Numerical simulation of polymeric extruded scaffolds under compression

Henrique A. Almeida* & Paulo J. Bártolo

Centre for Rapid and Sustainable Product Development, Centro Empresarial da Marinha Grande, Rua de Portugal - Zona Industrial, 2430-028
Marinha Grande, Portugal

* Corresponding author. Tel.: +351 244 569 441; fax: +351 244 569 444. E-mail address: henrique.almeida@ipleiria.pt

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. Scaffolds must be biocompatible, biodegradable, with appropriate porosity, pore structure and distribution, and optimal vascularization properties. Establishing a proper balance between porosity and mechanical performance is a critical design challenge for these scaffolds. This research work presents a numerical simulation strategy to study compressive behavior of scaffolds with different pore sizes. Cellular solid models were the models used for simulation purposes and its results agrees with the experimental data.

© 2013 The Authors. Published by Elsevier B.V. Selection and/or peer-review under responsibility of Professor Mamoru Mitsuishi and Professor Paulo Bartolo

Keywords: Tissue Engineering; Scaffold Design; Cellular Structures; Computational Modeling

1. Tissue Engineering

Tissue engineering is a multidisciplinary domain that can be described as “the application of the principles and methods of engineering and life sciences toward the fundamental understanding of structure-function relationships in normal and pathological mammalian tissues, and the development of biological substitutes to restore, maintain, or improve tissue and organ functions” [1-3].

The cell-seeded temporary scaffold approach is the most widely used strategy for tissue engineering [4, 5]. In this approach, living cells are obtained from a tissue harvest, from either the patient (autograft) or a different person (allograft), and cultured in vitro in a scaffold to manipulate cell functions and guiding new tissue formation, in order to obtain suitable biological constructs for transplantation [6, 7]. Scaffolds are critical elements allowing cell attachment, proliferation and differentiation, delivering and retaining cells and growth factors, enabling the diffusion of cell nutrients and oxygen, and the establishment of an appropriate mechano-biological environment for the cells to secrete their own extracellular matrices in an organized way [8, 9].

To achieve these goals, an ideal scaffold must satisfy several biological and mechanical requirements [1, 10]. They must be biocompatible and biodegradable structures with controlled degradation rate. Additionally, they must have appropriate strength and stiffness, and adequate surface finishing guaranteeing a good biomechanical coupling between the scaffold and the host tissue. Scaffolds must also be fully interconnected, highly porous structures with appropriate pore size, pore shape and pore distribution. Porosity is a key design parameter to ensure an adequate mass flow of nutrients and oxygen to the inside of the construct and metabolic waste and byproducts to the outside, without compromising its mechanical performance.
Computer-aided design and simulation is a critical tool to develop suitable scaffolds for tissue engineering. This paper explores the use of a Crushable Foam behavior model to describe the deformation of cellular scaffolds. Numerical results are compared with experimental compression data.

2. Scaffold Production

Scaffold units were produced using the Bioextruder system illustrated in Figure 1 [11]. This system enables the fabrication of scaffolds in a wide range of polymeric and polymer/ceramic materials and comprises two different deposition systems: one rotational system for multi-material deposition, acted by a pneumatic mechanism, and another one for a single material deposition using a screw to assist the deposition process. The rotational system has four reservoirs, two with temperature controlled and another two without. A wide range of nozzle diameters, ranging between 0.1 and 1 mm, can be used.

Scaffold units with rectangular pores were produced in Poly(ε-caprolactone) (PCL) using the single deposition mode (Figure 1). PCL pellets (CAPA 6500) with molecular weight of 50000 were obtained from Perstorp Caprolactones (Cheshire, United Kingdom). Rectangular prisms measuring 30 x 30 x 8 mm were initially designed with a 0º/90º architecture, using Solidworks (Dassault Systems). Scaffolds were produced with different pore sizes. Figure 2 shows the main design parameters considered, while Table 1 indicates the values of both design and processing parameters. An example of a PCL unit is illustrated in Figure 3. As previously reported, depending on the processing conditions, a difference between theoretical porosity and real porosity is achieved [12-14], though this difference was not considered for this research work.

3. Scaffold Compressive Testing

The produced scaffolds were submitted to compression tests. The constructs were cut into block-shaped specimens characterized by the following dimensions: 5 x 5 x 8 mm (length \( l \) x width \( w \) x height \( h_0 \)). All tests were carried out in dry state at a rate of 1 mm/min up to a strain value of 0.5, using an Instron 5566 testing system equipped with a 1 KN load cell. Five compression tests were considered for each group of design parameters.

The “apparent” stress was evaluated as the force \( F \), measured through the load cell divided by the total area of the apparent cross section of the scaffold \( A = l \times w \):

\[
\sigma = \frac{F}{A} \tag{1}
\]

while the strain \( \varepsilon \) was defined as the ratio between the scaffold height variation \( \Delta h \) (i.e. the vertical displacement equal to the cross head displacement), and the scaffold initial height \( h_0 \):

\[
\varepsilon = \frac{\Delta h}{h_0} \tag{2}
\]
Figures 4 and 5 illustrate in an experimental way the obtained compressive stress-strain curves.

![Fig. 4. Compression Stress-Strain curves for the five samples with a pore size of 450 μm.](image)

![Fig. 5. Compression Stress-Strain curves for the five samples with a pore size of 650 μm.](image)

Once determined the average stress-strain curves for each pore size, the compressive bulk modulus and the compressive tensile stress were evaluated. The compressive tensile stress corresponds to both the limit value of the scaffold’s elastic behavior and the starting point of the scaffold’s plastic behavior. The Maximum Tensile Stress, which represents the tensile cut-off stress in the numerical simulations, was also determined. The obtained data are indicated in Table 2.

**Table 2. Mechanical compressive properties of the extruded structures for different pore sizes.**

| Pore Size [μm] | Bulk Modulus [MPa] | Tensile Stress [MPa] | Maximum Stress [MPa] |
|---------------|---------------------|----------------------|----------------------|
| 450           | 51.05 ± 3.21        | 4.36 ± 0.27          | 13.20 ± 1.08         |
| 650           | 47.57 ± 5.51        | 2.59 ± 0.31          | 9.47 ± 0.53          |

4. Constitutive Equations for Structural Analysis

Many natural materials are not fully dense, i.e. they possess internal cavities similar to the structures considered for this research work. This type of design is intentional, since it reduces the structure’s density, and in some cases present optimal performance regarding mechanical solicitations [15]. An example of a biological cellular material is cancellous bone, which is designed to have a variable density, where regions subjected to higher stresses are denser [15]. By definition, a cellular solid is made up of an interconnected network of solid struts or plates, which form the edges and faces of cells [16]. According to this definition, polymeric and ceramic tissue engineering scaffolds can be considered as cellular structures.

The constitutive model for crushable foams is considered for the analysis of materials typically used in energy absorption structures. The crushable foam plasticity models present the following characteristics:

- are used to model the enhanced ability of a foam material to deform in compression, due to cell wall buckling processes. It is assumed that the resulting deformation is not instantaneously recoverable, ideally presenting a plastic behavior for short duration events;
- can be used to model the difference between a foam material's compressive strength and its much smaller tensile bearing capacity, resulting from the cell wall breakage in tension;
- must be used in conjunction with the linear elastic material model;
- can be used when rate-dependent effects are important;
- are intended to simulate material response under essentially monotonic loading.

Two phenomenological constitutive models are usually considered: the volumetric hardening model and the isotropic hardening model.

The volumetric hardening model was developed based on the different response foam structures usually experience in compression and tension. In compression, the ability of the material to volumetrically deform is enhanced by cell wall buckling processes, as described by Gibson and Ashby [16] and Maiti *et al* [17]. It is assumed that the resulting deformation is not instantaneously recoverable, ideally presenting a plastic behavior for short duration events. On the other hand, in tension, cell walls break rapidly, and as a result the tensile load bearing capacity of crushable foams may be considerably smaller than its compressive load bearing capacity. Under monotonic loading, the volumetric hardening model assumes perfectly plastic behavior for
pure shear and negative hydrostatic pressure stress states, while hardening takes place for positive hydrostatic pressure stress states.

The isotropic hardening model was originally developed for metallic foams by Deshpande and Fleck [18]. It assumes symmetric behavior in tension and compression, and the evolution of the yield surface is governed by an equivalent plastic strain, which contributes to both the volumetric plastic strain and the deviatoric plastic strain.

To implement this model, it is assumed that the Young’s modulus is constant and the stress elastic behavior is updated along time, as follows:

$$\sigma_{\text{trial}}^i = \sigma_{\text{eq}}^i + E\varepsilon_{\text{pl}}^{\text{eq}}(\Delta t)^{1/2}$$

(3)

The magnitudes of the principal stress values, $\sigma_{\text{trial}}^i$, $i = 1,3$ are then confirmed, to evaluate if the yield stress ($\sigma_{y}$) is exceeded. If so, they are scaled back to the yield surface, as follows:

$$\sigma_{y} < \left| \sigma_{\text{trial}}^i \right| \text{then } \sigma_{\text{trial}}^i = \sigma_{y} \left| \frac{\sigma_{\text{trial}}^i}{\sigma_{y}} \right|$$

(4)

After the scale of the principal values, the stress tensor is transformed back into the global system. The yield stress is a function of the natural logarithm of the relative volume $V$, i.e., the volumetric strain.

The mechanical behavior of crushable foams is known to be sensitive to the rate of straining. This effect can be introduced by either a piecewise linear law or the overstress power law model.

Scaffolds are polymer based, so the volumetric hardening model is considered. Additionally, two constitutive models were simultaneously used: a linear elastic behavior model for small deformations within the elastic domain, and a crushable foam behavior model for the high deformations in the plastic domain.

5. Structural Simulations and Results

For simulation purposes, scaffolds were assumed to be rectangular structures with the following dimensions: length ($l$); 2.5 mm; width ($w$); 2.5 mm and height ($h_0$) 4.0 mm. Additionally, a rigid body attached to the scaffold was considered simulating the machine’s clamp (Figure 6). A constant velocity of 0.1667 mm/ms was defined for the movement of the rigid block under compression. This value is 10000 higher than the experimental value (0.0001667 mm/ms). The reason for this velocity is related to the computational time, as it was not possible to undergo the simulations with the real compression velocity.

The mechanical properties for the rigid body were defined in such a way that the rigid body has sufficient strength to perform the scaffold’s compression without suffering any kind of deformation. A limit dislocation value was also defined for the rigid body. Once it reaches 50 % of the scaffold’s height, the compressive simulation is completed, as the strain value reaches the value of 1.

Figures 7 and 8 compare the obtained numerical fitted sigmoid stress-strain curves with the average experimental stress-strain curves for scaffolds with pore sizes of 450 $\mu$m and 650 $\mu$m. Results show that as the pore size increases, the compressive strength of the scaffolds decreases. It is also possible to observe that the numerical model does not allow to predict the densification phenomenon, resulting in the slight deviations between numerical and experimental results observed at the end of the compression test.
Fig. 8. Comparison between numerical and experimental results for scaffolds with pore size of 650 μm.

Figures 9 and 10 illustrate the stress behavior of the considered scaffolds for different time steps of the compressive test: 20 %, 40 %, 60 %, 80 % and 100 % compression.

Fig. 9. Compression levels of scaffolds with a pore size of 450 μm. a) 20% of compression, b) 40%, c) 60%, d) 80%, e) 100%.

Fig. 10. Compression levels of scaffolds with a pore size of 650 μm. a) 20% of compression, b) 40%, c) 60%, d) 80%, e) 100%.

Results show that the scaffold with a pore size of 450 μm presents the smallest bulging phenomenon, presenting the smallest deviation between the numerical and experimental stress-strain curves. Regarding the scaffold with a pore size of 650 μm, the scaffold presents a more balanced compression, except in the center of the scaffold, when compared to the other scaffold structure. The two structures tend to bulge outwards when undergoing the compressive simulations, presenting a good agreement between the numerical curves and the experimental curves in the plastic domain. The plot results also illustrate the mesh deformations during the compression test (the mesh becomes non-symmetric). This unbalanced meshed body results in an unbalanced bulging phenomenon, contributing to the deviation between numerical and experimental results at the densification phase.
6. Conclusions

Design strategies to produce optimized scaffolds represent a critical topic of research in the field of tissue engineering. This is an emergent domain covered by this research work.

Scaffolds were modeled using the crushable foam behavior model. Compression tests were numerically simulated and the obtained results compared with experimental ones. The effect of porosity was considered.

Results show that as the pore size increases, the compressive strength of the scaffolds decreases. The numerical and experimental results present a global good agreement throughout the compression cycle. In the linear elastic domain, the obtained experimental and numerical curves present an excellent agreement. Regarding the plastic domain, the obtained curves also present a good agreement, with slight deviations at the end of the compression cycle, which are essentially due to the difficulty of the numerical model to predict the densification phenomenon.

The slight deviations between the numerical and experimental curves can also be related to porosity differences as theoretical values were used for computer simulation, and to mesh deformations during the compression test, as the mesh is non-symmetric. This unbalanced meshed body results in an unbalanced bulging phenomenon.

Acknowledgements

This research was supported by the Portuguese Foundation for Science and Technology through both a PhD Grant (SFRH/BD/37604/2007) and the strategic project Pest-OF/EME/UI4044/2011. Authors also acknowledge the support of the European Commission through the Marie Curie Project “International Research Exchange for Biomedical Devices Design and Prototyping” “IREBID”.

References

[1] Tarawneh, A.M., Wettergreen, M. and Liebschner, M.A.K. (2012) “Computer-Aided Tissue Engineering: Benefiting from the Control Over Scaffold Micro-Architecture”, Computer-Aided Tissue Engineering, M. Liebschner & D. Kim (Eds.), Springer, Chapter 1: 1-25.

[2] Eshraghi, S. and Das, S. (2010) “Mechanical and microstructural properties of polycaprolactone scaffolds with one-dimensional, two-dimensional, and three-dimensional orthogonally oriented porous architectures produced by selective laser sintering”, Acta Biomaterialia, 6(7):2467-2476.

[3] Skalak, R. and Fox, C.F. (1988) “Tissue engineering”, Alan R. Liss, New York.

[4] Fuchs, J.R., Nasseri, B.A. and Vacanti, J.P. (2001) “Tissue engineering: a 21st century solution to surgical reconstruction”, Ann Thorac Surg, 72, 577-581, 2001.

[5] Liu, C.Z. and Czemanski, J.T. (2006) “On the development of biodegradable scaffolds for tissue engineering: a perspective”, Materials Science and Technology, 12:2479-2488.

[6] Melchels, F.P.W., Domingos, M.A.N., Klein, T.J., Malda, J., Bártolo, P.J. and Hutmacher, D.W. (2012) “Additive Manufacturing of Tissues and Organs”, Progress in Polymer Science, 37, 1079.

[7] Bártolo, P.J., Chua, C.K., Almeida, H.A., Chou, S.M. and Lim, A.S.C (2009) “Biomanufacturing for tissue engineering: present and future trends”, Virtual and Physical Prototyping, 4, 203.

[8] Bártolo, P.J., Kruth, J.P., Silva, J., Levy, G., Malshe, A., Rajurkar, K., Mitsuishi, M., Ciurana, J. and Leu, M. (2012) “Biomedical production of implants by additive electro-chemical and physical processes”, CIRP Annals – Manufacturing Technology, 61(2):635-655.

[9] Almeida, H.A. and Bártolo, P.J. (2010), “Virtual Topological Optimization of Scaffolds for Rapid Prototyping”, Medical Engineering and Physics, 32(7):775-782.

[10] Almeida, H.A. and Bártolo, P.J. (2012) “Structural and Vascular Analysis of Tissue Engineering Scaffolds: Part 1 – Numerical Fluid Analysis”, Computer-Aided Tissue Engineering, M. Liebscher & D. Kim (Eds.), Springer, Chapter 12: 183-207.

[11] Mateus, A.J., Almeida, H.A., Ferreira, N.M., Alves, N.M., Bártolo, P.J., Mota, C.M. and de Sousa, J.P. (2008), “BioExtrusion for Tissue Engineering Applications”, Virtual and Rapid Manufacturing, P.J. Bártolo et al (Eds.), Taylor&Francis:171-175.

[12] Domingos, M., Chiellini, F., Gloria, A., Ambrosio, L., Bartolo, P.J. and Chiellini, E. (2012) “Effect of process parameters of the properties of 3D bioextruder poly(e-caprolactone) scaffolds”, Rapid Prototyping Journal, 18(1):116-121.

[13] Domingos, M., Chiellini, F., Cometa, S., De Giglio, E., Grilo-Fernandes, E., Bártolo, P.J. and Chiellini, E. (2011) “Evaluation of in vitro degradation of PCL scaffolds fabricated via bioextrusion – Part 2: Influence of pore size and geometry”, Virtual and Physical Prototyping, 6, 157.

[14] Domingos, M., Chiellini, F., Cometa, S., Giglio, E., Grilo-Fernandes, E., Bártolo, P.J. and Chiellini, E. (2010) “Evaluation of in vitro degradation of PCL scaffolds via bioextrusion - Part 1: Influence of the degradation environment”, Virtual and Physical Prototyping, 5, 1.

[15] Meyers, M.A., Chen, P.Y., Lin, A.Y.M. and Seki, Y. (2008) “Biological materials: Structure and mechanical properties”, Progress in Materials Science, 53(1):1-206.

[16] Gibson, L.J. and Ashby, M.F. (1997) “Cellular Solids: Structure and Properties”, Second Edition, Cambridge University Press, Cambridge, U.K.

[17] Maiti, S.K., Gibson, L.J. and Ashby, M.F. (1984) “Deformation and Energy Absorption Diagrams for Cellular Solids” Acta Metallurgica, 32(11):1963-1975.

[18] Deshpande, V.S. and Fleck, N.A. (2000) “Isotropic Constitutive Model for Metallic Foams,” Journal of the Mechanics and Physics of Solids, 48:1253-1276.