Scientists bioprint tissue-like constructs capable of controlled, complex shape change

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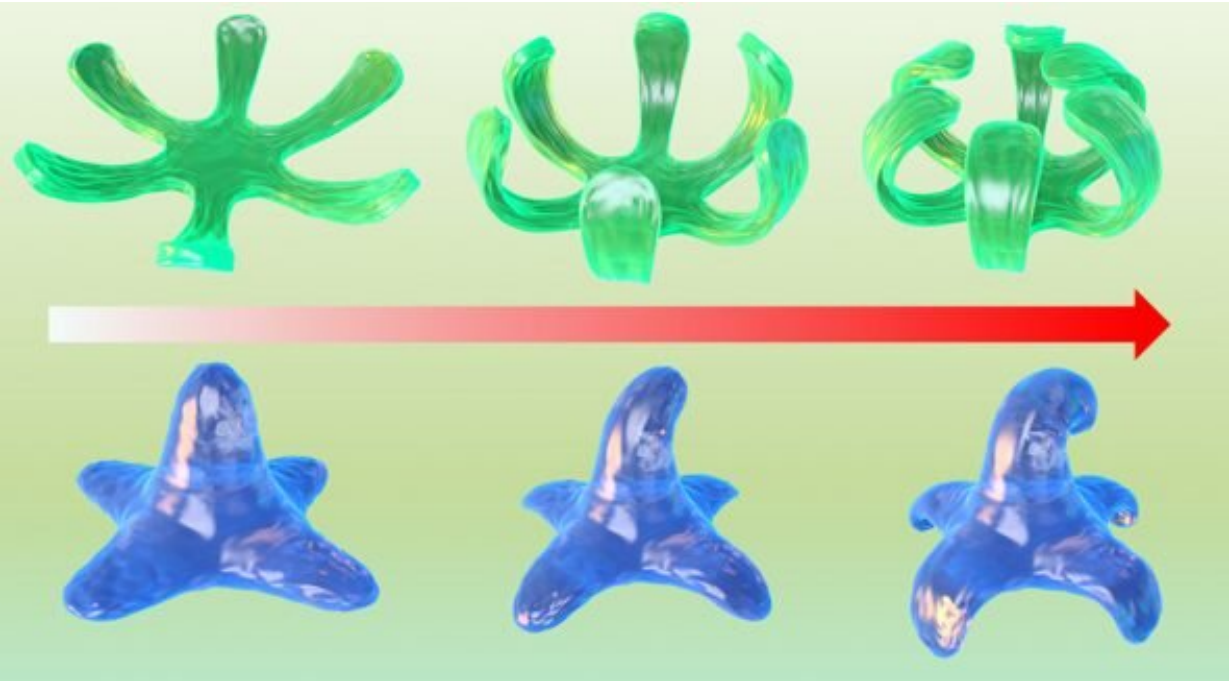

Bioprinted cell-rich bioconstructs showing controlled, complex 4D shape transformations. Credit: Eben Alsberg and Aixiang Ding

Where standard 3D printing uses a digital blueprint to manufacture an object out of materials like plastic or resin, 3D bioprinting manufactures biological parts and tissues out of living cells, or bioinks. A fourth dimension—shape transformation over time—can be achieved by incorporating materials that enable printed constructs to morph multiple

times in a preprogrammed or on-demand manner in response to external signals.

Bioprinting 4D constructs provides opportunities for scientists to better mimic the shape changes that occur during the development, healing and normal function of real tissues and fabricate complex structures.

A new study in the science journal *Advanced Materials* describes the development of a new cell-laden bioink, comprised of tightly-packed, flake-shaped microgels and living cells, for bioprinting 4D constructs. This new system enables the production of cell-rich bioconstructs that can change shape under physiological conditions.

Titled "Jammed Micro-Flake Hydrogel for Four-Dimensional Living Cell Bioprinting," the study is authored by engineers at the University of Illinois Chicago who created the bioink and conducted experiments of prototype hydrogels.

Their experiments resulted in a variety of complex bioconstructs with well-defined configurations and high cell viability, including a 4D cartilage-like tissue formation. Further designs demonstrate complex, multiple 3D-to-3D shape transformations in bioconstructs fabricated in a single printing.

"This bioink system provides the opportunity to print bioconstructs capable of achieving more sophisticated architectural changes over time than was previously possible. These cell-rich structures with pre-programmable and controllable shape morphing promise to better mimic the body's natural developmental processes and could help scientists conduct more accurate studies of tissue morphogenesis and achieve greater advances in tissue engineering," said study corresponding author Eben Alsberg, Richard and Loan Hill Chair, who has appointments in the departments of biomedical engineering, mechanical and industrial

engineering, pharmacology and regenerative medicine, and orthopedics.

Alsberg says the bioink advances previous technologies in several ways.

"The bioinks have what are called shear-thinning and rapid self-healing properties that enable smooth extrusion-based printing with high resolution and high fidelity without a supporting bath. The printed bioconstructs, after further stabilization by light-based crosslinking, remain intact while—for example—bending, twisting or undergoing any number of multiple deformations. With this system, cartilage-like tissues with complex shapes that evolve over time could be bioengineered," Alsberg said. "Another key achievement was engineering a system that enables fabrication of bioconstructs capable of undergoing complicated 3D-to-3D shape transformations."

"This is the first system that meets the demanding requirements of bioprinting 4D constructs: Load living cells in bioinks, enable printing of large complex structures, trigger shape transformation under physiological conditions, support long-term cell viability and facilitate desired cell functions such as tissue regeneration," said Aixiang Ding, postdoctoral research associate at UIC and the first author of the paper. "We are endeavoring to translate this system into clinical applications of tissue engineering, as there is a critical shortage of available donor tissues and organs."

UIC's Oju Jeon, David Cleveland, Kaelyn Gasvoda, Derrick Wells and Sang Jin Lee are co-authors of the paper.

More information: Aixiang Ding et al, Jammed Micro-Flake Hydrogel for Four-Dimensional Living Cell Bioprinting, *Advanced Materials* (2022). DOI: 10.1002/adma.202109394