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Open Source Software for the Automatic Design of Scaffold Structures for Tissue Engineering Applications

J. C. Dinis[a], T. F. Morais[b], P. H. J. Amorim[b], R. B. Ruben[a,c]*, H. A. Almeida[a,c], P. N. Inforçati[b], P. J. Bártolo[a,d], J.V.L. Silva[b]

[a] *Centre for Rapid and Sustainable Product Development, Polytechnic Institute of Leiria, Marinha Grande, Portugal*
[b] *Renato Archer Information Technology Center – CTI, Campinas, São Paulo, Brazil*
[c] *School of Technology and Management, Polytechnic Institute of Leiria, Leiria, Portugal*
[d] *Manchester Biomanufacturing Centre, School of Mechanical, Aerospace and Civil Engineering, Manchester Institute of Biotechnology, University of Manchester, UK*

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. 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. In this research work, an open source software tool for the design of scaffolds is presented.

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Keywords: Computer-Aided Scaffold Design, Open-source software, Tissue Engineering design, Cellular Materials Design, Additive Manufacturing.

* Corresponding author. Tel.: 351 244 820 300; fax: +351 244 820 310.
E-mail address: rui.ruben@ipleiria.pt

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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 [1-4].

Several researchers have studied the mechanical behaviour of scaffolds in order to ensure if their mechanical properties are adequate for a specific application in tissue engineering [5]. In the last years, several computational tools have been developed to support and aid the design of scaffolds for tissue engineering, such as the Computer-Aided Tissue Engineering (CATE) developed by Sun et al [6-8] and the Computer Aided System for Tissue Scaffolds (CASTS) developed by Naing et al [9, 10], and Computer Aided Design of Scaffolds developed by Almeida and Bártolo [11, 12]. The last computer tool integrates different routines and systems to support both the design and the fabrication of scaffolds through additive manufacturing.

In this research work, a new user-friendly software application that designs and manipulates scaffold geometries is presented. Its geometric database is based on triple periodic minimal surfaces. With this application, the user may define the porous size dimension and choose which type of triple periodic minimal surface will be used for the design of the scaffold.

2. Triple Periodic Minimal Surfaces

In the 1880s, Schwarz described the first periodic minimal surface [13-15]. A minimal surface is a surface that is locally area-minimizing, that is, a small piece has the smallest possible area for a surface spanning the boundary of that piece. The surfaces were generated using symmetry arguments: given a solution to a Plateau's problem for a polygon, and the reflections of the surface across the boundary lines also produce valid minimal surfaces that can be continuously joined to the original solution [15, 16]. Minimal periodic surfaces are the most studied hyperbolic surfaces. If a minimal surface has space group symmetry, it is periodic in three independent directions, so it is called Triple Periodic Minimal Surfaces.

Triple Periodic Minimal Surfaces are also biomimetic surfaces describing several natural shapes, such as lyotropic liquid crystals, zeolite sodalite crystal structures, diblock polymers, hyperbolic membranes (prolamellar structure of choloroplasts in plants), echinoderm plates (interface between the inorganic crystalline and organic amorphous matter in the skeleton), cubosomes and certain cell membranes [8, 11, 12, 16].

Five types of parametric hyperbolic surfaces were considered in our design database: (1) Schwartz P, (2) Schwartz D, (3) Gyroid, (4) Neovius, (5) W (iWP). They are defined mathematically as follows:

$$\cos(x) + \cos(y) + \cos(z) = 0 \tag{1}$$

$$\sin(x) * \sin(y) * \sin(z) + \sin(x) * \cos(y) * \cos(z) + \cos(x) * \sin(y) * \cos(z) + \cos(x) * \cos(y) * \sin(z) = 0 \tag{2}$$

$$\cos(x) * \sin(y) + \cos(y) * \sin(z) + \cos(z) * \sin(x) = 0 \tag{3}$$

$$3 * (\cos(x) + \cos(y) + \cos(z)) + 4 * \cos(x) * \cos(y) * \cos(z) = 0 \tag{4}$$

$$\cos(x) * \cos(y) + \cos(y) * \cos(z) + \cos(z) * \cos(x) - \cos(x) * \cos(y) * \cos(z) = 0 \tag{5}$$

3. Developed Software

As mentioned before, a user-friendly software application that designs and manipulates scaffold geometries was developed and the geometric database was defined with the previous equations. The software application was developed in Python, as one of the reasons for this choice is because it is considered a high level programming language, object-oriented, functional, dynamic and strong typing [17]. In the development process, the following libraries were used: VTK (Visualization Toolkit), numpy and wxPython libraries [18].

On opening, the users may choose the type of surface in which they want to build their scaffolds and define both porosity and size (Fig. 1). Once concluded the design process, the user may then export the geometry in a STL file format for further manipulation and/or production in one of the many additive manufacturing systems.

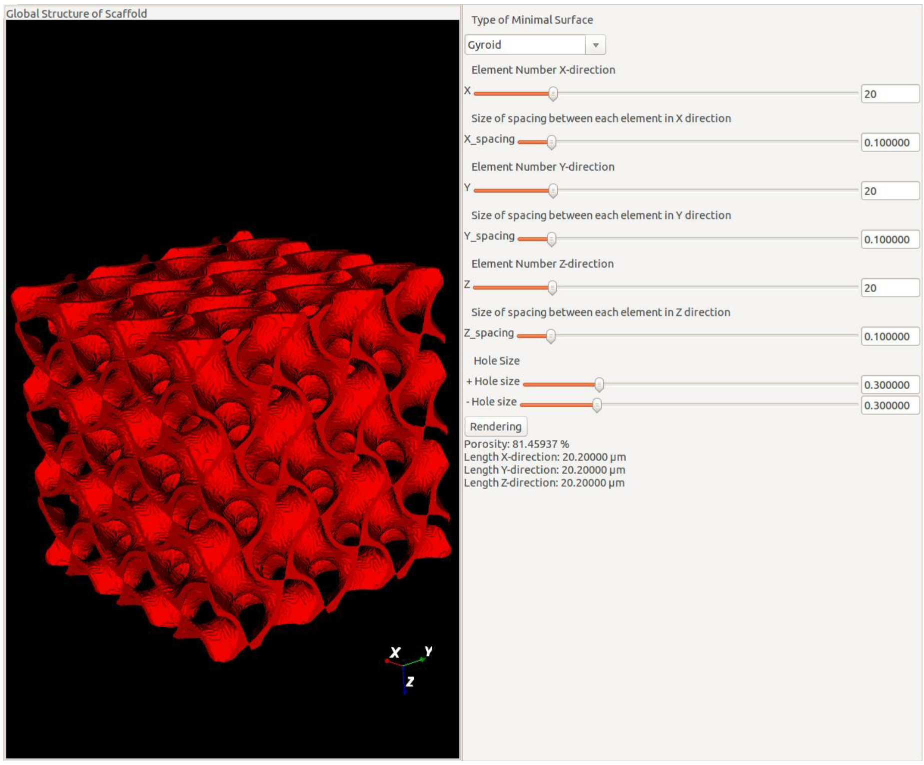


Fig. 1 Example of the “Interface Scaffold” developed in Python.

The porosity can be controlled using then by the following equation [11, 12]:

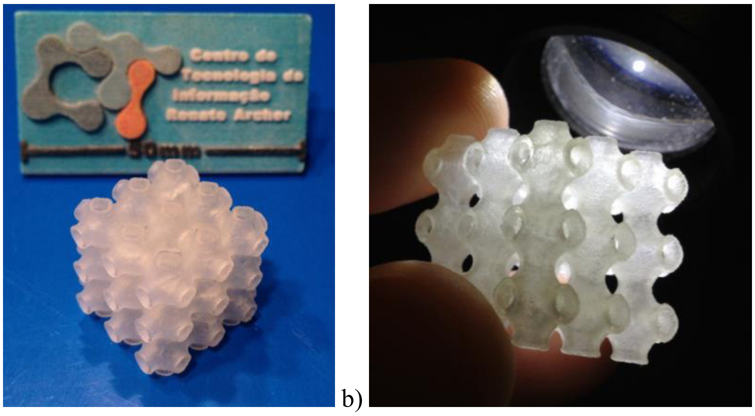
$$\eta = \frac{V_p}{V_s + V_p} \times 100 \tag{6}$$

where V_p and V_s is the volume of the porous and solid respectively.

During the design of the scaffold models, all the design parameters were maintained, only modifying the type of geometric surface. After designing the scaffold models with different surfaces and levels of porosity, the scaffolds were then produced on a *CONNEX 350* from *OBJET*. This equipment uses the *POLYJET* technology and works with photosensitive resin materials called *FullCure 720*. The thickness of each layer during production is of 30 µm.

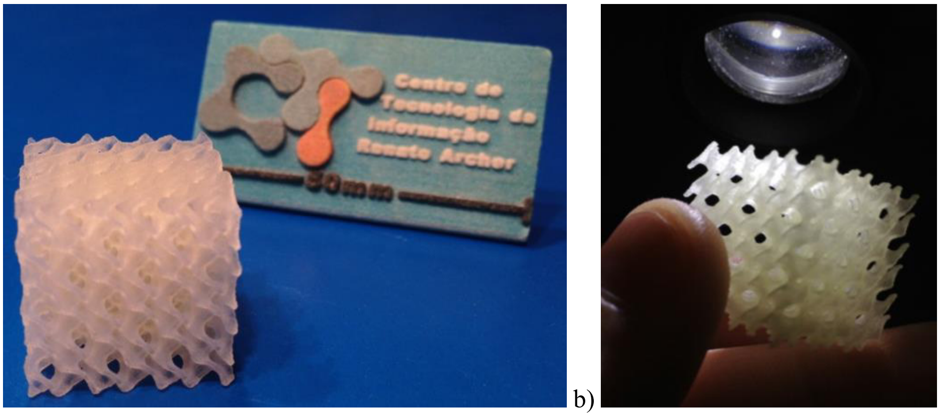
With the “Interface Scaffold” software is possible to obtain several Schwarz_P triply periodic minimal surface. In this case two of them were performed with 84% (+ hole size and – hole size equal to 0.3) and 78% (+ hole size and – hole size equal to 0.7 and 0.1) of porosity. The porosity was calculated by equation 6. The “+ hole size” and “- hole size” parameters were always equal for all type of structures. In figure 1 is possible to observe the Gyroid example with “+ hole size” and “- hole size” both equal to 0.3. In the Schwarz_P case, figure 2 presents the 3D printed model of one scaffold defined by equation 1.

Figure 3 presents a 3D printed model performed with a Schwartz_D surface (given by function 2). With the same parameter design, used before, the porosity is less than the Schwartz_P minimal surface. The porosity given by this surface is approximately 76.5% and 68 % respectively.



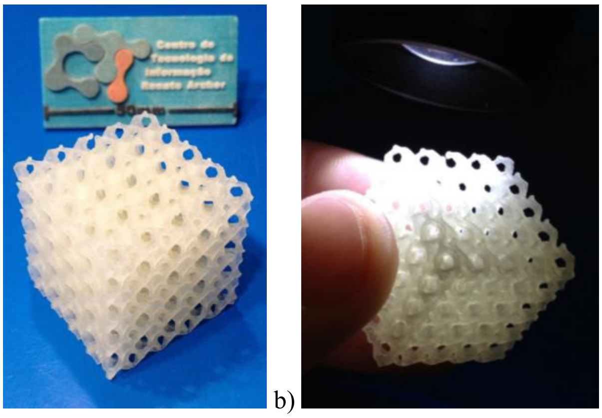
a) b)

Fig. 2. (a) Structure Schwarz_P printed in 3D; (b) Visualization of the pores.



a) b)

Fig. 3. (a) Structure Schwarz_D printed in 3D; (b) Visualization of the pores.



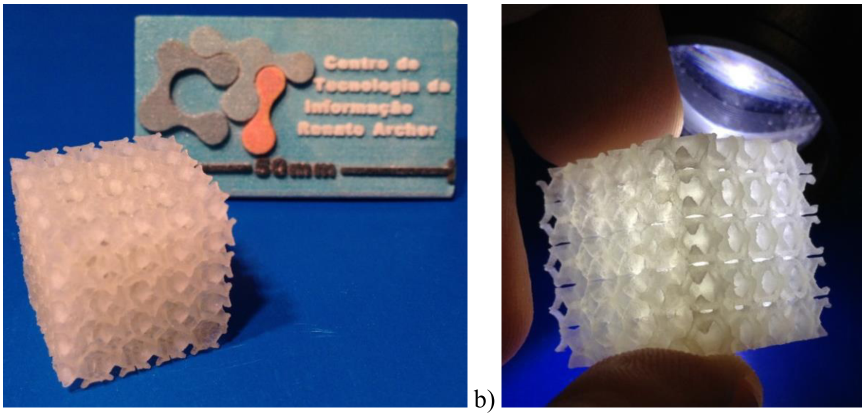
a) b)

Fig. 4. (a) Structure of Gyroid printed in 3D; (b) Visualization of pores.

Figure 4 presents the 3D model of a scaffold performed with a Gyroid surface model (given by function 3). For this structure, and always using the same parameters, the porosity is 81.5% (+ hole size and – hole size equal to 0.3) and 68% (+ hole size and – hole size equal to 0.7 and 0.1), respectively.

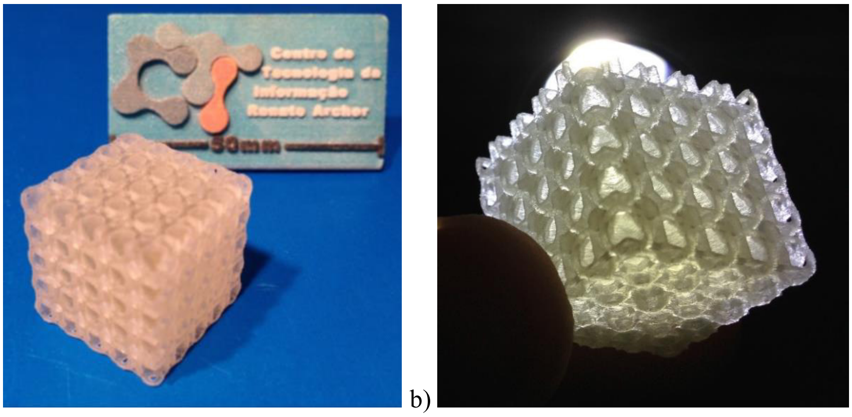
Figure 5 presents a 3D printed model of a scaffold performed with a Neovius surface (given by function 4). Neovius structure has higher porosity levels when compared to the previous models, in this case, the presenting levels of porosity are 87% and 82% respectively.

Figure 6 presents the 3D printed model of a scaffold performed with an IWP surface (given by function 5). For the same parameters of all other models, the IWP minimal surfaces present a 73% and 59% of porosity respectively.



a) b)

Fig. 5. (a) Structure Neovius printed in 3D; (b) Visualization of pores.



a) b)

Fig. 6. (a) Structure of IWP printed in 3D; (b) Visualization of pores.

4. Conclusion and future works

Advanced additive manufacturing technologies, namely Biomanufacturing, is using to fabricate scaffolds with controlled architecture for tissue engineering applications [19-21]. A scaffold should have a set of properties that provides mechanical support while simultaneously promoting tissue regeneration. Among these properties, scaffold permeability is a determinant factor as it plays a major role in the ability for cells to penetrate the porous media and for nutrients to diffuse. These technologies combined with computer aided design enable the production of 3D structures in a layer-by-layer fashion in a multitude of materials. Actual prediction of the effective mechanical properties of scaffolds is very important for tissue engineering applications [22-24].

With the aid of the developed software and its geometric database based on triply periodic minimal surface, one can obtain different highly complexity geometric models with different levels of porosity and permeability. By comparing all 5 models, the Neovius present the highest levels of porosity followed by the Gyroid, Schwartz_P, Schwartz_D and (IWP) respectively.

References

[1] R. Shalak, C. F. Fox; Preface. In: Tissue Engineering, eds. Alan R. Liss, New York; pp. 26- 29; 1988.
[2] R. Langer, J.P. Vacanti; tissue engineering; science; vol. 260; pp. 920-926; 1993.
[3] D. W. Hutmacher; scaffold design and fabrication technologies for engineering tissues-state of the art and future perspectives; J Biomat Sci-Polym E; vol 12; pp. 107- 124; 2001.
[4] Z. Fang, B. Starly, W. Sun; Computer-aided characterization for effective mechanical properties of porous tissue scaffolds; Computer-Aided Design; vol 37; pp. 65-72; 2005.
[5] C. Sandino, J. A. Planell, D. Lacroix; A finite element study of mechanical stimuli in scaffolds for bone tissue engineering; Journal of Biomechanics; vol 41; pp. 1005-1014; 2008.
[6] W. Sun, A. Darling, B. Starly, C. Gomez; Computer Aided Tissue Engineering Part II: Application to biomimetic modelling and design of tissue scaffolds; J. Biotechnology and applied Biochmistry; vol 39; pp. 49- 58; 2004.
[7] W. Sun, A. Darling, B. Starly, J. Nam; Computer Aided Tissue Engineering Part I: Overiew, scope and challenges ; J. Biotechnology and applied Biochmistry; vol 39; pp. 29- 47; 2004.
[8] W. Sun, P. Lal; Recent development on computer aided tissue engineering- a review; Computer Methods and Programs in Biomedicine; vol 67; pp. 85-103; 2002.
[9] M. W. Naing, C. K. Chua and K. F. Leong; Computer Aided Tissue Engineering Scaffold Fabrication; In: Virtual Prototyping & Bio-Manufacturing In Medical Applications ;B. Bidanda & P.J. Bártolo eds; Springer USA; pp. 67-85; 2008.
[10] M. W. Naing, C. K. Chua, K. F. Leong, and Y. Wang; Fabrication of customized scaffolds using computer-aided design and rapid prototyping techniques; Rapid Prototyping Journal; vol 11; Nº 4; pp. 249-259; 2005.
[11] H.A. Almeida & P.J. Bártolo (2012), Structural and Vascular Analysis of Tissue Engineering Scaffolds: Part 1 – Numerical Fluid Analysis, Computer-Aided Tissue Engineering, M. Liebschner (Ed.), Springer (ISBN: 978-1-61779-763-7), Chapter 12: 183-207.
[12] H.A. Almeida & P.J. Bártolo (2012), Structural and Vascular Analysis of Tissue Engineering Scaffolds: Part 2 – Topology Optimization, Computer-Aided Tissue Engineering, M. Liebschner (Ed.), Springer (ISBN: 978-1-61779-763-7), Chapter 13: 209-236.
[13] A. Schwarz, Gesammelte Mathematische Abhandlungen, Springer, Berlin, 1933.
[14] E. R. Neovius, "Bestimmung zweier spezieller periodischer Minimal • achen", Akad. Abhandlungen, Helsingfors, 1883.
[15] Information on http://www.indiana.edu/~minimal/archive/Triply/genus3.html.
[16] Hermann Karcher, Konrad Polthier, "Construction of Triply Periodic Minimal Surfaces", Phil. Trans. R. Soc. Lond. A 16 September 1996 vol. 354 no. 1715 2077–2104.
[17] Information on http://www.python.org/
[18] W. J. Schroeder, L. S. Avila, K. M. Martin, W. A. Hoffman, C.C, Law; The Visualization Toolkit; edit by Kitware, Inc.(2001).
[19] Information on http://archive.msri.org/about/sgp/jim/geom/level/library/triper/index.html
[20] Information on http://epinet.anu.edu.au/mathematics/minimal_surfaces.
[21] Ignacio Ochoa, José A. Sanz-Herrera, José M. García-Aznar, Manuel Doblaré, Darmawati Mohamad Yunos, Aldo R. Boccaccini; Permeability evaluation of 45S5 Bioglass-based scaffolds for bone tissue engineering; Journal of Biomechanics; vol. 42; pp.257-260; 2009.
[22] Claire G. Jeong, Huina Zhang, Scott J.Hollister; Three-dimensional poly(1,8-octanediol-co-citrate) scaffold pore shape and permeability effects on sub-cutaneous in vivo chondrogenesis using primary chondrocytes; Acta Biomaterialia; vol.7, pp.505-514; 2011.
[23] Anthony C. Jones, Christoph H. Arns , Adrian P. Sheppard, Dietmar W. Hutmacher, Bruce Milthorpe, Mark A. Knackstedt; Assessment of bone ingrowth into porous biomaterials using micro- computed tomography imaging; Biomaterials vol 28, pp. 2491- 2504, 2007.
[24] Anthony C. Jones, Bruce Milthorpe, Holger Averdunk, Ajay limaye, Tim J. Senden Arthur Skellariou, Adrian P. Sheppard, Rob M. Sok, Mark A. Knackstedt, Artur Brandwood, Dennis Rohner, Dietmar W. Hutmacher: Analysis of 3D bone ingrowth into polymer scaffolds via micro- computed tomography imaging; Biomaterials vol 25, pp. 4947- 4954, 2004.