THE POSITION OCCUPIED BY THE PRODUCTION OF HEAT, IN THE CHAIN OF PROCESSES CONSTITUTING A MUSCULAR CONTRACTION. BY A. V. HILL, B.A., *Fellow of Trinity College, Cambridge*[1].

(*From the Physiological Laboratory, Cambridge.*)

CONTENTS.

THE processes which occur in the response of a muscle to an electric excitation can be classed under three headings:—(a) those occurring *before*, (b) those occurring *during*, (c) those occurring *after*, the actual muscle twitch. It is possible, *a priori*, that the heat production should take place either,

(a) before, and in preparation for the mechanical response, or

(b) during, and in intimate connexion with it, or

(c) after, and in recovery from the effects of the twitch, and in preparation for the next.

For example, it is easy to suppose that (a) the heat is given out in some process whereby the tension of the muscle is suddenly increased, and that a twitch follows, consequent on this increase of tension. It may be, however, that (b) the heat is evolved in the actual process of

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[1] A large part of the work recorded in this paper was carried out during the tenure of the George Henry Lewes studentship.

doing work against a load. Finally it has often been suggested that the main body of the heat is (c) produced in a stage of "recovery" from the effects of an excitation: possibly the heat is liberated by the oxidation of products of activity, possibly by some chemical rebuilding of the unstable contractile molecules. The energy-changes, shown by the rise of temperature in an excited muscle, may occur in one, two, or even all of these stages. In any theory of contraction it is obviously necessary to know when the heat is evolved. The first Part of this paper deals with observations on the actual time at which the heat is set free, both in single twitches and prolonged contractions.

Much work has been done in connexion with the mechanical efficiency of a muscular contraction. In spite of the many observations, scarcely any clues have been gained as to the nature and position of the energy changes in the chain of processes constituting the intermediate mechanism of the muscle. It was my hope, when I started this investigation, that an exact consideration of the changes of mechanical efficiency under various conditions, together with an application of thermodynamical reasoning, might lead to some such clues. The second Part of this paper gives the experimental evidence which led to a somewhat unexpected development of this subject. It is important to compare with the heat liberated (H) not the *work done* (W) but the *maximum tension* set up (T). The mechanical "efficiency," W/H, varies with stimulus and load, but the ratio T/H remains constant. Various phenomena connected with this ratio, T/H, have been investigated.

Ordinary muscular movements are not twitches, but prolonged contractions of varying lengths. Both for this reason, and because of the bearing such observations have upon theories of muscular contraction, it is of interest to investigate the heat set free during complete tetanus. The degradation of energy necessary in order to keep up the tension for a given time varies according to the length of time during which the muscle has been contracted already, according to the state of fatigue, according to the temperature and several other factors. Experiments in this connexion are given in the third Part of the paper.

In Part IV is given the experimental evidence dealing with the changes of mechanical efficiency under variation of stimulus and load: there is also given a short mathematical proof that these changes can be deduced from the constancy of T/H, and the laws of mechanics.

PART I. THE TIME RELATIONS OF THE HEAT SET FREE
DURING MUSCULAR ACTIVITY.

In a previous paper[1] I have described the apparatus and methods used in determining the amount of heat set free in a muscular contraction. In the experiments given in this Part the instrument was used in two different forms :—

(A) As described in my previous paper, with the exception that the upper stimulating electrode lay above the thermo-electric junction.

(B) With the further modification that five thermo-electric junctions were introduced in series, as shown in Fig. 1.
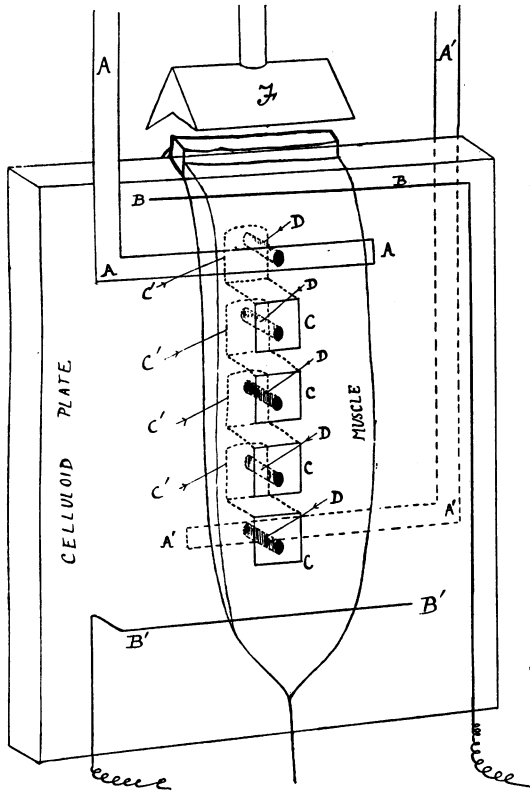

Fig. 1. *AAA, A'A'A'.* Copper terminals leading to coil. *BB, B'B'.* Upper and lower electrodes. *CCCC.* Copper plates on front side of celluloid. *C'C'C'C'.* Copper plates on back side of celluloid. *DDDDD.* Constantan plugs, forming thermo-electric junctions with copper plates. *F.* Clamp for holding muscle in position.

[1] A. V. Hill. This *Journal,* XL. p. 390. 1910.

In both cases a pair of muscles is used, either the two *semi-membranosi* or the two *sartorii* connected together by a piece of bone at their upper ends. The muscles rest astride of the celluloid plate, one being in contact with one set of junctions, the other with the opposite set. In either form of the instrument one of the pair is stimulated, the other is left unstimulated: thus the junction (or junctions) on one side of the celluloid plate is warmed, while the other is kept cool. Consequently a current goes round the copper coil connected to the copper terminals AA': and the Broca magnet system is twisted about a vertical axis. A spot of light is reflected from the mirror of the magnet system on to a scale, and when the muscle is stimulated this spot of light makes an excursion. The instrument used in its later form (B) has two advantages:—

(i) it is much more sensitive: there is five times the E.M.F. of the previous form for the same rise of temperature, and only a slight increase of resistance[1];

(ii) the junctions lie all along the muscle, and thus we obtain in a rough way the mean rise of temperature of the whole muscle: in the form (A) the rise of temperature is recorded at only one point.

The earlier form (A) has however one great advantage: the junction is so near the top of the muscle that no appreciable movement occurs over it when the muscle contracts. Thus differences of temperature along the muscle itself cause no error. In all the experiments in which the later form (B) of the instrument was employed, the muscle was kept stretched at a constant length and not allowed to contract: this error has not therefore been able to arise. The copper-constantan junctions are coated with celluloid or shellac varnish. In the more sensitive form, (B), of the instrument it is possible to use *sartorii* muscles: this is a great advantage, as the *sartorius* is a much longer and more uniform muscle than the *semi-membranosus*. With the earlier form, (A), it was impossible to use the *sartorius*: its heat capacity was so small that there was not enough heat to warm the junction sufficiently to obtain a reasonably large movement of the spot of light.

The object of moving the upper stimulating electrode above the top thermo-electric junction is as follows. The movements of the spot of light depend upon two factors:—

(i) the amount of heat produced;

(ii) the time relations of the heat production.

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[1] The resistance of each junction is about ·002 ohm: the resistance of the copper coil is about ·005 ohm. The instrument is therefore two or three times as sensitive.

We desire to find the actual time at which the heat is set free in muscular activity. We must therefore compare the movements of the spot of light, set up by the rise of temperature resulting from excitation of a normal muscle, with the movements caused by raising the temperature uniformly during a known period. If, for example, we wish to prove that in a muscle the heat is evolved uniformly for 1 sec., we must compare the movements of the spot of light when the muscle is excited with the movements caused by raising the temperature at a uniform rate for 1 sec., in a body of the same size and shape as the muscle, lying upon the junctions in the same way. This latter process was carried out as follows. The muscle, which had been used for the experiment, was killed while still in the instrument by over-excitation, fatigue, or lapse of time. It was then warmed either

(i) instantaneously, by passing an excessively strong induction shock through it; or

(ii) uniformly, for a known period, by "tetanising" it with excessively strong currents during that period.

The heat is produced in the dead muscle by the merely physical effects of the strong currents employed. For this purpose it is necessary to warm the muscle uniformly all over: hence,

(a) we must use a muscle of uniform cross-section: otherwise the rise of temperature will increase along the muscle as the cross-section decreases. I have therefore always used a *sartorius* when possible.

(b) the warming currents must pass uniformly down the whole of the muscle, at any rate through those parts which are close to the junctions. Hence it is necessary that the electrodes, which are used for warming as well as stimulating, should be beyond the upper and lower junctions respectively.

In this Part of the paper we are concerned with the time relations of the heat production, not with its actual or relative magnitude. We must observe therefore the time relations of the movements of the spot of light. The quantity observed, and used as a criterion, is the *time* after excitation at which the spot of light reaches its maximum displacement. This time can be taken, with considerable accuracy, by an observer standing behind the scale with a stop-watch. The great advantage of this time as a criterion is that it is an easily observed quantity which is independent of the *amount* of heat set free: whatever be the displacement of the spot of light caused by a heat production, instantaneous or of given duration but of variable magnitude, the "time to maximum displacement" is the same. In this respect the movements

of the spot of light are analogous to those of a pendulum: the period of oscillation of a pendulum of given length is independent of the actual magnitude of the oscillation. In form (A) of the instrument it is possible to use another time as a criterion: the spot of light returns to any given fraction of its maximum displacement in a time which is independent of the total heat set free. The fraction which I have usually taken is $\frac{1}{5}$: by doing so one evades the errors caused by the momentum of the magnet system swinging it back too far. In form (B) of the instrument the heat is lost so rapidly by conduction across the copper or constantan that momentum effects entirely mask the constancy of the "time to return to $\frac{1}{5}$." To prove the constancy of these times it is only necessary to refer to the following Table.

TABLE I.

Instrument A. Dead muscle warmed with single strong induction shocks.

Displacement of spot of light, in mm.	136	128	113	94	71	46	25	11
Time to maximum displacement, in secs.	6·7	6·9	6·9	6·9	6·9	6·9	6·8	6·9

Instrument B. Dead muscle warmed by tetanising for 1 sec.

Displacement of spot of light	392	293	283	252	163
Time to max. displacement	7·7	7·6	7·6	7·6	7·7

Instrument B. Dead muscle tetanised for ·08 sec.

Displacement of spot of light	99	79	64	52	38	24
Time to max. displacement	7·4	7·4	7·5	7·5	7·5	7·5

Instrument A. Dead muscle warmed by single induction shocks.

Displacement of spot of light	146	117	87	70	50	29
Time to return to $\frac{1}{5}$	28·6	29·5	29·2	29·2	29·6	29·3

N.B.—(i) It should be noted that these constant times are not in any way the periods of any free vibrations of the magnet system.

(ii) In order to obtain results comparable from time to time the spot of light should be brought on to the scale by twisting the quartz fibre, and not by the use of a powerful control magnet.

We now come to the main point of the method. If the heat production is prolonged the time taken by the spot of light to reach its maximum displacement is also prolonged. Let us suppose that for an instantaneous rise of temperature the "time to max. displacement" is 7·2 sec. using a muscle of given shape: this time can be observed, if necessary, when the muscle is dead. Then if the heat were liberated at a uniform rate for 2 sec. we should expect that the "time to max. displacement" would be about 8·2 sec. This can be shown experimentally, as is done in Table II. Thus if we observe in any live muscle that the

maximum displacement is reached t seconds later than it is for an instantaneous rise of temperature, we may conclude that the heat was given out for $2t$ seconds. See Table II.

TABLE II.

In these experiments dead muscles were warmed at a uniform rate for known times, by means of a tetanising current. For this purpose Mr Keith Lucas kindly lent me an apparatus, which has, on a uniformly rotating drum, two adjustable arms which can be made to open two knock-down keys at any required interval apart. One of these keys short-circuits the currents of the secondary coil: the other is placed in the primary circuit. The keys are closed in order, and the coil starts working. On opening the first key the induced currents are no longer short-circuited, but pass through the muscle: on opening the second key the primary circuit is broken. During the adjustable interval between the opening of the two keys the tetanising currents are passing through the muscle. In all cases the muscles were dead, and the apparatus was used in the form (B). Times are given in seconds. The "calculated times to max." were calculated as follows. The mean "time to max." for the shortest duration t_0 is taken as standard. Let us call it T. Then the calculated "time to max." for any other duration t is

$$\left[T + \frac{t - t_0}{2} \right] \text{ seconds.}$$

There is an exact concordance between "calculated" and "observed," especially for the shorter durations.

Exp. i.

Duration of heat production	0·08	1·0	2·0	4	7
Number of observations	28	5	6	7	6
Observed mean time to max.	6·95	7·46	7·8	8·84	10·52
Calculated time to max.	6·95	7·41	7·91	8·91	10·41

Exp. ii.

Duration of heat production	0·08	1·0	2	3	5	8
Number of observations	30	9	7	6	4	4
Observed mean time to max.	6·48	6·99	7·43	7·98	9·22	10·82
Calculated time to max.	6·48	6·94	7·44	7·94	9·44	10·44

Exp. iii.

Duration of heat production	0·05	1·0	2·0	4·0	7	10
Number of observations	30	5	6	4	3	4
Observed mean time to max.	6·77	7·26	7·87	8·92	10·6	12·05
Calculated time to max.	6·77	7·25	7·75	8·75	10·25	11·75

Here then, in this "time to maximum displacement," we have a criterion whereby we may determine the actual duration of any evolution of heat in a living muscle. By taking sufficient observations the results may be made very accurate.

All the preliminary observations were made in form (A) of the instrument: all later observations in form (B). As they confirm one

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another, I propose to give results obtained with both. Using the *semi-membranosus* in form (A), it is found that the "time to maximum displacement" for an instantaneous rise of temperature is always the same, if no control magnet is used. The mean of many readings is 7·7 sec. Similarly for the "time to return to $\frac{1}{6}$," where the mean of many readings is 29·2 sec. The observations made with form (A) of the instrument on living muscles are given in the next Table.

TABLE III.

Exp. i. Three normal muscles: observations with different strengths of stimuli. Left in O_2 several hours.

Heat produced	12	19	22	22	28	28	30		31
Time to max. displacement	8·0	7·6	7·6	7·6	8·0	7·6	7·7, 7·7, 7·5, 7·5		8·0
Heat produced	34	34	41	41	42	42	43	59	60	70
Time to max. displacement	7·6	7·7	7·5	7·3	7·3	7·6	7·6	7·2	7·8	7·7
Heat produced	72	64	70	80
Time to max. displacement	8·2	7·6	8·2	7·7

The mean value of all these "times to maximum" is 7·7 sec. The "probable mean error" of this result is ± ·051 sec.

Exp. ii. Fresh muscle: observations with different stimuli.

Heat produced	13	17	19	29·5	30	31	33	57
Time to max.	8·4	8·0	9·0	8·4	8·3	8·5	8·6	8·5

The mean value of these "times to max." is 8·46 sec. The "probable mean error" of the result is ± ·1 sec.

Exp. iii. Five normal muscles: observations with different strengths of stimuli. The heat productions greater than 37 were given by short tetani.

Heat produced	15	18	18	20·5	21	21	25	27
Time to return to $\frac{1}{6}$	31	30·2	30·4	30·2	30·4	30·4	29	31·4
Heat produced	28	28	28	29	30	30	30	30
Time to return to $\frac{1}{6}$	29·1	28·6	30·2	29·6	28·6	28	30·5	31·8
Heat produced	31	32	32	32·5	32·5	33	34	37
Time to return to $\frac{1}{6}$	31·2	28·5	30·5	30·2	30·4	30·6	29·9	30·7
Heat produced	72	93	109	117	130	133	169	213
Time to return to $\frac{1}{6}$	29·4	30·5	32·1	29·9	29·9	30·3	29·9	30·9
Heat produced	252	263	283
Time to return to $\frac{1}{6}$	30·3	29·9	30·3

The mean value of all these "times to return to $\frac{1}{6}$" is 30·2 sec. The "probable mean error" of this result is ± ·15 sec.

For an instantaneous rise of temperature the time to max. is 7·7 sec., and the time to return to $\frac{1}{6}$ is 29·2 sec.

From this Table it is seen that in the three muscles given in Exp. i the heat production is very rapid : the " time to max." is the same as for an instantaneous rise of temperature. In Exp. ii however the heat production takes 1·52 sec.: for the " time to max." is ·76 sec. greater than for an instantaneous rise. In Exp. iii again there is practically no heat set free after the initial outburst: if more than about 1 °/₀ of the total heat produced were liberated between the times 7·7 sec. and 30·2 sec. there would be more than 1 sec. difference between the actual and theoretical " time to return to $\frac{1}{6}$."

The subject obviously needed further investigation : all that had been shown hitherto was that in some muscles the heat was evolved very rapidly after excitation, while in others it might take 1·5 sec. The method was applied again, with the instrument in its more sensitive form (B). *Sartorii* muscles of *Rana temporaria* were always used. The experiments may be classed under two heads:

I.   Those referring to rapid twitches.
II.   Those referring to prolonged contractions.

Many observations, usually between 10 and 20, were taken on each occasion. It is impossible here to give every observation, so I have contented myself with giving the " probable[1] mean error " of each result. The mean of 20 readings is subject to only a very small error, and the degree to which any result may be trusted is shown by the small value of the probable mean error tabulated with it.

In the Tables given below times are in minutes, measured from the moment when the muscles were placed in the instrument: the " mean time to max.," the probable mean error of the result, and the duration of the heat production are given in seconds. The duration of the heat production is taken as twice the difference between the numbers.

(i)   The " time to max." observed.
(ii)   The " time to max.," t_0, for an instantaneous rise of temperature of the same muscle when dead.

It involves the assumption that the heat production occurs at a uniform rate, so long as it lasts. Probably, however, the rate of heat production in a twitch would start at a high value and fall off gradually

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[1] The probable mean error is calculated as follows. If t_1, $t_2...t_n$ be n readings of the " time to maximum displacement," the "mean time to max." is $y = \dfrac{t_1 + t_2 + ...t_n}{n}$, and the probable mean error of this result is $\pm \sqrt{\dfrac{(y - t_1)^2 + (y - t_2)^2 + ... + (y - t_n)^2}{n\,(n-1)}}$.

to zero, following some such equation as $\dfrac{dH}{dt} = \lambda e^{-kt}$; where H is the total heat set free, λ and k are certain constants.

In this case it can be shown[1] that the "time to max." is $(t_0 + 1/k)$: so that the duration obtained by the above method is $2/k$. This represents the period taken for about 86·5 % of the heat to be evolved. In any case, under whatever laws the heat is given off, the "duration" given in the Tables below is a valid measure of the degree to which the heat production is prolonged.

The columns marked "dead" refer to the observations made on an artificial instantaneous rise of temperature in the muscle, when dead.

From the experiments given in Table IV we may conclude:

(*a*)   Exps. i, ii, iii show that in a muscle left long enough in O_2 the heat production of a single twitch may become so rapid as to be practically instantaneous.

(*b*)   Exps. i to v show that, when a muscle is left in O_2, the heat production of a single twitch gradually becomes more rapid.   In Exp. i

TABLE IV.   *Experiments referring to rapid twitches.*

The effects of O_2, or want of O_2, on the duration of the heat production.

Exp. i.   Fresh muscle in O_2.   Each observation a tetanus of ·07 sec.

Time ...	90	100	200	Dead
Mean time to max.	7·30	7·38	7·13	7·11
Number of observations ...	9	26	20	15
Prob. mean error	± ·03	± ·034	± ·031	± ·045
Duration of heat production	·38	·54	·04	—

Exp. ii.   Each observation ·07 sec. tetanus.   Muscle in O_2.

Time	50	80	180	190	200	Dead
Mean time to max.	7·14	7·15	6·97	*	6·86	6·86
Number of observations	20	11	31	—	9	25
Prob. mean error	± ·036	± ·056	± ·037	—	± ·06	± ·023
Duration of H.P.	·56	·58	·22	—	0	—

* 100 shocks given at intervals of 2 sec.

[1] If t_0 be the "time to max." for instantaneous rise of temperature, and if H be the total heat evolved up to any time t, following any law whatever $H = f(t)$, then it may be shown from the results of Table II that the "time to max." will be very nearly

$$y = \frac{\displaystyle\int_{t=0}^{t=\infty} t\,dH}{\displaystyle\int_{t=0}^{t=\infty} dH}.$$

EXP. iii. Muscle left 15 hours in Ringer: then put in the instrument in *hydrogen*.

Time	90	110	155	180	190	267
Time to max.	7·06	7·16	7·13	*	7·20	6·92
Number of observations	20	20	21	—	13	30
Prob. mean error ...	± ·059	± ·032	± ·045	—	± ·036	± ·032
Duration of H.P. ...	1·12	1·32	1·26	—	1·40	·84
Time	310	375	385	435	490	Dead
Time to max.	6·90	6·83	6·84	6·79	6·82	6·50
Number of observations	15	21	10	12	13	33
Prob. mean error ... ,	± ·032	± ·028	± ·027	± ·030	± ·047	± ·026
Duration of H.P. ...	·80	·66	·68	·58	·64	—

* O_2 was admitted.

EXP. iv. Muscle left 15 hours in Ringer: in the instrument in air.

Time	165	195	255	270	315	330	360	Dead
Time to max.	7·05	*	7·02	6·95	6·95	†	6·96	6·95
Number of observations	16	—	14	18	21	—	20	28
Prob. mean error	± ·029	—	± ·042	± ·033	± ·043	—	± ·042	± ·019
Duration of H.P.	·20	—	·14	0	0	—	·02	—

* O_2 was admitted. † 20 sec. tetanus and 1 min. tetanus.

EXP. v. Muscle, after 27 hours in Ringer, and 13 in the instrument in *hydrogen*.

Time	780	790	800	820	840	850	935	1085	Dead
Time to max.	7·0	7·18	7·30	7·38	7·28	*	7·25	7·17	7·01
No. of observations	10	10	10	20	20	—	42	15	10
Prob. mean error	± ·07	± ·05	± ·07	± ·037	± ·031	—	± ·031	± ·033	± ·046
Duration of H.P.	0	·34	·58	·74	·54	—	·48	·32	—

* O_2 was admitted.

EXPS. vi, vii, viii and ix. Muscles in O_2.

Time	60	Dead	60	Dead	80	Dead	55	Dead
Mean time to max.	7·25	6·47	8·40	7·26	7·21	6·49	8·40	7·47
No. of observations	29	11	24	19	19	18	15	17
Prob. mean error	± ·04	± ·05	± ·03	± ·05	± ·05	± ·03	± ·045	± ·025
Duration of H.P.	1·56	—	2·28	—	1·44	—	1·86	—

EXP. x. Muscle in O_2.

Time	60	80	220	Dead
Mean time to max.	6·85	*	7·05	?
No. of observations	45	—	17	—
Prob. mean error ...	± ·027	—	± ·036	—
Duration of H.P. ...	x	—	$x + ·4$	—

* N_2 admitted.

the duration of the H.P. falls from ·54 sec. to 0: in Exp. ii from ·58 sec. to 0: in Exp. iii from 1·4 sec. to ·6 sec.: in Exp. iv from ·2 sec. to 0: in Exp. v from ·54 sec. to ·32 sec.

(c) Exps. iii, v, x show that when a muscle is left in hydrogen, or an atmosphere free of O_2, the heat production gradually becomes more prolonged: especially is this the case when the small amount of O_2 already in the muscle is used up by exercise (see in particular Exp. v). In Exp. iii the duration of the H.P. increases from 1·12 to 1·26 sec.: in Exp. v from 0 to ·74 sec.: in Exp. x by ·4 sec.

(d) Exp. iii shows a muscle in which five hours in O_2 only reduced the duration of the H.P. to about ·6 sec.

(e) Exps. vi to ix show muscles in which one hour in O_2 has reduced the duration of the H.P. no more than to 1·56 sec., 2·28 sec., 1·44 sec., and 1·86 sec. respectively.

The duration of the heat production of a single twitch is therefore a variable quantity. It may sometimes be reduced to a very small value by the presence of O_2: it may be increased by the absence of O_2, coupled with moderate amounts of exercise. The evolution of heat may, on the one hand, be practically instantaneous: it may, on the other hand, last as long as 2 sec., *i.e.* from four to ten times as long as the contraction itself.

We now come to a consideration of the duration of the evolution of heat in prolonged contractions. During a constant tetanus the rate of heat production is by no means constant, but falls off very rapidly at first. Curves connecting the total heat set free with the duration of the constant tetanus are given in Part III of this paper. (See Figs. 5 and 6, p. 29.) We must assume these results, in order to proceed. Using the formula given above (footnote p. 10), and supposing that in a tetanus every element of heat is set free *immediately after* the stimulus which liberated it, we can deduce the following approximate results. Let t_0 be the "time to max." for an instantaneous rise of temperature: then we shall have, for a living muscle,

Duration of tetanus in secs.	·25	·5	1·0	2·0	3	4	5	6	8
Time to max. = t_0 +		·10	·18	·37	·82	1·3	1·79	2·28	2·78	3·78

If we find that in the actual tetanus of a muscle the "time to max." is greater than

t_0 + (the number given in the second row of the Table),

then we shall conclude that the amount of heat set free by each element of excitation was not liberated immediately, but took a certain finite time for its evolution.

In Table V the "calculated least time to max," is the "time to max." that would have been observed, had each element of heat been given out immediately after the element of excitation that caused its liberation. The numbers marked "prolongation of H.P." are twice the difference between the observed "time to max." and the "calculated least time." They represent roughly, but in as valid a way as we can expect in our present stage of knowledge, the average degree to which the heat production is prolonged.

TABLE V. *Duration of heat production in prolonged contractions.*

EXP. i. Muscle in O_2. Mean time to max. for instantaneous rise of temperature $=6\cdot73$ sec. Time in minutes after putting in the instrument.

Time	90	115	182	192	202
Duration of tetanus	2 sec.	1 sec.	1 sec.	2 sec.	2 sec.
Number of observations	14	10	10	7	15
Mean time to max.	7·88	7·53	7·55	8·00	8·07
Calculated least time to max.	7·55	7·10	7·10	7·55	7·55
Prolongation of H.P.	·66	·84	·90	·90	1·04

EXP. ii. Muscle in O_2. Mean time to max. for instantaneous rise $=7\cdot14$ sec.

Duration of tetanus	1 sec.	2 sec.	3 sec.	3 sec.
Number of observations	15	11	7	7
Mean time to max.	7·93	8·38	8·86	9·39
Calculated least time to max.	7·51	7·96	8·44	8·44
Prolongation of H.P.	·84	·84	·84	1·90

EXP. iii. Muscle left 14 hours in O_2-free Ringer: put in instrument in H_2. Ten preliminary stimulations. Mean time to max. for instantaneous rise $=7\cdot14$ sec. Observations are of 1 sec. tetanus. Consecutive observations.

Observations	1 to 7	8 to 14	15 to 21	22 to 29	*	30 to 41
Mean time to max.	7·60	7·93	8·14	8·16	—	7·89
Calculated least time to max.	7·51	7·51	7·51	7·51	—	7·51
Prolongation of H.P.	·18	·84	1·26	1·30	—	·76

* O_2 put on. Next observation after 45 min.

EXP. iv. Muscle 1 hour in O_2. Mean time to max. $=6\cdot97$ sec. for instantaneous rise.

Duration of tetanus	·1	·2	·5	1·0	2·0	4	4	1	·5	1
Number of observations	12	3	8	3	2	1	1	1	5	2
Time to max. ...	7·47	7·53	7·60	7·87	8·5	9·2	9·3	8·0	7·68	8·0
Calcd. least time to max.	7·01	7·09	7·15	7·34	7·79	8·27	8·27	7·34	7·15	7·34
Prolongation of H.P.	·92	·88	·90	1·06	1·42	1·86	2·06	1·32	1·06	1·32

Duration of tetanus	2	4	2	1	·3	·2	·1	·2	·4	·8
Number of observations	1	1	1	1	2	1	1	1	1	1
Time to max. ...	8·5	9·2	8·5	7·9	7·7	7·5	7·4	7·4	7·7	7·8
Calcd. least time to max.	7·79	8·27	7·79	7·34	7·09	7·05	7·01	7·05	7·12	7·25
Prolongation of H.P.	1·42	1·86	1·42	1·12	1·21	·90	·78	·70	1·16	1·10

TABLE V (*continued*).

EXP. v. Left in H_2. 1 sec. tetanus.

Time	...	...	45	95	160	190
Time to max.		...	7·31	7·69	7·88	7·90
Number of observations			7	8	8	5

The heat production had its duration prolonged 1·18 sec., by 145 minutes in H_2.

EXP. vi. Muscle in O_2. Time to max. for instantaneous rise = 6·50 sec.

Duration of tetanus	...	·08	·30	1·0	2·0	4·0
Number of observations	...	13	12	10	12	7
Mean time to max.	...	6·82	6·89	7·20	7·61	8·49
Calculated least time to max.		6·50	6·59	6·87	7·32	8·28
Prolongation of H.P.	...	·64	·60	·66	·58	·42

EXP. vii. Muscle in air. 1 sec. tetanus. Time to max. for instantaneous rise = 6·62 sec.

        (i) After 1½ hours in air, "prolongation of H.P." = 1·84 sec.
        (ii) After 1½ hours more in O_2, ditto   = 2·98 sec.

From Table V we may conclude :

(*a*) In a tetanus the heat is never given out immediately on excitation. The element of heat liberated by any element of excitation is not completely evolved until a time from ·5 to 2 sec. after that element of excitation. In other words the H.P. lags behind the excitation causing it.

(*b*) Except in one exp. (Exp. iii) there is no direct evidence that O_2 shortens the duration of the H.P. in a tetanus : it is difficult to observe this, because the excitations necessary for the experiment gradually prolong the H.P. There is, however, fairly satisfactory evidence that the prolongation of the H.P. increases more rapidly in H_2 than in O_2.

Summary of Part I.

The problem of when the heat is evolved in muscular activity is one of fundamental importance, but unfortunately of considerable complexity. The apparatus used in the experiments given above can probably be considerably improved for the purposes of a further investigation. It should be possible, *e.g.*, to work with a capillary electrometer instead of a Broca magnet-system. However, until further work can be done, we may safely lay down certain general observations on the subject.

(1) The heat production of a single twitch usually occurs very rapidly—is complete in 0·1 sec.—in muscles left several hours in O_2.

(2) The heat production can be prolonged by leaving the muscle long in an atmosphere free of O_2.

(3) The heat production of a twitch may occupy as long as 2 sec.: much longer than the period covered by the mechanical effects of the twitch.

(4) In a tetanus the evolution of heat usually lags behind the excitation. It may be roughly 2·5 sec. behind, but generally it is, in a frog's *sartorius*, about 0·8 sec. behind. Each element of excitation causes a corresponding element of heat production, which is not complete till a moment from ·5 to 2·5 sec. after that element of excitation occurred.

These phenomena, incomplete as they are at present, seem to me to be of fundamental interest: they have bearings both upon general physiology and upon our conception of the nature of the muscular machine. A more general consideration of them is given later in the General Summary.

PART II. THE CONSTANCY OF THE RATIO BETWEEN THE HEAT PRODUCED AND THE INCREASE OF TENSION, IN A MUSCLE EXCITED ISOMETRICALLY.

It is well known that there is no simple relation between the work done in a muscle twitch and the heat set free. In other words, the "efficiency" of the muscular machine varies with (*a*) the load, (*b*) the number of fibres excited, (*c*) the strength of excitation of each fibre. The absence of any simple relation between work and heat, together with the considerations given in a later part of this paper[1], led me to the following series of experiments. These have shown that there is a direct proportion between the maximum increase of tension (T) set up during the activity of an isometric twitch, and the heat (H) evolved in the process; in other words T/H is constant, whatever be the initial tension, the number of fibres excited, or the strength of excitation of each fibre. This fact must be of fundamental importance in our theories of how, in the muscle, chemical energy is transformed into work.

Method. The muscles were situated in contact with the thermo-electric junctions in the usual fashion, in the muscle chamber[2] full of damp oxygen. The lower ends of the muscles were tied to silk threads, which passed through small holes in the base of the instrument and were attached to the lever used for measuring the tension. This lever stood on a shelf below the table, and recorded on a smoked drum. The

[1] Pp. 38, 39.

[2] The instrument was, for the rest of the paper, used in its earlier form A: see p. 3.

lever is shown in Fig. 2 : the figure explains itself. It was necessary for several purposes that the lever should be capable of being adjusted very delicately in a vertical direction. For example, such an adjustment makes it possible to vary the initial tension on the resting muscle with ease and accuracy. The lever was made for this purpose: it can be screwed up and down on a vertical brass rod, and can have its vertical displacement read on a scale. The spring can be fixed in any of the holes shown in the figure : thus the sensitivity of the instrument can be varied at will, for if the spring is moved to two . new holes further to the left, then the same increase of tension causes a greater movement of the lever. The muscle is attached to the string at X, which is so close to the axis that no appreciable short-ening of the muscle can occur. The instrument is calibrated by turning it upside down and hanging weights on it. Stimulation was by single induction shocks, or short tetani, and was carried out by the use of Mr Keith Lucas' apparatus described above (p. 7).
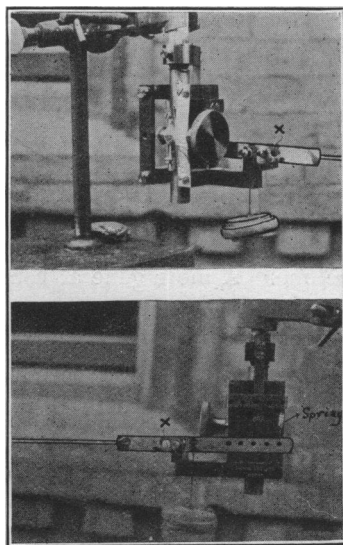

Fig. 2. The Tension Lever.

In warm weather the apparatus gave constant results for only very short times: since it is necessary in these comparative experiments to secure constancy as long as possible, I have had made [1] a water jacket, constructed of two concentric brass cylinders with a spiral of lead tubing between them [2]. Water is allowed to run by a siphon arrangement, through this lead tubing, whereby the temperature of the inside of the jacket is kept constant at a low value, within a few fractions of a degree. A hole is bored in front, to let in the light from a Nernst lamp.

Results. In the Tables below are given experiments demonstrating the constancy of T/H for variations of the three factors (i) initial

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[1] By the Cambridge Scientific Instrument Co., to whom, and to Mr Harper in particular, my thanks are due for the admirable way in which they have made the apparatus and carried out the alterations necessary for this research.

[2] The rest of the space between the cylinders is filled with water.

tension, (ii) number of fibres excited, (iii) degree of excitation of each fibre. In considering the constancy of T/H we must not expect a physical or mathematical accuracy : we must bear in mind that even if T/H may vary occasionally by as much as 10%, the mechanical efficiency W/H often varies as much as 700% for the same conditions of loading. Errors must inevitably be introduced because all these observations are made on a tissue in a changing state, and the changes are not always gradual, but sometimes occur abruptly. A long series of experiments has led me to believe that under all variations of the three factors T/H is constant, at any rate to a first approximation. A few of these experiments are given in the Tables below.

TABLE VI. *Variation of stimulus, which is a single induced shock. Constant initial tension.*

There is every reason to believe that variation of the strength of a single induced shock simply varies the *number* of fibres excited.

H = heat produced, measured in units of the galvanometer scale.

T = max. increase of tension set up, in gr. wt.

EXP. i. Temperature $5\cdot5°$ C. ($\pm0\cdot3°$ C.). Three hours after dissection. In O_2 Constant initial tension = 10·5 gr. wt. Observations in order of time.

Coil at (in cm.)	13·5	12	11	8	11·5	13	14	12·6	11·8	8·5
H	26	40·5	49	63	43·5	23	6	26·5	35	53
T	12	16·5	20·5	24·5	17·5	11·5	2·5	12·5	14·5	20
T/H	·46	·41	·42	·39	·40	·49	·41	·47	·42	·38

EXP. ii.

Coil at	16	13	15	16	13·5	7
H	20·5	42	30	22·5	34·5	47
T	12	23	18·5	12	18·5	24
T/H	·58	·55	·62	·53	·53	·51

EXP. iii. Temperature = 6·2° C. Three hours after dissection. Initial tension = 3 gr.

Coil at	20	24	22	12	18	23	18	10
H	24	10	19·5	30	23	13	22	32
T/H	·54	·53	·54	·57	·58	·52	·56	·52

[With regard to variation of stimulus the weak point of the heat-measuring instrument should be noted. The junction is at only one part of the muscle, the top end. Sub-maximal stimuli are apt to cause contraction of one part of the muscle and not of another, in which case the rise of temperature at one point is not a fair estimate of the total heat produced all over the muscle. Consequently, in some muscles, no constancy whatever can be obtained for T/H, for variation of the single shock: in these muscles T/H shows perfectly irregular changes as we change the strength of the stimulus. In only about half the muscles tested have I obtained the degree of constancy of T/H shown in the above Table. Usually if a muscle gives irregular results it can be made to give regular ones, by keeping it in the instrument for some time. The muscles have in all cases been treated with Ringer's solution, and it is known that this solution changes the excitability of muscles. Consequently irregular results are obtained, until the tissue has become accommodated all over to the new fluids bathing it.]

TABLE VII. *Muscle excited by a tetanus of very short duration. Variation of the period during which the muscle was excited. Constant initial tension.*

Duration of tetanus in seconds.

Coil giving about 42 shocks per sec.

Exp. i.

Duration of tetanus	·016	·031	·062
H	30	52·5	70
T/H	·80	·80	·79

Exp. ii.

Duration of tetanus	·0039	·0078	·016	·031	·039
H	12	21	28	33·5	39
T/H	2·52	2·70	2·47	2·50	2·38

Exp. iii.

Duration of tetanus	·008	·023	·031	·039	·078	·117
H	18·5	21	32	44	53	55
T/H	1·3	1·14	1·2	1·0	1·0	1·1

Exp. iv.

Duration of tetanus	·0039	·0156	·0234	·0390	·0078	·0156	·055	·07	·09
H	18	22·5	27	32	14·5	22	28	33	33
T/H	1·85	1·9	1·67	1·82	1·72	1·77	1·93	1·73	1·87

TABLE VIII. *Variation of initial tension. Constant stimulus.*

Initial tension in gr. wt.

Exp. i. Temperature 18° C.: tetanised ·05 sec.

Initial tension	3	18	33
H	34	32	24
T/H	1·46	1·45	1·48

Exp. ii. Tetanised ·055 sec.

Initial tension	5	11	26	30
H	29·5	26	21·5	24
T/H	2·34	2·54	2·51	2·3

Exp. iii. Temperature = 5·7° C. Single induction shocks.

Initial tension	45	5·5	45	12·5	20	36	3·5	20·5	12·5
H	65	51	68	60	61	68	56	67	56
T/H	·53	·57	·51	·56	·57	·49	·45	·49	·50

It is noticeable that there is a sudden fall of T/H between the 5th and 6th observations: but that both before and after this fall T/H is constant. Possibly a piece of the muscle had broken free, and although it still gave out heat it no longer aided in increasing the tension. These abrupt changes in T/H are not uncommon.

Exp. iv.

Initial tension	2	8·5	22	36	48	22	11	30
H	55	61	66	68	66	62	63	66
T/H	·83	·93	·87	·73	·68	·85	·85	·79

The results of Tables VI, VII, VIII may be expressed as follows:

(1)   Table VI shows that when a muscle is excited isometrically, at a constant initial tension, by a single stimulus of variable magnitude, the increase of tension is always proportional to the amount of heat evolved, whatever the strength of the stimulus.

(2)   Table VII treats of the effect of stimulating with a short tetanus, of length from ·1 to ·01 sec. The muscle, in these cases, receives in rapid succession from one to five shocks. However many shocks the muscle receives in a time not greater than ·1 sec., the increase of tension is always proportional to the amount of heat evolved.

(3)   Table VIII shows that when a muscle is excited by a constant stimulus, whether a single shock or a short tetanus, the increase of tension is exactly proportional to the heat evolved, whatever be the initial tension on the muscle.

We may now consider the bearing of these results.

1.   It is very probable that increasing the strength of a stimulus increases simply the *number* of fibres which react to that stimulus, and not the strength with which the individual fibre contracts. If this is so, Table III shows that however many fibres contract T/H is constant for the whole muscle, *and therefore T/H is the same for each individual fibre.*

Thus, at any given moment, the mechanism connecting the evolution of heat with the increase of tension is the same in every fibre.

2.   Stimuli may be " summed," and " summation of stimuli " implies that it is possible to increase the force of contraction of each single fibre in the muscle. Table IV then shows that *the increase of tension produced in a fibre during activity is exactly proportional to the quantity of heat evolved, however strongly that fibre may contract.*

3.   Increasing the initial tension on the whole muscle increases the tension and length of each fibre. Thus, during activity, *whatever be the initial resting tension and length of a fibre, that fibre acquires an increase of tension exactly proportional to the quantity of heat produced by it.*

These phenomena are of interest, and will be referred to again in a general discussion at the end of this paper.

We have considered so far the constancy of T/H under variation of the external conditions affecting a muscle, viz. stimulus and load.

We must now turn to a consideration of the effects of altering the internal conditions of the muscle itself, of varying the physical and chemical nature of the medium in which the muscular machine is working.

A. V. HILL.

(i) *The effect of time on a muscle in O_2.*

The main effect of time is a gradual decrease of the ratio T/H. This is best seen in the Table below.

TABLE IX.

Exp. i. Temperature $= 16 \cdot 5^\circ$ C. In O_2. Time in minutes.

Time since dissection			67	72	77	87	97	107	134	165
Coil at (in cm.)	...		10·5	10·5	10·5	10·0	9·5	9·2	8·5	8
H	...	...	51	50	49	49	45	45	44	45
T/H	...	...	1·24	1·26	1·24	1·18	1·25	1·23	1·19	1·05
Time since dissection			181	238	300	390	468	555	555	
Coil at (in cm.)	...		8	7·8	7·6	7·6	6·8	7	4	
H	...	...	43	41	37	31	30	23	22	
T/H	...	...	·99	·96	·89	·90	·87	·80	·87	

Exp. ii. Temperature $= 16 \cdot 5^\circ$ C. In O_2.

Time since dissection			80	143	143	200	270	440
Coil at	...	...	15	15	12	10·5	10	8·5
H ...	...	...	46	35	45	44	45	17·5
T/H	...	...	1·03	·89	·90	·83	·78	·57

Exp. iii. (a)   Temperature $= 9 \cdot 2^\circ$ C.   Time since dissection 100 minutes.   Coil at 13.
$H = 46$. $T/H = 1 \cdot 34$.

(b)   Same muscle kept for 60 minutes at $4 \cdot 3^\circ$ C.

(c)   Same muscle at $10 \cdot 0^\circ$ C.   Time since dissection 180 minutes.   Coil at 13.
$H = 43$. $T/H = 1 \cdot 08$.

This is a particularly good experiment, because the excitability has not fallen off appreciably between the observations: for the same shock produces approximately the same evolution of heat. The rise of temperature from $9 \cdot 2^\circ$ to $10 \cdot 0^\circ$ C. cannot explain the fall of T/H, because *ceteris paribus* a rise of temperature causes a rise of T/H.

Each value of T/H in this Table is the mean of several observations.

It is seen from Table IX and Fig. 3 that T/H falls off as time goes on. The fall is rapid about 2·5 hours after dissection, and after 4·5 hours the ratio falls off only very slowly. There is one possible source of error in these experiments. The excitability falls off very rapidly at higher temperatures, so that to obtain an approximately equal heat production we have to increase the shock: we must never increase this to an extent which is liable to warm the muscle or to produce contracture in some fibres. In Exp. iii however the excitability has been left unchanged, although 80 minutes have elapsed. Nevertheless T/H has fallen off as much as 19 %. Thus, even when the excitability of a muscle is maintained, the ratio T/H falls off very

.considerably as time goes on, both at high and low temperatures. Presumably this must be due to the absence of the blood stream, which either provides some chemical substance (other than O_2 which here is provided), or removes the products of activity.
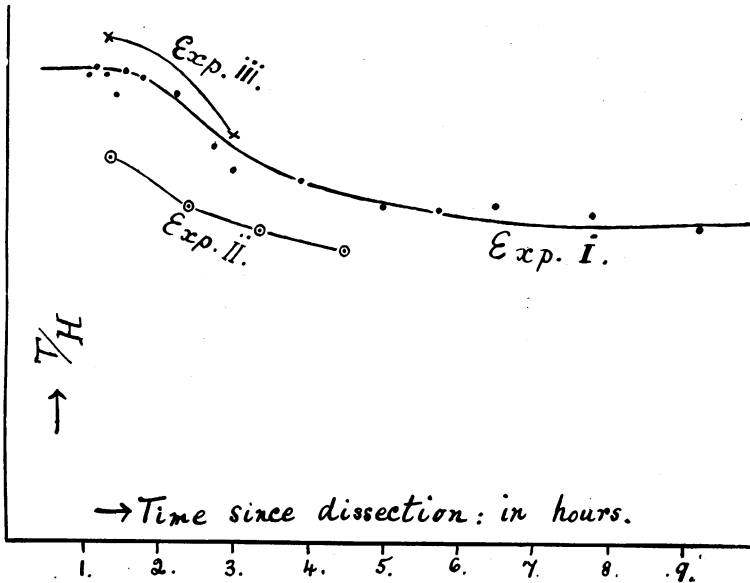

Fig. 3. To show decrease of T/H with time.

(ii) *The effects of fatigue.*

From experiments made in this connexion no very general conclusions can, at present, be drawn. In a perfectly fresh muscle T/H is, at first, largely reduced by a period of activity : it then remains, in spite of further fatigue, at a constant value until the muscle finally collapses. *Never have I observed any single case in which T/H has been increased by fatigue.* It is true that in a tetanus the same tension is kept up by a less heat production when the muscle has been subjected to previous excitation[1]. It is most necessary however to remember that we cannot apply results direct from the activity of a twitch to the activity of a tetanus : many mistakes have been made by doing so. For single twitches the increase of tension falls off under fatigue more rapidly than the heat produced. The final collapse of the muscle is possibly due to the sudden exhaustion of the supply of O_2 dissolved in it : for the

[1] See below p. 30, Table XII.

collapse takes place much earlier when the muscle is bathed in N_2. When parts of the muscle are almost dead, as seems to be the case in this state of final collapse, we can no longer trust an instrument which records the rise of temperature at only one point of the muscle. For this reason I have not been able, as yet, to give valid experiments to trace the effect of a high degree of fatigue upon the ratio T/H. I hope to do so later with the instrument in its form (B)[1], when it should be possible to give a fuller description of the effects of fatigue. At present one can say only that in a single twitch moderate degrees of fatigue generally lower, and never raise, the value of the ratio between increase of tension and heat set free.

We must beware of applying this statement to the effects of mild degrees of fatigue upon voluntary movements. Voluntary movements are not mere twitches : they are complexes of muscular contractions of many varied durations, produced by excitations of varying lengths sent out from the central nervous system. We cannot, without long and careful consideration, draw general conclusions from experiments such as these, as to the effects of fatigue upon the "efficiency" of voluntary movements. The efficiency (= work done ÷ total energy lost) depends upon two factors :

    (i)   the ratio T/H of a twitch,

    (ii) the ratio T/H in a tetanus, or prolonged contraction.

With sufficient knowledge of the effects of fatigue upon these two factors, for the case of every muscle involved in a given voluntary movement, it should be possible to predict the effects of fatigue upon the whole voluntary movement. We must remember that every muscle of any animal has different properties from the rest: some work more efficiently for rapid movements, some for slow. To say, as some text-books do, that because a frog's muscle evolves less heat in proportion to the height of contraction during a tetanus when it is fatigued, that therefore the voluntary movements of a man running are carried out more efficiently during fatigue, is absolutely inadequate and misleading. The whole problem is far more complex than such a statement would imply, and no general rules can at present be laid down.

(iii) *The influence of temperature.*

A rise of temperature increases very largely the value of T/H. That proportion of the degraded chemical energy which is transformed into the potential energy of increased tension is far greater at high

temperatures than at low. Since T/H falls off with time, and since it is necessary to cool the instrument for considerable periods before the whole is at a uniform temperature, we cannot write down with any appreciable accuracy any temperature coefficient of T/H.

TABLE X.

Exp. i. Coil at 13: time in minutes.

Time since dissection	60	100	135	180	270	330	360
Temperature ...	17°	9·2°	4·3°	10°	14·5°	22·5°	27°
T/H	1·55	1·34	1·17	1·08	1·07	1·52	1·46

Exp. ii.

Time since dissection	60	105	140	165	195
Temperature ...	17°	24·8°	28·5°	22·5°	18·5°
T/H	1·15	1·22	1·29	1·15	1·07

Exp. iii.

Time since dissection	120	180	255	315	360	390
Temperature ...	4°	4°	10·3°	19·2°	26·3°	30·5°
T/H	·60	·60	·62	·84	1·05	1·10

We know from p. 20 that T/H decreases as time goes on : hence, in Exp. iii, T/H has been very largely increased by a rise of temperature, *in spite of the time which has elapsed between the observations.* Looking at Exp. iii in this light, we can say that in the transformation of chemical energy into potential energy[1] in the muscle, at least twice as large a proportion of the total energy degraded is transformed into potential energy at 30° C. as at 4° C.

There is one general consideration which, to some extent, coordinates all these changes of T/H. It is well known that a fresh muscle gives a sharper, brisker, twitch than a stale muscle. In a muscle which is perfectly fresh the tension falls off again very soon after it has risen : while in one which is stale the tension remains constant for a noticeably longer period. The difference in the tension curves is shown in Fig. 4.

Now large amounts of heat have to be used per unit time in keeping up a tone: and contracture involves heat production[2]. Hence we should expect that in a single twitch heat has to be used to *keep up* the tension at its maximum value, as well as to raise it to that value. Thus, when the tension is more prolonged, H is increased while T remains constant. Thus T/H will be smaller when the tension curve is more prolonged.

[1] The potential energy due to increased tension.
[2] A. V. Hill. This *Journal*, XL. p. 395. 1910.

Now fatigue, lapse of time since dissection, and a low temperature all give prolonged curves of tension. This seems to me to be undoubtedly one of the factors which cause these changes in the value of T/H: *whenever the increase of tension is prolonged T/H has a smaller value.* I have noticed however, many times, that the duration of the increased tension is not the only factor which determines variations in the ratio T/H.
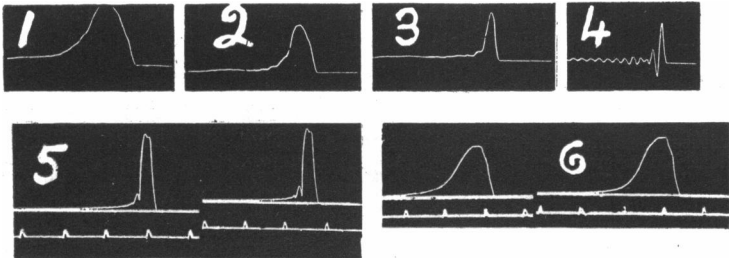

Fig. 4. To show change of tension curve, with change of T/H. *Nos.* 1, 2, 3, 4 *from the same muscle, at different temperatures.* No. 1, 4° C. $T/H = \cdot 6$: No. 2, 10·3° C. $T/H = \cdot 62$: No. 3, 19·2° C. $T/H = \cdot 84$: No. 4, 26·3° C. $T/H = 1\cdot05$. *Nos.* 5 *and* 6 *from the same muscle.* No. 5 fresh, $T/H = 1\cdot48$: No. 6 after fatigue, $T/H = 1\cdot29$.

Summary of Part II.

The inconstancy of the ratio W/H, where W is the mechanical work done in a twitch, and H is the heat set free, together with the considerations given in Part IV of this paper, led to an examination of the ratio T/H, where T is the maximum tension set up in a twitch. It was found that in an isometric muscle twitch *the ratio T/H is constant,* whether we vary

    (i)   the number of fibres contracting,

    (ii) the strength of contraction of each fibre,

    (iii) the initial resting tension on the muscle.

We may conclude (i) that T/H is the same for every fibre, (ii) that T/H is constant for any fibre however strongly that fibre contracts, (iii) that T/H is independent of the resting length and tension of any fibre.

Hence we shall deduce that the tension of an isometric muscle twitch is, theoretically, a far more important factor than the height of contraction. The tension refers to the potential energy of the active muscle, the height of contraction to the actual work done. Part IV

shows that the latter can, in general, be deduced from the former. Hence the important factor in our conceptions of the nature of the muscular machine *is the potential energy which is thrown suddenly into being* following an excitation. In a general sort of way there is a proportion between this increase of tension-energy during a twitch and the amount of heat set free.

An excitation liberates a certain amount of potential energy of increased tension: it liberates also a certain amount of heat energy; there is some degree of proportionality between these two.

The ratio T/H decreases in fatigue, by the action of time on a muscle isolated from its blood stream, and by lowering the temperature. A rise of 26° C. more than doubles the proportion of the total energy degraded which is turned into tension energy.

A further discussion of these results is given in the Summary of Part IV, and in the General Summary.

PART III. THE HEAT PRODUCED DURING THE TONE OF
COMPLETE TETANUS.

In Part II the experiments referred to single twitches only. In this Part the muscles have been tetanised for varying periods up to 2·5 sec. It is impossible to obtain very concordant results, with the instrument and muscles available, for periods much longer than this.

If a muscle is tetanised[1] for any period t_1 we can record
(i)   the curve of tension during that time,
(ii)   the total heat produced H_1.

When the period t_1 is not so long as to damage the muscle, the muscle may be tetanised again for a period t_2, and a similar tension curve recorded, the heat produced being H_2. Suppose t_2 to be greater than t_1: then in the process of keeping up the tension from the time t_1 to the time t_2 the quantity of heat set free is

$$\{H_2 - H_1\}.$$

Now t_1 and t_2 may be varied at will, so that we can observe exactly the relation between the duration of the tetanus and the total amount of heat set free in it. In practice however the following difficulty arises. Suppose that we tetanise for 1 sec. and that the tension recorded rises to 50 gr. wt.: if we then tetanise for 1·2 sec. the tension is generally a little less than before, say 47 gr. wt.; the previous

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[1] By Mr Keith Lucas' apparatus. See p. 7.

stimulation had, to a slight extent, exhausted the muscle. When there is no large difference between $T_{1\cdot2}$ and $T_{1\cdot0}$ we are justified in multiplying $H_{1\cdot2}$ by $T_{1\cdot0}/T_{1\cdot2}$, in order to "reduce" the value of the heat for the second tetanus to what it should be, had it shown an increase of tension equal to that set up by the previous tetanus. Then, and not until then, can we subtract $H_{1\cdot0}$ from $H_{1\cdot2}$, in order to obtain the heat set free by the tetanus which existed during the period from 1·0 sec. to 1·2 sec.

Let t be the time, measured from the beginning of a tetanus: let H be the total heat set free by a tetanus existing for that time. Then, by experiments of the type described above, it has been found possible to determine in the fresh muscle the relation[1] between H and t. This relation must be of fundamental importance in any theory of contraction: I have therefore given several experiments and figures, as the observations are generally of a higher degree of accuracy than the average physiological experiment. In all these cases the tension has remained constant during each tetanus, from the moment when it reached its maximum. Yet in every case $\frac{dH}{dt}$ starts at a very high value, and falls until it reaches a certain constant value. In other words a tetanus for the first 0·1 sec. produces far more heat than a tetanus for the second 0·1 sec.: while a tetanus during the period 1·5 sec. to 2 sec. produces exactly as much heat as a tetanus from 2 sec. to 2·5 sec.

The factors which cause this fall of $\frac{dH}{dt}$, and the final constant value attained by it, are undoubtedly fundamental properties of the muscle mechanism.

In the experiments to be given below certain points should be noticed.

(1) During the tetanus of a fresh active muscle, for a short period such as 2 sec., the tension should rise rapidly and remain constant until the tetanus ends. In some cases the tension, no doubt from exhaustion, falls off again directly the maximum has been reached. Whenever the tension curve showed that the tension had not remained constant during the tetanus, and therefore that the muscle was becoming somewhat exhausted, the observation was rejected. Only those observations are given in which the tension, having reached its maximum, remained constant.

(2) The muscles were, in all cases, in oxygen.

(3) Most of the observations were made on the *semi-membranosus* muscles of large male frogs, at room temperature (12° C. to 18° C.). Stimulation was tetanisation by an

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[1] It should be noticed that H is **not** the heat set free in time t, but the heat *set free by a tetanus of time t*. Part I of this paper shows that the heat production lags behind the excitation: H may be much greater than the heat set free *in* time t.

induction coil, 50 shocks per sec., with one volt in the primary circuit. Duration of tetanus in seconds.

(4) The "Reduced Value of H" was calculated as follows:

(a) Provided that there was no exhaustion of the muscle, and that successive observations of complete tetanus showed the same maximum tension, the reduced values of H in all observations were obtained by dividing H by the maximum tension of a complete tetanus. The reduced values of H represent therefore the heat that would be produced by various durations of a constant tetanus, in which the final tension set up is the unit of tension.

(b) If the values of T, the maximum tension of a complete tetanus, were falling off in consecutive observations, it became necessary to correct for this defect. This must be done for the two different cases :

(a) If the tetanus were of such a duration that the maximum tension was attained, the reduced value is taken as H/T, the heat produced per unit tension.

(β) If the tetanus were too short for the maximum tension to be reached, the reduced value of H is H/T_m, where T_m is the maximum tension that would have been set up if the tetanus had been continued. T_m is taken from the nearest observation, in point of time, which gave a value of the maximum tension.

Thus the reduced values of H *represent the heat produced during various lengths of a tetanus, in which the maximum tension set up* (or the maximum tension that would have been set up if the tetanus were continued long enough) *is the unit of tension.*

TABLE XI.

Exp. i.   Temp. $12.7°$ C.   Coil at 10.

Duration of tetanus, t ...	·33	·50	·70
Max. tension set up, $T \propto$	32	32·5	32
Heat produced, H, $\propto$ ...	72·5	85	103
"Reduced Value" of H ...	2·26	2·62	3·22

Results shown in Fig. 5.

Exp. ii.   The experiment was made backwards and forwards, *i.e.* with increasing and decreasing times, in order to eliminate the effects of fatigue.   See Fig. 6.

Duration of tetanus, t	·04	·08	·04	·08	·16	·32	·64	1·28	2·56	1·92
$T \propto$	26·7	33	26·2	33	38	39·5	39	38·8	38	37
$H \propto$	43	65	43	64·5	94·5	118	173	260	378	279
Reduced value of H...	1·09	1·64	1·09	1·63	2·39	2·99	4·45	6·7	9·95	7·54

Duration of tetanus, t	1·60	1·28	·96	·72	·48	·32	·24	·16	·12	·03
$T \propto$	36·2	35	34·3	33·2	32·4	31·7	30·5	28·1	25·5	22
$H \propto$	224	182	142	115	92	77	66	50	43	33
Reduced value of H...	6·2	5·2	4·15	3·45	2·84	2·43	2·13	1·61	1·38	1·06

Results shown in Fig. 6.

Exp. iii.

Duration t ...	2·0	1·3	0·9	0·5	0·3	0·15	0·08
T	20·1	20·0	19·4	19	18·8	17·1	14·2
H	248	169	135	87	69	46	33
Reduced value of H	12·3	8·45	6·95	4·6	3·65	2·45	1·75

Results shown in Fig. 5.

TABLE XI (*continued*).

Exp. iv.

		·08	·16	·32	·64	1·28
Duration *t*	...	·08	·16	·32	·64	1·28
T	...	16·7	19·5	19·6	19·0	18·2
H	...	47	54	67·5	89	127
Reduced value of *H*		2·4	2·75	3·45	4·7	7·0

Results shown in Fig. 6.

Exp. v.

Duration *t*	...	1·28	·64	·32	·16	·08	·04	·02
Reduced value of *H*		10·5	6·05	4·05	2·95	2·3	1·82	1·45

Results shown in Fig. 5.

Exp. vi.

Duration *t*	...	·016	·031	·047	·062	·078	·094	·109	·133	·172
Reduced value of *H*	1·65	2·6	3·8	4·6	5·7	6·35	6·05	6·35	6·9

Duration *t*	...	·273	·390	·545	·78	1·03	1·25	1·48	1·72	1·95
Reduced value of *H*	8·25	10·4	12·0	15·8	18·5	19·8	22·5	25·6	26

Results shown in Fig. 6.

Exp. vii.

Duration *t*	...	·008	·016	·023	·039	·047	·062	·078	·101	·133
Reduced value of *H*	1·12	1·64	1·68	2·2	2·25	2·85	3·55	3·95	4·65

Duration *t*	...	·172	·218	·273	·335	·405	·485	·570	·665
Reduced value of *H*	5·0	5·65	6·45	7·25	8·05	8·85	9·6	10·25

Results shown in Fig. 5.

Exp. viii.

Duration *t*	...	·016	·031	·062	·125	·250	·46	·92	1·84
Reduced value of *H*	3·0	5·25	7·0	10·8	15·0	21·4	29·5	44·7

Results shown in Fig. 5.

The tension set up by the muscle in this experiment varied from 73 gr. wt. for ·125 sec., to 67 gr. wt. for 1·84 sec. No large errors can have been introduced by "reducing" the value of *H*.

From the experiments given in Table XI, and shown graphically in Figs. 5 and 6, it is seen that the curve relating total heat produced to duration of tetanus rises rapidly at first, and then more slowly, until it becomes almost a straight line. After about $\frac{1}{2}$ sec. the heat set free is proportional to the duration of the tetanus producing it. Before that time however there was no such proportion. For example in Exp. ii a tetanus of ·2 sec. causes a H.P. proportional to 43, while a tetanus of ·4 sec. causes a H.P., not of 86, but only of 60. We cannot calculate the *rate* of heat production from these curves, for the heat production
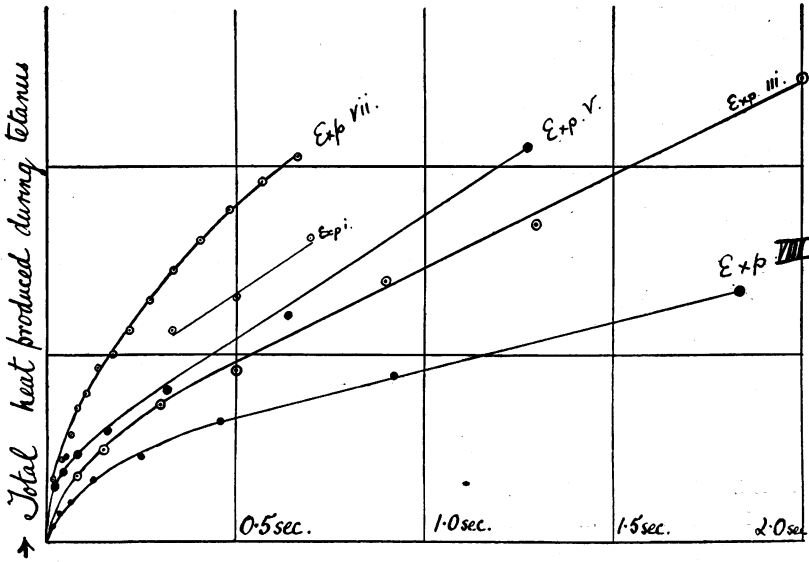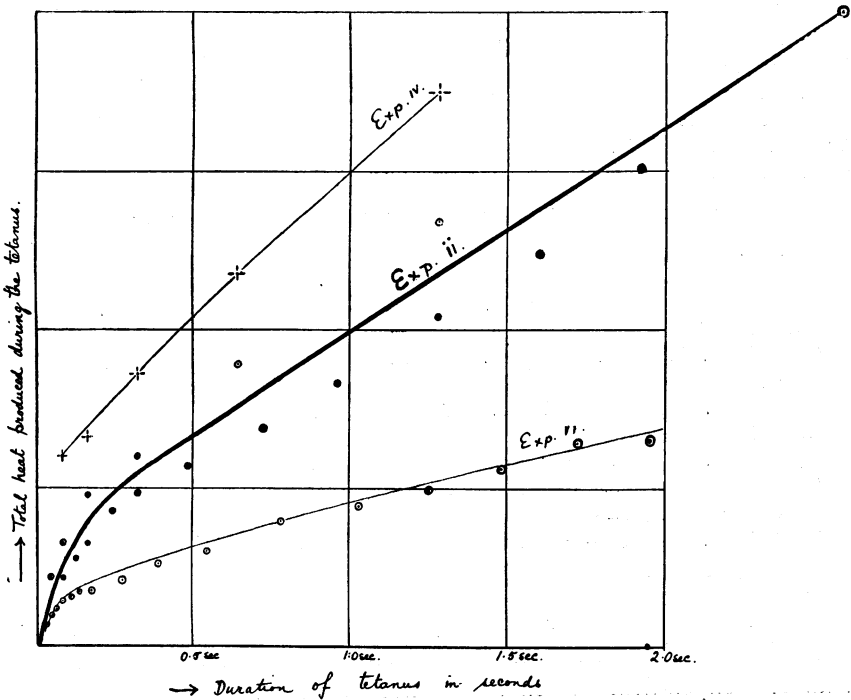
Fig. 5. Heat produced during tetanus.

Fig. 6. Heat produced during tetanus. Exp. ii was taken in both directions for increasing and decreasing times. The curve is drawn as the mean of the backward and forward readings.

lags behind the excitation, and the curves connect heat production with duration of excitation. To assume that the curves given in Figs. 5 and 6 are the same as curves connecting total heat set free with time measured from the beginning of tetanus, is to assume that every element of heat is given out immediately after the element of excitation that caused its liberation: which is not true (Part I). It is necessary to point out this error as it is a very natural one. Only very general statements may, as yet, be made as to the *rate* of evolution of heat in tetanus.

There are other somewhat curious phenomena observed in connexion with the heat produced during tetanus. These are given in the next Table.

TABLE XII.

Exp. i. *Variation of stimulus.* Duration of tetanus 0·8 sec.

Coil at, in cm.	10	4	14	12	10	8	6
Heat produced per unit tension $=\dfrac{H}{T}$	6·35	6·65	2·65	3·4	5·5	6·7	6·7

Exps. ii. *Effects of previous use upon the heat set free per unit of tension exerted.* Tetanus of 1 sec. In each experiment (a, b, c, d, e) the observations were made in order of time, at intervals of a few minutes.

(a) Heat per unit tension	4·7		4·5		4·1		4·05	3·95
(b) Heat per unit tension	8·9		8·4		8·0			
(c) Heat per unit tension	4·32		4·16		3·9		3·65	*	3·3
(d) Heat per unit tension	3·1	2·9	2·8	2·7	2·7	*	2·2
(e) Heat per unit tension	8·85		8·00		8·5		8·0	7·95

* Here several stimuli were given to the muscle, but unrecorded.

Exp. iii. *Effects of temperature upon the heat per unit tension.* The following observations were taken at intervals of about 25 minutes.

(a) Coil 10. Temperature 12·7° C. 0·33 sec. tetanus, $H/T = 2\cdot26$. 0·5 sec. tetanus, $H/T = 2\cdot62$. 0·7 sec. tetanus, $H/T = 3\cdot22$.

(b) Coil 10. Temperature 4·0° C. 0·7 sec. tetanus, $H/T = 2\cdot4$. 1·0 sec. tetanus, $H/T = 2\cdot5$.

(c) Coil 10. Temperature 1·5° C. 0·7 sec. tetanus, $H/T = 2\cdot08$. 1·0 sec. tetanus, $H/T = 2\cdot05$.

(d) Coil 10. Temp. $= 0\cdot2°$ C. 1 sec. tetanus, $H/T = 2\cdot54$.

(e) Coil 8·5. Temp. $= -1\cdot0°$ C. 1 sec. tetanus, $H/T = 2\cdot68$.

(f) Coil 8·5. Temp. $= -2\cdot4°$ C. 1 sec. tetanus, $H/T = 2\cdot07$.

(g) Coil 8·5. Temp. $= -3\cdot5°$ C. 1 sec. tetanus, $H/T = 2\cdot34$.

From Table XII we see:

(i) That the heat per unit tension, in a tetanus of given duration, is much less when the stimulus is less. It requires, proportionally, a far less expenditure of energy to keep up a tension of 10 gr. than

one of 50 gr. A muscle is working much more efficiently when exerting a small tension than when exerting a large tension. A muscle exerting a constant tension of 40 gr. may be using not merely twice the energy of a muscle exerting a force of 20 gr., but five or six times the amount.

(ii) A tension of given duration can be kept up by a muscle with a less expenditure of energy when the muscle has been subjected to previous stimulations. A fresh muscle works less efficiently in keeping up a tension than one which has been exercised already. As the stimulations are continued the ratio H/T becomes almost constant, and it is then that the observations given above (Table XI) have been made. Thus, when a muscle is fresh, moderate amounts of exercise make it work more economically[1] in keeping up a given tension: but further exercise then has little effect.

(iii) A fall of temperature decreases the value of H/T: *i.e.* a given tension is kept up more economically at a low temperature than at a high.

[(ii) and (iii) are probably due to the following cause. At low temperatures, and after moderate degrees of exercise, single twitches become more prolonged: it is easier therefore to secure "summation" at low temperatures and after exercise. This may explain the smaller amount of heat produced per unit tension under these conditions; if summation is produced easier probably less heat will be required for it.]

Summary of Part III.

It has been found possible to determine experimentally the relation between t, the duration of a tetanus, and H, the total heat set free in it. It has been shown that in a prolonged tetanus, the tetanus for the first $\frac{1}{10}$ sec. produces far more heat than the tetanus for the second $\frac{1}{10}$ sec., which again produces far more heat than the tetanus for the third $\frac{1}{10}$ sec.: and so on. Finally however, as the tetanus goes on, the heat produced by each $\frac{1}{10}$ sec. of it becomes the same. Expressed mathematically, $\frac{dH}{dt}$ starts at a high value, but falls rapidly until it reaches a constant value.

It has been shown in addition that the muscle works more economically in proportion to the tension it exerts, when it exerts a low tension than when it exerts a high. Further, that a fresh muscle works more economically in exerting a tension when it has received a

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[1] Exercise may reduce the heat required to keep up unit tension as much as 25 %.

moderate amount of stimulation: and that muscles exert a tension more economically at low temperatures than at high.

It will be the duty of further investigation to determine the bearing of these results upon our conceptions of the muscular machine.

PART IV. THE MECHANICAL EFFICIENCY OF A MUSCLE TWITCH.

It has been shown, by Fick[1] and others, that after excitation a muscle which is not allowed to contract undergoes a sudden change of tension, as seen graphically in Fig. 7. The curves of tension may be compared with the curves of contraction shown in the same figure. Thus, after excitation, a muscle changes its elastic constants: in
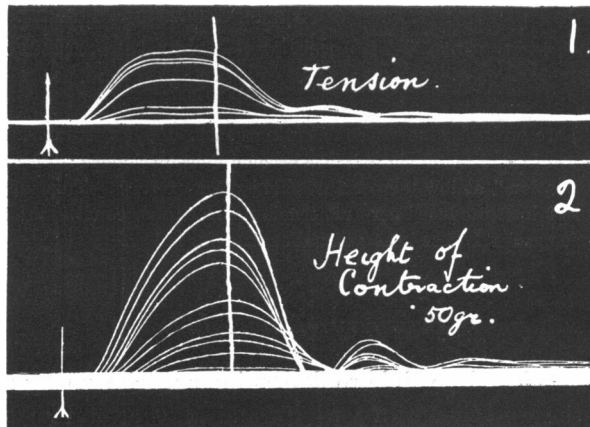
Fig. 7. No. 1. Curves of tension. No. 2. Curves of contraction.

particular its "natural length" diminishes, and consequently its tension is increased. This change of natural length has been brought about by some complex process in the fibres, but whatever be the nature of that process the facts are plain and obvious enough.

Before stimulation a muscle was at tension T_0: after stimulation its tension is $\{T_0 + T\}$, where T varies with the time according to the curves of Fig. 6. This increase of tension T is the sign of two things, (i) a decrease of the "natural length," and (ii) a change of the elastic

[1] See Biedermann, *Electro-physiology*, p. 82, Fig. 42.

coefficient. Both of these changes last, in a single twitch, only a very short time. The objects of this Part of the paper are:

(i) to give experiments determining as exactly as possible the variations of the mechanical efficiency under variation of stimulus and load;

(ii) to show that these variations can be deduced in general from the results of Part II, and elementary mechanical principles.

(i) *Experimental observations of the mechanical efficiency.*

In the Tables given below are shown experiments dealing with the relation between the work (W) done in a muscle twitch, and the heat produced (H). The mechanical efficiency, W/H, changes when we change the load or stimulus. The relation between W/H and the load lifted, or between W/H and the stimulus, has been investigated as accurately as possible with my instrument. The lower end of the muscle, instead of being attached to the tension lever, was tied to a light lever which measured the height of contraction. Near the axis of this lever was hung the load. Thus the momentum of the load did not come in, and the muscle contracted always against the same tension. In some experiments the load was "supported" before the contraction occurred: in others it was "unsupported," *i.e.* the tension on the muscle was the same both before and during contraction. There is a considerable difference between the results of the two cases. The weight lifted always fell again when the twitch was over: hence the work done reappeared chiefly in the muscle as heat. Thus H represents very nearly the total energy degraded, and W/H is the mechanical efficiency in the ordinary sense.

TABLE XIII. *Variation of load: constant stimulus.*

A. Load unsupported before contraction, *i.e.* muscle under initial tension equal to that of the load.

Exp. i. *Semi-membr.* muscle, attached to unsupported lever. Length of muscle slightly stretched, 3 cm. Weight of muscle 0·25 gr. Maximum contraction of muscle under tetanus = 0·75 cm.

Tension of load	...	0	1·43	4·29	7·15	11·44	17·16	22·9
H	... ...	?	25	29	31	34	36	37
Height of contraction		?	4·2	3·3	3·3	2·8	1·7	1·2
Efficiency $= W/H$	...	0	2·4	4·9	6·4	7·7	8·1	7·4

EXP. ii. Observations, taken in order.

Tension of load	0	10	20	30	40	50	60
Efficiency $= W/H$	0	·7	·9	1·18	1·27	1·27	1·37

EXP. iii.

Tension of load	0	10	20	30	40	50	60	80
Efficiency $= W/H$	0	1·77	2·53	3·35	3·80	4·03	4·61	4·89
Tension of load	100	120	140	160	180	200	220	240
Efficiency $= W/H$	5·20	5·56	5·73	5·51	5·49	4·76	4·52	4·13

EXP. iv.

Tension of load	0	40	80	100	120	60	80	120	70	80	60
Efficiency $= W/H$	0	2·78	4·01	4·25	4·27	3·58	3·82	4·08	3·68	3·93	3·27

These results are shown in Fig. 8.
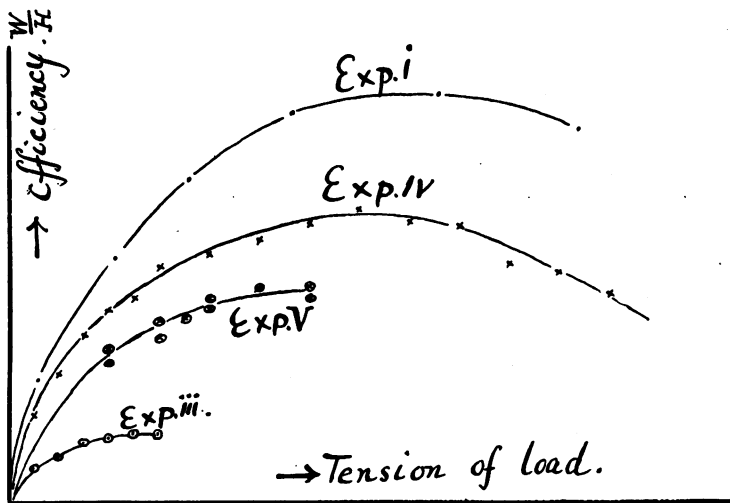
Fig. 8. Efficiency of unsupported muscle, with varying load.

B. Load supported before contraction, *i.e.* muscle under constant initial tension, independent of the load to be lifted.

EXP. v. Muscle under constant tension of 3 gr. wt. before contraction began; the tension it lifted when it did contract is given in the first row.

Tension during contraction	0	20	80	125	160	20	60	100	140
H	?	30	42	45	47	32	40	44·5	45·4
Height of contraction	?	3·4	1·7	·9	·2	3·0	1·9	1·0	·2
Efficiency $= W/H$	0	2·3	3·2	2·4	·68	1·9	2·8	2·3	·61
Tension during contraction	100	60	40	20	40	60	90	120	
H	44·5	39	38	33	37·5	39	42·5	43	
Height of contraction	1·0	1·8	2·2	2·9	2·1	1·7	1·1	·2	
Efficiency $= W/H$	2·3	2·8	2·3	1·8	2·3	2·6	2·3	·56	

The tensions were changed about irregularly, so that one might be sure that any effect of changed efficiency might not be due to a gradually appearing collapse of the muscle, due to fatigue.

Exp. vi.

Tension during contraction	0	30	50	70	90	110	130	150	170
Efficiency = W/H ...	0	4·0	5·4	5·6	6·2	5·8	5·6	3·5	1·1

Exp. vii.

Tension during contractn.	0	20	30	60	80	100	120	140	160	140	120
Efficiency = W/H ...	0	3·7	5·8	7·0	7·5	6·9	5·7	5·1	3·9	5·3	5·8
Tension during contractn.	100	80	60	40	20	40	60	20	40	60	80
Efficiency = W/H ...	6·2	6·2	5·7	4·2	2·9	4·2	5·3	2·8	3·8	4·4	4·2

In Exp. vii the efficiency is noticeably falling off under fatigue.

Exps. v, vi, and vii are shown in Fig. 9.
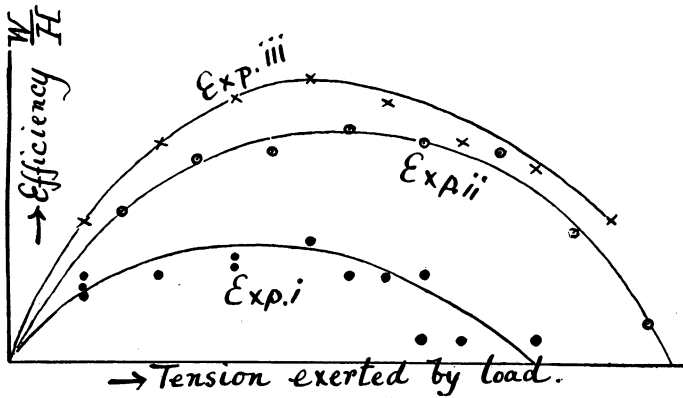
Fig. 9. Efficiency of supported muscle, with varying load.

TABLE XIV. *Efficiency under variation of stimulus.*

The total heat set free by a stimulus is a better measure of the strength of the stimulus than is the position of the secondary coil. I have therefore given in the first row the value of H, the variations of which have been produced by variation of stimulus.

A. *Unsupported muscles : constant tension.*

Exp. i. 10 gr. wt. tension.

H	23	35	44	23	48	36	18	53	18
Efficiency = W/H	5·5	4·75	4·2	5·6	4·0	4·36	5·7	3·6	5·6

Exp. ii.

H	24	36	47	57	59
Efficiency = W/H	8·1	6·1	6·0	5·3	5·4

Exp. iii.

H	115	90	78	40
Efficiency = W/H	4·2	4·47	4·6	6·7

Exp. iv.

H	16	50	80	111
Efficiency = W/H	9·0	6·25	5·4	4·9

3—2

Exp. v. *H*   12   35   43
         Efficiency = *W*/*H*   16·5   6·1   5·95
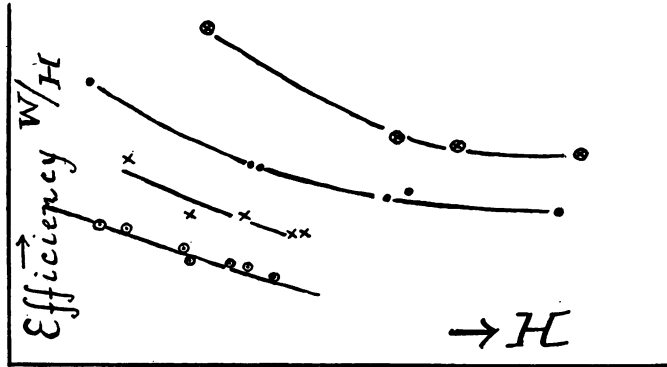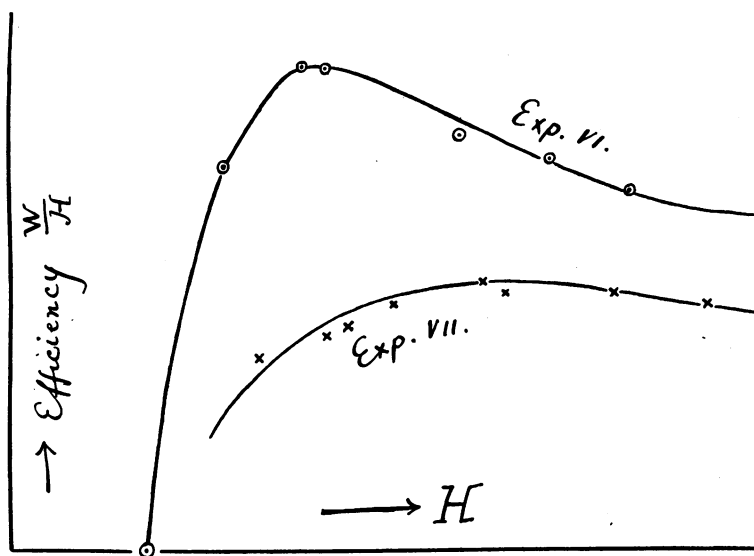
Exps. i to v are shown in Fig. 10.

Fig. 10. Efficiency of unsupported muscle, with varying stimulus.
     (*H*, the total heat produced, is plotted as the abscissa, being the best measure of the strength of the stimulus.)

B. *Supported muscles.*

Exp. vi. Tension of load 18 gr. wt.: 10 gr. of this was supported before contraction commenced.

H	6	9·5	13	14	20	24	27·5
Efficiency = *W*/*H*	0	1·7	2·15	2·14	1·85	1·75	1·6

Exp. vii. Tension of load 22 gr. wt.: 10 gr. of this was supported before contraction.

H	11	14	15	17	21	22	27	31
Efficiency = *W*/*H*	1·7	1·9	2·0	2·2	2·4	2·3	2·3	2·2

Exps. vi and vii are shown in Fig. 11.

From Tables XIII and XIV we may conclude :

(i) In an " unsupported " muscle the efficiency increases as the tension of the load increases, it reaches a maximum value, and at high tensions of the load shows a tendency to fall again.

(ii) In a " supported " muscle the efficiency increases as the tension of the load increases, reaches a maximum, and then falls again to zero.

(iii) In an " unsupported " muscle the efficiency decreases always as the stimulus is increased.

(iv) In a " supported " muscle the efficiency rises from zero, reaches a maximum, and then falls again, as the stimulus is increased.

Figs. 8, 9, 10, 11 are the graphical representations of these conclusions.

(ii) *Mathematical consideration of the results.*

The basis of this treatment is the assumption that the results of Part II of this paper can be applied to other than isometric twitches. We have shown that T/H is constant whatever the stimulus or tension in a muscle not allowed to contract. Thus a certain amount of heat energy must be evolved in order *to set up a certain new elastic state in the muscle.* Let us assume that this new elastic state, and not the tension itself, is really the fundamental quantity. Then we may suppose that the same new elastic state is set up by the same heat production whether the muscle be allowed to contract or not. When a muscle is excited a certain amount of energy, H, has to be used to

Fig. 11.   Efficiency of supported muscle, with varying stimulus.
        (H, the total heat produced, is plotted as the abscissa, being the best measure of
    the strength of the stimulus.)

change the natural length from l' to l and the coefficient of elasticity from E' to E. Let us assume that this is the case whether the new elastic body contracts, or not. In doing so we are advancing a hypothesis which can be tested only by its results: and the results in this case can be shown to be in accordance with facts. Whether the hypothesis be completely true, or not, the factors introduced must be of importance in determining variations of efficiency, and we see that,

to some degree at any rate, the mechanical efficiency is complicated by purely external conditions.

Let l be the " natural length " of a muscle which it strives to attain during the activity of a single twitch.

Let E be the coefficient of elasticity of the muscle during the active stage.

Let y be the initial length of the muscle before excitation.

Let x be the length of the muscle at the moment when the maximum height of contraction has been reached.

Let T_0 be the tension against which the muscle contracts: W the work done: H the heat set free: T the maximum increase of tension, in the sense used in Part II.

I propose to consider here only the case of the supported muscle, for variation of load or stimulus. The unsupported muscle can be treated in the same way, but owing to a certain complication[1] the algebra is long and uninteresting.

(a) *Supported muscle: variation of load.*

Here y, the resting natural length, is constant. We have, for the maximum height of contraction under tension T_0, the equation

$$T_0 = E\,(x - l)/l,$$
$$\therefore \quad x = T_0 l/E + l.$$

Hence the height of contraction, $y - x$, is

$$y - l - T_0 l/E,$$

and the work done,

$$W = T_0\,\{(y - l) - T_0 l/E\}.$$

Now, by Part II, T/H is constant.

Hence $H = CT$, where C is some constant.

But T is the maximum tension that would have been set up at length y, if the muscle had been excited isometrically.

$$\therefore \quad H = CT = CE\,(y - l)/l.$$

Hence the efficiency is

$$\frac{W}{H} = \frac{T_0\,(y - l) - T_0^2 l/E}{CE\,(y - l)/l}\ .$$

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[1] The complication in question is that the inactive muscle is not a perfectly elastic body. The extension is in no wise proportional to the tension, but less. This is due to the presence of connective tissue in the muscle; at high extensions due to heavy loads the connective tissue becomes taut, and being relatively inextensible disturbs the simplicity of the argument.

This expression contains only one variable, viz. T_0 the tension of the load: if it be plotted graphically with respect to T_0 we obtain a parabola as in Fig. 12.' There is an exact correspondence between this parabola and the curves given in Fig. 9 for the relation between efficiency and load.
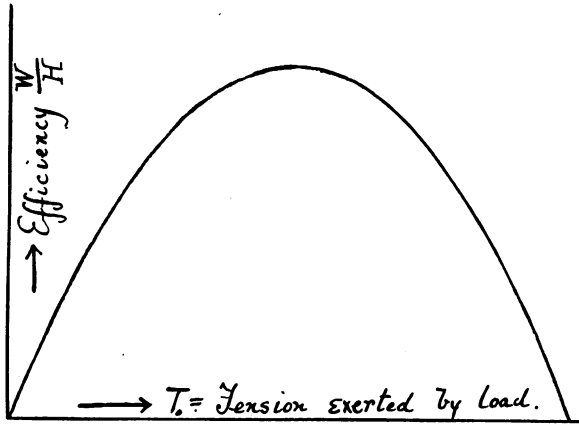

Fig. 12. Calculated efficiency of supported muscle : varying load. Cf. Fig. 9.

(b) Supported muscle: variation of stimulus.

One point must be noticed. Varying the stimulus varies simply the number of fibres contracting, and not the strength of contraction of each fibre. The natural length during activity is the same however many fibres are excited, being the active natural length of each fibre. Thus E, the coefficient of elasticity of the whole active muscle, is proportional to the number of fibres excited. Hence E is proportional to H, the total heat set free : for the total heat liberated is proportional to the number of fibres working. Let us put $E = \mu H$.

We must remember that unless the stimulation is greater than a certain limit the weight will never be lifted from the support. Hence W/H may be zero, for it cannot be negative. We have from (a) above

$$W = T_0 \{(y - l) - T_0 l/E\}.$$

Hence

$$\frac{W}{H} = \frac{T_0 (y - l)}{H} - \frac{T_0^2 l}{\mu H^2},$$

putting $E = \mu H$.

This contains one variable H, which is varied by varying the stimulus. It may be plotted with respect to H, and we obtain a curve as in Fig. 13. There is an exact correspondence between this curve and the curves given in Fig. 11 for the relation between efficiency and stimulus.
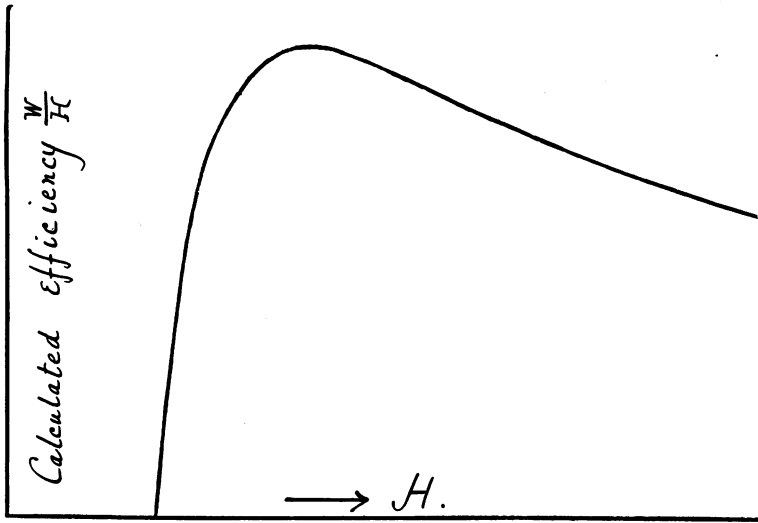

Fig. 13.   Calculated efficiency of supported muscle: varying stimulus.   Cf. Fig. 11.

We see therefore that there is an exact correspondence between theory and fact. Assuming the results of Part II we can deduce the changes of efficiency from the laws of elementary mechanics.

Summary of Part IV.

Experiments are given to show, as accurately as possible, the changes of the mechanical efficiency with variation of stimulus and load. It is assumed, in the mathematical portion, that the results of Part II can be applied to muscles which are allowed to contract, as well as those which are not. We suppose that a certain definite degradation of energy is necessary in an active muscle, in order that the muscle fibres may assume a new elastic condition, viz. a new decreased natural length and a new coefficient of elasticity. With this assumption it is possible to deduce the changes of the mechanical efficiency from the laws of mechanics.

It is thus seen that the mechanical efficiency is of no great importance in our investigations into the nature of the muscular machine. It depends upon three factors:

(i) the amount of potential energy (due to stretching) existing in the muscle before excitation occurs,

(ii) the ratio T/H,

(iii) the conditions of loading.

Further it is a variable quantity, and consequently of much less value than T/H, which is constant under all variations of the external conditions. The mechanical efficiency, though at first sight the obvious factor to investigate, turns out to be of no theoretical importance. What we need to investigate if we are to probe deeper into the thermo-dynamical mysteries of the muscle is not the mechanical efficiency W/H, but the ratio T/H, or—better still—the ratio existing between the potential energy liberated as increased tension in the muscle, and the total energy degraded. Now that proof has been afforded it seems obvious to a student of thermodynamics that such should be the case. The potential energy of increased tension is the work factor existing on the one hand: on the other hand we have the heat energy. It is indeed difficult to realise all the potential energy of increased tension as work, without loss, or without obtaining some work as well from the stretched state existing before excitation: but this makes no difference to our point of view. The true efficiency of the muscle is not W/H, but the ratio

$$\frac{\text{potential energy thrown into an active muscle by excitation}}{\text{total chemical energy liberated as heat}}.$$

To this factor future work must be applied. *The muscular machine is concerned with the transformations of chemical energy into the potential energy of increased tension*: the conditions of loading determine the amount of actual work accomplished, and therewith the mechanical efficiency.

General Summary.

A summary of the effects observed in each Part of this paper is given after that Part. Here we shall consider shortly the bearing of these results upon our conception of the nature of the muscular machine.

In Part II it has been shown that, in a muscle twitch, the increase

of tension is proportional to the rise of temperature. Now the rise of temperature must have been caused by some chemical reaction, of the type

$$A + B + C \longrightarrow ABC + \text{Heat.}$$

Hence we may conclude that the increase of tension is proportional to the extent of this chemical reaction. Now the tension may have been set up by one of two things: either

(a) by the heat itself (cf. Engelmann's theory of contraction): or,

(b) by the presence of some chemical bodies, liberated, broken off from a combined or adsorbed state, thrown into solution, by the stimulus.

If case (a) were the true condition of things, we should expect that the tension set up would be proportional to the amount of heat set free. If case (b) were the truth, we should look for a proportion between the tension set up, and the concentration of the chemical bodies setting it up. But the heat set free in a chemical reaction is proportional to the extent of that reaction: the heat liberated in an oxidation is proportional to the amount of substance oxidised. Hence in either case we should expect to obtain a constant ratio T/H: thus Part II does not enable us to decide between these rival theories. Let us turn therefore to Part I, which shows us that under certain conditions the heat production may take place long after the contraction is over. These experiments, if there be no unforeseen error in them, show conclusively that the heat does *not* set up the tension: the muscle is not a heat engine: for the heat may not have appeared until long after the tension has risen and fallen again. Hence we must conclude that the heat is set up by the presence of certain chemical bodies, which affect the colloidal tissues of the muscle in such a way as to set up a tension. On excitation therefore some substance A is liberated, which sets up a tension proportional to its concentration. A is then destroyed, or replaced in its original position, with an evolution of heat proportional to its amount.

Let us turn now to the action of oxygen: as is shown in Part I the presence of O_2 diminishes the duration of the reaction which gives out the heat,

$$A + B + C \longrightarrow ABC + \text{Heat.}$$

Hence we should expect O_2 to be one of the bodies participating in the reaction: for in that case the velocity would be, among other things, proportional to the concentration of free O_2 in the tissue. Thus, by increasing the O_2 tension in the tissue an atmosphere of O_2 would

decrease, and similarly an atmosphere of H_2 would increase, the duration of the heat production. In this connexion the experiments of Fletcher and Hopkins[1] on the oxidative removal of lactic acid are very suggestive. They found that the presence of O_2 removed lactic acid, and presumably replaced it in its former position in the tissues. Possibly O_2 treats other products of activity in the same way. On stimulation therefore certain molecules are thrown into solution, which before stimulation were lightly connected in some physical or chemical way with other bodies, so as to be inactive. The presence of these chemical molecules sets up a tension, possibly at certain colloidal membranes in the fibre: the tension falls off again, owing to the diffusion of these chemical molecules into the general free space of the fibre, away from the sensitive membranes: the molecules are then oxidised, or replaced in their original positions, under the action of O_2, with an evolution of heat proportional to the amount of those bodies present.

It is easy to explain the action of temperature upon the ratio T/H by some such scheme as this: the active chemical bodies have more effect upon the sensitive membranes at high temperature than at low, and hence T/H is greater and rises more rapidly: but they diffuse away faster, and hence the tension falls more sharply.

According to this conception, based upon these experiments, and sketched above, there are three stages in the process of muscular contraction:

(i) the liberation of certain molecules following an excitation:

(ii) the action of these molecules, on certain local structures, in producing a longitudinal tension:

(iii) the removal, or replacement, of these molecules.

Each of these three stages can be investigated with regard to a variety of factors: such factors are the presence or absence of salts, drugs, oxygen, the onset of fatigue, and variations of temperature acting upon the ratio T/H. A preliminary sketch of the methods available has been given in this paper: a complete investigation of these facts will give us more real insight into the nature of the muscular machine, and therewith of all living tissues, than any theories of contraction ever founded by ingenious minds upon insufficient knowledge.

[1] This *Journal*, xxxv. pp. 296, etc. 1907.