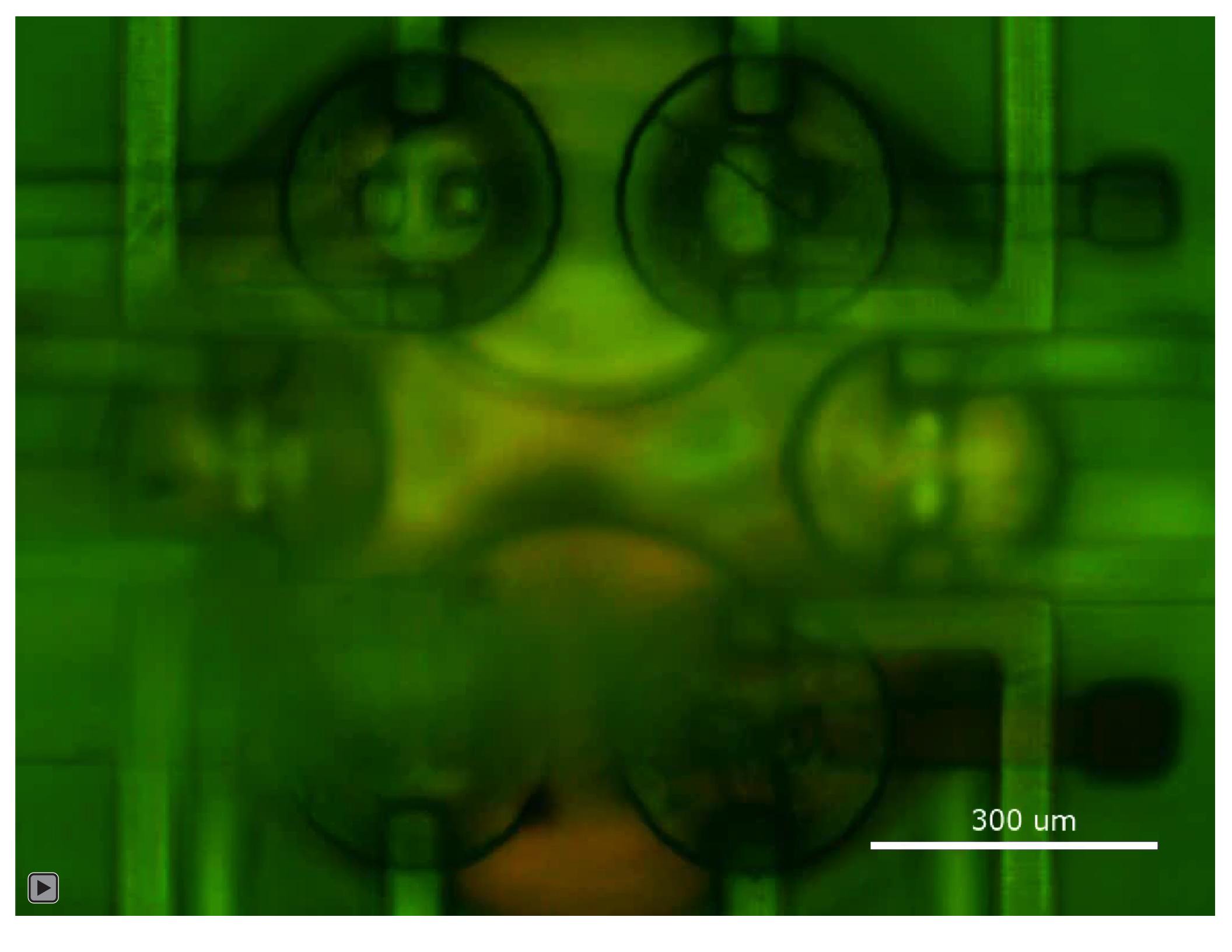


Selectable Ratio Mixer and Pump



Example ratios	
50:50	$3V_A + 3V_B$
83:17	$5V_A + V_B$





300 μ m

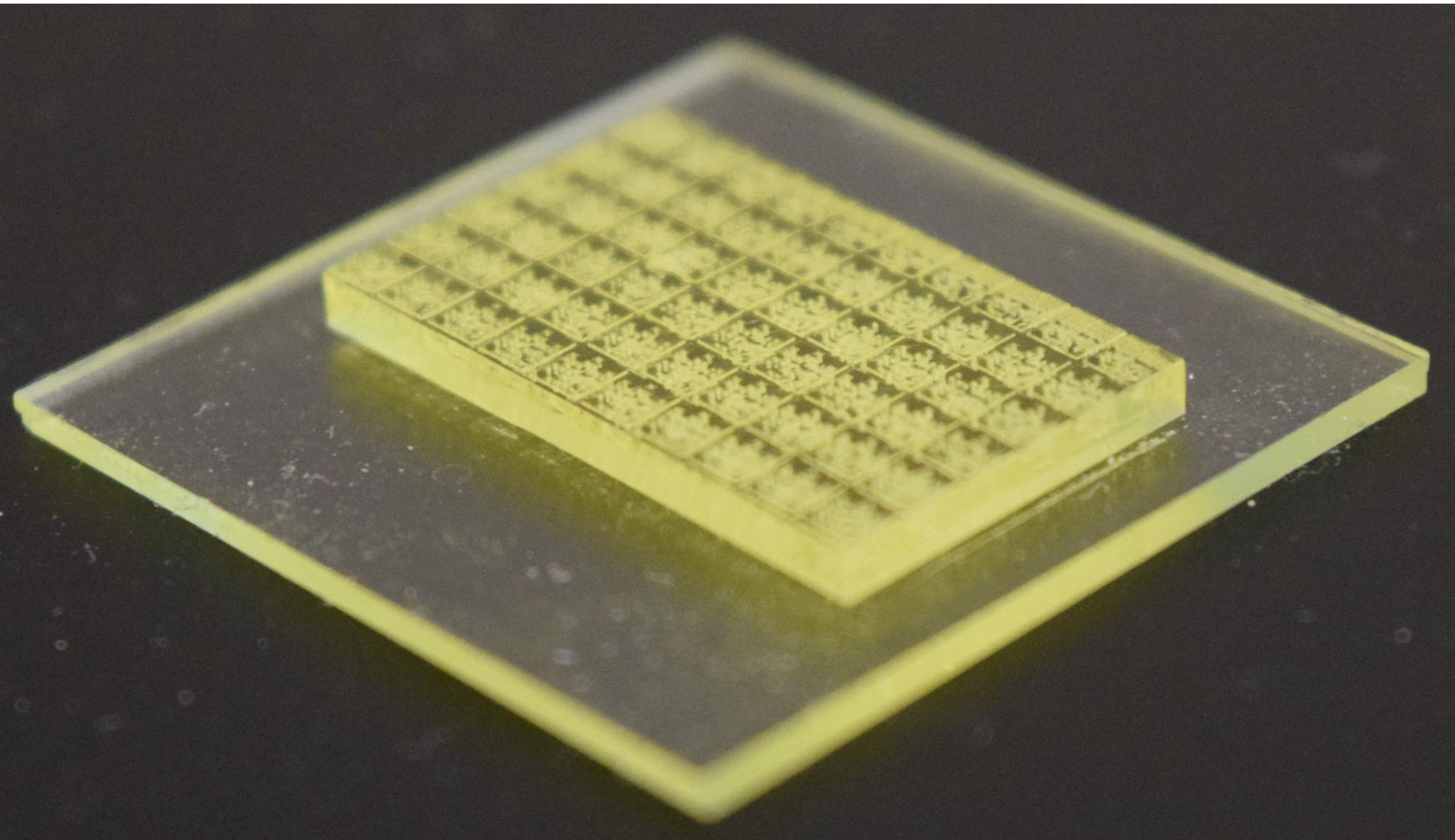


Effort

- 5 days
 - Decide to implement idea to final device
 - Experimental testing used to drive design modifications
- ~20 devices
 - 5 interface chips
 - 15 device chips
 - Multiple designs of each
 - Multiple rounds of testing

60 Selectable Ratio Mixer-Pumps

Print time: 30 minutes



Take Aways

- Microfluidics → It's all about the voids (interconnected network of microvoids)
- 3D Printer resolution specs ≠ achievable void size
- Achievable void size - channels
 - Z - resin optical properties: $\sim 2.3h_a$
 - XY - projected image resolution: 4 pixels
- High density interconnects, valves, pumps
- Small devices → parallel fabrication → manufacturing with 3D printing

Needs

- High resolution 3D printer
 - UV LED source
 - Complete control over operation of printer
- Resins
 - Small h_a
 - Must be tailored to emission spectrum
 - Open source
- Explore 3D structures
 - Get away from conventional 2D thinking
 - Components
 - Layout
 - Experiment-based exploration of parameter space and performance optimization
- Automated design
 - Library of standard components
 - Automated layout
 - Specify functional processes → automated design generation

Acknowledgements

- Radim Knob, postdoc
 - SEM images
- Bryce Bickham, sophomore
- Funding
 - NIH R01EB006124
 - NIH R15GM123405

Posters

- Hua Gong, T219k
High Density, Reversible 3D Printed Microfluidic Interconnects
- Mike Beauchamp, T184h
Microchip Electrophoresis of Preterm Birth Biomarkers in 3D Printed Devices
- Anna Nielson, M182h
Separation of a Panel of Preterm Birth Biomarkers Using Microchip Electrophoresis