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Constitutive equations for ligament and other soft tissue: evaluation by experiment

Abstract Ligaments, tendons and other soft tissues are nonlinearly viscoelastic. To discriminate among various constitutive equations which may be used to describe the tissue, appropriate experimental modalities are requisite. Ideally, testing should span physiologic ranges for load (or strain), load history (recovery and reloading), and load onset and duration, and a robust model will fit all data. Methods to expand the experimental window of time for relaxation and creep are presented and evaluated. The role of ramp, relaxation and recovery protocols is studied in the context of viscoelasticity describable by linear, quasi-linear, nonlinear superposition, Schapery, and multiple integral formulations. The advantages associated with testing protocols that expand the time windows for creep or relaxation are presented.

1 Introduction

Like other soft tissues in the body, tendons and ligaments exhibit viscoelastic or time-dependent behavior. When these tissues are held at a constant strain level, stress in the tissues decrease, a phenomenon called stress relaxation. Conversely, when held at a constant stress level, strains in the tissues increase, known as creep. Creep and relaxation are important components of tissue behavior, and an investigation of such behavior takes careful consideration. An optimal experiment extracts the maximum amount of useful information from the specimen being tested. This may often require performing multiple phases in the experiment, such as testing at various strain levels or strain rates, to robustly capture the true behavior. As an example, performing a single stress relaxation test on a specimen at one specific strain level will give information about the time-dependent nature of the specimen, but it fails to give any insight about linearity. Performing relaxation tests at multiple strain levels would be required to determine any nonlinear viscoelastic properties. It may also be necessary to perform viscoelastic tests at various strain rates, as any stress–strain curve generated will depend on the strain rate utilized during data collection. While a concave-up stress–strain curve is an indication of nonlinear behavior, a concave-down curve could be due to nonlinearity or to time dependence or both.

Careful planning is also required in order to determine which constitutive equation provides the best representation of the data. The purpose of this paper is not only to present constitutive equations for the modeling of soft tissues such as tendon and ligament, but also to suggest the means by which to evaluate the best choice

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of constitutive model by experimentation. In addition, methods to expand the time window of observation are discussed.

2 Constitutive equations

Several constitutive equations have been utilized in the analysis of soft tissue mechanics. Of the most popular are quasi-linear viscoelasticity (QLV) and nonlinear superposition. It is also possible to use linear superposition (over a restricted range of load or strain), Schapery nonlinear equations, and other single or multiple integral models. Determining which model to use to fit data requires careful thought and cogent experimental design.

A stress–strain curve in response to a constant strain rate reveals the stiffness of a material by its slope, and the material strength by the maximum load achieved. Such a plot also can reveal material nonlinearity. In study of biological tissue such as ligament, stress relaxation testing is frequently done in order to determine viscoelastic properties. A single relaxation test reveals viscoelastic behavior, if any exists. The shape of the relaxation function at a particular strain level is a quantitative measure of the viscoelastic response. The relaxation function is given by:

$$E(t) = \sigma(t)/\varepsilon_0, \tag{1}$$

where ε_0 is the constant strain level to which the ligament is pulled and $\sigma(t)$ is the stress, defined by:

$$\sigma(t) = F(t)/a_0. \tag{2}$$

Here, $F(t)$ is the force and a_0 is the undeformed area. It has been shown [1] that the shape of the curve can be approximated by the power law described as:

$$\frac{\sigma(t)}{\varepsilon_0} = At^{-n} \tag{3}$$

where A has units of Pa and t has units of seconds. This indicates that $E(t)$ can be approximated by a straight line on a plot of $\log[\sigma(t)/\varepsilon_0]$ versus $\log[t]$. The slopes of the straight lines of the relaxation data on these plots indicate the power, or n value, of the data, and thus the magnitude of n indicates how rapidly relaxation or recovery occurs in time. Power law damping such as this fits experimental data well, and the nonlinear behavior (single parameter n) is easier to distinguish than the three spectral damping commonly used with QLV.

A single relaxation curve does not adequately describe tissue behavior, however, as it does not reveal whether the material is nonlinear or linear, and gives no insight regarding the proper model to use. Any number of models can be made to fit a single relaxation curve. Model selection then requires the fitting of multiple curves to begin eliminating some options.

A protocol consisting of a stress–strain curve and a single relaxation test can reveal that a tissue is nonlinear and that it is viscoelastic, and can therefore falsify a linear elastic model (Fig. 1). Results of this type are
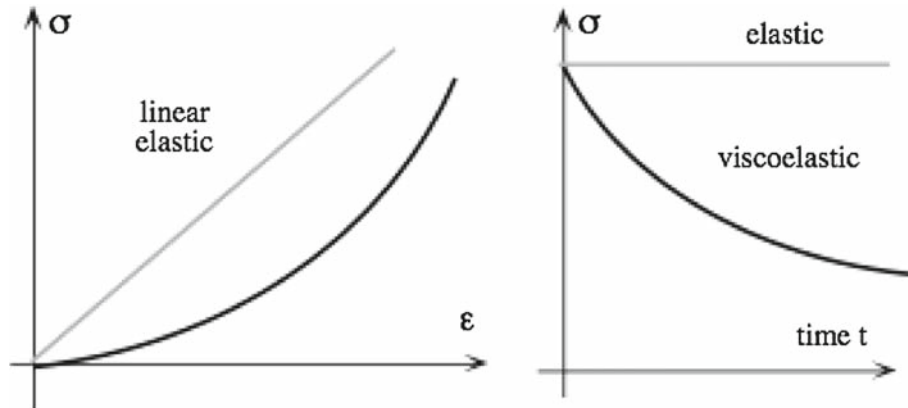

Fig. 1 A stress–strain curve at constant strain rate as shown demonstrates that the tissue is not linearly elastic, and a stress relaxation curve demonstrates that it is not elastic but viscoelastic
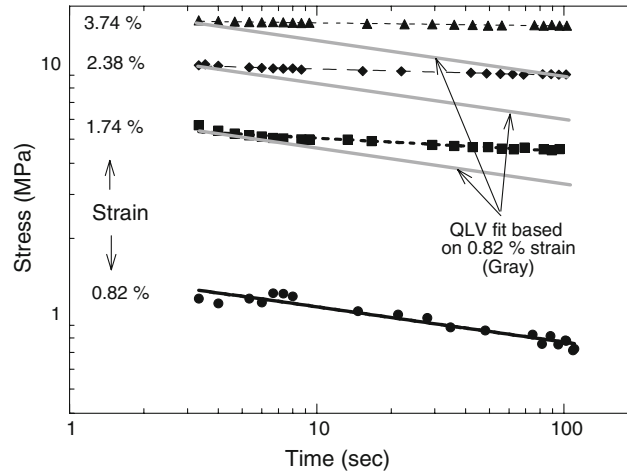
Fig. 2 Relaxation curves for different strain levels, adapted from Ref. [1]. If the curves are not parallel, data indicate that the behavior is not describable with QLV (see Eq. (7))

common in the biomechanics literature. However such a protocol cannot falsify a viscoelastic model including QLV and nonlinear superposition. By performing multiple relaxation tests over a wide range of applied strain levels (relative to a state with preload which may approximate that in nature) and plotting the resulting stress relaxation curves, any nonlinear viscoelasticity of the tissue becomes apparent and one can begin to discriminate among possible models. Also, relaxation rate changes at each strain may become apparent with multiple strain levels. This allows a comparison of models since a constant relaxation rate, independent of the level of applied strain, is implied in QLV Eq. (7), whereas a changing relaxation rate is allowed by the nonlinear models such as the nonlinear superposition and Schapery models. This is demonstrated in a rat ligament study in which stress relaxation was performed at a range of sub-damage strains (0.82, 1.74, 2.38, and 3.74%). The resulting curves (Fig. 2) demonstrated a dependence of the rate on strain which was not captured by a QLV model [1]. Similarly, in cornea [2], creep becomes more pronounced as stress increases. The behavior therefore does not follow quasi-linear viscoelasticity (QLV). Also, tendon [3] does not follow QLV because the relaxation rate depends on the strain level. Multiple relaxation tests at different strain levels can therefore verify or falsify linear or QLV models, but cannot falsify nonlinear models such as nonlinear superposition or the Schapery model. The presence of a varying relaxation rate is not enough to distinguish whether the nonlinear superposition or Schapery model (for example) is the strongest model; further examination is necessary.

A powerful way to further discriminate between models is to apply a more complex loading history. A simple method is to perform a multi-level stress relaxation test involving two different strains (Fig. 3a, b). For example, a relatively large strain can be imposed for a given length of time, followed by an immediate lowering or increase of the strain. Such step functions allow for easier model calculations, and their implications will be discussed in the following sections.

As nonlinear superposition [4], QLV [5–7], and Schapery [4,8] models have been used to describe tissue behavior, they will be further described here.

The basic form of the nonlinear superposition is:

$$\sigma(\varepsilon, t) = \int E\left[t - \tau, \varepsilon(\tau)\right] \frac{d\varepsilon(\tau)}{d\tau} d\tau, \tag{4}$$

but with the use of the discrete step strain function the nonlinear superposition prediction for stress response to a relaxation recovery protocol becomes:

$$\sigma(t) = \varepsilon_a E(t, \varepsilon_a) - (\varepsilon_a - \varepsilon_b) E(t - t_1, \varepsilon_b), \tag{5}$$

where t is the time from the start of stress relaxation at the first step strain, t_1 is the time at which recovery begins, ε_a denotes the first strain level, and ε_b denotes the second strain level. Because the relaxation modulus in Eq. (5) is a function of both time and strain, if a series of relaxation experiments is done at different strain levels, a material which obeys nonlinear superposition can exhibit relaxation curves which differ in magnitude and in shape as a function of strain.
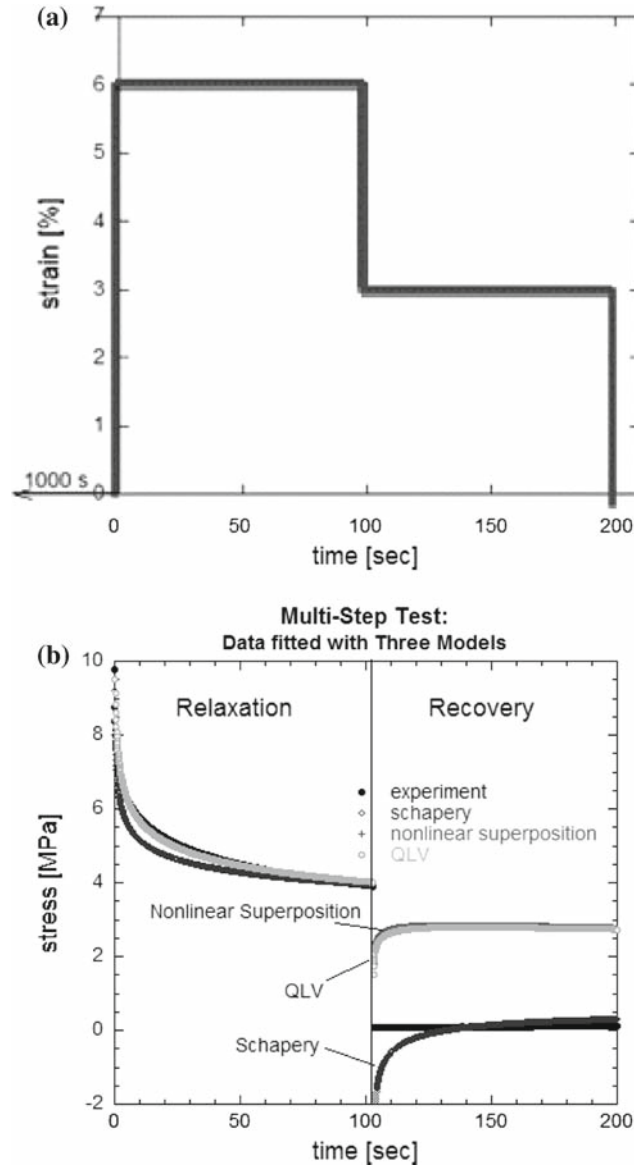
Fig. 3 a Multi-step strain history for relaxation and partial recovery and **b** resulting stress–strain curves from porcine digital flexor tendon, along with the resulting Schapery, Nonlinear Superposition, and QLV model predictions. Such a test can help indicate which nonlinear model is most appropriate

The basic equation for stress in QLV is:

$$\sigma(t) = \int_0^t E_t(t-\tau) \frac{d\sigma}{d\varepsilon} \frac{d\varepsilon(\tau)}{d\tau} d\tau. \tag{6}$$

QLV is a special case of nonlinear superposition in which the kernel is separable into a product, $E(t,\varepsilon) = E(t)g(\varepsilon)$, where $g(\varepsilon)$ represents the nonlinear strain dependence which is independent of time. With the kernel defined as such, the rate of stress relaxation (reflected in the definition of $E(t)$) is thus independent of the strain level, demonstrated in the gray fit lines in Fig. 3a. Since we are using discrete step strain functions, the integral reduces to:

$$\sigma(t) = (\varepsilon_a) E_t(t) g(\varepsilon_a) - (\varepsilon_a - \varepsilon_b) E_t(t - t_1) g(\varepsilon_b) \tag{7}$$

to describe the stress behavior predicted by QLV. The relaxation modulus in Eq. (7) is a product of functions of time and strain. Therefore if a series of relaxation experiments is done at different strain levels, a material which obeys QLV must exhibit relaxation curves which may differ in magnitude but have the same shape (time dependence). Also, recovery (the second term in Eq. (7)) must follow the same time dependence as relaxation in a material obeying QLV, because the time dependence is unchanged by multiplication by a strain-dependent number.

The general form of the Schapery nonlinear stress relaxation is given by:

$$\sigma(t) = h_e E_e + h_1 \int\limits_{0-}^{t} \Delta E(\rho - \rho') \frac{\mathrm{d}h_2}{\mathrm{d}\tau} \mathrm{d}\tau, \tag{8}$$

where h_e, h_1, and h_2 are strain-dependent material properties, ΔE is the transient component of the modulus (defined by $\Delta E \equiv E(t) - E_e$), E_e is the equilibrium or final value of the modulus (defined by $E_e = E(\infty)$), and ρ and ρ' are defined as follows:

$$\rho \equiv \int\limits_{0}^{t} \mathrm{d}t'/a_\varepsilon[\varepsilon(t')] \quad (a_\varepsilon > 0), \tag{9}$$

$$\rho' \equiv \rho(\tau) = \int\limits_{0}^{\tau} \mathrm{d}t'/a_\varepsilon[\varepsilon(t')] \tag{10}$$

where a_ε is an additional strain-dependent material property [9]. Physically, ρ can be regarded as an internal clock time which can depend on strain. Again, the use of step functions enables us to simplify the integral equation to

$$\sigma(t) = \left[h_e^b E_e + h_1^b h_2^b \Delta E \left(\frac{t - t_a}{a_\varepsilon^b} \right) \right] \varepsilon_b - \left(\frac{h_1^b}{h_1^a} \right) h_1^a h_2^a \left[\Delta E \left(\frac{t - t_a}{a_\varepsilon^b} \right) - \Delta E \left(\frac{t_a}{a_\varepsilon^a} + \frac{t - t_a}{a_\varepsilon^b} \right) \right] \varepsilon_a, \tag{11}$$

where "a" denotes the first strain level and "b" denotes the second, and t_a denotes the time at which the second step is invoked. The Schapery model's strain-dependent properties h_e, h_1, and h_2 are related to the Helmholtz free energy (specifically, third order and higher strain effects), and strain property a_ε is related to strain influences in free energy and entropy production. Further simplification of this equation is possible in tendon and ligament, since it has been determined that, for fibrous composite materials in isothermal testing conditions, $h_1 = a_\varepsilon = 1$ [9]. This leaves the equation for the two-step model as:

$$\sigma(t) = \left[h_e^b E_e + h_2^b \Delta E(t - t_a) \right] \varepsilon_b - h_2^a \left[\Delta E(t - t_a) - \Delta E(t) \right] \varepsilon_a. \tag{12}$$

As with nonlinear superposition, a material obeying the Schapery model can exhibit relaxation curves which differ in shape as a function of strain. Moreover the recovery behavior need not follow the shape of the relaxation curve at any strain.

All three of these single-integral equations are able to fit data from a single relaxation test at one strain of tendon or ligament well when the parameters in the model are taken from the data which they are fitting [4]. To determine which of these is the best model for the tissue, a more comprehensive testing protocol and corresponding predictions are necessary. The two-step protocol presented here is a good start towards determining more robust viscoelastic behavior. When the second strain level is lower than the first ($\varepsilon_b < \varepsilon_a$), the researcher gains information about both the relaxation behavior and the recovery behavior of the tissue. The recovery response is highly relevant to the function of tissue in the body because tissues are naturally subject to load–unload cycles. Further modifying the experiment to incorporate more complex loading histories, such as the use of a sinusoidal strain input, can determine if any of these models proves to accurately represent tissue behavior, but does so with additional complexity in calculations (as we no longer have step functions). It may also indicate that more complex models (i.e. multiple integral models) are required to capture the true behavior.
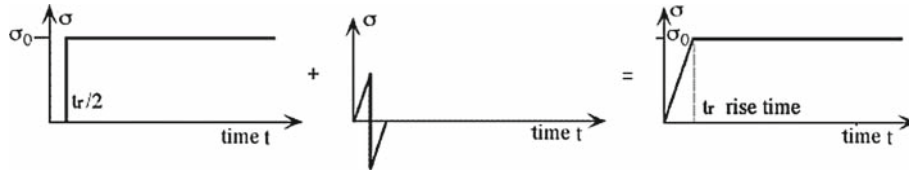
Fig. 4 Rise time as a superposition of an ideal step function and a doublet pulse

Previous experiments show that stress relaxation in ligament and other soft tissues occurs at different rates depending on the strain level [1,10]. Similarly, the rate of creep depends on the stress level [11]. Creep predictions based on relaxation are poor [1,12] if QLV is assumed. So to gain a more complete understanding of the viscoelastic properties of a tissue, both stress relaxation and creep tests must be performed, and these must be carried out in strategic fashion.

3 Rise time consideration

It is desirable to observe the viscoelastic properties of tissue over a window of time as wide as possible. Connective tissues in the body are subject to abrupt forces (corresponding to short times) during locomotion, sports activities, and overload leading to injury. Tissues are also subjected to a long-term component of load during activities such as standing over long time periods, since tendon and ligament are always stretched, never compressed. Therefore in order to capture the full physiologic behavior of soft tissues it is important to analyze behavior both at very short time periods and long time periods.

The window of observation during viscoelastic testing has limitations on both ends. The long end, which is the length of the test, is limited by several factors, including drift in the mechanical testing setup, time constraints of the experimenter, and accumulation of data. Testing of biological tissue further limits the duration of a test; fresh tissue cannot exist (unfrozen) outside of the body for indefinitely long test periods without degradation of various biological components. The short end of a test is dependent on machine capabilities (e.g., how fast it can apply the load) and data acquisition speed (e.g., how fast it can collect the first time points). By implementing a ramp speed that is as fast as physically possible with the test system and acquiring data at an appropriate rate, the window of experimental time scale can be extended by several decades (factors of ten) in the time scale without requiring unrealistically long tests. A wide window of time allows better discrimination among constitutive models because the shape of the relaxation curves is more clearly seen, and curve fitting in the presence of noise or biological variability is more robust. Faster ramp speeds are also more physiologically relevant, closer mimicking the quick loads implemented on tendons following muscle twitch, or compression of cartilage following a step, a jump or an impact.

When performing such viscoelastic tests, it is important to consider the effect of rise time, t_r, on the specimen in order to determine the appropriate time to begin utilizing data. Rise time is defined as the length of time required to reach the desired load level (strain level in the case of stress relaxation). A common conservative assumption [13] for an appropriate time is $10t_r$; this lengthy wait begins to greatly reduce the amount of data collected in the shortest time decades, leading to either very long tests or shrinking the window of observation, as well as a loss of information in the earliest time points. It is desirable, therefore, to determine the earliest time point at which the data can be plotted for observation. In the following, a demonstration of extension of data interpretation to shorter times is presented [14].

In the case of creep, the stress history can be considered a superposition of a shifted ideal step occurring at half the rise time ($t_r/2$) and a shaped pulse (see Fig. 4).

The stress history of the shifted ideal step can be written as:

$$\sigma(t) = \sigma_0 H(t - t_r/2), \tag{13}$$

where $\sigma(t)$ represents stress, $H(t)$ represents the Heaviside step function, σ_0 is the imposed initial stress, t is time, and t_r is the rise time. The corresponding strain response is:

$$\varepsilon(t) = \sigma_0 J(t - t_r/2), \tag{14}$$

where $\varepsilon(t)$ represents the strain in the specimen, and $J(t)$ is the creep compliance of the material. The shaped pulse is of the form:

$$\sigma_p(t) = \sigma_0 t/t_r \quad \text{for } 0 < t < t_r/2, \tag{15}$$

$$\sigma_p(t) = \sigma_0 t/t_r - \sigma_0 \quad \text{for } t_r/2 < t < t_r, \tag{16}$$

and can be approximated as the doublet $\Psi(t)$ for $t \gg t_r$. Since the integral of the doublet is the delta function, we can write:

$$\sigma_p(t) \approx \left(\sigma_o t_r^2/24\right)\Psi(t). \tag{17}$$

We can then, using the sifting property of the doublet, write:

$$E(t) \approx \sigma_0 J(t - t_r/2) + \left(\sigma_0 t_r^2/24\right)\left[d^2 J(t - t_r/2)/dt^2\right] \tag{18}$$

to describe the strain response. During interpretation of experiments, the second term may be neglected (as the magnitude of the creep curve is much larger than the curvature), and data may be taken starting at a time point that is a multiple of the rise time. The following is an example by which one can determine how soon data may be taken (at what multiple of the rise time) without incurring excessive error from the non-ideal step function.

Suppose, with J_0 constant, that

$$J(t) = J_0 (t/t_r)^n. \tag{19}$$

Then

$$\begin{aligned}
d^2 J(t)/dt^2 &= J_0 \left(n(n-1)/t_r^2\right)(t/t_r)^{n-2} \\
&= J_0 \left(n(n-1)/t_r^2\right)(t/t_r)^n (t/t_r)^{-2} \\
&= J(t)\left(n(n-1)/t_r^2\right)(t/t_r)^{-2}.
\end{aligned} \tag{20}$$

So for this case, the strain response is:

$$E(t) \approx \sigma_0 J(t - t_r/2)\left[1 + (1/24)(n(n-1)/2)((t - t_r/2)/t_r)^{-2}\right]. \tag{21}$$

Supposing Andrade creep (a particular form of power law), where $n = 1/3$,

$$E(t) \approx \sigma_0 J(t - t_r/2)\left[1 - (0.0046)((t - t_r/2)/t_r)^{-2}\right], \tag{22}$$

so even at time points as early as $5t_r/2$, deviation is less than 1% from the delayed step. Thus, data can be obtained at much earlier time points than the commonly used but conservative $10t_r$, further opening the window of observation by shortening the time scale of the earliest meaningful data.

Figure 5 helps demonstrate how choosing to begin collecting data at the shorter time point ($5/2t_r$) can allow for data collection over several decades within a reasonable duration of testing, which further allows for multiple test runs to be performed. Also, a wide window of time allows better discrimination among constitutive models. Consider a 0.1 s rise time, as shown in Fig. 5. This corresponds to a strain rate of 50%/s when stretching to 5% strain, so it is not unreasonably fast for most test systems. In the case of a 0.1 s rise time, data can be collected over three to four decades of time while still allowing time for multiple tests to be performed. On the other hand, if one extensive relaxation test is desired, it is possible to collect data over five decades of time (∼7 h) in a single day when data are collected at $5/2t_r$, whereas it would take more than a full day to complete the test over five decades (∼28 h) when data are collected beginning at $10t_r$. While many current test machines are capable of ramp times of 0.1 s or less, some models require more time to reach full strain capacity, which would further amplify the effect of using $5/2t_r$ as a starting time point rather than $10t_r$.

4 Analysis of ramp strain history

The experimental strain history for a relaxation test is not a mathematical step function since all experimental devices have some inertia. The initial part of the step can often be approximated as a ramp function. Moreover, ramp strain histories are often used to generate stress strain curves. The input is a ramp strain following a linear function of time and the output is stress versus time from which one plots a stress strain curve. In tests of linear materials, it is straightforward to analyze the ramp by Laplace transforms. Such an approach is inapplicable to nonlinear materials such as soft tissue. Therefore in the following, response to a ramp is analyzed by direct construction. Suppose the strain follows a ramp function, $\varepsilon(t) = Rt$, with R as the strain rate. To evaluate
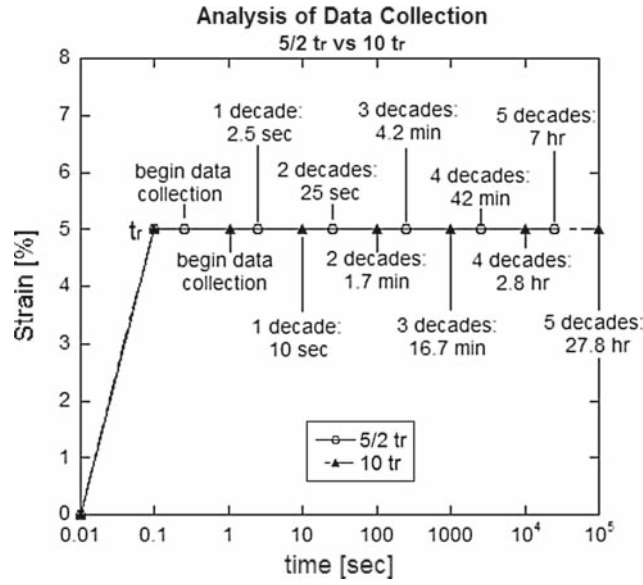
Fig. 5 Analysis of data collection. Using a stress relaxation example, we see the consequences of using a longer time point for data acquisition, including the amount of information lost in early tissue response. Time points defined above the line describe the timing of events when data collection begins at $5/2t_r$; time points defined below the line describe the timing of events when data collection begins at $10t_r$. Data collection over five decades is shown
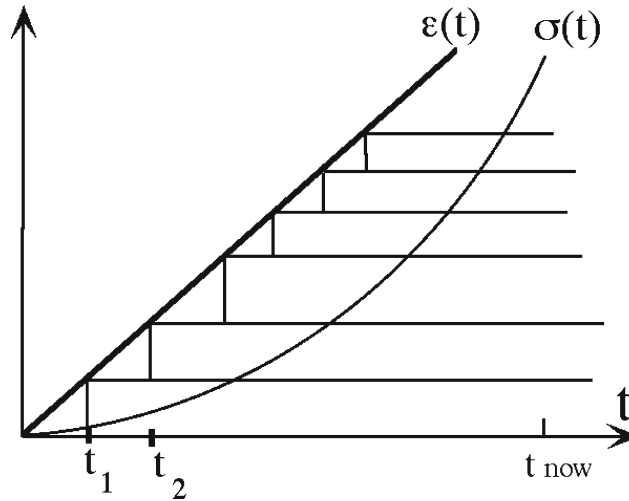

Fig. 6 Decomposition of a ramp function, strain versus time, into a series of step functions graphed along with the resulting stress versus time

integral forms of viscoelastic constitutive equations, write the strain history as a summation of Heaviside step functions H (Fig. 6),

$$\varepsilon(t) = 0H(t) + Rt_1 H(t - t_1) + R(t_1 - t_2)H(t - t_2) + \cdots, \tag{23}$$

$$\varepsilon(t) = R\Sigma_j \left(t_j - t_{j-1}\right) H(t - t_j). \tag{24}$$

For a material which obeys nonlinear superposition, the stress is written as a sum of increments, with $E(t, \varepsilon)$ as the relaxation function, considered as a Young's modulus,

$$\sigma(t) = R\Sigma_j \mathrm{d}\sigma = R\Sigma_j(t_j - t_{j-1})E(t - t_j, \varepsilon(t_j)). \tag{25}$$

For soft tissue, the relaxation modulus E is small at small strain, so its contribution to the stress strain curve in the initial region is also small. In the limit of small steps, the stress can be evaluated as a Stieltjes integral.

The slope of the stress–strain curve obtained from the ramp history (constant strain rate input) is, for a material which obeys nonlinear superposition,

$$d\sigma(t)/d\varepsilon = RE(t, \varepsilon). \tag{26}$$

If the material obeys QLV, the modulus function is separable into a time dependent part and a strain dependent part $E(t, \varepsilon) = E(t)g(\varepsilon)$, so

$$d\sigma(t)/d\varepsilon = RE(t)g(\varepsilon). \tag{27}$$

If the material is linearly viscoelastic, then

$$d\sigma(t)/d\varepsilon = RE(t). \tag{28}$$

For a linear viscoelastic material, the slope of the stress strain curve decreases with strain, since as strain increases, so does time; the material is time-dependent since it is viscoelastic.

As for discrimination between QLV and nonlinear superposition, the shape of the ramp response differs. The difference is likely to be most noticeable at small (physiologic) strains, near the origin of the graph. Ligament strain during normal bodily activity is typically below 4%: from 3.6% for squatting, to 1.7% for bicycling [15]. Comparing Eqs. (26) and (27), the slope depends on the modulus. The modulus depends on strain differently in QLV and in nonlinear superposition. Experiment shows that the effect of strain on the relaxation modulus is most pronounced at small (physiologic) strains. Therefore in a stress strain curve, the difference between QLV and the observed relaxation behavior of ligament will also be most pronounced at small strains. Unless a magnified view of this region is provided, the ramp protocol is inadequate to clearly distinguish behavior which follows QLV from behavior which follows nonlinear superposition.

In order to observe the viscoelastic behavior of soft tissues, the rate of the ramp in a stress relaxation or creep test should be as close as possible to a pure step [10]. In a test setting, it is impossible to achieve a perfect step scenario; most experimenters use the fastest ramp setting and assume a step function. Some authors have attempted to deal with the finite ramp issue by creating equations that work with the fast ramp time [8]. Other authors, however, have manipulated constitutive equations to accommodate slower ramp times. These authors slow the rate of the ramp so that it takes 18 s or more to reach the final strain [5,16], heading in the opposite direction from traditional experiment planning and interpretation of the ramp segment in rheology. More importantly, a loading time of 18 s is not physiologically realistic. Loading of tendon and ligaments during movement generally occurs much more quickly, closer to the experimental "step function" than the slower ramp.

Justifications for using the slower ramp times include the risk of overshoot, vibration, or poorly approximated strain histories [5,6,16]. However, it has been argued that the slow ramp time poses inherent issues regarding the considerable amount of relaxation occurring during the slow ramp phase [7] and that large errors can then occur in indirect fitting of the data [6]. If overshoot is a concern, it can usually be eliminated by controlling the gain of the servo amplifier in the test instrument. Any overshoot remaining can be modeled as a delta function in the input; its effect decreases with time as the derivative of the relaxation function, and is usually small.

Using a long ramp time greatly lengthens the amount of time necessary to perform experiments. Even if the experimenter begins taking data as soon as the ramp is finished, an 18 s ramp requires waiting at least 18 s from initiation of the input to gather uncoupled time dependent information. This has deleterious consequences in the length of time required to gather information over decades of time; a single decade of time requires three minutes, two decades lasts 30 min, three decades takes roughly five hours, and the fourth decade takes over 2 days to complete. If the experimenter waits either $2.5t_r$ or $10t_r$ to begin data collection, the problem becomes even more severe. Such lengthy testing prohibits the practice of multiple tests occurring in a single experiment, and limits the amount of information that can be gathered from a specimen, and is unnecessary given the ability of current testing technology. Furthermore, such long ramp times completely eliminate the gathering of data during early tissue response, limiting the amount of useful information gained during testing. Physiologically, the faster ramp better mimics loading in vivo, as most connective tissue occurs rapidly in the body during normal movement and injury scenarios. Thus, it is of great interest to gather information at early time points, which requires the use of a faster ramp.

5 Discussion

This paper discussed several of the more prevalent constitutive equations (quasi-linear viscoelasticity, nonlinear superposition, and Schapery models), as well as the means to falsify or discriminate between various models. Testing the tissue at a variety of strain (for stress relaxation) and stress (for creep) levels will not only reveal information regarding linearity, but also validate or falsify constitutive equations that may depend on constant relaxation or creep rates. Complex loading histories, such as a multi-step strain input during stress relaxation, or sinusoidal strain input, will further discriminate between models, as well as provide more detailed information about the tissue in question.

Also discussed were special experimental considerations including rise time and ramp strain history analysis that assist in the cogent design of experimental methods. It was shown through an example that data collection can be started at an earlier time point, $5/2t_r$ rather than $10t_r$, in order to collect data over more decades of time in a given time period and acquisition of data during early tissue response. This allows more of data to be acquired in a time that is reasonable for biological tissue, and allows multiple test runs to be performed on a given tissue in order to design more insightful experiments. The ramp itself was examined with regard to an appropriate speed; careful ramp history analysis leads to the conclusion that slow ramp times are not required and may hinder the investigation of viscoelastic tissue response. Utilizing a slow ramp significantly reduces the number of decades of time over which uncoupled, time-dependent data can be collected, as the earliest time point occurs much later than during fast ramp time experiments, which eliminates observation of early viscoelastic response. Overshoot and vibration generally have a very small effect during viscoelastic testing, and can be lessened by adjusting gain settings in the testing apparatus. A combination of utilizing the fastest ramp speed possible for the testing apparatus (with carefully adjusted control settings) and data collection beginning at an early time point ($5/2t_r$) leads to the maximum amount of information being collected in a reasonable amount of time and the most comprehensive analysis of the early tissue viscoelastic response. This allows for multiple tests to be performed on the same tissue in a single day to better discriminate between constitutive equations, and is more physiologically realistic.

Selecting the best constitutive equation data can better characterize soft tissue behavior using a given data set. Careful planning of experiments and analysis of results can lead to more robust models to predict the behavior. Performing viscoelastic tests at multiple stress or strain levels can validate or falsify the use of quasi-linear models. Further discrimination between single integral models (nonlinear superposition, Schapery, and QLV) can be facilitated by examining creep and relaxation behavior, as well as the recovery that follows. At this point, if no decision has been made (if more than one single integral model fits the data), it is possible to create more complex experiments, such as a sinusoidal input, to determine which of the single integral models provides the most robust fit. If none of the single integral models provides a robust fit, it may be necessary to use multiple integral models rather than a single integral model. Using the methods and analyses presented in this paper can aid in the design of experiments that are both informative and time efficient, and gather more physiologically relevant data.

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