

Energetics of Shortening Muscles in Twitches and Tetanic Contractions

II. Force-Determined Shortening Heat

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ABSTRACT The extra heat liberation accompanying muscular shortening, the force-determined shortening heat, is defined as the difference between the heat produced when shortening occurs and that produced in an isometric contraction developing the same amount of force and performing the same amount of internal work. Based on this definition, the initial energy production in twitches and tetanic contractions (E) is given by

$$E = A + f(P, t) + \alpha_F x + W,$$

where A is the activation heat, $f(P, t)$, the tension-related heat (a heat production associated with the development and maintenance of tension), $\alpha_F x$, the force-determined shortening heat, and W , the external work. It is demonstrated that this equation accurately accounts for the time-course of heat evolution and the total initial energy production in both twitches and tetani at 0°C. The force-determined shortening heat is liberated, during shortening, in direct proportion to (a) the distance shortened, and (b) the force against which shortening occurs. The normalized value of the force-determined shortening heat coefficient, α_F/P_o , is the same in both the twitch and the tetanus. Finally, this formulation of the muscle's energy production also accounts for the total energy production in afterload isotonic twitches at 20°C, where a Fenn effect is not demonstrable.

INTRODUCTION

In delineating the factors which determine or modify the energy usage by contracting muscle, the aim is to find a relationship which (a) accounts for the total energy liberated by the muscle as a function of load and other mechanical variables, (b) accounts for the time-course of the energy liberation, and (c) is

internally consistent under various circumstances such as changes in stimulus pattern or temperature. Such a formulation would furnish a thermodynamic reference to which theories of muscular contraction and its component processes must conform.

Historically, the problem has been dominated by the investigations of Fenn (1923, 1924) and Hill (1938). Hill's formulation for the heat production in a tetanus at 0°C (Hill, 1964 *a*) is accurate with regard to both the time course and the total amount of heat liberated (Aubert and Lebacqz, 1971; Homsher and Rall, 1973); however, the application of the concept of Hill's shortening heat to the twitch (Hill, 1949, 1964 *b*) results in inconsistency (Homsher and Rall, 1973). Likewise, Fenn's formulation (1923) is accurate for the total initial energy liberated in a twitch at 0°C, but it does not account for the time course of the energy liberation nor does it apply to isotonic twitches at higher temperatures.

The formulation should also correspond to functional distinctions. In skeletal muscles, excitation elicits the activity of two systems utilizing energy, the sarcoplasmic reticulum which splits ATP as the driving reaction for the calcium cycle, and the myofibrils which develop force and perform work. The former has been equated with the activation heat (Homsher et al., 1972; and Smith, 1972) and is accepted to be a constant term under usual conditions of activity. Thus, it is in the myofibrillar events that variable energy liberation occurs. The thick and thin filaments, upon interaction, form an enzyme system which hydrolyzes ATP. Heat production and chemical change show this to take place in the isometric situation. As the degree of interdigitation of A and I filaments is reduced by stretch, and thus in effect the enzyme concentration is diminished, the energy liberation is reduced in proportion (Homsher et al., 1972; Smith, 1972). Thus, the development and maintenance of tension per se require an energy expenditure. Variability of the total energy turnover results, apparently, from the variation in force development and the degree to which shortening occurs and work is performed. It is these relationships we seek to formulate.

In Hill's (1938) original definition of the shortening heat, the myothermal base line against which the shortening heat production was measured was that of an isometric contraction at the *length* to which the muscle shortened. In the interpretation of this investigation, we have assumed that the development and maintenance of *tension* require an expenditure of energy which is determined by that tension whether the muscle is shortening or isometric. Accordingly, we have redefined a *force-determined shortening heat* (SHF) as *the difference between the heat produced when shortening occurs and that produced in an isometric contraction which develops the same peak force and performs the same amount of internal work*. To avoid confusion with Hill's usage of the term "shortening heat" (SH), we shall speak of the force-determined shortening

heat (SHF) and denote its coefficient as α_F . On this basis, the energy liberation (E) by a contracting muscle is given as

$$E = A + f(P, t) + \alpha_F x + W, \quad (1)$$

in which $A + f(P, t)$ is the isometric heat production of a muscle developing a peak force P (composed of the activation heat A and the tension-related heat $f(P, t)$ [Homsher et al., 1972]), α_F , the force-determined shortening heat coefficient, x , the distance shortened, and W , the external work performed. In our practical use of the equation, internal work is, operationally, included in $f(P, t)$. Eq. 1 is similar to a formulation previously suggested by Mommaerts (1969).

It will be shown that our Eq. 1 (*a*) accounts for both the magnitude and time-course of energy liberation in both the twitch and tetanus, (*b*) is internally consistent with regard to the value of α_F in both situations, and (*c*) can account for the modification of the Fenn effect in twitches at elevated temperatures.

METHODS AND MATERIALS

The methods and materials employed in this study were the same as previously described (Homsher et al., 1972; Homsher and Rall, 1973).

RESULTS

Time-Course and Amount of SHF Produced in Afterloaded Isotonic Twitches

The first series of experiments were designed to learn whether or not there is an SHF production in an isotonic twitch, whether SHF is liberated in proportion to the distance shortened, and whether the SHF liberated during shortening is equal to the net SHF observed when relaxation is complete. By definition SHF is the difference between the heat produced by a muscle shortening against a force P , and that produced by an isometric contraction which develops a peak force equal to P . Therefore, experiments were performed in which the heat produced during an afterloaded isotonic twitch was compared to the heat produced in an isometric twitch at such a length beyond l_0 that the maximum isometric force equaled the force exerted by the afterload. In these experiments four muscle pairs were allowed to contract and relax against various afterloads. In addition, three pairs of muscles contracted against afterloads but, with the cessation of shortening, the afterload was caught and prevented from stretching the muscle back to its initial length.

Fig. 1 contains heat and displacement recordings of afterloaded isotonic twitches in which the afterload is prevented from dissipating its stored potential energy into the muscle as heat. Superimposed on the isotonic heat recordings (h_s) are the isometric heat recordings (h_i) which served as the base

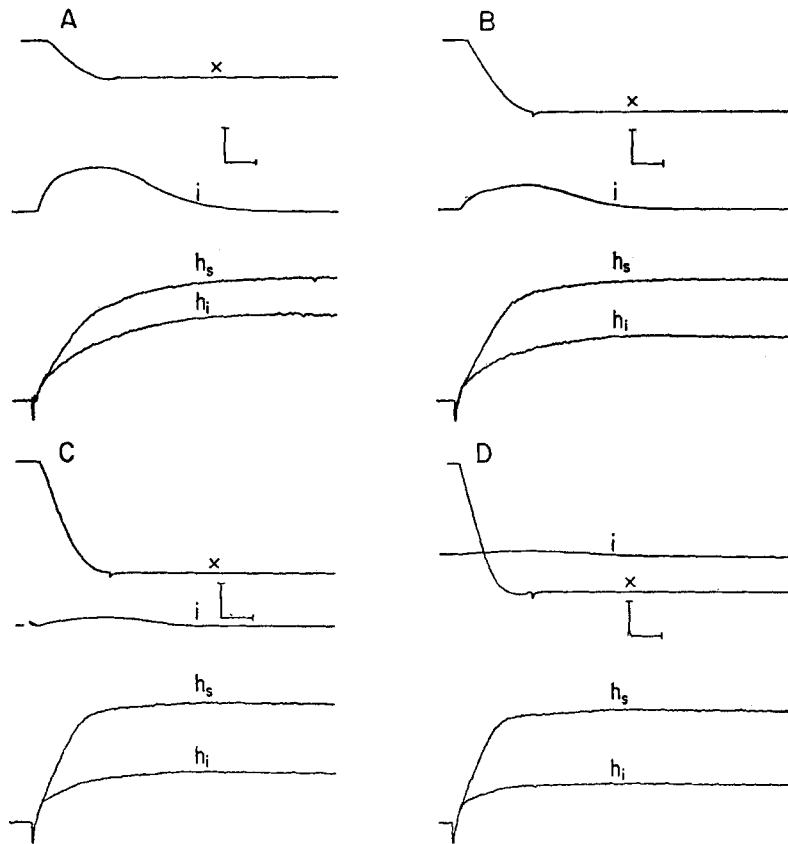


FIGURE 1. SHF production in afterloaded isotonic twitches and isometric contractions at lengths beyond l_0 . Each panel contains displacement, tension, and superimposed heat recordings of afterloaded isotonic twitches and their isometric controls. Panels A, B, C, and D correspond to afterloads of 50, 28, 10, and 2 g, respectively. The records labeled i are the isometric tension records, x , the displacement records, h_i , the isometric heat production, and h_s the isotonic heat production. Afterloads were not allowed to return the muscle length to l_0 during relaxation. In each panel the horizontal bar corresponds to 300 ms, and the vertical bar to 1.08 mm (x), 40 g (i), or 4.30 g-cm (h_i , h_s). The records are exactly as taken. Experiments were performed on thermopile E4. For this muscle pair M , 86.8 mg, l_0 , 2.1 cm, and P_{ot} , 104 g.

line against which SHF was measured. The isometric tension recordings are also shown. The muscles were first stretched to various lengths beyond l_0 and the isometric twitch heats and tensions (here 2, 10, 28, and 50 g) recorded to provide the myothermal base-line values against which SHF is measured. After resting at l_0 for 20–30 min, a control isometric contraction was performed to be certain that the condition of the muscle had not changed. The muscles then contracted against afterloads of 2, 10, 28, and 50 g. The superimposed myothermic records of Fig. 1 show two important features. First, when

shortening begins the records begin to diverge and as shortening continues the difference between the records increases. Second, upon cessation of shortening, the difference between the heat records becomes constant. Fig. 2, containing plots of the difference (SHF) between the isotonic and isometric heat records as a function of time, confirms these impressions. Therefore, upon shortening, extra heat, SHF, is liberated and when shortening ends, SHF reaches a final constant value. In Fig. 3, SHF is plotted as a function of the distance shortened. These graphs show that SHF is produced in proportion to the distance shortened and increases with the fractional afterload

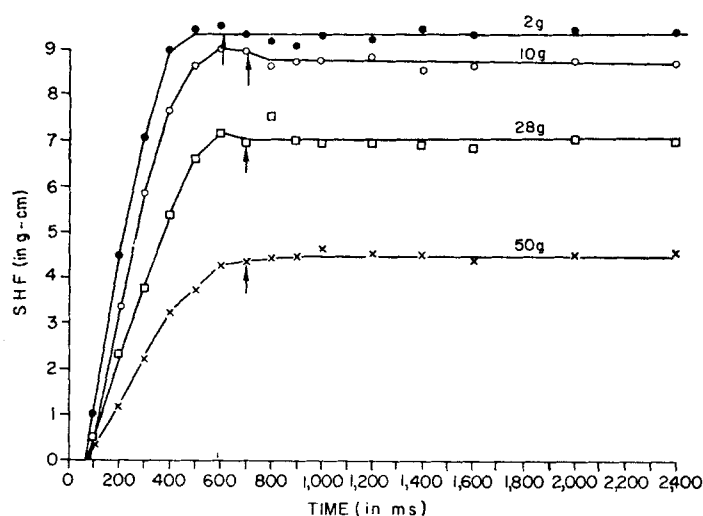


FIGURE 2. SHF production as a function of time after stimulation. For this graph the difference between h_s and h_i (Fig. 1) at a given afterload (SHF) was measured and corrected for the lag in the conduction of heat from the muscle to the thermopile. SHF was plotted as a function of time after stimulation. The vertical arrows in the graph indicate the cessation of shortening. The number above each plot is the afterload against which the muscle shortened.

(P/P_{oi}) . The slope of SHF vs. x can be used to calculate the normalized force-determined shortening heat coefficient from the time-course of shortening $(\alpha_F/P_{oi})_s$, and at afterloads of 2, 10, 28, and 50 g, was 0.22, 0.24, 0.28, and 0.30, respectively. Also from the total difference between the isotonic and isometric heat records at the end of relaxation, a *net* normalized force-determined shortening heat coefficient $(\alpha_F/P_{oi})_n$ can be calculated. At afterloads of 2, 10, 28, and 50 g $(\alpha_F/P_{oi})_n$ was 0.20, 0.22, 0.29, and 0.35, respectively. In seven pairs of muscles in which $(\alpha_F/P_{oi})_s$ was compared to $(\alpha_F/P_{oi})_n$, the ratio was 1.02 ± 0.02 (SE of mean, $n = 30$). When a regression analysis of $(\alpha_F/P_{oi})_s$ on $(\alpha_F/P_{oi})_n$ was performed it was found that

$$(\alpha_F/P_{oi})_s = -0.017 + 1.053 (\alpha_F/P_{oi})_n \quad (2)$$

In this regression analysis the correlation coefficient was 0.918, the intercept of Eq. 2 was not significantly different from zero ($P < 0.8$) and the slope was not significantly different from one ($P < 0.6$). Therefore, in a twitch, SHF is produced during shortening and is neither reabsorbed nor increased during relaxation.

Force-Determined Shortening Heat Obtained from Initial Heat Production in Twitches at 0°C by "Derived" Method

In the preceding section we have shown that SHF is produced during shortening and is neither reabsorbed or augmented during relaxation. Experiments are described below which were performed to determine the dependence of SHF on tension and to obtain accurate values of α_F/P_{oi} . Following the pattern first suggested by Gibbs et al., (1967), we used a format which employs the entire range of Eq. 1, and explicitly yields the SHF by a method we call the "derived" method. This technique involves measurements of the total initial twitch energy which are simpler to perform than time-course measurements, and which can be brought to considerable accuracy by the use of integrating thermopiles.

Muscles were allowed to shorten isotonicly against various afterloads ranging from 0.01 to 0.74 P_{oi} . The distance shortened, the external work performed, and the total initial energy liberation (heat plus external work, the load fell back against the muscle during relaxation) were measured. The total heat produced was obtained by subtracting the external work from the total energy liberated. After a series of isotonic twitches at various afterloads, a rest period of 20–30 min was given, and an isometric twitch series was performed at various lengths beyond l_o to vary P (as in Fig. 2 of Homsher et al., 1972).

A typical experiment is given in Fig. 4. Curve H_T is the total energy liberated, heat plus work, in afterloaded isotonic twitches as a function of the load. It corresponds to the classical Fenn effect (Fenn, 1923) in that at all loads the total energy seems to consist of the external work (shown by curve W_E) plus an approximately constant heat production ($H_T - W_E$). The line H vs. P is the relation between isometric twitch heat and force as varied by stretch beyond l_o . By our definition, force-determined shortening heat is the difference between a point on $H_T - W_E$ and the corresponding point on the H vs. P plot; i.e., SHF is the difference along any one vertical line within the shaded area. Visual inspection shows that, as would be expected, SHF ($= \alpha_F x$) increases at diminishing loads as x increases. The insert in Fig. 4 shows the values obtained for α_F/P_{oi} as a function of the relative afterload P/P_{oi} . From this it is clear that α_F/P_{oi} is a linear function of the relative afterload. Table I gives the means of all our determinations of α_F/P_{oi} and its load dependence obtained by the derived method. These results represent values from 17 pairs of muscles, 3 of which were studied on integrating thermopiles.

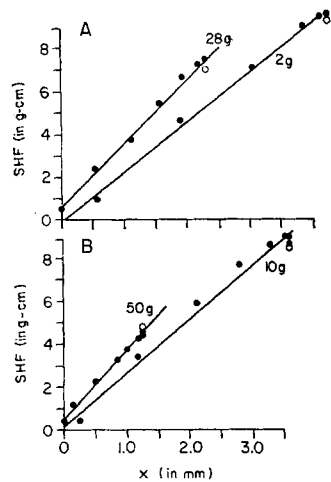


FIGURE 3

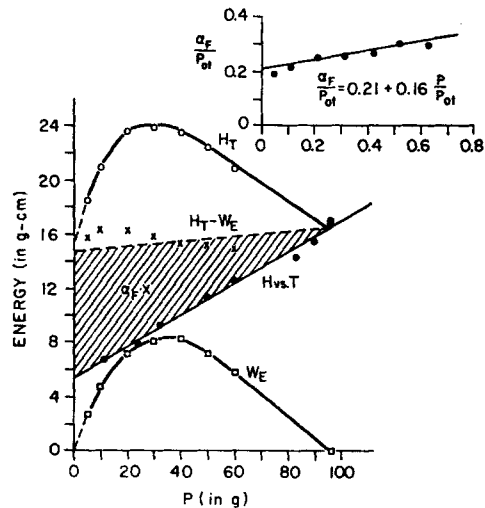


FIGURE 4

FIGURE 3. SHF production as a function of the distance shortened. In panel A, SHF production is plotted against the distance shortened in afterloaded isotonic contractions against 2 and 28 g; in panel B, against 10 and 50 g. Data were taken from Fig. 1. SHF values have been corrected for the lag in heat conduction from the muscle to the thermopile. The lines through the data are the result of linear regression analysis of SHF on x ; correlation coefficients for this regression at afterloads of 2, 10, 28, and 50 g are 0.997, 0.993, 0.996, and 0.997, respectively. The open circles (\circ) indicate the difference between h_s and h_i at the end of relaxation.

FIGURE 4. Determination of the force-determined shortening heat, $\alpha_F x$, in twitches at 0°C from the total initial energy liberation. This experiment was performed in a manner similar to that of Fig. 1. The muscle was first stretched to various lengths beyond l_0 and isometric heat and tension recorded and plotted as H vs. T . The correlation coefficient on this regression was 0.993. After a 30-min rest, heat production and shortening in a series of afterloaded isotonic twitches were recorded. The first twitch was against 60 g, the second against 50 g, etc. The series was repeated in reverse order after a 30-min rest period. Average difference between total heat produced at a given afterload in the two series was $3.1 \pm 1.6\%$ (SE of mean). Average values of total energy production in isotonic twitches are plotted as H_T and external work performed as W_E . The amount of shortening heat produced per centimeter of shortening, α_F , is calculated (as described in the text) and is normalized for maximum isometric twitch tension, α_F/P_{ot} . The values of α_F/P_{ot} are plotted as a function of relative load, P/P_{ot} , to determine the relationship between the shortening heat coefficient and relative load (inset). The equation obtained upon regression analysis is given in the inset and had a correlation coefficient of 0.927. In this experiment M was 100.8 mg and l_0 , 2.2 cm. Thermopile, W1.

Force-Determined Shortening Heat in a Tetanus

To learn whether or not SHF liberation is comparable in the twitch and tetanus, measurements of SHF production during tetanic shortening were made. For these experiments muscles were tetanized and allowed to shorten, against an ergometer, distances of 0.35, 0.50, 0.60, and 0.75 cm at velocities

TABLE I

SUMMARY OF THE MEASUREMENTS OF NORMALIZED FORCE-DETERMINED SHORTENING HEAT COEFFICIENT

From total initial twitch heat production at 0°C ($n = 17$)	$\alpha_F/P_{ot} = 0.20 (\pm 0.01) + 0.23 (\pm 0.02) (P/P_{ot})$
From short tetanic contractions at 0°C ($n = 5$)	$\alpha_F/P_o = 0.19 (\pm 0.01) + 0.27 (\pm 0.03) (P/P_o)$
From total initial twitch heat production at 20°C ($n = 5$)	$\alpha_F/P_{ot} = 0.22 (\pm 0.03) + 0.20 (\pm 0.05) (P/P_{ot})$
From calculations based on determinations of Hill's shortening heat (see text)	$\alpha_F/P_o = 0.20 + 0.25 (P/P_o)$

of 0.3, 0.6, 1.0, and 1.5 cm/s, respectively. Shortening began 30 ms after the first stimulus. The muscles' initial length and the duration of stimulation were so arranged that when shortening ceased, the redevelopment of isometric tension was approximately equal to the maximum tension developed during shortening (the average difference between the redeveloped and maximum tension during shortening was $0.8\% \pm 1.8\%$ (SEM) of P_o). The muscles' initial length (and duration of tetanic stimulation) at velocities of 0.3, 0.6, 1.0, and 1.5 cm/s were $l_o + 1$ mm (800 ms), $l_o + 2$ mm (500 ms), $l_o + 2.5$ mm (300 ms) and $l_o + 3$ mm (300 ms), respectively. After each tetanus the muscles were allowed to recover for 15–20 min. The myothermal base line for SHF determinations was the tetanic heat production by the isometrically contracting muscle developing the same maximum force as observed during shortening and tetanized for the same length of time. Obtaining the reference isometric contraction is complicated by the fact that tetanus tension recordings at lengths beyond l_o show a progressive rise in tension due to inhomogeneous sarcomere spacing at the tendinous ends of the muscle (Gordon et al., 1966). However, after correcting for the "creep" in tension, the twitch:tetanus ratio is independent of muscle length (Smith, 1972). In matching the isometric tension development to the tension of the isovelocity tetanus, the twitch:tetanus ratio, B , was measured at l_o (for experiments in Fig. 5, it was 0.91), and the muscle was stretched so that the twitch tension was B times the maximum tension seen in the isovelocity tetanus. The tension, displacement, and myothermal recordings from a typical experiment are shown in Fig. 5. The myothermal recordings show that (a) with shortening, the isovelocity heat trace departs from that of the isometric recording, (b) when shortening ends, there is a noticeable decline in the rate of heat production, (c) when shortening ends the difference between the isovelocity and isometric heat records becomes constant. In Fig. 6, the difference between the isovelocity and isometric heat

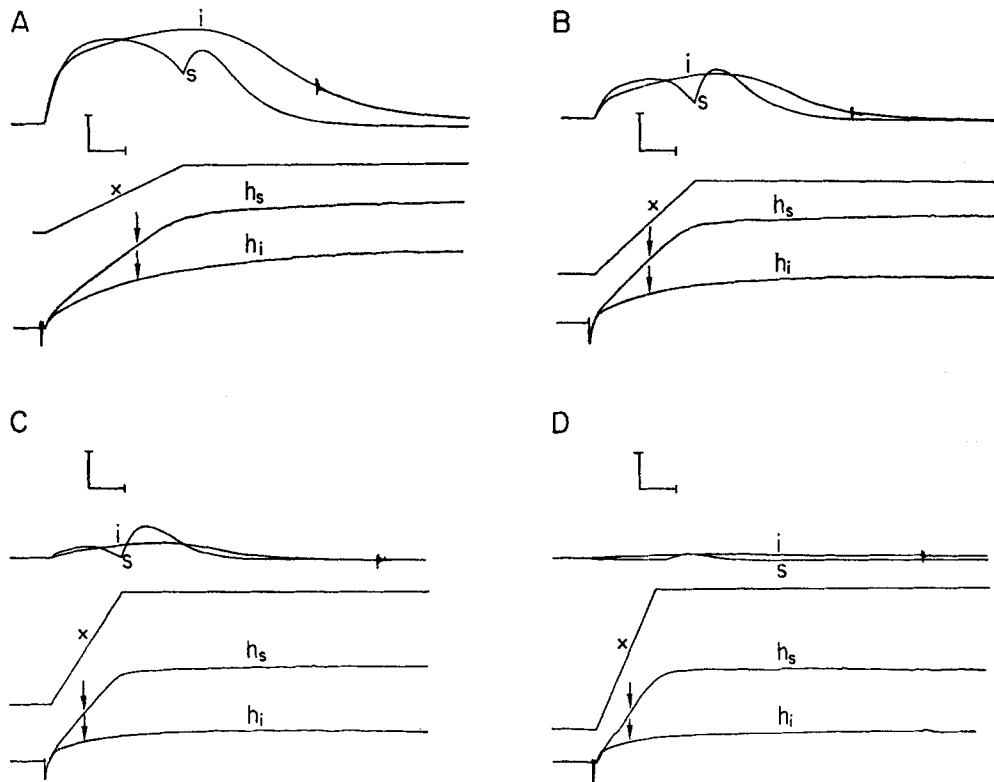


FIGURE 5. SHF production in a tetanus. Panels A, B, C, and D show the tension, displacement, and myothermal recordings obtained from isovelocity and isometric tetani. The velocity of shortening in A, B, C, and D is 0.3, 0.6, 1.0, and 1.5 cm/s, respectively. Records labeled *i* are the isometric tension records of muscles stretched beyond l_0 , *s*, tension records of isovelocity tetani, *x*, the displacement, h_s , the heat recording of the isovelocity tetanus, and h_i , the heat recording of the isometric tetanus. The heat recordings have been retouched to remove the stimulus artifacts. The horizontal bar in each panel corresponds to 300 ms, and the vertical bar to 20 g (tension, *i*, *s*), 2 mm (displacement, *x*), and 7.06 g-cm (heat, h_i , h_s). The average relative tension development (\bar{P}/P_0) during shortening at rates of 0.3, 0.6, 1.0, 1.5 cm/s was 0.39, 0.17, 0.05, and 0.00, respectively. The vertical arrows in the heat recordings indicate the last stimulus of the tetanus. The muscle length (and twitch tension at that length) at which the isometric tetani for panels A, B, C, and D were made was $l_0 + 4.5$ mm (41 g), $l_0 + 6.2$ mm (19 g), $l_0 + 8.6$ mm (5.4 g) and $l_0 + 9.2$ mm (0 g), respectively. These muscles had an l_0 of 2.0 cm, P_0 , 89 g, P_{oi} , 81 g, and a blotted weight of 74.0 mg.

production, corrected for the conduction of heat from muscle to thermopile, is plotted against time after beginning of stimulation, and the basic observations made from the original heat recordings are confirmed. Fig. 6 indicates that (a) the rate of heat production above the isometric rate increases with velocity, and (b) in a tetanus α_F has the same value during shortening as at the end of relaxation. This latter conclusion follows from the fact that shorten-

ing is a linear function of time and the extra heat production reaches a constant value at the end of shortening. When α_F/P_o is determined from these plots and a regression analysis of α_F/P_o against the average relative load (\bar{P}/P_o) during shortening is performed, it is found that $\alpha_F/P_o = 0.20 + 0.26 \bar{P}/P_o$ (correlation coefficient = 0.98) in this example. In five different pairs of muscles studied in this manner, α_F/P_o (for a tetanus) was not significantly different from α_F/P_{ot} (for a twitch) (see Table I). This result indicates that SHF liberation in the tetanus is the same as that observed in a twitch.

The value of α_F/P_o can also be calculated from the determinations of Hill's shortening heat, SH, in the preceding paper (Homsher and Rall, 1973). By definition Hill's shortening heat is the difference between the heat observed (h_{obs}) during shortening (lasting Δt seconds) and that during an isometric tetanus at l_o (stable maintenance heat rate = \dot{M}). Hence, $SH = h_{obs} - \dot{M}\Delta t$. By definition, force-determined shortening heat, SHF, is the difference between the heat observed during shortening (lasting Δt seconds) and that observed during an isometric contraction developing an equivalent force ($A + f[P, t]$). From the work of Homsher et al. (1972), it is known that in a tetanus the rate of activation heat production is $0.3\dot{M}$, and the rate of tension-related heat production is $0.7\dot{M} P/P_o$. Hence $SHF = h_{obs} - (0.3\dot{M}\Delta t + 0.7 \dot{M}\Delta t P/P_o)$. Subtracting SH from SHF gives

$$\alpha_F x - \alpha x = 0.7\dot{M}\Delta t (1 - P/P_o). \quad (2)$$

Substituting x/v (x is the distance shortened and v is the shortening velocity) for Δt and dividing both sides of Eq. 2 by x we obtain

$$\alpha_F - \alpha = \frac{0.7 \dot{M}}{v} (1 - P/P_o). \quad (3)$$

Since $\dot{M} = 0.035 P_o l_o/s$, $v = (P_o - P)b/(P + a)$, $b = l_o/4$, and $a = P_o/4$, we obtain

$$\alpha_F - \alpha = 0.025 P_o + 0.098 P. \quad (4)$$

As the preceding paper (Homsher and Rall, 1973) showed that $\alpha = 0.18 P_o + 0.15 P$, substitution of α in Eq. 4 gives $\alpha_F/P_o = 0.20 + 0.25 P/P_o$. This result shows that SHF calculated from muscles shortening after isometric tension has developed is the same as that observed at the beginning of a tetanus or in a twitch (see Table I).

SHF Production in Twitches at 20°C

In the studies so far described the variation of total energy liberation as a function of afterload has conformed to the Fenn effect as originally described

(Fenn, 1923, 1924). Data in the literature have indicated that there is no Fenn effect in cardiac muscle (Gibbs et al., 1967; Coleman, 1969). The same is true for amphibian skeletal muscles contracting at temperatures above 0°C (Hill, 1930; Fischer, 1931; Tigyi, 1959; Jöbsis and Duffield, 1967, and Chapman and Gibbs, 1972 *a*). These differences have made the concept of the Fenn effect and SH even more confusing, and in some cases methodological imperfections may have contributed (Hill and Woledge, 1962). We will next show that certain of these results can be reproduced and can be accounted for by the definition of force-determined shortening heat.

It has been shown (see Homsher et al., 1972, Table II) that when temperature is elevated neither the activation heat nor the tension-related heat in a twitch changes; i.e., if an isometrically contracting muscle develops 50 g of tension and liberates 2.5 mcal/g of heat at 0°C, it will do the same at 20°C. However, the contraction-relaxation time at 20°C is about $\frac{1}{10}$ of that at 0°C. The shortening velocity has a Q_{10} of 2–2.5 (Hill, 1938); thus, in an afterloaded isotonic twitch at 20°C, muscles will be able to shorten about five times faster than at 0°C, but will be activated for only $\frac{1}{10}$ as long. Hence muscles contracting against a given load at 20°C, will be able to shorten only half the distance as at 0°C. Consequently, a muscle will produce at 20°C, the same amount of activation heat and tension-related heat as at 0°C, but only half as much SHF and work. Therefore, as the afterload is reduced, the total energy production by isotonic twitches will decline more rapidly than at 0°C. These estimates are substantiated by the results of Fig. 7 in which a typical experiment on the effect of afterload on the total energy production at 20°C is shown. In this experiment, the muscle pair was given three stimuli at 250-ms intervals at each afterload and length on an integrating thermopile. As can be seen, the total energy output varies little for P/P_{oi} values between 1.0 and 0.5 whereas below that value, it declines. In addition, the maximum external work obtained was only about 16% of the isometric heat production at l_o as compared to a typical value of 40% at 0°C (see Fig. 4). The $(H_T - W_E)$ curve falls well above the H vs. T curve indicating the presence of a force-determining shortening heat, $\alpha_{F\lambda}$. If SHF is calculated as in Fig. 4, one obtains a plot of α_F/P_{oi} vs. P/P_{oi} which is given in the inset in Fig. 7. Again, there is a force-determined shortening heat, which like that at 0°C, shows a load dependence. The results of α_F/P_{oi} determinations in five separate pairs of muscles contracting at 20°C are given in Table I. The results are in good agreement with those values obtained at 0°C.

DISCUSSION

In defining those factors which regulate muscle energy output, a relationship should be obtained which accounts for the time-course and total amount of energy liberation in both the twitch and the tetanus. It has been demonstrated

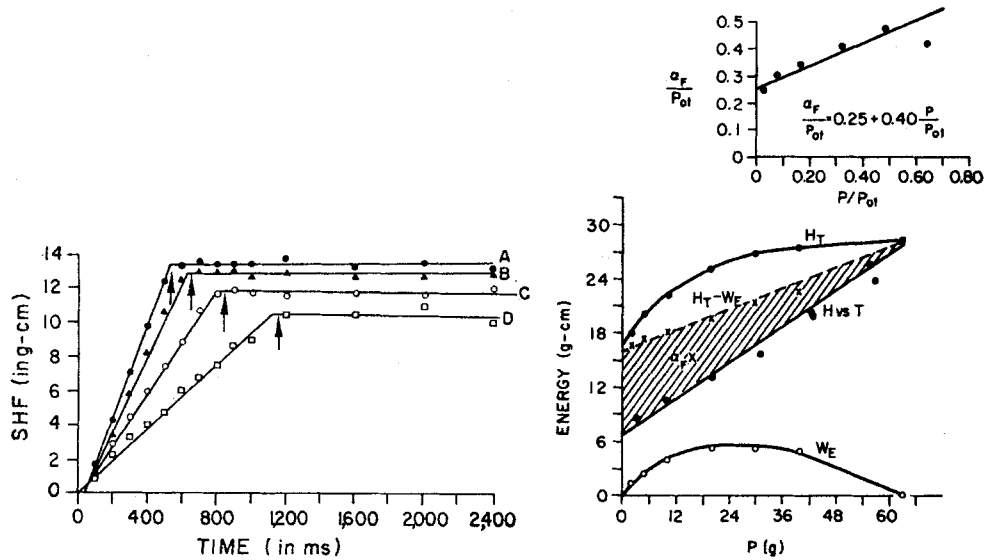


FIGURE 6

FIGURE 7

FIGURE 6. SHF production as a function of time after the beginning of stimulation in isovelocity tetani. Data for this figure were taken from Fig. 5. SHF is given by the difference between the heat production of shortening muscles developing a tension, P , and that of an isometric tetanus developing a tension equal to P . The data have been corrected for the lag in the conduction of heat from the muscle to the thermopile. The vertical arrow in the graph indicates the cessation of shortening. Plots A, B, C, and D correspond to muscles shortening at velocities of 1.5, 1.0, 0.6, and 0.3 cm/s, respectively.

FIGURE 7. Determination of the force-determined shortening heat in twitches at 20°C from total initial energy production. Experiment similar to that of Fig. 4. Three isotonic twitches (at 250-ms intervals) were recorded at afterloads of 40 g then 30 g, etc. Total initial energy, H_T , produced was measured on a calibrated integrating thermopile (W_2). Next, the muscle pair was stretched to various lengths beyond l_0 and performed three isometric twitches (at 250-ms intervals) at each length. Total isometric heat was then plotted against average isometric tension in the three twitches (yielding the regression line H vs. T ; correlation coefficient is 0.99). Total external work, W_E , was subtracted from H_T . The difference between the ($H_T - W_E$) value and the H vs. T value at a given load is the shortening heat, $\alpha_{F \times}$. The normalized shortening heat coefficient, α_F/P_{ot} , has been plotted against relative load, P/P_{ot} (inset). For this muscle pair, M was 75.4 mg, l_0 2.1 cm, and P_{ot} , at 0°C, 88 g.

(Homsher and Rall, 1973) that Hill's definitions of the activation heat, shortening heat, feedback heat, and work fail to accomplish these objectives. In our attempt to redefine those factors which do account for muscle energy liberation, several concepts were considered fundamental. First, since the external work performed by a muscle does not appear as heat until relaxation (or does not appear at all if contraction is against an ergometer), the basic problem was one of accounting for the *heat* production during contraction, specifically

during shortening. Second, the concept of an activation heat as an energy usage independent of myofibrillar energy consumption is well documented (Hill, 1950; Homsher et al., 1972; Smith, 1972, and Chapman and Gibbs, 1972 *b*). Third, the notion of an extra heat accompanying shortening seemed fundamental since the rate of heat production is markedly increased with shortening.

With shortening the rate of heat production increases, but *increases with respect to what?* Hill's original *definition* of SH considered the isometric heat rate at l_0 as the base line on the assumption that this heat production was equivalent to that involved in switching the muscle on and off, i.e., the activation heat. This assumption has been found to be incorrect (Smith, 1972; Homsher et al., 1972). Further, it has been demonstrated that using the activation heat as a base line for SH leads to the result that α in the twitch is different from that in the tetanus (Homsher and Rall, 1973). Earlier work (Aubert, 1956; Smith, 1972; Homsher et al., 1972) has shown that the development and maintenance of isometric tension results in a heat liberation which is directly proportional to the amount of tension and this heat is produced before relaxation (Homsher and Rall, 1973). In afterloaded isotonic contractions, muscles develop tension isometrically before shortening and may therefore evolve an amount of energy similar to that observed in a stretched muscle developing an equivalent force isometrically. For these reasons, it was *assumed* that the development of force by a contracting muscle (whether at a fixed length or shortening) obligates an expenditure of energy determined by that force. This amount of energy can be approximated by the relationship between heat and force in stretched isometrically contracting muscles. The heat associated with tension development and maintenance has been termed the tension-related heat and is designated as a general function of both force and time, $f(P, t)$. The tension-related heat is a function of (*a*) tension, since it is linearly dependent on tension in both the twitch and the tetanus, and (*b*) time, since it is evolved over a period of time and depends in its amount on the duration of stimulation. Approximation of $f(P, t)$ by measurement of the heat production in *stretched* muscles rather than foreshortened muscles was chosen since the latter produce an unknown amount of internal shortening (presumably evolving shortening heat and work). Since the stretched isometric contraction was assumed to produce the same amount of activation heat and tension-related heat as the shortening contraction, it became the base line against which force-determined shortening heat was measured. Using the activation heat plus the tension-related heat as a base line for the extra heat accompanying shortening, we have found that the time-course and total amount of energy liberated in *both* a twitch and tetanus could be described by a force-determined shortening heat and work. In addition, the magnitude of the normalized force-determined shortening heat coefficient was the same in both the twitch and the tetanus.

It is concluded that the energy liberation by a contracting muscle is accounted for by Eq. 1.

Having developed an equation which accurately predicts muscle energy liberation, in what way does it clarify our understanding of muscle energetics? First, this formulation makes superfluous any speculation that (*a*) in a twitch Hill's shortening heat is reabsorbed during relaxation (Carlson et al., 1963), (*b*) shortening heat is an entropy change (Kushmerick et al., 1969), and (*c*) shortening heat is reversed in a thermoneutral reaction during relaxation (Woledge, 1971). Such arguments are based on the assumption that Hill's concept of the shortening heat as defined in the tetanus is applicable to the twitch. It is not. Additionally, experiments (similar to those described in Figs. 4 and 5 D) in which the creatine phosphate hydrolysis was measured at the end of several contraction-relaxation cycles show that the activation heat, work, tension-related heat, and force-determined shortening heat have an appropriate metabolic equivalent (Rall et al., 1973; Homsher et al., manuscript in preparation).¹ Second, the definition of the force-determined shortening heat accounts for the disappearance of the Fenn effect at 20°C. The change in the relationship between total initial energy and relative tension when the temperature is elevated from 0°C to 20°C is not due to any alteration of the contractile mechanism. Rather, it apparently is a consequence of the differential in Q_{10} s of the shortening process and the activation and tension-related heat production. It is possible that this type of explanation may also apply to cardiac muscle energetics. Third, this formulation identifies tension development and maintenance as an important factor in determining muscle energy liberation, a view sometimes anticipated but never entered as a specific term in the energetic balance. Last, because of its accuracy and the relative ease of obtaining a base line against which the SHF and work can be measured, this approach should facilitate the design and execution of experiments testing the correlation between the time course of heat production and the hydrolysis of ATP and creatine phosphate.

To avoid misinterpretation of this empirical equation for the energy cost of contraction, several points should be emphasized. (*a*) The fact that the time-course and total energy liberation can be described by four separate terms does *not* imply that there are four separate mechanisms liberating energy. Our choice of Eq. 1 is, in fact, rather arbitrary as is any such formulation (Chapman and Gibbs, 1972 *b*). It is our guess that whereas activation heat is produced by the ATP hydrolysis accompanying the calcium cycle, the production of work, tension-related heat, and force-determined shortening heat are all derived from an ATP hydrolysis attendant to the attachment and/or motion of cross bridges and their rate of turnover would be regulated by the amount of calcium in the sarcoplasm and the load the muscle bears.

¹ Homsher, E., and J. A. Rall, W. F. H. M. Mommaerts, and A. Wallner. Manuscript in preparation.

(b) The fact that the isometric heat production of stretched muscles is taken as a base line against which SHF is measured does *not* imply that during shortening some cross bridges remain fixed, developing tension, while others cause shortening and work performance, both with an accompanying ATP hydrolysis. Such a model would not permit shortening to occur. (c) The fact that muscles which are stretched during contraction produce more tension than isometrically contracting muscles does *not* mean that these muscles should liberate more tension-related heat. Our empirical equation applies only to isometric and shortening conditions and hence relates to the kinetics of cross-bridges attachment and detachment under such conditions. The kinetics of cross-bridge cycling are likely to be substantially modified by stretching active muscles. (d) Although Eq. 1 designates the activation heat, tension development, shortening, and work as the primary determinants of the muscles' energy liberation, it should not be assumed that these are the only salient factors. For example, the amount of force-determined shortening heat produced during shortening appears to be dependent on the degree of myofibrillar overlap (Homsher and Rall, unpublished data). In addition, it is likely that the rate of SHF and tension-related heat production may be dependent on the amount of calcium in the sarcoplasm. Further examination of contracting muscles will be required to sort out all those factors that regulate a muscle's energy output.

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