Force, Velocity, and Power Changes During Normal and Potentiated Contractions of Cat Papillary Muscle

Y. Christopher Chiu, Edmond W. Ballou, and Lincoln E. Ford

The instantaneous force-velocity relations of cat papillary muscles were studied at different times in the twitch in normal and in postextrasystolic potentiated contractions. Fourteen to sixteen different loads were used to define each of the force-velocity curves. The curves were fitted by a least-squares procedure to the hyperbolic (Hill equation). The hyperbolae were extrapolated to obtain maximum velocity and isometric force and interpolated to obtain maximum power. All three of these values rose more quickly than developed force. Maximum velocity reached 77% of its peak at the earliest time studied, 20–25% of the time to peak force. Developed force achieved 22% of its final value at this time, while extrapolated isometric force and maximum power both reached 44% of their peak values. Postextrasystolic potentiation sufficient to produce a 1.5 to twofold increase in peak developed force produced less than a 20% increase in extrapolated maximum velocity. The results can be interpreted in terms of a model in which the maximum velocity of the contractile elements remains constant during the twitch. Variation in maximum velocity is attributed to a small internal load, equivalent to 6% of twitch force. Since maximum velocity is relatively constant, it does not give a good measure of changes in the force-velocity curves. By contrast, the extrapolated isometric force and maximum power are much more sensitive to changes in the force-velocity curves, and they vary in proportion to each other. The advantage of using interpolated maximum power rather than isometric force to define changes in the curves is that it can be normalized to muscle mass. (Circulation Research 1987;60:446-458)

When a muscle is stimulated electrically, its ability to contract rises and then falls. It is conceptually easy to imagine, therefore, that something called the "active state" might rise and fall with a characteristic time course, which then produces changes in the generation of force and shortening in the muscle. While the concept is simple, the attempts to measure "active state" have produced such conflicting results that the whole concept has fallen into disrepute. These conflicting results are generally attributed to the fact that the perturbation used to make the measurements frequently altered the active state. Another equally good reason is that many different parameters were being measured as a reflection of the active state, and some of these may have been inappropriate. A detailed review of the concept of the active state is beyond the scope of this experimental paper. The purpose of the present work is simply to study how the active mechanical properties — force and velocity of the muscle — change during a twitch without reference to the "active state." Since a muscle is able simultaneously to generate force and to shorten, measurement of either force or velocity has no meaning without the other, so the entire force-velocity curve is used to define the changes that occur during the twitch. To extend the range of force that can be studied, postextrasystolic potentiated contractions are used in addition to normal contractions. The difference between the present work and earlier studies of force-velocity relations is that the present measurements were made very shortly after a quick release to an isotonic load and measurements for a single curve were obtained at the same time in the twitch. It has long been recognized that to avoid the progressive change that occurs with continued shortening, the force-velocity relation should be measured immediately after a quick release to an isotonic load. In spite of this recognition, most of the studies, until recently, were performed with inertial levers, which cannot impose a rapid and critically damped tension step. To avoid the uncertainty of these types of experiments, we have made a servo system capable of imposing critically damped force steps completed within 1–2 milliseconds.

Materials and Methods

Preparation

Adult cats were anesthetized with intraperitoneal injections of 125–250 mg sodium pentobarbital and the hearts excised. Right ventricular papillary muscles were removed and gripped with platinum foil clips previously described. Holes in the clips were passed over hooks on the force transducer and motor to attach the muscle to the apparatus. Selected muscles were at least 5 mm long between the clips and had cross-sectional areas less than 1.0 mm². Experiments were performed in a modified Tyrodes solution.
solution containing a mM concentration of NaCl 118, KCl 4.7, MgSO\(_4\) 2.4, CaCl\(_2\) 2.5, NaH\(_2\)PO\(_4\) 1.2, NaHCO\(_3\) 22.5, glucose 5, and pH 7.4 at 26–28° C. The solutions were bubbled continuously with a gas mixture containing 5% CO\(_2\) and 95% O\(_2\). Stimuli were 1 millisecond duration square pulses applied through bright platinum electrodes in the bath parallel to the muscle. The stimulator consisted of a relay in series with a 12V power source and a potentiometer. The resistance of the potentiometer was adjusted to give slightly more than the minimum current required to produce maximum twitches.

**Protocol**

Muscles were stimulated regularly every 4 seconds. Twitch tension was measured at different lengths to define \(L_{\text{max}}\), the length at which maximum force developed. Force-velocity curves were measured at lengths between 88 and 90% \(L_{\text{max}}\). This length was chosen to minimize rest force and avoid the correction for the load borne by the parallel elastic element. Rest force was measured by applying a large shortening step to the unstimulated muscle.

To measure a force-velocity curve, releases to 16 different isotonic loads were made in 16 different contractures. These releases were made regularly every eighth contraction, with the muscle length being held constant for the intervening 7 twitches. An electronic circuit divided the isometric force recorded immediately before the step into 16 approximately equal loads, and a second circuit selected one of these isotonic loads to be applied to the muscle. The selection proceeded automatically from the lowest to the highest load. Occasionally, a step below zero load was not noticed during this automatic procedure, so that some force-velocity curves were determined from 15, or rarely 14, steps. When steps to high relative loads were applied late in relaxation, the muscle stopped shortening and occasionally began lengthening by the time velocity was measured, as described in “Results.”

These negative velocity points were not used in the data analysis. Releases to a series of 16 isotonic loads were made at one time in the twitch. The time was then changed and another series of 16 releases made. The time between stimulation and release was always some fixed multiple of 50 or 100 milliseconds, so force-velocity curves were typically measured at 100, 200, etc., or 150, 250, etc., milliseconds after stimulation.

When postextrasystolic potentiation was studied, control and potentiated twitches were alternated in a series so that any long-term drift in the preparation affected the control and potentiated twitches equally.

At the end of the experiments, the muscle was cut out of the clips and weighed. The cross-sectional area of \(L_{\text{max}}\) was determined as the weight/(1.05 \times \text{density}) with 1.05 taken as the density of the muscle. Developed force was divided by the cross-sectional area at \(L_{\text{max}}\) to obtain a measure of force/mm\(^2\).

**Recording**

All analyses were made from digital records obtained with a Digital Equipment Corp. PDP 11/10 computer equipped with an AR11 input/output device. The records were stored on floppy disks. Three signals were recorded: force, length, and an amplified length trace that was digitally differentiated to obtain velocity. The amplification of the second length signal was changed and another series of 16 releases made. The data were analyzed automatically from the lowest to the highest load so that the records were spliced. Recording was then stopped until 2 milliseconds before the step to the isotonic load so that the records were spliced. Recording was then continuous from 2 milliseconds before the step until 46 milliseconds after the onset of the step (Figure 1). Force and velocity data were then obtained from the recordings at 1 millisecond after completion of the force step (approximately 2–3 milliseconds after the initiation of the step) and at 7, 20, and 40 milliseconds after the initiation of the step. The data were averaged over a 1-millisecond period (6 data points), e.g., from 6.5–7.5 milliseconds after the onset of the step for the 7-millisecond point. Some records were obtained at one-fourth the usual recording rates, and in all experiments, slow recordings at one-fiftieth the usual rate were made of the isometric twitch to define its time course.

**Data Analysis**

The end-points of these experiments were force-velocity points obtained at different times in the contraction cycle. The 14–16 force-velocity points were fitted by a Newton-Raphson least-squares routine\(^4\) to the Hill equation.\(^2\) The form of the equation used was

\[
(P + a) \cdot (V + b) = c
\]

where \(P\) and \(V\) are force and velocity, respectively, and \(a, b,\) and \(c\) are the fitted parameters. For making more physiological comparisons, the extrapolated isometric force \((P_0)\), extrapolated maximum velocity \((V_{\text{max}})\), and interpolated maximum power \((PV_{\text{max}})\), de
FIGURE 1. Measurement of force-velocity properties. The three traces are (from top) length, force, and velocity determined by digital differentiation of a high gain length record. The points at which measurements were made are indicated by arrows on the records. BAS indicates a baseline period of recording at the time of stimulation. Recording was then stopped for 396 milliseconds. PRE indicates a 2-millisecond recording of the isometric force just before the step to the isotonic load. Recording is continued from this point until the end of the record. The remaining arrows indicate, respectively, force and velocity measurements at 1 millisecond after completion of the step, and 7, 20, and 40 milliseconds after the onset of the step. Sixteen such points were usually used to define the curves in the subsequent graphs.

Derived from a, b, and c, were used to define changes in the curves. These values were obtained from the fitted curves using the formulae:

\[ P_v = \frac{c}{b} - a \]  

\[ V_{max} = \frac{c}{a} - b \]  

\[ PV_{max} = a \cdot b + c - 2\sqrt{abc} \]

To illustrate the changes in power associated with changes in load, force-power as well as force-velocity curves are plotted. The power values were obtained by multiplying force times velocity.

Normalization of Data

To compensate for small variations in developed force in different contractions, relative forces were used in the fitting process, i.e., isotonic load divided by the developed isometric force measured immediately before the step. The absolute values of force, such as those plotted in Figure 2, were then determined by multiplying the relative force values by the average of the 16 isometric forces measured just before the releases. Force was normalized by cross-sectional area at \( L_{max} \), velocity and length by \( L_{max} \), and power by muscle mass. To compensate for differences between muscles, force, velocity, and power are sometimes expressed as percents of the corresponding reference values obtained just before the time of peak force.

Statistics

The Newton-Raphson least-squares routine used to fit the force velocity data minimized the variance, \( S^2 \), was defined by

\[ S^2 = (\bar{v} - \bar{v})^2/(n - 3) \]  

where \( \bar{v} \) is the observed velocity, \( \bar{v} \) is the value of velocity determined by the fitting procedure, and \( n \) is
The effects of this relatively low rest force are described in Appendix B. The reference values for normalizing the data are presented here. The results obtained with six muscles are described in Table 1. Rest force was assessed by applying a large shortening step to the unstimulated muscle and measuring the drop in force. The contractions were studied at 88-90% L\textsubscript{max} to the unstimulated muscle and measuring the drop in force and velocity were measured (1 millisecond after the 2-millisecond baseline (BAS); 2) the 2 milliseconds of isometric data immediately before the step (PRE); and 3) the times at which the force step was complete, before changes occur. On the other hand, such early velocities may not represent the velocity of the contractile element because of lightly damped series elastic recoil. In addition, velocity transients, although small, are likely to have some effect on the measured velocities at early times. In our experiments, the earliest time that these have consistently subsided was about 7 milliseconds after the initiation of the step. During this time, the muscle would have shortened by no more than 2% L\textsubscript{max}. In the rest of this paper, all the data presented were collected at 7 milliseconds after the initiation of the step. A force-velocity power curve, corresponding to the 7-millisecond force-velocity curve in Figure 2A, is shown in Figure 2B.

The results from a total of 45 force-velocity curves are presented here. The data for each curve were fitted to the hyperbolic Hill equation to obtain a mathematical description. The frequency distribution of the standard errors of the fitted curve are plotted in Figure 3. In the rest of this paper, all the data presented were collected at 7 milliseconds after the initiation of the step. A force-power curve, corresponding to the 7-millisecond force-velocity curve in Figure 2A, is shown in Figure 2B.

The results obtained with six muscles are described here. The dimensions of the muscles and their rest and developed forces at L\textsubscript{max} are given in Table 1. Rest force was assessed by applying a large shortening step to the unstimulated muscle and measuring the drop in force. The contractions were studied at 88-90% L\textsubscript{max} to the unstimulated muscle and measuring the drop in force and velocity were measured (1 millisecond after the completion of the step and 7, 20, and 40 milliseconds after the initiation of the step).

As shown in the records, the force step was completed within 1-2 milliseconds, while velocity continued to change during the entire recording period. The initial rapid shortening has been attributed to series elastic recoil and velocity transients of the contractile element.\textsuperscript{9} In most steps, the subsequent velocity declines progressively without attaining a constant value. As a result, the velocity varies substantially depending on the time of measurement of the step. Figure 2A shows 4 force-velocity curves with times of measurement at 1 millisecond after the completion of the step and at 7, 20, and 40 milliseconds after initiation of the step. Sixteen data points were used to construct each of these curves. The extrapolated V\textsubscript{max} for each point differed by about tenfold. In addition, curves at later times lost their hyperbolic characteristics. This illustrates the importance of measuring velocity instantaneously instead of averaging it over many milliseconds. Ideally, velocity should be measured as soon as the force step is complete, before changes occur. On the other hand, such early velocities may not represent the velocity of the contractile element because of lightly damped series elastic recoil.\textsuperscript{3} In addition, velocity transients,\textsuperscript{9} although small, are likely to have some effect on the measured velocities at early times. In our experiments, the earliest time that these have consistently subsided was about 7 milliseconds after the initiation of the step.\textsuperscript{9} During this time, the muscle would have shortened by no more than 2% L\textsubscript{max}. In the rest of this paper, all the data presented were collected at 7 milliseconds after the initiation of the step. A force-power curve, corresponding to the 7-millisecond force-velocity curve in Figure 2A, is shown in Figure 2B.

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### Table 1. Cat Papillary Muscle Dimensions and Forces

<table>
<thead>
<tr>
<th>Muscle number</th>
<th>L\textsubscript{max} (mm)</th>
<th>Cross-sectional area (mm\textsuperscript{2})</th>
<th>Force developed at L\textsubscript{max} (mN/mm\textsuperscript{2})</th>
<th>Rest force at L\textsubscript{max} (mN/mm\textsuperscript{2})</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5.0</td>
<td>0.95</td>
<td>48</td>
<td>5.4</td>
</tr>
<tr>
<td>2</td>
<td>6.0</td>
<td>0.92</td>
<td>39</td>
<td>6.8</td>
</tr>
<tr>
<td>3</td>
<td>6.4</td>
<td>0.97</td>
<td>37</td>
<td>2.9</td>
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<tr>
<td>4</td>
<td>5.4</td>
<td>0.35</td>
<td>51</td>
<td>4.1</td>
</tr>
<tr>
<td>5</td>
<td>6.0</td>
<td>0.19</td>
<td>37</td>
<td>5.0</td>
</tr>
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<td>6</td>
<td>5.3</td>
<td>0.50</td>
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<td>8.8</td>
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<tr>
<td>Mean</td>
<td></td>
<td>0.64</td>
<td>43.0</td>
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<td></td>
<td>0.22</td>
<td>2.4</td>
<td>0.82</td>
</tr>
</tbody>
</table>

the number of observations. The square root of this number, the standard error, was used to assess the quality of the fit.

### Results

The results obtained with six muscles are described here. The dimensions of the muscles and their rest and developed forces at L\textsubscript{max} are given in Table 1. Rest force was assessed by applying a large shortening step to the unstimulated muscle and measuring the drop in force. The contractions were studied at 88-90% L\textsubscript{max} to minimize the effects of rest force, which averaged less than 4% of the developed force at the length studied. The effects of this relatively low rest force are described in Appendix B. The reference values for normalizing the data are listed in Table 2, together with the times of measurement and the lengths studied. To compare muscles of different abilities, contractile parameters were normalized to values obtained just before the peak of the twitch. As shown, there is no systematic variation in any of the contractile parameters with changes in cross-sectional area.

A typical set of experimental records is shown in Figure 1. The uppermost trace is length, the next is force, and the third is velocity. The points marked by arrows on the record are 1) the 2-millisecond baseline (BAS); 2) the 2 milliseconds of isometric data immediately before the step (PRE); and 3) the times at which force and velocity were measured (1 millisecond after the completion of the step and 7, 20, and 40 milliseconds after the initiation of the step).

As shown in the records, the force step was completed within 1-2 milliseconds, while velocity continued to change during the entire recording period. The initial rapid shortening has been attributed to series elastic recoil and velocity transients of the contractile element.\textsuperscript{9} In most steps, the subsequent velocity declines progressively without attaining a constant value. As a result, the velocity varies substantially depending on the time of measurement of the step. Figure 2A shows 4 force-velocity curves with times of measurement at 1 millisecond after the completion of the step and at 7, 20, and 40 milliseconds after initiation of the step. Sixteen data points were used to construct each of these curves. The extrapolated V\textsubscript{max} for each point differed by about tenfold. In addition, curves at later times lost their hyperbolic characteristics. This illustrates the importance of measuring velocity instantaneously instead of averaging it over many milliseconds. Ideally, velocity should be measured as soon as the force step is complete, before changes occur. On the other hand, such early velocities may not represent the velocity of the contractile element because of lightly damped series elastic recoil.\textsuperscript{3} In addition, velocity transients,\textsuperscript{9} although small, are likely to have some effect on the measured velocities at early times. In our experiments, the earliest time that these have consistently subsided was about 7 milliseconds after the initiation of the step.\textsuperscript{9} During this time, the muscle would have shortened by no more than 2% L\textsubscript{max}. In the rest of this paper, all the data presented were collected at 7 milliseconds after the initiation of the step. A force-power curve, corresponding to the 7-millisecond force-velocity curve in Figure 2A, is shown in Figure 2B.

The results from a total of 45 force-velocity curves are presented here. The data for each curve were fitted to the hyperbolic Hill equation to obtain a mathematical description. The frequency distribution of the standard errors of the fitted curve are plotted in Figure 3. In addition, 11 of the 45 curves are shown individually in Figures 2, 4, and 7. These individual curves are identified by the numbers in the nomogram of Figure 3. This identification makes it possible to compare graphically

<table>
<thead>
<tr>
<th>Muscle number</th>
<th>Length studied (L/L\textsubscript{max})</th>
<th>Force developed at L (mN/mm\textsuperscript{2})</th>
<th>Rest force at L (mN/mm\textsuperscript{2})</th>
<th>Time to peak force (msec)</th>
<th>Time of reference study (msec)</th>
<th>Extraaloped isometric force (mN/mm\textsuperscript{2})</th>
<th>Maximum velocity (L\textsubscript{max}/s)</th>
<th>Maximum power (μW/g)</th>
<th>a/P_o</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.88</td>
<td>34.9</td>
<td>1.12</td>
<td>444</td>
<td>400</td>
<td>37.3</td>
<td>2.63</td>
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<td>0.70</td>
<td>460</td>
<td>400</td>
<td>25.0</td>
<td>2.11</td>
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<tr>
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<td>33.7</td>
<td>1.16</td>
<td>568</td>
<td>550</td>
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<tr>
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<td>18.0</td>
<td>0</td>
<td>620</td>
<td>450</td>
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<td>2.76</td>
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<td>0.24</td>
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</tbody>
</table>

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Changes in the Force-Velocity Relation With Time in the Twitch

Eight force-velocity curves measured at different times in the twitch are shown in Figure 4. Separate curves illustrating the dependence of power on force are also shown. The curves in Figures 4A and 4C were made during the rise of twitch force. The curves in Figures 4B and 4D were made during relaxation, when twitch force was falling. Velocities at all forces rose and fell with twitch force; however, maximum velocity changed to a much smaller extent than velocities at finite loads. The time course of changes of the contractile parameters is shown in Figure 5, where the three parameters of the force-velocity curves in Figure 4 are plotted together with twitch force as a percentage of the reference value (Table 2, muscle 1). At 25% of the time to peak force, maximum velocity had achieved 80% of its full value. At the same time, extrapolated isometric force and maximum power had each achieved approximately 40% of their highest values, and developed force had reached about 25% of its maximum. For all muscles studied at this early time, the average values for the four parameters were 77% for maximum velocity, 44% for maximum power, 44% for extrapolated isometric force, and 22% for developed twitch force.

Force-Velocity Curves in Relating Muscle

During relaxation, the fall of extrapolated isometric force led the fall of twitch force, just as it led the rise of twitch force early in the contraction. Some of the apparent fall was due to a rapid decline, and even reversal, of velocity that occurred in the 7-millisecond period between the onset of isotonic shortening and the
velocity measurements. Some records used to generate the data in Figure 4 are shown in Figure 6. Those in Figures 6A and 6B were made 100 milliseconds after the stimulus, during the rise of force, when force had achieved 24% of its full value. Those in Figures 6C and 6D were made 700 milliseconds after the stimulus, during relaxation, when force had fallen to 42% of its full value. Records 6A and 6C are paired with 6B and 6D to match the relative loads. With heavy relative loads applied early in the twitch, as in Figure 6B, velocity remained relatively constant during the period of recording. In all other cases (Figures 6A, C, and D), velocity fell during the period of recording. The fall was much greater during relaxation. With light loads, shortening nearly stopped during relaxation (Figure 6C), and with heavy loads (Fig 6D), shortening not only stopped but also reversed. With very heavy loads (not shown), the reversal began before the 7-millisecond period of recording so that velocities were negative. Thus, the ability of the relaxing muscle to shorten is impaired, probably because of shortening-induced deactivation. For this reason, data obtained later than the peak of the twitch were not used to describe changes in contractile capability.

Postextrasystolic Potentiation

To obtain a wider range of developed forces, 3 of the muscles (numbers 3, 5, and 6) were studied during postextrasystolic potentiation of the twitch force. Typical force-velocity curves obtained shortly before the peak of twitch force are shown in Figure 7. Twitch force, extrapolated isometric force, and maximum power were all increased nearly twofold by the potentiation. Maximum velocity increased by only about 15%.

Results From All Muscles

To compare the data from all 6 muscles, the values of maximum velocity, maximum power, and extrapolated isometric force for all muscles are plotted as a function of developed twitch force in Figure 8. To normalize for variation among muscles, the values were divided by a reference value obtained just before the time of peak twitch force, as in Figure 5. The reference values are given in Table 2.

The dashed line in each graph represents the value that each parameter would have if it had a one-to-one correspondence with twitch force. The use of potentiated twitches and different times in the twitch permitted a comparison of contractile parameters over a tenfold range of developed force. Maximum velocity varied by less than twofold over this range. A least-squares linear regression (solid line, Figure 8A) to all

![Figure 5](image-url)  
**Figure 5.** Changes in the force-velocity parameters with time. The solid curve indicates the time course of isometric twitch force. The other values are taken from the curves fitted to the data shown in Figure 5. All values, including twitch force, are normalized to reference values measured at 400 milliseconds, just before the time of peak twitch force.

![Figure 6](image-url)  
**Figure 6.** Differences in the time course of isotonic shortening during the twitch. Records A and B were made during the rise of force, records C and D during relaxation. In relaxing muscle, the velocities decreased substantially during the period of recording. In D, shortening stopped by 9 milliseconds, and lengthening restored the muscle to its original length at 36 milliseconds. The three traces in each panel are, from top to bottom, length, velocity, and force, respectively.

![Figure 7](image-url)  
**Figure 7.** Response to postextrasystolic potentiation: All force-velocity measurements were made during the rise of force at 450 milliseconds. Time to peak force 620 milliseconds. Muscle number 5.
Figure 8. Variations in contractile parameters with developed isometric twitch force. All values, including twitch force, are normalized to reference values measured shortly before the time of peak twitch force. Open symbols represent values obtained during the rise of twitch force. Closed symbols represent values obtained during potentiated contractions. Symbols with dot indicate values obtained during relaxation. Potentiated parameters were measured only during the rise of force, not during relaxation. The solid lines were fitted to the maximum power and extrapolated isometric force data for force-velocity curves measured during the rise of force (open symbols) only in B and C. The solid line in A was fitted to the maximum velocity values measured in both potentiated and non-potentiated contractions before the time of peak twitch force.

Discussion

The main conclusion of this study is that the contractile capability of isolated heart muscle, as measured by the force-velocity curves, is never constant; it changes continuously during the twitch. All parameters of the force-velocity curves change with time, but maximum velocity changes to a much lesser extent than maximum power, developed isometric force, or extrapolated isometric force. This finding raises the question of values except those measured during relaxation had a slope of 0.27.

The lines of correspondence in Figures 8B and 8C would, at first glance, appear to give a good general description of the maximum power and extrapolated maximum force data, suggesting that these two parameters varied in proportion to developed force. Closer inspection of the data shows, however, that almost all the values obtained during the rise of force lie above the line of correspondence, and those obtained during relaxation lie below the line. Changes in these values led the changes in twitch force throughout the twitch and correspond most closely to twitch force at the peak of the twitch when the values were changing most slowly. Thus, the line of correspondence gives a good description of the data only near the peak of the twitch when variations are produced by changes in potentiation. To obtain a numerical description of the changes in the two parameters during the rise of twitch force, these data were fitted with a least-squares linear regression (solid lines, Figures 8B and 8C). The slopes and intercepts for the two lines were almost identical, suggesting that maximum power and extrapolated maximum force change together. The correspondence between the two is better seen in Figure 9, where maximum power is plotted against extrapolated isometric force. The slope and intercept of the least-squares regression were 1.05 and 0.02, respectively, showing an almost exact correspondence. The correlation coefficient was 0.92.

Some data were obtained early in the potentiated twitches so that values from potentiated and nonpotentiated beats could be compared at the same level of extrapolated isometric force. As shown in Figure 8, the values for all parameters for potentiated and nonpotentiated twitches overlap in the region where the extrapolated isometric forces are the same.

HILL PARAMETERS. The Hill equation is a rectangular hyperbola and asymptotic to a force asymptote and a velocity asymptote, $a$ and $b$, respectively, in equation 1. As described in Appendix A, these asymptotes can be used to assess the presence of an internal load. Plots of these asymptotes are shown in Figure 10. There is a moderate amount of scatter in the data because these asymptotes are determined by large extrapolations of the fitted curves. The plot of $a$ vs. $P_o$ (Figure 10A) is reasonably well described by a linear regression axis with a slope of 0.52 and an intercept that was 39% of the reference value. The values of $b$, plotted in Figure 10B, show no dependence on isometric force; the correlation coefficient was $-0.18$. 

Discussion

The main conclusion of this study is that the contractile capability of isolated heart muscle, as measured by the force-velocity curves, is never constant; it changes continuously during the twitch. All parameters of the force-velocity curves change with time, but maximum velocity changes to a much lesser extent than maximum power, developed isometric force, or extrapolated isometric force. This finding raises the question of
whether a single parameter can be used to describe the force-velocity capabilities at any instant. Each of the parameters will be considered separately.

Maximum Velocity
As noted, maximum velocity changes much less than the other parameters of the force-velocity curves, so that it is a much less sensitive index of changes than the other parameters of the curves. In addition, because maximum velocity is defined by the intercept of the force-velocity curve with the velocity axis that it approaches tangentially, this parameter is very sensitive to small changes in load. As explained in Appendix A, all of the changes in maximum velocity measured here can be accounted for by a small (about 6% \( P_0 \)) internal load that cannot be measured directly. To the extent that this explanation is correct, maximum velocity of the contractile elements may not change at all. In an earlier analysis, \(^9\) we have shown that much of the decline in velocity with progressive shortening at a constant external load, as illustrated in Figures 1 and 2A, can be accounted for by an internal spring that becomes compressed during shortening. This conclusion that maximum velocity is very sensitive to small changes in load and that there may be small internal loads that cannot be measured directly suggests that changes in maximum velocity may not reliably signal changes in the contractile elements themselves.

Developed Isometric Force
The results of these experiments show that the zero velocity appropriate to the developed isometric force does not lie on the force-velocity curves except at the peak of the twitch, and it, therefore, does not signal changes in these curves. This phenomenon is well known because during an afterloaded contraction, in which the muscle is allowed to shorten as soon as force develops to equal the afterload, the velocity is much higher than would be expected if the contractile elements were near their isometric force level. The common explanation for this finding, dating from Hill’s investigation\(^10\) of active state, is that the contractile elements are moving, even when the overall muscle length is held constant, because the series elastic element length changes with force. Another mechanistic explanation derives from Huxley’s cross-bridge theory of contraction.\(^11\) This theory states that this relatively slow approach to full isometric force is caused by the relatively slow attachment of the force generating cross-bridges. When the muscle is allowed to shorten, however, all of the cross-bridges go into their steady-state cycling rate appropriate to the load within a very short time, so that the velocity appropriate to the load is achieved very rapidly. Undoubtedly both mechanisms are operative in the papillary muscle preparation as it was used here. Regardless of which mechanism predominates, it is clear that developed force lags behind extrapolated isometric force and, thus, doesn’t accurately reflect changes in the force-velocity properties of the preparation.

Extrapolated Isometric Force
This parameter changes as much as any other with changes in the force-velocity properties. As shown in Appendix A, when maximum velocity does not change, it is possible to obtain curves that superimpose by normalizing all forces to the isometric force appropriate to the curves. Thus, extrapolated isometric force is an excellent indicator of changes in the force-veloc-
ity relation. The disadvantage is that, like maximum velocity, it is determined by extrapolation of the curves to an axis that it approaches tangentially and is thus subject to errors in the extrapolation procedure.

**Maximum Power**

The present experiments show that maximum power changes in direct proportion to extrapolated isometric force. It can, therefore, be used in place of isometric force when the latter requires a large extrapolation. Because maximum power is determined by interpolation rather than extrapolation, it is subject to less error. It has some additional advantages in that it is a property that can be compared directly to quantities not measured in isolated muscle. For example, because power has the same dimension as energy rate, maximum power can be compared directly to oxygen uptake or substrate utilization to obtain efficiency in a way that force or velocity cannot.

A major advantage of the maximum power value in isolated muscle is that the values are directly comparable to similar values obtained in the intact ventricle without any geometric assumptions. To compare forces developed by muscles of different sizes, the forces are divided by cross-sectional area. To make a comparison with wall tension in the ventricle, it is necessary to know the ventricular diameter, fiber orientation, and region of the ventricular wall being considered. Similarly, muscle velocities are normalized to muscle length, and comparison with fractional shortening velocities in the ventricle requires that the region of the wall and fiber orientation be specified. By contrast, muscle power is normalized by dividing by (length \(\times\) cross-sectional area), equivalent to muscle volume or muscle mass. Weight-specific ventricular power measured as \([\text{pressure} \times \text{ejection rate}]/\text{muscle weight}\) for the intact ventricle requires no geometric specifications when being compared to weight-specific work rate in isolated muscle measured as \([\text{forces} \times \text{velocity}]/\text{muscle mass}\).

**Relation to Earlier Experiments**

The force-velocity relation in papillary muscles was originally studied by Abbott and Mommaerts\(^ {12}\) and later by Sonnenblick.\(^ {13,14}\) These early studies used afterloaded isotonic contractions in which muscle length was held constant until twitch force rose to a value determined by a preset afterload. When force reached that level, the muscle shortened under a constant isotonic afterload, and velocity was recorded soon after the onset of shortening. Each force-velocity point was determined at a different time in the twitch. The rationale for these experiments was that the muscle's contractile capability was defined by a single force-velocity curve that remained constant throughout the twitch. This rationale was based on experiments in skeletal muscle by Hill,\(^ {18}\) which he interpreted as showing that the "activation" in a muscle rose to a steady level early in a twitch and remained constant until well after the peak of the twitch. In this formulation, Hill postulated that the relatively slow rise of "isometric" force was due to the contractile elements not being isometric. Because the connections between the contractile elements and the apparatus were compliant (i.e., because there were series elastic elements), the contractile elements were shortening during the rise of force, and force was therefore below the expected isometric level. Several different experiments have disproved this hypothesis. Jewell and Wilkie\(^ {15}\) showed that the rise of tetanic force, calculated from the fully activated force-velocity relation and the compliance of series elastic elements, was much more rapid than observed. More recently, Cecchi et al.\(^ {17-19}\) have shown that the rise of tetanic force is not instantaneous when the sarcomeres are held isometric. All of these observations suggest that the major justification for using afterloaded contractions to define force-velocity properties was invalid.

Brutsaert et al.\(^ {10}\) have used very lightly afterloaded contractions to define maximum shortening velocity as a function of muscle length. By loading and unloading the muscle early in the course of shortening, they were able to vary the time in the twitch when the muscle reached a given length. Their plots of velocity vs. length nearly superimposed, even though the time when the muscle reached common length-velocity points differed. From these observations they concluded that there is a "unique force-velocity-length relation . . . independent of time." Our results do not agree with this conclusion. The likely explanation of their results is that maximum velocity tends to rise during the twitch, as shown in Figures 4, 5, and 8, while the process of shortening tends to decrease velocity, as shown in Figures 1 and 2, so that overall coincidence of the velocity length records is a balance between two competing factors. The main points to be derived from the disparity between our results and those of Brutsaert et al. are that the results and conclusions to be drawn from these types of experiments depend very heavily on the way the measurements are made and that failure to consider the multiple factors can lead to very different conclusions.

The series elastic elements caused an additional problem for the afterloaded contractions. Variations in series elastic element length at different afterloads resulted in each force-velocity point being recorded at a different contractile element length. This has not been a severe problem in skeletal muscle, where the technique was originally developed, because the series elastic compliance of skeletal muscle is much less than cardiac muscle and because there is a range of length where isometric force changes little with changes in length. The increased series element compliance in heart muscles occurs in large part because the muscles are much shorter, about one-sixth the length of skeletal muscle. If the absolute value of the compliance were the same in both preparations, the contractile elements would shorten about six times more in cardiac muscle than in skeletal muscle for a given force change. In the early studies, where the muscles were tied with thread, the contractile elements shortened substantially when
full isometric force was developed. In more recent studies, such as the present one, where the muscles are held by metal clips or clamps, the series elastic extension is about as much, so that the contractile elements shorten by 4–6% as twitch force develops. This is still a substantial amount when compared with the short working range of papillary muscle. The isometric force declines from its maximum, at $L_{\text{max}}$, to zero when length decreases to 75% of $L_{\text{max}}$. There are two important implications for the afterloaded studies being carried out over such a large extent of the functioning range of the muscle. First, the appropriate isometric force was different for each load and varied by as much as a factor of two. Second, the early experiments were frequently done at lengths where there was force borne by “parallel elastic elements” at rest. As the contractile elements shortened, some fraction of this load was transferred to them, and their load was not constant. The present experiments were carried out at a short length where there was very little rest force in the muscle. The rest force was not negligible, however, and the magnitude of the effect of a transfer of the load during the rise of force is calculated in Appendix B. In addition, the shortening that occurs during the time between the release and the velocity measurement is different at different loads and different times in the twitch. As explained in Appendix B, the effects of this shortening on the conclusions are very small.

The early studies of papillary muscle were criticized for all of the reasons described above. Quantitative estimates of the errors arising from each of these sources were published first by Hefner and Bowen and subsequently by Pollack. Jewell and Blinks pointed out that these problems could be avoided if the mechanical properties of the muscle were defined by force-velocity curves measured immediately after quick releases from the isometric state at different times in the twitch. The muscles would begin isotonic shortening at the same contractile element length and at the same time in the twitch for all loads. Experiments of this sort using lever systems produce large oscillations following the releases, and there is some evidence that these oscillations inactivate the muscle. An additional difficulty with the oscillations is that they make quantitative estimates of velocity very difficult. If sufficient time is allowed to elapse for the oscillations to die away, the muscles will have shortened to such an extent that the advantage of an “instantaneous” measurement described by Jewell and Blinks will not be obtained. Proper measurements, therefore, require the use of a critically clamped system that can change loads within a few milliseconds. Our earlier studies have shown, however, that the measurements cannot be made immediately after the isometric load is achieved because the velocity measurements are contaminated by some slow shortening of the lightly damped series elastic elements and because velocity transients obscure the steady state. Our earlier studies showed that the earliest time that an accurate measurement of the steady-state contractile element velocity can be made is 7 milliseconds. Even at this early time, it is apparent that velocity has declined somewhat as the result of the prior shortening, so that velocities are somewhat less than a true instantaneous measure would give. Since the decline in velocity is greatest at the lowest loads, the uncertainties created by these changes are greater for maximum velocity than other parameters of the curves.

Appendix A

Internal Load

Recent evidence in skinned skeletal muscle fibers has shown that maximum velocity does not change with changes in the level of activating calcium. The controversy surrounding this point (see review by Dolin and Ford) has largely been resolved. In addition, force-velocity curves obtained at two different calcium levels can be made to superimpose when the forces are scaled by a constant factor, as in Figure 11C. To the extent that the changes in the force-velocity relation seen in the present experiments are caused by changes in the level of calcium activation, changes in maximum velocity would not be expected.

The major difference between this expectation and our experimental results is that the experimental curves do not have a common maximum velocity. There are at least three possible explanations for this difference: 1) the changes in the force-velocity curves are not due solely to changes in calcium activation; 2) the effect of activating calcium may be different in papillary and skeletal muscle; and 3) there might be an internal load such that the contractile elements cannot be fully unloaded and maximum velocity cannot be achieved.

The analysis presented here is directed at this third possibility. It attempts to define whether the results can be accounted for by an internal load and, if so, how large the load would have to be. The basis for this analysis is shown graphically in Figure 11.

The two force-velocity curves in Figure 11A do not have the same measured maximum velocity at zero external load and so cannot be made to superimpose by scaling the external isotonic forces to the externally developed isometric force (Figure 11B). If the total force on the muscle is composed of the external load plus some fixed internal load, the curves can be made to superimpose if the total isotonic force (and not just the external force) is scaled to the total isometric force (Figure 11C). The available experimental techniques do not permit a direct measurement of the internal load, but if the differences in maximum velocity are due entirely to an internal load, the size of the load can be inferred from the fitted parameters of the force-velocity curves.

The force-velocity curves are rectangular hyperbolas asymptotic to values of force $(a)$ and velocity $(b)$ lying respectively to the left and below the origin. To make the curves superimpose in Figure 11C, only the values of force were scaled. The scaling did not alter the velocity asymptote $b$. Since the curves are identical after the scaling, the value of $b$ for both curves must be identical. In the presence of an internal load, which alters only force, the velocity asymptote $b$ is not affect-
A. ABSOLUTE FORCE

B. NORMALIZED TO EXTERNAL P₀

C. NORMALIZED TO TOTAL P₀

Figure 11. Effect of an internal load. Panel A shows the effect of a fixed internal load on force-velocity curves at two levels of activation. The measured $V_{\text{max}}$ for both are diminished and different, even though the true $V_{\text{max}}$ for the contractile elements is the same for both curves. Panel B shows that the curves cannot be made to superimpose by scaling the forces to the externally developed isometric force while Panel C shows that the curves can be made to superimpose by scaling the forces to the total load on the contractile elements.

ed. Therefore, a condition for the changes in $V_{\text{max}}$ to be due entirely to an internal load is that the values of $b$ remain constant. In contrast, asymptote $a$ was scaled in precisely the same manner as the rest of the force values so that the ratio $a/P₀$ was the same for the two curves. In the presence of an internal load ($i$), the true force asymptote for the contractile elements is equal to the apparent force asymptote, minus the internal load, $i$. In this case, the value $(a - i)/(P₀ + i)$ should equal a constant, $k$. A plot of $a$ vs. $P₀$ obtained for different curves should then yield a straight line with slope $k$ and intercept $(k + 1) \cdot i$. The value of the internal load $i$ would then be determined as the intercept divided by $(k + 1)$.

The data in Figure 10 show that, within experimental error, $b$ is constant, fulfilling the first condition for superimposing the curve. The plot of $a$ vs. $P₀$ is reasonably linear with a slope of 0.52 and an intercept of 39% of the reference value. The reference value in Table 2 is 0.23 $P₀$, so that the intercept has the value of 0.09 $P₀$ (i.e., 0.23 $P₀ \times 0.39$). The internal load is, therefore, 0.09 divided by 1.0 plus the slope (1.52 = 1 + 0.52) or about 0.06 $P₀$.

These considerations suggest that all of the changes in maximum velocity can be explained by an internal load equivalent to 6% of peak force in the nonpotentiated contractions. They do not prove the existence of such an internal load, but they do show that it is not necessary to postulate a change in contractile element maximum velocity to account for the observed changes in muscle maximum velocity.

Appendix B

Effects of Rest Tension

Although the tension on the muscles at rest was small, it was not negligible. Table 2 shows that rest tension was about 4% of peak twitch force. This is equivalent to 20% of developed force at the earliest time studied when developed force was one-fifth of the peak twitch force. The purpose of this appendix is to show that the effect of this rest tension on the conclusions about maximum velocity would have been small.

Since cardiac muscles can bear a load at rest, the contractile elements must be in parallel with a parallel elastic element. Our previous experiments showed that the arrangement of the viscoelastic elements is best represented by the Maxwell model. In this configuration, the contractile element is directly in parallel with the parallel element, and this pair is in series with the series elastic element. With this arrangement, the contractile element will shorten even if the ends of the muscle are held isometric. As twitch force develops, the parallel element shortens and bears less load. This load is transferred on to the contractile element. The issue to be discussed is the magnitude of the load transfer and its potential influence on the results. The quantity to be calculated is not the total load transferred but the increase in transferred load between the earliest time studied and the peak of the twitch.

Results from our previous experiments, as well as those of others, showed that the series and parallel
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elements can be described as exponential equations of the form
\[ T = T_0e^{(L-L_0)/k} - T_o \]  
(B1)

where \( T \) is the force at any length (\( L \)), \( T_o \) is the tension at reference length (\( L_o \)), \( T_0 \) is a force asymptote, and \( k \) is a length constant. In our experiments, the length constants were 0.05 and 0.02 \( L_{\text{max}} \) for the parallel and series spring, respectively, and \( T_o \) was negligible.

These values can be used to calculate the transfer of load between the two elements. At the earliest times studied, the developed force increased from 20 to 100%, the series elastic element would be stretched by 1.6 length constants or about 0.03 \( L_{\text{max}} \). Both the contractile and the parallel elements will thus be about 0.03 \( L_{\text{max}} \) shorter at the peak of the twitch than at the earliest times studied, and the force-velocity curves obtained at the peak of contraction should be corrected for the greater load transferred to the contractile elements at this shorter length. Similarly, the 3% change in \( L_{\text{max}} \) corresponds to the 0.6 length constant of the parallel elastic element. When it is shortened by this amount, 55% of the load on the parallel elastic elements is transferred to the contractile elements during the increase in tension from 20 to 100% of isometric force. The rest tension on the muscles at the lengths studied here averaged a little less than 4% of full isometric force. Some of this rest force was transferred to the contractile elements as developed force rose from 0 to 20% of full twitch value and so is common to all force-velocity curves and, therefore, need not be corrected for in making comparisons. Of the remaining amount, 55% (something less than 2% of the full isometric force) must be added to the measured loads at the peak of the twitch, when the force-velocity curves obtained at the time of peak force are compared with those measured early in the twitch. Substituting the value of 0.23 for \( kP \gamma \) (Table 2) in the force-velocity relation (equations 2 and 3) increases the extrapolated maximum velocity by about 12%, increasing slightly the difference between the maximum velocity at the two times.

A second transfer of load occurs after the release when the whole muscle shortens. During the 5–6 milliseconds between the completion of the step and the velocity measurement, the contractile elements could shorten as much as 0.01–0.015 \( L_{\text{max}} \), at the highest velocities (2.5 \( L_{\text{max}}/s \)). This is the maximum length difference for data points on the same curve at different loads and the same time in the twitch. The differences between velocities obtained at the same relative loads but different times in the twitch would be much less than this. For example, at the earliest time studied, the maximum velocity was 23% less than that at the peak of the twitch, so that the difference in the contractile element length shortening between the two times is 0.0023–0.0035 \( L_{\text{max}}/s \) \((0.23 \times (0.01–0.015))\). This difference is an order of magnitude smaller than the length difference caused by the isometric tension difference at different times. The main point of these calculations is that the effect of rest tension on maximum velocity is relatively small, when the muscles are studied at these short lengths.

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KEY WORDS: papillary muscle • force-velocity curves • isometric force • maximum power • maximum velocity
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