VISCOELASTIC-PLASTIC CONSTITUTIVE MODELS FOR BIODEGRADABLE THERMOPLASTICS USED TO PRODUCE SCAFFOLDS

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Abstract. A large range of biodegradable polymers are used to produce scaffolds for tissue engineering, which temporarily replace the biomechanical functions of a biologic tissue while it progressively regenerates its capacities. However, the mechanical behavior of biodegradable materials during its degradation, which is an important aspect of the scaffold design, is still an unexplored subject. The lack of design tools to predict long term behavior has limited the success of the biodegradable scaffolds. The considerations and the 4D numerical dimensioning methods presented here will help to overcome this limitation. For a biodegradable scaffold, performance decreases along its degradation, ideally in accordance to the regeneration of the biologic tissue, avoiding the stress shielding effect or the premature rupture. The viscoplastic constitutive models used in this work allow simulating the performance of biodegradable structures undergoing large deformations in the monotonic tests at different strain rates and it also enables to simulate hysteresis occurring in the unloading reloading cycles at different strain levels. Moreover, by setting the material parameters as functions of the degradation time, this enables the prediction of the mechanical behavior of complex 3D scaffolds during degradation time (the 4th dimension).

Keywords: scaffolds development, constitutive models, viscoplastic, biodegradable, plastics

1. INTRODUCTION

There are many biodegradable polymers commercially available to produce a wide variety of scaffolds, each of them with suitable properties according to the tissue they are supporting during regeneration. Different mechanical properties and degradation rates are possible among these polymers. However, each of these may have some shortcomings, which restrict its use in a specific application, due to inappropriate stiffness or degradation rate. Blending, copolymerization or composite techniques are extremely promising approaches, which can be used to tune the original mechanical and degradation properties of the polymers (Aslan *et al.*, 2000) according to the application requirements, enabling a range of mechanical properties and degradation rates. Many examples can be found from generic tissue engineering scaffolds (Levenberg and Langer, 2004), biodegradable ligaments (Vieira *et al.*, 2009), biodegradable endovascular (Soares, 2008) and urethral stents (Tamela and Talja, 2003). In nowadays 3D scaffolds can be printed with layers and parts of different biodegradable materials. These can then be coated with a biodegradable and bioactive material, to obtain a more intelligent surface in terms of cell mediated interaction. A complex geometry like these can be modeled in a commercial 3D drawing software and the mechanical behavior can be predicted by numerical simulation.

Biodegradable polymers can be classified as either naturally derived polymers or synthetic polymers. The most popular and important class of biodegradable synthetic polymers are aliphatic polyesters, such as polylactic acid (PLLA and PDLA), polyglycolic acid (PGA), polycaprolactone (PCL), polyhydoxyalkanoates (PHA's) and polyethylene oxide (PEO) among others. They can be processed as other thermoplastic materials. Natural polymers used in scaffolds include starch, collagen, silk, alginate, agarose, chitosan, fibrin, cellulosic, hyaluronic acid-based materials, among others. Some of these are bioactive material, and their degradation products can modulate the inflammatory response. However, these are more prone to enzymatic degradation than the synthetic biodegradable polymers, consequently the degradation kinetics depends more on the host. The synthetic polymers have that advantage of more predictable behavior evolution. New biodegradable material solutions are still arising every day.

The design process of these implantable biodegradable medical devices must contemplate the biocompatibility issues related to toxicity and the functional aspect related to mechanical considerations. In terms of mechanical dimensioning, one must consider not only the static strength and stiffness of the device, but also the long-term

mechanical behavior considering degradation. This degradation is defined as the time-dependent cumulative irreversible damage due to hydrolysis. When loading conditions are simple and the desired time for mechanical support is known, a "trial and error" approach may be sufficient to design reasonable reliable scaffolds. However, such studies represent a costly method of iterating the product dimensioning. Hence, in more complex situations, device designers and engineers can use numerical approaches to define the material formulation and geometry that will satisfy the immediate needs of symptomatic relief, without the occurrence of any degradation, using conventional 3D numerical analysis in iterative dimensioning. It is very important to mention that, nowadays, there isn't an established scientific method to develop a product made from biodegradable polymer. Thus, scientific contributions in this direction can aid the development of reliable biodegradable medical devices.

The failure criteria for maximum strength as a function of degradation time have traditionally been modeled according to a first order kinetics. The dimensioning of these devices can be complex, not only because the mechanical properties evolve during degradation, but also because these biodegradable materials cannot be modeled using only elastic constitutive equations (Soares, 2008). In more precise terms, the response of an elastic material implies that the loading and unloading paths coincide, the material responds instantaneously to an applied load. This behavior is time-independent and the material returns to its former unloaded configuration upon the removal of external loads. However, for example, Soares (2008) and Grabow *et al.* (2007) verified the nonlinear viscoelastic characteristics of PLA. Also, the experimental results for the researched biodegradable material (PLA-PCL blend in proportion 90:10), presented in a previous work (Vieira *et al.*, 2013) clearly demonstrate the non linear time-dependent mechanical behavior. Therefore, time-dependent constitutive models are required to simulate all those phenomena.

A constitutive model for a mechanical analysis is a relationship between the response of a body (for example, strain state) and the stress state due to the forces acting on the body, which can include the environmental effects. A wide variety of material behaviors can be described with a few different classes of constitutive equations. And the existing models can be divided into two categories: the equilibrium models and the time-dependent models (Bergström and Boyce, 1998). It is known that the stress in a biodegradable polymer after being subjected to a step in the applied strain will relax towards an equilibrium state (Miller and William, 1984). This equilibrium state can be represented by linear elastic or non linear elastic models, such as elasto-plastic or hyperelastic models. The response of an elastic or hyperelastic material implies that the loading and unloading paths coincide. Mechanical properties of biodegradable plastics are commonly assessed within the scope of linearized elasticity, despite the clear evidence that they can undergo large strains before breaking. Other inelastic or hyperelastic models are required to model those situations. Hence, given the nature of biodegradable polymers, classical models such as the neo-Hookean and Mooney-Rivlin models, for incompressible hyperelastic materials, have been used to predict mechanical behavior until rupture of non-degraded under quasi-static monotonic loading, for instance, some researchers applied this approach for PLA (Garlotta, 2001; Lunt, 1998). However, those approaches neglect changes in the properties of the material during degradation process. In the case of elasto-plastic models, after unloading phase, the material returns to an equilibrium sate, which includes some plastic strain. These types of models show at least one sliding element in its model formulation. Hence, the loading and unloading paths do not coincide. Although, these approaches neglect the time-dependent mechanical behavior, they can simulate the equilibrium response.

To account time dependency, dissipative elements must be used in the model formulation. The simplest viscoelastic models consider a linear combination of springs (using the Hooke's law) and dashpots (using Newtonian damper with linear viscosity). The classical examples of these simple models are the Maxwell and Kelvin–Voigt models, in which spring and dashpots are organized in series or in parallel, respectively. The elastic component is modeled using a single material parameter E (Young modulus) according to the Hooke's Law, $\sigma = E\varepsilon$. Analogously, the dissipative element uses a single material parameter η (viscosity) according to the equation $\sigma = \eta \; d\varepsilon/dt$. More complex variants of these simple models can be found at the literature. These models can simulate the non linear viscoelastic, viscoplastic and hysteretic nature of polymers. These models are based on the same concept of networks, combining elastic, sliding and dissipative elements, in order to simulate the equilibrium response of the material and the time-dependent deviation from equilibrium state. However, those approaches have been applied to predict the mechanical behavior of polymers neglecting changes in the properties of the material during the hydrolytic degradation process. Therefore, it is possible to find only few recent scientific contributions about this issue in the literature, mainly concerning biodegradable polymers (Khan and El-Sayed, 2012; Muliana and Rajagopal, 2012; Soares, 2008; Vieira *et al.*, 2011a).

Regarding the challenge presented above, in the following section of this work, the degradation process is discussed, demonstrating how these phenomena can be mathematically modeled. After that, a three-dimensional viscoplastic model developed by Bergström and Boyce (1998) is analyzed in terms of its potential and limitations to represent a complex load case scenario in a biodegradable material. Since this model assumes that the mechanical behavior is divided into an equilibrium network and a non-linear time-dependent network, it enables to simulate the monotonic tests of a biodegradable structure loaded under different strain rates. Also, it is possible to predict the hysteresis effects during unloading-reloading cycles at different strain levels. Furthermore a parametric study is presented, showing the evolution of the material model parameters during the hydrolytic degradation, and analyzing those parameters more sensible to this process. Finally, a method is proposed, based on this analysis, to simulate the three-dimensional viscoplastic mechanical behavior during hydrolytic degradation.

2. BIODEGRADATION AND EROSION

Usually, the most important degradation mechanism of biodegradable polymers is chemical degradation via hydrolysis (Göpferich, 1996). Due to hydrolytic or enzymatic chain scission, which occurs in the polymeric macromolecules, and the consequent reduction of molecular weight, the mechanical response of a biodegradable polymeric product will evolve during this process.

An important distinction must be made between erosion and degradation. Both are irreversible processes. The erosion process can be described by phenomenological diffusion-reaction mechanisms. An aqueous media diffuses into the polymeric material while oligomeric products diffuse outwards to be then bio-assimilated by the host environment. Then, we have material erosion with correspondent mass loss. To fully model the erosion process, a complex mathematical model is needed to account for all the reaction steps and for the structural and morphologic details. The parameters in such a model require extensive experimentation. Numerical techniques have been used (ex: Göpferich and Langer, 1993) to solve the corresponding equations for devices in the context of drug release systems. However, these models were unable to predict the mechanical properties evolution of the device.

On the other hand, the degree of degradation refers to mechanical damage, with negligible mass loss, and depends on hydrolysis. Polymer degradation is the first step of the erosion phenomenon, where the mechanical properties are significantly reduced. Within the polymeric matrix, hydrolytic reactions take place, mediated by water and/or enzymes, converting these very long polymer chains into shorter water-soluble fragments. Hydrolytic degradation can be estimated by measuring the evolution of molecular weight, by gel permeation chromatography (GPC), or the tensile strength evolution (by universal tensile testing). The complete erosion of the polymer is known to take substantially longer than the complete loss of tensile strength.

2.1 Diffusion

After immersion of a biodegradable polymeric device in an aqueous medium, the very first event which occurs is water uptake, up to a saturation of water concentration that depends on the hydrophilicity of the polymer, its crystalline degree, the temperature and pH of the media. This step is accompanied by swelling. The intrusion of water then triggers the chemical polymer degradation. While water diffuses rapidly well inside the material, enzymes are large molecules unable to do it, and so they degrade at surface. The penetrating water rapidly creates a negative gradient of water concentrations from the surface to the centre as expected from a pure diffusion viewpoint. Diffusion of small molecules like water is rather fast as compared with degradation that can take several months. Therefore, one can consider that hydrolysis of ester bonds starts homogeneously along the volume from the beginning (Li *et al.*, 1990). The water concentration (*w*) along the the three directions (*x, y* and *z*), and during the incubation time (*t*), is determined using Fick's Law, presented for 3D:

$$\frac{dw}{dt} = D_1 \frac{\partial^2 w}{\partial x^2} + D_2 \frac{\partial^2 w}{\partial y^2} + D_3 \frac{\partial^2 w}{\partial z^2} \qquad (1)$$

In the case of isotropic polymers, diffusion has no preferential direction, and $D_1 = D_2 = D_3 = D$.

2.2 Hydrolysis

The macromolecular skeleton of many polymers comprises chemical bonds that can go through hydrolysis in the presence of water molecules, leading to chain scissions. In the case of aliphatic polyesters, these scissions occur at the ester groups. A general consequence of such process is the lowering of the plastic flow ability of the polymer, causing the change of a ductile and tough behavior into a brittle one. In Fig. 1, it is presented a scheme of the most common hydrolysis mechanism. Each polymer molecule, with its own carboxylic and alcohol end groups, is broken in two, randomly in the middle at a given ester group. Hence, the number of carboxylic end groups will increase with degradation time, while the molecules are being splited by hydrolysis. Hydrolysis has traditionally been modeled using a first order kinetics equation based on the kinetic mechanism of hydrolysis, according to the Michaelis–Menten scheme (Bellenger *et al.*, 1995). According to Farrar and Gillson (2002), the following first-order Eq. (2) describes the hydrolytic process related to the carboxyl end groups (*C*), the hydrolysis rate constant (*k*), ester concentration (*e*) and water concentration (*w*), during the degradation time (*t*):

$$\frac{dC}{dt} = kewC = uC \qquad (2)$$

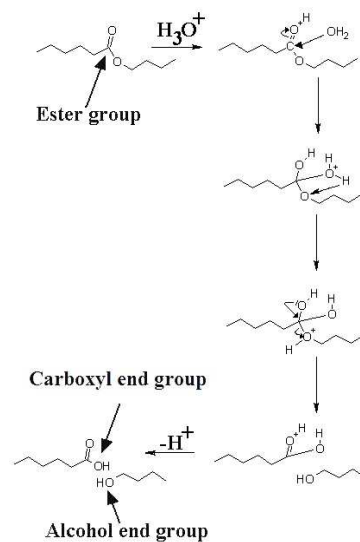where *u* is the mean hydrolysis rate of the material.

Figure 1. Acid catalyzed hydrolysis mechanism (Vieira *et al.*, 2011a)

Using the molecular weight, and since the concentrations of carboxyl end groups are given by $C=1/M_n$; the Eq. (2) becomes Eq. (3):

$$M_{n_t} = M_{n_0}\, exp^{-ut} \tag{3}$$

where M_{nt} and M_{n0} are the number-average molecular weight, at a given time t and initially at t=0, respectively. This equation leads to a relationship $M_n = f(t)$. It has been shown by Vieira *et al.* (2011a) that the fracture strength follows the same trend as the molecular weight, described by Eq. (4):

$$\sigma_t = \sigma_0\, exp^{-ut} \tag{4}$$

Hydrolysis rate u is affected by the temperature or mechanical stress, molecular structure, ester group density as well as by the degradation media. Temperature will increase the hydrolysis rate constant k, which is associated to the probability of bond scissions, due to excitement of the molecules. In this work, the temperature is kept constant as in the human body, i.e. at the homeostatic value of around 37°C. However, it is important to highlight that the influence of the mechanical environment in the degradation rate has been also reported by some researchers (Miller and William, 1984). Similarly to temperature, stress also increases the probability of bond scissions, but in the present case, no loads were applied during the degradation process. Concerning the degradation dependence on the degradation media, some authors reported that the degradation rate of PLA and blends of PLA-PCL was significantly affected by some enzymes (Gan et al., 1999; Williams 1981). The pH of the aqueous media also affects the degradation reaction rates (Tsuji and Ikada, 1998; Tsuji and Ikada, 2000; Tsuji and Nakahara, 2001). Again, in the present work, pH can be considered constant. Also, in the human body, pH is kept at a homeostatic value. For these reasons, it was considered that the hydrolysis rate constant k was constant over time. Since water diffusion is much faster than hydrolysis, it is usually assumed that water is spread out uniformly in the sample volume (i.e. no diffusion control) (Göpferich, 1996). Hence w is constant in the early stages of the reaction along the volume. In this early stage of erosion, when mechanical strength droops significantly, also the ester concentration e is nearly constant, because the macromolecules remain macro, despite the scissions, which occur randomly in the ester groups (Göpferich and Langer, 1993). Therefore, the degradation rate, $u=kwe$, was considered constant during degradation. In some cases this assumption is not valid because of heterogeneous diffusion, or the presence of a complex three-dimensional stress field, which evolves during the degradation process. However, it is possible to relate damage with strength values and to molecular weight. Thus, the hydrolytic damage d was defined by Vieira *et al.* (2011a), according to Eq. (5):

$$d = 1 - \frac{\sigma}{\sigma_0} = 1 - \frac{M_{n_t}}{M_{n_0}} = 1 - exp^{-ut} \tag{5}$$

To simulate the evolution of the mechanical behavior of biodegradable polymers, the constitutive models must be adapted accordingly to hydrolytic damage.

2.3 Hydrolytic degradation: simulation methods

Recent developments of hyperelastic constitutive models enable the modeling of biodegradable structures during degradation (Soares *et al.*, 2010; Vieira *et al.*, 2011b) considering that the constitutive model parameters are changed according to hydrolytic damage. More recently, a nonlinear viscoelastic model was used to simulate the time-dependent performance of biodegradable structures (Muliana and Rajagopal, 2012). In that work, the authors considered that hydrolytic damage depends on the deviatoric strain tensor and the concentration of water. Thus, at each time increment step, damage must be calculated in the material point of the continuous model. First water concentration at each material point is updated based on Fick's Law. Then the hydrolytic damage is updated as function of the deviatoric strain tensor. Finally, the constitutive relation is updated at each time increment. This method enables to model the relaxation behavior (or creep) during degradation, and it is reasonably good to model moderate deformations. However, in many applications, the mechanical behavior of biodegradable polymers should be analyzed considering large deformation theories (Khan and El-Sayed, 2012). Thus Khan and El-Sayed (2012) developed a phenomenological constitutive viscoelastic-plastic model, which is able to predict the response of biodegradable polymers under large deformations. The model consists of a nonlinear elastic spring element acting in parallel with a variable number of Maxwell elements. The hyperelastic response of both springs in the elastic branch and in the Maxwell branch is governed by the Ogden-type free energy function. The model was based on the phenomenological approach and some of its capabilities, mainly at large deformations, require experimental validation. These types of methods allow the four-dimensional modeling, where the fourth dimension is the time. Yet, the characteristic time of degradation is different from the characteristic viscoelastic time for stress relaxation or creep. If the material has viscoelastic attributes, then the degradation time couples with the time-dependent mechanical behavior of the material. Stretching induces stress relaxation with time by means of viscous flow of the material. Besides, in parallel, stretching induces chemical scissions of the molecules, which provide an additive pathway for relaxation (Khan and El-Sayed, 2012).

The viscoplastic constitutive model used in this work, the Bergström-Boyce model (Bergström and Boyce, 1998) allows simulating the performance of polymers undergoing large deformations. On the other hand, it is a physical inspired polymer model. An important motivation for using physically based constitutive theory to simulate the mechanical behavior of a polymer is that the model can be calibrated through a relative small set of simple mechanical tests, such as uniaxial loading, and enables accurate predictions for other loading cases (Bergström et al., 2002). Together, it enables to simulate the monotonic tests of polymers at different strain rates and it also enables to simulate hysteresis, which occurs under unloading-reloading cycles at different strain levels (Bergström et al., 2002). Unlike the other material models, which were used and adapted to simulate the mechanical behavior during degradation, the Bergström-Boyce model, since it is viscoplastic, enables to simulate the irreversible accumulation of plastic strain. This phenomenon leads dimension instability and consequent design problems. Therefore, in this work, a parametric study is presented for a polymeric blend of PLA-PCL, showing the evolution of the material model parameters during hydrolytic degradation, and analyzing those parameters more sensible to this process. In this investigation, based on experimental results, the limitation and potentialities of the Bergström-Boyce model to simulate a biodegradable polymer over large range deformations under hydrolytic biodegradation are evaluated. Finally, a method is proposed, based on this analysis, to simulate the three-dimensional viscoplastic mechanical behavior during hydrolytic degradation. From the author's knowledge, few methods were developed to predict the mechanical behavior during hydrolytic degradation. These are based on hyperelastic models (Soares *et al.*, 2010; Vieira *et al.*, 2011a) , or quasi-linear viscoelastic models (Muliana and Rajagopal, 2012), or phenomenological viscoplastic models (Khan and El-Sayed, 2012). However the calibration and validation of these methods was restricted to moderate deformations. On the other hand, in the present work, a method based on a viscoplastic model, physical inspired on the polymeric microstructure, was calibrated and validated for large deformations.

3. BERGSTRÖM AND BOYCE'S MODEL

In the constitutive model, the mechanical behavior is decomposed into two parts: an equilibrium response, modeled by a hyperelastic constitutive model (defined as Network A), and a time-dependent deviation from equilibrium, defined by a viscoplastic constitutive model (defined as Network B) as shown by Fig. 2.
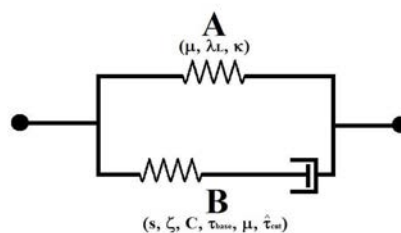

Figure 2. Rheological representation of Bergström-Boyce model, adapted from (Bergström and Boyce, 1998)

In fact the Network B is composed of an elastic element (also modeled by a hyperelastic constitutive model) in series with a time-dependent element, which acts to relieve the strain of the Network A in function of the time. According to the rheological representation of the constitutive model, shown in Fig. 2, the material is modeled as two polymer networks acting in parallel (Bergström and Boyce, 1998). Finite deformation continuum mechanics requires the specification of reference and deformed configurations. Let X denotes the components of a Cartesian vector specifying a material point in the reference configuration. Then x(X, t) denotes the same material point in the deformed configuration, and represents the motion of this material point. The total deformation gradient is defined by Eq. (6):

$$F = F_{ij} = \frac{\partial x_i}{\partial X_j}$$

(6)

Since deformation in Network A is the same of Network B, then $F = F_A = F_B$. The deformation gradient in Network B can be further decomposed into a plastic deformation followed by an elastic deformation ($F_B = F^e{}_B F^p{}_B$), where the plastic deformation represents the configuration obtained by a complete virtual elastic unloading of Network B to a stress free state. The response of Network A is given by the Arruda-Boyce model (Arruda and Boyce, 1993), also known as eight-chain model. The Arruda-Boyce eight-chain hyperelastic model is an extension of the neo-Hookean model, which takes non-linear Langevin chain statistics into account when deriving the strain energy density function. The stress response of the eight-chain model is given as:

$$\sigma_A = \frac{\mu}{J \bar{\lambda}^*} \cdot \frac{\mathcal{L}^{-1}(\bar{\lambda}^*/\lambda_L)}{\mathcal{L}^{-1}(1/\lambda_L)} \operatorname{dev}[B^*] + \kappa(J - 1)I$$

(7)

where μ is the shear modulus, κ the bulk modulus, and λ_L is the limiting chain stretch. I is the second order identity tensor. $\mathcal{L}^{-1}(x)$ is the inverse Langevin function, where $\mathcal{L}(x)=[\coth(x) - 1/x]$, is the Langevin function. According to Gaussian statistics the shear modulus μ is calculated as $\mu = NbT$, where N is the number of polymer chains per unit volume, b is the Boltzmann constant, and T is temperature (Arruda and Boyce, 1993). The Jacobian is defined as $J=\det[F]$. $\bar{\lambda}^*$ is the applied chain stretch, which can be calculated from:

$$\bar{\lambda}^* = \sqrt{\frac{\operatorname{tr} B^*}{3}}$$

(8)

$B^* = J^{-2/3}B = J^{-2/3}FF^T$ is the distortional left Cauchy-Green tensor and σ_A is the Cauchy stress tensor (also known as true stress tensor) acting in Network A. The stress on Network B is also given by the eight-chain model:

$$\sigma_B = \frac{s\mu}{J_B^e \overline{\lambda_B^{e\,*}}} \cdot \frac{\mathcal{L}^{-1}(\overline{\lambda_B^{e\,*}}/\lambda_L)}{\mathcal{L}^{-1}(1/\lambda_L)} \operatorname{dev}[B_B^{e\,*}] + \kappa(J_B^e - 1)I$$

(9)

where s is a dimensionless material parameter, which specifies the shear modulus of Network B relative to Network A, and $\overline{\lambda_B^{e\,*}}$ is the chain stretch in the elastic part of Network B. Using this representation, the total Cauchy stress tensor $\sigma_= \sigma_A + \sigma_B$. The velocity gradient in Network B, $L_B = \dot{F}_B F_B^{-1}$, and the deformation gradient in Network B can be decomposed into elastic and viscoplastic components ($F_B = F^e{}_B F^p{}_B$). Hence:

$$L_B = \left[\frac{d}{dt}\left(F_B^e F_B^p\right)\right]\left(F_B^e F_B^p\right)^{-1} = \left[\dot{F}_B^e F_B^p + F_B^e \dot{F}_B^p\right]\left(F_B^p\right)^{-1}\left(F_B^e\right)^{-1} =$$
$$= \dot{F}_B^e (F_B^e)^{-1} + F_B^e \dot{F}_B^p \left(F_B^p\right)^{-1}\left(F_B^e\right)^{-1} = L_B^e + F_B^e L_B^p (F_B^e)^{-1} = L_B^e + \widetilde{L_B^p}$$

(10)

where the velocity gradient L can be decomposed into the sum of stretch rate and spin tensors, D and W respectively:

$$L_B^p = \dot{F}_B^p \left(F_B^p\right)^{-1} = D_B^p + W_B^p$$

(11)

$$\widetilde{L_B^p} = \widetilde{D_B^p} + \widetilde{W_B^p}$$

(12)

To ensure the unloading unique, the viscous spin tensor is prescribed zero, i.e. $\widetilde{W_B^p} \equiv 0$, according to (Bergström and Boyce, 1998; Bergström *et al.*, 2002). The rate of viscoplastic deformation of Network B is constitutively prescribed by:

$$\widetilde{L_B^p} = \widetilde{D_B^p} = \dot{\gamma}_B N_B = \dot{\gamma}_B \frac{\text{dev}[\sigma_B]}{\tau} = \dot{\gamma}_B \frac{\text{dev}[\sigma_B]}{\|\text{dev}[\sigma_B]\|_F} \tag{13}$$

where N_B gives the direction of the driving stress state of the relaxed configuration and $\dot{\gamma}_B$ is an effective creep rate. $\tau = \|\text{dev}[\sigma_B]\|_F$ is the effective stress, which drives the viscous flow. The time derivative of F_B^p can be derived as follows:

$$\widetilde{L_B^p} = F_B^e \dot{F}_B^p (F_B^p)^{-1} (F_B^e)^{-1} = \dot{\gamma}_B N_B \tag{14}$$

and:

$$\dot{F}_B^p = \dot{\gamma}_B (F_B^e)^{-1} \frac{\text{dev}[\sigma_B]}{\|\text{dev}[\sigma_B]\|_F} F_B^e F_B^p \tag{15}$$

The effective creep rate-equation for viscous flow is given by (Bergström and Boyce, 1998; Bergström *et al.*, 2002):

$$\dot{\gamma}_B = \dot{\gamma}_0 \left(\overline{\lambda_B^p} - 1 + \xi\right)^C \left[R\left(\frac{\tau}{\tau_{base}} - \hat{\tau}_{cut}\right) \right]^m \tag{16}$$

where $\dot{\gamma}_0 = 1$ is a constant introduced to ensure dimensional consistency, $R(x) = [(x + |x|)/2]$ is the ramp function, $\hat{\tau}_{cut}$ is a cut-off stress such that no flow will occur for values lower than the cut-off stress, τ_{base} represents the flow resistance, m is a positive stress exponential, ξ is a strain adjustment factor, C is a strain exponential constant, which is restricted at the interval [-1, 0], and (Bergström and Boyce, 1998):

$$\overline{\lambda_B^p} = \sqrt{\frac{\text{tr}[F_B^p F_B^{p^T}]}{3}} \tag{17}$$

4. EXPERIMENTAL ANALYSES AND NUMERICAL SIMULATIONS

Suture fibers of PLA–PCL (composition 90:10, with 400 μm in diameter) were provided by *Chirmax*. First, non degraded specimens were evaluated. Three test specimens of 100mm long were cut for each experimental set. The distance between the grips was set to 50 mm and, non degraded specimens were monotonically tensile tested in a universal testing machine (TIRAtest 2705), with a load cell of 500 N and grips commonly used in fiber testing, at displacement rates of 500 mm/min and 15 mm/min.

In addition to these monotonic tensile tests, one cyclic test was done using the same setup, with a load displacement rate of 50mm/min and unload displacement rate of 5mm/min. The first cycle was loaded up to 0.7 mm, then reloaded up to 1.5 mm, 3 mm, 4.5 and 6 mm in the 5th cycle. The unloading between each cycle was conducted until reach a stress free state. Second, the fiber specimens were placed in 50 ml test tubes and submitted to four different degradation steps (0, 2, 4 and 8 weeks) under phosphate buffer solution (PBS) at constant temperature (37 ◦C). A similar monotonic tensile test, at displacement rate of 250 mm/min, was performed on dry specimens (24 h in incubator at 37 ◦C) at the end of each degradation step.

The experimental results, published in previous work (Vieira *et al.*, 2013; Vieira *et al.*, 2011a), exposed the nonlinear time-dependent mechanical behavior of PLA-PCL suture fibers. Based on these results (the average of three tests), the inverse analyses to identify the parameters of the viscoplastic model was done using MCalibration™ software (from *Veryst Engineering*). The inverse parameterization technique used to minimize the difference between the experimental results and the model predictions was the Nelder-Mead method, which is implemented in the MCalibration™ software. In addition, a parametric study for all the parameters was performed using 3 sets of values (low, mean and high), where the mean corresponds to the value determined by inverse parameterization, and where the low and high values correspond to deviations of more or less 10 percent of the mean value. This parametric study enabled to identify the most sensitive parameters of the material model for the prediction of the experimental results. After that, another inverse parameterization was done where the two active parameters were those most sensitive, while the other parameters were set to averaged values obtained in the previous inverse analyses. After determining the two most sensitive parameters at each degradation step, they were fitted by linear regression as function of the degradation damage *d* model as defined by Vieira *et al.* (2011a). Finally, the predictions using the two most sensitive parameters at each degradation step, calculated by the correspondent linear regression, were compared to the experimental results. It is important to highlight that only the results of monotonic tensile tests at 250 mm/min were used in the analyses to identify the parameters of the viscoplastic model during hydrolytic degradation.

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5. RESULTS AND DISCUSSION

In the Fig. 3a) it is possible to observe that the evaluated viscoplastic model was able to simulate the time-dependent nature of the polymer in this range of strain rates. By using these two loading cases in the inverse analyses, the coefficient of determination R^2 was very close to 1(one), meaning that the model was able to predict the mechanical behavior of the polymer at different strain rates very accurately.

In the Fig. 3b), it is possible to identify that the evaluated viscoplastic model was also able to simulate the hysteric effect commonly observed in polymers. By using cyclic unloading-reloading and monotonic loading cases in the inverse analyses, the coefficient of determination R^2 was still very close to 1(one).
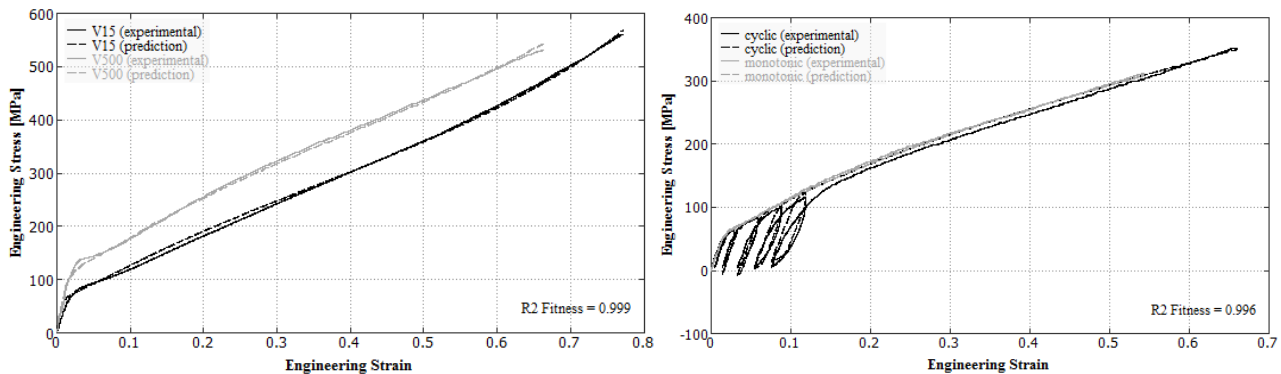

Figure 3. Experimental results of non degraded PLA-PCL fiber, and prediction via viscoplastic Bergström-Boyce model a) monotonic tensile test at two displacement rates (500 and 15mm/min), b) cyclic tensile test

From Fig. 4 it is possible to see that the evaluated viscoplastic model was also able to simulate the non-linear mechanical behavior until rupture in monotonic tensile test at different hydrolytic degradation steps, with the coefficient of determination R^2 always above 0.995. Although precision is slightly reduced with hydrolytic degradation time. Comparing to hyperelastic models such as the Neo-Hookean or the Arruda-Boyce models, the coefficient of determination R^2 does not reach 0.98, and reduces considerably during the hydrolytic degradation time (R^2 does not reach 0.8 after 8 weeks of hydrolytic degradation). Thus, the coefficient of determination is much higher for the Bergström-Boyce models (after 8 weeks of hydrolytic degradation R^2 is 0.995).
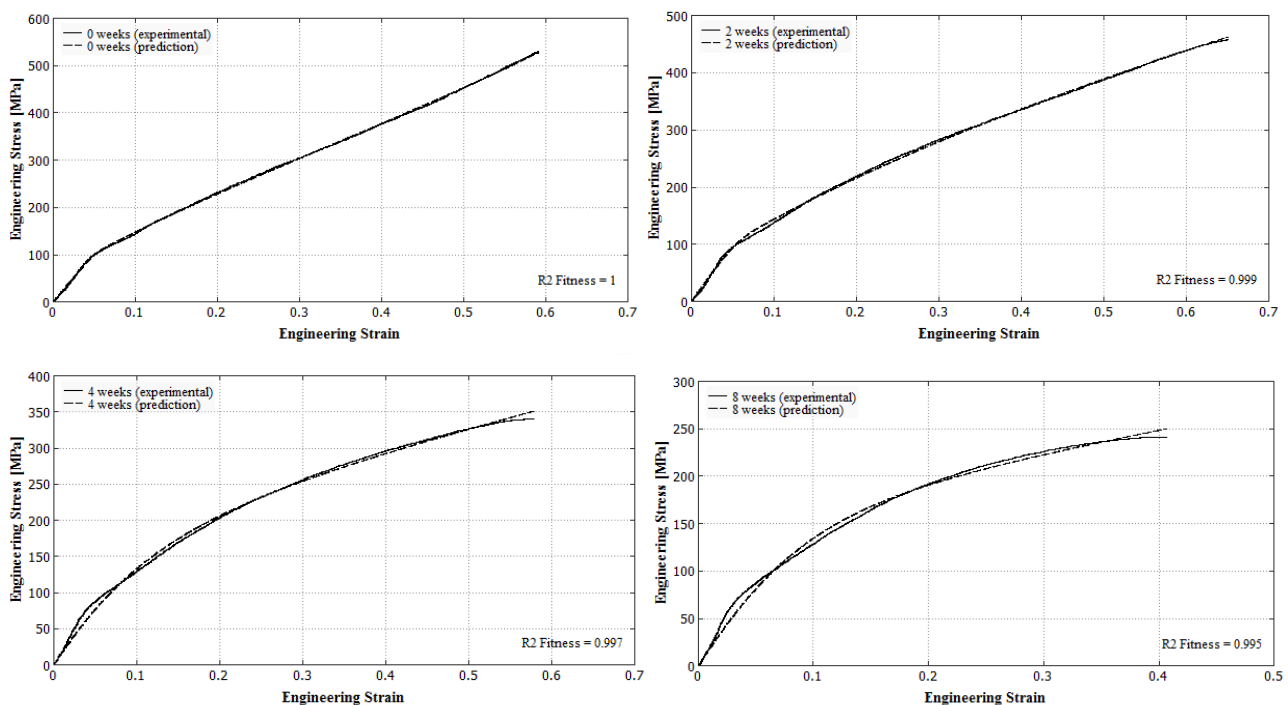

Figure 4. Experimental results of monotic tensile test at 250 mm/min of PLA-PCL fiber, and prediction via viscoplastic Bergström-Boyce model, after 0, 2, 4 and 8 weeks of hydrolytic degradation

In the Tab. 1, a list of the material model parameters, which are used on the predictions of the mechanical behavior during hydrolytic degradation, are presented at each degradation step.

Table 1. List of the model parameters determined by inverse parameterization at each hydrolytic degradation step

Model parameters	0 weeks	2 weeks	4 weeks	8 weeks
μ - Shear modulus of network A	355.439	331.842	256.811	192.686
λ_L - Locking stretch	1.55813	5.18064	9.99997	5.42087
κ - Bulk modulus	59137.1	52603.8	2522.86	10961.5
s - Relative stiffness of network B	0.994461	1.03951	1.40451	2.27284
ξ - Strain adjustment factor	0.286773	0.189326	0.500236	0.482787
C - Strain exponential	-0.48398	-0.54034	-0.00815	-1.8e-08
τ_{base} - Flow resistance	48.2916	94.9219	1645.91	1402.44
m - Stress exponential	13.4184	5.68314	1.1001	1.34039
$\hat{\tau}_{cut}$ - Normalized cut-off stress for flow	0.008102	0.009484	4.17e-06	0.003313

Based on the parametric study, it is concluded that the shear modulus μ is the most sensitive parameter of the Bergström-Boyce model, for all the hydrolytic degradation steps. The locking stretch λ_L is another sensitive parameter, which was studied. We verify that deviations from the determined value affect the prediction, mainly at higher stress levels. However, since the hydrolytic degraded specimens break at lower stress levels, this parameter becomes almost insensitive in the predictions of the mechanical behavior of the polymer after two weeks of hydrolytic degradation and forward. Also the flow resistance τ_{base} is sensitive to deviations. Although it is much less sensitive than the shear modulus μ, it is observed great changes of its value during the degradation process. On the other hand, stress exponential m is also sensitive to deviations, but its value remains in the same order of magnitude. The strain exponential C is nearly insensitive for values close to zero. The correlation with experimental results decreases for values close to -1 (minus one). This same trend was observed by Bergström *et al.* (2002), in the case o UHMWPE, where the optimal value of the material parameter C was very close to zero. However, for elastomeric materials, the same parameter C has a value close to -1 (minus one) (Bergström and Boyce, 1998). Hence the magnitude of the plastic flow rate is nearly independent on the strain level. Based on these observations, it was performed another inverse analysis, considering only these two variable parameters: the shear modulus μ and the flow resistance τ_{base}. The other parameters were set constant during the hydrolytic degradation process, assuming averaged values determined from the different hydrolytic degradation steps, which were calculated in the previous inverse analyses. The parameters determined by this way are shown in Tab. 2.

Table 2 List of the material model parameters determined by inverse parameterization at each hydrolytic degradation step, with only two active parameters (the shear modulus μ and the flow resistance τ_{base})

Model parameters	0 weeks	2 weeks	4 weeks	8 weeks
μ - Shear modulus of network A	408.062	335.217	261.177	211.162
λ_L - Locking stretch	5	5	5	5
κ - Bulk modulus	30000	30000	30000	30000
s - Relative stiffness of network B	1.5	1.5	1.5	1.5
ξ - Strain adjustment factor	0.4	0.4	0.4	0.4
C - Strain exponential	-0.25	-0.25	-0.25	-0.25
τ_{base} - Flow resistance	32.109	139.271	209.505	287.162
m - Stress exponential	3	3	3	3
$\hat{\tau}_{cut}$ - Normalized cut-off stress for flow	0.005	0.005	0.005	0.005

As it can be seen, the material was assumed to be nearly incompressible, since the bulk modulus κ used, which represents the resistance to volume changes, is very high from the beginning of the hydrolytic degradation process until eight weeks. Furthermore, using higher values of shear modulus will have a negligible effect on the prediction, while a small value will decrease the correlation between the prediction and the experimental results. It was observed that the shear modulus decreases nearly linear with the hydrolytic damage. This same trend was also reported in a previous work (Vieira *et al.*, 2011a), where the neo-Hookean, Mooney-Rivlin and second reduced hyperelastic models were used to predict the mechanical behavior of the same biodegradable polymer. Muliana and Rajagopal (20012) also assumed in their own viscoelastic model that shear modulus decreases with hydrolytic degradation, i.e. hydrolytic degradation softens the polymers. On the order hand, Soares (2008) reported that the material becomes less viscous during hydrolytic degradation, and returns faster to an equilibrium state. This assumption is also consistent to the results of this work, where the flow resistance τ_{base} increases nearly linear with the hydrolytic damage. This may be explained by the

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reduction of the mobility of the polymer chains during hydrolytic degradation, which becomes more brittle and resistant to flow.
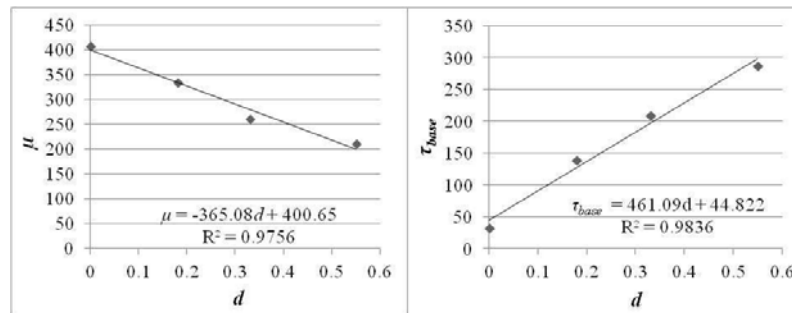

Figure 5. Evolution of the material parameters of the Bergtröm-Boyce model, shear modulus μ and flow resistance τ_{base}, during hydrolytic degradation

The linear fitting of these two parameters (the shear modulus μ and the flow resistance τ_{base}) as function of the hydrolytic damage d is shown in the Fig. 5. A good correlation of the linear fitting was demonstrated, with the coefficient of determination R^2 above 0.97 for both parameters. Based on these linear equations, the shear modulus $\mu(d)$ and the flow resistance $\tau_{base}(d)$ were calculated, and they are shown in Tab. 3.

Table 3 List of the shear modulus μ and the flow resistance τ_{base} used at each hydrolytic degradation step, determined by the linear fitting equation as function of hydrolytic damage

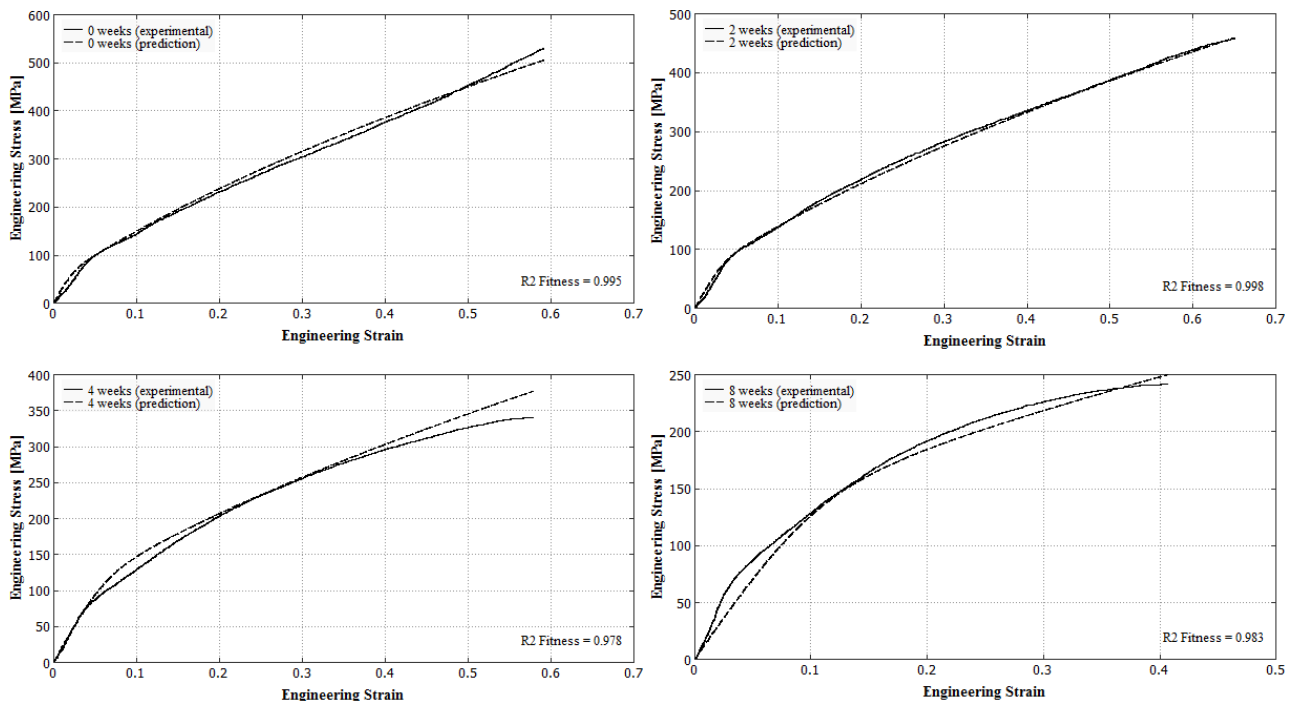| Model parameters	0 weeks	2 weeks	4 weeks	8 weeks
μ - Shear modulus of network A	400.65	334.936	280.174	199.856
τ_{base} - Flow resistance	44.822	127.818	196.982	298.422

Figure 6. Experimental results of monotic tensile test at 250 mm/min of PLA-PCL fiber, and prediction via viscoplastic Bergström-Boyce model, after two weeks of hydrolytic degradation

Then these values were used together with the other material model parameters values previously assumed constant during hydrolytic degradation, to predict the mechanical behavior of the polymer during hydrolytic degradation. The basic assumption in this formulation consists on the introduction of the hydrolytic damage scalar field, which does not change the nature of the constitutive law, and the model still exhibits viscoplastic constitutive behavior at any

hydrolytic degradation step. A comparison of these predictions against the experimental monotonic tensile test results, at different hydrolytic degradation steps is shown in Fig. 6. Although the result of these predictions, using the proposed method to estimate the material model parameters, is less accurate than the initial predictions, using the inverse analyses of all the parameters, the result has still a satisfactory correlation, with the coefficient of determination R^2 above 0.98. However, based on this method, two of the parameters are functions of the hydrolytic damage d, while the other parameters remain constant during hydrolytic degradation.

6. CONCLUSIONS

Biodegradable polymers, as conventional polymers are known by their non-linear and time-dependent mechanical behavior. The method presented in this work is the first one based on a viscoplastic constitutive model validated experimentally for large deformations. Although the application of this method was only demonstrated, in the present work, for this particular blend, the authors had evaluated the method for other biodegradable polymers, such PDO and PGA. Furthermore, this can still be extended to other thermoplastic biodegradable materials, since the Bergström-Boyce model was originally developed for engineering rubbers, but was also used to predict the mechanical behavior of other thermoplastics and other soft materials with both non-linear and time-dependent mechanical behavior. Although this model is much more complex than the hyperelastic models usually used to model the mechanical behavior of biodegradable polymer, it enables to simulate realistic loading cases usually similar to those in service. These in service loading cases comprise loading at various rates, and cyclic loading above yielding. Hence, the investigated material model is able to capture the more significant phenomena, which occur in biodegradable polymers, such as relaxation and creep, hysteresis and plastic strain accumulation with hydrolytic biodegradation. In fact, this could be confirmed using the proposed method to predict the mechanical behavior of biodegradable polymers based on the Bergtröm-Boyce constitutive model. For this method, the shear modulus μ and the flow resistance τ_{base} are linear functions of the hydrolytic damage, while the other material model parameters remain constant during the hydrolytic degradation process. . Comparing to experimental results at different hydrolytic degradation steps, the prediction were accurate until more than half life (d=0.5). Above this, the assumption of homogeneous degradation process and constant hydrolytic degradation rate will be less valid. Therefore, the proposed method is an important tool to be used in the design and dimensioning of biodegradable devices, such as scaffolds, according to mechanical and durability requirements. The simple modeling technique presented here allows preclinical evaluation of the functional compatibility, and the optimization by comparison of different solutions in terms of long-term biomechanical behavior. These constitutive models can be implemented in commercial finite element software and the material parameters can be changed as function of hydrolytic damage. In addition, a failure criterion could be associated with these parameters. These can be also applied to more complicated numerical models in 3D applications.

The present investigation can be further updated to more detailed models, which consider the hydrolytic degradation rate dependence on the stress state and the presence of enzymes. In these more complicated problems, hydrolytic damage will depend not only on the biodegradation time, but also on the hydrolysis kinetic constant; no longer constants but now time, geometry, biodegradation media and stress state dependent. In these cases, hydrolytic damage will be a local internal variable, which varies along the volume and must be calculated previously at each material point and at each biodegradation step. However, the proposed adaptation of the studied constitutive model is still valid from there forward.

7. ACKNOWLEDGEMENTS

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