3D Printing Strategies for Hard Tissues

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Rice University

3rd Annual 3D Printing & Biofabrication Workshop: Virtual Event

November 13, 2020

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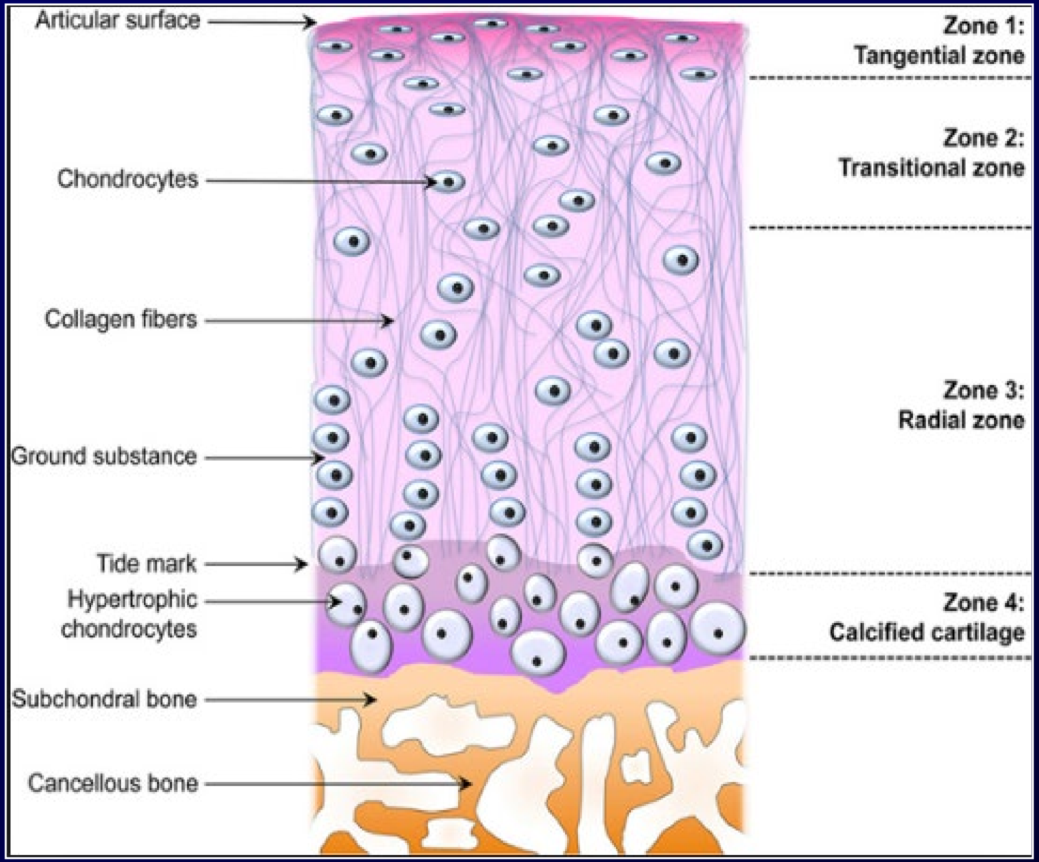
Cartilage and Bone Tissues



Complex structural, mechanical, and biological properties of bone and cartilage tissues require unique combinations and gradients of materials

Mosher TJ. Clin Sports Med. 2006 Oct 1;25(4):843–66. Harris J, et al. Arthrosc J Arthrosc Relat Surg. 2010;26(6):841–52.

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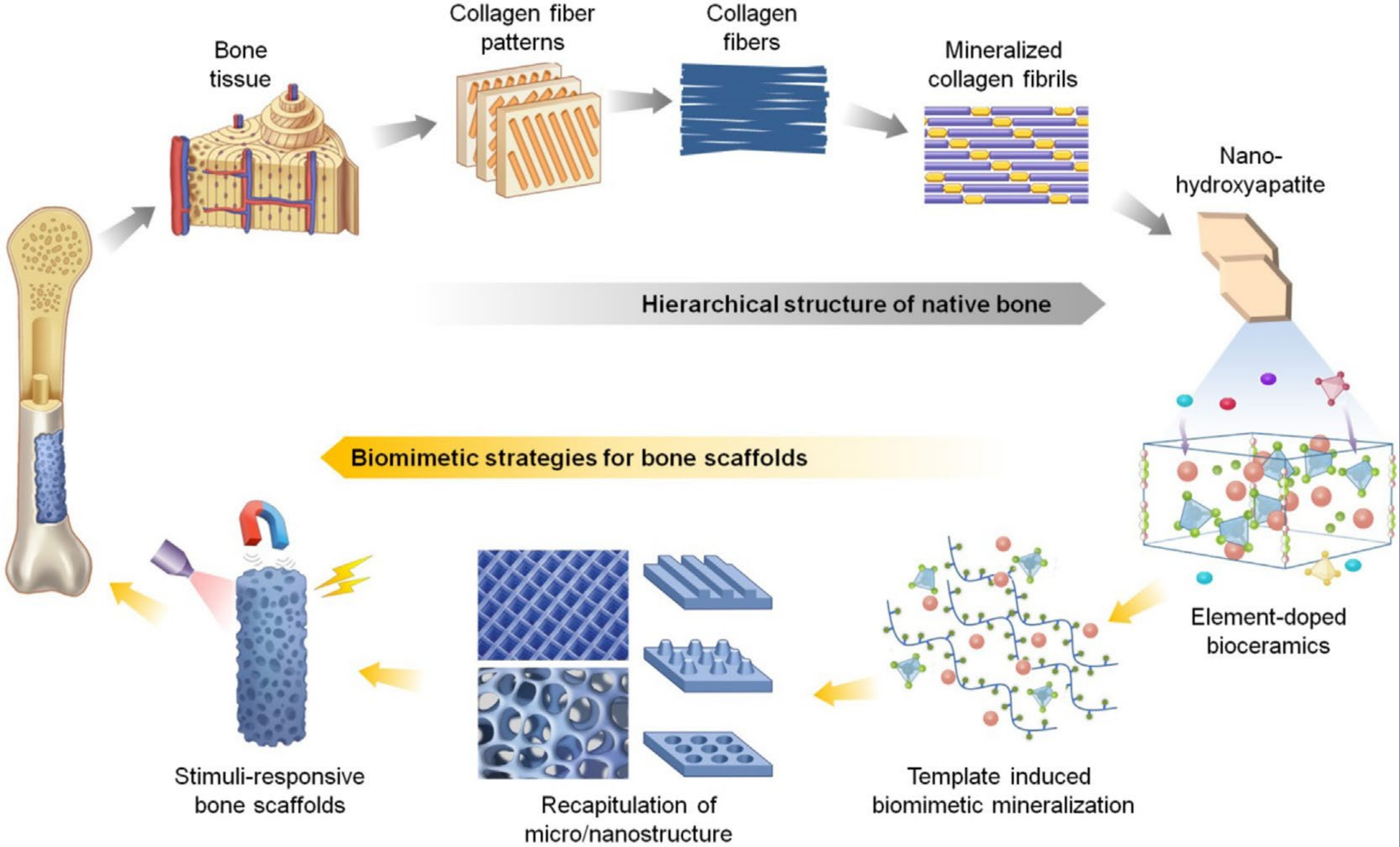
Biomimetic Scaffolds



Recent biomaterials advances enabled production of hierarchically designed tissue engineering scaffolds.

Du et al., Biomaterials, 2019

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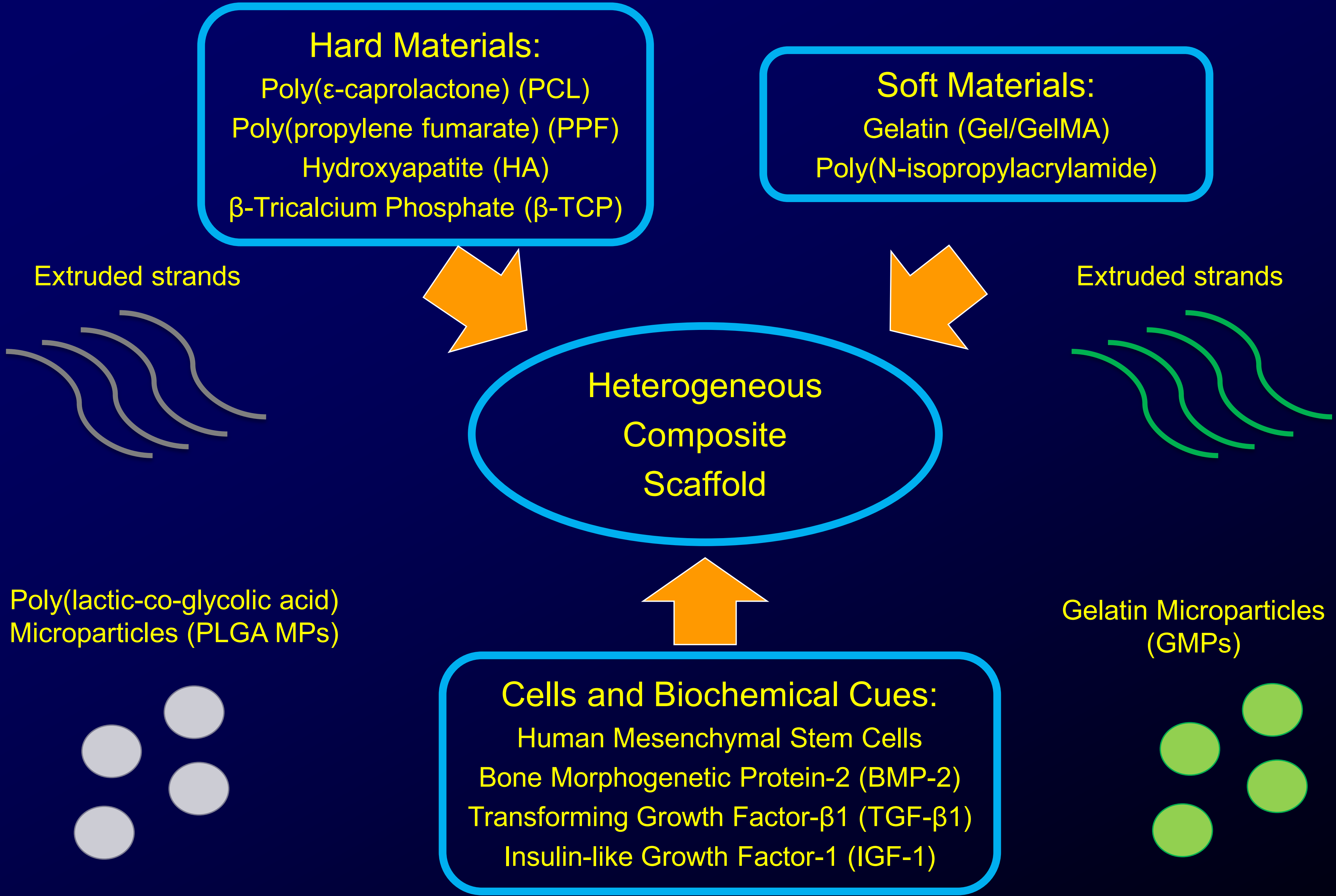
Hard Materials:
Poly(ε-caprolactone) (PCL)
Poly(propylene fumarate) (PPF)
Hydroxyapatite (HA)
β-Tricalcium Phosphate (β-TCP)
Soft Materials:
Gelatin (Gel/GelMA)
Poly(N-isopropylacrylamide)
Extruded strands
Extruded strands
Heterogeneous
Composite
Scaffold
Poly(lactic-co-glycolic acid)
Microparticles (PLGA MPs)
Gelatin Microparticles
(GMPs)
Cells and Biochemical Cues:
Human Mesenchymal Stem Cells
Bone Morphogenetic Protein-2 (BMP-2)
Transforming Growth Factor-β1 (TGF-β1)
Insulin-like Growth Factor-1 (IGF-1)

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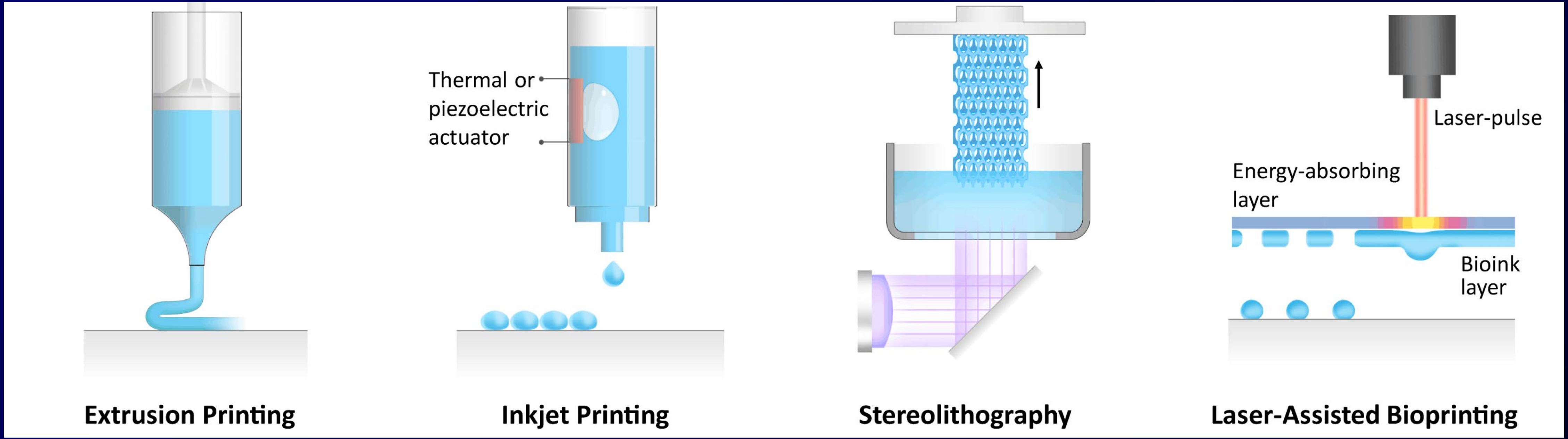
Bioprinting



Various 3D printing modalities available, each with different resolution, printing speeds, material compatibility, and other properties that affect bioink choices and scaffold fabrication.

Bedell, Navara, & Du et al., Chem. Rev., *2020*

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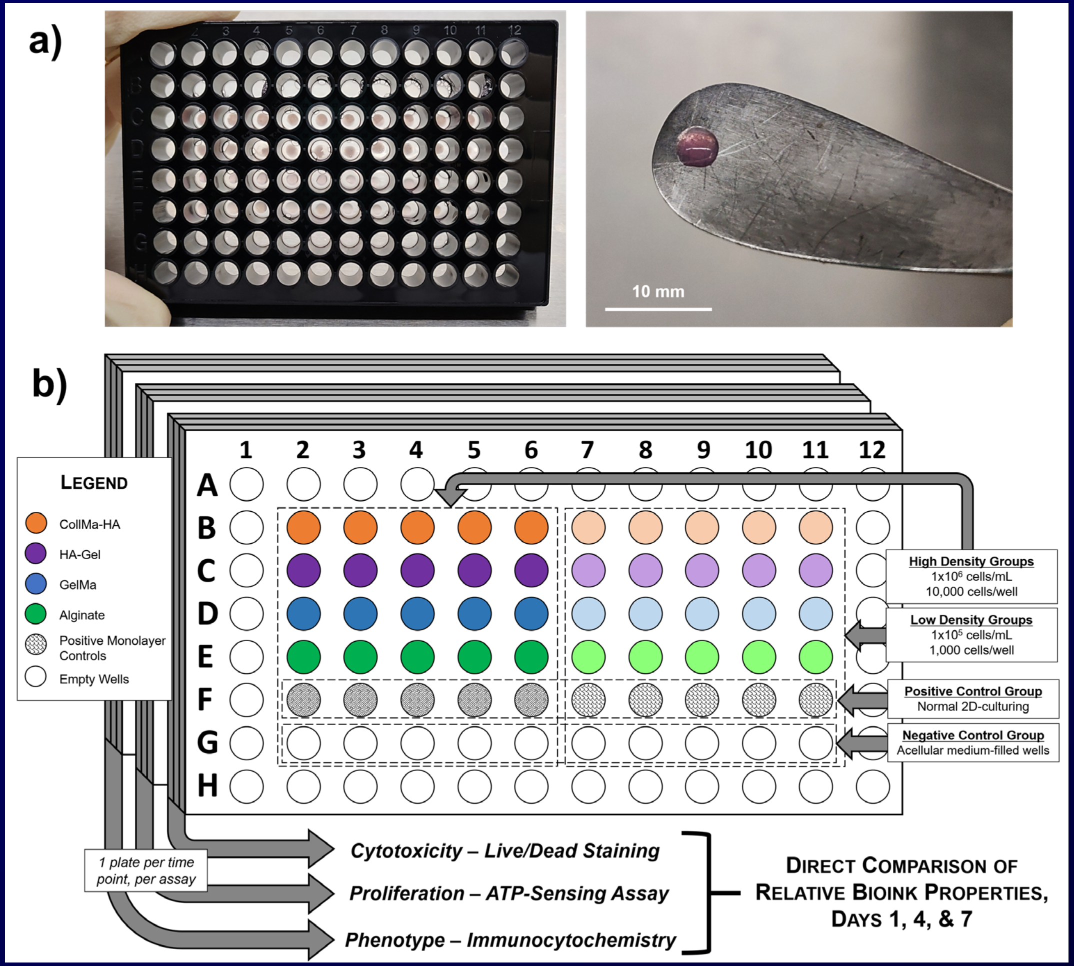
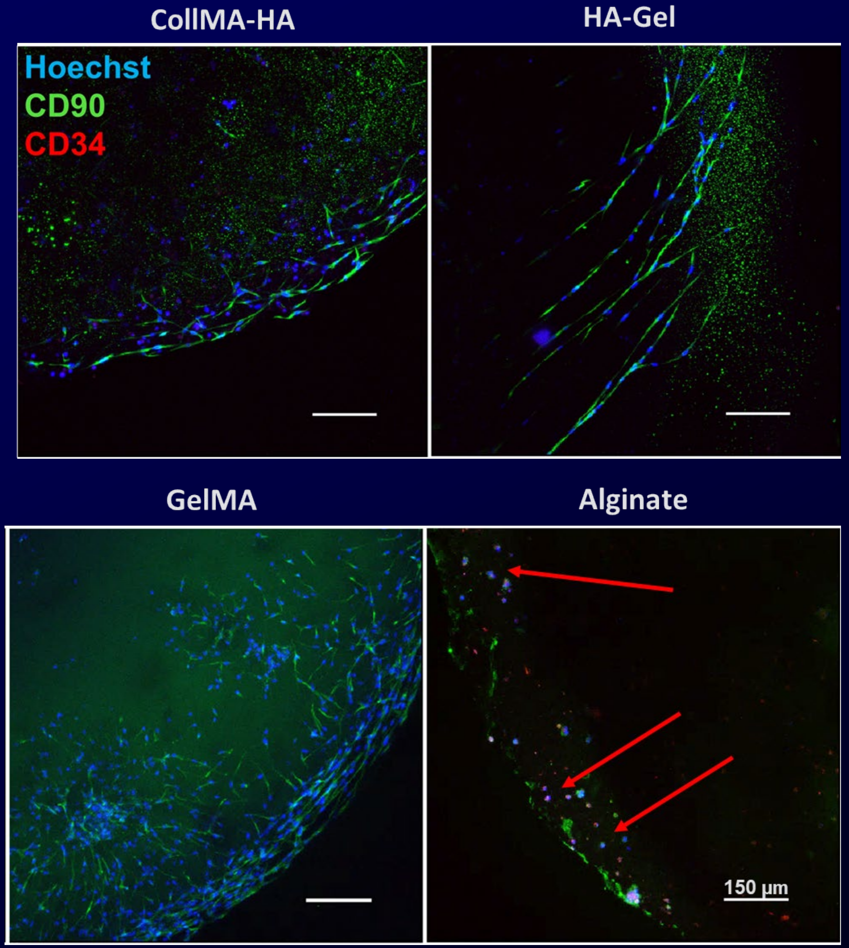
Cell-Laden Hydrogel Bioinks





A high-throughput method to quantify and compare the biocompatibility and phenotypical effects of bioink formulations for 3D bioprinting.

Bedell et al., Bioprinting, 2020

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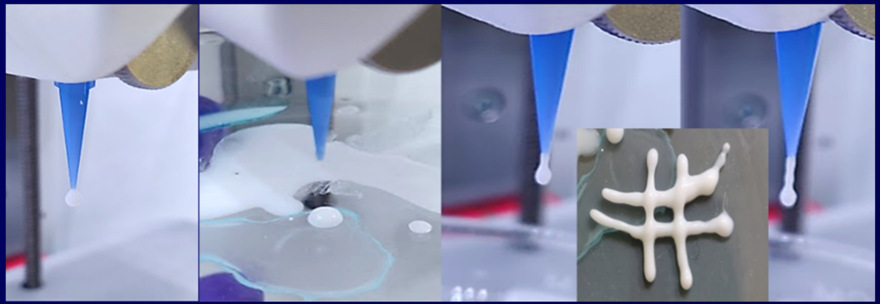
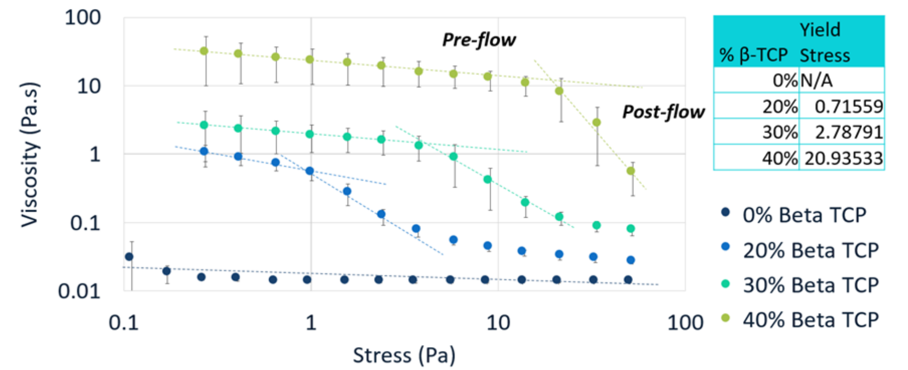
Printability Assessment

Filament Formation

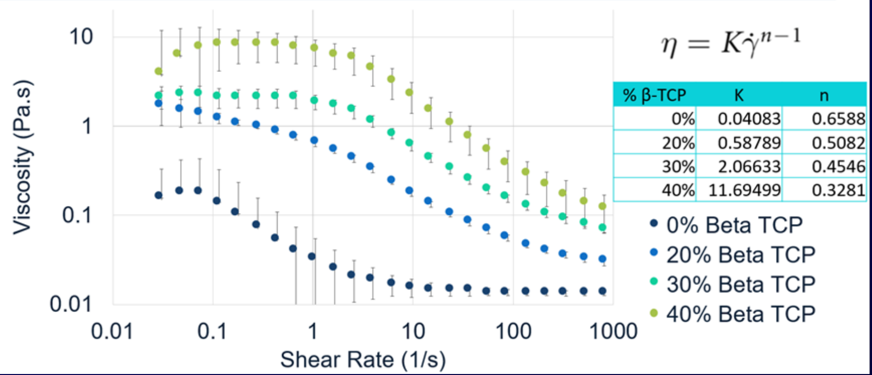


Flow Initiation



% β-TCP	Yield Stress
0%	N/A
20%	0.71559
30%	2.78791
40%	20.93533

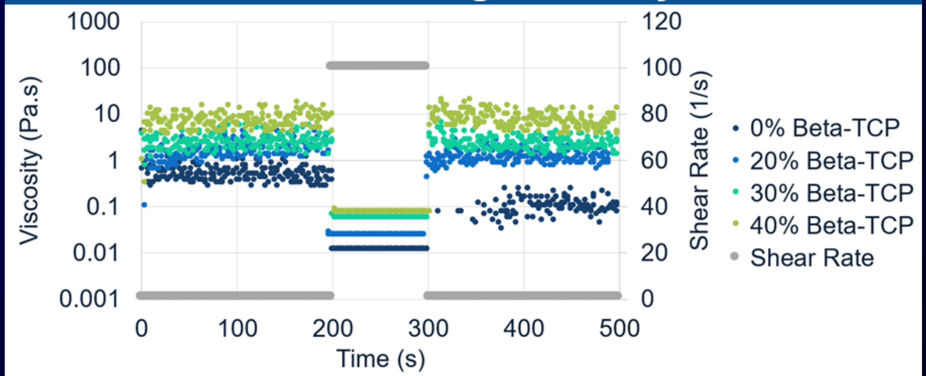
Shear Assessment



$$\eta = K\dot{\gamma}^{n-1}$$

% β-TCP	K	n
0%	0.04083	0.6588
20%	0.58789	0.5082
30%	2.06633	0.4546
40%	11.69499	0.3281

Post-Printing Recovery



Addition of ceramic nanopowder components can modulate shear-thinning, viscosity, and shear-recovery properties.

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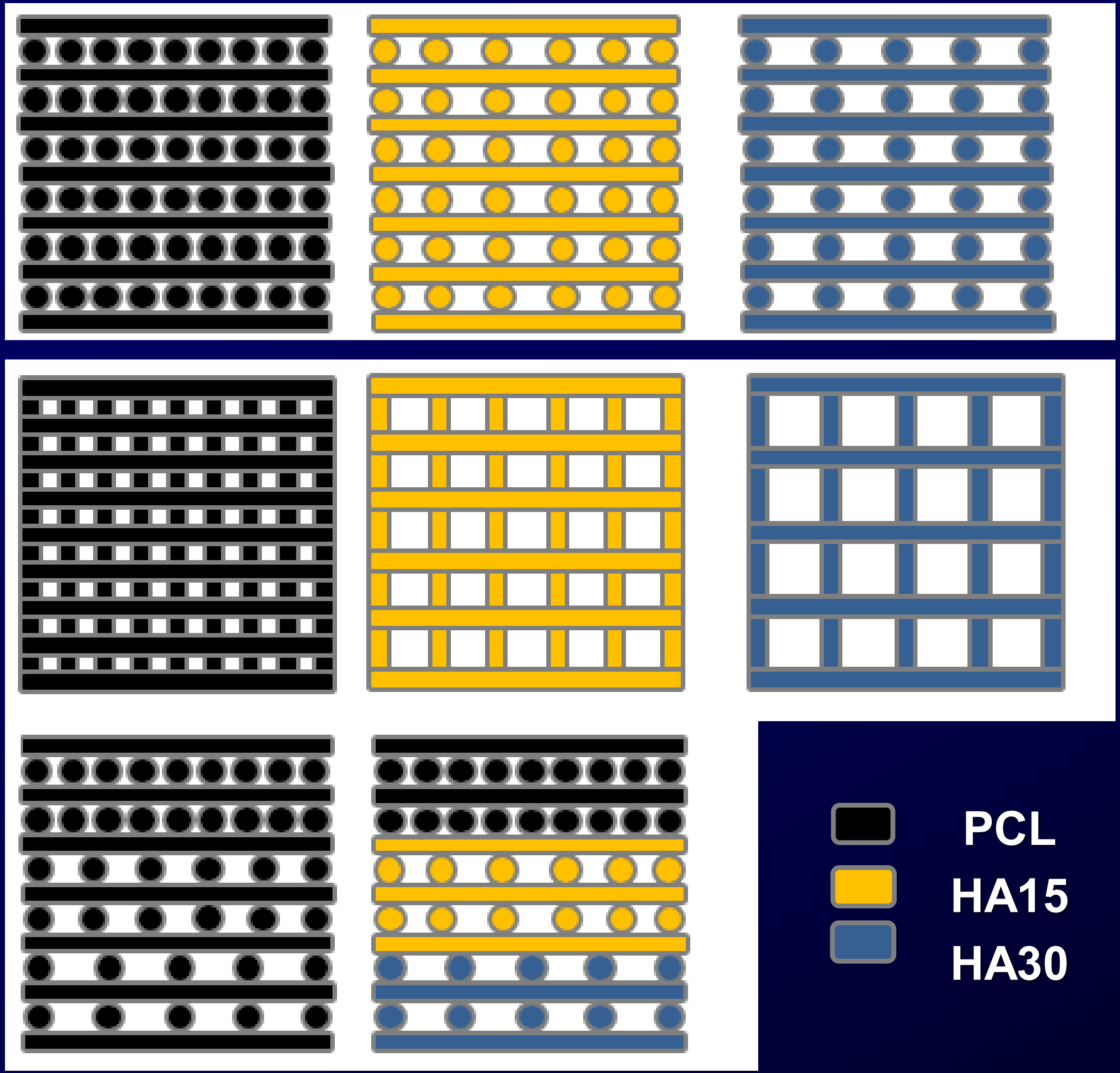
Scaffold Design Scheme



(L⟶R) 0.2 mm, 0.5 mm, 0.9 mm fiber spacing (top view)

(L⟶R) 0.2 mm, 0.5 mm, 0.9 mm fiber spacing (side view)

(L⟶R) Porosity gradient, dual gradient (side view)

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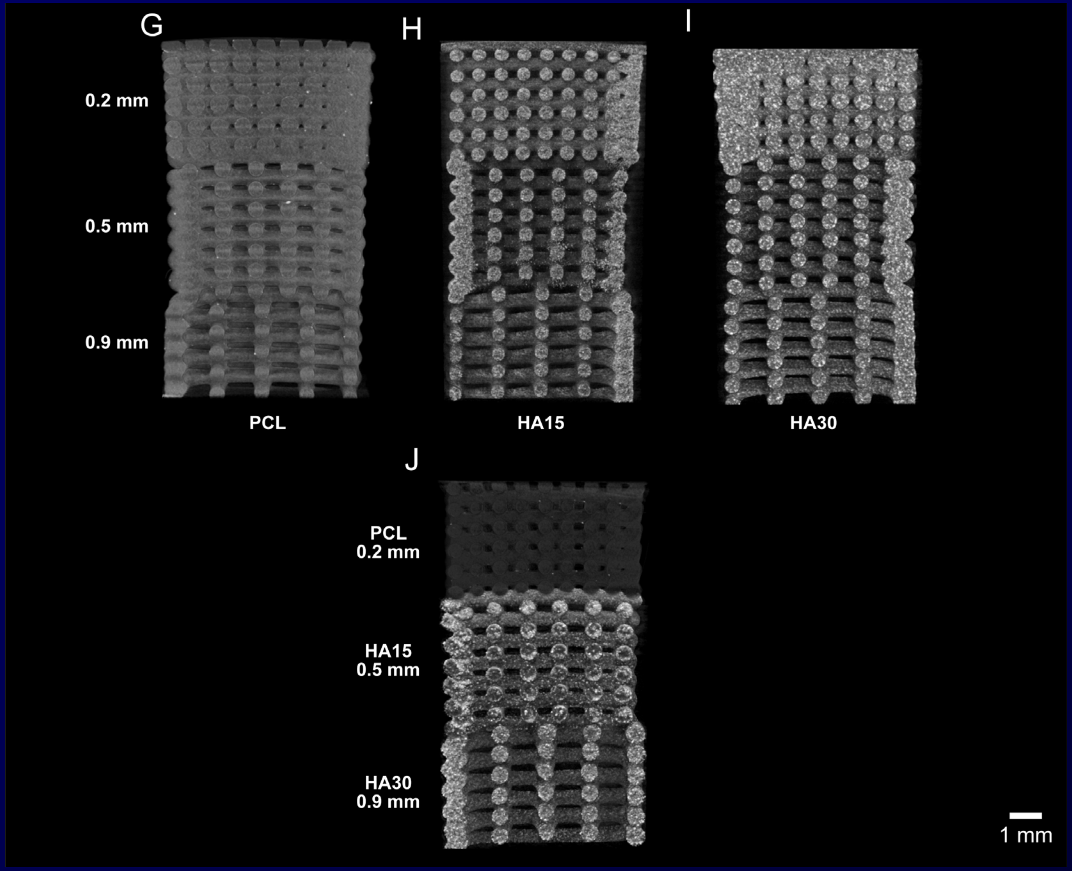
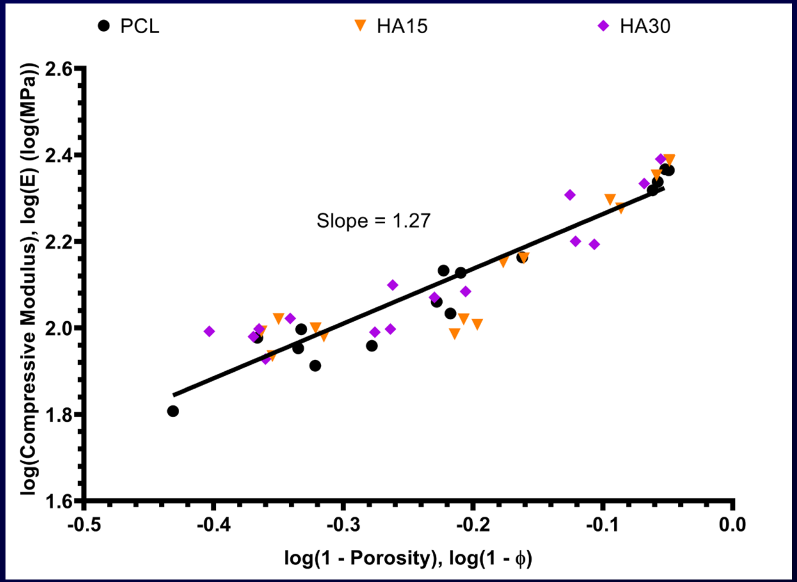
3DP Vertical Gradient Scaffolds





$$E \sim (1 - \phi)^{1.27}$$

Porosity and dual ceramic/porosity vertical gradients were readily incorporated within 3DP scaffolds.

Bittner et al., Acta Biomaterialia, 2019

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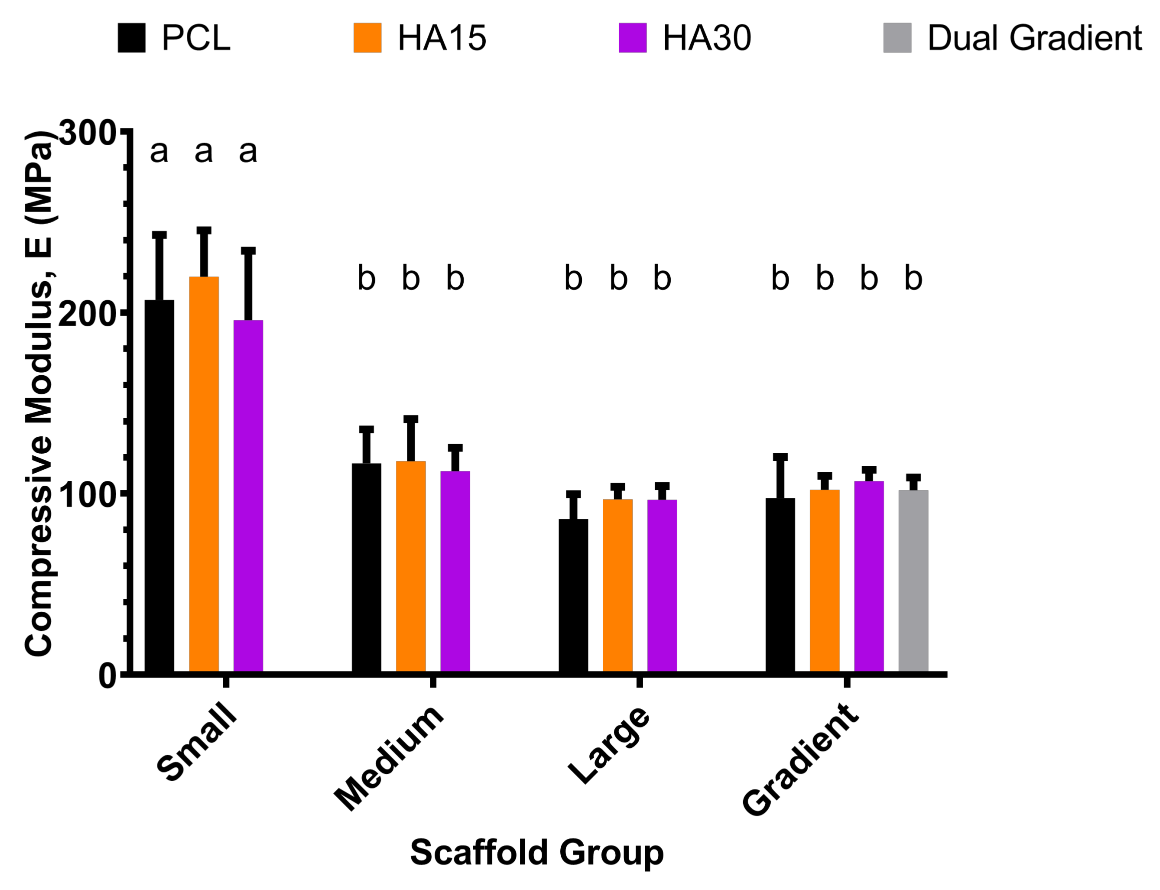
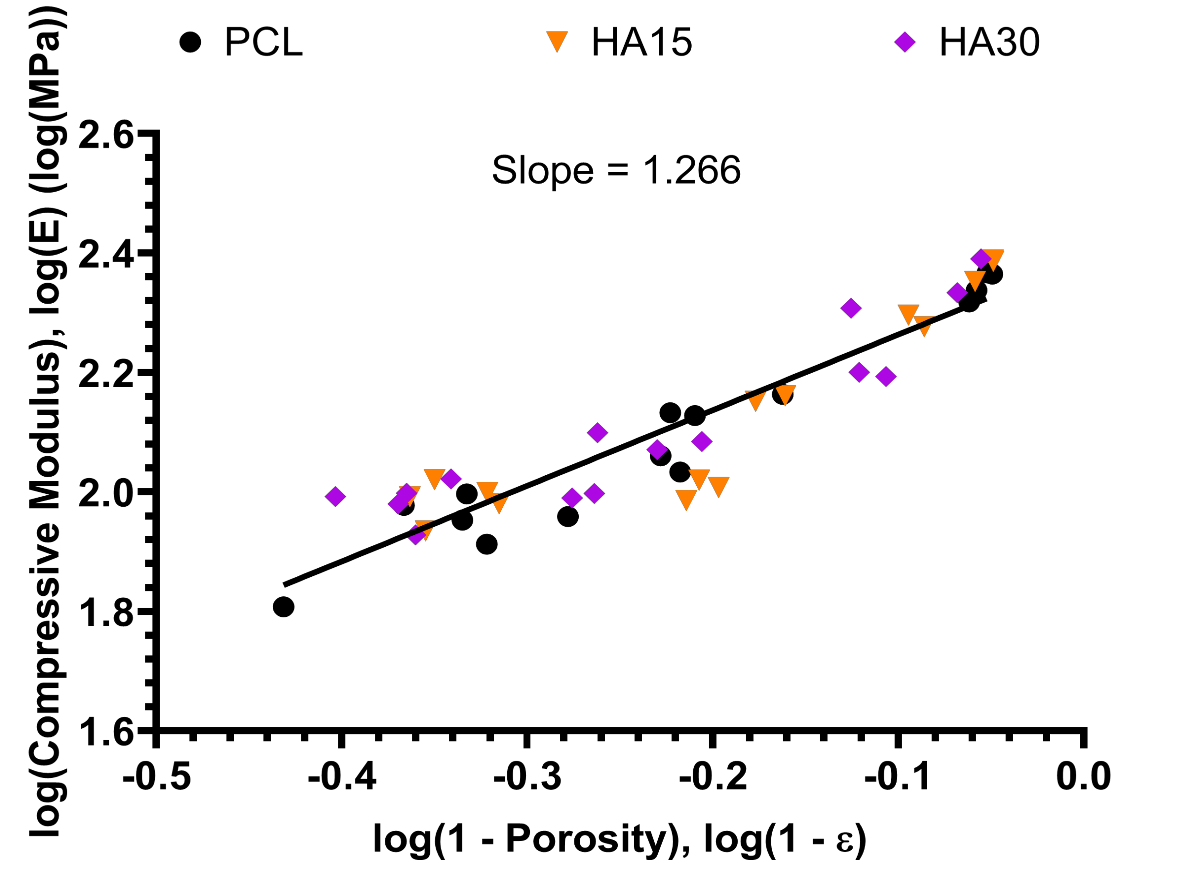
3DP Vertical Gradient Scaffolds





Compressive properties decreased with increasing porosity for uniform scaffolds

Bittner et al., Acta Biomaterialia, 2019

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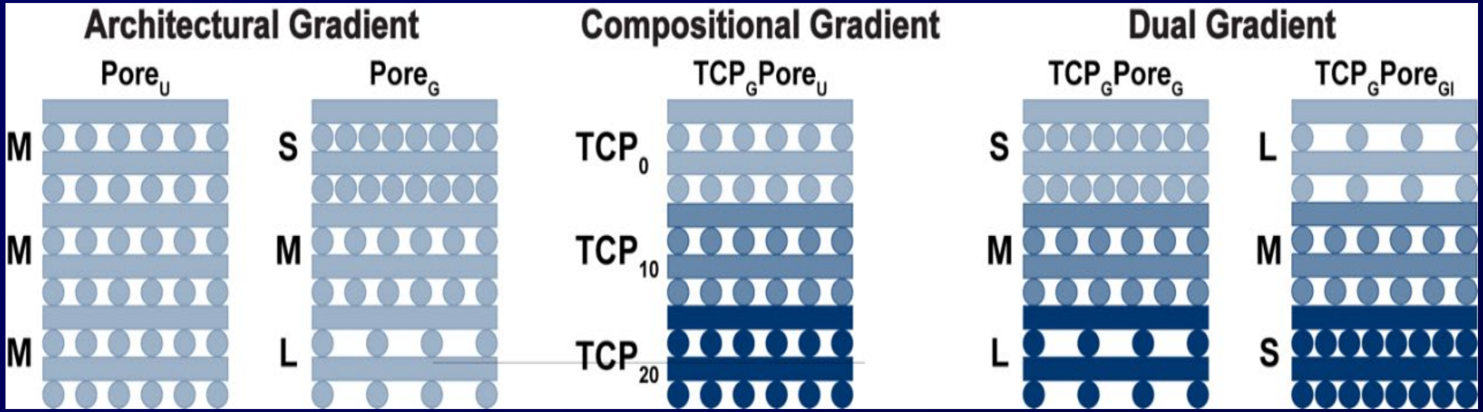
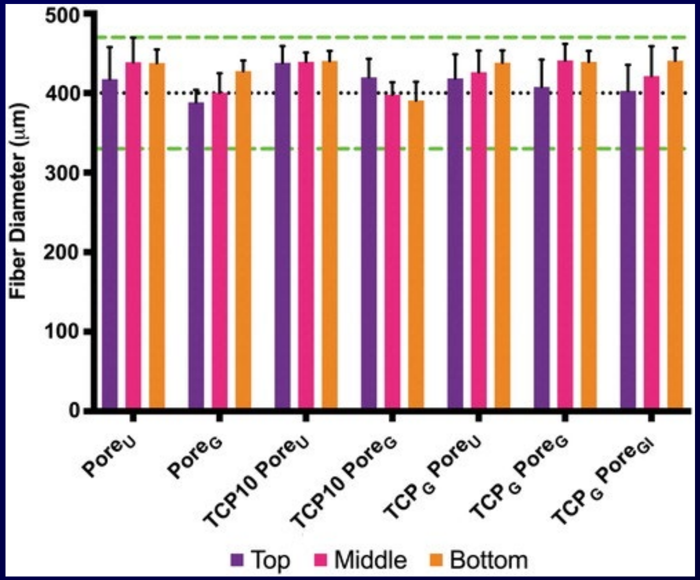
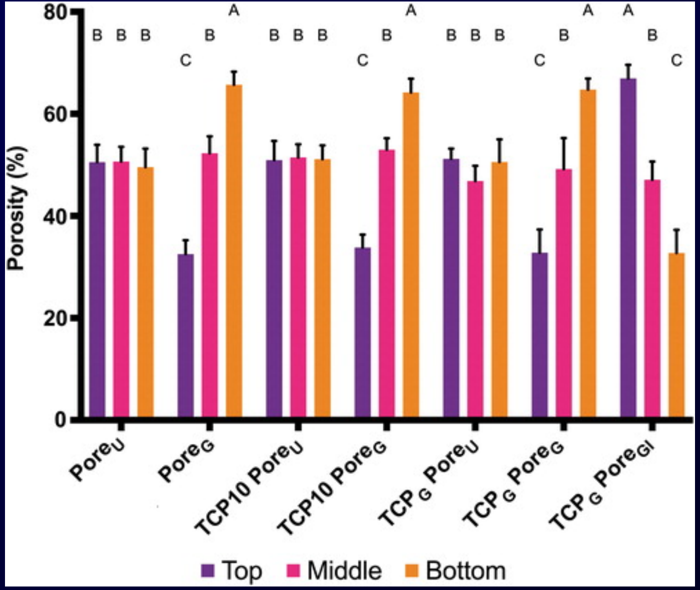
3D Gradient Cell Phenotypes







Scaffolds can be fabricated in a reproducible manner to create pore size and ceramic content gradients

Smith et al., Tissue Eng. Part A, 2020.

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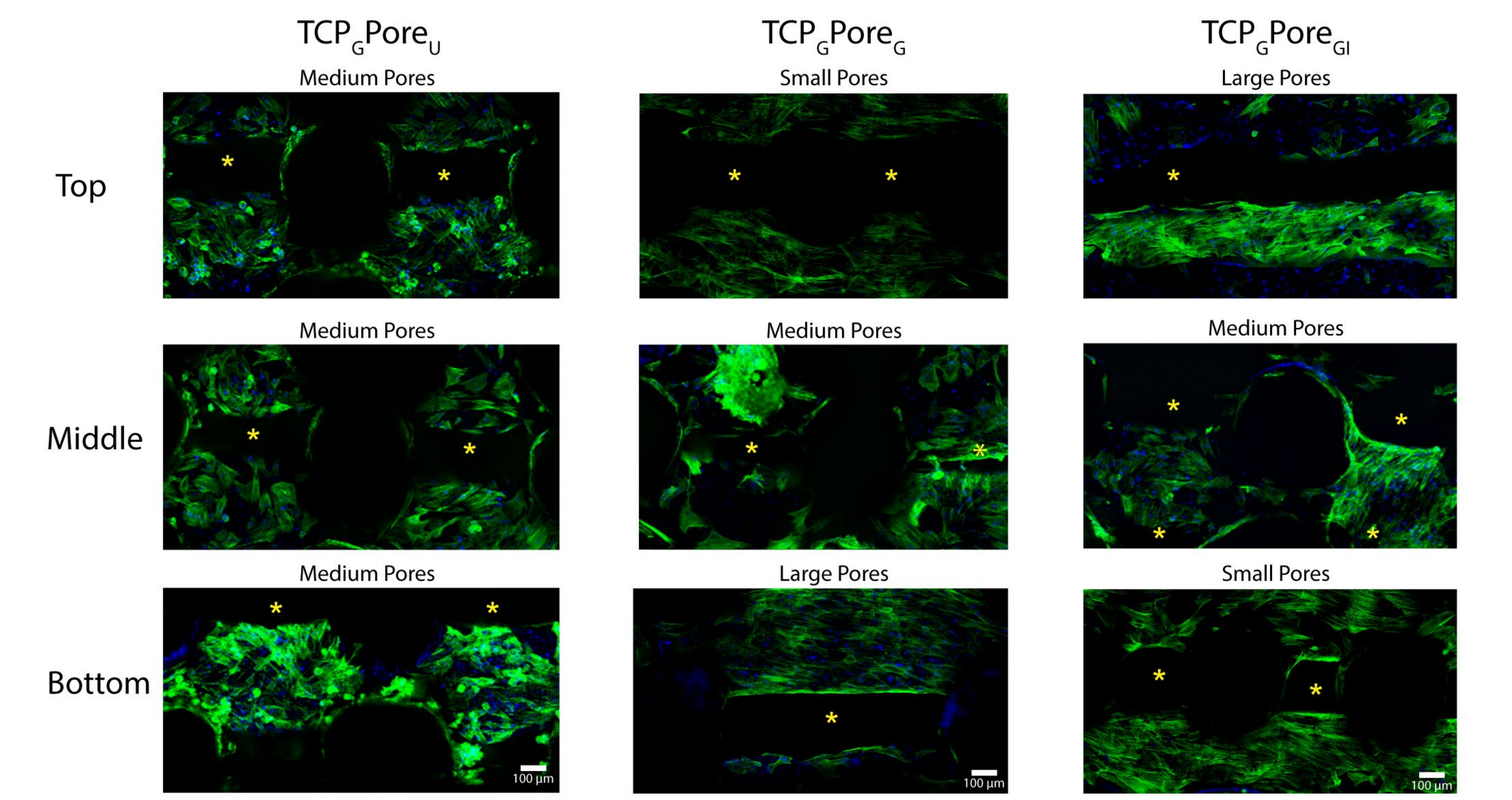
3D Gradient Cell Phenotypes



3D distribution of rabbit MSCs within 3DP vertical dual ceramic/porosity gradient scaffolds.

Smith et al., Tissue Eng. Part A, 2020.

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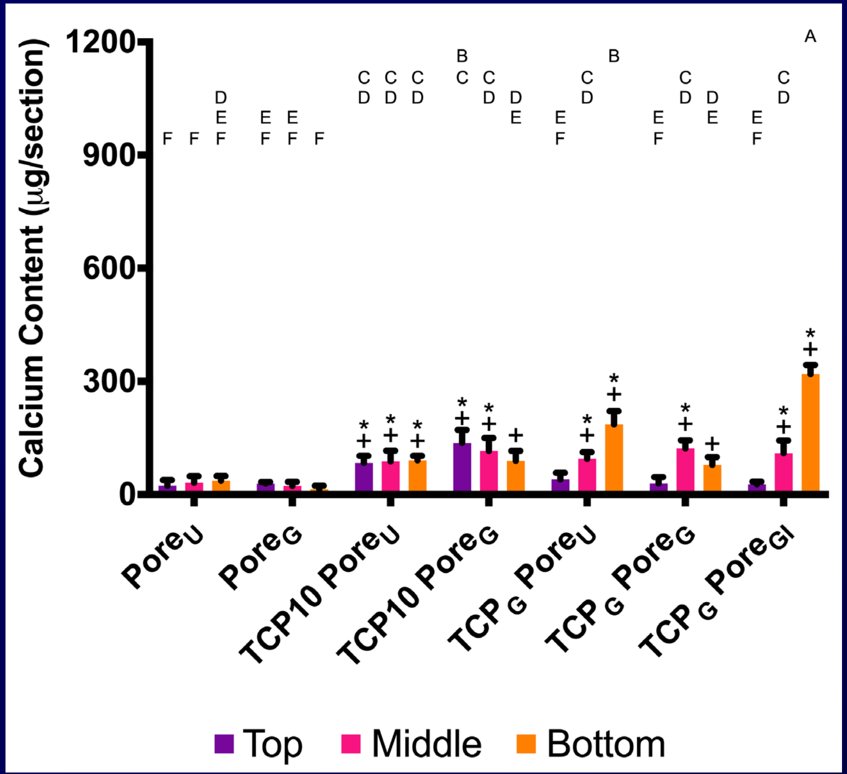
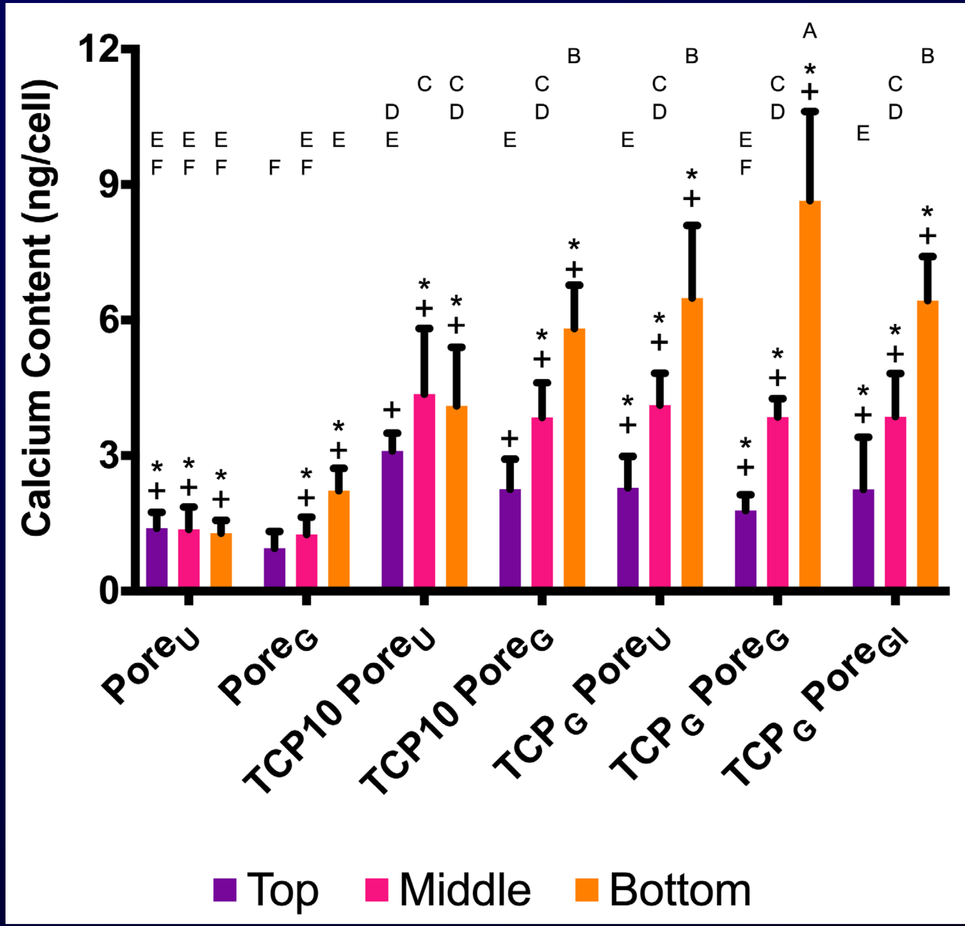
3D Gradient Cell Phenotypes



Acellular Constructs
Day 28

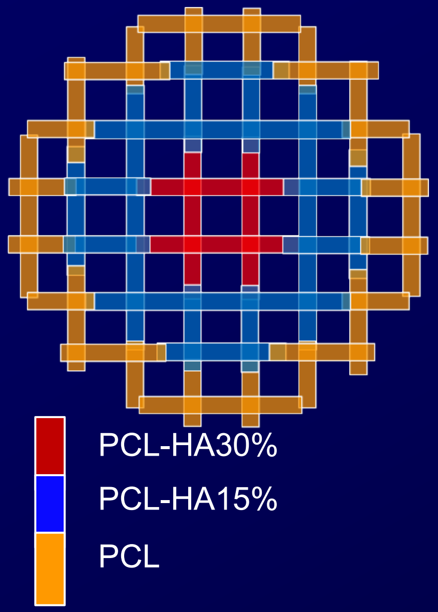


Directed osteogenic differentiation & spatial segregation with 3DP architectural and compositional gradients.

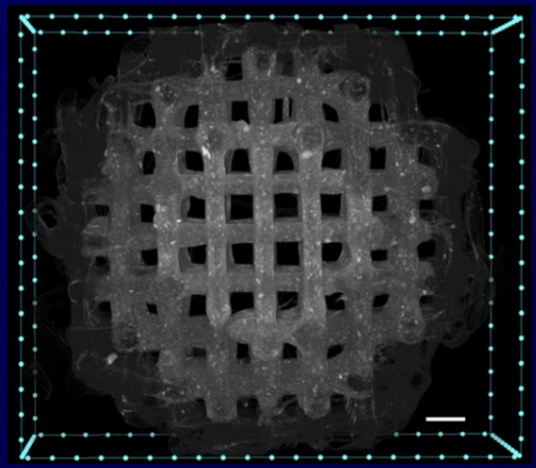
Smith et al., Tissue Eng. Part A, 2019

Complex Horizontal Gradients

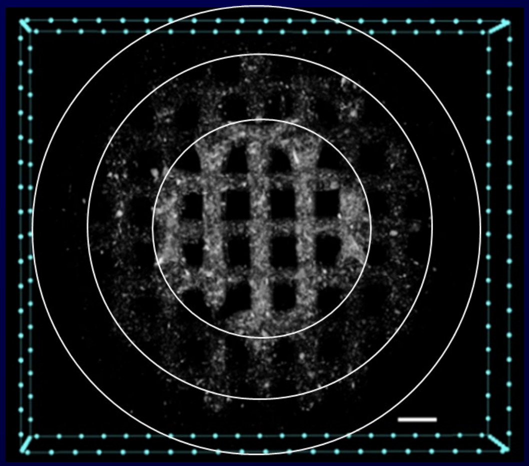
Printing pattern



Printed scaffold



HA distribution



Scale bar: 500 μm

Printing methodology allows the highly precise deposition of the different compositions within the same layer of the scaffolds

Diaz-Gomez et al., Tissue Eng. Part C: Methods, 2019

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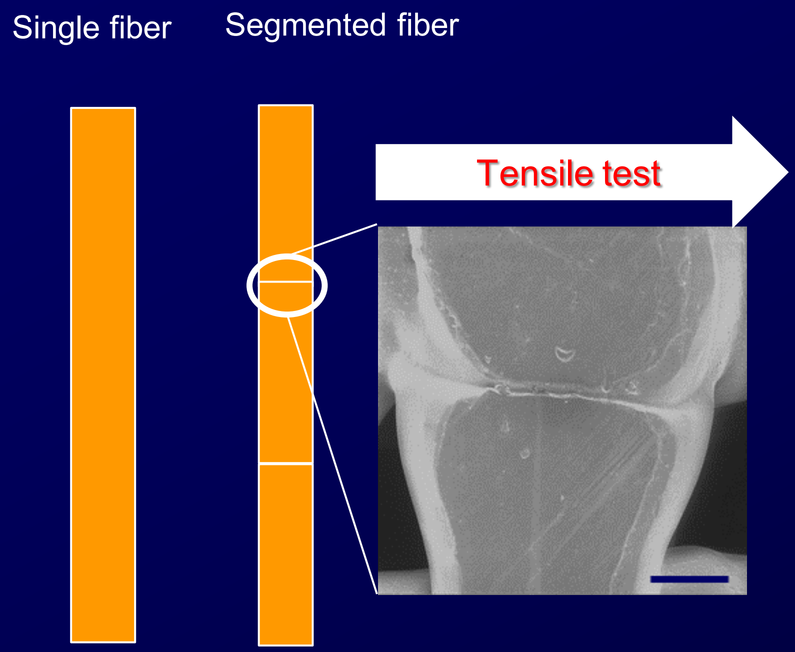
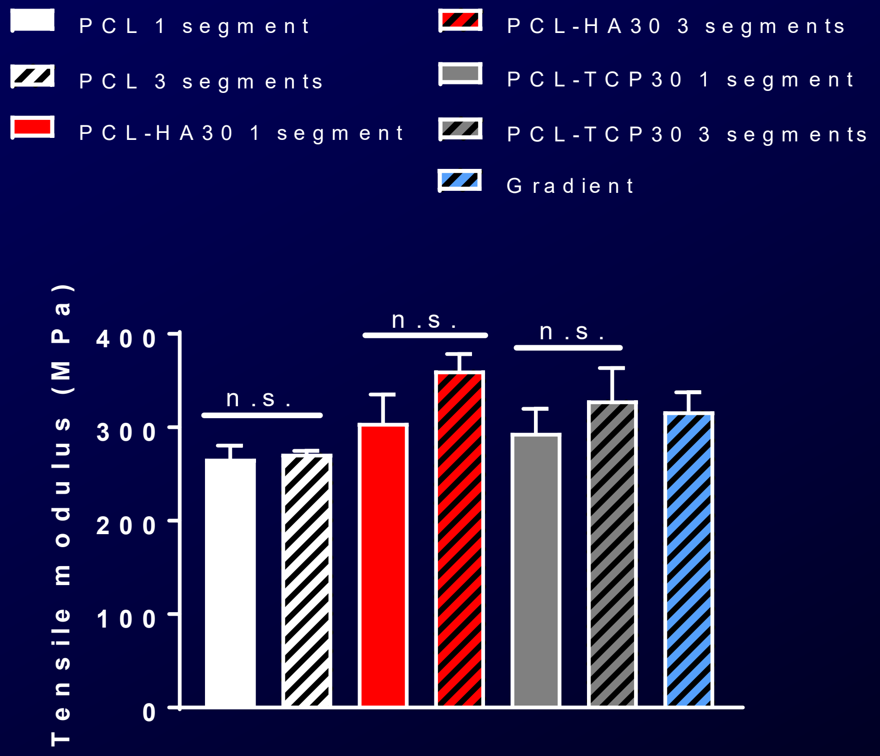
Tensile Properties of Segmented Fibers





The sequential segmented printing does not significantly compromise the mechanical properties of the fiber

Diaz-Gomez et al., Tissue Eng. Part C: Methods, 2019

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3DP Horizontal Gradient Scaffolds

Can’t play media

Multimaterial segmental fiber printing for dual ceramic/porosity horizontal gradients.

Diaz-Gomez et al., Tissue Eng. Part C: Methods, 2019

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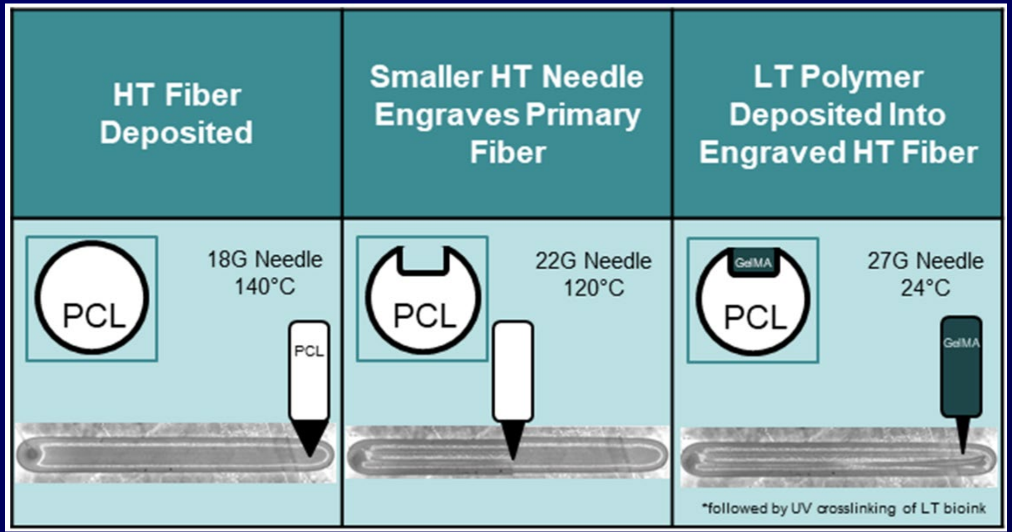
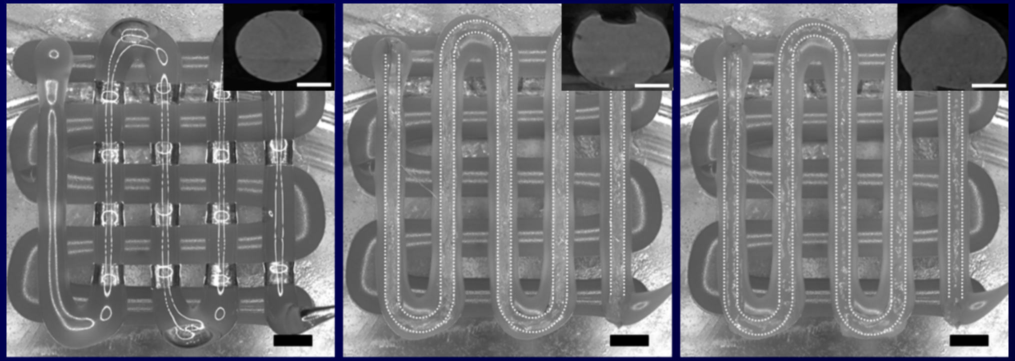
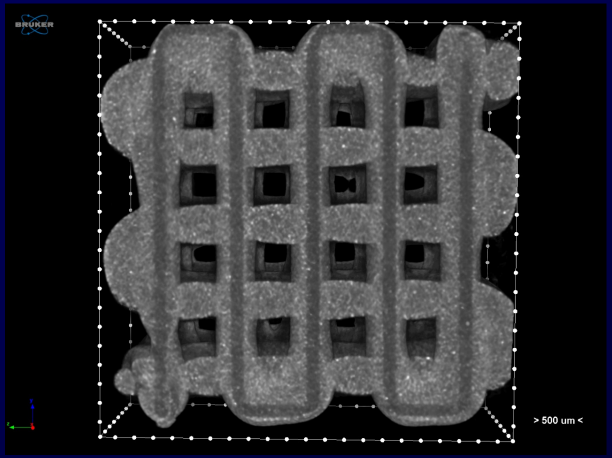
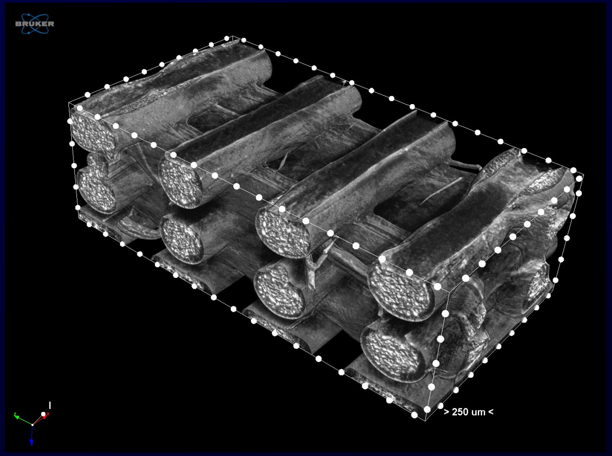
3DP Engraved Fiber Scaffolds





PCL Printing Engraving GelMA Printing





Engraving provides customized architecture to incorporate multiple materials in single filaments.

Diaz-Gomez et al., Bioprinting, 2020.

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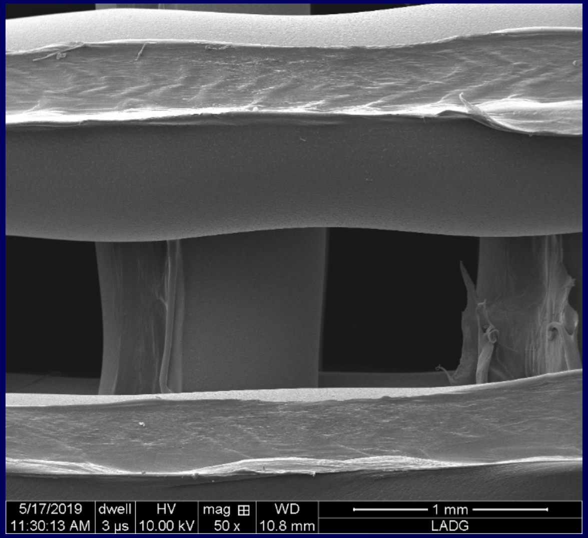
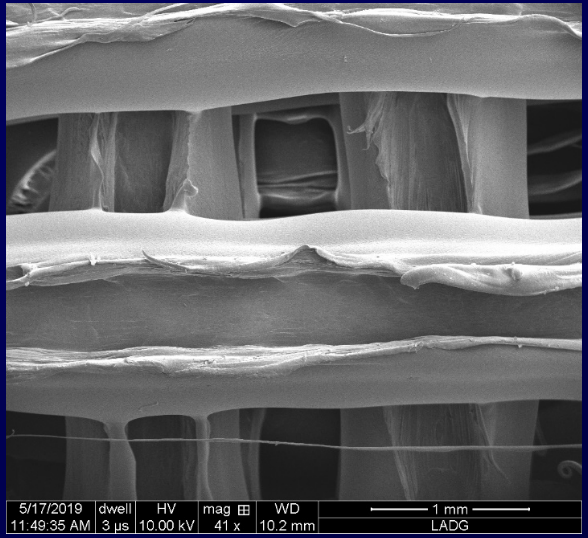
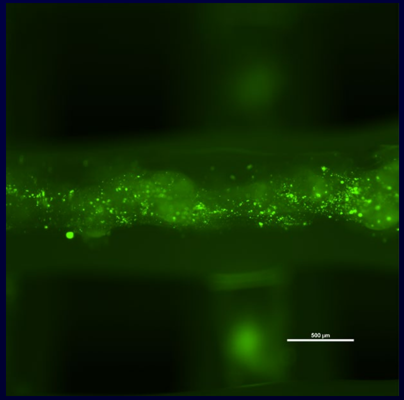
3DP Engraved Fiber Scaffolds



0.4 mm Height



0.5 mm Height



Varying engraving height allowed for printing of different amounts of filling materials, including bioinks with live cells or other temperature/material sensitive components.

Diaz-Gomez et al., Bioprinting, 2020.

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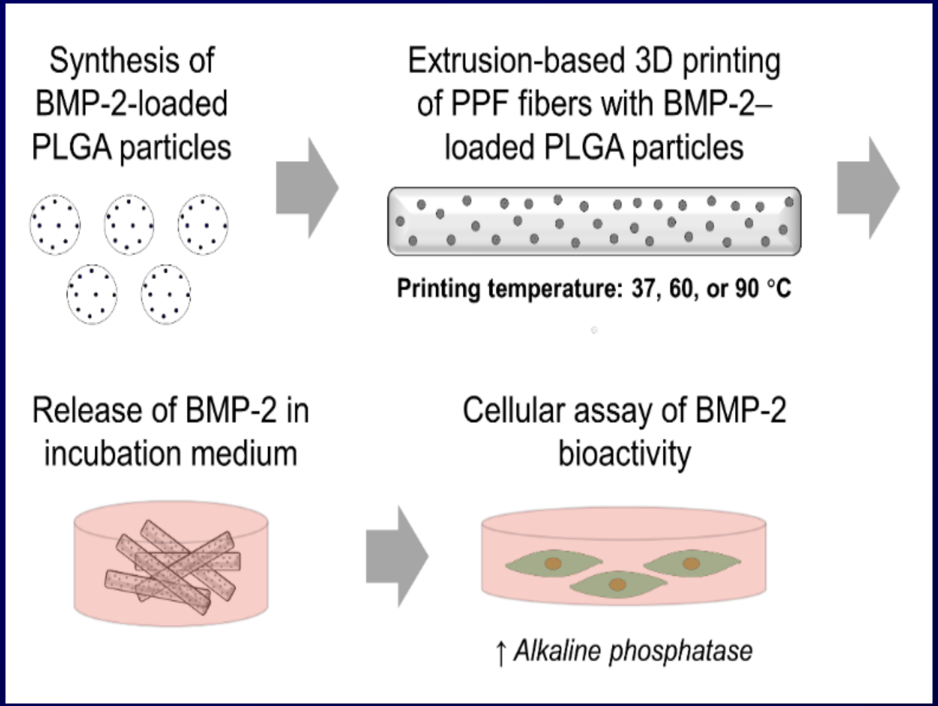
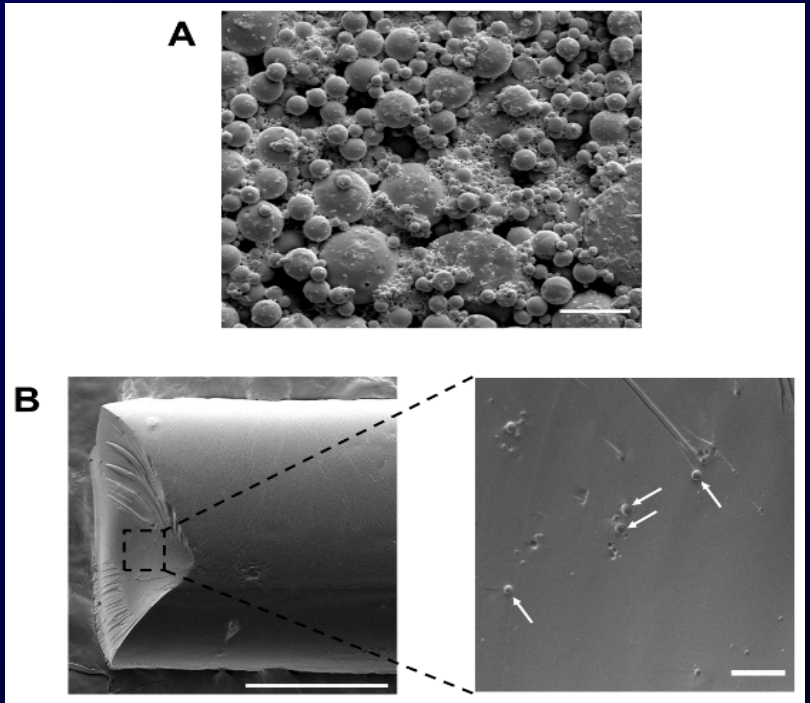
Microparticle Delivery via 3DP





PLGA microparticles can encapsulate BMP-2 growth factors which can be incorporated into 3D-printed hard polymers.

Koons et al., in prep.

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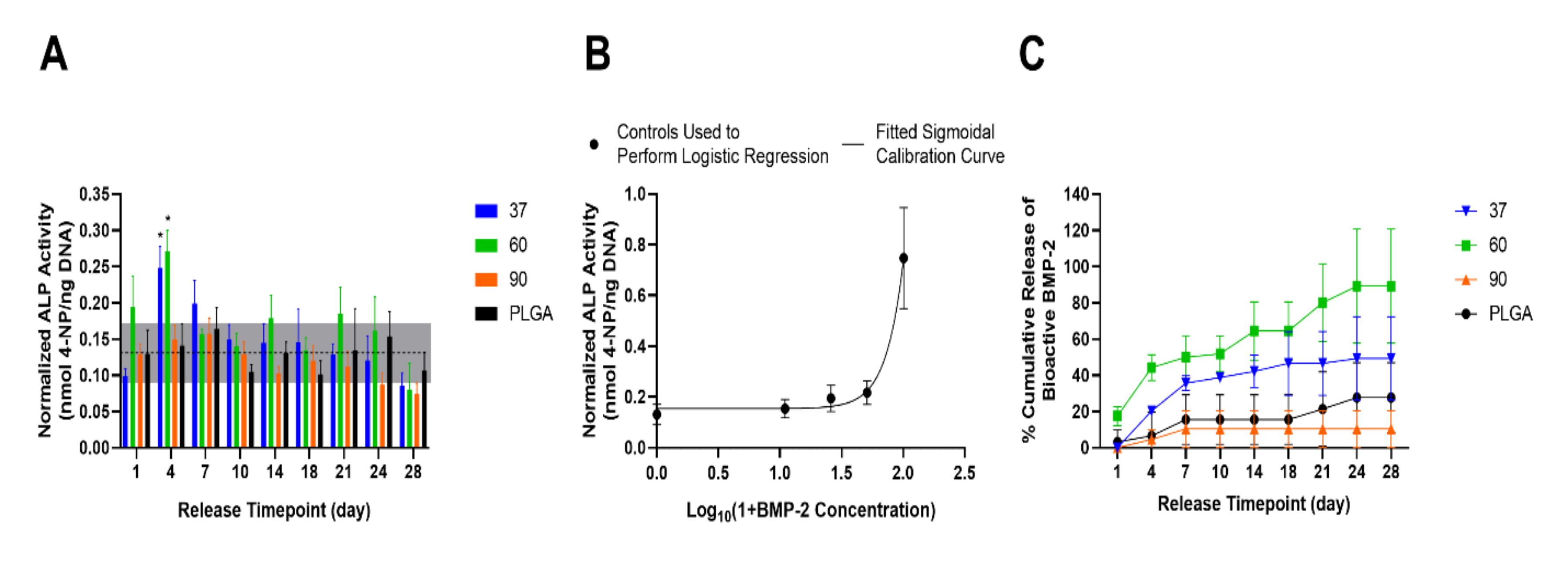
Microparticle Delivery via 3DP



Printing temperature effects bioactivity of encapsulated growth factors.

Koons et al., in prep.

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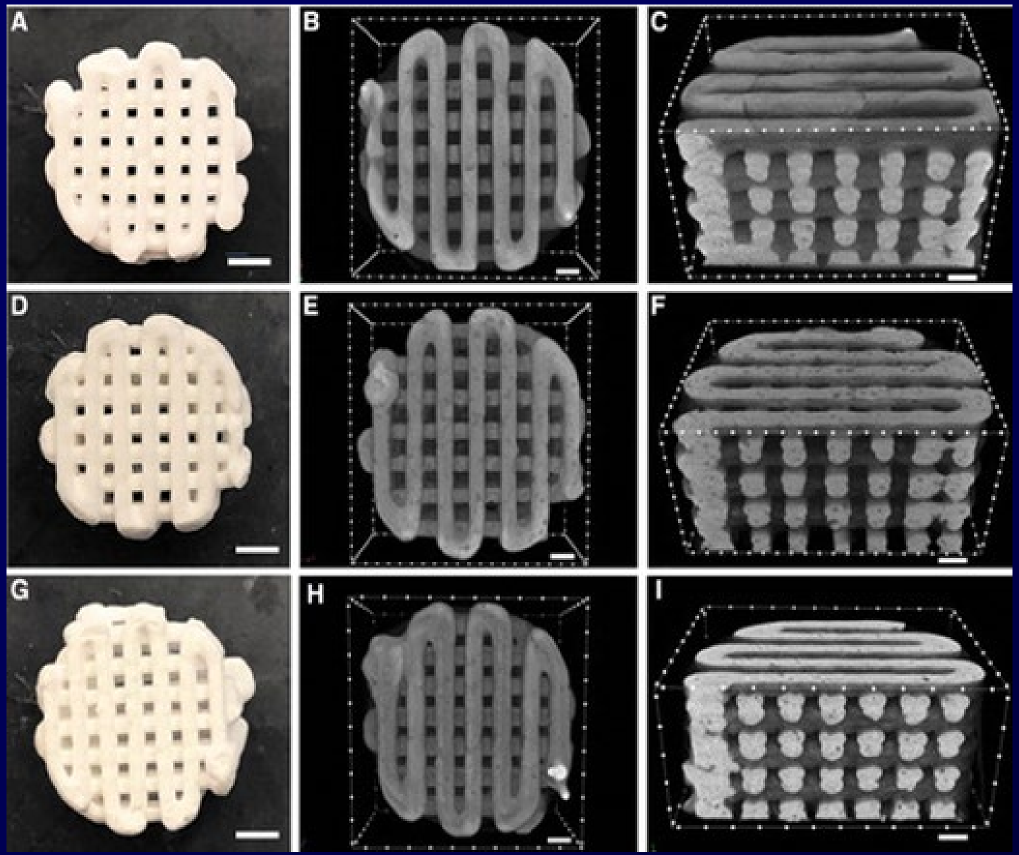
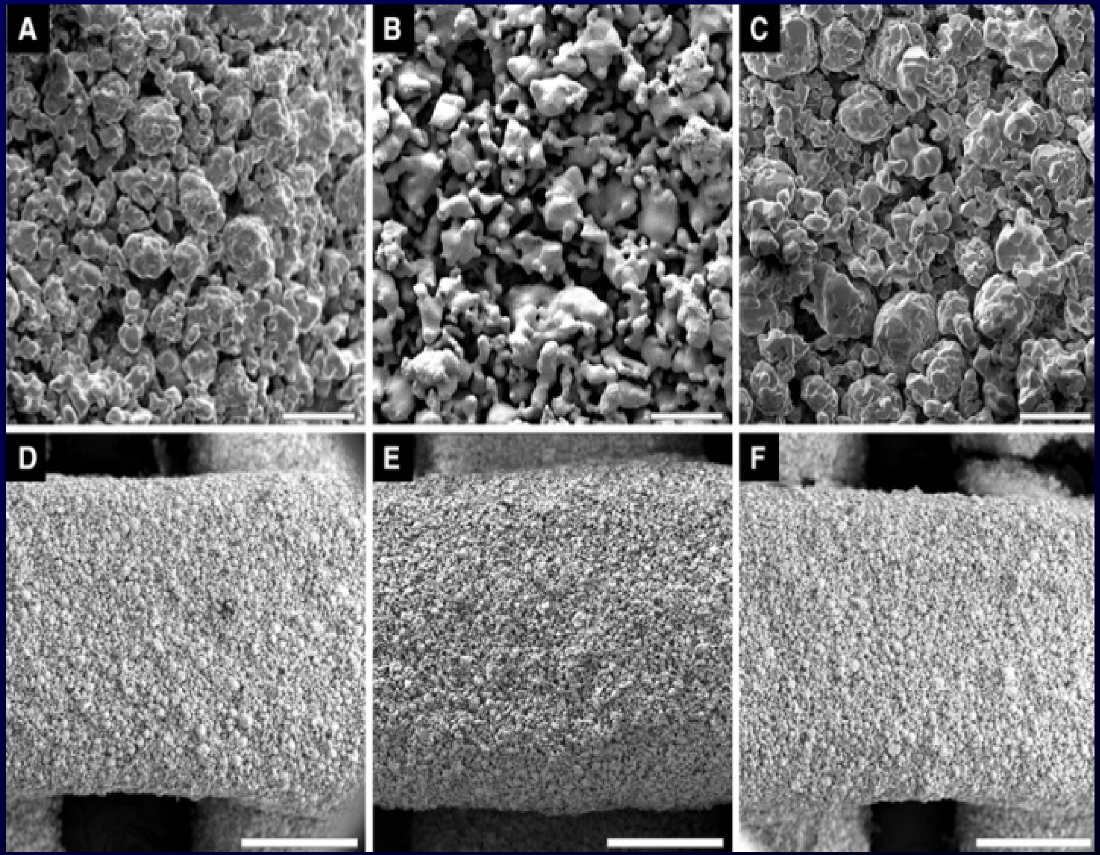
Ceramic-Based Ink





Engraving provides customized architecture to incorporate multiple materials in single filaments.

Diaz-Gomez et al., Tissue Eng. Part C: Methods, 2020

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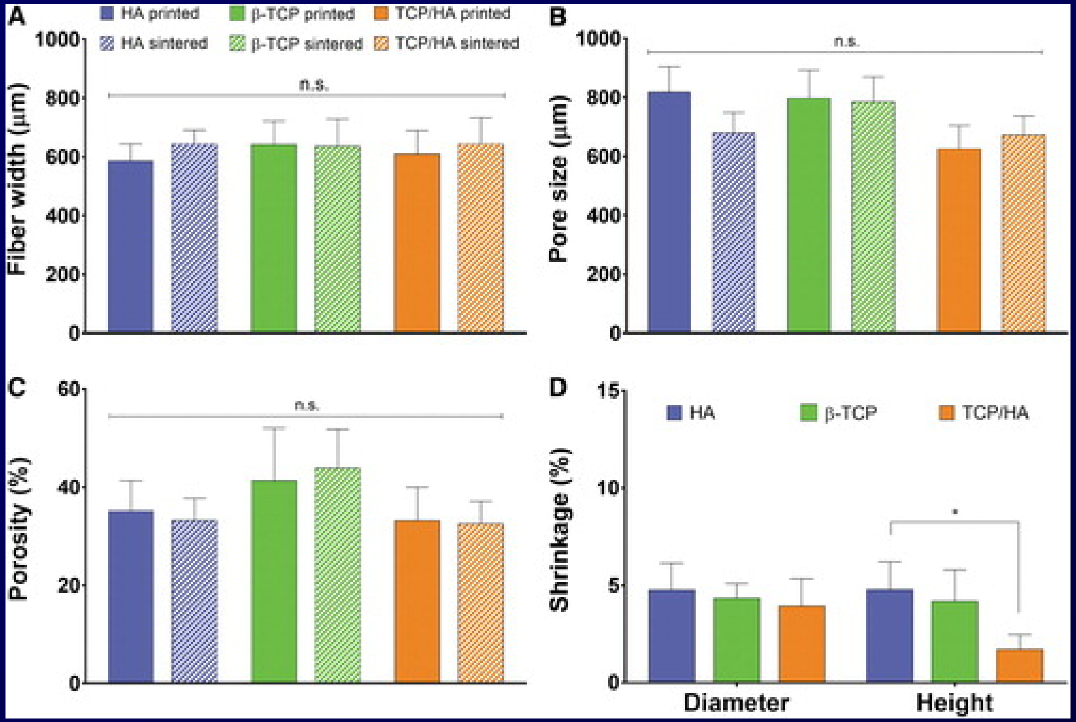
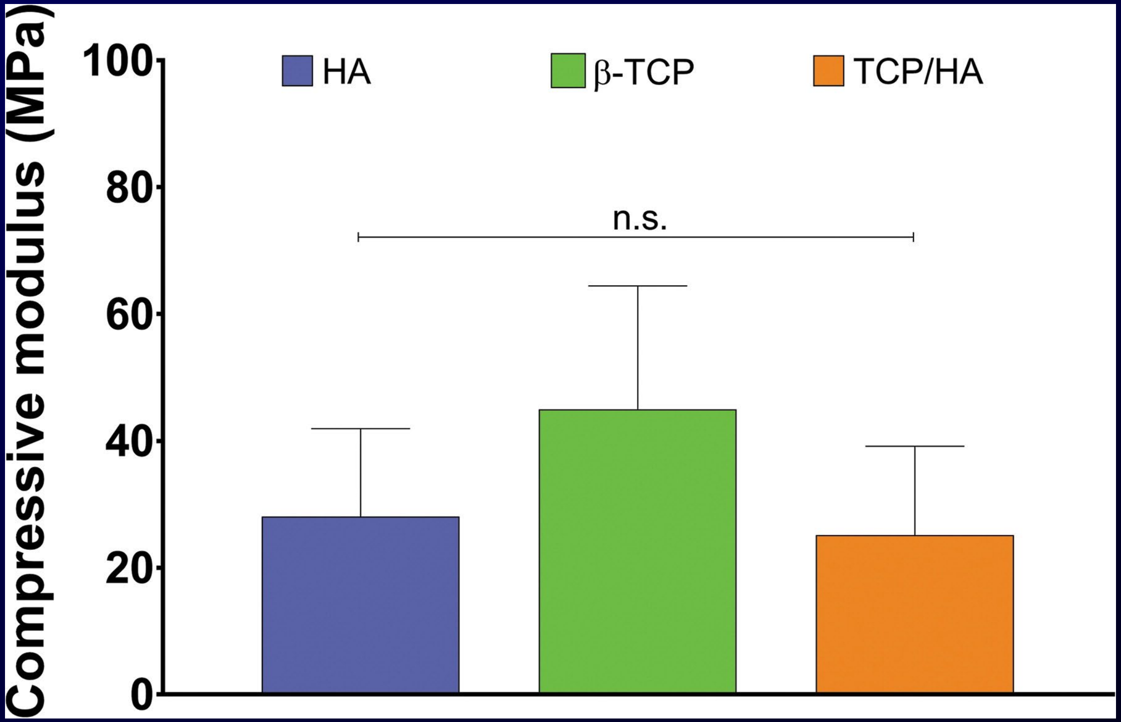
Ceramic-Based Ink





Ceramic-based inks can be printed reliably and predictably with controllable pore sizes and porosity, leading to strong mechanical properties.

Diaz-Gomez et al., Tissue Eng. Part C: Methods, 2020

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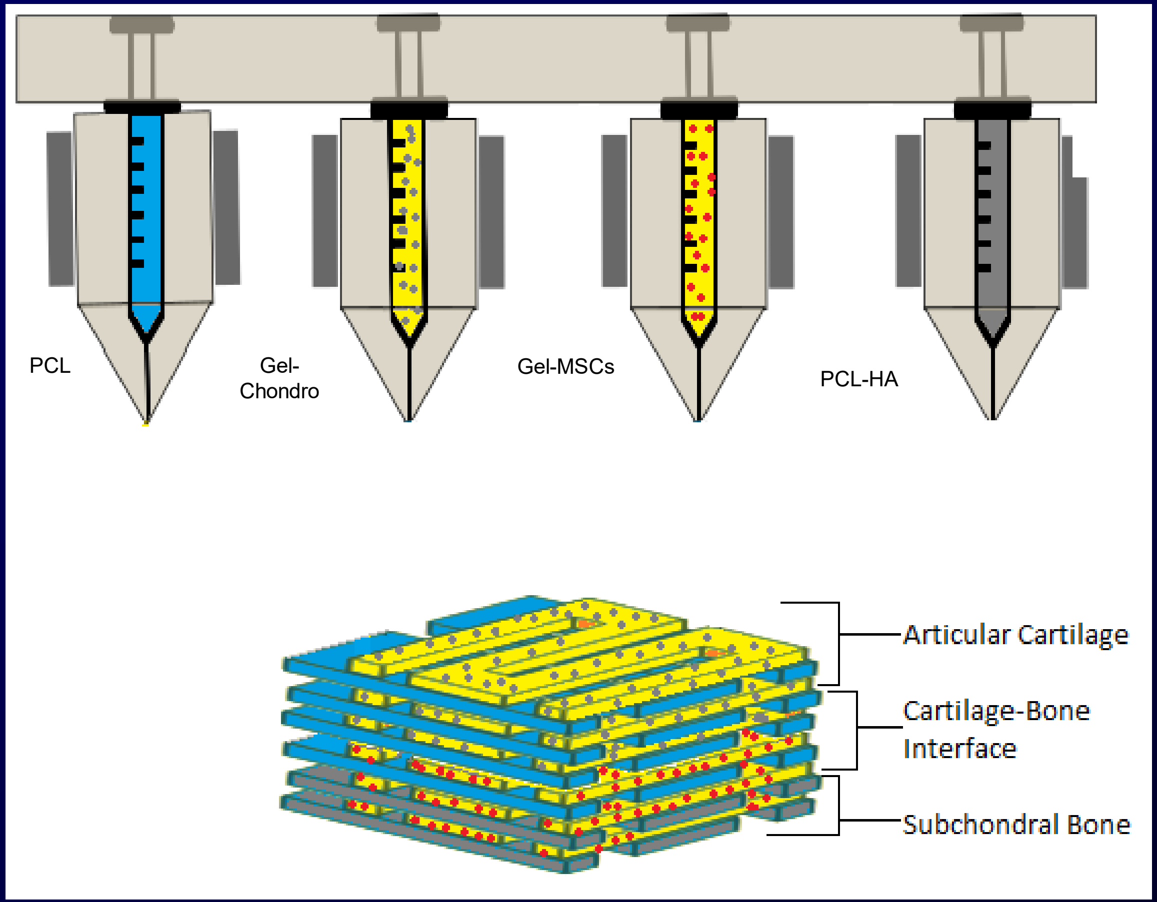
Ideal Scaffold Designs



Ideal scaffold requires combination of custom bioinks and architecture, especially in complex tissues.

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UNIVERSITY OF MARYLAND • RICE UNIVERSITY • WAKE FOREST UNIVERSITY

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