ON THE ORIGIN OF
THE INITIAL HEAT IN MUSCULAR
CONTRACTION

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It has been shown by HARTREE & HILL (1, 2) and by FISCHER (3), that the first stage of the heat production of working muscles, the "initial heat" of HILL, may be subdivided into three phases (see fig. 1).
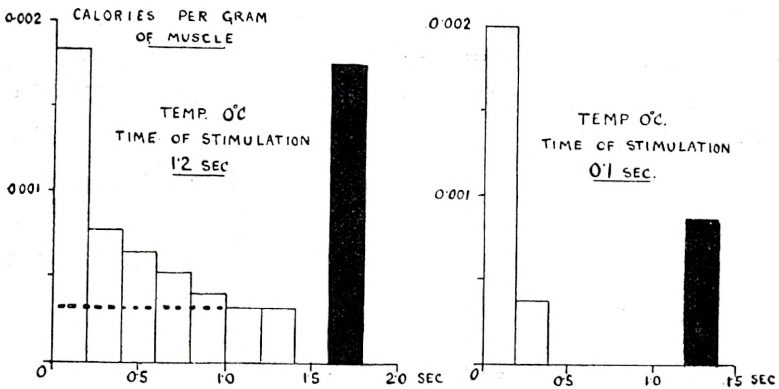

Fig. 1.

According to the generally accepted explanation of the shape of the curve as given by HARTREE & HILL the first phase coincides with the development of tension, the second is due to the subsequent maintenance of tension, and the third to dissipation of potential energy into heat. In a twitch, of course, only the first and the third phase are present. Now a closer examination of the heat production shows that the heat developed in the second phase is proportional to the duration of the stimulus. HARTREE & HILL (4)

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propose the term "tension-time"-production for the ability of muscle to maintain a given tension during a certain time. The product tension × time may be represented graphically as the area of the isometric tension curve, $\int T dt$, where T means tension and t the time. Thus if the total initial heat is H and E the potential energy dissipated into heat we have

$$H = bx + E;$$

in this equation the link bx represent tension-time, x being the duration of stimulus and b the constant tension maintained. This equation has been accepted by Fenn (5, 6) in the form $E = A + Bt$ and more recently also by Abramson, who, to the equation of Johansson (7) $U = s + tZ$ where U means the total amount of energy liberated, s and t constants, and Z the duration of contraction, added a third link on the right side making allowance for the state of shortening in which the muscle has to contract. Abramson's (8) equation is the following

$$U = k_1 + k_2\, TZ + k_3\, Tr;$$

here U is the energy spent, T the tension, Z duration of stimulus, $r = l_0 - l_1$, ($l_0 = $ the resting length of muscle), and k_1, k_2, k_3 constants.

The authors here cited agree in the opinion that in a tetanic contraction the expenditure of energy is in the main used for the maintenance and not for the development of tension. Hartree & Hill add that in a twitch, on the contrary, the energy is spent on setting up tension only.

We cannot admit, however, that this point of view is

permissible. The equations may be arithmetically correct, but they give no physical nor physiological meaning at all, because physics operates with nominated figures. It is the link bx or Bt resp. $k_2 TZ$, the link of maintenance, which makes the trouble. The product (tension × time) has, as pointed out by HILL, the same dimension as momentum, i. e. (mass × velocity). This cannot be denied, but as potential energy has the same dimension as heat we obtain from $(H - E) = bx$, when taking the dimensions on both sides, a new equation of the appearence $L^2 MT^{-2} = LMT^{-1}$; and such an equation must be erroneous. In ABRAMSON's equation the last link, Tr, has the same dimension as have H and E, r being a length and T a force, and it is thus suffering from the same error as is the original equation of HARTREE & HILL.

This from a physiological point of view serious error seems to arise firstly from the shape of the heat curves as given by FISCHER and by HARTREE & HILL, secondly from a misconception of the term maintenance as applied to muscular activity. We will consider this lastnamed contention first.

Maintenance in the proper sense of the word bears upon a stationary or continuous process and not upon a discontinuous or rhytmic one. But a rhytmic physiological process may appear continuous if the single responses are developed at such a rate that the preceding one has not had time to disappear. The apparently steady state may be represented by a straight or by waved curve according to the respective duration of the refractory period of the object concerned, the time occupied for the development of the response, and the time demanded for recovery. Now in the case of muscle it cannot be doubted that we have

to do with a pseudocontinuous process belonging to the lastnamed kind, and this point is essential. If a true steady state was realized tension might develop in some way or other, and it might then be maintained by means of quite another reaction, which not necessarily had any relation to development of tension. In the second case, however, the pseudocontinuous state involves a rhytmic development of tension caused by the same fundamental process. It might perhaps be objected that the state of tension once established might claim less expenditure of energy in response to the following stimuli in order to be kept "constant". This conception, however, is in opposition to the "all-or-none" principle which demands that each single reaction of any muscular fibre is maximal.

If we stimulate an excised muscle under isometric conditions with a single induction shock we will obtain a curve of the well-known shape shown in fig. 2. The duration of the whole reaction and the slope of the ascending as well as the descending branch of the curve may vary under varying experimental conditions e. g. temperatur changes, but we never find the ascending and the descending crus of the curve connected by a plateau. The muscle can set up tension, and the tension once established may immediately perform external work or may degenerate into heat, but the muscle cannot store tension. It must, therefore, be due to experimental errors when HILL finds the third phase in initial heat dependent on the duration of stimulus, provided that this increase in heat production depends on dissipation of potential energy. When, on the other hand, several observers have found the heat production in the second phase proportional to time, this observation may certainly be right in

spite of the misunderstanding dealt with above, but the mutual dependence of heat and duration of stimulus is only indirect and does not always appear. It wil according to the "all-or-none" principle be found only when the rhytm of stimulus is regular; the amount of heat liberated depending really on the number of effective stimuli and not directly on the time elapsed (RIESSER and Co-workers).

Returning to the consideration of the shape of the heatcurve we consider it justifiable to believe that it is the initial abrupt rise of the curve which must be held responsible for the untenable dis-

Fig. 2.

tinction between development and maintenance of tension. This being so, it would seem worth while to seek for some cause which might explain the initial strong outburst of heat or at least that part of it by which it exceeds the level corresponding to the second phase. So far as we are aware, the explanation must be sought and may be found in the structure of the muscles. The histological structure of muscle has not hitherto been recognized according to its importance, although it may be taken as a mere chance if thermodynamic investigations on muscle undertaken without regard to its structure should prove to give reliable results.

Before entering more closely into the problem here concerned it will be convenient to recall how a skeletal muscle is built up. The muscular belly consists of bundles bound together by means of coarser connective tissue,
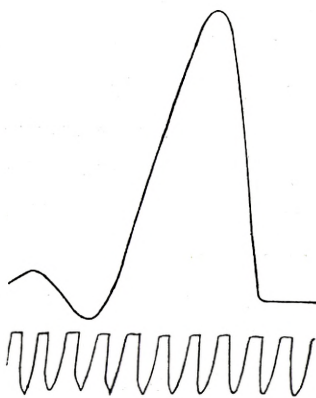
each bundle comprises a number of fasciculi, the lenghts of which are usually shorter than the whole belly. The fasciculus again consists of muscular fibres, the histological elements of muscular tissue, connected by sparse connective tissue. The shapes and dimensions of the fibres in the frogs sartorius, the muscle most commonly used for physiological experiments, have been envestigated repeatedly, some few years ago by LINDHARD, who found (9) that most of the fibres were not cylindrical but conical and sometimes spindle-shaped. The fibres did not proceed from one end of the muscle to the other, only the thick end of the fibre was attached to the tendon, the other tapering end was found somewhere in the endomysium. In a 27.9 mm. long sartorius the average length of the fasciculi was 25.5 mm. and the average length of 117 fibres was 17.2 mm., in a 26 mm. long sartorius the length of the fibres was found varying between 5.2 and 24.0 mm. The thickness of the single fibre as measured near the two ends varied very much as well in the individual fibre as when different fibres were compared. No constant relation between length and thickness was found, as the following figures will show:

Length in mm   13.5   14.8   25.5   15.1   18.2   13.1   14.4   21.5
Thickness in μ 9—104 46—122 9—101 49—107 9—61 21—80 46—168 24—128

The fibre is surrounded by a homogeneous membrane, the sarcolemma, and subdivided transversly by numerous fenestrated membranes (Membranes of KRAUSE) by which it must be assumed to be inserted into the surrounding connective tissue (HÄGGQVIST (10, 11)). The endomysium must again be regarded as a network continuous through the whole muscular belly and without any interruption

passing into the tendons. When the fibre is treated with suitable reagents the membranes of KRAUSE may be dissolved and the fibre may break up into discs (discs of BOWMAN) only some few μ in height.

If we imagine a muscle consisting of parallel cylindrical contractile rods inserted with both ends in tendons, such a muscle will, when stimulated and prevented from shortening, not change its shape, nor will the individual fibres change in length or shape. An actual sartorius, on the contrary, will when stimulated change its shape, even when isometrically arranged, as seen by several observers. This change may be due to mutual displacement of the histological elements only, leading to a new state of equilibrium corresponding to the tensions caused by stimulation, and such a displacement must in fact be assumed to take place as soon as the tensions vary; but also the individual fibre must vary, if not necessarily in length yet always in shape. When a fibre is excited at constant length the tension developed must be constant on the unity of cross-section or proportional to the area of the cross-section; and the consequence of this distribution of the tension must be that the shape of the fibre is altered until we obtain a new state of equilibrium in which the tensions on each cross-section are equal without regard to the size of the area.

In order to obtain an adequate idea of the changes in conformation of an isolated muscular fibre during isometric contraction we choose as an example a fibre shaped as a right circular truncated cone of the length of 20 mm. having at the thick and the thin end a diameter of $^1/_{10}$ and $^1/_{60}$ mm. respectively and being perfectly elastic. We will first let the fibre shorten to $^1/_3$ of its original resting length. The shape of the fibre will still be that of a trun-

cated cone but the radius in each sectional area at right angle to the axis of the cone will be multiplied by $\sqrt{3}$. If we then stretch the contracted fibre to its original resting length, we may calculate the resulting change in configuration.

To this purpose we make a section through the axis of the fibre and place a rightangled coordinate system in the sectional area in such a manner that the point of intersection of the axes is in the centre of the thin end, and the x-axis falls along the axis of the cone. (Fig. 3.)

Then the generator-line L_1 of the original resting fibre obeys the equation

$$y_1 = \frac{1}{480}(x_1 + 4) \tag{1}$$

while the generator-line L in the shortened fibre will obey the equation

$$y = \frac{\sqrt{3}}{160}\left(x + \frac{4}{3}\right). \tag{2}$$

If we consider a volume-element of the shortened fibre situated between two sections at right angles to the x-axis in the points x and $x + dx$ the height of this segment, dx, when the fibre is stretched will be multiplied by $1 + \frac{\alpha}{y^2}$, while its radius is divided by $\sqrt{1 + \frac{\alpha}{y^2}}$, α being a constant depending on the coefficient of elasticity of the fibre. After stretching we have the abscissa of the element considered

$$\xi = \int_0^x \left(1 + \frac{\alpha}{y^2}\right) dx = \int_0^x \left(1 + \frac{\alpha\, 160^2}{3\left(x + \frac{4}{3}\right)^2}\right) dx$$

or

$$\xi = \frac{160}{3}\sqrt{3}\,y - \frac{\alpha \cdot 160 \cdot \sqrt{3}}{3\,y} - \frac{4}{3} + \alpha \cdot 6400. \tag{3}$$

This equation in addition to

$$\eta = \frac{y}{\sqrt{1 + \dfrac{\alpha}{y^2}}}$$

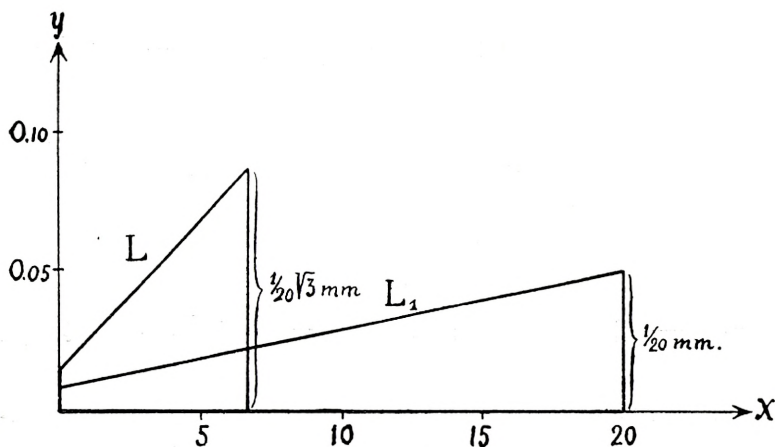will determine the "meridian" in the rotation-body arrived

Fig. 3.

at by stretching the contracted fibre. As we must have $\xi = 20$ for $y = \dfrac{\sqrt{3}}{20}$, we find $\alpha = \dfrac{1}{400}$, which value sub-stituted in the above equation gives

$$\xi = \frac{160}{3}\sqrt{3}\,y - \frac{2\sqrt{3}}{15\,y} + \frac{44}{3}$$

and

$$\eta = \frac{y}{\sqrt{1 + \dfrac{1}{400\,y^2}}}$$

which is thus the final appearence of the equation deter-
mining the "meridian"-curve in the case examined. The
curve determined in this way is shown in Fig. 4.

Every cross-section of the fibre will in an isometric
contraction move towards the big end and the displace-
ment $\varDelta$ may be found from the equation

$$\varDelta = \xi - 3x = \xi - 3\left[\frac{y \cdot 160}{\sqrt{3}} - \frac{4}{3}\right] = -\frac{320}{3}\sqrt{3}\,y - \frac{2\sqrt{3}}{15y} + \frac{56}{3};$$

the maximum value for $\varDelta$ corresponds to $y = \frac{1}{40}\sqrt{2}$, and
hence

$$\varDelta_{\max} = \frac{56}{3} - \frac{16}{3}\sqrt{6} = 5.60\,\text{mm.}$$

The corresponding values for ξ, η are

$$\xi = \frac{44}{3} - \frac{4}{3}\sqrt{6} = 11.40\,\text{mm.}, \qquad \eta = \frac{1}{120}\sqrt{6} = 0.0204\,\text{mm.}$$

The cross-section which undergoes maximum of dis-
placement is lying between the elements that shorten and
those which are passively stretched during isometric con-
traction of the fibre, and this cross-section is the only one
the radius of which remains unaltered. In the resting fibre
this cross-section is situated at a distance $x_1 = 4\sqrt{6} - 4$
$= 5.80$ mm. from the thin end of the fibre, in the isome-
tric contracting fiber, as shown above, it is placed at
$\xi = 11.40$ mm. from the thin end.

Thus the big end of the fibre will shorten and do
work, but part of this work will be stored as an increase
in potential energy in the thin end. If now the gain of
the thin end of the fibre was equal to the loss of the big

end, the deformation of the fibre would not involve any loss of potential energy, but this condition is not fulfilled. In fact the loss of energy in the big end is greater than the increase in the thin end, and the difference must appear as heat. To make this clear we will consider a simplified case.

We imagine two elastic strings of the same material with the length l but with different cross-sections such that when stretched to twice their resting length their tensions will be 1 and 2 respectively. If these two strings are fastened in such a way that they meet one another when
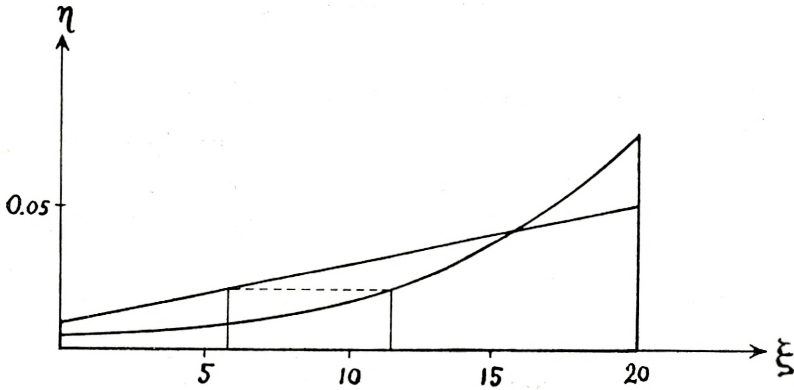
Fig. 4.

their length is doubled, and when in this position they are connected together and then released we will see that the big one shortens while the thin one is stretched until the tension is equal between the two points of insertion. The tension of equilibrium may be found from the equation

$$1 + x = 2(1 - x) \quad \text{or} \quad x = {}^1/_3,$$

when x is the increase in tension of the thin string. When, as is true for perfectly elastic bodies, the tension is proportional to the increase in length also the length of the

thin string will increase by $a = \frac{1}{3}$. Under these conditions
the potential energy gained by the thin string may be
found from the equation

$$E_1 = \int_0^a (1+x)\,dx,$$

or, for $a = \frac{1}{3}$, $E_1 = \frac{7}{18}$, while the energy-loss of the thick
string is

$$E_2 = 2\int_0^a (1-x)\,dx,$$

and, for $a = \frac{1}{3}$, $E_2 = \frac{10}{18}$. Hence the potential energy
dissipated which must appear as heat is $E = E_2 - E_1 = \frac{1}{6}$.

We will now return to our muscular fibre. Assuming
that the maximal tension of frogs muscle at resting length
is 6 kg/cm^2, and that $20\,\%$ of the sectional area is occu-
pied by connective tissue, then the maximum tension of
the contractile substance proper is 7.5 kg/cm^2.

If we imagine that each volume-element (transverse seg-
ment) of the contracted fibre is stretched to its original
height, then the whole fibre must assume its original length
and shape and under this assumption the content of po-
tential energy of the fibre will be greater than will be the
case if it is allowed to assume the form shown in fig. 4.
It is the difference between these two amounts of potential
energy which appears as heat. This difference may be
calculated as shown below.

Under the first assumption each volume-element is
stretched to its treble length. If we assume the maximum
isometric tension of the fibre to be 0.075 kg/mm^2 the
infinitesimal work by stretching is:

$$dE_1 = \frac{1}{2} \cdot 0.075 \cdot \frac{\pi y^2}{3} \cdot 2\,dx$$

or, by the aid of (2)

$$dE_1 = \frac{3\pi}{1024 \cdot 10^3} \left(x + \frac{4}{3}\right)^2 dx.$$

Thus the potential energy of the fibre after stretching is:

$$E_1 = \frac{3\pi}{1024 \cdot 10^3} \int_0^{\frac{20}{3}} \left(x + \frac{4}{3}\right)^2 dx = \frac{215}{432} \cdot \pi \cdot 10^{-3}\ \text{kg mm.}$$

If we now consider the second case in which the contracted fibre is passively stretched to its original length, being allowed to assume its natural shape as shown in fig. 4, we have:

The value of α corresponding to stretching of the fibre to the length x is found from (3), if we substitute $\xi = x$ and $y = \frac{\sqrt{3}}{20}$; the calculation gives

$$\alpha = \frac{3x - 20}{16000}.$$

α is proportional to the force k necessary to perform the stretching of the fibre, and their relation may be found, if we consider an isometric contracted volume-element, which gives the equations

$$1 + \frac{\alpha}{y^2} = 3 \quad \text{and} \quad k = 0.075 \cdot \frac{\pi y^2}{3}.$$

Thus

$$k = \frac{\pi}{80}\,\alpha.$$

The work done when stretching the fibre to the original length is:

$$E_2 = \frac{\pi}{80\cdot 16000} \int_{\frac{20}{3}}^{20} (3x-20)\,dx = \frac{\pi}{4800}\ \text{kg mm.}$$

Thus the extra heat due to deformation of the isometric contracted fibre is

$$Q = (E_1 - E_2)\cdot \frac{1}{426.5} = \frac{\pi}{3456}\cdot\frac{1}{426.5} = 2.130\times 10^{-6}\ \text{cal.}$$

The volume of the fibre being $V = 6.26\times 10^{-5}\ \text{cm}^3$, we have further the extra heat per cm^3 fibre $Q_0 = 0.0340$ cal./cm^3.

For a fibre of the length of 6 mm., the diameters of which at the thick and at the thin end are 0.1 mm. and 0.03 mm. respectively we find in the manner described

$$Q = 0.451\times 10^{-6}\ \text{cal.}$$
$$V = 2.18\ \times 10^{-5}\ \text{cm}^3.$$
$$Q_0 = 0.0207\ \text{cal./cm}^3.$$

And the same calculation gives for a fibre of the length 15 mm. and the diameters 0.11 and 0.05 mm.

$$Q = 0.829\times 10^{-6}\ \text{cal.}$$
$$V = 7.89\ \times 10^{-5}\ \text{cm}^3.$$
$$Q_0 = 0.0105\ \text{cal./cm}^3.$$

The maximum tension of frogs muscle is in these cal-

culations considered to be 6 kg/cm². The correctness of this figure may be disputable, but if anybody want to obtain the values corresponding to e. g. 3 kg/cm² it is only to divide the results given here by two.

When these figures are compared with the figures of HARTREE & HILL in fig. 1, it is easily seen that the calculated extra heat is much larger than the observed first phase. It is evident, however, that exact figures cannot be obtained, and further that the calculated value must be too high. In the fascicle the fibres are not moving freely, but as mentioned above they are fastened by means of KRAUSE's membranes to the intrafascicular connective tissue which must of course yield an increasing resistance against the displacement of the muscular discs. Further, the amount of heat must vary with the shape and dimensions of the fibre. On the other hand, it is evident that a deformation of the fibres takes place during contraction, that this deformation involves a loss of potential energy, which appears as heat, an that this heat production is of such an order of magnitude that it may easily explain the surplus of heat appearing in the first phase of the heat-curve. Thus a part of the heat produced during contraction must be supposed not to be of chemical origin but due to mechanical causes. This point of view cannot at present be proved to be correct; as, however, the explanation given by previous authors is obviously erroneous, and as the explanation given in this paper may elucidate also other points in muscular contraction it deserves to be taken under consideration.

Under truly isometric conditions the heat production must thus be supposed to be proportional to the number of stimuli and the mechanical part of the heat must be

only small. The deformation of the fibre between each
two stimuli being negligible and the potential energy dissi-
pated even so. If on the other hand the loaded muscle is
allowed to shorten the "deformation-heat" must be greater
than in the isometric contraction. When the muscle shor-
tens every new stimulus must cause a renewed effort to
adapt the shape of the fibres to the length of muscle,
and even when the single alteration is only slight the sum
may be considerable. The surplus heat due to the cause
here proposed will vary with the extent of shortening and
with the load. It is probable, therefore, that this "defor-
mation-heat" will suffice to explain the otherwise quite
mysterious extra heat production of a muscle doing work
during shortening shown by Hartree & Hill (12) as the
only remnant of the theories of Fenn. During relaxation no
heat production from this origin is to be expected. In a
twitch the tension will be less if the muscle is allowed to
shorten and thus the "deformation-heat" will diminish, on
the other hand the change in shape will be greater and
thus tend to increase the heat of deformation. It is possible,
of course, that these opposite tendencies may be of equal
size, but it is still more probable that existing differences
will disappear within the wide limits of error of the myo-
thermic methods.

The point of view here given involves some consequen-
ces with regard to the conception of muscular efficiency.
Twenty years ago A. V. Hill (13) defined the true, theore-
tical efficiency of muscle as the relation between the po-
tential energy thrown into the fibre by excitation and the
total heat production. If we consider the first tracing in
fig. 1 it is evident that the constant level in the second
phase which we must regard as equal to the heat loss

necessary to develop the potential energy represented by the black rectangle is only a little more than 0.0003 cal., while the black rightangle itself correspond to 0.00175 cal. But before this constant relation has been etablished 0.0025 cal. are wasted owing in the main to the mutual displacement of the fasciculi and to the changes in shape of the fibres engaged in the contraction. It is evident too that the transitional state in the muscle corresponding to the changes described above is not instantaneous but relatively protracted as compared with the time occupied by a twitch (cfr. the second tracing in fig. 1), and thus the maximum tension in a muscle cannot be arrived at in a twitch. In the isolated fibre, on the other hand, we found that a certain cross-section remained unaltered during the changes in shape of the fibre when contracting at constant length. The tension on this cross-section must represent the final maximal tension of the whole fibre, and we may thus according to HILL define the theoretical maximum efficiency in a twitch as

$$\frac{\text{(Tension of unaltered cross-section)} \times \text{(maximum of shortening)}}{\text{Total heat} - \text{(the heat owing to deformation of the fibre)}}.$$

This magnitude is as yet quite unknown. The efficiency of the muscle has no theoretical interest being dependent on the histological structure of the individual specimen. As the stimuli in rhytmic stimulation must be regarded as having individually the same effect, and as the maximum tension of the fibre, which is determined by the unaltered cross-section, once established, does not increase by continued stimulation, while the heat production depends on the number of stimuli, the efficiency of the socalled tetanus has no real meaning.

SUMMARY

It is shown that the usually accepted explanation of the initial heat-curve of an isometric muscle cannot be maintained.

It is not permissible from an energetic point of view to distinguish between development and maintenance of tension.

It is shown that the deformation of the muscular fibre during contraction may be responsible for the surplus heat in the first phase of heat production, and it is made probable, that the extra heat, which appears when the muscle is doing work while shortening, may be derived from the same source.

The consequences of this point of view with regard to the efficiency of muscular contraction are mentioned briefly.

References.

1. HARTREE & HILL: Journ. Physiol. 54, 84. 1920.
2.   —   : Ibid. 55, 133. 1921.
3. FISCHER: Pflüger's Arch. 219, 514. 1928.
4. HARTREE & HILL: Journ. Physiol. 54, Proceedings 16. Octbr. 1920.
5. FENN: Journ. Physiol. 58, 175. 1923—24.
6. — : Ibid. 58, 373. 1923—24.
7. JOHANSSON: Skand. Arch. f. Physiol. 11, 273. 1901.
8. ABRAMSON: Arbeitsphysiologie 1, 480. 1929.
9. LINDHARD: Physiol. Papers ded. to A. KROGH, Copenhagen 1926, p. 188.
10. HÄGGQVIST: Anat. Anz. 53, 273. 1920.
11.   —   : Zeitschr. f. mikr. anat. Forsch. 4, 605. 1926.
12. HARTREE & HILL: Proc. Roy. Soc. B 104, 1. 1928.
13. HILL: Journ. Physiol. 42, 1. 1911.

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