Joseph M. DeSimone, PhD

Department of Radiology

Department of Chemical Engineering

Department of Chemistry (by courtesy)

Graduate School of Business (by courtesy)

Stanford University

Presentation at the US Patent and Trademark Office TC 2800 Virtual Tech Fair, May 18, 2021

Academic Career

THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL

NC STATE UNIVERSITY

- Mentored 80 PhD students
  - 50% women and those underrepresented in STEM
- 80+ postdocs

Stanford University

NATIONAL GEOGRAPHIC

Entrepreneurial Career

MICELL TECHNOLOGIES

Abbott A Promise for Life

BioStent, Inc

Advanced Chemotherapy TECHNOLOGIES

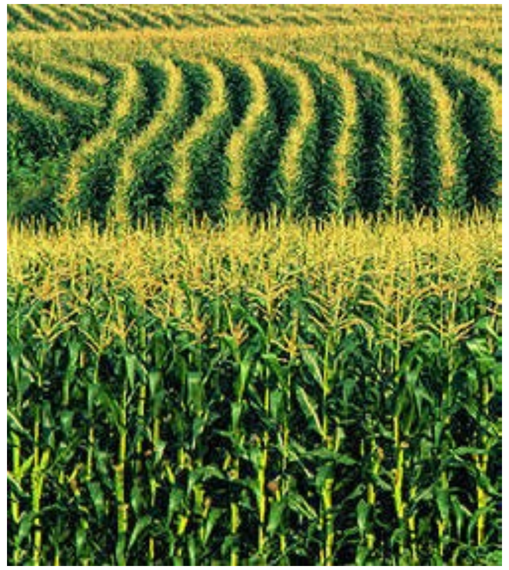
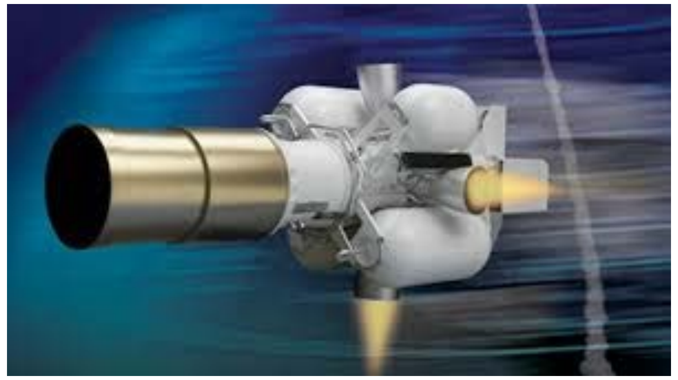
LIQUIDIA TECHNOLOGIES

BLUE CURRENT

Carbon

Innovation Drives the Global Economy





"Research is an expression of faith in the possibility of progress. The drive that leads scholars to study a topic has to include the belief that new things can be discovered, that newer can be better, and that greater depth of understanding is achievable. Research, especially academic research, is a form of optimism about the human condition."

Henry Rosovsky: The University: An Owners Manual

Convergence as a strategy to drive innovation

- National Academies study

NATIONAL ACADEMY OF SCIENCES

NATIONAL ACADEMY OF ENGINEERING

Extend to social sciences, humanities and performing arts

NATIONAL ACADEMY OF MEDICINE

CHERISHING KNOWLEDGE · SHAPING THE FUTURE · FOUNDED 1780
AMERICAN ACADEMY OF ARTS & SCIENCES

- The coming together of different fields of study through collaboration and the integration of approaches that were originally viewed as distinct and potentially contradictory.

- "…convergence is a blueprint for innovation…"

Convergence: Facilitating Transdisciplinary Integration of Life Sciences, Physical Sciences, Engineering, and Beyond; National Academies Press: Washington D.C., 2014. (Committee Chair)

Convergence & Diversity

EDITORIAL

INNOVATION

Driving Convergence with Human Diversity

– Joseph M. DeSimone and Crista L. Farrell

- “We learn the most from those we have the least in common with.”
- “History shows that the most innovative solutions often arise from diverse teams composed of talented individuals with different areas of expertise, backgrounds, and life experiences.”
- “Without being intentional about human diversity, we risk detracting from the opportunity that exists to achieve innovation and societal impact through convergent science.”

www.ScienceTranslationalMedicine.org 28 May 2014 Vol 6 Issue 238 238ed11

Emily
Stein

Cooper
Shea

Brian
Lee, PhD

Gabriel
Lipkowitz

Gloria
Chyr

Netra
Rajesh

Madison
Driskill

Audrey
Shih

DeSimone Lab

Stanford

Rhys
De Sota

Tim
Samuelson

Harrison
Lin

Kaiwen
Hsiao, PhD

Alex
Abramson, PhD

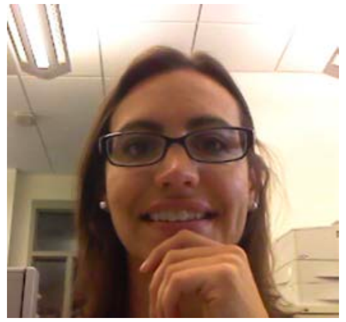
Michael
Zhang, MD

Sydney
Stoker, DDS

Ayinwi
Muma

Leah
Brickson

Shaomin
Tian, PhD



Jillian
Perry, PhD

Gunilla
Jacobson, PhD

Maria
Dulay, PhD

Crista
Farrell

Sofia
Gonzales


Carbon
PRIDE
LOVE

In this lab, WE BELIEVE

SCIENCE
is real

LOVE
is love

BLACK LIVES
matter

KINDNESS is
everything

WOMEN'S RIGHTS
are human rights

DISABILITIES
deserve accessibility

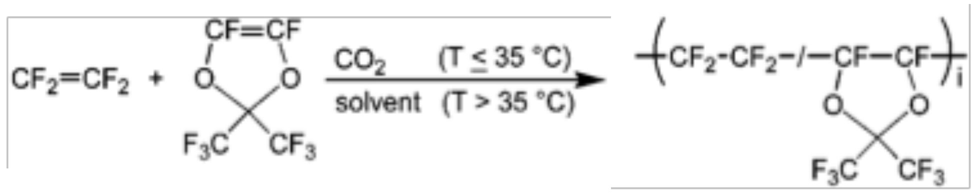
IMMIGRANTS
are welcome

We need to leave the
PLANET
better than we found it

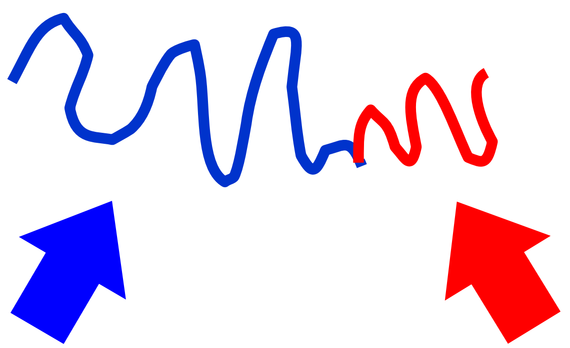
EVERY MOMENT
counts

Synthetic Organic Chemistry Integrated with Novel Processes

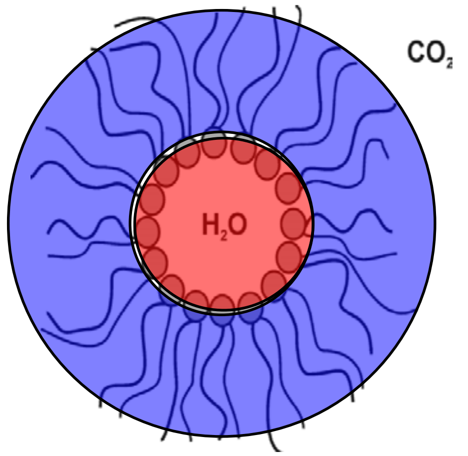
- **Novel fluoropolymers & Surfactants**



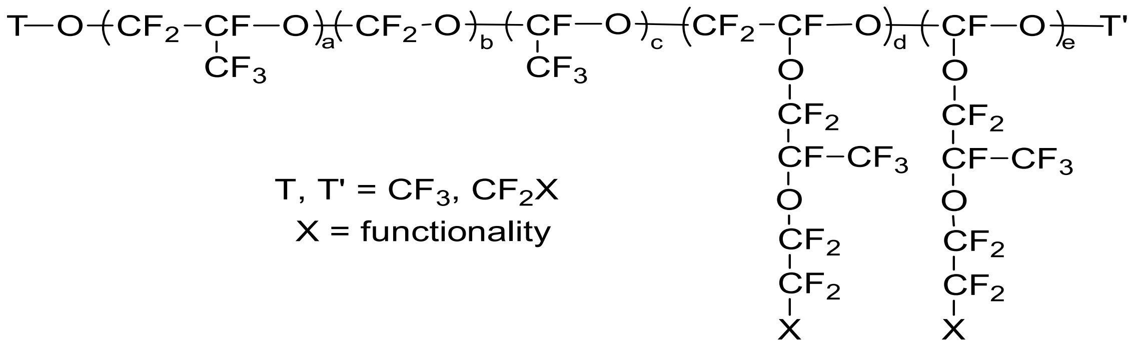
Polymerizations in Supercritical CO_2



“CO_2-philic” “CO_2-phobic”

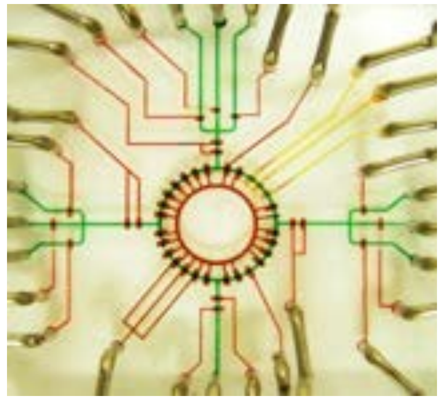


Science **1992**, *257*, 945
Science **1994**, 265, 356
Langmuir **1995**, 11, 4241
Science **1996**, *274*, 2049
Nature **1997**, *389*, 368
Macromolecules **1999**, *32*, 8224
J. Am. Chem. Soc. **2001**, *123*, 7199
Langmuir **2004**, 20, 1065
Macromolecules **2006**, *39*, 3427
Macromolecules **2009**, *42*, 148.

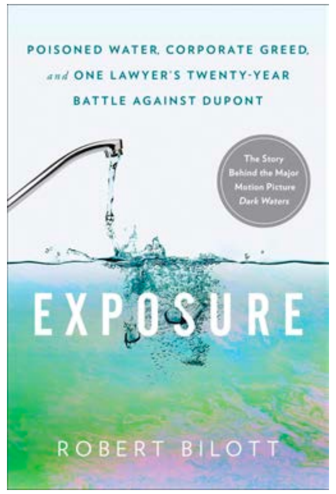


Synthesis of “Liquid Teflon” in CO_2

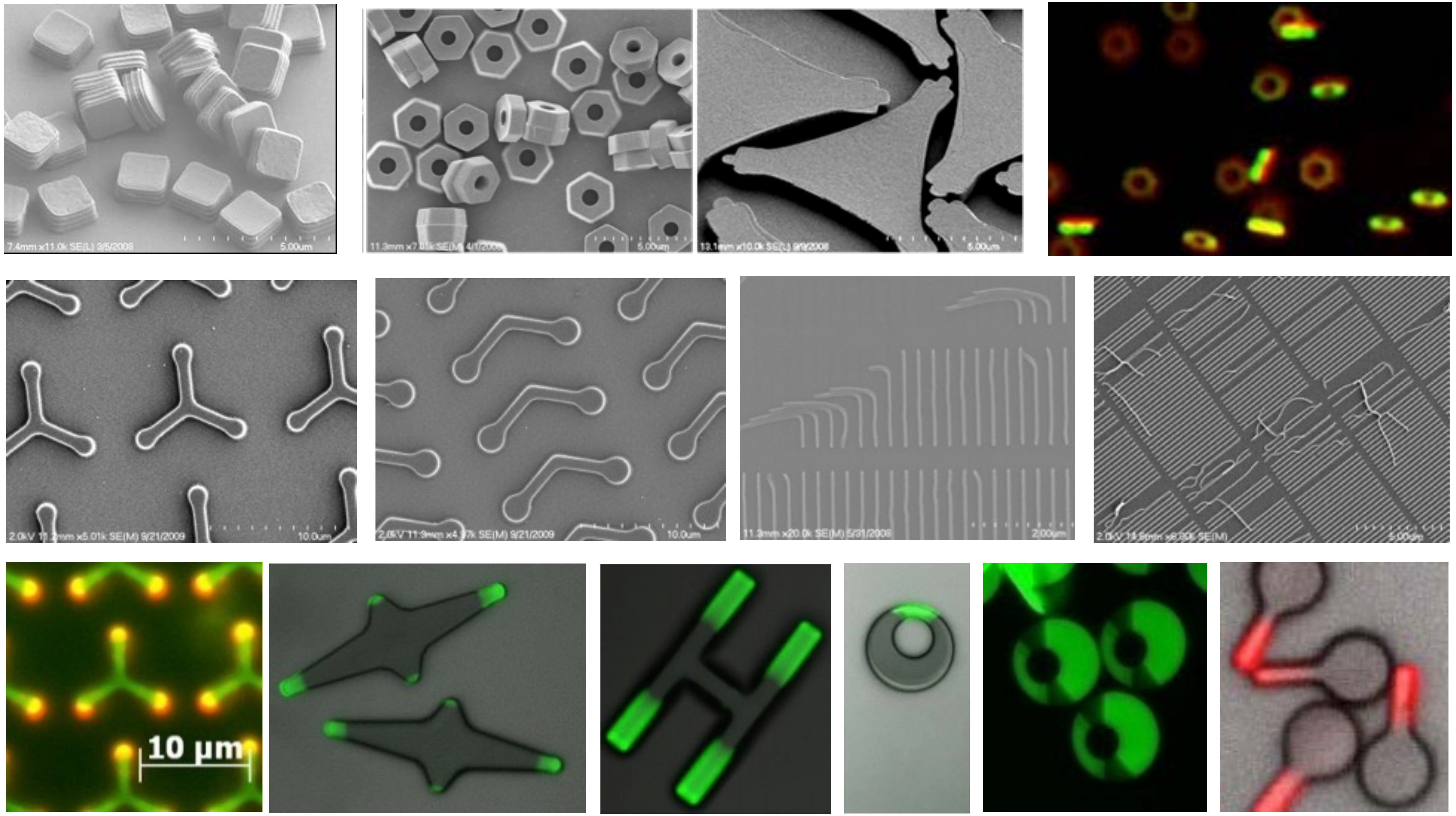
- **Merging Lithography with Therapeutics, Vaccines and More…**



Presidential Green Chemistry Challenge:
1997 Academic Award



Extremely Uniform, Shape-Specific Particles with a Wide Range of Spatio-Chemical Composition Control

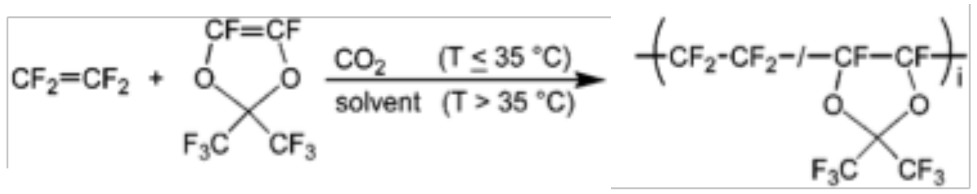


"Scalable, Shape-Specific, Top-Down Fabrication Methods for the Synthesis of Engineered Colloidal Particles"; Merkel, Herlihy, Nunes, Orgel, Rolland, DeSimone. *Langmuir* **2010**, *26 (16)*, 13086

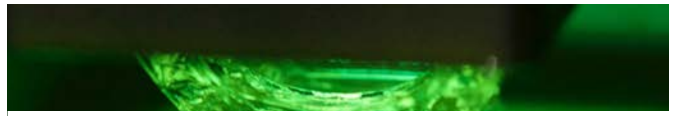
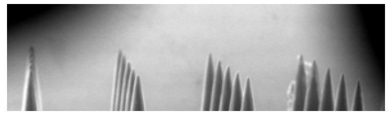
WELCOME
TO THE
NASDAQ FAMILY
Now Listed on Nasdaq
LIQUIDIA
TECHNOLOGIES
LQDA NasdaqListed
Nasdaq
changedirection.org
FLIX ORIGINAL COMEDY SPECIAL
M JEFFERIES
HIS IS ME NOW
NOW
AMING | NETFLIX
FELL FR
THE NEW

Synthetic Organic Chemistry Integrated with Novel Processes

- **Novel fluoropolymers & Surfactants**

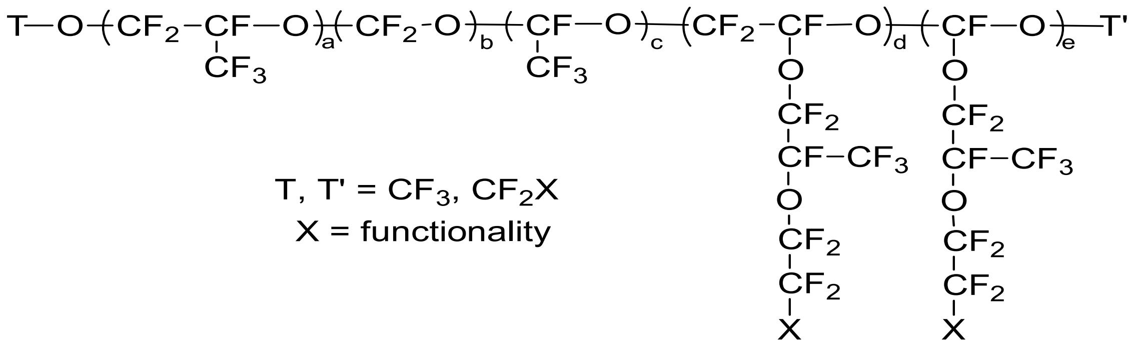


Polymerizations in Supercritical CO_2

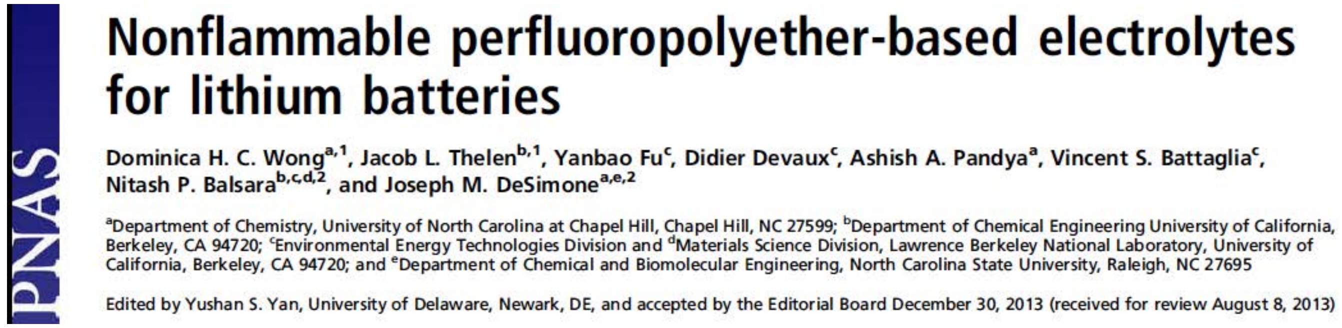
carbon

Science **2015**, *347*, 1349-1352
TED2015, Vancouver



Synthesis of “Liquid Teflon” in CO_2

“Optically Transparent, Amphiphilic Networks Based on Blends of PFPEs and PEG”; *J. Am. Chem. Soc.* **2008**, *130*, 14244



PNAS

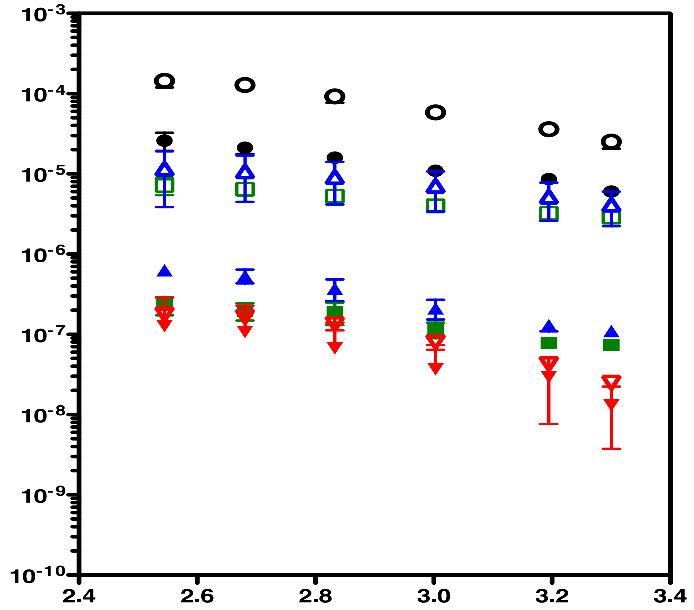
Nonflammable perfluoropolyether-based electrolytes for lithium batteries

Dominica H. C. Wong[a,1], Jacob L. Thelen[b,1], Yanbao Fu[c], Didier Devaux[c], Ashish A. Pandya[a], Vincent S. Battaglia[c], Nitash P. Balsara[b,c,d,2], and Joseph M. DeSimone[a,e,2]

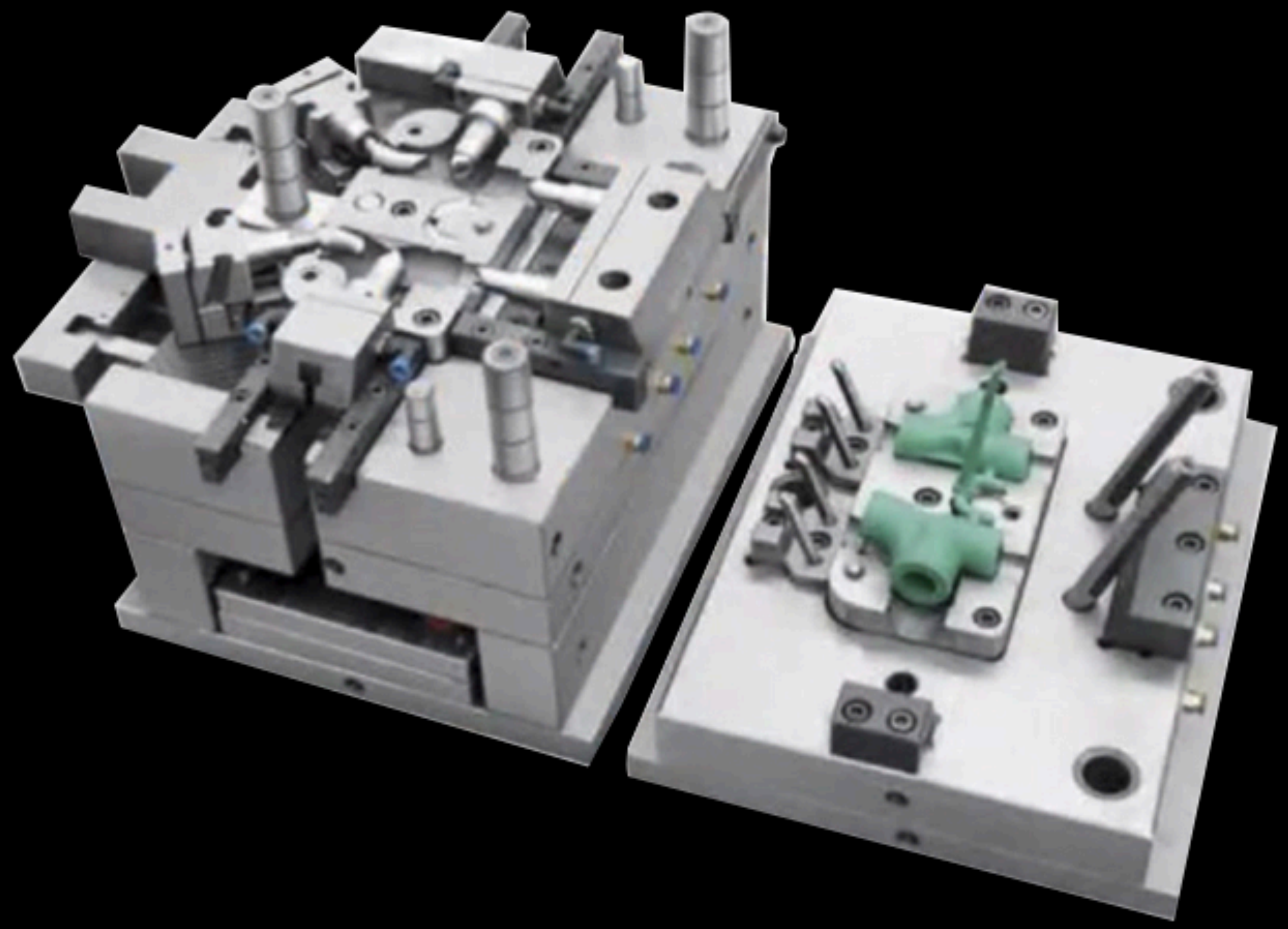
[a]Department of Chemistry, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599; [b]Department of Chemical Engineering University of California, Berkeley, CA 94720; [c]Environmental Energy Technologies Division and [d]Materials Science Division, Lawrence Berkeley National Laboratory, University of California, Berkeley, CA 94720; and [e]Department of Chemical and Biomolecular Engineering, North Carolina State University, Raleigh, NC 27695

Edited by Yushan S. Yan, University of Delaware, Newark, DE, and accepted by the Editorial Board December 30, 2013 (received for review August 8, 2013)

BLUE CURRENT



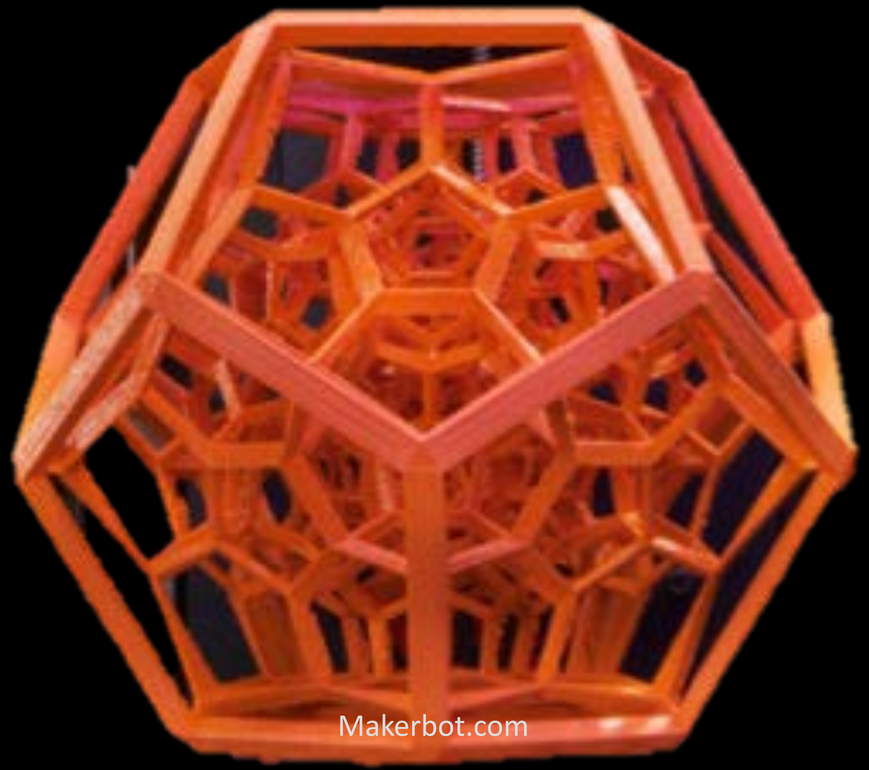
Casting / molding was invented 7,000 years ago



Injection molding $330B

Why 3D printing?
(a digital printing technology)

- Complexity is free
- Unlimited design space
- Zero lead time
- Precise replication from scanner
- Compact, portable manufacturing
- Zero skill manufacturing
- Empowering to everyone…

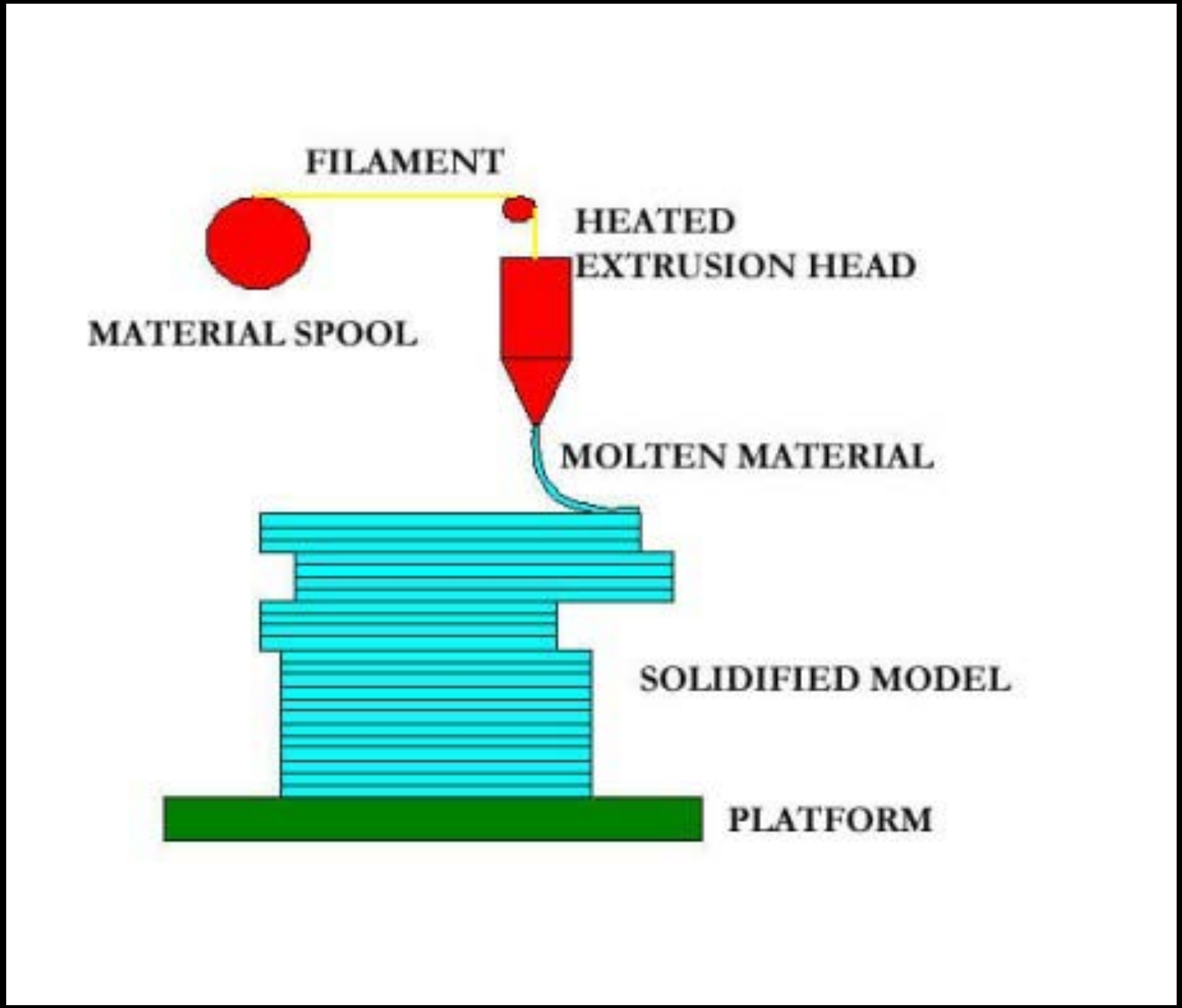


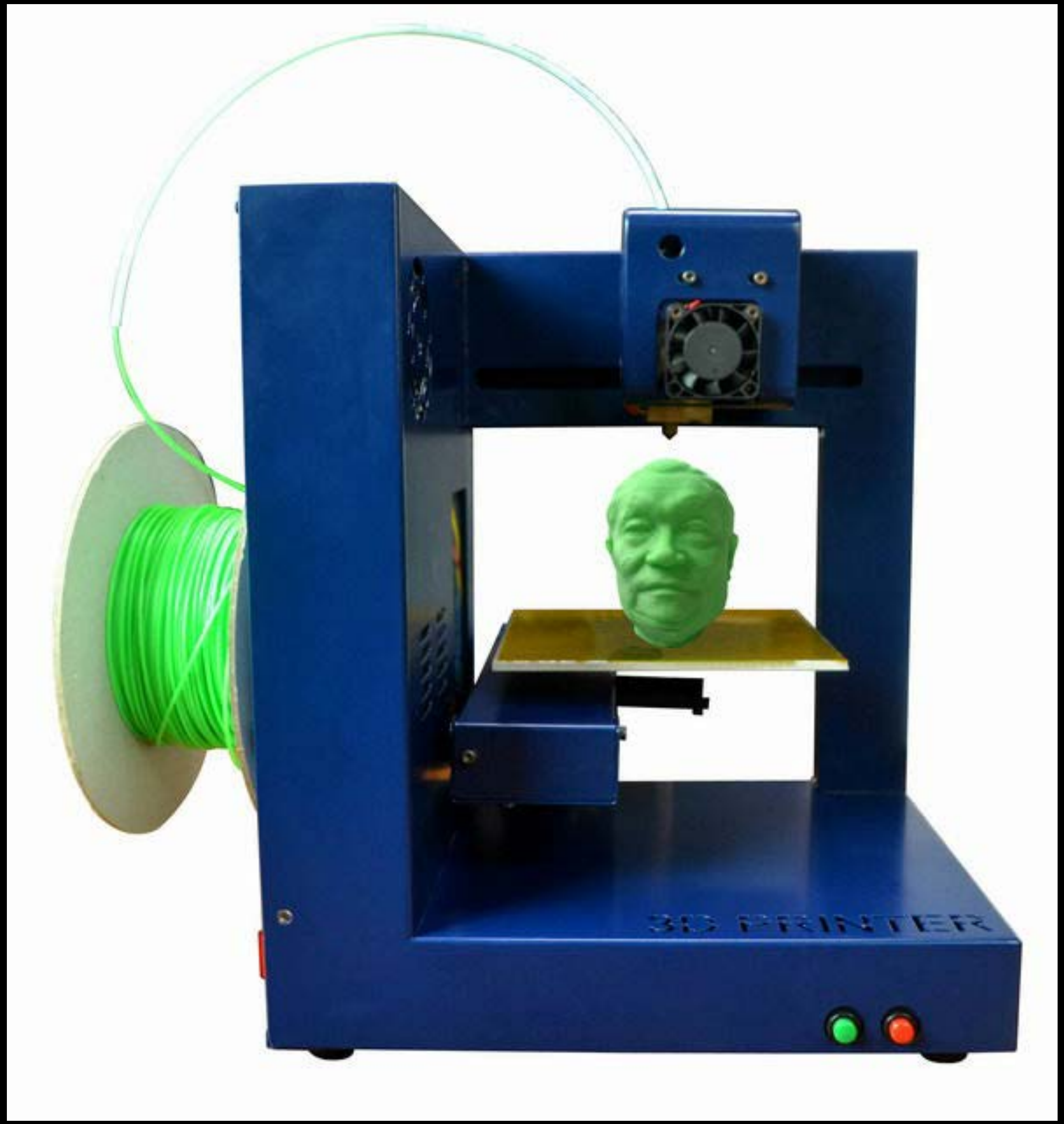
Adapted from *Fabricated: The New World of 3D Printing*

Polymer-Based 3D Printing Processes

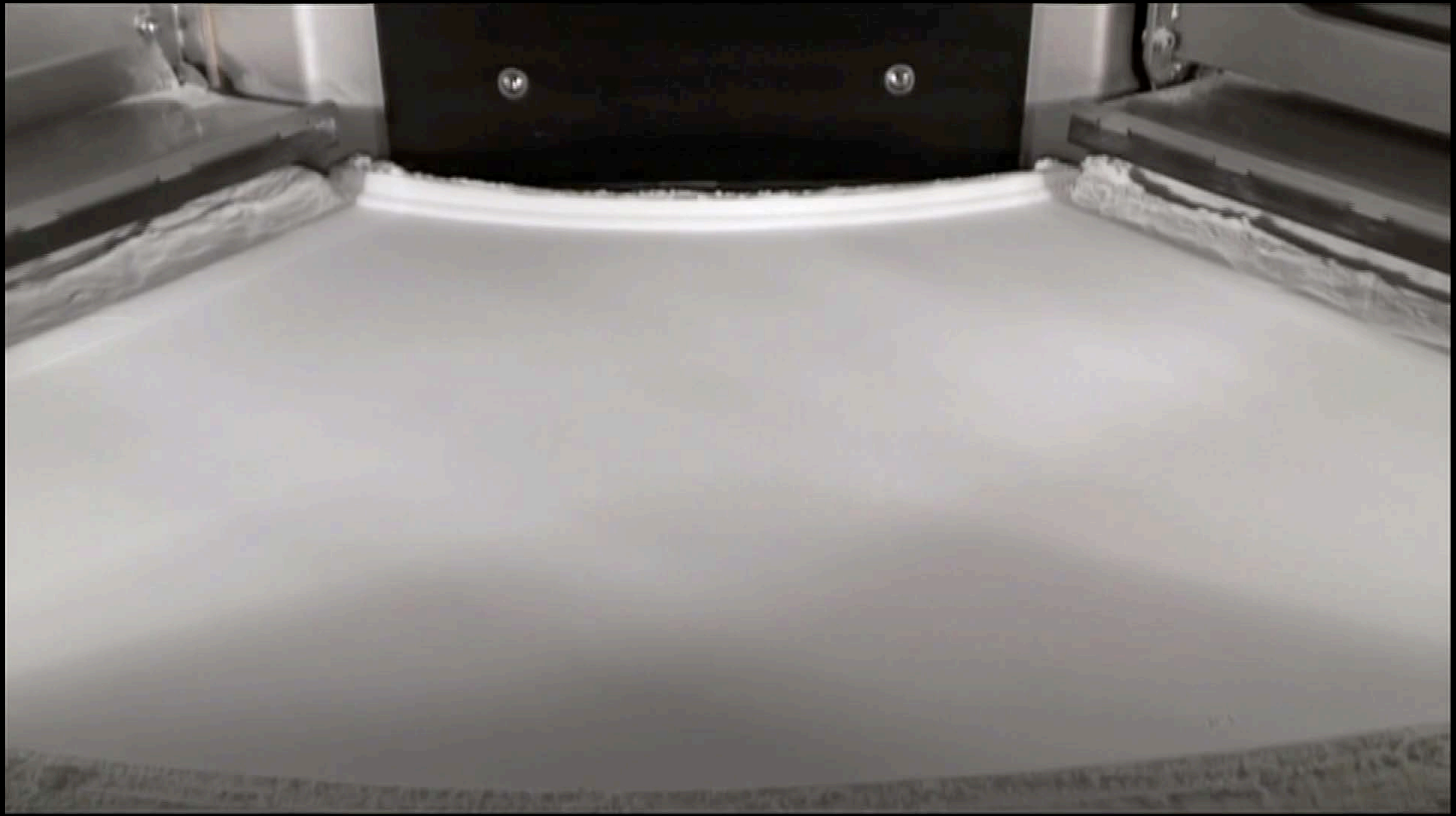
	Extrusion	Powder Bed Fusion	Binder Jetting	Material Jetting	Photo-Polymerization
Tradename	FDM	SLS	Binder Jetting	Polyjet	SLA
Description	Heated material selectively dispensed through a nozzle	Laser selectively fuses regions of powder bed	Liquid bonding agent selectively deposited to join powder	Droplets of build material selectively deposited	Liquid polymer selectively cured by laser or DLP
Example Printer	Stratasys	EOS 3DS MJF	3DS ZCorp	Objet 3DS Polyjet	3DS Envisiontec

Extrusion Technology





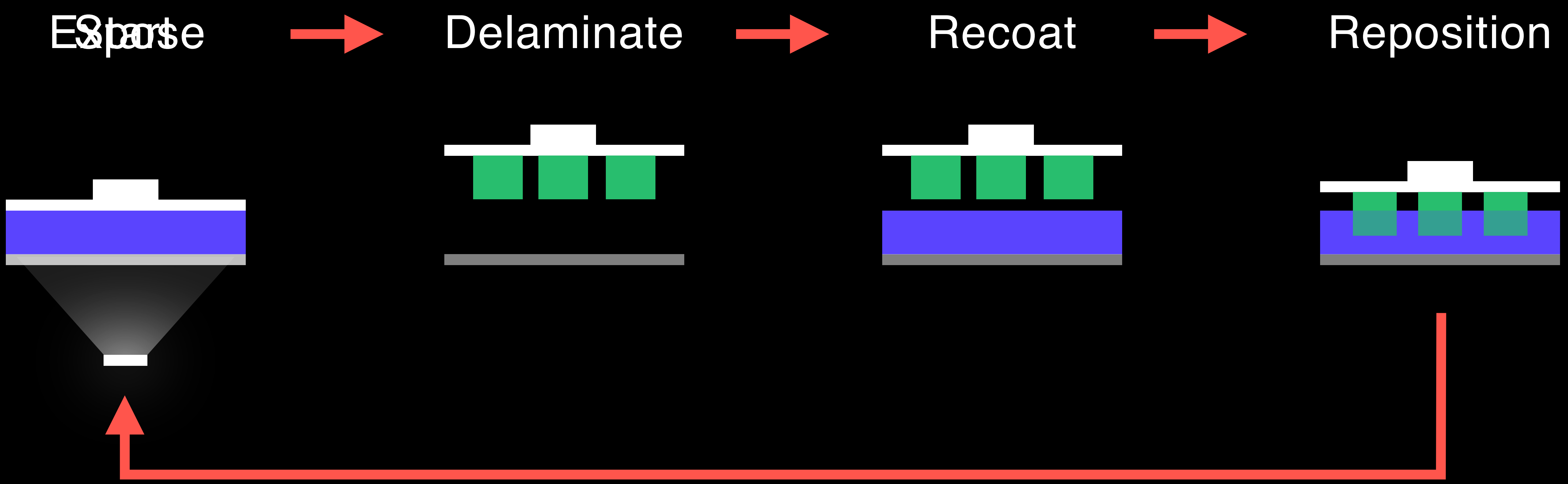
Powder Bed Fusion Technology



- Slow — typically 1-3 mm/hr; build takes hours
- Prototype-quality — shale effect
- Limited functionality, low Tg plastics
- Materials too expensive, lots of waste

Original Photo-polymerization Technology (circa 1980)

Traditional Mechanical Approach for resin renewal



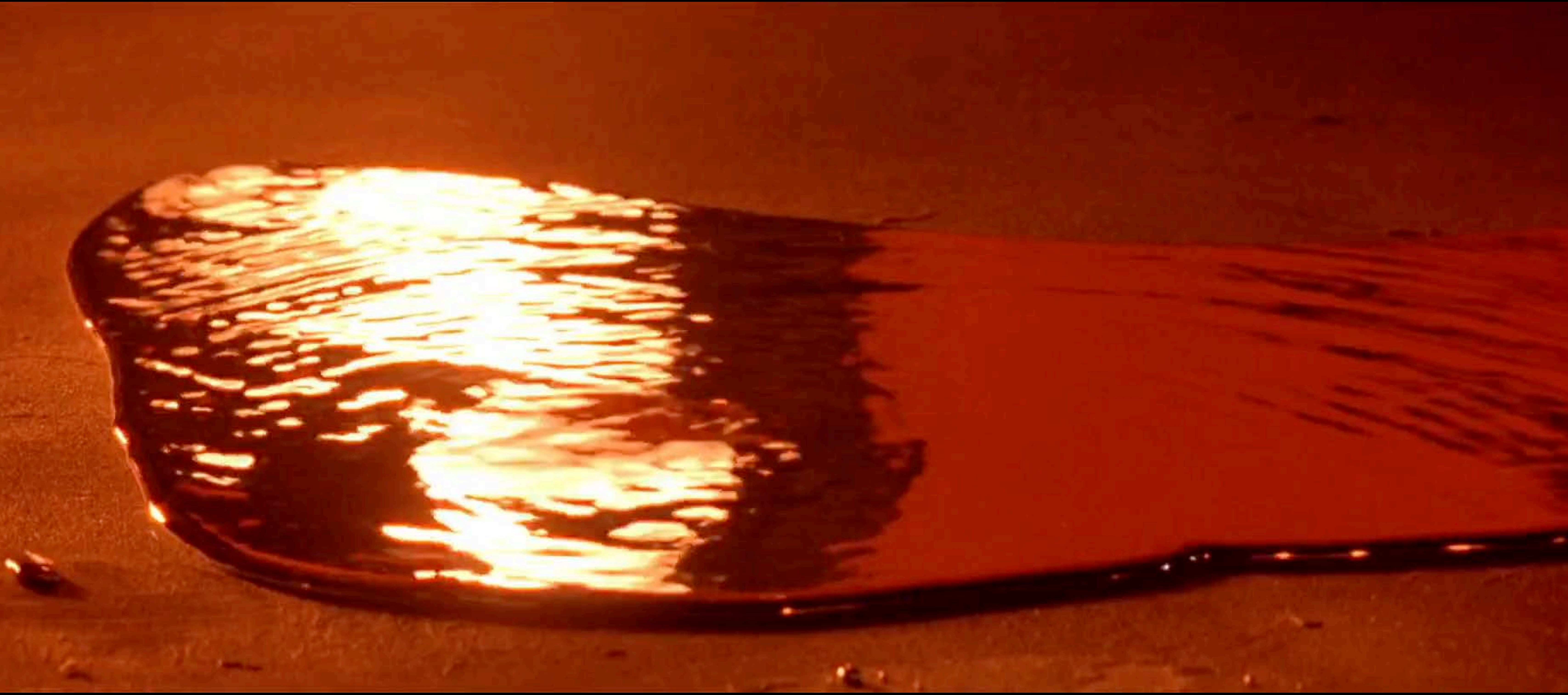
2D PRINTING OVER AND OVER

3D Prints Take Forever

Printed Parts exhibit Anisotropy

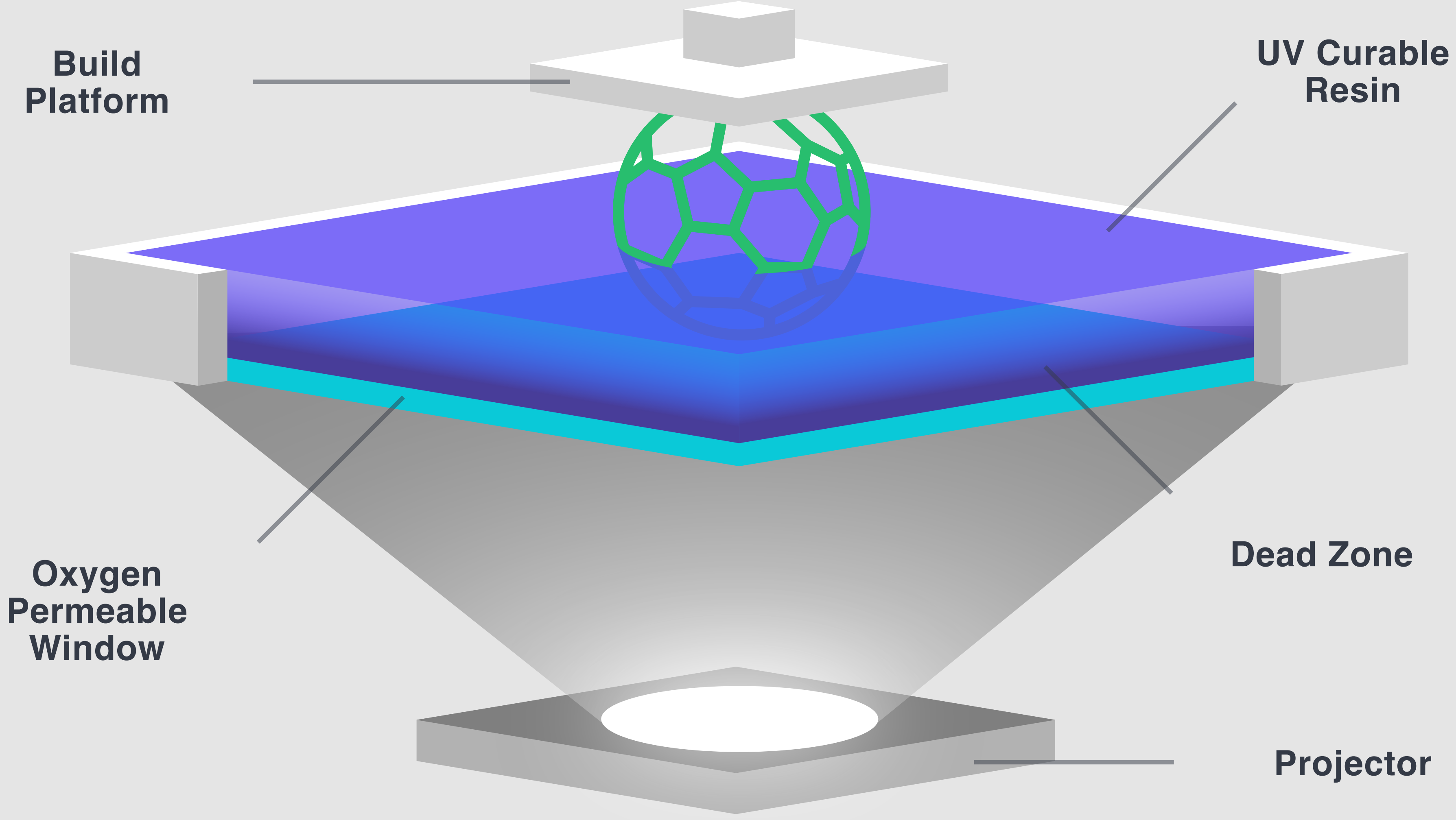
Layers or Particles are Not Fully Fused

Material Choices are Far Too Limited

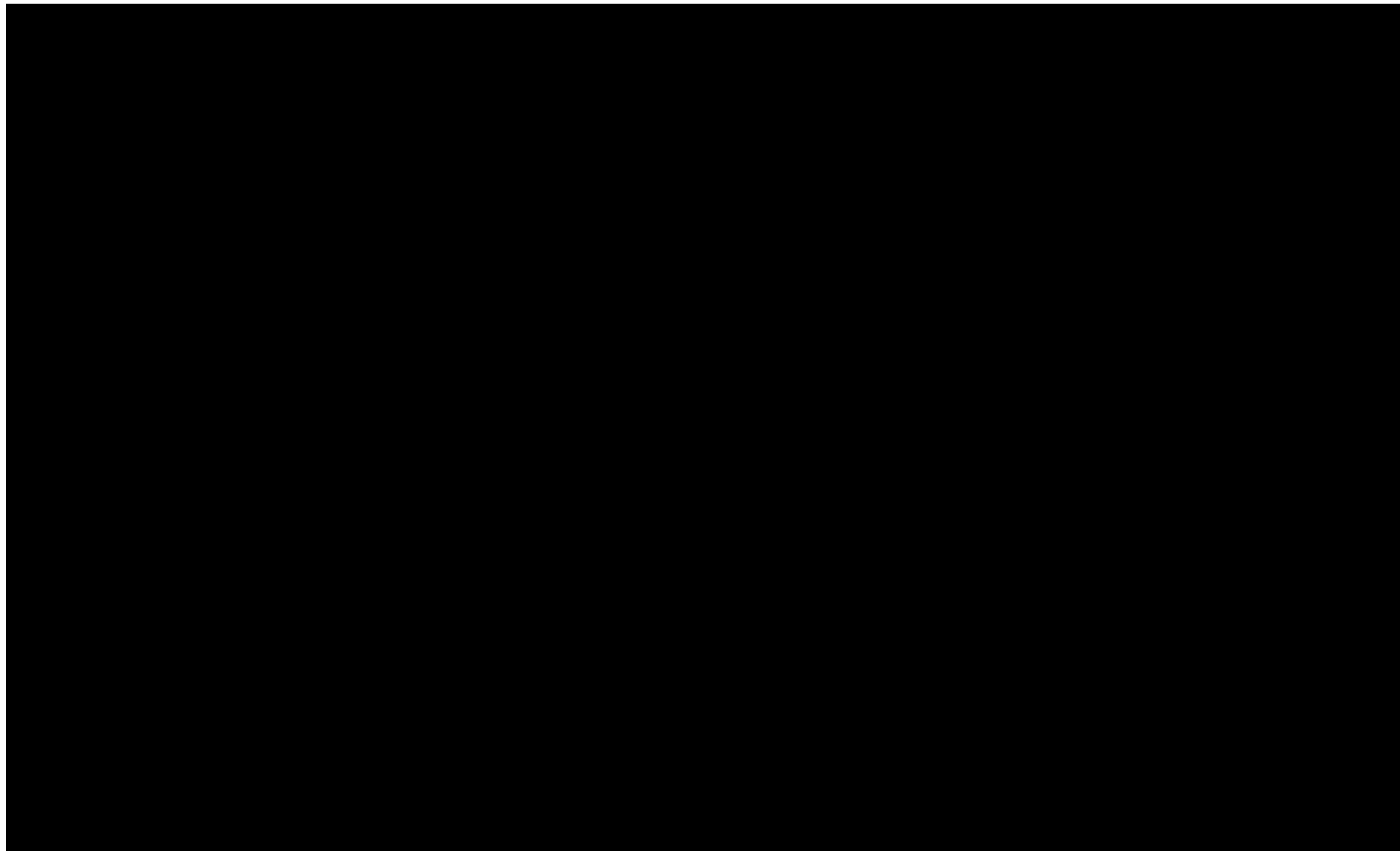


Terminator 2: Judgment Day
Tri-Star Pictures

Science **2015**, *347*(6228), 1349-1352

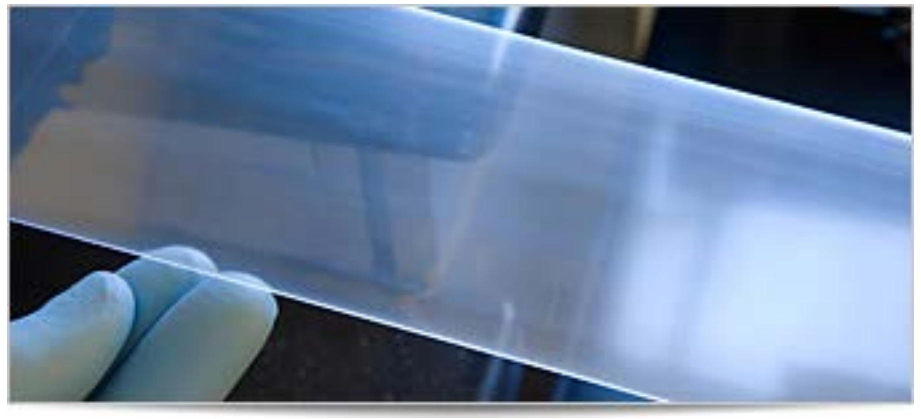



Carbon

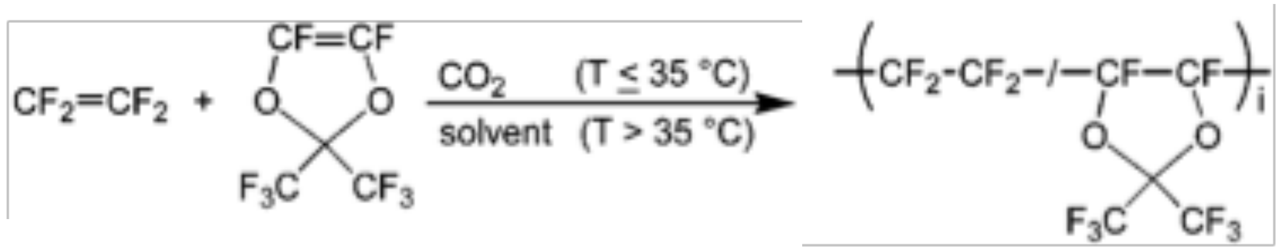


Key Features of the CLIP Window

Science **2015**, *347*(6228), 1349-1352



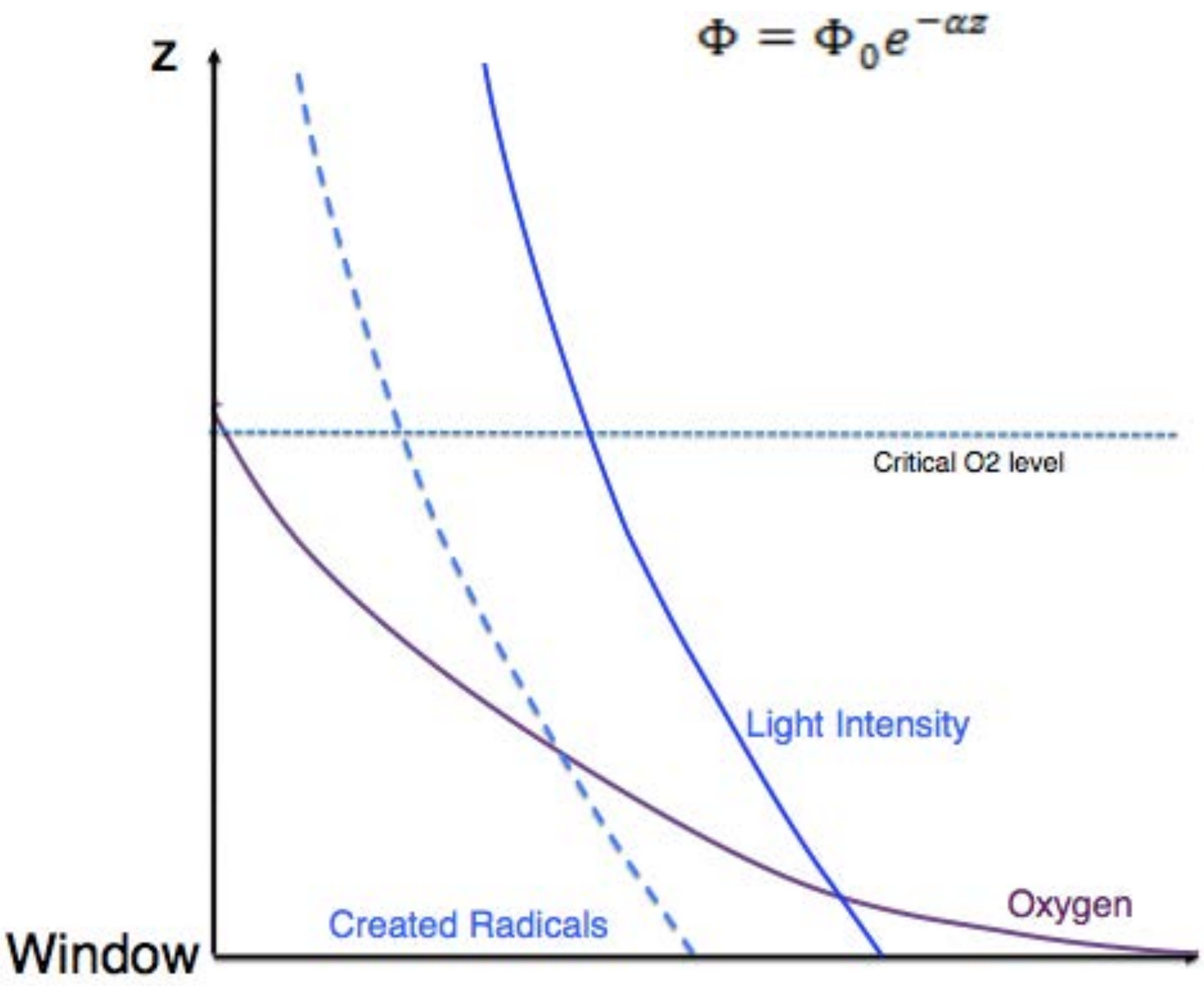
Polymerizations in Supercritical CO_2



Science **1992**, *257*, 945
Macromolecules **2003,** *36*, 7107

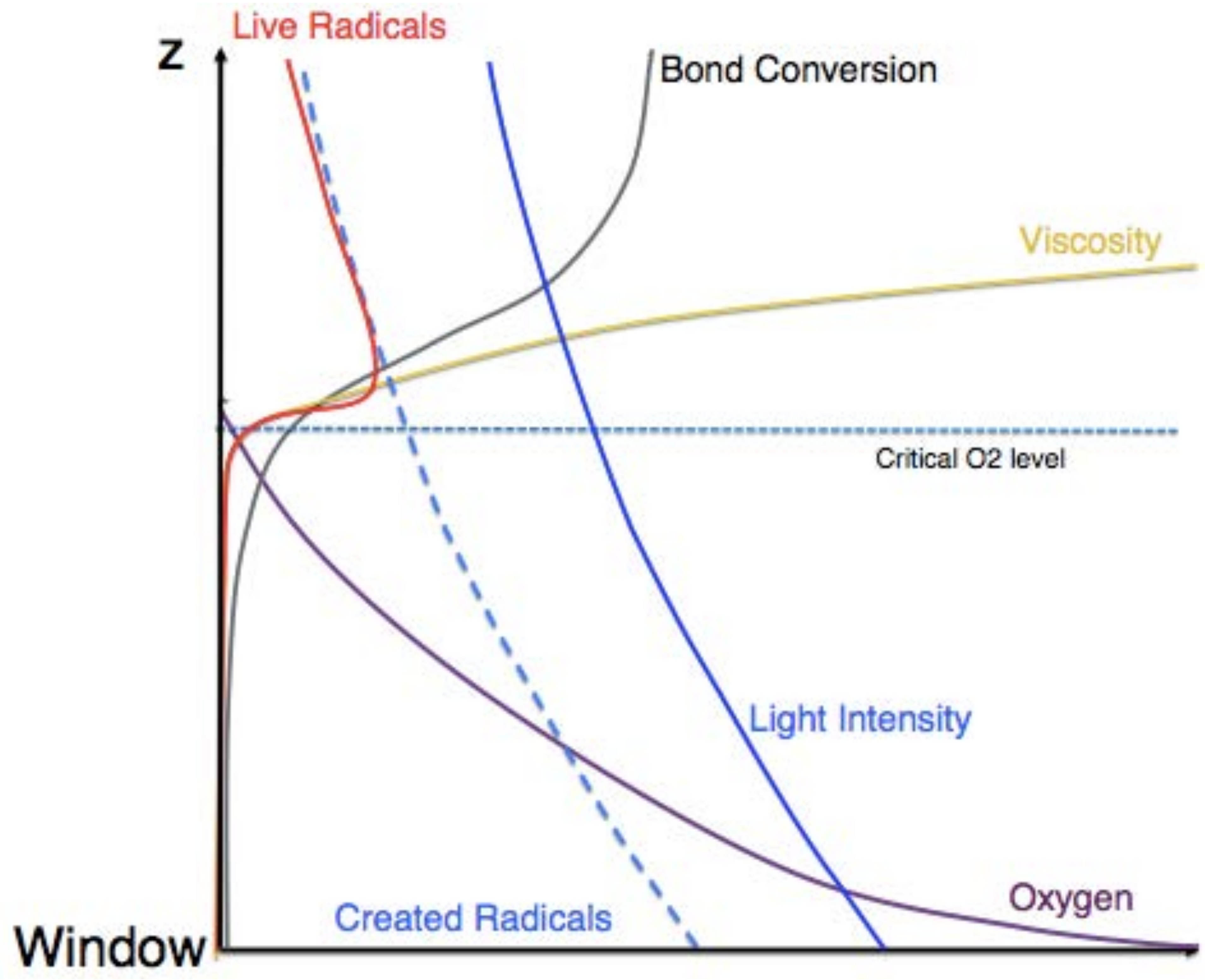
- Optically transparent at 385 nm
- Highly permeable to oxygen
- Chemically resistant to a wide range of organic liquids
- Thermally stable
- Photochemically stable
- Mechanically strong and durable
- Works well for small areas, not for areas > 10 cm^2 due to "drumming"

At the Interface



$$PI \xrightarrow{hv} PI^* \xrightarrow{k_d} 2R\cdot$$
$$R\cdot + M \xrightarrow{k_i} RM\cdot$$
$$RM_n\cdot + M \xrightarrow{k_p} RM_{n+1}\cdot$$
$$PI \xrightarrow{hv} PI^* + O_2 \xrightarrow{k_Q} Quenching$$
$$RM\cdot + O_2 \xrightarrow{k_O} RMOO\cdot$$

At the Interface



$$PI \overset{h\nu}{\rightarrow} PI^* \overset{k_d}{\rightarrow} 2R\cdot$$

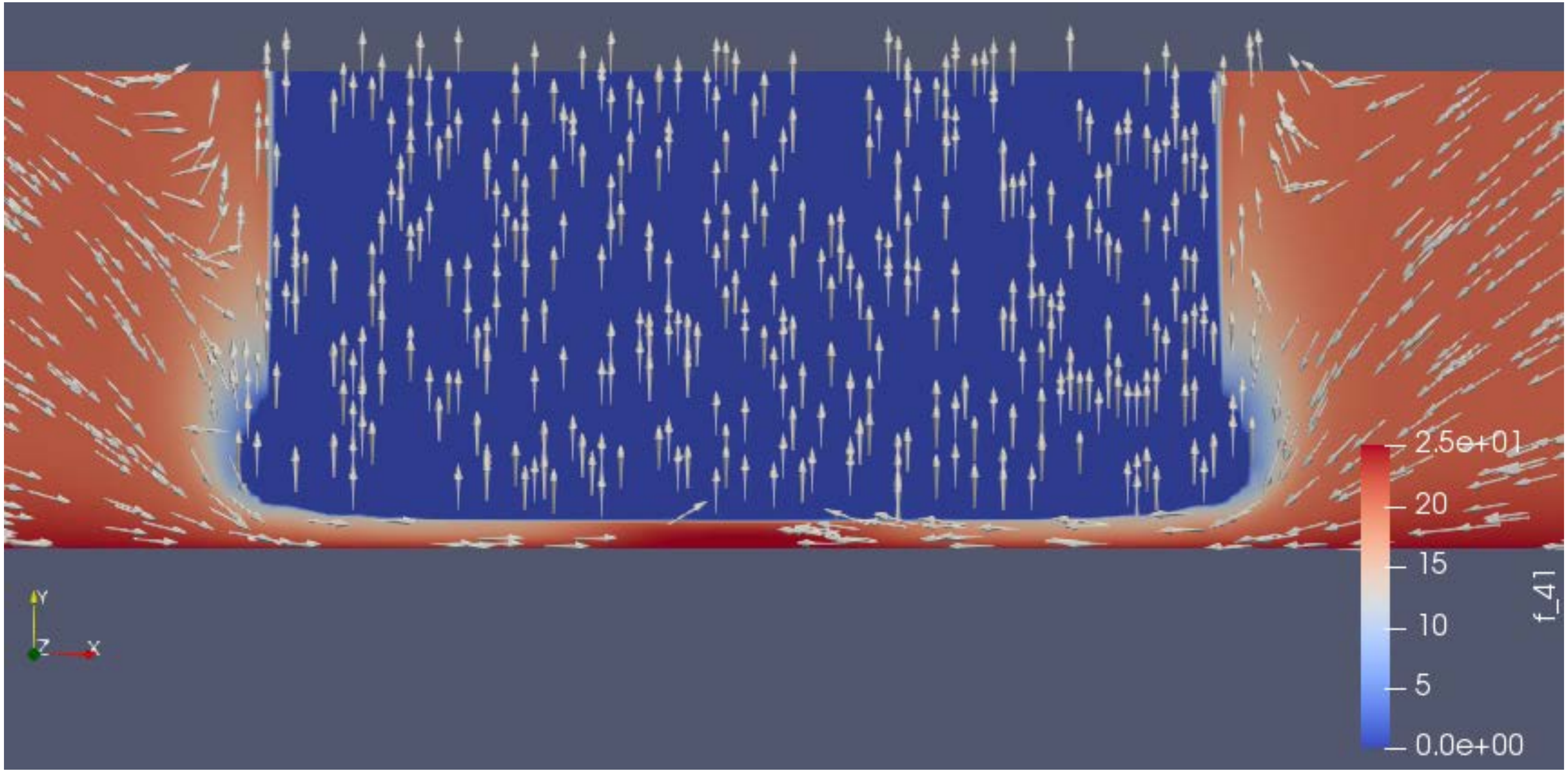
$$R\cdot + M \overset{k_i}{\rightarrow} RM\cdot$$

$$RM_n\cdot + M \overset{k_p}{\rightarrow} RM_{n+1}\cdot$$

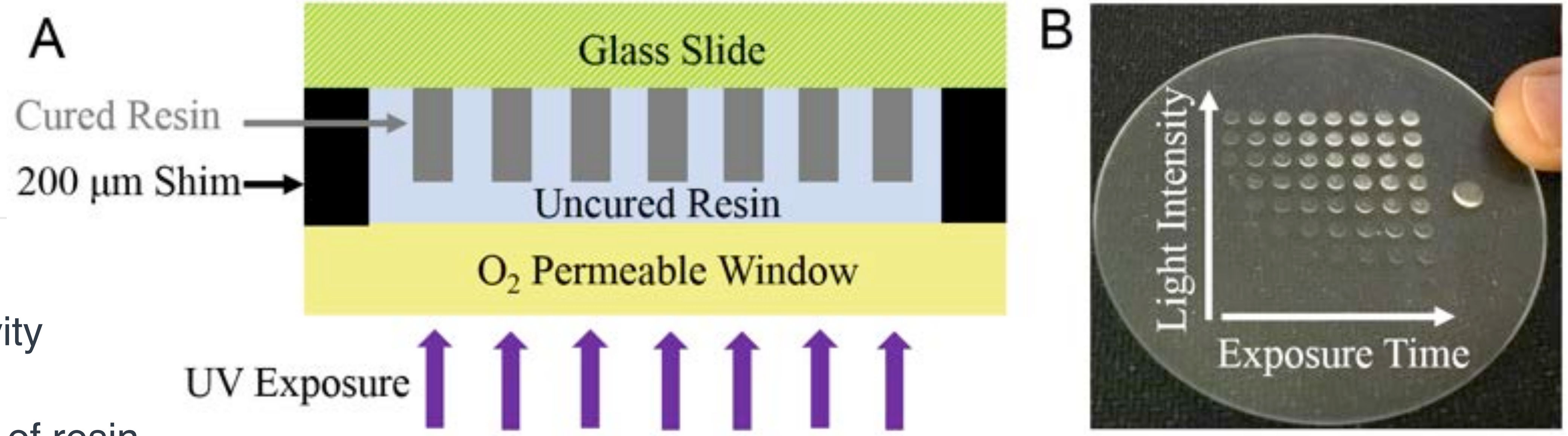
$$PI \overset{h\nu}{\rightarrow} PI^* + O_2 \overset{k_Q}{\rightarrow} Quenching$$

$$RM\cdot + O_2 \overset{k_O}{\rightarrow} RMOO\cdot$$

FEA simulation: O_2 and resin flow



Print Planner

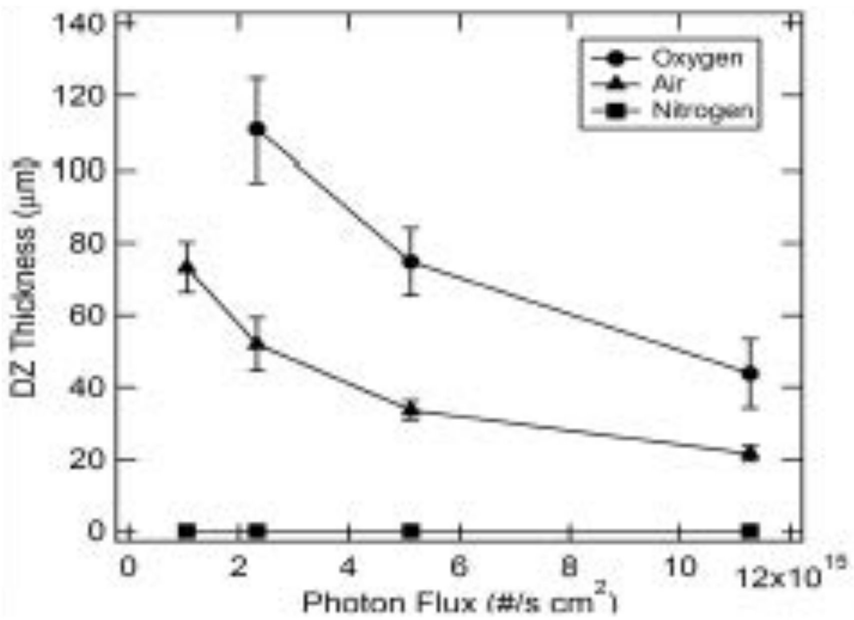


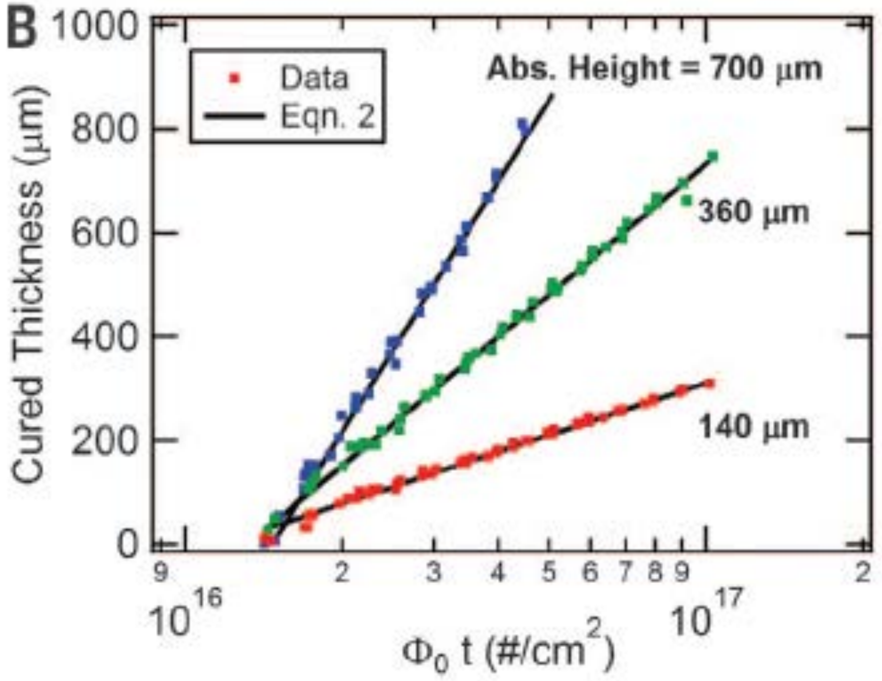
Resin properties

- Dose-to-cure
- Molar absorptivity
- Viscosity
- Green strength of resin

Machine configuration

- Available light intensity
- Oxygen flux
- Pixel size





Part geometry

- Cross-sectional area
- Cavities
- “Hero” surface orientation

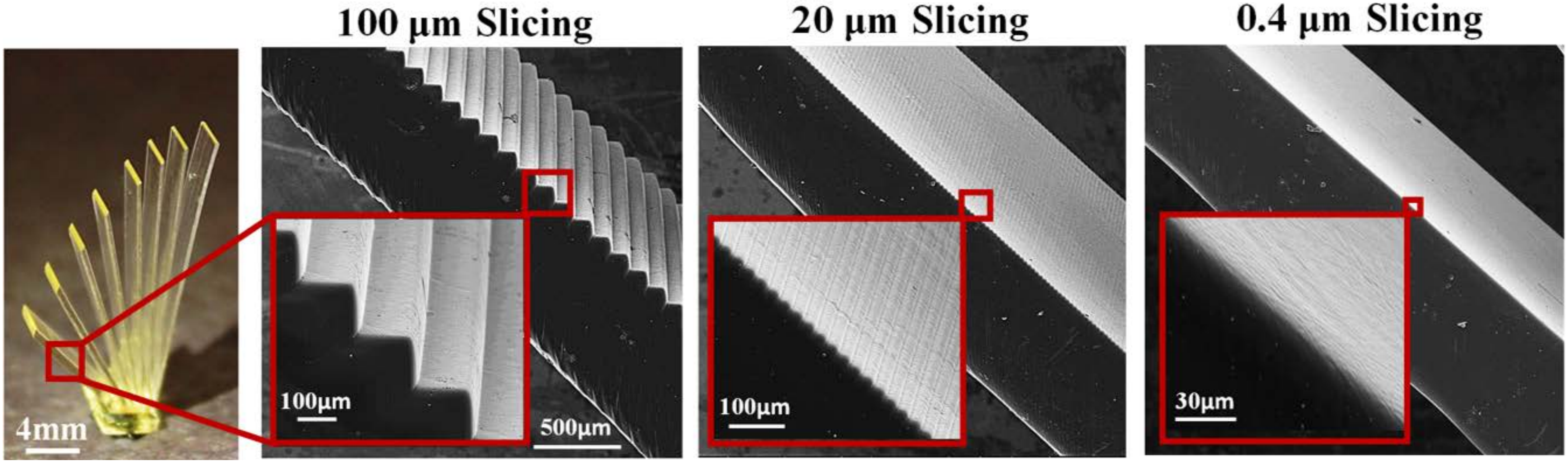
Desired operating conditions

- Accuracy
- Trade-off between resolution and speed
- Use of latent heat
- General Purpose Printer mode vs Manufacturing mode

“Print Button”

Surface Roughness with CLIP

PNAS | October 18, 2016 | vol. 113 | no. 42 | 11703–11708



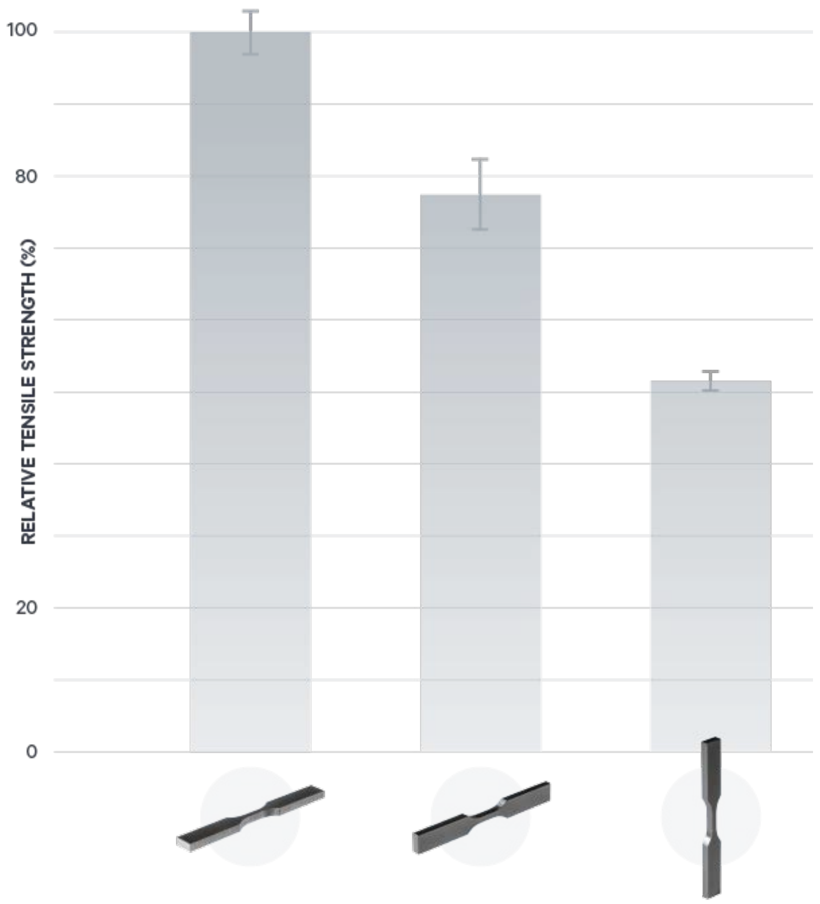
Slicing (μm)	R_a (μm): 20°	R_a (μm): 90°	R_{Sm} (μm): 20°	Experimental Step Height (μm)
100	13.78 ± 0.79	0.006 ± 0.001	145.65 ± 0.42	92.23 ± 6.01
20	0.82 ± 0.03	0.006 ± 0.001	28.74 ± 0.22	18.20 ± 1.19
0.4	0.012 ± 0.004	0.005 ± 0.001	0.72 ± 0.06	0.45 ± 0.05

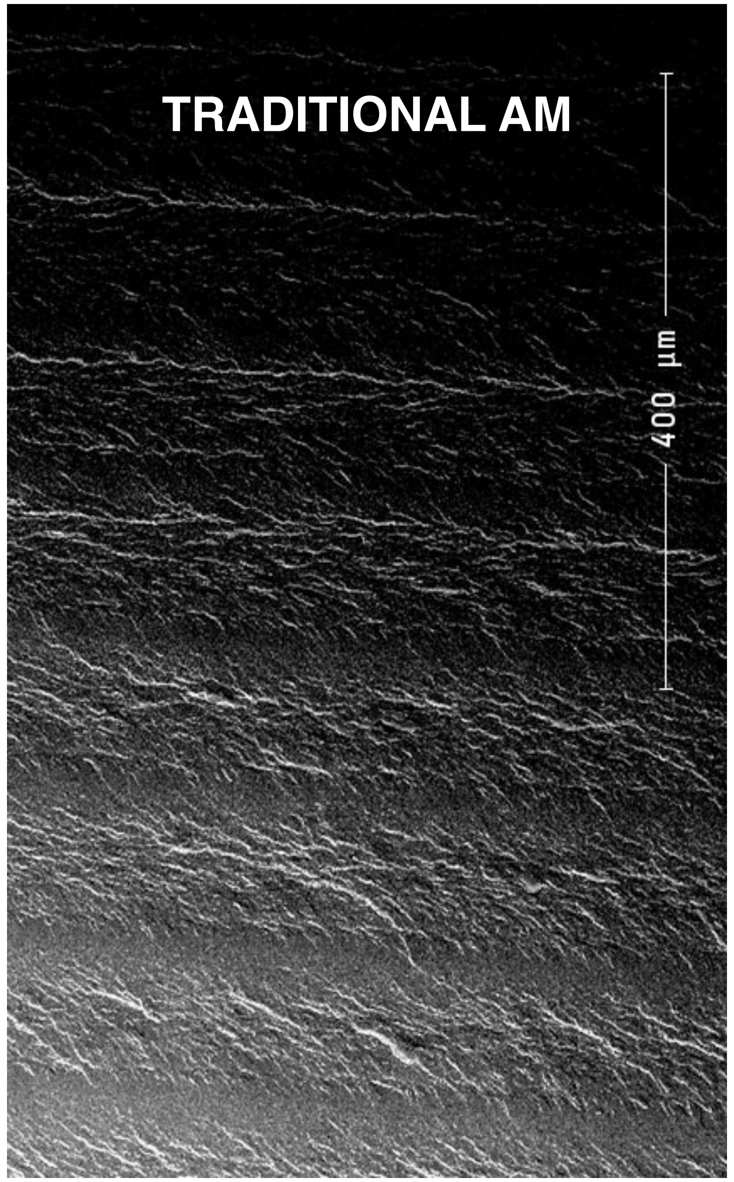
Open Book Fabrication Time: 31.21 min
Build Speed: 40 mm/hr.

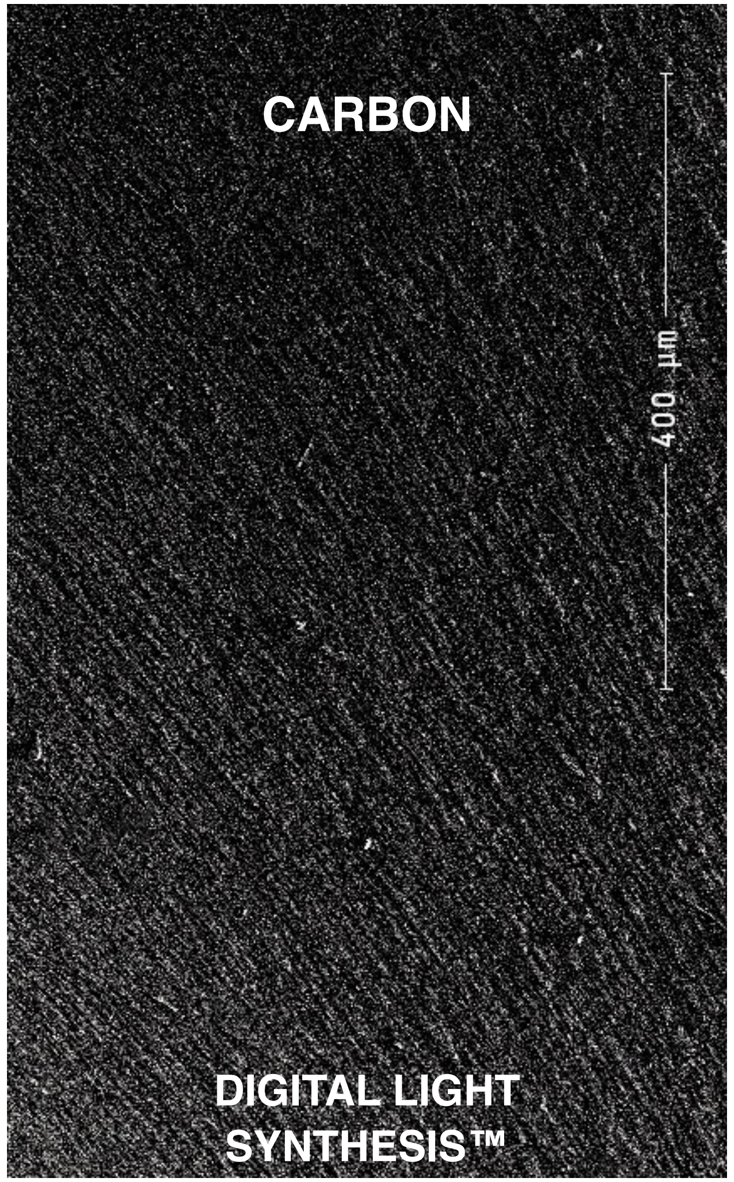
UNC Chemistry Lab

Consistent and Predictable Isotropic Mechanical Properties

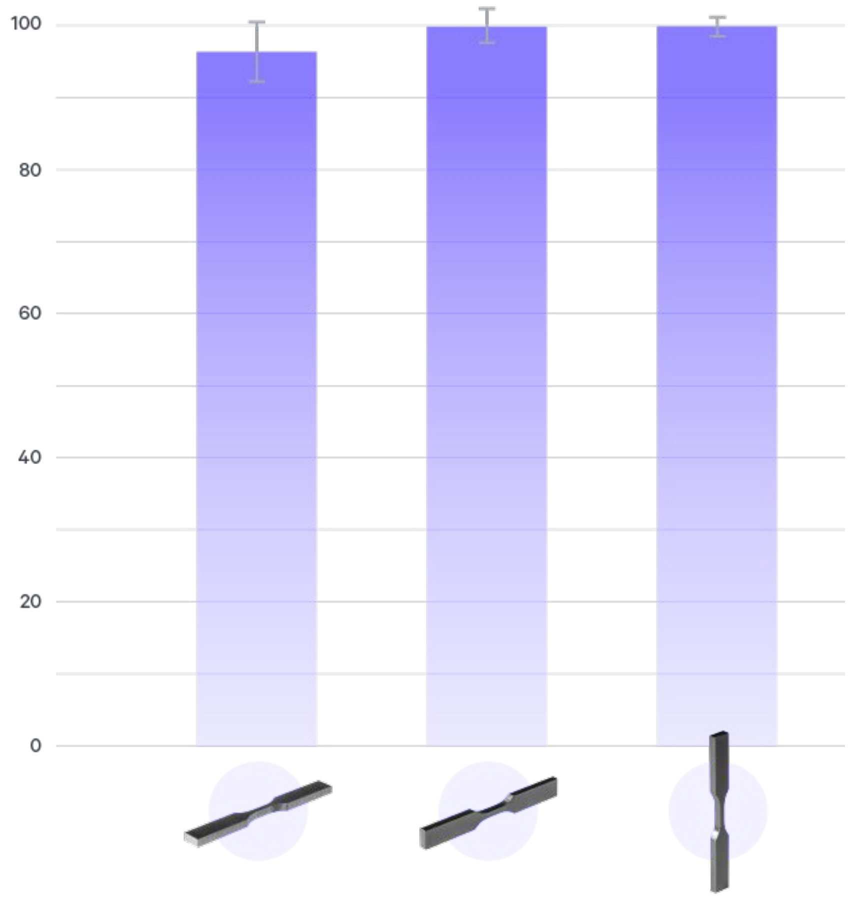
TRADITIONAL AM







CARBON



Data centric

Digital thread maintained through each unit operation

Design files are local and can be encrypted

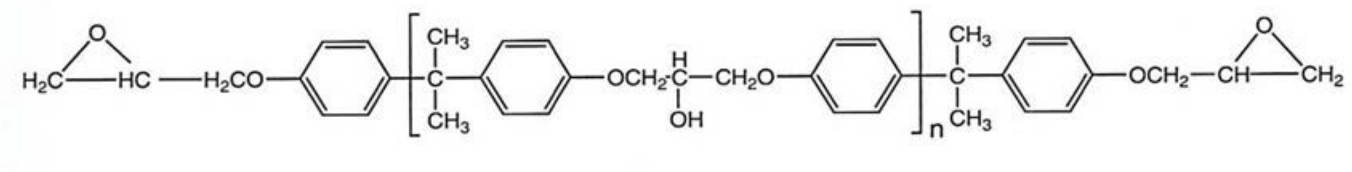
Analytics & Business Intelligence

OTA software upgrades

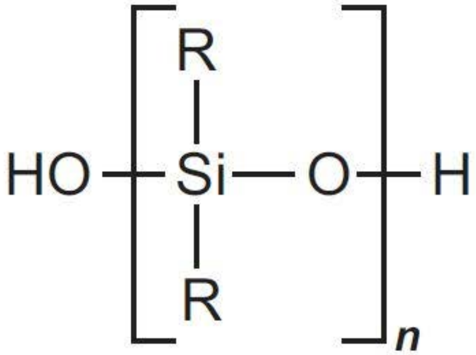
M2

SMART PART WASHER

L1

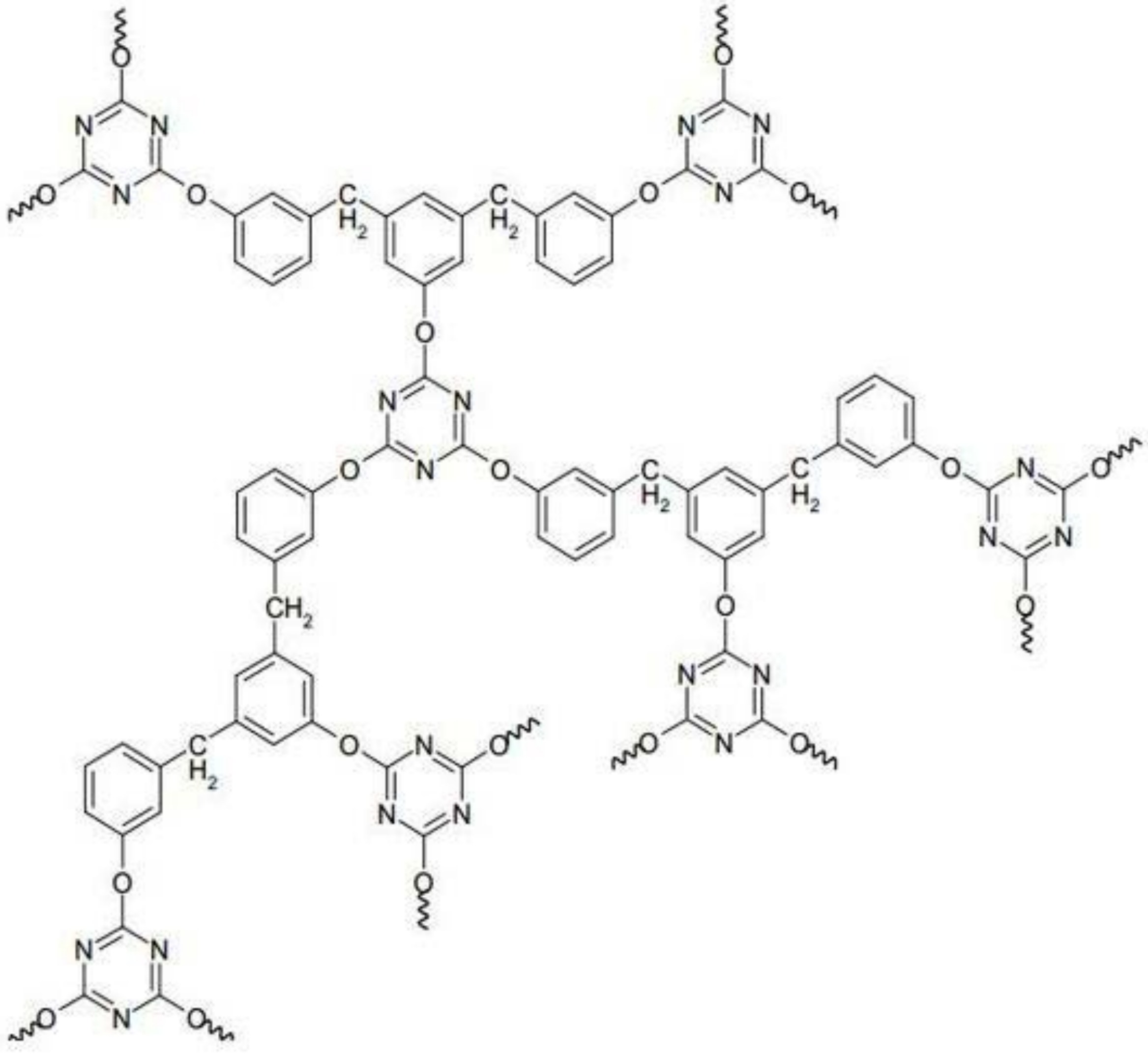


EPOXY

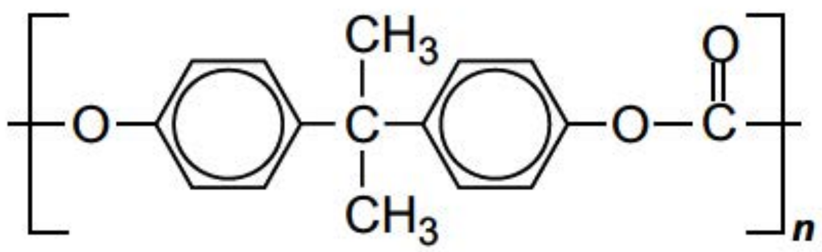


SILICONE

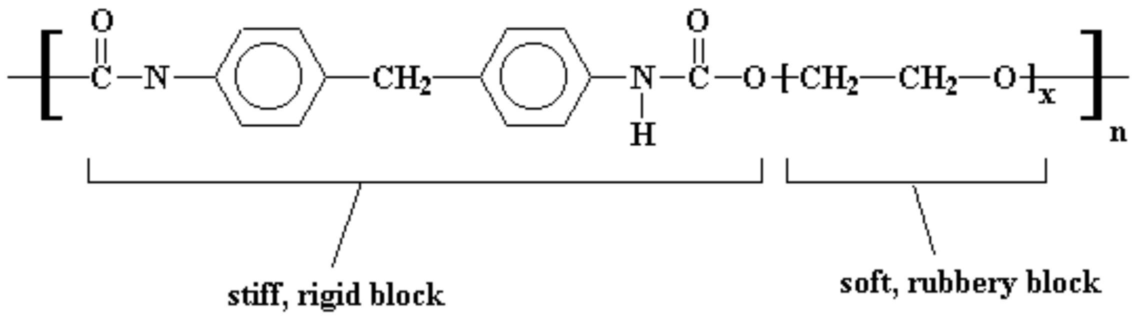
Most polymers are not light curable. How can we adapt other chemistries to a broader platform?



CYANATE ESTER NETWORK



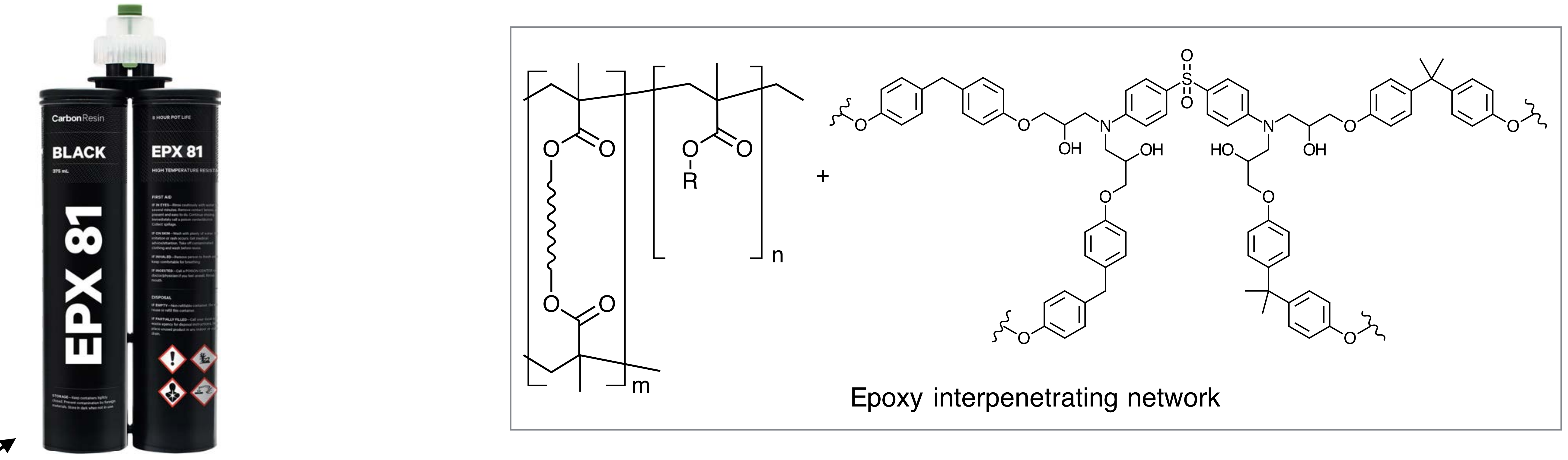
POLYCARBONATE

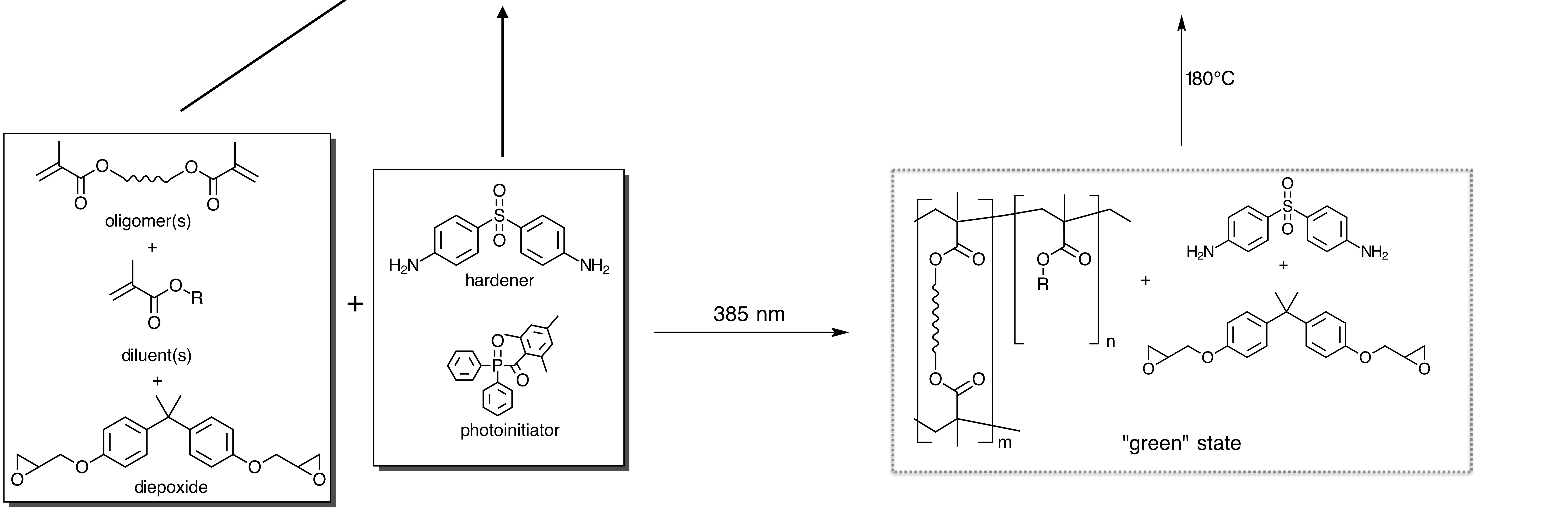


POLYURETHANE

Dual cure resins

EPX Epoxy


CarbonResin
BLACK
EPX 81
EPX 81
Epoxy interpenetrating network
180°C


oligomer(s)
+
diluent(s)
+
diepoxide
+
hardener
photoinitiator
385 nm
"green" state

RPU-130

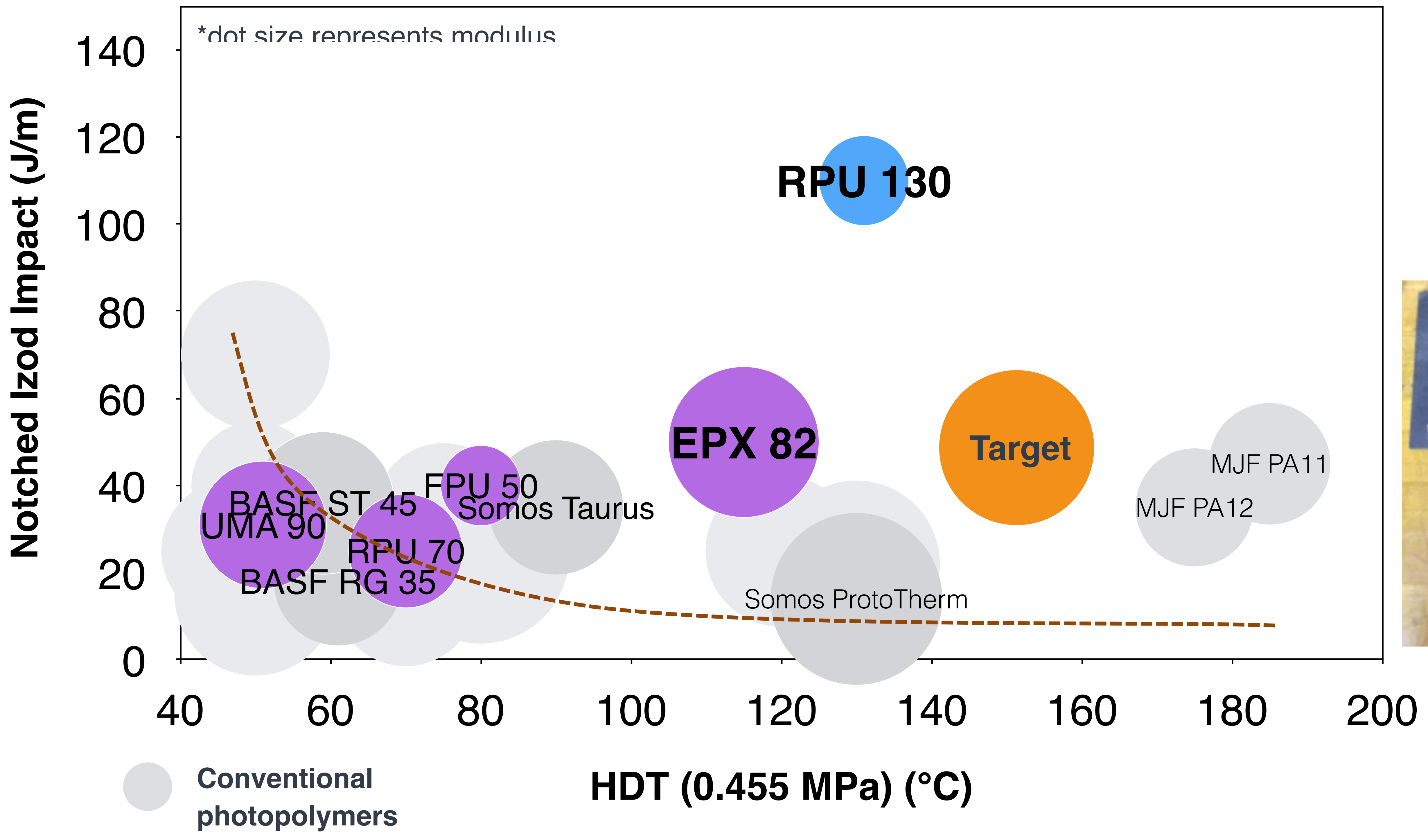
Excellent temperature & impact resistance
Comparable to unfilled thermoplastics

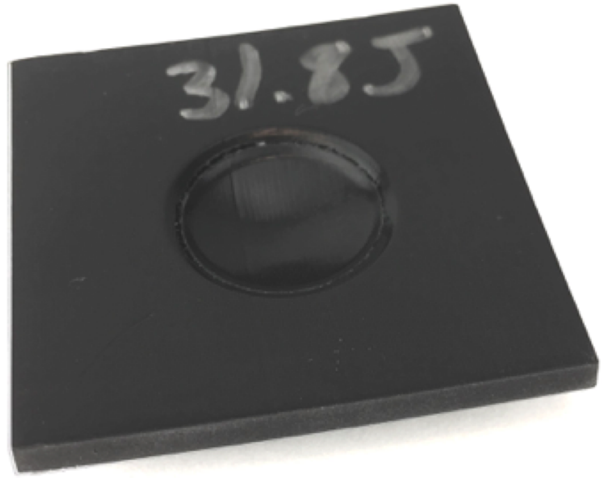
TENSILE MODULUS	1000 MPa
TENSILE YIELD STRENGTH	30 MPa
ELONGATION AT BREAK	>50%
CHARPY IMPACT (NOTCHED, RT)	10 kJ/m²
IZOD IMPACT (NOTCHED, -40°C)	50 J/m
GARDNER IMPACT (TEST GC, RT)	~20 J
HEAT DEFLECTION TEMPERATURE	120°C+

Passes interior/exterior thermal cycling
Passes interior chemical resistance
Passes interior odor & fogging

RPU 130

Tough, temperature- and impact-resistant polyurethane
25% **bio-based feedstock** (propanediol polyol)





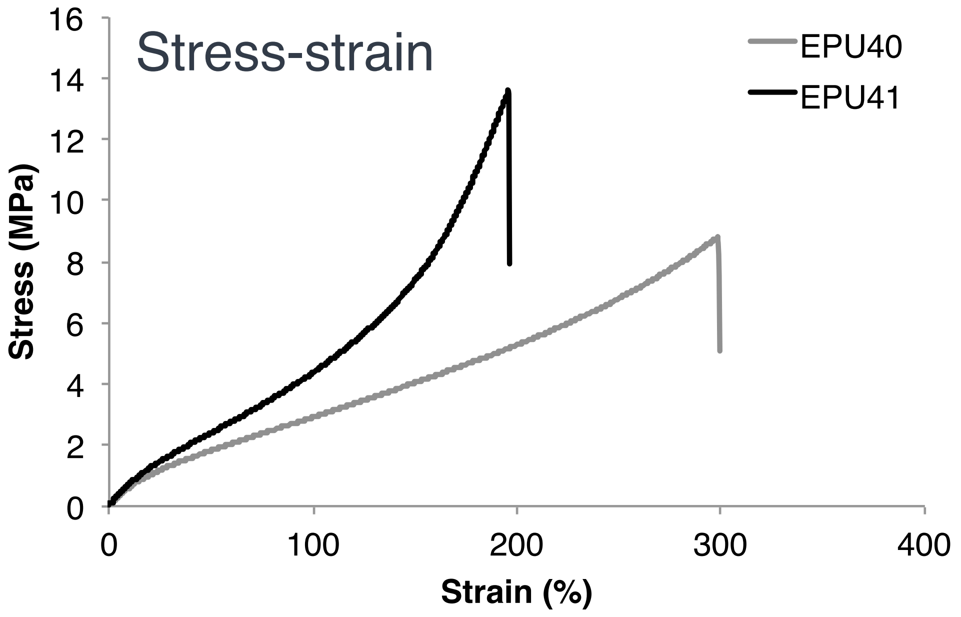
RPU 130 (ductile at 30J)

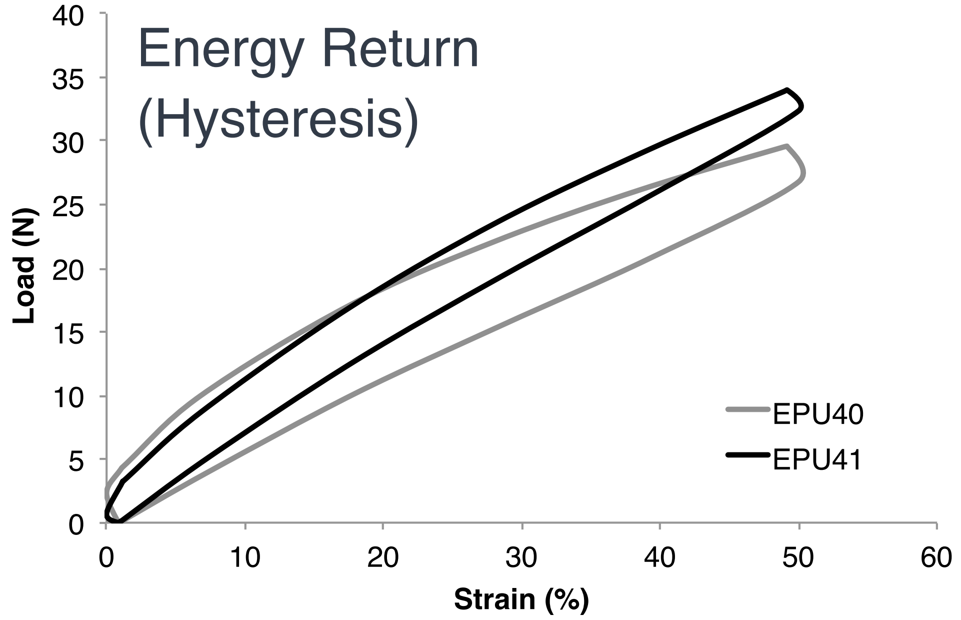
HP MJF PA12 (fail at 10J)

EPU40 & EPU41 Elastomeric Polyurethanes

EPU41 is our next-generation elastomeric engineering material. It has higher energy return and improved cold temperature performance, making it useful in a variety of industrial and consumer applications.

	EPU40	EPU41
SHORE HARDNESS	69A	76A
ELONGATION AT BREAK	300%	190%
TEAR STRENGTH	26 kN/m	19 kN/m
ULTIMATE TENSILE STRENGTH	9 MPa	13 MPa
ENERGY RETURN	72%	84%
GLASS TRANSITION TEMPERATURE	8°C	-9°C





Resins To Fit Design Needs

EPX 82
Automotive

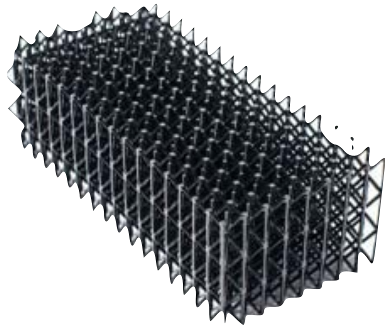
FPU 50
Enclosures

CE 221
Fluidics

RPU 70
Nozzles

SIL 30
Padding

EPU 41
Energy return



EPU 40
Impact absorption

DPR 10
Models

MPU 100
Medical

RPU 130
Consumer

Data centric

Digital thread maintained through each unit operation

Design files are local and can be encrypted

Analytics & Business Intelligence

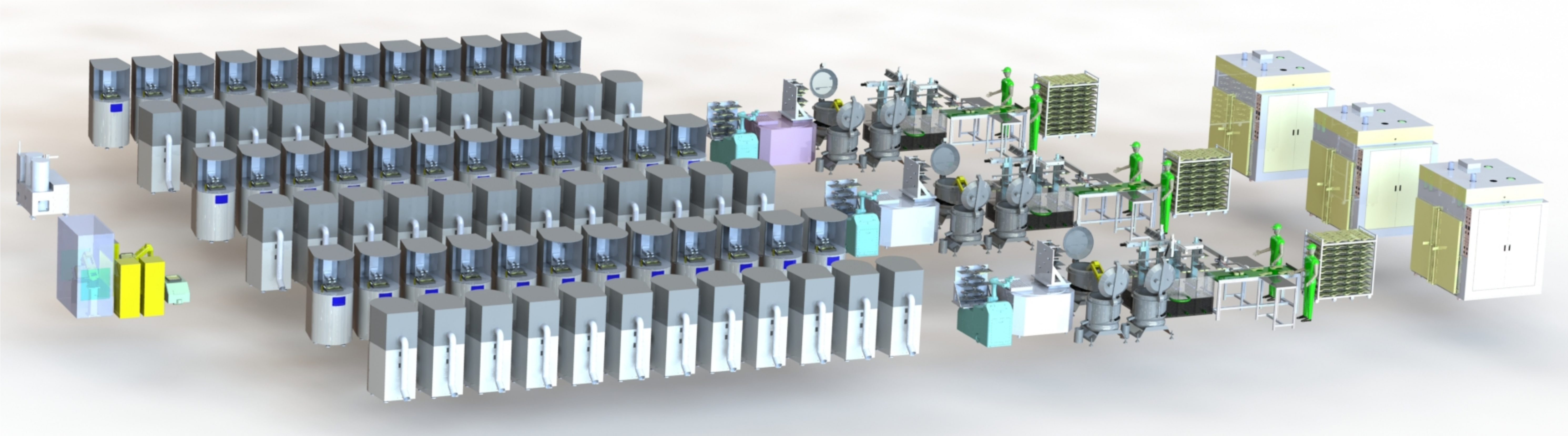
OTA software upgrades

M2

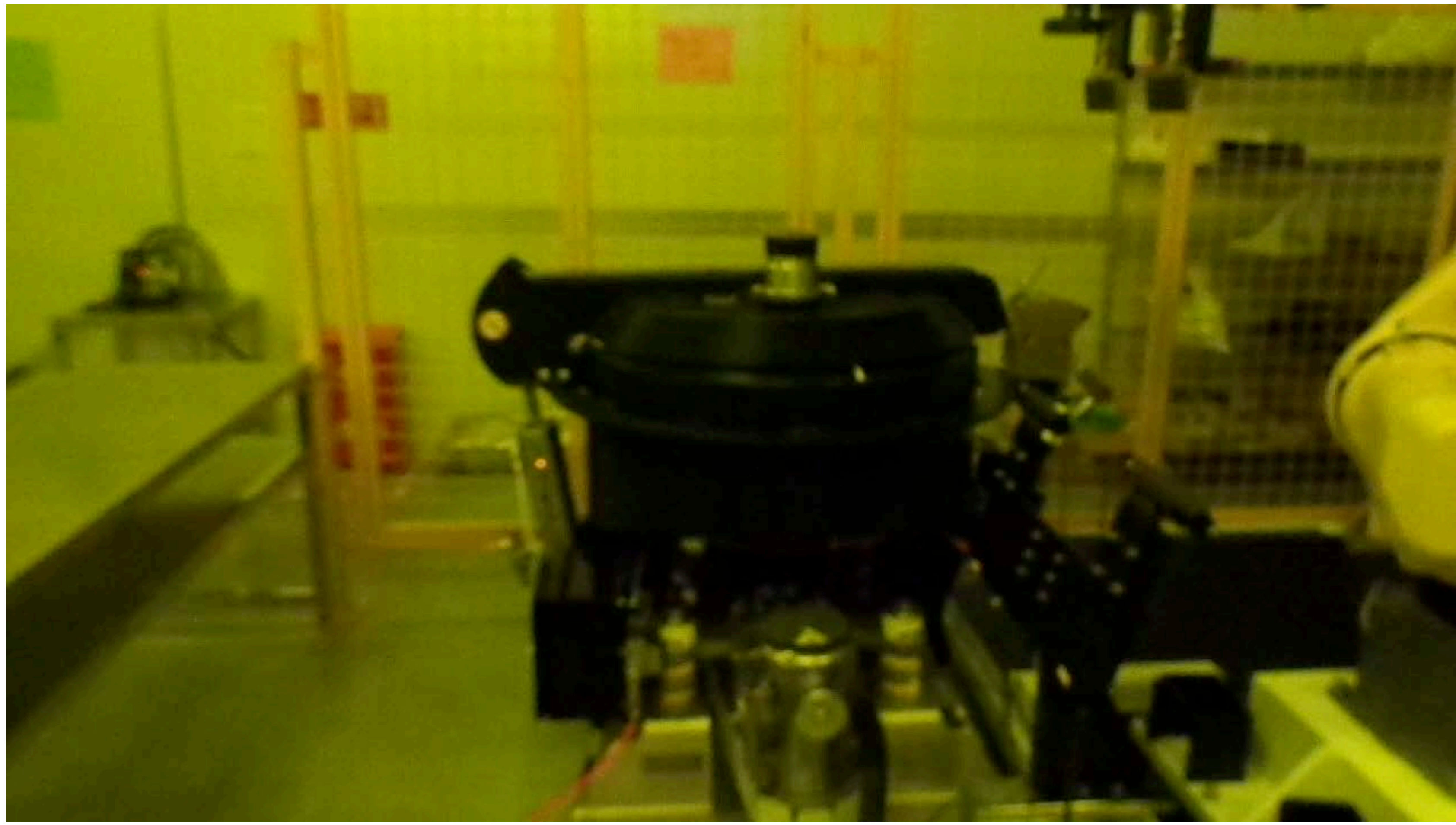
SMART PART WASHER

L1

Digital Factory of the Future

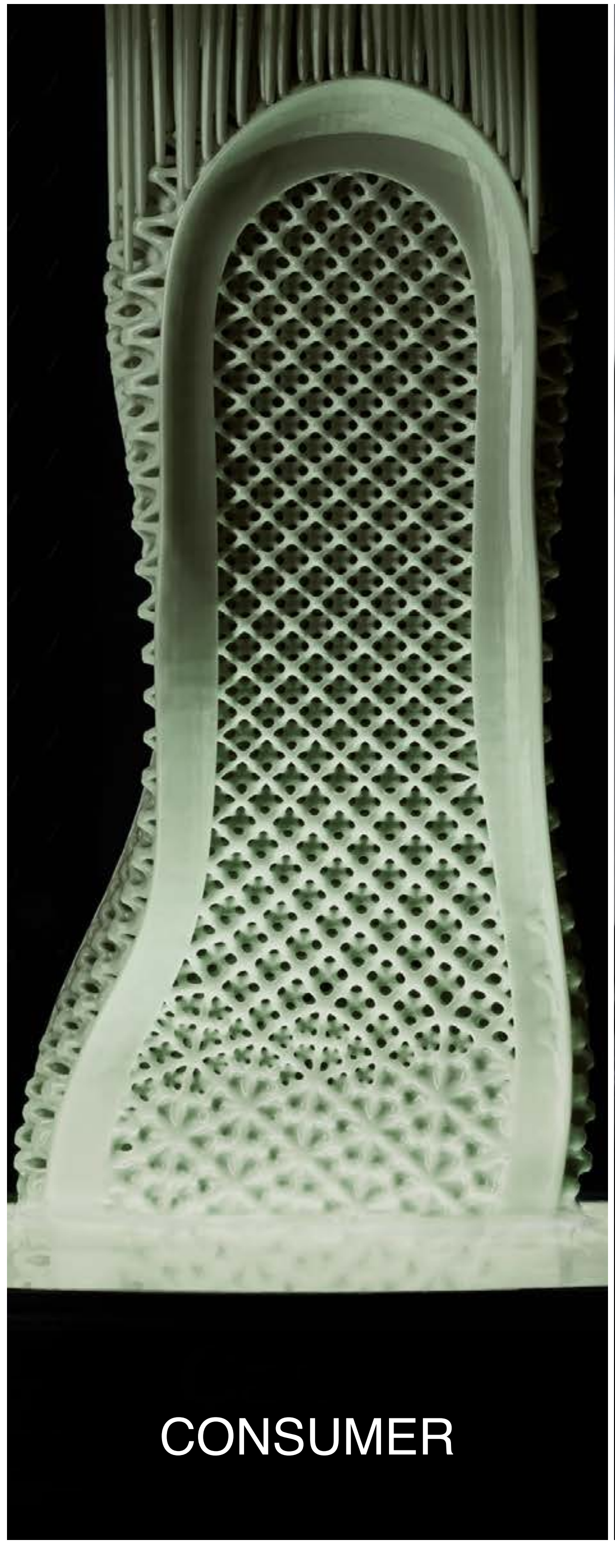


Unit Operations
Mixing
Printing
Platform Spinning
Part Removal
Inert Baking


Carbon


Making what the world needs

Challenge what’s acceptable.
Create extraordinary.


CONSUMER

AUTOMOTIVE

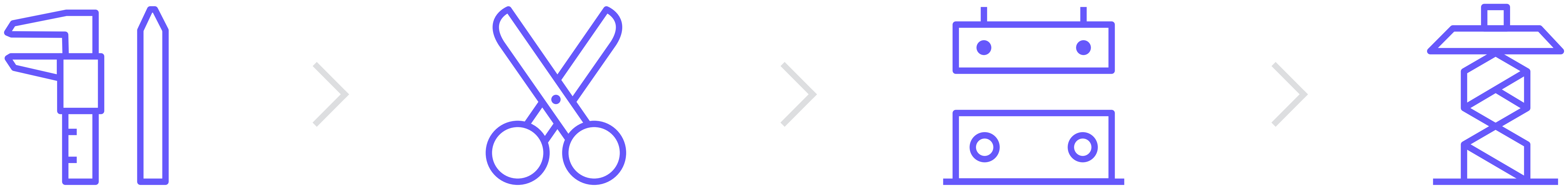
INDUSTRIAL

(MICRO)ELECTRONICS

HEALTHCARE

Going Digital

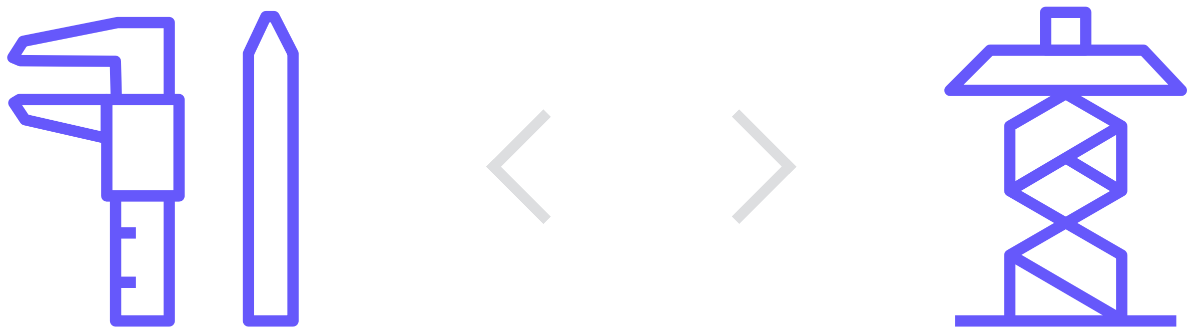
DIS-INTERMEDIATION OF PRODUCT DEVELOPMENT CYCLES



DESIGN | PROTOTYPE | TOOLING | MANUFACTURE

Going Digital

DIS-INTERMEDIATION OF PRODUCT DEVELOPMENT CYCLES



DESIGN	MANUFACTURE

Thermoformed Aligners

Our Expanding Portfolio of Dental Resins and Markets

Family: **Model production**
Resin: Carbon's DPR 10

Family: **Impression trays**
Resin: Dreve Fotodent® tray for Carbon printers

Family: **Surgical guides**
Resin: Whip Mix Surgical Guides for carbon printers

Family: **Denture base**
Resin: DENTCA Denture Base II for Carbon print

Family: **Gingiva masks**
Resin: Dreve Fotodent® gingiva for Carbon printers

Family: **Denture teeth**
Resin: DENTCA Denture Teeth for Carbon printers

First FDA-cleared 3D printed dentures

Carbon

FIRST FDA-CLEARED 3D PRINTED DENTURES

Dentures

Dentsply Sirona

Lucitone Digital Print

DENTURES

FIRST FDA CLEARED 3D PRINTED DENTURES TO EXCEED HIGH-IMPACT STANDARDS

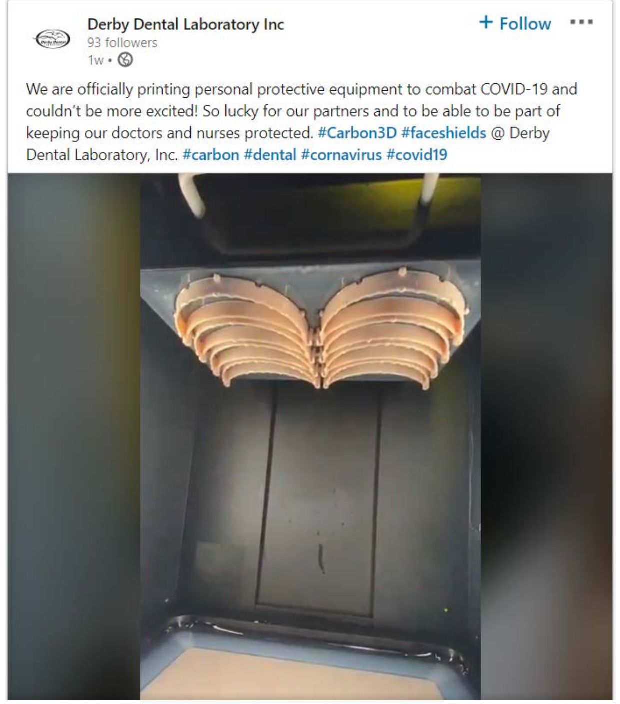
Making what the world needs

Challenge what’s acceptable.
Create extraordinary.


Carbon

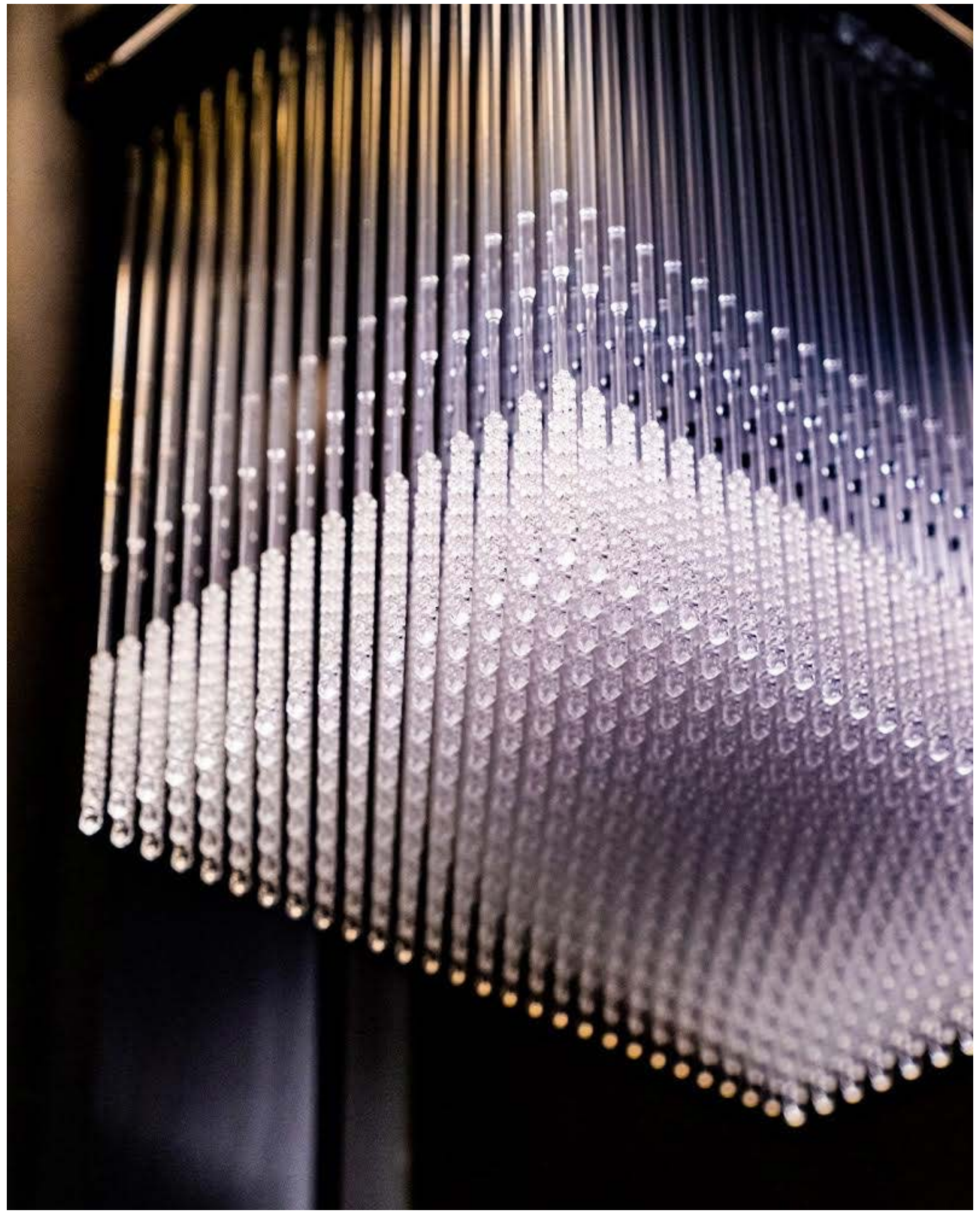
Face Shields Summary

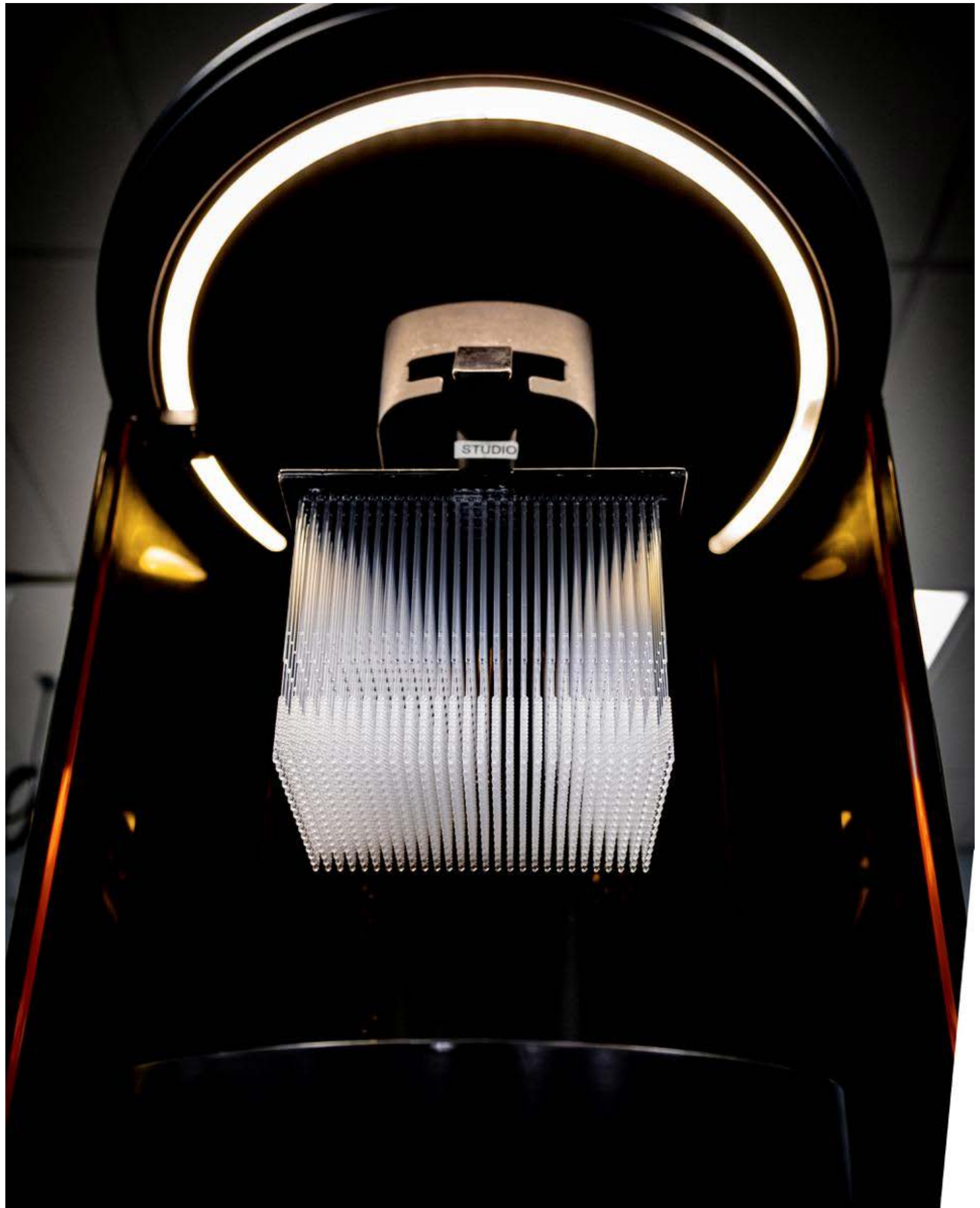
Byrnes Dental Laboratory donates 100s of face shields to local facilities

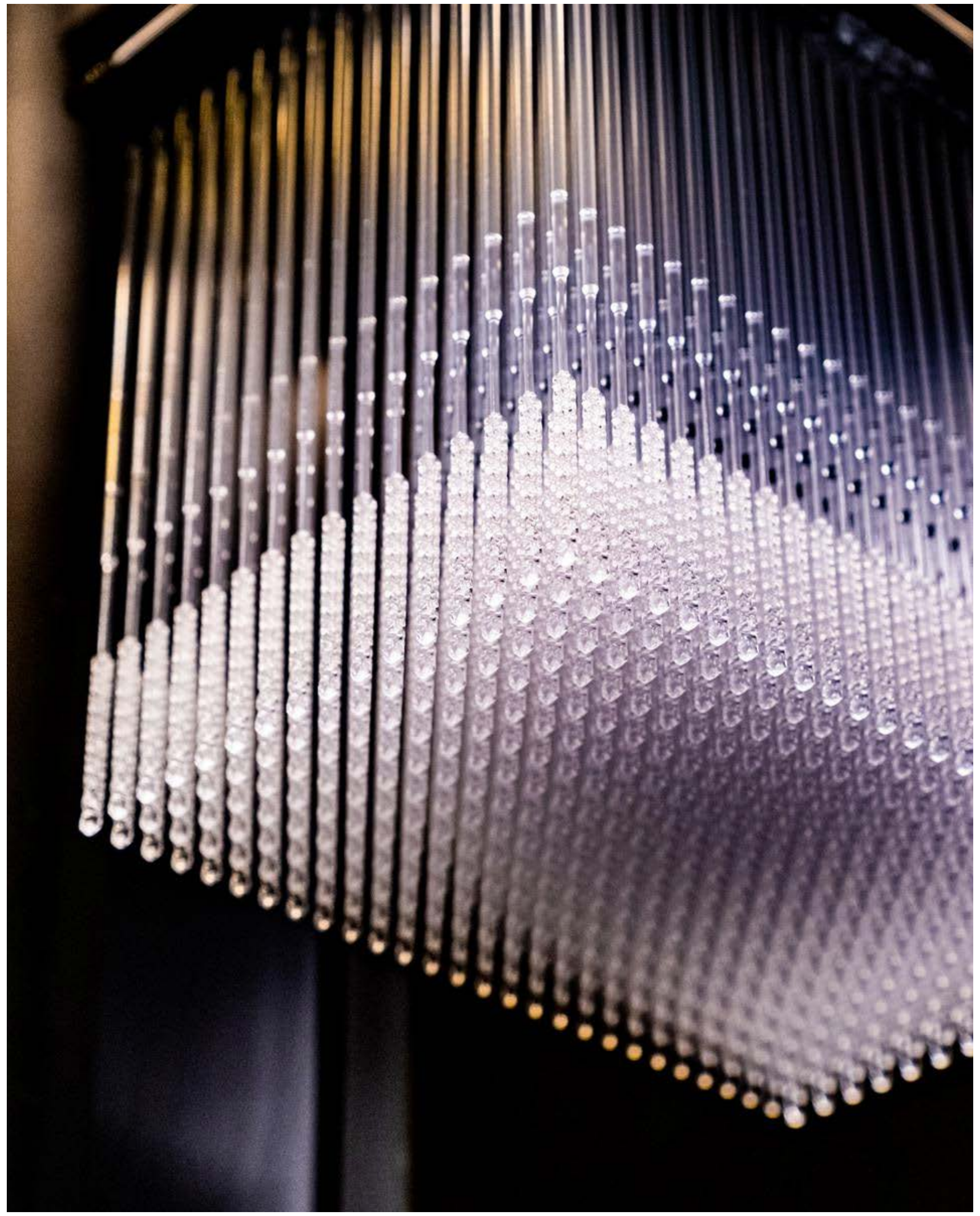


Face Shields Produced by Apex Dental Sleep Laboratory

Resolution Medical Lattice Swabs, Crafted with Carbon™ Technology



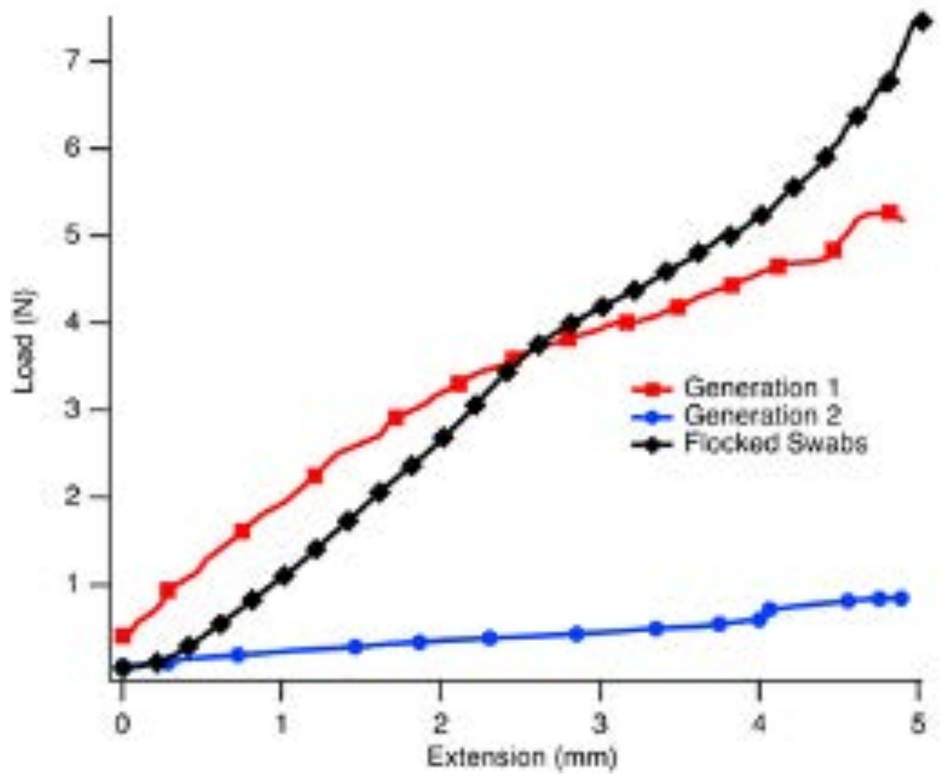




Generation 2 Design

The Rapid Deployment of a 3D Printed "Latticed" Nasopharyngeal Swab for COVID-19 Testing Made Using Digital Light Synthesis

Carbon
Resolution Medical
Stanford Medicine:



		Generation 1 +	Generation 1 −	
Control	+	6	1	7
Control	−	2	147	149
		8	148	156

κ = 0.790 (0.56-1.00 at 95% CI)

		Generation 2 +	Generation 2 −	
Control	+	21	1	22
Control	−	2	217	219
		23	218	241

κ = 0.928 (0.84-1.00 at 95% CI)

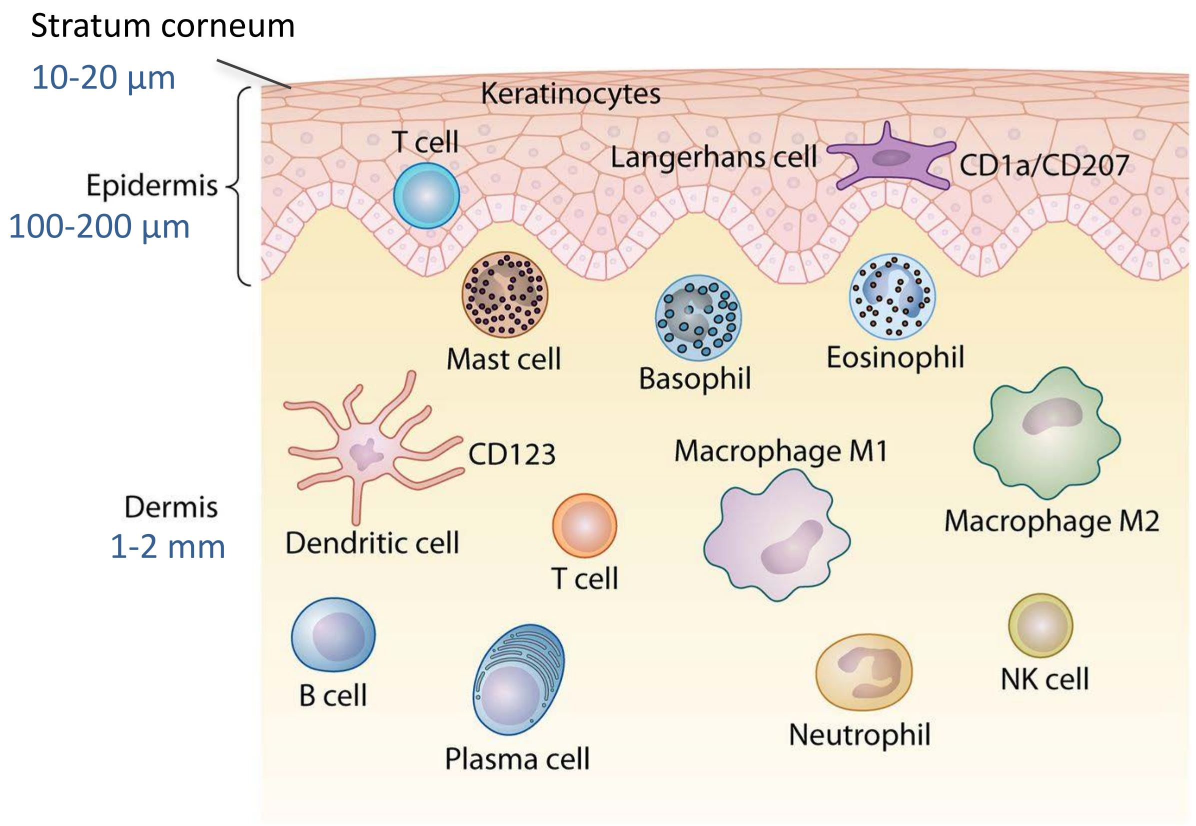
medRxiv THE PREPRINT SERVER FOR HEALTH SCIENCES

doi: https://doi.org/10.1101/2020.05.25.20112201 Posted May 27, 2020.

Addressing Unmet Needs in CLIP

Advances in printing	Faster printing	Multiple material printing	High resolution printing
Advances in resins	Recyclable resins	Composites	Bio-absorbable resins
Advances in software	Topology optimization & Software Controlled Chemical Reactions to Grow Parts	Cloud & circular economy	Imaging & bespoke products

Intradermal and Transdermal Vaccination



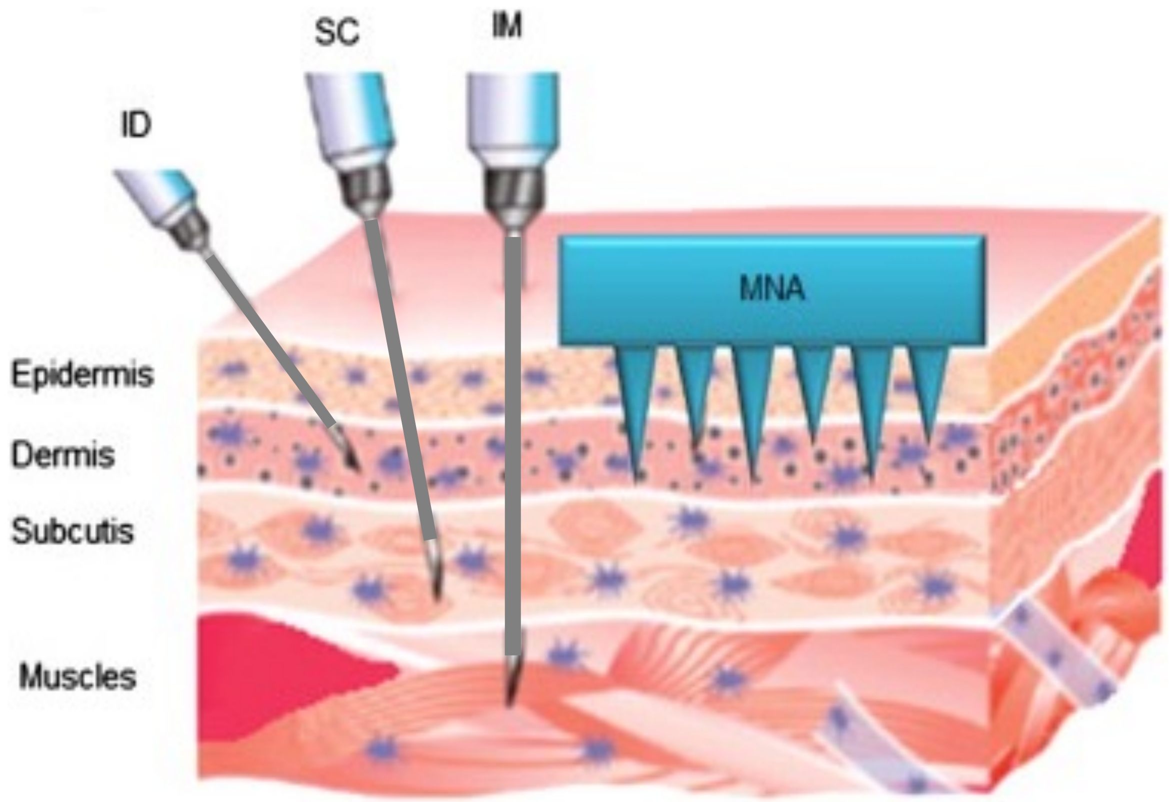
Juarez Antonio Simões Quaresma Clin. Microbiol. Rev. 2019

<u>Advantages</u>

- Skin rich in immune cells
- Dose sparing

<u>Challenges</u>

- Penetration of stratum corneum
- Precise injection into the skin requires professional training

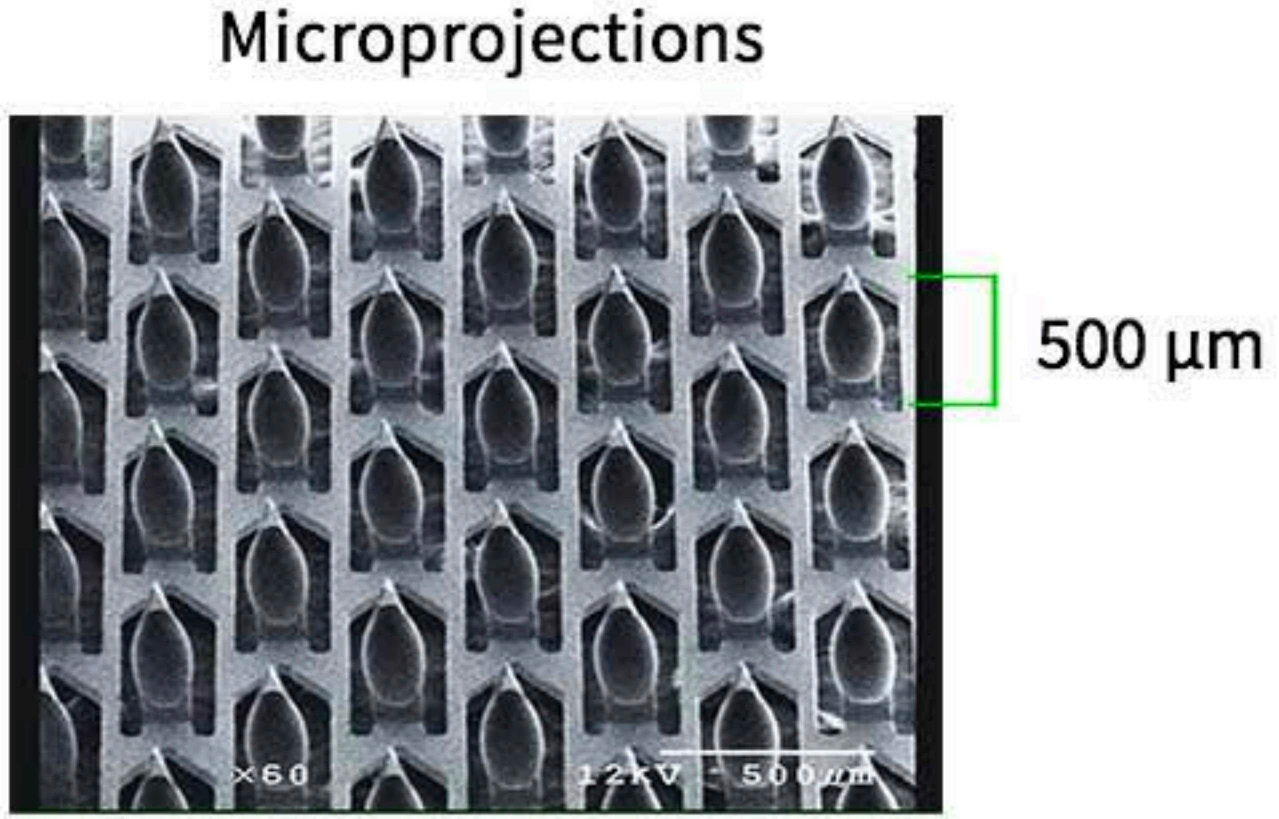


Microneedles

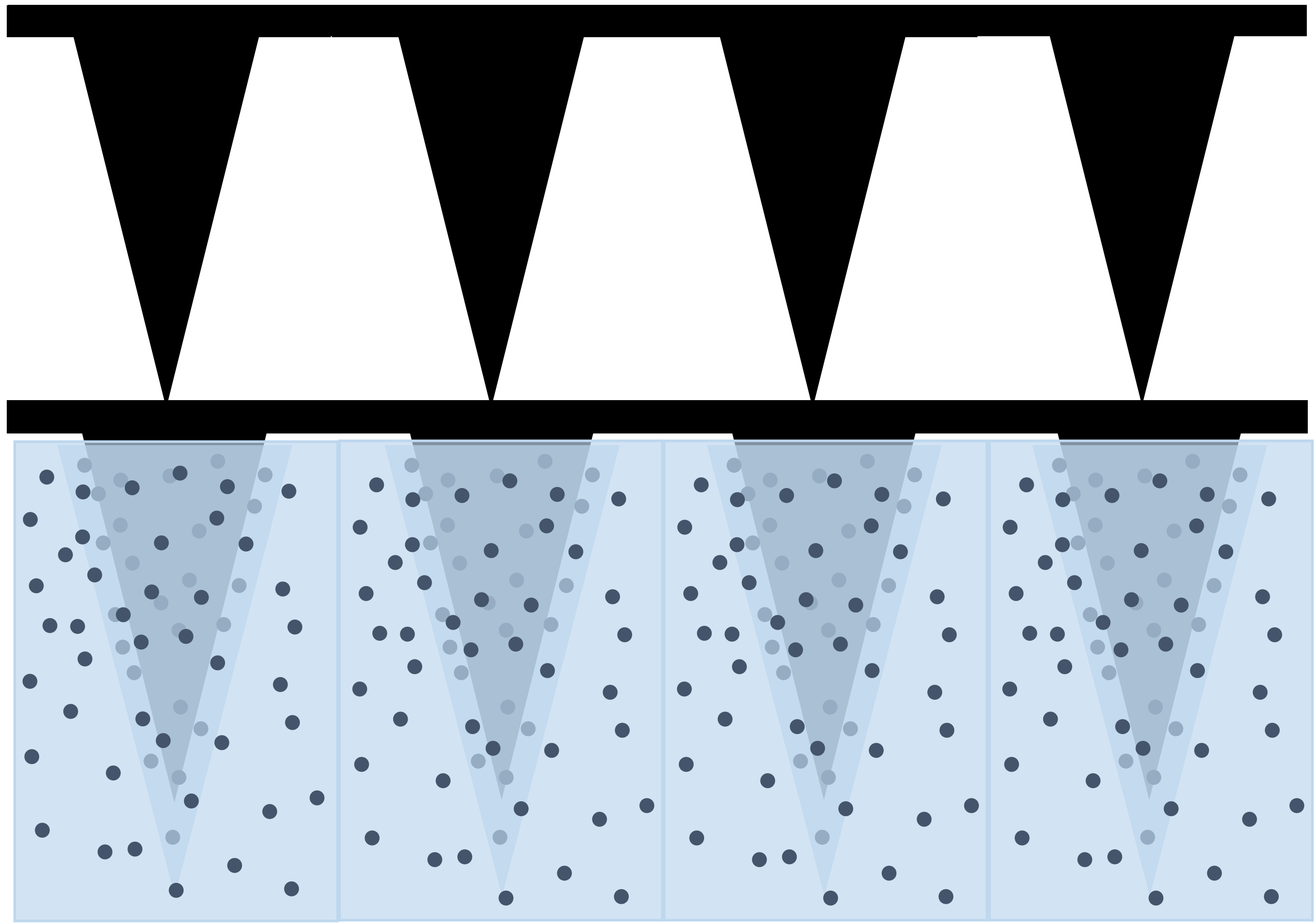
- Micron-scale projections that penetrate stratum corneum
- Allow delivery of both small and large, hydrophilic vaccine components
- Minimally invasive
- Self-administration

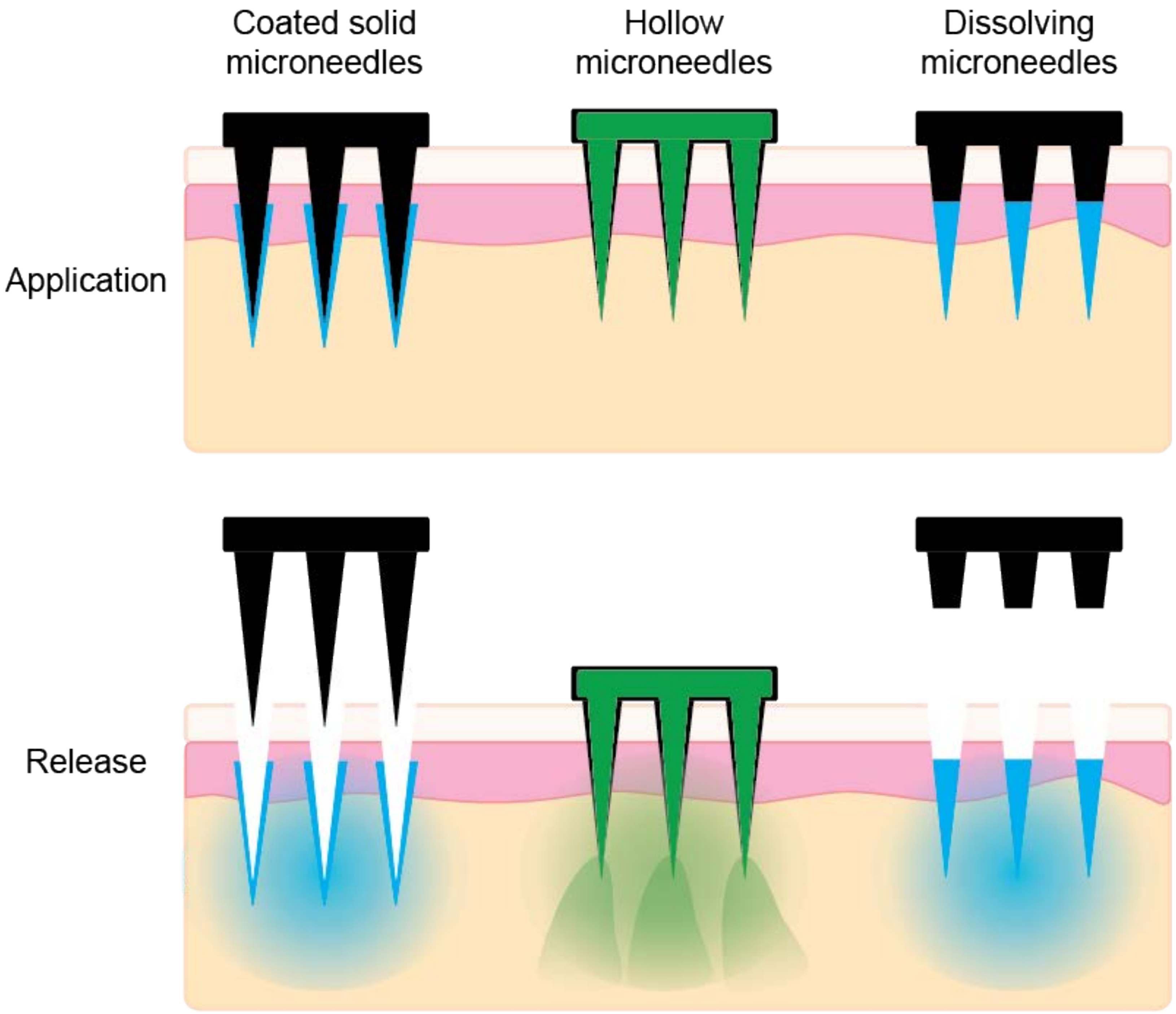
“Microneedles for drug and vaccine delivery”
Mark R. Prausnitz et. al. *Adv Drug Deliv Rev.* **2012,** 64, 1547.

- Current microneedle fabrication methods:
  - Photolithographic processes
  - Silicon etching
  - Laser cutting
  - Metal electroplating
  - Metal electropolishing
  - Micro-molding
    - Limitations:
      - Design, geometries, molded needle quality, and materials
      - Loss of the fidelity & limited geometries



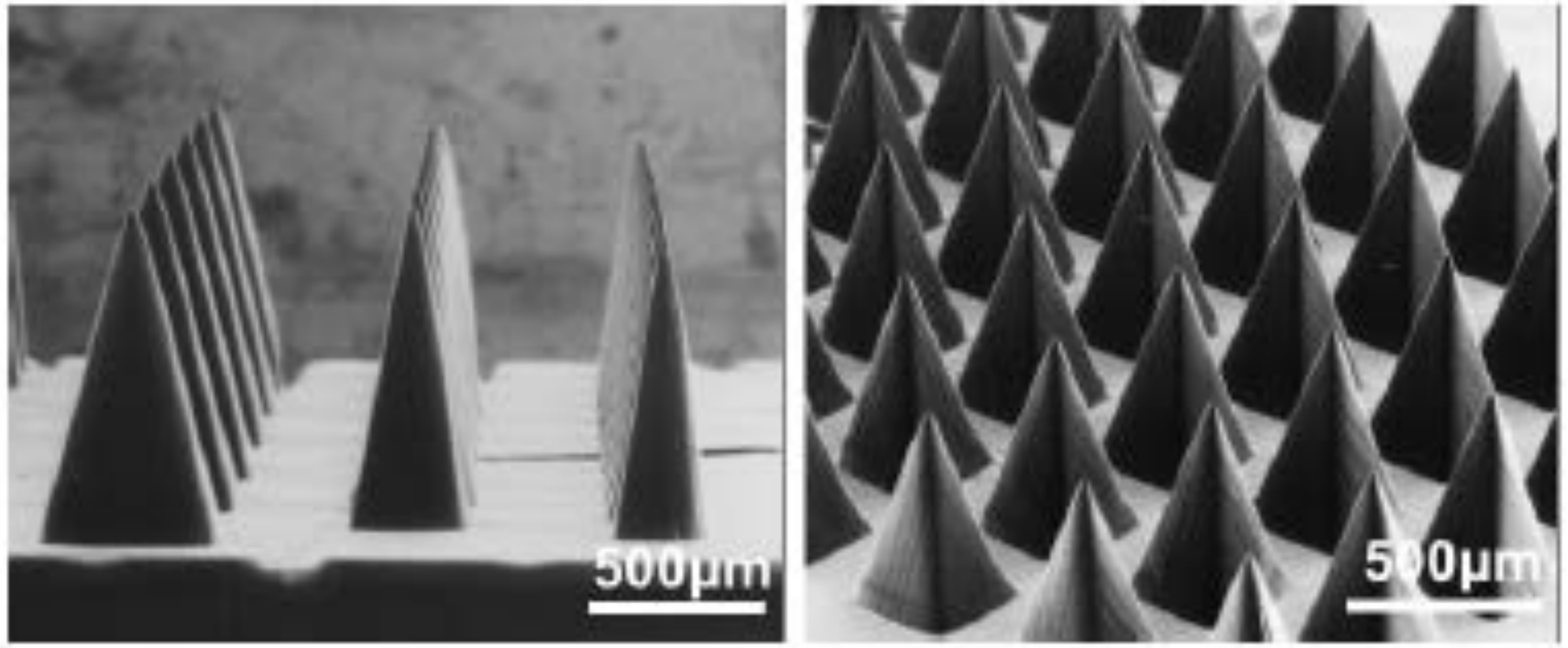
Microneedle Classes

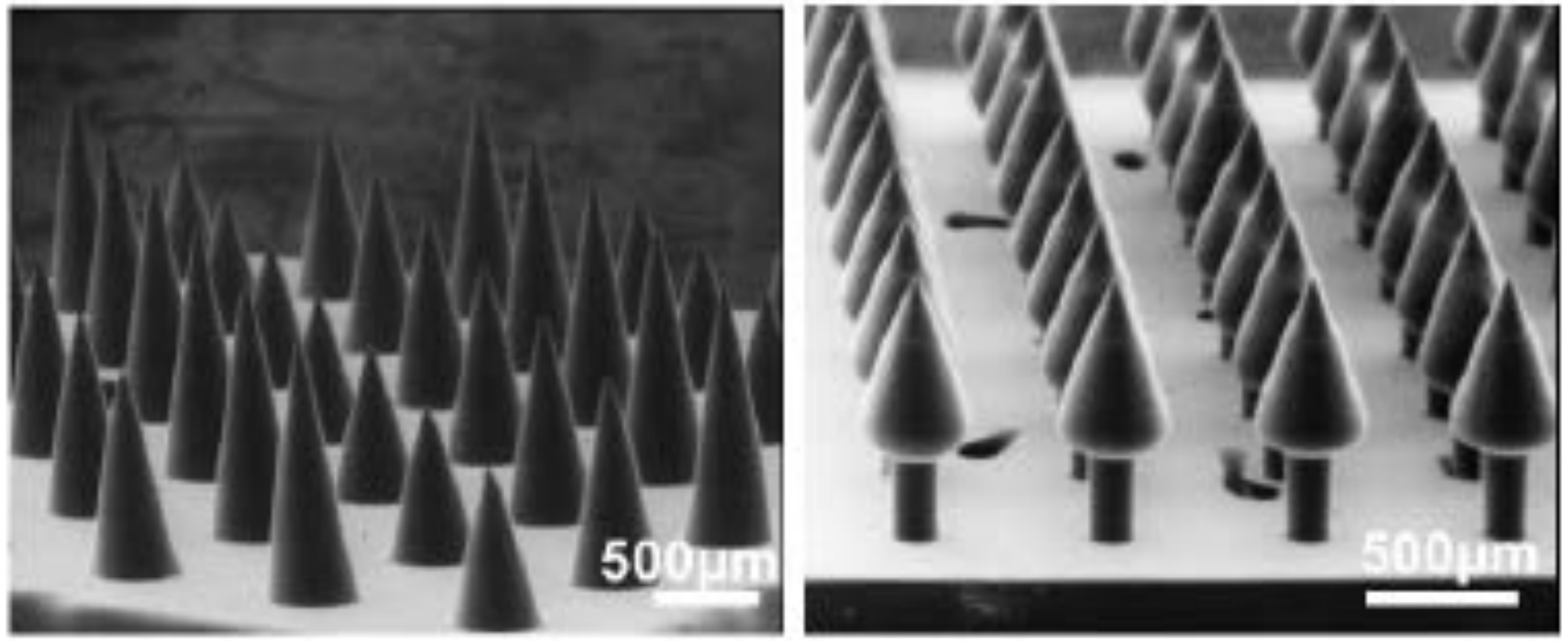


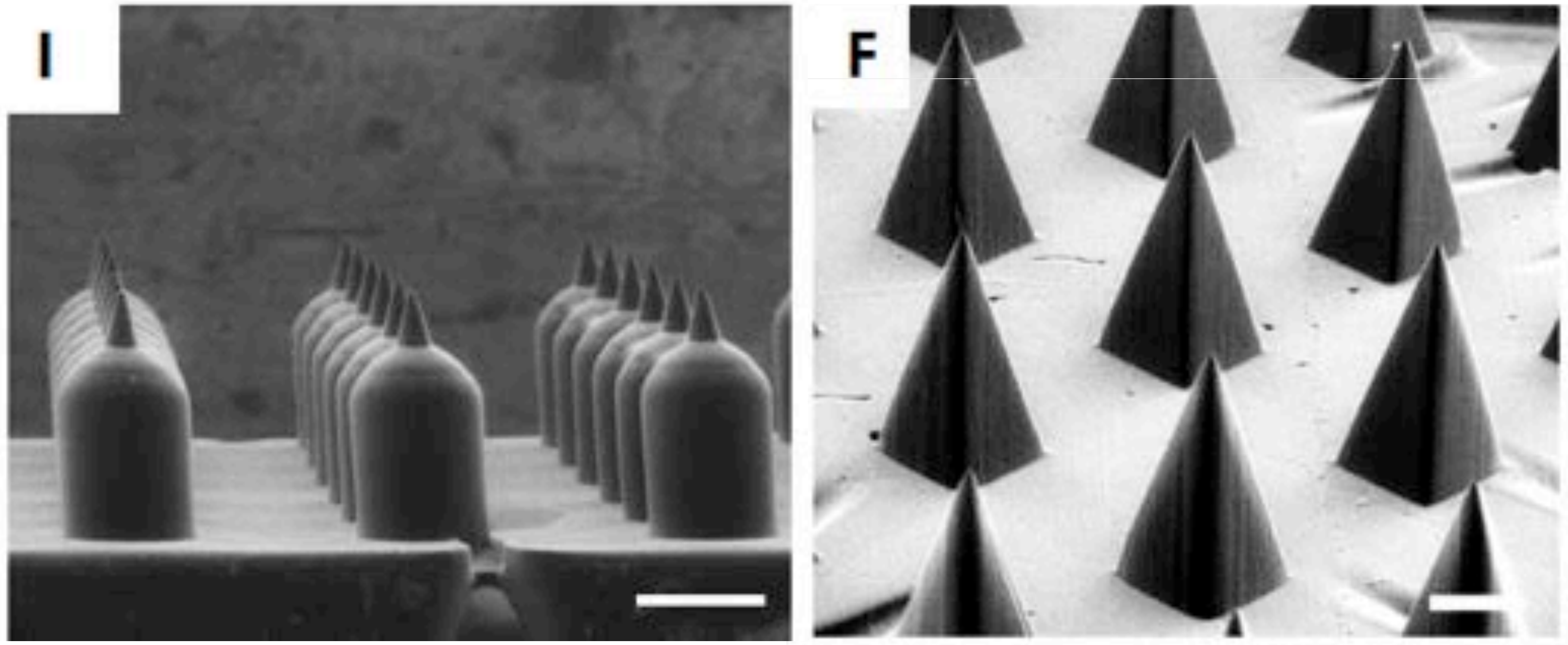


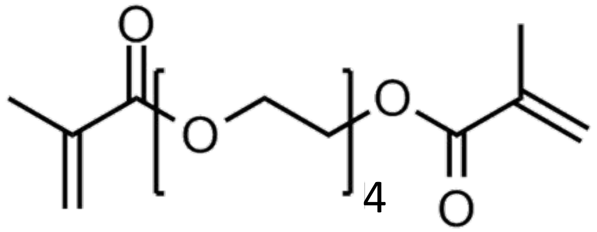
Micro-needles Via CLIP with 20 um Pixels

Tumbleston et. al (2015), *Science* ; Johnson et. al (2016), PLOS One.

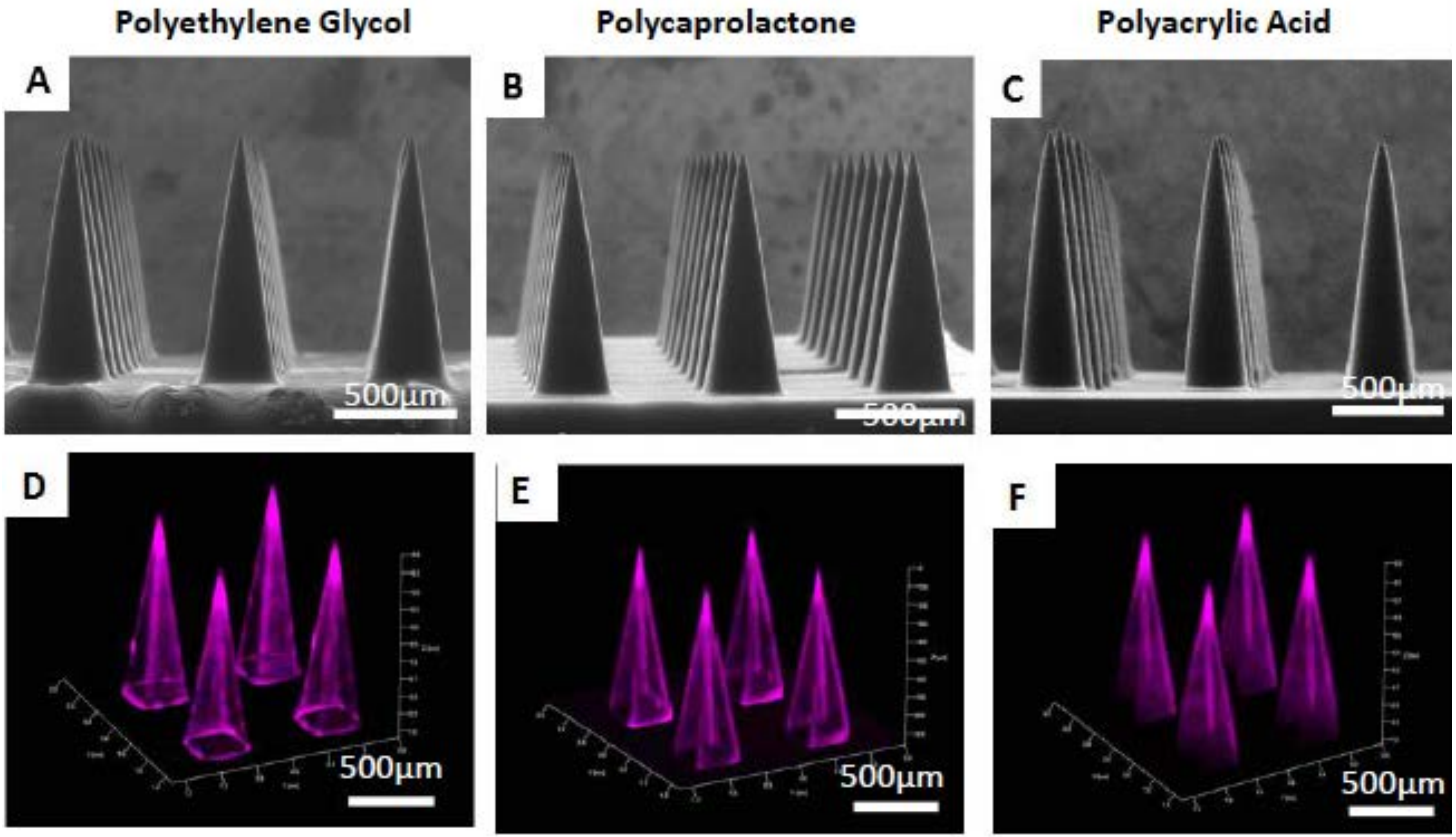




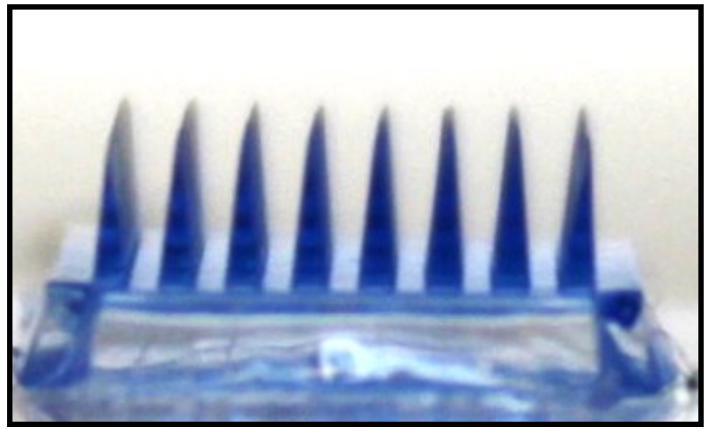




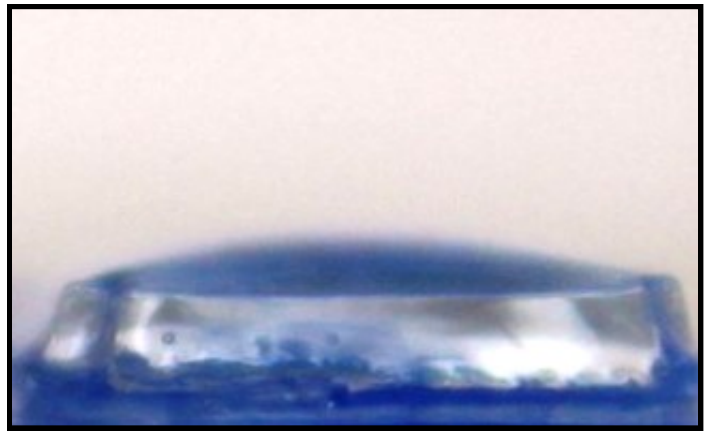
Micro-needles Via CLIP with Different Materials



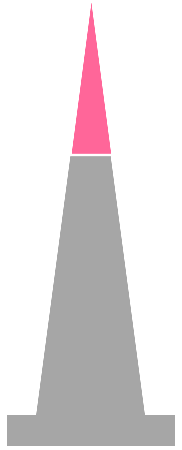
Micro-needles Via CLIP with Different Materials

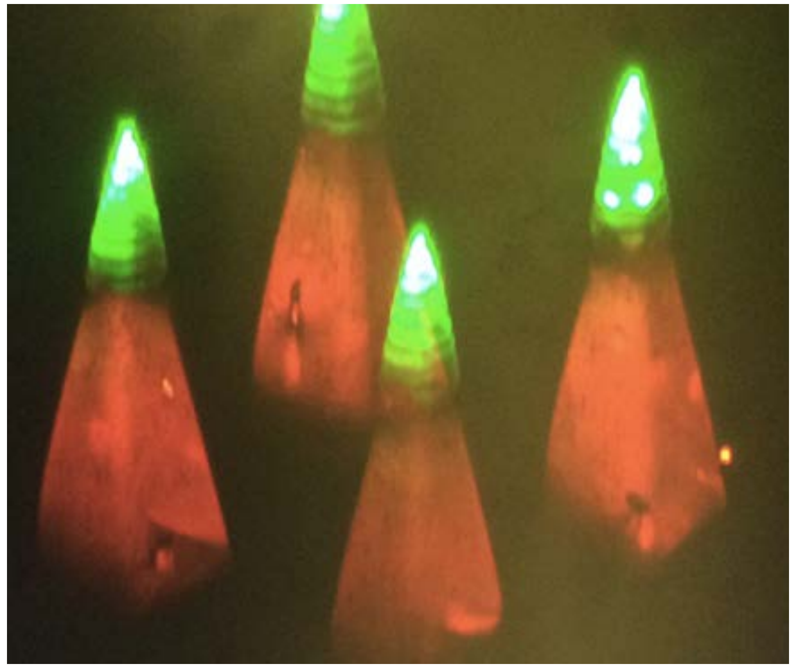


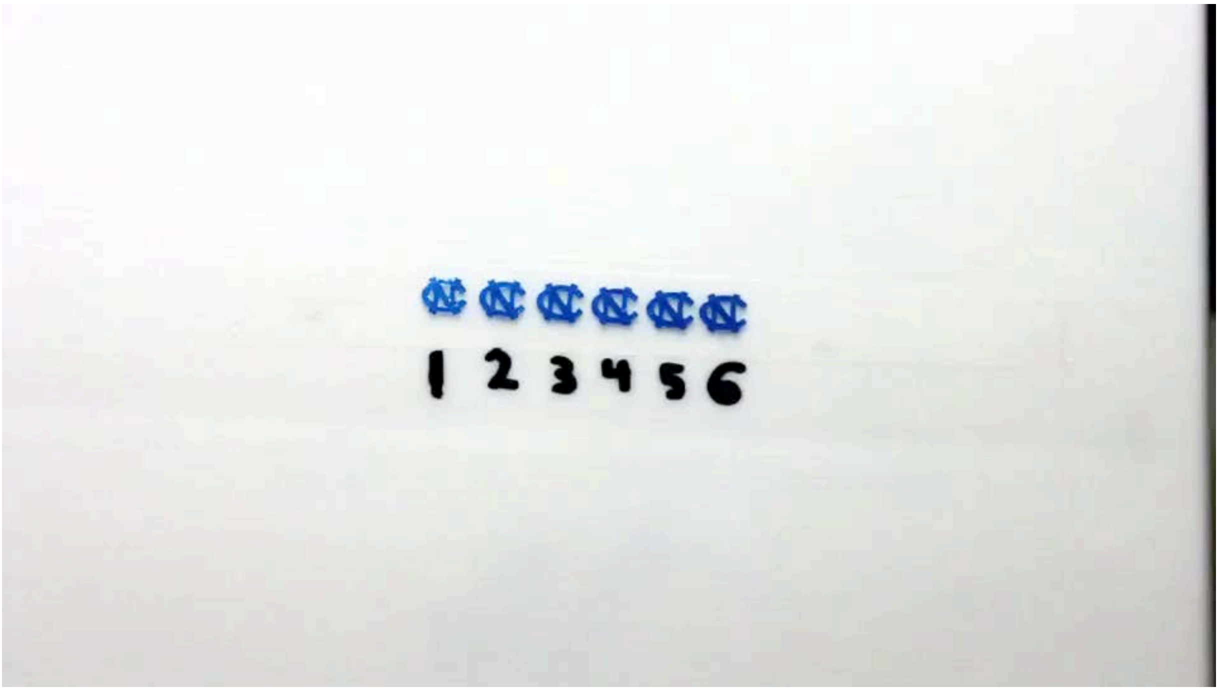
Dissolvable PAA microneedles

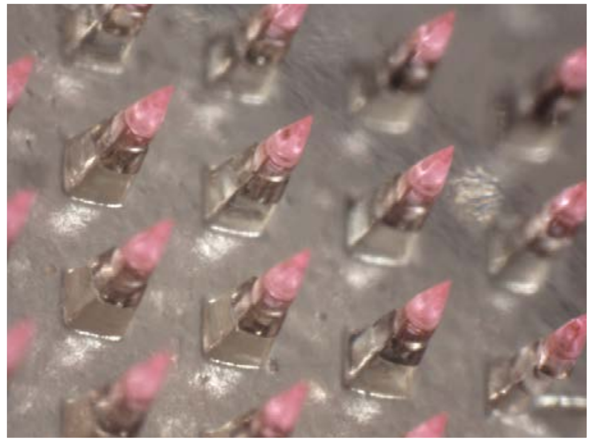


After 5 min in Saline

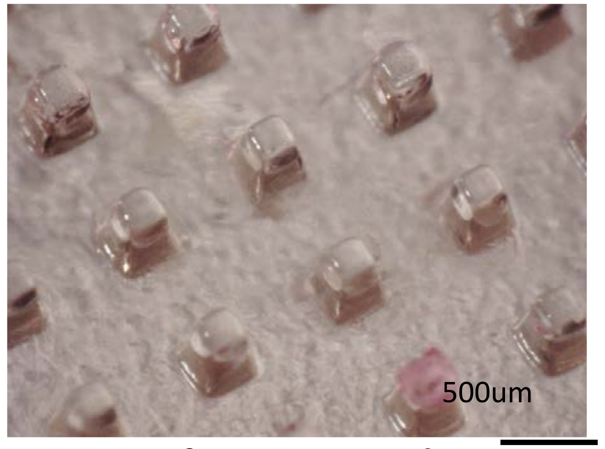






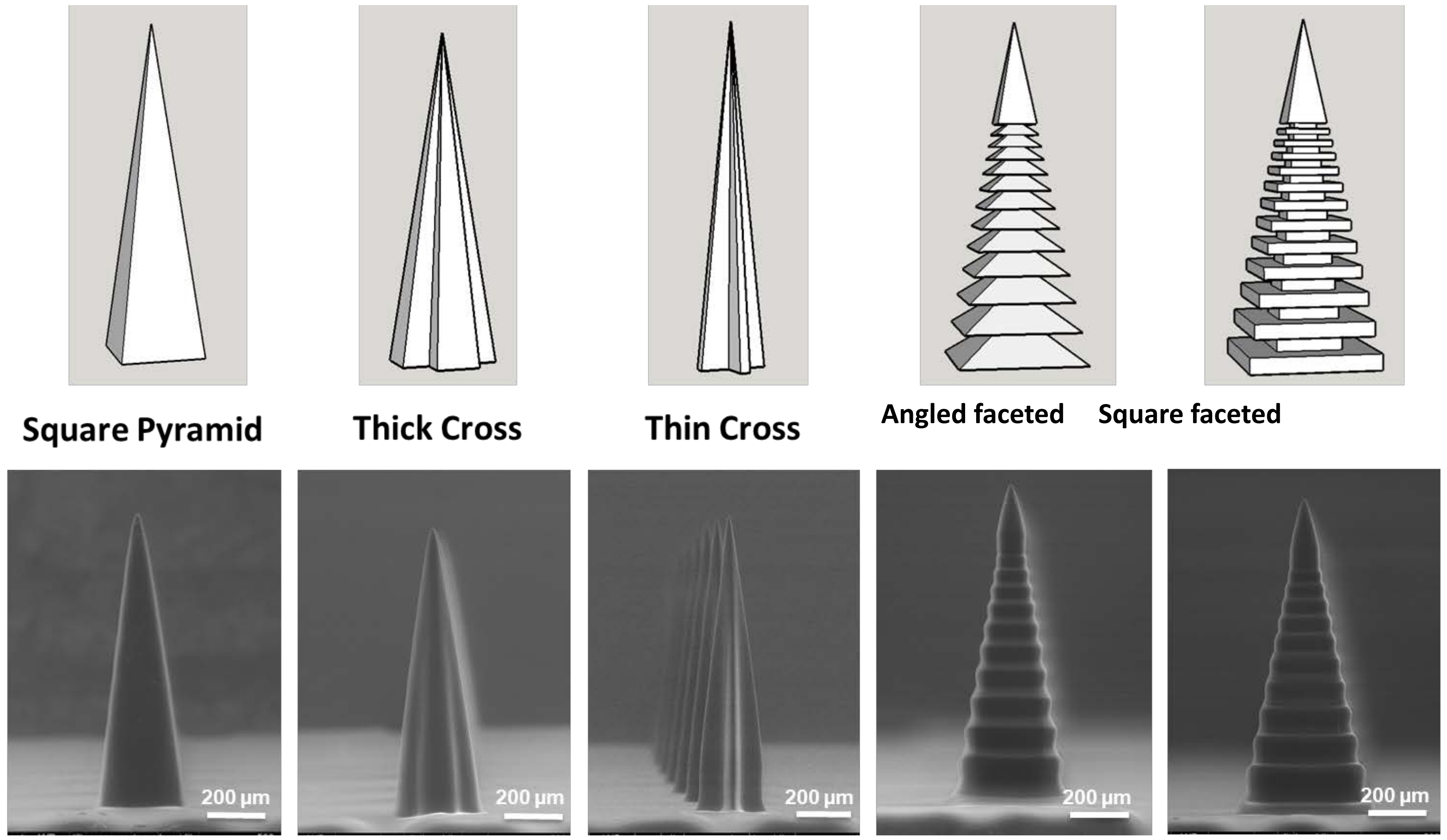


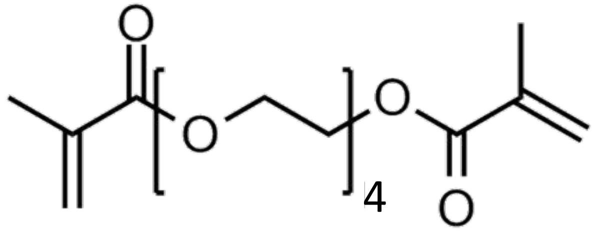
Pre-Skin Application

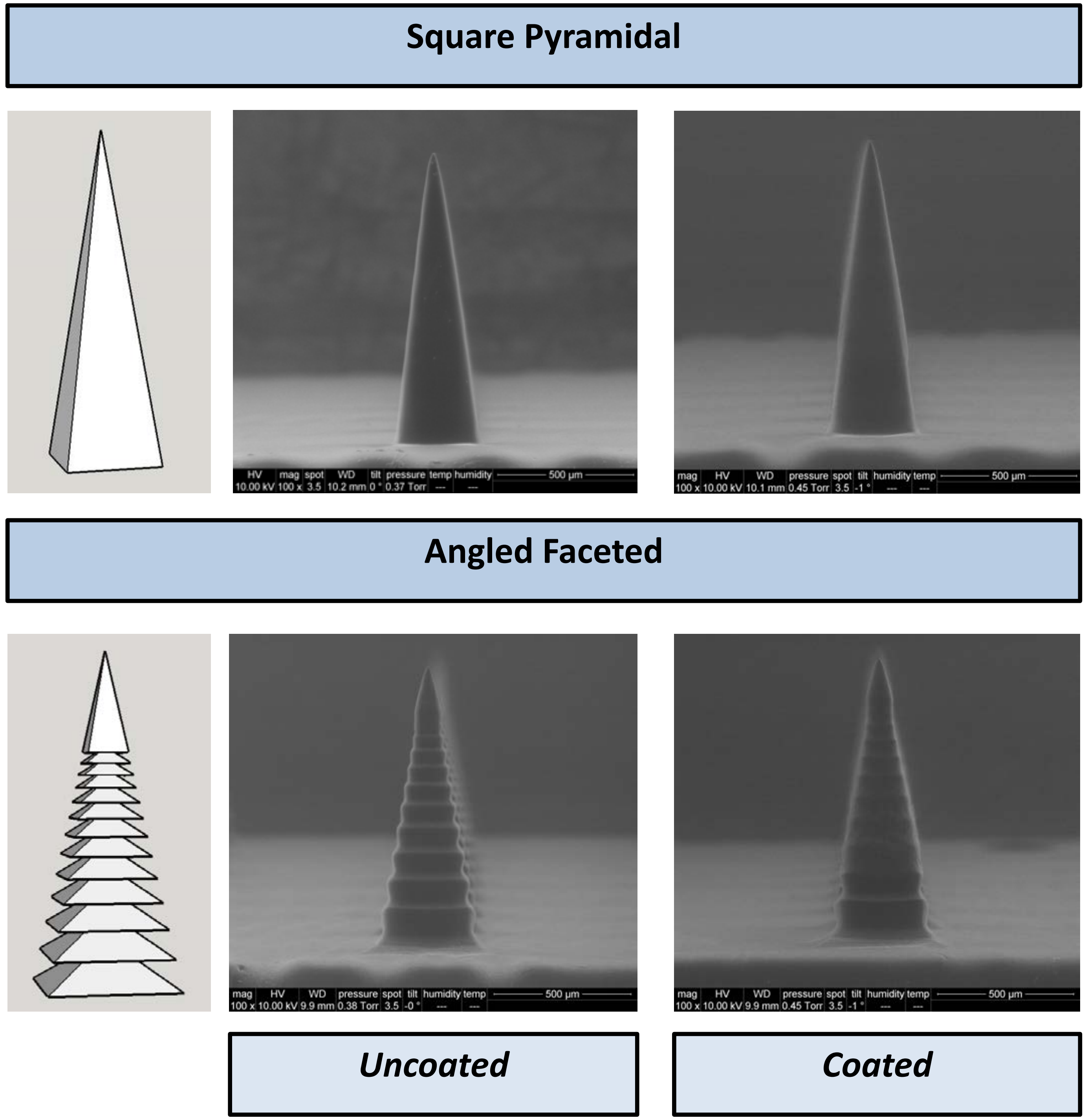


After 5 min in skin

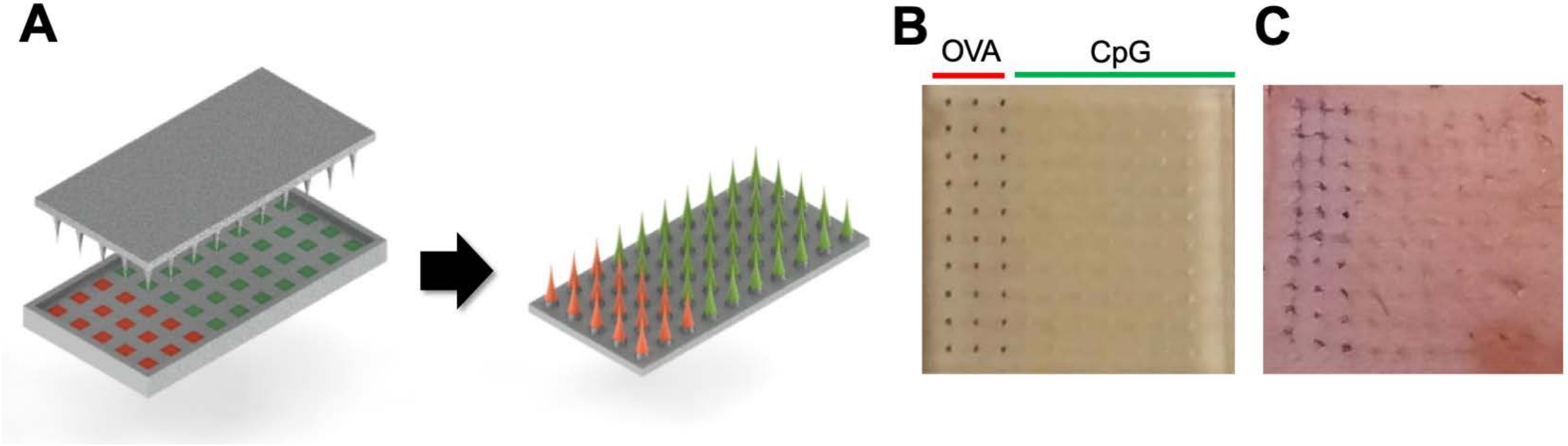
Novel Geometric Designs with 20 um Pixels





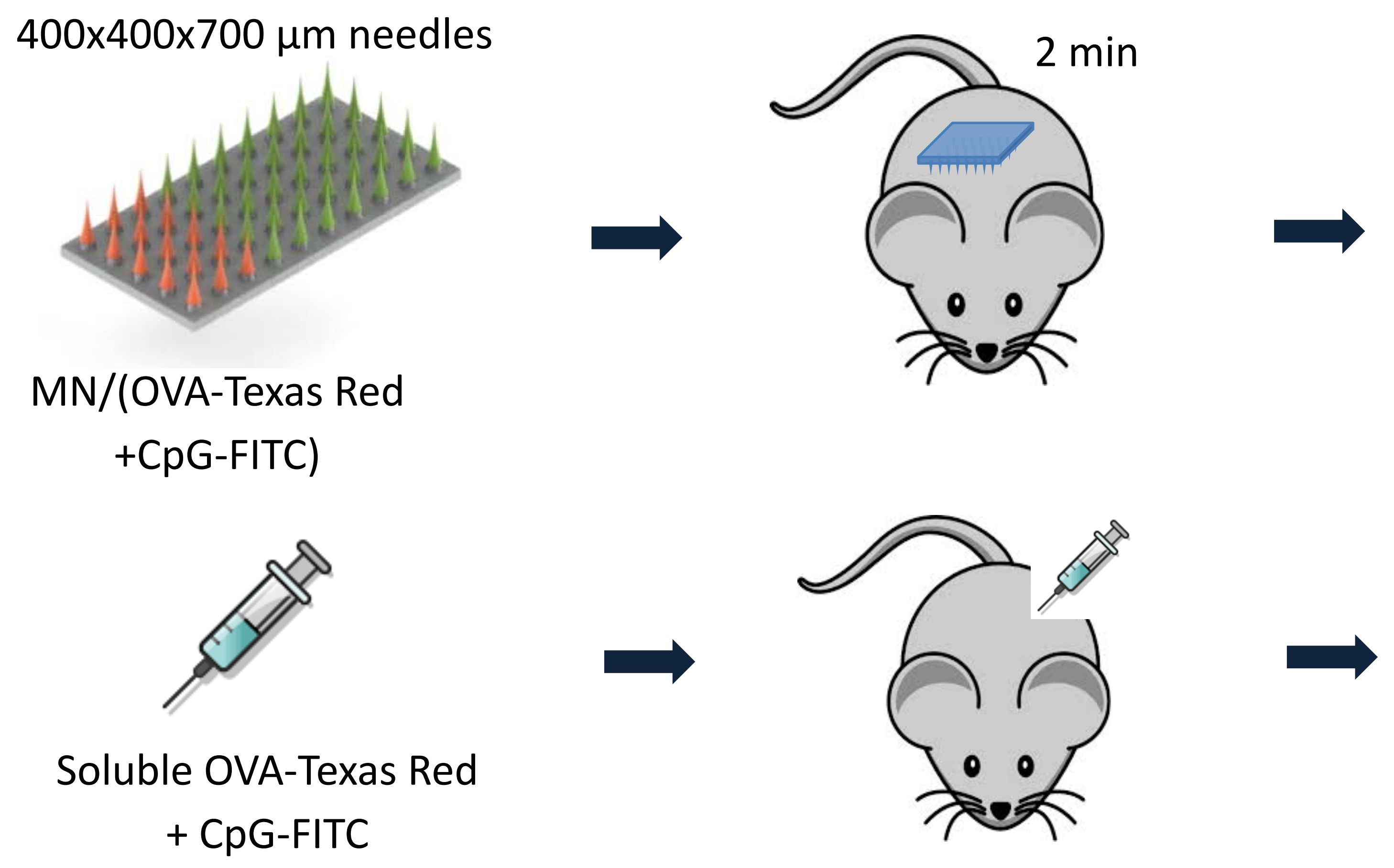


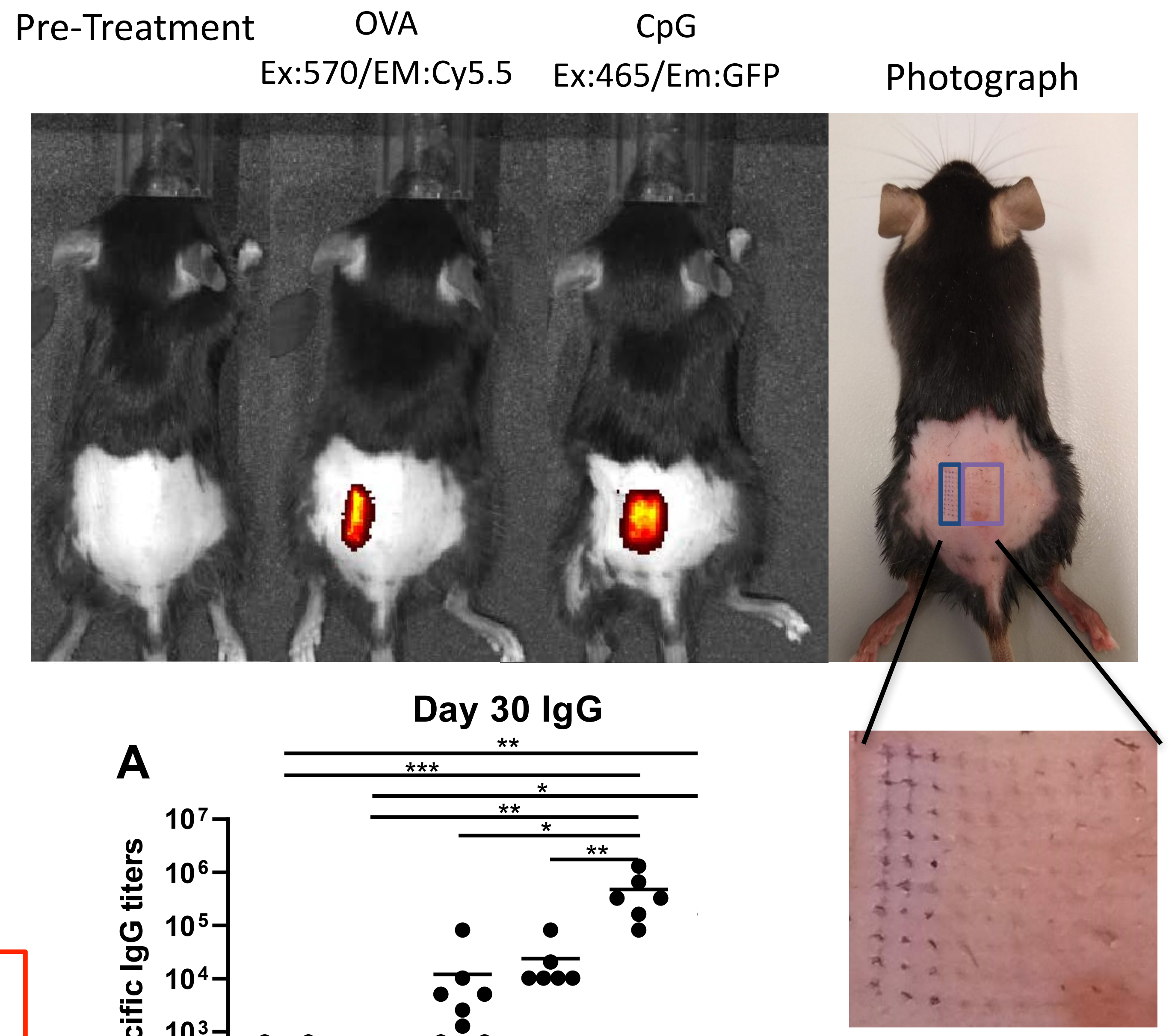
Solid Microneedle Vaccine Delivery

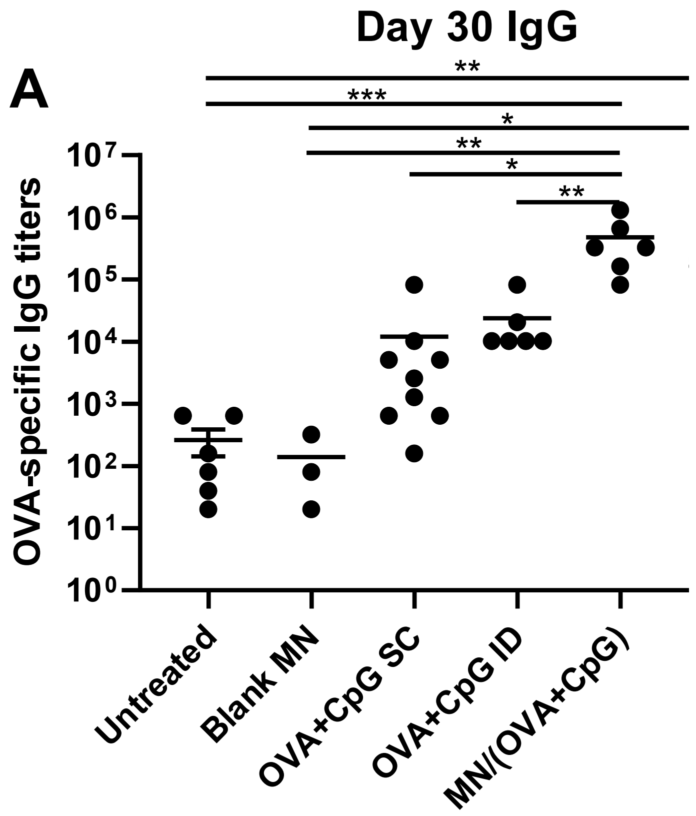


Vaccine stabilized as a thin film in vitrified sugar matrix (should be) stable for 24 months at 25 °C

Vaccine Kinetics: Tracking Cargo Delivery in Mice







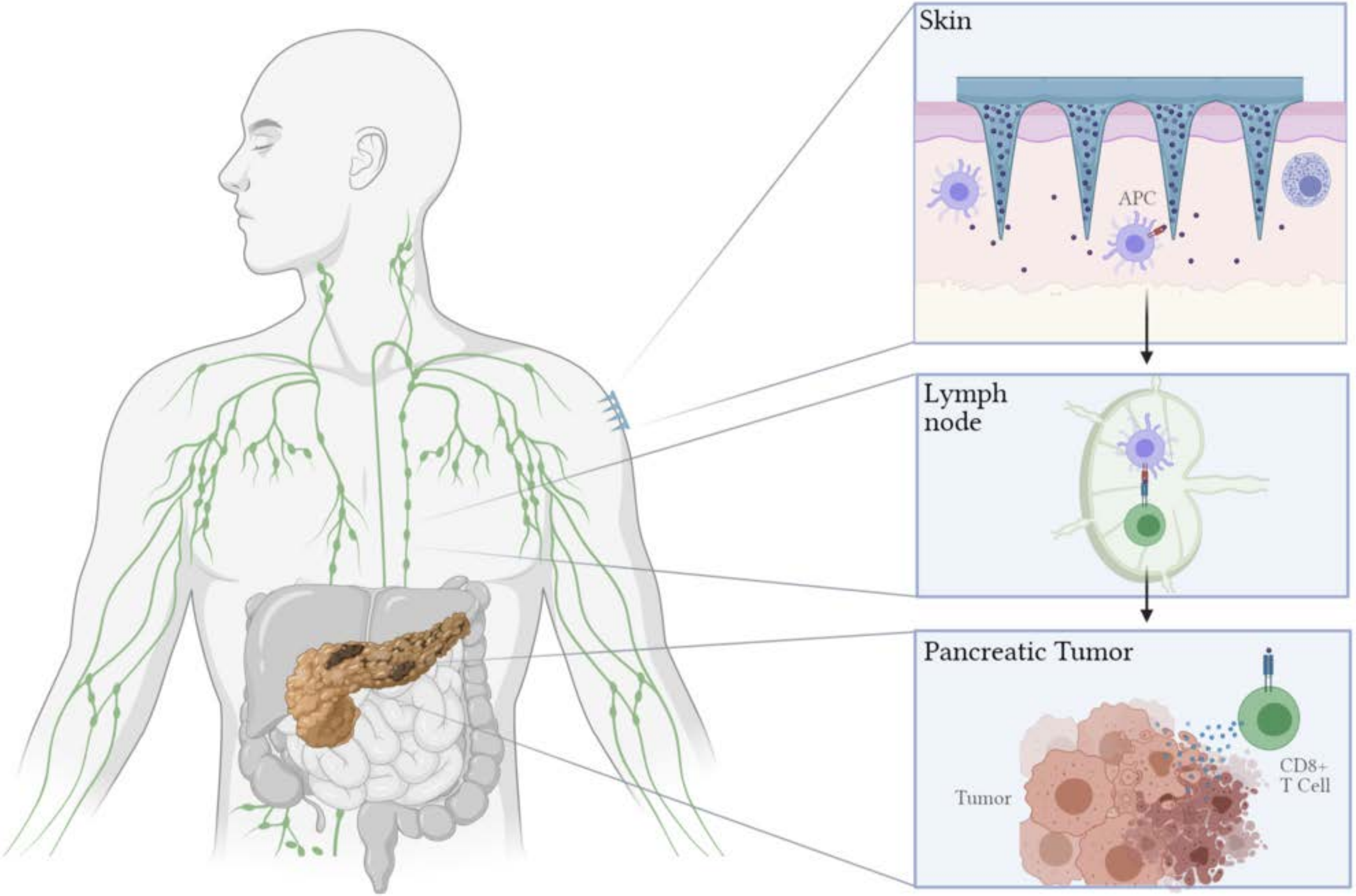
- MN-based vaccine induced 50X higher antigen-specific antibody response after boost

What the world needs now…

- Deliver whatever suite of antigen(s) and adjuvant(s) that are needed
- Cold chain independent
- Prime-plus-boost in single dose
- Self-administerable
- Scaleable to billions of doses

Design Vaccines on the Means of Delivery

Cancer Vaccines Delivered via Microneedles



A Future Fabricated with Light