A QUANTITATIVE COMPARISON BETWEEN THE ENERGY LIBERATED AND THE WORK PERFORMED BY THE ISOLATED SARTORIUS MUSCLE OF THE FROG. By WALLACE O. FENN.

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THIS work is the result of a suggestion by Prof. A. V. Hill that the heat production of muscles allowed to shorten and do work should be re-investigated by means of the improved myothermal methods which he and Hartree(1) have developed and have applied with such success to muscles in isometric contraction. As shown by their work on the difficult problem of the thermo-elastic effect(2), this technique makes it possible to allow muscles to shorten without errors due to slipping over the junctions provided strict precautions be taken to insure uniformity of temperature. The primary object of the experiments was to measure the maximum efficiency attainable with a frog's muscle under ideal conditions of load, etc. This has been done and the result shows an astonishingly low efficiency. The experiments, moreover, have led to important modifications of some of the fundamental and accepted principles of muscle physiology. In particular it can now be shown that there is a fairly good quantitative relation between the heat production of muscles and the work which they perform, and that a muscle which does work liberates, *ipso facto*, an extra supply of energy which does not appear in an isometric contraction. Having reached this rather novel point of view, it was a surprise to find that in its essentials it was not new but was urged by A. Fick 30 years ago, without, however, a satisfactory experimental basis. For this reason the history of the subject is of interest.

Heidenhain(3) first showed that if increasing weights were hung on a muscle (not after-loaded) then the heat production caused by the contraction of the muscle and the lifting of the weight increased with increase in the weight. Both Fick(4) and Heidenhain(3) added to this fact the observation that the heat also increased with the load even if the muscle always contracted from the same initial position. This was accomplished either by after-loading the muscle or by the use of Fick's inertia lever. Fick, in consideration of the increase in heat which he obtained with increase in work, endeavoured to find out whether the mechanical potential energy set up during an isometric contraction could be used for mechanical work, or whether, when the muscle shortened and did work there was an extra equivalent amount of chemical energy liberated in the muscle. A complete answer to this question has not yet been found. It had been shown by Heidenhain(3) that a muscle gave off more heat in an isometric twitch than in a freely shortening twitch under varying loads, but this might mean merely that the process of shortening had prevented the development of the potential energy. Consequently Fick(5) arranged to hold the muscle in the isometric position until the maximum tension had been developed and then to release it to shorten "mit Wurf." Under these circumstances he found more heat in the muscle when allowed to shorten than when shortening was prevented altogether. He concluded that in muscle mechanical potential energy is not produced beforehand by chemical processes, being then available for doing mechanical work, but that in all probability the chemical process accompanying the mechanical effect occurs at the time when the mechanical effect is produced. This conclusion of Fick's might have been accepted, but Schenck(6) did not have much success in confirming his experiments except under special conditions. Greife(7) agreed with Heidenhain(3), Fick(8) and Schenck(6) that an isometric contraction gave in general more heat than an isotonic, but both Fick and Heidenhain found certain cases in which an isotonic contraction under a heavy load gave slightly more heat than an isometric contraction(9, 10). Blix(11), however, insisted that the isometric contraction always gave more heat than the isotonic, the reason being that the average length of the muscle was greater when the muscle was held fast than when shortening was permitted. In Fick's final paper on the subject(12) he arranged, with the use of Blix's myographion, first to let the muscle do work during stimulation and then to stretch it during stimulation. He found always less heat produced when work was done on the muscle than when the muscle did work. He concluded, therefore, "that it is the actual process of doing positive mechanical work, *i.e.* of shortening under tension, which is responsible, in muscle, for the chief expenditure of chemical energy." This conclusion, it now appears, was entirely correct, but it is an extremely difficult one to prove conclusively on a gastrocnemius or any similar muscle (cf. p. 196). Frank(13), in a review of the subject, therefore accepted Blix's hypothesis that variations in heat were due merely to variations in the length of the muscle.

Later A. V. Hill(14,15), by improvements in the technique, made it appear that the earlier experiments were not very reliable and apparently settled the question once for all in favour of Blix by finding that the gastrocnemius and semimembranosus muscles gave off less heat in an isotonic contraction (without load) than in an isometric one, and that they gave off no more heat when shortening "mit Wurf" at the point of maximum tension (Fick's experiment) than when shortening was prevented altogether. Thus the view came to be accepted that on stimulation a muscle developed a given amount of heat and a given amount of elastic potential energy, both varying with the length of the fibres of the muscle. The amount of elastic potential energy which could be recovered as work depended merely upon the art of the experimenter in arranging his levers and had no relation to the total energy liberated. Tension was therefore regarded as the sole product of a muscular contraction.

Method. The method employed was that of Hartree and A. V. Hill(1). It will suffice here to indicate only certain modifications of their procedure. Most of the experiments were done with the large Paschen galvanometer supplied by the Cambridge and Paul Instrument Company, and purchased for the purpose by the generosity of the Rockefeller Institute for Medical Research, New York City, to whom grateful acknowledgment is made. For some of this work a combined thermopile and muscle chamber like that described by Hartree and Hill was used, but for the most part a somewhat simpler piece of apparatus of different design was employed. It is shown in Fig. 1. Its chief advantage is that, apart from the thermopile itself, it can be made very simply out of a rubber stopper, a test tube and some glass tubing. There is also less danger of leaks than with the ebonite box type and, due to the relative thinness of the glass walls, temperature equilibrium is attained more rapidly. The thermopile proper was made by electroplating silver upon constantan according to the method of W. H. Wilson(16) and was well insulated with shellac. The method of Hartree and Hill for calibrating the muscle had to be modified somewhat to suit a different set of apparatus. It consisted essentially in running an alternating current of known strength through the muscle for a known length of time. Current from the same source was used for stimulating the muscle where short tetani were wanted. The strength of the current was adjusted by means of a transformer and potentiometer and was measured by means of a special type of milliammeter in series with the muscle. The milliammeter consisted of a heating coil of very fine insulated constantan wire (670 ohms) wound around the "hot" junctions of the thermopile which was used by Hill in his investigations on the heat associated with the transmission of the nervous impulse (17). The leads of this thermopile could be connected with the galvanometer and the deflection produced by a given current in the heating coil determined. A previous calibration of this milliammeter with a direct current of known strength and duration enabled the deflection produced by an alternating current to be read in absolute units if the sensitivity of the galvanometer were also determined. The resistance of the muscle was measured by substituting a known resistance for the muscle in the alternating heating circuit and varying it until the same deflection was obtained on the galvanometer, *i.e.* until the same current flowed, as when the muscle was used. In practice a measurement of the current was made with any known resistance and the resistance of the muscle could then be accurately calculated in obvious ways. The weight of the muscle between the electrodes was taken after each experiment.

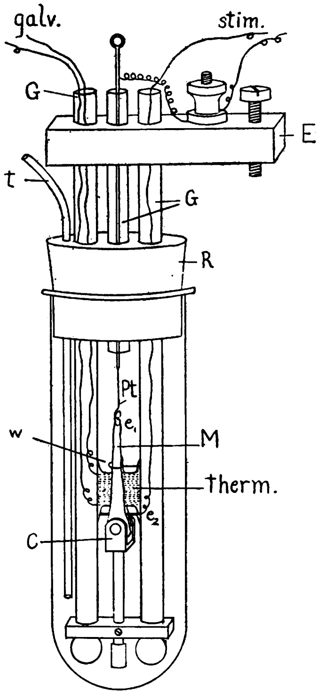

Fig. 1. Thermopile and muscle chamber. Through the rubber stopper, *R*, of a large test tube pass three glass tubes, *G*. Between these the thermopile (therm.) is fastened by means of shellac and well insulated from the muscle by shellac. The leads from the thermopile to the galvanometer pass through two holes in one of the glass tubes. The lower stimulating electrode consists of a platinum bar, e_2, between the two muscles. It is connected to the stimulating circuit by means of a copper wire leading up through the other glass tube. The upper stimulating electrode, e_1, consists of a piece of platinum wire, *Pt*, bent into an 8-shaped loop at one end, which is tied between the two muscles and soldered to a fine steel rod at the other end. This rod serves to make mechanical connection with the lever and electrical connection with the electrode. *E* is an ebonite block by which the whole apparatus is secured upright in the water bath; *w* is a platinum wire guide for the muscle to insure good contact with the thermopile; *t* is a fine glass tube through which Ringer's solution or oxygen can be introduced into the chamber; *C* is an ebonite clamp to hold the muscle; it is secured to the glass rods by means of an ebonite bar at the base and a silver plated set screw. The whole apparatus is sunk well beneath the surface of the water bath which is stirred by a continuous current of air. The two glass tubes which conduct the wires to the surface are filled with paraffin to prevent leakage through the holes blown for the wires or through the external openings.

Many of the phenomena described do not depend in any degree upon the accuracy of the calibration; they could be described equally well in terms of the galvanometer deflection. In others, as will be seen, the accuracy of the result depends upon the determination of the heat in absolute units. Now the calibration procedure can be carried out nominally with any accuracy desired, but its significance always depends upon whether the artificial heating is exactly similar to the natural heating in distribution. It is exceedingly difficult to say just where musculature ends and tendon begins and to place an electrode on this exact spot in such a way that only the musculature will be heated by the current. It is equally difficult to correct for any error in the position of the electrode by measurements. Because of the difficulty of adjusting a ring electrode such as that used by Hartree and Hill for a muscle which must move freely through it, I have substituted a platinum vane tied between the ends of the two muscles (Fig. 1). Part of this vane certainly extends beyond the tendon to the musculature, but if it did not there would be an equal probability of error due to a warming of the tendon and to excessive production of heat in a poor contact between electrode and muscle. The accuracy of the calibration is also dependent upon the uniformity in the cross section of the muscle (which makes a gastrocnemius difficult to use) because the heat per unit length of muscle varies inversely as the cross section in an electrical calibration but directly as the cross section in a natural contraction. Attempts to control this error by measurements of the electrical resistance of different known lengths of the sartorius muscle have given rather variable results owing to the difficulties involved in measuring the short lengths accurately, but when averaged together they tend to show that the muscle is uniform in cross section, becoming correspondingly thinner where it becomes wider. This error must certainly be negligible in Hartree and Hill's experiments where both ends of the muscle can be neglected (see below). Another calibration error lies in the possibility of a shrinking or swelling of the muscle after killing with chloroform with a consequent change in its heat capacity and its position on the thermopile. Simple observation makes it appear probable that this error is usually negligible although the muscle occasionally shortens markedly under the influence of chloroform if not restrained.

The calibration is more difficult in these experiments where the total absolute amount of heat in the whole muscle must be known (in order to be compared with the total work done) than it is in Hartree and Hill's experiments where the force and heat developed *in the same length of muscle* are observed and where consequently any part of the muscle which projects beyond the electrodes at either end may be disregarded, provided that the natural heat produced there is far enough away from the thermo-junctions to be unable of itself to affect the readings. The total error in the calibration in my experiments from all these causes cannot be accurately stated in figures, but it is believed that it could not by any possibility exceed 10 p.c. even in the small muscles; this is not serious for the purposes at hand. One specimen of *Rana esc.* was used. All the others were *R. temp.* or toads.

1. *Increase in total energy liberated with increase in work performed.*

The first experiments performed were a repetition of some made by Heidenhain and Fick. Any ordinary isotonic lever is used for recording the height of the contractions. A 25 or 50 gm. weight is hung on the lever so that the tension on the muscle is 5 to 10 gm. and its length only slightly exceeds its resting value. Any increase in the weight on the lever is supported by an after-loading screw. Short maximal tetani or maximal break shocks were used throughout for stimulating. In the contraction, energy which appears as mechanical work is stored temporarily in the lifted weight and reappears in the muscle as heat when the muscle relaxes and lowers the weight. The energy lost when the lever hits the after-loading screw has been calculated from the velocity of the weight at this moment, as measured from records of the contraction on a moving drum, and has been found to be negligible. Thus the galvanometer deflection represents the total energy mobilised as a result of the contraction. By means of the calibration this can be calculated in absolute units (ergs).

The protocol of a typical experiment is given in Table I in order to make the procedure clear. The results of another experiment are plotted in Fig. 2. The important points to be noted are, (1) that less heat is

TABLE I. Increase of heat with increase of work: typical exp.

Weight on lever gm.	Galvanometer deflection mm.		Height of contraction on drum cm.		Av. work Ergs × 10^4	Av. heat Ergs × 10^4	Efficiency W/H %
50	312	295	6·1	6·1	1·26	9·3	13·5
100	364	322	4·7	4·4	1·88	10·5	17·9
200	412	338	2·5	2·1	**1·90**	**11·5**	16·5
300	276	286	0·5	0·5	0·62	8·6	7·2
∞	238	↑	0	↑	0	7·3	0

Frog. Maximal alternating stimulus for 1/5 secs. At room temperature, viz. 7·5° C. Shortening = height on drum × 0·163. Work (ergs) = 981 × wt. on lever × height on drum × 0·0413 (lever factor). Heat (ergs) = mm. deflection × 306·2 (ergs per mm. from calibration). Two readings taken at each weight, first in ascending, then in descending order of weights as indicated by the arrows. Heat and work are expressed in units of 10,000 ergs. Weights in excess of 50 gm. were after-loaded. Maxima in heavy type.

liberated in the isometric contraction than in any of those where shortening is allowed, (2) that the increase in heat (above the isometric heat) is roughly parallel to the work done, and (3) that the process in the muscle

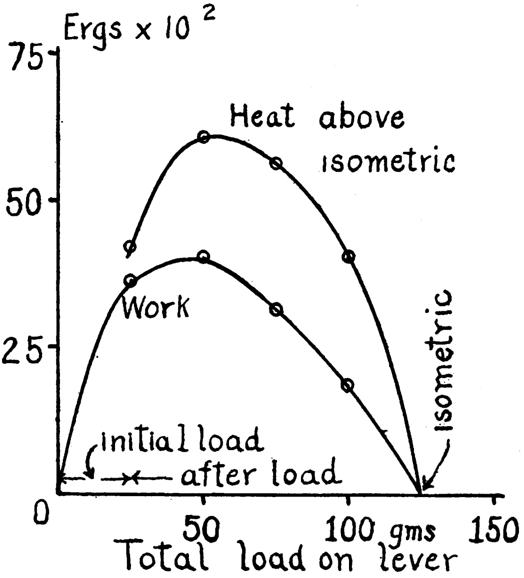

Fig. 2. Variations of work and heat (ordinates) in units of 100 ergs in isotonic contractions against increasing loads (abscissæ). The heat curve represents only the heat *in excess* of the isometric which was 193×10^2 ergs. Thus the isometric heat is made to coincide arbitrarily with the line of zero work. The muscle arm of the lever is 4·7 times the weight arm. Weight in excess of 25 gm. after-loaded. Muscle stimulated with maximal break shocks. Maximum efficiency of the initial process, $38{\cdot}7 \div (193+61) = 15{\cdot}2\ \%$.

which causes this extra liberation of energy takes place after the stimulus is over (break shocks) and hence after the number of fibres brought into activity is presumably completely determined. This experiment supports the contention of Fick that work as well as tension is a product of the muscular reaction and it is much clearer evidence than can be obtained with the gastrocnemius muscle where the heat increases with increasing load but does not decrease again to the isometric.

Further data are given in Tables II and III. In some experiments the muscle was stimulated with a short tetanus; in others with a maximal break shock. The result is always the same, although the range of weights used may not always be sufficient to represent both sides of the maximum. In all, some 60 experiments of this type have been recorded. Typical variations of the heat with variations of work have always been found except in a few cases when the muscle showed obvious signs of fatigue.

TABLE II. Increase of heat with increase of work.
(Summary of four exps. similar to that in Table I.)

Weight on lever gm.	Frog. 6·7° C.		Frog. 7·5° C.		Toad. 8° C.		Frog. 8·5° C.	
	Work	Heat	Work	Heat	Work	Heat	Work	Heat
50	1·30	10·1	1·46	14·9	0·26	1·45	0·58	5·03
100	**2·01**	13·1	2·62	**17·1**	0·24	1·37	**0·74**	**5·64**
200	1·56	**14·4**	**3·26**	16·4	0·02	1·14	0·42	5·50
300	0·18	9·6	1·79	14·5	—	—	0·12	4·82
∞	0	9·2	0	11·5	0	1·14	0	4·57
	0·5 sec.		0·5 sec.		0·2 sec.		Break shocks	

All exps. at room temperature, with a pair of sartorius muscles. Tension on muscle during contraction ¼ that of weight. Initial tension of muscle therefore 50/4 or 12·5 gm. Maxima in heavy type. Work and heat expressed in units of 10,000 ergs. Isotonic lever, after-loaded.

TABLE III. Increase of heat with increase of work.
(Summary of three exps. similar to that in Table I.)

	Toad. 8° C.		Frog. 0° C.		Frog. 8·5° C.	
25	4·3	**24·1**	3·5	23·4	3·1	**43·8**
50	**5·1**	20·7	**3·9**	**25·4**	**4·1**	38·5
75	4·3	18·3	3·2	24·9	3·9	37·4
100	2·4	14·4	1·8	23·2	3·0	35·0
150	0·2	13·1	0	19·3	0	29·6
	0	13·8		—		—
	0·2 sec.		Break shocks		Break shocks	

Work and heat are averages of 2, 4 and 8 series respectively in alternating directions. Tension on muscle ¼ of weights given. Initial tension 6·25 gm. Maxima in heavy type. Units of 1000 ergs. Isotonic lever, after-loaded.

TABLE IV. Increase of heat with increase of work: constant shortening.
(Summary of six exps. similar to Fig. 3.)

	Exp. 1		Exp. 2		Exp. 3		Exp. 4	
25	—	—	—	—	1·49	70·2	1·51	50·4
50	4·0	153	4·3	97	3·03	72·6	3·08	55·0
75	5·7	138	6·2	110	4·57	75·6	**4·65**	**58·4**
100	7·4	163	8·0	130	6·11	78·8	3·99	56·8
125	9·0	167	9·9	138	7·64	**80·3**	—	—
150	10·7	170	10·3	**143**	**8·19**	79·4	—	—
175	**12·4**	**171**	**10·5**	138	7·47	76·1	—	—
200	9·8	165	5·6	117	—	—	—	—
Isom. *l*	0	133	0	84	0	57·0	0	42·5
Isom. *s*	0	—	0	86	0	—	0	35·2
	0·5 sec., 8·4° C., 2·66 mm. shortening; muscle 0·19 gm.		0·4 sec., 0° C., 3·0 mm. shortening; muscle 0·25 gm.		0·2 sec., 8·2° C., 2·5 mm. shortening; muscle 0·26 gm.		0·2 sec., 0° C., 2·6 mm. shortening; muscle 0·18 gm.	

Frog. Tension on muscle during shortening ¼ that of weight given. The isometric heat in the long and the short positions is given where possible. Initial tension is represented by the smallest weight in each series. Each figure is the average of two series of ascending and descending weights respectively. When the work ceases to increase in proportion to the increase in weight, the shortening is incomplete. Maxima in heavy type. Units of 1000 ergs.

Blix (11) would explain the increase in heat with increase in load as due to an increased average length of fibre during the contraction. This might have explained the initial rise but cannot account for the subsequent fall of the curve toward the isometric level: on the other hand, the change in the heat is always proportional in a general way to the work. The work is equal to the product of the tension, T, under which the muscle shortens and the absolute amount of shortening, s. As the load increases from 0 to infinity, Ts must pass through a maximum, since at zero weight $T = 0$ and at infinite weight (isometric) $s = 0$. With small loads the muscle shortens so much and so rapidly that maximum tension cannot be developed. With large loads the maximum tension is developed but the amount of shortening of which the muscle is capable before relaxation begins is very small.

2. *Increase in the total energy liberated when increasing loads are lifted to a constant height.*

In these experiments it is arranged that the muscle should shorten under different loads only between two fixed positions, the "long" position and the "short" position, the amount of shortening allowed being only 2 or 3 mm. A diagram of the apparatus designed for this purpose will be published later. In contraction the muscle lifts the weight from the long position to the short, and in relaxation the weight stretches the muscle again to the long position.

The purpose of this modification of the experiments described in the preceding section is to make possible a more accurate analysis of the factors of length, tension, shortening, etc., which together determine the amount of energy liberated in a muscle as a result of a given stimulus. The advantages of the procedure are as follows:

1. The amount of shortening remains constant over a considerable range of weights: hence variations in energy liberated must be due to variations in length of fibre, tension of the muscle during shortening, or speed of shortening.

2. Over this same range the maximum possible change of heat due to mere change in the length of the fibres can be determined by measuring the heat produced in an isometric contraction at each of these positions. Thus, if the increase in heat due to an increase of load is much greater than the difference in the isometric heat at the long and short positions, then it is certain that the mere length of fibre is not the dominant factor.

3. The change in shape of the muscle is also constant (until the weight becomes too heavy to lift to the required height) so that the irreversible "viscous" loss (cf. Hartree and Hill(2)) becomes proportional to the various speeds of shortening and lengthening, and hence its absolute

value for each weight can be estimated roughly by permitting the muscle to shorten from the long to the short position without being stimulated, then pulling it back immediately to the long position with a weight which is just adequate for the purpose, and measuring the resulting galvanometer deflection. Incidentally this procedure controls any large errors which might arise due to differences of temperature along the muscle. Usually one obtains a deflection of about 5 mm. which is perhaps 2 p.c. of the deflection obtained when the muscle contracts. This is so small that it has been neglected in recording the results, but if allowed for it would merely increase the amount of external work performed. This irreversible loss may of course be greater in a stimulated muscle than in a resting one, but no method has suggested itself of determining this point. When measured in this way on an unstimulated muscle the speed of shortening is somewhat less than in a contraction under the smallest weights, but the speed of lengthening is greater than in a stimulated muscle. A correction for the speed of the change of shape therefore would not significantly alter the above estimate that the irreversible "viscous" loss amounts to less than 5 p.c. of the total energy liberated.

4. This procedure also certifies that if the weight lifted is so small that the muscle cannot develop its maximum tension during the shortening, that tension can still be developed when the contraction becomes isometric at its shorter length.

5. When the muscle is *in situ* in the body of the frog it also contracts between fixed limits which are in a rough way comparable to those used experimentally.

In measuring the isometric heat in the "long" and "short" positions the muscle must also be calibrated in both positions. The calibration constants so obtained show that on the average 1·05 times as much heat must be liberated in the long position as in the short position in order to produce the same galvanometer deflection. This is because a stretched muscle is thinner on the thermopile. The "long" calibration is of course used for all readings where work is done, because the muscle is in that position throughout the duration of the galvanometer deflection (4 secs.) except for the first second or less.

The results of a typical experiment with limited shortening are plotted in Fig. 3. In general the curves may be regarded as comparable to those in Fig. 2 except that the ascending limb of both the heat and the work curves has been "sliced" off by the arbitrary limitation of the amount of shortening permitted. In Fig. 3, however, the base line of the work curve (work = 0) is plotted so as to coincide with the point on the axis of ordinates representing the heat produced by shortening under zero load. In Fig. 2, on the other hand, the level of zero work coincides with the level of isometric heat. This change is made in Fig. 3 in order that the ratio between the slopes of the heat and the work curves can be seen at a glance. In this experiment the ratio is 2·7. In 32 similar curves which have been obtained the average of this ratio was 2·3, *i.e.* the increase of energy liberated was 2·3 times as great as the increase in work. In this average, two or three experiments have been neglected where the ratio was practically zero, due very evidently to the extreme fatigue of the muscle as shown by a very low and rapidly falling heat output and work output. Data from four normal experiments are summarised in Table IV (*supra*). In an experiment like that in Fig. 3 it is impossible to start with zero weight because the muscle must be made to return to its original length promptly. The curves have

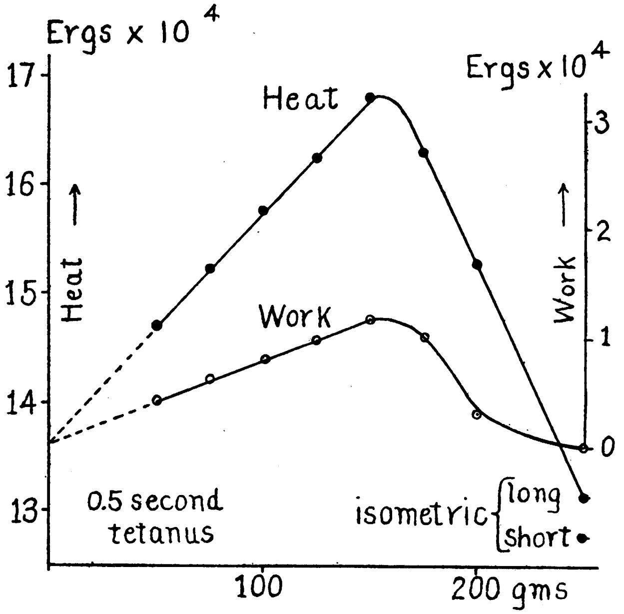

Fig. 3. Exp. similar to that in Fig. 2 except that the amount of shortening was limited to 2·66 mm. The heat curve has been extrapolated to the ordinate of zero load and the base line of the work curve is made to coincide arbitrarily with this point. The work curve falls off at the point where the load becomes too heavy to be lifted the full distance. Weights in excess of 50 gm. after-loaded. Muscle arm on lever four times weight arm. Weight of muscle between electrodes 0·19 gm. Temp. = 8·4° C. Results of four other similar experiments given in Table IV.

been prolonged, however (dotted), to the vertical axis. Even at this extrapolated point there is usually more energy liberated than in an isometric contraction at either the long or the short position, but the difference is not large. As the weight lifted is increased the work must increase in direct proportion, *i.e.* as a straight line, as long as the height to which the weight is lifted remains constant. When the weight becomes too heavy for the muscle to lift the required height the work curve falls off and finally decreases to 0 when the contraction becomes isometric. Usually, as in Fig. 3, the heat also increases approximately as a straight line until the maximum is reached and then decreases rapidly to the isometric level. Frequently the heat curve maximum occurs at a slightly lower weight than the work curve maximum. Examples of this may be found in Tables II, III and IV. This is probably to be explained by minor complications due to length of fibre and "viscous" loss. The mechanical efficiency (work divided by total energy liberated) disregarding the recovery heat production, is seldom over 10 p.c. in these experiments on account of the arbitrary limitation of the amount of shortening. The efficiency can readily be calculated from Table IV.

It was found by Evans and Hill(18) that the heat produced by the sartorius muscle in isometric contractions was greatest when the length of the muscle was approximately equal to its length in the frog. I have repeated their experiments with several muscles stimulated with break shocks and short tetani and can entirely confirm their conclusion. Moreover, I have had occasion to measure the isometric heat production in 14 experiments in the long and short positions, representing a change in length of 2½ to 3 mm. or about 10 p.c. of the length of the muscle. In five of these the heat production was 5 p.c. more in the long position than in the short; in nine it was 11 p.c. less. The initial tension was always between 6 and 12 gm. which is not far from the tension of the muscle in the body when the leg is extended. Thus in four muscles I have found that an initial tension of 9, 12, 19 and 25 gm. stretched the muscle to 102, 100, 106 and 110 p.c. respectively of their several normal extended lengths in the frog. Accurate measurements of muscle lengths are admittedly difficult to make, but it seems not unfair to say from these facts that in my experiments the muscles have worked over a range of lengths which is approximately normal. Any deviation from the normal length of the muscle diminishes the heat liberated isometrically on a given stimulus. It is perhaps worth emphasising that the proportionality between isometric heat and muscle length, or the area of certain longitudinal surfaces, which is so often quoted as an argument in favour of the surface tension theory of muscular contraction, is true only over a very limited range.

Summary. 1. When a muscle is made to lift increasing weights through a constant small distance, comparable to the normal amount of shortening in the frog, the increase in energy liberated tends to be on the average 2·3 times the increase in work, *i.e.* it is proportional to the tension under which the shortening takes place. Complications due to fibre length and irreversible "viscous" loss can be largely ruled out.

2. When a muscle shortens 2 or 3 mm. under some tension the energy liberated is greater than the time average of the isometric heat for all the lengths through which the muscle passes in shortening. When there is no weight on the muscle this is usually but not always true.

3. *Increase in total energy liberated caused by increased degree of shortening under a constant load.*

It has been shown above that the heat production of muscles increases when increasing loads are lifted through the same distance. Evidence will now be presented that the converse is also true, *i.e.* that the heat production of muscles is increased when the same load is lifted through increasing distances.

The amount of shortening was varied by adjusting the proper screw. Each series started with no shortening, *i.e.* isometric. The shortening was then increased at random until the weight could be lifted no higher, after which the shortening was decreased again step by step to the isometric. The results obtained with 100, 50 and 25 gm. on the lever using the same muscle are plotted in Fig. 4. The curves H_{100}, H_{50} and H_{25} show the increase in heat above the isometric with the three different weights; the broken lines W_{100}, W_{50} and W_{25} represent the corresponding increase in work. There is a tendency for the curves to reach a maximum, but it is obviously a fair approximation to the truth to say that, with a given weight, the increase in heat is proportional to the shortening. Furthermore, the rate of increase of heat with increased shortening is roughly proportional to the tension under which the muscle shortens. As far as the muscle is concerned, the two factors which determine the amount of work performed are the amount of shortening and the tension during shortening. This experiment, of itself, proves that it is neither one of these factors alone but rather their product, *i.e.* the work, which determines the increase in the heat production[1].

As the shortening increases the time average of the length decreases.

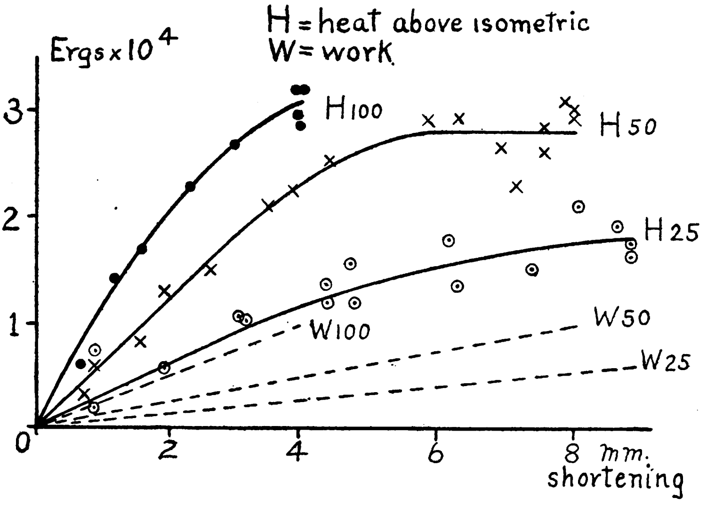

Fig. 4. Increased heat obtained with increased shortening under constant loads. The results of three series are plotted in which the muscle shortened under 100, 50 and 25 gm. (on the lever) respectively, the tension on the muscle being only one-quarter of this. The curves marked H_{100}, H_{50} and H_{25} show the heat liberated in excess of $5{\cdot}6 \times 10^4$ ergs, which was the isometric value. The corresponding work performed is plotted in the broken lines marked W_{100}, W_{50} and W_{25}. Duration of stimulus, 0·2 sec. Frog's muscle, weighing 0·33 gm. between electrodes. Temp. 0° C. At the point where the muscle has shortened 4 mm. it has lifted 100 gm. 1 mm. and the work in ergs is $981 \times 100 \times 0{\cdot}1 = 0{\cdot}981 \times 10^4$ ergs.

When the shortening is greatest (8 mm. in Fig. 4) this factor might cause a significant decrease in the heat obtained due to the decrease in the isometric heat production at shorter lengths, even as Blix suggested. This complication may account for the fact that the heat production does not continue to increase at the same rate as the amount of shortening is increased but tends to approach a maximum. Obviously, however, the idea of Blix that length determines heat production can have at most only a small share in the explanation of these curves, for in general the greater the shortening the greater the heat.

Data for eight other essentially similar curves with various weights and various durations of stimulus have been obtained. Care was taken

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[1] I have frequently referred to the total energy liberated rather loosely as the heat production. The two terms are synonymous only when the energy which appears as mechanical work is reabsorbed by the muscle as heat in relaxation.

in all cases that the strength of the stimulus should be maximal in order to avoid the possibility of stimulating more fibres after the muscle began to shorten. In one very fatigued muscle no increase and if anything a decrease of heat with increased shortening was noted. I have repeatedly observed that the whole mechanism by which excess heat is liberated in accordance with the work done is thrown out of action by fatigue.

4. *Increase in total energy liberated due to increase of work on an inertia lever.*

The lever which has been used for these experiments is one described by A. V. Hill(19) and similar to that used by Doi(20) in investigating the maximum work of frog's muscle. It consists essentially of a steel rod carrying equilibrated masses at either end. At one end is hung a rider of 1 to 5 gm. weight. The "equivalent mass" against which the muscle pulls can be increased by moving the point of attachment of the muscle nearer to the fulcrum. The lever records its movement on a smoked drum so that the height to which the weight is lifted and hence the work done can be calculated. A similar lever has been used by Meyerhof(21) who made simultaneous determinations of the amount of lactic acid produced by the muscle.

In order to measure the heat liberated by the muscle it must be made to return to its original length within about 1 second after stimulation. If it takes 4 secs. for the galvanometer to reach its maximum deflection it can be shown that a small change in the calibration constant due to the shortening of the muscle during the first second will have no appreciable effect on the maximum deflection recorded. In order to pull the muscle back, therefore, after it has shortened, a simple isotonic lever with a small weight has been used in conjunction with the inertia lever as shown in the inset (Fig. 5). In relaxation the inertia lever continues to lift its weight while the isotonic lever falls back with the muscle to its original position. Later, of course, the inertia lever falls back also. The energy used by the muscle in imparting an acceleration to the inertia lever is not, therefore, reabsorbed as heat in the muscle, and in order to determine the total energy liberated in the muscle as a result of the stimulus it is necessary to add the work done on the inertia lever to the heat detected in the muscle. The latter includes, of course, the work done on the isotonic lever, for this is reabsorbed by the muscle in relaxation.

In each experiment the results of two series of observations are averaged. One series starts with an infinite equivalent mass (isometric) and ends with the smallest equivalent mass, while the other series is similar but in reverse order. The results of such an experiment are shown in Fig. 5 where the work, and the extra heat liberated because of this

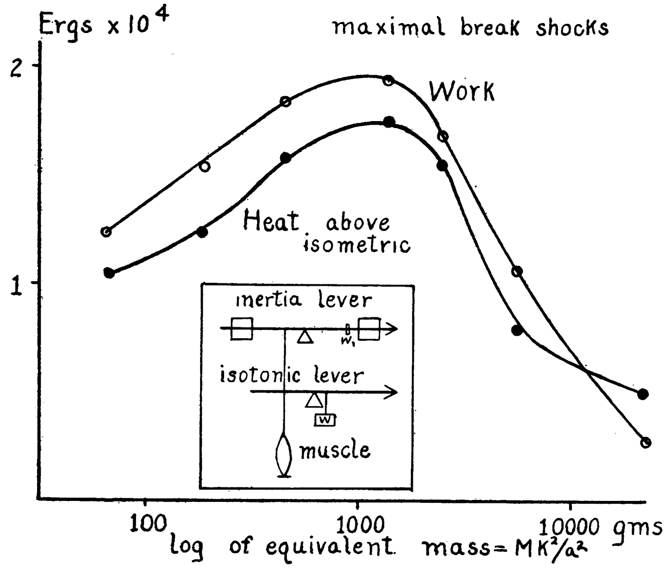

Fig. 5. Energy liberated in excess of isometric, and the work performed when a muscle is stimulated with maximal break shocks and made to shorten against an inertia lever. "Equivalent mass" of lever increased by moving point of attachment of muscle farther away from fulcrum. "Equivalent masses" are represented as abscissæ; logarithms have been used merely for convenience in plotting. At large equivalent masses the work done on the isotonic lever is practically negligible, but at small equivalent masses it becomes a large fraction of the whole. Isometric heat 97,300 ergs. Room temp. =8·5° C. Weight of muscle between electrodes 0·26 gm. Each point is the average of six determinations on the same muscle.

work (heat above isometric), both in units of 10,000 ergs, are plotted as ordinates over the logarithms of the equivalent masses as abscissæ. The nearer the point of attachment of the muscle to the fulcrum, the greater the equivalent mass, the less the shortening of the muscle, the slower the shortening, and the greater the tension on the muscle. In this experiment, within the limits of error of the calibration, the extra heat liberated is equal to the work done. This is frequently, but by no means always, the case. This particular experiment was selected for plotting because break shocks were used for stimulating, thus proving that the excess heat due to the work done may be liberated after the stimulus is over and hence cannot be due to an increased number of fibres brought into contraction.

Averaging the results of 33 experiments like that recorded in Fig. 5 it is found that the extra heat is 1·3 times as great as the work performed at the optimum equivalent mass. Averaging similarly 36 experiments like that in Fig. 2 in which increasing weights on an *isotonic* lever were lifted by a muscle it was found that the extra heat liberated was 1·8 times as great as the work done with the optimum weight. The difference between 1·8 on the isotonic lever and 1·3 on the inertia lever is significant and is due largely to the fact that in the experiment with the isotonic lever the muscle had to let the weight down again in relaxation. It will be shown in another paper that there is an extra expenditure of energy involved in lowering a weight in relaxation which will account for the difference mentioned. A small part of the difference might be due to the fact that the maximum mechanical efficiency of a contraction on the inertia lever is 20 p.c. greater than the maximum on the isotonic lever, *i.e.* there is more work done on the inertia lever for the same amount of heat. The maximum energy liberated on the isotonic lever tends to be greater, however, than on the inertia lever, showing definitely that some other factor such as that mentioned must be involved.

In Table V the results of seven other experiments similar to that in Fig. 5 are summarised. Similar experiments have been averaged together. In all but the last two the heat is at a maximum at the smallest

TABLE V. Increase of heat with increase of work on inertia lever.
(Summary of seven exps.)

Exps. 1, 2 and 3			Exps. 4 and 5			Exps. 6 and 7		
Equiv. mass (kilos.)	Work	Excess heat	Equiv. mass (kilos.)	Work	Excess heat	Equiv. mass (kilos.)	Work	Excess heat
0·32	62	111	0·78	68	**122**	0·36	217	276
0·46	64	**111**	1·12	69	117	0·80	264	420
0·72	65	108	1·75	**70**	114	1·42	288	493
1·29	**66**	97	3·13	69	107	3·19	**306**	**508**
1·85	63	86	4·48	67	100	5·67	281	460
2·89	59	85	7·01	64	88	12·76	236	352
5·15	49	59	12·46	53	64	—	—	—
11·58	28	33	28·00	40	41	—	—	—
46·34	12	16	112·2	18	12	—	—	—
Isom. 33,400 ergs, 0·5 sec. Av. of 8 dets. on 3 muscles at 7° C.			Isom. 28,800 ergs, 0·4 and 0·5 sec. Av. of 6 dets. on 2 muscles at 0° C.			Isom. 103,500 ergs, 0·5 sec. Av. of 4 dets. on 2 muscles at 7° C.		

Excess heat is total heat minus isometric heat. Work and heat in units of 100 ergs. All at room temperature unless at 0° C. Similar experiments only have been averaged together.

equivalent mass used, where the work is slightly below the maximum. The same thing can be observed in experiments on the isotonic lever as shown in Tables II, III and IV, where the maximum heat production frequently occurs with a slightly smaller load than the maximum work. In Exps. 6 and 7 in Table V the muscles used were stronger than in the other experiments. Their average maximum work is nearly five times as large and the optimum equivalent mass is also larger.

In one experiment with the inertia lever at 6·7° C. I have been able to show that an increase in the duration of the stimulus from 0·05 to 0·7 sec. increased the optimum equivalent mass from 40 or 80 to 5670 gm., although the maximum efficiency was just 20 p.c. in both cases. In another similar experiment at 0° C., an increase in the duration of the stimulus from 0·05 to 0·5 sec. increased the optimum equivalent mass from 1400 to 3150 gm. and increased the maximum efficiency slightly from 14 p.c. to 15·5 p.c. The experiments were conducted by using first one duration of stimulus and then the other in alternation in order to eliminate changes due to fatigue.

The interpretation of the curves in Fig. 5 is as follows. The work performed by a muscle in any contraction is equal to the product of the average tension of the muscle by the amount of shortening. As the equivalent mass is decreased the amount of shortening increases and becomes so rapid that the tension of the muscle decreases and approaches zero. Conversely as the equivalent mass is increased the tension increases, but the amount of shortening which can be accomplished before the stimulus is over and relaxation begins decreases and approaches zero (isometric). Hence the product of shortening and tension, *i.e.* work, must pass through a maximum at a certain optimum equivalent mass, for this product is necessarily equal to zero at infinitely large or infinitely small equivalent masses. If the stimulus were continued until a given amount of shortening were accomplished, as in Hill's experiments with human arm muscles pulling against an inertia device (22), there would be no optimum equivalent mass but the work would continue to increase indefinitely with the mass. It will be important to find out to what extent the theoretical interpretation of Hill's curves will require modification in the light of the knowledge that the shortening of a stimulated muscle is not comparable to the shortening of a stretched spring but is more like the behaviour of an electric motor. If the muscle were like a spring it would possess a given amount of potential energy which, if it did not appear as work, would necessarily appear as heat in some irreversible "viscous" process involved in the change of shape. If, however, the muscle were like an electric motor it would develop less energy where the equivalent mass was small and it would be unnecessary to postulate a large frictional loss. It remains for future investigation, however, to prove the applicability of these experiments on frogs to human muscles.

Summary. 1. When a muscle shortens against an inertia lever it liberates more energy than in an isometric contraction. This excess energy liberated is on the average 1·3 times as great as the work performed.

2. For a given duration of stimulus there is an optimum equivalent mass at which the maximum work is done with maximum efficiency. The optimum equivalent mass is greater for a long stimulus than for a short one.

5. *The mechanical efficiency of isolated sartorius muscles.*

The direct measurement of the mechanical anaerobic efficiency of isolated muscles has been made by Meyerhof(21), using a determination of the amount of lactic acid produced by the muscle as a measure of the total energy liberated. He arrived at an estimate of 45–50 p.c. after endeavouring to allow for the fatigue which was an inevitable part of his method due to the necessity of stimulating the muscles many times in order to develop enough lactic acid for an accurate measurement. Fick ((9), p. 221) found efficiencies of about 25 p.c. by the thermo-electric method, without however a satisfactory method of calibrating the muscle and so of translating the galvanometer deflection into absolute units.

It had been supposed for two reasons that the efficiency might be as high as 75 p.c. if the energy used in oxidative recovery was disregarded, *i.e.* if the energy expenditure was calculated from the initial heat production as given by the galvanometer deflection. The reasons for this prediction were, firstly, that oxidative efficiencies have been recorded in man as high as 30 p.c. Assuming, with A. V. Hill(23), that the oxidative heat production is 1·5 times the initial heat production, the total heat would be 2·5 times the initial heat and the anaerobic efficiency would be 2·5 × 30 p.c. or 75 p.c. The second reason originated from a consideration of the theoretical maximum work of a frog's muscle as measured by the area under the curve obtained by plotting the maximum isometric tension of the muscle for a given stimulus against the corresponding length of the muscle. This theoretical maximum work was found by A. V. Hill(14) to be a large fraction of the initial heat production. If then the muscle could be so loaded that it could attain the maximum tension at every stage in its shortening, when stimulated, then the mechanical work done would be equal to that calculated from the length-tension diagram and the efficiency would be high. It was hoped that an approximation to an ideal condition of loading could be obtained with the inertia lever.

The actual results obtained did not verify the predictions (see Table VI). Each figure there given is the maximum efficiency obtained with one of the pairs of muscles used. The measurements covered a period from August to May and the temperature varied from 0° to 15° C. The differences due to temperature were not larger than the differences due to varying conditions of the muscles so that no temperature effect can be observed. The muscles worked on both an isotonic and an inertia lever. The results are arranged in the order of magnitude so that the first figure represents the maximum. Muscles of toads appear to be somewhat more efficient than those of frogs. This may be correlated with the slower movements of the former, the frog being built for speed rather than efficiency. The efficiencies recorded on the inertia lever are somewhat higher than those on the isotonic lever. An average of the efficiencies obtained when the same muscle was used on both kinds of levers shows that the isotonic lever gives efficiencies only 79 p.c. as high as the inertia lever.

TABLE VI. Mechanical efficiency of isolated muscles working on isotonic and inertia levers.

Frog.	Isotonic:	28, 26, 25, 23, 21, 19, 19, 17, 16, 14, 13. Av. 20 %.
	Inertia:	32, 27, 27, 26, 25, 25, 23, 23, 23, 23, 22, 22, 21, 21, 20, 20, 16. Av. 23 %.
Toad.	Isotonic:	25, 22, 19, 18. Av. 21 %.
	Inertia:	40, 36, 31, 31, 25, 22, 17. Av. 29 %.

Each figure represents the highest value which could be obtained from one muscle in a large number of trials.

On the whole the efficiency of an isolated sartorius muscle of the frog may be taken to be between 25 and 30 p.c. This means an *oxidative* efficiency only two-fifths as great, *i.e.* 10 to 12 p.c., which is only one-half or one-third as great as the oxidative efficiencies usually recorded on man. Possibly the frog is to be regarded as a very inefficient animal compared to man, being built for quick movements at low temperatures where man's muscles would move more slowly and waste less energy in change of shape. Possibly also abnormalities caused by the removal of the muscle from the body may have something to do with the low efficiencies obtained.

The reasons why the predictions of a high efficiency were not realised are twofold:

1. As shown by A. V. Hill(24) and Meyerhof(21) the theoretical maximum work cannot be attained in practice in a single contraction unless sufficient time is allowed at each length for the maximum tension to be developed. Even on the inertia lever Doi(20) found that this condition does not obtain. Hill states that the theoretical maximum work

equals 1/6 *Tl*, *T* being the maximum isometric tension and *l* the length of the muscle. Doi found that the maximum work performed was only 1/25 or 1/20 *Tl*.

2. Hill's predictions of a high efficiency were based upon the hitherto commonly accepted assumption that the energy liberated depends entirely upon the nature of the stimulus and the initial condition of the muscle, and is independent of the weight lifted. If this had been so the experiments would have justified his use of the graph in which isometric tension is plotted against length for predicting the behaviour of a muscle when allowed to shorten. Thus, if the efficiencies recorded in Table VI be recalculated, substituting the isometric heat for the total energy actually liberated at the point of maximum efficiency, much higher efficiencies are obtained. This can be done roughly on the assumption that the excess heat liberated is 1·3 times the work performed on the inertia lever. Now the highest efficiency recorded in Table VI is 40 p.c.[1] for a toad. The total energy may be taken as 100, the work as 40, and the excess heat above the isometric as 1·3 × 40 or 52. The isometric heat would then be 100 − 52 or 48 and the efficiency, if heat had been independent of work, would have been 40/48 or 83 p.c. Similarly taking 32 p.c., the highest individual record for a frog, it can be calculated that the isometric heat would have been 100 − (1·3 × 32) or 58, and the efficiency would have been 32/58 or 55 p.c.

But while these considerations justify the predictions on the evidence then available they raise another more fundamental question, for the existence of this excess energy liberation appears to be incompatible with the assumption that a stimulated muscle is a new elastic body possessing elastic potential energy. The shortening of a muscle appears to be an active process and not merely analogous to the release of a spring previously stretched. The energy used in the performance of work is developed at the time when the work is done and does not represent potential energy already developed before shortening begins. Hence estimates of the work which a muscle can do cannot logically be based upon evidence obtained from isometric contractions.

Summary. The *oxidative* efficiency of an isolated frog's sartorius muscle is only 10 to 12 p.c.

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[1] This figure is to be accepted with some caution because it has never been repeated on another muscle. This animal, however, was the largest and most healthy toad which I had an opportunity of using and it repeatedly gave efficiencies of this order of magnitude.

6. *Comparison between gastrocnemius and sartorius muscles.*

All the earlier work on the heat production of muscles allowed to shorten and do work was done on the gastrocnemius or semimembranosus muscles or the preparation described by Fick((9), p. 11), consisting of the inner side of the thigh joining the pelvis and the knee. All the differences between my results on the sartorius muscle and earlier ones can be reduced to the fact that the isometric heat has previously been found too high relative to the isotonic heat. It seems probable that this difference is an anatomical one and is due to the fact that an "isometric" contraction of a non-parallel-fibred muscle like the gastrocnemius is not isometric at all as far as the individual fibres are concerned. When such a muscle is stimulated with the two ends held fast there appears to be a change in shape which necessarily implies a shortening of some fibres with a consequent stretching of other fibres or of the tendon. The isometric contraction of the gastrocnemius muscle is, therefore, a contraction in which there is a slight shortening of the individual muscle fibres under maximal tension. Taking the thin parallel-fibred sartorius muscle as the best available example of a single muscle fibre and admitting my experiments on this muscle as evidence of its behaviour, it becomes clear why the isometric contraction of the gastrocnemius should liberate relatively too much heat, for in the sartorius even a very slight shortening if carried out under maximal tension causes a considerable excess heat liberation. It can be calculated, for example, from the data in Table I that a shortening of 0·8 mm., or about 3 p.c. (0·5 cm. on the drum), under a tension of 300 gm. (on the lever) increased the heat production 18 p.c. above the isometric. Similarly Hartree and Hill, in their experiments (unpublished) on the sartorius muscle, have found that a muscle tied "isometrically" with a thread gives off notably more heat than one similarly stimulated but tied with an inextensible wire. The thread stretches enough to enable the muscle to do an appreciable amount of work and hence to liberate a corresponding extra amount of heat. For these reasons the anatomical structure of a muscle, the arrangement of its fibres, the elasticity of its tendon, etc., has much to do with the relative amounts of isotonic and isometric heat.

There must be few, if any, muscular contractions in the living body which can really be carried out isometrically; there is always some bulging or twisting of the muscle which implies more or less shortening of the fibres. It is probable that even in a sartorius muscle the contraction is not really isometric unless the muscle is so stimulated that all the fibres are brought into activity simultaneously. Thus Bethe(25) has recently shown by a photographic method that in a muscle stimulated through its nerve a wave of contraction passes over the muscles in such a way that fibres remote from the origin of the wave are stretched before the wave reaches them by the contraction of fibres nearer the origin. In a muscle stimulated, as in my experiments, by an alternating current running from one end of the muscle to the other this initial stretching fails to occur. It will be interesting to confirm this view by measurements of the isometric heat of sartorius muscles stimulated in various ways with maximal stimuli of constant duration.

Prof. Hill has suggested to me that these same considerations may explain the observations of Hartree and Hill(26) that the isometric heat frequently decreases though the maximum tension remains the same, when the strength of the stimulating current is increased above the maximal. With a current just maximal some fibres might be stimulated slightly sooner than others, perhaps due to a better supply of nerve fibres, and would thus have an opportunity of shortening slightly in contraction. A still stronger stimulus might well prevent this shortening by bringing all the fibres into activity simultaneously.

In order to make certain that my results do not differ from the older results merely because of some modification in the method, I have repeated some of my experiments using a pair of gastrocnemius muscles in place of the sartorius and I have had no difficulty in confirming the older work in the following essential points.

1. As the after-load is increased the heat production continues to increase until the maximum is reached at infinite load, *i.e.* isometric. This I suggest is due to the fact that there is considerable shortening of the fibres even in an isometric contraction. In the few experiments which I have tried I have not been able to confirm the observation of Heidenhain and Fick(20) that the heat passes sometimes through a slight maximum just before the isometric is reached, thus suggesting the type of curve which I have found invariably on the sartorius. If their observations are trusted, however, in spite of Blix's emphatic denial of them, they may be taken as evidence that the increase of heat with increase of work is a factor in the gastrocnemius curves even though the factor of fibre length may also be important.

2. With a single gastrocnemius muscle I have repeated and confirmed Hill's experiment(14) in which the muscle was prevented from shortening for increasing times after stimulation with a consequent increase in the

heat production. In my experiment, as in Fick's (5), there was evidence of a maximum in the heat production just before the contraction became isometric (at point of maximum tension). Schenck (6) found this maximum only under special conditions when neither the tension nor the shortening was too small. This fits in perfectly with the idea that the isotonic heat is at a maximum under conditions which make the work maximal also and it doubtless accounts for Hill's result with an unloaded muscle in which the isometric contraction gave the maximum heat.

Hill (14) has shown that the theoretical maximum work (the area of the tension-length diagram) of a sartorius muscle is 1/6 the product of the isometric tension *T*, at the greatest length, and the length of the muscle *l*. In the gastrocnemius, Meyerhof (21) has found that the theoretical maximum work is only 1/14 or 1/17 of *Tl*. Hill suggests (unpublished) that this difference is also a matter of anatomy. *T* is the sum—or the resultant—of the tension of the individual fibres of the muscle; *l* the average length of one of them. If the length of the fibres of the gastrocnemius is only 6/14 or 6/17 that of the muscle while the length of the sartorius fibres is equal to that of the whole muscle, the difference is completely resolved.

It is already well known that the sartorius with its straight fibres is adapted for long quick movements under light loads, while the gastrocnemius with its diagonal fibres is adapted for the development of high tension with very little shortening. It seems possible that the gastrocnemius would be assisted in developing a high tension by the slight shortening of the fibres which always takes place in its supposedly isometric contraction and the consequent liberation of an extra supply of energy. Thus Hill (14) has observed that a 35 p.c. greater tension can be developed by a stimulated muscle at a given length if it has had to do work before reaching that length. The peculiar significance of this fact for the gastrocnemius and similar muscles now becomes apparent.

From this discussion it appears likely that the results which have been described for a sartorius muscle are equally applicable to other types of muscle but are obscured at times by complications arising out of anatomical differences. Because of the fact that the sartorius muscle, particularly when stimulated directly with a maximal stimulus is a better representation of a single muscle fibre than a gastrocnemius muscle, I would claim for my experiments greater significance as a basis for an understanding of the nature of the contractile process.

Application to the heart. It is a familiar fact (27, 28) that the oxygen consumption increases with increase in the work of the heart, whether it is the pressure or the output which is varied. Similarly, it can now be shown that the energy liberated by the frog's skeletal muscle varies with the work, whether it is the load or the shortening which is increased. I have shown that this phenomenon in skeletal muscle *cannot* be explained by changes in the length of the muscle fibres and that the significant factors are rather the amount of shortening of the fibres and the tension under which this shortening takes place. It is possible, indeed probable, that these same two factors (the product of which is work) determine the energy liberated and hence the oxygen consumption of the heart. The advantage to the heart of a greater initial volume may thus be due not to a greater length of fibre *per se* but rather to more nearly optimal mechanical conditions of working caused by an increased tension of the fibres during shortening (for the same arterial pressure) and a decreased amount of shortening (for the same volume output).

It is impossible at present to evaluate the true effect of fibre length on the energy liberated "isometrically" on account of the inevitable shortening which must occur, particularly in the heart. Even if fibre length had *no* effect on the energy liberated, an increase in the length of the whole muscle (in the gastrocnemius and heart at least) might be expected to cause the energy to pass through a maximum, as it is observed to do, for in stretching the muscle, the "isometric" shortening of the fibres approaches zero while the tension during that shortening approaches infinity. *All* the effect of fibre length on energy output cannot be explained in this way unless there is likewise an "isometric" shortening of fibres in the sartorius sufficient to explain the same phenomenon in that muscle.

The all-or-none law.

If a muscle *fibre* contracts at all as a result of a stimulus, the tension developed, the work done, and the energy liberated by that contraction will be (1) independent of the strength of the stimulus, and (2) dependent only upon the initial physiological and mechanical conditions which obtain in the muscle. This I take to be the commonly accepted statement of the all-or-none law as applied to muscles. Hartree and Hill(26) brought forward an apparent exception to item (1) when they observed that the heat production of a muscle is frequently slightly less with supermaximal stimuli than with maximal stimuli, showing that the contraction is not quite independent of the stimulus. This cannot now be regarded as necessarily an exception for a possible alternative explanation of the observation has been suggested above.

My experiments show, however, that item (2) in the above statement of the law is emphatically incorrect for the total energy can be varied markedly by changes in the tension and length of the muscle which occur *after* the stimulus is over. The energy of the contraction is dependent not only upon the initial conditions of the muscle but also upon the conditions which obtain during and for some time after the stimulus.

It is to some extent a corollary of the all-or-none law that variations in the energy output of a whole muscle for a given duration of contraction are due to variations in the number of active fibres. It now appears, however, that there is another regulatory mechanism within each individual fibre which, within certain limits, is able to adapt the energy output to the work done. When we lift a weight, therefore, two regulatory mechanisms are in operation. One is dependent upon the nervous system and acts by stimulating more and more fibres according to need. It can therefore vary the total energy liberated by small steps over a wide range of values, each step representing the contribution of a single fibre. The other mechanism is independent of the nervous system and works merely by virtue of the fundamental nature of the muscle machine, whatever that may be. By its means the energy output of each individual fibre can be promptly and more or less precisely adjusted to its work. This second mechanism may be regarded as a sort of fine adjustment, instantaneously active but capable of producing only relatively small variations in energy output.

Summary. 1. The all-or-none law, as applied to muscles, must be confined to the statement that the total energy liberated in a contraction of a single muscle fibre is independent of the strength of the stimulus.

2. The energy expenditure of a single muscle fibre can be varied by changes in the mechanical conditions of the muscle which occur *after* the stimulus is over.

The general nature of the contractile mechanism.

It is hoped that in the preceding pages convincing evidence has been presented to show that the initial heat produced in a muscle by stimulation is not dependent merely upon the number of fibres stimulated, but also upon the amount of shortening and the tension under which the shortening takes place. In mathematical terms, and rather inaccurately,

$$H = in + kTs.$$

This means that H, the total energy liberated as a result of the contraction, is equal to the sum of two products, the factors of the first being i, the heat produced by the isometric contraction of a single fibre and n the number of fibres stimulated and the factors of the second product being T, the tension of the muscle during the shortening, s the amount of shortening, and a constant, k, with a value usually between 1 and 2. In a later paper reasons will be given for believing that when the complications due to the lowering of the weight in relaxation can be properly allowed for the value of k is very nearly 1, *i.e.* the excess heat produced is very nearly equal to the work done.

The general nature of the muscular mechanism as elucidated by these experiments can be made clear by an analogy to an electric motor in which the energy used increases with the work done in an entirely automatic manner depending upon the intrinsic properties of the motor. When the load on the motor is increased it slows down, the back E.M.F. which it develops is decreased and more current passes through the coils. Conversely when the motor runs idle it develops a large back E.M.F. so that the current becomes very small. The necessity of providing a muscle with a mechanism of this general type makes new demands upon theories of muscular contraction which at present neither the surface tension nor the water absorption theories seem able to meet.

SUMMARY.

1. The older work on the heat production of muscles allowed to shorten has been repeated and extended with the use of the sartorius muscle of the frog instead of the gastrocnemius. Quite different results have been obtained which are apparently due to differences in the anatomical structure of the two muscles.

2. On account of the greater anatomical simplicity of the sartorius muscle it is regarded as a better example of a single muscle fibre and hence greater theoretical significance is claimed for the results obtained with it. Consequently important modifications of some of the fundamental and accepted principles of muscle physiology have become necessary.

3. When a muscle lifts increasing weights to a constant height, the increase in heat obtained is roughly proportional to the tension under which the muscle shortens (*i.e.* the weight).

4. When a muscle lifts the same weight through increasing heights the increase in heat obtained is roughly proportional to the amount of shortening.

5. Since the product of tension during shortening and the amount of shortening, is work, the increase in heat becomes roughly proportional to the work.

6. Whenever a muscle shortens upon stimulation and does work in lifting a weight, an extra amount of energy is mobilised which does not appear in an isometric contraction. Hence less energy is liberated in an isometric contraction than in any contraction in which the muscle is allowed to shorten.

7. When a muscle is made to do work on an inertia lever against varying equivalent masses so that the tension under which it shortens and the amount of shortening vary simultaneously the excess heat is still roughly proportional to the work done.

8. The anaerobic efficiency of the sartorius muscle of a frog is very low, only about 25 to 30 p.c. at most. The oxidative efficiency is therefore only about 10 to 12 p.c.

9. The energy liberated by the contraction of a single muscle fibre for a given stimulus is not dependent solely upon the initial mechanical and physiological condition of the muscle but can be modified by the nature of the load which the muscle discovers it must lift after the stimulus is over. The all-or-none law of muscular contraction must be qualified from this point of view.

10. The experiments provide a new explanation of the parallelism between the work of the heart and its oxygen consumption.

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