

The heat of shortening and the dynamic constants of muscle

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The hope was recently expressed (Hill 1937, p. 116) that with the development of a more accurate and rapid technique for muscle heat measurement, a much more consistent picture might emerge of the energy relations of muscles shortening (or lengthening) and doing positive (or negative) work. This hope has been realized, and some astonishingly simple and accurate relations have been found, relations, moreover, which (among other things) determine the effect of load on speed of shortening, allow the form of the isometric contraction to be predicted, and are the basis of the so-called "visco-elasticity" of skeletal muscle. This paper is divided into three parts. In Part I further developments of the technique are described: everything has depended on the technique, so no apology is needed for a rather full description of it and of the precautions necessary. In Part II the results themselves are described and discussed. In Part III the "visco-elastic" properties of active muscle are shown to be a consequence of the properties described in Part II.

PART I. METHODS OF MEASURING THE ENERGY LIBERATION OF MUSCLE

(a) *Galvanometer system.* In the earlier stages of the present work a single moving-coil galvanometer of rather short period (0.2–0.3 sec.) was employed, as described in the previous paper (Hill 1937, pp. 115 and 131). Such a galvanometer, however, was far slower than the thermopile, and the interpretation of records obtained by it was difficult, or impossible, without laborious numerical analysis. The galvanometer could not be made quicker without reducing its sensitivity too much; amplification therefore was necessary if recording was to be quick enough.

Now the rise of temperature which it was particularly desired to measure was that associated with shortening, which in a muscle 3 cm. long allowed

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to shorten 5 mm. proved to be of the order of $1-2 \times 10^{-3}$ °C. The thermopiles gave about $1500 \mu\text{V}$ per 1°C , so the change to be observed was of the order of $1.5-3 \mu\text{V}$. If this was to be determined to within 4%, it was necessary to avoid disturbances greater than $0.06-0.12 \mu\text{V}$.

It is frequently asked why amplification by thermionic valves is not used. Dr Otto Schmitt of St Louis advises me that the present limit of direct measurement with valves, even for the relatively slow processes involved in this work, is of the order of $0.3 \mu\text{V}$, so the direct method would not be nearly accurate enough. Indirect methods might be used, involving some special arrangement designed essentially to transform up the small potential difference, in the low impedance of the thermopile, to a larger potential difference, in an impedance more comparable with the input impedance of a valve. This impedance matching might be carried out in several ways, the simplest of which would involve frequency or amplitude modulation of a carrier oscillation and subsequent amplification at high audio- or radio-frequency. Such a technique, however, although in principle about ten times better than present galvanometric methods, is not at present available and would have to be developed.

The alternative of building a finer thermopile with many more junctions, and using direct amplification, might have a better chance of success. Since a valve has a very high input impedance, a high resistance thermopile could be used. If it were possible to build a thermopile with 500 couples, not by soldering where the limit has already been nearly reached, but perhaps by electrodeposition, or sputtering of the active metals upon a thin former and subsequently slicing the film into a thin continuous spiral, the desired sensitivity could be achieved. The construction, however, of so fine a thermopile would require much time and effort, without any certainty of ultimate success. One may conclude, therefore, that valve amplification may indeed be applicable to measurements of muscle heat, but not with present instruments or methods (see also p. 155 below).

It was decided, therefore, to fall back on the older method of amplifying the deflection of the galvanometer by photo-electric means, the light returning from the mirror falling upon a differential photo-cell and producing a current which deflected a second galvanometer of short period (Hill 1932, 1934*a, b*; Downing and Hill 1935). The secondary galvanometer gave 20-25 times the deflexion of the primary galvanometer. The resulting sensitivity was unnecessarily high, and an adjustable fraction of the current from the photo-cell was "fed back" into the primary galvanometer in order to make it quicker, more stable and less sensitive (cf. Watton 1935, Appendix by Hill). By this the sensitivity could be set to the value required,

and any unnecessary sensitivity was not wasted but used to make the system quicker and more stable.

The secondary galvanometer, constructed by Mr A. C. Downing, was of the type recently described (Hill 1937, Appendix I), but with much stiffer suspension (above and below) and so a very short period.

Period: 0.053 sec.

Internal resistance: 120 ohms.

External resistance for critical damping: 500 ohms.

Coil dimensions: $24 \times 1 \times 1$ mm.; weight 54 mg.

Wire: 30μ copper, 100 turns.

Suspension: 16μ phosphor bronze, 5 mm. at each end.

Mirror: $3\frac{1}{2} \times 1\frac{1}{2}$ mm.

Sensitivity at 2 m. distance, nearly damped: 1 mm. = 3.4×10^{-8} amp.

It was mounted on a Julius suspension and was perfectly steady. Records were made from it on a camera drum moving at 8 or 13 cm./sec. The lower half of the light beam was intercepted by mirrors and observed simultaneously on a scale.

The primary galvanometer, constructed by Mr Downing, was of the same type but suited to a lower resistance circuit and of longer period.

Period: 0.0965 sec.

Internal resistance: 44 ohms.

External resistance for critical damping: 70 ohms.

Coil dimensions: $24 \times 1.3 \times 0.5$ mm.

Wire: 40μ silver, 50 turns.

Suspension: 16μ phosphor bronze, 12 mm. at each end.

Mirror: $3\frac{1}{2} \times 2$ mm.

Sensitivity at 2 m. distance: 1 mm. = 2.8×10^{-8} amp.

It was adjusted for the greatest possible stability, by aligning the coil with the suspension. With the high amplification employed, the stability was at first insufficient (at the top of a building in London), and the primary galvanometer, lamp, lenses and photo-cell were mounted together on a teak stand floating on mercury in a trough 78×40 cm. in size (cf. Downing, Gerard and Hill 1926). A little thick oil on the top of the mercury helped to damp oscillations. With appropriate feed-back of the photo-current the stability was now sufficient, and when the laboratory was quiet the amplified deflexion could be read on a photographic record to 0.1 mm.

A 12 V, 36 W motor head-lamp was used with large accumulators to provide the illumination. A large condensing lens focused the light on the galvanometer mirror, from which it was focused again on the two halves of a large photo-cell of the rectifying type ("GMBH electro-cell") arranged differentially (in opposition in parallel). The platform on which galvanometer, lamp, photo-cell, etc. floated was heavily loaded. The

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photo-current was led to the pair of resistance boxes shown in fig. 1 by which the feed-back was regulated. R_1 was usually kept at 1000 ohms: the impedance of the photo-cell was high so this did not matter, and it was undesirable to lose sensitivity by short-circuiting the thermopile with a lower resistance. The feed-back was regulated by adjusting R_2 , as shown by the example in Table I.

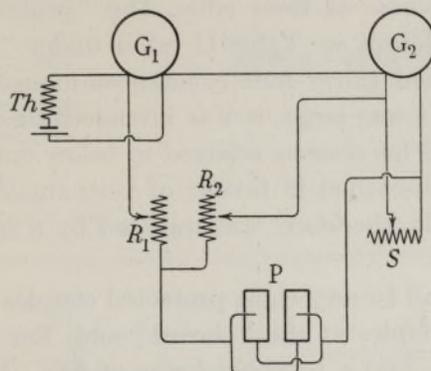


FIG. 1. Circuit of coupled galvanometers: G_1 primary, throwing light on to photo-cell; G_2 secondary. P , rectifying photo-cell, two halves arranged in opposition in parallel. R_1 and R_2 , resistances for adjusting the feed-back to G_1 . S , shunt to G_2 for adjusting damping. Th , thermopile connected to G_1 .

TABLE I. DEFLEXION OF SECONDARY GALVANOMETER G_2 FOR $1 \mu\text{A}$ IN PRIMARY GALVANOMETER G_1

R_1 (ohms)	0	1000	1000	1000	1000	1000
R_2 (ohms)	1000	1000	300	100	50	0
Deflexion (mm.)	28	51	104	230	350	800
Period of G_1 (msec.)	18	24	35	52	63	96

The period was calculated from that observed without "feed-back", assuming it to be proportional to the square root of the sensitivity.

It was found that the damping of the whole system could be sufficiently adjusted by the shunt S of G_2 . Critical damping is not wanted. It is better, indeed, for quickness, to use the system rather underdamped, for the heat production of muscle occurs relatively slowly, and no overshooting occurs. For working at 0°C , where the heat production is rather small, R_2 was usually about 130 ohms and the period of G_1 about 50 msec. This gave sufficient stability, and the amplified deflexion to a constant current was nearly complete in 35–40 msec. For higher temperatures R_2 , and the feed-back, could be made greater, and the period of G_1 reduced to 35–40 msec., with an amplified deflexion nearly complete in 30 msec. The system,

therefore, was fast enough to allow the thermopile current to be recorded with very little lag. For most purposes a full numerical analysis of records was not needed, which greatly simplified and quickened the research.

(b) *Thermopile*. The three instruments particularly used were similar to the one described before (Hill 1937). All were "protected" against the errors due to movement by having a sufficient set of dummy couples, or of similar constantan wires, at their ends. The "protection" seems to be very effective. For details see Table II below under "Calibration".

Thermopile P. 2 had thirty-four constantan-manganin couples in the "protected" part. It was large, it was intended for the sartorii of large Hungarian frogs, and for reasons referred to below under "Muscle" these large muscles were discarded in favour of very small ones from English frogs. This thermopile, therefore, was replaced by a smaller one. It gave $1286\mu\text{V}$ per 1°C .

Thermopile P. 4 had twenty-eight protected couples of constantan-iron, sixteen protecting couples at the "thread" end, four protecting couples at the "clamp" end, and a total thickness of 55μ . It gave $1415\mu\text{V}$ per 1°C . Having iron instead of manganin, it had a higher thermo-e.m.f. and a lower resistance. It is short—total length, including electrodes, 20 mm.—and suited any frog's sartorius, however small. The insulation was usually very good, in spite of its thinness. If leaks appeared, the thermopile was dried, thinly painted with very dilute bakelite varnish ("yacht varnish"), dried under a lamp and the dried varnish scraped off. The high insulating properties of the mica were in this way restored without thickening it. The insulation was so good, although only 20μ thick, that condenser discharges of 400 V, $0.03\mu\text{F}$, for the purpose of "control heating", gave momentary disturbances only of the order of 1 mm. Stimuli showed no disturbance at all unless the air in the room was damp. This instrument was used in most of the experiments (Dec. 1937–May 1938).

Thermopile P. 5 shown in fig. 2 has forty-two protected couples, is about 45μ thick, and gives $1628\mu\text{V}$ per 1°C . Being of constantan-manganin, and rather thinner, it has a higher resistance and is actually rather less sensitive than P. 4. It is very flat and so designed that a small frog's sartorius pair lies, and moves, very accurately in the groove (4 mm. wide) containing the hot junctions. Mechanically, and for quickness, it is the best instrument hitherto constructed. It has the same good insulation, but only 16μ thick, as P. 4. It was used in the later experiments.

The quickness of response of thermopile P. 5 to a sudden rise of temperature of the muscle on it, when connected to the coupled galvanometer system described above, is shown by curve *E* in fig. 3. For comparison

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previous "heating-control" curves are given, as described in the legend. Curve *A*, from the original paper by Hill and Hartree (1920*a*), rises so slowly that it had to be plotted on one-third the time scale. The increase in speed, illustrated in fig. 3, has made possible the experiments described

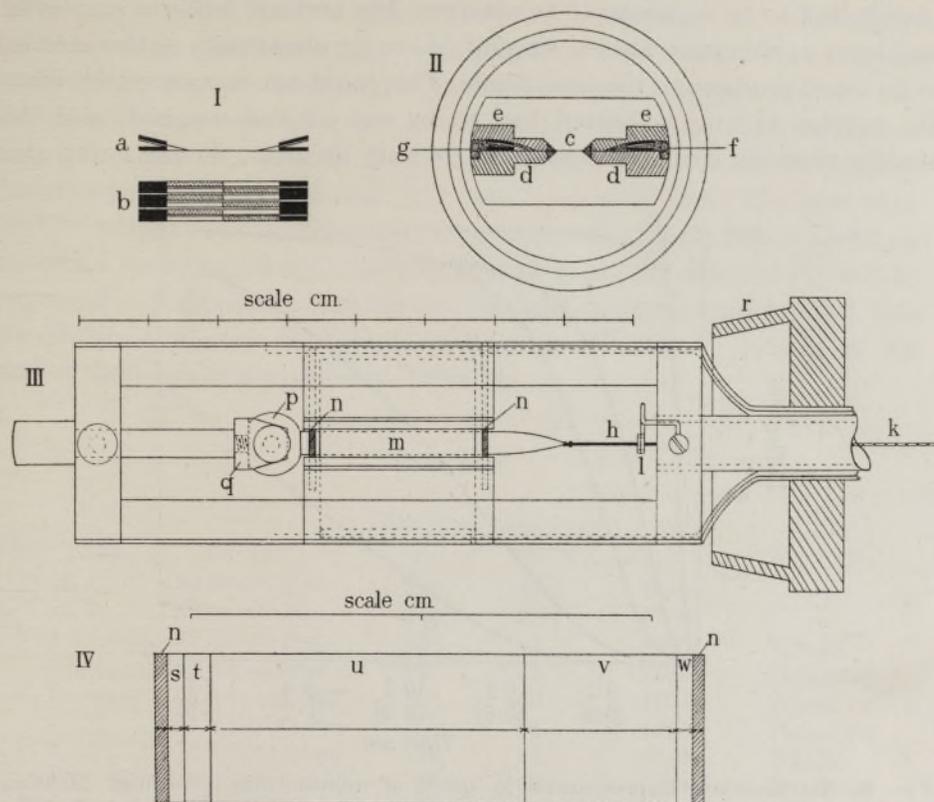


FIG. 2. Thermopile P. 5 (A. C. Downing). I and II to show construction and mounting of thermopile element. III, complete instrument with muscle. IV, enlarged diagram of central part of thermopile element. I: *a*, end view; *b*, side view, of manganin-constantan couples, with "loaded" cold junctions. Alternate cold junctions raised to avoid short circuit. II: *c*, end-view of thermopile element between insulated brass flanges *dd* and bakelite *ee*, 4 mm. exposed for contact with muscles; *f*, stimulating leads; *g*, thermopile leads. III: *h*, thread to chain *k* and muscle *m* on thermopile; *l*, silver ring to guide thread; *n*, platinum electrodes; *p*, pelvic bone and acetabula in clamp *q*; *r*, tapered brass block to carry insulated brass cover, holding 105 c.c. of Ringer's fluid which is stirred by bubbling oxygen. Before observation the fluid is removed. IV: central portion of element, 23.6 mm. long, 45 μ thick. Left to right: *n*, electrode; *s*, mica alone; *t*, three insulated constantan dummies; *u*, forty-two insulated manganin-constantan couples; *v*, twenty insulated constantan dummies allowing a 29% "protected" shortening of muscle; *w*, mica alone; *n*, electrode. Resistance 68 ohms, sensitivity 1628 μ V/1° C. The couples are of 44 s.w.g. (81 μ) wire, rolled to 12 μ after hard soldering. The cold junctions are "loaded" with soft solder for 4 mm. outwards to slow their warming up by conduction.

in Part II: the adoption of the "protected" thermopile has made them accurate.

(c) *Calibration.* In the present investigation heat and work had to be directly compared, so calibration of heat deflexions in absolute units of energy had to be as accurate as possible. The method hitherto employed had been to liberate a known amount of energy electrically in the muscle, in its usual position on the thermopile. This could not be very exact, since the portion of muscle heated had to be cut off and weighed, and the heating near the electrodes could not be very uniform. It was found also

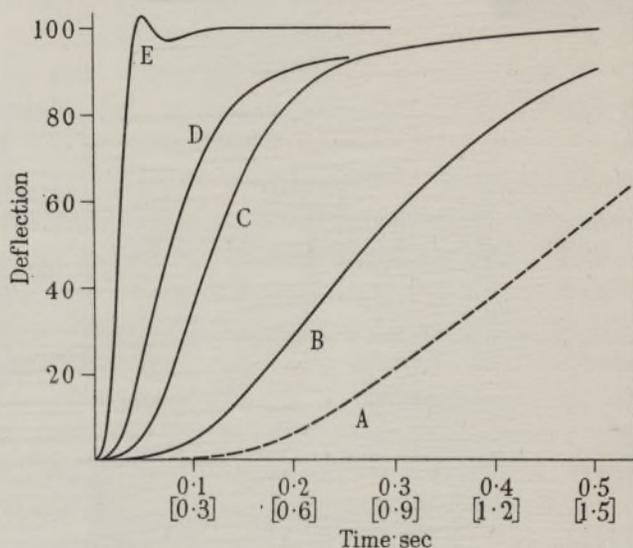


FIG. 3. To illustrate improvement in speed of myothermic recording. Heating controls. *A*, 0.1 sec. heating, Hill and Hartree (1920*a*), lower time scale; *B* to *E*, upper time scale. *B*, Hartree (1933), 0.05 sec. heating, thermopile W.H. 2 (Table II), moving magnet galvanometer. *C*, ditto, Moll (0.19 sec.) "micro" galvanometer. *D*, Hill (1937 unpublished), instantaneous heating, thermopile P. 2, Hungarian frog, 0.22 sec. galvanometer. *E*, (present research), instantaneous heating, thermopile P. 5, English frog, coupled galvanometers.

that the same amount of electrical energy in different forms (e.g. in single condenser discharges of different voltage and capacity, or in repetitive discharges) did not give precisely the same readings, probably owing to more or less of the energy being liberated near the electrodes with the different forms of discharge. This direct method of calibration had the advantage that it made automatic allowance for heat capacity and heat loss in the instrument. The present thermopiles, however, are so thin that their heat capacity is very small, and the deflexions are so rapid that there

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is no time for any significant heat loss. It was more accurate therefore—and much simpler—to calibrate them once and for all by direct observation of the e.m.f. per 1° C difference of temperature between hot and cold junctions, and to allow for the heat capacity in each case.

The e.m.f. per 1° C was determined by connecting the thermopile, through a high resistance, to a quick galvanometer (period 0.2 sec.), and transferring it rapidly, between two baths, from one temperature to another. The temperatures were read with a standard thermometer, the transference took only a second, and the galvanometer gave an immediate reading. The thermopile is so thin that its "hot" junctions take the new temperature within a few milliseconds, while its "cold" junctions are so deeply embedded under metal and insulator that they are not affected for several seconds. The deflexions are calibrated by introducing a known e.m.f. into the circuit, and very consistent readings are obtained. Details of the various thermopiles are given in Table II.

TABLE II

Thermopile	Couples	Thickness Resistance		e.m.f. $\mu\text{V}/1^\circ\text{C}$	Remarks
		μ	ohms		
W.H. 1	88 const.-iron	210	22.5	3640	—
W.H. 2	66 const.-iron	240	23.7	2775	—
P. 1	92 const.-iron	125	61	4200	Whole
	64 const.-iron	125	45	3100	Protected
P. 2	54 const.-mang.	55	69	1997	Whole
	34 const.-mang.	55	44	1291	Protected
P. 3	52 const.-mang.	70	84	2010	Whole
	32 const.-mang.	70	52	1228	Protected
P. 4	48 const.-iron	55	55	2445	Whole
	28 const.-iron	55	32	1415	Protected
P. 5	42 const.-mang.	45	68	1628	Protected

The W.H. thermopiles are those used by Hartree in his latest researches (Hartree 1932, 1933). The P. thermopiles are "protected" ones, P. 1 being the instrument recently described (Hill 1937).

The allowance for the heat capacity of the thermopile is illustrated in the following example:

Thermopile P. 5, 12μ of wire, 33μ of mica and bakelite. $\rho c = (0.85 \times 12 + 0.63 \times 33)/45 = 0.69$. ρc for muscle = 0.92. Hence 45μ of thermopile is equivalent in heat capacity to 34μ of muscle. Muscle pair, 90 mg., 3 cm. long, $3\frac{1}{2}$ mm. wide, average thickness 820μ . Thus 1° temperature rise of muscle gives $820/854 = 0.96^\circ$ temperature rise of thermopile after equilibration. Hence 1° C of muscle gives $0.96 \times 1628 = 1564\mu\text{V}$, and 1 cal./g. of muscle gives $1564/0.88 = 1778\mu\text{V}$.

In each experiment, and usually on each sheet of records, the sensitivity of the system was measured by introducing $\pm 10 \mu\text{V}$ in the galvanometer-thermopile circuit. If 30 mm. deflexion = $10 \mu\text{V}$, 1 mm. = $0.333 \mu\text{V}$ = (in the above example) 0.187×10^{-3} cal./g. This was a usual sensitivity for 0°C . For higher temperatures one-half to one-third of this was sufficient. The records were read to $\frac{1}{10}$ mm. For comparison with the work, which is measured in g. cm., the heat in cal./g. is multiplied by $42,600 \times$ (weight of muscle). The muscle was cut off at its tendons and weighed at the end of an experiment.

In the method of calibration adopted it is necessary that the thermo-e.m.f. per 1°C should be the same at the temperature of the experiment as at that of calibration. This was tested with a manganin-constantan couple and found to be the case.

(d) *Mechanical arrangements.* For an investigation of the present kind the use of a thread to connect muscle to lever is objectionable, because of its extensibility. The muscle shortens more than intended, it does work in stretching the thread and this work appears as heat in relaxation. A wire is better, but it is difficult to make a wire, which has to be manipulated, remain straight, and a bent wire stretches by straightening and is as bad as a thread. Fine chains, therefore, were used for all connexions. Chains intended for jewellery can be bought at Woolworth's Stores for a few pence, and some of these are excellent. They are only half as extensible as the best thread in the range of loads considered, they show no after-extension as a thread does, they are perfectly flexible, they hang quite straight, and they can be adjusted precisely to be just tight. The best chain found consisted of small plane elliptical links, long axis 2 mm., short axis 1 mm., of chromium-plated brass wire, weighing about 16 mg./cm. length.

It is necessary, for accurate work, to be sure of the initial tension of the muscle. A light isotonic lever was constructed, on which the muscle pulled twenty-two times as far out as the load. To avoid friction the lever was mounted on miniature ball-bearings (G.M.B.). The load on this lever determined the initial tension. It was connected by a chain to the main isotonic lever, or to the isometric lever, above it. It had a thin bamboo pointer which was used to record movement on a smoked drum.

The main isotonic lever was of aluminium strip and was mounted on ball-bearings. It provided the after-load. The weight in its pan was 18.3 times the force it produced on the muscle. Its stand had two adjustable screw stops, one at each end, the first to hold the after-load till shortening began, the second to adjust the amount of shortening allowed. It was equipped with two electromagnets, one for holding the lever up, i.e. in the initial position, one for holding it down, i.e. in the final position. The

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magnets were connected to the lever by threads, or later by chains. The first one maintained the contraction isometric until it was released by opening a key, when the muscle was able to shorten isotonicly through the distance required. The moment of release was determined, in relation to the beginning and end of stimulation, by a third arm on Lucas's revolving contact breaker. If this magnet was not used, the contraction was isotonic (after-loaded) from the start. The other magnet was actuated, when required, by the contact of the lever with the second stop. By it the main weight could be held up, and not lowered by the muscle in relaxation: the muscle, in that case, relaxed under the initial load only.

The isometric lever was adjusted by a separate rack and pinion, mounted on the same stand as the rest, and was disengaged when the main isotonic lever was in use. The chains and the isometric lever together permitted 0.93 mm. shortening when the muscle developed a force of 100 g.

The whole arrangement was mounted on a Palmer screw stand, by which it could be raised or lowered precisely as required.

It was important to make sure that, under the conditions of its use, the system of levers employed developed no considerable kinetic energy. Otherwise the work done by the muscle would be greater than that calculated from the load and the shortening. This was tested as follows. At time t sec. let y cm. be the displacement from its zero position of the point of attachment of the muscle to the lever, and let P grams weight be the static load on the muscle due to the weights employed. Let $\frac{1}{2}M(dy/dt)^2$ be the kinetic energy of the whole moving system, where M is its "equivalent mass" and has to be determined. Let us suddenly release the chain from the muscle (at $t = 0$ and $y = 0$) and record, on a rapidly moving drum, what happens. The work done by the weights is Pgy ergs, and if the bearings be assumed frictionless—as they nearly are—this is transformed into kinetic energy. Hence,

$$\frac{1}{2}M(dy/dt)^2 = Pgy$$

or, on integration

$$y = \frac{1}{2}Pgt^2/M.$$

Experiments showed that $\sqrt{y/t}$ was constant, from which M could be determined. Its actual value was about 1 g. This does not include the mass of the chain (about 1 g.) or the equivalent mass of the weights in the pans. The latter can be calculated: for example, 100 g. on the "after" lever is equivalent to $100/(18.3)^2 = 0.3$ g.: 100 g. on the "initial" lever to $100/22^2 = 0.2$ g.

Let us see what effect this has. High velocities occur only with small loads. At 0° C the highest velocity of shortening observed, with a small

load (total equivalent mass, say, 2.5 g.), was about 4 cm./sec. The kinetic energy is $\frac{1}{2} \times 2.5 \times 4^2 = 20$ ergs = 0.020 g. cm. This is quite negligible compared with the energy, or work, liberated by the muscle. At 20° C, with a rather larger load, equivalent mass (say) 3.0 g., a higher velocity, say 10 cm./sec., might be reached: the kinetic energy would be $\frac{1}{2} \times 3 \times 10^2 = 150$ ergs = 0.153 g. cm.: this is still negligible compared with the energy liberated by the muscle. With heavier weights on the levers, the equivalent mass is rather greater: with 500 g. on the "main" lever and 50 g. on the "initial" lever it would be 3.6 g., but with this, even at a higher temperature, the velocity of shortening would be low, and the kinetic energy would remain negligible. For the muscles employed, therefore, and the velocities they attained, the lever system was nearly enough "isotonic"; it discharged its role of maintaining a constant pull on the muscle, its kinetic energy was negligible.

The isometric lever and the chain were not quite as inextensible as could be wished: but a long connexion is inevitable when the muscle is mounted on a thermopile, and the complication of an optical lever and photographic recording was to be avoided with so much else to attend to. Moreover it will be shown below that the elastic portion of the muscle itself must be stretched 2-3 mm. in a maximal tetanus: which is several times as much as the stretch of lever and chain. Work is done by the muscle in stretching lever and chain, e.g., for 100 g. tension developed, assuming the extension given above and normal elasticity, $\frac{1}{2} \times 100 \times 0.093 = 4.65$ g. cm. This appears in the muscle as heat during relaxation: it would warm a muscle of 120 mg. about 10⁻³° C: it provides a considerable part of the relaxation heat observed after an isometric contraction.

(e) *The muscle.* At first it was intended to use the rather large sartorii of Hungarian frogs with thermopile P. 2. A pair of these had an average weight of 500 mg., an average length of 45 mm., and each had an average thickness of about 1 mm. It was found, however, that irregularities of the heat records occurred in contraction, and particularly in relaxation, which could be ascribed to no other cause than non-uniformity of the heat production and of the speed of relaxation. The muscles were prepared as carefully as possible, but still the irregularities persisted. To get rid of them, either a muscle which contracted more uniformly and was less affected by manipulation, or a much thinner one in which thermal equilibration was quicker, was needed. For both reasons recourse was had to the sartorii of small English frogs, averaging in weight about 80 mg. the pair, in length 32 mm., in thickness 0.35 mm.

Since the time taken in thermal equilibration depends on the square of

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the thickness, it is diminished to one-eighth by using the thinner muscles; and the sartorii of English frogs (which also can be obtained in better condition) seem to be less affected by experimental procedure. Being thinner, moreover, the initial soaking with Ringer's solution, and the oxygen supply, are more effective. A final advantage is that, whereas the connective tissue covering (epimysium) is thick and strong in Hungarian sartorii, it is thin and almost imperceptible in English ones. This connective tissue slows conduction of heat to the thermopile, and adds to its heat capacity. It is dangerous to try to dissect it away, for there is risk of injury to the surface fibres, and if these are made inexcitable, being (say) 50μ thick, they will add greatly to the heat capacity of the thermopile and render conduction much slower. Even a single layer of injured fibres, on each face of a rapid thermopile such as P. 5, with a heat capacity equal to only 34μ of muscle, would slow it in the ratio of $(134/34)^2$, i.e. about 15 times: and a layer of injured fibres, by liberating potassium ions, would be likely to affect the fibres beneath it, and so lead to even worse results. For exact registration of the time relations of its heat production a muscle must be quite uninjured at its surface. The sartorius of a small English frog is well adapted to myothermic experiments, but very few muscles are. For accurate work, a muscle must be a regular band of tissue, very thin, contracting and shortening straight and uniformly, and quite uninjured in its preparation. Otherwise, with the present very sensitive instruments, anomalous or absurd results may be obtained.

The thermopiles have been made even quicker than predicted in the previous paper by the use of the thin muscles. The curve in fig. 1*a* (Hill 1937) was calculated for a thermopile of equivalent half thickness $b = 0.0014$ cm., with a muscle of thickness $a = 0.1$ cm. on each face. With thermopile P. 5, $b = 0.0017$ cm.; a pair of muscles of 80 mg., 30 mm. long and $3\frac{1}{2}$ mm. wide, has $a = 0.04$ cm. For $a/b = 0.04/0.0017 = 23$ the following performance can be calculated:

% of full e.m.f.	60	65	70	75	80	85	90	95	$97\frac{1}{2}$
Time (msec.)	3.2	4.4	6.0	8.2	12	19	35	84	150

This assumes no heat loss by conduction, etc., and no warming of the cold junctions of the thermopile. Actually such changes, though small, are not quite negligible, and their effect is to make the later stages of temperature equilibration apparently rather more rapid.

The thermopile is now about as thin as it seems possible—or even useful—to make it. By employing an even thinner muscle the thermopile response could be quickened still more. It is doubtful, however, whether

any significant advantage would be gained by increasing the nominal speed of the thermopile, for it is impossible to eliminate altogether the layer of fluid between muscle and thermopile, and if this were as little even as 5μ thick on each face, it would, by increasing the heat capacity from the equivalent of 34μ of muscle to one of 47μ , slow the attainment of temperature equilibrium in the ratio of $(34/47)^2$, i.e. to about one half. Moreover, as shown above, the connective tissue on the surface of the muscle must provide a certain delay. In small active young frogs, preferably females, this connective tissue layer is thinner: but it cannot be avoided altogether. It is doubtful, therefore, whether a thinner thermopile would give any significantly better results.

It might be suggested that a single thermocouple stuck right into the muscle, as in the experiments on a frog's gastrocnemius (Hill 1931*a*; Cattell 1932), would be quicker than a thermopile. It would in fact be far slower, even if the small e.m.f. of a single couple could be recorded rapidly enough: for it could not fail to injure several fibres around it, and these by liberating potassium would affect the excitability of others, and the couple, however thin itself, would be surrounded by a relatively large region of inert tissue. This would not be thick enough to have much effect on the magnitude of the final reading, but it would greatly slow its attainment. The present thermopile is as thin as a single muscle fibre, and no arrangement involving thermal conduction through inexcitable fibres can compete with it.

For similar reasons the surface of the muscle and the surface of the thermopile must be very plane, and no muscle with a "belly" on it could be used. When the muscle develops a tension there must be no tendency to pull away from the thermopile, or to suck in fluid to fill up hollows. Such hollows would greatly hinder conduction. The muscle should lie as straight and as uniformly as possible: it should move backward and forward as though in guides. The ring *l* (fig. 2) helps to keep the muscle true in its movement. The acetabula are slightly off the middle line of the muscle, and it is best to fit the clamp slightly to one side on its rod to make the muscle lie true in its groove. The screws of the clamp allow the bone to be adjusted to and fro so that the muscles are equally in contact with the two faces. Such precautions are not insignificant: they are of major importance for accurate results. Hartree in his last paper (1933) insisted on their necessity, and that is increased by the use of the present thin thermopiles. In some of the earlier experiments the photographic records of the heat were very sharp, showing by obvious angles the moments when shortening began or ended, or when the stimulus ceased.

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In others, unaccountably then, this sharpness did not appear. In the former the thermal contact of active muscle with thermopile must have been good, in the latter poor. Once it was realized that such precautions as are detailed above must be and can be taken, all the records have been sharp. It is possible to see on the heat record, within 0.01 sec., the moment at which shortening is permitted and the extra heat associated with shortening begins.

The dissection of the muscle is important, and no unnecessary bits of tissue should be left attached to it. The pelvic bone should be cleared of other muscle, so that the sheet of tendon to the sartorius is clearly seen. If the muscle does not lie straight and flat enough on the thermopile it had better be discarded, for the results will be suspect. It should be soaked in position on the thermopile, preferably loose so that Ringer's solution can get at both sides of it, for several hours before use, so as to avoid the inexcitability investigated by Dulière and Horton and by Horton (1929, 1930). If it begins to fail, the experiment should be stopped and the muscle soaked again, or discarded. Otherwise it may be contracting in parts, and anomalous results will occur. Before the Ringer's solution is withdrawn the muscle should be tightened to press out fluid from between it and the thermopile: and the solution should be sucked out slowly so as to draw away unnecessary fluid by capillarity. Then before records are begun several contractions should be allowed, to enable the muscle to come into regular and uniform mechanical and thermal contact with the thermopile. Other such precautions will occur to the experimenter, who will realize that without rather perfect thermal contact between muscle and thermopile the results of laborious experiments and calculations may be largely wasted.

(f) *The effect of a non-contracting layer of muscle on the transfer of heat to the thermopile.* We have referred above to the anomalies which may be produced in the heat records by a layer of non-contracting, or imperfectly contracting muscle. The two most serious cases, and others are intermediate between them, are:

- (i) a layer of inert material, fluid, connective tissue, or inexcitable fibres, between muscle and thermopile;
- (ii) a layer of inexcitable fibres on the outside, where injury may have occurred in dissection.

In both cases the deflexion is reduced, but the more important effect is on the apparent time at which the heat is set free.

(i) Let a pair of muscles, each of thickness a , have each an *inner* non-contracting layer of thickness b' in contact with a thermopile of thick-

ness $2b$. Then in the equations of the previous paper (Hill 1937) a is to be replaced by $(a - b')$, b by $(b + b')$. The effect can be seen approximately at once, viz. to make the apparent thickness of the thermopile $2(b + b')$ instead of $2b$, which would slow the rise of temperature of the hot junctions in the ratio of $b^2/(b + b')^2$. Now b is very small, e.g. 0.0017 cm. for thermopile P. 5, so that if a layer 0.01 cm. thick (only about two fibres) failed to respond the early temperature rise of the thermopile would be slowed $(0.0117/0.0017)^2 = 21$ times. A considerable delayed heat production would apparently result. For example, as a rough estimate, in a 0.2 sec. tetanus at 25° C, in which the initial heat is really all liberated in about 0.3 sec., some 50% of that heat would appear to be delayed. At 0° C, where initial heat is produced far more slowly, the error would not be so obvious. There is no way, however, of avoiding it except to ensure that the surface of the muscle contains normal active fibres in close thermal contact with the thermopile.

(ii) For the case of a muscle of which a thin *outer* layer does not contract, let us take contracting muscle and thermopile together and call their thickness b , and let the thickness of the outer non-contracting layer be a . Then the analysis of the previous paper (p. 119) is applicable. We suppose b to be warmed suddenly at $t = 0$ to temperature y_0 . The temperature of the thermopile (at $x = 0$) at subsequent times is

$$\sum_{n=-\infty}^{n=+\infty} \frac{y_0}{2\sqrt{(k\pi t)}} \int_{-b}^{+b} e^{-[\xi - 2n(a+b)]^2/4kt} d\xi.$$

Putting $a/b = \gamma$, and transforming, this becomes

y_0 [1 - the sum of the areas of the probability integral* between $0.5b/\sqrt{(kt)}$ and $(0.5 + \gamma)b/\sqrt{(kt)}$: between $(1.5 + \gamma)b/\sqrt{(kt)}$ and $(1.5 + 2\gamma)b/\sqrt{(kt)}$: between $(2.5 + 2\gamma)b/\sqrt{(kt)}$ and $(2.5 + 3\gamma)b/\sqrt{(kt)}$: etc.].

Take $\gamma = a/b = \frac{1}{10}$, i.e. suppose that the outer $\frac{1}{11}$ part of the muscle produces no heat. Consider a muscle 1.1 mm. thick on each face of the thermopile, i.e. put $b = 0.1$ cm., and take $k = 1.35 \times 10^{-3}$. Then the curve of fig. 4 can be calculated, showing how a rise of temperature of 1.10 produced by the sudden heating of the inside $\frac{10}{11}$ of the muscle drops in a few seconds to 1.00 as the heat is redistributed. For a muscle 1 mm. thick on each face of the thermopile, 1.2 sec. is required for the temperature to fall half way to its final level. Thus apparent "delayed negative heat" may readily be observed in a muscle the outside of which is not functioning.

$$* \frac{2}{\sqrt{\pi}} \int_0^x e^{-x^2} dx.$$

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With a thick muscle the effect may continue for several seconds. It was frequently observed with sartorii of Hungarian frogs, and provided one reason for discarding them. The conclusion that this delayed negative heat is not a genuine physiological phenomenon was confirmed by the fact that its time relations, at different temperatures, agreed in general with calculation. With the thinner muscles of English frogs thermal equilibration is much quicker: the time taken to any stage is proportional to the square of the thickness. Thus in fig. 4, for a muscle 0.4 mm. thick, the times should be divided by $(1.1/0.4)^2 = 7.6$, so the whole process would be half complete in 0.16 sec., 90% complete in 0.36 sec. It can still sometimes be seen, but the muscles of English frogs appear to behave more uniformly and it is seldom troublesome.

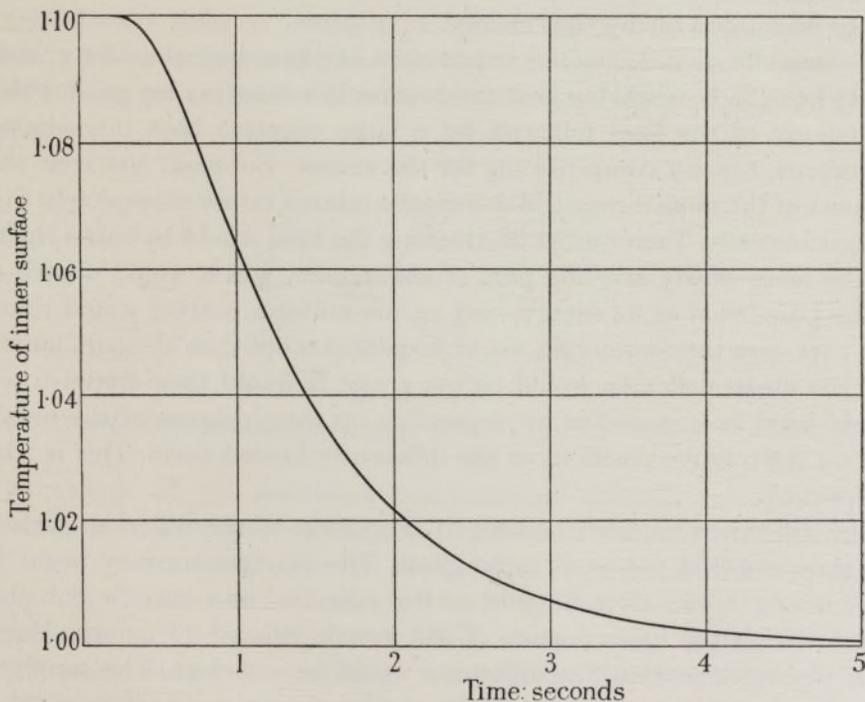


FIG. 4. To show subsequent fall of temperature of the inner surface of a muscle, 1.1 mm. thick, after instantaneous heating of the inner 1.0 mm. only; the outer 0.1 mm. not being heated, except by subsequent conduction with cooling of the inner part. Initial rise of temperature 1.10: final rise of temperature 1.00.

The delayed negative heat observed by Hartree (1932) is another matter altogether: it occurs much later—between 4 and 40 sec. at 0° C in a thin muscle—and cannot be due to any error of the kind here discussed.

The effect of non-uniform heating occurs very obviously in one special case, and explains a phenomenon which was, for a time, very hard to understand. When a muscle lifts a load isotonicly for a limited distance, and then comes against a stop, subsequent lengthening in relaxation is very rapid. The tension developed by the muscle, while contracting against the stop, may be considerably greater than the load, and in relaxation the weight begins to drop only when the tension is already falling rapidly. The energy of the load, i.e. the work done in lifting it, then appears suddenly in the muscle as heat (see fig. 8 below) and a very sharp upstroke occurs on the photographic record. This upstroke often shows two striking anomalies (see p. 169 below):

- (i) it is greater than can be accounted for by the energy of the weight, and
- (ii) it is followed by a rapid fall (in a second or two) to a level which *can* be accounted for by that energy.

If these effects were genuine expressions of physiological activity, there would have to be a sudden heat production in relaxation far greater than the energy of the load followed by a large negative heat immediately afterwards, exactly compensating for the excess. Suppose, however, that the part of the muscle near the thermopile relaxes rather more slowly than the part outside. Then during lengthening the load would be borne chiefly by the more slowly relaxing part of the muscle, which would absorb an undue proportion of its energy, and so non-uniform heating would result. The part near the thermopile would be heated more than the part outside and the initial deflexion would be too great: it would then diminish to a steady level in a second or so, depending on the thickness of the muscle and on the relative positions of the differently heated parts. This is what is observed.

The difference required in time of relaxation of the different parts of the muscle would not need to be great. The lengthening may begin (at 0° C) nearly 1 sec. after the end of the stimulus, and may be complete in 0.1 sec. If the inner portion of the muscle relaxed 10% more slowly than the outer portion, the difference would be sufficient. The supply of oxygen to, and the loss of CO₂ from, the inner portion is not so rapid as for the outer portion, which might be the cause of it. The fact that, after thermal equilibration, the extra deflexion observed in relaxation is closely accounted for by the energy of the load gives one confidence in this explanation of the anomalies observed.

(g) *On the possibility of using a resistance thermometer for muscle heat measurements.* All successful work hitherto on the heat production of isolated muscle (or nerve) has employed thermocouples or thermopiles.

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An obvious suggestion is that a resistance thermometer might be used. A wire with a large temperature coefficient of resistance is made one arm of a bridge. At any given temperature the bridge is balanced with a galvanometer: a rise of temperature of the muscle raises the resistance of the wire, throws the bridge out of balance and causes a deflexion of the galvanometer.

The sensitivity of a given resistance thermometer is directly proportional to the e.m.f. employed in its bridge. Both might be increased indefinitely were it not for the heat liberated in the resistance wire itself. In practice, if that heat is too great, disturbances occur which render the increase of sensitivity useless. In myothermic experiments such disturbances are particularly obvious, for the muscle (for quickness of recording) must lie in close contact with the heated wire, and differences of temperature are set up between different points in it. When the muscle contracts cooler regions come in contact with the wire, and the negative effect of these may entirely mask the positive effect due to the heat production of the muscle itself.

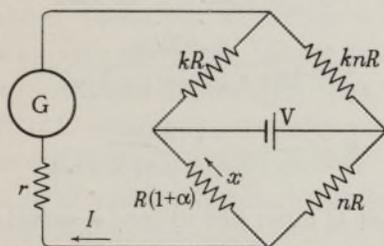


FIG. 5. Bridge for resistance thermometer (arm $R(1 + \alpha)$), in balance when $\alpha = 0$.

The theory of the resistance thermometer applied to myothermic experiments is given below: in its ordinary form it is shown to have no advantage in sensitivity over the thermopile, and certain disadvantages. This prediction was tested experimentally by constructing a resistance thermometer of 10μ platinum wire and using it with a pair of frog's sartorii under optimum conditions (see below). Its sensitivity was less than that of a thermopile, even when disturbances due to the heat set free in it were so great as to render it useless. A resistance thermometer of extremely thin strip or film would be better adapted than a thermopile, particularly with alternating current, to valve amplification. The conditions of its employment are discussed. It might be badly disturbed by stimulation of the muscle, by "calibration", or even by action potentials.

The bridge shown in fig. 5 is in balance when α is zero. We suppose that the muscle lies in close thermal (but not electrical) contact with the

wire of resistance R , and that when it contracts its heat production warms the wire and so increases its resistance to $R(1 + \alpha)$. The quantity α is very small, which simplifies the calculation. Let V be the battery voltage, r the resistance of the galvanometer, x the current in the wire R , E and I respectively the e.m.f. across and the current through the galvanometer. Then, sufficiently nearly,

$$I = \frac{V\alpha}{(1+n)[R(1+k)+r(1+1/n)]}, \quad (1)$$

$$E = \frac{V\alpha}{(1+n)[R(1+k)/r+(1+1/n)]}, \quad (2)$$

$$x = \frac{V}{R(1+n)}. \quad (3)$$

Let the maximum allowable rate of heat production in the wire R be Q watts. Then

$$Q = Rx^2 = V^2/R(1+n)^2.$$

Substituting for $V/(1+n)$ in (1) and (2), we find

$$I = \frac{\alpha\sqrt{(RQ)}}{R(1+k)+r(1+1/n)}, \quad (1')$$

$$E = \frac{\alpha\sqrt{(RQ)}}{R(1+k)/r+(1+1/n)}. \quad (2')$$

With the limitation that Q must not exceed a certain value, we require to make I , or E , as great as possible.

It is clear from (1') that by making n large and/or k small we can increase I . For the greatest conceivable advantage take $k = 0$ and $n = \infty$. Then

$$I = \frac{\alpha\sqrt{(RQ)}}{R+r}.$$

This, if R is variable, can be shown to be greatest when $R = r$, when it becomes

$$I = \frac{1}{2}\alpha\sqrt{(Q/r)}. \quad (4)$$

Now the current sensitivity of a well-designed galvanometer of given period is approximately proportional to the square root of its resistance, so that the maximum deflexion resulting from a current I in a galvanometer of resistance r is proportional to $I\sqrt{r}$, which from (4) is proportional to $\frac{1}{2}\alpha\sqrt{Q}$ and is therefore independent of r . Hence we can take any convenient sensitive galvanometer of given period and the maximum deflexion will be about the same.

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To find an approximate upper limit to the permissible current in the bridge, let us take Q to be equal to the rate of resting heat production of a frog's sartorius muscle in oxygen at room temperature. This is of the order (calculated from Hill 1928) of 4×10^{-5} W. The resting heat production of a muscle at 20° C, with an ordinary thermopile, gives a steady deflexion of the same order of size as that caused ballistically by a single twitch, and a rate of heat production in the wire greater than this would almost certainly cause disturbances when the muscle contracted.

Let us calculate the current sensitivity per 1° C so that α becomes the temperature coefficient of resistance. The highest value of α given in Kaye and Laby's Tables is 6.2×10^{-3} , for iron and for nickel. The value for platinum, a metal which would be more convenient for very fine wires, is 3.8×10^{-3} . With $\alpha = 6.2 \times 10^{-3}$, $Q = 4 \times 10^{-5}$, and $r = 40$, the maximum current through the galvanometer, per 1° C, becomes (from equation (4))

$$I = 3.1 \times 10^{-6} \text{ amp.}$$

The thermopile (P. 4) chiefly used in the present work has a resistance of 32 ohms and gives about $1400 \mu\text{V}/1^\circ$ C, which with a galvanometer of 40 ohms provides about 20×10^{-6} amp., about 6 times as much as the resistance thermometer. Another thermopile, with more couples, but not so thin, gives $3640 \mu\text{V}/1^\circ$ C with a lower resistance. It would be nearly 20 times as sensitive as the resistance thermometer. It might be suggested that the limiting value of Q taken above is rather too low: the sensitivity, however, is proportional only to the square root of Q , so that to equal the sensitivity even of the thin thermopile, the resistance thermometer would require a current producing heat at 36 times the rate assumed above. This would probably cause intolerable disturbances. The thermopile has no errors at all of this kind. In the calculation we have taken throughout the most favourable conditions. We conclude, therefore, that the thermopile has a far higher current sensitivity than the resistance thermometer for myothermic experiments. Incidentally, being differential, it is not affected by gradual changes of temperature: a resistance bridge would require continual readjustment unless designed to be differential.

We have assumed that the resistance thermometer is employed with a galvanometer, in the same way as the thermopile. It is possible that the resistance element might be constructed of exceedingly fine wire or strip, or of metal film sputtered on mica, and so give a higher volt sensitivity suitable for use with amplifier and oscillograph. Employed in this way it would have the advantage that an alternating current could be used in the bridge, which would be easier to amplify than the direct current

produced by a thermopile. From (2') above the maximum possible e.m.f. can be calculated as before by putting $\alpha = 3.8 \times 10^{-3}$ (for platinum), $Q = 4 \times 10^{-5}$, $k = 0$ and $n = \infty$: r is now the input impedance of the first valve which may be taken as infinite compared with R . Hence, for 1°C rise of temperature,

$$E = \alpha \sqrt{RQ} = 24 \times 10^{-6} \sqrt{R}.$$

The volt sensitivity, therefore, increases as the square root of the resistance of the element, so the latter resistance should be as great as possible. The specific resistance of platinum is about 11×10^{-6} . A wire, therefore, 4 cm. long and 10μ in diameter has a resistance of 154 ohms, giving (from above) about $300 \mu\text{V}/^\circ \text{C}$. With Wollaston wire of 2μ diameter the resistance would be 25 times and the volt sensitivity 5 times as great, say $1500 \mu\text{V}/^\circ \text{C}$. If it were possible to construct a film of sputtered platinum on mica, of resistance 100,000 ohms, the volt sensitivity would be about $4000 \mu\text{V}/^\circ \text{C}$. This is nearly three times as great as that of the best thermopile made with very fine rolled wire, but about equal to that of thicker thermopiles with more couples.

If, therefore, such resistance elements could be constructed they would have a high volt sensitivity, and the advantage that they could be used with alternating current. They would certainly have a very small heat capacity, and so would allow very rapid recording. It is probable, however, that far more serious errors might result from leakage of the stimulus than with a low-resistance circuit. The insulation (for quickness) must certainly be thin, and even if its resistance were infinite it would allow a capacitative leak between the muscle and the resistance element. A wet muscle separated by only (say) $10\text{--}20 \mu$ of insulation (as in the present thermopiles) from the conducting system is subjected to stimuli of several volts, and—if control heating is needed—to a condenser discharge of several hundred volts. An insulation resistance of 20 megohms (and more could not be expected after soaking in Ringer's solution) might allow only 1 part in 200 of an e.m.f. applied to the muscle, to appear between the ends of a 100,000 ohms strip. With a 6 V stimulus, however, this would be 60 mV, thousands of times greater than the quantity to be observed, and a considerable part of it would be amplified: with "control heating" the disturbance would be still greater. Even with a low resistance element, if its insulation is not very good, a discharge between the ends of the muscle may be slightly short-circuited through insulation and galvanometer, and appreciable disturbance may occur. For that reason it has always been evident that the insulation of a thermopile must be kept high. With a

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high resistance circuit, however, and amplification, leakage of stimulating (and *a fortiori* of heating) current could scarcely fail to disturb the recording system.

It might be suggested that the muscle could be stimulated through its nerve, and not directly. With indirect stimulation, however, of the frog's sartorius, or of any similar muscle, owing to the difficulty of preparing the nerve without injury, there could be no certainty that *the whole* of the muscle would respond equally. For an accurate study of the time relations of the heat production it is essential that the whole muscle should contract together: otherwise heat flow from one part to another may mask the true effects. Even, however, if indirect stimulation were permissible, the action potential of the muscle itself might leak, either directly, or through the very high capacitance of the muscle separated from the element by only $10\ \mu$ of mica, into the recording system. Action potentials of 20 mV, separated by only $10\ \mu$ of wet mica from a high resistance connected to an amplifier, might of themselves alone produce disturbances greater than the $4\text{--}8\ \mu\text{V}$ which is the whole quantity to be measured. It might be possible to design an amplifier to avoid the effect of such leaks, but its design would be complex, and with the very large disturbances to be expected, particularly in direct stimulation, no certainty of success could be predicted.

We may conclude, therefore, that for measurement of muscle heat:

(a) a resistance element, when used with a galvanometer, is far inferior to a thermopile;

(b) a resistance element to be used with alternating current and valve amplification must have a very high resistance;

(c) with an element of high resistance, leaks and disturbances from stimuli, and even from action currents, might prove prohibitive;

(d) and therefore that the use of a resistance thermometer, instead of a thermopile, would probably require years of experimental development, with no security of ultimate success.

It seems better to carry on with the efficient thermopiles and galvanometers already available.

PART II. THE HEAT OF SHORTENING AND LENGTHENING AND THE INFLUENCE OF LOAD ON THE RATE OF ENERGY LIBERATION

(a) *The extra heat associated with shortening.* When a muscle mounted on a thermopile, in the manner and with the precautions described above,

is tetanized isometrically, the galvanometer record of its heat production is similar to curves *A* and *E*, fig. 6, and curves *A*, *E* and *K*, fig. 7. If it is allowed to shorten isotonicly under a small load, the record rises initially more rapidly, as in curves *B*, *C* and *D*, fig. 6, and then becomes approximately parallel to the isometric curve. The extra deflexion is proportional to the amount of shortening allowed.

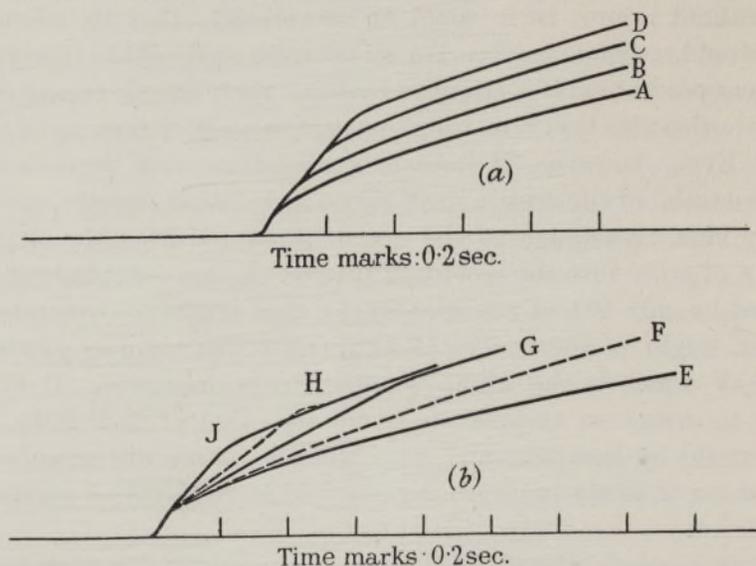


FIG. 6. Heat production during isotonic shortening from the start. Curves traced from galvanometer records and superimposed. Tetanus at 0°C : muscle $32\frac{1}{2}$ mm. long, 88 mg.: time, 0.2 sec. (a) Upper. Shortening different distances under constant load 1.9 g.: *A*, isometric; *B*, 3.4 mm.; *C*, 6.5 mm.; *D*, 9.6 mm. (b) Lower. Shortening constant distance 6.5 mm. under different loads: *E*, isometric; *F*, 31.9 g.; *G*, 23.7 g.; *H*, 12.8 g.; *J*, 1.9 g.

If a muscle is stimulated isometrically and then suddenly released under a small load, it shortens rapidly and during its shortening the galvanometer gives a quick extra deflexion. In fig. 7 (*c*), *K* represents the heat deflexion for a contraction which is isometric throughout: *L* for a contraction which is isometric at first, with release at 1.8 sec. followed by 9.1 mm. shortening under 2.9 g. load: *M* for a similar release at 0.95 sec.: *N* for the same release at the start. The extra deflexion is the same whenever the release occurs, provided that the contraction is fully maintained. It is proportional to the amount of shortening allowed, as is seen from fig. 7 (*a*), curves *A* to *D*.

This sudden extra deflexion of the record implies a sudden increment in the rate of heat production of the muscle. The increase of heat rate is

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proportional to the speed of shortening and stops when the shortening of the contractile component stops: the total extra heat is proportional to the total shortening. If the load is small, the speed of shortening is high and the increment in the heat rate is large: if the load is greater, the speed of shortening is less and the increment in the heat rate is smaller. In fig. 6 (b), curve *E* represents the same isometric contraction (45 g. tension) as *A*: *J*, *H*, *G* and *F* represent isotonic contractions of 6.5 mm., released at the start, under 1.9, 12.8, 23.7 and 31.9 g. respectively. With the greatest load the shortening was not complete in the time. The heat rate was greater the less the load and the more rapid the shortening: but the total extra

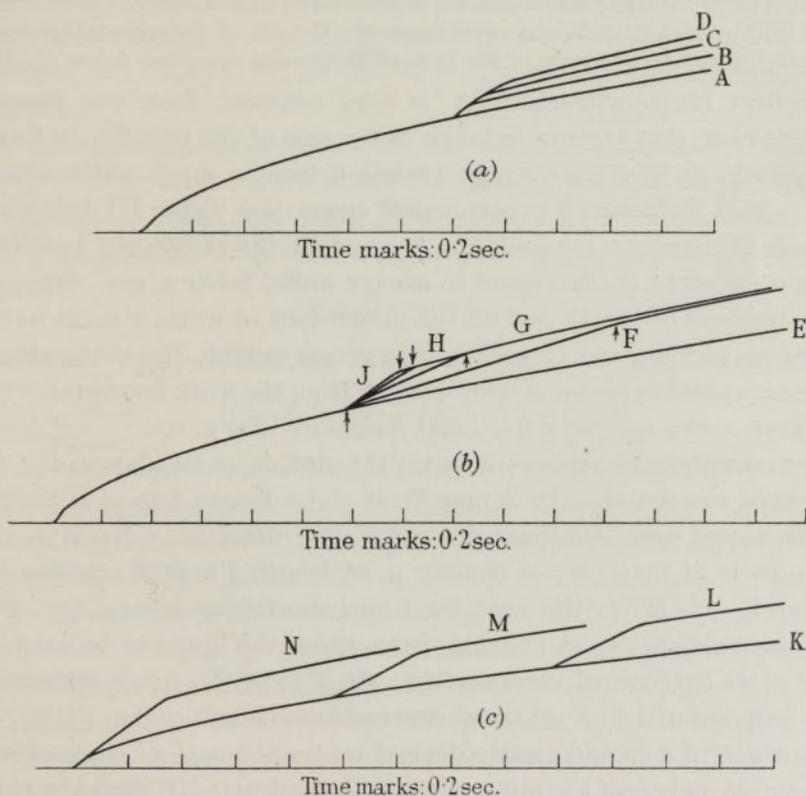


FIG. 7. Heat production in isotonic shortening, released during isometric contraction. Curves traced from galvanometer records and superimposed. Tetanus at 0°C : muscle, (a) and (b) 29.5 mm., 89 mg., (c) 30 mm., 87 mg.; time 0.2 sec. (a) *Upper*. Release at 1.2 sec., shortening different distances under constant load 3.0 g.: *A*, isometric; *B*, 1.9 mm.; *C*, 3.6 mm.; *D*, 5.2 mm. (b) *Middle*. Release at 1.2 sec., shortening constant distance 5.2 mm. under different loads: *E*, isometric (45 g.); *F*, 24.9 g.; *G*, 13.9 g.; *H*, 5.7 g.; *J*, 3.0 g. End of shortening shown by arrows. (c) *Lower*. Isometric (*K*); release at 1.8 sec. (*L*), 0.95 sec. (*M*), and start (*N*), shortening constant distance 9.1 mm. against constant load 2.9 g.

heat was the same in each case. In fig. 7 (*b*) curve *E* represents the same isometric contraction (43 g. tension) as *A*; *J*, *H*, *G* and *F* represent isotonic contractions of 5.2 mm., released at 1.2 sec., under 3.0, 5.7, 13.9 and 24.9 g. respectively. Again the extra heat rate is less with the greater load, but the total amount of heat is the same.

With a greater load, proportionally more work is done by a muscle in shortening more slowly a given distance, but *the total heat for shortening remains unaltered*. Thus when a muscle shortens it liberates extra energy in two independent forms, (i) heat for shortening proportional to the shortening, and (ii) mechanical work.

The evidence for these conclusions is illustrated in figs. 6 and 7. The curves were traced from actual records and superimposed. Details of the calculation required for an accurate determination of the heat of shortening are given below (p. 171).

The heat for shortening 1 cm. is very constant from one muscle to another, when due account is taken of the size of the muscle. In fourteen experiments at 0° C its average variation from a mean value was only 13%, which includes all experimental errors (see Table III below). Let a muscle shorten by an amount x cm., and let the shortening heat (which is proportional to x), expressed in energy units, be ax g. cm. Since x has the dimensions of length and ax the dimensions of work, a must have the dimensions of force and we reckon it in grams weight. The shortening heat can be expressed *as though* it were derived from the work done in shortening a distance x cm. against a frictional resistance of a g. wt.

The quantity a clearly depends on the size, in particular on the cross-section, of the muscle. In a muscle of given length but of n times the cross-sectional area, the heat for shortening must be n times as great. In a muscle of mass M , of density ρ , of length l and of uniform cross-section A , $A = M/\rho l$: the heat for x cm. shortening is ax g. cm., so the apparent resistance to shortening, from which the heat can be calculated, is a/A g. wt./sq. cm. of cross-section. At 0° C in the frog's sartorius the mean value of a/A in a maximal contraction is about 400 g. wt./sq. cm.

The value of a should clearly depend on the strength of contraction: if, for example, only half the fibres of a muscle contracted, a would be reduced to one-half. The simplest measure of the strength of contraction is P_0 , the full isometric tension. We should expect a/P_0 to be constant. In eleven experiments the mean value of a/P_0 was about 0.25, and the average variation from the mean was only 10%. a is not very easy to measure and a considerable part of this 10% must be experimental error. Thus the apparent resistance to shortening bears a rather constant ratio to the maximum force which a muscle can exert.

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The ratio a/P_0 is constant, or nearly constant, not only from one muscle to another, but at different temperatures. At a higher temperature a is greater, but P_0 is greater too. Thus a/P_0 may be regarded, at least as a first approximation, as a natural constant for frog's muscle. If a frog's sartorius can exert a maximum force P_0 , then in shortening a distance x it will liberate heat approximately equal to $P_0x/4$ g. cm., which is independent (i) of the speed of shortening, (ii) of the work done, and (iii) of the temperature.

(b) *The rate of energy liberation during shortening.* We have seen that in shortening a distance x cm., extra heat ax g. cm. is set free. If P g. be the load lifted, the work done is Px g. cm. Thus the total energy, in excess of isometric, is $(P+a)x$ g. cm. The rate of extra energy liberation, therefore, is $(P+a) dx/dt$, or $(P+a)v$, if v be the velocity (cm./sec.) of shortening.

It is found experimentally that the rate of extra energy liberation, $(P+a)v$, is a rather exact linear function of the load P , increasing as P diminishes, being zero when $P=P_0$ in an isometric contraction and having its greatest value for zero load (see fig. 11 below). We may write therefore

$$(P+a)v = b(P_0 - P), \quad (1)$$

where b is a constant defining the absolute rate of energy liberation. This may be written

$$(P+a)(v+b) = (P_0+a)b = \text{const.} \quad (2)$$

Equation (2) relates speed and load in an isotonic shortening; it can be verified separately without any thermal measurements: this will be referred to later (p. 177). It represents a rectangular hyperbola with asymptotes at $P = -a$, $v = -b$.

The constant b is of the dimensions of a velocity (cm./sec.) and, when due account is taken of the dimensions of the muscle, is very constant at a given temperature. If a muscle of given cross-section be n times as long, then v , the velocity of shortening, will obviously be n times as great under a given load. Hence b also should be proportional to the length l of the muscle. At 0°C in the frog's sartorius the mean value of b/l was about 0.33/sec. (Table III below), and the average variation from the mean in eleven experiments was only 9%. Of this variation a considerable part must have been due to experimental error, so that the real variation is less. Thus b/l is constant, or nearly constant, from one muscle to another at a given temperature.

It is well known that muscles can shorten, and give out energy, much more quickly at a higher temperature. It was expected therefore that b

would increase with temperature. This was verified experimentally and b was found to be increased about 2.05 times for a rise of 10° C.

(c) *The energy absorbed during lengthening.* In the experiments illustrated in fig. 7 during an isometric contraction a muscle was released and allowed to shorten and do work. The converse experiment has been made (fig. 13 below): a muscle was allowed to contract isotonicly through a limited distance, and then a load somewhat greater than the isometric tension was applied to it. The muscle lengthened and work was done upon it by the load. The questions to be answered were:

(i) Is there a negative heat of lengthening, the converse of the positive heat of shortening?

(ii) Is the work done by the load in falling simply transformed into heat, or is it absorbed, or dealt with in some other way?

In principle, equation (2) above, viz. $(P+a)(v+b) = (P_0+a)b$, could apply just as well to lengthening as to shortening. For shortening v is positive and P is less than P_0 , as we know. In isometric contraction v is zero and $P = P_0$. In lengthening v is negative and P should be greater than P_0 . Now the fact that the force exerted during lengthening is larger than in isometric contraction, and is greater the more rapid the lengthening, has been known since Fick (1882), and was examined in detail by Wyman (1926) and by Levin and Wyman (1927). This qualitative confirmation that equation (2) applies to lengthening as well as to shortening encouraged one to proceed.

The difficulty in making thermal experiments on lengthening is that, unless the speed of lengthening is very low, the force developed will be too great for the muscle to bear. For $v = -b$, i.e. for a speed of lengthening only about one-quarter of the maximum speed of shortening, equation (2) shows that P should be infinite. Even for $v = -b/6$ (in an ordinary frog's sartorius, about 1.6 mm./sec.) P should be $1.25 P_0$. The reason why high tensions must be avoided is that active muscle apparently "gives", or "relaxes", or "slips", rather like a wire strained beyond its elastic limit, if the force is too great (see Gasser and Hill 1924, p. 412). No damage is necessarily done to the muscle, and the active state is set up again as soon as the force is reduced. For the moment, however, a rapid "give" or "slip" occurs when the load is too great, and the work done by the load is degraded directly into heat, as it is in ordinary relaxation when the stimulus ends (see fig. 8 below).

It is necessary, therefore, to work with loads not very much greater than the isometric tension, and such loads are bound to stretch the muscle rather slowly. The extra heat for lengthening x cm. should be $-ax$ g. cm.:

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but x must be small if the stretch is to be slow and the contraction not unduly prolonged: the heat therefore is bound to be small, and to appear only slowly. Moreover, it is apt to be masked by heat produced irreversibly through "give" or "slip" of parts of the muscle. With the additional complication that the isometric heat rate varies somewhat with length, it has proved impossible as yet to give a decisive answer to the question—Is the heat of lengthening negative and equal to $-ax$ g. cm.? The evidence (see below, p. 179 and figs. 13 and 14) inclines to the view that it is negative, but the experimental determination of its absolute amount has proved, as yet, to be too difficult. Perhaps another muscle (e.g. of a tortoise, cf. Wyman (1926), or a dog-fish, cf. Levin and Wyman (1927)), or a frog's muscle at another season, might provide less difficulty.

The second question—Is the work done in stretching the muscle transformed into heat, or is it dealt with in some other way?—can be answered decisively (see below, p. 180 and fig. 14). It is not transformed into heat unless the load is too great and "give" or "slip" occurs. With a suitable load, e.g. of 60 g. on a muscle capable of an isometric tension of 50 g., giving a rate of stretch of about 1.4 mm./sec., the work done may disappear, almost or entirely, with little or no remainder as heat. With greater loads, however, and quicker stretches, a large fraction of the work done by the load in falling is transformed into heat and causes a rapid upstroke of the galvanometer.

It may be asked—What happens to this work? The answer might be that we must think of some mechanism like that of a tramway motor, capable of acting as a dynamo and feeding back current to the mains in running down hill. The true answer, however, as we shall see below, may well be that the work *is* transformed into heat, but the rise of tension associated with stretching diminishes the rate of energy liberation of the muscle so much that the positive heat associated with the degradation of work is balanced by the diminished heat production of the muscle. It is not necessary to suppose that any part of the mechanism is really reversed: only that it is slowed.

(d) *The nature of the heat of shortening and the mechanism of the energy control.* The exactness of the relations described above invites the question of their nature and mechanism. Is the heat of shortening simply degraded work, done in overcoming a constant resistance a ? if so, it should occur also as positive heat in lengthening, since processes which degrade work into heat act equally in both directions. The question cannot be answered decisively until that of the heat in lengthening has been finally settled. If the heat of shortening were degraded work, if a were a constant internal

resistance, we might expect it, as viscosity is, to be largely reduced by a rise of temperature: actually it is increased somewhat, in proportion to the strength of contraction. It is difficult to think of a force of this kind which might be present in muscle.

An objection to the idea that a might represent a real, irreversible frictional resistance to shortening, or lengthening, is that, if it did, there should be a difference $2a$ between the loads (i) at which a muscle just shortens, and (ii) at which it just lengthens. $2a$ is a fairly large quantity, about half the isometric tension: the difference in question, if it exists, is certainly much smaller than this. If, however, the heat of shortening be due to a "reversible" change, in the sense at least that its sign is reversed in lengthening, and if a be only an apparent resistance, then we must think of some physical process which gives out heat in shortening, absorbs heat in lengthening. Consider, for example, the case of surface tension. This has a negative temperature coefficient, so that heat is given out when an area exhibiting surface tension contracts and does work, absorbed when the area is made to expand. The surface tension, for example, of benzene at T° K is given as $\sigma_T = \sigma_0 - 0.146(T - T_0)$. The heat given out, therefore, in an air-benzene surface is $T \times 0.146$ ergs/sq. cm. of contraction, which at 0° C is 40 ergs or about 0.04 g. cm. Or we might speculate about the heat given out when chemical affinities are satisfied by the folding up of myosin chains during muscular shortening (cf. Astbury 1938), and the heat absorbed when the molecules are drawn apart again. Without, however, a more concrete picture of the actual muscular mechanism, it is not very useful to speculate further. It is sufficient to realize that plausible theories can be invented to imitate this property of muscle.

The control exercised by the tension P existing in the muscle at any moment, on the rate of its energy expenditure at that moment, may be due to some such mechanism as the following. Imagine that the chemical transformations associated with the state of activity in muscle occur by combination at, or by the catalytic effect of, or perhaps by passage through, certain active points in the molecular machinery, the number of which is determined by the tension existing in the muscle at the moment. We can imagine that when the force in the muscle is high the affinities of more of these points are being satisfied by the attractions they exert on one another, and that fewer of them are available to take part in chemical transformation. When the tension is low the affinities of less of these points are being satisfied by mutual attraction, and more of them are exposed to chemical reaction. The rate at which chemical transformation

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would occur, and therefore at which energy would be liberated, would be directly proportional to the number of exposed affinities or catalytic groups, and so would be a linear function of the force exerted by the muscle, increasing as the force diminished.

The isometric contraction, on this view, does not present a special case. Let the rate of total energy expenditure by a muscle exerting a force P_1 be H_1 , and exerting a force P_2 be H_2 : then the experiments referred to above have shown that

$$H_1 - H_2 = b(P_2 - P_1).$$

If H_1 is greater than H_2 it is because, on this view, more chemically reactive points are exposed when the tension of the muscle is less. In an isometric contraction the rate of heat production is H_0 , corresponding to tension P_0 . If the load is lowered to P_1 the muscle shortens and does work, more energy is required, and more energy is actually liberated through an increase, proportional to $(P_0 - P_1)$, in the number of chemically reactive points. If the load is raised to P_2 the muscle lengthens and does negative work (work is done on it), less energy is required, and less energy is actually liberated since the number of chemically active points is diminished proportionally to $(P_2 - P_0)$.

The question, therefore—Where does the work done on the muscle in lengthening go to?—is answered. By raising the tension one causes a decrease in the rate of chemical transformation in the muscle. It is not necessary to imagine any actual reversal in the direction of chemical reaction during lengthening: only a slowing of the reaction normally accompanying activity. It has never been found, even with more rapid stretches, that the total energy rate of the muscle is negative: it is less than the isometric energy rate but still positive. Lengthening, therefore, and negative work, do not cause a reversal, but only a slowing, of the processes associated with activity.

The high temperature coefficient of the constant b is presumably the resultant effect of the temperature coefficients of the chemical reactions by which the energy is liberated. For a given tension in the muscle the number of chemically reactive regions may be the same at different temperatures: if so, the temperature coefficient of b is simply that of the chemical processes. Possibly, however, for a given tension, the number of reactive spots may alter somewhat with temperature: if so, the temperature coefficient of b is a mixture of both effects. As defined above, b is a linear velocity (cm./sec.): but if $n(P_2 - P_1)$ be the actual increase in the number of reactive spots, in passing from a higher tension P_2 to a lower tension P_1 , then b/n is a rate of energy liberation. We have no idea what

n may be and it is simpler to leave matters as they are, remembering that b is expressed in cm./sec. simply because, for convenience, the number of active spots is taken as equal, and not merely proportional, to $(P_2 - P_1)$.

The isometric heat rate at 0° C, between 0.8 and 1.8 sec. from the beginning of stimulation, when the tension has become steady, lies consistently between 2 and 4×10^{-3} , with a mean of about 3×10^{-3} cal./g. \times sec. = 128 g. cm./g. \times sec. The extra heat rate associated with shortening is greatest when $P = 0$, when it is of the order of 500 g. cm./g. \times sec. Thus during the limited interval of shortening under zero load the total heat rate may be 5 times as great as during an isometric contraction. The effect, therefore, of rapid shortening on the heat production is large.

During lengthening the work done *by* the muscle is negative, so the work done *on* the muscle must be subtracted from the observed heat to give the energy actually liberated by the muscle. The net energy rate of the muscle, so calculated, would become zero if $-Pv$, the rate of doing work on the muscle, became equal to the isometric heat rate, which—taking its mean value at 0° C—is 128 g. cm./g. \times sec. With the usual values for 0° C of a , a/P_0 and b , it can be calculated that $Pv = -128$ g. cm./g. \times sec. when $P/P_0 = 1.30$ and $v = -0.2b$. These represent a load 30% greater than the isometric tension, a speed of lengthening in an ordinary frog's sartorius of about 2 mm./sec. This may explain why a discontinuity occurs, and the muscle "gives" or "relaxes", with a load not very much greater than isometric. The total energy rate by the muscle gets reduced too nearly to zero, and the contraction cannot be maintained. In terms of our hypothesis, an increased tension on the muscle may obliterate all the chemically reactive points of the mechanism, chemical transformation may become impossible, energy liberation may cease, and the muscle may relax as though the stimulus had been stopped. Mechanically this is what happens, as is easy to verify by suddenly subjecting a fully contracting muscle to a load (say) 50% greater than the isometric tension: and it is interesting that it should happen in the very region of loads where calculation would predict it.

At a higher temperature the isometric heat rate is greater, but b is greater too. "Reversible" lengthening, therefore, can be quicker, but the relative load, P/P_0 , at which the discontinuity occurs should be about the same.

(e) *Shortening heat and relaxation heat during an isometric contraction.* In the heat records of isometric contractions in figs. 6, 7, 8, 13 and 14, the upstroke at the beginning is very similar to that in records of contractions in which shortening is permitted: but smaller. This, as will be shown below,

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is almost certainly due to shortening of a contractile component of the muscle, stretching (a) an elastic component of the muscle, (b) its tendons, (c) the connexions to the isometric lever, and (d) the lever itself. The quick upstroke at the beginning represents "shortening heat". The work done in stretching these several elastic bodies remains as mechanical potential energy until relaxation occurs, when it appears as heat. It is the origin of the obvious "hump" on the heat record which occurs in relaxation (see fig. 8, curve A, below). This "hump" is not the only source of heat during relaxation but is a considerable part of it. It can be reduced by fixing the muscle rigidly at its ends, so that less work is done against elastic forces, but it is doubtful whether it can be altogether abolished. The muscle may have within itself a genuine undamped elastic component: its machinery may be elastic. (See p. 187 below.)

The heat rate during isometric contraction and relaxation is largely affected by these mechanical factors. The present instruments are capable of providing a much more accurate analysis of the initial heat than any hitherto published. It is hoped to complete such an analysis in the near future, with adequate control of the mechanical conditions affecting the heat.

(f) *The sudden fall in the heat rate at the end of stimulation.* With the present instruments the moment at which a stimulus stops can easily be detected on the heat records by an "angle", i.e. by a sudden change of slope. It is clear that the heat rate immediately begins to drop as soon as stimulation ends. An analysis of the records makes the drop very obvious, and simultaneous isometric mechanical records show that the tension is fully maintained for some tenths of a second (at 0° C) afterwards.

In a twitch provoked by a single shock the heat has a high rate at first, declining gradually to zero. The visible mechanical effect, however, only gradually reaches its maximum. It is natural, therefore, that in a maintained tetanus the full tension should remain for some moments after the heat rate has begun to fall. The earlier events in the chain of chemical processes accompanying muscular activity, although producing heat, may not necessarily be those which are responsible for the maintenance of tension.

(g) *The heat of relaxation after an isotonic contraction.* When a muscle contracts and relaxes isotonicly the work done on the load during shortening appears in the muscle as heat during relaxation. If the load be great the work is considerable and the deflexion when relaxation occurs is sudden and large. This deflexion is quantitatively equivalent to the work.

In fig. 8, B is the heat record of the isotonic contraction of a muscle lifting a large load, and shortening slowly as shown by the mechanical

record *b* below. As soon as the shortening was complete the large after-load was held up, by the device described above (p. 145), and the muscle relaxed very late, when its tension had fallen to a low value equal to the small initial load. The heat record *B* showed only a very small "hump" corresponding to the degradation to heat of the potential energy of its elastic component as the tension of the muscle relaxed.

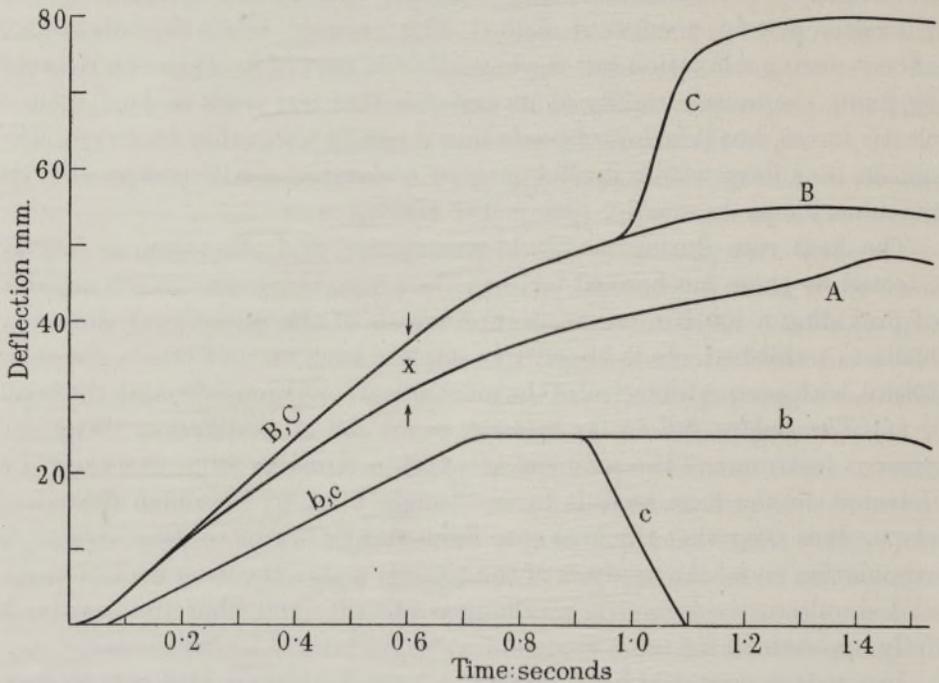


FIG. 8. Relaxation heat in isometric and isotonic contractions. *A*, *B* and *C*, galvanometer records of heat in 0.6 sec. tetanus at 0° C with initial load 3.6 g. Muscle 196 mg. *A*, isometric; *B*, isotonic, after-load 38.6 g., held up; *C*, isotonic, same after-load but free. *B* and *C* rise faster than *A*, owing to the shortening heat. When the muscle lengthens under the load, the energy of the load (the work done by the muscle on it) appears as heat: hence the rapid upstroke in *C* during relaxation: *C* rises above *B* by an amount equal to the work. Efficiency, 30.5%. Mechanical records below, with corresponding letters. Relaxation under the small initial load only (*b*) was very delayed. Note the small relaxation "hump" on the heat record *A* of the isometric contraction. All records are means of a pair in a series and reverse. *X*, end of stimulus.

When the load was free to fall as the muscle relaxed, the mechanical record was *c* and the heat record *C*. The rise of the heat record coincides in time with the fall of the load, and the maximum height of *C* above *B* represents a production of heat equal to the work of the load in falling. This equality is not always apparent. Sometimes the sudden rise of the

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heat record is greater than the work, but in such cases it is followed by a rather rapid fall apparently representing an absorption of heat. The time to complete this subsequent fall is of the same order of size as that calculated (see p. 152 above) for the redistribution of heat unevenly produced in the muscle. When the difference between *B* and *C* has become steady it corresponds to the work. Relaxation is very sudden with large loads, and if the inner layer of muscle, that nearer the thermopile, relaxed slightly later than the outer layer, it would be stretched by the falling load and would receive more than its fair share of the energy of the latter: this would then be redistributed by conduction, but only after it had affected the thermopile. The anomaly has no physiological significance; it is an excellent example, however, of the traps which beset myothermic experiments. Without a critical examination it might have led to very peculiar conclusions about heat production and absorption during relaxation. The facts are really quite simple: the energy of the load, and the energy of any stretched bodies in series with the muscle, are turned straight into heat when the muscle relaxes.

In fig. 8, curve *A* represents an isometric contraction: it is lower than *B* for the isotonic contraction, owing to shortening heat in the latter. Relaxation is later in the isometric contraction. The small "hump" to the right represents elastic energy which is turned into heat when relaxation occurs.

The stimulus ended at *X*, and a small change in the slope of the isometric heat record can just be detected there, representing a fall in the rate of heat production. The "angle" is less obvious than it often is.

The mechanical efficiency, i.e. (work)/(total energy), was high in the experiment of fig. 8, viz. 30.5%. This was due to the fact that the load was small enough for the muscle to lift it a considerable distance, and yet large enough for the muscle to have to go on lifting it till after the stimulus ended. Efficiencies up to 35% have been observed. These efficiencies, of course, cover only the initial process: if the recovery process were included they would be about half as great. Frog's muscle seems to be rather inefficient as compared with human muscle. It is interesting that higher efficiencies have been obtained with isotonic contractions than with the Levin-Wyman apparatus: see Hartree and Hill (1928*a*, p. 243, etc.).

(*h*) *The effect of length on the isometric heat rate.* From the heat records of "isometric long" and "isometric short" contractions (figs. 6, 7, 8, 13, 14), and from the differences plotted in figs. 9 and 10, it is seen that the heat rate is greater at the shorter length. In figs. 9 and 10, curves *E*, the change of isometric heat rate is plotted as a function of the distance the muscle

had shortened. Many series of this kind have been made, and they consistently show that the isometric heat rate becomes greater as the length becomes less, reaches a maximum, and then becomes less again at still smaller lengths. The relation has been examined only incidentally, in order to provide the necessary correction in the calculation of the shortening heat: it has been studied in detail by Brown and Katz, in relation to the tension of the muscle: they will report on it elsewhere.

The effect is not due at all to the heat of shortening, for shortening was complete long before the isometric heat rate was measured. The present experiments throw no light on its nature. It is certainly genuine, and directly contradicts a number of earlier observations by various authors: the difference is presumably due to the errors which the present methods, and particularly the protected thermopile, were designed to avoid. Blix (1902), for example, concluded that muscle heat increased and diminished with the length of the fibres, and was a surface—not a volume—effect. Hill (1913) found in a tetanus that the heat was less the more a muscle was allowed to shorten, and Evans and Hill (1914) and Hill (1925) concluded that this was true for all durations of stimulus.

All these results were obtained by reading the maximum deflexion of a galvanometer, none of them by measuring the slope of a continuous record of the heat. The existence of the shortening heat was not known, and any mechanical work was added automatically to the total heat when the muscle relaxed. A protected thermopile was not used, though an attempt was made by Hill (1913) to avoid some of the errors which it avoids by the use of a "conical" thermopile. Considerable temperature differences may have existed between different points of the muscle. The results anyhow seem to be wrong, and the moral may be drawn that all earlier experiments on the heat production of muscles allowed to shorten are suspect, and should now be repeated.

Fenn and Latchford (1933) found a slight increase in the difference (heat for 0.4 sec. tetanus—heat for 0.2 tetanus) with decrease of length. Fischer (1935) determined the heat for maintenance of tension by subtracting the heat for a tetanus just long enough for maximum tension to be developed from the heat for a much longer tetanus. He found a rise in the heat for maintenance as the length was diminished and then a fall. Hill (1925) had obtained similar results. The effect depends to some degree on the definition of the "resting length".

Experimental evidence

(i) *The heat of shortening.* The evidence for the heat of shortening is various: some of it was illustrated in figs. 6 and 7. The determination of its absolute amount has been made in three ways:

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(a) by a complete numerical analysis of the rate of heat production, before, during and after shortening;

(b) by calculating the increment in the rate of heat production, when shortening is permitted, from the increased slope of the heat record, and comparing this with the rate of shortening;

(c) by measuring the total upward displacement of a heat record, as the result of a given total shortening.

All three methods are complicated by the fact that the extra heat for shortening is measured as an excess above the isometric level, and the isometric heat rate is somewhat different at different lengths. For accuracy it is necessary to make some allowance for this. Since the isometric heat rate varies rather rapidly at first, when stimulation begins, and then becomes more constant, the allowance is more accurate for later releases than for shortening at the start.

All three methods have led to the same conclusions: (a) is laborious, and with the quickness of the present instruments it has no significant advantage over the others; (b) is easily applied and is quite satisfactory: the allowance, however, for varying heat rate with length is not so accurate as in (c); (c) seems to give the best and most consistent results and was adopted in all the later experiments. Details of its applications are given in figs. 9 and 10 and their legends.

The muscle is stimulated isometrically and then released after its full tension is developed. It shortens the required amount and becomes isometric again. It might be supposed that if the instruments had no lag the reading at the moment when visible shortening ended would give the heat of shortening. This is not so. When a muscle is released, part of the shortening observed is that of the elastic component, previously stretched by the contractile component in the preliminary isometric phase; when the muscle again becomes isometric at the shorter length, its contractile component goes on shortening, and stretching the elastic component, until the full tension is developed. Thus when shortening is checked the isotonic heat record continues at first to rise faster than the isometric, but at a rapidly decreasing rate. This necessitates the extrapolation described in the legend of fig. 9.

After this extrapolation, it remains to allow for the mean extra heat rate (isometric), over the range of shortening considered. The lighter the load, the less will be the time taken in shortening and the smaller the correction required. The observed excess heat rates are plotted and a mean calculated for the range of lengths involved: this is multiplied by the observed time of shortening, and the product subtracted from the extra deflexion at the

extrapolated end of shortening. No correction is applied for the time occupied in subsequent "isometric shortening": the correction must be

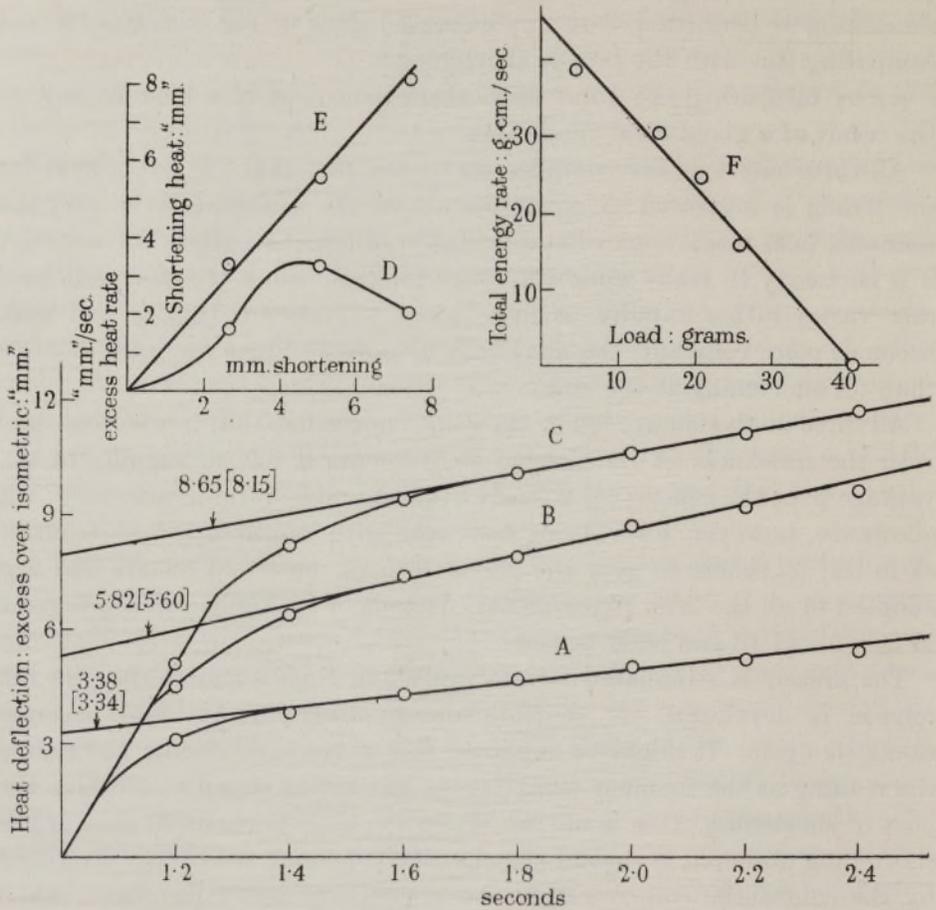


FIG. 9. To illustrate the calculation of the heat of shortening. *A*, *B* and *C*, heat deflexions (mm.) in excess of isometric for 2.65, 5.05 and 7.40 mm. shortening under 4.6 g. load, after quick release at 1.0 sec. Curves extrapolated back to end of shortening, shown by arrows: extrapolated deflexion in mm. Slow rise after end of shortening due partly to lag of instruments, but chiefly to continued shortening of contractile component against elastic component. Curve *D*, excess heat rate (above isometric), when steady, as function of length. From this, the mean excess heat rate over the range of shortening was calculated for *A*, *B* and *C*, and a correction applied to the extrapolated deflexion at the end of shortening. The result is shown in square brackets, e.g. [8.15], and plotted in *E* against the amount of shortening. *Result*. $a = 10.7$ g. wt. = 383 g./sq. cm.; $a/P_0 = 0.24$. In *F* the total energy rate in another series is plotted against the load: result, $b = 1.12$ cm./sec. = 0.325 length/sec. *Experimental details*. 0°C ; thermopile P. 5; muscle 101 mg., $34\frac{1}{2}$ mm.; mean of series and reverse. 1 mm. heat deflexion = 0.936 g. cm. = 0.218×10^{-3} cal./g. Average heat rate, isometric, 1-2 sec., 12.2 mm. deflexion/sec.

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small and would be difficult to make. The result gives the corrected heat of shortening. Plotting this in g. cm. against cm. of shortening a straight line is obtained, the slope of which is a . This proportionality of shortening heat to distance shortened has been obtained many times: the evidence is all similar to that of curves F in figs. 9 and 10.

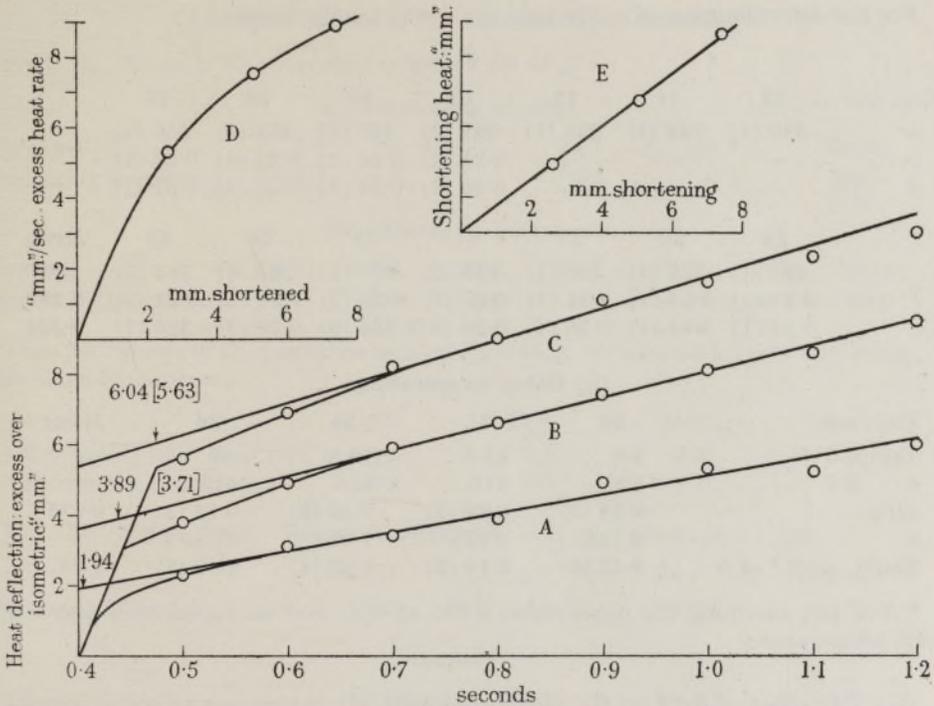


FIG. 10. To illustrate the calculation of the heat of shortening. Same muscle as for fig. 9 but at 13°C and initial load 7.3 g. See legend of fig. 9. Result. $a = 14.3$ g. wt. = 513 g./sq. cm.; $a/P_0 = 0.193$. Experimental details. 1 mm. heat deflexion = 1.895 g. cm. = 0.442×10^{-3} cal./g. Average heat rate, isometric, 0.4–0.9 sec., 36.6 mm. deflexion/sec.

Table III contains all the valid results obtained, with weighting factors allotted according to the nature of the experiment. Considering the smallness of the quantities observed the results are rather consistent, and the mean values of the "dynamic constants" there given would seem to be reasonably certain for the case of the frog's sartorius. It will be interesting to determine the same constants in other muscles. Most muscles are unsuited to thermal experiments of this kind, but for them the indirect method is available, involving only the measurement of the speed of shortening at a series of different loads (see p. 177 below).

TABLE III. THE DYNAMIC CONSTANTS OF ENGLISH FROG'S SARTORIUS MUSCLE

a is given in g. wt./sq. cm. of muscle cross-section.

a/P_0 is a number without dimensions.

b is given in (muscle length)/sec.

The numbers in brackets are the "weights" used in calculating the means.

For the determination of a , the load lifted was usually small.

(i) 0° C								
Exp. no. ...	13	14	15	16	20	22	23	
a	330 (1)	344 (1)	255 (1)	362 (2)	420 (1)	453 (1)	550 (1)	
a/P_0	—	—	—	0.21 (2)	0.24 (1)	0.28 (1)	0.23 (1)	
b	—	—	—	0.38 (2)	0.34 (1)	0.36 (1)	0.32 (1)	
	24	26	27	31	33	34	39	Mean
	493 (1)	326 (1)	380 (1)	418 (3)	470 (3)	365 (3)	383 (3)	399
	0.27 (1)	0.31 (1)	0.31 (1)	0.27 (3)	0.28 (3)	0.24 (3)	0.24 (3)	0.257
	0.34 (1)	0.41 (1)	0.38 (1)	0.28 (3)	0.335 (3)	0.30 (3)	0.325 (3)	0.331

(ii) Other temperatures

Exp. no. ...	36	37	38	39	Mean
Temp. 0° C	8.9	13.5	19.8	13	
a	590	613	415	513	
a/P_0	0.28 (3)	0.29 (3)	0.18 (3)	0.19 (3)	0.235
b	0.735	0.935	1.09	0.815	
Temp. coeff.* of b	2.45 (2)	2.16 (3)	1.82 (4)	2.00 (3)	2.05

* For 10°, assuming the mean value 0.331 at 0° C and an exponential increase with temperature.

(ii) *The effect of load on the shortening heat.* In a number of experiments the extra heat for shortening was determined with several different loads, i.e. at several speeds of shortening, and with very different amounts of work done. Release was either at the start, or later, and the methods of calculating the shortening heat were various. The shortening heat was always about the same, whatever the load, the speed, or the work. In three of the latest experiments the method used was that described in detail in the preceding section, which is probably the best, and five series gave the results in Table IV. They are summarized at the end of the Table. With the smallest loads the shortening heat seems to be rather less than with higher loads: with loads more than 25% of the isometric tension it is practically constant. The difference is scarcely significant and may be due to some consistent error. The experiments and calculations for the slower shortenings cannot be very exact since the shortening heat is rather small, and when it is spread over a longer time more allowance has to be

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made for the change of heat rate with length, and the allowance is rather precarious. It may be that the difference with the lighter loads is genuine, but in any case it is very small, when compared with the great difference in respect of mechanical work.

TABLE IV. EXTRA HEAT FOR SHORTENING WITH DIFFERENT LOADS

All heats are given in mm. galvanometer deflexion

Exp. 33. Temp. 0° C. Isometric tension $P_0 = 45$ g.

(i) Shortening at start

Load (g.)	1.9	12.8	23.7	31.9	Mean
Shortening heat (mm.)	6.8	8.1	9.2	8.8	8.2

(ii) Release at 1.2 sec.

Load (g.)	2.7	7.3	12.5	18.3	23.7	31.9	Mean
Shortening heat (mm.)	7.1	7.7	8.3	9.0	8.6	9.2	8.15

Exp. 34. Temp. 0° C. Isometric tension $P_0 = 44$ g. Release at 1.2 sec. Two series, with washing between.

Load (g.)	3.0	13.9	24.9	Mean
(1) Shortening heat (mm.)	6.4	7.2	8.2	7.3
(2) Shortening heat (mm.)	7.2	8.0	8.4	7.9

Exp. 35. Temp. 8.9° C. Isometric tension $P_0 = 41$ g. Release at 0.4 sec.

Load (g.)	7.1	18.1	24.6	Mean
Shortening heat (mm.)	5.5	6.2	6.1	5.9

Summary

Load (g.)	1-10	10-20	20-30	30+
Shortening heat: average % of mean	89	102	108	104

The general conclusion is borne out by a considerable number of other incidental results. For example: (i) the total heat rate has been found to increase linearly with the rate of shortening (varied by altering the load); (ii) the shortening heat, when determined for a larger load but not for a smaller one, has been found to be of the usual order of size as given in Table III; (iii) in one experiment at 0° C, for some unknown reason, no allowance was necessary for difference of heat rate, short and long: in this experiment the following total deflexions were observed at 2.0 sec., for 5.6 mm. shortening, release at the start.

Isometric: 31.1 mm.

Isotonic: 2.5 g., 37.9 mm.; 8.0 g., 39.5 mm.; 16.2 g., 38.5 mm.; 24.4 g., 38.1 mm.

The cumulative effect of this evidence is rather convincing, and as a first approximation at least we may conclude that the heat for shortening is independent of the load, the speed and the work.

(iii) *The rate of energy liberation as a function of load.* It is now established that, in shortening a distance x , extra heat is liberated equal to ax g. cm. The work done is Px g. cm.: the total excess energy liberated is $(P+a)x$: the rate of excess energy liberation therefore is $(P+a)v$, v being dx/dt .

In a number of experiments, with a series of different loads, with a already determined (as above) by thermal measurements, and with v read off directly from the mechanical records, the quantity $(P+a)v$ was plotted against P with the result shown, for the last seven experiments, in fig. 11. A linear relation clearly exists between the energy rate and the load, both at 0°C and at higher temperatures. Thus

$$(P+a)v = b(P_0 - P),$$

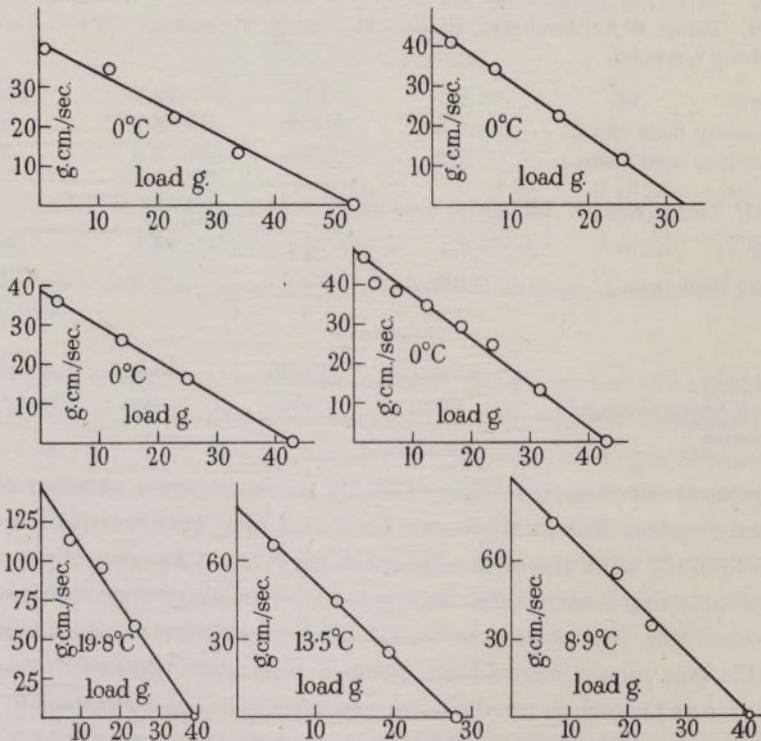


FIG. 11. Relation between excess energy liberation per second and load. From the last seven experiments made, without selection. Horizontally, total load lifted = P . Vertically $(P+a)v$, where a was calculated from the heat of shortening ($=ax$) observed in the same experiment, and $v (=dx/dt)$ was the speed of shortening observed under load P .

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where b is a constant and P_0 is the isometric tension. The values of b obtained in the present research are given in Table III. The temperature coefficient for 10°C is about 2.05.

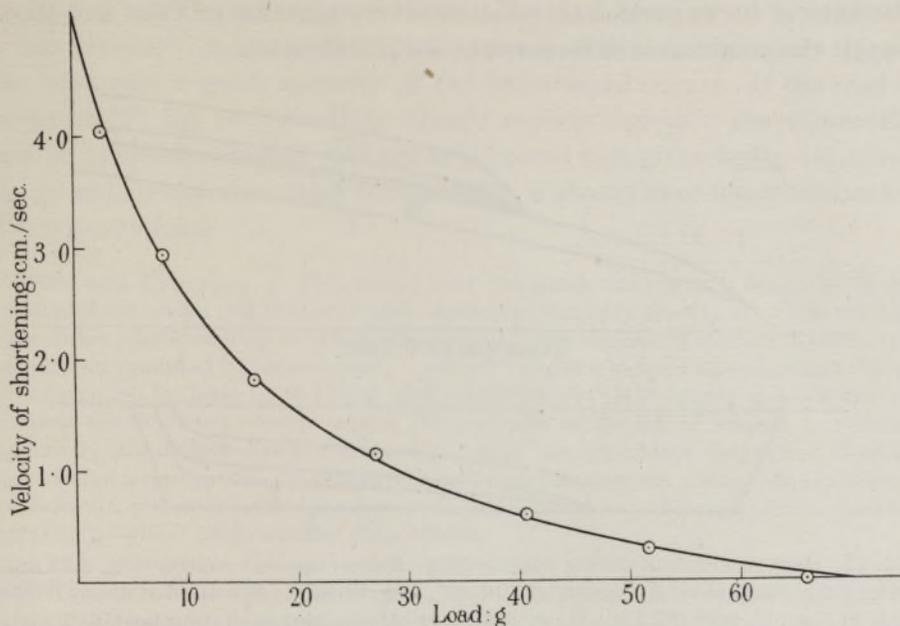


FIG. 12. Relation between load (g. wt.) and speed of shortening (cm./sec.) in isotonic contraction. Each circle is the mean of two observations in a series and reverse. Muscle, 165 mg., 38 mm., in Ringer's solution at 0°C . Tetanus 11.4 shocks/sec.: observations at 4 min. intervals: 5.6 mm. shortening. The curve is calculated from the equation $(P + 14.35)(v + 1.03) = 87.6$. Hence $a = 14.35$ g. wt. = 357 g./sq. cm., $a/P_0 = 0.22$, $b = 1.03$ cm./sec. = 0.27 length/sec.

(iv) *The relation between load and speed of shortening in an isotonic contraction.* The linear relation described in the preceding section involves one thermal measurement, that of the shortening heat from which a is derived, and the proof, by thermal measurements, that a is the same for different loads. The resulting equation, however, written $(P + a)(v + b) = \text{const.}$ can be verified by purely mechanical measurements, and the constants a and b can be derived, without thermal measurements at all, by fitting the equation to the observations of P and v . It is important that the values of a and b so derived are similar to those directly obtained by the method already described: in particular that, when observations by both methods are available, the value of a deduced from the shortening heat is the same as that obtained by fitting the equation to the P - v measurements.

An example of the relation between speed and load in an isotonic shortening is shown by the experimental points in fig. 12, together with a curve calculated from the equation with the constants given in the legend. The fit is good, and the constants are similar to those of Table III. The form of the experimental relation is very like that of Fenn and Marsh (1935): the equation is different, but see p. 183 below.

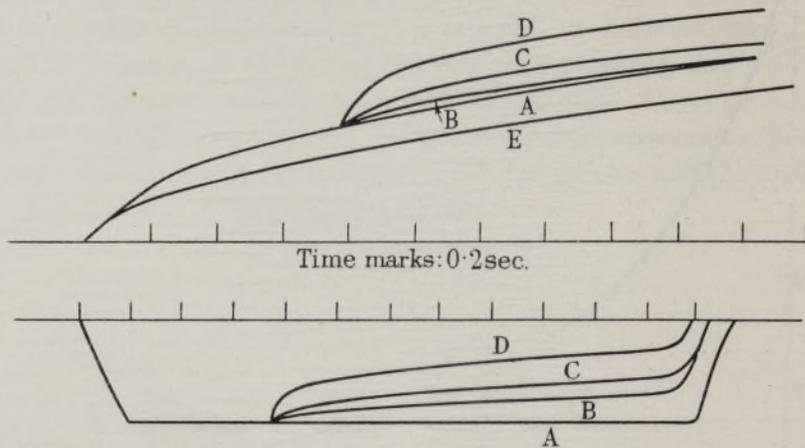


FIG. 13. Heat production during lengthening. *Below*: isotonic contraction, 5.75 mm., under 2.5 g. load; then *A*, "isometric short", 40 g. tension; *B*, loaded at about 0.8 sec. with 51.7 g.; *C*, with 57.2 g.; *D*, with 62.6 g. *Above*: corresponding heat deflexions: also *E*, "isometric long": traced from actual records and superimposed. Note that in later stages *B*, *C* and *D* have a rather less slope than *A* and about the same as *E*. Tetanus, 2 sec.; 0° C; muscle 30 mm. long, 97 mg.; time 0.2 sec.

A further investigation of the relation between load and speed is being made by Katz and by Barer on the muscles of frogs, tortoises and marine animals, in order to obtain a wider survey of the dynamic constants of muscle.

The greatest velocity of shortening, viz. at zero load, from the equation, is bP_0/a . With the mean constants of Table III, for the frog's sartorius, this is $0.331/0.257 = 1.29 \times (\text{muscle length})/\text{sec.}$, with a temperature coefficient of about 2.05 for 10° C. The greatest rate of extra energy liberation is also with zero load; its mean value at 0° C is $av_{\max} = 399 \times 1.29 \text{ g. cm./c.c.} \times \text{sec.} = 399 \times 1.29 \times 0.95 \text{ g. cm./g.} \times \text{sec.} = 490 \text{ g. cm./g.} \times \text{sec.} = 11.5 \times 10^{-3} \text{ cal./g.} \times \text{sec.}$ This is about 4 times as large as the isometric heat rate.

(v) *The heat and energy liberation during lengthening.* Typical heat and mechanical records, for a muscle lengthening under a load rather greater than the isometric tension, are given in fig. 13. The "isometric short" tension was about 41 g., the "isometric long" tension, not recorded, was probably somewhat larger. The heat rate, "isometric short", was rather

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greater than "isometric long", which is a complication in interpreting the results of lengthening.

The immediate effect of subjecting a frog's muscle to a load greater than it can bear is to cause it to lengthen, rather rapidly at first, and then, if the load is not too great, more slowly. The first more rapid lengthening is "irreversible", in the sense that the energy of the load is largely turned into heat, and a quick upstroke of the heat record occurs. If the load is too great (*F*, fig. 14 below) the muscle rapidly "gives", the contractile state so to speak collapses, and the heat record (not given in fig. 14) shows a large and sudden rise rather like that (fig. 8 above) in ordinary relaxation with a heavy load.

Gasser and Hill (1924, p. 411) found that the quick stretch of a tetanized frog's muscle did not cause the tension to rise suddenly, but only slowly, after the stretch, to the value corresponding to the greater length. They suggested that some structure, produced or modified by stimulation, "yielded" under a sudden rise of tension. With the longitudinal muscle of the body wall of *Holothuria* (Hill 1926*b*) a quick stretch produces the expected rise of tension, the converse of the fall of tension on release: apparently this muscle does not so readily "give" on stretching. Levin and Wyman (1927) found large increases in tension on stretching the muscles of dog-fish, *Holothuria* and *Echinus*, but only small increases with those of tortoise and crab. Some muscles apparently "give" more readily than others.

With a smaller load, after the first "irreversible" lengthening, the muscle proceeds to lower the load by a process apparently similar to, but the converse of, ordinary isotonic shortening. During this phase the energy of the load does not reappear as heat, and the heat record runs approximately parallel to that of an isometric contraction. In curves *B* and *C*, fig. 13, the muscle, while lengthening slowly, appears to give out heat at a rate definitely less than "isometric short", about the same as "isometric long", slightly less than would correspond to the isometric rate at the intermediate length at which it is at any moment. This slight deficit, if genuine, is to be attributed to the negative heat of lengthening, the converse of the positive heat of shortening. It occurs so slowly, however, and is so small, that it has proved impossible to measure it, or even to be quite sure of its existence. The process cannot be made to occur more quickly (at any rate in frog's muscle) without increasing the load, and that causes "irreversible" lengthening which disguises the whole effect.

There is no doubt, however, of the main conclusion, viz. that the rate of energy liberation by the muscle is considerably diminished during lengthening under a load. In fig. 14 the heat record (*C*) of the muscle lowering a load appears, as in fig. 13, to rise slightly less rapidly than the isometric heat records, either long (*A*) or short (*B*), due to the negative

heat of lengthening. From the observed heat has been subtracted the work done by the load on the muscle. The difference is shown by *D*. The immediate drop is due to the fact that part of the energy of the load is instantly used to stretch the elastic component of the muscle. After that, *D* rises considerably more slowly than *A* or *B* throughout its course. But *D* represents the total energy given out by the muscle, which—as is seen—is much less in lowering a load.

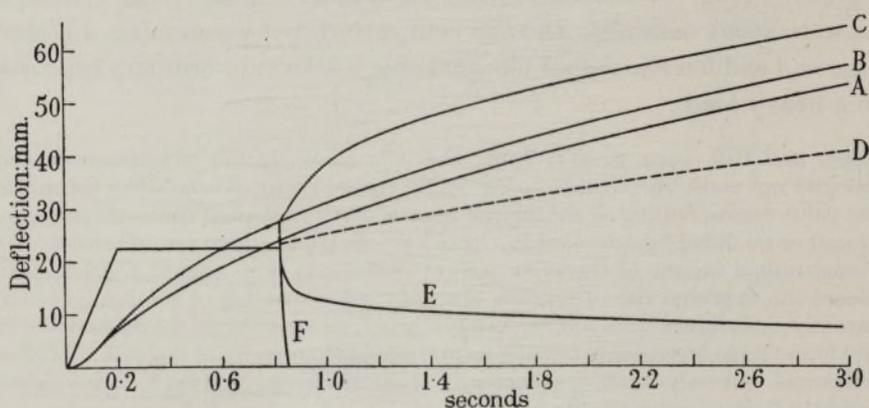


FIG. 14. Heat production during lengthening. *A*, heat record of isometric contraction ("isometric long"). *B*, heat record of shortening 5.6 mm. under 2.2 g., followed by "isometric short". *B* is above *A* because of the shortening heat. *C*, heat record of contraction similar to *B*, but loaded at 0.82 sec. with 58.6 g. *E*, mechanical record of shortening under 2.2 g., followed by lengthening under 58.6 g. Note the rapid fall at first, accompanied by a rapid heat deflexion (*C*), and the slow lengthening later, accompanied by a heat rate slightly less than in *A* and *B*. *D*, net energy liberated during lengthening, i.e. (heat) - (work): note that this rises much more slowly than *B* and *C*. *F*, sudden "give" of muscle under 68.2 g., accompanied by a very large and sudden heat deflexion (not shown). Each record is the mean of a pair, in series and reverse. Tetanus, 3 sec.; 0° C; muscle 29 mm. long, 89 mg.

This experiment has been made many times, and the result is always the same unless the load is so great that immediate "irreversible" relaxation occurs. The linear relation, therefore, shown in fig. 11 above between energy rate and load, can be continued to the right, i.e. to loads greater than the isometric tension, and to negative rates of extra energy liberation. No attempt has been made to verify the relation quantitatively in this region, but this might possibly be done. It should not be too difficult to get indirect evidence by continuing the experimental relation between load and speed (fig. 12 above) to loads greater than isometric, to see whether the equation $(P+a)(v+b) = \text{const.}$ applies also to the extension.

PART III. THE VISCO-ELASTIC PROPERTIES OF ACTIVE MUSCLE

The idea of muscle "viscosity" was proposed, in its modern form, by Hill (1922) to account for the decrease of force with increase of speed in the shortening of human arm muscles. This relation between force and speed of shortening does not depend upon any intervention of the nervous system, it is an intrinsic property of muscle itself, as Gasser and Hill (1924) found with isolated muscles and many have found since. Whether it is due to "viscosity" or not, this decrease of force with increase of speed is one of the major factors in the dynamics of muscle.

In a general way many of the facts had long been known. Fick, for example, was aware that a tetanized muscle did less work if it shortened more quickly against a smaller mass, and had supposed (1882, p. 67) that a greater part of the energy of its elastic forces was then used in overcoming internal resistances and degraded into heat. These internal resistances, he wrote (p. 130), were naturally greater the more rapid the movement. Blix (1893), to account for after-extension, likened the resting muscle to a spring moving in a viscous fluid. There had been, nevertheless, no very precise formulation of the problem, and little attention had been paid to it. Since 1922, however, much work has been done, and the term "visco-elasticity of muscle", although implying a theory which is certainly imperfect, has served at least to provoke many new experiments and to focus attention on a very real and important problem.

It may be useful, since a rather drastic change is now being proposed in our view of the "visco-elasticity" of muscle, to refer here to papers published in the last 16 years on the subject.

A. *On human muscle*: Hill (1922, 1926*a*, 1934*c*); Hansen and Lindhard (1923); Lupton (1922, 1923); Furusawa, Hill and Parkinson (1927); Best and Partridge (1928); Dickinson (1928, 1929); Müller (1930); Fenn (1930*a*, *b*, 1931*a*, *b*, 1932); Fenn, Brody and Petrilli (1931); Fenn and Garvey (1934).

B. *On isolated unstriated muscle*: Hill (1926*a*, *b*); Winton (1930, 1937); Levin and Wyman (1927); Sulzer (1928, 1929); Bozler (1930, 1931, 1933, 1936); Bayliss, Boyland and Ritchie (1930); van Overbeek (1931); de Nayer and Bouckaert (1932); Postma (1933); Jordan (1933); Bouckaert and Delrue (1934); Shukow (1936).

C. *On isolated striated muscle*: Gasser and Hill (1924); Hill (1926*a*, 1931*b*); Levin and Wyman (1927); Bouckaert, Capellen and de Blende (1930); Petit (1931); Oinuma and Hayashi (1932); Cattell and Edwards (1932); Stevens and Snodgrass (1933); Stevens and Metcalf (1934); Brown (1934); Fenn and Marsh (1935); Fenn (1936); Hursh (1938).

D. *General*: Weber (1933, p. 139); Jordan (1935).

E. *On the effect of work and shortening on the heat production of muscle*: Fenn (1923, 1924); Azuma (1924); Hartree (1925, 1928); Hill (1925, 1930); Wyman (1926); Hartree and Hill (1928*a, b*); Martin (1928); Cattell (1932); Feng (1932); Fenn and Latchford (1933).

The following facts are clear:

(i) active muscle, at least as ordinarily prepared and used, contains an undamped elastic element: if, during maintained isometric contraction, the muscle be instantaneously released, the tension does not fall to zero unless the amount of release be sufficient to allow the undamped element to reach its natural length;

(ii) active muscle contains an apparently damped element, in series with the undamped elastic one; the former, if allowed to shorten, exerts a force which is smaller the faster the shortening, until at a certain speed it exerts no force at all: at more than that speed it cannot shorten; conversely, if made to lengthen, it exerts a force which is greater the faster the lengthening, until at a certain speed it "gives" like a wire stressed beyond the elastic limit;

(iii) resting muscle contains the elastic element (i), but only to a minor degree the apparently damped element (ii);

(iv) the active state is set up much more rapidly than the isometric tension, as is shown by applying a quick stretch at various moments after a stimulus.

Various suggestions have been made to account for the facts. The first and obvious one that muscle is endowed with "viscosity", resisting change of shape, was soon found to require that the viscosity should be very much higher during activity than at rest—at least in striated muscle. It was unlikely, therefore, that simple viscosity alone was involved: more likely, that a molecular rearrangement had to occur when an active muscle altered its shape. Fenn, however, in 1923, had found that when a muscle shortened and did work it gave out more total energy than when it remained isometric: he has several times insisted that this—called by others the Fenn effect—is probably the basis of the apparent viscosity. In a recent paper (Fenn and Marsh 1935) he showed experimentally that the relation between speed of shortening and load in an isotonic contraction cannot be deduced from the simple hypothesis of a two-component, (undamped elastic)-(damped elastic) system. He found, however, satisfactory agreement with an equation which assumed that the true internal muscle force fell off exponentially as the velocity increased. Why it should do so he could not explain, but he argued that the rate of development of "shortening energy" from chemical potential energy is of paramount

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importance in determining how fast a muscle can shorten under a given load. Less clearly defined, his view was much the same as the present one.

The relation found experimentally by Fenn and Marsh between speed of shortening and force exerted in an isotonic contraction is the same as that shown in fig. 12, to which, as we have seen, the equation

$$(P+a)(v+b) = \text{a constant}$$

applies. Their only experiment at 0° C of which details are given is in their Table I, p. 284, and the equation

$$(P+450)(v+0.35) = 870$$

gives a very satisfactory fit.* The values $a = 450$ g./sq. cm. and $b = 0.35$ length/sec. agree well with those found on English frogs here. Fenn and Marsh give mean values of the constants of their equation, for frog's sartorii at 0° C and at 23° C. Calculating a mean curve from these constants, it is possible to fit the equation $(P+a)(v+b) = \text{const.}$ to the curve, at 0° C with considerable accuracy, at 23° C with sufficient. Numbers recalculated from the present equation and plotted in Fenn's way lie on good straight lines. The equations are not the same, but the experiments on shortening alone cannot decide between them. The values of the constants a and b which give the best fit are

$$0^\circ \text{ C: } a = 640 \text{ g./sq. cm.}, b = 0.59 \text{ length/sec.}$$

$$a/\text{mean } P_0 = 0.38.$$

$$23^\circ \text{ C: } a = 740 \text{ g./sq. cm.}, b = 1.82 \text{ length/sec.}$$

$$a/\text{mean } P_0 = 0.26.$$

Without the original data this roundabout calculation from the means, via Fenn's equation, cannot be very precise, but the result is satisfactory in three ways:

(i) in giving values of a and b of the same order of size as have been found in London on different frogs;

(ii) in showing little effect of temperature on a/P_0 ; and

(iii) in showing a large increase of b with rise of temperature.

It is clear, therefore, that the results of Fenn and Marsh are entirely consistent with those recorded above, and that the simpler equation $(P+a)(v+b) = \text{const.}$ may be regarded as correctly describing the shortening of muscle under constant load. The great virtue of constant load is simply that it eliminates one variable, it avoids change of length

* Professor Fenn, in a private communication, states that all the velocities and shortenings with his frog lever are given twice as great as they ought to be.

of the undamped elastic component. If load be not constant, then the elastic element will vary in length as the load varies: to it we can then apply the ordinary rules for elastic bodies. To the contractile component (better so-called than "damped elastic") the characteristic equation still applies, P and v no longer being constants in any contraction, but functions of the time related to one another by the characteristic equation. The apparent "damping" of the contractile component lies in those factors which determine its characteristic equation, viz., as Fenn has maintained, in the manner in which the energy supply is regulated.

The experiments on heat and energy in lengthening (figs. 13 and 14 above) make it impossible any longer to regard "viscosity" as the primary cause of the effects observed in active muscle. During lengthening, at not too high a speed, the rate of heat production is certainly not greater than in an isometric contraction and is probably slightly less. If "viscosity" were the chief reason for the slow lengthening, it would undoubtedly be greater. The rate of energy liberation by a muscle is considerably diminished during lengthening, considerably increased during shortening: these facts find no explanation in the "viscosity" hypothesis, but themselves provide an explanation of the other facts on which the "viscosity" hypothesis was based. As Fenn has pointed out, simple viscosity should provide a linear relation between speed and load: it has long been recognized that the actual relation is not linear. It was always possible, however, in a complex histological structure like muscle, and with a "viscosity" which might really depend on the reorganization of the protein molecules in new crystalline patterns as the muscle altered its shape (Hill 1931*b*, p. 120), that a less simple relation between load and speed might be found. The "viscosity" hypothesis, therefore, must be dismissed, not for these reasons but because it gives no explanation of the large alterations of heat and energy liberation during shortening and lengthening, and because, from those alterations themselves can be deduced, as a necessary consequence, the facts which the "viscosity" hypothesis was intended to explain. The muscle may still have visco-elastic properties, but they are less important in its behaviour than the other properties of shortening heat and energy regulation which we have discussed.

The general conclusion, therefore, is plain. The active muscle is still a two-component system, consisting of an undamped purely elastic element, in series with a contractile element governed by the characteristic equation $(P+a)(v+b) = \text{const.}$ There may be, indeed there must be, visco-elastic and probably purely viscous elements as well. Convincing evidence for these, in the resting—at any rate in the dead—muscle, is found in the

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irreversible thermo-elastic effects (Hill and Hartree 1920*b*; Feng 1932; Meyer and Picken 1937) and perhaps in the phenomena of prolonged after-extension (cf. Winton 1930). Their contribution, however, is small in the active striated muscle, compared with that of the two main components: in the unstriated muscle genuine viscous and visco-elastic factors may conceivably be more important. The active striated muscle, however, is chiefly a contractile element governed by the characteristic equation, in series with a purely elastic element.

It is not necessary here to attempt to show how all the so-called visco-elastic properties of striated muscle can be derived from the conception of a two-component system: many of them obviously can: others, particularly in the case of twitches or short tetani, require special assumptions as to the manner and speed of disappearance of the active state of the contractile component when a stimulus ends. The maintained contraction is simpler. Three examples of that are of special interest:

(a) the form of the isometric contraction, the rate of development of which can be deduced quantitatively from known values of a and b and of c , the amount of stretch of the elastic component;

(b) the form of the force-distance curves (Levin-Wyman), during shortening at constant speed;

(c) the greatest rate of doing work.

(a) *The isometric contraction.* Assume that the contractile component, of initial length l_c , stretches the elastic component, of initial length l_e , the subsequent lengths at time t being y_c and y_e respectively. Assume further:

(i) that the active state of the contractile component, defined by the equation $(P+a)(v+b) = \text{const.}$, is set up instantaneously on stimulation, and maintained by a tetanus: Gasser and Hill (1924) showed that it is certainly set up very rapidly;

(ii) that the elastic component is perfectly elastic, so that the force P is proportional to the stretch $(y_e - l_e)$, i.e. $P = \alpha(y_e - l_e)$, where α is constant; and

(iii) that the amount of shortening of the contractile component is small enough to allow P_0 , the full tension at any of the lengths involved, to remain sensibly constant.

In an isometric contraction the rate of shortening of the contractile part is equal to the rate of lengthening of the elastic part, so that

$$v = -dy_c/dt = dy_e/dt = (dP/dt)/\alpha.$$

Substituting for v in the characteristic equation and multiplying by α , we obtain

$$(P+a)(dP/dt + \alpha b) = \text{const.} = (P_0+a)\alpha b. \quad (1)$$

Consider the equation

$$\log_e \left(\frac{1}{1 - P/P_0} \right) - \frac{P/P_0}{1 + a/P_0} = \frac{t\alpha b/P_0}{1 + a/P_0}.$$

This is a solution of equation (1), as is seen by differentiating, and it satisfies the initial and final conditions that $P = 0$ at $t = 0$ and $P = P_0$ at $t = \infty$. Hence it represents the form of the isometric contraction, i.e. P as a function of t . The right-hand side can be simplified, since $P_0/\alpha =$ the amount of stretch of the elastic component under the full isometric tension $= c$. Replacing natural by common logarithms the equation then becomes

$$\log_{10} \left(\frac{1}{1 - P/P_0} \right) - \frac{0.4343P/P_0}{1 + a/P_0} = \frac{0.4343tb/c}{1 + a/P_0}. \quad (2)$$

Now we have seen that a/P_0 is approximately constant from one muscle to another and from one temperature to another, so that for frog's skeletal muscle $(1 + a/P_0)$ is usually about 1.25. At 0°C the mean value of b is about 0.35 (length)/sec. and c depends on the amount of tendon, on the force developed and on the elasticity of the lever used to record the response: according to Gasser and Hill c is about 0.1 to $0.15 \times$ (length). We have found it usually rather less: for the sake of calculation let us take $c = 0.1 \times$ (length). Then for the frog's sartorius at 0°C the isometric tension should develop according to the equation

$$\log_{10} \left(\frac{1}{1 - P/P_0} \right) - 0.3474P/P_0 = 1.216t.$$

For 16°C , assuming a/P_0 to be the same, b to be increased three times and c to become 0.12 (the force exerted being rather greater), the left-hand side of this equation remains unaltered, the right-hand side becomes $3.04t$. In fig. 15 two curves are drawn, for 0° and 16°C , from these equations. They are exactly similar to isometric contractions experimentally observed.

Direct evidence for the agreement of calculated and observed isometric contractions will be given in a later paper by Katz.

Gasser and Hill (1924) and Hill (1926*b*), from their experiments on quick releases during maintained contraction, concluded that the "process determining the speed of redevelopment of tension after release is identical with that determining the speed of initial development of tension". According to the present theory this is necessarily the case, for in both, i.e. in initial development and in redevelopment of tension, the contractile component has to shorten against the increasing force of the elastic component. Apart from the fact that P_0 might be rather less in re-

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development at a shorter length—which would alter c —the equations would be identical.

A simple test of the theory was made by taking advantage of the fact that, in equation (2), c can be increased arbitrarily at will by placing an elastic connexion between the muscle and the lever. If c is increased, t will be increased in the same proportion and the contraction, remaining exactly similar, will be slowed. This was easily verified. Further, by increasing c by a known amount and finding the ratio of the times for a given development of tension, the absolute value of c can be determined without a quick release. These experiments will be described in more detail elsewhere by Katz.

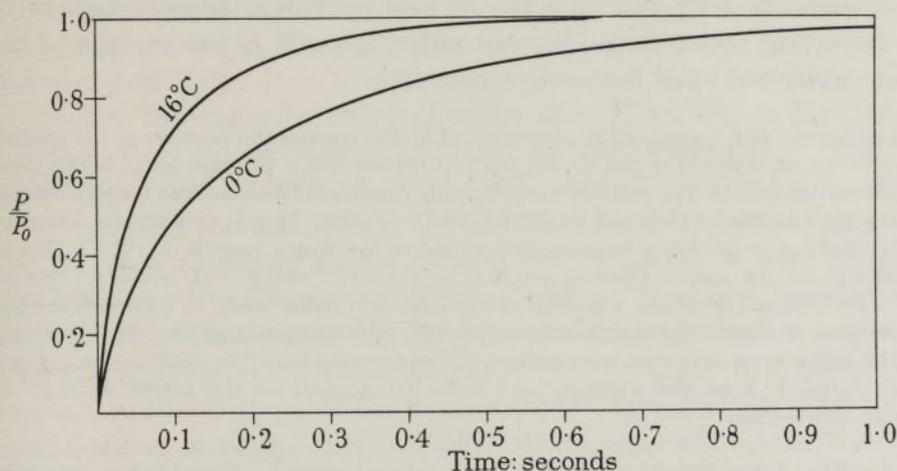


FIG. 15. Isometric contractions of frog's sartorius at 0° and 16° C; calculated from equation (2) with the constants given in the text.

The shortening of the contractile component and the lengthening of the elastic component in an isometric contraction should have two thermal consequences which are readily verified (cf. p. 167 above):

(i) during relaxation the stretched elastic component should shorten against the falling tension of the contractile component, and its potential energy should be transformed into heat;

(ii) during the initial development of tension the contractile component should liberate extra heat for shortening, which would exaggerate the early rate of heat production.

As regards (i), assuming perfect elasticity, the potential energy is $P_0c/2$, which if $c = 0.1 \times \text{length}$ becomes $0.05P_0 \times \text{length}$. In a typical muscle of 100 mg., 3 cm. long, developing a force of 60 g., this is 9 g. cm., or 1.9×10^{-3} cal./g., a fairly considerable amount. The "hump" on the heat

record which regularly occurs in relaxation, at the time when the tension is falling, is just of this order of quantities. The whole of the relaxation heat does not occur in this hump, but a large part of it does. According to Hartree and Hill (1928*b*, p. 12) the relaxation heat after a tetanus is about $0.12P_0 \times \text{length}$, and about one-half of this must have been derived from the potential energy of the stretched elastic component. The remainder is presumably an accompaniment of the disappearance of activity in the contractile component.

As regards (ii), if the contractile element shortens by an amount $0.1 \times (\text{muscle length})$, it should give out shortening heat $0.1a \times (\text{length})$. In the above example, assuming $a/P_0 = 0.25$, $a = 15 \text{ g.}$, so the shortening heat comes to 4.5 g. cm. or $0.95 \times 10^{-3} \text{ cal./g.}$ This is large enough to be an important factor in causing the early high rate in the analysis of the heat production of an isometric contraction.

The matter can be put more generally. Let the contractile portion of the muscle shorten by nl , stretching the elastic portion, where n is a fraction and l is the total length of the muscle. The total extra energy liberated will be nla as heat for shortening, plus $nlP_0/2$ as work: total $nla + nlP_0/2 = nla(1 + P_0/2a)$. If $a/P_0 = 0.25$, this becomes $3nla$. Taking a as 400 g./sq. cm. (mean value for frog's muscle at 0°C), this is $1200nl \text{ g. cm./sq. cm.} = 1200n \text{ g. cm./c.c.} = 27n \times 10^{-3} \text{ cal./g.}$ If $n = 0.1$, this is $2.7 \times 10^{-3} \text{ cal./g.}$, of which $\frac{1}{3}$ is shortening heat appearing early in contraction, $\frac{2}{3}$ is work done in stretching the elastic component, which appears as heat in relaxation.

The ratio, in an isometric contraction, of "shortening heat" to "relaxation hump" is $1 : P_0/2a$, $1 : 2$ on the average, and does not depend on the actual amount of elastic shortening.

(*b*) *The force-distance relation at constant speed.* Consider a muscle tetanized isometrically till its full tension is developed, and then released at constant velocity with the Levin-Wyman apparatus. With the same symbols as for (*a*) above and $u = \text{velocity of shortening}$, we have:

$$u = -dy_c/dt - dy_e/dt = \text{constant},$$

$$v = -dy_c/dt,$$

$$P = \alpha(y_e - l_e),$$

$$\therefore -dy_c/dt = u + dy_e/dt = u + (dP/dt)/\alpha.$$

Substituting in the characteristic equation and multiplying by α ,

$$(P + a)(dP/dt + \alpha u + \alpha b) = \text{const.} = (P_u + a)\alpha(u + b), \quad (3)$$

where P_u is the steady force corresponding to velocity u . (It is assumed that the amount of shortening is not so great that P_0 sensibly changes.)

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This is the same as equation (1) above with $(u+b)$ instead of b and P_u instead of P_0 . The boundary conditions are now, (i) at $t = 0$, $P = P_0$, and (ii) at $t = \infty$, $P = P_u$. Note that P_u can be calculated from the characteristic equation, $(P_u + a)(u + b) = (P_0 + a)b$.

Consider the equation

$$(P_0 - P) + (P_u + a) \log_e \left(\frac{P_0 - P_u}{P - P_u} \right) = P_0(b + u)t/c, \quad (4)$$

where c , as before, is the amount of stretch of the elastic component under the full isometric tension P_0 . This is a solution of equation (3), as is seen by differentiating: and it satisfies the initial condition that $P = P_0$ at $t = 0$, and the final condition that $P = P_u$ at $t = \infty$. Hence it represents the relation between P and t during shortening of the whole muscle at constant velocity u .

Consider the case of a frog's sartorius at 0°C , for which $P_0 = 100 \text{ g.}$, $a = 25 \text{ g.}$, $b = 1 \text{ cm./sec.}$ and $c = 0.25 \text{ cm.}$, and let us calculate a family of "indicator" curves, similar to those of Levin and Wyman (1927), for a set of velocities $u = 0.25, 0.5, 1, 2, 3$ and 5 cm./sec. The result is shown in fig. 16. It is obviously similar to such sets of curves as were given in figs. 2, 6 and 10 of Levin and Wyman's paper. In actual practice the amount of shortening necessary before a steady force is reached is so large that P_0 is less than at the start. The curve for $u = 0$ in fig. 16 is horizontal: in practice it will slope downwards somewhat from the left. This slight complication, however, does not disguise the main effect, viz. that the general form of the indicator curves, for a set of constant velocities, can be deduced from the theory of the two-component system, with values of a , b and c found by independent methods.

Details of experiments made with the Levin-Wyman apparatus to test the theory will be published elsewhere by Shapiro.

(c) *The greatest rate of doing work.* The rate of doing work is Pv , which from the characteristic equation becomes $bP[(P_0 + a)/(P + a) - 1]$. This can be shown to be a maximum when $P/a = \sqrt{(1 + P_0/a) - 1}$. The usual value of a/P_0 in the frog's sartorius is about 0.25: inserting this, $P/a = \sqrt{5} - 1 = 1.24$, or since $P_0/a = 4$, $P/P_0 = 0.31$: thus the greatest rate of doing work should occur with a load equal to about 0.3 of the full isometric tension. For different values of a/P_0 in the neighbourhood of the mean, the value of P/P_0 giving the greatest work rate varies only slightly:

a/P_0	0.15	0.20	0.25	0.30	0.35
Optimum P/P_0	0.27	0.29	0.31	0.32	0.34

Thus in any practical case the greatest rate of doing work will occur with a load about $\frac{3}{10}$ of the maximum force. This may have practical applications.

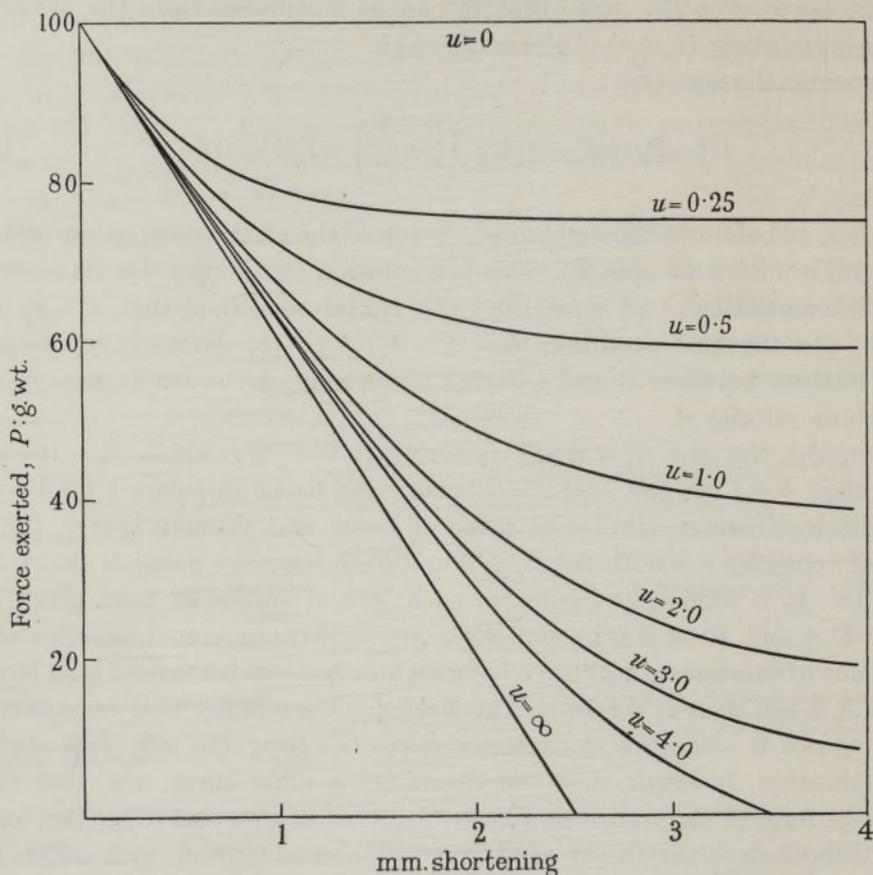


FIG. 16. Force-distance curves, for constant speeds of shortening during a fully developed tetanus, as made by the Levin-Wyman apparatus; calculated for 0°C from equation (4), with the constants given in the text. Speeds given in cm./sec. on the curves.

The active state of muscle. It has generally been assumed that the simplest "unit" of muscle activity is the twitch, and that all maintained activity can be regarded as due to the fusion or summation, partial or complete, of twitches. This view has something to commend it from the point of view of excitation, but from that of energy exchange it is simpler to think of muscle as having two states, that of rest and that of maximal maintained activity. During rest the source of energy is cut off completely from the contractile mechanism. During a tetanus of sufficient frequency the barrier is removed and the two are steadily connected: energy is set

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free in maintaining the active state, and if shortening occurs extra energy is liberated for shortening and as mechanical work. When the stimulus ends the barrier begins to fall, there is a rapid decrease in the rate of heat production, and in a short time the contractile mechanism is again isolated from the energy source.

After a single shock the conditions are more complex and the analysis is more difficult. The barrier is raised, the active state rapidly sets in, the contractile part of the muscle begins to shorten and stretch the elastic part, an external force is gradually developed, and shortening may occur according to the mechanical conditions. The barrier, however, begins to fall again, the energy supply is gradually cut off and the active state disappears. The energy relations, heat and work, of a twitch are complicated by the movements of the barrier, i.e. by a process which has more to do with excitation—or the immediate result of excitation—than with the properties of the active state.

For the present purpose, therefore, we have considered a muscle as having two states, (A) that of rest with the low heat production of rest, (B) that of activity with (i) the high heat production of activity, and (ii) the capacity for shortening and doing work governed by the characteristic equation and its corresponding energy relations. We have not been concerned with the process of transformation from one state to the other, but have assumed that the active state is set up very rapidly after the first shock—for this there is strong experimental evidence—and that it is steadily maintained by a tetanus of sufficiently high, but not actually very high, frequency.

Gasser and Hill (1924) examined the onset and disappearance of the "fundamental mechanical response" in a twitch, by applying a quick stretch at various moments before and during contraction. They found that its intensity reaches its maximum very early after the shock, and passes off continuously thereafter. The energy liberated in a twitch, as well as in a tetanus, is affected by mechanical conditions existing during contraction (Hill 1930), and a few preliminary experiments with the present equipment have shown that in a twitch in which shortening is allowed the heat is given out earlier than in an isometric one.

It is clear that the energy of a twitch is not set free in a single "all-or-none" outburst, but continues to appear at a decreasing rate as the "barrier" is lowered, and is affected by shortening and work as is the energy in a maintained contraction. The twitch, however, is much more complex than the maintained contraction and needs to be specially investigated. Further exploration of its energy relations may throw light

on the manner in which the "energy store" is linked to the "contractile mechanism" during activity.

SUMMARY

Part I

1. A coupled galvanometer system is described which is sensitive enough for muscle heat measurements with a deflexion time of 30–50 msec. Its sensitivity and period can be regulated by an adjustable feed-back. Used with a "protected" thermopile 45μ thick, it is rapid enough to allow the initial heat to be read from the records in absolute units and (for most purposes) without analysis.

2. The great advantage, in speed and accuracy, of using a very thin muscle, and the anomalies caused by non-uniform contraction and relaxation, are discussed.

3. The possibility is considered of using a resistance thermometer instead of a thermopile. Very serious difficulties are foreseen.

Part II

4. When a muscle shortens, in a tetanically maintained contraction, it liberates extra energy in two forms, (i) as "shortening heat", in amount proportional to the shortening, and (ii) as external mechanical work. The shortening heat is independent of the load, and therefore of the work done and the speed of shortening.

5. The rate of energy liberation at any moment, i.e. of work + heat, is a linear function of the load, increasing as the load diminishes.

6. The "dynamic constants" of muscle, in a maintained contraction, are defined and measured. They are

a , the shortening heat per cm. of shortening;

P_0 , the isometric tension;

b , the increase of energy rate per g. wt. decrease of load.

At any temperature these quantities are very constant: a/P_0 is independent of temperature, b has a temperature coefficient of about 2.05 per 10° C.

7. A "characteristic equation" is deduced, for the speed of shortening v under a load P , viz. $(P+a)(v+b) = \text{const.}$ This equation is very accurately obeyed. By fitting it to observations of v and P , the same constants a and b are obtained as are given by heat measurements.

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8. When a contracting muscle is made to lengthen gradually by applying a load rather greater than the isometric tension, there appears to be a negative heat of lengthening and the total energy given out by the muscle is less than in an isometric contraction. The energy relations in lengthening are the converse of those in shortening and seem to be governed by the same rules.

9. The nature of the shortening heat, and the mechanism by which the energy rate is governed by the load are discussed. It is suggested that the chemical processes by which energy is liberated involve certain active points in the molecular machinery, and that when these are occupied in attracting one another and producing a tension they are not available to take part in chemical reaction.

10. The work done by a muscle in raising a load, or in overcoming any elastic resistance, is transformed into heat in relaxation.

11. There is a sudden drop in the heat rate directly the stimulus ends, and before visible relaxation occurs.

12. The effect of muscle length on the isometric heat rate is described.

Part III

13. The "visco-elasticity" of contracting muscle is shown to be the property of a two-component system, the one component being undamped and elastic, the other being governed by the characteristic equation $(P+a)(v+b) = \text{const.}$ and its corresponding energy relations. The fact that an active muscle shortens more slowly under a greater force is due, not to "viscosity" but, as Fenn has claimed, to the manner in which the energy liberation is regulated. A large force causes a low energy rate, which results in a low speed.

14. From this can be deduced (i) the form of the isometric contraction, (ii) the form of the force-distance curves made, at constant velocity, by the Levin-Wyman apparatus, and (iii) that the greatest rate of doing external work should occur with a load equal to about 30 % of the isometric tension.

15. The active state of muscle is discussed.

REFERENCES

- Astbury, W. T. 1938 *Trans. Faraday Soc.* **34**, 377.
 Azuma, R. 1924 *Proc. Roy. Soc. B*, **96**, 338.
 Bayliss, L. E., Boyland, E. and Ritchie, A. D. 1930 *Proc. Roy. Soc. B*, **106**, 363.
 Best, C. H. and Partridge, R. C. 1928 *Proc. Roy. Soc. B*, **103**, 218.

- Blix, M. 1893 *Skand. Arch. Physiol.* **4**, 399.
 — 1902 *Skand. Arch. Physiol.* **12**, 52.
 Bouckaert, J. P., Capellen, L. and de Blende, J. 1930 *J. Physiol.* **69**, 473.
 Bouckaert, J. P. and Delrue, G. 1934 *Arch. int. Physiol.* **38**, 109.
 Bözler, E. 1930 *Z. vergl. Physiol.* **12**, 579.
 — 1931 *Z. vergl. Physiol.* **14**, 429.
 — 1933 *Protoplasma*, **19**, 293.
 — 1936 *Cold Spring Harbor Symposium on Quantitative Biology*, **4**, 260.
 Brown, D. E. S. 1934 *J. Cell. Comp. Physiol.* **4**, 257.
 Cattell, McK. 1932 *J. Physiol.* **75**, 264.
 Cattell, McK. and Edwards, D. J. 1932 *J. Cell. Comp. Physiol.* **1**, 11.
 Dickinson, S. 1928 *Proc. Roy. Soc. B*, **103**, 225.
 — 1929 *J. Physiol.* **67**, 242.
 Downing, A. C., Gerard, R. W. and Hill, A. V. 1926 *Proc. Roy. Soc. B*, **100**, 223.
 Downing, A. C. and Hill, A. V. 1935 *J. Sci. Instrum.* **12**, 91.
 Dulière, W. and Horton, H. V. 1929 *J. Physiol.* **67**, 152.
 Evans, C. L. and Hill, A. V. 1914 *J. Physiol.* **49**, 10.
 Feng, T. P. 1932 *J. Physiol.* **74**, 455.
 Fenn, W. O. 1923 *J. Physiol.* **58**, 175.
 — 1924 *J. Physiol.* **58**, 373.
 — 1930a *Amer. J. Physiol.* **92**, 583.
 — 1930b *Amer. J. Physiol.* **93**, 433.
 — 1931a *Sci. Mon., N.Y.*, **32**, 346.
 — 1931b *Amer. J. Physiol.* **97**, 1.
 — 1932 *Pflüg. Arch. ges. Physiol.* **229**, 354.
 — 1936 *Cold Spring Harbor Symposium on Quantitative Biology*, **4**, 233.
 Fenn, W. O., Brody, H. and Petrilli, A. 1931 *Amer. J. Physiol.* **97**, 1.
 Fenn, W. O. and Garvey, P. H. 1934 *J. Clin. Invest.* **13**, 383.
 Fenn, W. O. and Latchford, W. B. 1933 *J. Physiol.* **80**, 213.
 Fenn, W. O. and Marsh, B. S. 1935 *J. Physiol.* **85**, 277.
 Fick, A. 1882 "Mech. Arbeit u. Wärmeentwicklung b. d. Muskelthätigkeit."
 Leipzig: Brockhaus.
 Fischer, E. 1935 *J. Cell. Comp. Physiol.* **5**, 441.
 Furusawa, K., Hill, A. V. and Parkinson, J. L. 1927 *Proc. Roy. Soc. B*, **102**, 29
 and 43.
 Gasser, H. S. and Hill, A. V. 1924 *Proc. Roy. Soc. B*, **96**, 398.
 Hansen, T. E. and Lindhard, J. 1923 *J. Physiol.* **57**, 287.
 Hartree, W. 1925 *J. Physiol.* **60**, 269.
 — 1928 *J. Physiol.* **65**, 385.
 — 1932 *J. Physiol.* **75**, 273; **77**, 103.
 — 1933 *J. Physiol.* **79**, 492.
 Hartree, W. and Hill, A. V. 1928a *Proc. Roy. Soc. B*, **103**, 234.
 — — 1928b *Proc. Roy. Soc. B*, **104**, 1.
 Hill, A. V. 1913 *J. Physiol.* **47**, 305.
 — 1922 *J. Physiol.* **56**, 19.
 — 1925 *J. Physiol.* **60**, 237.
 — 1926a *Proc. Roy. Soc. B*, **100**, 87.
 — 1926b *Proc. Roy. Soc. B*, **100**, 108.
 — 1928 *Proc. Roy. Soc. B*, **103**, 138.
 — 1930 *Proc. Roy. Soc. B*, **107**, 115.
 — 1931a *Proc. Roy. Soc. B*, **109**, 267.
 — 1931b "Adventures in Biophysics." University of Pennsylvania Press.

The heat of shortening and the dynamic constants of muscle 195

- Hill, A. V. 1932 *Proc. Roy. Soc. B*, **111**, 106.
 — 1934a *Nature, Lond.*, **133**, 685; and **134**, 289.
 — 1934b *J. Sci. Instrum.* **11**, 281.
 — 1934c *J. Physiol.* **82**, 207.
 — 1937 *Proc. Roy. Soc. B*, **124**, 114.
- Hill, A. V. and Hartree, W. 1920a *J. Physiol.* **54**, 84.
 — — 1920b. *Philos. Trans. B*, **210**, 153.
- Horton, H. V. 1930 *J. Physiol.* **70**, 389.
- Hursh, J. B. 1938 *J. Cell. Comp. Physiol.* **11**, 333.
- Jordan, H. J. 1933. Quoted from *Ber. ges. Physiol.* **74**, 59.
 — 1935 *Verhand. Koninkl. Akad. Wetensch. Amsterdam*, **15**, 214.
- Levin, A. and Wyman, J. 1927 *Proc. Roy. Soc. B*, **101**, 218.
- Lupton, H. 1922 *J. Physiol.* **57**, 68.
 — 1923 *J. Physiol.* **57**, 337.
- Martin, D. S. 1928 *Amer. J. Physiol.* **83**, 543.
- Meyer, K. H. and Picken, L. E. R. 1937 *Proc. Roy. Soc. B*, **124**, 29.
- Müller, E. A. 1930 *Arbeitsphysiologie*, **3**, 298.
- de Nayer, P. and Bouckaert, J. P. 1932 *Arch. int. Physiol.* **35**, 9.
- Oinuma, S. and Hayashi, K. 1932 Quoted from *Ber. ges. Physiol.* **69**, 679.
- van Overbeek, J. 1931 *Z. vergl. Physiol.* **15**, 784.
- Petit, J. L. 1931 *Arch. int. Physiol.* **34**, 113 and 139.
- Postma, W. 1933 Quoted from *Ber. ges. Physiol.* **74**, 58.
- Shukow, E. K. 1936 Quoted from *Ber. ges. Physiol.* **96**, 38.
- Stevens, H. C. and Metcalf, R. P. 1934 *Amer. J. Physiol.* **107**, 568.
- Stevens, H. C. and Snodgrass, J. M. 1933 *Amer. J. Physiol.* **104**, 276.
- Sulzer, R. 1928 *Z. Biol.* **87**, 472.
 — 1929 *Z. Biol.* **88**, 604.
- Watton, W. L. 1935 *J. Sci. Instrum.* **12**, 115.
- Weber, H. H. 1933 *Ergebn. Physiol.* **36**, 109.
- Winton, F. R. 1930 *J. Physiol.* **69**, 393.
 — 1937 *J. Physiol.* **88**, 492.
- Wyman, J. 1926 *J. Physiol.* **61**, 337.
-