Mechanical Control of the
Rising Phase of Contraction of Frog
Skeletal and Cardiac Muscle

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ABSTRACT The effect of shortening on contractile activity was studied in experiments in which shortening during the rising phase of an isotonic contraction was suddenly stopped. At the same muscle length and the same time after stimulation the rise in tension was much faster, if preceded by shortening, than during an isometric contraction, demonstrating an increase in contractile activity. In this experiment the rate of tension rise determined in various phases of contraction was proportional to the rate of isotonic shortening at the same time after stimulation. Therefore, the time course of the isotonic rising phase could be derived from the tension rise after shortening. The rate of isotonic shortening was found to be unrelated to the tension generated at various lengths and to correspond closely to the activation process induced by shortening. The length response explains differences between isotonic and isometric contractions with regard to energy release (Fenn effect) and time relations. These results extend previous work which showed that shortening during later phases of a twitch prolongs, while lengthening abbreviates contraction. Thus the length responses, which have been called shortening activation and lengthening deactivation, control activity throughout an isotonic twitch.

INTRODUCTION
In the frog heart a diminution of the load during an isotonic twitch prolongs and an increase in load abbreviates twitch (2). These opposing effects have been called, respectively, shortening activation and lengthening deactivation. The same results were obtained for frog skeletal and mammalian cardiac muscle (unpublished). However, mechanical interventions changed the duration of activity only if applied during the late part of the rising phase and during relaxation. In the work presented here we examined the question of whether changes in length influence contractile activity also during the earlier part of the twitch. For this purpose, shortening in a contraction which started isotonically was suddenly stopped and the subsequent rise in tension was compared with that during an isometric contraction at the same muscle length and the same time after stimulation. The rate of tension rise was used as a measure of the state of activity of the muscle. These and other experiments showed that shortening increases not only the duration, but also the strength of contractile activity.
This result is in sharp conflict with generally accepted views, according to which shortening as well as lengthening has a relaxing effect (see reference 7, p. 172). This contention is based mainly on two types of observations. It was found that after release during the rising phase of an isometric twitch, tension did not rise as high as during an isometric control twitch at the shorter length (6, 8, 11), an effect that has been interpreted as a weakening of contractile activity. However, it seems that a complete recovery of tension could hardly be expected after the loss of mechanical energy during shortening, because the muscle would have to make up for this loss at a time when activity was diminishing in a normal twitch. Moreover, records of this type of experiment (8, 12) show that the tension rise after the release was faster and larger than in a control twitch during the same phase of the twitch, observations which argue more for activation than the reverse.

Another argument for a relaxing action of shortening is based on the observation of Jewell and Wilkie (10) that the isometric phase of relaxation of an afterloaded twitch starts earlier and is faster than during an isometric twitch, the more so, the larger the previous shortening. It has been assumed (4–8, 11) that these effects are due to the previous shortening. However, it has been shown by Jewell and Wilkie that acceleration of relaxation is due not to shortening but to the elongation of the muscle during the isotonic phase of relaxation.

The early beginning of the isometric phase of relaxation also is not due to the previous shortening per se. It is fully explained by the rapidity of isotonic relaxation. This interpretation is confirmed by the fact that the beginning is actually delayed with large preloads, as shown by graphs of previous authors (4, 12). This is so because isometric relaxation then begins before the rapid phase of isotonic relaxation. As pointed out previously (2), the early onset and acceleration of isometric relaxation during afterloaded twitches can be explained as being due to lengthening deactivation. The mistaken conclusion that these phenomena show deactivation by shortening is due to failure to recognize that transient length changes involve two changes in opposite directions, which have to be considered separately. In work on skeletal and cardiac muscle it has been shown that the two changes produce separate and opposite responses which may partly cancel each other and that the direction of the response is determined by the last of the length changes (unpublished observations). Therefore, the effect of transient shortening is due not to shortening but to lengthening.

**MATERIALS AND METHODS**

The sartorius of very small frogs and rings of the frog ventricle, dissected as described previously (1), were used. The muscles were attached vertically by a thin copper wire to a lever above the muscle. The lever was 7 cm long and was made of thin aluminum sheet. For stimulation Pt electrodes were used, the cathode being placed near the middle of the muscle for the sartorius, at one end for the ventricle.

The lever was attached to a torque motor, as described previously (2). The motor was improved by diminishing the mass of the coil by more than 95%. The force acting on the muscle was monitored by recording the current through the torque motor. The force could be changed during a contraction by a digital pulse generator (W-P Instruments). Movements of the lever reached 90% deflection in 10 ms or less, depending on
the state of the muscle. For recording movements a photoelectric transducer, or a
displacement transducer based on absorption of Eddy current (Kaman Sciences Corp.,
Colorado Springs, Colo.), was used. Both types of transducers were highly linear. To
record isometrically, a rod attached to a force transducer was placed below the muscle
lever near the attachment of the muscle. The compliance of the system was 5 μm/g. For
recording, a storage oscilloscope and a Polaroid camera were used.

In the experiments reported the starting load or resting tension was varied between
5% and 30% of maximum twitch tension without changing the nature of the results. To
obtain uniform twitches, supermaximal stimuli were applied twice a minute. Tetani
were produced by stimulating for 0.3 s at a frequency of 25 Hz. Their magnitude
usually dropped less than 1% in 10 min if they were repeated once a minute.

The magnitude of the effects reported, except for the staircase, was very uniform.
Each type of experiment was carried out with more than 10 preparations and repeated
several times with each muscle. The physiological solution used contained in millimoles
per liter: NaCl 113; KCl 2.5; CaCl₂ 1.5; Na-acetate 2; Na-phosphate buffer (pH 7.2) 2. It
was bubbled with O₂. The temperature was 1°C.

RESULTS

Isotonic-Isometric Contractions

Experiments designed to study the question of whether a length change during
the rising phase of a contraction alters contractile activity are based on the
following consideration. If such an alteration is produced and if it persists after
shortening is stopped, the steepness of tension rise should be different from
that during a purely isometric contraction, provided the comparison is made at
the same length and the same time after stimulation. The following experiment
was designed to study this question. A rod connected to a force transducer was
placed below the lever and adjusted so that the load was fully supported
without stretching the muscle. An isometric contraction was then recorded.
Before each of the following contractions the load was increased, thereby
extending the muscle and allowing the muscle to shorten various distances
before the contraction became isometric. Shortening always stopped at the
same length. Changes in length and tension were recorded.

Fig. 1 clearly shows that the tension rise was steeper, if preceded by
shortening, than was the corresponding phase of an isometric contraction of
cardiac and skeletal muscle. In the graphs the rates of tension rise with and
without previous shortening and isotonic shortening were plotted against time.
In some phases of contraction the tension rise after shortening was several
times faster than during an isometric contraction at the same length and the
same time after stimulation. It is also important that the rate of tension rise was
increased during the whole rising phase, showing that the activating effect of
shortening had a long duration.

There were characteristic differences, between different types of muscles in
the effects of stopping shortening. During twitches of the sartorius the rate of
tension rise after shortening was the same as during a large part of the rising
phase (Fig. 1 B). During a tetanus the rate was constant at first, but later
became larger (Fig. 1 D). In the ventricle the rate first increased then decreased.
These differences are significant because they are related to differences in the
time course of isotonic contraction. The first part of the rising phase was S-shaped in the ventricle. In the sartorius, shortening became linear 50 ms after the stimulus during a twitch, but the linear range varied from 50% to 80% of total shortening in different muscles. During repetitive stimulation the slope of the rising phase was exactly the same as during a twitch and, at small loads, the

![Graphs A, C, and E superimposed. Upper family of curves: length. Top line is length at which shortening stopped. Lower family: tension developed after shortening stopped; on extreme left, a purely isometric contraction. A, twitches of sartorius; loads ranged from 80 to 700 g force (gf) cm\(^{-2}\). C, brief tetani of sartorius, loads from 60 to 450 gf, cm\(^{-2}\). E, twitches of ventricle, loads from 0.6 to 4 g. Calibration for A and C on left, tension in 1 kgf-cm\(^{-2}\); for E, 5 gf. Calibration on right, length in millimeters. Graphs B, D, and F were obtained from records on left. Circles: rate of tension rise after shortening stopped. Triangles: rate of tension rise during isometric contraction at the same time after stimulation. Interrupted line: isotonic shortening at intermediate load. Ordinate of graphs on left: rate of tension rise in kgf-cm\(^{-2}\)-s\(^{-1}\) for B and D; gf-s\(^{-1}\) for F; on right: length in mm. Time in seconds.

Figure 1. Isotonic-isometric contractions in which the load varied but shortening stopped at the same length. In records A, C, and E several contractions were superimposed. Upper family of curves: length. Top line is length at which shortening stopped. Lower family: tension developed after shortening stopped; on extreme left, a purely isometric contraction. A, twitches of sartorius; loads ranged from 80 to 700 g force (gf) cm\(^{-2}\). C, brief tetani of sartorius, loads from 60 to 450 gf, cm\(^{-2}\). E, twitches of ventricle, loads from 0.6 to 4 g. Calibration for A and C on left, tension in 1 kgf-cm\(^{-2}\); for E, 5 gf. Calibration on right, length in millimeters. Graphs B, D, and F were obtained from records on left. Circles: rate of tension rise after shortening stopped. Triangles: rate of tension rise during isometric contraction at the same time after stimulation. Interrupted line: isotonic shortening at intermediate load. Ordinate of graphs on left: rate of tension rise in kgf-cm\(^{-2}\)-s\(^{-1}\) for B and D; gf-s\(^{-1}\) for F; on right: length in mm. Time in seconds.
linear range then was further extended. However, at large loads the rate of shortening later accelerated until about 80% of maximal shortening was reached, as illustrated in Figs. 1 and 2. The fact that the slope of the rising phase is not increased by repetitive stimulation confirms the generally accepted view that the amount of Ca released in skeletal muscle fibers saturates the contractile mechanism. This argues against the assumption that shortening activation is due to release of Ca.

In the experiment illustrated in Fig. 1 the comparison between the rate of tension rise after shortening and the time course of isotonic contraction was complicated by the fact that the load was different in successive twitches. Therefore, in another type of experiment the rod attached to the force transducer was at first adjusted as in the previous experiment and an isometric contraction was recorded, but before each subsequent contraction the rod was lowered while the load remained unchanged, so that again the muscle could...
shorten various distances before the contraction became isometric (Fig. 2). To determine the relation between the rate of tension rise after shortening and the rate of isotonic shortening, the ratio of these values was plotted against time in the graphs of Fig. 2. Within the limits of accuracy of the measurements this ratio was constant in the ventricle during the whole, and in the sartorius during most, of the rising phase. Thus the rate of tension rise after shortening was generally proportional to the previous rate of shortening.

In another modification of these experiments, contractions were almost entirely isometric but isotonic shortening was permitted in various phases for a very short time. Shortening by less than 0.5% accelerated the subsequent rise in tension.

The magnitude of shortening activation can also be expressed quantitatively by adding the tension which would have been produced under isometric conditions during the period of shortening to the tension produced later after movement was stopped and comparing this sum with the tension developed in an isometric contraction. This sum was 45–53% larger in twitches of the sartorius, 21–30% larger in the ventricle, than the peak tension during isometric twitches if determined shortly after the point of inflexion of the isometric twitch.

Effect of Passive Changes in Length

By changing the load during a twitch the effect of shortening as well as lengthening can be determined. In the experiment illustrated in Fig. 3, three twitches of the ventricle were superimposed: an experimental twitch during which the load was increased or decreased, and twitches at the low and high loads. In this way the shortening after the change in load could be compared with that during a control at the same load during the same time. After diminishing the load, shortening was at first faster than during the control with the lower load, but became later more nearly parallel. The amount of shortening after the change in load was 15% larger than in the control at the same load and during the same time. An increase in load had the opposite effect. These observations confirm that shortening increases contractile activity and show, furthermore, that lengthening has the opposite effect. In addition to these effects, diminution of the load late during the rising phase prolonged, and increase of the load during this phase abbreviated the twitch as reported previously (2).

Staircase

Ritchie and Wilkie (13) previously observed that the staircase effect in the sartorius is larger for auxotonic than isometric twitches. This difference was still larger if isotonic and isometric twitches were compared. After a rest period of 1 h the size and duration of successive isotonic twitches sometimes increased more than 50%, but the slope of the rising phase remained exactly constant in the sartorius (Fig. 4). This is important because it shows that the increase in response was entirely due to a prolongation of activity. In cardiac muscle, on the contrary, the rising phase became steeper under the same conditions. This difference undoubtedly reflects the fact that during the staircase internal Ca increases in the heart (14), not in the skeletal muscle (15).
DISCUSSION

Role of Length Responses in Muscle Mechanics

The results described above show that after a period of shortening under otherwise identical conditions, the rise of tension is faster than in a purely isometric contraction. This is not a momentary effect, but lasts during the whole rising phase. Evidence has also been presented that passive extension during the rising phase of an isotonic twitch slows shortening and that passive shortening has the opposite effect. These results are an extension of previous studies, which have shown that passive shortening during later phases of a twitch prolongs, and passive extension abbreviates, the isotonic twitch of cardiac and skeletal muscles (reference 2 and unpublished observations). These responses, which have been called, respectively, shortening activation and lengthening deactivation, evidently control mechanical activity throughout the isotonic twitch.

The length responses described explain the large differences in the time course of the isotonic and isometric twitches. That these differences are not simply due to physical conditions is evident from the observations on the
staircase effect described above, which show that activity during the rising phase lasts longer in the isotonic than in the isometric twitch. The prolongation of activity must be assumed to be caused by shortening activation, which acts as positive feedback during the rising phase. Lengthening deactivating similarly produces positive feedback during relaxation and therefore explains the rapidity of isotonic relaxation.

The discovery of the length responses may clarify other aspects of muscle mechanics. Jewell and Wilkie (9) have calculated the rise in tension from the force-velocity and load-extension curves on the basis of a model in which the contractile elements are in series with an elastic element. It was found that the rise in tension during a tetanic contraction was much slower than predicted from the model. This discrepancy can be explained by shortening activation which comes into play in the measurement of shortening velocity. This factor also explains that the rise in tension is faster after release than at the beginning of the isometric contraction.

The velocity of isotonic shortening and the rate of tension rise after shortening directly depend on the strength of contractile activity. Therefore, it seems reasonable to expect that these values, determined at the same time, are proportional to each other in different phases of a contraction. It has been shown above that this is true for most parts of the rising phase (Fig. 2). Therefore, the time course of isotonic shortening can be determined by integration from tension records such as those in Fig. 2 A. Specifically, the observation that in the sartorius the rate of tension rise after shortening is constant at the beginning of a twitch explains the linearity of shortening during this time. During tetani, shortening may accelerate after a linear start. This corresponds to the increase in the rate of tension rise after shortening in the second half of the rising phase (Fig. 2 C). Finally, in cardiac muscle this rate first rises, then falls, in agreement with the S shape of the rising phase (Fig. 2 D).

The linearity of the rising phase of the isotonic twitch of the sartorius raises an important question. The linear range may extend over 15% of muscle length during a twitch, and more than 20% during a tetanus. This range must be expected to include part of the ascending and descending branches of the active length-tension diagram, an assumption which has been verified experimentally. Therefore, overlap of filaments is not important in the control of isotonic shortening; the most important factor evidently is shortening activation.

Significance of Length Responses for Energetics

The finding that at the same length and the same time after stimulation tension rises much faster in an isotonic-isometric contraction than during a purely isometric contraction can only signify that metabolic activity is increased by shortening. This conclusion agrees well with the energetics of contraction, specifically, the well-known difference in heat production between isotonic and isometric twitches and, more generally, with shortening heat. In fact, shortening activation and shortening heat should be considered to be two aspects of the same phenomenon.

Nature of Length Responses

Length responses have been demonstrated most directly during contractures of
cardiac muscle (1, 3). Under appropriate conditions shortening activation and
lengthening deactivation can be observed under these conditions, but slow
responses of a different character can also be obtained. It is particularly
important that extension and shortening always produce opposite effects as in
normal muscles. This result, the delay in lengthening deactivation, and the
long duration of all the effects observed so far preclude a simple mechanical
explanation of the length responses. It is also significant that such responses
can be obtained in muscles immersed in isosmotic potassium solutions and,
therefore, must be assumed to be due to an intracellular mechanism. As
pointed out above, it is unlikely that the shortening activation is due to release
of Ca.

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REFERENCES

1. Bozler, E. 1972. Feedback in the contractile mechanism of the frog heart. J. Gen.
Physiol. 60:239–247.
2. Bozler, E. 1975. Mechanical control of the time-course of contraction of the frog
heart. J. Gen. Physiol. 65:329–344.
3. Bozler, E., and J. F. Delahayes. 1973. Mechanical and electrical oscillations in
cardiac muscle of the turtle. J. Gen. Physiol. 62:523–538.
4. Brady, A. J. 1965. Time and displacement dependence of cardiac contractility:
problems in defining the active state and force velocity relations. Fed. Proc.
24:1410–1420.
5. Brady, A. J. 1972. Mechanics of the myocardium. In The Mammalian Myocardium.
G. A. Langer and A. J. Brady, editors. John Wiley & Sons, New York.
6. Briden, K. L., and N. R. Alpert. 1972. The effect of shortening on the time course
of active state decay. J. Gen. Physiol. 60:202–220.
7. Brutserd, D. L. 1974. The force velocity-length-time interaction of cardiac muscle.
Physiological Basis of Starling’s Law of the Heart. Ciba Foundation, London.
8. Edman, K. A. P. 1975. Mechanical deactivation induced by active shortening in
isolated muscle fibers of the frog. J. Physiol. (Lond.). 246:255–275.
9. Jewell, B. R., and D. R. Wilkie. 1958. An analysis of the mechanical components
in muscle. J. Physiol. (Lond.). 143:513–540.
10. Jewell, B. R., and D. R. Wilkie. 1960. The mechanical properties of relaxing
muscle. J. Physiol. (Lond.). 152:30–47.
11. Julian, F. J., and R. L. Moss. 1976. The concept of active state in striated muscle.
Circ. Res. 38:53–59.
12. Kaufmann, R. L., R. M. Bayer, and C. Harnasch. 1972. Autoregulation of
contractility in the myocardial cell. Pfluegers Arch. Eur. J. Physiol. 332:96–116.
13. Ritchie, J. M., and D. R. Wilkie. 1955. The effect of previous stimulation on the
active state of muscle. J. Physiol. (Lond.). 130:488–496.
14. Sands, S. D., and S. Winegrad. 1970. Treppe and total calcium content of the frog
ventricle. Am. J. Physiol. 218:908–910.
15. Winegrad, S. 1970. The intracellular site of Ca activation of contraction in frog
skeletal muscle. J. Gen. Physiol. 55:77–88.