Why Bioprint Biological Structures?

Today, we can culture cells in 3D, generate spheroids and complex organoids, and harness their natural capacity for self-organization. Why, then, should we also want to print biological structures? The answer begins where simply allowing cells to grow is no longer enough: when we need to define precisely where cells are positioned, what they interact with, and how complex the architecture of the resulting model should be.

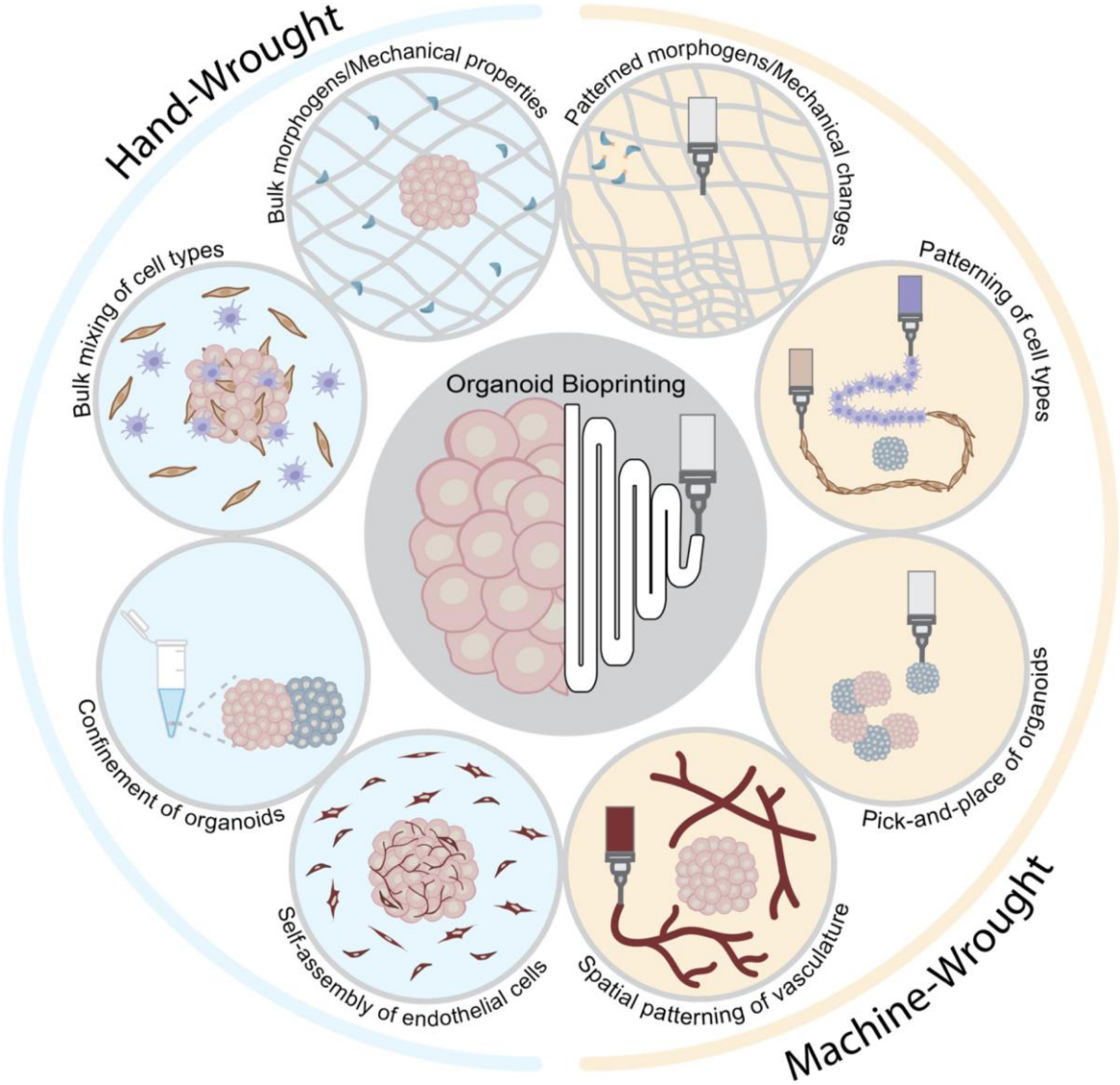


Fig. 1. From self-organization to controlled architecture in 3D biological models. Bioprinting complements the natural self-organization of organoids by enabling spatial control over their microenvironment—including mechanical properties and biochemical signals, the distribution of cell types and organoids, and the incorporation of vascular structures. Adapted from Zhang et al., 2025 [1].

A 3D model is not automatically a tissue

The transition from conventional adherent 2D cell cultures to 3D models has fundamentally transformed the possibilities of cell biology. Spheroids and organoids allow cells to interact in a three-dimensional environment, produce their own extracellular matrix, differentiate, and, to some extent, spontaneously organize into structures resembling native tissues.

This capacity for self-organization is one of the greatest strengths of 3D models. Yet we always harness it under conditions that we create ourselves—using a scaffold, an extracellular matrix, or a carefully selected cellular environment. The more complex the tissue we seek to reproduce, the more important the relationships between different cell types, structures, and the surrounding microenvironment become.

In native tissue, what matters is not only which cells are present, but also where individual cell populations are located, how far apart they are, which interfaces they form, what mechanical and chemical conditions they experience, and how they communicate. Spatial organization is a fundamental property of functional tissue.

This is where the limitations of spontaneous self-organization alone begin to emerge. Organoids can vary in size, shape, and internal organization, and they cannot always reproduce the larger-scale architecture of native tissues.

An increasingly important direction is therefore to combine organoid technologies with bioprinting. While organoids harness the natural ability of cells to organize themselves, bioprinting adds another layer: design and control over spatial organization.

Bioprinting adds design

This may be the most important answer to the question of why we should print biological structures.

Bioprinting is not simply a way to place cells in 3D. It makes it possible to define a structure in advance—the positioning of cells, their spatial relationships, and their integration into the resulting model. It enables the creation of functional architecture. Cells, cell aggregates, organoids, and biomaterials can thus become building blocks that are spatially arranged to address a specific biological question.

We may want to create an interface between two tissue types. Position different cell populations in precisely defined regions. Design the shape and dimensions of a construct. Combine different biomaterials. Or provide space for channels and a future vascular network.

Modern bioprinting is therefore moving beyond simply depositing successive layers of material toward controlling the spatial organization of living systems. Review articles identify the ability to control the localization of cells, matrix components, morphogens, different cell populations, and vascular elements as one of the major opportunities in contemporary biofabrication [1].

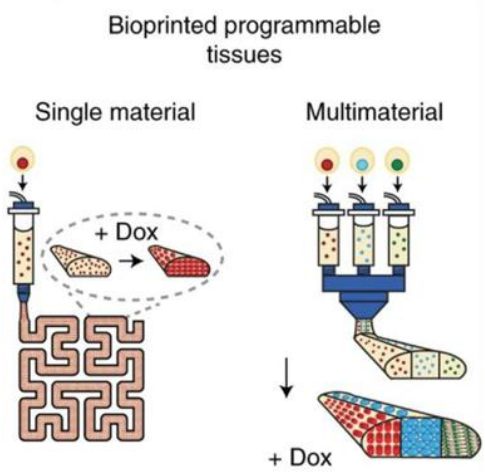


Fig. 2. Bioprinting enables control over the spatial organization of a biological model. In addition to printing a single material, multiple materials and cell populations can be combined to create defined architectures in more complex tissue models. Adapted from Zhang et al., 2025 [1].

Biology needs more than a flat surface—it needs space. Conventional 3D printing typically builds structures by successively depositing material along fixed axes. When fabricating complex biological structures, however, it is useful to control not only the position but also the direction from which cells and biomaterials are deposited. Multi-axis bioprinting adds degrees of freedom, enabling work with complex geometries and printing onto existing 3D structures from different directions [2].

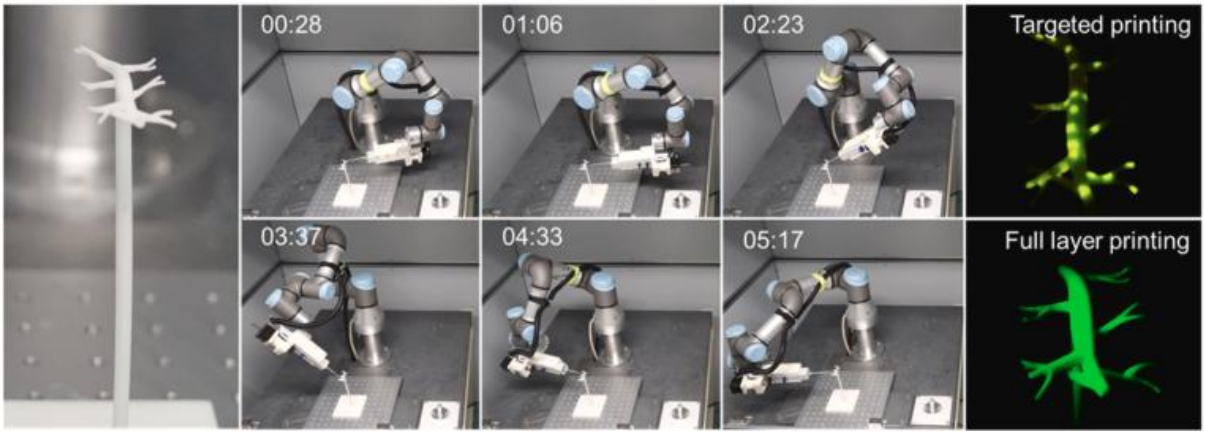


Fig. 3. Multi-axis robotic bioprinting enables targeted deposition of cells onto complex 3D structures from different directions. Six degrees of freedom extend the capabilities of conventional layer-by-layer printing along Cartesian axes and allow deposition onto pre-existing three-dimensional scaffolds. Adapted from Zhang et al., 2022 [2].

The BioAssemblyBot from Advanced Solutions is based on this principle. Its six-axis robotic arm replaces a conventional printhead restricted to motion along Cartesian axes. The manufacturer summarizes the concept simply: “Biology is not square.”

Six-axis motion enables not only conventional additive deposition but also contour printing, work with more complex geometries, and targeted deposition of materials or cells onto existing 3D structures and curved surfaces [3].

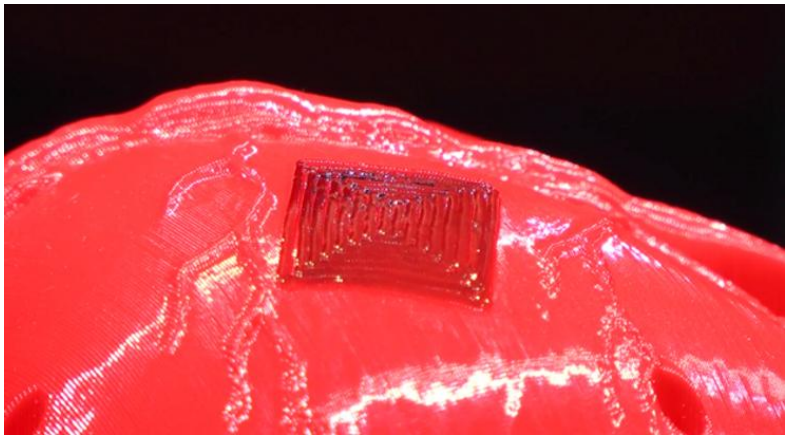


Fig. 4. Printing directly onto a complex curved surface using the BioAssemblyBot. The system first scans the geometry of an existing 3D object and then allows the printing path to be adapted to its surface. The image shows a structure printed onto a heart model. Source: Advanced Solutions [3].

From shape to function

A more complex shape alone does not necessarily make a better biological model.

The purpose of controlled architecture is to move from geometry to function.

Native tissues consist of several cell populations arranged in specific spatial relationships. Barriers, gradients, contact zones, and mechanically distinct environments arise between individual compartments. These relationships, in turn, influence migration, differentiation, signaling, and responses to drugs.

One important direction in biofabrication is therefore compartmentalization—the deliberate creation of distinct yet interconnected regions within a single model.

Bioprinting can bring together multiple cell types, biomaterials, bioactive factors, or preformed biological building blocks within a spatially defined tissue architecture. Combining bioprinting with organoids is one promising way to integrate the natural self-organization of cells with control over the arrangement of the resulting model [4].

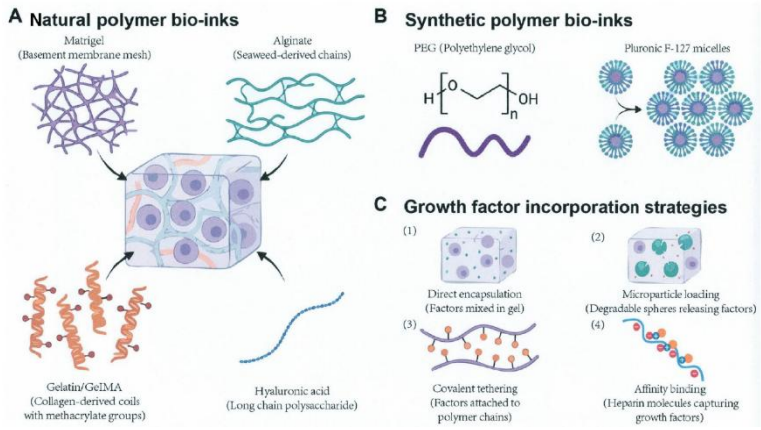


Fig. 5. Examples of bioink composition and functionalization for 3D bioprinting. Bioinks may combine natural or synthetic polymer components with bioactive factors, whose incorporation into the material provides additional control over the properties of the cellular microenvironment. Source: [4].

The larger the structure, the greater the challenge: transport

As 3D models increase in size, another fundamental limitation emerges.

Cells need oxygen and nutrients, while metabolic waste products must be removed. In small structures, transport can occur predominantly by diffusion. However, as the distance between cells and the surrounding medium increases, oxygen and nutrient gradients develop, and hypoxic or even necrotic regions may appear inside the 3D construct.

Insufficient transport is a well-recognized limitation of larger 3D tissue models. In certain bioprinted hydrogel constructs, practical diffusion limits for nutrient and gas exchange are on the order of hundreds of micrometers. In a recent protocol for organ-scale 3D bioprinting, the authors use a range of approximately 200–300 µm. They also emphasize the need to design structures that keep cells within this transport distance, for example through channels or porous architecture [5].

This also matters experimentally. Hypoxia or cell death within a model may not reflect a property of the tissue or disease being studied. Instead, it may be an artifact of the culture system itself.

A larger, biologically more complex model therefore needs more than correctly positioned cells.

It needs a solution for transport.

Vascularization: from structure to a functional system

In the body, the vascular system addresses this challenge. Vascularization not only supplies oxygen and nutrients and removes metabolites; through endothelial and perivascular cells, it also contributes to tissue homeostasis and communication with surrounding cells. Establishing relevant microvasculature is therefore a key step in developing more complex 3D models [6].

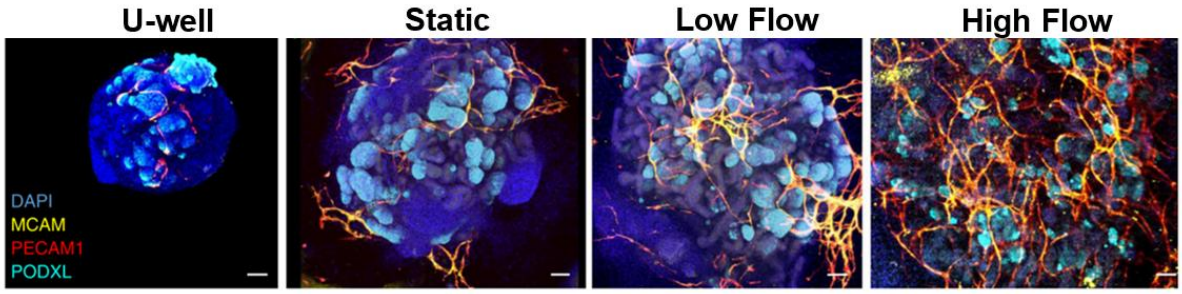


Fig. 6. Effect of flow on organoid vascularization. Microfluidically controlled flow influences the development of vascular networks; in the model studied, higher flow resulted in more extensive vascularization than static conditions. Adapted from Strobel et al., 2023 [6].

This is where biofabrication, organoid culture and printing technologies, microfluidics, and vascular biology converge. Current approaches combine vascularization, 3D bioprinting, and perfusion systems to create not only vascular structures but also functional transport within the model [7].

For example, Advanced Solutions combines its BioAssemblyBot platform with Angiomics Human Microvessels—fragments of intact human microvessels that can be pipetted or bioprinted into a 3D model and used to develop microvascular networks [8].

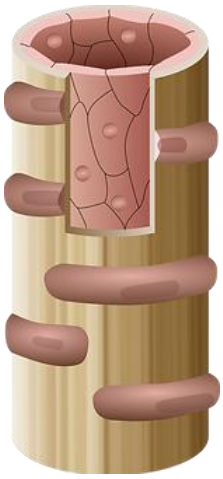


Fig. 7. Angiomics Human Microvessels—fragments of intact human microvessels for vascularizing 3D models. They retain the structure and cellular composition of the original microvessel, including cells of the perivascular niche, and can form interconnected microvascular networks after incorporation into a 3D culture. Source: Advanced Solutions [8].

At this point, the original question—"why print?"—takes on another dimension. It is no longer only about the shape of a tissue, but about designing an environment in which individual biological components can grow, communicate, and form a functional system of living structures.

Bioprinting does not end when printing is complete

As 3D models become more complex, the role of the bioprinter also changes. Creating a structure is no longer sufficient: an experiment may involve multiple materials, cell populations, and additional steps during cultivation.

The BioAssemblyBot therefore integrates bioprinting with robotic handling and automation. Interchangeable tools allow different operations to be combined within a single workflow, while BioApps Maker can link experimental steps into an automated protocol [9].

DESIGN → BUILD → CULTURE → ANALYZE

Let biology grow—and give it structure

The purpose of bioprinting is not to replace the natural self-organization of cells. Its strength lies in combining both principles: biology generates complexity, while engineering adds control over space, architecture, and experimental conditions [10]. Not to prevent cells from organizing themselves, but to determine where and under what conditions that organization takes place.



Fig. 8. Interchangeable BioAssemblyBot Hands extend the capabilities of the BioAssemblyBot platform beyond 3D bioprinting alone. Different tools allow printing, dispensing, pipetting, scanning, and object manipulation to be combined within a single robotic system. Source: Advanced Solutions [9].

References

[1] Zhang D, Huerta-López C, Heilshorn SC. Organoid bioprinting to pattern the matrix microenvironment. Curr Opin Biomed Eng. 2025 Sep;35:100607. doi: 10.1016/j.cobme.2025.100607. Epub 2025 Jun 5. PMID: 40717815; PMCID: PMC12288624.

[2] Zhang Z, Wu C, Dai C, Shi Q, Fang G, Xie D, Zhao X, Liu YJ, Wang CCL, Wang XJ. A multi-axis robot-based bioprinting system supporting natural cell function preservation and cardiac tissue fabrication. Bioact Mater. 2022 Feb 19;18:138-150. doi: 10.1016/j.bioactmat.2022.02.009. PMID: 35387155; PMCID: PMC8961309.

[3] From Scanning to 3D Bioprinting - BAB Does It All, https://www.advancedsolutions.com/post/scanning-to-3d-bioprinting

[4] Zhang Y, Huang Z, Wang B, Li B, Yang Y. Three-dimensional bioprinted organoids: advances and clinical translation. Regen Biomater. 2026 Jun 30;13:rbag142. doi: 10.1093/rb/rbag142. PMID: 42502268; PMCID: PMC13401513.

[5] Qiao T, He C, Xia P, Liu G, Sun Y, Sun M, Wang Y, Cheng Y, Yu M, He Y. Bioink design for organ-scale projection-based 3D bioprinting. Nat Protoc. 2026 Mar;21(3):894-923. doi: 10.1038/s41596-025-01221-0. Epub 2025 Jul 30. PMID: 40739021.

[6] Strobel HA, Moss SM, Hoying JB. Vascularized Tissue Organoids. Bioengineering (Basel). 2023 Jan 17;10(2):124. doi: 10.3390/bioengineering10020124. PMID: 36829618; PMCID: PMC9951914.

[7] Nwokoye PN, Abilez OJ. Bioengineering methods for vascularizing organoids. Cell Rep Methods. 2024 Jun 17;4(6):100779. doi: 10.1016/j.crmeth.2024.100779. Epub 2024 May 16. PMID: 38759654; PMCID: PMC11228284.

[8] A Genuine Vascularization Solution**,** https://www.advancedsolutions.com/microvessels

[9] Can I get a hand?, https://www.advancedsolutions.com/bioassemblybot-hands-overview

[10] Huang, M.S., Christakopoulos, F., Roth, J.G. *et al.* Organoid bioprinting: from cells to functional tissues. *Nat Rev Bioeng* **3**, 126–142 (2025). doi: 10.1038/s44222-024-00268-0