Instantaneous Force-Velocity-Length Determinants in the Contraction of Heart Muscle

By Edmund H. Sonnenblick, M.D.

The inverse relation between force and velocity of shortening comprises one of the most fundamental properties of the contractile system of muscle. This force-velocity relation was first defined for skeletal muscle relative to one initial muscle length. Subsequently, Abbott and Wilkie demonstrated that the same inverse relation applies at any instant during the course of contraction if modifications are made to account for instantaneous changes in muscle length as the muscle shortens. Recently, using the cat papillary muscle, the force-velocity relation, relative to initial muscle length, has also been demonstrated in heart muscle. These studies have allowed a mechanical definition of the manner in which myocardial force generation is altered by changing initial muscle length. Increasing initial muscle length has been shown to increase the maximum isometric force generated by the muscle (P₀), but not to change the maximum velocity of shortening of the unloaded muscle (Vₘₐₓ). In contrast, inotropic interventions which alter the contractile state of the muscle at a constant initial muscle length, such as changing frequency of contraction or the addition of norepinephrine, have been found to increase Vₘₐₓ, with or without a change in P₀. However, the basic question remains whether velocity of shortening of heart muscle at any instant during the course of contraction depends on the muscle length at that instant in time in the same manner that the initial velocity of shortening is determined by the initial muscle length from which the contraction began.

This question assumes added pertinence in extending principles of muscle mechanics to the intact ventricle. Fry and co-workers have studied the relations of force and velocity in the whole heart and have assumed the measurement of velocity, tension, and muscle length at any given instant during contraction to be of use in the analysis of the performance of the intact myocardium. More recently, this concept of instantaneous force, velocity, and length relations has been applied further to the analysis of factors which modify the contractile state of the intact ventricle in man.

The purpose of this report is to present data obtained from the cat papillary muscle which supports the view that the force-velocity relation is of value not only in describing shortening of heart muscle at a given initial muscle length, but by applying the force-velocity relation appropriate to a changing muscle length at any instant during contraction, this relation may be shown to pertain throughout muscle shortening. Thus, in heart muscle, the course of contraction has been found to be uniquely described by the instantaneous relations of force, velocity, and muscle length during shortening. This application of instantaneous force-velocity-length relations allows for a more generalized analysis of contraction in heart muscle than is afforded by the use of initial muscle length relative to force and velocity alone.

Methods

The papillary muscles from the right ventricles of cats anesthetized with sodium pentobarbital (25 mg/kg) have been employed in these studies. Muscles ranged in length from 6.5 to 13.0 mm with a calculated average cross-sectional area of 0.6 to 1.4 mm². Papillary muscles were suspended in Krebs solution equilibrated with 5% CO₂ in O₂. Experiments were done at temperatures ranging from 19 to 30°C, but in most experiments the temperature was 21 to 22°C. The papillary muscle was arranged so as to re-

From the Cardiology Branch, National Heart Institute, Bethesda, Maryland.
Accepted for publication October 29, 1964.

Circulation Research, Vol. XVI, May 1965
cord force and displacement simultaneously. The lower end of the muscle was firmly held by a spring-loaded lucite clip which formed the end of a rigid stainless steel extension of a force transducer (Statham G1-4-350). At its upper end, the free tendinous end of the muscle was tied (Ethicon 0000 noncapillary silk) to a straight wire connection from an isotonic lever system which was used to measure displacement. Details of this preparation have been presented previously.

A photodiode was employed to measure displacement of the lever. This lever, fabricated from magnesium for maximum stiffness and minimal mass, has a lever ratio of 20:1, an experimentally measured equivalent mass of 60 mg, and a sensitivity to 3 μ. Afterloads, applied across the fulcrum of the lever, were suspended through a distensible rubber connection to further minimize inertia.

The muscle was stimulated by platinum plates (2.0 by 0.5 cm) placed parallel to the muscle, using an American Electronics stimulator (model 104A). Superthreshold stimuli (approximately 5 v for 3 msec) were used with frequencies of 6 to 12 per minute. Muscles handled in this manner routinely developed maximum forces of 600 to 1000 g/cm² and remained stable for periods longer than 24 hours.

The displacement of the isotonic lever and the force delivered to the force transducer were electrically differentiated through R.C. circuits (time constant 1.0 msec) and all signals, along with the stimulation artifact, were recorded on a Sanborn multichannel oscillograph (model 350 series). A recording paper speed of 100 mm/sec was routinely employed. For added time resolution, these signals could be led into dual channel Tetronix oscilloscope (model 502) and photographed at high speed.

This arrangement of the papillary muscle allowed for the controlled study of the relation between developed force, velocity of shortening, and muscle length during the course of afterloaded isotonic contraction. The initial muscle length was established by a preload and fixed by a micrometer stop above the free end of the lever. Afterloads could then be added to the lever, but these were encountered by the muscle only with the onset of contraction. For purpose of calculation, the preload plus the afterload comprised the total load during shortening. Generally the preload was 5% or less of maximally developed force (P₀), and in no instance did it exceed 10% of P₀.

Results

The relation of instantaneous velocity of
FIGURE 2
A. Relation of initial velocity of shortening (ordinate) and afterload (abscissa) from experiment as shown in figure 1. See text. $P_0$ (isometric force) = 8.6 g/mm. The inverse relation of force and velocity may be noted. B. Relation of extent of shortening on abscissa and afterload (tension) on the ordinate for experiment similar to that portrayed in figure 1. Initial muscle length 9 mm. Note that with increasing tension (afterload) the extent of shortening decreases. The points A, B, C, and D illustrate the contractions shown in figure 3. Note that each of the contractions has the same load but initiate from different muscle lengths. Nevertheless the muscle shortens to the same end point (X), regardless of the point from which the contraction started.

FIGURE 3
The course of isotonic shortening and velocity of shortening are shown as functions of time after stimulation. In each instance the total load is 2.3 g. From A to D, the length from which the contraction begins has been decreased as in figure 2B. See text.
shortening to instantaneous muscle length and load was explored in detail in eleven cat papillary muscles. The data presented are taken from one of the experiments but are entirely representative of all eleven.

The relation between initial velocity of shortening and load was determined in each case. The initial muscle length was established by a preload, generally 0.3 g, and the initial muscle length fixed by a stop above the lever tip. Following stimulation, after a brief latency (35 to 40 msec at 21°C), the muscle starts to develop force. When this force equals the load, shortening begins. The course of muscle shortening with increasing loads is seen in figure 1, A to H. Maximum velocity of shortening for each contraction is rapidly but not instantly established. Velocity of shortening then declines as the muscle continues to shorten. When the afterload is increased progressively (fig. 1), the initial maximum velocity of shortening decreases. The inverse relation between the initial velocity of shortening and load (force) comprises the well known force-velocity relation as graphed in figure 2A.

In figures 3 and 4, the relation of instantaneous muscle length to velocity of shortening is depicted. As an example, initial muscle length has been established in this instance at 9.0 mm with an 0.3 g preload. The course of contraction with a 2.0 g afterload is seen in figure 3A and is graphically portrayed in figure 2B, point A. Following force development equal to the load, the muscle shortens with a constant load to point X. The course and velocity of shortening for this afterloaded contraction is given in figure 3A. If the total load is then kept constant, but initial muscle length decreased, for example to point B on figure 2B, the course and velocity of shortening occurs as given in figure 3, panel B. The latency from stimulation to the onset of shortening is now longer and peak velocity (d/dt) is less. However, the minimum length to which the muscle shortens is virtually the same in both instances. In panel C and D of figure 3, initial muscle length has been further shortened and again the muscle shortens essentially to the same point. However, in some experiments, the muscle which started shortening from the shorter initial length was found to shorten somewhat further than the muscle shortening from the longer length. This was most prominent in depressed muscles, as attested to by a maximum developed force (P_o) of 2 to 3 g/mm² in contrast to a P_o of 6 to 8 g/mm² in nondepressed muscles. Further, when temperature was raised from 21 to 30°C, the duration of contraction was abbreviated (Q_102.1 ± 0.2) and under these conditions the muscle shortening from the longer length tended to relax prior to shortening to the

---

**Figure 1**

A. Velocity of shortening has been plotted as a function of instantaneous muscle length in mm during contraction. Plot obtained from tracings as in figure 3. Initial muscle length has been decreased progressively but total load kept constant. Note that after a brief delay, the course of velocity as a function of length is independent of the length at which contraction began. B. Velocity of shortening as a function of time after stimulation with decreasing initial muscle length. The complete divergence of these curves is evident.

*Circulation Research, Vol. XVI, May 1965*
same final length. Thus, the generality noted above applies only as long as the duration of contraction (duration of active state) is not abbreviated.

Within broad limits, the velocity of shortening at any instant during contraction is found to be a function of muscle length at that instant and not the length at which shortening began. In figure 4A, the velocity of shortening has been plotted as an instantaneous function of muscle length during the course of shortening for the contractions shown in figure 3. Contractions starting at both longer and shorter muscle lengths, but with constant loads, have been compared in figure 3A and D. One finds in this case that the decline in velocity of shortening as the muscle shortens depends in general on the muscle length at any instant during contraction (fig. 4A). Further, it is clear that velocity of shortening under these conditions is not declining as a function of time, since the muscle in figure 3A and D reaches the same length at different times, but still with the same velocity of shortening. This generality does not appear to hold, however, for the initial period of shortening in which a brief relatively steady state velocity is generally observed. Further, a finite time is clearly necessary for the assumption of maximum velocity of shortening.

As velocity of shortening (dl/dt) declines pari passu with a decrease in instantaneous muscle length, some divergence from the common dl/dt pathway noted in figure 4A is found toward the end of the contraction as the active state declines. Indeed, a divergence from the common velocity of shortening pathway serves to identify a decline in the active state. This divergence of dl/dt, which is very slight in figure 4A, is increased somewhat as temperature rises. Nevertheless the common pathway of velocity with constant load remains during the greater part of contraction.

Since instantaneous power (W) equals the force (or load) times the velocity, (P.dl/dt), the curves of figure 4A and B, also represent instantaneous contractile element power as functions of muscle length (fig. 4A) and time after stimulation (fig. 4B).

If velocity of shortening at different muscle lengths is plotted relative to time it is found that the velocity is less at any given time after

![Figure 5](image-url)

*The relation of instantaneous force-velocity and length. Obtained from the experiment in figure 1. The instantaneous lengths are noted on the graph.*
FIGURE 6
Effects of increasing frequency of contraction on the course and velocity of isotonic shortening. Preload 0.3 g; afterload 4.0 g. See figure 7.

stimulation for the shorter than for the longer muscle (fig. 4B). Since velocity of shortening is length dependent, the reason for this separation of velocity-time curves resides largely in the fact that less time is required for the shorter muscle to attain a given length than for the longer muscle.

If the instantaneous velocity-length relation of figure 4A is valid it should be possible to construct a family of force-velocity curves representing multiple instantaneous lengths from the contractions of a single force-velocity curve starting from one muscle length (figure 5). As has previously been noted for force-velocity curves determined at multiple initial muscle lengths, the curves relating force and velocity at several instants in time during contraction converge toward a common maximum velocity ($V_{max}$) but have multiple maximum forces ($P_o$) which decrease as a function of instantaneous muscle length.

The curve relating instantaneous muscle length and velocity may be altered by (inotropic) agents which alter the contractile state of the muscle. In figures 6 and 7, the effects of increasing frequency of contraction are shown while in figures 8 and 9, the effects of
norepinephrine are depicted. In both instances, the instantaneous velocity at any muscle length is increased by the inotropic intervention. Under these conditions, the shift in the curves relating instantaneous velocity and muscle length defines an augmentation of the contractile state of the muscle. This may be contrasted to the case (fig. 4) where only initial muscle length was altered and a single velocity-length curve resulted.

In contrast to the velocity-length plot (figs. 7A and 9A), the plot of instantaneous velocity against time after stimulation (figs. 7B and 9B) demonstrates how in response to an inotropic intervention, the velocity of shortening is augmented initially but declines more rapidly as the duration of active state (active contraction) is abbreviated. When initial muscle length was altered, velocity relative to length declined toward a common end point and no abbreviation of the active state duration was evident.

Discussion

In extending A. V. Hill's pioneer work on skeletal muscle to heart muscle, it was shown that, at any one initial muscle length, velocity of muscle shortening is a function of the load carried. At the onset of a contraction, contractile elements shorten at the expense of elastic components with the development of force. Once this generated force equals the imposed load (afterload), the series elastic component remains constant in length as a function of the constant load and subsequent muscle shortening reflects the shortening of contractile elements alone. Thus, the force-velocity relation describes the activity of the contractile elements independently of the series elastic elements.

Using the cat papillary muscle, it has been shown that the force-velocity relation of heart muscle resembles that of skeletal muscle. However, this relation describing initial velocity of shortening as a function of load at one muscle length during tetanic (prolonged) stimulation, requires some modification when applied to heart muscle. The present data indicate that performance of the contractile element in heart muscle is dependent on four variables: force, velocity, instantaneous muscle length, and time (duration of active state). The first three parameters pertain to the intensity of the active state. The duration of active state is also an important consideration. In terms of Hill's model for active muscle, contractile elements are fully activated shortly after stimulation during isometric

*The active state may be defined as a mechanical measure of those chemical processes which generate force or shortening in the muscle. When these processes are fully active, the active state may be said to be maximal.
contraction. Since, when the muscle is first activated, force is very small, the contractile elements shorten at maximum velocity (V_{max}). As shortening of the contractile elements proceeds, the elastic components in series with them are stretched and externally manifest force is progressively generated. With the increase in force, contractile element velocity falls, in accordance with the force-velocity relation. This process continues until force is so great that velocity reaches zero and P_o is manifest. Thus, during every isometric contraction, contractile element velocity moves down along its given force-velocity curve even though no external muscle shortening may occur. Even under isometric conditions, some decrease in the length of the contractile elements also occurs as the series elastic component is stretched. Therefore, the velocity of shortening of the contractile system decreases as a result of a decrease in contractile element length as well as an increase in force.

In skeletal muscle, activation may be summated so that adequate time is assured for the development of maximum force (P_o). In heart muscle where summation of stimuli is not possible, P_o may not be manifest unless steps are taken to prolong the duration of the maximal active state, as for example, by lowering temperature. If the duration of the active state were limited, the contractile elements would still begin to shorten at maximal velocity (V_{max}) shortly after stimulation. Contractile element velocity would then decrease as force increases due to stretching of the series elastic component, the decline in contractile element velocity following the force-velocity curve. However, at the time at which the active state begins to decline, the velocity of the contractile component of shortening would depart from the tetanic force-velocity curve and a force less than P_o would ultimately be generated. In the present study, the influence of time (duration of active state) has been largely offset by working at 21°C where the active state is prolonged so that P_o may be approached. This is attested to by: 1) the hyperbolic force-velocity curves obtained (fig. 1); 2) the plateau of the shortening curves (fig. 2); 3) the relation of velocity to length (vide infra); and 4) the fact that the muscle will shorten to the same point independent of the length at which shortening began. At 37°C, the duration of active state is abbreviated and undoubtedly this abbreviation plays an important role in limiting force development and muscle shortening at physiological temperatures.

The force-velocity curve in skeletal muscle, as conceived by Hill, refers to one initial muscle length. However, Abbott and Wilkie have demonstrated that if velocity is studied as a function of muscle length during a given contraction, the validity of the Hill equation...
FORCE-VELOCITY-LENGTH RELATIONS

FIGURE 10

A three-dimensional representation of the relations of load (force), velocity, and muscle length. Plotted from the data in figure 5. On the base are shown load (force) and muscle length; on the vertical axis is velocity of shortening. The basal plane, then, is the length-tension relation; the plane on the right face, the force-velocity relation; and the plane on the left face, the velocity-length relation. The course of a single afterloaded contraction may be plotted relative to this construct. Thus, a muscle activated at point A would rapidly have the active state of its contractile elements increased to point B. The shortening of the contractile elements at the expense of the series elastic elements generates force. With the increased force, contractile element velocity falls (point B to C). This represents the isometric phase of the contraction. At C, the force equals the load and shortening begins. In shortening (points C to H), the load is constant and the instantaneous velocity of shortening decreases as muscle length decreases. An exception would apply if the active state were to decline prematurely. In that case, the velocity would fall away from the plane represented by these curves and fall, e.g., E to K. Such occurs as temperature is increased. This representation of the instantaneous force-velocity and length relation comprises one contractile state of the muscle. A change in the contractile state is represented by a change in the coordinate of velocity (Vmax) with or without a change in the length-tension (P0) coordinates. Again, for any given contraction the same principles as described above apply.

holds at all muscle lengths during contraction as well as the initial length.

The present study has demonstrated that in heart muscle, for a given contractile state, once shortening has begun the instantaneous velocity of shortening becomes a function of instantaneous muscle length, essentially independent of the point at which shortening began. That this might occur in heart muscle as previously demonstrated in skeletal muscle4 has been suggested by Fry. On this basis, Fry has constructed a theoretical three-dimensional relation between force-velocity and length of the contracting intact ventricle. The present data support the validity of such a suggestion. In figure 10, the force-velocity-length relations in figure 5 have been expressed as a three-dimensional construct. However, certain minor limitations to this generality exist. As may be noted in figures 3, 6, and 8, with an initiation of shortening, velocity does not decrease as a function of muscle length until some shortening has already ensued. This initial phase of relatively steady-state shortening has been commented upon for both frog sartorius and rat dia-
phragm, and is not readily accounted for on a theoretical basis. As Ritchie has noted, acceleration would not explain this phenomenon. This observation might suggest that activation of the contractile system in heart muscle is time dependent and not complete until later in the contraction. This is a clear possibility which is receiving further exploration.

While the velocity-length curve with a constant load is essentially independent of initial muscle length under the conditions of these experiments, this would not be the case if the duration of the active state were abbreviated, as occurs at higher temperature. Under this latter circumstance the velocity at shorter muscle lengths would fall abruptly as contractile element activity ceased. In terms of the force-velocity curve, at one initial muscle length, velocity of shortening at high loads would be lower than anticipated from a hyperbolic force-velocity curve and maximum force would be less than P_o. The force-velocity curve remains valid at smaller loads under these conditions and a decline in active state would be attested to by deviation from this curve (fig. 10). The important corollary of this is that velocity of shortening during contraction may decrease as a function of both time and shortening, either because the maximal active state is decreasing, or the muscle is moving to a shorter instantaneous length and to a force-velocity curve appropriate to that shorter length. The present study would support the latter view as the primary determinant of the decrease in velocity observed as the muscle shortens.

Previously it has been demonstrated that the force-velocity relation in heart muscle, unlike skeletal muscle, is not unique. In addition to changing muscle length which alters P_o, without a change in the maximum velocity (V_max) of the muscle, at any one muscle length, factors such as heart rate, norepinephrine, calcium, and strophanthidin increase V_max with variable effects on P_o. In changing V_max the basic contractile state of the muscle is altered.

The present data serve to extend these previously demonstrated relations between force and velocity at an initial muscle length to force and velocity at an instantaneous length during a given contraction. The usefulness of such findings has been demonstrated in evaluating the effects of heart rate or catecholamines on the contractile state of the intact human ventricle. In these experiments, the relative velocity of movement of tantalum clips sewn to the ventricular surface was studied. By measuring velocity with which the clips approached one another at one ventricular size, the effects of altering initial ventricular volume on velocity were obviated and intraventricular pressure became a constant function of intramyocardial wall tension. In this manner, the effects of heart rate and catecholamines on the instantaneous force and velocity characteristics of the intact heart have been studied and a shift upward and to the right of the relation of instantaneous force and velocity has been demonstrated. The present study serves to demonstrate the theoretical validity of such measurements and helps to validate the use of instantaneous force-velocity relations in more fully evaluating the contractile state of the intact heart.

Summary

The relations of force and velocity during the course of shortening of heart muscle have been explored using the cat papillary muscle. It has been shown that at any instant during contraction the course of muscle shortening is described by the instantaneous relations of force-velocity and muscle length. The three dimensional force-velocity length diagram allows for greater generalization in the analysis of contraction of heart muscle than has been afforded by the analysis of force and velocity relative to initial muscle length alone, and provides a useful construct for portraying a given contractile state of heart muscle. A change in the velocity coordinate of this diagram (V_max) with or without a change in the force coordinate (P_o) serves to define a change in the contractile state of heart muscle.
Acknowledgment
The excellent technical assistance of Miss Michael Ann Callahan is gratefully acknowledged.

References
Instantaneous Force-Velocity-Length Determinants in the Contraction of Heart Muscle

EDMUND H. SONNENBLICK

Circ Res. 1965;16:441-451
doi: 10.1161/01.RES.16.5.441

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1965 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/16/5/441

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation Research can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation Research is online at:
http://circres.ahajournals.org/subscriptions/