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Journal of Computational Design and Engineering 3 (2016) 385–397

www.elsevier.com/locate/jcde

Geometric and mechanical properties evaluation of scaffolds for bone tissue applications designing by a reaction-diffusion models and manufactured with a material jetting system

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Received 25 July 2015; received in revised form 17 June 2016; accepted 26 June 2016
Available online 30 June 2016

Abstract

Scaffolds are essential in bone tissue engineering, as they provide support to cells and growth factors necessary to regenerate tissue. In addition, they meet the mechanical function of the bone while it regenerates. Currently, the multiple methods for designing and manufacturing scaffolds are based on regular structures from a unit cell that repeats in a given domain. However, these methods do not resemble the actual structure of the trabecular bone which may work against osseous tissue regeneration. To explore the design of porous structures with similar mechanical properties to native bone, a geometric generation scheme from a reaction-diffusion model and its manufacturing via a material jetting system is proposed. This article presents the methodology used, the geometric characteristics and the modulus of elasticity of the scaffolds designed and manufactured. The method proposed shows its potential to generate structures that allow to control the basic scaffold properties for bone tissue engineering such as the width of the channels and porosity. The mechanical properties of our scaffolds are similar to trabecular tissue present in vertebrae and tibia bones. Tests on the manufactured scaffolds show that it is necessary to consider the orientation of the object relative to the printing system because the channel geometry, mechanical properties and roughness are heavily influenced by the position of the surface analyzed with respect to the printing axis. A possible line for future work may be the establishment of a set of guidelines to consider the effects of manufacturing processes in designing stages.

Keywords: Bone scaffold; Reaction-diffusion models; Additive manufacturing; Porous structures

1. Introduction

Bones are formed by connective tissue with specialized cells as osteocytes, osteoblasts, and osteoclasts immersed in an extracellular matrix composed mainly by minerals (hydroxyapatite), proteins (collagen, cytokines, osteonectin, osteopontin, osteocalcin, osteoinductive proteins, sialoproteins, proteoglycans, phosphoproteins, and phospholipids) and water. Osseous tissue has not only mechanical but synthetic and metabolic roles. Bones must provide protection for internal organs, support and define the shape of mammals and interact with muscles and tendons to generate movement [1]. The synthetic function includes the production of blood cells [2] and the metabolic function is to storage calcium, phosphorus, growth factors and fat [3]. Osseous tissue is prone to suffer multiple conditions triggered by extreme mechanical loads or hormonal insufficiencies, among other causes. In those cases, osseous tissue has a high capacity of healing without scar material [4]. Medical procedures such as immobilization and surgery

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Peer review under responsibility of Society of CAD/CAM Engineers.

http://dx.doi.org/10.1016/j.jcde.2016.06.006

suffice, most of the time, to achieve regeneration. However, about 10% of the cases require the use of additional support such as autografts, allografts or fixation devices to help the healing process [5]. Whereas these procedures require donors, are expensive or imply certain risks, bone tissue engineering is necessary.

Scaffolds, cells seeding and growth factors are the main strategies used in tissue engineering [6]. Considering the mechanical function of bones, scaffolds are a very important component to successfully maintain, replace and improve bone tissue functions when necessary. Particular mechanical properties that characterize bones are modulus of elasticity, tensile strength, fracture toughness, Poisson's ratio, elongation percentage, etc. For all these reasons, scaffolds should be as close as possible to the replaced tissue from a mechanical point of view. This is necessary to avoid problems like osteopenia due to the use of bone grafts that are stiffer than the original bones [7] or new fractures due to low strength.

One of the major objectives of bone tissue engineering is to achieve similar geometries to those of trabecular bone. To date, there are several methodologies for scaffold design based on regular and irregular structures [8]. The most constructive approaches are based on regular arrangements: an internal geometry filled with a periodic distribution of unit cells. Unit cells are constructed with computer-aided design (CAD) tools using design primitives like cylinders, spheres, cones, blocks organized in rectangular or radial layouts [9]. The advantages of such regular porous structures allow for easier modeling, physical simulation and manufacturing. Besides the unit cell approach, there are parameterized models using mathematical functions to generate implicit surfaces with porosity gradients [10]. It should be noted that those methodologies can be complemented by optimization techniques to improve the mechanical strength or permeability [11–16]. Although, periodic or regular porous structures can be relatively sophisticated, they are still limited to represent the structures present in nature [8,11]. On the other hand, irregular structures are obtained from fractal curves or clinical images. For example, space-filling curves, continuous fractal curves that cover domains like planes or tridimensional spaces can create irregular architectures that are not generally achieved in models made with unit cell approaches [17]. Furthermore, variable porous structures can be acquired directly from computed tomography bone scans [18–20]. Finally, designed structures can be fabricated using additive manufacturing methods such as SLA, SLS, FDM, 3D Printing and many others [21].

Although most of the work on bone scaffold modeling is supported on regular porous structures, it is important to consider that some studies show that imposing the same shear stresses might not be adequate for bone scaffold regeneration. Regeneration and remodeling of osseous tissue is not only caused by a high value of stress or strain but also by differences or gradients of those signals in nearby sections of bone tissue [22,23]. This raises the possibility that irregular structures may be better to stimulate tissue regeneration due to less uniform stress distributions than those observed in regular structures. Another possible explanation for the irregular structure visible in trabecular bone is that regular structures have a tendency to exhibit catastrophic failure opposite to irregular structures [24]. As a result, biomimetic design has been introduced and widely used as an alternative method for irregular porous structure modeling. However, a faithful reproduction of the structures present in nature, in most cases, is not strictly necessary: a simpler approach to the achievement of a biomimetic design to mimic tissues or organs functionality is the global variation of porosity of the different regions according to a natural reference model [8,25].

The reaction-diffusion models proposed by Turing [26] are some of the best known and widely used mathematical theories to describe processes of patterns formation in biology. They describe geometric patterns generation from at least two substances called morphogens; these substances have the capacity to diffuse in the environment and react with each other. Compared to other models that only consider diffusion processes, the inclusion of the reaction term between morphogens allows patterns formation regardless of the initial distribution of the substances that generate them [27]. Reaction-diffusion models are used to model behavior pattern formation in living organisms [27,28] and bone formation processes [29–31]. On the other hand, it is possible that reaction-diffusion systems can be implemented in numerical methods to provide faster pattern generation and geometry control than those supported on particle-based methods [32].

This paper explores the modeling of geometric structures by reaction-diffusion models and the geometric and mechanical properties of these structures produced by additive manufacturing processes. For this purpose, porous structures are obtained from a Schnakenberg reaction-diffusion model. Later, those structures are fabricated using an additive manufacturing system and the capacity of these systems to reproduce the modeled geometry is estimated. Finally, structure stiffness is established by measuring its modulus of elasticity. Results show that different geometrical characteristics of porous structures are possible by varying the parameters of the reaction-diffusion system. Additive manufacturing systems can reproduce complex geometries depending on the geometrical feature size; and, the modulus of elasticity is determined by the structure geometry and specific characteristics of the selected manufacturing process.

2. Materials and methods

The design and fabrication process of a porous structure that can be used as scaffold in bone tissue engineering is illustrated in Fig. 1. Based on a reaction-diffusion model, a geometric pattern is generated in a specific domain. In this work, the domains used were cube-shaped, cylindrical or wedge-shaped. More complex shapes that resemble complete bones or portions of them may be used if required. From the pattern obtained, solid (resembling trabeculae) or void (representing pores) portions inside the domain are defined. Once this process is completed, a model of the scaffold geometry is obtained and it can be taken to manufacture using an additive manufacturing process.