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Textile Processes for Engineering Tissues with Biomimetic Architectures and Properties

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Abstract

Textile technologies, in which fibers containing biological factors and cells are formed and assembled into constructs with biomimetic properties, have attracted significant attention in the field of tissue engineering. This article highlights the most prominent advancements of the field in the areas of fiber fabrication and construct engineering.

Keywords

Biofabrication; Textile technologies; Fiber-based techniques; Biomaterials; Scaffolds; Tissue engineering

Directing cellular growth with functional tissues

Engineering functional tissues requires fabricating constructs that can provide suitable biological, chemical, mechanical, and architectural features to direct cellular growth. Many human tissues, such as musculoskeletal, cardiac, and connective tissues, possess a fibrillar architecture that offers interesting physical characteristics such as anisotropic mechanical properties [1]. Thus, engineered fibrous constructs can potentially recreate these characteristics. Such structures can be potentially generated using direct-write bioprinting and textile processes [2]. These technologies can also create finely tuned patterns, which are essential for creating highly organized tissues such as different muscles.

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In direct-write printing, polymeric or hydrogel fibers are extruded through a nozzle and deposited in a predefined pattern to form a construct [3]. In textile processes, these fibers are fabricated and then assembled into 2-dimensional (2D) fabrics and 3-dimensional (3D) constructs with tunable properties. Textile-based constructs were first used in tissue engineering to fabricate scaffolds with tailored mechanical properties [2]. For example, 3D weaving strategies have been developed to create constructs with properties similar to native cartilage (Figure 1a). Such porous engineered composite scaffolds uniquely combine the potential for load-bearing and cell-based tissue regeneration after implantation [4].

Fabricating cell-laden fibers

To be able to control the cellular distribution and physical properties, cell-laden fibers should be used during the assembly process [5]. Among different biomaterials used as cell-carriers, hydrogels, which are 3D polymeric networks with high water content, provide a nurturing environment for cellular growth and maturation [6]. Thus, cell-laden hydrogel fibers with different morphologies and from a number of materials, have been fabricated using wet spinning, microfluidic spinning, and interfacial complexation [7]. In all of these processes, the pre-polymer is exposed to the crosslinking reagent to quickly form solid fibers. However, natural polymers and protein-based materials are not usually rapidly crosslinkable. Thus, strategies based on sacrificial templates have been proposed for engineering protein-based fibers (Figure 1b) [8]. In these methods, the targeted protein solution is either surrounded by a sacrificial sheath or mixed with a rapidly but reversibly crosslinkable hydrogel such as alginate. Once the template is formed, the entrapped proteins will be crosslinked, and the sacrificial template can be removed to leave a hydrogel fiber. These techniques have been successfully employed to fabricate stable protein-based fibers [8].

Another challenge in the direct-write printing of constructs is controlling the distribution of encapsulated cells or biological factors. Thus, platforms for creating coded fibers have been engineered and can be connected to multiple pre-polymer sources. Their flow rates were adjusted by computer-controlled valves such that the targeted compound can be positioned at any arbitrary location within the fiber (Figure 1c) [9]. This spider-inspired microfluidic platform could also fabricate multi-material fibers with different topographies.

Textile processes in modular tissue engineering

Textile processes are two-step methods, in which fibers are first formed and then assembled into constructs. Creating patterns of different cells and biological factors is easier using this method than with 3D printing because multimaterial printing methods are not well established. Fibers serve as the building blocks (modules) of the engineered fabrics and can be provided with various functionality that could later be incorporated into the fabricated constructs. Compared with 3D printing, textile processes, including braiding, weaving, and knitting, can simultaneously tune mechanical properties and control the distribution of various compounds/functions [1]. Mechanically strong fibers have been fabricated from synthetic polymers and have been loaded with drugs and growth factors. These fibers have been assembled into 3D scaffolds with biomimetic physical properties for applications such

as muscle, tendon, ligament, blood vessel, and skin tissue engineering. Furthermore, the fiber topography can direct cellular growth and orientation in the construct once seeded with cells [9]. However, in these scaffolds, the cellular distribution cannot be controlled.

Hydrogels are excellent cell carriers for engineering many soft tissues, but their ultimate tensile strength is often low. Thus, their assembly using textile processes has been challenging. There are only a few examples of successful fabrication of fabrics from hydrogel fibers. In one example, Onoe *et al.* designed a microweaving machine to weave cell-laden hydrogel fibers (Figure 1d) [10]. In another example, hydrogel fibers were reinforced with sacrificial alginate templates that could withstand mechanical stress applied during weaving and braiding and thus fabricated constructs with clinically relevant dimensions (Figure 1e) [8]. The extensive efforts for engineering cell-laden hydrogel fibers and then assembling them using textile processes has also failed to address these key challenges because hydrogels are not mechanically strong to withstand the applied stresses during the fabrication process. Furthermore, engineered constructs are too soft to offer mechanical strength comparable to human musculoskeletal tissues (ultimate tensile strength >10-1000 MPa).

Thus, polymeric fabrics with proper mechanical strength should somehow be mixed with hydrogels that support 3D cellular growth. The properties of niches suitable for cellular growth and function can be different from the tissue-level mechanical properties. Therefore, new methods that can tailor the physicochemical properties at both the cell and the tissue levels independently would be useful. Recently, one study described engineered 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 multi-step 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]. Toward 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 independent 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, and ligaments.

In addition, along with the advancements in the field of flexible electronics and in fabricating electrical systems on non-conventional platforms, smart fibers can be engineered that can stimulate better tissue formation or subsequent monitoring the 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 surgical meshes with regenerative properties.

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Figure 1.

Various platforms for engineering cell-laden fibers and constructs. (a) 3D woven scaffolds for cartilage tissue engineering. (i) Fluorescent image of a freshly seeded construct. (ii-iii) Architecture of a typical woven structure formed by interlocking multiple layers of two perpendicularly oriented sets of in-plane fibres in the z-direction; cross-sectional view of the Y–Z plane (ii); cross-sectional view of the X–Z plane (iii) [4]. (b) The use of sacrificial alginate templates for engineering protein-based hydrogels. Schematic of fiber fabrication platform (i) and the fiber formation process (ii). Typical fabricated alginate-protein (gelatin methacryloyl) hybrid fibers Alginate: GelMA (2%:10% w/v) (iii) and GelMA (10%) after alginate removal showing that the overall shape and geometry was presented (iv) [8]. (c) A biomimetic platform for engineering coded fibers (i). Micrographs showing multicomponent fibers (ii), (iii). Fabricated grooved hydrogel fibers for guiding cellular growth (iv) [9]. (d) A microweaving machine for the fabrication of hydrogel-fabrics (i) and a typical fabricated hydrogel fabrics (ii) [10]. (e) centimeter scale hydrogel fabrics with predefined patterns formed using a weaving machine [8]. (f) Fabrication of composite fibers by coating a polymeric fibers with a layer of cell-laden hydrogel (i). A typical composite fiber by two separate layers of microbead-laden hydrogel (ii). Micrograph showing a typical braided construct from composite fibers (iii) [11].