Received: 8 October 2018 | Revised: 8 April 2020 | Accepted: 12 April 2020
DOI: 10.1002/pen.25402

ARTICLE

POLYMER ENGINEERING AND SCIENCE
WILEY

Numerical approach to simulate the mechanical behavior of biodegradable structures considering degradation time and heterogeneous stress field

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Funding information
Conselho Nacional de Desenvolvimento Científico e Tecnológico, Grant/Award Number: 406553/2016-5; Fundação de Amparo à Pesquisa do Estado de São Paulo, Grant/Award Number: 2016/03555-1

Abstract

Biodegradable polymers are widely used to manufacture biodegradable devices, such as those used in regenerative medicine. In many cases, nonuniform degradation can arise from nonuniform stress fields. The developed numerical methodology can simulate the mechanical behavior of three-dimensional structures subjected to loads during degradation after a given degradation time, thus providing a valuable tool for pre validation of biodegradable devices. Degradation rate was assumed as linear function of the local von Mises stress. Material model parameters change as degradation proceeds and hydrolytic damage increases. Hence, shear modulus of the neo-Hookean constitutive model was assumed as linear function of hydrolytic damage. The methodology was developed in a finite elements' framework using ABAQUS/Standard. The local hydrolytic damage and the consequent shear modulus evolutions were calculated by means of a user material subroutine. The stress field affects locally the kinetics of degradation and the evolution of hydrolytic damage. Thus, local hydrolytic damage and the material parameter are updated at each time step to recalculate stress and strain fields at the inputted degradation time. The aim of this work was to allow the simulation of biodegradable devices subjected to both mechanical and chemical environments.

KEYWORDS

biodegradable polymers, constitutive model, hydrolysis, mechanical behavior, simulation

1 | INTRODUCTION

Currently, there is a wide variety of commercial biodegradable polymers with the most diverse properties. They are commonly used to produce regenerative medical devices, such as scaffolds, for many different applications. Scaffolds can temporarily replace the biomechanical functions of a biological tissue while polymer degradation and tissue recovery occur simultaneously. Biodegradable polymers are applied in bone screws, drug delivery devices, tissue engineering scaffolds, stents, articular cartilage regeneration, among others, as reviewed by Ulery et al.[1] In the case of scaffolds, these must have a structure with controlled porosity for a successful regeneration of tissues. This porosity allows cells migration into the device and promotes angiogenesis and cells nutrition.[2]

Biodegradable polymers can be classified as either natural or synthetic. Among the natural class are starch, collagen, silk, alginate, agarose, chitosan, fibrin, cellulosic, hyaluronic acid-based materials, among others.

Among synthetic biodegradable polymers, aliphatic polyesters, such as poly(lactic acid) (PLA), poly(glycolic acid) (PGA), polycaprolactone (PCL), polyhydoxyalkanoates (PHA), and poly(ethylene oxide) (PEO), belong to the most important group. Each biodegradable polymer has unique properties, such as stiffness and degradation rate. They can be combined to tune their properties according to design requirements. The main advantage of using biodegradable polymers in regenerative medicine is that degradation products are naturally absorbed by the human body and consequently avoid an additional surgery for device removal. Since each application require a certain degradation profile and mechanical behavior, different biodegradable polymers can be selected and combined (such as blends, copolymers and composites) in order to adjust its degradation profile and mechanical properties according to the desired functions.

Biodegradable polymers are prone to undergo degradation (photo, thermal, mechanical, or chemical degradation). The most important degradation mechanism is chemical degradation by hydrolysis, which occurs due to the presence of water and enzymes.[3] First, it is important to distinguish between erosion and degradation. Both are progressive and irreversible processes. Erosion can be modeled as a diffusion-reaction process.[3] Initially, water diffusion into the material occurs. When hydrolysis begins, macromolecules of the polymer start being divided into smaller fragments, so-called oligomers. Depending on the polymer nature and on its thickness, diffusion can be faster or slower than hydrolysis reaction. Fick's law is generally used to model the diffusion process. When diffusion is very slow compared to hydrolysis, or in the case of thick structures, hydrolysis occurs mainly near the surface, whereas the bulk material is only slightly hydrolyzed. As the surface is eroded and loose material, the hydrolysis moves into the material core. On the other hand, when diffusion is faster than hydrolysis, or in the case of thin or porous structures, the molecular weight decreases occurs homogeneously throughout the entire volume. This process continues until oligomers are small enough to be soluble and then diffuse outward, leading to erosion and material mass loss.[3] On the other hand, degradation is due to the chemical reaction called hydrolysis and can be catalyzed by the presence of water, with or without enzymes. This chemical reaction causes the division of macromolecules and results in the reduction of mechanical performance of the polymer, known as hydrolytic damage. This damage can be estimated by analyzing the molecular weight of the polymer, through size exclusion chromatography or gel permeation chromatography (GPC), or the evolution of mechanical strength, using universal mechanical testing. Therefore, degradation is an initial step of the erosion phenomenon. The complete erosion of the polymer takes much more time than the complete loss of tensile strength.[4] Erosion, on the other hand, can be estimated by measuring, for example, the mass loss or the drug release kinetics, or the production of CO_2 (in the case of composting).

The simplest kinetic hypothesis to describe hydrolysis considers a random scission. A first-order differential equation describes the increase of carboxylic acid end groups. However, due to its simplicity, this model is unable to describe, for example, oligomer diffusion and mass loss. Nor even the autocatalytic effect and the accelerated degradation at the core due to the newly formed carboxylic acid end groups that cause a local decrease in pH. Furthermore, chain scissions provide extra mobility for the polymer chains to reorganize, enabling recrystallization. Hence, this simple model is also unable to describe the degradation differences between amorphous and crystalline regions, and the chain scissions induced crystallization. To model erosion, a complex mathematical model is needed to account for all these steps and for all the structural and morphological details. Over recent years, more advanced models were developed to predict the evolution of molecular weight along the volume. These models range from empirical to phenomenological or deterministic to stochastic models. In a recent work of Sevim and Pan,[5] the erosion model considers autocatalytic hydrolysis, oligomer production and their diffusion, together with erosion (bulk and surface) using the Monte Carlo modeling methods and a set of differential equations. Zhang et al.[6] also consider crystallization induced by polymer chain scissions, because of an increased mobility of polymer chains while its molecular weight is reducing. Interactions between microscopic hydrolysis, the mesoscopic formation of cavities due to autocatalysis, and macroscopic diffusion of oligomers, are considered in this complicated multiscale model that uses cellular automata and Monte Carlo methods. Although these approaches to model polymer erosion were able to predict the heterogeneous evolution of molecular weight, crystallinity, and mass during erosion, hence enabling to understand transitions between bulk and surface erosion, none of these were able to predict the mechanical behavior evolution of the device. These processes need to be related to the material performance at the macroscopic scale. Thus, they must be combined with constitutive models for that purpose. These erosion models are commonly used to describe drug release kinetics. Changes in molecular weight along the volume during degradation were measured in many studies. However, there were very few attempts to model lifetime predictions[7] in terms of mechanical performance.

In design, the prediction of mechanical behavior of materials is of great importance, and constitutive relations are used. In the case of biomedical devices, apart from biological compatibility, these devices shall be also functional compatible in terms of mechanical performance. Therefore, degradation rate must be compatible to tissue regeneration. Mechanical stability during tissue healing process is one of the main aspects in tissue engineering. Hence, it is fundamental to know the mechanical behavior of the device during degradation.[2] As shown in a previous work,[4] the mass loss is very small when, in the initial phase of erosion, molecular weight, and mechanical strength are strongly reduced.

In the case of biodegradable eco-friendly devices, these must sustain their mechanical functions during its life cycle. Most of the initial uses for PLA were focused on biomedical applications and therefore most of research associated with hydrolytic degradation of PLA was done in aqueous or biological media. In the work of Mitchell and Hirt,[8] degradation of PLA fibers was also studied outside an aqueous media, testing different levels of relative humidity. The first-order random scission model and an autocatalytic model were used in the work of Mitchell and Hirt[8] to predict the evolution of molecular weight, and both provided a reasonable fit of experimental data.

The initial mechanical behavior of biodegradable polymers can be modeled using constitutive models applied to conventional polymers. However, the hydrolytic damage is ignored. In literature there are still few studies[4,9-19] regarding methodologies able to simulate the mechanical behavior of biodegradable polymers combined with hydrolytic degradation. Two main approaches were used on those studies. On one group of methodologies,[4,9-14] the material parameters of the constitutive models vary depending on a scalar field, which quantifies the hydrolytic chemical degradation and its hydrolytic damage. However, degradation rate depends on local variables such as temperature, humidity, the stress state (or deformation), degree of crystallinity, pH, which may vary throughout the volume. All these variables can also be considered fields. This way, it is interesting to use methodologies that combine constitutive models and hydrolysis kinetic models that depend on such fields. So, it is possible to predict the mechanical behavior of biodegradable polymeric structures at a given degradation time, with complex geometry and boundary conditions and with gradients of temperature, humidity, crystallinity, etc. Different constitutive models, other than the linear elastic model, were use on these approaches. In fact, most of biodegradable polymers present a nonlinear mechanical behavior, and hence the linear elastic model is not suitable for most cases,[11] specially at large deformations. On another group of approaches[15,17-19] the linear elastic model was used, and the evolution of Young´s modulus is modeled considering chain scissions and the consequent formation of cavities and recrystallization in a Representative Volume Element (RVE) at a microscale (atomic level). These approaches can represent the significant lag between the reduction of Young´s modulus after the reduction of the molecular weight, generally observed in most polymers. These approaches can also represent the increase of Young´s modulus in the initial phase of degradation due to an increase of crystallinity. It is important to underline that these approaches[15,17-19] do not consider the influence of stress field on degradation kinetics. A recent approach presented by Guo et al.,[16] uses a birth-death element method. Accordingly, elements become inactive when a local variable, related to mass loss, reaches a limit value. In this work,[16] the rate of mass loss is stress dependent. Therefore, this method is not coupled to degradation kinetics but to erosion kinetics, since mechanical performance reduction is a consequence of material volume decrease. This approach[16] is more realistic to model surface erosion in polymers.

This work presents a new methodology, using the constitutive neo-Hookean hyperelastic model combined with a simple hydrolysis kinetic model that describes the hydrolytic damage evolution that depends on the stress field. Some previous works show the influence of static and/or dynamic stress/strain and cracking[16,20-25] on hydrolysis rate.

2 | MODELING HYDROLYTIC CHEMICAL DEGRADATION

As discussed, the presence of water activates hydrolysis of covalent chemical bonds on biodegradable polymers. This phenomenon causes irreversible changes in polymers mechanical behavior, since its chains are divided into smaller molecules. Initially, diffusion of water into the polymer creates a water concentration gradient from surface to the core. As discussed above, in many cases, when the dimensions are small enough, saturation is faster than degradation time and bulk erosion is dominant. In these cases, diffusion can be considered instantaneous and water is uniformly distributed along the volume from the beginning of degradation. In this work, water diffusion was considered constant along the volume.

For aliphatic polyesters (such as PLA, PGA, PCL, etc.) the polymer chains are formed by a sequence of ester groups with a carboxylic radical and an alcohol group at each end. According to the first-order random scission model,[26] macromolecules are randomly divided in two, at any ester group, during hydrolysis. Hence, the number of terminal carboxyl groups will increase during this process. According to Laycock et al.,[7] random scission controls the early stage of hydrolysis, leading to a rapid loss of strength. As discussed above, this process can be easily modeled using a first-order equation:

$$\frac{dc}{dt} = kewc = uc \tag{1}$$

where c is the concentration of carboxylic groups, t is the degradation time, k is the hydrolysis rate constant, e is the concentration of ester groups, and w is the concentration of water in the polymer. The product $u = kew$ is the polymer hydrolytic degradation rate. As $c = 1/M_n$, where M_n is the number average molecular weight of the polymer, after integration Equation (1) becomes:

$$M_{nt} = M_{n0}\exp(-ut) \tag{2}$$

where M_{nt} is the number average molecular weight at a given degradation time and M_{n0} is the initial number average molecular weight of the polymer before degradation. These microstructural changes results in a molecular weight reduction and, consequently, decrease in the microstructural dependent material properties. Mechanical behavior will evolve during degradation, due to hydrolysis, as can be seen from Figure 1A). Mechanical properties, such as strength, strain at failure and toughness, will decrease. According to Vieira et al.,[4] mechanical strength follows the same trend of molecular weight, as can be observed in Figure 1B), and can be predicted by the following equation:

$$S_t = S_0\exp(-ut) = S_0\exp(-kwet) \tag{3}$$

where S_t is the strength of the polymer at degradation time t and S_0 is the initial strength.

Hydrolytic damage d_h can be defined as the ratio between the initial molecular weight of the nondegraded material and the molecular weight at a given degradation time.[4] Thus, from Equations (2) and (3), we have:

$$d_h = 1 - \frac{M_{nt}}{M_{n0}} = 1 - \frac{S_t}{S_0} = 1 - \exp(-ut) = 1 - \exp(-kewt) \tag{4}$$

Therefore, hydrolytic damage has a value between zero (nondegraded) and one (fully degraded). When strength decreases to half of its initial value, hydrolytic damage is equal to 50% (ie, $d_h = 0.5$). Commonly found in literature, the term "*half-life*" of a biodegradable structure is an important design functional requirement and corresponds to the degradation time needed to reduce the structural strength to half of its original value. In this work, this simple model to predict the molecular weight distribution, and hence the hydrolytic damage, will enable the link between chemical damage and the evolution of constitutive model parameters. As mentioned above, other more sophisticated models could be used to describe the polymer degradation and the heterogenous evolution of molecular weight. However, these must be adapted to consider the stress/strain effect on degradation.

As already mentioned, the degradation rate u, according to Equation (1), is influenced by several factors. As discussed above, for bulk erosion, water diffusion is much faster than hydrolysis, and it is therefore possible to consider water concentration w uniformly distributed and constant from the beginning of degradation.[27] The concentration of ester groups, e, can also be statistically considered uniformly distributed along the volume. Furthermore, this can also be assumed constant during the initial phase of degradation, since macromolecules remain macro despite their multiple random scissions.[28] Finally, the hydrolysis rate constant k measures the probability of bonds scissions. Temperature, for example, will increase the hydrolytic rate constant, k, due to excitation

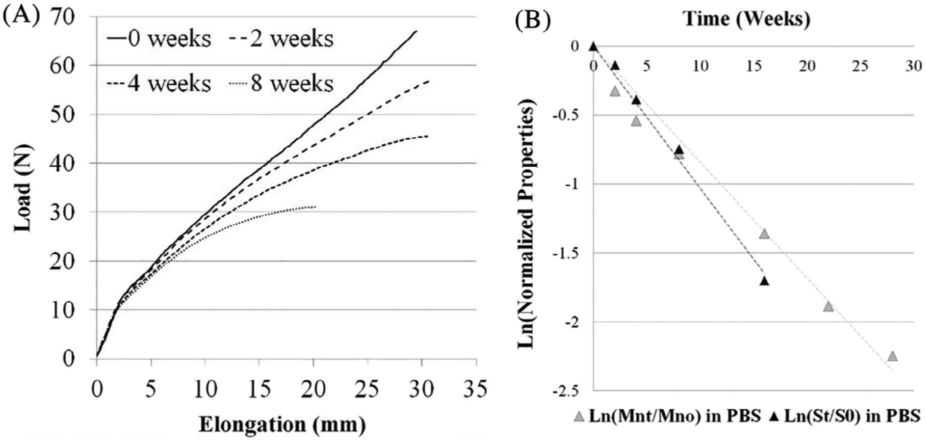

FIGURE 1 A, Results of tensile tests in poly(lactic acid)-polycaprolactone (PLA-PCL) fibers. B, Evolution of normalized molecular weight and normalized tensile strength during the degradation of PLA-PCL fibers (adapted from ref. [4])

of molecules.[29-31] The influence of mechanical stress (or strain) on degradation rate was studied in previous works.[16,20-25,32] Analogously to the temperature, stress (or strain) applied during polymer degradation is expected to increase the hydrolysis rate constant k, since there will be an increased probability of bonds scission. The aqueous degradation media also influences the hydrolytic rate constant, k. Some works reported that certain enzymes affect degradation rates of some biodegradable polymers.[33,34] On the other hand, according to Tsuji et al., the hydrolytic rate constant, k, is affected by pH of aqueous medium.[35-37] If water, temperature, stress field, and degradation medium are constant along the volume of an amorphous polymer and during degradation, then the hydrolytic rate constant, k, can be assumed constant and uniformly distributed. Thus, degradation rate, u, can be considered constant along degradation and uniformly distributed. Assuming these hypotheses, the methodology to simulate the mechanical behavior during degradation becomes simplified, since the evolution of the mechanical properties is homogeneous along the polymer. In this work, degradation rate will be considered heterogeneous along the volume, due to a heterogeneous stress field. The hypothesis of instantaneous diffusion in an amorphous polymer with no autocatalysis was considered, and the premise that temperature and degradation media are constant during time and along the volume. On the other hand, stress field will vary along the volume, considering generic geometries and boundary conditions. Therefore, each region will have a different degradation rate, u. Degradation rate will be higher in regions of stress concentration. Hence, hydrolytic damage, d_h, is a scalar field.

3 | CONSTITUTIVE MODEL

A load acting on a solid generates stress, which results in changes of its original shape. This mechanical relationship between stress and strain can be expressed by means of a constitutive model, which will be different for each type of material. For polymers, which exhibit nonlinear stress-strain relationship, the classic linear elastic model is generally not suitable for large deformations.

Recent works on methodologies to simulate the mechanical behavior of biodegradable polymeric structures during degradation are based on hyperelastic models,[4,10,11] on viscoelastic nonlinear models[12-14] and on viscoplastic models.[9] These methodologies consider changes in material parameters of constitutive models according to the hydrolytic damage. The introduction of a scalar field representing the hydrolytic damage, d_h, does not change the nature of the constitutive law.

In previous works,[10-12] a constitutive framework for biodegradable polymers was formulated, were the degradation process introduces another mechanism of entropy production due to chain scissions. They also assumed the existence of a scalar field, $d_h(\mathrm{x}, t)$, that represents the degree of degradation which has a value between zero (nondegraded) and one (fully degraded). In these works, the time derivative of this scalar field depends on the local state of deformation. In another previous work of Muliana et al.[13] was also analyzed the mechanical response of polymers when subjected to mechanical loading coupled with diffusion of water. They also adopt the deformation-dependent rate of degradation of Soares et al.[10,11] and its modification to incorporate the degradation dependence due to local concentration of water, $w(\mathrm{x},t)$. The equation that governs the diffusion of water through the polymer was assumed to follow the Fick's law.

In those works, since degradation is spatial dependent and locally changes the material properties, the polymer that is initially isotropic and homogenous becomes heterogeneous. However, in those works,[10-13] an empirical approach to describe the hydrolysis kinetics was used. Therefore, the hydrolytic damage is an internal variable that cannot be measured and can only be determined by fitting experimental results. In other works,[4,9] a physically inspired model to describe the hydrolysis kinetics, based on the random scission hypothesis, was used to describe the hydrolytic damage evolution. In those, hydrolytic damage can be measured by determining the molecular weight or the strength evolution. This enables to validate the methodology by determining the hydrolytic damage. d_h, based on measurements of strength or molecular weight, according to Equation (4). However, in those works,[4,9] based on experimental results where specimens degraded without any load, the influence of a heterogeneous stress field and a water concentration field was not considered. Methodologies like those[4,9] involving the simulation of three-dimensional (3D) structures considering the degradation time are called 4D approaches. In this work, as discussed above, hydrolytic damage evolves heterogeneously throughout the volume, similarly, to works,[10-13] but using the first-order random scission model to describe the hydrolytic damage evolution. Furthermore, in this work the neo-Hookean hyperelastic model is used.

As other hyperelastic models, neo-Hookean model is used to predict the relaxed configuration of polymers after loading, especially those having a more ductile and nonlinear behavior, such as elastomers. They can reproduce the "S" shape of stress vs strain curve. Mechanical properties of hyperelastic materials are usually represented in terms of strain energy density, W. Generalizing to a 3D representation, a generic hyperelastic constitutive relation can be presented in terms of the first Piola-Kirchhoff stress tensor **P**, where W is a scalar function of the deformation gradient $\mathbf{F} = \partial x_i / \partial X_j$ (where x_i is the vector of the current position of a point in the material and X_j is the vector of the same point in the nondeformed configuration):

$$\mathbf{P}_{ij} = \frac{\partial W}{\partial \mathbf{F}_{ij}} \tag{5}$$

or in terms of Cauchy stress tensor **T**:

$$\mathbf{T}_{ij} = \frac{1}{J}\mathbf{F}_{ik}\frac{\partial W}{\partial \mathbf{F}_{kj}} \tag{6}$$

where $J = \det \mathbf{F}$ is the Jacobian which represents the volume change ($J = 1$ for incompressible material). Hyperelastic constitutive relations are usually defined in terms of invariants of the left Cauchy-Green deformation tensor $\mathbf{B} = \mathbf{F}.\mathbf{F}^{\mathrm{T}}$. The three invariants are defined as:

$$I_B = \mathrm{tr}\left(\mathbf{B}_{ij}\right) = \mathbf{B}_{kk} = \lambda_1^2 + \lambda_2^2 + \lambda_3^2 \tag{7}$$

$$II_B = \frac{1}{2}\left[{I_B}^2 - \mathbf{B}_{ik}\mathbf{B}_{ki}\right] = \lambda_1^2\lambda_2^2 + \lambda_2^2\lambda_3^2 + \lambda_3^2\lambda_1^2 \tag{8}$$

$$III_B = |\mathbf{B}_{kk}| = J^2 = \lambda_1^2\lambda_2^2\lambda_3^2 \tag{9}$$

where λ_i, ($i = 1, 2, 3$) are the eigenvalues of **F**, the so-called principal stretches. Many polymeric materials are nearly incompressible. Therefore, the deviatoric left Cauchy-Green tensor (responsible for distortions) is more conveniently used:

$$\overline{\mathbf{B}}_{ij} = \mathbf{B}_{ij} - \frac{1}{3}\mathbf{B}_{kk}\delta_{ij} \tag{10}$$

that is, neglecting the volumetric part of the strain tensor (responsible for volume changes):

$$\frac{1}{3}\mathbf{B}_{kk}\delta_{ij} \tag{11}$$

where δ_{ij} is the Kronecker delta. Therefore, an alternative set of invariants of the deviatoric left Cauchy-Green tensor is commonly used:

$$\overline{I_B} = J^{-2/3} I_B \tag{12}$$

$$\overline{II_B} = J^{-4/3} II_B \tag{13}$$

Based on this set of invariants, a common presentation for the strain energy density of the neo-Hookean model is:

$$W\left(\overline{I_B}, \overline{II_B}, J\right) = C_{10}\left(\overline{I_B} - 3\right) + d(J-1)^2 \tag{14}$$

where C_{10} is the material parameter related to distortion (the shear modulus $\mu = 2.C_{10}$) and d is the material parameter related to volume change (the bulk modulus $\kappa = 2/d$ and $d = 0$ for incompressible material). Integrating according to Equation (6), the neo-Hookean constitutive model is defined by:

$$\mathbf{T}_{ij} = \frac{2C_{10}}{J^{5/3}}\left(\mathbf{B}_{ij} - \frac{1}{3}\mathbf{B}_{kk}\delta_{ij}\right) + 2d(J-1)\delta_{ij} \tag{15}$$

Vieira et al.[38] proposed a methodology where the shear modulus of the material is a function of hydrolytic damage $\mu(d_h)$. Since hydrolytic damage (and molecular weight distribution) changes during degradation, shear modulus will change accordingly. This methodology was able to simulate the mechanical behavior of biodegradable polymeric structures using hyperelastic constitutive models. However, in that work, stress field was considered constant. The intention was to simulate the monotonic tensile tests of cylinders (constant cross section) at different degradation stages, occurring without any load.

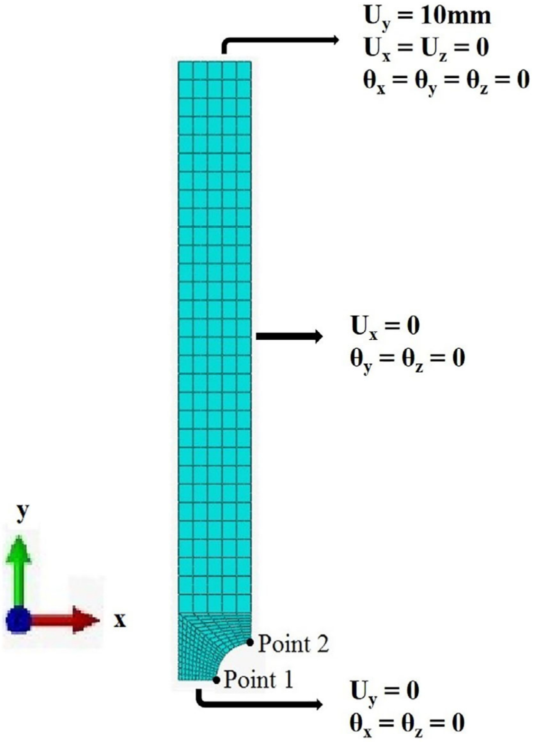

FIGURE 2 Three-dimensional (3D) model used for simulation with boundary conditions [Color figure can be viewed at wileyonlinelibrary.com]

The present work follows the same reasoning of Vieira et al.[38] for the hyperelastic neo-Hookean model, but considering loads applied during degradation and a different geometry. Hence, stress field is no longer homogeneous along the volume. This will influence the degradation rate of the material at each region of the solid. Therefore, after some degradation time, each region of the structure will behave differently, since there are some regions more degraded than others.

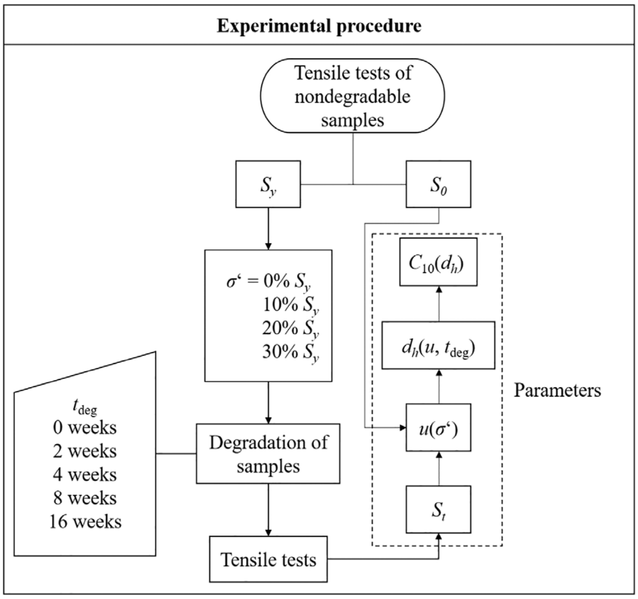

FIGURE 3 Flowchart of experimental operations required to acquire material parameters and relationships

4 | METHODS

As in Vieira et al.,[38] the present work presents a methodology implemented in ABAQUS/Standard finite element software, using the neo-Hookean constitutive model. The implementation was also performed using a user material subroutine (UMAT). The coupon was 200 mm long, having 25 mm in width, 2 mm in thickness, and the central hole has 12 mm in diameter. Then, 978 elements C3D20R were used in a model representing a quarter of the coupon, according to Figure 2, considering symmetry in planes *x*-*z* e *y*-*z*. Two different case studies were analyzed in this work. In the first case, referred as isometric loading, an axial load is applied by controlling a constant displacement of 10 mm of the top surface, symmetry condition on *y* axes on the right surface and symmetry condition on the *x* axes on the lower surface, according to Figure 2. In the second case, referred as isotonic loading, an axial load is applied by controlling a constant load of 5.200 N on the top surface and imposing the same symmetry boundary conditions on the right and lower surface. This load corresponds to a displacement of 10 mm in the first day of degradation. The material was considered almost incompressible $(d < <0)$. A convergence study was performed in order to determine the minimum number of elements and the maximum time increment Δt for each iteration that enables results to converge to asymptotic values. The time increment Δt used for each iteration was 1 day.

From experimental test results, it is possible to obtain the necessary parameters used in the developed

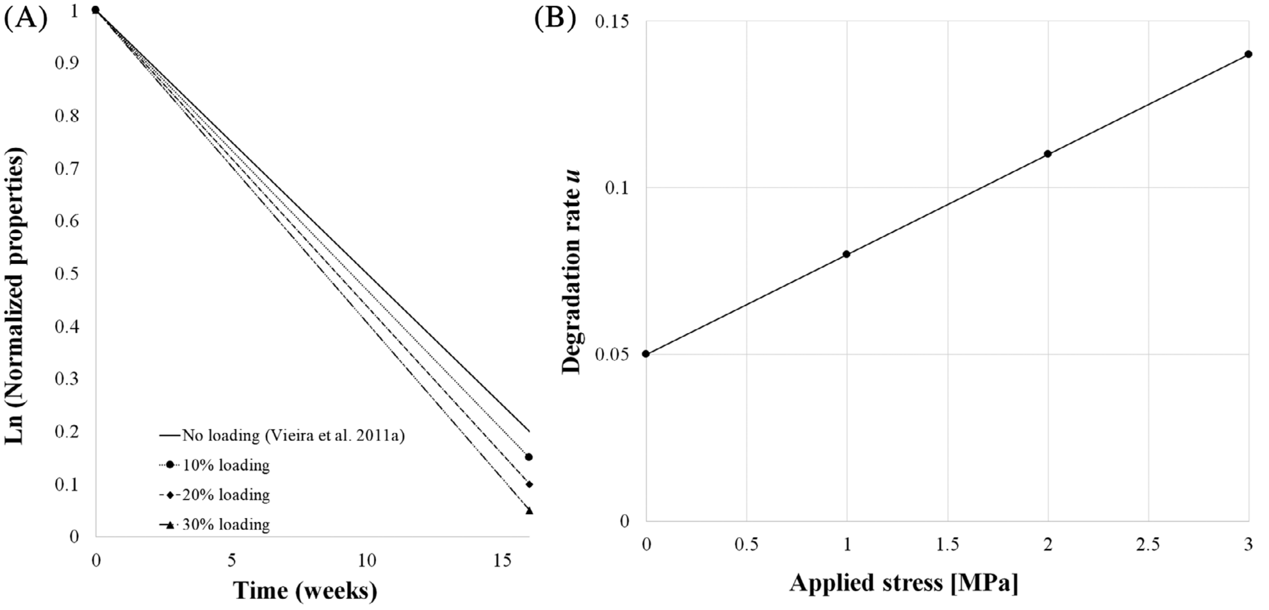

FIGURE 4 A, Normalized strength (S_t/S_0) during degradation of a generic biodegradable polymer. B, Evolution of the degradation rate u with applied uniaxial stress σ' during the degradation

subroutine. Figure 3 illustrates the flowchart of experimental operations required to obtain the necessary parameters and relationships to be used in this numerical methodology. To determine the variation of the degradation rate $u(\sigma')$ as a function of the stress field, the coupon bars subjected to different constant loads during degradation, are placed in a thermostatic bath with a degradation media. In the case of a uniaxial load, stress (ie, load divided by the cross-sectional area) is equal to the von Mises equivalent stress σ'. The uniaxial stress must be lower than the yield stress of the material S_y (eg, 0%, 10%, 20%, and 30%), to promote a very slow creep. This way, time to failure due to creep is much higher than degradation time. Otherwise, two coupled phenomena will lead to failure, the viscous flow, and the chemical bonds scissions. It is important to recall that generic polymers have viscoplastic attributes and subsequently degradation is related with the time-dependent mechanical behavior of the material. Furthermore, if diffusion of water is also considered, the problem leads to three different time histories associated with diffusion of water, viscoplastic flow, and hydrolytic degradation itself.

After the degradation period (0, 2, 4, 8, and 16 weeks, for example, depending on materials used and temperature) the coupons are tested to measure strength of the material and to characterize its mechanical behavior. Degradation experiments using different biodegradable polymers under tension are currently being performed and will be presented in future works. Considering several stages of degradation, it is possible to determine the evolution of mechanical strength during degradation. Degradation rate is defined by the slope of the linear fit when results are presented in a semilogarithm scale of strength normalized to its nondegraded value (S_t/S_o) vs degradation time (according to Equation (3)).

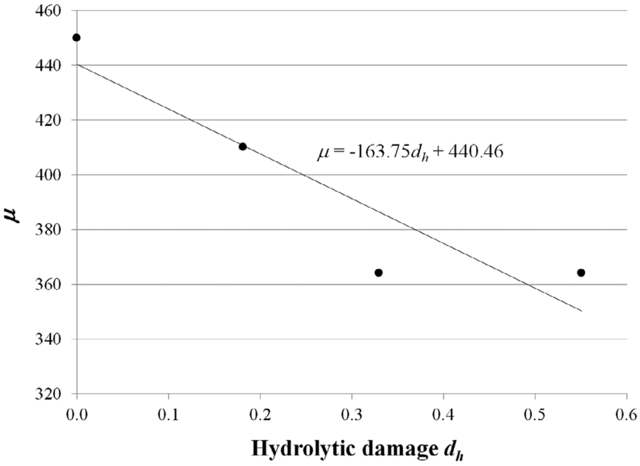

FIGURE 5 Evolution of the material parameter μ for the neo-Hookean model during degradation (adapted from ref. [4])

TABLE 1 UMAT calibration parameters

Parameters	Reference
$C_{10} = \mu/2 = (-163.75 \times d_h + 440.46)/2$	[4]
$d = 6.8e\text{-}4$	[4]
$u = \sigma' \times 0.03 + 0.05$	Hypothetical values

Abbreviation: UMAT, user material subroutine.

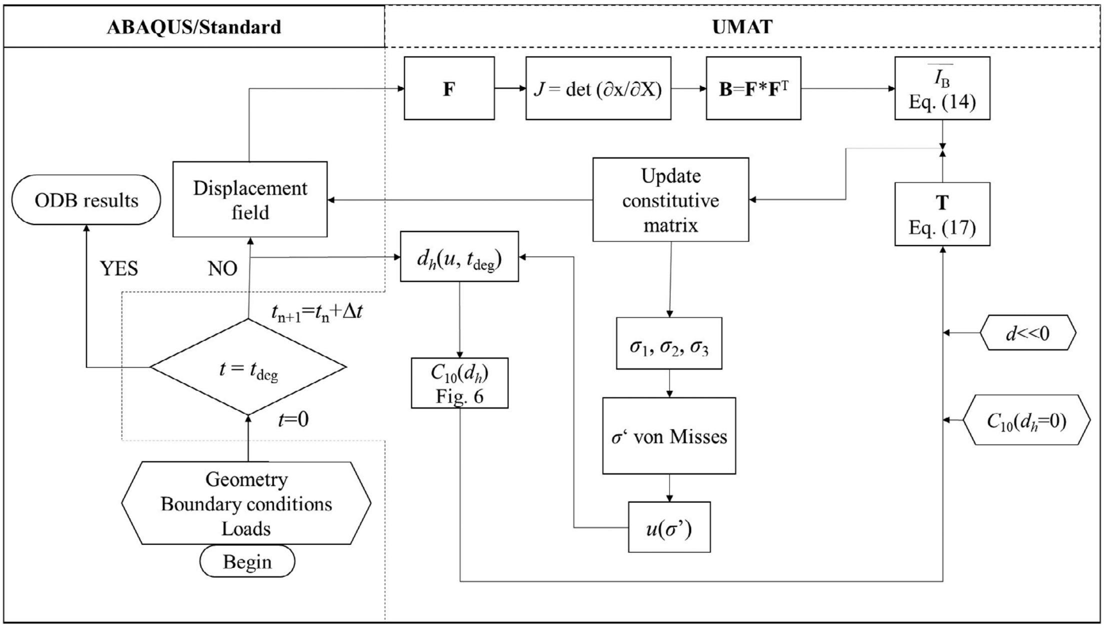

FIGURE 6 Operations flowchart developed by user material subroutine (UMAT)

Vieira et al.[4] established a relationship between the normalized strength and degradation time, for a PLA-PCL polymer blend (90:10) subjected to degradation without any load applied during degradation (see Figure 1B). In this work it was assumed that a greater degradation rate (or greater slope) occurs for a greater

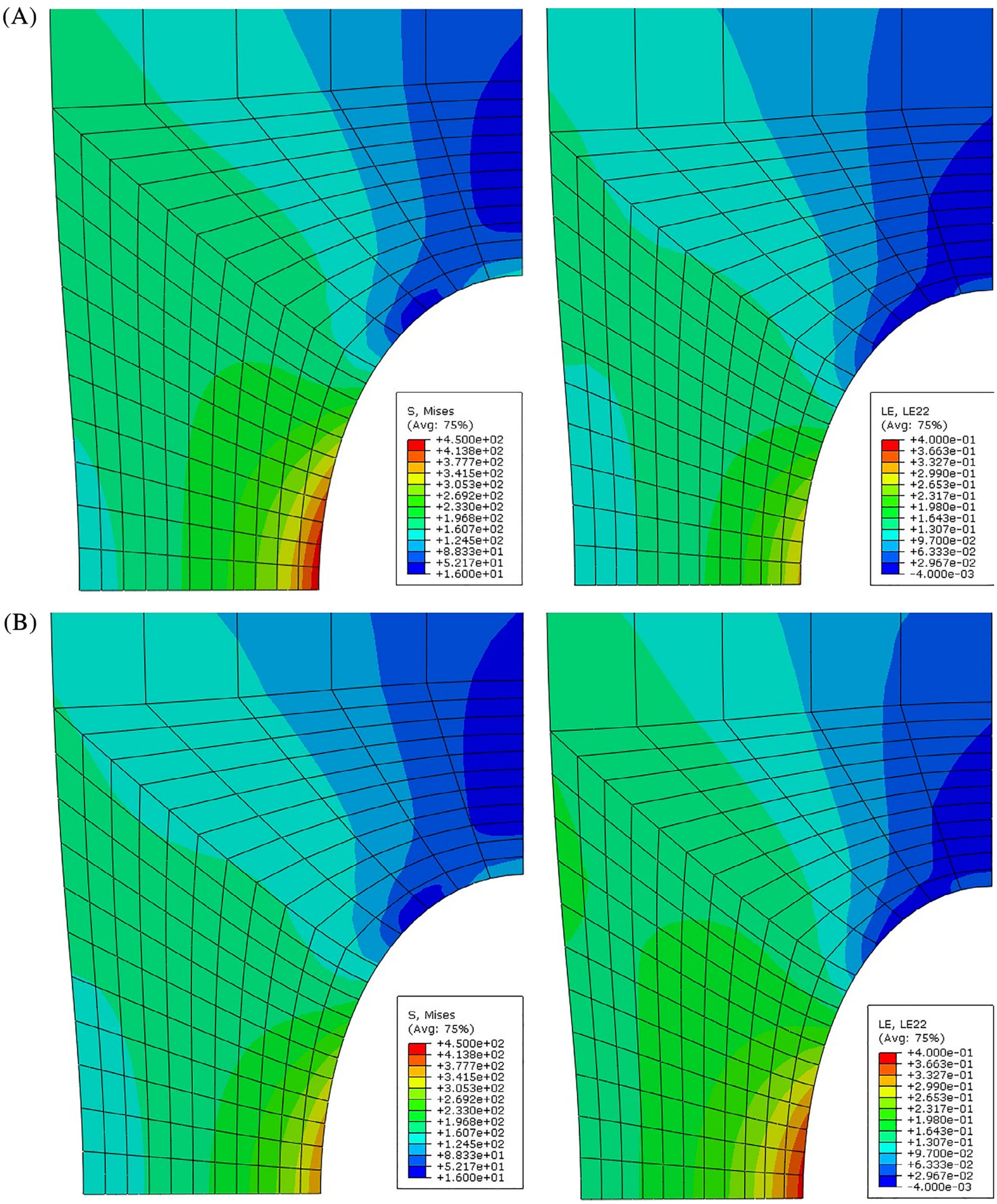

FIGURE 7 Evolution of von Mises stress (left) and axial strain (right) at different stages of degradation: A, 0 weeks and B, 16 weeks [Color figure can be viewed at wileyonlinelibrary.com]

constant load applied during degradation, as shown in Figure 4A. Having experimental results for several levels of constant load applied during degradation (eg, 0%, 10%, 20%, and 30% of S_y), it is possible to represent the curve of degradation rate u vs applied stress σ' and fit these experimental points. In this work, it was assumed a linear increase of the degradation rate as function of the applied stress, as shown in Figure 4B. In the work of Guo et al.,[16] erosion and mass loss rate was also assumed a linear function of a stress invariant. In another example of Soares et al.,[11] hydrolytic damage increasing rate ($\partial d_h/\partial t$) varies linearly with deformation.

Vieira et al.[4] determined the shear modulus ($\mu = 2.C_{10}$) for different degradation stages, or levels of hydrolytic damage, by inverse parameterization of experimental monotonic tensile test results. Linear fitting was a reasonable approximation between experimental results to represent the decrease of shear modulus and consequent material softening. In the work of Soares et al.,[10] it was assumed a linear decrease of shear modulus. In the method developed by Muliana and Rajagopal,[13] the authors also assumed in their methodology that shear modulus decreases due to hydrolytic degradation.

The developed UMAT uses the material parameters C_{10} and d as input data for a nondegraded material. Considering the geometry (see Figure 2), loading and boundary conditions, ABAQUS, initially calculates, in a first iteration, the displacement gradient. The numerical algorithm is implemented at each Gaussian (material) point in the finite element analyses. Based on this, the UMAT routine calculates the deformation gradient **F**, the Jacobian J and finally the left Cauchy-Green deformation tensor **B**. Knowing the initial material parameters C_{10} and d for a nondegraded material, then it calculates the Cauchy stress tensor through Equation (15). Then, it updates the constitutive matrix to recalculate the displacement field for the next time increment Δt. On the other hand, knowing the degradation rate at a certain von Mises stress, it is possible to obtain the hydrolytic damage at a given element after some degradation time Δt, through Equation (4). As in the work of Vieira et al.,[38] the UMAT calculates the material parameter as a function of the local hydrolytic damage d_h at a given Gaussian (material) point within the element at a determined time increment. It then updates the material parameter C_{10}, in each element, based on the evolution shown in Figure 5, considering the parameter d constant, that is, $d << 0$ (remains nearly incompressible). The routine follows until the accumulated time is equal to the inputted degradation time. The flowchart of this methodology and operations performed by ABAQUS and UMAT are shown in Figure 6. Finally, ABAQUS generates an ODB (Output Data Base) file. Thus, it is possible to obtain the graphics of distribution of equivalent von Mises stress, hydrolytic damage d_h and the material parameter C_{10}.

In the present work, the values of material parameters, $C_{10}(d_h)$ and d, were obtained in literature[38] and the hypothetic relation for the degradation rate as a function of the equivalent stress, $u(\sigma')$, are presented in Table 1. Although these relations have not been obtained experimentally, they provide possible values for a real biodegradable polymer. Knowing that higher stresses increase its rate of degradation, the relation shown in Figure 4B was considered. The evolution of the material parameter, μ, during degradation, was adapted form Vieira et al.,[4] and can be observed in Figure 5.

5 | RESULTS AND DISCUSSION

The methodology used different stages of degradation: 0 until 16 weeks (112 days) to do the analysis. Figure 7 (left) shows the numerical results for the isometric loading case in a region of the finite element model near the geometric discontinuity were the highest von Mises stresses were obtained. As expected, the higher stress values are present in the region near the sample hole, indicated in Figure 2 at point 1. In this point 1, the polymer degrades faster when compared to point 2, leading to further lower values of stress as the polymer becomes more compliant. In Figure 8, it is possible to observe the time-dependent stress evolution at points 1 and 2, exhibiting a *stress relaxation*. The evolution of shear modulus, for the isometric loading case, is shown in Figure 9. Since we have a heterogeneous stress field due to the geometric discontinuity, an initial homogeneous

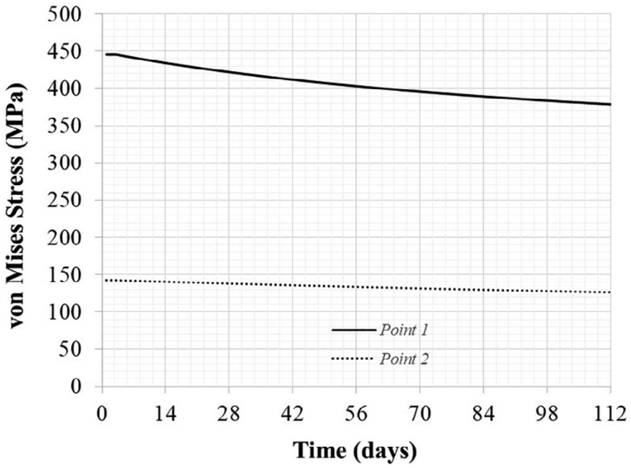

FIGURE 8 Evolution of von Mises stress at points 1 and 2 during degradation until 16 weeks (112 days) in isometric condition

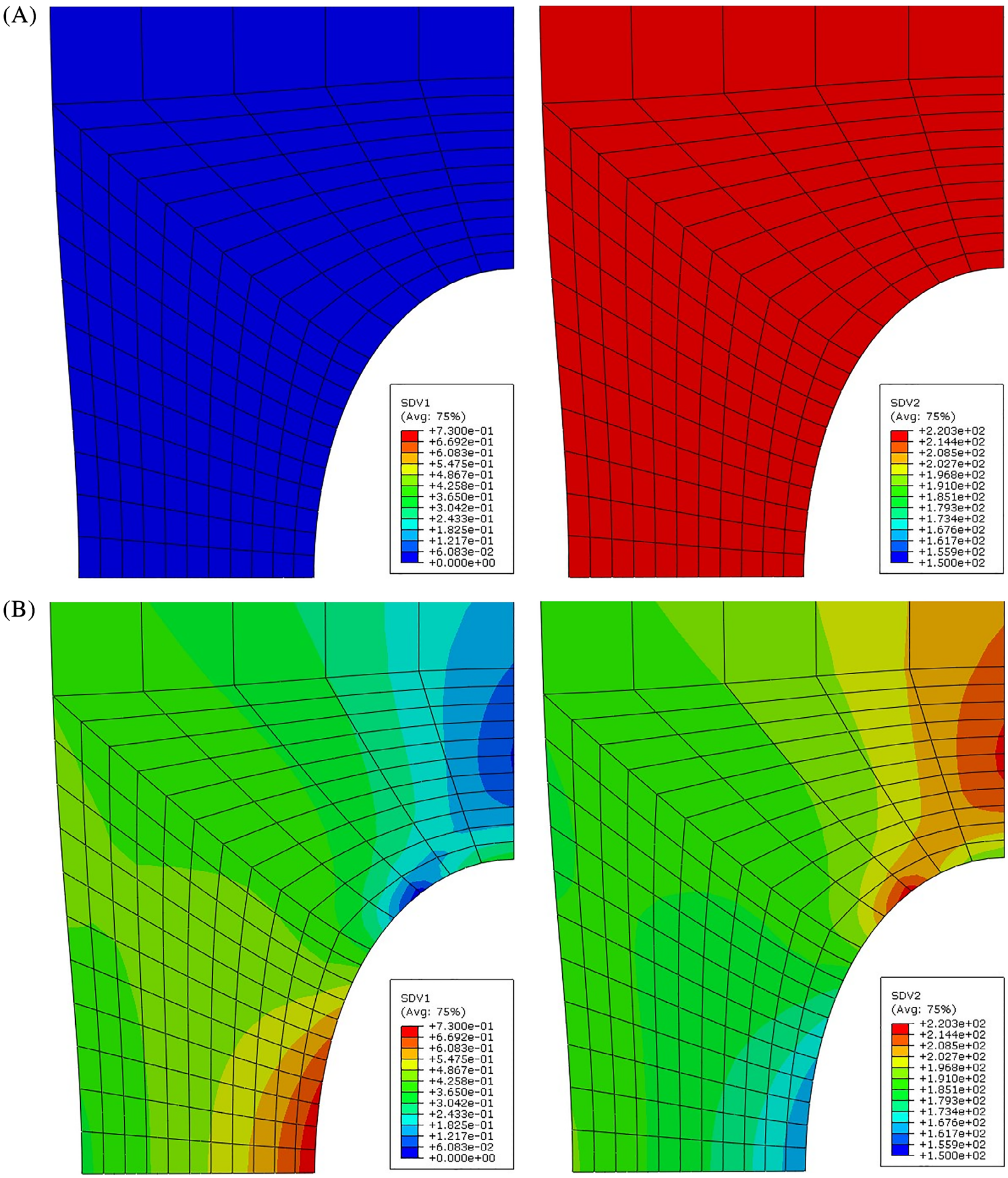

FIGURE 9 Evolution of hydrolytic damage d_h (left) and C_{10} parameter (right) for different stages of degradation: A, 0 weeks and B, 16 weeks for the isometric condition [Color figure can be viewed at wileyonlinelibrary.com]

material becomes heterogeneous, as shown in Figure 9. As anticipated, at point 1, where von Mises stress is higher, shear modulus is lower and softens faster when compared to point 2.

Hydrolytic damage, d_h, is zero in the initial moment and increases during hydrolytic degradation. Furthermore, a heterogeneous hydrolytic damage field is shown in Figure 9. In point 1, where von Mises stress is higher,

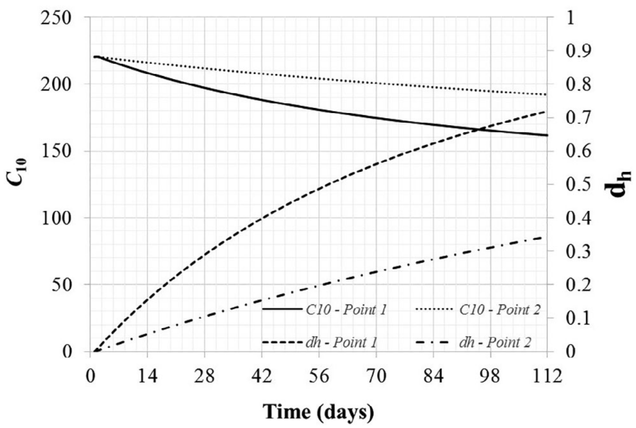

FIGURE 10 Evolution of C_{10} parameter (left) and hydrolytic damage d_h (right) at points 1 and 2 during degradation until 16 weeks (112 days) in isometric condition

hydrolytic damage is higher in comparison to point 2. Figure 10 shows the evolution of hydrolytic damage, d_h, and shear modulus, C_{10}, at points 1 and 2 during degradation for the isometric loading condition. To validate this methodology, several samples can be collected in different regions, near and far from the hole, to measure the molecular weight. Hence, hydrolytic damage at each region can be determined from Equation (4) by measuring the molecular weight evolution of the polymer.

Figure 7 (right) shows the numerical results for the isotonic loading case in a region near the geometric discontinuity that presented the highest values of axial strains. As expected, the highest strain values occur in the region near the sample hole, indicated in Figure 2 at point 1. In this point 1, the polymer degrades faster relatively to point 2 (indicated in Figure 2), leading to a further higher value of axial strain as the polymer becomes more compliant. It was possible to observe that the time-dependent strain evolution in the axial direction at points 1 and 2 exhibit a *creep elongation*. The evolution of hydrolytic damage, d_h, and shear modulus, C_{10}, at points 1 and 2 during the degradation, for the isotonic loading case was identical to the isometric loading case, since the hyperelastic model is completely reversible and time independent. On the other hand, the 10 mm displacement imposed on the top face in the isometric condition corresponds to 5.200 N in the isotonic condition. As predicted, at point 1, where axial strain is higher, shear modulus is lower and softens faster when compared to point 2. Furthermore, at point 1, where axial strain is higher, the hydrolytic damage is higher in comparison to point 2. These two different conditions enable to visualize two different aspects of the "time-dependent" behavior due to hydrolysis.

6 | CONCLUSIONS

To predict or simulate the mechanical behavior of biodegradable structures during hydrolytic degradation is a complex problem. However, it is a very pertinent problem in the design of biodegradable devices. This article presents a methodology able to predict the mechanical behavior of biodegradable polymers. In the presented approach, shear modulus of the neo-Hookean constitutive model depends on hydrolytic damage, which depends on the local degradation rate related to the local stress state. Although the material parameters values used are hypothetic, the authors believe that this "5D" methodology can be applied to any biodegradable polymer that exhibits an hyperelastic behavior. This approach can easily be implemented using experimental results after in vitro incubation in aqueous media (constant temperature and pH) for different degradation stages and with different constant loads applied during degradation, and subsequent monotonic tensile tests. In a future work, authors will present experimental results for different biodegradable materials, with different degradation rates, that will allow to calibrate the material parameters and relations. This methodology will be also validated based on experimental results, where specimens with the geometry used in this work will degrade with a constant load. To measure hydrolytic damage, small material samples will be collected from different regions of the specimen and its molecular weight will be determined by GPC.

When scaffolds are implanted to temporarily replace a biologic tissue, they undergo degradation through hydrolysis and in most cases, are submitted to heterogeneous stress fields. Hence, this approach can provide new insights to the design of biodegradable devices and its prevalidation of functional (mechanical and durability) requirements. It enables to simulate the mechanical behavior in a virtual environment at any given degradation time, and it simplifies the iterative process of dimensioning-verification, avoiding the trial and error approach commonly used in these applications.

Finally, similar methodologies can use different models to describe the heterogenous evolution of molecular weight. Or even other constitutive models, with different degrees of complexity and features, may be used to predict the 3D mechanical behavior of biodegradable polymers at any given degradation time. Elastoplastic or viscoplastic constitutive models, enable more realistic results in the case of cyclic loading if one wants to study the cumulative plastic strain and the resultant loosening of the scaffold. In a future work, other constitutive models will be used. However, to use those models, additional experimental tests are needed to calibrate the material parameters, such as cyclic quasi-static unloading-reloading tests, monotonic tests at different strain rates or creep/relaxation test.

ACKNOWLEDGMENTS

The authors would like to thank FAPESP for funding the project (grant number 2016/03555-1) and CNPq for funding the project (grant number 406553/2016-5).

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How to cite this article: Taguti MVH, Françoso A, Ribeiro ML, Vieira AFC. Numerical approach to simulate the mechanical behavior of biodegradable structures considering degradation time and heterogeneous stress field. *Polym Eng Sci*. 2020;60:1566–1578. https://doi.org/10.1002/pen.25402