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Probabilistic constitutive law for damage in ligaments

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ABSTRACT

A new constitutive equation is presented to describe the damage evolution process in parallel-fibered collagenous tissues such as ligaments. The model is formulated by accounting for the fibrous structure of the tissues. The tissue's stress is defined as the average of the collagen fiber's stresses. The fibers are assumed to be undulated and straightened out at different stretches that are randomly defined according to a Weibull distribution. After becoming straight, each collagen fiber is assumed to be linear elastic. Damage is defined as a reduction in collagen fiber's stiffness and occurs at different stretches that are also randomly defined by a Weibull distribution. Due to the lack of experimental data, the predictions of the constitutive equation are analyzed by varying the values of its structural parameters. Moreover, the results are compared with the available stress–strain data in the biomechanics literature that evaluate damage produced by subfailure stretches in rat medial collateral ligaments.

1. Introduction

Injuries to ligaments can be classified according to their severity as first-, second-, and third-degree sprains. With a first-degree sprain, the ligament is overstretched but the joint remains stable. A second-degree sprain occurs when the ligament is partially torn and moderately affects the joint stability. A third-degree sprain is the most debilitating ligament injury. It consists of a complete rupture of the ligament and causes severe joint instability. While third-degree sprains are the most severe pathology of ligaments, first- and second-degree sprains are the most common. Indeed, epidemiological studies have estimated that more than 85% of ligamentous injuries consist of first- and second-degree sprains [2].

Despite their high incidence, few experimental studies have been conducted on ligaments to analyze changes in structural properties [16,22,21] and mechanical properties [26] when microtrauma and partial tears occur. Panjabi et al. [22] investigated the influence of subfailure injuries on the structural properties of rabbit anterior cruciate ligaments (ACLs). The ultimate load, ultimate deformation, and energy absorbed at failure were seen not to change profoundly following a subfailure injury defined as 80% of the ultimate deformation of the contralateral control ligaments. The shape of the load-deformation curve, however, was noted to be remarkably different with major changes observed in the toe region. In a follow-up study, Panjabi and Courtney [21] found that the same subfailure injury at high speed produced an increase in the ultimate deformation.

The most comprehensive study of subfailure damage has been conducted on rat medial collateral ligaments (MCLs) by Provenzano et al. [26]. The authors analyzed the effects of different subfailure stretches on the tensile stress–strain curves. In their experiments, the specimens were stretched to subfailure stretches by performing tensile tests, unloaded and allowed to recover for a time 300 times greater than the duration of the test to avoid a viscoelastic creep-recovery response before being reloaded. After recovery, the specimens were stretched again until complete failure of the specimen occurred. These experiments are different than experiments (e.g. hysteresis and preconditioning) in which the specimens are cyclically loaded and unloaded to the same initial stretch by using the same strain rate. The stress–strain curves during reloading that followed the creep-recovery were observed to change when the subfailure stretches exceeded a threshold stretch corresponding to 5.14%. The toe region was noted to be elongated while the tangent modulus and the tensile strength were found to decrease with increasing subfailure strain.

Because of the difficulties in studying experimentally the damage evolution process in ligaments, constitutive equations need to be formulated to enhance our understanding of the injury mechanisms and to guide the design of appropriate experiments. Several structural [14,11,17,33,7] and phenomenological [3,27,19,20,5] constitutive equations have been proposed to describe the damage evolution process in collagenous tissues. All these equations can successfully fit the three regions (toe, linear, and failure regions) of the experimental stress–strain curves while some [27,19,20,5] can also describe other mechanical behaviors that are typical of soft tissues. For example, the finite-strain damage constitutive model proposed by Rodriguez et al. [27] can also reproduce the reduction in stiffness between loading and unloading paths in each straining

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cycle. The anisotropic elasto-damage constitutive model developed by Natali et al. [19] captures the increase in stiffness at low strain values due to cyclic loading. More recently, Natali et al. [20] and Ciarletta and Ben Amar [5] have presented damage constitutive models which also consider the viscoelasticity of soft tissues. However, none of the cited models can predict the effect of subfailure stretches (prolonged toe region, decrease in ultimate stress and tangent modulus) as observed and defined by Provenzano et al. in their experimental studies [26].

In this study, a new probabilistic model for damage of parallel-fibered collagenous tissues is presented. The mechanical response of the tissues is assumed to be determined by their comprising collagen fibers. Damage is defined as a reduction in straight collagen fiber's stiffness, which occurs at randomly defined stretches. The proposed model can not only reproduce the toe, linear, and failure regions of the stress–strain curve in ligaments but, unlike previous models, it can also predict the changes in the stress–strain curve such as prolonged toe region, decrease in tensile strength and tangent modulus that are determined by subfailure stretches. The predictive capabilities of the model are investigated by studying the effect of the structural parameters on the tensile behavior of ligaments and by using published tensile data [26].

2. Model formulation

2.1. Preliminaries and basic assumptions

Ligamentous tissues can be regarded as composite materials consisting of collagen fibers and elastin fibers embedded in a proteoglycan-rich matrix, the so-called *ground substance*. Collagen, which occupies 65%–80% of the total dry weight of ligaments, is the main load carrying component. Elastin constitutes less than 1% of the dry weight of ligaments and is responsible for elastic recovery. Water occupies 60–70% of the tissue's total weight [1].

Collagen has a hierarchical structure: collagen molecules are packed together to form collagen fibrils, collagen fibrils aggregate to form collagen fibers and collagen fibers are arranged in fascicles [13]. The collagen fibers are wavy when unstrained and gradually lose their waviness under strain [10]. Moreover, they exhibit a linear elastic behavior [28].

To describe the tensile behavior of ligaments, a structural one-dimensional model is presented hereafter. In the model formulation, the collagen fibers are assumed to be the only ligaments' component that determines their mechanical behavior. Collagen fibers are assumed to be linear elastic and parallel to the ligaments' loading direction. They are wavy and gradually become straight and damaged under strain. Each collagen fiber reduces its stiffness at different damage stretches. The ligament's stress is defined as the average of the stresses of the constituent collagen fibers. Elastin contribution is neglected due to its small amount. Moreover, the ground substance and its interaction with the collagen fibers are ignored.

2.2. Collagen fiber and ligament stretch

The ligament is assumed to be made of N parallel collagen fibers, where N is a non-negative integer. The collagen fibers are defined randomly by their straightening stretches according to a Weibull distribution [31]. The Weibull distribution is a one-tailed continuos probability distribution widely used in reliability and life data analysis due to its versatility. It has three parameters – the so-called shape, scale and location parameters – that can be varied to mimic the behavior of other probability distributions such as, for example, the exponential distribution. The probability density function (PDF) of a Weibull random variable Λ_s is

$$p(\Lambda_s;\alpha_s,\beta_s,\gamma_s)=\begin{cases}0 & \text{for } \Lambda_s<\gamma_s,\\ \dfrac{\alpha_s}{\beta_s}\left(\dfrac{\Lambda_s-\gamma_s}{\beta_s}\right)^{\alpha_s-1}e^{-\left(\frac{\Lambda_s-\gamma_s}{\beta_s}\right)^{\alpha_s}} & \text{for } \Lambda_s\geq\gamma_s,\end{cases} \tag{1}$$

where Λ_s is the fiber's straightening stretch, $\alpha_s>0$ is the shape parameter, $\beta_s>0$ is the scale parameter, and $\gamma_s>0$ is the location parameter. The cumulative distribution function associated with (1) is

$$P(\Lambda_s;\alpha_s,\beta_s,\gamma_s)=\begin{cases}0 & \text{for } \Lambda_s<\gamma_s,\\ 1-e^{-\left(\frac{\Lambda_s-\gamma_s}{\beta_s}\right)^{\alpha_s}} & \text{for } \Lambda_s\geq\gamma_s.\end{cases} \tag{2}$$

By inverting Eq. (2) for $\Lambda_s\geq\gamma_s$, one obtains the following relation:

$$\Lambda_s(P;\alpha_s,\beta_s,\gamma_s)=\gamma_s+\beta_s[-\ln(1-P)]^{1/\alpha_s}. \tag{3}$$

Eq. (3) can be used to generate randomly distributed collagen fibers by generating their associated straightening stretches. Let $\Lambda_s^{(i)}$ be the straightening stretch of ith collagen fiber ($i=1,2,\ldots,N$). Then, $\Lambda_s^{(i)}$ can be defined as

$$\Lambda_s^{(i)}(P_s^{(i)};\alpha_s,\beta_s,\gamma_s)=\gamma_s+\beta_s[-\ln(1-P_s^{(i)})]^{1/\alpha_s}, \tag{4}$$

where $P_s^{(i)}$ is a random number between 0 and 1.

Let Λ be the overall stretch of the ligament. Each collagen fiber is stretched only after losing its waviness. Thus, the stretch of ith collagen fiber, which is denoted by $\Lambda^{(i)}$, is computed relative to its straightening stretch, $\Lambda_s^{(i)}$, and is defined as $\Lambda^{(i)}=\Lambda/\Lambda_s^{(i)}$.

2.3. Damage and collagen fiber stress

Damage is assumed to be a stretch controlled process. The ith collagen fiber possesses M damage stretches, where M is a non-negative integer. These stretches are randomly generated by using a Weibull distribution. Thus, the jth subfailure stretch ($j=1,2,\ldots,M$) of the ith collagen fiber is given by

$$\Lambda_d^{(j)}(P_d^{(j)};\alpha_d,\beta_d,\gamma_d)=\gamma_d+\beta_d[-\ln(1-P_d^{(j)})]^{1/\alpha_d}, \tag{5}$$

where $P_d^{(j)}$ is a random number between 0 and 1, $\alpha_d>0$, $\beta_d>0$, and $\gamma_d>0$ are the shape, scale, and location parameter of the Weibull distribution, respectively.

Each collagen fiber is linearly elastic with stiffness K. It reduces its original stiffness by a factor $0\leq D\leq 1$ when damage occurs. This reduction in stiffness can be attributed to breakage of fibrils in each collagen fiber. The limit $D=0$ describes the complete failure of the collagen fiber while the limit $D=1$ represents the case in which the collagen fiber is not damaged.

Thus, the stress of ith collagen fiber, which is denoted by $\sigma^{(i)}$, is defined as

$$\sigma^{(i)}=\begin{cases}0 & \text{for } \Lambda^{(i)}\leq 1 \text{ (i.e. wavy fiber)},\\ K(\Lambda^{(i)}-1) & \text{for } 1<\Lambda^{(i)}<\Lambda_d^{(j)} \text{ (i.e. straight, undamaged fiber)},\\ D^jK(\Lambda^{(i)}-1) & \text{for } \Lambda^{(i)}\geq\Lambda_d^{(j)} \text{ (i.e. straight, damaged fiber)},\end{cases} \tag{6}$$

where $1\leq j\leq M$ and $\Lambda_d^{(1)}\leq\Lambda_d^{(2)}\leq\cdots\leq\Lambda_d^{(M)}$. It must be noted that D^j denotes the exponentiation with base D and exponent j. Fig. 1 illustrates an example of stress–stretch curve for a single straight collagen fiber that is damaged $j=5$ times at five different stretches, $\Lambda_d^{(1)}$, $\Lambda_d^{(2)}$, $\Lambda_d^{(3)}$, $\Lambda_d^{(4)}$, and $\Lambda_d^{(5)}$. In this example, the initial stiffness K of the collagen fiber is reduced to D^jK at each $\Lambda_d^{(j)}$ and D has been set to be equal to $1/2$.

The overall stress of the ligament is defined as the average of the stresses of the N collagen fibers. Thus, it is given by

$$\sigma=\frac{1}{N}\sum_{i=1}^{N}\sigma^{(i)}. \tag{7}$$

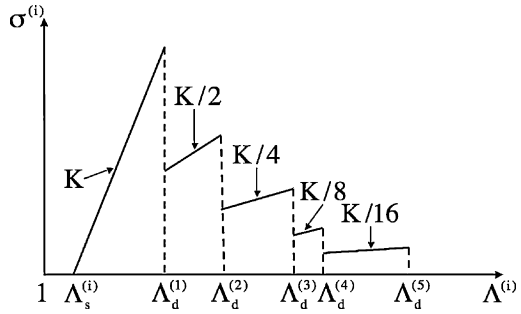

Fig. 1. Example of stress–stretch relation for the ith collagen fiber. In this example, damage occurs at five stretches, $\Lambda_d^{(j)}$ with $j = 1 \ldots 5$, and causes a reduction in stiffness by a factor D chosen to be equal to $1/2$.

Thus, the tensile behavior of the ligament can be described by (4)–(7) and, hence, require the following set of parameters $\{K, D, \alpha_s, \beta_s, \gamma_s, \alpha_d, \beta_d, \gamma_d, N, \text{and } M\}$. Below it will be explained how the number of parameters can be reduced and computed by using experimental data.

3. Results

In order to demonstrate the capability of the model, the number N of collagen fibers that constitute the ligament has been chosen to be 10^5. It needs to be noted that this number does not represent the effective number of fibers that occupy the ligamentous substance. Indeed, in the numerical implementation of the model, no differences are noticed in the value of the stress σ defined by (7) when the number N is increased. The number M of damage stretches in straight collagen fibers can be related to the number of fibrils that could break thus producing a reduction in collagen fiber's stiffness. M has been set to be 100 since approximately hundreds of fibrils make up a single collagen fiber. The straightening stretches of the collagen fibers and damage stretches of each straight collagen fiber have been computed by transforming uniform deviates generated by using Park and Miller's Minimal Standard generator with an additional shuffle [23,24] into Weibull distributed deviates via Eqs. (4) and (5).

Published experimental data by Provenzano et al. [26] on rat MCLs have motivated the formulation of the proposed model and have been used to validate its predictions. The stress–strain data reported in Fig. 5F [26] have been digitized and employed to determine values of the model parameters. The results of the curve fitting performed by minimizing the sum of the squared differences between the predicted and measured values of the ligament's stress via the Differential Evolution code [25] are shown in Fig. 2. The Differential Evolution is a robust genetic-type algorithm [9] that can be used to minimize any kind of function with any kind of constraints defined on continuos, discrete, and mixed search spaces. The values of the material parameters obtained are $K = 1059$ MPa, $\alpha_s = 1.000$, $\beta_s = 0.0273$, $\alpha_d = 2.052$, $\beta_d = 0.2357$, and $D = 0.8992$ ($R^2 = 0.99$). These parameters provide a unique minimum in the parameter space defined by the following intervals: $0 \le K \le 10,000$, $1 \le \alpha_s \le 10$, $0 \le \beta_s \le 10$, $1 \le \alpha_d \le 10$, $0 \le \beta_d \le 10$, and $0 \le D \le 1$. The set of parameters computed via the minimization are computed so that they can then be varied for studying the effect of each structural parameter on the overall stress–stretch response. It was assumed that the location parameter, γ_s, of the Weibull distribution that describes the collagen fibers' straightening process is equal to 1. Such assumption is physically sound and implies that the collagen fibers cannot become straight under compression, i.e. when the stretch is less than 1. The location parameter, γ_d, of the Weibull distribution that defines the damage stretches of the collagen fiber has been fixed to be 1.0514. This is the stretch value corresponding to the 5.14% strain at which damage occurs in rat MCLs [26].

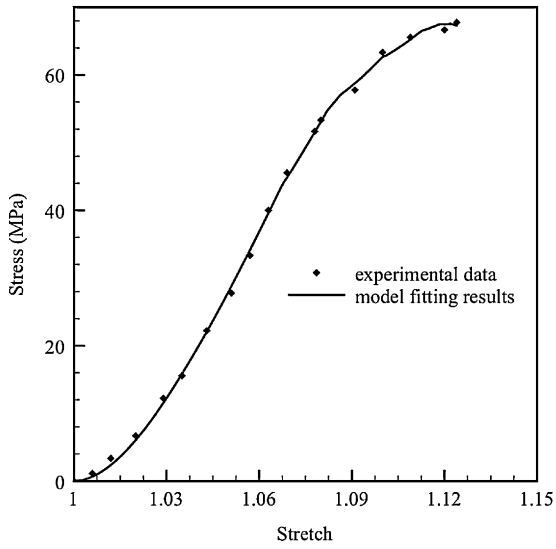

Fig. 2. Model fit to tensile experimental data.

Due to the lack of combined mechanical and histological experimental data on partial and complete failure of collagenous tissues, the predictive capabilities of the constitutive model have been studied by varying the values of its structural parameters within bounds that are dictated by their physical meaning. The values of the parameters, which are not varied in all these predictions, have been fixed to the values obtained by curve fitting the experimental data published by Provenzano et al. [26]. The effect of different subfailure stretches on the stress–stretch curves of ligaments are illustrated in Fig. 3. The stress–stretch curve for a ligament obtained during first loading up to a given subfailure stretch is assumed to be equal to the stress–stretch curve of its corresponding contralateral control ligament (up to that subfailure stretch) in agreement with the experiments. The first loading curve in Fig. 3 is plotted for the values of the material parameters obtained from the curve fitting procedure described above and using the data collected on the

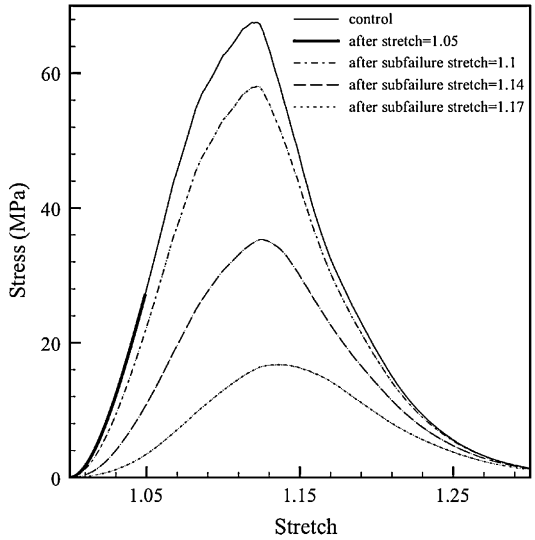

Fig. 3. Model prediction for different values of subfailure stretches. The first loading curve (continuos line) is plotted for the values of the material parameters obtained from curve fitting. The different second loading curves (bold and dashed lines) are then predicted by computing how many fibrils are broken in the collagen fibers during the first loading up to subfailure stretches equal to 1.05, 1.1, 1.14, and 1.17.

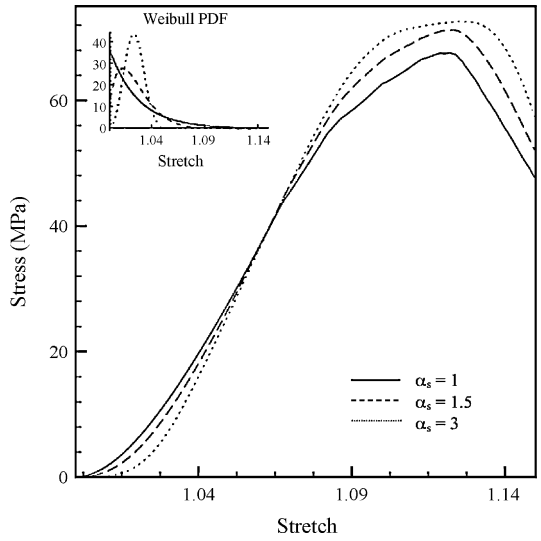

Fig. 4. Model prediction and associated Weibull PDF defining collagen fiber straightening process for different values of α_s.

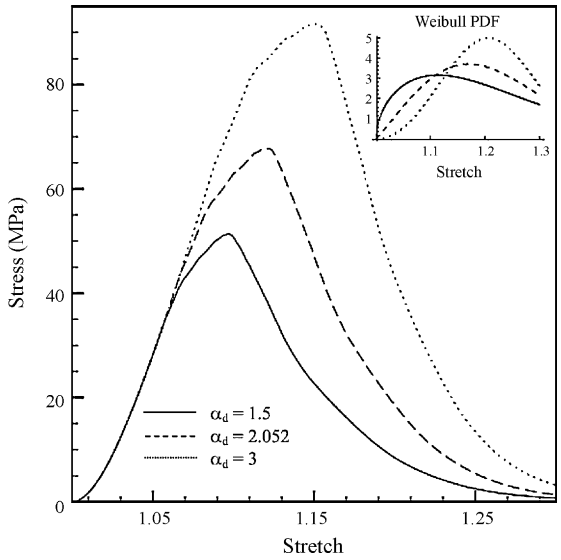

Fig. 6. Model prediction and associated Weibull PDF defining collagen fiber damage process for different values of α_d.

contralateral control ligament. The different second loading curves depicted in Fig. 3 are then predicted by computing how many fibrils are broken in the collagen fibers during the first loading up to subfailure stretches equal to 1.05, 1.1, 1.14, and 1.17. The results are comparable with the experimental data [26] in which damage, which appears for a subfailure stretch higher that 1.05, was characterized by a more prolonged toe region and a reduction in tangent modulus and ultimate stress.

In Figs. 4 and 5, the stress–stretch curves predicted by the model are depicted for various values of the shape parameter, α_s, and scale parameter, β_s, of the Weibull distribution that describes the fiber straightening process. It can be seen that, by changing these parameters, the toe region of the stress–stretch curve changes. As the value of α_s increases, more collagen fibers become straight at a greater stretch, which corresponds to the stretch at which the Weibull PDF has a maximum. The resulting stress–stretch curve has a more prolonged toe region, increased stiffness, and greater ultimate stress (Fig. 4). As the value of β_s increases, the Weibull PDF becomes flatter implying that the straightening process of collagen fibers become slower since the straightening stretches of collagen fibers are more evenly distributed. Thus, the toe region is also prolonged but both the stiffness and the ultimate stress decrease since the probability of fibers being straight and, hence, supporting load also decreases (Fig. 5).

In Figs. 6 and 7, the stress–stretch curve is presented for different values of the shape parameter, α_d, and scale parameter, β_d, of the Weibull distribution that defines the damage stretches of individual collagen fibers. By varying these parameters, the failure region of the stress–stretch curve changes while the toe region remains unaffected. As the value of α_d increases, the Weibull PDF becomes sharper and its maximum value shifts to the right. This indicates that straight fibers are damaged at larger stretches and sudden failure is more probable. Therefore, greater failure stretch, tensile strength and a sharper stress–stretch curve are associated with a greater value of α_d. As the value of β_d increases, the maximum value of Weibull PDF also shifts to the right but the function appears flatter. This results in greater failure stretch and ultimate strength and more gradual failure process.

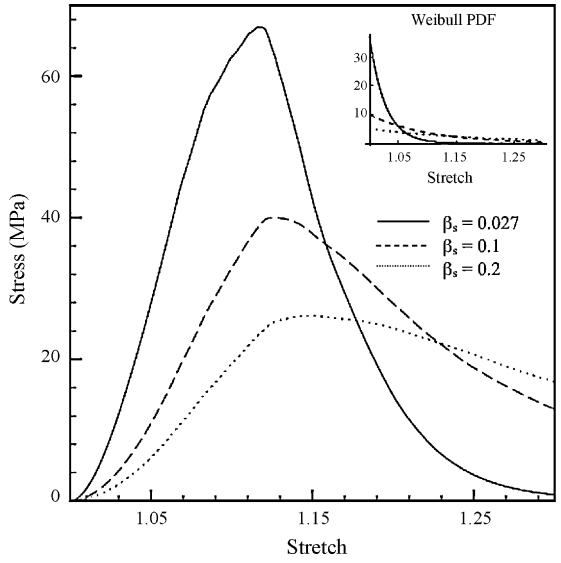

Fig. 5. Model prediction and associated Weibull PDF defining collagen fiber straightening process for different values of β_s.

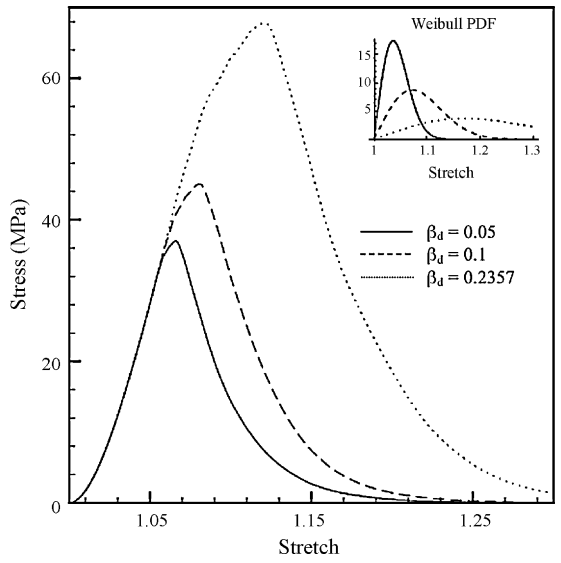

Fig. 7. Model prediction and associated Weibull PDF defining collagen fiber damage process for different values of β_d.

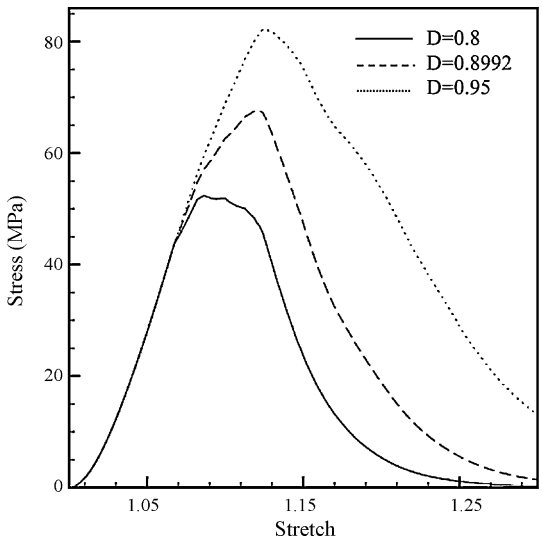

Fig. 8. Model prediction for different values of D.

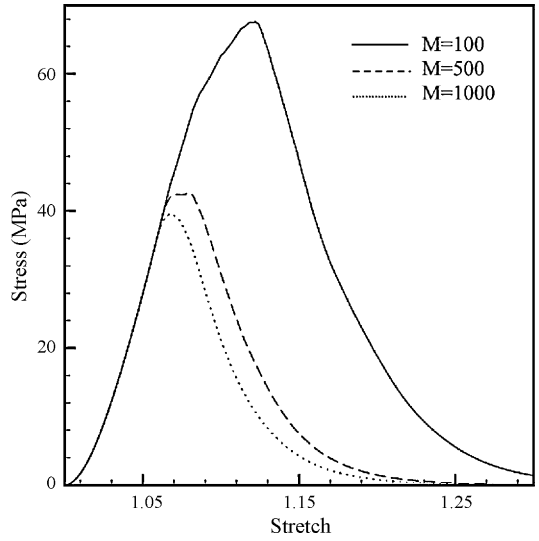

Fig. 9. Model prediction for different values of M.

In Fig. 8, the stress–stretch curves are depicted for different values of the stiffness reduction parameter, D. One can observe that as D increases, the stress sustained by the tissue increases. For a fixed M, high values of D indicate that little damage is produced in straight collagen fibers and, hence, their stiffness is slightly reduced. By changing the number of damage stretches, M, in a straight collagen fiber the model can reproduce different failure modes as shown in Fig. 9. Precisely, for low values of M, the failure region of the stress–strain curve has a more jagged appearance that is often observed during tensile tests. One must also observe that when $M \to \infty$ or $D \to 0$ in (6), the current model becomes similar to a previous model that describes complete failure in ligaments [7].

4. Discussion

A novel probabilistic constitutive equation for damage in parallel-fibered collagenous tissues such as ligaments has been formulated. The constitutive equation has been shown to successfully reproduce the stress–stretch curves for rat MCLs (see Fig. 2) and the changes in such curves determined by subfailure stretches (see Fig. 3). The only experimental data available in the literature on damage in ligaments [26] have been used to determine the values of six model parameters by using the Differential Evolution algorithm. The fitting parameters have been then varied for analyzing their role on predicting the tensile damage behavior in ligaments.

Determining the values of all the parameters uniquely by curve fitting only one macroscopic stress–strain curve is not possible unless restrictions are imposed on such parameters. However, the authors believe that, by combined micro- and macro-experiments, one could determine independently the values of subsets of parameters. Moreover, because the parameters are directly related to the tissue's structure, they are physically meaningful. Therefore, when finding the parameter values by minimizing the sum of squared residuals, restrictions can be imposed as dictated by their physical significance.

Two Weibull distributions have been selected to randomly generate straightening stretches of collagen fibers and damage stretches in each collagen fiber. These one-tailed distributions have been preferred over two-tailed distributions (e.g. Gaussian distribution) because they do not describe unrealistic scenarios in which collagen fibers are straight, support load, and are damaged when the stretch is less than one. The location parameters of the Weibull distributions have been fixed to reduce the number of model parameters and obtain a unique solution via the minimization process. Specifically, γ_s has been set to 1. This assumption implies that every collagen fiber is wavy in the initial configuration. In addition, γ_d was fixed to 1.0514. One must note that this collagen fiber's stretch value corresponds to 5.14% ligament's strain at which damage occurs [26]. However, the authors speculate that damage at the collagen fiber level may manifest at a lower strain than damage at the tissue's level and, hence, γ_d may have a lower value.

The parameters in the Weibull distributions, $\{\alpha_s, \beta_s, \gamma_s, \alpha_d, \beta_d, \gamma_d\}$ as well as the collagen fiber's stiffness, K, and its reduction, D, could be determined by designing appropriate experiments as described hereafter. For example, recent experiments by Hansen et al. [10] have shown that information about the straightening process of collagen fibers can be correlated with tensile stress–strain data by using optical coherence tomography. Hurschler et al. [12] have used the results of the above cited experiments to compute the parameters of a micro-structual model in which the straightening process is also defined by means of a Weibull distribution. They have shown that the location parameter can be uniquely determined when enough experimental data for the toe region of the stress–strain curve are available. The collagen fiber stiffness as well as its reduction due to damage could be determined by using x-ray diffraction techniques as previously done by Sasaki and Odajima [28] or, alternatively, by atomic force microscopy.

Three-dimensional constitutive equations are necessary to accurately describe the mechanical behavior of ligaments [32]. Although the proposed model is one-dimensional, one must note that it can be extended to a three-dimensional model by using Lanir's structural approach for soft tissues [15] as previously suggested by De Vita and Slaughter [6,7]. Information on collagen fiber orientation in ligaments and three-dimensional experimental data are needed to finally test a generalized three-dimensional structural model.

More experiments need to be conducted to study the damage evolution in collagenous tissues and evaluate the predictive capabilities of proposed model. The model successfully fits the available stress–stretch data and describes the prolonged toe region, decrease in tangent modulus and ultimate stress observed after subfailure stretches reported for MCLs. However, when used to *predict* the stress after a subfailure stretch corresponding to approximately 9% strain as reported by Provenzano et al. [26] (see Fig. 5), the computed stresses are overestimated. These predictions could be due to the assumption that collagen fibers are damaged at a

stretch equal to 1.0514 when tissue's damage has been reported to occur. However, if collagen fibers are assumed to experience damage at a stretch that is lower than 1.0514, the predicted stresses will have lower values.

The model predictions suggest that other mechanisms such as, for example, breaking of collagen intermolecular cross-links, interfibrillar cross-links, and debonding of fibrils from the proteoglycan-rich matrix need to be incorporated into structural models to accurately predict damage in ligaments. The shape of the toe region, tangent modulus, and tensile strength of collagenous tissues depend on the presence of collagen cross-links both at the molecular and fibrillar level [4,8]. Moreover, the mechanical role of the ground substance needs to be considered since its removal from collagenous tissues causes a decrease in tangent moduli and nominal stresses [18] as observed in damaged ligaments by Provenzano et al. [26]. Finally, according to Screen et al. [29,30], the proteoglycan content affects the sliding between adjacent collagen fibers believed to be responsible for failure of fascicles.

The proposed model does not account for the short-term and long-term viscoelasticity experimentally observed in ligamentous tissues. Therefore, it cannot describe viscoelastic phenomena such as the effect of strain rate, hysteresis, creep, and relaxation. To our knowledge, little work has been done in developing constitutive models that can capture both the damage and viscoelasticity of ligaments [20,5]. Ongoing studies include the development of a structural constitutive model that describes viscoelastic phenomena by assuming that elastic collagen fibers are embedded in a viscoelastic ground substance.

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Conflict of interest statement

The authors acknowledge that they do not have any financial and personal relationships with other people or organisations that could inappropriately influence (bias) their work.

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