Volumetric Bioprinting

Alex Nottegar

MICRO-722: 3D Printing with Light

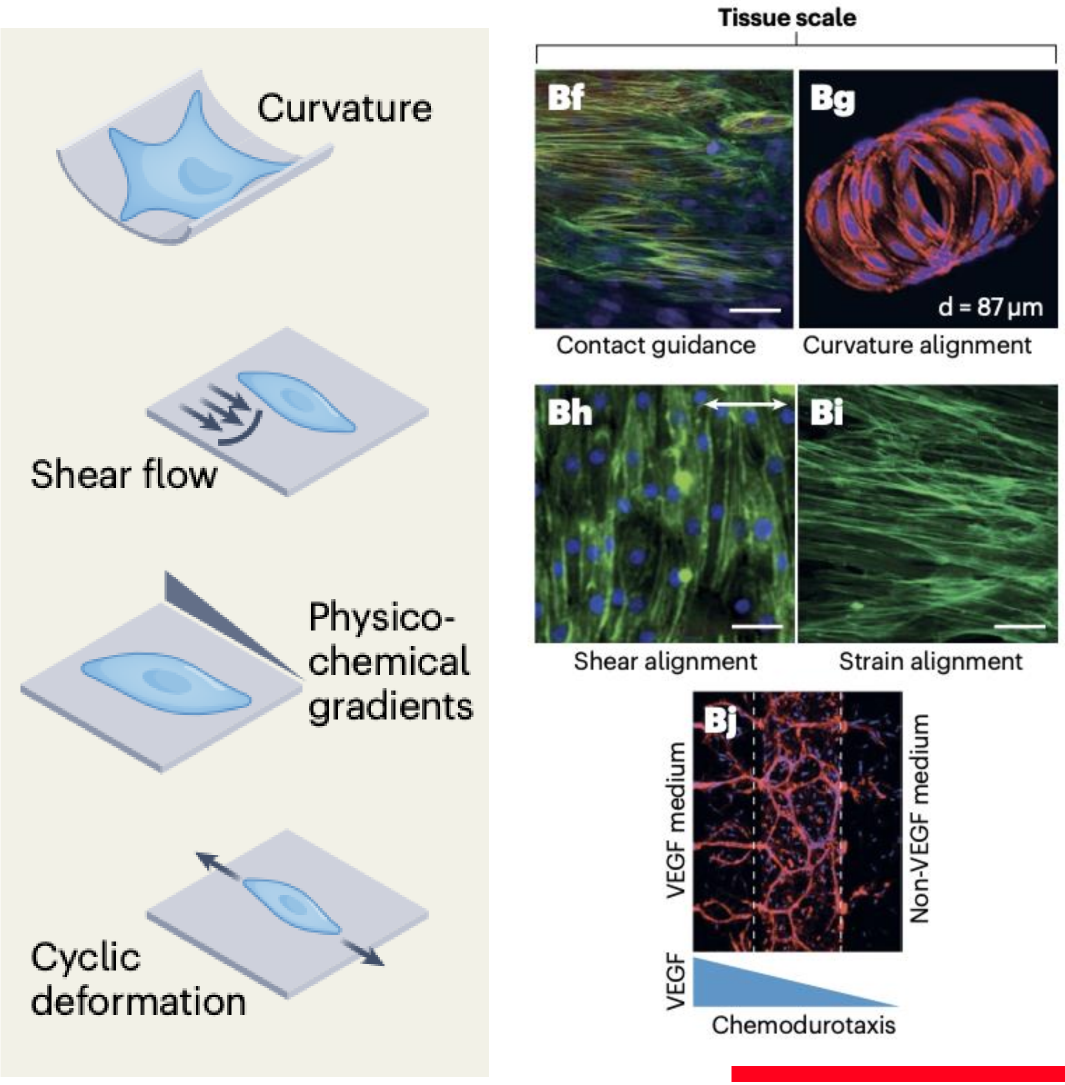
EPFL

Volumetric Bioprinting of Complex Living-Tissue Constructs within Seconds

Paulina Nuñez Bernal, Paul Delrot, Damien Loterie, Yang Li, Jos Malda, Christophe Moser, and Riccardo Levato**

Structural Anisotropy in Living Tissues

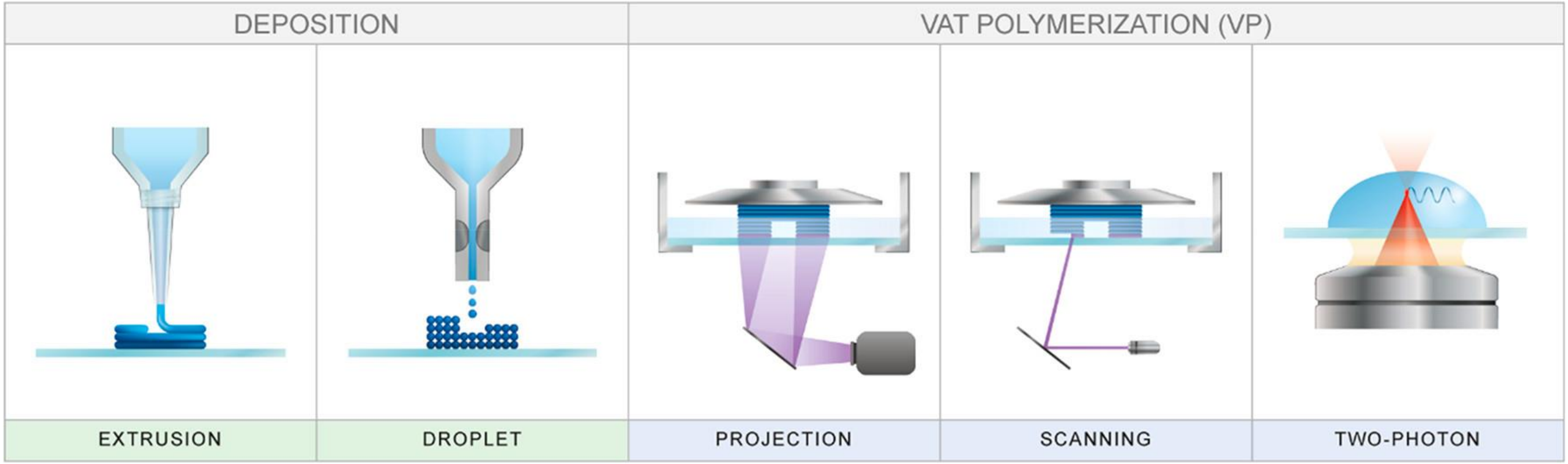
- Biological tissues are structurally anisotropic, meaning their properties vary in 3D space (collagen alignment in tendons, osteon orientation in bone)
- This directional organization influences cell behavior, nutrient transport, and the tissue functionality
- Replicating native anisotropy is essential for fabricating biomimetic organs with mimic the structure and function of native tissue



Nature Reviews Bioengineering, 2025

EPFL

Conventional Bioprinting Methods

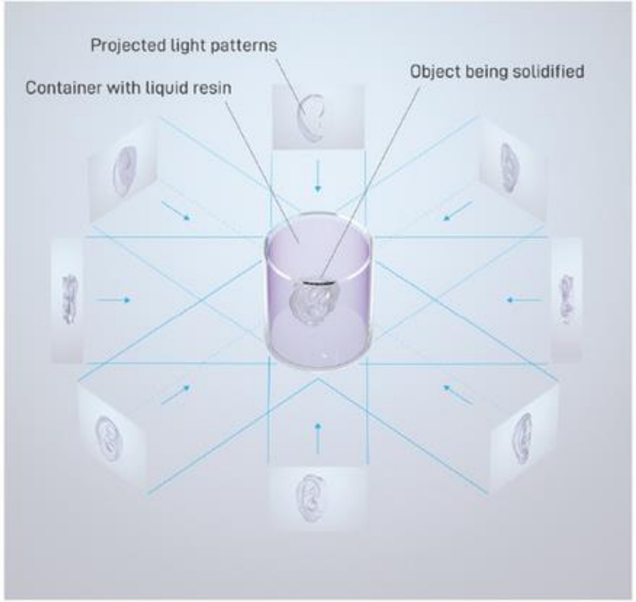


Chemical Reviews, 2020

Limitations:

- Layer-by-layer methods lead to surface artifacts
- Take considerable time; especially for larger sized grafts
- Required sacrificial support materials to print complex structures
- Extrusion based methods can impair cell functionality due to high shear stresses

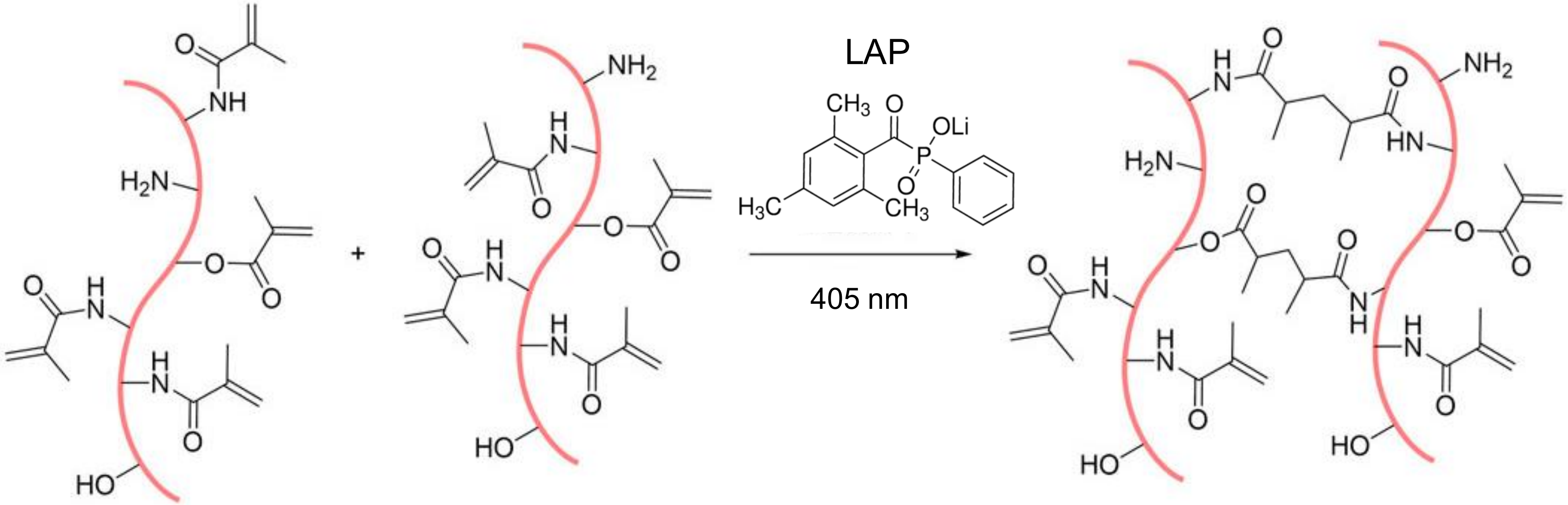
Volumetric Bioprinting



Volumetric Bioprinting:

- Photo-crosslinking of cell-laden resin
- Printing of entire object at once; rather than point-by-point or layer-by-layer
- Fast printing times causes less stress to cells
- Complex structures without supports

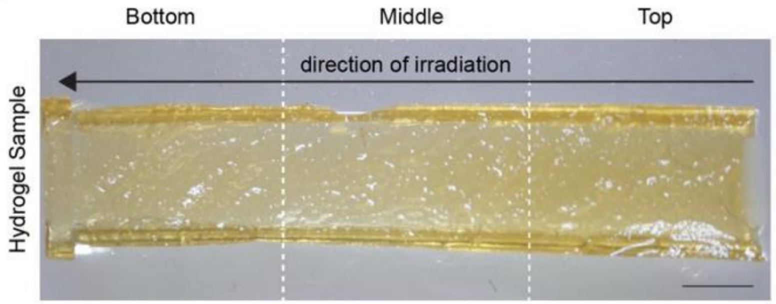
GelRESIN



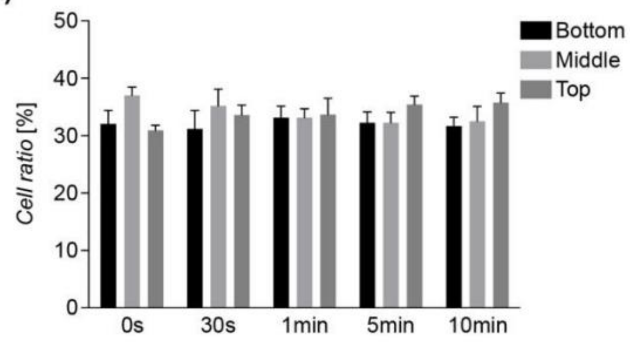
Methacrylated gelatine (GelMA) chains

Crosslinked GelMA hydrogel

A)

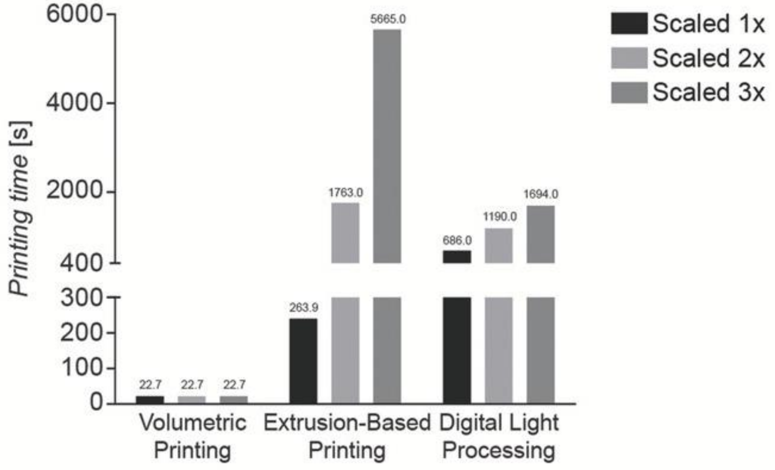


B)



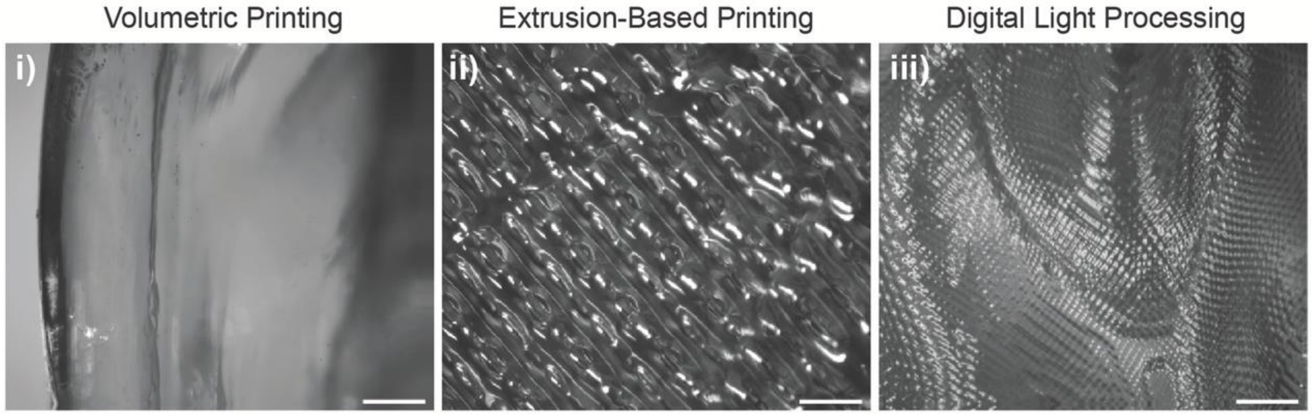
Volumetric Additive Manufacturing

Fast print times independent of size

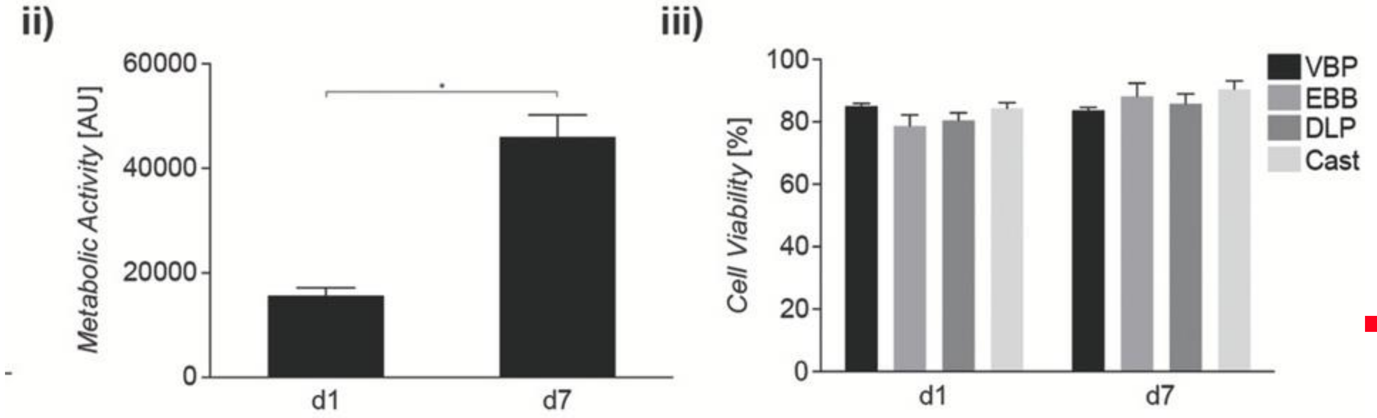


$t \sim d^3$ $t \sim d$

Artifact-free surface finish

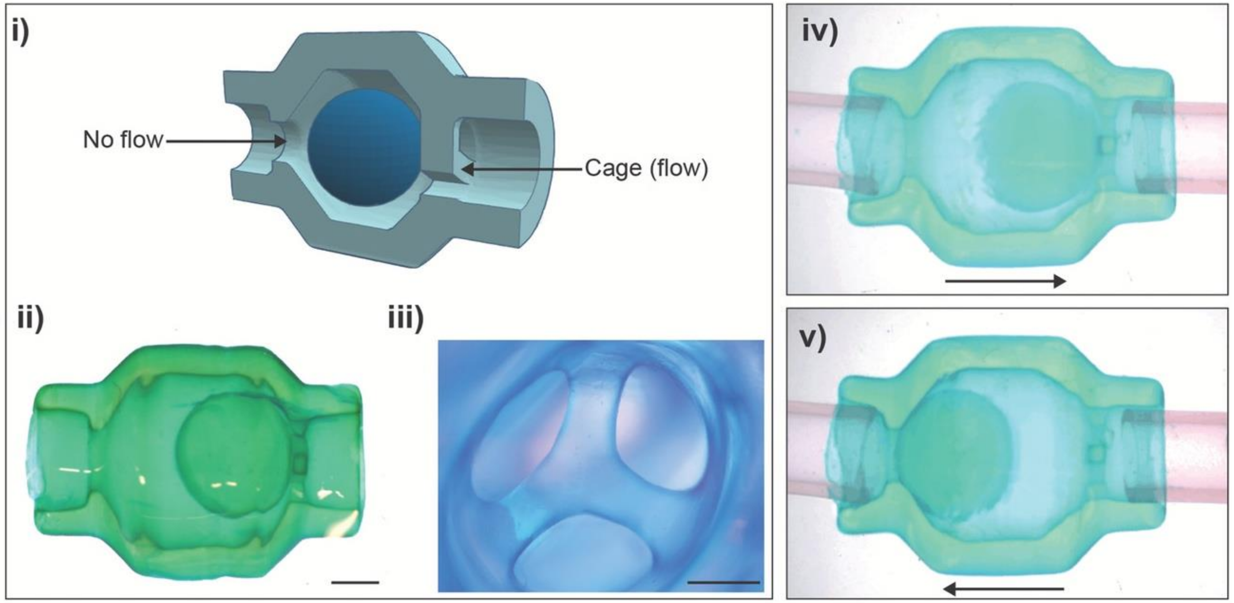


High cell viability and functionality

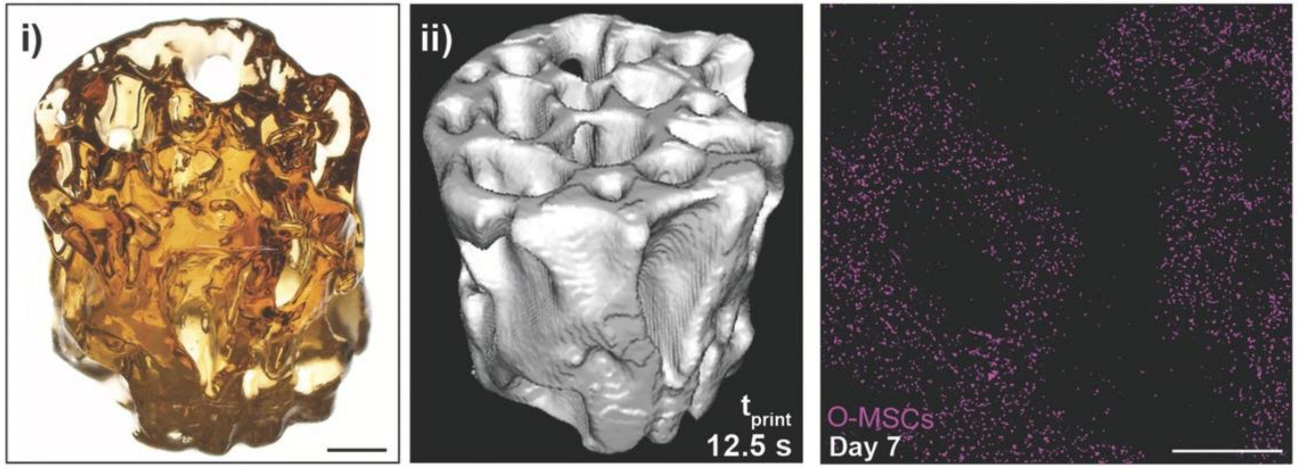


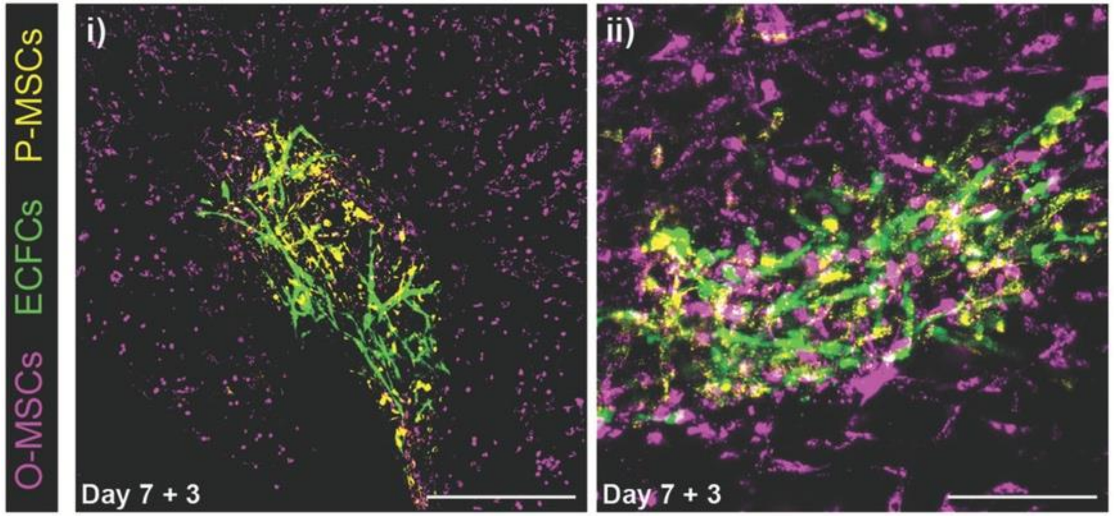
Volumetric Additive Manufacturing

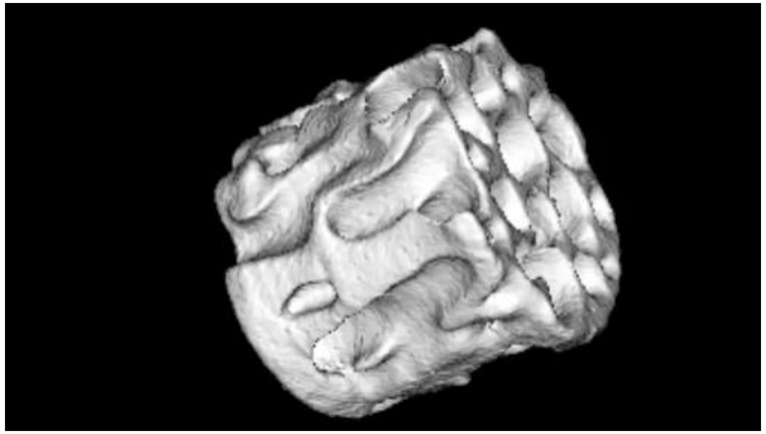
Complex; support-free; free-floating structures



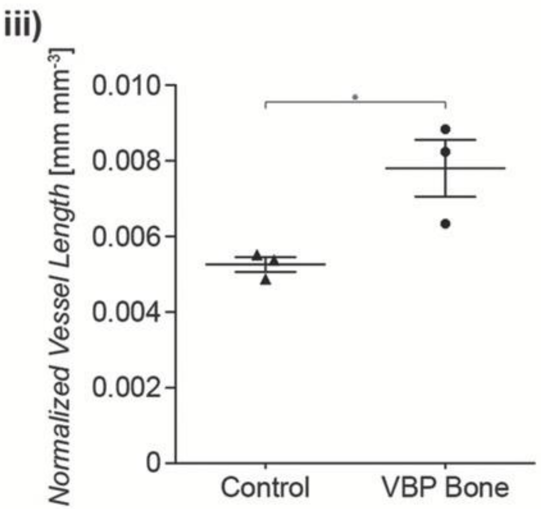
Trabecular Bone Model





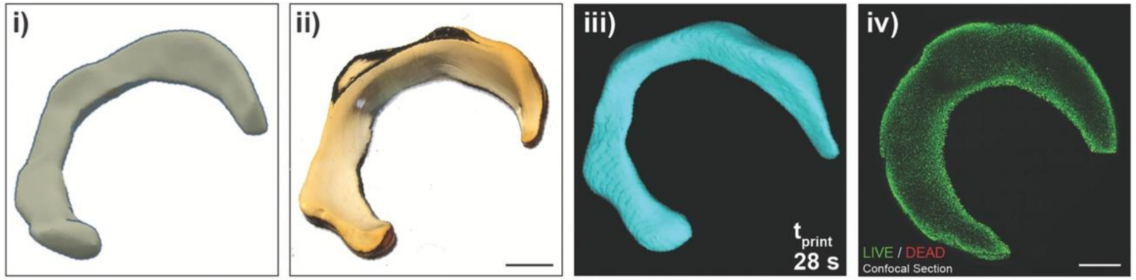


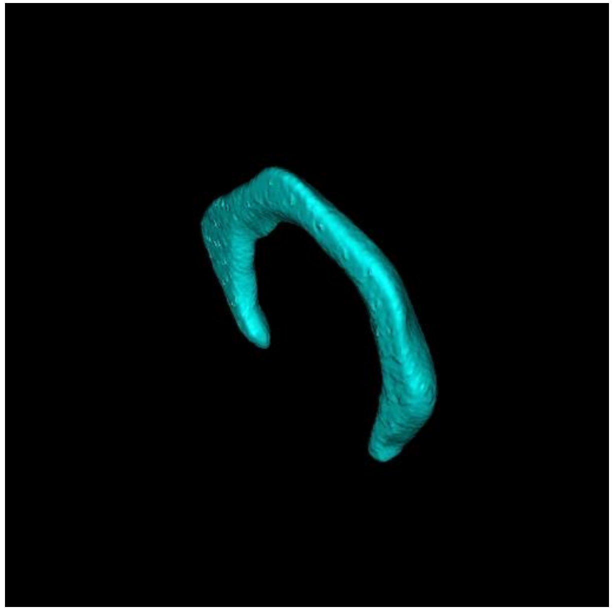
- Bioprinted structure was primed in an osteogenic medium
- Complex porous network was perfused with ECFCs and MSCs
- Forms highly vascularized network

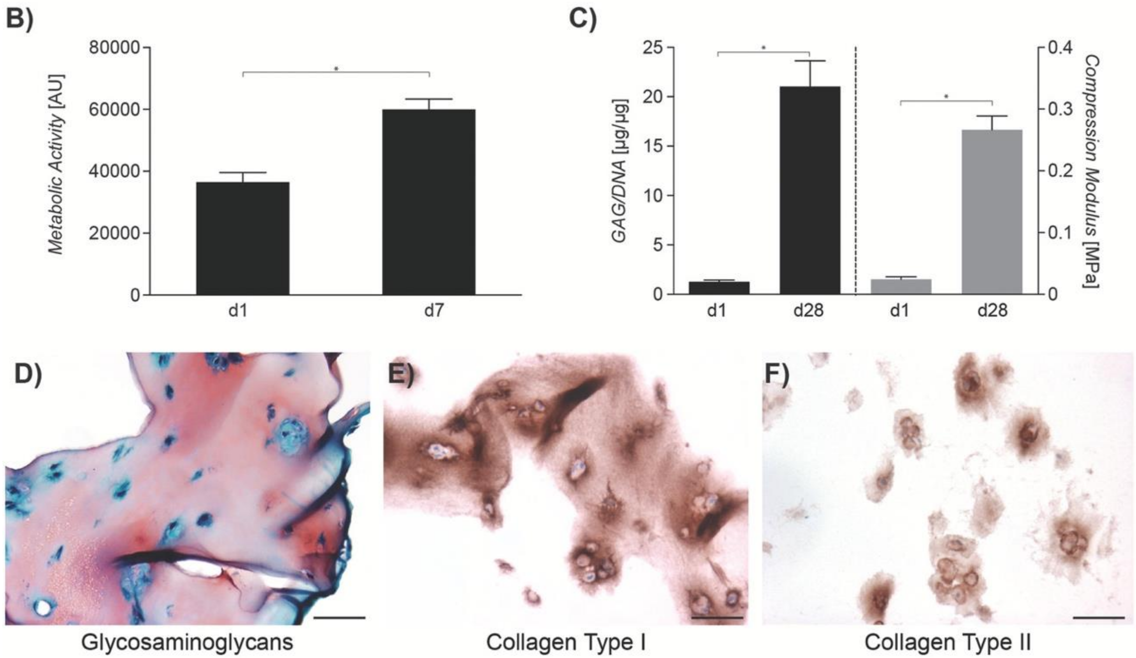


EPFL

Meniscal Graft







- 10^7 ACPCs mL^{-1}
- High cell viability and metabolic activity
- Cells deposit neo-fibrocartilage matrix leading to increase in construct mechanical properties
- High amount of collagen type I and minor amounts of type II analogous to native tissue

Conclusions

- Volumetric bioprinting enables the fabrication of entire, cell-laden 3D structures within seconds, a major advance over layer-by-layer bioprinting
- High cell viability (>85%) and functional tissue formation, including bone- and cartilage-like constructs
- Free-form, centimeter-scale architectures are produced without support materials with fine structural fidelity and improved surface finish

Adaptive and context-aware volumetric printing

https://doi.org/10.1038/s41586-025-09436-7

Received: 5 December 2024

Accepted: 21 July 2025

Published online: 3 September 2025

Open access

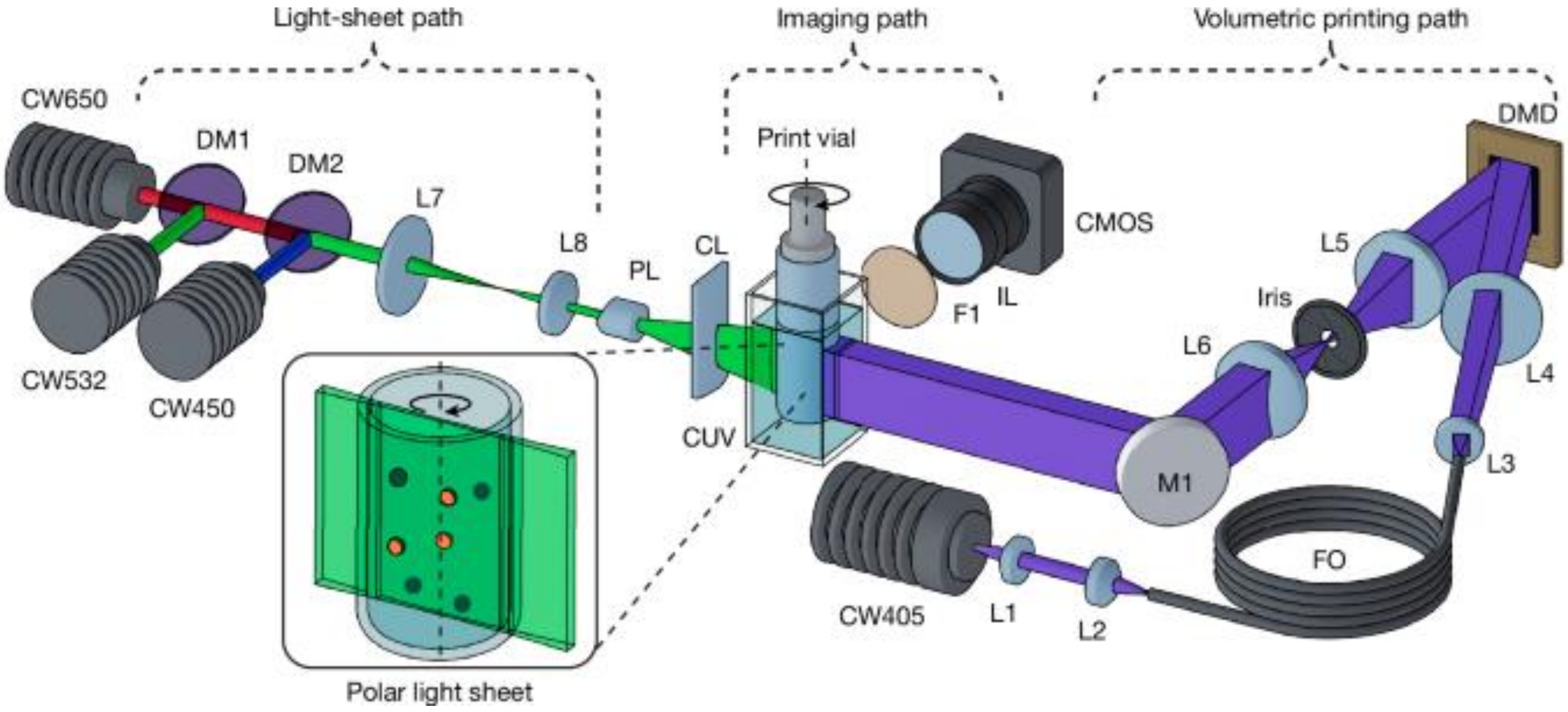
Check for updates

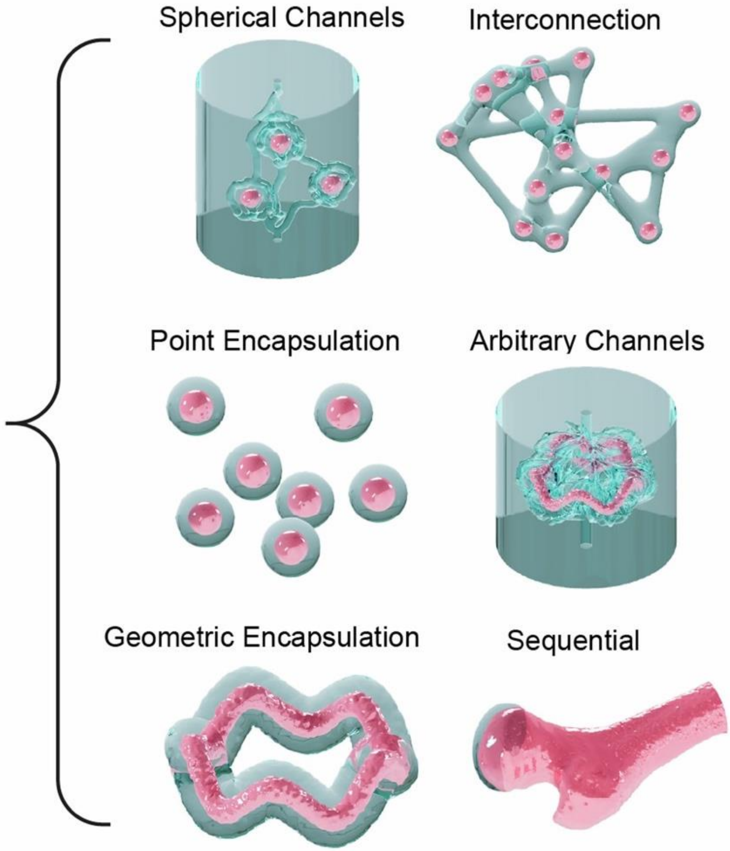
Sammy Florczak[1,2], Gabriel Größbacher[1], Davide Ribezzi[1], Alessia Longoni[1], Marième Gueye[1], Estée Grandidier[1], Jos Malda[1,2] & Riccardo Levato[1,2]✉

We introduce Generative, Adaptive, Context-Aware 3D Printing (GRACE), a new approach combining 3D imaging, computer vision and parametric modelling to create tailored, context-aware geometries using volumetric additive manufacturing. GRACE rapidly and automatically generates complex structures capable of conforming directly around features ranging from cellular to macroscopic scales with minimal user intervention. Here we demonstrate its versatility in applications ranging from synthetic objects to biofabrication, including adaptive vascular-like geometries around cell-laden bioinks, resulting in improved functionality. GRACE also enables precise alignment of sequential prints, as well as the detection and overprinting of opaque surfaces through shadow correction. Compatible with various printing modalities[1–4], GRACE transcends traditional additive manufacturing limitations in automating overprinting and adapting the printed designs to the content of the printable material. This opens new possibilities in tissue engineering and regenerative medicine.

GRACE

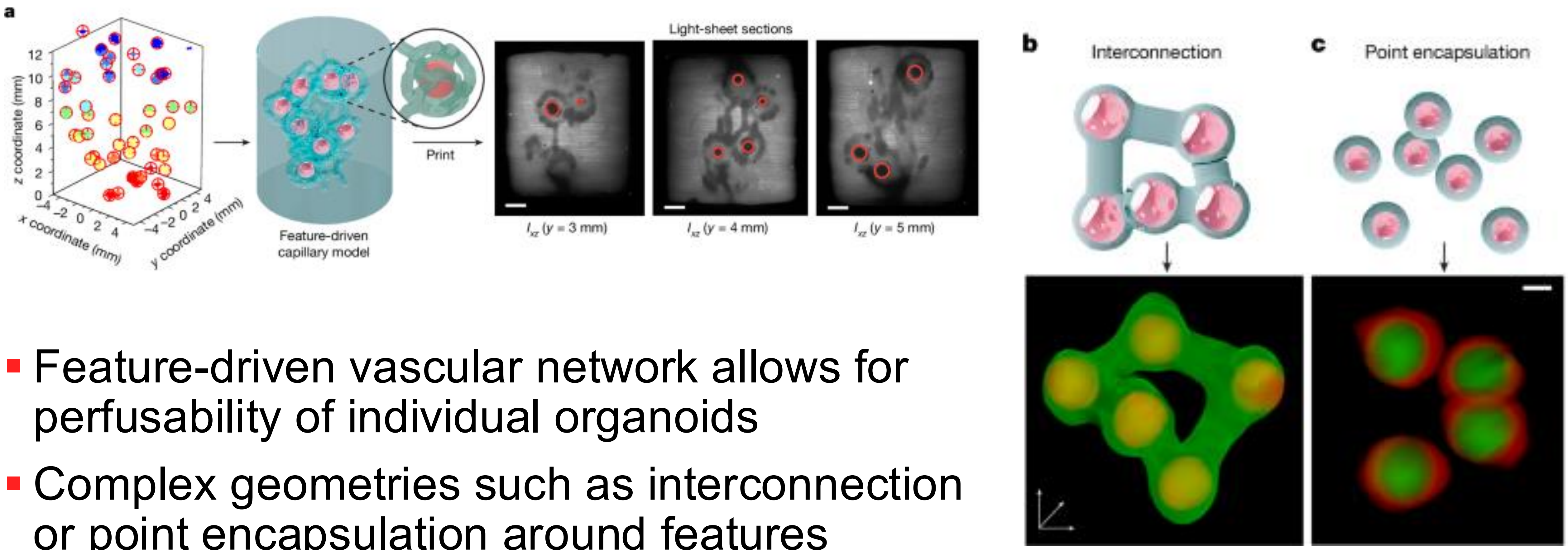
Generative, adaptive, context-aware 3D printing





light sheet scanning → parametric model → volumetric printing

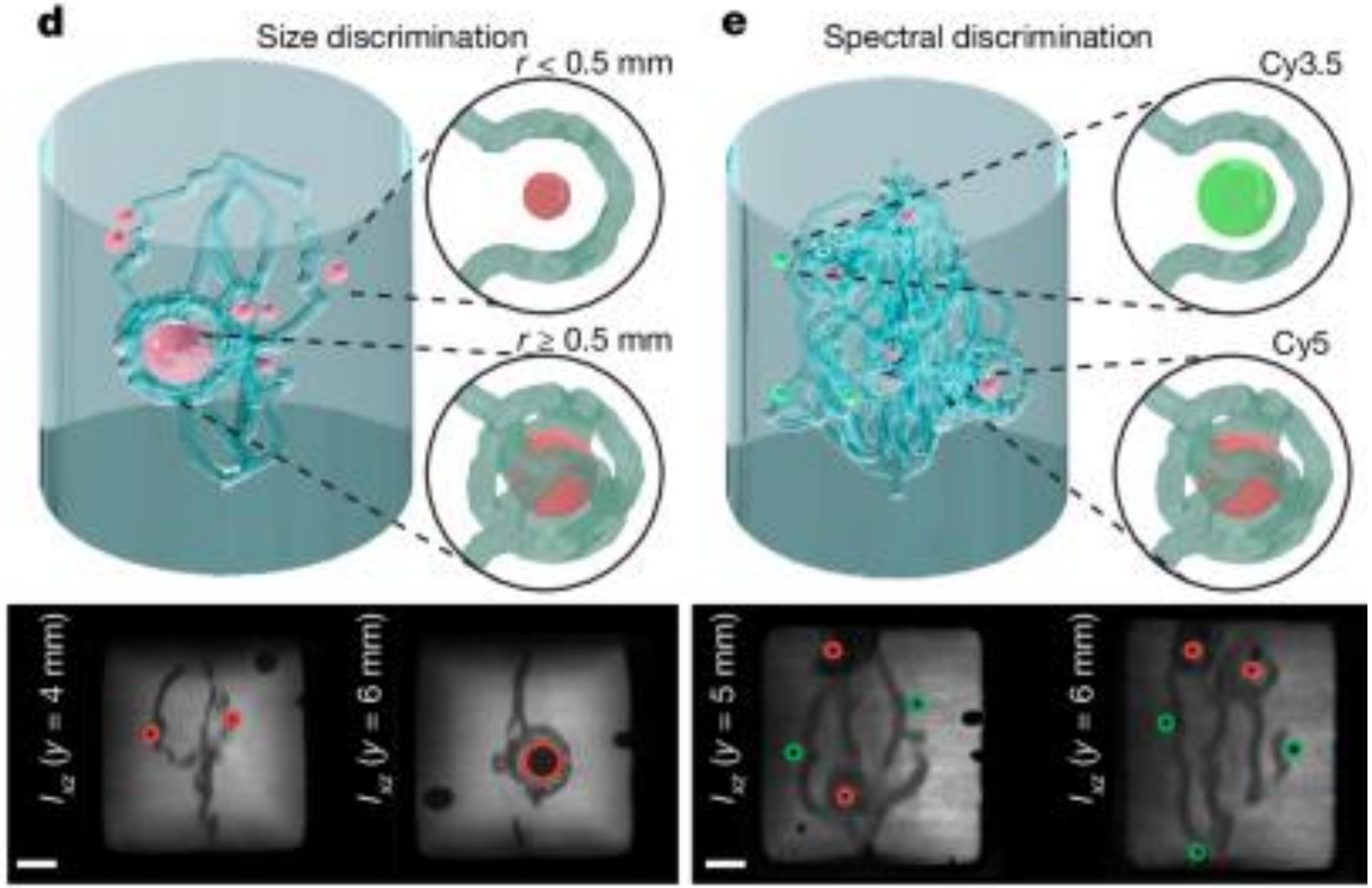
Feature-driven Complex Geometries



- Feature-driven vascular network allows for perfusability of individual organoids
- Complex geometries such as interconnection or point encapsulation around features

EPFL

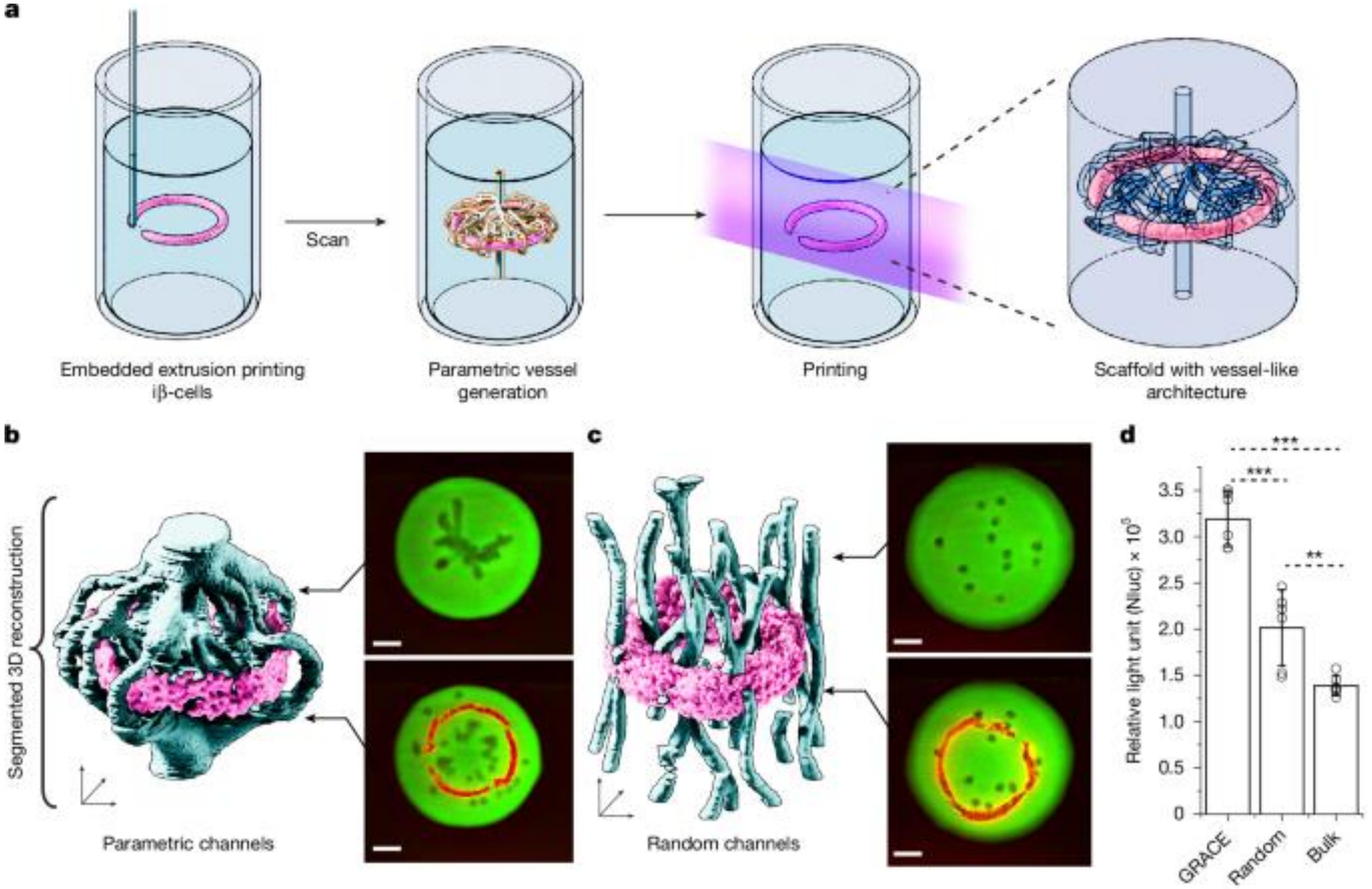
Parametric Discrimination



- Ability to discriminate between size or spectral signal of features

Vascularization of Cellular Structures

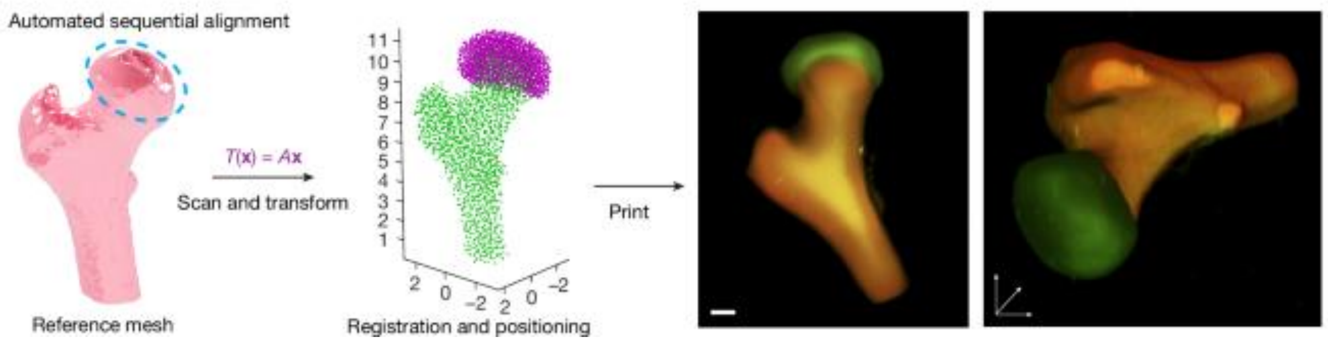
- Ability to fabricate adaptive geometries of vessel-like channels around living cells
- Embedded Extrusion of highly cellularized torus structures of iβ-cells
- Vascular networks generated and printed around toruses
- Superior mass transport with adaptive geometries

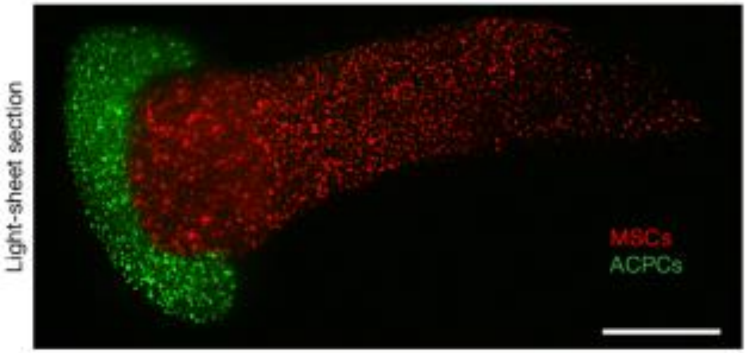


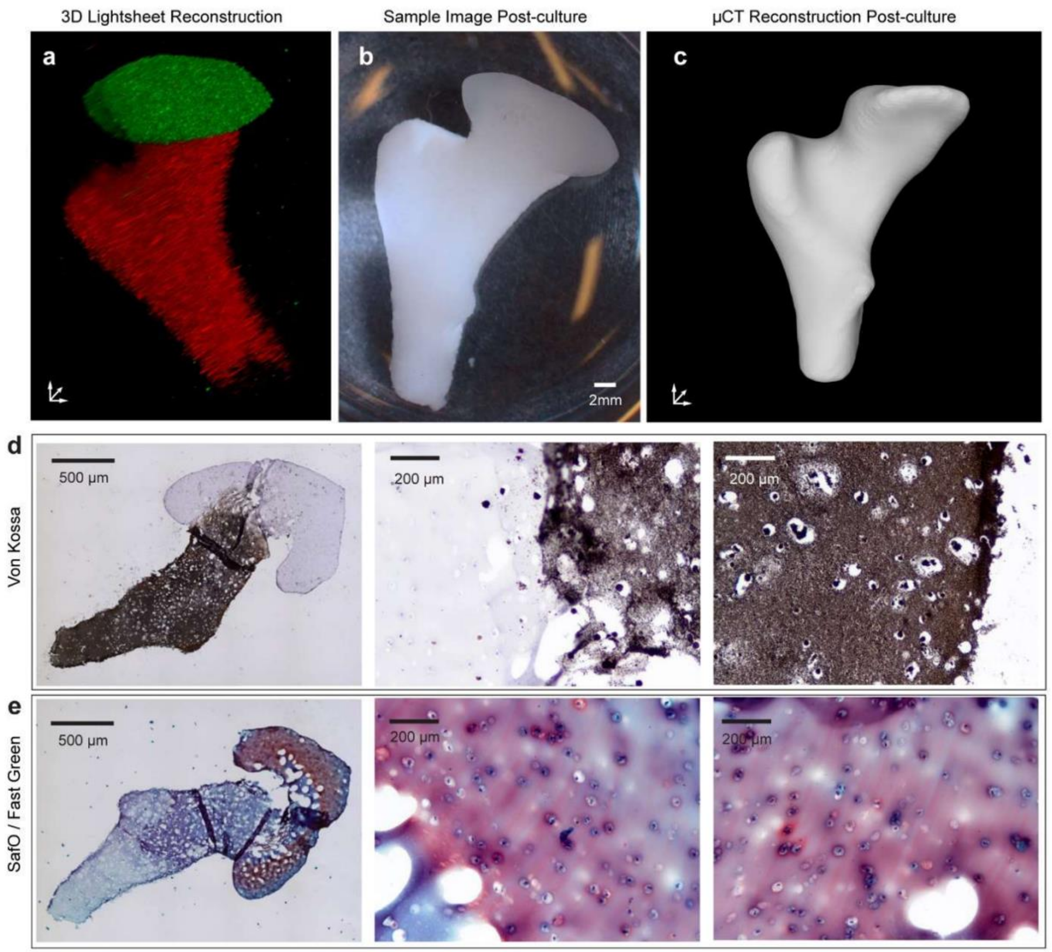
EPFL

Over-printing Auto Alignment

Two component cell-laden bone and cartilage model







histology after 4 weeks

Conclusions

- Enables real-time, autonomous geometry generation tailored to the printing context
- Prints complex and biologically relevant structures that conform to embedded features
- Performs automatic overprinting and precise alignment of sequential prints

Future of Volumetric Bioprinting:

- Scale for patient-specific grafts and organ-level constructs
- Future uses in *in vitro* disease modeling, regenerative medicine, tissue engineering and personalized therapy testing