properties. Therefore, new methods that can tailor the physicochemical properties at both cell and tissue levels independently would be useful. Recently, one study described the engineering of composite fibers with a mechanically strong core from synthetic polymers covered with a layer of cell-laden hydrogel (Figure 1F) [11]. Upon their assembly, both the mechanical properties of the constructs and the distribution of cells could be controlled at the same time. The mechanical properties of these constructs, like tensile stress, tensile strength, Young's modulus, and elongation at break, could be easily tailored across several orders of magnitude to match the values for various tissues. In addition, the presence of a hydrogel layer, which could be tailored independently, created the opportunity to optimize its characteristics without affecting the properties of the entire construct.

The multistep fabrication of these composite fibers creates the opportunity to add functionalities to the engineered tissue. For example, the polymeric fibers can be used for controlled release of biological factors and cues to direct cellular growth and differentiation [12]. To this end, drug-eluting polymer-based sutures have been engineered that could be employed for many tissue engineering applications.

Envisioned Future Opportunities for the Use of Textile Platforms in Tissue Engineering

Overall, fiber-based technologies have emerged as a strong tool for various tissue engineering applications that can address many of the unmet needs in the field. It is expected that the similarity of braided and woven constructs to native muscle, tendon, ligament, and myocardium will eventually generate functional musculoskeletal tissues and cardiac patches. The combination of these technologies with advanced biomaterials will enable the development of more advanced scaffolds and engineered tissues. The possibility of tuning tissue-level properties independently of cell-level properties by using composite fibers and simultaneously controlling and directing cellular distribution, growth, and alignment is a unique capability that is essential for engineering load-bearing and highly organized tissues such as muscle, cardiac tissue, and ligaments.

In addition, along with advances in the field of flexible electronics and in fabricating electrical systems on nonconventional platforms, smart fibers can be engineered that can stimulate better tissue formation or subsequent monitoring of cellular function in culture [13]. Such characteristics could be important for engineering tissues such as cardiac and muscle tissues whose function depends on their electrophysiological activity. These aims can be achieved by engineering composite fibers with multiple independent compartments and their assembly using textile processes.

Fibers and textile technologies can also be used in regenerative medicine and cell therapies as drug and cell carriers. Similarly, textile technologies can be used in regenerative medicine through engineering advances of surgical meshes with regenerative properties.

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Special Issue: Biofabrication

Forum

Towards Single-Step Biofabrication of Organs on a Chip via 3D Printing

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Organ-on-a-chip engineering employs microfabrication of living

tissues within microscale fluid channels to create constructs that closely mimic human organs. With the advent of 3D printing, we predict that single-step fabrication of these devices will enable rapid design and cost-effective iterations in the development stage, facilitating rapid innovation in this field.

Goal of Organ-on-a-Chip Engineering

Organs on a chip are microengineered tissues cultured within microfluidic devices that serve as bioreactors [1]. These systems are specifically designed and fabricated to mimic the structure of human tissues better than current models, which largely rely on traditional static 2D systems. The field has seen recent success in modeling the blood–brain barrier, lung, intestinal ('gut on a chip'), and cancer tissue. These systems can ultimately be used to better understand human organs and disease, screen drugs for safety and efficacy, and generate replacements for damaged or diseased organs.

3D printing has demonstrated a strong promise to revolutionize numerous fields, including microfluidics and tissue engineering research, by enabling rapid, versatile, and customizable fabrication of a multitude of different objects (Box 1). Here we discuss recent progress using 3D printing in two fields relevant to organ-on-a-chip engineering–microfluidics and tissue engineering–as well as the potential to apply 3D printing to single-step fabrication of organ-on-a-chip devices.

3D-Printed Microfluidics

Traditionally, microfluidic devices are fabricated using UV lithography to generate a master of raised structures and soft lithography to create an imprint of those structures in an elastomer such as polydimethylsiloxane (PDMS) followed by a bonding step to seal the imprint to a glass slide, creating microfluidic channels. However, this approach requires several labor-intensive steps and specialized equipment, making the process inaccessible for many research laboratories and preventing rapid iteration of designs.

3D printing for microfluidic device fabrication takes advantage of the capabilities of 3D printing to rapidly generate microscale fluid channels within a few hours using simple, user-friendly equipment such as commercially available 'desktop-style' 3D printers [2]. This approach facilitates a rapid iterative design and fabrication process and improves interdisciplinary accessibility to microfluidics-based research, which may accelerate innovation in organ-on-a-chip engineering.

Further, 3D printing allows fabrication of 'truly 3D' channel geometries; that is, fluid channels with 3D complexity in contrast to the traditional '2½D' devices in which 2D channel designs are simply projected into the third dimension. Added 3D complexity can facilitate additional microfluidic capabilities, such as more efficient micromixing [3].

Several types of 3D printers have been proposed for printing microfluidic chips. Stereolithography uses a liquid resin material that is readily removed from the channels post-printing, but the channel resolution is limited with this method. By contrast, extrusion printing offers high resolution but requires the use of support materials that must be removed post-printing; sacrificial support materials have been employed to address this challenge.

The biocompatibility of 3D-printed microfluidic platforms is a critical challenge when moving toward organ-on-a-chip devices, necessitating the use of printable materials that are nontoxic and, for some applications, facilitate cell attachment on the printed surface. Biocompatible materials are available and have been demonstrated in several studies to facilitate cell culture of 3D micropatterned cellular constructs [4] and dental pulp stem cells [5] for tissue engineering applications.

There has also been a push toward a 'body on a chip' in which multiple organs are organized on a single chip to better model the multiorgan interactions that occur *in vivo*. In this respect, microfluidic circuits may be 3D printed and later seeded with cells or bioprinted with a cell lining to mimic human vasculature.

3D-Printed Living Tissues within Microfluidic Devices

Bioprinting is an extension of 3D printing in which living cells are mixed with scaffold materials to create a 'bioink' that is then deposited into a 3D construct; this has been applied to a range of tissues [6–8]. Bioprinting offers the ability to create a 3D biomimetic tissue by patterning cells and, in some approaches, multiple cell types with precise and reproducible spatial control. Several approaches have been proposed,

Box 1. 3D Printing Technologies

3D printing uses a computer-aided design model to deposit materials layer by layer, generating a 3D structure. Two of the most common types of 3D printing are stereolithography and extrusion-based printing. Stereolithography uses a photocurable liquid resin material that, on exposure to UV light, solidifies into a solid material. UV light is applied using either a laser in a raster pattern or digital light projection to expose each 2D layer, iterated in a layer-by-layer fashion to generate a 3D structure.

Extrusion-based bioprinting involves depositing a material either in a continuous filament (fused deposition modeling) or in droplets (inkjet printing) to generate each layer. Hybrid approaches combine multiple categories of printing. One example is the polyjet 3D printing approach (commercialized by Stratasys Ltd), which involves inkjet printing of a photocurable material that is solidified by UV flood exposure after each layer is deposited. Interesting applications include 3D printing of microfluidic devices as well as living tissues.

3D printing is also referred to as rapid prototyping because it enables quick succession of model generation, testing, and redesign. From this perspective, 3D printing will serve as a powerful tool in the coming years to facilitate rapid innovation in several fields, including organ-on-a-chip engineering.