

# Using biofabrication to integrate multi-scalar architecture into tissue engineered constructs

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Replicating the composition and structure of natural tissues using cell-laden hydrogel constructs is considered a highly promising strategy for developing functional tissue replacements. The formation, maturation, and maintenance of native tissues rely on a variety of dynamic processes, where cells experience precisely regulated physical and chemical cues over time and space. These interactions play a crucial role in tissue development. However, despite notable progress in tissue engineering and regenerative medicine, current approaches still struggle to replicate these intricate, dynamic processes at a scale suitable for clinical applications.

In recent decades, biofabrication has seen significant advancements, leading to the development of cutting-edge technologies that offer precise spatial control in the fabrication of both acellular biomaterials (biomaterial inks) and cell-laden hydrogel-based materials (bioinks). These innovations have been instrumental in creating constructs that more accurately mimic the native tissue microenvironment. This presentation will highlight recent research from my laboratory that explores sacrificial biofabrication techniques for generating highly organized, high-resolution structures within large hydrogel constructs. Additionally, I will introduce novel programmable sacrificial bioinks designed to enable spatial and temporal control over architectural features during fabrication.

Our work integrates multiple biofabrication techniques, such as extrusion, lithography, and volumetric approaches, applied to various hydrogel-based biomaterials. A key breakthrough in this research is the development of a dynamic bioinks with programmable physio-mechanical properties. This feature allows either precise control over the timing of architecture introduction into hydrogel constructs, or dynamically stiffening the microenvironment of the hydrogel over time. Specifically, the dynamic properties better recapitulate the native dynamic matrix remodelling process, able to dictate and influence cell function.