



Short communication

Effective method for multi-scale gradient porous scaffold design and fabrication

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ABSTRACT

Function-based modeling is a highly flexible porous scaffold design approach for use in tissue engineering. It was recently proposed as a valid tool for constructing cellular structures by providing a compact representation of complex structures. However, current approaches have some limitations with regard to combining multiple function-based substructures. In this short communication, we propose an effective method for combination operations of multiple substructures based on given substructures and boundaries. With this proposed method, a functional gradient porous scaffold (FGPS) with multi-scale substructures could be easily constructed and directly fabricated by using additive manufacturing techniques.

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1. Introduction

There are two major problems when using conventional CAD-based design for porous structures [1]: (1) the manual operations are time-consuming; and (2) there are limitations with regard to controlling the pore geometry spatial distribution. Thus, function-based scaffold design has attracted interest for tissue engineering.

Considerable effort has been made on function-based scaffold design and fabrication for use in tissue engineering. Yoo proposed an effective method for constructing porous scaffolds using distance field (DF) and TPMS-based functions [1–3]. Melchels et al. [4] analyzed the porous structures and mechanical properties of gyroid and diamond architectures. Kapfer et al. [5] proposed the TPMS-based sheet solids that could provide a relatively high stiffness with a high porosity. The lattice porous structures proposed by Pasko et al. [6] and the cellular structures proposed by Fryazinov et al. [7] were function-based structures for use in tissue engineering. Function-based modeling allows scaffold architectures to be easily described by using a single mathematical inequality (e.g. $\phi(x, y, z) \geq 0$), with freedom to introduce different pore shapes and architectural features, including porosity gradients [8]. As a highly flexible approach, a complex scaffold structure can readily be generated as a CAD file and is suitable for additive manufacturing techniques [2–4,8].

Gradients in pore geometry are recommended for those optimized scaffold structures that are to be used to form multiple tissues and tissue interfaces [3]. In vitro, reduced porosity stimulates osteogenesis by

suppressing cell proliferation and promoting cell aggregation. In vivo, increased porosity results in cell ingrowth.

Although some strategies for simple functional gradient porosities have been proposed [1–8], there remain some limitations with these current approaches: (1) combining multiple function-based substructures for constructing a FGPS was not considered; and (2) transitions between adjacent substructures were not considered. In this short communication, we propose an effective method to overcome these limitations.

2. Material and methods

2.1. Combination operation for FGPS design

Two substructures that are represented by $\phi_1 \geq 0$ and $\phi_2 \geq 0$ can be combined by

$$\phi_c = \phi_1 \oplus_k^{b(x,y,z)} \phi_2 = \frac{1}{1 + e^{k \cdot b(x,y,z)}} \phi_1 + \frac{1}{1 + e^{-k \cdot b(x,y,z)}} \phi_2 \quad (1)$$

where \oplus denotes the combination operation, $\phi_c \geq 0$ represents the resulting structure, $b(x, y, z) = 0$ is the boundary between the two substructures, and the parameter k controls the transition gradient between them.

Using Eq. (1), we place the substructure $\phi_1 \geq 0$ in the region $b(x, y, z) < 0$ and the substructure $\phi_2 \geq 0$ in the region $b(x, y, z) > 0$. The resulting structure comprising these two substructures is represented by $\phi_c \geq 0$.

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2.2. Fabrication of FGPS

The resulting model was constructed and then exported as an STL file using Wolfram Mathematica 9.0 software. The product was directly manufactured using the three-dimensional printing (3DP) system Objet30 Pro (Israel) with Objet VeroWhitePlus (material). The 3D model was fabricated by stacking the 2D patterns. This system could judge where to place support materials and where to place main materials based on the STL file. Finally, the support materials were removed by a water flushing device provided with this system.

3. Results and discussion

3.1. Combination operation

We combined two porous scaffolds with a cylindrical boundary to construct a FGPS. The first substructure (diamond architecture [4]) with a porosity of 32% was defined as a network solid [5]:

$$\phi_1 = -(\cos(1.5x)\cos(1.5y)\cos(1.5z) - \sin(1.5x)\sin(1.5y)\sin(1.5z) - 0.3). \quad (2)$$

The second substructure (gyroid architecture [4]) with a porosity of 67.6% was defined as a sheet solid [5]:

$$\phi_2 = -((\cos(0.5x)\sin(0.5y) + \cos(0.5y)\sin(0.5z) + \cos(0.5z)\sin(0.5x))^2 - 0.5^2). \quad (3)$$

Then, the boundary between these two substructures was defined as a cylindrical surface with a radius of 16 mm:

$$b_1 = 16^2 - (x^2 + y^2) = 0. \quad (4)$$

Based on Eq. (1), we had

$$\phi = \phi_1 \oplus_{k^1} \phi_2. \quad (5)$$

The resulting scaffold was defined by

$$(\phi \geq 0) \cap (20^2 - (x^2 + y^2) \geq 0) \quad (6)$$

where $20^2 - (x^2 + y^2) = 0$ was the external surface of the scaffold with a radius of 20 mm.

By setting $k = 1$ and $k = 0.02$, the resulting scaffolds are shown in Fig. 1. With a larger value of k , the transition between the two substructures will be more abrupt. This scaffold can be applied as a femur-mimetic structure that has a dense cortical shell and a porous cancellous interior [2]. The detailed codes for constructing the resulting scaffold using Mathematica 9.0 software are shown in Appendix 1.

3.2. Recursive combination operation

Furthermore, the combination operations could be recursively applied:

$$\phi_c = (\phi_1 \oplus_{k_1}^{b_1(x,y,z)} \phi_2) \oplus_{k_2}^{b_2(x,y,z)} \phi_3. \quad (7)$$

For example, the third substructure (primitive architecture [8]) $\phi_3 \geq 0$ with a porosity of 54.6% could be defined as a sheet solid:

$$\phi_3 = -((\cos(0.75x) + \cos(0.75y) + \cos(0.75z))^2 - 0.8^2). \quad (8)$$

The resulting scaffold constructed using Eq. (5) was combined with this structure by

$$\phi_c = \phi \oplus_k^{b_2} \phi_3. \quad (9)$$

The new scaffold was then defined by

$$(\phi_c \geq 0) \cap (20^2 - (x^2 + y^2) \geq 0). \quad (10)$$

By setting $k = 1$ and $b_2 = y$, the new scaffold with different gradient porosities is shown in Fig. 2(a). The codes for these operations are shown in Appendix 2. Therefore, a complex FGPS could be effectively constructed based on these recursive combination operations. Using the 3DP technique, this product was fabricated as shown in Fig. 2(b).

3.3. Multi-scale scaffold structure

Integrating mesoscale porosity with three-dimensional continuous macropores is of particular importance because it combines high specific surface area with high flux and pore accessibility desired [9]. A mesoscale porous structure and a macroscale porous structure can be respectively constructed by using our combination operations and subsequently integrated by using Boolean operations.

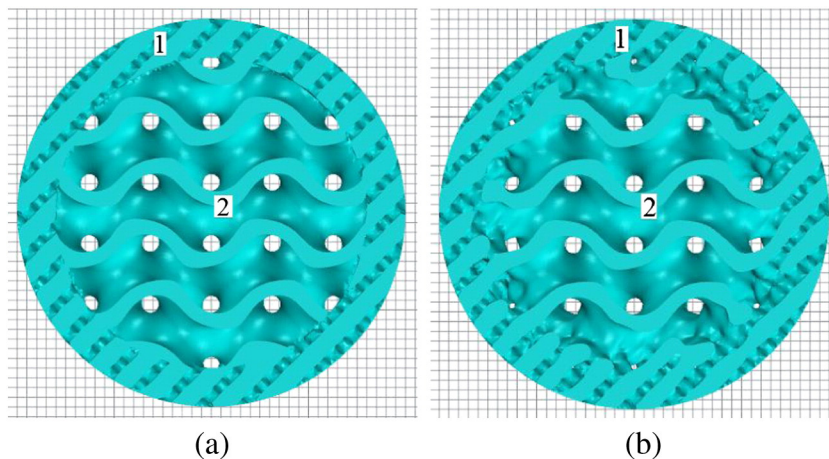


Fig. 1. FGPS with an abrupt transition between two substructures (1 and 2) when $k = 1$ (a) and a gradual transition when $k = 0.02$ (b). Substructures 1 and 2 were defined, respectively, by $\phi_1 \geq 0$ and $\phi_2 \geq 0$ (see Eqs. (2) and (3)).

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