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Design of tissue engineering scaffolds based on hyperbolic surfaces: Structural numerical evaluation

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ABSTRACT

Tissue engineering represents a new field aiming at developing biological substitutes to restore, maintain, or improve tissue functions. In this approach, scaffolds provide a temporary mechanical and vascular support for tissue regeneration while tissue in-growth is being formed. These scaffolds must be biocompatible, biodegradable, with appropriate porosity, pore structure and distribution, and optimal vascularization with both surface and structural compatibility. The challenge is to establish a proper balance between porosity and mechanical performance of scaffolds.

This work investigates the use of two different types of triple periodic minimal surfaces, Schwarz and Schoen, in order to design better biomimetic scaffolds with high surface-to-volume ratio, high porosity and good mechanical properties. The mechanical behaviour of these structures is assessed through the finite element method software Abaqus. The effect of two parametric parameters (thickness and surface radius) is also evaluated regarding its porosity and mechanical behaviour.

1. Introduction

In tissue engineering, the formation of tissue with desirable properties strongly relies on the mechanical properties of the scaffolds at a macroscopic and microscopic level. Macroscopically, the scaffold must bear loads to provide stability to tissues while it is being formed fulfilling its volume maintenance function. At the microscopic level, both cell growth and differentiation and ultimate tissue formation are dependent on the mechanical input to cells. Thus, the scaffold must be able to withstand specific loads and transmit them in an appropriate way to the growing and surrounding cells and tissues.

Ideally, scaffolds must be biocompatible, biodegradable with a degradation rate matching the regeneration rate of the new tissue, highly porous structures with full interconnectivity between pores, with appropriate mechanical properties and surface characteristics [1].

The design of optimized scaffolds for tissue engineering is a key topic of research, as the complex macro- and micro-architectures required for a scaffold depends on the mechanical properties, and the physical and molecular stimulations of the surrounding tissue at the defect site. One way to achieve such designs is to create a library of unit cells (the scaffold is assumed to be a repeating, tessellating unit structure), which can be assembled through specific computational tools proposed by several authors [2–6].

Naing et al. [6] proposed a CAD system of structures based on convex polyhedral units for additive manufacturing applications. This computational tool named *Computer Aided System for Tissue Scaffolds* (*CASTS*) consists of a basic library of units that can assemble uniform matrices of various shapes. Each open cellular unit is a unique configuration of linked struts. This system, together with an algorithm allowing the designer to specify the unit cell and the required dimensions, is able to automatically generate a structure suitable for tissue engineering applications. Sanz-Herrera et al. [7] characterized a specific family of scaffolds based on a *Face-Cubic Centred* (*FCC*) arrangement of empty pores, leading to an analytical formulae of porosity and specific surface. The effective behaviour of these scaffolds was evaluated in terms of its mechanical properties and permeability, through the asymptotic homogenization theory applied to a representative volume element identified with the *FCC* unit cell. The homogenization theory, which is complex in its implementation, has been used by several authors to simulate the behaviour of scaffolds for tissue engineering applications [1].

Almeida and Bártolo [8,9] used a computational tool called *CADS* (*Computer Aided Design of Scaffolds*), based on the finite element method and knowledge based tools to predict the mechanical and

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vascular behaviour of varying regular basic scaffold units, as a function of porosity and pore topology. Almeida and Bártolo [10] also proposed a topological optimization strategy to find out the best material use for a construct subject to either a single load or a multiple load distribution. The proposed topological optimization scheme enables the design of ideal topological architectures for scaffolds maximizing its mechanical behaviour.

Most of the works on scaffold designs for tissue engineering applications are based on either cubic lattices with straight edges and sharp corners or shapes obtained through Boolean operations with geometric primitives. This work explores the design of scaffolds with high surface-to-volume ratios, facilitating cell proliferation and cell–cell interactions, maximizing both porosity and mechanical performance. Two types of parametric hyperbolic surfaces (Schwarz and Schoen's I-WP surfaces) are considered, and the effect of two design parameters (surface thickness and radius) is investigated. These hyperbolic surfaces enable the design of biomorphic scaffolds facilitating cell attachment, migration and proliferation.

2. Triply periodic minimal surfaces

2.1. Definition

Hyperbolic surfaces are interesting in the design of biomimetic scaffolds as they commonly exist in natural structures. Amongst the various hyperbolic surfaces with an average negative Gaussian curve, the Triple Periodic Minimal Surfaces (TPMS) are the most investigated ones [11–14].

TPMS describe several natural shapes, such as lyotropic liquid crystals, zeolite sodalite crystal structures, diblock polymers, hyperbolic membranes (found in the prolamellar body of plants), cubosomes and certain cell membranes [11–14]. In the biomanufacturing field, TPMS allow the design of scaffolds with very high surface-to-area ratios enhancing cell proliferation.

2.2. Periodic surface modelling

A periodic surface can be defined through the following mathematical model [15–19]:

$$\phi(r)=\sum_{k=1}^{K} M_k \cos\left[\frac{2\pi(L_k\cdot r)}{\beta_k+Ps_k}\right] \tag{1}$$

where r is the location vector in the Euclidean space, L_k is the k lattice vector in the reciprocal space, M_k is the magnitude factor, β_k is the wavelength of periods and Ps_k is the phase shift [15–19].

In the TPM case, the Weierstrass formula can be used to describe these surfaces in a parametric way [15–19]:

$$\begin{cases} x = Re\displaystyle\int_{\omega 0}^{\omega 1} e^{i\theta}(1-\omega^2)R(\omega)d\omega \\ y = Im\displaystyle\int_{\omega 0}^{\omega 1} e^{i\theta}(1+\omega^2)R(\omega)d\omega \\ z = -Re\displaystyle\int_{\omega 0}^{\omega 1} e^{i\theta}(2\omega^2)R(\omega)d\omega \end{cases} \tag{2}$$

where ω is a complex variable, θ is the so-called Bonnet angle, and $R(\omega)$, Re and Im are geometric functions which varies for different surfaces.

Important sub-classes of TPMS are the so-called Schwarz primitive and Schoen's I-WP surfaces, considered in this research work.

2.3. Schwarz TPMS Primitives

A periodic Schwarz primitive surface can be mathematically described by the following nodal approximation [15–19]:

$$\phi(r)=M_p\left[\cos\left(\frac{2\pi x}{\beta_x}\right)+\cos\left(\frac{2\pi y}{\beta_y}\right)+\cos\left(\frac{2\pi z}{\beta_z}\right)\right] \tag{3}$$

Since the previous equation only defines the surface model, the solid geometric modelling of the Schwarz units were obtained using a commercially available CAD software (*Solidworks 2012* from *Dassault Systemes*, *www.3ds.com*) through offset and thickening operations in order to obtain solid models for production and simulation. Through these operations, the solid geometric modelling enables to define two important modelling constraint parameters: thickness and radius. Based on these two modelling parameters, two sub-models were defined:

- Thickness (the obtained models varied their thickness while maintaining the same geometric radius as illustrated in Fig. 1(a)).
- Radius (the obtained models varied their radius while maintaining the same geometric thickness as illustrated in Fig. 1(b)).

The variation of these parameters enables changes to the architecture of each basic unit of a scaffold, varying its porosity, degradation kinetics and mechanical behaviour (Fig. 1).

2.4. Schoen TPMS Primitives

The mathematical description of a Schoen's I-WP surface is given by the following nodal approximation [15–19]:

$$\phi(r)=M_1\left[\begin{array}{l} 2\cos\left(\frac{2\pi x}{\beta_x}\right)\cos\left(\frac{2\pi y}{\beta_y}\right)+2\cos\left(\frac{2\pi y}{\beta_y}\right)\cos\left(\frac{2\pi z}{\beta_z}\right) \\ 2\cos\left(\frac{2\pi z}{\beta_z}\right)\cos\left(\frac{2\pi x}{\beta_x}\right) \\ -\cos\left(\frac{4\pi x}{\beta_x}\right)-\cos\left(\frac{4\pi y}{\beta_y}\right)+\cos\left(\frac{4\pi z}{\beta_z}\right) \end{array}\right] \tag{4}$$

Similarly to the Schwarz solid modelling, the solid Schoen units were obtained through the same offset and thickening operations. By varying the thickness (Fig. 2(a)) and radius (Fig. 2(b)) values, different solid configurations can be obtained as illustrated in Fig. 2.

3. Scaffold modelling using TPMS basic units

There are many approaches for mapping the basic unit into arbitrary units. Fig. 3 illustrates the Boolean operations through addition of the repeating units into an arbitrary unit with thickness variation resulting in a scaffold with a thickness gradient.

Melchels et al. [19] presented a scaffold design methodology using TPMS geometries. They used the *K3DSurf* v.0.6.2 software developed by *Abderrahman Taha* (http://k3dsurf.sourceforge.net) to generate the CAD models that describe the well-known TPMS geometries of Gyroid architectures [20]. The gradient in pore size and porosity of the Gyroid structure was introduced by adding a linear term to the equation for the Z-values. They also demonstrated for the Gyroid architectures, the stress and strain are much more homogeneously distributed throughout the structure than for cubic regular architectures. Later on, they assessed the influence of the scaffold pore architecture on cell seeding and static culturing by comparing a computer designed Gyroid architecture fabricated by Stereolithography, with a random pore architecture resulting from Salt Leaching [21]. These scaffolds presented random pore architectures in terms of distribution and size. The scaffolds produced by