THE REGULATION OF THE SUPPLY OF ENERGY IN MUSCULAR CONTRACTION. By W. HARTREE[1] AND A. V. HILL.

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CONTENTS.

In 1914 an investigation was carried out by one of us (1) of the heat produced in the prolonged isometric contraction of a frog's sartorius muscle. The observations were made at room temperature, viz. at about 15° C. At that time the preponderating effect of temperature was not realised, and no particular notice was taken of small changes of temperature: it was difficult moreover with the apparatus employed then to work with any great accuracy at any temperature other than that of the room: it seemed desirable therefore to confirm and amplify the 1913 results by the method described in our recent paper (2) which makes it possible to work with equal ease at all temperatures. This investigation has led (*a*) to a theory of the physico-chemical mechanism regulating the supply of energy in an excited muscle, and (*b*) to a general relation between the mechanical and thermal responses, for all durations of stimulus.

Method. The heat was determined by the employment of the nickel-gold thermopile referred to in our previous paper (2). A calibration experiment was carried out in each case, on the dead muscle, to enable the heat produced to be expressed in absolute measure. This method of calibration is entirely satisfactory, the galvanometer deflections being under all conditions directly proportional to the rate of heat-production by the warming current, and to the duration of the warming. There is no basis for Snyder's (7) suggestion that "electrical currents passing

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through the dead muscle may activate... oxidations in the disintegrating tissues," and so lead to errors. Such errors, if they existed, would not remain exactly proportional to the amount of electrical energy liberated in the muscle over long periods of time, and under all conditions. The whole of this investigation depends upon an accurate measurement of the quantities observed in absolute units of heat or work, and the method of calculating the sensitivity adopted by Snyder would in our case lead to a result 300 p.c. too large, and render the investigation worthless.

The heat H liberated in any portion of muscle of length l and of mass m has, for reasons given below, been expressed in terms either of H/l or of H/m, *i.e.* in terms of heat per centimetre length, or of heat per gram. Heat has usually been expressed in gram-centimetres instead of calories, partly because a gram-centimetre is a more convenient size of unit in dealing with muscles, and partly because by this means a direct comparison is possible between the thermal and the mechanical response. Gram-centimetres can be reduced to calories by dividing by 4.24×10^4. The temperature of the muscle was varied by varying the temperature of the water inside the Dewar flask. The rise of tension T of the stimulated muscle was recorded on a moving surface, either (*a*) by an ordinary writing tension-lever, or (*b*) usually, in order to ensure greater quickness and accuracy of response, by photographic means (2. p. 116). In a number of experiments the tension in the longer contractions began to fall appreciably before the stimulus ceased: such experiments have been neglected.

The stimulus employed was always maximal, and produced either by a single induction shock, or by a single phase alternating current of 90 periods per second, giving therefore 180 stimuli per second. Its E.M.F. could be varied as required, and the heat produced by it determined if necessary: as a matter of fact the heating effect of the stimulating current was always negligible. The frequency of stimulation was not varied, since it was shown in a previous paper[1] that the frequency is without effect on the heat production, provided the tetanus is complete.

It should be noted that the "heat" referred to in this paper is that liberated in the initial three phases (2. p. 126) of the contraction, and includes none (or practically none) of that produced in the fourth recovery phase. It is read directly as the maximum deflection of the galvanometer, corrected if necessary in the longer contractions for the (small) loss of heat occurring before the maximum is reached. The recovery heat-production takes place too slowly to have any appreciable effect in the first few seconds involved.

The contractions have been isometric throughout. There is no particular virtue in the isometric contraction except that it eliminates one variable (the length of the muscle) and leaves the observer free to examine the elastic changes in the muscle uncomplicated by a change of length. The simple relation found below between the heat-production, the duration of the stimulus, and the mechanical response, could never have been established by a study of the more complicated case of a muscle allowed to shorten. The thermometric apparatus now available makes it possible to work on muscles allowed to shorten, without danger of disturbances produced by differences of temperatures along their length, and in a later paper we hope to deal with forms of contraction other than the isometric. Here we consider only the simplest case.

The method of conducting the experiment was as follows. As soon as the muscle had settled down to a constant temperature on the thermopile, usually in oxygen but sometimes in oxygenated Ringer's solution, it was given a few preliminary shocks and then a series of stimuli, increasing in duration from a single shock up to (say) two seconds, and diminishing again to a single shock. Each stimulus therefore was given twice, once in the increasing and once in the decreasing series, and an attempt made to eliminate the effects of fatigue by taking the mean of the two readings. After such a series, which was taken as representative of one temperature, the series was sometimes repeated at another temperature. It was often found that the results at a second temperature were unsatisfactory, owing to depreciation in the condition of the muscle due to the severe exercise, and such results have been neglected. Indeed it is probably best in general to trust to experiments made on fresh muscles, and to use a pair of muscles at one temperature only. In all the experiments given here, only the first series is given. By expressing the results in absolute units one experiment is made directly comparable with another. The method of eliminating the effects of fatigue by repeating the observations in the reverse order is very satisfactory, as is shown by the strikingly straight ends to the curves of Fig. 1. The results have been expressed in four ways:

a. By considering only H/m, the heat produced per gram of muscle in a maximal contraction, and paying no attention to the tension. The relation between H/m and x, the duration of the stimulus, is shown in Fig. 1, for five different temperatures. This relation will lead us to a hypothesis as to the manner in which the supply of energy is regulated in the muscle.

b. By considering H/Tl, the heat produced per centimetre length of muscle per gram weight of tension set up.

c. By considering H as a function of x and T. It will be shown that the heat liberated is the sum of two quantities, one being proportional to the duration of the stimulus, and the other to the potential energy set up.

d. By considering the "tension-time" set up. The "tension-time" is defined as the area of an isometric tension-time curve (3) and is of the dimensions of momentum (mass × velocity). It is equal to the momentum set up by the muscle in pulling horizontally at a large freely suspended mass. We shall show that a muscle excited isometrically by a prolonged stimulus liberates "tension-time" at a constant rate from the start: we shall then give the relation between the tension-time and the heat-production.

1. THE RELATION BETWEEN HEAT-PRODUCTION AND DURATION OF STIMULUS.

After a prolonged series of maximal stimuli at one temperature, followed by an interval of about an hour to allow the muscle to settle down to another temperature, the conditions of the muscle are apt to be lowered and less heat to be evolved from a given stimulus. It is

TABLE I. The relation between heat-production, duration of stimulus, and temperature. Many observations were made, at various times of year, but owing to the inadvisability of comparing observations made at one season with those made at another we have given here all the experiments made between May 22nd and August 10th and those only. Heat production given in gram-centimetres (not calories) per gram of muscle. Observations given so, [250], have been obtained by interpolation. The means at each temperature are plotted in Fig. 1.

Temp. C.	Month	Duration of stimulus: seconds											
		·00	·01	·02	·05	·10	·20	·40	·80	1·2	1·6	2·0	2·4
0°	May	[219]	215	224	255	288	343	445	610	720	835	950	1060
,,	July	275	273	280	321	380	495	650	895	1120	1320	1500	1660
5°	May	[207]	214	256	309	366	486	690	995	1230	1470	1700	1930
,,	July	215	[223]	265	315	381	518	740	1130	1410	1650	1900	[2110]
10°	May	[165]	210	264	382	495	715	990	1470	1880	2250	2610	—
,,	July	192	[247]	310	495	700	1040	1560	2140	2700	3250	3750	—
,,	Aug.	169	[196]	245	324	416	600	890	1270	1530	1810	2100	—
15°	June	192	219	283	430	610	880	1310	1980	2650	3330	[3950]	—
,,	July	138	[155]	246	360	485	740	1085	1680	2240	2840	3430	—
,,	,,	152	200	337	520	798	1200	1670	2470	3200	3900	4680	—
20°	May	[122]	150	260	415	605	945	1400	2250	3170	4040	—	—
,,	July	117	138	283	530	830	1270	1720	2610	3450	4300	—	—
,,	,,	123	159	300	555	805	1250	1850	2940	4000	5050	—	—
,,	,,	128	[154]	295	545	830	1220	1780	2700	3600	4600	—	—

inadvisable therefore to make observations at different temperatures on the same muscles. Our procedure has been to express the heat-production in calories (or gram-centimetres) per gram of muscle, and to assume that the average condition of a fresh muscle (in a large number
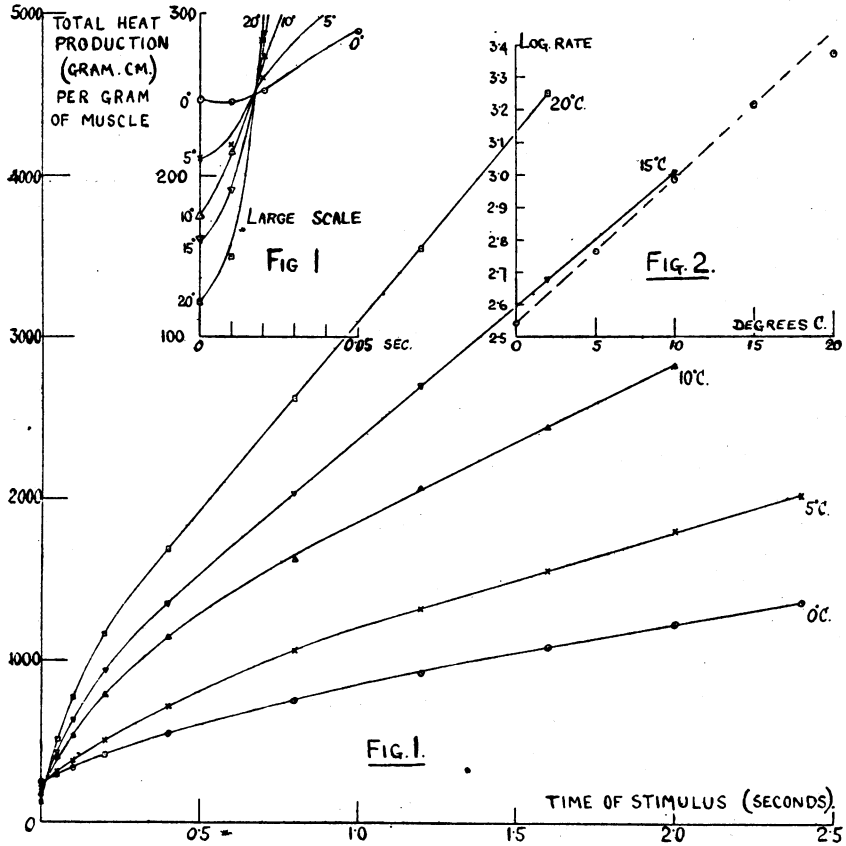

Fig. 1. Relation between heat-production H, duration of stimulus x, and temperature. The larger diagram shows the curves up to 2·0 seconds on a small scale; the upper diagram on the left shows the initial shape of the curves up to 0·05 second, on ten times the scale.

Fig. 2. Temperature coefficient of the rate of heat-production when a steady state has been reached. Horizontally temperature, vertically the logarithm of the heat-production per gram, per second duration of stimulus, as measured from the curves of Fig. 1.

of experiments) is constant for a given time of year. The results of a number of experiments are given in Table I, and taking the average of several experiments at each temperature they are shown graphically in Fig. 1. It should be noted that Fig. 1 does not give the relation between

heat-production and time, but between heat-production and duration of stimulus: the heat produced by a stimulus at any given moment does not appear *at* that moment (2. p. 111). We propose therefore to adopt the symbol x to denote duration of stimulus and t to denote time. It is seen from Fig. 1:

(1) that in a prolonged stimulus there is an extensive outburst of heat as the result of the first moment of the stimulus, and that successive equal periods of stimulation produce progressively smaller effects until the heat produced per second of stimulation attains a constant value;

(2) that the single maximal shock (represented by x = 0, *i.e.* zero duration of stimulus) gives considerably more heat at low temperatures than at high, while a longer stimulus gives far more heat at high temperatures than at low. The curves cross at about 0·017 second duration of stimulus: in other words a change of temperature has little or no effect on the energy liberated in a maximal stimulus lasting for 0·017 second.

The final steady value of the heat produced per gram of muscle per second of stimulus $\frac{1}{m}.(dH/dx)$, represented by the final slope of the curves in Fig. 1, has the following values:

Temp.	0° C.	5° C.	10° C.	15° C.	20° C.	25° C.	30° C.	35° C.	37° C.
gm. cm.	350	585	980	1640	2740	[4580]	[7650]	[12800]	[15700]
Calories	0·0083	0·0138	0·023	0·039	0·065	[0·108]	[0·18]	[0·30]	[0·37]

These values have been smoothed off by the aid of the temperature coefficient, found as shown below, and the numbers in square brackets extrapolated by its aid. The temperature coefficient is found as follows: the production of heat in the final steady state per gram of muscle per second of stimulus $\frac{1}{m}.(dH/dx)$ is read off from the final slopes of the curves, and it is found that the effect of a rise of temperature of 10° C. is to increase it 2·8 times over the range 0° C. to 15° C. This is shown in Fig. 2 where the logarithm of this quantity is plotted against temperature and shown to give a straight line. The rate therefore at which a stimulus liberates heat is governed by a temperature coefficient of the same size and exponential type as is an ordinary chemical reaction, and we may expect therefore that the regulation of the supply of energy to the muscle in a prolonged contraction is chemical in nature.

Various important questions arise in connection with these results:

(*a*) Why do the earlier shocks of a stimulus cause so much greater a liberation of energy than the later ones? (*b*) What is the nature of the final steady outflow of energy under a prolonged stimulus? (*c*) Why does an increase in the frequency of stimulation (1. p. 317) have no

effect on this steady outflow? (*d*) Why does a rise of temperature have so large an effect in increasing this steady outflow? (*e*) Why does a rise of temperature decrease the heat produced as the result of a single shock?

These questions go to the root of the problem of summation of contractions, and any theory of muscular activity must face them. We do not propose here to do more than indicate the lines on which we feel an explanation should proceed, the *type* of mechanism by which we believe the supply of energy is regulated in the muscle.

Imagine an elastic bag connected by a narrow pipe to a large reservoir of compressed air: the bag stretches and takes up air until the pressure in it is equal to that of the reservoir. A valve in the bag is now opened and the air rushes out, in large amount at first and then at a diminishing speed, until the rate of the outflow reaches a steady value determined by the size of the pipe connecting the bag to the reservoir. Similarly, interpreting this mechanical model in a chemical sense, let us suppose the muscle to possess a store (endowed with certain "elastic" properties to be described later) of the chemical bodies whose explosive liberation is the immediate cause of the mechanical response. This store is momentarily opened by a shock, *e.g.* by means of a momentary change in the permeability of its surface, and the chemical bodies [*e.g.* lactic acid] appear outside and cause the mechanical response. Following stimuli produce a similar though smaller outflow, as the elastic store becomes depleted. Simultaneously the store begins to be replenished along certain channels, not mechanical but chemical in nature, from the larger reservoir of available sugar or glycogen in the muscle. The mechanical model can be represented by the upper diagram of Fig. 3, while the hypothesis can be given a more concrete chemical form as in the lower diagram. Let us suppose that contraction is due to the appearance of a chemical
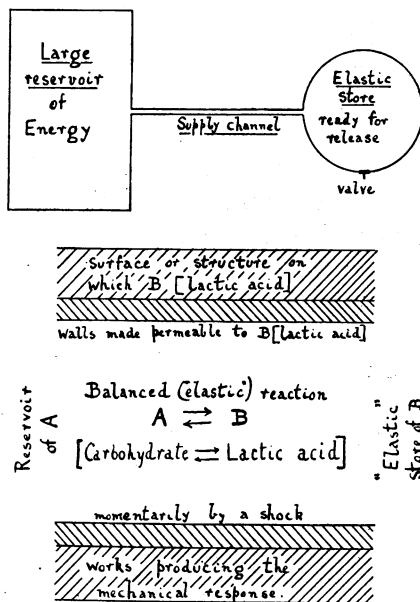

Fig. 3. Diagram of mechanism regulating the supply of energy in the muscle. Upper figure mechanical model, lower figure proposed chemical system.

body B [lactic acid] in the neighbourhood of certain surfaces or colloidal networks of the muscle and that in relaxation B is removed from the seat of its action by some physical or chemical means (*e.g.* neutralisation). Let us suppose next that B is produced from some chemical body A, of which there is a large supply in the muscle; these hypotheses are not *ad hoc*, they are generalisations from previous work on the lactic acid and heat-production of muscle. In the system shown in Fig. 3, the large reservoir represents a large store of the body A: the supply channel is the chemical reaction (under the agency of a katalyst) A →B and the "elasticity" of the store of the body B is provided by the balanced nature of the reaction A ⇌ B. We may suppose that the equilibrium exists inside some narrow space whose boundaries are impermeable to the active agent B [lactic acid]. A shock causes in these boundaries a momentary rise of permeability to B, this rise of permeability being manifested by the electric change; B immediately passes out: once outside it causes a rise of tension in the colloidal system there, and the mechanical response ensues. Relaxation is then produced by the neutralisation, removal, or combination of B, with an evolution of heat (the heat produced in relaxation, as we have shown elsewhere[2]) and then in the presence of oxygen B is removed by oxidation, or by restoration to its previous position inside the "reservoir," or by both[8].

In the meantime, owing to the loss of B, the equilibrium A ⇌ B has been upset and more A proceeds to be transformed into it. If now the shock be repeated the amount of B which passes out, and the amount of heat produced in consequence are less, because the concentration of B has not yet attained its previous value, and there is less of it ready to pass out. If a third shock be applied still less of B passes out, and if the shocks be repeated at short intervals the space in which the equilibrium A ⇌ B previously existed will be kept depleted of B: consequently the rate at which heat is liberated and B appears outside will be determined entirely by the rate at which the reaction A →B can go on, and not at all on the frequency of stimulation. The velocity of this reaction will depend upon the temperature, in the same way as that of other chemical reactions, so we should expect the rate of production of heat during the steady state to be affected by temperature as in the manner observed.

According to this scheme, which in detail is capable of wide modification, the heat is produced by any or all of the three causes: (*a*) by the breakdown A → B; (*b*) by the action of B on the colloidal system outside; and (*c*) by the neutralisation, removal, or combination of B in relaxation. Each of these factors would give us an amount of heat proportional to

the extent of the breakdown A → B, so that the production of B from A should be proportional to the liberation of heat.

The "elastic" property with which it is essential to endow the system to explain the sudden outburst of energy at the beginning of excitation is a necessary consequence of the balanced nature of the reaction. So long as B is at a low "pressure" (*i.e.* concentration) the reaction goes →, diminishing in speed as the pressure of B increases. Finally a considerable amount of B is formed, and equilibrium is attained, the store of B being available for immediate explosive release on the application of a stimulus.

The hypothesis sketched above (*a*) is in general agreement with what is already known as to the chemical and physical accompaniments of muscular activity; (*b*) explains the greater effect of the earlier stimuli, the final steady state attained, and the independence of frequency of excitation; (*c*) explains the large effect of temperature on the rate of heat-production during the steady state; and (*d*) explains the effect of a fall of temperature in increasing the heat-production following a single maximal shock: *the change of permeability caused by the single shock lasts longer at the lower temperature* (as does the electric response) *and therefore allows more B to escape,* and *so more heat to appear.*

We believe that this general hypothesis will be found to give a consistent picture of the facts. We have purposely avoided making it too definite, as this can be done only after more specific chemical investigations have been made. Considerations of energy can never enable one to describe the precise mechanism but only the general sequence of events. With the aid of subsidiary hypothesis however it is possible to fit a large number of ascertained facts into the scheme: *e.g.* the onset of chloroform rigor may be supposed to be due to a permanent change in the permeability of the walls caused, *e.g.*, by the solvent effect of the chloroform; or the steady resting liberation of energy of a muscle to a small resting permeability of the walls: or the fact that less energy is liberated when the muscle is allowed to shorten to the fact that the area of the walls is smaller, and less energy can escape: or the prolonged contraction and evolution of heat induced by a shock after treatment with veratrine to a great increase in the time during which the permeability of the walls enclosing the store of B (lactic acid) is maintained. The reader can easily supply further examples for himself.

The absolute value of the rate of liberation of energy is of general, rather than of specific interest. The quantities given above represent, at various temperatures, the maximum sustained rate of output of energy

of which the muscle is capable. The observations have not been continued beyond 20°, owing to the rapid depreciation of a frog's muscle kept at higher temperatures. If however we extrapolate to 37° by means of the temperature coefficient we find that at 37° (if it did not go into rigor) the frog's sartorius muscle could attain a maximum sustained rate of output of energy of 0·37 calorie per gram of muscle per second. This does not include any heat produced in oxidative recovery processes, but only that liberated in the initial breakdown. Including the recovery processes the sustained rate would be about 0·70 calorie per gram per second.

2. THE HEAT-PRODUCTION IN RELATION TO THE TENSION DEVELOPED AND MAINTAINED.

This was investigated previously at 15° C. (1). The heat H was determined as before in any length l of muscle (either the whole length or the length between the electrodes) and divided by T the maximum tension set up. It is clear that H must be divided by l, otherwise H/T has no absolute meaning, since by increasing the length of the muscle —but not the cross-section—we can increase H without increasing T. A change in cross-section however affects both H and T equally in a maximal contraction, so need not be considered. Moreover if T be measured in grams wt. and l in cm., Tl is obtained in gram cm., so that if H be expressed (as has been done here) in gram cm. H/Tl becomes a *number* of no dimensions.

The values of H/Tl were observed on fresh muscles for stimuli increasing in duration from that of a single shock up to 2·0 seconds, and decreasing again to a single shock, and the mean was taken of the two values of H/Tl for each duration. If a second series be taken the values of H/Tl may differ appreciably from those recorded in the first series: in other words, employing the term "efficiency" in the loose sense of

$$\frac{\text{(tension maintained)}}{\text{(energy supplied in maintaining it)}}$$

the "efficiency" of the muscle has changed as the result of exercise. It is inadvisable therefore to perform more than one series of experiments on the same muscle, so that experiments at different temperatures must be made on different muscles. Hence to avoid errors due to variations in individual muscles it is necessary (a) to compare results obtained at one time of year only, and (b) to make a large number of experiments. The results of our experiments are collected in groups in Table II. It is seen that the "efficiency" of the muscle in developing and maintaining

a prolonged tension is less in July than in May or November. The bearing of this fact is discussed below, but for the moment it is clearly better to avoid taking the means of numbers differing as widely as those in

TABLE II. Relation between H/Tl and x for various constant temperatures, where H is total heat produced in length l of muscle, T is the maximum tension developed, and x is the duration of the stimulus in seconds. H and Tl are both expressed in gram cm. so that the quantities given in the Table are simple numbers.

		Duration of stimulus: seconds										
Temp. C.	Month	·00	·01	·02	·05	·1	·2	·4	·8	1·2	1·6	2·0
0°	May	—	·190	·200	·207	·220	·241	·287	·381	·462	·550	·609
,,	,,	—	—	·190	·196	·209	·230	·277	·353	·425	·495	·572
,,	,,	—	184	·191	·197	·205	·221	·270	·368	·436	·510	·558
,,	,,	—	·180	·182	·185	·201	·218	·264	·345	·410	·484	·550
,,	July	·296	·300	·304	·305	·330	·370	·425	·530	·626	·708	·790
,,	Aug.	·320	—	·325	·345	·362	·368	·416	·495	·570	·615	·695
,,	Nov.	·240	·242	·244	·260	·280	·302	·360	·440	·520	·580	·640
5°	May	—	·177	·190	·207	·225	·272	·345	·471	·570	·685	·748
,,	,,	—	·201	·211	·221	·240	·285	·365	·525	·655	·760	·890
,,	,,	—	·170	·188	·207	·228	·270	·347	·479	·585	·696	·810
,,	July	·252	—	·270	·287	·305	·350	·424	·590	·745	·858	·985
,,	Aug.	·260	—	·263	·274	·271	·320	·386	·510	·602	·725	·795
,,	Nov.	·260	·262	·265	·285	·310	·360	·440	·580	·680	·765	·850
10°	May	—	·198	·215	·243	·269	·330	·445	·611	·780	·925	1·100
,,	,,	—	·209	·213	·229	·238	·282	·384	·565	·706	·840	·981
,,	,,	—	·183	·196	·220	·255	·322	·410	·593	·760	·890	1·030
,,	July	·310	—	·330	·367	·410	·502	·588	·860	1·110	1·340	1·570
,,	Aug.	·236	—	·261	·295	·325	·378	·490	·645	·845	1·000	1·170
,,	Nov.	·280	·284	·290	·305	·340	·410	·540	·775	1·020	1·260	1·470
15°	May	—	—	—	·244	·275	·342	·468	·704	·930	1·120	1·320
,,	,,	—	—	—	·224	·251	·309	·425	·640	·841	1·045	1·230
,,	,,	—	·169	·179	·213	·246	·312	·435	·649	·871	1·062	1·295
,,	July	·260	—	·304	·354	·390	·476	·655	1·010	1·340	1·670	1·980
,,	,,	·265	·265	·320	·369	·438	·542	·700	1·050	1·360	1·670	2·000
,,	Dec.	·210	·250	·275	·330	·380	·460	·600	·870	1·140	1·400	1·660
20°	May	—	[·181]	·201	·225	·280	·381	·598	·940	1·290	1·570	1·910
,,	,,	—	·166	·177	·210	·240	·337	·481	·756	1·035	1·340	1·650
,,	,,	—	·170	·195	·239	·292	·390	·579	·924	1·230	1·580	1·900
,,	July	·226	·241	·302	·387	·460	·628	·885	1·440	1·940	2·300	—

Table II, and we have averaged the May results only in Fig. 4. In that figure the values of H/Tl are plotted against x, the duration of the stimulus, for various constant temperatures. From the figure we see:

(a) that H/Tl for a shock or a very short stimulus, is practically unaffected by a change of temperature, the curves for different temperatures all starting at about the same point;

(b) that the curve relating H/Tl to x the duration of the stimulus rapidly becomes linear, *the rate of heat-production* becoming proportional to the tension maintained;

(c) that a rise of temperature increases and a fall of temperature diminishes the value of H/Tl for a given x, the " efficiency" of the muscle in maintaining a force being much decreased by a rise of temperature.

With regard to (a), the fact that the value of H/Tl observed in the case of a single shock is independent of temperature, contradicts an observation made by one of us ten years ago with much less efficient
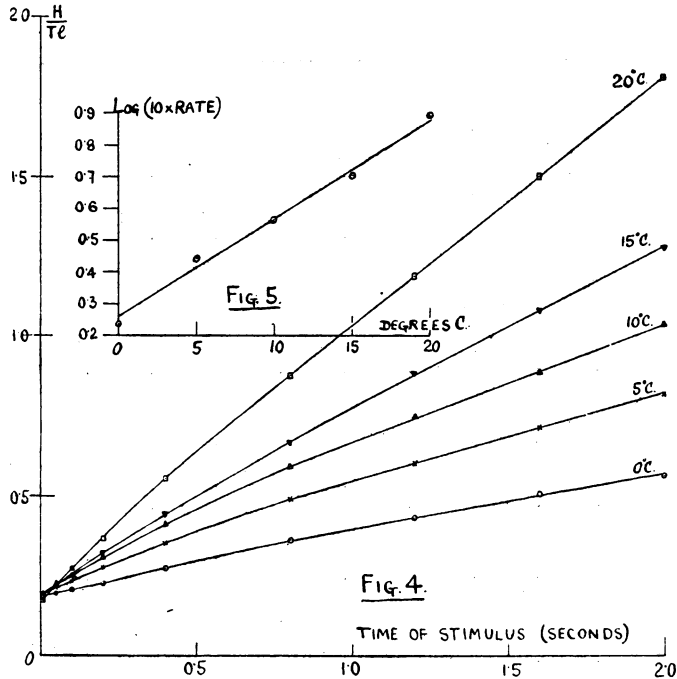

Fig. 4. Relation between H/Tl and duration of stimulus, for different temperatures. The curves all start from the same point, corresponding to H = Tl/5·5, and rapidly become linear.

Fig. 5. Temperature coefficient of rate of heat-production per cm. of muscle per gram weight of tension maintained. Horizontally temperature, vertically logarithm of the above quantity. Note the linear relation which corresponds to an increase of 2·0 times for a rise of 10° C.

methods(9), though as a matter of fact it adds another argument to the general conclusions of that paper that the tension bears a constant relation to the heat-production for a wide variation of the external conditions. The erroneous nature of the conclusion drawn then, that H/T diminishes as the temperature is raised, was probably due to a tension-lever, with too much inertia, " overshooting" in the more rapid

twitches at a higher temperature, and to the relatively large effects of fatigue in the case of a muscle raised to such temperatures as 26° or 28° C. Whatever be the explanation however of the previous erroneous result there can be no doubt that in fact H/Tl in a single isometric twitch is very nearly, if not quite, independent of temperature[1]. If the maximum tension set up be proportional to the total quantity of the body B [lactic acid] allowed to escape as the result of a stimulus, we might expect the tension to be proportional to the heat-production. In any case the observed constancy of H/Tl is further evidence that the tension developed in an isometric contraction is the most fundamental expression of the mechanical response.

With regard to (*b*), the observation that H/Tl rapidly becomes a linear function of the duration of stimulus confirms the results of two previous papers (9. p. 30 and 1. p. 320) over the whole range of temperatures investigated. It seems probable that a prolonged stimulus sets up a steady stream of the body B which acts upon the sensitive protein substances outside and is "removed" in the processes of relaxation at a steady rate, the tension at any moment being proportional to the amount still present. When a steady state is attained, as much B is liberated per second as is removed, and a steady concentration is maintained in the "active" spaces of the muscle so long as the supply and the removal are not interfered with. Thus the tension maintained should become proportional to the *rate* of heat-production.

With regard to (*c*) we may express the effect of temperature more exactly, as we did above in the case of the heat-production. The steady slopes attained by the curves of Fig. 4 were measured up and their logarithms taken: the numbers obtained, which are the logarithms of the rate of increase of H/Tl per second of stimulus, are plotted against temperature in Fig. 5. The result is a straight line, showing that the rate of increase of H/Tl per second of stimulus has a temperature coefficient of the same exponential type as an ordinary chemical reaction, increasing 2·0 times for a rise of 10° C. A similar calculation from the

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[1] Prof. Meyerhof of Kiel (who saw the MS. of this paper) expressed privately to one of us a belief that this conclusion might, on further investigation, prove inconsistent with the facts. Since this paper was written we have therefore investigated the question again in a different manner, making readings of H/Tl on the *same* muscle at a succession of different temperatures. It is possible to do this if only a few shocks be given at each temperature, for then the muscle may maintain its condition for long periods. The experiments themselves will be described in a later paper, but it may be stated here that they are entirely consistent with the conclusion that H/Tl in a twitch is independent of temperature.

July results of Table II gives a temperature coefficient of about 2·6, and from the November results a temperature coefficient of about 2·4. We may take the mean temperature coefficient as being about 2·3. Before discussing the meaning of this high temperature coefficient we should note that the rate of increase of H/Tl per second of stimulus is of the dimensions minus one in time, and represents a *rate of proportional change*, e.g. it is of the same order of dimensions as the velocity constant k of the chemical reaction, $X \to Y$ in which $d[Y]/dt = k[X]$. Thus the rate of increase of H/Tl is a quantity which, unlike some quantities, we can reasonably endow with a temperature coefficient of the usual type and the fact that it is so high suggests that the velocity of some chemical reaction is the basis of it. Now if a constant stream of the chemical body B [lactic acid] is passing out, accompanied by a constant production of heat, its effect at any given spot—which depends upon its concentration there at the moment—is determined not only by the rate at which it is being supplied but by the rate at which it is being removed. The rate of removal will presumably be governed by some equation of the type (rate of removal) = k (concentration still present), while when the steady state is attained we must necessarily have (rate of removal) = (rate of supply). Thus during the steady state we should expect to find

(rate of supply of B) = k (concentration of B)

or since the rate of supply of B is measured by the rate of production of heat, and the concentration of B by the tension set up,

(rate of production of heat) = k (tension set up).

This agrees with the observed facts. Now suppose for the moment that the constant k is practically unaffected by the temperature, or in other words that the removal of B [lactic acid] is of a simple physical nature (*e.g.* diffusion). Then our last equation would show that in the final steady state the rate of production of heat divided by the tension set up should also be practically unaffected by the temperature. Our experiments show that this is not the case, and we must conclude rather that the constant k is largely affected by the temperature, or in other words that the removal of B is effected by chemical means. Thus *the high temperature coefficient of the rate of increase H/Tl with duration of stimulus points to the fact that the process of relaxation is due to removal of the active agent in contraction from the seat of its action by some chemical means.* This last deduction can be made in another way which is a striking confirmation of the general validity of the hypothesis sketched above. It is well known that the course of the mechanical response is consider-

ably affected by temperature, and we have shown (2. p. 117) that the "rate of relaxation" is increased about 2·2 times by a rise of 10° C. Thus the constant k defining the rate of removal of the active agent in the contraction might be expected to increase about 2·2 times for a rise of 10° C. and this agrees well with the mean value 2·3 of the temperature coefficient actually found for H/Tl. We may conclude therefore that the higher "efficiency" of the muscle in maintaining a force at a lower temperature is due to the fact that the fundamental processes accompanying relaxation go on much more slowly at a lower temperature, being in fact chemical processes of some kind with a high temperature coefficient.

The absolute value of the steady heat-production, per second of stimulus, per centimetre length of muscle, per gram weight of tension maintained, was given in the previous paper(1) as being 15×10^{-6} calories at 15° C. The values for 15° C. deduced from the above Tables have an average for May, July and November, of about 14×10^{-6} calories, which is in satisfactory agreement with the previous value obtained with very different apparatus. It is possible now to state the value of this quantity at all temperatures, as is done in Table III.

TABLE III. Absolute values of heat-production per cm. length of muscle, per gram weight of tension maintained, per second stimulus, in a prolonged contraction (d/dx H/Tl). Mean values taken for May, July and November, for sartorius of *Rana temp.* Mean temperatures coefficient found = 2·3 for 10° C. The values above 20° C. were obtained by extrapolation with the aid of the observed temperature coefficient.

Temp.	0° C.	5° C.	10° C.	15° C.	20° C.	25° C.	30° C.	35° C.	37° C.
Calories × 10⁻⁶	4·1	6·2	9·4	14	22	[33]	[50]	[75]	[87]
Gram cm.	0·17	0·26	0·40	0·61	0·92	[1·4]	[2·1]	[3·2]	[3·7]

According to previous work(4) the potential energy of an excited muscle is about Tl/6, and this has been confirmed by recent work of Meyerhof's(5) and by the results given in the next part of this paper: hence in order to *maintain* a state of potential energy E in a muscle, the following amounts of energy have to be supplied per second.

Temp.	0° C.	5° C.	10° C.	15° C.	20° C.	25° C.	30° C.	35° C.	37° C.
Energy supplied per second = E ×	1·0	1·6	2·4	3·7	5·5	[8·4]	[13]	[19]	[22]

This shows the extraordinary inefficiency of the prolonged contraction of striated muscle at higher temperatures. It should be noted that the calculation takes no account of the energy wasted in recovery processes, so that taking the complete process into account the numbers given above should be about doubled. It would be interesting to compare

these numbers with those deduced from the oxygen consumption of a man holding a heavy weight.

Since the relative economy with which a force is maintained by a muscle is, physiologically speaking, a very important quantity, it is desirable to have a term to denote it. The amount of heat liberated per second of stimulus, in maintaining a force T in a length l, viz. $(dH/dx)/Tl$, the quantity given in the last row of Table III is clearly a measure of the wastefulness of the muscle in the process, and we may denote its reciprocal $(Tl)/(dH/dx)$ by the term "*the efficiency of a muscle in maintaining a constant force*." The efficiency of the muscle in maintaining a constant force is decreased very largely by a rise of temperature, to the extent of 2·3 times (on the average) for a rise of 10° C. It is affected also by a variety of other factors. For example, the immediate result of exercise is to increase the efficiency of the muscle in maintaining a constant force, and to diminish the speed of response, while the July frog (which is in better condition and "training" and exhibits a more rapid twitch than the May or November one) shows a smaller efficiency. We may generalise by saying that any factor which slows the chemical processes accompanying relaxation will increase the efficiency of the muscle in maintaining a force. This generalisation has obvious physiological applications. Some muscles, *e.g.* unstriated muscles, relax exceedingly slowly, and these are the muscles occupied chiefly in maintaining a force for a long time: their high efficiency in so doing is a direct consequence of the slowness of their relaxation processes. Supposing the single twitch of all muscles to be produced with the same high efficiency, it is obvious that the muscle whose twitch takes 1000 times as long to run its course will maintain a force over a long period with 1000 times the efficiency. Or again, it is well known to athletes that heavy and exhausting exercise is very bad training for sports, such as sprint-running or jumping, where great quickness is required: the training which leads to quickness of contraction and relaxation is directly opposed to that which leads to economy, and immunity from fatigue, in slow, prolonged and heavy movements.

3. The heat-production in relation to the potential energy developed and the duration of the stimulus.

It was shown in Part 1 that H, the total initial heat-production, becomes a linear function of x, the duration of the stimulus, as x is increased. In Part 2 it was shown that H/Tl similarly becomes a linear function of x. It should be noted however that H, or H/Tl, does not

immediately become a linear function of x, and the divergence from the linear relation is considerable at the start, as is seen in Figs. 1 and 4. It is clear that H is made up of two factors, one of which is proportional to the duration of the stimulus. The question then arises, what is the second factor? Now a muscle has two functions, dynamical and statical, viz. (*a*) the production of potential energy to enable the animal to do work if required, and (*b*) the maintenance of a force to enable the animal to carry loads, to support itself, or to preserve its posture. These functions of a muscle are independent ones, and we might expect them to correspond to two different factors in the heat-production. If this be so, we should hope to find that H = (some function of the duration of the stimulus) + (some function of the potential energy developed). Now, as the stimulus is continued, the potential energy reaches a maximum and remains constant, while the heat-production H becomes a linear function of x the duration of the stimulus. Hence we might expect to find:

$$H = bx + \text{(some function of the potential energy E)}$$

where b is some constant, depending on the temperature. In a previous paper (4. p. 461) it was shown that the potential energy developed in a muscle on excitation, as measured by the quantity Tl/6, is a fairly large fraction of the initial heat-production, amounting for a stimulus of 0·075 seconds, and under a moderate initial tension, to about 75 p.c. of the heat-production. This result has been confirmed by Meyerhof (5. p. 278) who finds, employing a different method and a different muscle, that on the average the potential energy of an excited muscle is about 80 p.c. of the total initial heat-production, being anywhere between 75 and 100 p.c. A further confirmation of the same fact is given by the experiments recorded in Table II and Fig. 4, where it is seen that for very short durations of stimulus the quantity H/Tl is the same for all temperatures and has, for the May results, the value (about) 0·18. Thus for the May results Tl/6 is about 93 p.c. of the total initial heat-production, at all temperatures. The previous value (75 p.c.) was also obtained in May and was for a stimulus lasting 0·075 second; reference to the 15° C. curve in Fig. 4 shows that a stimulus of 0·075 second gives a value of H/Tl of 0·23, corresponding to a value of Tl/6 equal to 73 p.c. of the heat-production. The agreement is very good, and it is obvious now that to ensure the highest efficiency the shortest possible stimulus should be employed, so that for a single shock and employing the English frog in May we may say that 93 p.c. is the value

of the efficiency as measured by the quantity Tl/6H. Practically therefore the initial heat-production is equal to the potential energy developed, or in other words practically the whole of the energy liberated by a muscle in the initial stages (*i.e.* apart from "recovery") of a twitch passes through the phase of potential energy before it appears finally as heat[1]. Returning to our original argument therefore we should expect to find, $H = bx + E$, or in other words the heat-production to be the sum of two factors, one equal to the potential energy developed, and the other to the duration of the stimulus multiplied by some appropriate constant. We have tested this deduction in the following manner, and so obtained a striking confirmation of the theory.

In all the experiments made in May the heat-production per gram of muscle has been plotted against x the duration of the stimulus, as in Fig. 1, and the final steady slope of the curve read off. H/m finally becomes equal, for large values of x, to $bx +$ (some constant). Now b having been determined, the quantity $(H/m - bx)$ can be calculated for all durations of stimulus from the observed values of H and x, and the mean values of $(H/m - bx)$ for each temperature are given in Table IV. In the same Table are given the mean values of Tl/m. It is obvious at once that at all temperatures $(H/m - bx)$ and Tl/m increase together and reach a maximum at or near the same duration of stimulus. The two quantities are plotted against one another in Fig. 6, when it is seen:

(*a*) that up to a certain limit of Tl/m, *i.e.* up to a certain duration of stimulus, $(H/m - bx)$ is directly proportional to Tl/m;

(*b*) that beyond this duration, *i.e.* for larger values of Tl/m, the curve bends upwards, the ratio of $(H/m - bx)$ to Tl/m increasing.

The same facts are shown by the results of July, Aug., Nov. and Dec.

Over the fairly wide range where $(H/m - bx)$ is proportional to Tl/m, the constant of the proportion, viz. $k = \dfrac{H/m - bx}{Tl/m}$, is practically the same for all temperatures, and has the value 1/5·5. The fact that k is independent of temperature suggests that it has some real physical significance, while the agreement found between this quantity and the constant, 1/6, in Tl/6, the expression for the potential energy, is striking evidence that, at any rate for the shorter durations of stimulus, the quantity $(H/m - bx)$ really does represent the potential energy developed

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[1] It will be seen that the values of H/Tl given in Table II for months other than May (July, Aug., Nov. and Dec.) are considerably higher, averaging (for zero duration of stimulus) 0·26. This lower value corresponds to Tl/6 = 0·64 H. It may be that at other times of year the "efficiency" is really lower; or it may be that the potential energy is really greater than Tl/6.

in the muscle. The expression Tl/6 for the potential energy of a stimulated muscle was only intended to apply to the case of a single shock or a very short stimulus, and seeing that (H/m − bx) is equal, or approximately equal, to the potential energy of the muscle, so expressed, in the shorter stimuli, it is natural to assume that in the longer stimuli

TABLE IV. H/m is the heat-production per gram of muscle, b is the final steady rate of heat-production in a prolonged stimulus, x the duration of stimulus, T the maximum tension developed, l the length of the muscle, and m its mass. The means given are the results of 13 experiments on fresh muscles made in May.

|		Duration Secs.							
		·01	·02	·05	·10	·20	·40	·80	1·20
0° C. b = 307	H/m − bx	213	221	236	254	281	317	355	359
	Tl/m	1170	1200	1290	1370	1490	1590	1660	1680
5° C. b = 525	H/m − bx	199	236	272	304	368	446	520	523
	Tl/m	1130	1260	1400	1550	1730	1860	1920	1930
10° C. b = 733	H/m − bx	197	234	286	324	399	491	555	—
	Tl/m	1035	1180	1400	1580	1730	1870	1910	—
15° C. b = 1450	H/m − bx	193	280	356	413	502	580	—	—
	Tl/m	1210	1710	1950	2160	2380	2400	—	—
20° C. b = 1910	H/m − bx	160	235	311	380	484	497	490	—
	Tl/m	1020	1410	1750	2050	2230	2280	2310	—
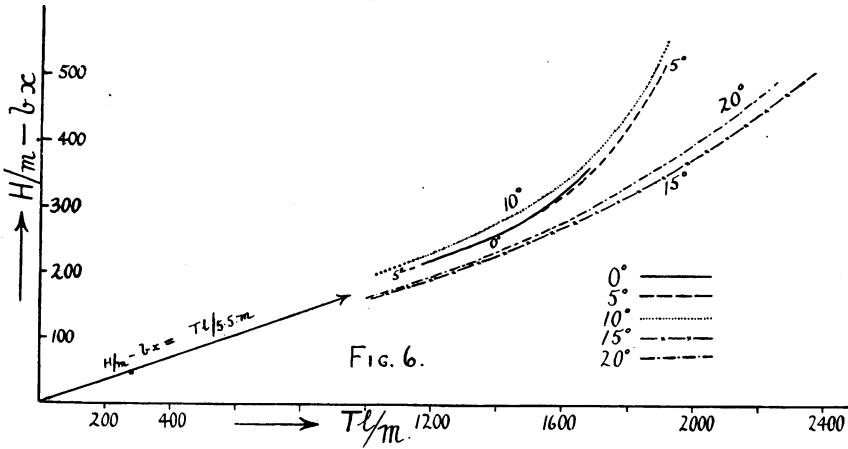
Fig. 6. Relation between (H/m − bx) and Tl/m. For description of symbols and discussion see text.

also the true measure of the potential energy set up is (H/m − bx). It is probable that in the longer stimuli the actual work which could be obtained from a muscle is less than (H/m − bx), because the viscous flow of the muscle under a prolonged tension may have degraded a considerable part of the potential energy into heat(10); nevertheless we may regard (H/m − bx) as representing either the actual potential energy

(as in the shorter stimuli), or as energy which has passed through the phase of mechanical potential energy before being degraded into heat by the viscous flow of the muscle under a prolonged contraction.

We may conclude therefore that the two separate functions of a muscle, the production of work, and the maintenance of a force, are reflected in two separate factors in the heat production. The total energy set free by a muscle in an isometric contraction is the sum of two separate quantities, (1) the energy appearing in, or passing through the phase of potential energy; and (2) an amount of energy proportional to the duration of the stimulus; and may be expressed in an equation,

$$H = bx + E$$

where H is the heat set free, x is the duration of the stimulus, b is a constant characteristic of the muscle, its temperature, etc., and E is the potential energy produced in it. In a short stimulus the energy appears almost entirely in the potential energy term, as mechanical energy ready to do work if required. In a long stimulus the energy is used almost entirely in maintaining the contraction.

This result bears upon our views of the nature of the chemical breakdown preceding and initiating the contraction. It has been argued [11] that since the energy of the breakdown of glucose into lactic acid is only some 16 p.c. of the heat given out by the muscle in liberating that lactic acid, the precursor of lactic acid in the muscle is not glucose, but something possessing considerably more chemical energy. It would seem however that the total energy liberated in a twitch is little, if at all, greater than the potential energy. The latter is probably provided by the action of lactic acid (the body B, discussed in Part 1 above) on some "active" structure or surface, and the loss of this potential energy in relaxation is presumably one source of the heat. Indeed we have shown [2] that a considerable proportion of the heat appears during the process of relaxation, in the case of a very short stimulus some 30 p.c. of it. Let us suppose that in a twitch the following processes occur in order:

(1) The permeability of the walls enclosing the "ready" store of lactic acid is increased by the shock, the lactic acid passes out, acts upon the "sensitive structure" of the muscle, liberating potential energy E and heat H_1.

(2) Carbohydrate breaks down to replace the lactic acid lost, with production of heat H_2.

(3) Relaxation sets in, the lactic acid is removed from the sensitive structure by some anaerobic chemical or physico-chemical process unknown, with production of heat H_3.

(4) Finally in the presence of oxygen the lactic acid is replaced in its previous position as carbohydrate (Meyerhof(5),(8)), about $\frac{1}{3}$ or $\frac{1}{4}$ of it however being lost in the process in supplying energy to "restore" the chemical condition of the muscle, and in giving out the "recovery heat-production"(12). According to this scheme the total heat given out in the initial as distinguished from the recovery phases is:

$$H = H_1 + H_2 + H_3$$

which is approximately equal to the potential energy E. The heat H_1 is liberated during the development of the mechanical response, the heat H_3 during its disappearance; while H_2, the heat derived from the reaction, carbohydrate $\rightarrow$ lactic acid, is liberated at some time unknown. If we adopt this scheme of the events happening in muscle we are relieved from the necessity of finding a lactic acid precursor other than carbohydrate, a chemical problem often and vainly attempted. We are reduced rather to finding a non-oxidative chemical or physico-chemical reaction capable of seizing on and "removing" lactic acid from the sensitive structures or surfaces of the muscle, and then of delivering up the lactic acid it has seized upon to the later and gradual processes of oxidative recovery. If we suppose that the bodies capable of combining with, and so of removing, the lactic acid, are limited in amount we can explain the existence of the "lactic acid maximum" as being due to the cessation of the reaction, carbohydrate $\rightarrow$ lactic acid, as soon as the products of the reaction begin to appear in a free form: and the slower relaxation of a muscle subjected to fatigue or the action of acid would then be due to the partial saturation of the bodies whose function it is to seize upon the lactic acid and so to reverse the process of contraction.

This view agrees largely with that of Meyerhof(14) who says: "Lactic acid is produced explosively at the 'verkürzungsorten': this releases a process possessing considerable free energy, whereby the elastic condition of the smallest fibrils is changed: the lactic acid is then removed by the attraction of the surrounding muscle-plasma, with an affinity at least as great as that of its original attraction to the fibrils." Meyerhof also looks for the energy liberated in contraction not in the energy of a built up precursor, but in that set free in the actions whereby lactic acid is attracted to and removed from the "sensitive" protein bodies of the muscle.

4. THE TENSION-TIME PRODUCTION OF MUSCLE.

It was shown above (Part 2) that once a steady state has been reached the total heat produced in any interval is proportional to the

force maintained multiplied by the time during which it is maintained. The hope of finding some simple expression for the mechanical response, proportional to the heat-production from the beginning of the stimulus and not merely after a steady state has been attained, led us to examine the properties of the "tension-time," a quantity which is defined as the area of the isometric tension-time curve, or mathematically as $\int Tdt$ where T is the tension developed and t the time. As a matter of fact, as is shown in Fig. 8, the "tension-time" is not exactly proportional to the heat-production; indeed the results of Part 3 would not be true if it were. The experimental investigation however of the properties of the tension-time has led to a striking simple relation.

It might at first appear that the tension-time is an artificial conception; as a matter of fact it is anything but artificial, and represents an important mechanical property of the muscle. Suppose that we have a large mass hanging at rest on a long vertical string; let us attach to it an inextensible horizontal string connected to a muscle, and stimulate the muscle. The momentum (mass × velocity) produced in the mass is equal to the tension-time produced by the muscle, and the faculty of a muscle for producing motion in heavy masses is determined therefore by its faculty for producing what we have here called "tension-time." This quantity can be determined experimentally in various ways, *e.g.* by allowing the muscle to accelerate a heavy mass, and measuring the momentum set up; the most accurate method however is the indirect one of making it record an isometric tension curve on a uniformly moving surface, and measuring the area of this curve. This method we have adopted throughout the present investigation, using either mechanical or photographic recording of the tension curves.

If we apply to the muscle a series of maximal stimuli starting from a single shock, increasing in duration up to two or three seconds, and returning down the series again to the single shock, we obtain a set of isometric tension-time curves whose areas can be measured up and recorded just as the heat-production in the experiments described above. There is no need here to give such a series of isometric curves, as they are similar to those recorded on p. 116 of our previous paper (2). If now the means of the two observations at any one duration be taken, in order to eliminate fatigue, we get the series of results which are recorded in Table V and shown graphically in Fig. 7. In order to make the results with different muscles comparable with one another it is necessary that the quantity determined as above should be independent of the dimensions of the muscle, and this we have secured by employing instead of the tension T the quantity Tl/m where l is the length and m the mass

of any portion of the muscle, this quantity being proportional to the tension developed per sq. cm. of cross-section of the muscle. The numbers in Table V and the curves in Fig. 7 have been given only up to 0·54 second duration of stimulus; in every experiment carried out (including

TABLE V. Tension-time production against duration of stimulus, for different temperatures. The tension has been expressed in terms of Tl/m (which is proportional to the tension per sq. cm. of cross-section), in order to make the results with different muscles comparable. [T is in grams-weight, l in cm., m in grams, and time in seconds.]

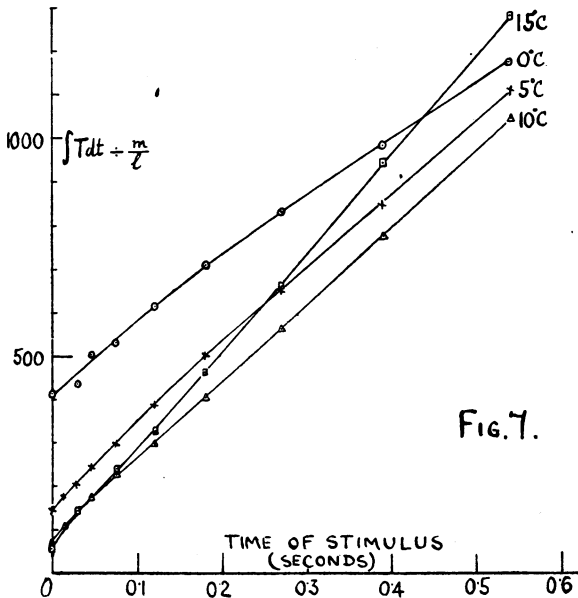|			Duration of stimulus								
Temp.	Month	Shock	0·015	0·030	0·045	0·075	0·12	0·18	0·27	0·39	0·54
0° C.	Oct.	418	409	425	500	525	598	695	815	945	1110
	Nov.	410	—	439	[512]	538	626	725	845	1009	1231
5° C.	Oct.	153	172	217	256	300	386	491	630	810	1100
	Nov.	139	175	193	231	295	387	513	670	870	1120
10° C.	Sept.	58	99	127	161	220	279	394	549	—	—
	Oct.	88	137	192	220	268	355	470	641	—	—
	Nov.	60	94	117	149	199	253	347	491	680	920
15° C.	Dec.	61	—	141	—	235	315	442	636	900	1230
	Dec.	61	—	153	—	246	340	481	693	980	1330

Fig. 7. Relation between "tension-time" (vertically) and duration of stimulus (horizontally). Note linearity of relation at all temperatures.

several with time of stimulus up to two or three seconds) the curves could not be distinguished from straight lines (especially at higher temperatures), and it seemed unnecessary to continue the curves further. Although the curve for each individual experiment approximates nearly

to a straight line there is not a very close agreement between the results of different experiments. This is due in part to the effect exercised by the condition of the muscle, but principally to the great effect of the initial tension, a factor the importance of which was not realised at the time these experiments were made (13). From Fig. 7 we see:

(a) that for a single shock the tension-time is very considerably increased by a fall of temperature; for long durations however the curves tend to cross, and more tension-time to be produced by the warmer muscle;

(b) that at all temperatures the relation between the tension-time and the duration of the stimulus is linear from the start.
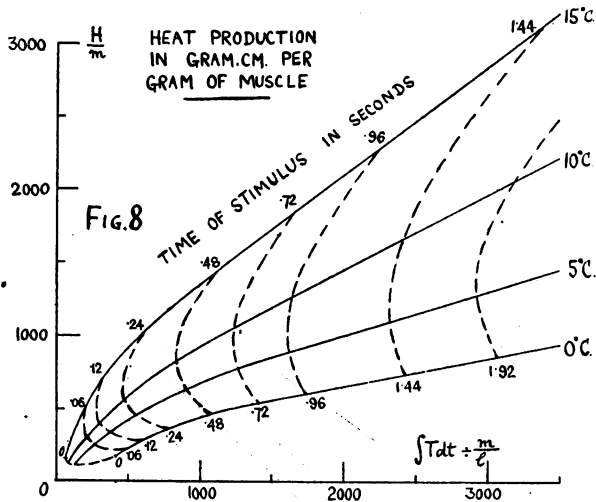

Fig. 8. Relation between heat and tension-time. Vertically, H/m in gram cm. per gram of muscle; horizontally, tension-time multiplied by length per gram of muscle. The full curves are for constant temperatures, the broken curves for constant duration of stimulus. The diagram shows the average results deduced from several experiments, made in Oct. and Dec.

The effect of temperature on the contraction resulting from a single shock is a combined consequence of the facts (i) that more energy is liberated by a single shock at a lower temperature and (ii) that a given quantity of energy causes, at a lower temperature, a more prolonged contraction. The opposite effect of temperature in the case of the longer stimulus is due to the fact that in this case far more energy is liberated at the higher temperature, and this more than compensates for the more rapid passing off of the effect of a given amount of it. The linearity of the relation shown in Fig. 7 is good, if empirical, evidence that the tension-time has some real physical (or physiological) significance in the economy of the muscle.

We will turn now to a short account of experiments in which simultaneous observations were made of the heat and of the tension-time produced by a muscle. The experiments were carried out in the usual manner, the heat H being measured in gram cm. of work per gram of muscle, and the tension-time in terms of $\int Tl \, dt/m$. The results are shown in Fig. 8, where we have plotted the two quantities concerned against one another (i) for constant temperature, and (ii) for constant duration of stimulus. For constant temperature and increasing duration of stimulus the relation between the heat and tension-time rapidly becomes linear, while for constant duration and increasing temperature the relation follows the curious broken curves shown in the figure. We are unable at present to draw any obvious deduction from these curves, but the striking linearity of the relation shown in Fig. 7 between tension-time and duration of stimulus suggests that the former has some real physiological significance, in which case its relation to the heat-production as given in Fig. 8 may be of value in some future investigation. In any case Fig. 8 shows in a convenient form the relation between the four quantities, heat, tension-time, duration of stimulus, and temperature, any two of these being determinable from the curves as soon as the other two are given.

Summary.

1. A single maximal shock produces considerably more heat at a lower temperature: a tetanic stimulus of about ·017 second duration produces practically the same heat at all temperatures; a longer stimulus produces far more heat at a higher temperature.

2. In a prolonged maximal contraction there is a sudden outburst of heat for the first moment of the stimulus, succeeding elements of the stimulus producing less and less effect until a steady state is reached in which heat is produced at a constant rate. In this final steady state the rate of heat-production has a temperature coefficient of the exponential type, increasing 2·8 times for a rise of 10° C.

3. For a single shock H/Tl has the same value for all temperatures, thus confirming the view that the tension developed in an isometric twitch is the best measure of the mechanical response. [H is heat-production, T is tension developed, l is length of muscle.] H/Tl increases as the stimulus is continued, becoming finally a linear function of the duration of the stimulus; in other words the heat-production becomes proportional to the force maintained. In this final steady state the rate of heat-production per unit of force maintained is largely increased by a rise of temperature, having an exponential temperature coefficient of 2·3 per 10° C.

4. In a contraction the heat produced is the sum of two factors, corresponding to the two functions of a muscle of maintaining a force and of doing work. This may be expressed by the formula $H = bx + E$, where E is the measure of the potential energy produced, x is the duration of the stimulus and b a constant characteristic of the muscle and its condition. This is the most general relation known between the mechanical and the thermal response.

5. The tension-time (the area of an isometric tension-time curve) is a linear function of the duration of the stimulus, from the first moment of the stimulus. For short durations it is less, for long durations it is greater at a higher temperature (cf. Fig. 8).

6. The heat produced per gram of muscle, per second of stimulus, in the final steady state of a prolonged isometric contraction, is given (p. 138) in absolute units of heat for a variety of temperatures.

7. The heat produced per cm. length of muscle, per gram wt. of tension maintained, per second of stimulus, in the final steady state, is given (p. 147) in absolute units. The results show a very low "efficiency" of the striated muscle in *maintaining a constant force*, especially at higher temperatures. On the other hand in a single twitch the "efficiency" in *producing potential energy*, as expressed by $\frac{1}{2}Tl/H$, is very high, approximately to unity.

8. The "efficiency" of the muscle in maintaining a constant force is increased by a fall of temperature, or by any other factor tending to increase the duration of the twitch resulting from a single shock. It is lowered by any factor increasing the quickness of the muscular response. These facts explain the high efficiency of the unstriated muscle in maintaining a constant force.

9. A physico-chemical mechanism is suggested to account for the manner in which the supply of energy is regulated in the muscle.

REFERENCES.

(1) A. V. Hill. This Journ. 47, p. 305. 1913.
(2) Hartree and A. V. Hill. Ibid. 54, p. 84. 1920.
(3) Hartree and A. V. Hill. Proc. Physiol. Soc. p. liv. This Journ. 54. 1920.
(4) A. V. Hill. This Journ. 46, p. 455. 1913.
(5) Meyerhof. Pflüger's Arch. 182, p. 275. 1920.
(6) Hartree and A. V. Hill. Phil Trans. B. 210, p. 153. 1920.
(7) Snyder. Amer. Journ. Physiol. 44, p. 424. 1917.
(8) Meyerhof. Pflüger's Arch. 185, p. 31. 1920.
(9) A. V. Hill. This Journ. 42, p. 22. 1911.
(10) Hartree and A. V. Hill. Phil. Trans. Roy. Soc. 210, p. 153. 1920.
(11) A. V. Hill. Ergbn. d. Physiol. 15, p. 372. 1916.
(12) A. V. Hill. This Journ. 46, p. 79. 1913.
(13) Doi. Ibid. 54, p. 222. 1920.
(14) Meyerhof. Naturwissenschaften, 35, p. 700. 1920.