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# A 3D finite element model to predict the arcade-like collagen structure in a layered PCL scaffold for cartilage tissue engineering

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**KEYWORDS** cartilage; collagen fibres; tissue engineering; anisotropy; finite element modelling

## 1. Introduction

Recently, tissue engineering strategies have been increased in order to mimic as closely as possible the environment of the native tissue, improving the regeneration of its structure and function. Previous experiments of cartilage tissue engineering used scaffolds with a homogeneous structure. However, the zonal organization in constructs has been shown to develop functional tissues with better biomechanical and biochemical properties. McCullen et al. (2012) studied the scaffold with a trilaminar structure of fibres showed that the heterogeneous organization have superior features when compared with the homogeneous scaffolds. Similarly, Steele et al. 2014 demonstrate that bilayered cartilage scaffolds have zonal differences in cellular proliferation, biochemical composition and gene expression. The directional organization of collagen fibres in the scaffolds strongly influences the anisotropic mechanical behaviour of the tissue, since the collagen fibres are the major responsible for its mechanical strength. The main goal of this study is to present new results related with a new anisotropic finite element (FE) model to mimic the growth and the remodelling of collagen fibres in a zonal organized polycaprolactone (PCL) scaffold for cartilage tissue engineering.

## 2. Methods

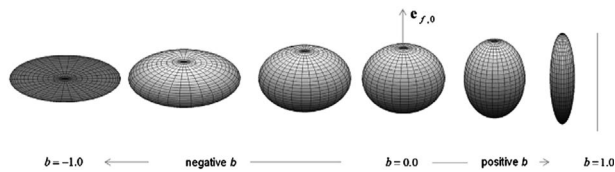
Using a FE computational tool, called *V-Biomech* (Cortez et al., 2016), two anisotropic approaches were combined and implemented in a previous mathematical formulation to simulate the transport of nutrients, the cell growth kinetics, the extracellular synthesis and the remodelling of the biphasic mechanical properties inside of a hydrogel. Considering the scaffold as incompressible, the description of its energy function  $\bar{W}_{total}$  is:

$$\bar{W}_{total} = \bar{W}_{iso} + \bar{W}_{aniso}^{COL} + \bar{W}_{aniso}^{PCL}$$

where  $\bar{W}_{iso}$  is associated with the isotropic component and defined by the neo-Hookean constitutive model. A new remodelling algorithm ( $\bar{W}_{aniso}^{COL}$ ) based on the distribution of the collagen fibres around a reference direction modelled by parameter  $b \in [-1, +1]$  (details in Figure 1) is introduced to simulate the reorientation and redistribution of collagen fibres, which grow and evolve throughout the cultivation time.

Their alignment was determined by the directions of the positive principal strains (Driessen et al., 2004; Wilson et al., 2006). In addition, the initial anisotropic structure with PCL fibres distributed in a depth manner was modelled following the Holzapfel's model (Holzapfel et al., 2000) and defined by  $\bar{W}_{aniso}^{PCL}$ . Based on literature data for PCL hydrogels, the Young modulus ( $E$ ), the Poisson's ratio ( $\nu$ ), the initial permeability ( $K_p$ ) and the initial fluid volume fraction ( $n_f$ ) were defined with the values presented in Table 1. All anisotropic constitutive parameters were determined by experimental results.

A quarter of a 3D disc shape scaffold with 5 mm diameter and 5 mm height was modelled as a biphasic material and meshed with 540 27-node hexahedral finite elements. Three different layers were defined with PCL fibres horizontally and vertically aligned in the superficial and deep zones, respectively, and randomly oriented in the middle zone of the scaffold. The construct was simulated as being submerged in a standard culturing environment with continuous concentrations in the scaffold-medium interface to promote the chondrocyte differentiation and the production of collagen. To evaluate the new biphasic fibre-reinforced model for a layered PCL scaffold, a compressive loading regime at physiological strain level (15% of displacement with a frequency of 1 Hz) was performed. The fields of the distribution of fibres, the associated reference directions and the maximum principal strains were investigated.



**Figure 1.** Three-dimensional graphical representation of the ellipsoidal distribution of fibres distribution around an initial reference direction  $e_{f,0}$ .

**Table 1.** Model parameters used in simulations.

Parameter	Value
$E$ (kPa)	9.5
$\nu$	0.3
$K_p$ (mm <sup>4</sup> /N.s)	60.0
$n_f$	0.8

### 3. Results and discussion

Analysing the fields of the compressive strains generated, a maximum of 0.15 MPa was observed in the superficial zone (Figure 2), being useful to align the collagen fibres parallel to the surface.

Under deformation, fibres rotate to the direction, which can resist more. In the superficial zone, fibres showed an isotropic distribution ( $b = 1.0$ , see Figure 1) in the direction parallel to the surface and a fibre reference direction, which was initially defined in the vertical direction, aligned perpendicular to the loading direction (Figure 3).

### 4. Conclusions

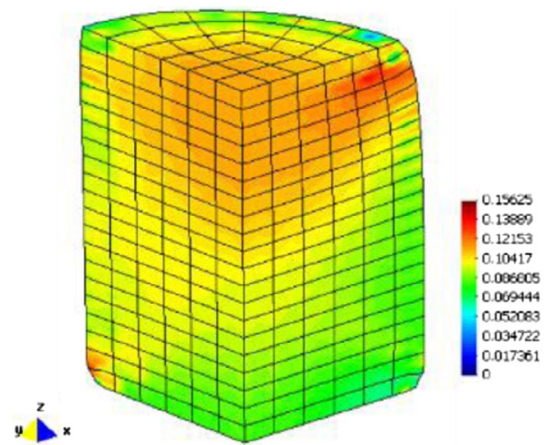
The FE model presented in this work allows to analyse, in a numerical way, the evolution of collagen fibres and their orientation in the three zones of a layered PCL scaffold, helping to a better understand of the experimental tests in cartilage tissue engineering

### Acknowledgements

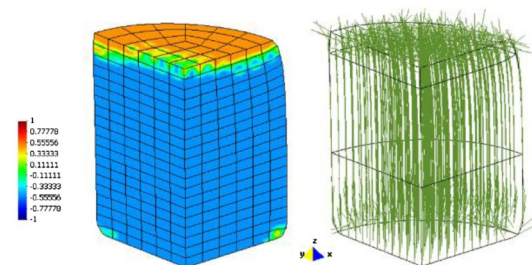
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**Figure 2.** Spatial gradients of the maximum principal strain on the tissue engineered cartilage scaffold.



**Figure 3** Distribution of collagen fibres (left), defined by the  $b$  parameter, and the associated reference vectors (right) This result is related with the initial direction of the PCL fibres, which were defined as aligned in the  $x$ -direction.

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