

Rapid Scanningless 3D Printing: Vision, Status, and Research Needs

Shaochen Chen, PhD

Professor of NanoEngineering and Bioengineering

Co-Director, Biomaterials and Tissue Engineering Center (BMTec)

Institute of Engineering in Medicine (IEM)

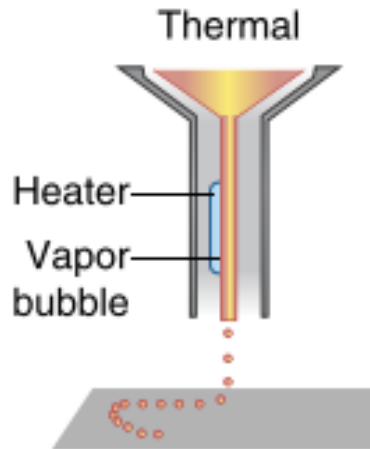
Clinical and Translational Research Institute (CTRI)

University of California, San Diego

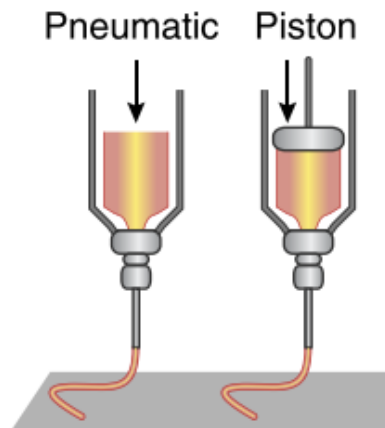


Scanning 3D Printing Technologies

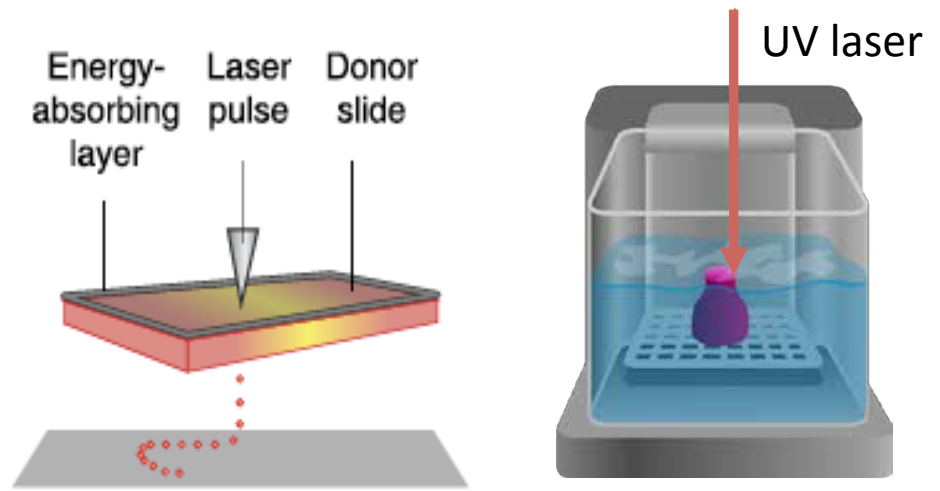
Inject-based



Extrusion-based



Light-assisted

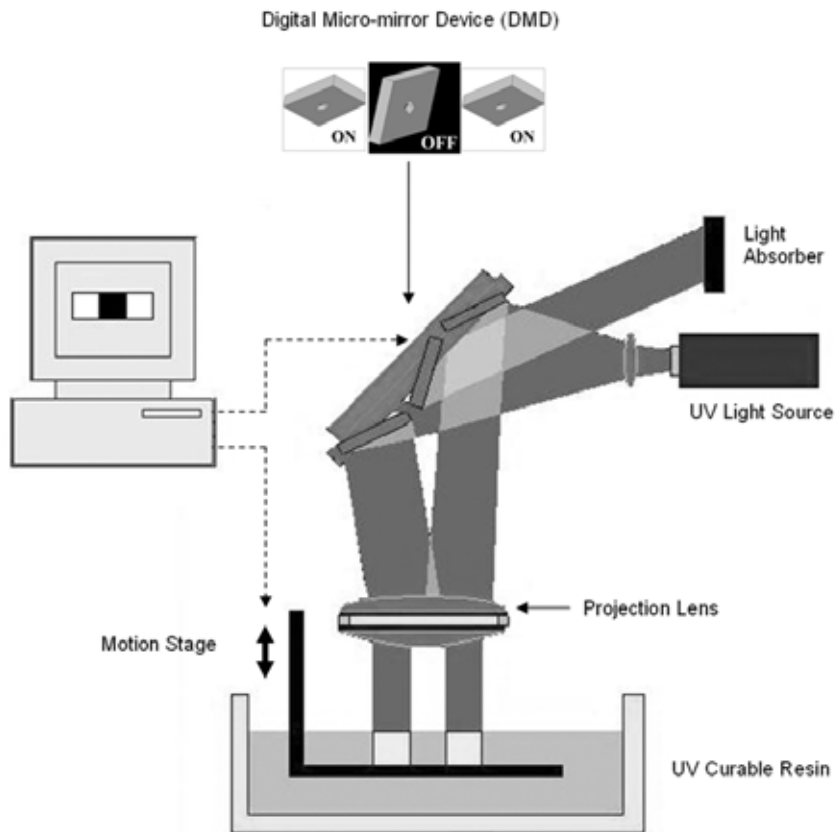


Murphy SV and Atala A. Nat Biotechnol. 2014

Mapilli, Lu, Chen,
Roy, *J. Biomed. Mat.
Research* (2005)

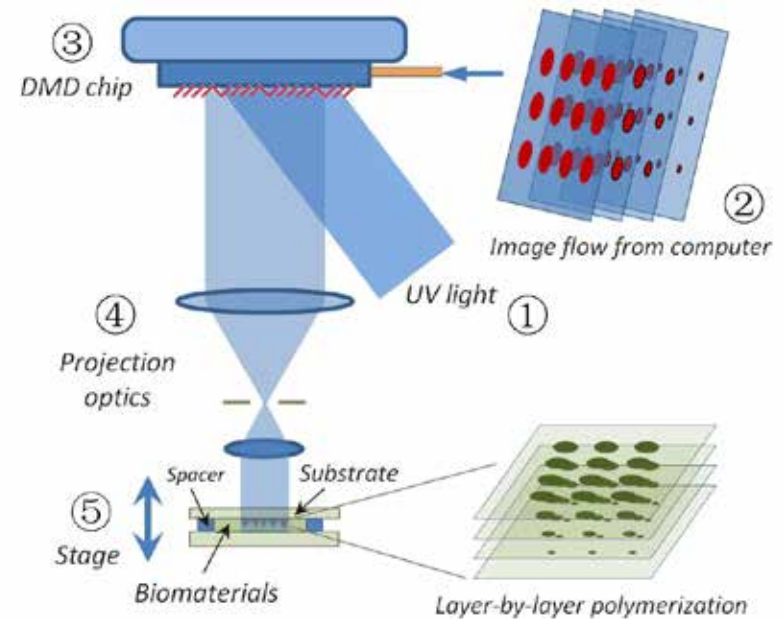
Scanningless 3D Printing Technologies

Layer-by-layer Projection Printing



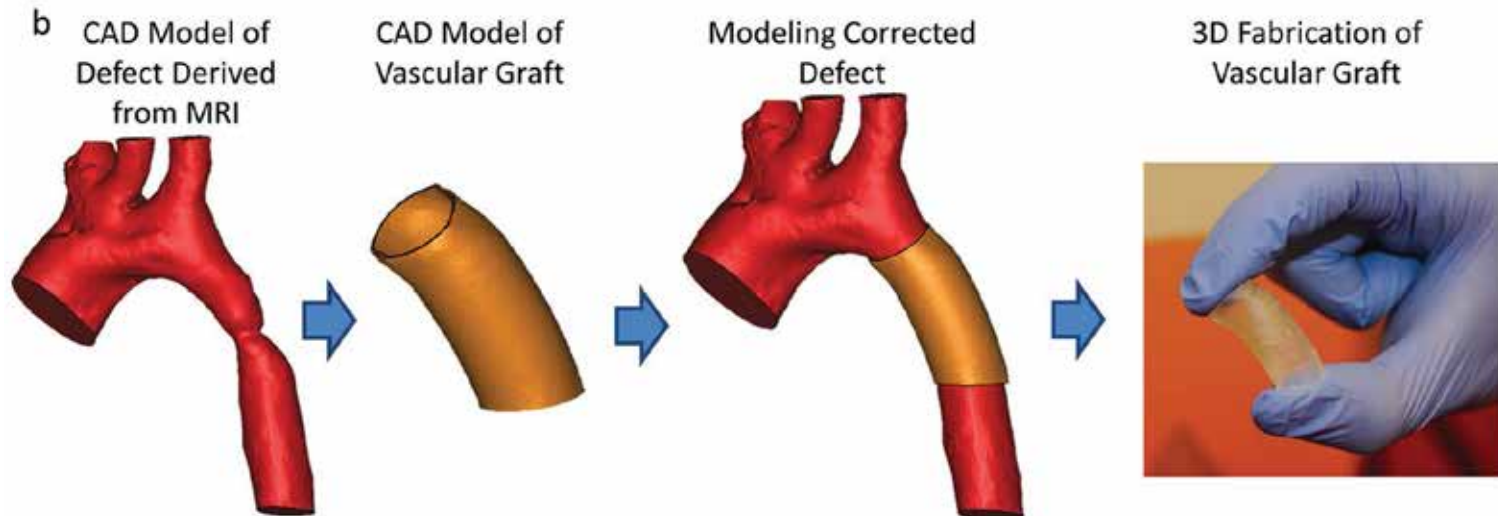
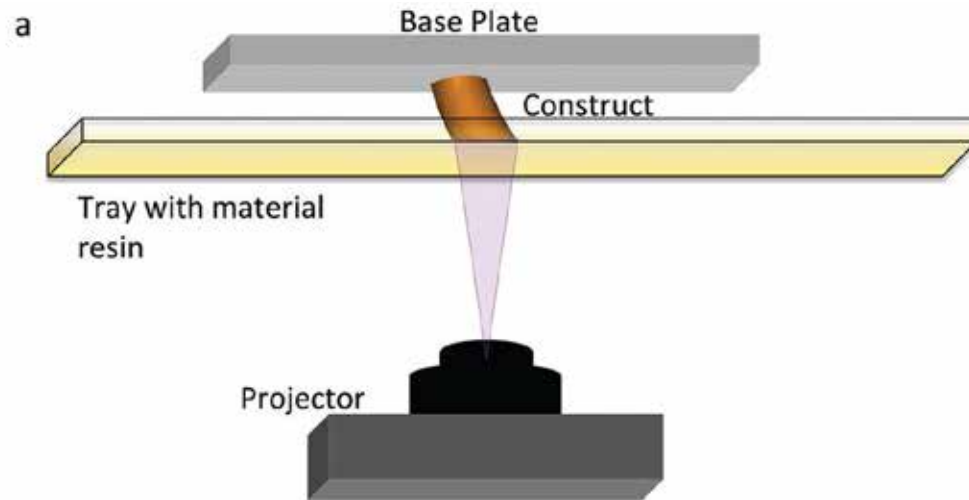
Lu, Mapili, Chen, and Roy, *J. Biomedical Materials Research*, 2006

Dynamic, Continuous Projection Printing

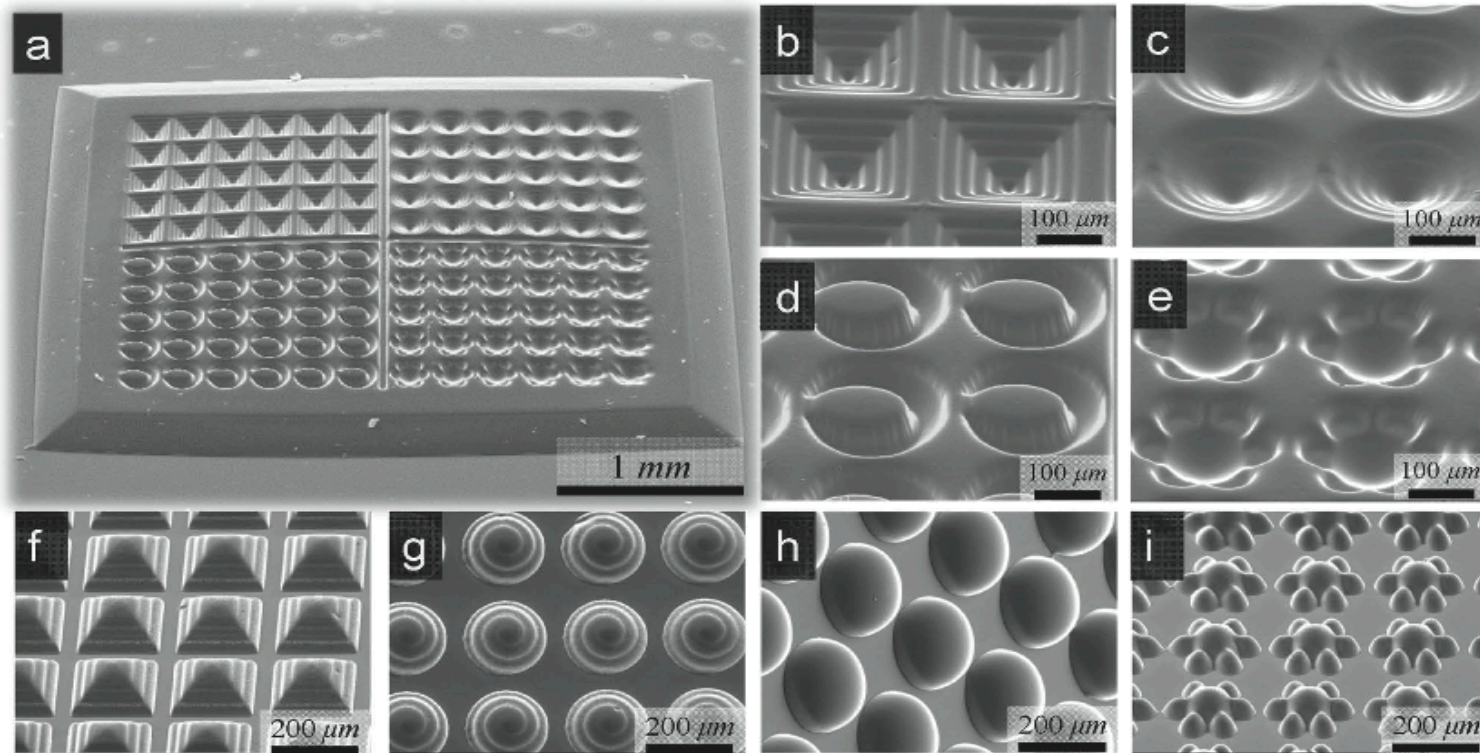


Zhang, Qu, Soman, Hribar, Lee, Chen, He, *Advanced Materials*, 2012.

DLP Printing of Vascular Grafts



Complex 3D Array with Smooth Sidewalls



Pyramid

Spiral

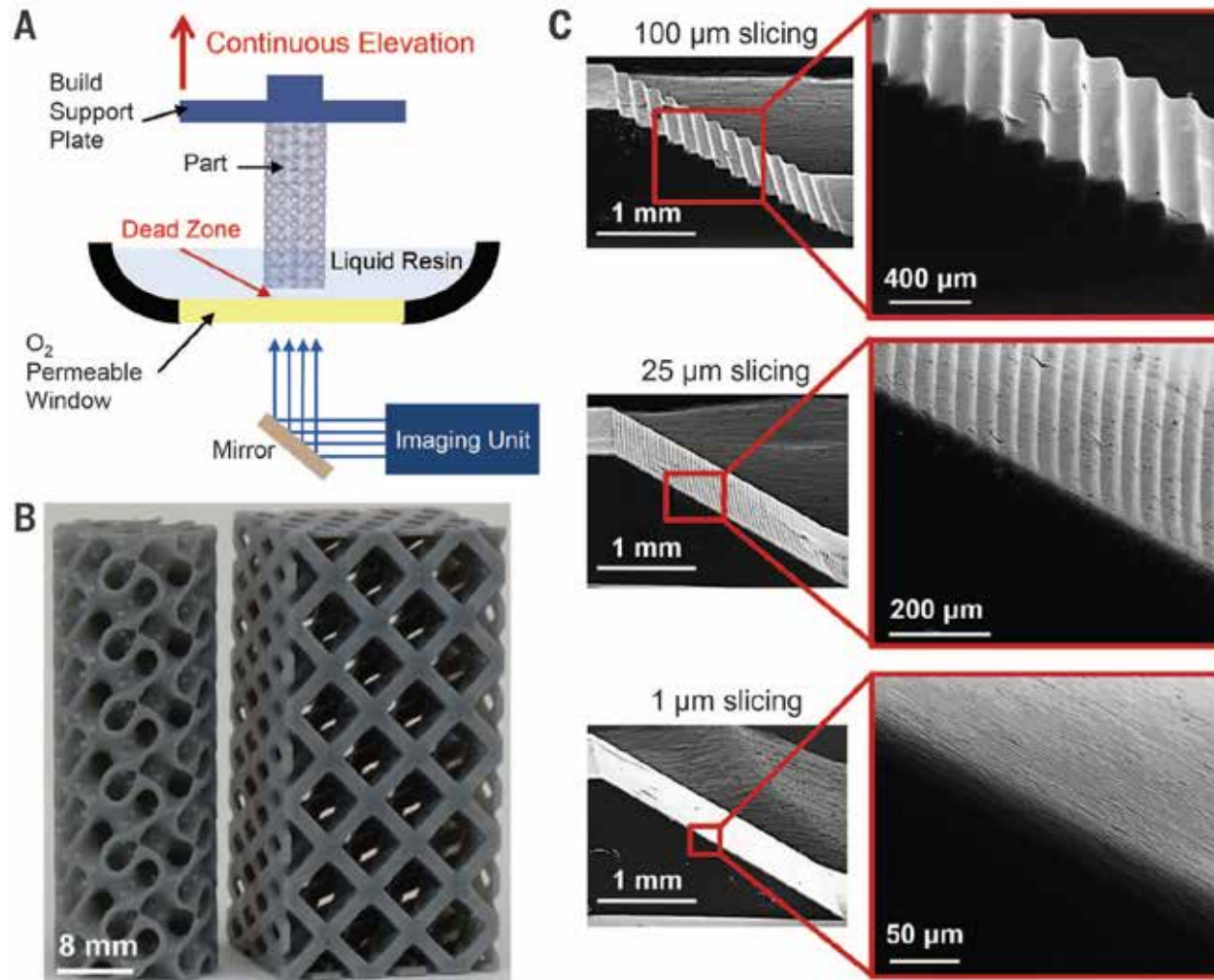
Dome

Flower

Continuous printing is key to eliminate artificial interfaces between drops and layers in nozzle-based 3D printing.

Zhang, Qu, Soman, Hribar, Lee, Chen, He, *Advanced Materials*, 24 (31), 4266-4270 (2012).

Continuous Liquid Interface Production

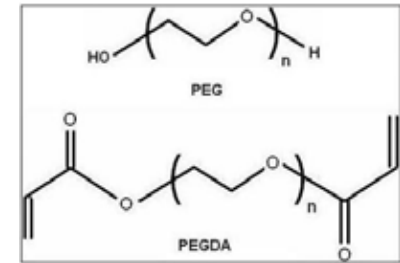


Tumbleston, J.R. et al (Joe DeSimone at UNC) , *Science*, 2015.

Materials Used for 3D Printing

- **Poly(ethylene glycol) Diacrylate (PEGDA)**

- Photo-crosslinkable
- Tunable mechanical properties
- Nontoxic, non-immunogenic
- Can be chemically modified (i.e., RGD, heparan sulfates)

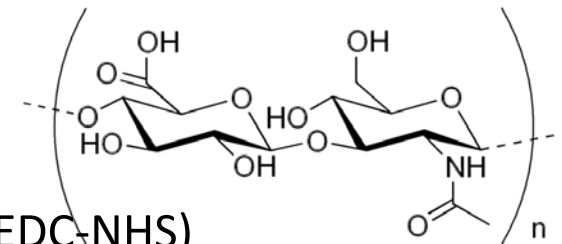


- **Gelatin Methacrylate (GelMA)**

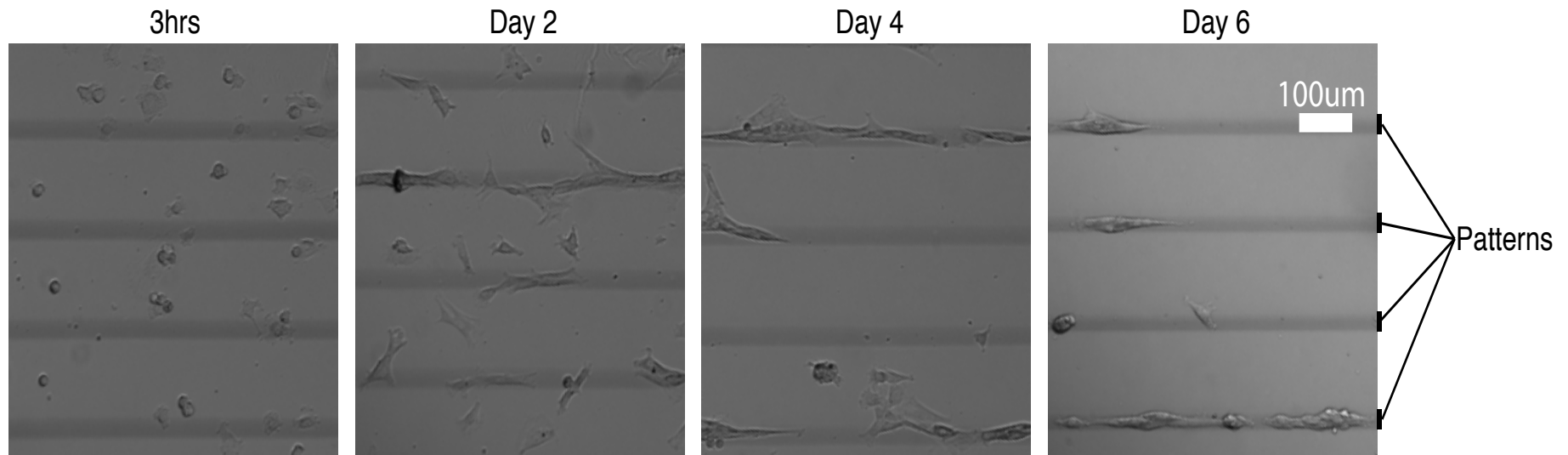
- Biodegradable
- Cell adhesive

- **Hyaluronic Acid (HA)**

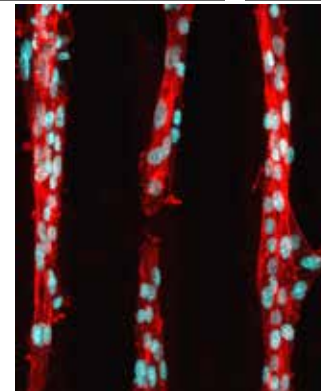
- Biodegradable
- Cell adhesive if covalently functionalized with a cell-adhesive protein (e.g. laminin using EDC-NHS)



Cell Alignment on Stiffness-Patterned Hydrogel



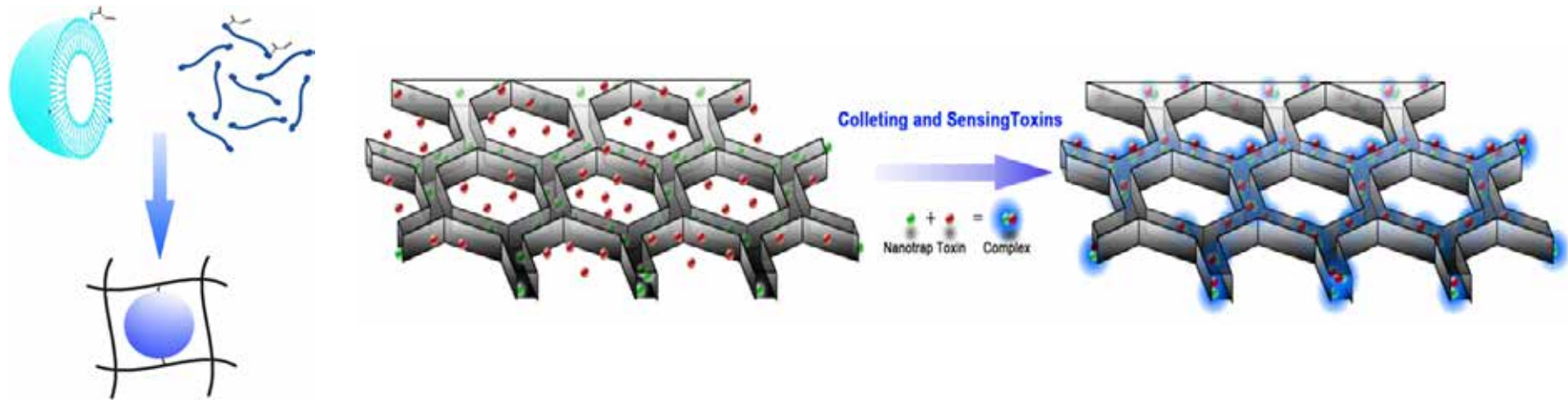
In vitro cell migration. A7R5 smooth muscle cells show migration to the stiffer regions patterned by the digital plasmonic patterning method.



Fluorescent staining shows their actin (red) and nuclei (cyan).

Wen, Vincent, Choi, Fuhrmann, Hribar, Chen, Engler, *Nature Materials*, 13, 979-987, 2014
Hribar, Choi, Ondeck, Engler, Chen, *Advanced Functional Materials*, 24, 4922-4926, 2014

Nanoparticles-enabled 3D Detoxification

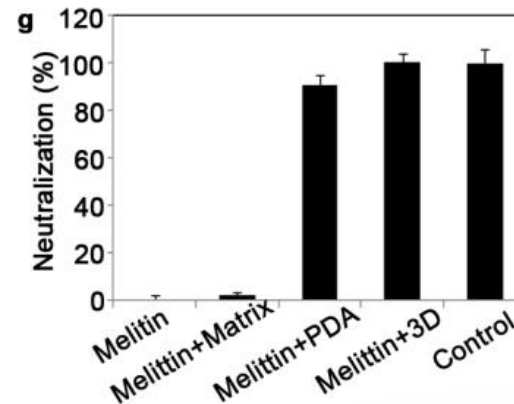
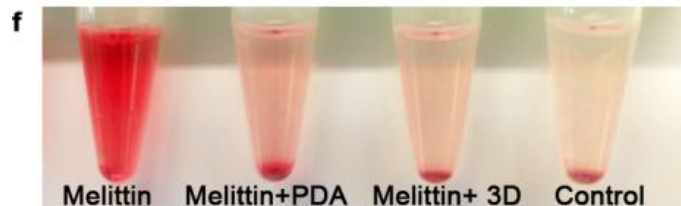
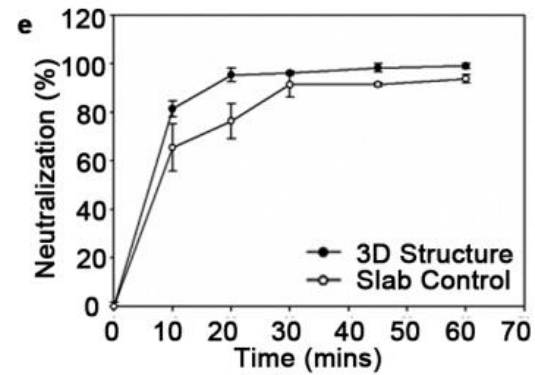
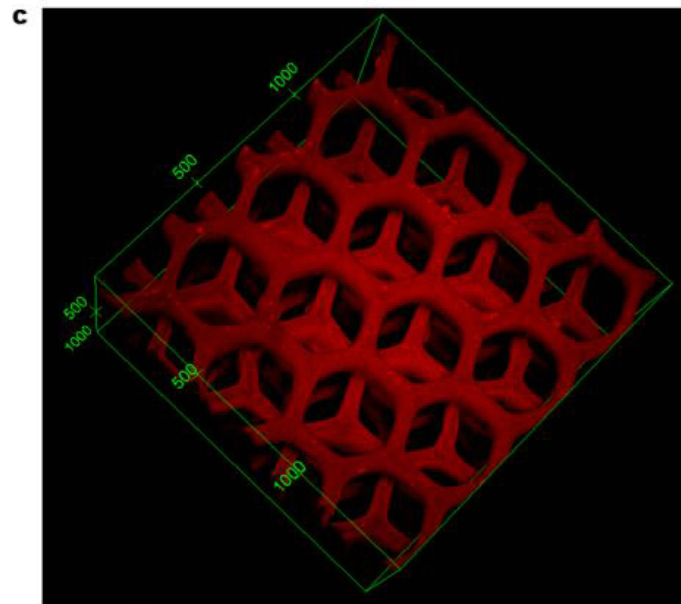
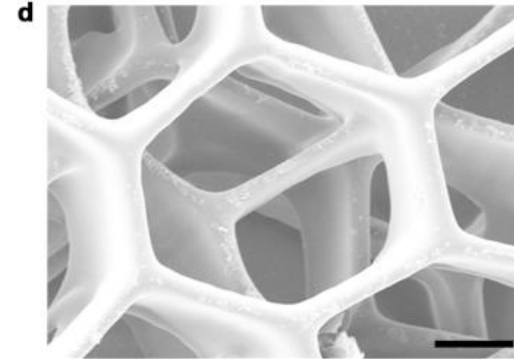
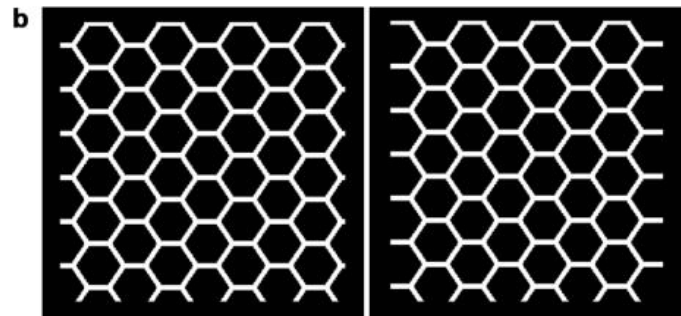


Polydiacetylene (PDA) nanoparticles (green) are installed in PEGDA hydrogel matrix (grey) with liver-mimetic 3D structure fabricated by 3D printing.

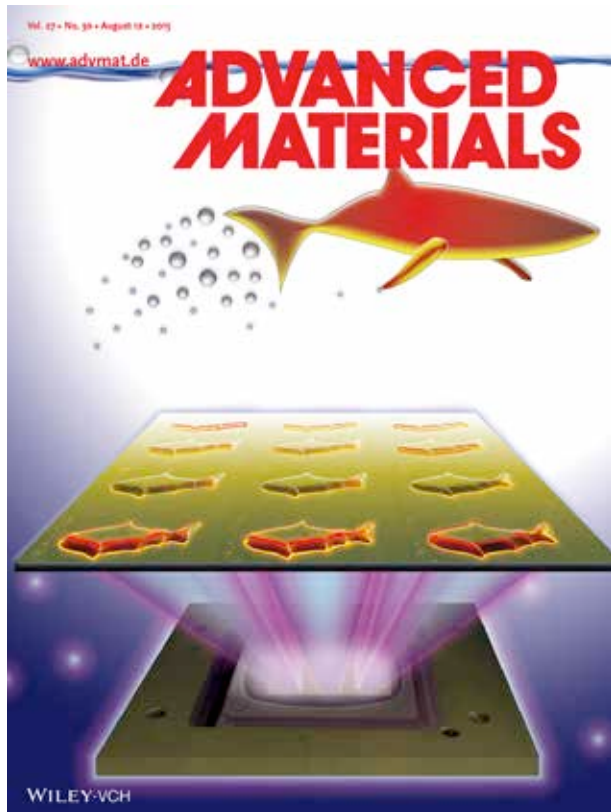
The PDA NPs can attract, capture and sense toxins (red), while the 3D matrix with modified liver lobule structure allows toxins to be trapped efficiently.

Gou, Qu, Zhu, Xiang, Yang, Zhang, Wei, and Chen, *Nature Communications*, 5: 3774, 2014

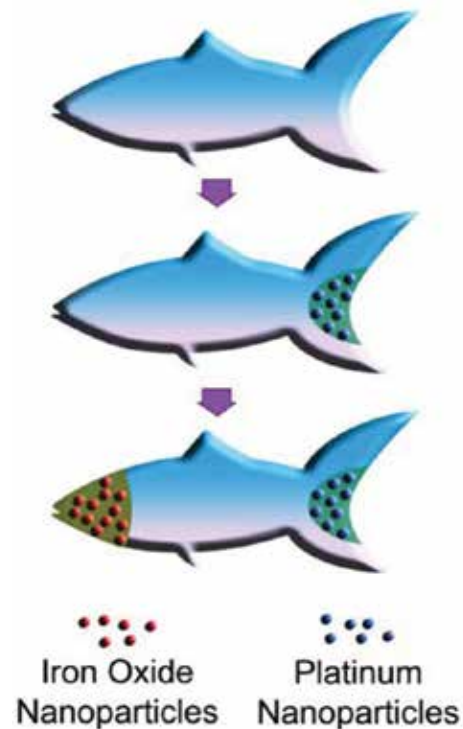
Liver-mimic 3D Detoxification



3D-printed Artificial Micro-fish



Inside Cover Image

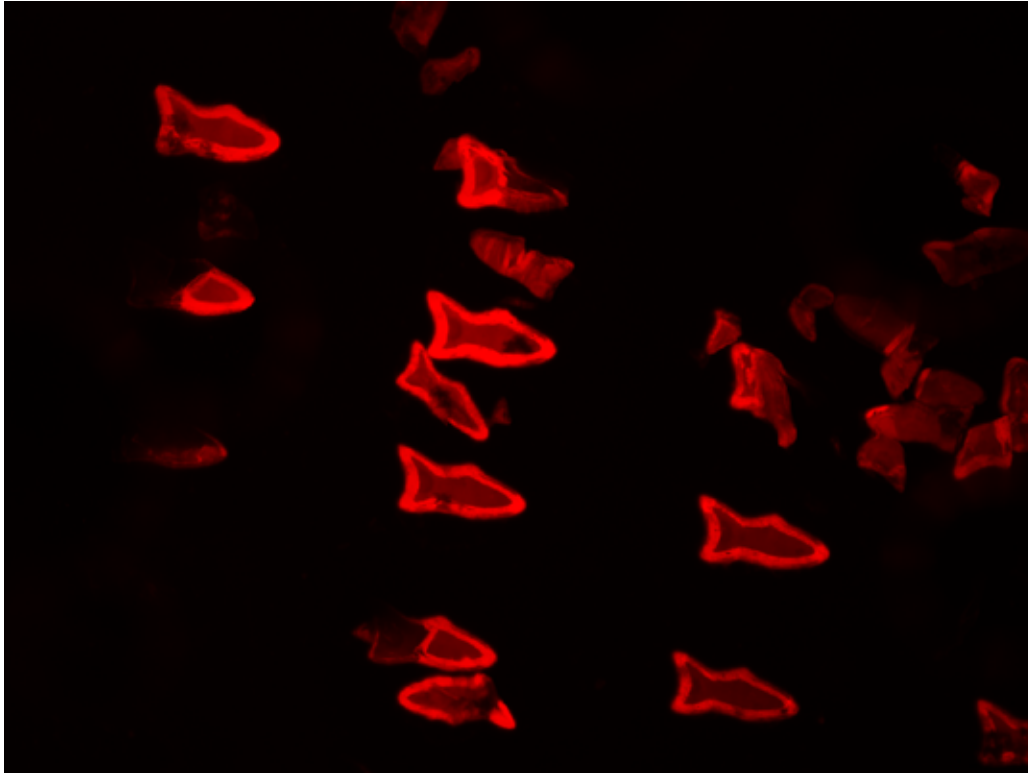


Fish-shaped microrobots

- Swim in liquids
- Chemically powered
- Magnetically guided
- Detoxify the toxins

Zhu et al, *Advanced Materials*, 27, 4411 (2015)

3D-printed Micro-fish to Remove Toxin



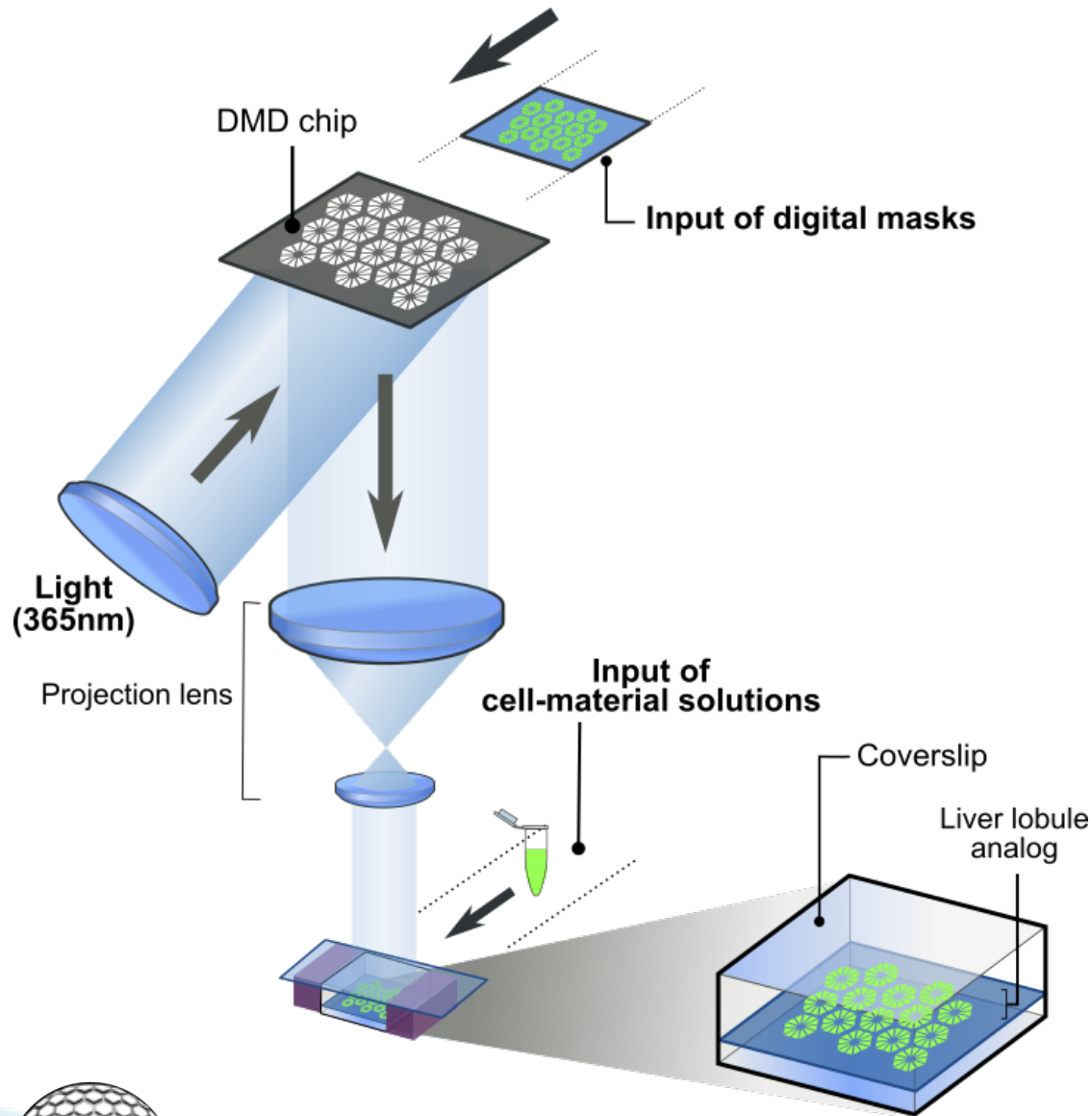
Nano-robots:

- Self-propelled
- Sensing
- Drug delivery
- Nano-surgery

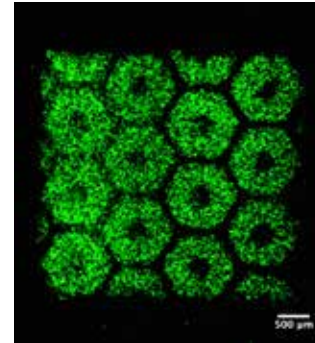
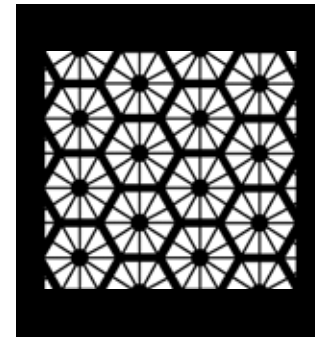
Zhu et al, *Advanced Materials*, 27, 4411 (2015)

Press report by *The Wall Street Journal*, *The Washington Post*, *Forbes*, *BBC News*, etc

3D Bioprinting of Human Liver Tissues



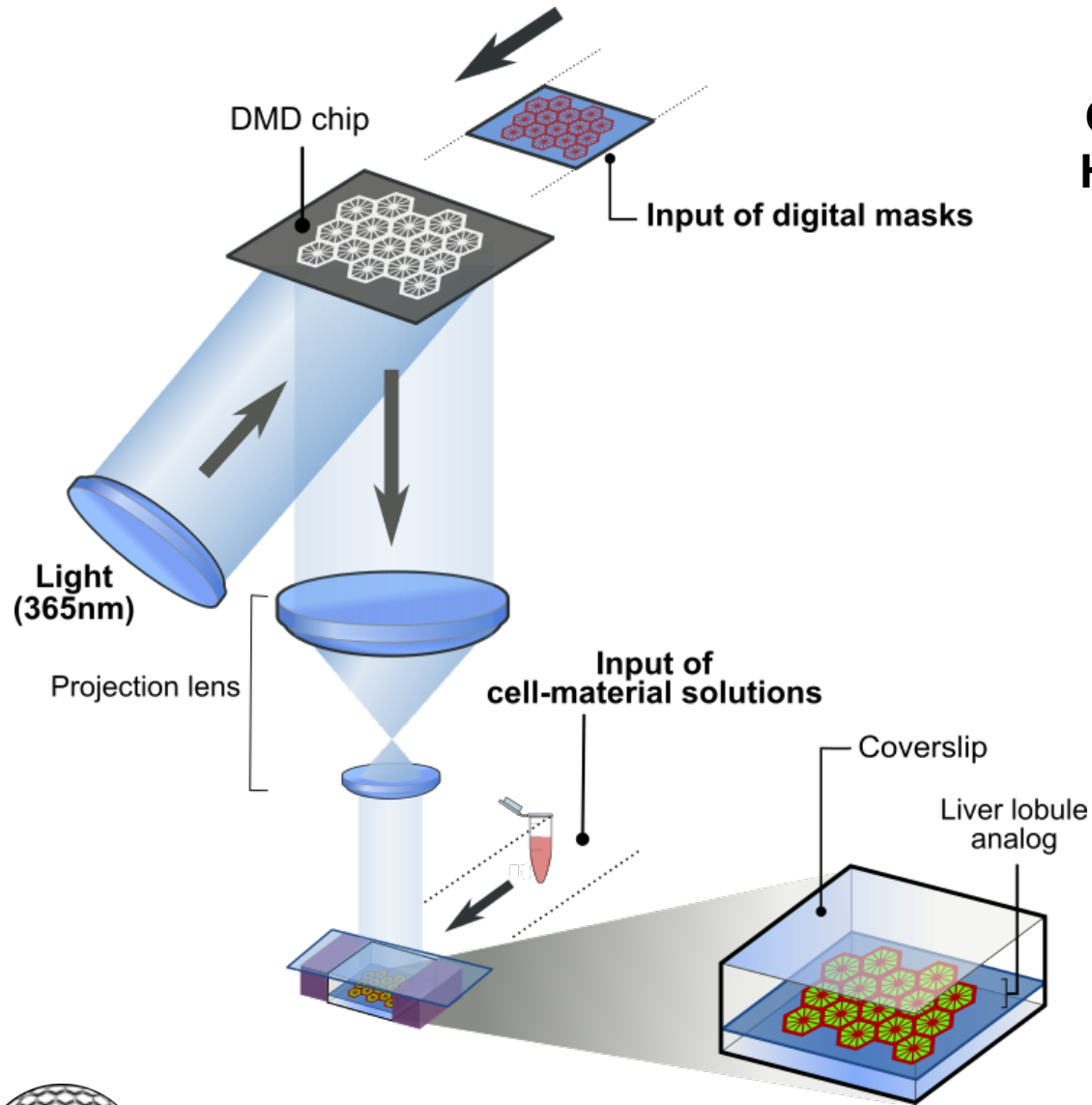
Cells: hiPSC-HPCs
Hydrogel: GelMA



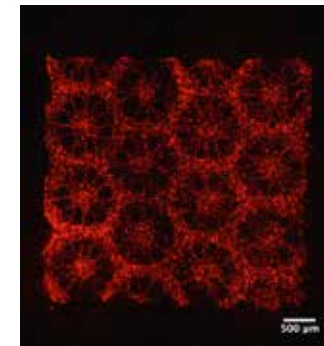
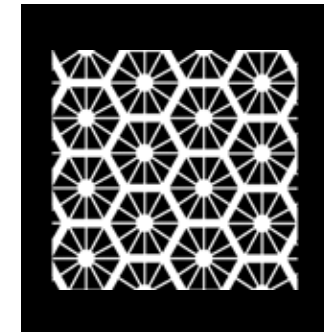
Printed in 1 second



Two-Step Bioprinting



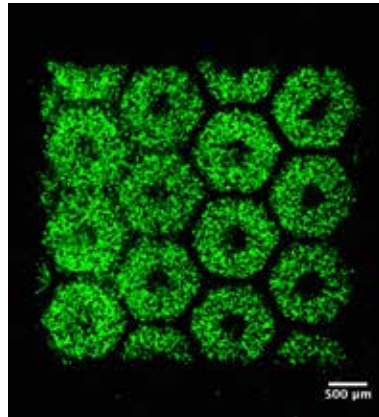
Cells: HUVEC and ADSC
Hydrogel: GelMA with HA



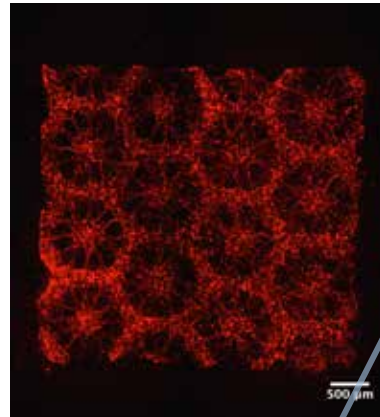
Printed in 1 second



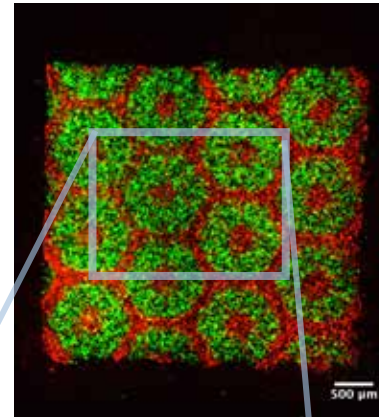
Bioprinted Hepatic Construct



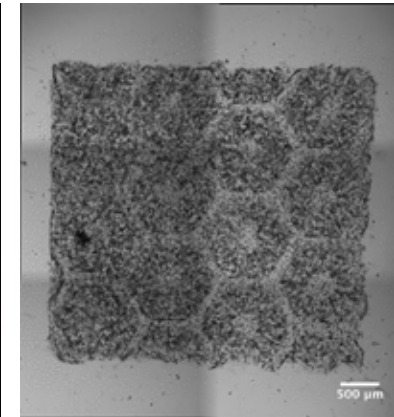
hiPSC-HPCs



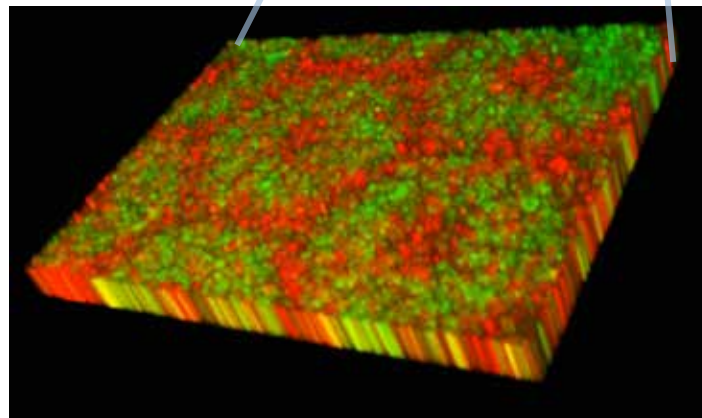
HUVEC and ADSC



Merge

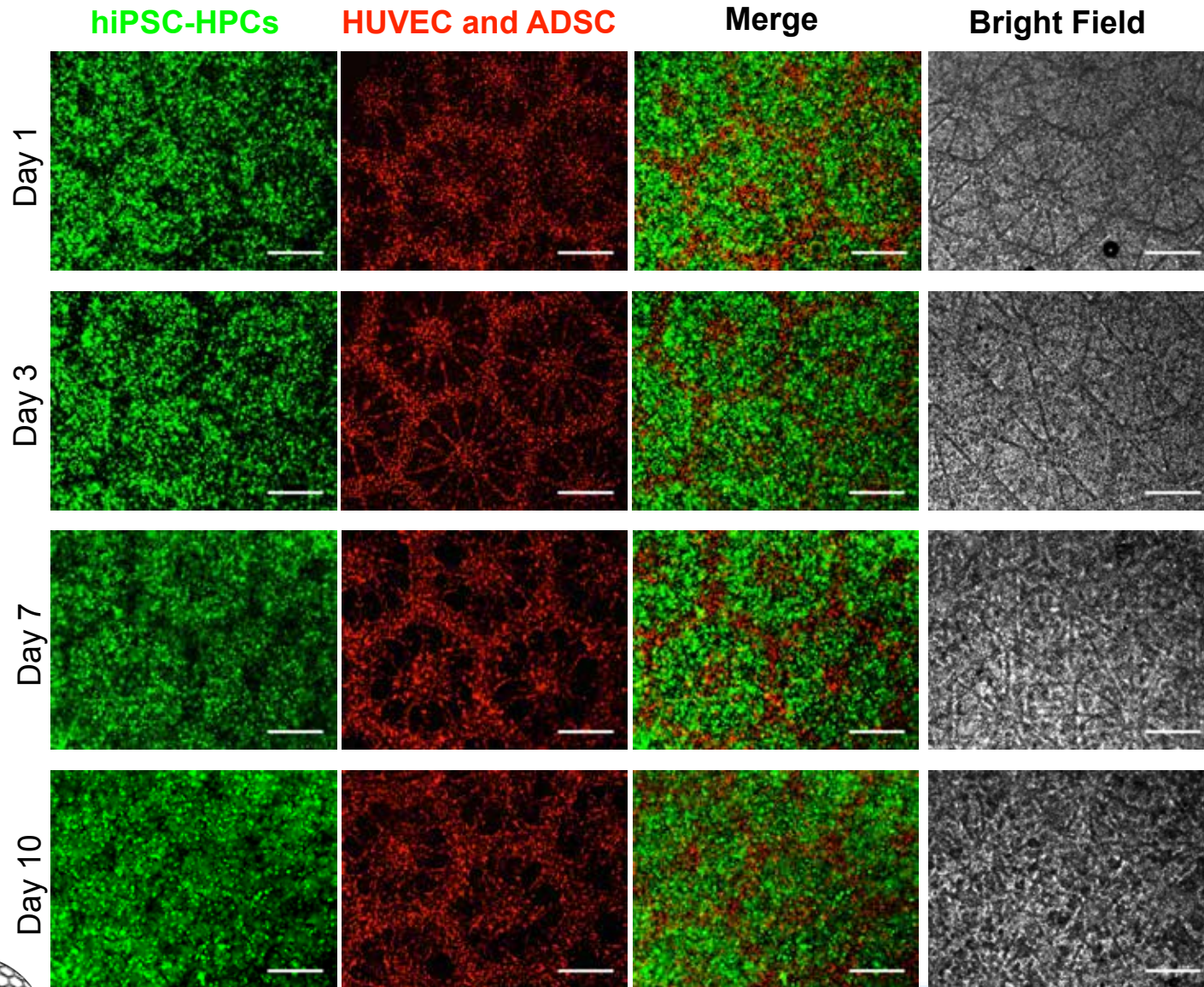


Bright Field

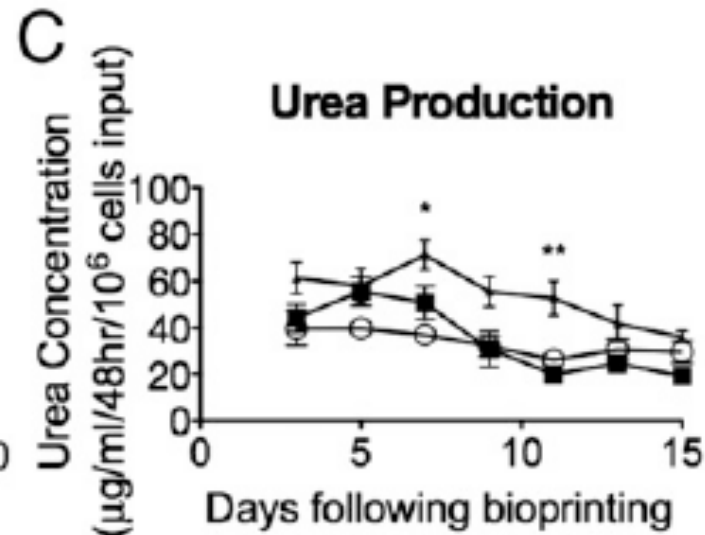
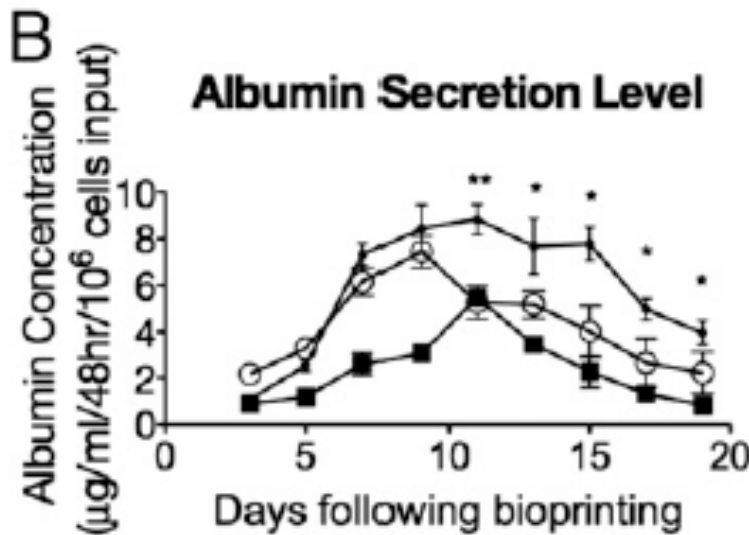
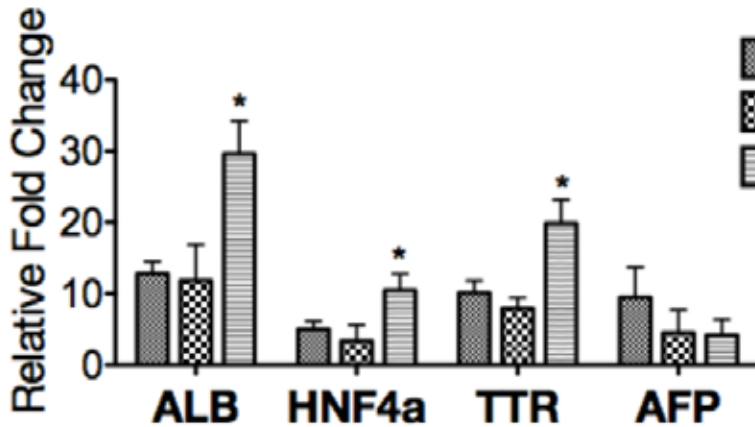


3D reconstruction

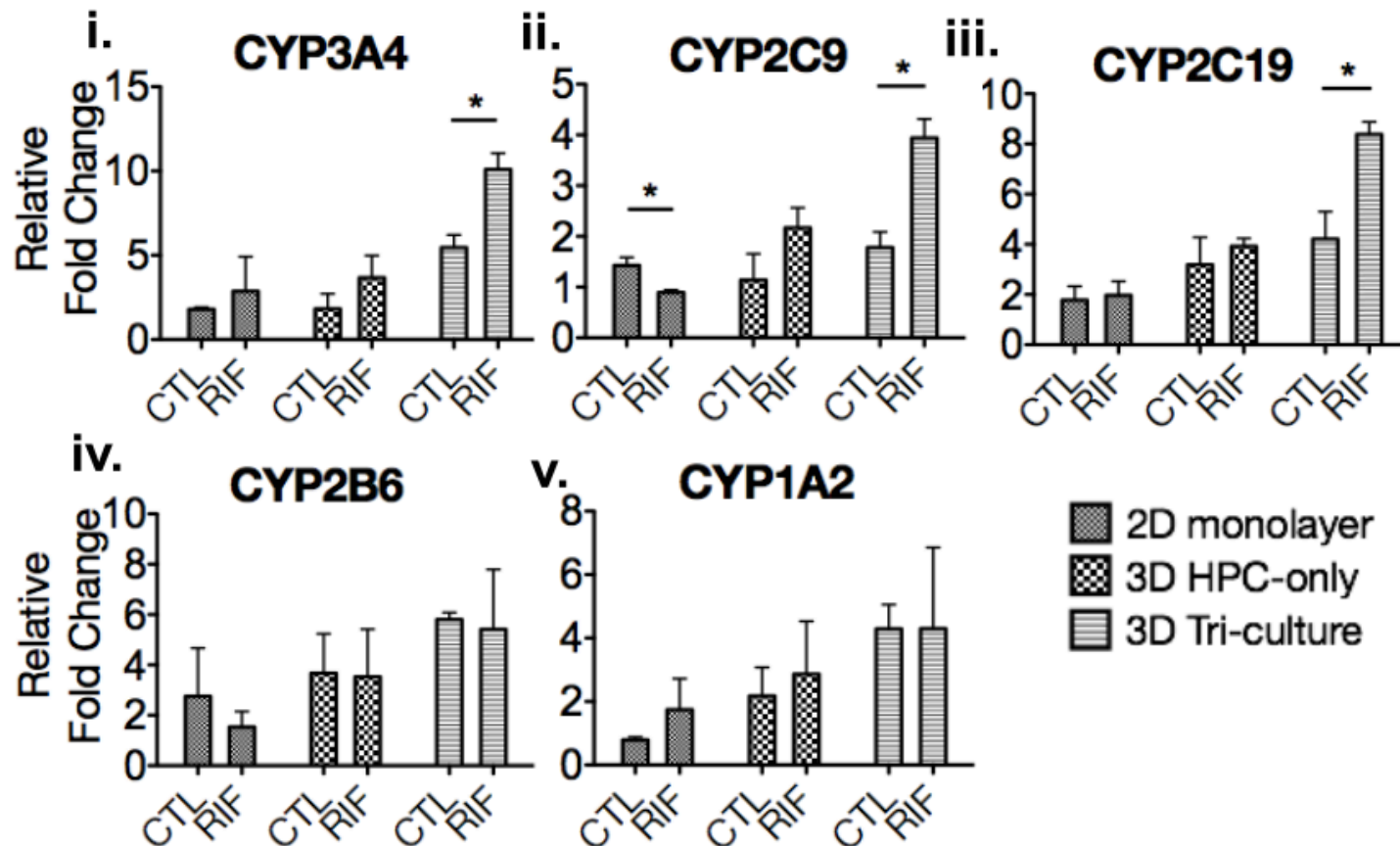
Pattern Maintenance Post-printing



Liver-specific Genes and Functions



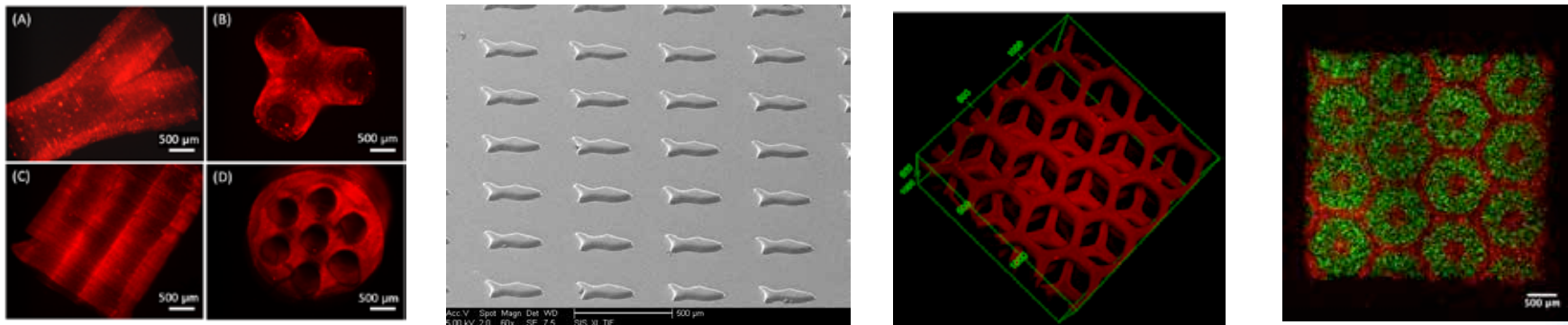
Expression Levels of Key Enzymes in Drug Testing



- hiPSC-HPCs in 3D triculture have the highest average expression levels of CYPs
- Rifampicin (antibiotics) treating led to significant increase in CYP3A4, 2C9, 2C19 in 3D triculture, but not in 2D or 3D-HPC only models.

Summary

- Light-based scanningless 3D printing approaches offer a rapid printing speed with microscale resolution.
- BioPrinting allows direct-write of 3D, novel, biomimetic biological scaffolds with control of chemical, biological, and mechanical properties:
 - porosity, shape, stiffness, Poisson ratio
 - chemical composition
 - cell encapsulation
- A variety of biopolymers (e.g. PEG, GelMA, HA) can be used for precision tissue models (*in vivo* and *in vitro*)



Gaps and Research Needs

- Multiple materials parallel printing,
- Multiple cells continuous printing
- Develop viable collaboration with medical doctor and biologists
- Develop novel biomaterials for tissue engineering and regenerative medicine
- Develop effective vascularization strategies to keep engineered tissues alive
- High-throughput manufacturing

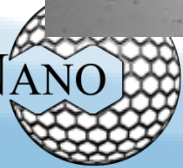
Science Outreach: 1-second Photo



High school students in the hydrogel (pictures with permission)



BIONANO



Italian National TV Producer

Public talk show for bioprinting UC San Diego