Modeling Muscle's Nonlinear Viscoelastic Dynamics

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***Abstract*— Muscle's contractile properties are complicated by its viscoelastic properties. Failure of early viscoelastic muscle models led to Hill's force-velocity relation embodied as the contractile element. Adopting a particular force-velocity relation to describe muscle is neither easy, nor unique [1]. Time-varying elastance based models of the left ventricle have been popular since the idea was presented in 1969 [2]. This paper investigates adoption of the time-varying elastance concept to describe the viscoelastic properties of muscle. It will be shown that a time-varying elastance must be extended to a time, length, and velocity dependent elastance. Results show how a generalized force generator description of muscle [3] may be used to realistically model muscle's viscoelasticity.**

I. Introduction

DESCRIBING muscle as a mechanical spring has origins as early as 1674, when Mayow described muscle as an elastic material that changes due to metabolic processes [4]. Weber viewed muscle as an elastic spring whose stiffness varies depending on whether it is in a passive or active state [5]. Chauveau and Laulanié also considered muscle as an elastic spring with time-dependent stiffness, and proposed that shortening velocity affects force generation [6], [7]. Purely elastic models were subsequently refuted on thermodynamic grounds [8]. Stress relaxation and creep displayed by muscle are not explained by a simple viscoelastic model [9]. Hill reintroduced viscoelastic muscle models after observing that external work done accelerating an inertial load was inversely related to shortening velocity [10]. Series two-element viscoelastic models (Maxwell) are unbounded in length when subjected to a step change in force, and parallel (Voigt) models yield infinite force when subjected to step changes in length. Fenn found that energy release by muscle differs for isometric versus shortening muscle [11]. The concept of describing muscle as elastic material survived Mayow, but not the requirement that muscle elastance change with metabolic processes.

Subsequently, Hill developed the contractile element embodied as an empirical hyperbolic relation between muscle force (load) and shortening velocity [12]. Currently, lumped muscle contraction models are typically based on the contractile element. The contractile element is defined from two muscle variables, force and velocity. A previous study showed that evaluation of muscle's contractile properties via variables may not be unique [1]. Alternatively, a generalized force generator model permits computation of the parameter muscle elastance that may more accurately reflect muscle's contractile properties [3].

This study attempts to identify the underlying mechanisms that result in muscle's viscoelastic properties. Although the work uses data measured from twitch contractions of cardiac muscle, similar behavior is exhibited by all striated muscle. Consequently, this approach may be useful in modeling the approximately 650 muscles in the human body.

II. Methods

Time-varying elastance. Muscle force, f_m, is related to muscle length, ℓ_m by a time-varying elastance, $E_m(t)$:

$$E_m(t) = \frac{f_m(t)}{\ell_m(t) - \ell_c} \tag{1}$$

where ℓ_c is the constant muscle length corresponding to zero generated force. Muscle is thereby viewed as a spring whose stiffness varies with time, according to biochemical processes within the muscle ultrastructure. This relation is analogous to the time-varying elastance description for the left ventricle, relating ventricular pressure and volume [2].

Solving eq. 1 for muscle length ℓ_m and taking the derivative with respect to time gives velocity of shortening $d\ell_m/dt$:

$$\frac{d\ell_m}{dt} = \frac{1}{E_m}\frac{df_m}{dt} - \frac{f_m}{{E_m}^2}\frac{dE_m}{dt} + \frac{d\ell_c}{dt} \tag{2}$$

Time and length-varying elastance. Broadening the concept of a time-varying elastance to a time and length-varying elastance:

$$E_m(t, \ell_m) = \frac{f_m(t)}{\ell_m(t) - \ell_c} \tag{3}$$

yields the following expression for velocity of shortening:

$$\frac{d\ell_m}{dt} = \frac{1}{E_m}\frac{df_m}{dt} - \frac{f_m}{{E_m}^2}\left[\frac{\partial E_m}{\partial \ell_m}\frac{d\ell_m}{dt} + \frac{\partial E_m}{\partial t}\right] + \frac{d\ell_c}{dt} \tag{4}$$

Brady muscle experiments. Force and length data from the literature [13] were used in this modeling study. Papillary muscles were isolated from the right ventricles of rabbits or cats. Muscles ranged in weight from 0.3–5 mg, in length from 3–10 mm and were no greater than 1 mm in diameter. Muscles were bathed in oxygenated perfusate maintained at 22°C. Force was measured with a capacitance force transducer, and length with photoelectric cells detecting motion of a lever attached to the muscle. Imposed length changes were implemented with an ergometer built from a modified loudspeaker voice coil.

A recent model of muscle contraction [3], defined as follows, was compared to the time-varying elastance model.

This work was supported, in part, by a grant from the Howard Hughes Medical Institute.

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978-1-4244-7929-0/14/$26.00 ©2014 IEEE

Generalized force model. Muscle force f_m is described as a function of time t and muscle length l_m according to:

$$f_m(t, l_m) = a(l_m - b)^2 + (c\, l_m - d) f(t) \qquad (5)$$

Generated force results from the sum of passive and active components. a is a measure of passive muscle elastance and b corresponds to muscle length at zero force. Parameters a and b describe force resulting from stretch of the passive, unstimulated muscle. Parameters c and d describe muscle's active force generation. c, the length dependent component, is directly related to the muscle's contractile state, and varies with changes in inotropy. The length independent term, d, is constant for a particular muscle strip. The model exhibits muscle's force-length relation [14].

$f(t)$ describes the time course of active force generation:

$$f(t) = \frac{(1 - e^{-(\frac{t}{\tau_c})^\alpha}) e^{-(\frac{t-t_b}{\tau_r})^\alpha}}{(1 - e^{-(\frac{t_p}{\tau_c})^\alpha}) e^{-(\frac{t_p - t_b}{\tau_r})^\alpha}}, \quad t_b < t < 1 \qquad (6)$$

τ_c and τ_r are time constants characterizing the contraction (force increase) and relaxation (force decrease) processes related to myofilament crossbridge bond formation and detachment, respectively. α is a measure of the overall rate of these processes. The denominator normalizes $f(t)$ between the values 0–1. The combination of passive and active terms yields an analytical function describing muscle force as a function of both time and muscle length. t_b is a time constant derived from t_p, τ_c, τ_r and α:

$$t_b = t_p \left\{ 1 - \left(\frac{\tau_r}{\tau_c}\right)^{\frac{\alpha}{\alpha-1}} \left[\frac{e^{-(\frac{t_p}{\tau_c})^\alpha}}{1 - e^{-(\frac{t_p}{\tau_c})^\alpha}} \right]^{\frac{1}{\alpha-1}} \right\} \qquad (7)$$

and is close to the time to peak force, t_p, in magnitude.

The activation function $f(t)$ was modified to include velocity dependence, allowing it to reflect an altered number of attached crossbridge bonds:

$$F(t, v_m) = f(t) + k_1 v_m(t) + k_2 v_m(t - \tau) \qquad (8)$$

k_1 and k_2 describe how the number of bonds varies with muscle velocity at time t, and delayed τ after t. Muscle elastance, E_m, defined as $\partial f_m / \partial l_m$, was computed as

$$E_m(t, l_m) = 2a(l_m - b) + cf(t) \qquad (9)$$

Table I shows model parameters extracted from one papillary muscle. Detailed explanation of parameter extraction from experimental force curves is presented in [3].

III. Results

Brady [13] measured isometric muscle force for papillary muscles that were quickly released or stretched to a second isometric length during the twitch contraction. Fig. 1 shows quick release curves measured from one muscle. The topmost force curve corresponds to the isometric twitch at the initial muscle length. Other curves show how muscle force can drop to zero depending on the magnitude of the change in muscle length and its velocity of shortening. If the time-varying elastance (eq. 1) is subjected to a quick release (eq. 2), generated muscle force simply traverses from one isometric force curve (corresponding to the longer, initial length) to the other (final, shorter length), as shown in fig. 2. The model exhibits no velocity dependent force deactivation.

TABLE I

Model parameters extracted from one muscle strip.

Constant	Value [units]
a	1.861 [mN/mm^2]
b	7.956 [mm]
c	19.2 [mN/mm]
d	158.1 [mN]
τ_c	0.19 [s]
t_p	0.45 [s]
τ_r	0.3 [s]
α	2
$k_1 = k_2$	0.01 [s/mm]
τ	0.01 [s]

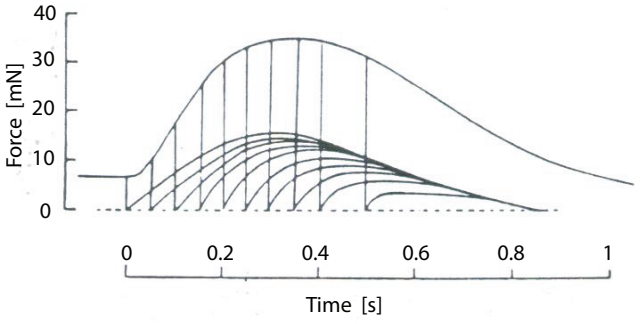

Fig. 1. Measured quick release force curves from the literature, adapted from [13]. Quick length changes varied in magnitude and speed, since the amount of release required to drop the force to zero depends on the force at the time of release.

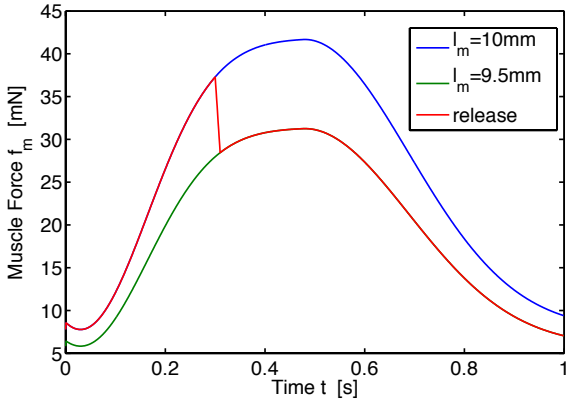

Fig. 2. Calculated quick release experiment performed on the time-varying elastance model of eq. 1. Muscle length of 10 mm was released 5% over 10 msec. No force deactivation occurs for this model.

Allowing muscle elastance to vary both with time and muscle length (eq. 3) yields a more complicated expression for velocity of shortening (eq. 4). Figure 3 shows quick release computed for the time and length dependent elastance model. The term $\partial E_m / \partial \ell_m$ represents how muscle stiffness changes with muscle length, and was taken to

be 20 mN/mm^2. This model now shows extensive force deactivation.

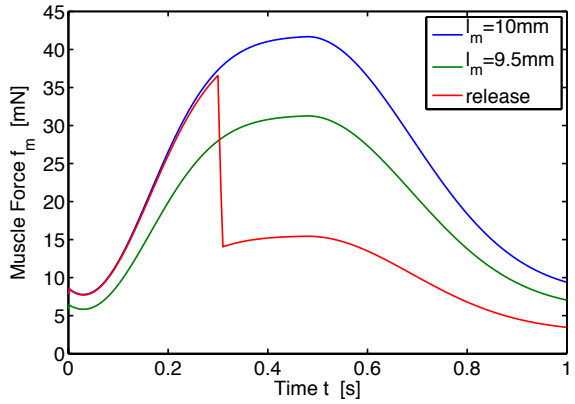

Fig. 3. Calculated quick release experiment performed on the time and length-varying elastance model of eq. 3. Muscle length of 10 mm was released 5% over 10 msec. Force deactivation occurs for this model.

Figure 4 shows papillary muscles subjected to quick stretches [13]. Shown are 5% stretches for muscle with initial length of 5.5 mm. The force response resembles stress relaxation of a 3-element standard linear solid, a viscoelastic model with a spring in parallel with the series combination of another spring and dashpot. The goal is to identify these elements with physiological significance. As expected, the time-varying elastance (eq. 1) shows no force overshoot, or subsequent stress relaxation, but merely traverses from one isometric force curve to the other (not shown).

Fig. 5 shows quick stretch performed on the time- and length-varying elastance (eq. 4). As shown, $\partial E_m/\partial \ell_m$ provides force overshoot beyond the isometric level. However, no subsequent force deactivation is present.

Fig. 6 shows quick release and quick stretch experiments computed from the generalized force model (eqs. 5 and 8). The dashed curves denote isometric force at the initial and final muscle lengths. For quick release, muscle force drops below the shorter isometric level, showing force deactivation and subsequent force recovery. After quick stretch, muscle force is initially higher than the longer isometric level, with subsequent recovery. Muscle experiments show a slower

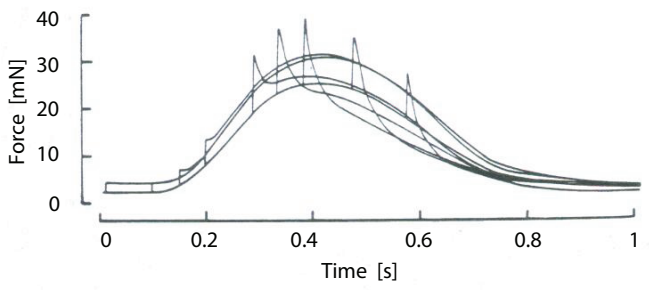

Fig. 4. Measured quick stretch force curves from the literature, adapted from [13]. The muscle was stretched 5% from initial length of 5.5 mm.

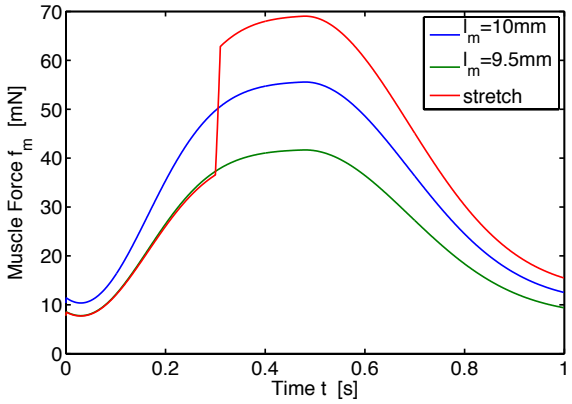

Fig. 5. Calculated quick stretch experiment performed on the time and length-varying elastance model of eq. 3 using eq. 4. Muscle length of 10 mm was stretched 5% over 10 msec. Muscle force overshoot is present, but stress relaxation is not for this model. $\partial E_m/\partial \ell_m$=15 mN/mm^2.

force recovery after the length change than those predicted by the model, suggesting that quick changes in muscle length directly affect the muscle's ability to form crossbridge bonds and generate force.

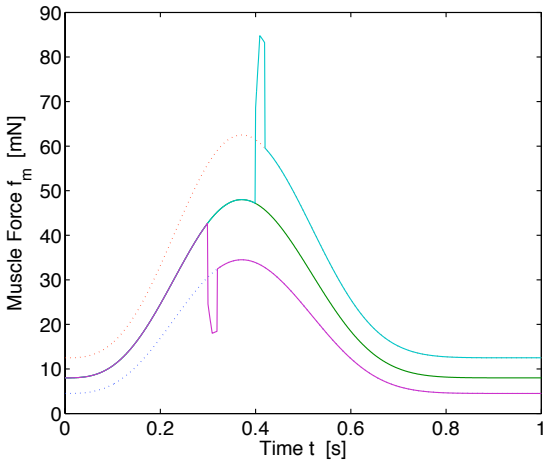

Fig. 6. Calculated quick release and stretch experiments computed for 5% changes in muscle length performed over 0.01s. Initial muscle length is 10mm. The dashed curves describe isometric force at the shorter (9.5mm) and longer (10.5mm) muscle lengths.

IV. Discussion

Modeling muscle with a time-varying elastance is attractive in its simplicity. Adopting a time-varying elastance curve *a priori*, however, fixes the muscle's contractile properties. Experimental data suggest that muscle's instantaneous loading conditions change its elastance. For example, x-ray diffraction data suggest widespread bond detachment with quick release. Both quick releases and stretches of 2% of sarcomere length produce large, rapid drops in the 14.3nm x-ray diffraction intensities [15], suggesting increased disorder in the contractile process with enhanced crossbridge detachment. Such enhanced disorder, coupled with the drop

of muscle force to zero, is strong evidence for universal bond detachment following quick release. The same trend of increased bond disorder is observed for the quick stretch diffraction pattern. Aequorin signals from ventricular papillary muscle corresponding to free calcium ion, believed to have been released from detached bonds, also suggest increased bond disorder during quick stretch and release experiments [16]. During slower length changes, such as isotonic conditions, mammalian papillary muscle shows significantly greater aequorin signals than for isometric contraction, indicating increased amount of free calcium ion and suggesting enhanced detachment of bonds, and that relaxation occurs earlier when muscle shortens than for the isometric case [17]. Clearly, muscle's nonlinear viscoelastic properties arise from ultrastructural dynamics.

Like muscle, the muscle model of eq. 5 is dynamic and varies with loading conditions. Although not shown, muscle elastance can be calculated from eq. 5 by taking the partial derivative with respect to muscle length, the traditional definition of elastance, shown in eq. 9 [3]. Elastance calculated in this way is also dynamic, and varies with loading conditions, varying with time, muscle length, and velocity of shortening.

V. Conclusions

A time-varying elastance based model of muscle contraction is unable to describe either muscle force overshoot or undershoot accompanying quick changes in muscle length. This purely elastic model demonstrates no viscoelastic properties. Making the elastance time and length varying embodies the model with force overshoot, in essence changing the predefined stiffness to some other pre-defined state. However, the model is insufficiently dynamic to show force recovery that resembles stress relaxation. Equation 5 provides a more realistic model of muscle's nonlinear viscoelasticity.

The muscle model of eq. 5 embodies muscle dynamics that are directly related to heart dynamics. For example, the Frank-Starling relation for the heart's preload arises from muscle's force-length relation. Increased muscle force, and thereby ventricular pressure, has both a passive component due to increased muscle stretch and an active component due to the formation of crossbridge bonds within the muscle. Although not shown in this paper, the model possesses an inverse force-velocity relation that translates to the heart's sensitivity to afterload. At higher pressures, the ventricle is forced to eject blood more slowly, thereby reducing cardiac output. Inotropic changes influence calcium ion availability in the muscle, which controls the number of bonds formed.

Lumped muscle models are commonly based on Hill's contractile element, embodied as a particular force-velocity relation. Studies have shown that the measured force-velocity relation varies with loading conditions [13], [18], [1]. Maximum velocity of shortening of the contractile element cannot be distinguished from a shift due to a change in muscle length, thereby invalidating it as an index of contractility [19]. Similarly, modeling showed that the entire force-velocity curve is also not unique for a particular contractile state and loading condition [1]. It is interesting to note that eq. 5 possess an inverse force-velocity relation without assumption of such; it arises from the model's force generating mechanism.

Results suggest that the time constants τ_c and τ_r are associated with the normal cycling of crossbridge bonds. If an imposed muscle length change is faster than this process, muscle stiffness is dictated by the current number of attached bonds, leading to increased stiffness. The quick length change then disrupts the bond formation process, leading to force deactivation, with subsequent recovery via normal bond cycling. The dynamic model of eq. 5 permits description of these ultrastructural processes. Since parameters have physiological significance, this model may provide new insight into muscle contraction dynamics.

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