

Sweet Science: 3D Printed Sugar Templates for Regenerative Medicine

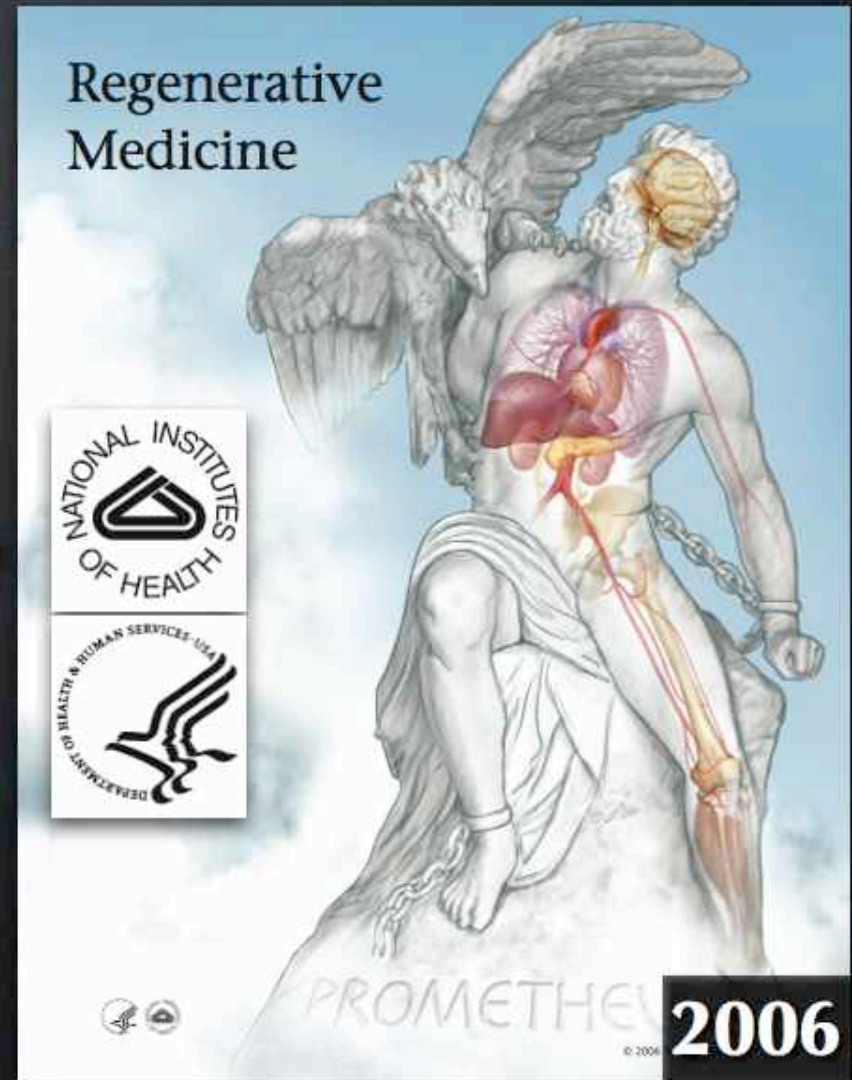
Jordan S. Miller¹, Kelly R. Stevens², Michael T. Yang¹, Brendon M. Baker¹, Duc-Huy T. Nguyen¹, Daniel M. Cohen¹, Esteban Toro¹, Alice A. Chen², Peter A. Galie¹, Xiang Yu¹, Ritika Chaturvedi¹, Sangeeta Bhatia², Christopher S. Chen¹

1. Department of Bioengineering, University of Pennsylvania, Philadelphia, PA, USA

2. Massachusetts Institute of Technology, Cambridge, MA, USA

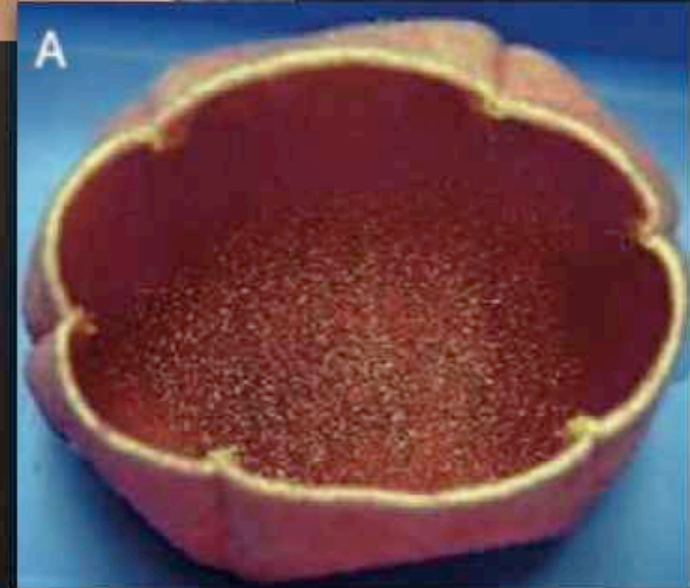
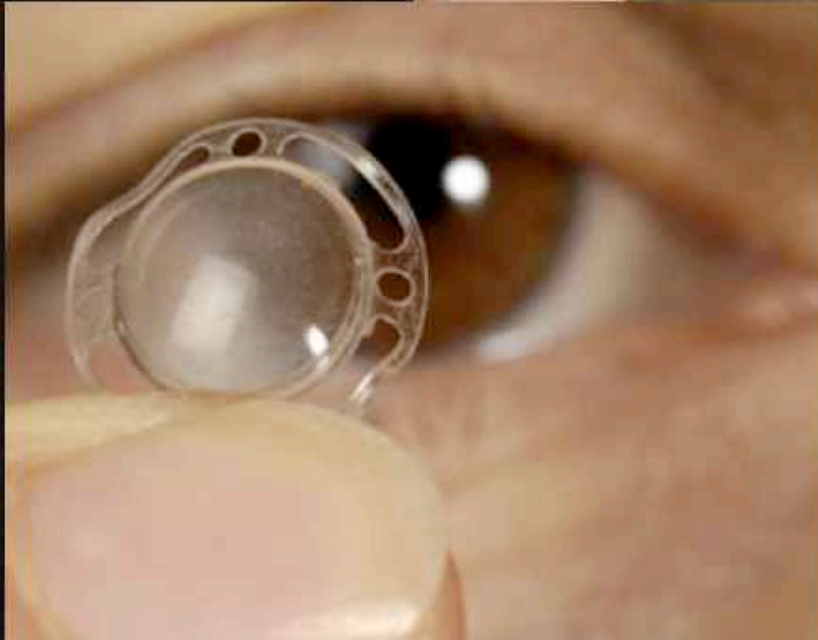


Tissue Engineering → Regenerative Medicine



Cells Outperform Devices.

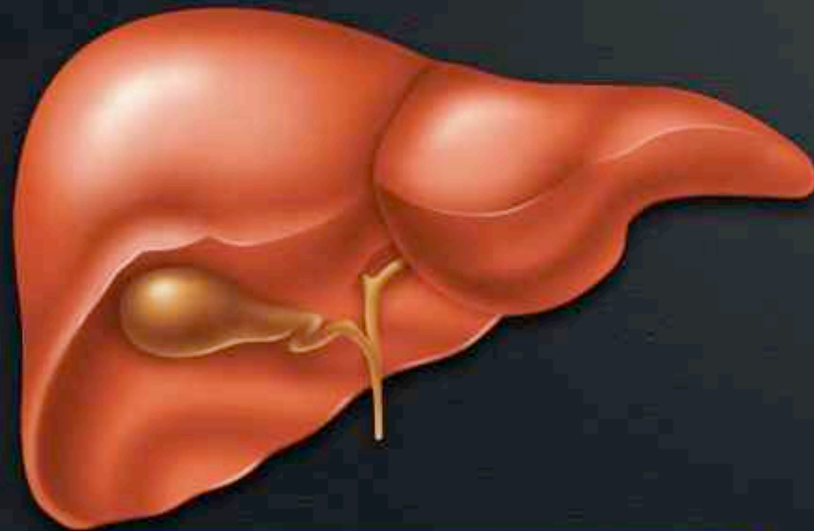
Some Successes in Regenerative Medicine



Yannas IV+. *Science* 1982; 215:174-6.
Heimbach D+. *Ann. Surg.* 1988; 208(3):313-20. Nishida+. *NEJM* 2004; 351(12):1187-96.
Yannas IV. *Chembiochem* 2004; 5(1):26-39. Atala+. *Lancet* 2006; 367:1241-6.

Solid Organs have Multiscale Vasculature

Human Liver



3.5 lbs (1.6 kg)
1.5 L volume
750 mL vasculature

Mouse Liver

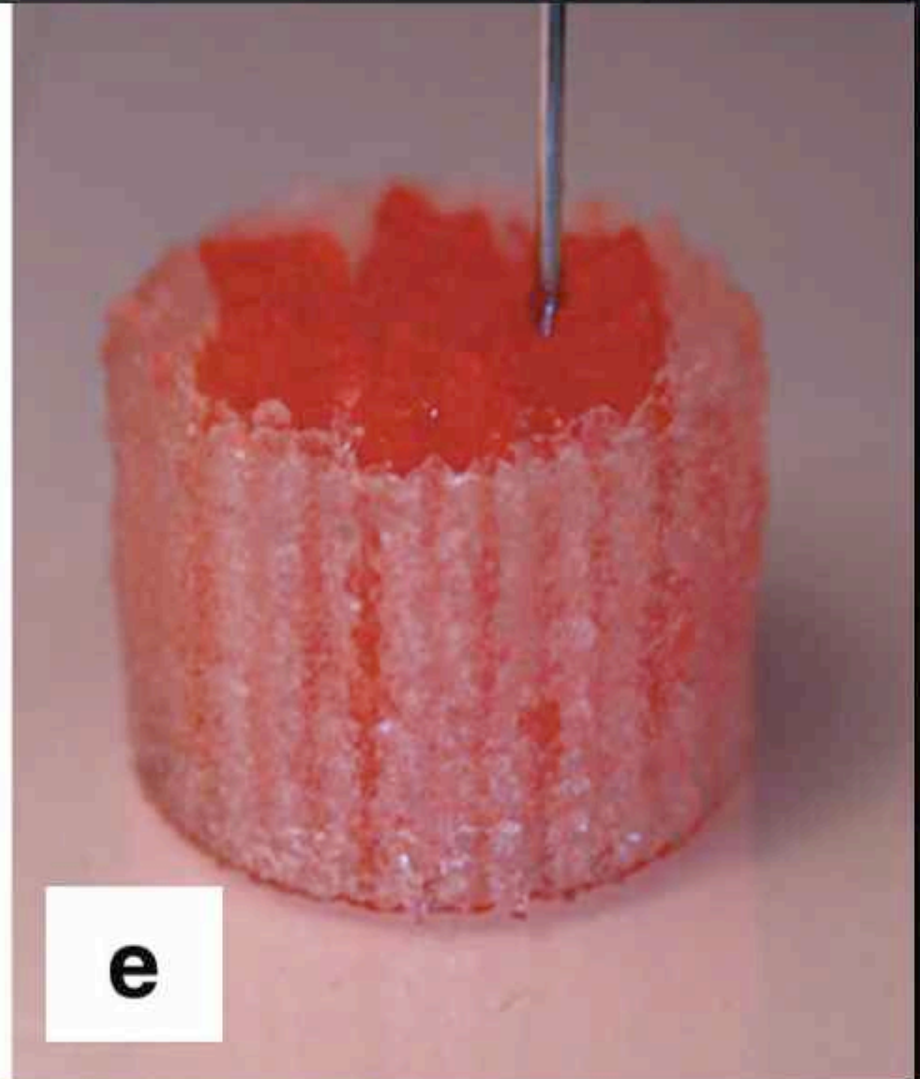
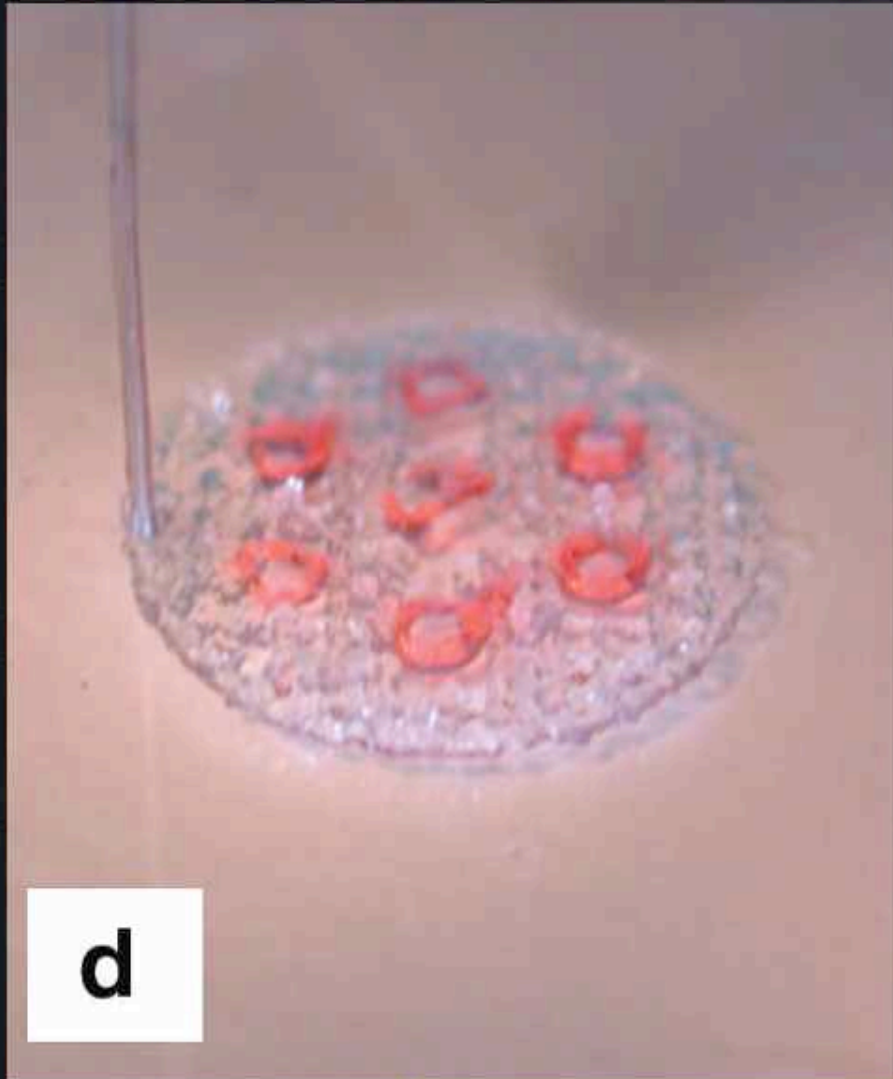


μ CT of mouse liver vasculature, 2 lobes
processed data from Bhatia lab, MIT

<http://zdsolutions.it/>

Andersen V+. *Alcohol Alcohol* 2000; 35(5):531-2.

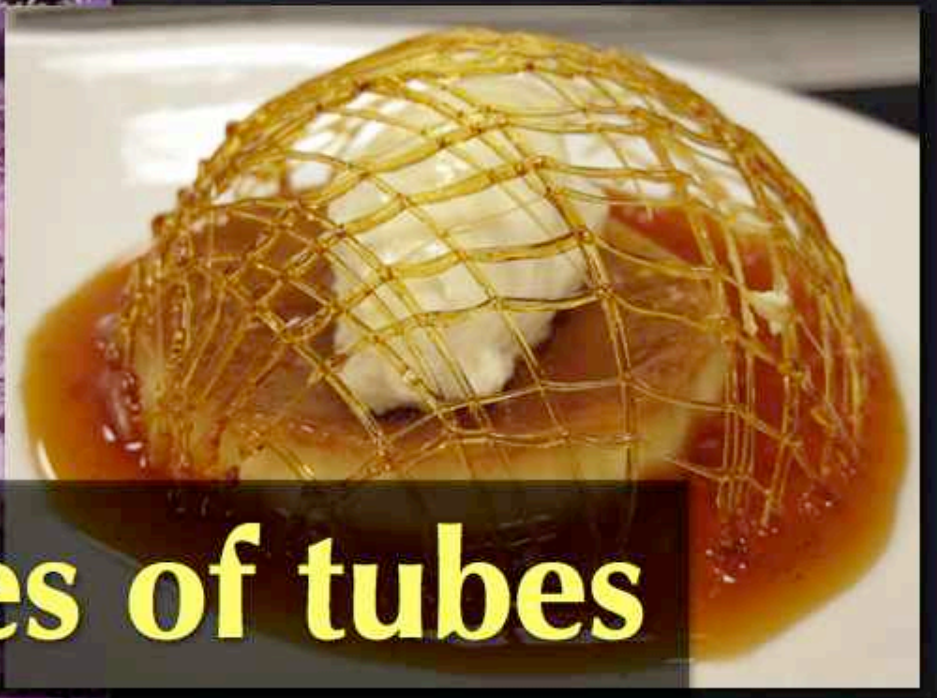
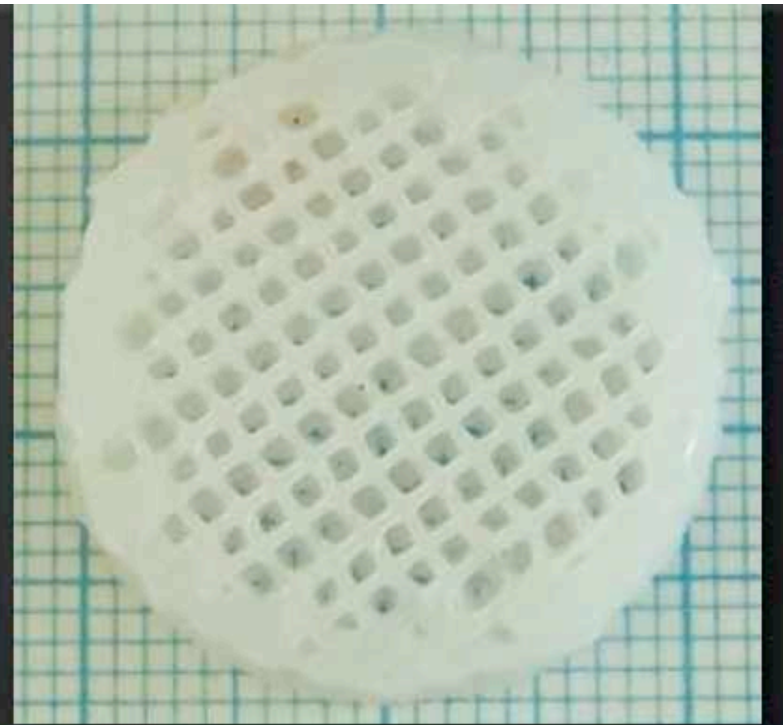
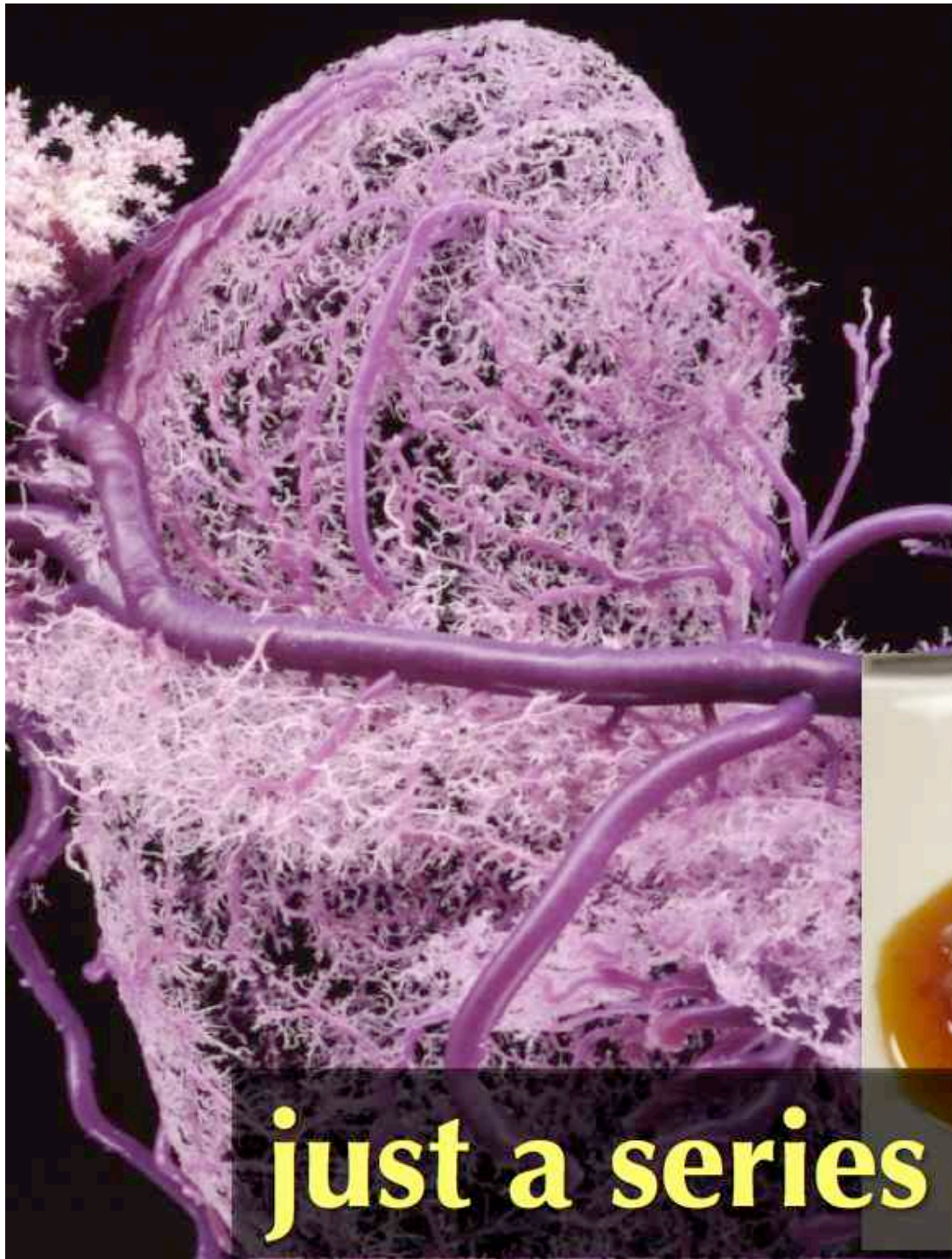
Bioprinting Cells and Gel



Hypoxia, Shear Stress, Cell Type and Gel Type limitations are major challenges

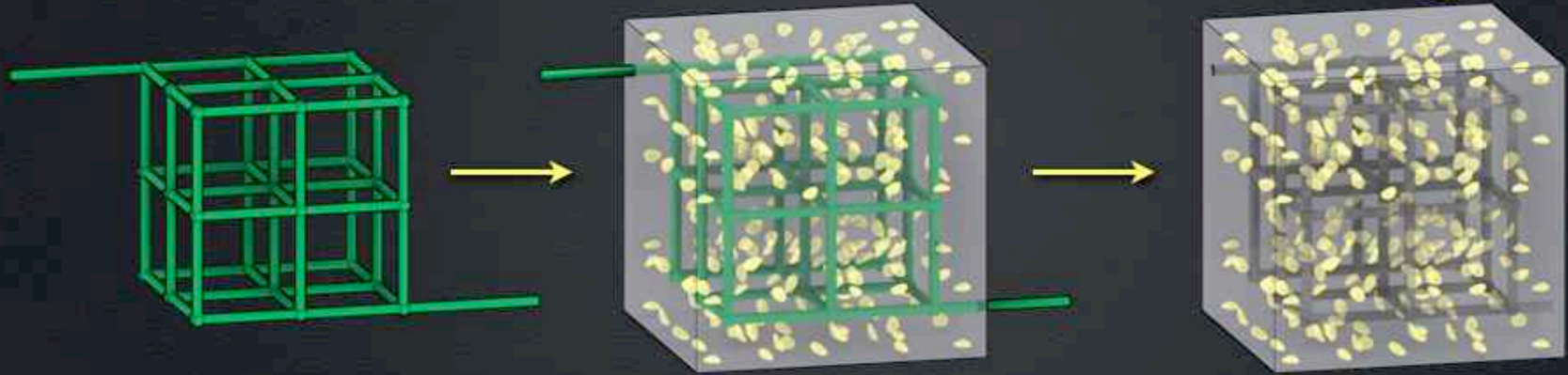
Wang, et al. (2010). Tissue Engineering PART B, 16(2), 189–197.





just a series of tubes

Functional 3D Vasculature with Living Cells



3D Printed,
Filament Network

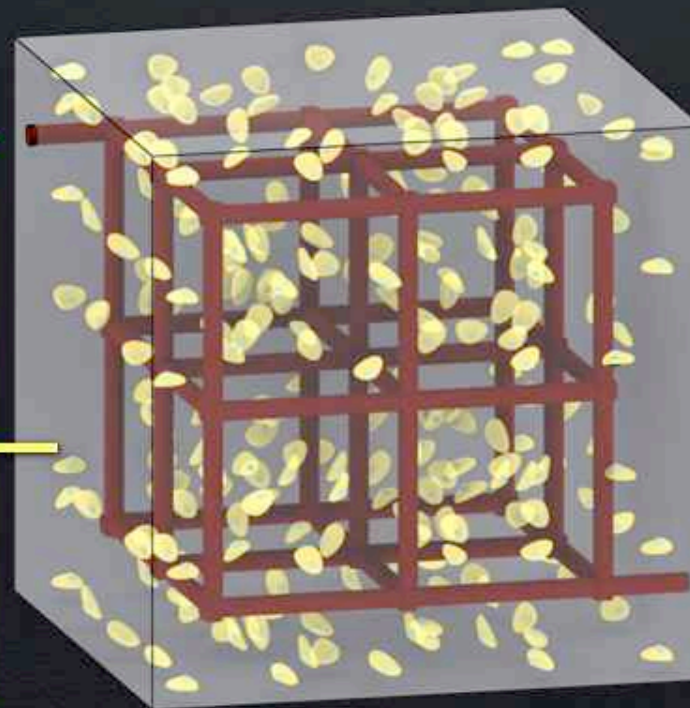
Encapsulate Network
and Living Cells

Dissolve Network

Place in
Media

Flow

Any Biogel
Fibrin
Collagen
Matrigel
Agarose
ECM Mimics



Rhymes with Stratasys



Me: "Hi, I'd like to buy one of your awesome machines, rip out the internals and replace it with my own modifications. Can you send me the schematics?"

Company: ".....uh..."



Science ♥'s Open Hardware

Open source is why Science works.

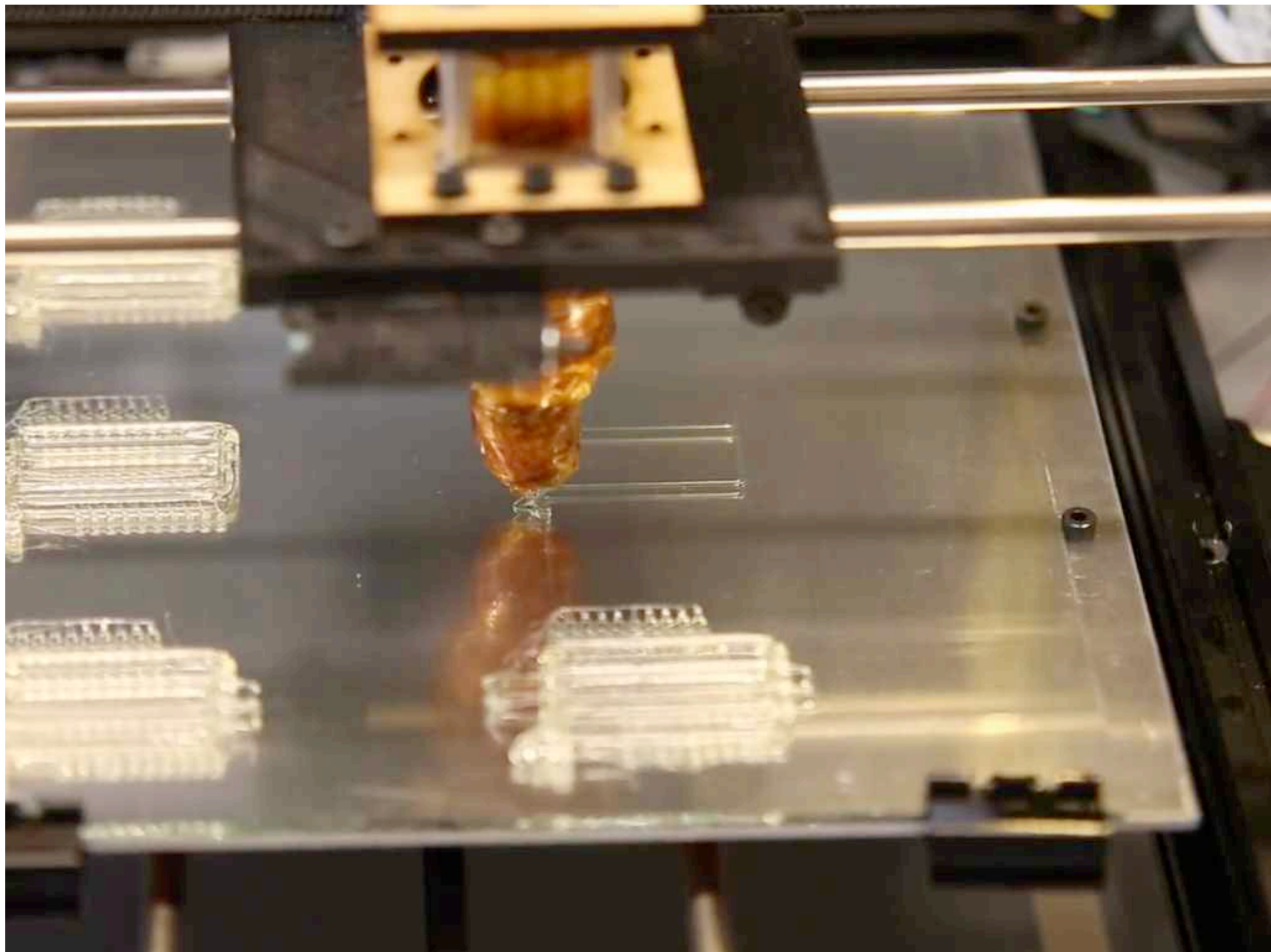
Open source gives you zero overhead to find collaborators everywhere in the world.

Open source defines the standards on which the future is built.

Closed source robs the future of ingenuity.

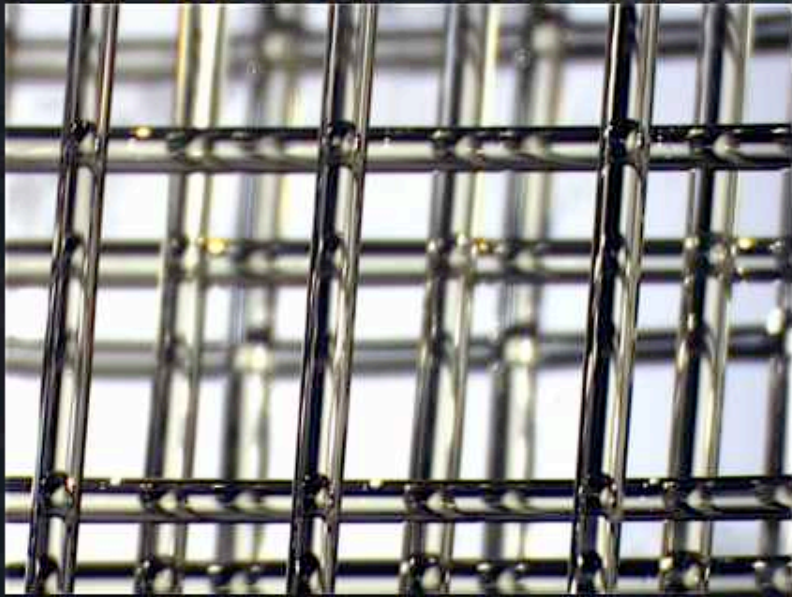
Closed source prevents the radical remixing and experimenting that are the hallmark of major advances.

Closed source makes you easy to forget.

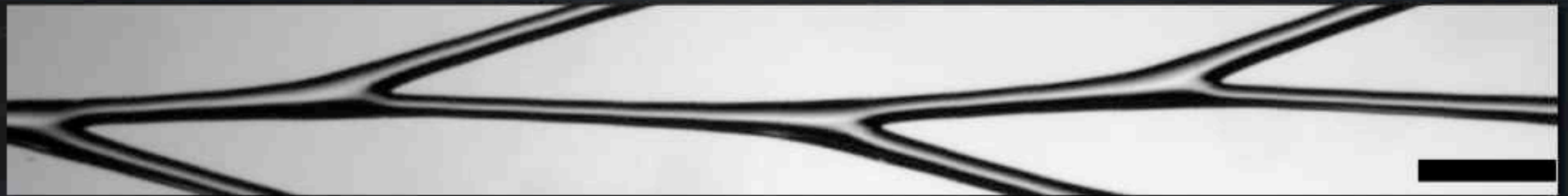


Reproducible Printing of Glass Lattice Architectures

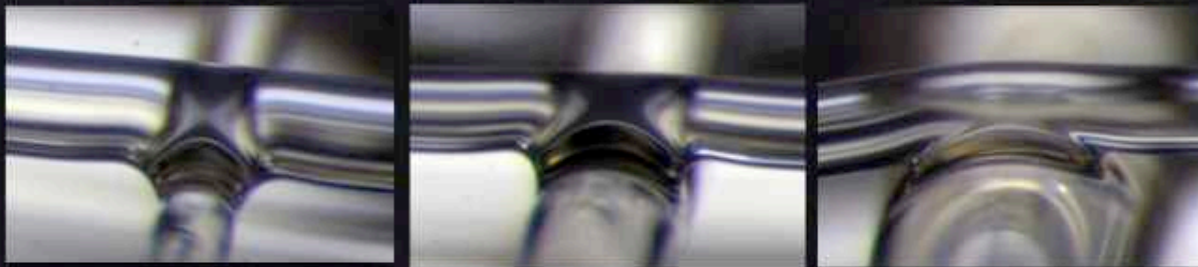
Multilayer



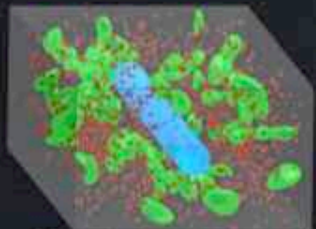
Multiscale



Smooth Interfilament Fusions



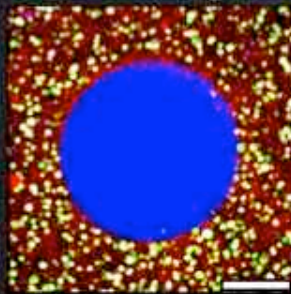
Casting Channels Yields Perfusable Cellularized Tissue Constructs in any ECM



Matrix (red beads)
Cells (EGFP)
Lumen (blue beads)

Agarose

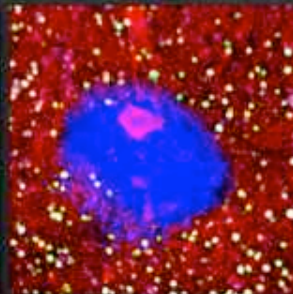
chain entangled



cross-section

Alginate

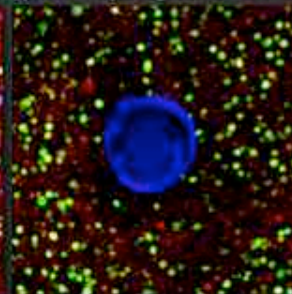
ionic



cross-section

PEG

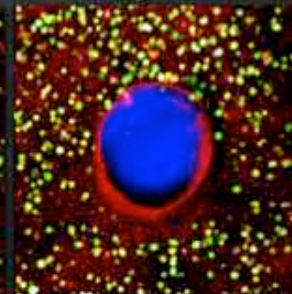
photopolymerized



cross-section

Fibrin

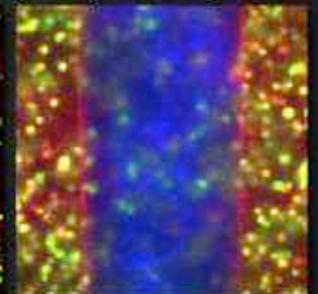
enzymatic



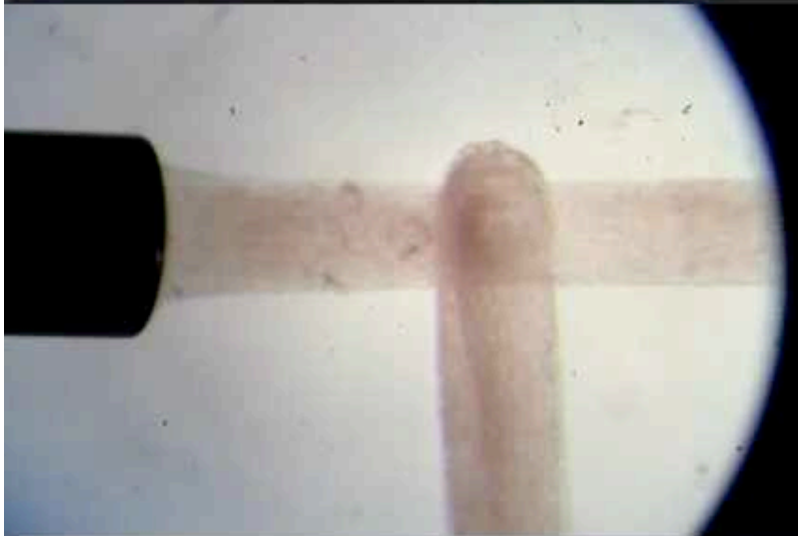
cross-section

Matrigel

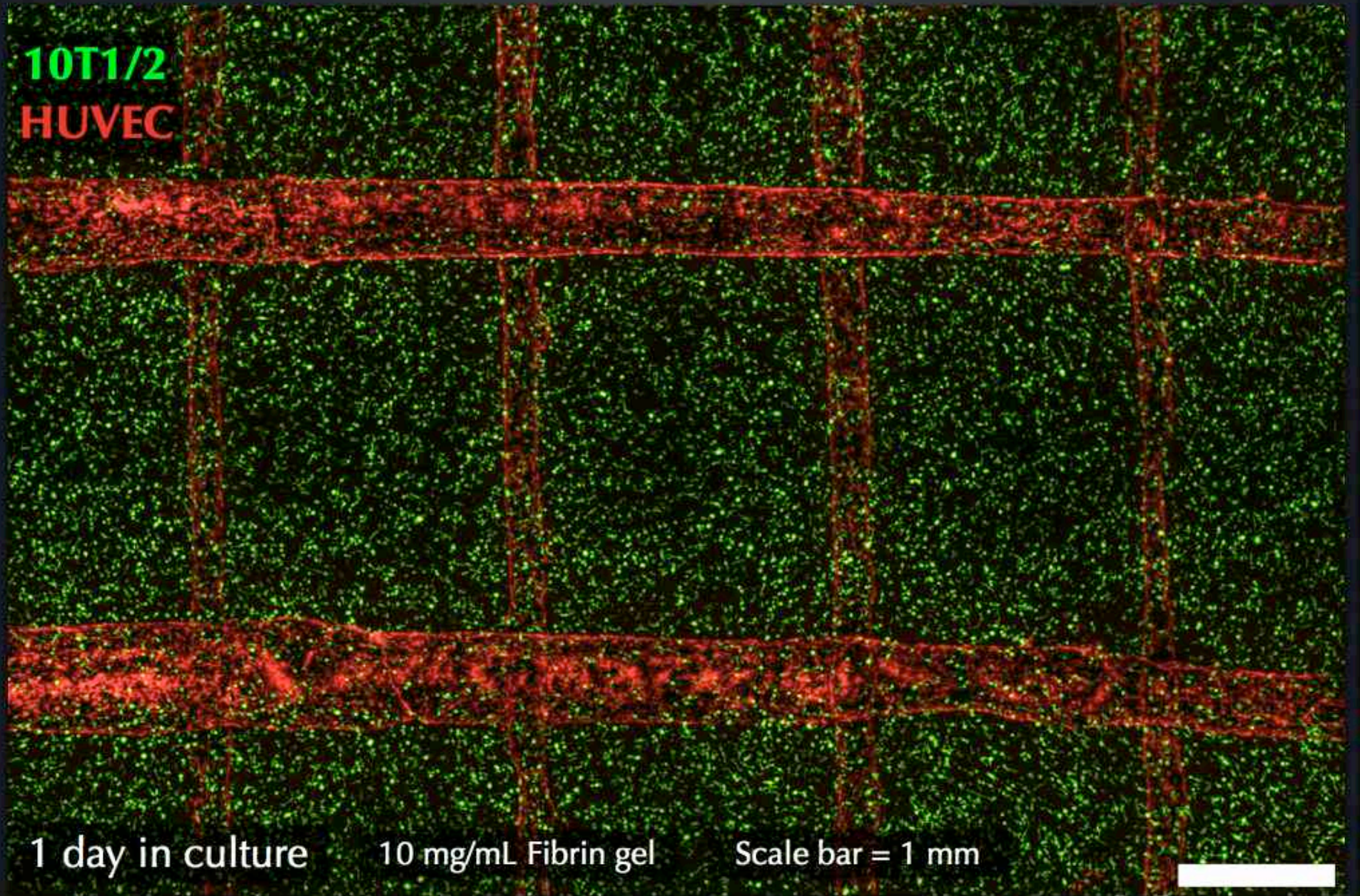
precipitated protein



top-view



Endothelialization of the Vasculature

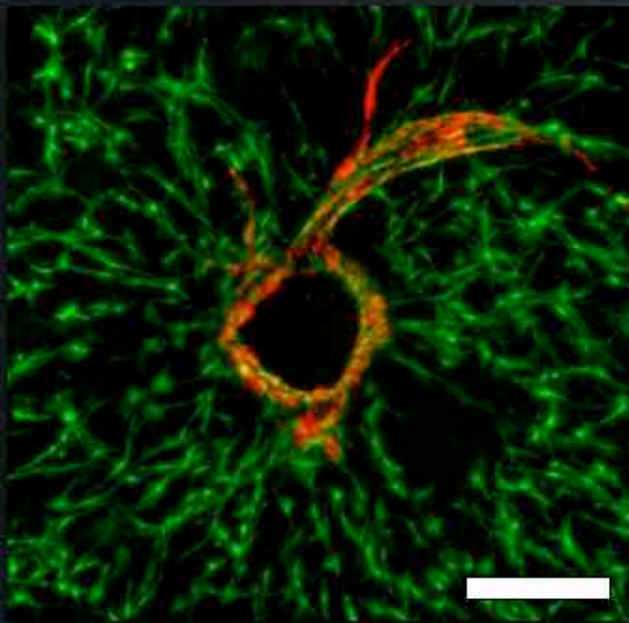


Endothelial Cells Sprout from Patterned Channels

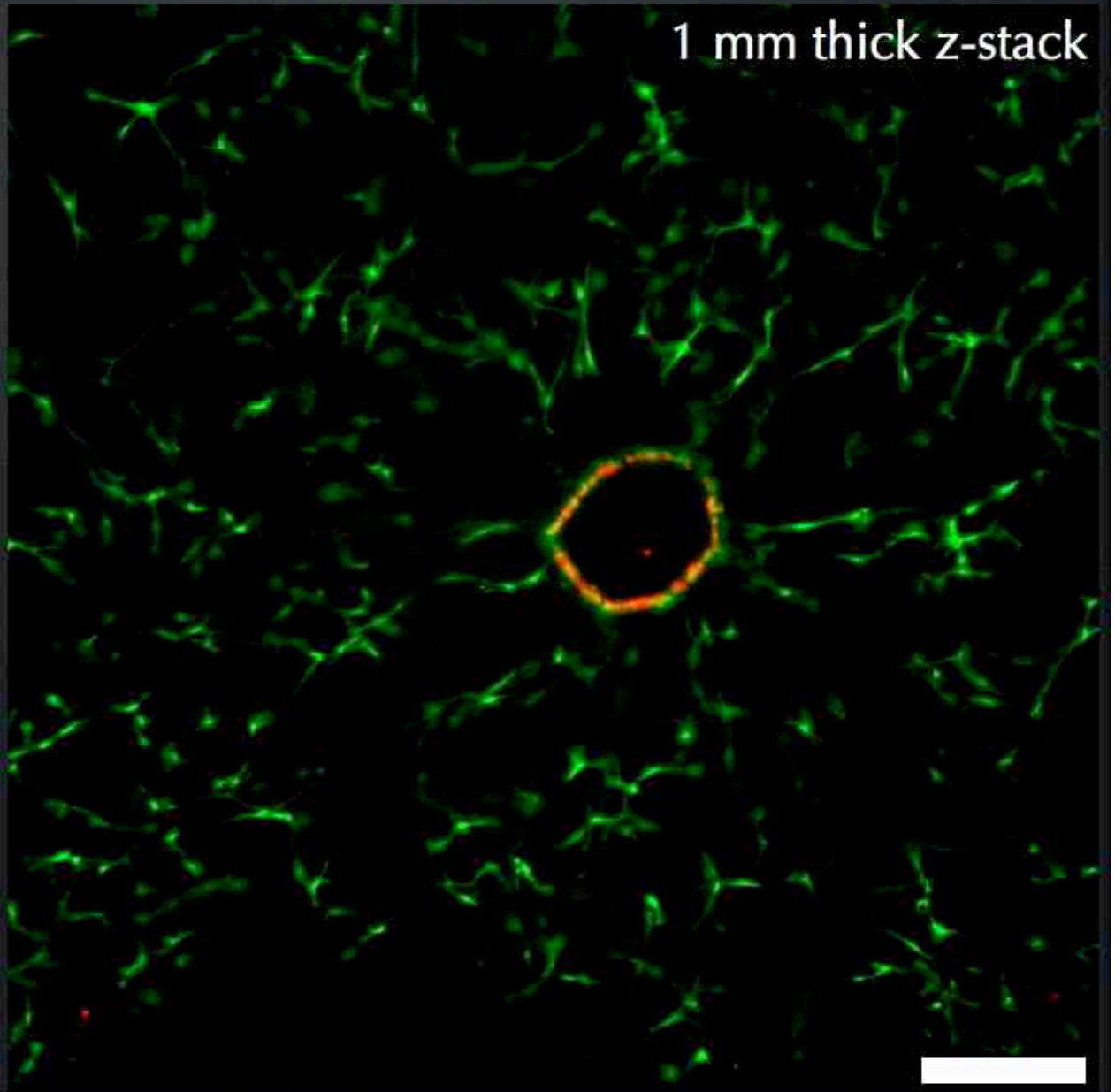
10T1/2

HUVEC

Partial z-stack



1 mm thick z-stack



9 days in culture
***with Serum and GFs**

10 mg/mL Fibrin gel
Scale bar = 200 μ m

Rapid casting of patterned vascular networks for perfusable engineered three-dimensional tissues

Jordan S. Miller¹, Kelly R. Stevens², Michael T. Yang¹, Brendon M. Baker¹, Duc-Huy T. Nguyen¹, Daniel M. Cohen¹, Esteban Toro¹, Alice A. Chen², Peter A. Galie¹, Xiang Yu¹, Ritika Chaturvedi¹, Sangeeta N. Bhatia^{2,3,4} and Christopher S. Chen^{1*}

Acknowledgements

We thank the large number of open source and related projects that critically facilitated this work, including Arduino.cc, RepRap.org, MakerBot.com, Replicat.org, MakerGear.com, Ultimachine.com, Hive76.org, Python.org, Hugin.SourceForge.net, ImageMagick.org, Blender.org, Enblend.sourceforge.net, NIH ImageJ, and Fiji.sc. We thank R. J. Vlacich and C. D. Thompson for assistance with precision pneumatic extrusion, A. Dominguez for assistance with red blood cell isolation, and Y-J. Chen for assistance with transduction. This work was supported in part by grants from the US National Institutes of Health (EB00262, EB08396, GM74048), the Penn Center for Engineering Cells and Regeneration, and the American Heart Association-Jon Holden DeHaan Foundation. Individual fellowship support was provided by R. L. Kirschstein National Research Service Awards from NIH (J.S.M., HL099031; K.R.S., DK091007), the National Science Foundation IGERT program (M.T.Y., DGE-0221664), and the American Heart Association (X.Y., 10POST4220014).

Science ♥'s Open Hardware

Open source is why Science works.

Open source gives you zero overhead to find collaborators everywhere in the world.

Science needs open technology platforms, not appliances.

Appliances rob the future of ingenuity.

Closed source prevents the radical remixing and experimenting that are the hallmark of major advances.

Closed source makes you easy to forget.

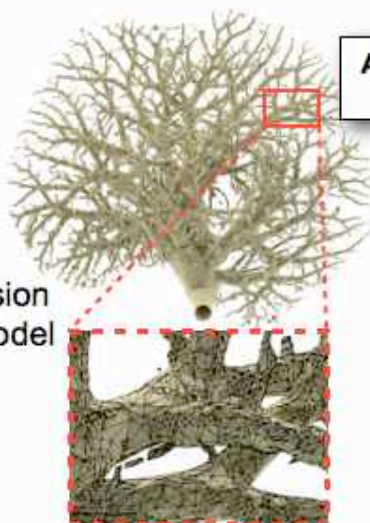
a Naturally Derived Vascular Architectures

Organ/Tissue of Interest



μCT Angiography
and Volumetric Extraction

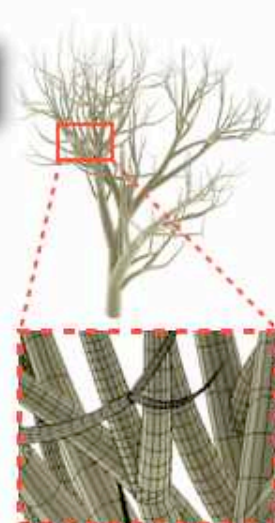
Conversion
to 3D Model



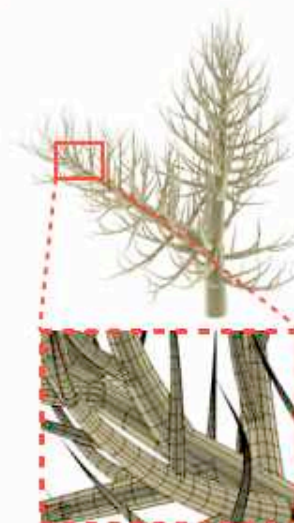
3D Surface Map

Architectural
Analysis

b Synthetic, Computer Generated and Parametrized Vascular Architectures

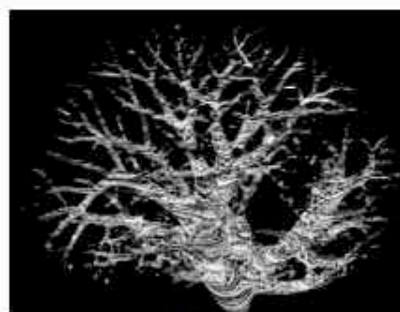


3D Surface Map



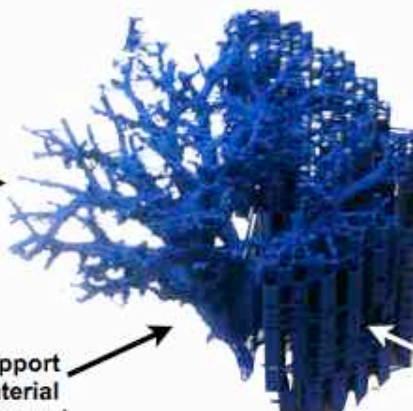
3D Surface Map

c 3D Printed Natural or Synthetic Architectures for Vascular Casting



Virtual Slicing
and Digital Cleanup

3D Print the
Sacrificial
Architecture

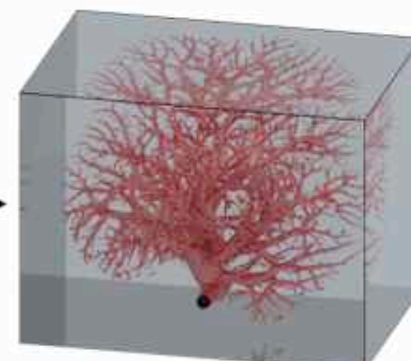


Support
Material
Removed

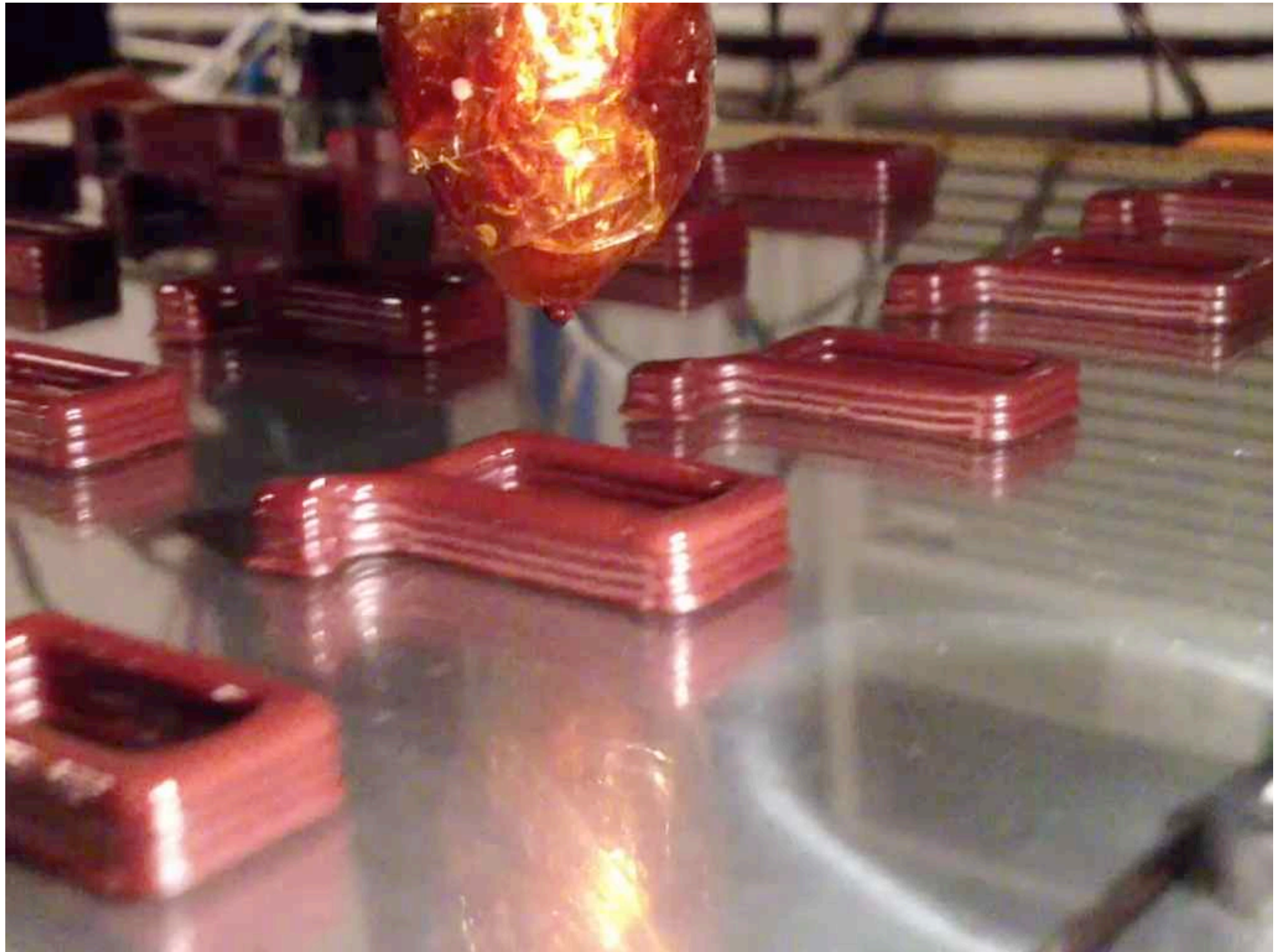
Physical
Cleanup

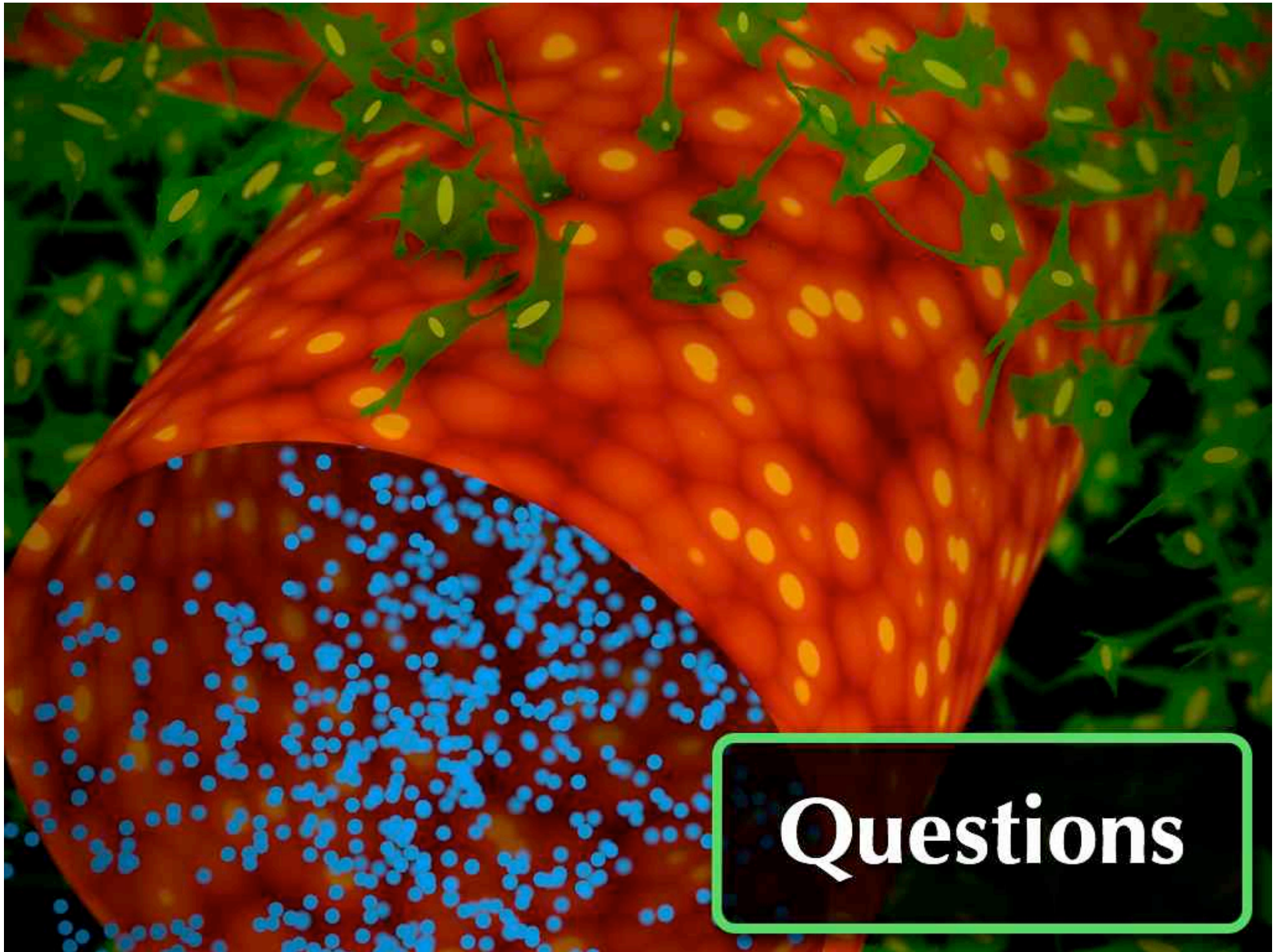
Temporary
Support
Material

Vascular
Casting
in Hydrogel



Patterned Vascular
Architecture in Hydrogel





Questions