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Novel real function based method to construct heterogeneous porous scaffolds and additive manufacturing for use in medical engineering

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ABSTRACT

Heterogeneous porous scaffolds have important applications in biomedical engineering, as they can mimic the structures of natural tissues to achieve the corresponding properties. Here, we introduce a new and easy to implement real function based method for constructing complex, heterogeneous porous structures, including hybrid structures, stochastic structures, functionally gradient structures, and multi-scale structures, or their combinations (e.g., hybrid multi-scale structures). Based on micro-CT data, a femur-mimetic structure with gradient morphology was constructed using our method and fabricated using stereolithography. Results showed that our method could generate gradient porosity or gradient specific surfaces and be sufficiently flexible for use with micro-CT data and additive manufacturing (AM) techniques.

1. Introduction

Biological cell behaviours are governed by their interactions with their environment. These interactions, including cell-cell and cell-extracellular matrix contacts, are key regulators of cell survival, proliferation, and differentiation. Both the molecular compositions of these contact locations and their spatial distributions affect cell behaviours [1]. Thus, constructing three-dimensional (3D) heterogeneous open-channelled scaffolds that mimic these complex in vivo arrangements in the cellular environment is an ongoing pursuit in tissue engineering [2].

CAD and AM techniques have significantly improved the capability to construct porous scaffolds by controlling their microstructural features, which has led to an increased interest in developing innovative scaffold architecture designs and fabrications [3]. Numerous mathematically defined methods have been proposed for scaffold design, such as real function based methods [4], implicit surface based (ISB) methods [3], and triply periodic minimal surfaces (TPMS) methods [5]. The resulting porous models can be, although are not limited to, type P, G, and D structures [6,7], I-WP, F-RD, Tubular-P, and Tubular-G structures [8,9], TPMS-based sheet solids [10], lattice porous structures and cylindrical rods [11], and cellular structures [12]. Even earlier, triply-periodic materials were discussed in soft materials, including biomorphic synthetic materials and biological structures [13,14]. Examples of these structures are shown in Fig. 1. In contrast to conventional methods, such as salt-leaching [15] and phase separation [16], these methods provide for constructing structures using simple mathematical inequalities that can accurately control structural features [9].

However, current mathematically defined models have regular appearances that are difficult to use for replacing natural tissues, although some strategies have been implemented to achieve simple gradient porosities [6,8], such as by linearly defining porosities based on a single TPMS-based structure type.

This paper is an extension of our previous work in which we constructed hybrid structures based on given subspace boundaries [4]. However, it is easier to construct heterogeneous structures based on control points when the boundaries are unknown. Here, we firstly constructed Voronoi cells based on control points to obtain desired convex or non-convex subspaces, and then to assign basic substructures in these subspaces using real weight functions. Second, to implement our method, we constructed four kinds of heterogeneous structures, including hybrid structures, stochastic structures, functionally gradient structures, and multi-scale structures. Our overall intent was to generate gradient morphologies with different structure types and complex transition boundaries in an easy to implement manner. As an important application, we showed how our method could be used to construct biomimetic scaffolds based on micro-CT data and fabricated them using AM techniques.

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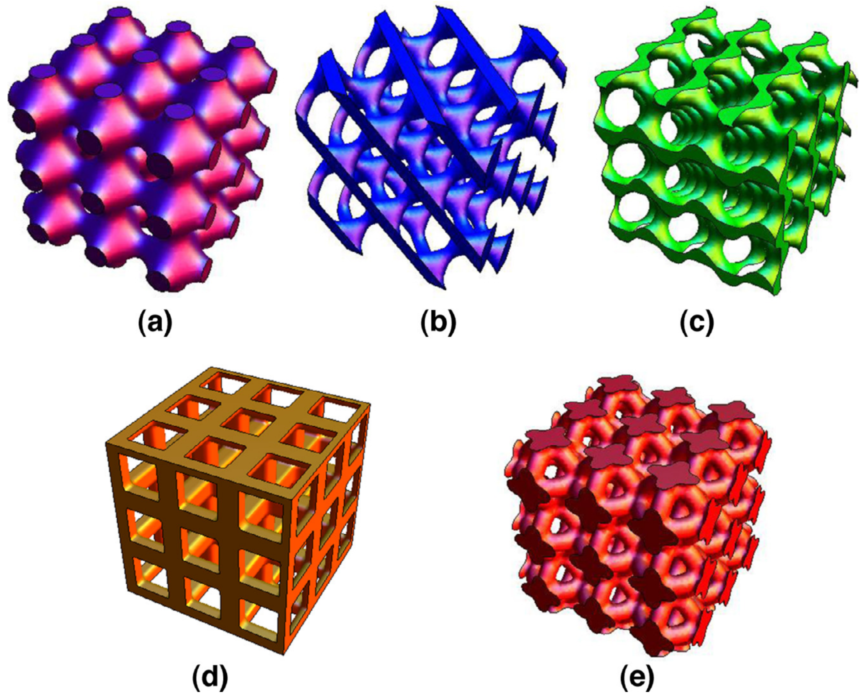

Fig. 1. Basic mathematically defined porous structure types (a) P [5], (b) D [6], (c) G [6], (d) L [11], and (e) T [12,17].

2. Methodology

2.1. Basic porous structures

Examples of some basic porous structures are shown in Fig. 1, which are represented by the following real functions.

Primitive (type P) TPMS [5]:

$$\phi_P = \cos(ax) + \cos(by) + \cos(cz) + d \quad (1)$$

Diamond (type D) TPMS [6]:

$$\phi_D = \cos(ax)\cos(by)\cos(cz) - \sin(ax)\sin(by)\sin(cz) + d \quad (2)$$

Gyroid (type G) TPMS [6]:

$$\phi_G = \cos(ax)\sin(by) + \cos(by)\sin(cz) + \cos(cz)\sin(ax) + d \quad (3)$$

Lattice (type L) structure [11]:

$$\begin{aligned} sx &= \sin(ax) + d \\ sy &= \sin(by) + d \\ sz &= \sin(cz) + d \\ mx &= \min(sy, sz) \\ my &= \min(sx, sz) \\ mz &= \min(sy, sx) \\ \phi_L &= \max(mx, my, mz) \end{aligned} \quad (4)$$

and Torus (type T) structure [12,17]:

$$\begin{aligned} sx &= \frac{t}{\pi}\arcsin\left(\sin\left(\pi\frac{x}{t}\right)\right) \\ sy &= \frac{t}{\pi}\arcsin\left(\sin\left(\pi\frac{y}{t}\right)\right) \\ sz &= \frac{t}{\pi}\arcsin\left(\sin\left(\pi\frac{z}{t}\right)\right) \\ mx &= h^2 - sx^2 - sy^2 - sz^2 - r^2 + 2r\sqrt{sy^2 + sz^2} \\ my &= h^2 - sx^2 - sy^2 - sz^2 - r^2 + 2r\sqrt{sz^2 + sx^2} \\ mz &= h^2 - sx^2 - sy^2 - sz^2 - r^2 + 2r\sqrt{sy^2 + sx^2} \\ \phi_T &= \max(mx, my, mz) \end{aligned} \quad (5)$$

Using these real functions, an inequality of $\phi \geq 0$ represents the solids, and $\phi < 0$ represents the pores. The parameters a, b, and c control pore size and specific surface in the x, y, and z directions, respectively. Parameter d controls porosity [4]. Parameters t, h, and r are the period, thickness, and radius of a torus, respectively [12]. sx, sy, sz, mx, my, and mz are intermediate variables.

2.2. Designing heterogeneous porous structures

A heterogeneous porous structure can be constructed based on the basic architectures described above using a real function based method. A user can provide some arbitrarily chosen number of 3D control points within a structure domain. Using our method, subspaces comprising each point are constructed, after which given basic architectures with desired porosities and pore shapes can be assigned to these subspaces. Our method also considers smooth transitions between adjacent substructures, while keeping the overall operations simple.

We define a heterogeneous structure by

$$\phi = \sum_{i=1}^{n} w_i(x) \cdot \phi_i(x) \geq 0 \quad (6)$$

The weight functions, $w_i(x)$, are defined by

$$w_i(x) = \frac{\exp(-k_i\|x - x_i\|^2)}{\sum_{j=1}^{n} \exp(-k_j\|x - x_j\|^2)} \quad (7)$$

where point x_i lies in the ith subspace, the ith substructure of $\phi_i \geq 0$ (not limited to types P, D, G, L, or T) is assigned to the ith subspace, the parameters $k_i > 0$ control the transition gradients, n is the number of control points, and x denotes the 3D spatial coordinate (x, y, z). The resulting heterogeneous porous structure is represented by $\phi \geq 0$.

Eq. (7) has some desirable properties, such as forming a partition of unity, i.e., $\sum_i w_i(x) = 1$, and a non-zero-denominator. Below, we explain the subspace assignment mechanisms of using Eqs. (6) and (7).

For two different points x_1 and x_2, by setting $k_1 = k_2 = k > 0$, in the region $\exp(-k\|x - x_1\|^2) > \exp(-k\|x - x_2\|^2)$, then we have

$$-\|x - x_2\|^2 + \|x - x_1\|^2 < 0 \quad (8)$$

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