Medical Engineering & Physics 33 (2011) 1056–1063

Contents lists available at ScienceDirect

Medical Engineering & Physics

journal homepage: www.elsevier.com/locate/medengphy

A mathematical model for creep, relaxation and strain stiffening in parallel-fibered collagenous tissues

Ratchada Sopakayang[a], Raffaella De Vita[b,*]

[a] Department of Mechanical Engineering, Faculty of Engineering, Ubon Ratchathani University, Warinchumrap, Ubon Ratchathani 34190, Thailand
[b] Mechanics of Soft Biological Systems Laboratory, 202 Norris Hall, Department of Engineering Science and Mechanics, Virginia Tech, Blacksburg, VA 24061, USA

ARTICLE INFO

Article history:
Received 13 September 2010
Received in revised form 16 February 2011
Accepted 22 April 2011

Keywords:
Constitutive model
Creep
Relaxation
Strain-stiffening
Viscoelasticity
Ligaments
Tendons

ABSTRACT

A simple model is presented for the description of relaxation, creep, and strain stiffening phenomena that are observed in parallel-fibered collagenous tissues such as ligaments and tendons. In the model formulation, the tissues are assumed to be composed of collagen fibers aligned along their physiological loading direction. The collagen fibers are gradually recruited under strain and are arranged in parallel with a Maxwell element which accounts for the viscoelasticity of the proteoglycan-rich matrix. Once straight, the collagen fibers are assumed to behave as linear elastic springs. Experimental data published by Hingorani et al. [1] are used to estimate the five model parameters by fitting relaxation and strain stiffening data and the predictions are evaluated by using creep data. The influence of each parameter on describing relaxation, creep, and strain stiffening is presented. The modeling results demonstrate that, by considering the fibers' recruitment and assuming that the matrix is linear viscoelastic, a conceptually simple model can describe relaxation, creep, and strain stiffening phenomena in ligaments and tendons.

1. Introduction

Collagenous tissues such as ligaments and tendons are characterized by long-term viscoelastic properties. They exhibit a slow continuous increase in strain over time, or creep, when subjected to a constant stress and a slow continuous decrease in stress over time, or stress relaxation, when subjected to a constant strain. The micro-structural origin of the long-term viscoelasticity of these tissues is still unknown and subject of debate among experts in biomechanics. Synchrotron X-ray scattering studies coupled with mechanical testing have indicated that the collagen fibers, which constitute the main load bearing components of the tissues, may be intrinsically viscoelastic [2] and that the interface between the collagen fibers and the surrounding proteoglycan-rich matrix may also determine the viscoelasticity of the tissues [3]. In many studies, however, the viscoelasticity of the tissues has been attributed to the proteoglycan-rich matrix that surrounds the collagen fibers [4–7].

The difference in the experimental findings suggests the need for more studies aimed at understanding the mechanisms that control the long-term viscoelasticity in ligaments and tendons. As suggested early by Fung [8] and experimentally observed by Thornton et al. [9] and Gupta et al. [7], different structural components of the tissues and their organization are responsible for different viscoelastic phenomena: the recruitment of collagen fibers governs creep [9] while sliding between collagen fibrils/fibers due to the presence of the proteoglycan-rich matrix is predominant in relaxation [7]. Together with histo-mechanical experiments, mathematical models that are formulated by accounting for the micro-structure of collagenous tissues can help in elucidating the relative role of different components of these tissues in determining their long-term viscoelasticity.

The most successful viscoelastic models for creep and relaxation in collagenous tissues are the quasi-linear viscoelastic (QLV) models introduced by Fung [8]. Despite their enormous success, the QLV models have been shown to have limitations since they cannot account for creep rate and relaxation rate dependency as exhibited by ligaments at high stress and strain levels, respectively [10] and, most importantly, cannot interrelate creep and relaxation [11,12]. Nonlinear viscoelastic theories, such as Schapery's theory and the modified superposition method, have been proposed to overcome some of the limitations of the QLV models [13]. Both the QLV models and the newly proposed models are, however, phenomenological models with parameters that lack physical meaning and do not relate to the micro-structural changes that are associated with creep and relaxation.

The long-term viscoelasticity of ligaments and tendons has been described by several structurally based constitutive models [9,14–22]. However, only in the linear viscoelastic model proposed by Thornton et al. [9] creep was predicted from relaxation and this

* Corresponding author. Tel.: +1 540 231 5905.
E-mail addresses: ratchada@vt.edu (R. Sopakayang), devita@vt.edu (R. De Vita).

1350-4533/$ – see front matter © 2011 IPEM. Published by Elsevier Ltd. All rights reserved.
doi:10.1016/j.medengphy.2011.04.012

was accomplished by accounting for the recruitment of collagen fibers. By performing histological studies, the authors observed that the collagen fibers were gradually recruited during creep due to the increase in strain over time. Moreover, they found that during relaxation only a discrete group of fibers was recruited at the fixed constant strain. Their model was, however, formulated by assuming a specific geometry for the ligaments and arrangement of the wavy collagen fibers.

A simple constitutive framework for modeling relaxation and creep including the strain stiffening in parallel-fibered collagenous tissues is presented. The collagen fibers are assumed to be oriented along the physiological direction of loading. They gradually lose their waviness and become straight under strain at which point they behave as linear elastic springs. The collagen fibers are arranged in parallel with the surrounding matrix that exhibits a Maxwell-type viscoelastic behavior. The model parameters that define the relaxation and strain stiffening phenomena are estimated by using published experimental data by Hingorani et al. [1] on rabbit medial collateral ligaments and are then used to predict creep. The influence of each parameter on describing the long-term viscoelastic properties of collagenous tissues is also analyzed.

2. Model formulation

In this study, the overall viscoelastic behavior of ligaments and tendons is assumed to be determined by their major components: the collagen fibers and the intervening proteoglycan-rich matrix. The collagen fibers are assumed to be aligned along the direction of loading. They are wavy when unstrained and become gradually straight as the overall tissue's strain increases. After becoming straight, the collagen fibers behave as linear elastic springs with equal elastic modulus. The proteoglycan-rich matrix is assumed to behave as a Maxwell-type viscoelastic material, which is described by a linear elastic spring and linear viscous dashpot arranged in series. A schematic of the proposed model, which is described in detail hereafter, is shown in Fig. 1.

2.1. Modeling framework

Ligaments and tendons are modeled as parallel arrangements of linear elastic collagen fibers, each having different waviness, and a linear viscoelastic proteoglycan-rich matrix. Then, the total stress of the tissue, $\sigma(t)$, where t denotes the time, is given by

$$\sigma(t) = \sigma_f(t) + \sigma_m(t), \tag{1}$$

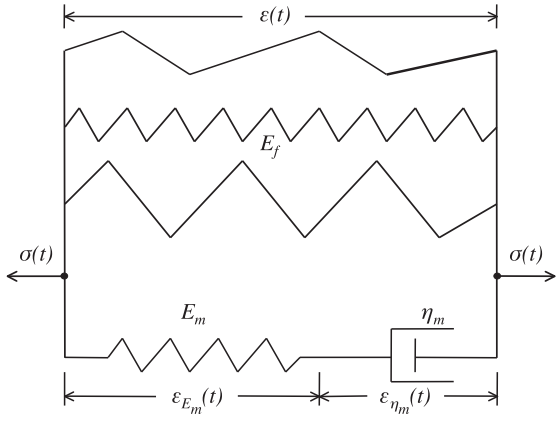

Fig. 1. Schematic of the viscoelastic model.

where $\sigma_f(t)$ is the stress of the collagen fibers and $\sigma_m(t)$ is the stress of the matrix. Moreover, the strain of the tissue, $\varepsilon(t)$, is

$$\varepsilon(t) = \varepsilon_f(t) = \varepsilon_m(t), \tag{2}$$

where $\varepsilon_f(t)$ is the strain of the fibers and $\varepsilon_m(t)$ is the strain of the matrix.

Due to the arrangement in series of the elastic spring and viscous dashpot of the matrix, one has that

$$\sigma_m(t) = \sigma_{E_m}(t) = \sigma_{\eta_m}(t), \tag{3}$$

where $\sigma_{E_m}(t)$ and $\sigma_{\eta_m}(t)$ are the elastic and viscous stresses of the matrix, respectively. Furthermore, the strain of the matrix, $\varepsilon_m(t)$, is

$$\varepsilon_m(t) = \varepsilon_{E_m}(t) + \varepsilon_{\eta_m}(t), \tag{4}$$

where $\varepsilon_{E_m}(t)$ and $\varepsilon_{\eta_m}(t)$ are the strain of the spring and the strain of the viscous dashpot for the matrix, respectively.

The elastic stress of the matrix is defined as

$$\sigma_{E_m}(t) = E_m \varepsilon_{E_m}(t) \tag{5}$$

where E_m denotes the elastic modulus of the matrix. The viscous stress of the matrix is defined as

$$\sigma_{\eta_m}(t) = \eta_m \varepsilon'_{\eta_m}(t), \tag{6}$$

where η_m denotes the viscous modulus of the matrix and a prime denotes the differentiation with respect to t.

After noting that $\sigma_m(t) = \sigma_{E_m}(t)$ from Eq. (3) and that $\sigma_m(t) = \sigma(t) - \sigma_f(t)$ from Eq. (1), Eq. (5) can be rewritten as

$$\varepsilon_{E_m}(t) = \frac{\sigma(t) - \sigma_f(t)}{E_m}. \tag{7}$$

Moreover, since $\varepsilon_{\eta_m}(t) = \varepsilon_m(t) - \varepsilon_{E_m}(t)$ from Eq. (4) and $\varepsilon(t) = \varepsilon_m(t)$ from Eq. (2), Eq. (6) becomes

$$\sigma_{\eta_m}(t) = \eta_m \varepsilon'(t) - \eta_m \varepsilon'_{E_m}(t). \tag{8}$$

By recalling that $\sigma_m(t) = \sigma_{\eta_m}(t)$ from Eq. (3) and using Eq. (8), Eq. (1) takes the form

$$\sigma(t) = \sigma_f(t) + \eta_m \varepsilon'(t) - \eta_m \varepsilon'_{E_m}(t). \tag{9}$$

Finally, after computing $\varepsilon'_{E_m}(t)$ from Eq. (7) and substituting the resulting expression into Eq. (9) one obtains the governing equation for the system described in Fig. 1

$$\sigma'(t) + \frac{E_m}{\eta_m}\sigma(t) = \sigma_f'(t) + \frac{E_m}{\eta_m}\sigma_f(t) + E_m \varepsilon'(t). \tag{10}$$

The ratio η_m/E_m is a characteristic time, τ, usually called the *relaxation time*. The above governing equation can be then rewritten as

$$\sigma'(t) + \frac{\sigma(t)}{\tau} = \sigma_f'(t) + \frac{\sigma_f(t)}{\tau} + E_m \varepsilon'(t). \tag{11}$$

It must be noted that Eq. (11) is derived solely by considering the arrangement of the constituents of the tissue as depicted in Fig. 1 and the Maxwell-type viscoelastic behavior of the matrix defined in Eqs. (5) and (6). In other words, no assumption on the constitutive behavior of the collagen fibers and, thus, on the stress of the collagen fibers, $\sigma_f(t)$, has been made to derive Eq. (11). Once the stress of collagen fibers, $\sigma_f(t)$, is defined, the governing Eq. (11) with appropriate initial condition can be used to describe relaxation, creep, and strain stiffening phenomena.

2.2. Stress of collagen fibers

The stress of the fibrous component of the tissue, $\sigma_f(t)$, is defined by using a structural approach as previously done by other investigators [23–25]. The collagen fibers are assumed to become straight

at different strains, $\varepsilon_s \geq 0$, defined by the following Weibull probability density function

$$p(\varepsilon_s) = \frac{\alpha}{\beta}\left(\frac{\varepsilon_s}{\beta}\right)^{\alpha-1} e^{-(\varepsilon_s/\beta)^{\alpha}} \quad \text{with} \quad \int_0^{\infty} p(\varepsilon_s)d\varepsilon_s = 1, \tag{12}$$

where $\alpha > 0$ is the so-called *shape parameter* and $\beta > 0$ is the so-called *scale parameter*. The stress of the collagen fibers is given by

$$\sigma_f(t) = \int_0^{\varepsilon(t)} E_f(\varepsilon(t) - \varepsilon_s)p(\varepsilon_s)d\varepsilon_s, \tag{13}$$

where E_f denotes the elastic modulus of each straight collagen fiber. The above equation can also be written as (see Appendix A)

$$\sigma_f(t) = E_f\left[\varepsilon(t) - \frac{\beta}{\alpha}\gamma\left(\frac{1}{\alpha}, \left(\frac{\varepsilon(t)}{\beta}\right)^{\alpha}\right)\right], \tag{14}$$

where

$$\gamma(x, y) = \int_0^y \xi^{x-1}e^{-\xi}d\xi \tag{15}$$

is the so-called *lower incomplete gamma function*.

2.3. Relaxation

Relaxation is a continuous decrease in stress that is observed in collagenous tissues when they are subjected to a constant strain. First, one must note that for any strain history, $\varepsilon(t)$, the solution to the governing Eq. (11) is

$$\sigma(t) = \sigma_f(t) + \frac{\int_0^t E_m\varepsilon\prime(t)e^{t/\tau}dt + C}{e^{t/\tau}}, \tag{16}$$

where C is a constant that is determined by the initial condition. In order to describe relaxation by using Eq. (16), the strain history of the tissue, $\varepsilon(t)$, is assumed to have the form

$$\varepsilon(t) = \begin{cases} at & \text{for } 0 \leq t < t_0, \\ \varepsilon_0 & \text{for } t \geq t_0, \end{cases} \tag{17}$$

where a, ε_0 and t_0 are constants and $at_0 = \varepsilon_0$. For $0 \leq t < t_0$, $\varepsilon'(t) = a$ and, hence, Eq. (16) takes the form

$$\sigma(t) = \sigma_f(t) + E_m a\tau[1 - e^{-(t/\tau)}] + Ce^{-(t/\tau)}. \tag{18}$$

By imposing the initial condition $\sigma(0) = 0$ and noting that $\varepsilon(0) = 0$, one obtains that $C = 0$ in Eq. (18). Therefore, in the interval $0 \leq t < t_0$, the stress of the tissue is

$$\sigma(t) = \sigma_f(t) + E_m a\tau[1 - e^{-(t/\tau)}]. \tag{19}$$

For $t > t_0$, $\varepsilon(t) = \varepsilon_0$ and $\varepsilon'(t) = 0$ so that Eq. (16) becomes

$$\sigma(t) = \sigma_f(t) + Ce^{-(t/\tau)}. \tag{20}$$

By using the initial condition $\sigma(t_0) = \sigma_f(t_0) + E_m a\tau[1 - e^{-(t_0/\tau)}]$ computed by using Eqs. (19) and (20), one obtains that

$$C = E_m a\tau(e^{(t_0/\tau)} - 1). \tag{21}$$

For $t > t_0$, the stress of the tissue can be written as

$$\sigma(t) = \sigma_f(t) + E_m a\tau\left(e^{((t_0-t)/\tau)} - e^{-(t/\tau)}\right). \tag{22}$$

The above equation describes the relaxation that is exhibited by the tissue when a constant strain ε_0 is applied. In this case, the stress of the collagen fibers, $\sigma_f(t)$, defined by Eq. (14) is constant and has the form

$$\sigma_f(t) = E_f\left[\varepsilon_0 - \frac{\beta}{\alpha}\gamma\left(\frac{1}{\alpha}, \left(\frac{\varepsilon_0}{\beta}\right)^{\alpha}\right)\right]. \tag{23}$$

2.4. Nonlinear strain stiffening behavior

A nonlinear strain stiffening behavior is observed in collagenous tissues subjected to a constantly increasing strain. As already noted, the solution to Eq. (11), for any strain history, is

$$\sigma(t) = \sigma_f(t) + \frac{\int_0^t E_m\varepsilon\prime(t)e^{t/\tau}dt + C}{e^{t/\tau}}. \tag{24}$$

In this case, the strain history has the form $\varepsilon(t) = bt$ for $t > 0$ where b is a constant. Moreover, since the initial condition is $\sigma(0) = 0$ and, thus, $\varepsilon(0) = 0$, it follows that $C = 0$ in Eq. (24) so that the stress of the tissue is

$$\sigma(t) = \sigma_f(t) + E_m b\tau[1 - e^{-(t/\tau)}]. \tag{25}$$

2.5. Creep

Creep is a continuous deformation of the tissue under constant stress. In this case, the governing Eq. (11) needs to be solved to compute the strain of the tissue, $\varepsilon(t)$. Firstly, by applying Leibniz's rule for differentiation of an integral to Eq. (13) one obtains that

$$\sigma_f\prime(t) = E_f\varepsilon\prime(t)\int_0^{\varepsilon} p(\varepsilon_s)d\varepsilon_s. \tag{26}$$

It must be noted that for $p(\varepsilon_s)$ defined by Eq. (12), $\int_0^{\varepsilon} p(\varepsilon_s)d\varepsilon_s = 1 - e^{-(\varepsilon/\beta)^{\alpha}}$, which is the Weibull cumulative density function. Thus, Eq. (26) can be written as

$$\sigma_f\prime(t) = E_f\varepsilon\prime(t)(1 - e^{-(\varepsilon/\beta)^{\alpha}}). \tag{27}$$

By using Eq. (27), the governing Eq. (11) can be rewritten as

$$\varepsilon\prime(t) = \frac{\sigma\prime(t) + (\sigma(t)/\tau) - (\sigma_f/\tau)}{E_f(1 - e^{-(\varepsilon/\beta)^{\alpha}}) + E_m}. \tag{28}$$

Eqs. (27) and (28) form a system of ordinary differential equations that can be solved numerically to find $\varepsilon(t)$ and $\sigma_f(t)$ after assigning the initial conditions.

In order to describe creep, the stress history of the tissue, $\sigma(t)$, is assumed to have the form

$$\sigma(t) = \begin{cases} ct & \text{for } 0 \leq t < t_0, \\ \sigma_0 & \text{for } t \geq t_0, \end{cases} \tag{29}$$

where c, σ_0, and t_0 are constants and $ct_0 = \sigma_0$.

For $0 \leq t < t_0$, $\sigma'(t) = c$ and $\sigma(t) = ct$. Then, Eq. (28) becomes

$$\varepsilon\prime(t) = \frac{c + (ct/\tau) - (\sigma_f/\tau)}{E_f(1 - e^{-(\varepsilon/\beta)^{\alpha}}) + E_m}, \tag{30}$$

which can be solved numerically together with Eq. (27) to find the strain of the tissue, $\varepsilon(t)$, by imposing the initial conditions $\varepsilon(0) = 0$ and $\sigma_f(0) = 0$.

For all $t > t_0$, $\sigma(t) = \sigma_0$ and $\sigma'(t) = 0$. Thus, Eq. (28) takes the form

$$\varepsilon\prime(t) = \frac{(\sigma_0/\tau) - (\sigma_f/\tau)}{E_f(1 - e^{-(\varepsilon/\beta)^{\alpha}}) + E_m}. \tag{31}$$

The above equation and Eq. (27) form a system of ordinary differential equations that can be solved numerically to determine the creep response of the tissue under constant stress σ_0. The initial conditions, $\varepsilon(t_0)$ and $\sigma_f(t_0)$, can be obtained from experimental data and by using Eq. (13).

3. Results

There were 5 parameters $\{E_f, \alpha, \beta, E_m, \tau\}$ that needed to be computed to describe the viscoelastic properties of ligaments and tendons by using the proposed modeling framework. Due to the

lack of a *complete* set of experimental data on both relaxation, creep, and strain stiffening phenomena, published results by Hingorani et al. [1] on rabbit medial collateral ligaments were used to analyze the capability of the model. To the authors' knowledge, these data together with similar data published by the same group [10] were the only complete set of data published in the biomechanics literature that interrelated creep and relaxation. Thornton et al. [9] also presented interrelated relaxation and creep data but, in their manuscript, the information about the strain rate used in their experimental protocol was omitted. For this reason, these data could not be used to validate the proposed model.

In the above-cited study [1], stress relaxation experimental data were collected by subjecting the ligament to a constant strain, $\varepsilon_0 = 0.81\%$, along its physiological loading direction. Creep experimental data were also collected by subjecting the contralateral ligament to a constant stress, $\sigma_0 = 2.98$ MPa, along the physiological loading direction. The constant stress value used during creep was chosen to be the peak stress observed during relaxation at $\varepsilon_0 = 0.81\%$ in order to compare relaxation and creep responses. Moreover, isochronal stress–strain data were derived from relaxation data collected at different constant strain values at the same time, $t = 2.4$ s. The relaxation data were then successfully fitted by the equation $\sigma = 2.4488t^{-0.2619}$ with $R^2 = 0.9769$, the creep data by the equation $\varepsilon = 0.60681t^{0.13927}$ with $R^2 = 0.9977$, and the stress–strain curve that described the strain-stiffening phenomenon by the equation $\sigma = 4.095\varepsilon^{1.835}$ with $R^2 = 0.9984$ [1]. These three equations were used in this study to generate the relaxation, strain-stiffening, and creep data that were needed to compute the model parameters and evaluate its prediction. The authors used this approach since digitizing the data from the published graphs would have introduced errors with a high level of uncertainty.

The two parameters, E_m and τ, which characterized the mechanical response of the proteoglycan-rich matrix, and the constant stress of the collagen fibers, σ_f, were evaluated by curve fitting Eq. (22) to the stress relaxation data generated by the equation $\sigma = 2.4488t^{-0.2619}$ and published by Hingorani et al. [1]. It must be noted that $\varepsilon_0 = 0.81\%$ and, therefore, $t_0 = 0.081$ in Eq. (22) since the experiments were conducted at a constant strain rate, $\varepsilon'(t) = a = 10\%/\text{s}$. The curve fitting was performed by employing the Levenberg–Marquardt nonlinear least squares algorithm implemented in Matlab (The MathWorks, Inc.) without imposing restrictions on E_m, τ, and σ_f. The results of the curve fitting are shown in Fig. 2. The parameters were uniquely determined to be $E_m = 130.4$ MPa, $\tau = 14.91$ s, and $\sigma_f = 0.7962$ MPa with $R^2 = 0.9719$.

The three parameters, E_f, α, and β, which defined the response of the collagen fibers, were then computed by curve fitting Eq. (25) with Eq. (13) to the nonlinear stress–strain data describing strain-stiffening presented by Hingorani et al. [1]. The strain history was $\varepsilon(t) = bt$, where $b = 10\%/\text{s}$, and $E_m = 130.4$ MPa and $\tau = 14.91$ s.

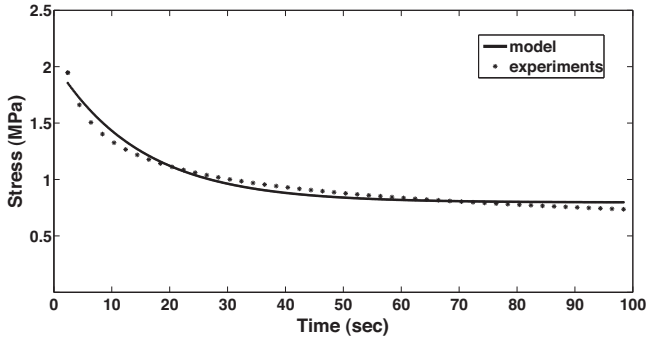

Fig. 2. Stress relaxation data [1] and model fit with $E_m = 130.4$ MPa, $\tau = 14.91$ s, and $\sigma_f = 0.7962$ MPa ($R^2 = 0.9719$).

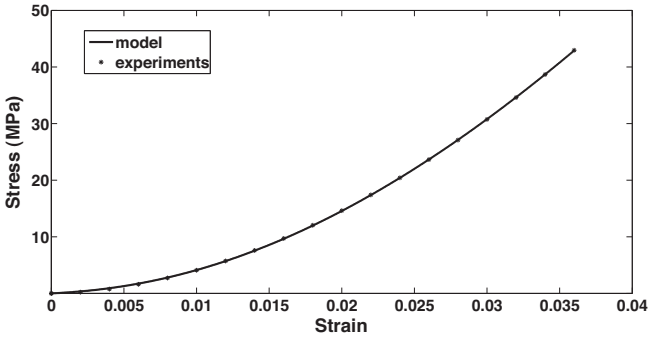

Fig. 3. Nonlinear elastic stress–strain data describing strain stiffening [1] and model fit with $E_f = 3536$ MPa, $\alpha = 1.189$, and $\beta = 0.04124$ ($R^2 \approx 1$).

The parameters were uniquely estimated to be $E_f = 3536$ MPa, $\alpha = 1.189$, and $\beta = 0.04124$ by using the Levenberg–Marquardt nonlinear least squares algorithm with no restriction on the parameters ($R^2 \approx 1$). In Fig. 3, the stress–strain data generated by the equation $\sigma = 4.095\varepsilon^{1.835}$ and the model fit were reported.

After determining all the model parameters, the creep behavior was *predicted* by numerically solving the system of ordinary differential equations formed by Eqs. (27) and (31) with $\sigma_0 = 2.98$ MPa as dictated by the experiments. The initial conditions were obtained from the experimental data for $t_0 = 2.4$ s, $\varepsilon(t_0) = 0.69\%$, and $\sigma_f(t_0)$ computed from Eq. (14). Fig. 4 presents the creep data generated by using the equation $\varepsilon = 0.60681t^{0.13927}$ [1] and the model prediction with $E_m = 130.4$ MPa, $\tau = 14.91$ s, $E_f = 3536$ MPa, $\alpha = 1.189$, and $\beta = 0.04124$ as previously computed by fitting relaxation and strain stiffening data ($R^2 = 0.67$).

The effect of the model parameters in illustrating relaxation and creep responses was studied by varying their numerical values. The parameters that were not varied were fixed to the numerical values computed by curve fitting the published relaxation and stress–strain data [1]. Figs. 5 and 7 illustrate the influence of E_m on the relaxation and creep phenomena. One could observe that as E_m increased, the peak stress and the stress over time increased while creep remained almost unchanged. As shown in Figs. 6 and 8, changes in τ influenced relaxation and creep similarly: both creep and relation reached faster a steady state value of strain and stress as τ decreased. In Fig. 9, the creep response was presented for different values of the fiber's elastic modulus, E_f. It could be noted that as E_f increased, the strain of the tissue decreased over time.

Finally, the effects of the shape and scale parameters of the Weibull distribution that described the recruitment of collagen fibers during creep were analyzed. The creep behavior for different values of the shape parameter α is shown in Fig. 10 while the corresponding Weibull probability density function is presented in Fig. 11. It can be seen from Figs. 10 and 11 that, for smaller values of

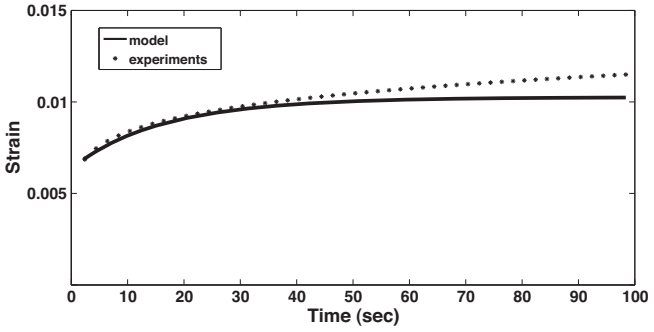

Fig. 4. Creep data [1] and model prediction for values of the parameters computed by curve fitting relaxation and strain-stiffening data ($R^2 = 0.67$).

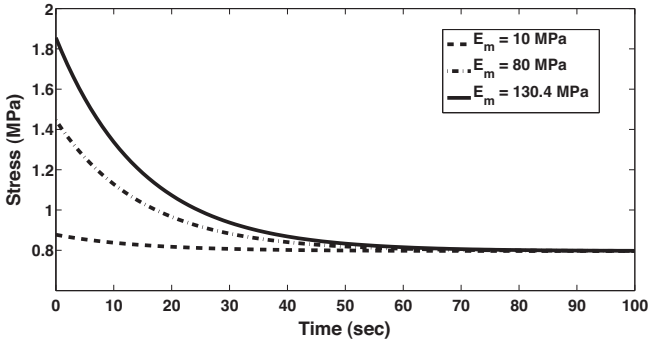

Fig. 5. Influence of the elastic modulus of the proteoglycan-rich matrix, E_m, on relaxation.

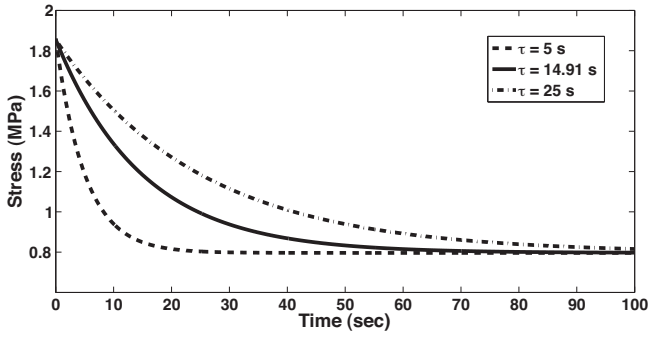

Fig. 6. Influence of the relaxation time, $\tau = \eta_m/E_m$, on relaxation.

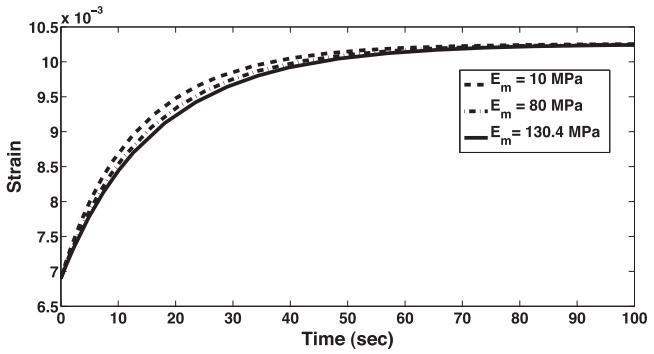

Fig. 7. Influence of the elastic modulus of the proteoglycan-rich matrix, E_m, on creep.

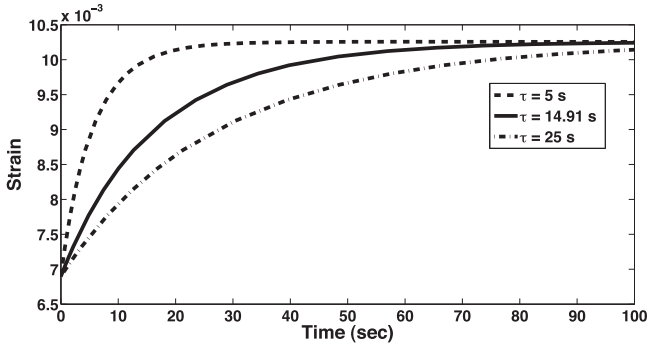

Fig. 8. Influence of the relaxation time, $\tau = \eta_m/E_m$, on creep.

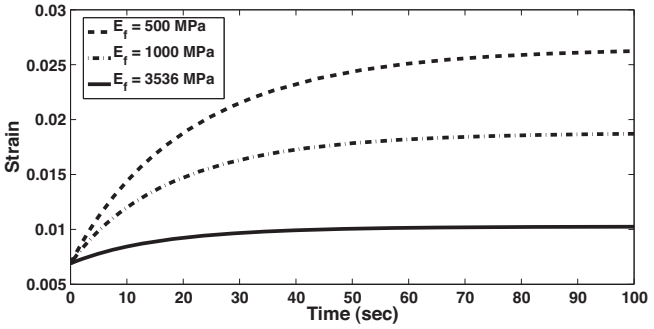

Fig. 9. Influence of the elastic modulus of the collagen fiber, E_f, on creep.

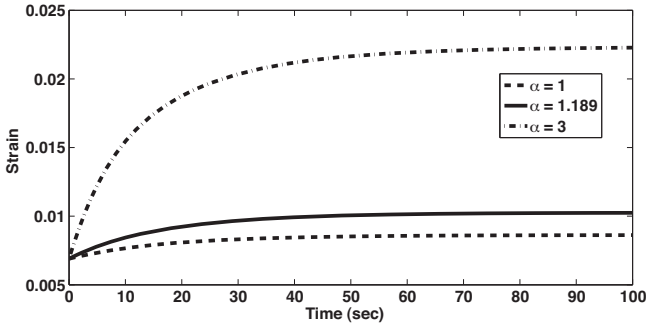

Fig. 10. Effect of the shape parameter, α, of the Weibull probability density function on creep.

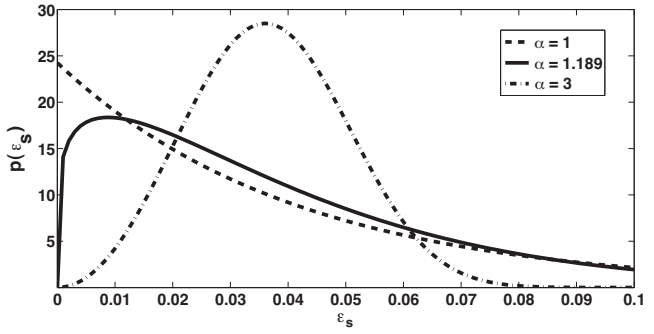

Fig. 11. Effect of the shape parameter, α, on the Weibull probability density function.

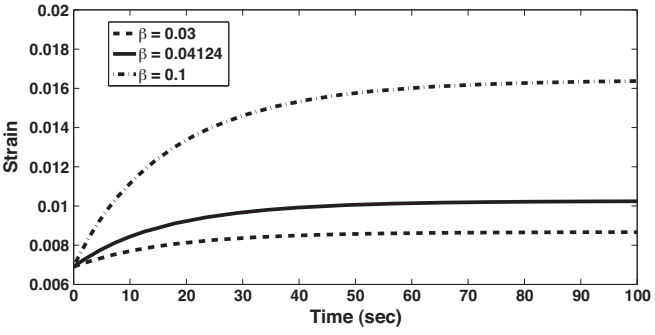

Fig. 12. Effect of the scale parameter, β, of the Weibull probability density function on creep.

α, more collagen fibers were recruited at lower values of the strain and the strain over time increased less while the tissue reached a steady state faster. Similarly, in Figs. 11 and 12 one could observe that as the scale parameter β increased, the collagen fibers were recruited more uniformly. Therefore, the strain of the tissue over time increased more and reached a greater steady state value as presented in Fig. 12.

4. Discussion and conclusions

A simple model was presented to describe relaxation, creep, and strain-stiffening phenomena in parallel-fibered collagenous tissues. The model, which is schematically presented in Fig. 1, was formulated by accounting for the mechanical contributions of the collagen fibers comprising the tissues and the proteoglycan-rich matrix that surrounds the collagen fibers. In agreement with experimental observations and histo-mechanical studies, the recruitment of collagen fibers was assumed to be responsible for the creep response of the tissues [9] while the relaxation response was mainly determined by the viscoelasticity of the proteoglycan-rich matrix [7]. Due to the lack of experimental data, the model parameters were estimated by using published data on rabbit medial collateral ligaments [1]. Although the results obtained were promising, additional experimental data were needed to fully validate the model and its predictions. For this reason, by varying the model parameters within the range of values obtained from curve fitting the experimental data, the model predictions were also presented.

Several structurally based models have been proposed to describe the long-term viscoelasticity of ligaments and tendons [9,26,14]. Unlike the cited models, the proposed model could describe relaxation and creep including the strain-stiffening phenomenon. The simple formulation presented here took into account important structural features of the tissues: the collagen fibers are gradually recruited during creep while the proteoglycan-rich matrix is mainly responsible for relaxation. The nonlinear strain-stiffening behavior typically observed in these tissues was described by assuming that the nonlinearity in the toe region of the stress–strain curve is determined by the gradual recruitment of collagen fibers.

The results of curve fitting the model to the relaxation and strain-stiffening data presented by Hingorani et al. [1] are presented in Figs. 2 and 3 and the prediction of the creep response is presented in Fig. 4. The elastic modulus and viscous modulus of the proteoglycan-rich matrix were found to be $E_m = 130.4$ MPa and $\eta_m = \tau E_m = 1944$ MPa s. The elastic modulus of the collagen fibers, E_f, was estimated to be 3.5 GPa which is within the range of values reported in the literature [27]. This value is, however, higher that the values for the elastic modulus of collagen fibers reported in similar studies on structural models for ligaments and tendons [28,24,25,29]. In the cited studies, the collagen fibers were assumed to be the only components of the tissues and, since the contribution of the proteoglycan-rich matrix was neglected, the elastic modulus of the collagen fibers was underestimated. In a mechanical model by Ault and Hoffman [30], in which both the collagen fibers and intervening matrix were considered responsible for the overall mechanical behavior of collagenous tissues, the elastic modulus of the collagen fibers (~2 GPa) was found to be comparable to the one found in this study, but the elastic modulus of the matrix (~0.25 GPa) was found to be much higher. This difference in the elastic modulus of the matrix can be attributed to the different assumptions made in the models. Indeed, Ault and Hoffman assumed that the matrix is a linear elastic material while in this study the matrix is a Maxwell-type viscoelastic material described by the elastic and viscous moduli. The shape parameter α and scale parameters β defined the strain-based

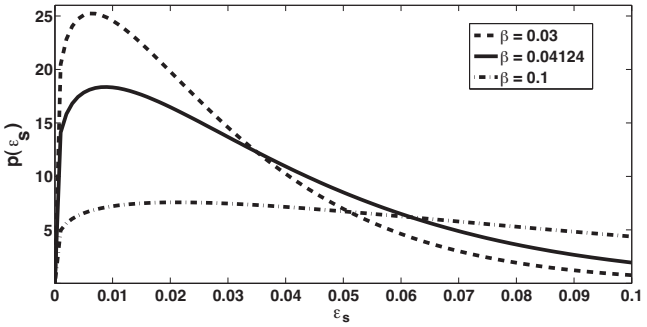

Fig. 13. Effect of the shape parameter, β, of the Weibull probability density function on creep.

recruitment process of collagen fibers during strain-stiffening and creep phenomena. The values computed by fitting the experimental data collected on rabbit medial collateral ligaments suggested that several fibers were straight and thus contributed to the total stress already at very small strains (see Fig. 11 or 13, continuous line).

While the model displayed a good agreement with the experimental data, there were limitations that needed to be discussed. The curve fittings were performed by using the data generated by the equations given by Hingorani et al. [1] and not by using the original published data. Clearly, this introduced some errors in the determination of the numerical values of the parameters. The model with the parameters computed from fitting relaxation and strain-stiffening data was then used to *predict* the creep phenomenon. The comparison with the experimental data shown in Fig. 4 indicated that the strain in the tissue reached a steady state much faster in the model prediction than in the experimental study with an error of 11.5% at $t = 100$ s. The value of the relaxation time, τ, was responsible for determining the time interval required to achieve a steady value of the strain as shown in Fig. 8.

The effects of the model parameters in illustrating relaxation and creep are shown in Figs. 5–13. The parameters that defined the relaxation response were the elastic modulus of the proteoglycan-rich matrix, E_m, and the relaxation time, $\tau = \eta_m/E_m$. In Fig. 5 the relaxation response was shown for different numerical values of E_m and in Fig. 6 for different numerical values of τ while the values of the remaining parameters were fixed. As E_m increased, the initial stress of the tissue during relaxation also increased, but the time needed to reach a steady stress value remained unaltered (Fig. 5) and was only affected by changes in τ (Fig. 6). These parametric studies clearly illustrated that the relaxation phenomenon was determined in the model solely by the viscoelasticity of the proteoglycan-rich matrix, in agreement with recent experimental findings [7].

The model parameters E_f, α, β, τ, and E_m were also varied to analyze their influence on creep. In Figs. 7 and 8, the creep response was presented for different numerical values of the elastic modulus of the proteoglycan-rich matrix, E_m, while the other parameters were kept fixed. One could note that when E_m increased, the strain during creep appeared to become steady slightly later in time. The steady value of strain corresponded to the total strain of the collagen fibers. On the other hand, the model parameter $\tau = \eta_m/E_m$ significantly influenced the creep behavior: as τ increased, the viscous modulus of the proteoglycan-rich matrix also increased and the strain reached a steady value later in time. These results demonstrated that the behavior of the tissue during creep, as described by the model, was affected mainly by the viscosity of the proteoglycan-rich matrix and only slightly by its elasticity.

The elastic modulus of the collagen fiber, E_f, clearly affected the creep response of the tissue. From Fig. 9, one could note that as the collagen fiber became stiffer, the strain over time decreased during creep and, thus, the overall tissue was more elastic and less viscoelastic as expected. In Figs. 10 and 11 and Figs. 12 and 13, the creep responses and the corresponding probability density functions that defined the recruitment of collagen fibers were presented for different values of the shape parameter, α, and the scale parameter, β, respectively, as previously described. As α increased, more collagen fibers became straight earlier, at lower values of the strain of the tissue (Fig. 11) and, as expected, the strain of the tissue during creep increased (Fig. 10). By changing the values of β, the probability density function described different modes of recruitment: as β increased the collagen fibers became straight more gradually and, as a consequence, the strain of the tissue over time was greater. These findings emphasized the importance of incorporating the recruitment of collagen fibers in the proposed model to reproduce the creep behavior.

Although the model prediction of creep did not match the data very well, the studies on the influence of the model parameters on creep (Figs. 7–10 and 12) suggested that the model could fit the creep data with a set of parameters not computed from fitting relaxation and strain stiffening data. It is possible that by using the original relaxation data instead of the power law models used by Hingorani et al. [1] a better fit to relaxation and prediction of creep would have been obtained. It is speculated that the introduction of secondary relaxation and creep, which involve irreversible damage of the tissues, will be necessary to enhance the performance of the current model.

One assumption made in formulating the model was that the collagen fibers and the proteoglycan-rich matrix were both strained when the entire tissue was strained due to their arrangement in parallel (see Fig. 1). This was different from what was assumed in a viscoelastic model for relaxation presented in a recent study by Gupta et al. [7], which focuses mainly on bridging the microstructural and mechanical properties of the collagenous tissues using state-of-the art experimental methods. In their model, the cross-linked fibrils, the inter-fiber and inter-fibrillar matrices were arranged in series and, thus, deformed with the entire tissue but independently. In our model, when the crimped and straight collagen fibers were strained, the proteoglycan-rich matrix that surrounded them was also strained and, thus, were not independent. But, in agreement with the studies by Gupta et al. [7], the strain of the collagen fibers and the matrix were different due to the strain-controlled recruitment of the fiber. According to our model the sliding between the fibers, which was represented by the Maxwell-type viscoelastic element, was responsible for the mechanical response of the tissue when the collagen fibers were crimped.

It is worth noticing that, while the model presented here was for parallel-fibered collagenous tissues, it could be extended to describe the viscoelasticity of other connective tissues having specific material symmetry or random networks of collagen fibers, as already done by one of the authors [24]. The orientation of collagen fibers was shown not to affect the time-dependent properties of connective tissues [3]. Therefore, experimental methods such as those pioneered by Sacks [31] to incorporate information about the orientation of collagen fibers into structural models for nonlinear elastic properties of thick soft tissues could be also extended to viscoelastic models.

Acknowledgment

This material is based upon work supported by the National Science Foundation under Grant No. 0932024.

Appendix A. Stress of collagen fibers

From Eq. (13), which represents the stress of the collagen fibers, it easily follows that

$$\frac{\sigma_f(t)}{E_f} = \varepsilon(t)\int_0^{\varepsilon(t)} p(\varepsilon_s)d\varepsilon_s - \int_0^{\varepsilon(t)} \varepsilon_s p(\varepsilon_s)d\varepsilon_s, \tag{A.1}$$

where $p(\varepsilon_s)$ is the Weibull probability density function already defined in Eq. (12). Moreover, it must be noted that

$$\int_0^{\varepsilon(t)} p(\varepsilon_s)d\varepsilon_s = 1 - e^{-(\varepsilon(t)/\beta)^\alpha}, \tag{A.2}$$

which is the so-called *Weibull cumulative distribution function*.

Let $\xi = \left(\frac{\varepsilon_s}{\beta}\right)^\alpha$. Then, $d\xi = \frac{\alpha}{\beta}\left(\frac{\varepsilon_s}{\beta}\right)^{\alpha-1} d\varepsilon_s$ so that

$$\begin{aligned}\int_0^{\varepsilon(t)} \varepsilon_s p(\varepsilon_s)d\varepsilon_s &= \int_0^{\varepsilon(t)} \varepsilon_s \frac{\alpha}{\beta}\left(\frac{\varepsilon_s}{\beta}\right)^{\alpha-1} e^{-(\varepsilon_s/\beta)^\alpha} d\varepsilon_s \\ &= \beta\int_0^{(\varepsilon(t)/\beta)^\alpha} \xi^{1/\alpha} e^{-\xi}\, d\xi.\end{aligned} \tag{A.3}$$

By recalling that the *lower incomplete gamma function* is defined as

$$\gamma(x,y) = \int_0^y \xi^{x-1}e^{-\xi}d\xi, \tag{A.4}$$

one obtains that

$$\int_0^{(\varepsilon(t)/\beta)^\alpha} \xi^{1/\alpha} e^{-\xi}\, d\xi = \gamma\left(\frac{1}{\alpha}+1, \left(\frac{\varepsilon(t)}{\beta}\right)^\alpha\right). \tag{A.5}$$

Moreover, by applying the following formula

$$\gamma(x,y) = (x-1)\gamma(x-1,y) - y^{x-1}e^{-y}, \tag{A.6}$$

one has that

$$\gamma\left(\frac{1}{\alpha}+1, \left(\frac{\varepsilon(t)}{\beta}\right)^\alpha\right) = \frac{1}{\alpha}\gamma\left(\frac{1}{\alpha}, \left(\frac{\varepsilon(t)}{\beta}\right)^\alpha\right) - \frac{\varepsilon(t)}{\beta}e^{-(\varepsilon(t)/\beta)^\alpha}. \tag{A.7}$$

Finally, Eq. (A.1) can be rewritten as

$$\sigma_f(t) = E_f\left[\varepsilon(t) - \frac{\beta}{\alpha}\gamma\left(\frac{1}{\alpha}, \left(\frac{\varepsilon(t)}{\beta}\right)^\alpha\right)\right]. \tag{A.8}$$

Conflict of interest statement

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

References

[1] Hingorani RV, Provenzano PP, Lakes RS, Escarcega A, Vanderby R. Nonlinear viscoelasticity in rabbit medial collateral ligament. Annals of Biomedical Engineering 2004;32:306–12.
[2] Puxkandl R, Zizak I, Paris O, Keckes J, Tesch W, Bernstorff S, et al. Viscoelastic properties of collagen: synchrotron radiation investigations and structural model. Philosophical Transactions The Royal Society of London Series B Biological Sciences 2002;357:191–7.
[3] Purslow PP, Wess TJ, Hukins DW. Collagen orientation and molecular spacing during creep and stress–relaxation in soft connective tissues. Journal of Experimental Biology 1998;201:135–42.
[4] Minns RJ, Soden PD, Jackson DS. The role of the fibrous components and ground substance in the mechanical properties of biological tissues: a preliminary investigation. Journal of Biomechanics 1973;6:153–65.
[5] Chimich D, Shrive N, Frank C, Marchuk L, Bray R. Water content alters viscoelastic behaviour of the normal adolescent rabbit medial collateral ligament. Journal of Biomechanics 1992;25:831–7.

[6] Elliott DM, Robinson PS, Gimbel JA, Sarver JJ, Abboud JA, Iozzo RV, et al. Effect of altered matrix proteins on quasilinear viscoelastic properties in transgenic mouse tail tendons. Annals of Biomedical Engineering 2003;31: 599–605.
[7] Gupta HS, Seto J, Krauss S, Boesecke P, Screen HRC. In situ multi-level analysis of viscoelastic deformation mechanisms in tendon collagen. Journal of Structural Biology 2010;169:183–91.
[8] Fung YC. Biomechanics: mechanical properties of living tissues. New York: Springer-Verlag; 1993.
[9] Thornton GM, Frank CB, Shrive NG. Ligament creep can be predicted from stress relaxation by incorporating fiber recruitment. Journal of Rheology 2001;45:493–507.
[10] Provenzano P, Lakes R, Keenan T, Vanderby R. Nonlinear ligament viscoelasticity. Annals of Biomedical Engineering 2001;29:908–14.
[11] Thornton GM, Oliynyk A, Frank CB, Shrive NG. Ligament creep cannot be predicted from stress relaxation at low stress: a biomechanical study of the rabbit medial collateral ligament. Journal of Orthopaedic Research 1997;15: 652–6.
[12] Lakes RS, Vanderby R. Interrelation of creep and relaxation: a modeling approach for ligaments. Journal of Biomechanical Engineering 1999;121:612–5.
[13] Provenzano PP, Heisey D, Hayashi K, Lakes R, Vanderby JR. Subfailure damage in ligament: a structural and cellular evaluation. Journal of Applied Physiology 2002;92:362–71.
[14] Decraemer WF, Maes MA, Vanhuyse VJ, Vanpeperstraete P. A non-linear viscoelastic constitutive equation for soft biological tissues based upon a structural model. Journal of Biomechanics 1980;13:559–64.
[15] Woo SLY. Mechanical properties of tendons and ligaments I. Quasi-static and nonlinear viscoelastic properties. Biorheology 1982;19:385–96.
[16] Flaud P, Quemada D. A structural viscoelastic model for soft tissues. Biorheology 1988;25:95–105.
[17] Johnson GA, Livesay GA, Woo SLY, Rajagopal KR. A single integral finite strain viscoelastic model of ligaments and tendons. Journal of Biomechanical Engineering 1996;118:221–6.
[18] Sverdlik A, Lanir Y. Time-dependent mechanical behavior of sheep digital tendons, including the effects of preconditioning. Journal of Biomechanical Engineering 2002;124:78–84.
[19] Vena P, Gastaldi D, Contro R. A constituent-based model for the non linear viscoelastic behaviour of ligaments. Journal of Biomechanical Engineering 2006;128:449–57.
[20] Ciarletta P, Micera S, Accoto D, Dario P. A novel microstructural approach in tendon viscoelastic modelling at the fibrillar level. Journal of Biomechanics 2006;39:2034–42.
[21] Ciarletta P, Amar B. A finite dissipative theory of temporary interfibrillar bridges in the extracellular matrix of ligaments and tendons. Journal of The Royal Society Interface 2009;6:909–24.
[22] Einat R, Lanir Y. Recruitment viscoelasticity of the tendon. Journal of Biomechanical Engineering 2009;131:111008.
[23] Lanir Y. A structural theory for the homogeneous biaxial stress–strain relationship in flat collageneous tissues. Journal of Biomechanics 1979;12:423–36.
[24] De Vita R, Slaughter WS. A structural constitutive model for the strain rate-dependent behavior of anterior cruciate ligaments. International Journal of Solids and Structures 2006;43:1561–70.
[25] De Vita R, Slaughter WS. A constitutive equation for the failure behavior of medial collateral ligaments. Biomechanics and Modeling in Mechanobiology 2007;6:189–97.
[26] Lanir Y. A microstructural model for the rheology of mammalian tendon. Journal of Biomechanical Engineering 1980;102:332–9.
[27] Fratzl P. Collagen: structure and mechanics. Heidelberg: Springer; 2008.
[28] Belkoff SM, Haut RC. A structural model used to evaluate the changing microstructure of maturing rat skin. Journal of Biomechanics 1991;24:711–20.
[29] Guo Z, De Vita R. Probabilistic constitutive law for damage in ligaments. Medical Engineering & Physics 2009;31:1104–9.
[30] Ault HK, Hoffman AH. A composite micromechanical model for connective tissues: part I—theory. Journal of Biomechanical Engineering 1992;114:142–6.
[31] Sacks SM. Incorporation of SALS-derived fiber orientation data into a structural constitutive model for planar collagenous tissues. Journal of Biomechanical Engineering 2003;25:280–7.