Interfacial transport

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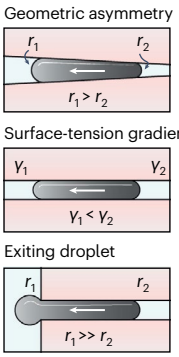
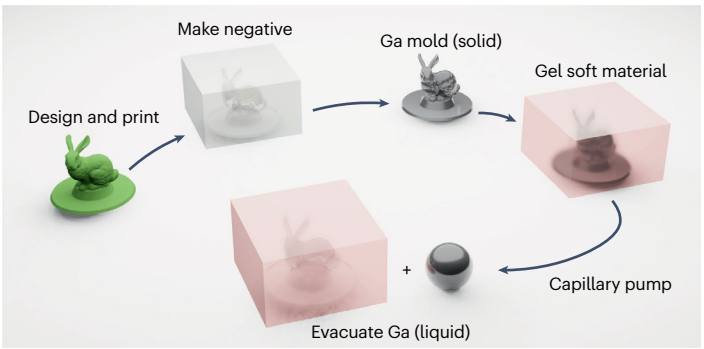
Molding multiscale biological structures via capillary action





The biological functions of natural tissues are regulated by the multiscale arrangement of cellular and extracellular material. Engineering biological tissues, therefore, requires a process design that aims to replicate these structures across multiple length and time scales. 3D printing techniques, such as two-photon lithography, can print complex architectures with biomaterials such as hydrogels, but cannot currently be used with natural extracellular matrices. Alternatively, sacrificial-template-based molding has been largely used with extracellular matrices, but current processes operate at a specific target length scale. Thus, a key challenge is developing a template that can provide the desired accuracy of complex shapes spanning different length scales without undermining the structural integrity of the soft biological materials.

Now, Christopher Chen, Subramanian Sundaram and co-workers report the use of gallium (Ga)-based engineered sacrificial capillary pumps for evacuation (ESCAPE) during the molding process to produce complex shapes in soft natural hydrogels, operating across both the cellular scale (micrometers) and millimeter scale. The authors stress the importance of deploying Ga as a templating material due to its specific properties; a melting point (approximately 30 °C) close to the temperature of cell cultures allows it to be used as both an injectable liquid and solid cast, while a tunable surface oxide layer allows for capillary action to drive the demolding process.

Unidirectional capillary pumping of liquid Ga is driven by a Laplace pressure gradient in the natural hydrogel channel, where the Laplace pressure is $2\gamma/r$, where γ is the surface tension and r is the radius of curvature. The capillary-driven evacuation can be caused by either a channel asymmetry or a gradient in the surface tension. The authors note that to avoid potential Ga droplet entrapment inside the soft gel channels, the surrounding material's elastic modulus must be greater than $3\gamma/r$.

The overall process consists of the following steps. First, the desired structure is designed and printed, followed by negative molding with a soft elastomer (here, polydimethylsiloxane). The method and materials used for the first two steps do not affect the final result of the overall methodology. Subsequently, liquid Ga is fed into the negative mold to generate the cast. The desired extracellular matrix is then polymerized around the Ga cast and, finally, the Ga is liquefied and pumped out via unidirectional capillary action. The authors applied this exciting methodology to fabricate hierarchical vascular trees and epithelial ducts, demonstrating its capabilities in accurately reproducing fine features at around 10–50 µm, up to the millimeter scale.

The ESCAPE method represents an important advance in both the precision and stability of fabrication in biomimetic tissue engineering. This approach could potentially open new avenues for developing biologically based tissues that closely replicate the functions and structural complexities of natural organs by facilitating the creation of multiscale biological forms in natural extracellular matrices.

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