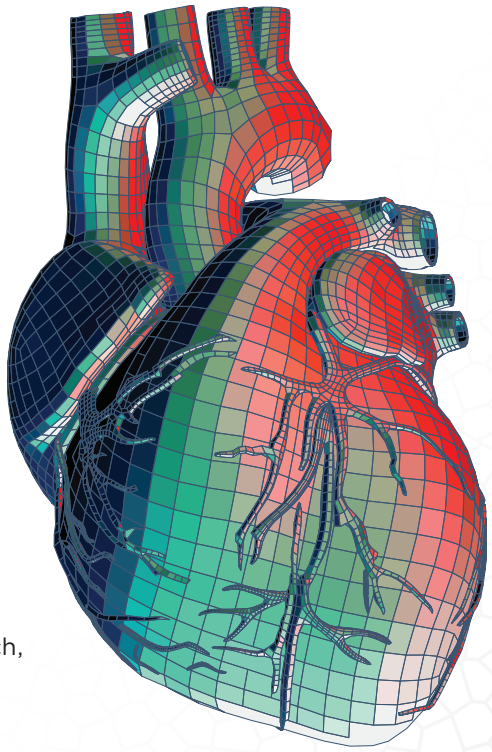
FLUIDFORM™
THE REGENERATIVE MEDICINE COMPANY

THE PATHWAY TO ENGINEERING TISSUE AND ORGANS

BACKGROUND



Ubiquitous availability of human tissue for drug discovery, surgical repair, and organ replacement will fundamentally transform human health. Cardiovascular disease alone accounts for 18 million deaths globally per year with organ transplantation representing a curative, but highly limited therapy. Billions of dollars are spent on the development on drugs that ultimately fail in expensive late-stage human clinical trials, typically from toxicity to the liver, heart, or kidneys.

The ability to generate tissues and eventual organs will revolutionize medicine. Drugs could be tested on human tissue before expensive clinical trials while damaged or diseased organs can be repaired or replaced. Many attempts have been made using classic manufacturing techniques to build tissue, however they cannot recapitulate its immense 3D structural complexity. Where traditional methods failed, 3D printing is able to create complex geometries that are impossible otherwise. Successful tissue fabrication is dependent on the simultaneous success of 3D printing, synthetic and stem cell biology, advanced materials science, AI and more. After over a decade of research, it has become apparent that there are key tissue engineering challenges that we must overcome to build tissues for research, repair, and replacement. These challenges are:

1. Creating tissues using the materials that are native and recognizable to the human body.
2. Printing tissues with an assembly method that can recapitulate the complex structures of the body.
3. Printing tissues that can develop function similar to native counterparts.
4. Scale the printing method to make clinically relevant sized tissues.

The first challenge alone has presented enough of a roadblock to prevent researchers from tackling the subsequent ones. This is due to how the typical 3D printing of thermoplastics does not translate effectively to printing the soft proteins that make up the human body. Researchers have been forced to make such huge compromises to their bioprinting materials and structure that achieving functional tissues has remained beyond reach.

Research has shown that without improved biofabrication methods, advances in related fields such as developmental and synthetic biology, robotics, and others will ultimately fall short of being able to manufacture human tissue. **FluidForm's FRESH printing technology solves this problem and subsequent challenges, ushering in the next generation of medicine.**

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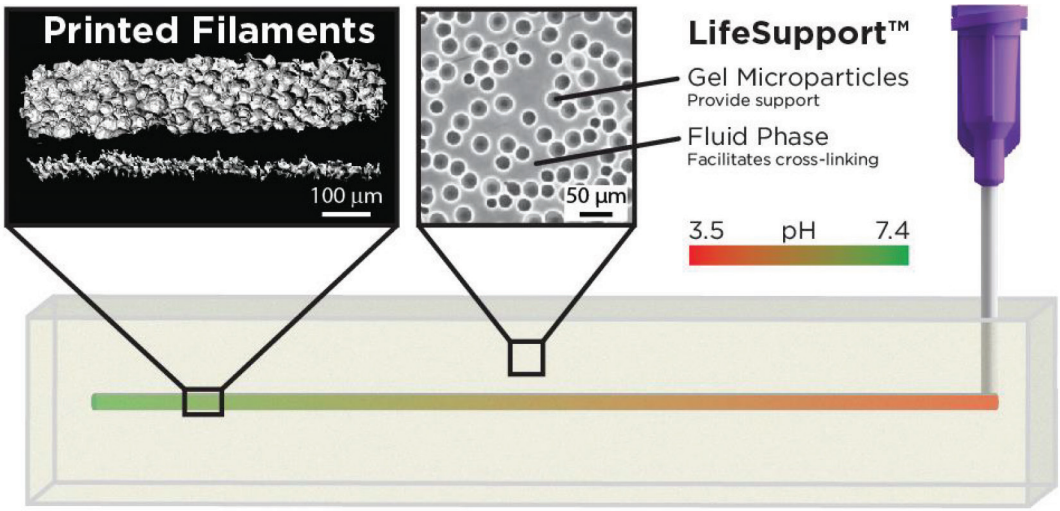
FRESH

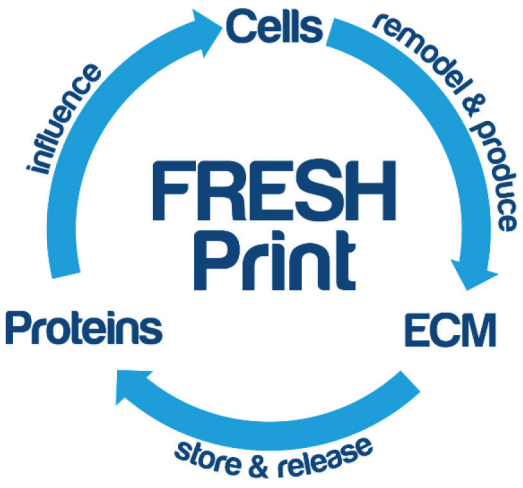
By modifying the bioprinting environment instead of the material, FluidForm can 3D print the proteins and cells native to the human body at high resolution. FRESH stands for Freeform Reversible Embedding of Suspended Hydrogels. The key innovation with FRESH is printing inside a sacrificial support bath instead of open air. Printing into a support bath physically maintains the positions of the soft proteins and cells while they gel into the proper shape without deforming.



HOW FRESH SOLVES THE 4 MAJOR CHALLENGES

1) USE THE RIGHT MATERIALS:

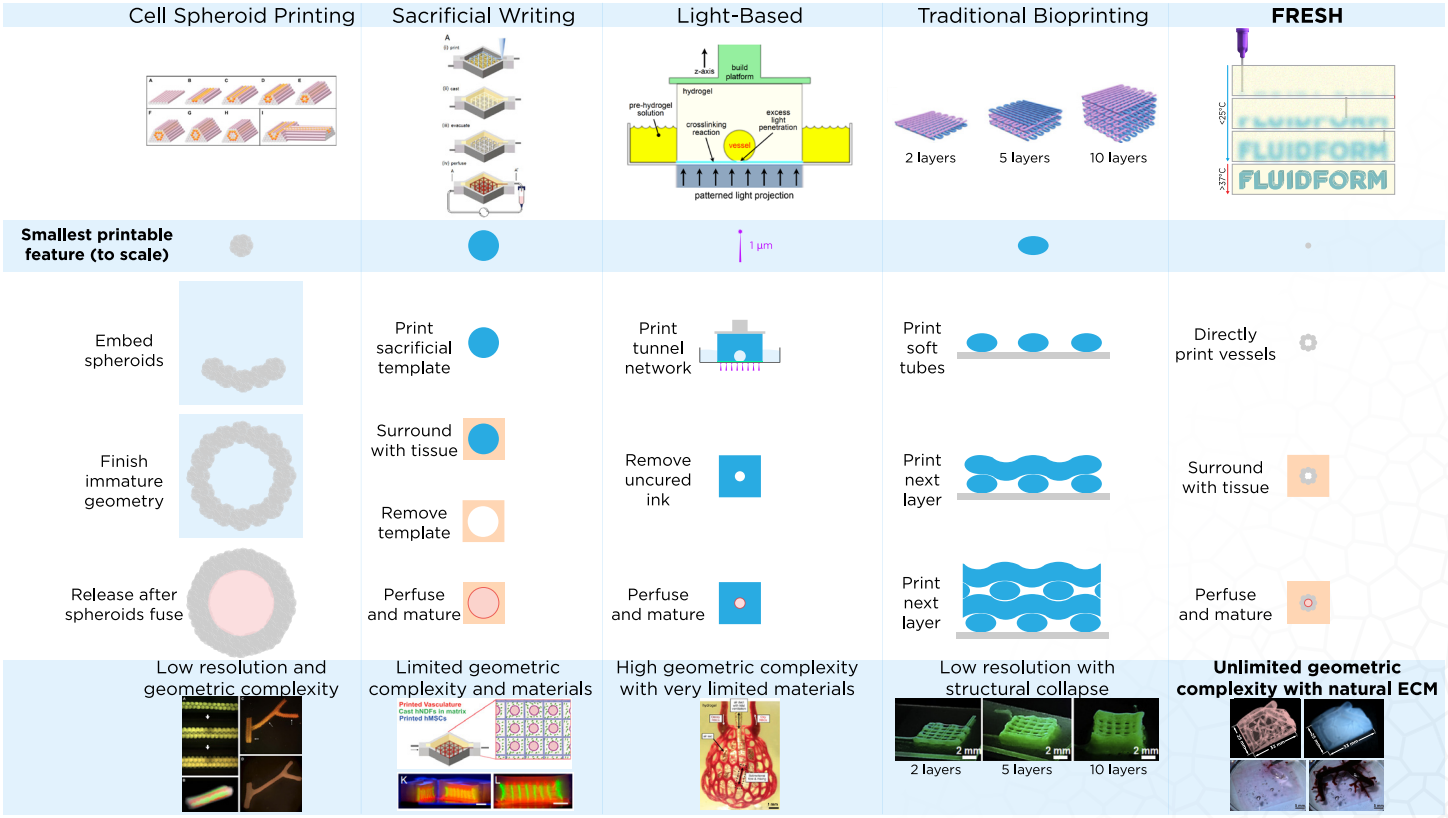
There are a litany of cells and proteins in every single tissue of the body. There is an interdependent relationship between cells, signaling molecules, and the extracellular matrix (ECM) that surround cells. Historically, bioprinters modified materials to be printable in air, compromising their physiological relevance. Instead of the UV light and high temperature that legacy bioprinting techniques use, **FRESH allows FluidForm to print cells and ECM proteins by using the gelation chemistry of the body** (ionic, pH, enzymatic). Not only can these materials and cells all be printed together, they can be additionally functionalized with other proteins that help guide a tissue to develop properly.



2) USE THE RIGHT ASSEMBLY METHOD:

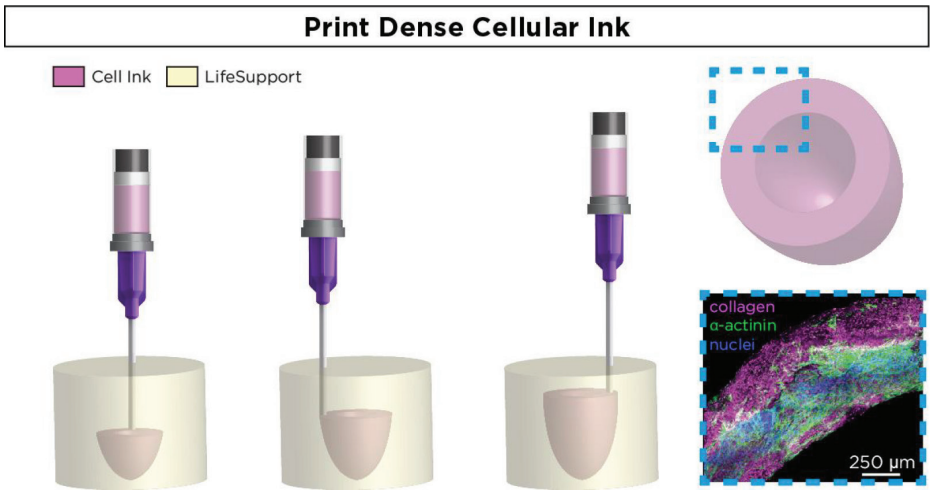
Structure and function are highly intertwined throughout biology. For there to be proper tissue function, there must be proper tissue structure such as the alignment of muscle fibers. Bioprinters must also be able to assemble the materials the same way the body builds with them from the ground up. FRESH is capable of achieving both control over spatial alignment, as well as printing soft deformable materials, without modifying them, at high resolution. Using FRESH, chemistries that were previously impossible to print become possible. This is due to the bioink-support bath interface that allows for chemical interactions to occur, like pH changes, that are not possible in open air. Collagen, the major structural protein of the human body, can now be assembled and aligned in any 3D shape by causing it to undergo pH-triggered gelation when FRESH printed. **This allows FRESH to be the only way to assemble the most physiologically relevant cells and materials into any geometry.**

Comparison of Traditional Bioprinting Methods to FRESH



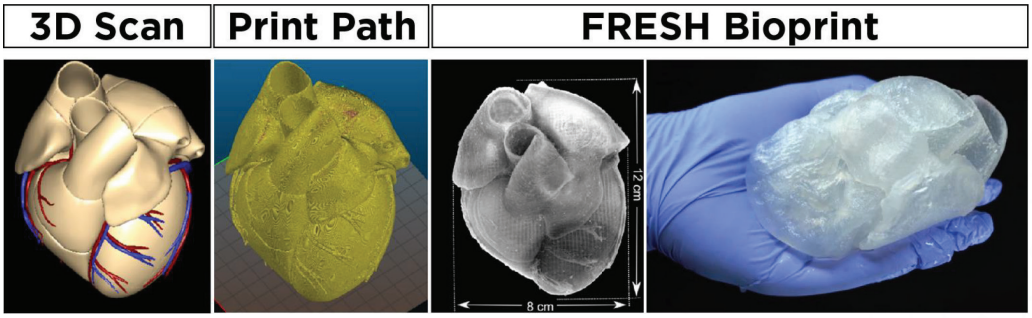
3) DEVELOP THE RIGHT FUNCTION:

The ultimate goal of 3D bioprinting is to create functional tissue, and at FluidForm one of those is contractile heart muscle. Just like the tissues of the body, engineered tissues need to have high cellular density to achieve native functionality. Traditional bioprinters fail here in two key ways. First, they dilute their bioinks with additives to make them more rigid in air. Second, these bioinks have a very low cell density compared to tissues in the body, as a huge portion of the material must be a thickener to give the print any structure. FRESH allows for bioprinting bioinks with over ten times the cell density of traditional bioinks, as cells can make up the vast majority (>90%) of the material printed. The end result is the printing of heart muscle tissue so dense, aligned, and large, it begins to beat like the native heart. **Printing cell dense materials allows FluidForm to build tissues that develop a next level of function for drug testing and regenerative medicine.**



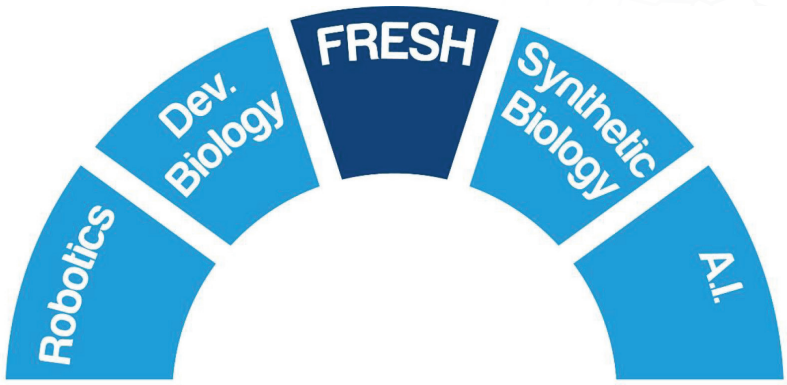
4) SCALE TO ORGAN SIZE:

It is critical that a bioprinting method's core technology can expand from the scale of 1 cm^3 required for biopharma tissue models to greater than 1 L^3 required for implantable tissue. Traditional bioprinters cannot build structures bigger than a postage stamp, **FRESH has already been scaled to organ size, demonstrated by printing a full-scale heart model**. With FRESH the limiting factor to printing organ-sized tissues is not the printer, but culturing enough cells.



CONCLUSION

FluidForm's FRESH technology overcomes core challenges to the future building of tissues and organs, providing a resolution ten times higher than traditional extrusion-based bioprinting methods while using cells and materials native to the human body. FRESH already allows for the assembling of tissues with such high cell density as to generate spontaneous function for improved drug testing and tissue replacement. By bridging the gap between biology and manufacturing, FluidForm is positioned to build tissues for drug discovery, surgical repair, and organ replacement



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