Non-homogeneous Compression Testing of Bioresorbable Amorphous Polymers and Identification of Constitutive Parameters for PLGA

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Abstract. Bioresorbable materials have shown promising results in medical applications (suture anchors, interference screws, craniofacial plates etc). In order to design products made of bioresorbable materials a deep understanding of the thermo-mechanical response behavior of such materials is required. In this paper, a suitable testing program involving numerical simulation, experimental tests and identification of constitutive parameter is proposed.
Keywords: bioresorbable polymers, compression testing, identification of constitutive parameters, PLGA

INTRODUCTION

Polymers such as poly(lactic acid), PLA, poly(glycolic acid), PGA, and copolymers like poly(lactic-co-glycolic acid), PLGA, have been used extensively in the production of medical implants (Ikada and Tsuji, 2000). A remarkable characteristic of these materials is the capacity to degrade by undergoing the chemical process of hydrolysis, which promotes the scission of polymer chains when attacked by water. The products of this reaction can be absorbed and metabolized by the human body. Degradation, absorption as well as the compatibility of thermo-mechanical properties with body tissues are essential characteristics of bioresorbable polymers, resulting in their successful usage in medical procedures. These materials have presented promising results as medical devices (suture anchors, interference screws, craniofacial plates etc).

In order to design products made of bioresorbable polymers a deep understanding of the thermo-mechanical response behavior of such materials is required. Several constitutive models recently found in the literature aim at representing many of the intricate characteristics of polymers, namely those features related to bioresorbable materials. However, there is a lack of data available in the literature that can be employed accordingly in numerical simulations. Thus, a suitable testing program involving numerical simulation, experimental tests and identification of constitutive parameters is essential in the design and analysis of products.

By considering a constitutive model previously developed (de Castro and Fancello, 2017a), and few modifications introduced to it, in the current paper a proposal of mechanical testing and procedure for identification of some constitutive parameters is presented. First, the incremental version of the model is briefly described . Further, the experimental tests performed aiming at the evaluation of compressive response of PLGA samples are discussed. A systematic procedure for identification of constitutive parameters is then introduced, followed by the results obtained with this procedure and final conclusions.

CONSTITUTIVE MODEL

The constitutive model presented here aims at representing the elasto-viscoplastic mechanical behavior of bioresorbable polymers subject to coupled ductile-hydrolytic degradation. The model follows the framework of the so-called variational constitutive updates (Ortiz and Stainier, 1999) and its mathematical formulation has been discussed in detail in previous publications (de Castro, 2017; de Castro and Fancello, 2017a,b). For the sake of clearness, the incremental formulation used in this work will be briefly outlined.

The constitutive updates framework is set down by a minimization procedure involving the incremental potentials $\mathcal{W}(\mathcal{E}_{n+1})$, $\bar{\mathcal{W}}(\mathcal{E}_{n+1})$ and the set of state variables $\mathcal{E}_{n+1} = \{\mathbf{C}_{n+1}, \mathbf{Z}_{n+1}\}$. Thus, the themo-mechanical problem is defined by

$$\bar{\mathcal{W}}(\mathcal{E}_{n+1}) = \min_{\mathbf{Z}_{n+1}} \mathcal{W}(\mathcal{E}_{n+1}), \quad \mathcal{W}(\mathcal{E}_{n+1}) = [W(\mathcal{E}_{n+1}) - W(\mathcal{E}_n)] + \Delta t \phi^*, \quad \mathbf{S}_{n+1} \equiv 2\frac{\partial \bar{\mathcal{W}}}{\partial \mathbf{C}_{n+1}}, \tag{1}$$

where $\mathbf{C}_{n+1}$ is the right Cauchy-Green deformation tensor, $\mathbf{Z}_{n+1}$ is the set of dissipative variables, W is the Helmholtz free energy, ϕ^* is the incremental dissipative function and $\mathbf{S}_{n+1}$ is the second Piola-Kirchhoff. In the current proposal, the

following functional forms were chosen

$$W = W^e + U + W^p, \qquad W^e = \mu \hat{\varepsilon}^e_{n+1}, \qquad U = \frac{1}{2} K (\ln J)^2, \qquad W^p = H \left[\frac{(e^{n\,\alpha} - 1)}{n} - \alpha \right], \tag{2}$$

$$\phi^* = (1 - d_{n+1}) \sigma_Y \dot{\alpha} + \frac{c f_A(\alpha_{n+1})}{\eta + 1} \left(\frac{\dot{\alpha}}{c} \right)^{\eta+1} + Y_{n+1} \dot{d}^p + \frac{R}{2 (1 - d_{n+\theta})^n (Y_{n+\gamma} + g)^{m-1}} \left(\dot{d}^h \right)^2 - g \dot{d}^h, \tag{3}$$

$$f_A(\alpha_{n+1}) = s_\infty + e^{-s_z \alpha_{n+1}} \left[(s_0 - s_\infty) \cosh(s_b \alpha_{n+1}) + s_g \sinh(s_b \alpha_{n+1}) \right], \tag{4}$$

where W^e, U, W^p are respectively the isochoric-elastic , volumetric-elastic and plastic contributions of the free energy potetial, $\hat{\varepsilon}^e_{n+1}$ is the elastic logarithmic strain, $J = (\det \mathbf{C})^{1/2}$, α is the internal variable associated with the isotropic hardening, and $d_{n+\theta}$ and $Y_{n+\gamma}$ are intermediate values (within the timestep) of the total damage variable and its corresponding thermodynamic force. Furthermore, the following approaches are employed $\dot{\alpha} = \Delta\alpha/\Delta t$, $\dot{d}^h = \Delta d^h/\Delta t$, and two important parametrizations are adopted, first for the evolution of ductile damage variable, $\dot{d}^p = \dot{\alpha}(Y^S/N)$, and second for the plastic velocity gradient $\mathbf{D}^p = \dot{\alpha}\mathbf{M}$, where $\dot{\alpha}$ and $\mathbf{M}$ are respectively the amplitude and the direction tensor related to $\mathbf{D}^p$. In Eq. (3), the first two expressions are related to the viscoplastic response of the model, the third one is associated with the ductile damage and the last two drive the hydrolytic degradation process. By following Farias et al. (2017), the function $f_A(\alpha_{n+1})$ is associated with the plastic flow resistance of the material, allowing for the effect of initial hardening and post-yielding softening.

Considering Eqs. (2), (3) and (4), one will find a total of 18 constitutive parameters. The parameters μ and K are the shear and bulk elasticity modulus, σ_Y is the initial yield stress, H and n are the modulus and exponential parameters of the hardening model, η and c are related to viscoplastic parameters associated with Perzyna function, s_∞, s_0, s_g, s_z and s_b are related to the plastic flow resistance, and the sets R, g, n, m and S, N are respectively the hydrolytic degradation and ductile damage constants. These variables should be then characterized by experimental and identification procedures.

The solution of the constitutive problem can be obtained by finding initially the values of $\Delta\alpha$, Δd^h, $\mathbf{M}$. The direction tensor $\mathbf{M}$ is obtained analytically, resulting in $\mathbf{M} = \sqrt{3/2} \ln \hat{\mathbf{C}}^{pr}_{n+1} / \| \ln \hat{\mathbf{C}}^{pr}_{n+1} \|$, where $\hat{\mathbf{C}}^{pr}_{n+1}$ is a predictor for the isochoric right Cauchy-Green deformation tensor. The variables $\Delta\alpha$, Δd^h are obtained by solving the residuals $r_1 = \frac{\partial W}{\partial \Delta\alpha}$, $r_2 = \frac{\partial W}{\partial \Delta d^h}$. Thus, by updating Δd^p, it is possible to compute the stress update $\mathbf{S}_{n+1}$, as well as the Cauchy stress tensor $\boldsymbol{\sigma}_{n+1}$[1].

EXPERIMENTAL PROCEDURE

A series of compressive tests was carried out in order to evaluate the mechanical response (viscoplastic behavior) of PLGA 85/15 samples, as well as to make available a set of experimental data for the identification procedure of constitutive parameters. Samples were machined from injected-molded conical parts, resulting in cylindrical specimens with nominal dimensions of 6×6 mm. To avoid undesirable strain localizations during the test procedure (a common onset caused by turning marks and imperfections), the cylindrical surface of the specimens was additionally polished by using a 1500 grit sandpaper.

Tests were performed in a servohydraulic machine (MTS Bionix) where a special compression test rig (Sonnenhohl, 2015) was assembled. While being deformed, the variation of sample height was measure by a Linear Variable Differential Transformer (LVDT) fixed directly to the compression device, then reducing measurement errors caused by machine compliance. Moreover, samples deformation occurring throughout the test was recorded by using a video camera system.

Another important aspect to be pointed out is that the specimens were placed directly in contact with the compression surfaces of the device without using any lubrication. By avoiding the use of lubrication, there is a reduction of typical instabilities observed in PLGA specimens often produced by localized deformations. In this case, non-homogeneities induced by the lack of lubrication, for example barreling, are preferable to material instabilities.

The experiment was performed for three different nominal strain rates (0.01 s^{-1}, 0.001 s^{-1} and 0.0001 s^{-1}). A total of nine samples were evaluated, three samples for each rate. The resulting load vs. displacement curves obtained with the tests are shown in Figure 3.

IDENTIFICATION OF CONSTITUTIVE PARAMETERS

Optimization-based parameter identification makes use of optimization algorithms and identification frameworks in order to find the best set of constitutive parameters. Gradient-based and Gradient-free algorithms have been tested in

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[1] $\boldsymbol{\sigma} = J^{-1} \mathbf{F} \mathbf{S} \mathbf{F}^T$, where $\mathbf{F}$ is the deformation gradient tensor

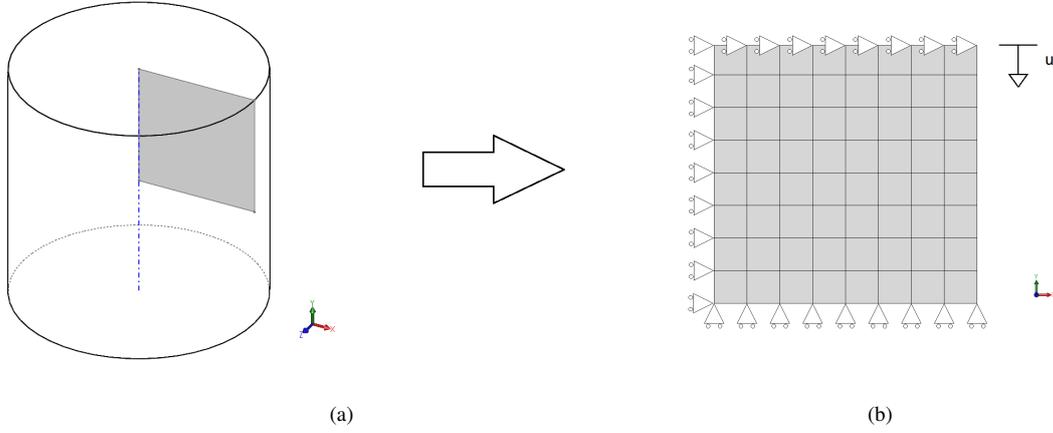(a)   (b)

Figure 1: FE Model

this type of problem. In general, gradient-based methods have a good convergence rate, but do not perform well when continuity of the derivatives or convexity are not guaranteed. Gradient-free methods are a category of methods that does not require the evaluation of derivatives, but makes use of some heuristics in order to find a minimum. Hybrid approaches use gradient-based and gradient-free methods in different steps of the optimization procedure in pursuance of trade-offs between exploration capability of gradient-free methods and convergence rate of the gradient-based methods. The choice of the best method is an on-going discussion and appears to be problem-specific. A review of multi-objective optimization algorithms and objective functions can be seen in Vaz Jr. et al. (2015) , Zhou et al. (2015) and Cui et al. (2017). In the present work we follow the hybrid approach presented in Vaz Jr. et al. (2015), where a a Particle Swarm Optimization (PSO) algorithm was employed in pursuance of broadening the search space and the Nelder-Mead method (Nelder and Mead, 1965), a simplex-based method, is used as a local search procedure.

The constitutive model in analysis requires 18 parameters to be fully characterized. However, due to the lack of data regarding damage and degradation mechanisms, in the present work only 12 parameters related to the assumed elastic-viscoplastic material behavior are identified, that is,

$$\mathbf{x} = [\mu, K, \sigma_Y, H, n, \eta, \mathsf{c}, s_\infty, s_0, s_g, s_z, s_b].$$

The strategy used to identify the constitutive parameters is performed by means of a curve-fitting procedure. The curve-fitting is carried out with an optimization procedure, where the set of constitutive parameters is estimated based on the minimization of an objective function that takes into account the difference between the results from experimental and numerically-simulated compression tests. In this way, experiments are simulated using an in-house Finite Element (FE) code, in which the above-mentioned constitutive model was implemented.

The FE model makes use of symmetry assumptions. A two dimensional axissymmetric model is used to represent the cylindrical body of the test specimens, as shown in Figure 1. Tests on mesh sensitivity and time discretization sensitivity were performed: an 8-node quadrilateral element was chosen with 300 equally-spaced time increments. Axial displacement is directly prescribed on the top-most nodes and no contact formulation was employed in this model. At the end of the simulation the resulting compression force is retrieved. A force-displacement curve is obtained for each of the three strain rates and the three curves are compared simultaneously to the corresponding experimental result.

The error function $f(\mathbf{x})$ between experimental (EXP) and simulated (SIM) curves is given by the root-mean-square error:

$$f(\mathbf{x}) = \sqrt{\frac{1}{n}\sum_{i=1}^{n}(F_i^{EXP} - F_i^{SIM})^2}, \tag{5}$$

where F is the axial compression force and n is the number of data points for each curve. Three error curves are obtained, one for each strain rate. This constitutes a multi-objective optimization problem and is transformed into a single objective problem using the weighted sum method. The optimization problem is formally presented as:

$$\mathbf{x}^{\mathrm{opt}} = \arg\min_{\mathbf{x} \in \mathcal{K}} \sum_{j=1}^{m} \omega_j f_j(\mathbf{x}) \qquad \mathcal{K} = \{\ \mathbf{x}\ \mid\ x_k > 0, k = 1 \text{ to } 12\} \tag{6}$$

where m is the number of objective functions and ω_j are weights. In this case, all weights were chosen as 1.0.

In order to explore the search space and avoid local minima, the number of particles of the PSO algorithm must be reasonably high. Since each particle requires that three FE simulations be carried out (one for each strain rate), the procedure could become computationally expensive. Thus, the number of particles must be restrained in such a way the entire procedure remains in an acceptable time frame to optimize the parameters.

Analyzing the data from the video recording and the force-displacement curves, it can be observed that localization effects and subsequent barreling of the test specimen only happen after the peak force. Prior to that the displacement field can be approximated to a homogeneous case. Assuming the hypothesis of homogeneity allows the usage of a one-dimensional simulation, significantly reducing computational time.

For small displacements (0 to 0.2 mm), no rate dependent behavior is observed. This kind of behavior is stronger for intermediate values of displacement (0.2 to 0.8 mm), and weak for higher values (0.8 to 1.7 mm). These observations together with the homogeneity hypothesis leads to the following calibration procedure:

1. The first step is to define the region where homogeneity is an admissible hypothesis. This region is divided in a linear, rate-independent part and the part where yield and rate dependency occurs. In the linear region (0 to 0.15mm), the optimization procedure is applied to find the elastic parameters μ and K while the others remains constant.

2. The second step is to apply the optimization procedure with all the remaining parameters to the whole homogeneous region (0 to 0.3mm), as a mean to get a rough initial estimation of the search space.

3. The third step consists of applying the optimization procedure to the whole compression (0 to 1.7mm) with the FE model using the estimated search space from the previous step. The particle number is diminished so that this step can be accomplished in reasonable time. If the objective function did not improve by at least 10% from the previous steps for four consecutive steps the PSO algorithm is stopped.

4. A fourth optimization step is applied in order to refine the results, now utilizing the Nelder-Mead optimization algorithm, until a tolerance criteria is met.

The optimization algorithms and the identification procedure were implemented in a in-house FORTRAN code. The above mentioned procedure is shown in the following diagrams (Figure 2).

RESULTS AND DISCUSSION

Experimental results are presented in Figure 3. As it occurs with other glassy polymers, PLGA 85/15 compression test exhibit stress softening after yielding followed by hardening at larger strains. For the high strain rate a continuous loss in resistance is observed from 0.4 to 0.6mm instead of the hardening behavior observed in low and medium strain rates. This could be an indicative of thermal effects as exhibited in Ames et al. (2009), not considered in the present model.

The results of the optimization procedure are presented in Figure 4. Separating the search in two stages (homogeneous and finite element) permits having a wide search space and a high number of particles in the first stage and narrowing the search space in the second. This permits the usage of the global search ability of PSO while in a reasonable time frame. After the optimization procedure the complete list of identified parameters is :

$$\mu = 860.61 \quad K = 4000.00 \quad \sigma_y = 60.00 \quad H = 0.0077 \quad n = 0.100 \quad \eta = 0.2025$$
$$c = 0.2790 \quad s_\infty = 3.1516 \quad s_0 = 50.00 \quad s_g = 200.00 \quad s_z = 820.00 \quad s_b = 799.45$$

The results show a complex stress-strain distribution where a strong localization occurs in the center of the specimen and also the formation of shear bands as it can be seen in Figure 4 b.

In Figure 5 the error between experimental and simulated forces is shown. For small displacements the identification procedure has good agreement with the experimental results. In the middle displacement range, where rate-dependency is stronger, the procedure is less effective in finding a good fit for all rates simultaneously. The peak force followed by softening is particularly difficult to identify. In the region of higher values of displacement, the procedure could capture both the hardening aspect and its rate dependencies. The continuous loss in resistance observed for the high strain rate (c) could not be represented using the current model. Further testing would be beneficial to understand this intricate behavior.

It is worth mentioning the non-uniqueness of the solution. The parameters σ_y and s_∞,for example, produced the same behavior in the compression curves so that another combination of these could produce equal values for the objective
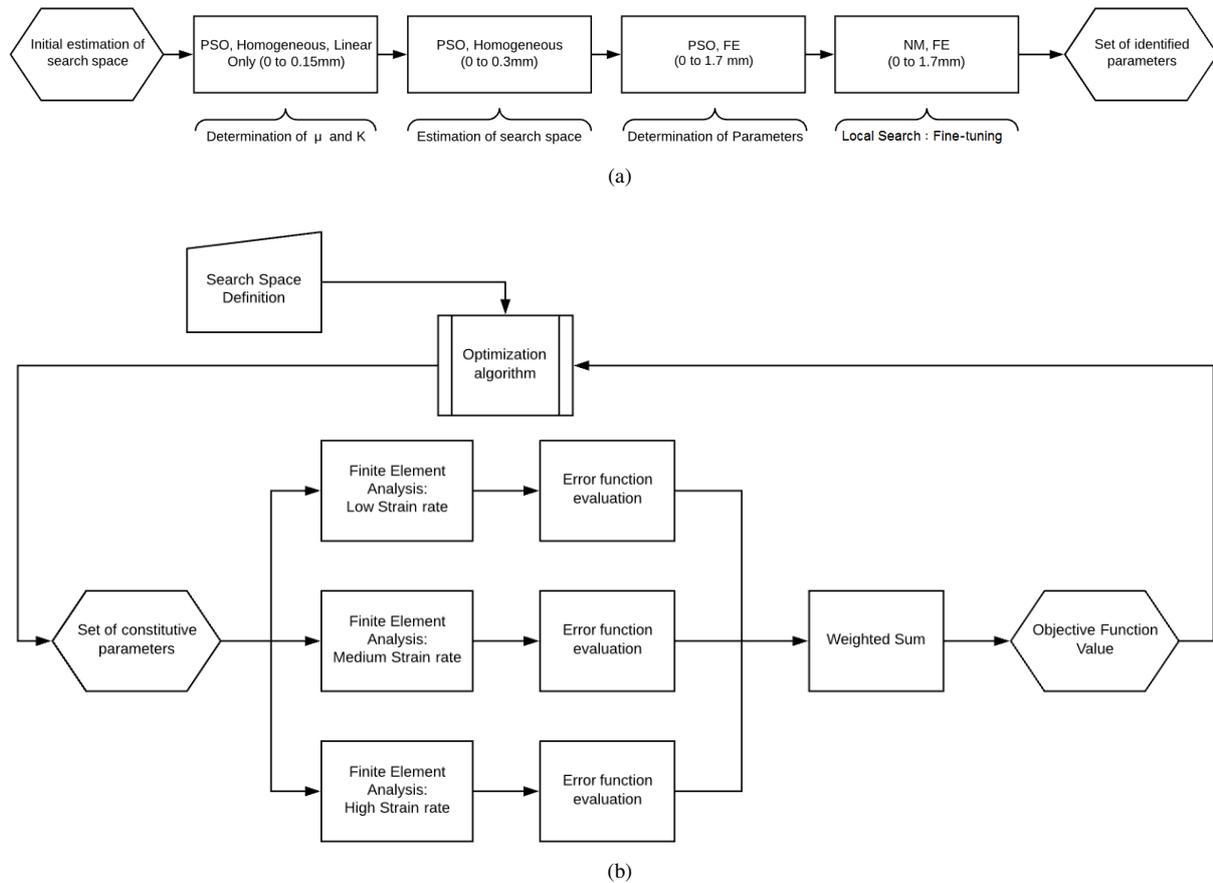
Figure 2: (a) Identification procedure diagram.(b) Objective function evaluation diagram

function. Further experimental testing could solve this issue or by adopting another flow-rule that does not produce this conflict.

Depending on the combination of values for constitutive parameters, the Finite Element Method could fail to achieve convergence, thus impairing the evaluation of the objective function. Convergence issues are especially present when steep softening occurs and denotes the sensibility of the viscoplastic parameters (η and c) and the plastic flow resistance parameters (s_∞, s_0, s_g, s_z and s_b) not only individually but as a set. Lack of convergency in a simulation was handled in the optimization algorithm by assigning a high value to the objective function. While this is acceptable when using the PSO algorithm, the Nelder-Mead method will fail, further emphasizing the need of defining a well-behaved search-space and how the hybrid approach can mitigate this difficulty.

Identification of constitutive parameters is significantly different for homogeneous and heterogeneous stress/strains fields. Structural effects adds another layer of complexity from an identification standpoint since the intrinsic behavior of the material can be overshadowed by geometric and localization effects. As stated earlier, barreling of the specimen was preferred than material instabilities and allowed more consistent results, this , however, implicated in a computational intensive and time consuming calibration procedure.

CONCLUSION

Compressive tests were performed for three strain rates in samples of PLGA 85/15. An optimization procedure was carried out in order to identify constitutive material parameters. The constitutive model is able to represent rate-sensitivity and softening of the material. Other functions for the plastic flow resistance could be tested in order to better simulate the softening behavior and avoid numerical difficulties that arise from the exponential formulation. For small and large axial displacements the proposed identification procedure for the model found good agreement with experimental results.
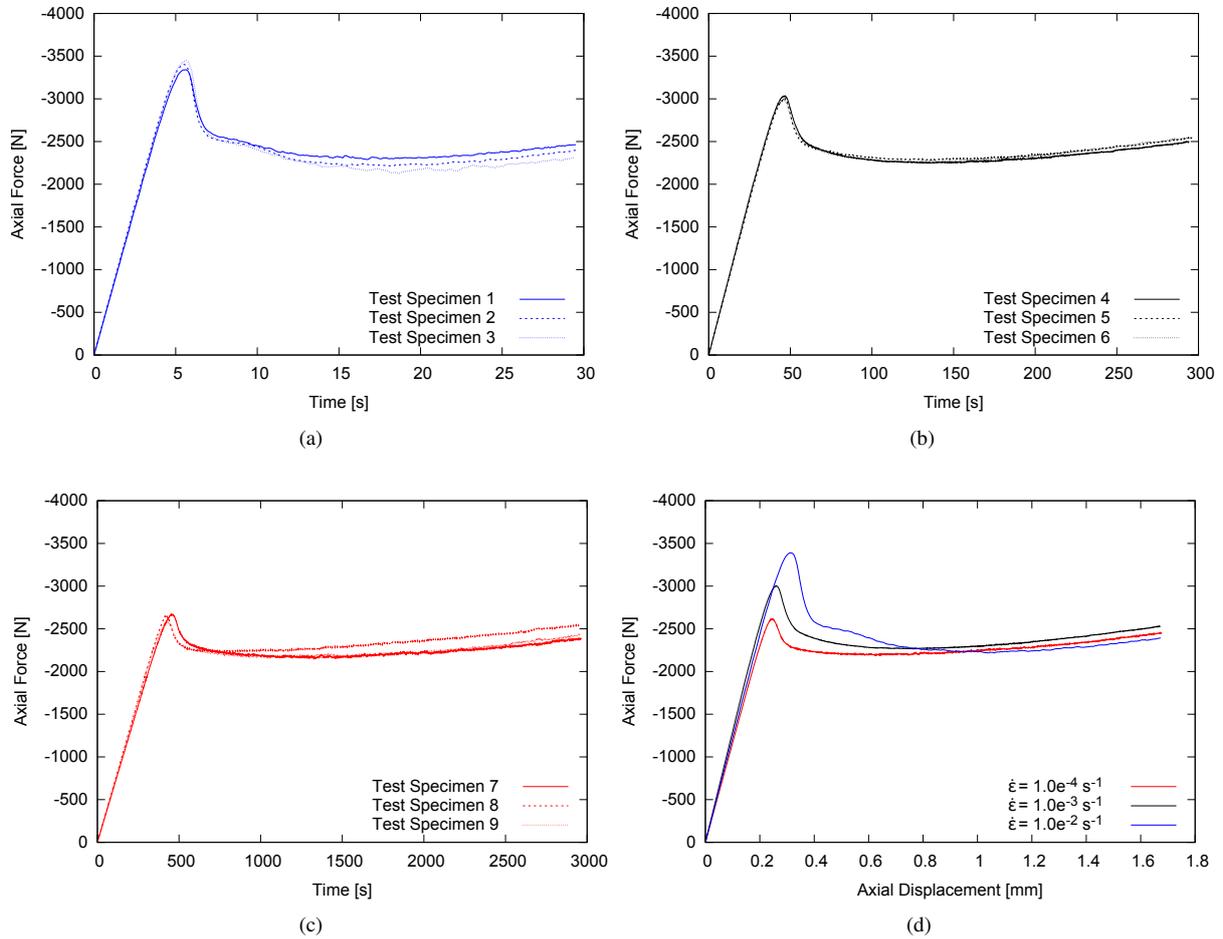
Figure 3: Experimental Results: Compression force for different strain rates (a) $\dot{\varepsilon} = 1.0 \times 10^{-2}$/s , (b) $\dot{\varepsilon} = 1.0 \times 10^{-3}$/s, (c) $\dot{\varepsilon} = 1.0 \times 10^{-4}$/s and (d) mean results for each strain rate.
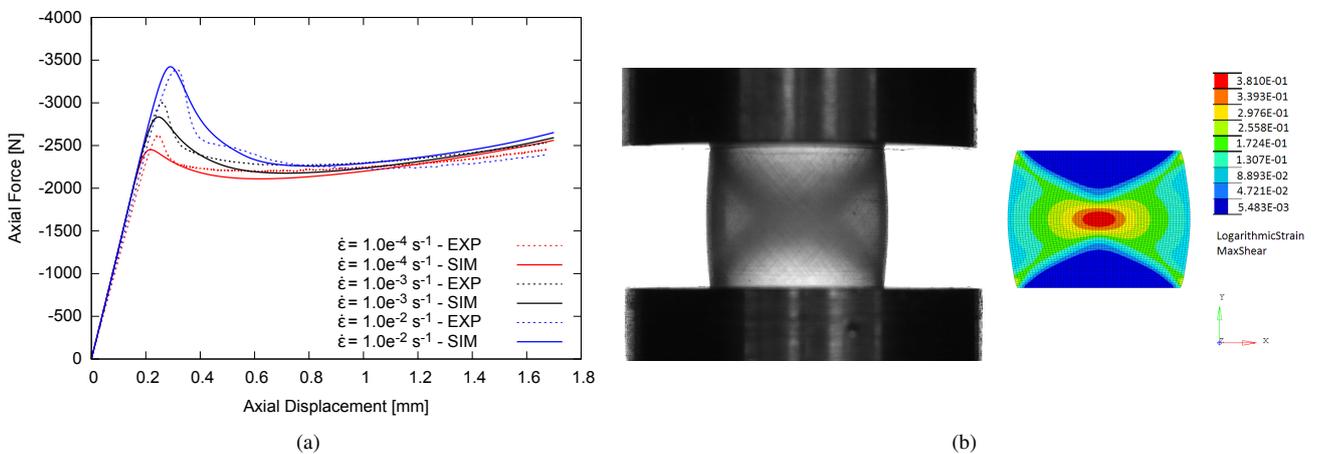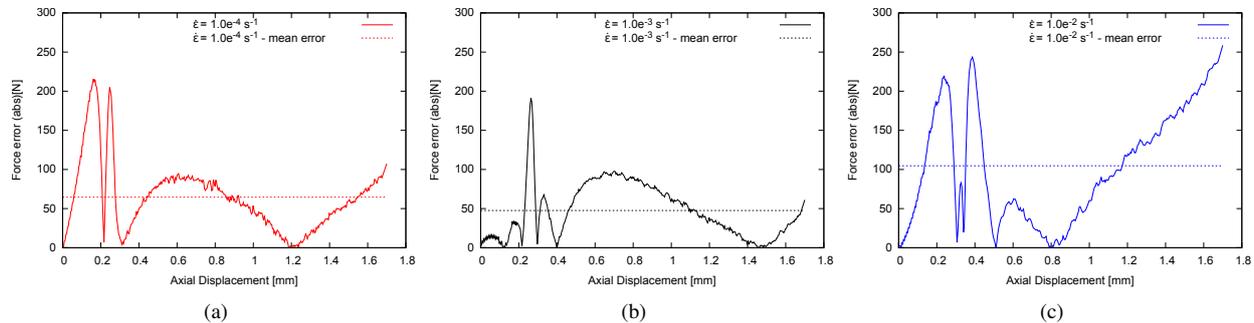

Figure 4: Compression tests at three different strain rates. (a) Comparison of the experiment and the fitted curves, (b) Test specimen and Finite Element Model: Maximum Shear Strain.

Figure 5: Absolute error between F^{EXP} and F^{SIM}

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RESPONSIBILITY NOTICE

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