An Improved Method to Analyze the Stress Relaxation of Ligaments Following a Finite Ramp Time Based on the Quasi-Linear Viscoelastic Theory

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The quasi-linear viscoelastic (QLV) theory proposed by Fung (1972) has been frequently used to model the nonlinear time- and history-dependent viscoelastic behavior of many soft tissues. It is common to use five constants to describe the instantaneous elastic response (constants A and B) and reduced relaxation function (constants C, τ_1, and τ_2) on experiments with finite ramp times followed by stress relaxation to equilibrium. However, a limitation is that the theory is based on a step change in strain which is not possible to perform experimentally. Accounting for this limitation may result in regression algorithms that converge poorly and yield nonunique solutions with highly variable constants, especially for long ramp times (Kwan et al. 1993). The goal of the present study was to introduce an improved approach to obtain the constants for QLV theory that converges to a unique solution with minimal variability. Six goat femur-medial collateral ligament-tibia complexes were subjected to a uniaxial tension test (ramp time of 18.4 s) followed by one hour of stress relaxation. The convoluted QLV constitutive equation was simultaneously curve-fit to the ramping and relaxation portions of the data ($r^2 > 0.99$). Confidence intervals of the constants were generated from a bootstrapping analysis and revealed that constants were distributed within 1% of their median values. For validation, the determined constants were used to predict peak stresses from a separate cyclic stress relaxation test with averaged errors across all specimens measuring less than 6.3±6.0% of the experimental values. For comparison, an analysis that assumed an instantaneous ramp time was also performed and the constants obtained for the two approaches were compared. Significant differences were observed for constants B, C, τ_1, and τ_2, with τ_1 differing by an order of magnitude. By taking into account the ramping phase of the experiment, the approach allows for viscoelastic properties to be determined independent of the strain rate applied. Thus, the results obtained from different laboratories and from different tissues may be compared. [DOI: 10.1115/1.1645528]

Introduction

The nonlinear time- and history-dependent viscoelastic behavior of soft biological tissues has been widely described by the quasi-linear viscoelastic (QLV) theory formulated by Fung (1972) [1–12]. This theory has been adopted for modeling the viscoelastic behavior of ligaments and tendons by many laboratories [9,13–17]. In our laboratory, the QLV theory has been successfully used for modeling the viscoelastic properties of the canine medial collateral ligament (MCL) [18], the porcine anterior cruciate ligament [19], and the human patellar tendon [20].

In the QLV theory, the reduced relaxation function, with constants C, τ_1, and τ_2, describes the time-dependent stress relaxation of a tissue normalized by the stress at the time of a step input of strain. Since it is experimentally impossible to apply a step increase in strain, many previous investigators have applied extensions at relatively high rates. Nevertheless, this approach proves to be technically challenging as it is difficult to measure strain accurately. On the other hand, others have modified the analysis to account for finite ramp times in order to better approximate solutions. These methods include normalization procedures, iterative techniques, as well as extrapolation and deconvolution [2,7,19,21,22]. However, these methods are still dependent on fast ramp times (~0.01 to 0.1 s) and therefore may be affected by the errors associated with high extension rates (eg., overshoot, vibration, poorly approximated strain histories) [14]. Previously, a two-step regression approach was used by our laboratory to improve the mathematical representation of the experimentally obtained reduced relaxation function [19]. Because two physically significant constants (B and τ_1) become highly correlated with this approach, it should be recognized that regression algorithms may fail to converge for certain applications. Further, the obtained solutions may be non-unique and constants may be highly sensitive to systematic deviations between the model and experimental data as well as random noise.

Therefore, the objective of this study was to develop an improved analytical method to obtain the constants of QLV theory (A, B, C, τ_1, and τ_2). By simultaneously curve-fitting the QLV constitutive equation (i.e., convolution integral of the instantaneous elastic response and reduced relaxation function) to the ramping and relaxation portions of the data from a static stress-relaxation test, algorithms converge to unique solutions with minimal variability of the constants for long ramp times. Therefore, the actual strain history can be accurately approximated and errors resulting from fast extension rates can be avoided. Six goat femur-medial collateral ligament-tibia complexes were subjected to a uniaxial tension test (ramp time of 18.4 s) followed by one hour of

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stress relaxation. A bootstrapping analysis was performed to assess the sensitivity of the constants to systematic deviations between the model and experimental data, random noise, and numerical instabilities. For validation, the constants obtained were used to predict the results of a separate cyclic stress relaxation experiment. For comparison, an analysis that assumed an instantaneous ramp time was also performed and the constants obtained for the two approaches were compared.

Materials and Methods

Experimental Studies. Six femur-MCL-tibia complexes (FMTCs) were obtained from six Sannen breed goats (wt. 38.0 $\pm$4.7 kg; mean$\pm$sd). These specimens were contra-lateral sham-operated controls used in a separate study of the structure and function of the healing MCL in response to a combined ACL/MCL injury [23]. As the focus of this paper is to present an analytical approach, please refer to the referenced articles for details regarding experimental methodology including specimen preparation, cross-sectional area measurement, strain tracking, and set-up for mechanical testing [24–28]. As described in our previous study, the cross-sectional area of the MCL was measured to be 8.6 ± 1.7 mm^2 (mean$\pm$SD) [23]. Our experimental protocol is also described previously [23]. Briefly, each specimen was attached to a materials testing machine (Instron™) within a saline bath that was kept at a constant 37°C. Each specimen was preloaded to 2 N and the gauge length was zeroed. This was followed by preconditioning between 0 and 1.5 mm of extension. Prior to each test, specimens were held at a zero-load position and allowed to equilibrate within the saline bath for one hour.

Each FMTC then underwent a static stress relaxation test whereby specimens were elongated to 3 mm at 10 mm/min and held for a period of 60 min [23]. Preliminary tests revealed that 3 mm of elongation resulted in midsubstance strains less than 5%. An elongation rate of 10 mm/min was chosen to represent a typical rate for tensile testing protocols. Thus, the time until peak load was $t_0=18.4$ s. Strain increased linearly with time, thus this elongation rate resulted in an average midsubstance strain rate, γ, of 0.15%/s. The advantage of utilizing a slow strain rate is that the actual strain history can be well approximated by a linear ramp followed by a hold at a constant strain magnitude. Thus, the errors associated with fast strain rates are avoided (eg., overshoot, vibration, poorly approximated strain histories) [14]. For these data, the total percentage of stress relaxation was defined as the difference between the peak stress at t_0 and the stress measured at the end of the test, normalized by the peak stress. The nonlinear stress-strain curve was determined from the ramping phase of this test.

Following one hour of recovery, a second test was performed to measure the cyclic stress relaxation behavior of the MCL. In this test, each FMTC was subjected to eight cycles of elongation between 2 and 3 mm at 10 mm/min and the corresponding peak and valley stresses were recorded. This corresponded to physiologic strains of approximately 1 to 3.5%, respectively. Data was collected at a constant rate of 5 Hz throughout all tests.

Quasilinear Viscoelastic Theory. The QLV theory assumes that the stress relaxation behavior of soft-tissue can be expressed as:

$$\sigma(t)=G(t)*\sigma^{c}(\varepsilon) \tag{1}$$

where $\sigma^{c}(\varepsilon)$ is the instantaneous elastic response, i.e., the maximum stress in response to an instantaneous step input of strain, ε. $G(t)$ is the reduced relaxation function that represents the time-dependent stress response of the tissue normalized by the stress at the time of the step input of strain [i.e., $t=0^{+}$, such that $G(t)=\sigma(t)/\sigma(0^{+})$, and $G(0^{+})=1$].

Using the Boltzmann superposition principle, the stress at time t, $\sigma(t)$, is given by the convolution integral of the strain history and $G(t)$:

$$\sigma(t)=\int_{-\infty}^{t} G(t-\tau)\frac{\partial\sigma^{e}(\varepsilon)}{\partial\varepsilon}\frac{\partial\varepsilon}{\partial\tau}\partial\tau \tag{2}$$

In the experimental setting, we can assume that the history begins at $t=0$. For soft tissues whose σ-ε relationship and hysteresis are not overly sensitive to strain rate, Fung has proposed the following expression for $G(t)$ based upon a continuous spectrum of relaxation:

$$G(t)=\frac{1+C[E_1(t/\tau_2)-E_1(t/\tau_1)]}{1+C\ln(\tau_2/\tau_1)} \tag{3}$$

where $E_1(y)=\int_y^{\infty}e^{-z}/z dz$ is the exponential integral, and C, τ_1, and τ_2 are material constants. An exponential approximation has been chosen to describe the instantaneous elastic response:

$$\sigma^{e}(\varepsilon)=A(e^{B\varepsilon}-1) \tag{4}$$

where A and B are material constants [29].

Approaches for Constant Estimation. For the current approach (which will be termed ''strain history approach'' throughout the remainder of this paper), the stress resulting from a ramp phase with a constant strain rate γ over the times $0<t<t_0$ can be written by substituting Eqs. (3) and (4) into Eq. (2):

$$\sigma(t:0<t<t_0,\theta)=\frac{AB\gamma}{1+C\ln(\tau_2/\tau_1)}\int_0^{t}\{1+\mathrm{C}(E_1[(\mathrm{t}-\tau)/\tau_2]-E_1[(t-\tau)/\tau_1])\}e^{\mathrm{B}\gamma\tau}\partial\tau \tag{5}$$

where $\theta=\{\mathrm{A,B,C},\tau_1,\tau_2\}$.

Similarly, the subsequent stress relaxation from t_0 to $t=\infty$, can be described as

$$\sigma(t:t\geq \mathrm{t}_0,\theta)=\frac{AB\gamma}{1+C\ln(\tau_2/\tau_1)}\int_0^{t_0}\{1+\mathrm{C}(E_1[(t-\tau)/\tau_2]-E_1[(t-\tau)/\tau_1])\}e^{\mathrm{B}\gamma\tau}\partial\tau \tag{6}$$

For a set of experimental data, the ramping portion of the data was defined as $(t_i,\mathbf{R_i})$, from $0<t_i<t_0$ and the relaxation data as $(t_i,\mathbf{S_i})$, from t_0 to $t=\infty$. Thus, the sums of squares difference between the experimentally obtained data and the theory can be expressed as:

$$f(\theta)=\sum_i[\mathbf{R_i}-\sigma(t_i:0<t_i<t_0,\theta)]^2 \tag{7}$$

and

$$g(\theta)=\sum_i[\mathbf{S_i}-\sigma(t_i:t_0\leq t_i<t,\theta)]^2 \tag{8}$$

Since Eqs. (7) and (8) are both functions of θ, the strain history approach minimizes these equations simultaneously using a nonlinear optimization algorithm. The algorithm used in this study was a Levenberg-Marquardt algorithm that was modified to minimize $f(\theta)+g(\theta)$. The code for this algorithm was written using Mathematica (Wolfram Research, Inc. Champaign, IL), and was largely based on the algorithm outlined in the book *Numerical Recipes in C* [30].

This strain history approach gives a direct fit of Eqs. (7) and (8) to the experimental data with no modification of the theory or normalization of the data. Assuming that the theory provides a perfect Gaussian curve-fit of the data and a global minimum of $f(\theta)+g(\theta)$ can be uniquely determined, the constants obtained that describe the instantaneous elastic response (A and B) and the spectrum of relaxation (C, τ_1, and τ_2) would be those obtained if a true step-elongation were to have been applied. This is because the actual strain history can be well approximated at slow extension rates. However, further analysis of the strain history approach revealed that curve-fits were non-Gaussian and constants A and τ_1

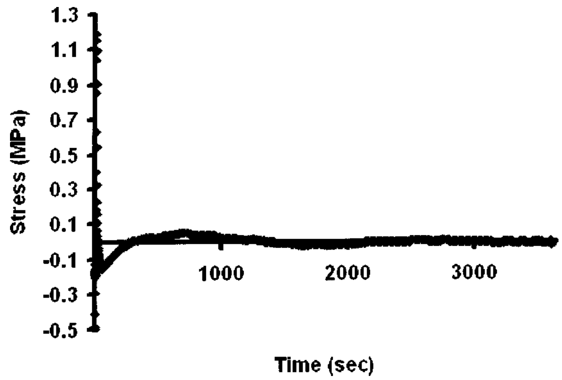

Fig. 1 A typical residual plot demonstrating systematic deviations of the model and experimental data

became significantly correlated as ramp time increases. Since constant A is not required to describe the reduced relaxation following ramping at a constant strain rate [19], it was held fixed for each individual regression analysis. Its value was determined by curve-fitting Eq. (4) to the ramping portion of the experimental data. This is further justified by previous work which has shown that the stress-strain curves of ligaments are insensitive to strain rates ranging over four decades [31].

The initial guess was determined from a preliminary analysis. To ensure global convergence, the initial guess for each constant was multiplied by a random factor between 0.1 and 10 and the regression analysis was performed. This was done 100 times and the guess that produced the lowest minimum of the objective function was the guess chosen for all subsequent analyses. It was found that the algorithm was relatively insensitive to the initial guess; that is, the algorithm consistently converged to a unique solution which was assumed to be the global minimum.

Because the curve-fits were non-Gaussian, it was necessary to assess the variability of constants that may result from systematic deviations between the model and the experimental data, experimental noise, and numerical instabilities. This study used a bootstrapping analysis that was previously described by Yin et al. [32]. First, the data from each specimen was curve-fit individually using the theory. Residual plots for each specimen were then curve-fit with a polynomial function to obtain a pool of curves representing systematic error (Fig. 1). Taking the difference between the systematic error curves and the residuals allowed for a random noise distribution for each specimen to be obtained (Fig. 2). Finally, a randomly selected systematic error curve and random error distribution were added to predicted stresses that were obtained by curve-fitting the theory to averaged experimental data. This created a set of data whose systematic error and random noise distributions were representative of those that could be observed experimentally. Constants A, B, C, τ_1, and τ_2 for this new data set were obtained using the strain history approach. One-hundred new data sets were generated using this methodology and 95% confidence intervals for each constant were obtained.

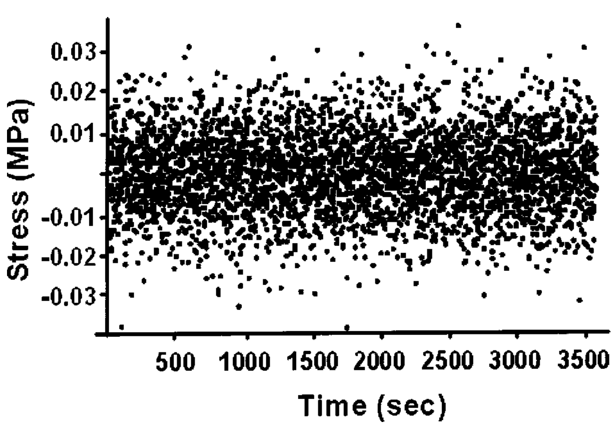

Fig. 2 A typical random error plot with distribution 0±0.00874 (mean±SD)

If the variability of a constant with respect to its median value (i.e., the difference between upper bound of the interval and the median, normalized by the median) was large (eg., >5%), then that constant is sensitive to systematic deviations between the model and the experimental data, experimental noise, and numerical instabilities. Thus, there would be less confidence that the solutions obtained from an individual regression analysis were meaningful since a data set with a slightly different distribution of random noise or systematic error may result in a completely different solution.

For validation of the constants, the ability of QLV theory to predict the results of the cyclic stress relaxation test using the constants obtained from the 60-min stress relaxation test was assessed. The constants A, B, C, τ_1, and τ_2 describing each specimen were separately substituted into Eq. (2) to obtain the specific equation describing the stress response of each goat FMTC. Using a previously described approximated cyclic strain-time history based [18], the peak stresses obtained from Eq. (2) were then compared to those obtained experimentally during the cyclic stress relaxation test for each specimen.

For comparison, the strain history approach was compared to another approach to estimate the five constants of Eqs. (3) and (4). The instantaneous assumption approach as described by Woo et al. (1981) assumes that the ramping phase of the stress relaxation tests occurred instantaneously [18]. Therefore, G(t) and $\sigma^c(\varepsilon)$ are assumed to be separable functions. Constants can be obtained by fitting Eq. (4) to $(\varepsilon_i, \mathbf{R_i})$, where $\varepsilon_i = \gamma t_i$ is the experimental strain from $0 < t < t_0$, and fitting Eq. (5) to $(t_i, \mathbf{s_i})$, where $\mathbf{s_i}$ is equal to $\mathbf{S_i}$ normalized by the stress at t_0. Thus, this approach does not account for relaxation that occurred during ramping which may result in increasingly erred estimates of constants as ramp times increase [33].

As the results from the bootstrapping analysis showed relatively small variations in the constants between the two approaches, solutions obtained for each individual regression analysis were considered to be stable. Thus, solutions obtained from curve-fitting each individual specimen's data with the two approaches could be compared. A nonparameteric two-tailed Wilcoxon sign-rank test and z-score statistic were used for statistical comparison and to calculate p-values. Significance was set at $p < 0.05$.

Results

During the ramping phase of the test, the stress-strain curves exhibited linear behavior up to approximately 1.5% strain. Afterward, the curve became nonlinear with the stress at the end of the ramping phase measuring 15.3±5.4 MPa. The stress-relaxation phase was nonlinear with respect to time as the largest percentage of relaxation occurred in the first 10 min. After, 40 min the rate of relaxation had diminished, with only a 0.6±0.4% reduction over the remaining 20 min of the test. At 60 min, the total amount of stress relaxation was 31.9±11.5%.

A typical curve-fit to the ramping and stress relaxation portions of the experimental data using the strain history approach is detailed in Fig. 3. These data were fit with an overall r^2 value greater than 0.99. Similarly, the instantaneous assumption approach was able to achieve separate fits of these data with good quality ($r^2 > 0.99$ for both portions). In terms of the constants describing the instantaneous elastic response, the confidence intervals for constant A obtained from the boot-strapping analysis were 5.8:6.0 MPa (lower bound 95% CI:upper bound 95% CI) for both approaches as they both determine constant A in the same manner. All values for constant A were within 1.7% of its median value.

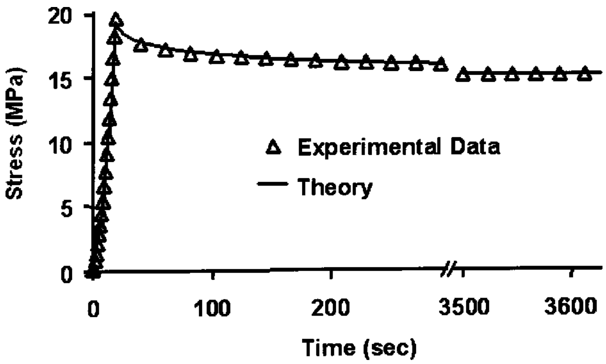

Fig. 3 A typical curve fit using the strain history approach to experimental data (γ=0.15%/s during ramping)

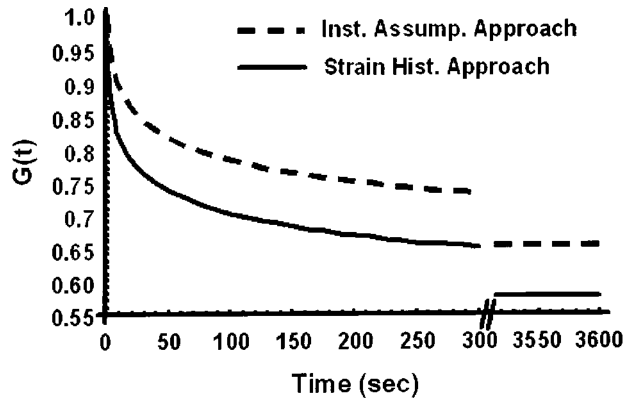

Fig. 4 The reduced relaxation function as determined using the instantaneous assumption approach and the strain history approach

Table 1 Constants describing the instantaneous elastic response obtained by curve-fitting individual specimens using the strain history and instantaneous assumption approaches. * significant difference between the two approaches ($p<0.05$).

	A (MPa)		B	
Specimen #	Strain History	Inst. Assum.	Strain History	Inst. Assum.
997	6.75	6.75	73.5	61.8
965	3.04	3.04	78.5	76.3
422	2.75	2.75	76.8	75.5
41	7.19	7.19	41.6	38.5
26	32.86	32.86	13.9	13.5
19	5.65	5.65	34.0	33.1
Mean±SD	9.7±11.5	9.7±11.5	53.1±27.0*	49.8±25.4

For constant B, the confidence intervals for the strain history approach and instantaneous assumption approach were 47.2:48.2 versus 45.7:46.4, respectively. For each approach, all constants were determined within approximately 1% of their median values. In terms of the constants describing the reduced relaxation function, the bootstrapping analysis yielded confidence intervals for constant C from the strain history approach and the instantaneous assumption approach to be 0.0721:0.0724 versus 0.0680:0.0680, respectively. Thus, all values determined for this constant were within 1% of the median values for both approaches. Similarly, the confidence intervals for constants τ_1 (0.62 s:0.63 s versus 2.01 s:2.02 s) and τ_2 (1469 s:1488 s versus 2138 s:2145 s) for the strain history versus instantaneous assumption approaches also determined values to be within 1% of their median values, respectively.

As the boot-strapping analysis demonstrated minimal sensitivity of the obtained constants, it was deemed that the solutions to both approaches are stable. Thus, the constants obtained for each individual specimen's data can be compared statistically. The results of those analyses are presented in Tables 1 and 2. It should be noted that these were paired comparisons and the high standard deviations are the result of inter-specimen variability. For these data it is important to consider whether a particular constant was determined to be either consistently higher or lower for specimens when determined using the strain history approach (Tables 1 and 2).

In terms of the solutions obtained from curve-fits of each individual specimen's data, constant B was determined to be significantly greater when obtained using the strain history approach (53.1±27.0; mean±SD) compared to the instantaneous assumption approach (49.8±25.4), indicating a more nonlinear instantaneous elastic response ($p<0.05$; Table 1). For the constants describing the reduced relaxation function, the strain history approach consistently estimated significantly higher values for constant C (0.089±0.057 versus 0.076±0.053) for each individual specimen ($p<0.05$). Estimates for constant τ_1 obtained using the strain history approach (0.54±0.15 s) were an order of magnitude lower than those obtained using the instantaneous assumption approach (2.13±0.98 s; $p<0.05$). Further, estimates for constant τ_2 were also significantly lower when determined with the strain history approach (1602±581 s versus 2222±821 s; $p<0.05$). Thus, it can be seen that the strain history approach consistently predicts a reduced relaxation function with a greater percentage of relaxation, steeper initial slope, and earlier time to reach equilibrium (Fig. 4).

For validation, the constants A, B, C, τ_1, and τ_2 obtained from the strain history approach could accurately describe the experimental data of the cyclic stress relaxation test for each specimen. Error between the prediction and experimental data ranged from 0.2% to 2.9% for the best prediction (Fig. 5*a*) and 9.3% to 16.2% for the worst prediction (Fig. 5*b*). In general, the prediction of the initial peak stress was the most erred for all specimens. Nonetheless, the average error for this peak measured only 6.3±6.0% across all specimens.

Table 2 Constants describing the reduced relaxation function obtained by curve-fitting individual specimens using the strain history and instantaneous assumption approaches. * significant difference between the two approaches ($p<0.05$).

	C		τ_1 (sec)		τ_2 (sec)	
Specimen #	Strain History	Inst. Assum.	Strain History	Inst. Assum.	Strain History	Inst. Assum.
997	0.204	0.183	0.30	3.29	1972	2451
965	0.055	0.047	0.64	2.07	1997	2685
422	0.071	0.058	0.63	1.85	896	1163
41	0.084	0.073	0.54	2.97	2248	3030
26	0.066	0.050	0.44	0.51	1587	2786
19	0.056	0.045	0.70	2.09	910	1218
Mean±SD	0.089±0.057*	0.076±0.053	0.54±0.15*	2.13±0.98	1602±581*	2222±821

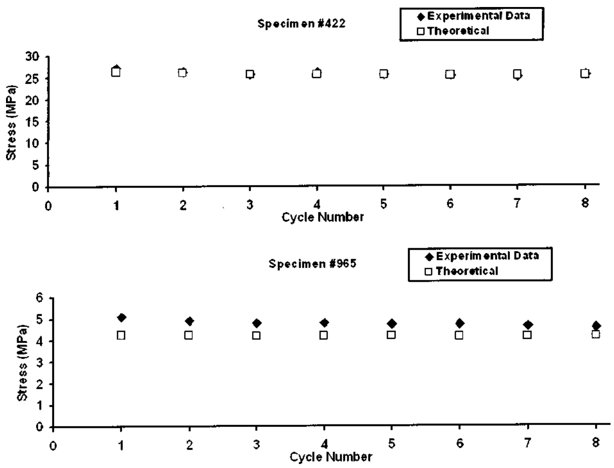

Fig. 5 Prediction of the peak stresses of a cyclic loading history based on the constants obtained from the stress relaxation experiment using the strain history approach for individual specimens (*a*) best prediction; (*b*) worst prediction

Table 3 Constants describing the instantaneous elastic response and reduced relaxation function obtained by curve-fitting individual specimens using the approach described by Kwan et al. (1993). ψ denotes convergence failure of the algorithm, for which the constants obtained for the iteration prior to failure are reported.

Specimen #	A (MPa)	B	C	τ_1 (sec)	τ_2 (sec)
997$^{\psi}$	<1E−10	2.1E+07	0.173	4.87	2287
965$^{\psi}$	15.62	36.3	0.068	5.25E−06	1275
422	10.95	46.2	0.071	9.05E−05	1568
41$^{\psi}$	<1E−10	2.5E+07	0.072	4.16	3186
26	1.68	90.0	0.071	1.34E−04	1657
19	2.67E−10	548.5	0.046	1.52	1197

Discussion

In this study, an improved analytical method to obtain the constants of Fung's QLV theory (A, B, C, τ_1, and τ_2) was presented. The current approach takes into account the ramping portion of the experiment; therefore, removing the assumption of a step change in strain. The strain history approach enabled us to fit the entire experiment (i.e., the stress versus time data from the ramping phase to the stress relaxation portion of the stress relaxation test). The key finding was that the regression algorithm converged to a unique solution that was stable and validated by predicting the stress response of a separate experiment. By comparing the set of constants for individual specimens to those obtained for the instantaneous assumption approach, the effect of the assumption of a step change was elucidated.

Previous studies using QLV theory together with the assumption of a step change in strain do not account for the relaxation that occurred during ramping and base normalization of experimental data on an underestimated peak stress [11,33,34]. As a result, constants C and τ_1 are significantly underestimated and overestimated, respectively [33]. The current approach improves the estimates of these constants. The constant C was significantly higher and constant τ_1 was an order of magnitude lower than those determined using the instantaneous assumption approach. Further, the strain history approach estimates a more nonlinear instantaneous elastic response as indicated by the higher value for constant B. All of these improved approximations result from accounting for the strain history during ramping.

In spite of the fact that the ramp time used in this study is 1–2 orders of magnitude longer than those used previously, the constants obtained using the strain history approach are similar to those reported previously for ligaments and tendons [17,18,20,35]. Most importantly, the determination of constant τ_1, which has been shown to be the most sensitive to the experimental ramp time, was on the same order of magnitude as these previous studies [33]. Further, the ability for the model to predict the results of a second experiment for validation of the constants was similar to that reported by Woo et al., 1981 whose constants were also determined based on data with a ramp time that was 2 orders of magnitude shorter than that used in this study. While this theory is only an approximation and no approach can guarantee that the obtained constants are "true," the fact that the strain history approach was able to estimate reasonable constants based on data with a ramp time 1–2 orders of magnitude slower than previous studies is a significant advancement. Thus, issues associated with fast strain rates can be avoided (eg., overshoot, vibration, poorly approximated strain histories) [14].

Previously our laboratory had used a two-step regression approach to obtain better estimates of the constants (A, B, C, τ_1, and τ_2) based on experiments with finite ramp times [19]. For this approach, however, two physically significant constants, B and τ_1, are highly correlated. As a result, regression algorithms either fail to converge or converge to solutions that are sensitive to systematic deviations between the theory and the experimental data for certain applications. This is demonstrated in Table 3 where the constants (A, B, C, τ_1, and τ_2) were determined for each individual specimen using this approach. Convergence failed for three of six specimens and the constants A, B, and τ_1 spanned more than 10 orders of magnitude.

A similar issue (i.e., the correlation of constants A and τ_1) was observed using the strain history approach. It was found that a relatively similar curve-fit could be achieved when both constants A and τ_1 are increased and decreased by the same percentage of their original value, respectively. Thus, this study chose to fix constant A based on work from two previous studies. One study showed that constant A is unnecessary to describe the reduced stress relaxation following a finite ramp time, and the other demonstrated that the stress-strain curve of ligaments is relatively insensitive to strain-rates ranging over 4 decades [19,31]. This allowed for a significant improvement of the variability displayed for the obtained constants when compared to that of Kwan et al. (1993). It should be noted that this study did not compare to other approaches that account for the loading portion of the experiment as these approaches are fundamentally based on short ramp times [2,7,22]. These approaches were not developed to apply to the experimental protocol utilized in this study, but will perform adequately when applied appropriately.

For tissues whose stress-strain curve is sensitive to strain-rate, an alternative means to determine constant A may be necessary. For this case, a high strain-rate experiment may still be required to determine constant A, but the remaining constants could be determined utilizing a second slower strain rate experiment along with the approach described in this study. Although this methodology would still require accurate high-speed measurements of stress and strain to determine constant A, the errors caused by the inability of a testing machine to accurately perform a ramp and hold test at high strain rates can still be avoided.

Because of the stability of the solutions obtained using the strain history approach, constants obtained from curve-fitting individual specimen's data can be compared. Thus, the strain history approach may prove to be an important analytical tool when making statistical comparisons of the viscoelastic properties obtained from different laboratories or from different tissues. In addition, researchers can focus on collecting accurate measurements of stress and strain at slower strain rates while still having the ability to determine meaningful constants describing the viscoelastic behavior of their specimens. We believe the strain history approach may allow for differences in the constants to be determined that may have otherwise been unobserved due to the effects of a finite ramp time or performing experiments at fast strain rates. This may eventually allow for more accurate comparisons of the constants describing injured, diseased, or treated tissues versus those of normal tissues so that researchers can quantitatively measure differences in viscoelastic behavior. In the future, we hope to use this approach to determine the differences in the viscoelastic behaviors of healing and sham operated MCLs.

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