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# Optimization of scaffold design for bone tissue engineering: A computational and experimental study

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ABSTRACT

In bone tissue engineering, the scaffold has not only to allow the diffusion of cells, nutrients and oxygen but also provide adequate mechanical support. One way to ensure the scaffold has the right properties is to use computational tools to design such a scaffold coupled with additive manufacturing to build the scaffolds to the resulting optimized design specifications. In this study a topology optimization algorithm is proposed as a technique to design scaffolds that meet specific requirements for mass transport and mechanical load bearing. Several micro-structures obtained computationally are presented. Designed scaffolds were then built using selective laser sintering and the actual features of the fabricated scaffolds were measured and compared to the designed values. It was possible to obtain scaffolds with an internal geometry that reasonably matched the computational design (within 14% of porosity target, 40% for strut size and 55% for throat size in the building direction and 15% for strut size and 17% for throat size perpendicular to the building direction). These results support the use of these kind of computational algorithms to design optimized scaffolds with specific target properties and confirm the value of these techniques for bone tissue engineering.



## 1. Introduction

Scaffolds for bone tissue engineering must be highly permeable in order to promote cell proliferation and differentiation as well as allowing oxygen, nutrient and metabolic waste diffusion, but they have also to provide the necessary mechanical support [1–3], which will depend upon anatomic location. Assuming bone is adapted to its load bearing function, the elastic constants of normal healthy bone can provide a design target for a specific anatomic application. Under such assumption, there will be circumstances where the elastic properties should be maximized, but other applications where only a minimum of stiffness may be required, as in completely contained defects [4]. In addition, permeability has been demonstrated in many cases to be associated with higher bone regeneration [5–8]. Indeed, permeability is important for bone regeneration not only because higher values improve bone ingrowth but also because inadequate values may induce the formation of cartilaginous tissue instead of bone [9,10]. Several studies on bone scaffold have focused on permeability as a key parameter [11,12], including a number of authors who have been focused on the development of computational tools, as well as measuring systems for permeability analysis [11,13–16].

The objective of this work is to develop an optimization tool able to design scaffolds that can achieve a target performance with respect to stiffness and permeability, having in mind the goal of designing scaffolds for specific clinical applications. The problem consists of a material distribution problem based on topology optimization of structures [17]. The idea of designing the scaffold microstructure based on topology optimization has also been explored by other researchers. Some of the first studies were presented by Hollister and co-workers [6,18]. It was demonstrated that tissue regeneration depends on scaffold architecture parameters like porosity and permeability and consequently the control of scaffold architecture may help explain the relationship of scaffold architecture to biological behavior. Although it was not for a tissue engineering application, Guest and Prévost have also proposed a work on topology optimization to design periodic porous structures with maximum effective permeability and prescribed flow properties [19]. More recently, Li's research group has presented studies on scaffold design based on topology optimization [20,21].

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In the present study a topology optimization approach is presented as a tool to design bone scaffolds for given mechanical conditions (strain field) and/or required permeability. Several computational results, concerning different optimization scenarios, will be presented. Some of the resulting designs were built from an implantable biomaterial, polycaprolactone-4%hydroxyapatite (PCL-4%HA), using a selective laser sintering (SLS) system [22] and the actual features of the scaffolds, including the pore interconnection sizes (here called *throats* for simplification), strut sizes and porosity, were assessed experimentally in comparison to the optimally designed features. The paper represents a departure from previous works since here a complete study including scaffold optimization for elasticity and permeability, SLS fabrication and experimental validation is done. The study of this chain from design to manufacture demonstrates the unique challenges inherent in optimizing scaffold architecture and subsequently fabricating the scaffold to replicate the original complex, optimized design.

## 2. Materials and methods

### *2.1. Scaffolds design – topology optimization*

Topology optimization consists of defining pore and material regions within a given design domain [17]. Here, the design domain is a unit cell which repeated periodically in the three-dimensional space defines the scaffold microstructure, assumed as a periodic porous media (Fig. 1). The quantity of material allowed to distribute within the unit cell defines the volume fraction (or inversely the porosity) of the scaffold. In this work it is assumed scaffolds are homogeneous with periodic structure. However, the scaffold could be heterogeneous and designed “region by region” [23]. The permeability and elastic properties of this periodic media are computed using an asymptotic homogenization method as described for instance by Guedes and Kikuchi [24].

To compute the permeability properties, the problem of a fluid flowing through a porous media is described by a 2nd order differential equation which is obtained by a combination of the Darcy Law and the balance of steady state flow [14]. Its integral form is described by Eq. (1), where $\boldsymbol{K}$ is the second order tensor of the medium permeability coefficients (m$^2$), $P$ is the hydraulic pressure (Pa), $\mu$ is the fluid viscosity (Pa s), $\Phi$ is an admissible arbitrary smooth weight function (see for example [25]), $\boldsymbol{f}$ is the quantity of fluid being removed or generated by volume (s$^{-1}$) and $\bar{\boldsymbol{q}}$ is the Darcy flux on the boundary $\Gamma_q$ (m/s):

$$\int_\Omega K_{ij}\frac{\partial P}{\partial x_j}\frac{d\phi}{\partial x_i}d\Omega-\int_\Omega \phi f\mu d\Omega-\int_{\Gamma_q}\bar{q}\phi\mu d\Gamma=0,\quad \forall\phi \ \ admissible \tag{1}$$

Other authors have derived Darcy’s Law from homogenization [19,26,27], with the difference that these have utilized Stokes flow as the basis for expanding the homogenization description whereas here Darcy’s law is directly used to expand the description. The formulation in Eq. (1), however, provides for easier computation of sensitivity derivatives and is thus easier to implement in the topology optimization algorithm.

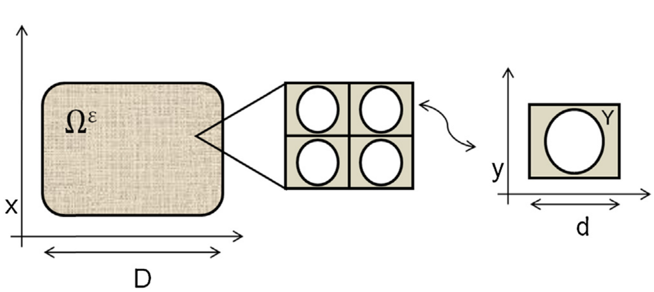


**Fig. 1.** Homogenization theory. Left, domain of the scaffold $\Omega^\varepsilon$; center, detail of the domain; right, unit cell Y; d, characteristic length scale of the microstructure size, represented by y; D, characteristic length scale of the scaffold, represented by x; $\varepsilon$, ratio between d and D.

For elastic properties let us consider the elasticity problem in its integral form (see for example [25]), where $\boldsymbol{E}$ is the fourth order tensor of elastic coefficients (Pa), $\boldsymbol{u}$ is the displacement field (m), $\boldsymbol{v}$ is the virtual displacement field, $\boldsymbol{b}$ represents the body forces (N/m$^3$) and $\boldsymbol{t}$ the traction on the boundary $\boldsymbol{\Gamma_t}$ (N/m$^2$).

$$\int_\Omega E_{ijkm}\frac{\partial u_k}{\partial x_m}\frac{\partial v_i}{\partial x_j}d\Omega-\int_\Omega b_i v_i d\Omega-\int_{\Gamma_i} t_i v_i d\Gamma,\quad \forall v_i \ \ admissible \tag{2}$$

The homogenization method “upscales” the problems described by Eqs. (1) and (2), converting the domain into a homogenized equivalent one, avoiding the complex task of analyzing the details of a periodic material. Using the method described by Guedes and Kikuchi [24], the equivalent permeability and elastic coefficients are obtained, respectively, by:

$$k^H_{im}=\frac{1}{Y}\int_y K_{ij}\left(\delta_{jm}-\frac{\partial x^m}{\partial y_j}\right)dY \tag{3}$$

$$E^H_{ijkm}=\frac{1}{|\text{¥}|}\int_{\text{¥}} E_{pqrs}\left(\partial_{rk}\partial_{sm}\frac{\partial\bar{x}^{km}_r}{\partial y_s}\right)\left(\partial_{pi}\partial_{qj}\frac{\partial\bar{x}^{ij}_p}{\partial y_q}\right)d\,\text{¥} \tag{4}$$

The $\chi$ functions in Eq. (3) represent the microstructure pressure perturbations for a unit average pressure gradient in each direction and are the solution of a series of problems in the microstructure:

$$\int_Y K_{ij}\frac{\partial x^m}{\partial y_j}\frac{\partial\phi}{\partial y_i}dY=-\int_Y k_{im}\frac{\partial\phi}{\partial y_i}dY\quad\forall\phi\,\text{admissible} \tag{5}$$

Equivalently, the $\bar{x}$ functions, in Eq. (4), represent the deformation modes for a unit cell subject to six unit average strains (3 normal and 3 shear), given by the solutions of the following set of problems in the microstructure:

$$\int_{\text{¥}} E_{ijrs}\frac{\partial\bar{\chi}^{km}_r}{\partial y_s}\frac{\partial v_i}{\partial y_j}=\int_{\text{¥}} E_{ijkm}\frac{\partial v_i}{\partial y_j}dY\quad\forall\ v_i\ \ \text{admissible} \tag{6}$$

These problems are solved on the domain of the unit cell by the finite elements method (FEM), using a MATLAB code. The unit cell is discretized in a 20 × 20 × 20 mesh of 8-node brick elements. To define the topology of the unit cell, a continuous “density field” ρ is associated to each finite element and its value is 1 if the finite element corresponds to a material region and 0 if it is void. This means that each element has a characterizing density value and, based on that value, each element’s mechanical and permeability properties are defined by a power law, where $K^0 = 1$, $E^0 = 10$ and $n$ is chosen as between 4 and 6:

$$k=(1-\rho)^n K^0 \qquad E=\rho^n E^0 \tag{7}$$

The final geometry will preferably only have 0 and 1 densities corresponding to material and void elements. In fact, this way of defining the material law corresponds to the SIMP (solid isotropic material with penalization) model [17], which leads the design variable $\rho$ to its extreme values, 0 or 1, once a suitable exponent $n$ is chosen. Material elements will have null permeability and maximum elasticity and void elements the other way around.

The homogenized properties are normalized to $K^0$, the “void permeability” and $E^0$, the base material elastic properties. While to obtain the effective elasticity, one only needs to multiply the resulting $E$ by the value of the elasticity of the base material ($E_{\text{base}}$), for permeability it is more complex since the permeability for the