35th Annual International Conference of the IEEE EMBS
Osaka, Japan, 3 - 7 July, 2013

Cardiac Muscle Strip Model Parameters and Muscle Elastance

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***Abstract*— A recent functional model of the left ventricle as a pressure generator that is time and volume dependent [1] was adapted to describe the mechanical aspects of heart muscle contraction. Muscle's complex dynamics develop from a single equation based on the formation and relaxation of crossbridge bonds. Muscle is modeled as a force generator that is time and length dependent. This equation permits the calculation of muscle elastance via $E_m = \partial f_m / \partial l_m$ from muscle force and length, both as functions of time. This muscle model is defined independently from load properties, and elastance is dynamic and reflects changing numbers of crossbridge bonds. The model parameters were extracted from measured force and length data from cat papillary muscle experiments in the literature [2]. The purpose of this paper is to present in some detail how to describe a particular muscle strip from measured data. The resulting model is tested under a wide range of mechanical conditions, such as isometric and isotonic contractions for normal and varied inotropic state, and muscle velocity is computed for different loads. Computed results compare favorably with similar measurements from the literature. The resulting lumped muscle model is a compact, yet comprehensive functional description of muscle dynamics.**

I. Introduction

MUSCLE is a dynamic tissue that embodies, at a minimum, a direct relation between muscle length and force, an indirect relation between load and velocity of shortening, and large variation with contractile state. Creating models of muscle that are equally dynamic is challenging. Muscle dynamics are directly related to heart performance, for example, the inverse relation between muscle force and velocity of shortening is directly related to how high arterial pressure (afterload) requires low velocity of ventricular ejection, which leads to low cardiac output.

A recent study presented a new functional description of the heart, proposing a single analytical function built from parameters extracted from animal experiments [1]. This compact model was found capable of describing the heart's response to changes in preload, afterload, and contractile state. This same approach was adapted to describe cardiac muscle strip [3].

Although the model has been presented in some detail [3], this paper presents the method of application for description of a particular muscle strip. Also shown is how instantaneous muscle elastance may be computed from the model, and how this elastance is dynamic under varied loading conditions.

This work was supported, in part, by a NASA Connecticut Space Grant Consortium Faculty Research Grant

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II. Methods

Sonnenblick muscle experiments [2]. Papillary muscles were isolated from the right ventricles of 0.5–1.5 kg cats. Muscles ranged from 7–13 mm in length with cross-sectional areas of 0.7–1.5 mm^2. Muscles were bathed in buffered Krebs-Ringer solution, and temperature was maintained at 21–25° C. Muscle tension (generated force) was measured with a Statham GI-1-1000 tension transducer, and muscle length was controlled by a custom electromechanical system. Muscles were stimulated with a Grass S4C impulse generator. Muscle tension and length were recorded on an oscilloscope and a Sanborn oscillograph.

Muscle model. Muscle force f_m is described as a function of time t and muscle length l_m according to [3]:

$$f_m(t, l_m) = a(l_m - b)^2 + (c\, l_m - d) f(t) \qquad (1)$$

Generated force results from the sum of passive and active components, shown on the left and right sides of the plus sign in eq. 1, respectively. The passive term, to the left of the plus sign, includes model parameters a and b, which are derived from passive muscle force, as described below. a is a measure of passive muscle elastance. b corresponds to muscle length at zero force. Parameters a and b describe force resulting from stretch of the passive, unstimulated muscle.

The active term, to the right of the plus sign, includes model parameters c and d, which are derived from muscle's active force measurements. 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 function $f(t)$ describes the time course of active force generation, a product of contraction and relaxation exponentials related to myofilament crossbridge bond formation and detachment, respectively:

$$f(t) = \frac{(1 - e^{-(\frac{t}{\tau_c})^\alpha}) e^{-(\frac{t - t_b}{\tau_r})^\alpha}}{(1 - e^{-(\frac{t_p}{\tau_c})^\alpha}) e^{-(\frac{t_p - t_b}{\tau_r})^\alpha}}, \quad t_b < t < 1 \qquad (2)$$

τ_c and τ_r are time constants characterizing the contraction (force increase) and relaxation (force decrease) processes, respectively, while 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:

$$t_b = t_p \left\{ 1 - \left(\frac{\tau_r}{\tau_c} \right)^{\frac{\alpha}{\alpha - 1}} \left[\frac{e^{-(\frac{t_p}{\tau_c})^\alpha}}{1 - e^{-(\frac{t_p}{\tau_c})^\alpha}} \right]^{\frac{1}{\alpha - 1}} \right\} \qquad (3)$$

TABLE I

MODEL PARAMETERS EXTRACTED FROM ONE MUSCLE STRIP.

Constant	Value [units]
a	1.861 [mN/mm]
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

and is close to the time to peak force, t_p, in magnitude. Muscle elastance, E_m, defined as $\partial f_m / \partial l_m$, was computed as

$$E_m(t, l_m) = 2a(l_m - b) + cf(t) \tag{4}$$

III. RESULTS

Isometric muscle force measurements were obtained from [2]. Passive and active isometric forces were measured from these force vs. time plots for various values of fixed muscle length. Figure 1 shows passive force f_p measured on a 10 mm long muscle strip (lower curve) and the difference between peak force (top curve) and f_p, denoted active force f_a (middle curve). f_p was fitted to the function $a(l_m - b)^2$ using MATLAB's nonlinear regression algorithm, giving the parameter values of a and b shown in Table I. f_a was fitted to the function $c\,l_m - d$ using MATLAB's linear regression algorithm, giving c and d.

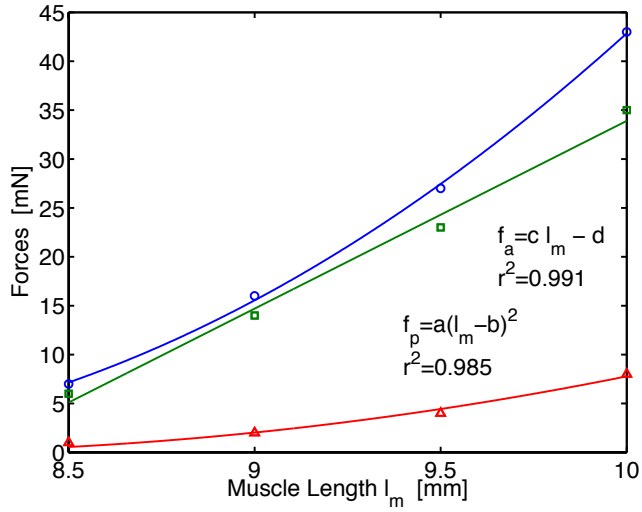

Fig. 1. Total force (top), active force f_a (middle) and passive force f_p (bottom) measured at different initial muscle lengths l_m. Measured forces are shown with data markers. Solid curves show linear active and nonlinear passive force curve fits.

The activation function $f(t)$ in eq. 1 represents the buildup of crossbridge bonds during contraction and the dissolution of bonds during relaxation of the muscle. The time constants τ_c and τ_r may be determined from experimental isometric force curves by examining the rising and falling (respectively) phases of isometric force plotted versus time. The time constant t_p is time to peak pressure and is directly measured from the isometric force curve. $f(t)$ measured from one muscle strip is shown in fig. 2. The shape of the isometric force curve, and consequently for $f(t)$, is little affected by changes in heart rate or inotropy, such as varied calcium ion or addition of norepinephrine [2]. At the same time, shape does vary from muscle strip to muscle strip, suggesting that these model time constants need to be determined once for a particular muscle.

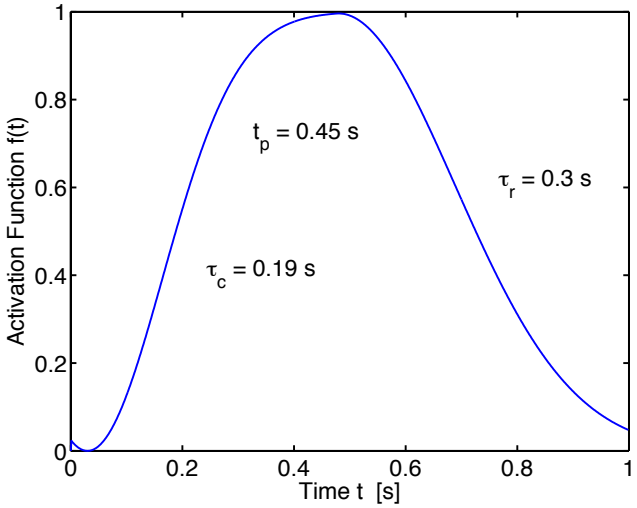

Fig. 2. Muscle activation function $f(t)$ and values of parameters τ_c, τ_r and t_p for one muscle strip.

Figure 3 shows how well the model (eq. 1) and extracted model parameters (Table I) describe measured isometric force for one muscle strip. Dotted curves denote measured forces and solid curves are computed from the model. One equation and one set of parameters is able to describe the entire set of isometric force curves.

Isotonic contractions attach the muscle strip to a fixed, sub-maximal load against which it is allowed to shorten. The muscle model was subjected to isotonic loading conditions, shown in fig. 4. Plotted are muscle length and force for seven different muscle loads. The muscle begins contracting isometrically. When muscle force exceeds the load's weight, the muscle lifts the load, shortening. With time, the muscle lengthens back to its original length and then relaxes isometrically. The control model parameters for the 10 mm long muscle strip were used.

Initial velocity of shortening was computed by taking the tangent to the muscle length curve at the start of the isotonic shortening phase. Plotting initial velocity of shortening, v_m, versus muscle load computed from the muscle model yields the hyperbolic force-velocity relations shown in fig. 5. This shape arises from the model without any additional assumptions about shortening velocity, and without the need to assume a hyperbolic function. The topmost curve is for control conditions and initial muscle length of 10 mm. The middle curve keeps muscle length at 10 mm, but reduces the muscle's contractile state, or inotropy, by decreasing

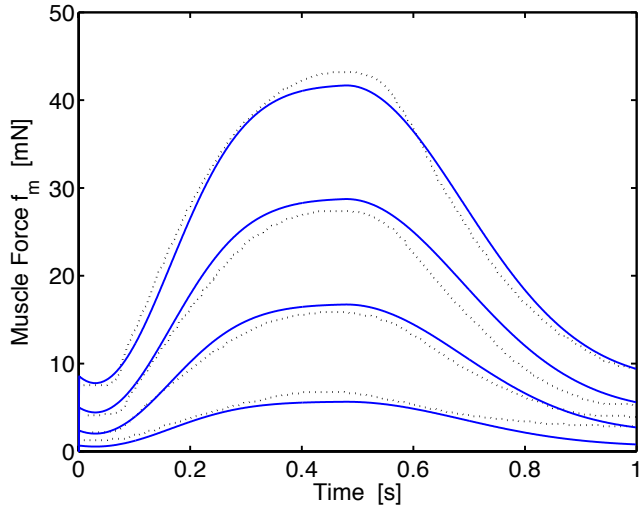

Fig. 3. Measured isometric force curves (dotted), and modeled (solid) with eq. 1 using the parameter values in Table I. Muscle lengths are 8.5, 9, 9.5 and 10 mm.

the model parameter c by 10%. This is akin to having a weakened muscle from reduced calcium ion availability. As shown, a different force-velocity relation results from this change in contractile state. The bottommost curve was computed for the control value of c, but for a shorter initial muscle length. We see that the force-velocity relation is sensitive to contractile state and loading conditions.

Muscle elastance computed via eq. 4 was found to be strongly dependent on contractile state and loading conditions. Fig. 6 shows elastance $E_m(t)$ computed for isometric and isotonic conditions for the control muscle with length 10 mm, for the same muscle with reduced contractile state, and for the control muscle at initial muscle length of 9 mm. As shown, muscle elastance varies widely. For example, the topmost curve (blue) corresponds to the control muscle at initial length of 10 mm under isometric conditions. The green curve below it corresponds to the same muscle under isotonic conditions. As the muscle is permitted to shorten, the change in muscle length decreases muscle elastance, thought to be due to having fewer crossbridge bonds attached. Similarly, the two bottommost curves are the isometric and isotonic twitches for the control muscle at a shorter initial length (9 mm). In between these two cases are the isometric and isotonic curves for the muscle at 10 mm initial length but with reduced contractile state. Each elastance curve is unique; the dynamic model yields muscle elastance that is as dynamic as the natural system.

IV. Discussion

The muscle model (eq. 1) is built from isometric force curves, yet it possesses the extensive dynamic behavior of muscle strip. The model embodies the main features of heart muscle dynamics, which are directly related to heart dynamics. The Frank-Starling relation for the heart, including both increased isovolumic pressure and increased ventricular

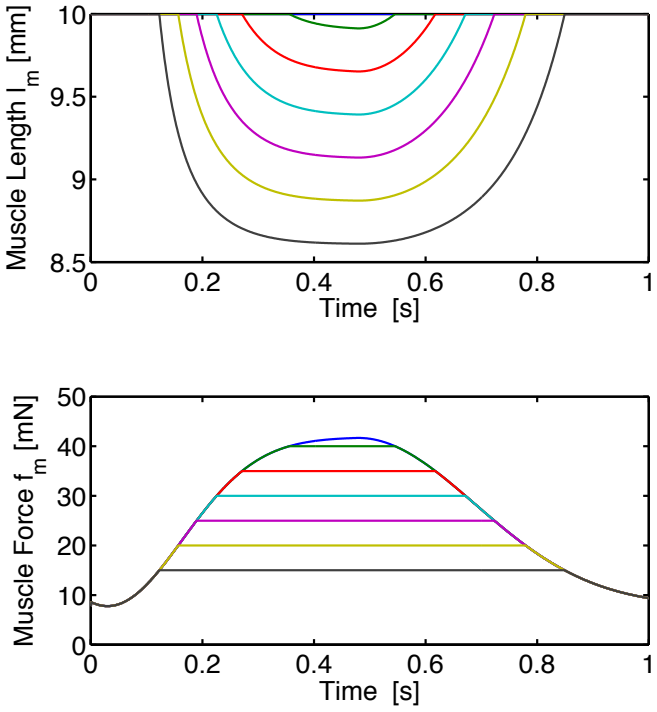

Fig. 4. Isotonic contractions computed from eq. 1 using the same model parameters as the isometric case (top force curve) for initial muscle length 10 mm, and for isotonic conditions for several loads. Plotted is muscle length (top) and muscle force (below).

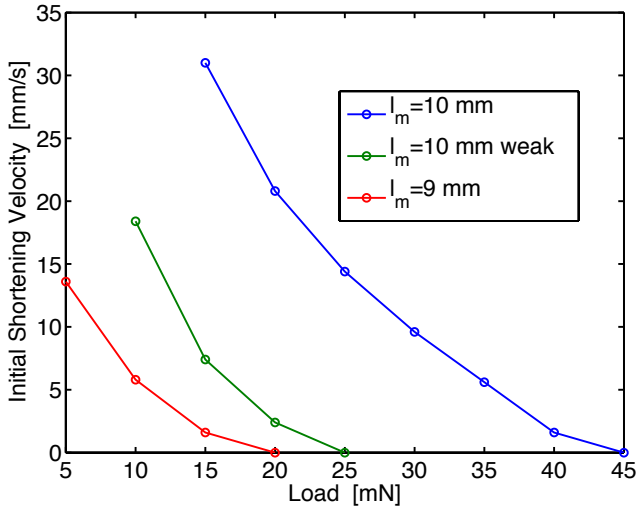

Fig. 5. Initial shortening velocity during isotonic conditions plotted as a function of load, giving Hill's inverse force-velocity relation for muscle [4].

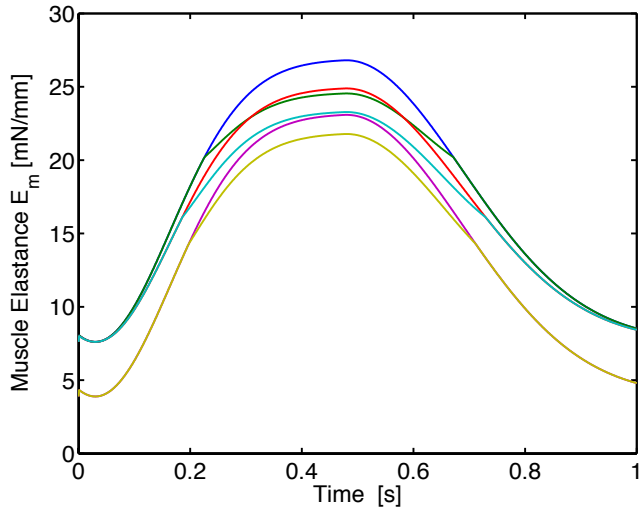

Fig. 6. Muscle elastance $E_m(t)$ computed for the control muscle with initial length 10 mm under isometric conditions (topmost blue curve) and for isotonic conditions (green curve). Other curves arise from a shortened muscle (9 mm) or from reduced contractile state.

outflow during ejecting beats when the heart is filled more, arises from muscle's force-length relation. The model has both passive (related to a and b) and active (related to c and d) elastic properties that describe stretching of the elastic heart chamber, plus active generation of force due to formation of muscular crossbridge bonds. As preload of the heart increases, both passive and active terms contribute; the former from increased chamber stretch and the latter from muscle's force-length relation, believed to be due to more optimal myofilament overlap permitting formation of more crossbridge bonds [5].

Muscle elastance arises from both passive and active muscle elastance terms, the former related to model parameters a and b, and the latter related to c, both of which vary with muscle length, and hence ventricular volume. The need to divide ventricular elastance into passive and active components has been proposed by other investigators [6]. In this model, the passive term corresponds to increased stretching of the passive elastic chamber and the active term to changes in stiffness associated with the active formation of crossbridge bonds.

Increased afterload (arterial pressure) requires the ventricle to operate at a higher pressure (force) and, therefore, with decreased outflow (velocity). Since blood ejection requires work, less energy is available compared to the non-ejecting heart beat and the beat duration is shorter.

Inotropic changes are believed to influence calcium ion availability, which is thought to control the number of crossbridge bonds formed within the heart muscle. This property is dictated in the model by parameter c, which modifies the force-length relation. As expected, muscle elastance computed using eq. 4 is directly related to parameter c, reflecting the heart's contractile state.

V. Conclusions

A single equation can be used to describe heart muscle. Modeling a particular muscle requires extraction of model parameters from measured isometric force curves at several fixed muscle lengths. The resulting model can describe both normal and pathological muscles under isometric and isotonic conditions.

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 [7], [8], a result substantiated by these model studies. Maximum velocity of shortening of the contractile element cannot be distinguished from a shift due to change in muscle length, thereby invalidating it as an index of contractility [9]. Similarly, modeling showed that the entire force-velocity curve is also not unique for a particular contractile state and loading condition [3].

This model provides a dynamic measure of muscle elastance that seems to uniquely characterize the muscle's contractile state. In addition, measuring model parameters from a set of isometric force curves is much easier than measuring the force-velocity relation for a particular muscle. This model may be useful for characterizing the mechanical performance of an individual muscle, or as a compact description of muscle for a larger physiological model. It appears to meet the goal of describing muscle as an elastic material that changes due to metabolic processes, a goal recognized as early as 1674 by Mayow [10].

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