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A STUDY OF THE PHENOMENA AND CAUSATION OF HEAT-CONTRACTION OF SKELETAL MUSCLE.

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IV. *A Study of the Phenomena and Causation of Heat-contraction of Skeletal Muscle.*

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Communicated by W. D. Halliburton, *F.R.S.*

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In the course of some experiments† to determine the influence of a rise of temperature upon the length of muscle stretched by different loads, we observed in a few cases that as the temperature rose, the ordinary heat contraction was followed by a second. This second contraction was less in extent than the first, and exerted only a slight force, for it was readily cut out, or even replaced by an elongation, when the tension was increased. In all these early experiments the muscle preparation employed was a frog's gastrocnemius, or a combined semitendinosus and gracilis preparation, and we were at first unable to obtain the same result when using the sartorius. We accordingly determined to investigate fully the conditions under which it was to be observed. At first we directed our attention to differences in anatomical structure, which might explain the difference in behaviour of the two muscles, and of these the most notable is the presence of a large tendinous insertion, arranged in a typical manner on the surface and in the interior of the gastrocnemius. The shrinkage of tendon when a piece is dropped into boiling water is a well-known phenomenon. It is limited to a shortening of the fibres in the direction of their length, and has been studied by Engelmann‡ and by Hermann.§

We soon found, however, that this could not explain the difference found, for in muscle the second contraction commences between 47° C. and 50° C., whereas the contraction of tendon does not commence until about 62° C. is reached.

The true cause of the discrepancy was soon found to lie in the instrumental defects of the apparatus we were using for magnifying the contractions. When we were dealing with a comparatively powerful muscle like the gastrocnemius a certain

* MS. returned to authors for compression 18 June, 1897, and received back January 13, 1899.

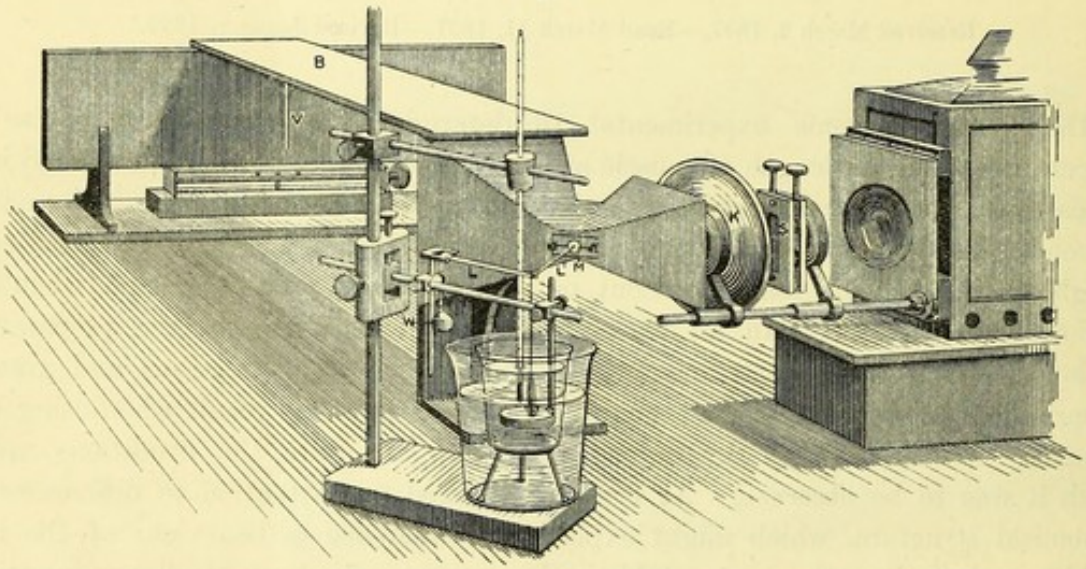
† 'Journ. Physiol.,' 1897, vol. 21, p. 353.

‡ Pflüger's 'Archiv,' 1873, vol. 7, *vide* footnotes on pp. 177 and 179.

§ *Idem*, 1873, vol. 7, p. 417.

amount of friction did not prevent the production of the second contraction. When, on the other hand, a sartorius is experimented upon, the force that this second contraction exerts is much weaker, and is soon prevented from producing any effect if too much friction be present. We at once obtained a similar result with the sartorius by making apparatus where the inertia of the moving parts was brought to a minimum, and friction, as nearly as possible, abolished. We have attained this result and at the same time retained the power of magnifying the movements to any degree we wished, by making use of a photographic method of recording, and by applying the necessary tension by means of a weak spiral spring, whose weight was supported from above. The main details of the apparatus employed in most of our experiments are shown in fig. 1.

Fig. 1.



The lower end of the muscle is firmly pinned down to a small cork base fitted to the lower end of a brass rod. The upper end is attached, by a waxed thread, to the extremity of a short lever, L, which is made to exert an upward pull upon the muscle by means of the weight, W. By this arrangement the tension of the muscle could be reduced, if required, to almost any extent. Resting on the lever, L, immediately above the point of attachment of the muscle, is a second very light lever, whose other extremity is fixed perpendicularly to the centre of a small circular mirror, M. This mirror moves round a horizontal axis in the plane of its reflecting surface. Any change in length of the muscle thus produces a proportionate rotation of the mirror. The movements of the mirror, and therefore of the muscle, are then recorded in the ordinary way. For this purpose a narrow horizontal slit, S, is brightly illuminated by means of a projecting lantern, and the light passing through it is collected by a lens, K, and falls on the surface of the mirror, whence it is reflected to fall across a vertical slit, V, placed at some distance from the mirror A photo-

graphic plate, held vertically, is driven across the slit, V, at any convenient rate, and only the strip of plate immediately behind the slit is thus exposed. The image of the slit, S, is carefully focussed on the plate and all light, other than that reflected from the mirror, M, is thoroughly screened from the plate. The mirror is set at an angle of 45° to the direction of the rays passing through the slit, S, and the rays are thus reflected at right angles to their first direction.

In those experiments in which we wished to employ high tensions, we have used a spiral spring fixed vertically above the muscle, to which it was attached by a fine wire. By varying the extension of the spring, or by using springs of different strengths, the tension on the muscle could be conveniently varied. The tension throughout any experiment remained constant, for we employed long springs, and the shortening of the muscle in our experiments was negligible in comparison to the length of the spring.

The metal L-piece and the muscle are surrounded by fluid by bringing up a small beaker containing the fluid. This small beaker is in its turn held in a larger beaker, which acts as a water-bath, and is heated by a gas-burner or by the passage of an electric current through it.

The temperature at any given time is recorded upon our tracings by blocking out the light at the slit, S, for a short time, and therefore appears as a break upon the continuity of the line forming the tracing. As a rule we have recorded each rise of either two or five degrees.

We have in all cases employed a sartorius preparation on account of its thinness, so that we might feel sure that the temperature was the same throughout the whole thickness of the muscle. We have also ensured the same result by making the temperature rise very slowly. In some cases a rise of 50° C. has been brought about in half-an-hour, in other cases it has been so slow as to extend over 2½ hours.

Of fluids in which to immerse the muscle, we have employed either a 0·75 per cent. NaCl solution or defibrinated ox-blood diluted with four times its volume of the above NaCl solution. As is known from the researches of Locke* and others "physiological salt-solution" is by no means an indifferent fluid to frog muscle, so that in all the tracings we are reproducing here the diluted blood solution has been employed. In a few preliminary experiments we determined that muscles kept in this fluid for, in some cases, longer than an hour, retained their irritability perfectly and produced a "simple muscle-curve" of a perfectly normal character.

As a typical curve, illustrating the various contractions, we have observed, when experimenting upon fresh and excitable frog's muscles by this method, we may take that of Exp. 23, fig. 2. In this record there are four distinct contractions:—

(1.) The first contraction commences at 28° C., its rate is much accelerated at 32° C., and it is completed shortly after 40° C. is reached. It is then followed by a fairly rapid and extensive relaxation.

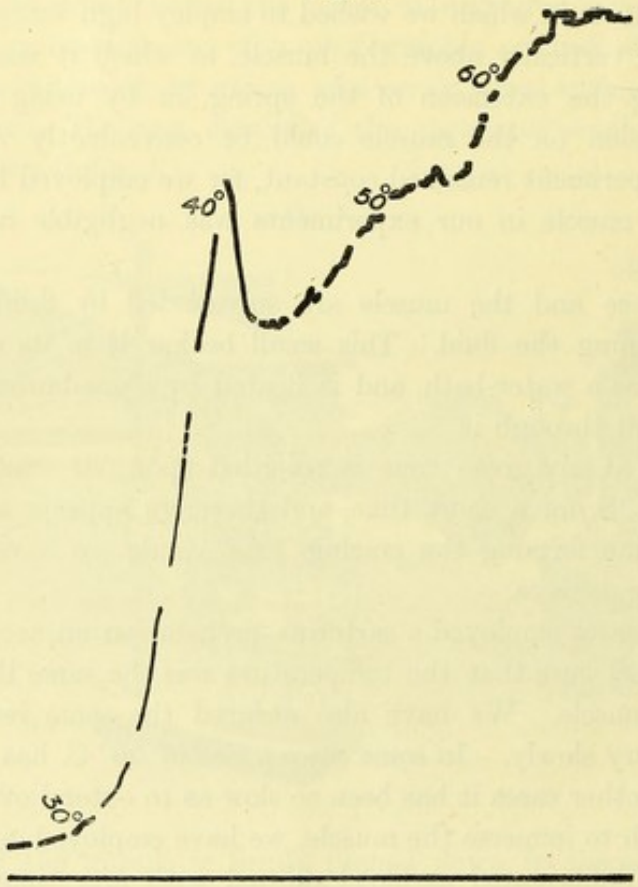
* Pflüger's 'Archiv,' 1893, vol. 54, p. 501.

(2.) The second commences at 44° C., its main effect is produced at a slightly higher temperature, and it is completed at about 50° C.

(3.) The third begins at 55° C. and is complete soon after 60° C.

(4.) The fourth commences at 63° C., and, in this tracing, is not very prominently marked.

Fig. 2.



Experiment 23. Freshly prepared sartorius of frog. Each break in the curve represents a rise of 2° C. Total duration of experiment 32 minutes. Magnification, 10-fold. Length of sartorius, 17·5 millims.

	Temperature limits.	Amount of shortening.
	° C.	millims.
First contraction. . . .	29–40	8·7
Second „	44–50	2·0
Third „	55–62	1·7
Fourth „	63–64	0·4

Total shortening 10·7 millims.

Of these contractions the first is the one which has been chiefly studied by previous workers at this subject.

Pickford* found that if the gastrocnemius of a frog were immersed for a few seconds in water at 82° C., or for several minutes in water at 37°·5 C., it passed into a condition of heat-rigor, and completely lost its excitability. If now the muscle were removed from the warm water, he described the irritability as returning completely after a few minutes, and that a complete resolution of the rigor occurred. Schiff† also stated that if the lower limb of a frog be immersed for 1 minute in water at 45° C. it became perfectly rigid, but recovered in about 4 minutes after cooling. Wundt‡ was able to confirm these observations only so far as the production of rigor was concerned, but was never able to obtain recovery. Kühne§ criticises these results, especially because these observers had immersed the muscle in water, a medium which was shown to exert a very harmful effect upon muscle, and, by itself alone, to lead to a contraction. Like Wundt, Kühne was never able to observe any recovery of irritability after heat-rigor had been completely established. He showed‖ that a muscle kept for some time at 37°·5 C., until its irritability was quite lost, never recovered on cooling. If kept still longer at this temperature it became acid, and he considered that this latter change was in reality the onset of rigor-mortis, which had been accelerated by the higher temperature. He showed¶ that the legs of a living frog became rigid if they were immersed for a time in a fluid kept at 40° C. The circulation through the muscles, as judged by that of the web, became slowed, but was not stopped by this immersion. If the frog were kept for some days the circulation quite recovered, the muscles were found alkaline to litmus, but never regained their excitability. Kühne found that muscle-plasma, prepared from the frog, gave a coagulum when heated to 40° C., but he regarded the process as practically the same as that produced much more slowly in muscle heated to 30° C. He supposed that the same was the case with living muscle, and considered that the main difference between a muscle which had passed into rigor-mortis and one which had become rigid due to the action of heat, was that, in the latter case, the rigidity and opacity were rather more pronounced. He further stated that a muscle which had already passed into rigor-mortis became more opaque when it was heated to 45° C. Alsothat a muscle which had gone into rigor at 40° C. became more stiff and opaque when heated a short time to 45° C. The conclusion** he ultimately arrives at is that rigor-mortis and the rigor occurring suddenly at 40° C. are to be considered as identical in nature, and that only the coagulation occurring at 45° C. could be termed a heat-rigor.

* 'Zeitschr. für rat. Medicin.' N. F. I., p. 110.
† 'Lehrbuch der Physiologie,' p. 44.
‡ Wundt, 'Die Lehre von der Muskelbewegung,' p. 66.
§ 'Myologische Untersuchungen.' Leipzig, 1860, p. 173.
‖ *Loc. cit.*, p. 179.
¶ *Loc. cit.*, p. 180.
** *Loc. cit.*, p. 193.

In a series of papers, SCHMULEWITSCH records some experiments bearing upon this question. He used a gastrocnemius preparation immersed in a bath of 0·65 per cent. sodium chloride, which was gradually warmed. He describes* two distinct processes as being set up :—

(*a*) A physical change. If the solution surrounding a muscle be warmed from 2° C. to 28° C. the muscle shortens, and again lengthens when the solution is cooled. This change was only obtained with muscles still retaining their irritability. If this were lost the reverse effect was obtained, *i.e.*, it behaved as an inorganic body.

(*b*) A physiological change. This expresses itself as two contractions. If a muscle be heated to 28° C., and kept at this temperature for a time, a contraction followed by an elongation occurs. The whole change at times lasted 4 minutes, the muscle remaining irritable the whole time. If the temperature be raised to 35° C., a second contraction occurs, but of shorter duration than the first. The muscle still remains irritable. At 40° or 41° C. the muscle enters into heat-rigidity, and its irritability is lost.

SCHMULEWITSCH assigned the contraction to a specific action of the temperature at the two points named, and only obtained them from irritable muscle.

In another series of experiments SCHMULEWITSCH shows† that the power a frog's muscle possesses of performing work is increased as its temperature is raised to about 33° C., but that with a further rise is diminished, until at a temperature varying from 38° C. to 41°·5 C. for different preparations the power is completely lost.

MAREY‡ examined the condition of frog's muscle warmed to about 35° C. He found that they still remained excitable to electrical stimuli, though with each single twitch the relaxation remained incomplete. These results he explained as caused by the coagulation of "myosin."

BOUDET§ found a contraction in a frog's gastrocnemius commencing at about 27° C. and reaching its maximum when the muscle had passed into rigidity. As the temperature was raised he found the elasticity to increase and to become more perfect.

MORIGGIA‖ found that if heat-contraction be checked soon after its commencement an almost complete recovery took place in about half-an-hour.

An important paper dealing with this question has been published by GOTSCHLICH.¶

* 'Compt. Rend.,' vol. 68, p. 936, 1869, and 'Centralbl. f. d. med. Wissenschaften,' vol. 5, p. 81, 1867.

† 'Medizin. Jahrbücher,' vol. 15, p. 3, 1868; Wien. 'Journ. de l'Anat. et de la Physiol.,' vol. 5, p. 27, 1868.

‡ 'Du mouvement dans les fonctions de la vie,' p. 354, fig. 3. Paris, 1868.

§ "De l'élasticité musculaire," 'Thèse pour le doctorat en Médecine,' p. 31. Paris, 1880.

‖ MORIGGIA, MOLESCHOTT 'Untersuchungen,' vol. 14, p. 386, 1892.

¶ GOTSCHLICH, Pflüger's 'Archiv,' vol. 54, p. 109, 1893.

He employed exclusively the sartorius of the frog, loaded with 2 to 3 grams, and suspended in an air-chamber, the temperature of which could be raised by heating an outer water-jacket.

He states that heat-rigor (Wärmestarre) can be brought about in two ways—either by heating for a short time to a temperature between 45° and 50° C., or by heating for a longer time at 35° C. As soon as the contraction was once obtained no further contraction resulted on considerably prolonging the time in the second case, nor by raising the temperature a little higher in the first. At a temperature of 65° to 75° C. he at times observed a second shortening, which he thought was due in all probability to a coagulation of the serum proteids contained in the muscle. In opposition to SCHMULEWITSCH, he was never able to observe a contraction by keeping a muscle at 27° or 28° C., even when the temperature was kept at this point as long as half-an-hour. If the muscle were cooled after it had been completely brought into a state of heat-rigor, it showed no tendency to elongate, and a second warming to 45° or 50° C. caused no further shortening; the length of the muscle remained absolutely unaltered.*

In the next place GOTSCHLICH enters largely into the consideration of a condition which he speaks of as "thermal persisting-contraction" (thermische Dauerverkürzung). He notes that a frog's muscle begins to contract at a temperature "far below that at which rigidity is produced," and proceeds to inquire as to what would happen if the muscle were cooled after being allowed to partially shorten. We may briefly summarise his main conclusions upon this state in the following statements:—

1. The muscle is more or less shortened.

2. The muscle slowly, but in the end completely, returns to its original length.

3. That on re-warming the muscle behaves exactly as an intact muscle, and, moreover, the condition may be repeated a number of times. The recovery of length is much accelerated by increasing the load.

4. Irritability is considerably diminished during the heat-shortening but can be tolerably retained even when marked shortening is present.

If cooled and stretched the muscle is still irritable, and may still remain so if the process be repeated (in one case three times). The loss of irritability need not be very marked.

5. The extensibility and elasticity are markedly altered and differ according to the length of time the warming has been continued.

6. The condition may be brought about in two ways: (*a*) by allowing a relatively high temperature, about 40° C., to act for a short time; (*b*) by exposing the muscle to a lower temperature, viz., about 35° C., for a longer time.

7. The muscle is not, however, brought into quite the same condition by these two methods. It shows differences in extensibility and in the time required to elongate.

8. The important factor to be considered in the production of this state is that of

* *Loc. cit.*, p. 124.

time; but that the action of a temperature of 40° C. for a few seconds produces practically the same result as a stay of some minutes at a lower temperature. (It is important to note in this connection that, by the method GOTSCHLICH uses, in order to expose a muscle to a temperature of 40° C. the rise must be gradual, for the muscle is suspended in air.)

9. He ultimately concludes* that this condition is of the same nature as heat-rigor, *i.e.*, it is qualitatively an incomplete rigor, and that the processes underlying the two conditions are chemical in nature, the one being an earlier phase of the other.

Before we proceed to a discussion of the results we have obtained, it will be convenient to consider the different proteids obtainable from muscle, for their temperatures of coagulation play an important part in the interpretation we place upon our results. Our knowledge is chiefly derived from the experiments of KÜHNE† and HALLIBURTON,‡ which have recently been extended and modified in many important particulars by v. FÜRTH.§ These proteids, for the case of frog muscle, may be arranged in a series as follows :—

(1.) An albumin (myo-albumin of HALLIBURTON), which coagulates at 73° C. This is only present in small quantities, and by v. FÜRTH is considered as an impurity due to admixture with a little blood-serum or lymph.

(2.) Myoglobulin (HALLIBURTON). This again is only present in small quantities. v. FÜRTH considers that it is in reality a small quantity of the next proteid remaining in solution after most has been precipitated.

(3.) Myosinogen (HALLIBURTON), or myogen (v. FÜRTH). This is the most important proteid. It is chiefly coagulated at a temperature of 56° C. The limits given by v. FÜRTH‖ for the coagulation temperature of a salt-free solution are from 55° to 65° C., with a maximum precipitation at about 58° C. Weak solutions require a rather higher temperature.

(4.) Paramyosinogen (HALLIBURTON), musculin (HAMMARSTEN), or myosin (KÜHNE and v. FÜRTH). Forms a high proportion of the total proteid and coagulates at about 47° C. The temperature limits found by v. FÜRTH¶ are, from 44° to 47° C. an opalescence and clouding, and a precipitate from 47° to 50° C.

(5.) Soluble myogen-fibrin (v. FÜRTH). This proteid is present in considerable quantities in frog's muscle-plasma. Its solutions begin to cloud when a temperature of 30° C. is reached, and give a coagulum between 32° and 40° C.

* *Loc. cit.*, pp. 154, 155.

† 'Myologische Untersuchungen,' 1860. 'Ueber das Protaplasma und die Contractilität,' Leipzig, 1864. MÜLLER'S 'Archiv,' 1859.

‡ 'Journ. of Physiol,' vol. 8, p. 133, 1887.

§ 'Arch. f. exp. Path. u. Pharm.,' vol. 36, p. 231, 1895.

‖ *Loc. cit.*, p. 243.

¶ *Loc. cit.*, p. 238.

The maximum effect is produced at 35° C. The coagulation-temperature is markedly affected by the quantity of salt present in the solution.

(6.) A nucleo-proteid (PEKELHARING*) which is only present in small quantities.

In the muscle-plasma of the rabbit there is one very important difference, viz., that soluble myogen-fibrin, if present at all, is only present in quite minimal quantities. The main proteids, if not the only ones characteristic of muscle, are then myogen and myosin (v. FÜRTH), and in addition for frog's muscle-plasma, soluble myogen-fibrin. Another important point relates to the formation, from these proteids, of coagulated varieties, *i.e.*, forms of proteid insoluble in the ordinary saline media. According to v. FÜRTH, the change which myosin (paramyosinogen) undergoes is directly into an insoluble form, which he terms myosin-fibrin. For myogen (myosinogen) the change is more complex. Apparently myogen, in the first instance, becomes changed into a soluble proteid, viz., the soluble myogen-fibrin we have already described. This change is remarkably rapid at about 40° C., but much less so at a slightly lower temperature. Soluble-myogen-fibrin, in its turn, is converted into an insoluble proteid, myogen-fibrin, and thus the series of changes of myogen are completed.

In addition to these proteids there are still other chemical substances in muscle to be taken into account when we are studying the effect of heat upon muscle. These are the fibrous tissue forming the peri- and endo-mysium and the sarcolemma sheaths. The sarcolemma is a substance which has been shown by EWALD† to closely resemble elastin in its solubilities. HALLIBURTON describes a proteid of the globulin class, giving a heat-coagulum at 75° C., as being present in the ground-substance of connective tissue.

With regard to the influence of heat upon tendon and upon elastic tissue, we have in the first place the work of HERMANN,‡ who found that tendon began to contract at 65° C. and finished at 75° C. In this connection we reproduce a tracing we have obtained from a thin tendon taken from the mouse's tail (fig. 4), from which it is seen that the contraction begins at 60° C., is complete at about 64° C., and is followed by a rapid elongation terminating in rupture soon after 65° C. The load in this experiment was about 1 gram.

The influence of heat upon elastic tissue has been studied, among others, by GOTSCHLICH,§ who found that a piece of ligamentum nuchæ shortened on heating and lengthened on cooling for all temperatures up to 65° C. Between 65° C. and 75° C. another contraction occurs which does not disappear on cooling. A closely analogous behaviour was observed by him‖ in a muscle which had been previously brought by heat into a condition of heat-rigor.

* 'Zeitschr. f. Physiol. Chem.,' vol. 22, p. 245, 1896.

† 'Zeitschr. f. Biol.,' vol. 26, p. 1, 1889.

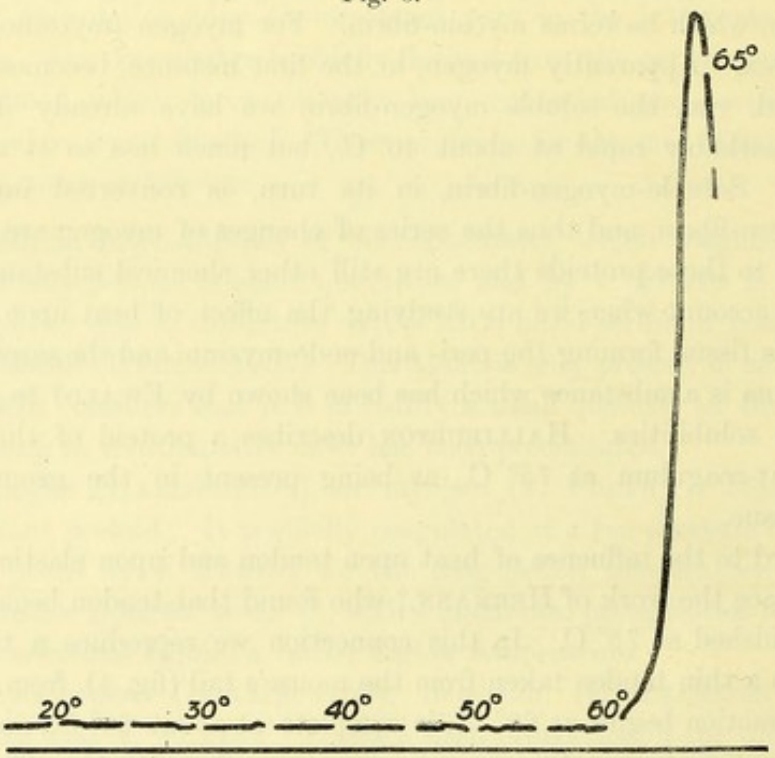
‡ *Loc. cit.*

§ *Loc. cit.*, p. 116.

‖ PFLÜGER'S 'Archiv,' vol. 55, p. 339, 1894.

If we examine the tracing (fig. 2) which we have given as a typical result of our experiments, bearing in mind the different proteids present in frog's muscle and the temperatures at which they coagulate, we immediately note an exact correspondence between the two results. At each of the three temperatures where the proteids soluble myogen-fibrin, myosin, and myogen coagulate, we find a corresponding contraction of the sartorius. And, moreover, this contraction corresponds in all its minutiæ with the range of temperature for each proteid-coagulation. At a temperature at which the coagulation commences, and V. FÜRTH obtained a clouding of his solutions, we find a contraction occurring, small in amount and slow in progress,

Fig. 3.



Exp. 38.—Mouse tendon. Each break on the curve records a rise of 5° C. Total duration of experiment 29 min. 5 secs. Magnification, 10-fold. Length of tendon, 19 millims. Contraction commenced at 60° C., but chiefly occurred when 63° C. was reached. Total shortening, 9·4 millims.

and as the temperature rises to that at which proteid-coagulation is rapid, so too our tracings show a rapid contraction, which gradually falls off as all the proteid becomes coagulated. This is true for each of the three contractions observed. With regard to the fourth contraction, which is frequently more apparent than in fig. 2, we find that it exactly corresponds with the behaviour of white-fibrous or yellow-elastic tissue similarly heated.

We consequently draw the following conclusions :—

(1.) The different contractions given by a muscle as its temperature is gradually

raised from 30° C. to 80° C. are caused by the successive coagulations of its proteids.

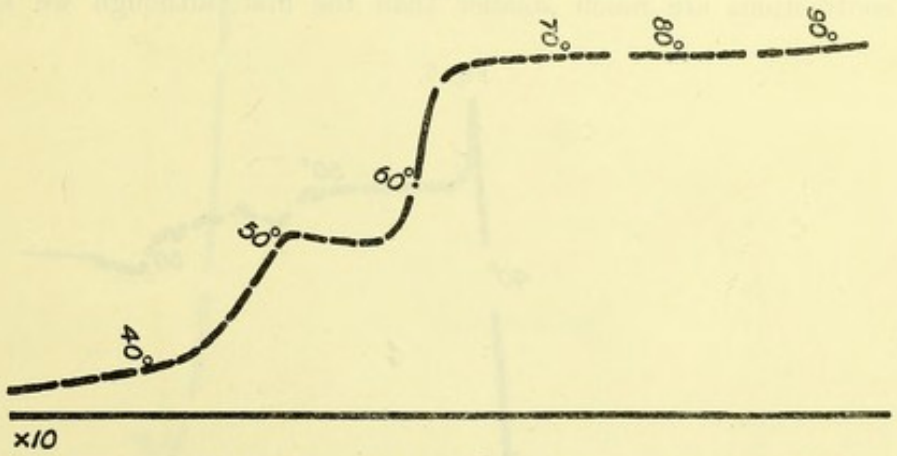
(2.) This is the cause not only of the contractions occurring at 47° and 58° C. but also for that produced in frog's muscle at 34° C., and to which the term heat-contraction or heat-shortening is usually restricted.

This view requires consideration and criticism from many directions. In the first place it gains strong confirmation from the study of—

The Behaviour of Muscles of Warm-blooded Animals when Heated.

Bernard* found that the muscles of a rabbit became rigid when the chamber containing the animal was heated until its temperature rose to about 50° C. Kühne†

Fig. 4.



Exp. 52.—Fresh gastrocnemius of mouse. Each break on curve represents a rise of 2° C. Total duration of experiment, 40 mins. 1 sec. Magnification, 10. Length of muscle, 13·0 millims.

	Temperature limits.	Amount of contraction.
	° C.	millims.
First contraction	43–51	1·7
Second ,, ...	58–63	2·4

Total shortening, 4·1 millims.

found that the muscles of a rabbit or dog did not become rigid until the temperature reached 49° or 50° C., a temperature which, as he pointed out, corresponds with that necessary to produce the first coagulation in the muscle-plasma of these animals.

* Quoted by Kühne, 'Myologische Untersuchungen,' p. 194.

† *Loc. cit.*, p. 194.

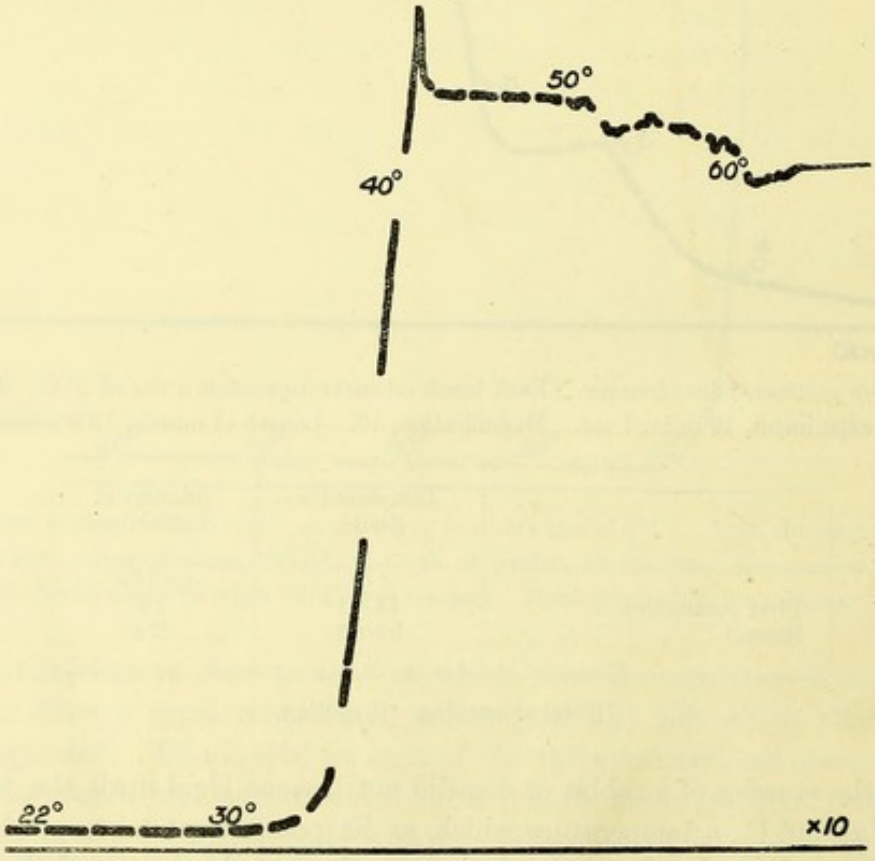
He found further that in the case of the pigeon the temperature necessary was still higher, viz., 53° C.

On testing mammalian muscle by the method we have described we find that it only gives two contractions, the first commencing at 44° C. and the second at 58° C. Mammalian muscle therefore differs from frog's muscle in not giving a contraction at 34° C. This exactly coincides with the fact that fresh extracts of mammalian muscle contain no soluble myogen-fibrin. The two contractions which are obtained correspond in their temperatures to the coagulations of the two proteids obtainable from mammalian muscle. This is shown in fig. 4.

The Meaning of the Variability in the Occurrence and in the Amount of the Contractions Obtained at Temperatures above 40° *C.*

In examining the tracings given by frog's muscle it is observed that the second and third contractions are much smaller than the first, although we know that

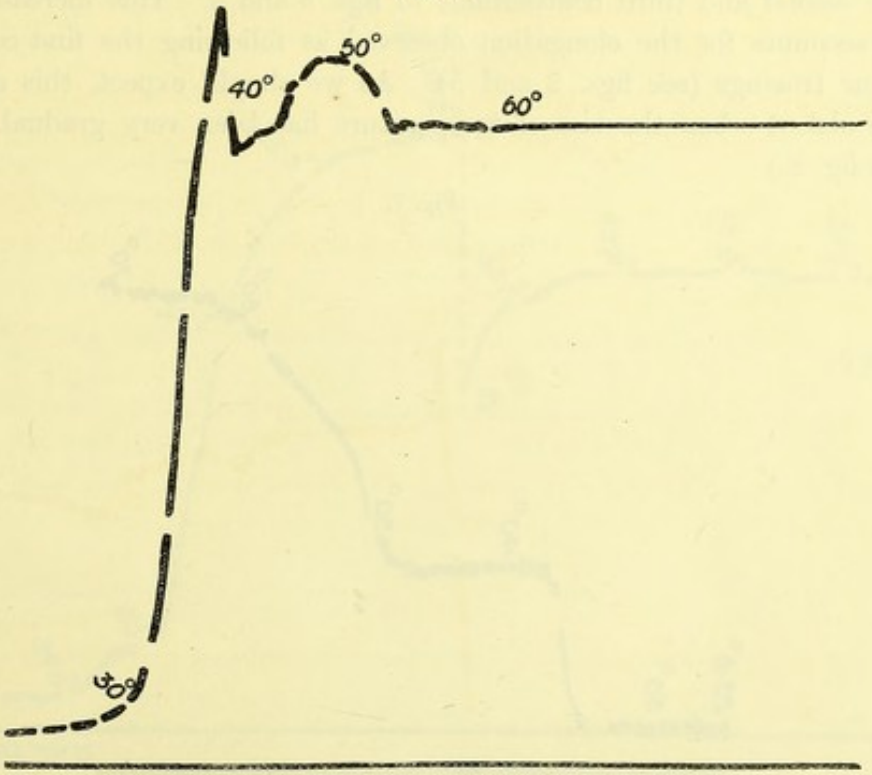
Fig. 5.



Exp. 24.—Sartorius of frog. Each break on curve represents a rise of 2° C. Total duration of experiment, 23 mins. Magnification, 10. Length of muscle, 21 millims. This tracing shows a contraction of 10·8 millims. from 33° to 41° C., an elongation from 51° to 53° C., followed by a slight contraction and a second elongation at 59° C.

the amounts of proteid coagulating at those temperatures are even greater than that at 34° C. In attempting to explain this result there are at least two factors to be taken into consideration. In the first place the forces producing the second and later contractions are acting on a tissue which is already in a state of strong contraction. In many cases, for instance, the sartorius has shortened to one-half its original length during the first heat-contraction. In the second place the forces producing the later contractions are very feeble, and in many cases are even unable to

Fig. 6.



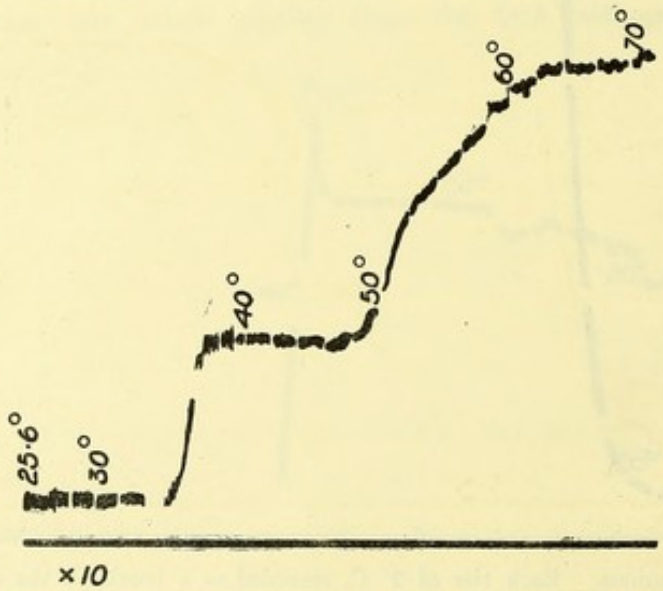
Exp. 25.—Frog's sartorious. Each rise of 2° C. recorded as a break on the curve. Total duration, 21 mins. Magnification, 10. Length of muscle, 19 millims. This tracing shows a contraction of 9·4 millims. from 30° to 39° C., a second contraction from 41° to 50° C., and a relaxation from 52° to 55° C.

overcome the slight tensions we have employed in our experiments. We have invariably found that when the first contraction is well marked the later ones are only slightly shown or even absent altogether, unless the tension acting on the muscle has been sufficient to produce an elongation after the first contraction has ceased. That the first mentioned is the chief cause of the small amount of these later contractions is proved by the fact that when the first contraction does not occur, a condition which, as we shall see, may be brought about in two ways, the later contractions then produce a marked effect (see figs. 7 and 9).

There is yet another condition, set up by the first contraction, which modifies the

appearance of the later ones, namely, an increase in the extensibility caused by the proteid coagulation. This change has already been recorded by GOTSCHLICH and others, and we have been able to show, by experimenting with higher loads, that a very decided increase in extensibility occurs with each proteid coagulation.* The contraction, therefore, in each case is the resultant of two changes in condition, the one tending to shorten, the other, the increase in extensibility, tending to result in elongation. With small loads the result is, as a rule, a shortening, unless the muscle be already in a marked degree shortened, when elongation may occur. This we see for the second and third contractions in figs. 5 and 6. This increase in extensibility also accounts for the elongation observed as following the first contraction in many of our tracings (see figs. 2 and 5). As we should expect, this elongation is completely absent when the rise of temperature has been very gradual. (Compare fig. 2 with fig. 8.)

Fig. 7.



Exp. 58.—Frog's sartorius, which had been heated to 34° C. for 65 mins. 24 hrs. previously. It was then kept in cold dilute blood, and on the following morning was distinctly opaque; it gave a distinct but slight contraction on tetanisation. It was passively stretched, and the tracing (fig. 7) taken. Each break on the curve records a rise of 2° C. There is a contraction commencing at 33° C., though much less than that given by a fresh muscle. A second contraction begins at 48° C., and is much more marked than in the case of a fresh muscle.

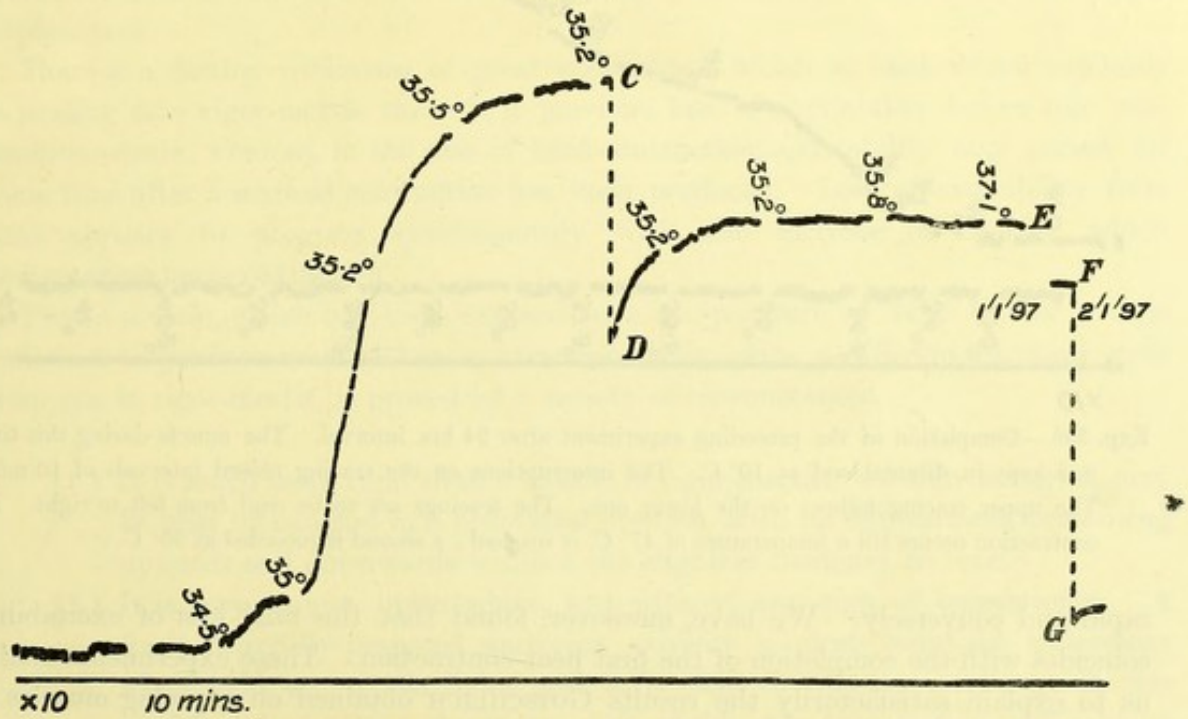
The First Contraction may be Completely Effected at the Lowest Temperature at which Solutions of Soluble Myogen-fibrin can be Coagulated.

If the explanation of heat-contraction we offer is the correct one, it must be possible to cause the whole of the first contraction at the lowest temperature at which soluble

* 'Journ. Physiol.,' 1897, vol. 21, p. 353.

myogen-fibrin will coagulate, and we have accordingly tested this experimentally. We find that the onset of the first contraction is in complete accordance with what we know of the coagulation of proteid solutions when they are heated. It is known that a proteid may be completely coagulated at the temperature at which its solution first shows a clouding. With this point in view we have examined saline extracts of frog's muscle, and have found that the lowest temperature at which soluble myogen-fibrin can be completely coagulated is 34°·5 C., though solutions from different muscles show slight individual differences. This precisely coincides with the results we have

Fig. 8.

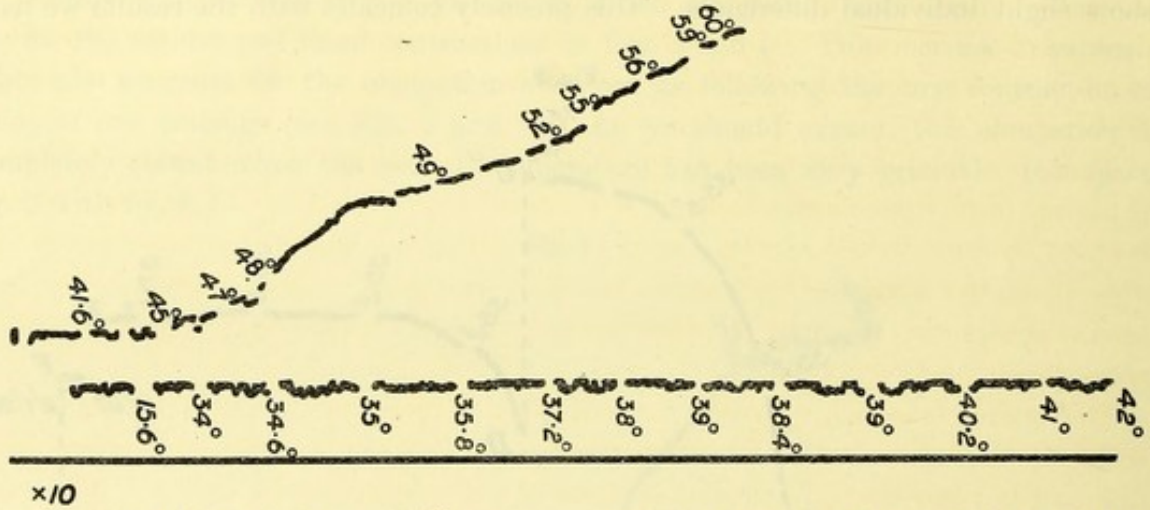


Exp. 59*a*.—Frog's sartorius. The breaks on the record represent intervals of 10 mins. Total duration, 2 hrs. 17 mins. This experiment, taken with Exp. 59*b*, shows that the whole of the first contraction can be brought about at 35° C., though it requires some time. There is no recovery on allowing the muscle to stand 24 hrs. At C, the muscle was passively stretched to D. At E, the experiment was broken off for 24 hrs., when the muscle was found to have elongated to F. It was then passively stretched to G, and the tracing, fig. 9, taken.

obtained with frog's muscle when experimenting to determine the lowest temperature at which heat-contraction can be produced. We show two tracings illustrating this. In the first, fig. 7, the muscle had been previously heated for 65 mins. to 34° C. At the end of that time it still gave a slight contraction on tetanisation, though it had become opaque. The proteid had not been completely precipitated at this temperature, and a small contraction occurred when the temperature rose above 34° C., and simultaneously an increase in the opacity was observed. In the latter part of Exp. 59 (fig. 9) the first contraction is completely cut out, the muscle having been kept at

about 35° C. for more than 2 hours. In these two tracings we would call attention to the marked contractions caused by the later proteid coagulations. We have confirmed these results in several other experiments. The muscle invariably behaves as if the proteid coagulation were the sole cause of the heat-contraction. If exposed to a temperature at which soluble myogen-fibrin coagulates quickly the contraction is

Fig. 9.



Exp. 59*b*.—Completion of the preceding experiment after 24 hrs. interval. The muscle during this time was kept in dilute blood at 10° C. The interruptions on the tracing record intervals of 10 mins. The upper tracing follows on the lower one. The tracings are to be read from left to right. No contraction occurs till a temperature of 47° C. is reached; a second is recorded at 55° C.

rapid and conversely. We have, moreover, found that the final loss of excitability coincides with the completion of the first heat-contraction. These experiments enable us to explain satisfactorily the results GOTSCHLICH obtained on exposing muscles to conditions producing partial heat-contraction. He thereby only caused partial coagulation of the soluble myogen-fibrin, and thus the muscle retained its normal properties to a corresponding degree.

Are Heat-rigor and Rigor-mortis Identical?

We have in the next place to consider KÜHNE's view that the first heat-contraction is in reality rigor-mortis, the onset of which has been accelerated by the high temperature. The constancy of the temperature at which this contraction occurs is greatly against this view, for it is highly improbable that a contraction which takes many minutes, even hours, to occur at temperatures just below 30° C. should have precisely the same physical causation as one which commences instantly at a temperature only 4 degrees higher. On the other hand, the ascription of this contraction to the heat-coagulation of soluble myogen-fibrin entirely does away with

our difficulties in this direction. We have already seen that KÜHNE considered the opacity produced in muscle exposed for a time to a temperature of 45° or 46° C. to be due to the production of a heat-coagulum, so that, at any rate for the second contraction, we are forced to the conclusion that the cause is the formation of a heat-coagulum. Another fact which is against the rigor-mortis view lies in the marked difference in time required to bring about complete heat-contraction when the muscle is exposed to the two temperatures of 34°·5 C. and 38° C. This difference in time is immediately explicable by the known influence of these two temperatures upon solutions of soluble myogen-fibrin; whereas, if rigor-mortis were the process at work, it would simply stand out as a curious fact without any immediate and simple explanation.

There is a further difference of great significance which is, that where a muscle is passing into rigor-mortis there is a previous loss of excitability before any contraction occurs, whereas, in the case of heat-contraction, excitability may persist for some time after a marked contraction has been produced. Loss of excitability from heat appears to progress synchronously with the increase of opacity, which accompanies heat-contraction.

That a muscle, which has been exposed to a temperature of 34°·5 C., for a time sufficient to produce marked heat-contraction, is in quite a different physical state from one in rigor-mortis, is proved by a variety of circumstances.

(1.) It is much more rigid than a muscle in rigor-mortis. A thin sartorius may be held by one end in a horizontal position, with its flat surfaces presenting upwards and downwards without the slightest tendency to bend.

(2.) It is very opaque, quite white, and without any sign of translucency. A fresh, carefully-prepared sartorius exhibits a most beautiful iridescence when held up to the light, and it is easy to observe a change in this produced by quite a short stay in a fluid at a temperature sufficient to cause heat-contraction.

(3.) The opacity produced during rigor-mortis is of quite a different character. It has more the appearance of finely-ground glass than the dense white opacity of a muscle that has been heated. Moreover, in rigor-mortis the distribution of the opacity is in patches, and it is very rare to find a muscle that does not show this patchy appearance, even after it has been kept for days.

(4.) The behaviour of these muscles to dilute hydrochloric acid (0·2 per cent.) is quite different to that observed with fresh or with rigor-mortis muscles. There is produced a distinct lessening of the opacity, which is readily observed at the thin edges; but even after prolonged action there still persists a good deal of opacity, much more so than remains in the case of rigor-mortis or fresh muscles.

(5.) A muscle that has passed into rigor-mortis, when treated as in our experiments, will give heat-contractions, though, as we shall show in a paper we hope to publish shortly, the form of those contractions is greatly affected by the stage which the muscle has reached in rigor-mortis.

In connection with the production of opacity when a muscle is heated, we must point out that as soon as any contraction takes place some opacity is to be observed, but the amount of opacity by no means runs parallel to the extent of the contraction. If the muscle be examined as soon as marked contraction has occurred, only a slight degree of opacity can be detected; whereas, when the full extent of the heat-contraction at 35° C. has been brought about, the opacity is most decided. The first precipitation of proteid apparently produces the greatest shortening. v. FÜRTH showed that at 30° C. myogen was converted fairly rapidly into soluble myogen-fibrin, and we are inclined to account for some of the opacity at the end of the first heat-contraction as being due to a further formation of soluble myogen-fibrin and its subsequent coagulation. This supposition is confirmed in that the third contraction, which we consider to be due to coagulation of myogen, is never well marked, and this is especially the case when the first contraction has been brought about slowly. The amount of contraction at 56° C. is small, even when the muscle is passively extended just before that temperature is reached.

Does a Muscle Show any Recovery from Heat-rigor?

We may now turn our attention to the question of the amount of recovery which has been observed after a muscle has been caused to contract by heat. GOTSCHLICH* apparently regards it as fairly complete, but we have never been able to observe the return of so large a proportion of the original excitability as he appears to have found in muscle which has been exposed to 35°·5 C. We have found that if the temperature be kept at the point at which it just causes contraction, the muscle remains excitable for a considerable time, but that the amount of possible contraction, as measured after a return to a lower temperature, gradually diminishes. If the experiment be broken off at any time before excitability disappears, the amount of contraction with maximum induced shocks does increase, but never in any degree attains to that given by the muscle before heating. In this connection some experiments recorded by SCHMULEWITSCH† are of considerable interest. In one experiment (No. 23) a gastrocnemius was loaded with a tension of 50 grams, and the heights of contraction with maximal induction shocks recorded. It was immersed in a bath of normal saline solution at 16° C., a twitch recorded, then heated quickly to 36° C. and another twitch, very much smaller, recorded. It was then rapidly cooled to 15° C.

* See his remarks in his first paper, p. 133.

† 'Mediz. Jahrbücher,' vol. 15, p. 13, 1868; Wien.

and again stimulated. This warming and cooling was repeated three times. On examining his records we noted that after each warming the height of contraction was markedly diminished, showing that recovery was far from complete, a conclusion confirmed by several other experiments of the same nature.

The best explanation of these various results seems to be that, on the one hand, soluble myogen-fibrin is not rapidly precipitated at a temperature of 34°·5 C., and, on the other hand, that the fact that some of it is coagulated in a muscle does not prevent that muscle from contracting when stimulated, though the amount of the contraction becomes distinctly restricted. The presence of soluble myogen-fibrin appears to be a necessary condition of the contraction of frog's muscle, for we have always obtained a heat-contraction at 35° C. in those cases where a small amount of irritability persisted after the previous application of heat, which was sufficient to produce incomplete heat-contraction.

Heat-contraction is a process quite distinct from the ordinary Contraction of Muscle.

That heat-contraction and the normal contraction of muscle are quite distinct processes, is well brought out by studying the effect of heat upon a fatigued muscle. We found that a completely fatigued muscle, when heated, gave contractions quite corresponding to those yielded by a fresh muscle. The total amount of heat-contraction as a rule exceeded that obtained by tetanising a muscle with maximal stimuli. If, moreover, a muscle be gradually heated whilst it is being tetanised, though fatigue very rapidly sets in as the temperature rises, and in spite of the rapid elongation thus occurring, as the temperature reaches 35° C. heat-contraction takes place in the usual manner.

As further confirmation of the complete difference between the two processes, we found that muscles which had lost their excitability to electrical, chemical, or thermal stimuli gave heat-contractions in no way distinguishable from those given by excitable muscles. Curarised muscles also give the same results as non-curarised.

The Cause of the Shortening.

In considering the mode in which the production of a heat-coagulum could determine a contraction, we have to consider two possibilities. Either the physical coagulation is simultaneously accompanied by a chemical change similar in nature to that underlying a normal contraction, or the proteid coagulation may set up a fresh series of physical conditions which in themselves are sufficient to determine a contraction. We shall not be in a satisfactory position to fully answer this question until we know more of the structure of a muscle from the mechanical point of view. There is, however, a method of producing proteid precipitation in a muscle which may aid in throwing light upon the process. KÜHNE* observed that a solution of

* 'Myologische Untersuchungen,' p. 130.

potassium sulphocyanide caused a strong contraction of a muscle when applied directly to it, and that this contraction was accompanied by a precipitation of the proteids as evidenced by the production of opacity.

We have employed this salt and confirmed KÜHNE's observation. The muscle shortens greatly on being immersed in this solution, and becomes very opaque. It presents exactly the appearance of a muscle which has been heated to 40° C. If, now, that same muscle be gradually heated, as in our experiments, we find that practically no heat-contractions occur, and such as do occur are probably due to quite small quantities of proteid still uncoagulated.

Ammonium sulphocyanide we found to exert no effect upon the production of heat contractions. Thus the action of potassium sulphocyanide favours the view that heat-contraction is caused by the purely physical precipitation of a proteid by heat. Other facts which also point to the same conclusion are: (1) The heat-contraction produced in rigor-mortis muscle; and (2) The contractions produced in fresh muscle at about 47° C. and 58° C. It is, moreover, probable that the precipitation of the proteids in one insoluble form during rigor-mortis is the sole physical cause forming the basis of that contraction.

On the other view, viz., that the physical is accompanied by a chemical change which latter is the true cause of the actual contraction, we have the series of observations with regard to the production of an acid reaction during heat-contraction. This change was first observed by DU BOIS REYMOND, and confirmed by KÜHNE* in many particulars, though he notes that a muscle in heat-rigor need not show an acid reaction. He moreover found that with the heat-coagulation of frog's muscle-plasma the reaction might or might not become acid. In our experiments we have found that commonly the muscle gives an acid reaction when heat-rigidity is well established, though cases in which an alkaline reaction is found are far from rare. In one case in which we examined the reaction of frog's muscle-plasma dissolved in 0·75 per cent. NaCl as it was gradually heated, we were quite unable to determine any change whatever in its reaction to litmus.

In conclusion, we would point out—

(1.) That our experiments lend strong support to the results obtained by v. FÜRTH as to the proteids of muscle.

(2.) That they tend to show that the different proteids are actually present as such in living muscle. That when we are examining a saline extract of muscle we are examining proteids actually present in living muscle, not disintegration products of more complex bodies.

(3.) That they offer valuable evidence in a positive direction as to the much-vexed question of fractional heat-coagulation.

* *Loc. cit.*, p. 184.