ON THE TIME-RELATIONS OF THE EXCITATORY PROCESS IN THE VENTRICLE OF THE HEART OF THE FROG.

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INTRODUCTION.

THE purpose of the present research is to study the order and succession of the phenomena which accompany or are associated with the excitatory state in the ventricle of the heart of the frog. It is intended to be introductory to further investigations of the excitatory process in plants and animals.

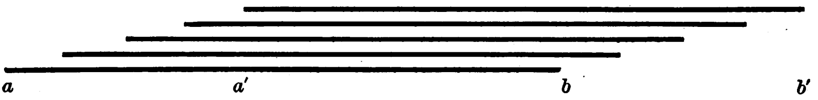
As regards voluntary muscle it has been established that each single contraction, whether it occurs by itself or forms part of a tetanic series, is preceded in each structural element by a state of excitation marked by diminished excitability and electrical disturbance, and that the relation between the invisible molecular change in the living substance of which these are the signs, and the succeeding changes of form, are so intimate that the former must certainly be regarded as the indispensable antecedent of the other. That this is so, has been learnt by investigation of the times (as measured from the moment of excitation) at which each several change (whether of excitability or of electrical or mechanical condition) begins, culminates, and ends. The guiding principles to be observed in these investigations have been laid down by our great leaders, Helmholtz, Donders, du Bois-Reymond, and the methods to be followed have been exemplified in their researches, and fruitfully applied, in various directions by their successors. As regards the subject now before us we owe most to the labours of Engelmann, whose researches on the propagation of the wave of contraction in the ventricle, on the electromotive properties of the resting heart, and on the electrical changes which immediately follow excitation, leave little more to be done. The facts he has observed so laboriously and recorded with such exactitude, serve as the starting point for the experimental work of which we now present the results. Before doing so, however, the reader must be put in possession of the existing state of knowledge of the subject.

I. *The time-relations of the Ventricular Contraction.*

By the following simple and conclusive experiment Engelmann has shown that the change by which each muscular element of the heart substance passes from the state of relaxation into that of contraction, is propagated from element to element with equal facility in every direction. The ventricle of a frog just killed is cut into bits in such a way that each bit, the end one excepted, is united with its neighbour on either side by a bridge of muscular substance less than a millimeter wide. The ventricle is then left for an hour or so in the moist chamber until the living tissue, of which the excitability is at first much impaired, has recovered from the immediate effects of the injury. It is then observed that, if the bits have been so cut that one of the terminal ones is united with the beating auricle and the other forms the apex, the strip pulsates rhythmically, the contraction beginning from the auricle and extending, after the manner of the peristaltic contraction of the intestine, from link to link of the chain of living substance. If the preparation is severed from the auricle there are no spontaneous pulsations, but contraction can be induced in any part of it by the passing of an induction shock, and it passes along the chain with equal facility and at equal rate in either direction. In repeating this experiment Engelmann found that the result was the same whatever the direction of the snips. So that in respect of propagation every part of the ventricular substance would appear to be equally endowed: there are no special channels of conduction.

In the chain of snips of contractile tissue, Engelmann found that the rate of propagation of the wave of contraction was sometimes so slow that it could be watched by the eye. In the most favourable cases it did not exceed twenty millimeters per second, but in the living heart he believes that it is undoubtedly faster, for an injury of which the first effect is to abolish the conductivity of the tissue, can scarcely be supposed to leave it eventually normal. Thus even if it be admitted that in the entire ventricle the rate of propagation is no greater than twenty millimeters per second, it is clear that in a ventricle of ordinary size the time occupied in the spread of the contractile change from the base to the whole of the living substance of the ventricle could not exceed a fifth of a second.

If it were possible to determine how long each individual element of the contractile substance remains in action after each excitation, and to deduct from this period the time occupied in the spread of the contractile change from its centre or centres of origin to the whole organ, the difference would express the duration of the systolic contraction. And conversely, if it were possible to determine how long the whole ventricle is in contraction and also the time required in the normal ventricle for the propagation of the contractile change from base to apex, its duration in each individual element could be accurately determined. That this is so, will be at once seen from the diagram. If the horizontal lines be understood to represent the periods during which as many individual contractile elements at different distances from the auriculo-ventricular groove are in action, it is evident that the time during which the whole organ is in contraction corresponds to the distance *a′ b*, that is to the period of action of each individual fibre *minus* the period of spread.



To the best of our knowledge the only data from which the duration of the ventricular systole can be learnt are the very scanty ones which are contained in the well-known research of E. Cyon on the influence of temperature on the heart[1]. This paper does not, indeed, contain any measurements, but it is stated generally that between 0° C. and 18° C. (see p. 110) the sum of the periods occupied by the heart in active contraction in a unit of time is constant and independent of the frequency of the beats. What this sum is, is not stated, but from the facsimiles of the graphic records it may be deduced that it amounts to about 12″ in every minute: consequently, as at 7° C. there are about eight beats per minute, and at 14° C. about twice as many, the duration of the systole must be about one and a half seconds at the former temperature, and three quarters of a second at the latter. If therefore we assume that between these temperatures the ventricle occupies a whole second in contraction, and that one-tenth of a second is lost in propagation, each individual contractile element must be at least eleven-tenths in action. But for our present purpose such conjectural estimates are of no value. To determine the time-relation between the excitatory and contractile change in the ventricle, it is necessary

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[1] "Ueber den Einfluss der Temperaturänderungen auf Zahl, Dauer, und Stärke der Herzschläge," von Dr E. Cyon. Ludwig's *Arbeiten*, 1866, p. 77.

to measure their duration in the same heart and if not at the same time, under the same conditions.

In 1856, **Kölliker** and H. **Müller**[1] made the important discovery that the "negative variation" can be observed in the beating heart. They found that when the ventricle, after having been cut off on the auricular side of the groove, was placed on the electrodes of the multiplier with the cut surface against one pad and the apex against the other, the needle swung one way when the heart was at rest, the opposite way during the systole. They then proceeded to apply to the pulsating heart the nerve of a rheoscopic limb of a frog. It was found that if very excitable preparations were used, whether the nerve was laid across the ventricle or in the direction of its length[2], the muscles of the limb contracted "a scarcely perceptible time before the systole of the ventricle," and further, that in certain cases, a second feebler twitch was observed at the beginning of the diastole, which was considered by the authors as dependent on a positive variation of the muscle current of the ventricle coincident with its relaxation.

The discovery remained fruitless until 1872, when **Donders** published the paper[3] on "secondary contraction from the heart," which served as the basis for all that has been done since. **Donders** confirmed the observations of **Kölliker** and **Müller**, and by the skilful application of the graphic method, determined the time-relations of the phenomena with the greatest accuracy. He found that in addition to the systolic twitch of the rheoscopic limb, its muscles contract whenever the nerve is brought into contact with the surface of the heart, and in many cases also when it is withdrawn—observing at the same time that the make and break contractions were not always present, and that their occurrence appeared to be in relation with the degree in which the surface of the heart had been exposed to external influences. Well aware of the bearing of his experimental results on the "pre-existence question," he with admirable caution, refrained from even putting into words the inference suggested by them, namely,

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[1] "Nachweis der negativen Schwankung des Muskelstroms am natürlich sich contrahirenden Muskel." *Verhandlungen der physicalisch-medicinischen Gesellschaft in Würzburg,* Band VI. p. 528.

[2] In the first experiment the nerve was applied to a cut and to a natural surface. Subsequently it was found that this was of no importance. The nerve was placed "quer über die Mitte der vorderen Fläche der Kammer, so dass er nach dem linken Herzrande anlag."

[3] "Rustende spierstroom en secundaire contractie, uitgaande van het hart." *Onderz. physiol. lab. Utrecht.* Derde reeks I. 1872, p. 256.

that (to quote from Engelmann[1]) "the surface of the uninjured heart exhibits no differences of electric tension." The investigation of the electromotive phenomena of the ventricle was next taken up by Engelmann in 1873, who discontinued the use of the physiological rheoscope and had recourse to the reflecting galvanometer with compensation. In this way the truth of the inference we have quoted was established by the most carefully conducted measurements, into the details of which it is unnecessary to enter, considering that the all-important fact which was established by them—the electrical equality of the surface of the heart—does not admit of being disputed.

As regards the duration and other time-relations of the excitatory electrical change or variation[2] of the heart ventricle, the earliest experiments were made by Engelmann in 1874 (see Engelmann, 'Ueber das Verhalten des thätigen Herzens." Pflüger's *Archiv*, Band XVII. p. 68). They were however not published until much later (after the communication of our first paper to the Royal Society). The first published research on the subject was by Dr Marchand of Halle (Marchand, "Beiträge zur Kenntniss der Reizwelle und Contractionswelle des Herzmuskels." Pflüger's *Archiv*, Band XV. p. 511). As these researches have a direct bearing on questions to be hereafter considered, they must be discussed at some length.

Dr Marchand's mode of observation was to excite the ventricle-apex preparation, after connecting it with the galvanometric circuit by contacts at its apex and base, by passing induction shocks in the neighbourhood, first of the one then of the other electrode, compensating whatever difference of potential might manifest itself between the two contacts, in the usual way. A Bernstein's differential rheotome was introduced into the galvanometric circuit, by means of which that circuit could be closed for a limited period of time (usually one-tenth of a second) at any required moment after excitation. In this way the course of the variation (*Verlauf der Reizwelle*) was investigated in each successive phase of its duration. In the tables which accompany the paper Dr Marchand has given the readings of the galvanometer and the rate of revolution of the rheotome, and the readings of its scale, leaving it to the reader to

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[1] "De electromotorische verschijnselen der spierzelfstandigheid van het hart." *Onderzoekingen*, &c. Derde reeks III. p. 106.

[2] We have found it convenient to continue to use the term "variation" to denote the excitatory electrical change, notwithstanding the misconception on which its first employment was founded.

translate these data into time. The general character of the results obtained may be judged of by the following table, which represents No. XVII., an observation selected by the author as typical. (See p. 527.)

Readings of the scale[1] of Bernstein's rheotome	3	1	97	94	90	80
Time after excitation of opening of galvanometer circuit	0″·03	0·05	0·12	0·16	0·22	0·37
Deflection of galvanometer	0	− 1	− 4·5	− 1·5	+ 2	+ 1
Readings of the scale of Bernstein's rheotome	65	50	40	30	20	10
Time after excitation of opening of galvanometer circuit	0·60	0·72	0·97	1·07	1·27	1·42
Deflection of galvanometer	+ 1	+ 2·5	+ 4	+ 3	+ 1	+ 0·5

The group of observations, of which No. XVII. is taken as an example, agree with each other in this respect, that in every instance the variation consists of two phases, in the first of which the contact nearest to the seat of excitation becomes negative to the more remote one. As regards the time at which the transition occurs, that is, the relative durations of the two phases, there are great discrepancies. The galvanometer readings are moreover very small and irregular. In another smaller group of which No. XXIII. may serve as a specimen, the second phase is wanting, the excited region remaining throughout negative to the other led-off surface. From these data Dr Marchand concludes (1) That when the ventricle-apex preparation is led off at base and apex, the excitatory phenomena (the *Reizwelle*) vary according to the seat of excitation in such a way that "if the preparation is excited at the apex, the first deflections indicate an ascending current, the subsequent ones a descending, and that if the excitation is at the base, the direction is reversed" (p. 530). This reversal, however, does not always occur (p. 532). (2) That the duration of the variation usually exceeds a second, and is always more than half a second—and this whether reversal takes place or not. Thus in

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[1] Each division of the scale corresponds to $\frac{1}{100}$ revolution; the times given in the second line of the table have been calculated by us from the reading in the first line. The "closing time" of the rheotome was in Exp. XVII. 0″·08, and the duration of a revolution 1″·5.

Experiment IV. to which Dr Marchand refers as an example of a variation of one phase, it lasted 1″·4. (3) That the wave of excitation precedes the wave of contraction, the former manifesting itself three or four-hundredths of a second after excitation, the latter not until a fifth or sixth of a second.

The author believes that the two phases of the variation (or to use his own term, of the *Doppelschwankung*) are the expression of the "progress of a wave of negative tension from the seat of excitation," but he leaves the question of the rate of propagation of the wave and the duration of negativity at any given point over which it passes undetermined. On this latter point he says: "The two phases of the excitatory variation cannot be isolated from each other, inasmuch as they partially cover each other. This would only be possible if the preparation were of such a length that the variation should be completely over at one end (*i. e.* at one contact) before it began at the other. As, however, the curve which is the expression of the successive deflections observed in the successive stages of a variation always exhibits two maxima on opposite sides with an intervening point of indifference, it is really the sum of two curves of which the true length and true maxima are unknown, and it is not possible to determine at what time the maximum is attained and when the whole variation terminates. To arrive at these results, the curves might be used which represent simple variations (*i. e.* not *Doppelschwankungen*). But in doing so it must be borne in mind that each such curve probably also contains another latent."

Here the author contents himself with bringing the reader face to face with phenomena which he admits himself unable to explain. From another part of the paper we learn that the rate of propagation of the contraction wave is more than 100 millimeters per second. If therefore, as the author on good ground believes, the excitation wave precedes the contraction wave, it must have the same rate of propagation. Hence in the case of the ventricle, it would arrive at the base four-hundredths of a second after starting from the apex. This being so, how does the propagation of "a wave of negative tension" explain the fact that the "transition," that is the indifference point between the first and second phase, occurs according to Experiment XVII., more than half a second after excitation? Again, how are we helped by it to understand the fact observed in Experiment IV., that the apex remains persistently negative during the whole variation, not attaining its maximum until 1·3 seconds after excitation? Both facts may admit of explanation, but they receive none from Dr Marchand.

We have now to return to the more recently published researches of Prof. Engelmann already referred to, the importance and value of which makes it necessary to give as complete an account of them as our space will allow. As regards the method employed it is only necessary to say that ventricles cut off below the auriculo-ventricular furrow were used, and that the observations were made with the aid of Bernstein's rheotome.

In 47 out of 78 preparations, in each of which the ventricle was excited at a point near to one of the leading-off electrodes, remote from the other, it was found that "the nearer of the two became, on excitation, first negative then positive to the more remote." In 31 cases the second effect was wanting. The result was the same whether the contacts were at base and apex or on opposite sides of the ventricle, whence it was concluded that "jeder Theil des Kammermuskels während der Erregung vorübergehend negativ electromotorisch wirksam wird, und dass diese Negativität sich vom Ort der Reizung nach allen Richtungen durch die Kammer fortpflanzt" (p. 78).

In the next section the results of actual observations are given in the form of curves, of which the abscissae represent the times after excitation at which the observations were made and the ordinates of the deflections observed. The first of these curves is the mean result of 33 experiments, in all of which there was "*Doppelschwankung*," *i.e.* the variation consisted of two phases as above described. It shows that in these experiments (in which the ventricle was excited at the apex and led off by two contacts, of which one was near the apex and at a distance of two millimeters from the seat of excitation, and the other at the base and three millimeters from its fellow) the two leading-off contacts were isoelectrical until 0''·06 after excitation. From that moment the negativity of the nearer contact rapidly increased, culminating at 0''·16, and then as suddenly declined and was succeeded by positivity which attained its maximum at 0''·3 and had completely subsided by half a second after excitation. Another curve relating to ten observations in which the distance from the seat of excitation to the nearer contact was very short, and in which consequently the variation began immediately after the excitation, exhibited the same phases and the same sudden reversal of the direction of the electromotive force, due "no doubt to the arrival of the negative wave at the second or more remote of the two electrodes" (p. 79). As however it was always observed that the positive effect was much smaller than the negative, it seemed necessary to assume that the "negative wave reaches the second electrode before it has attained its maximum at the first" (p. 78).

The total duration (Gesammtdauer) of the electrical effect of excitation is estimated at 0″·43 when the variation consists of two phases, but only 0″·21 when it consists of a negative phase only; and hence the author concludes that the local duration (örtliche Dauer) of negativity does not exceed 0″·2.

The rate of propagation of the negative wave was not found by Engelmann to be in any instance as great as 50 millimeters per second. In general it was only 20 mm. per second, but in two perfectly fresh preparations it was above 40 mm. (p. 91). The mode of observation was as follows:—the interval of time between excitation and the beginning of the variation was measured in a sufficient number of cases in which the distance from the seat of excitation to the nearest leading-off contact was known. By then deducting the shorter from the longer distances, and writing each of the differences over the difference in time corresponding to it, fractions were obtained which of course expressed the rate (number of millims. per second) at which the effect would have passed from the nearer to the further contact. Another estimate of the rate of propagation was based on the assumption that it corresponds to the ratio of the distance between the leading-off electrodes to the time-interval between the negative and positive maxima of the variation—it being supposed that the interval would express the time occupied in the progress of the wave from the one contact to the other[1].

I. THE EXCITATORY VARIATION IN THE UNINJURED STANNIUS' PREPARATION.

An account of the construction of the rheotome and the mode of using it for the purpose of investigating, during successive short intervals of time, the variations of intensity and direction of currents passing through it, will be found in an Appendix at the end of this paper. For the present purpose the galvanometric circuit, in which the rheotome is interpolated, has the arrangement shown in the figure.

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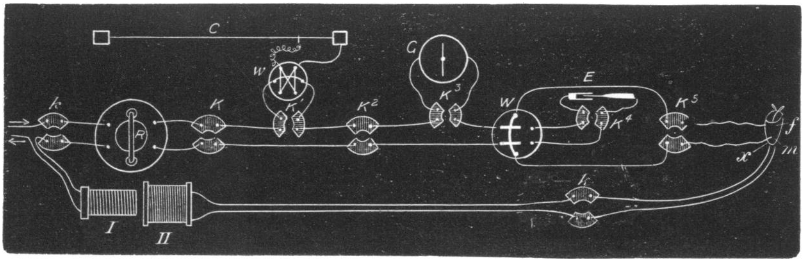
[1] Prof. Engelmann's results as to the "refractory period" and as to the electromotive force of the variation will be referred to under their proper heads.



When the keys *K*, K^1, K^2, K^3 and K^5 are open, and the switch *W* is in the position shown, any current between *f* and *m* passes through the galvanometer *G*, the compensator *C*, and the rheotome *R*. Only one of the four pairs of mercury pools of the rheotome is used, so that the circuit is closed once in each revolution. The binding screws for the outer pools of the rheotome (only one of which contains mercury) are connected with the key *k*, the wire from one of the blocks of which passes directly to one pole of a battery of two Groves. The other wire leads to the opposite pole first through the primary coil of the induction apparatus, and secondly through a mercurial contact (not shown in the diagram) which, so long as no current is passing through the primary coil, remains closed so as to short-circuit the terminals of the secondary coil, but is opened by the action of an electro-magnet whenever the primary current is closed. As however this does not happen until the closing induction current is over, this current is without effect on the preparation. The key k' in the secondary circuit is of such construction that it remains closed when not held open by the observer. The first step in every observation is to close the key *K* and adjust the slider of the compensator, having first turned the reverser *w* in the proper direction, so that the needle is at zero. The rheotome having been set by a table previously calculated for the period after excitation to be investigated, and allowed to revolve, the key *K* is opened, when if all is in order, the needle will be motionless. The key k' is then opened, and closed again the moment that the click of the electro-magnetic lever is heard. As it is of great advantage to possess a general knowledge of the character of the variation before beginning a rheotome experiment, a preliminary observation should always be made with the capillary electrometer (*E*). For this purpose the key *K* is closed and the switch *W* turned to the right. The galvanometer used is one made by Elliott Bros. It has a resistance of

5244 ohms, and when adjusted for the greatest attainable sensibility, $\frac{1}{1000}$ Daniell gives with a resistance in the circuit of 13,000,000,000 ohms, a deflection of one degree of the scale. We find that a sensibility which is about a third of this is suitable for our purpose. We adjust for a deflection of 350 divisions for an electromotive force of $\frac{1}{1000}$ Daniell and resistance of 10,000 ohms in addition to that of the galvanometer.

The electrodes have the following construction:—each consists of a U-shaped tube containing saturated solution of zinc sulphate, about six millims. in diameter, which is supported by a brass holder. In one limb of the tube is plunged a zinc wire which is hammered out into an oar-shaped end, and the surface so obtained is carefully polished and amalgamated. The other end of the wire is held by a clip which forms part of the holder. The other limb of the U contains a short bit of tube filled with kaolin moistened with solution of zinc sulphate. The top of this tube projects 3 or 4 millimeters from the tube which contains it. On this projecting part a mass of kaolin moistened with three quarters per cent. solution of salt, shaped like the head of a bird, is supported. When the electrode is in use, this is in contact with the surface of the preparation by the tip of the beak. These electrodes have a resistance of about 8000 ohms.

In our earlier experiments the preparation was so placed on a support of cork, the surface of which was covered with wax mass, that the ventral surface of the ventricle was exposed. The preparation was irrigated with a mixture of defibrinated frog's blood and 0·75 per cent. solution of chloride of sodium. In the first experiment the leading-off electrodes and the exciting wires (*x*) were in line, *x* being at the apex of the ventricle. One of the leading-off electrodes (*m*) was at a distance of one and a half millims. from *x*, in the direction of the base of the ventricle, the other (*f*) one and a half further in the same direction. The distance of the secondary coil from the primary was six centims.

The character of the variation was first investigated with the aid of the capillary electrometer. As so observed, the excitatory effect consisted in a movement of the mercury column which immediately followed the excitation and was in a direction indicating that the contact *m* became negative. This was succeeded, after an interval, by a movement in the opposite direction. The extent of each movement was about three degrees of the electrometer scale.

[1] The results of the observations of the rheotome, of which the rate of revolution was one in twelve seconds, were as follows:—When the

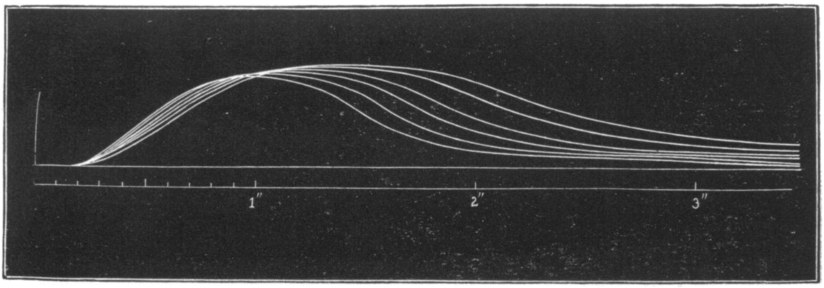
period of closure of the galvanometer circuit ended at 0″·05 after excitation, a slight negative deflection was just visible: when it ended at 0″·08 the deflection was −10 divisions of the galvanometer scale: at 0″·11, −7: at 0″·14, −trace. Hence, as the closing time lasted 0″·06, the duration of the negative phase was about $\frac{3}{100}''$. This was followed by a period of 1″·32 during which the surface of the heart remained isoelectrical. From 1″·4 after excitation to 1″·7 it was positive, *i.e.* the apex became positive to the base. The contraction of the ventricle was then recorded graphically. Its duration was found to be 1″·11. Relaxation had fully begun between 1″·36 and 1″·56 after excitation.

[2] In a second heart, the initial phase began at 0″·04 and lasted until 0″·35, after which there was a period of equipotentiality of one second, the terminal phase beginning at 1″·3 and lasting until 1″·7 after excitation. In these two experiments the positive and negative deflections were of nearly equal extent. The period of closure was 0″·06 throughout, the temperature 16°·5 C. to 17° C.

The observations just related exemplify the phenomena which present themselves in the uninjured ventricle, when special precautions are not employed to counteract the irregularities due to external influences.

On repeating the last observation, using the same preparation, it was found that the time at which the terminal phase began was later; and this was apparently due to the cooling of the room and consequently of the heart. In order to secure uniformity of temperature in future observations, the following arrangement for supporting the preparation was adopted. A cylindrical brass box, eight centimeters long by two in diameter, rests by its lower end on a wide support. Near its lower end it communicates by a long flexible tube with a reservoir of water, the temperature of which can be varied at will, and which flows out by a tube at the upper end into a receptacle. The upper end of the cylinder presents a hollow surface corresponding in form to that of the heart, so that the organ is in proximity with as large a surface of metal as possible, contact between the metal and the preparation being prevented by a coating of lacquer. A few preliminary trials with this contrivance assured us that by means of it we could control the temperature so as to obviate the irregularities previously observed.

From Experiment [1] and others similar, we had learnt that there is a close agreement between the duration of the systole of the ventricle and that of the variation, of which we regard the 'terminal phase' as the final act. To determine how far this apparent coincidence of the terminal phase with the beginning of the relaxation of the ventricle was constant, the first step was to obtain better information than previously existed as to the influence of changes of temperature on the duration of the ventricular contraction. For this purpose all that was necessary was to measure the duration of the systole in a Stannius' preparation, as excited by a single induction shock. The results so obtained will be best understood by an inspection of the curves, the facsimiles of which follow.



By comparison of these curves it will be seen that in the inhibited frog heart, the duration of the ventricular contraction varies according to temperature in such a way that between 12° C. and 18° C., each degree corresponds approximately to a tenth of a second of duration. This statement having been found to be applicable to all the hearts examined (specimens of *Rana esculenta* which had been in the laboratory all the winter but were in a healthy state) we were in a position to examine the relation between the phenomena. If it were found that the duration of the variation, *i.e.* of the period intervening between the initial phase and the terminal phase, also diminished between 12° and 18° by one tenth of a second for every degree of temperature, it might be considered as proved that the electrical change and the muscular contraction were correlative phenomena. The length of this period was determined in four Stannius' preparations which were excited and led off in exactly the same way as in previous experiments with this difference, that in each case two measurements were made, the first at a temperature of 12°, the second at 17°. In accordance with what has been said it was to be anticipated that the terminal phase would occur at the higher temperature about half a second sooner than at the lower. The results were as follows:—

[3]	Greatest negative deflection.	Greatest positive deflection.
Preparation I.	″ ″	″ ″
At 12° C.	from 0·1 to 0·2	from 1·9 to 2·0
At 17° C.	„ 0·1 „ 0·2	„ 1·5 „ 1·6
Preparation II.		
At 12° C.	„ 0·1 „ 0·2	„ 2·0 „ 2·1
At 17° C.	„ 0·1 „ 0·3	„ 1·6 „ 1·7
Preparation III.		
At 12° C.	„ 0·1 „ 0·2	„ 2·1 „ 2·2
At 17° C.	„ 0·1 „ 0·2	„ 1·6 „ 1·7
Preparation IV.		
At 12° C.	„ 0·1 „ 0·2	„ 1·9 „ 2·0
At 17° C.	„ 0·1 „ 0·2	„ 1·4 „ 1·5

The table shows that in the first two cases the maximum of the positive phase occurred about 0″·4 sooner at 17° than at 12°, and in the other two 0″·5 sooner, giving a mean of 0″·45. The following table gives the rheotome readings[1] of preparation II.

[4]	0″·1	0″·2	0″·3	0″·4	0″·5	0″·6	0″·7	0″·8	0″·9	1″·0	1″·1	1″·2
At 12°.	−12	−20	−10	0	0	0	0	0	0	0	0	0
At 17°.	−10	−15	0	0	0	0	0	0	0	0	0	0

	1″·3	1″·4	1″·5	1″·6	1″·7	1″·8	1″·9	2″·0	2″·1	2″·2	2″·3	2″·4
At 12°.	0	0	0	0	0	0	0	0	0	+3	+5	0
At 17°.	0	0	0	+1	+2	+3	+2	0	0	0	0	0

So far therefore as these observations go it is evident that the duration of the variation and that of the contraction are similarly influenced by change of temperature.

All experiments which have been made since the adoption of the arrangement above described for securing uniformity of temperature during the period of observation, have shown that the normal character of the variation is in conformity with [1], that is to say, that when the seat of excitation is nearer to one of the leading-off contacts than to the other, the former becomes negative to the latter at the beginning (initial phase), and positive at the end (terminal phase), and that during the relatively long intervening period, the two contacts are nearly equipotential (isoelectrical interval).

The excitatory process in the normal ventricle preparation presents characters which correspond in the main with those observed in the inhibited entire heart. As regards the duration of the

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[1] That these readings are small as compared with others given subsequently, is due to the circumstance that in the earlier experiments finely pointed electrodes were used.

systole, our observations show that its duration is the same for the same temperature. Thus at 12° C. the duration was found to be 2″·1, at 18°, 1″·6, giving as before a difference of 0″·5 for 6° C. difference of temperature. It was also found that when the same heart was measured at the same temperature in the inhibited state and again as a ventricle apex preparation, the time was the same. Before observing the variation it is necessary to allow time for the decline of the immediate effects of the section. Immediately after the ventricle apex has been prepared, the cut surface is of course negative to the natural surface, but, as will be seen in a subsequent paragraph, the difference rapidly diminishes. The variation is also modified in the manner to be described in a future section, but eventually recovers its natural characters. The time required to accomplish this is from half an hour to an hour, after which the variation observed when the preparation is led off in the usual manner differs but little from that of the uninjured inhibited heart.

Such being the general character of the variation, it will be convenient to state provisionally what significance is to be attached to it. In accordance with the well-known facts relating to other excitable structures, and particularly those observed by Engelmann as to the heart, and by Bernstein[1] as to muscle, the initial phase may be understood as signifying that immediately after excitation, the excited part becomes negative to other parts, and consequently that the contact nearest the seat of excitation becomes in the first instance negative to the other. As regards the terminal phase, its coincidence in time with the relaxation of the ventricle appears to us to indicate that, as the initial phase certainly corresponds with the beginning of the period of electrical change, so its close is marked by an opposite electrical condition; in other words, it seemed probable that the equipotentiality of the surface during the greater part of the ventricular contraction does not mean, as Engelmann supposed, that all is over, and that the electrical disturbance[2] merely precedes the systole and ceases with its commencement, but only that during the period in question the electromotive forces in action are nearly balanced, this state of equilibrium persisting until, towards the end of the systole, they again manifest themselves in an electrical difference between the two contacts

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[1] Bernstein, *Untersuch. über den Erregungsvorgang im Nerven- u. Muskelsysteme.* Section 2, p. 47.

[2] It will be seen in the next paragraph that the "initial phase" corresponds to the whole variation as observed by Engelmann.

opposed in sign to that by which the systole was ushered in. It further appeared to be probable that the occurrence of the terminal phase at the close of the period of excitation might be explained on the supposition that at that time, electrical activity had ceased at the contact nearest the point of excitation, but continued at the one more remote. If this were the case, it is clear that by so changing the relations of the leading-off contacts to the seat of excitation that the contact which before was most remote should now become nearest, both phases of the variation would be reversed in sign[1].

The following observations serve to exemplify this statement:—

[5] A Stannius' heart, led off at base (contact *f*, ventral surface, near auriculo-ventricular groove) and at apex (contact *m*, same surface, three millims. from *f*). Exciting electrodes (x) at apex and (x') at groove. By a switch, opening shocks could be directed either through x or x'. Difference of potential between m and f, 0·0. Temperature of heart 15° C. Observations were made alternately after excitation at x and x' as shown in the table. Duration of period of closure of galvanometer circuit 0″·1. The numbers given in the Table are the time-intervals between the moment of excitation and the end of the period of closure.

Time after excitation of opening of circuit,	0″·04	0″·06	0″·08	0″·10	0″·12	0″·14	0″·16	0″·18	0″·20
Excitation at x,	0	−7	−28	−40	−48	−45	−31	−20	−8
Excitation at x',	0	+1	+7	+20	+40	+41	+39	+30	+15

Time after excitation of opening of circuit,	0″·22	0″·24	....	1″·20	1″·40	1″·60	1″·70	1″·80	1″·90
Excitation at x,	−2	0	....	0	0	+6	+15	+10	0
Excitation at x',	+4	0	....	−1	−8	−9	−12	+3	0

During a period of about a second between 0″·22 and 1″·2, the contacts were equipotential.

[6] Stannius' heart, led off and excited as above. Difference between m and f −0·0002 D. Period of closure 0″·1.

Time after excitation of opening of circuit,	0″·04	0″·06	0″·08	0″·12	0″·16	0″·20	0″·24	......	1″·4	1″·6	1″·7	1″·8	1″·9	2″·0
Excitation at x,	0	−4	−10	−30	−29	−11	0	....		+2	+5	+10	+6	0
Excitation at x',	0	+4	+9	+19	+11	+33	0	......	0	−2	−3	−9	+4	0

Between 0″·2 and 1″·4 the contacts were equipotential.

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[1] A corresponding statement was made by Marchand (Pflüger's *Archiv*, Vol. xv. p. 530) as follows:—"The direction of the deflection which followed the excitation corresponded to a wave of negative tension starting from the seat of excitation: if therefore the excitation was at the apex, the first deflection was such as to indicate an ascending current, which was followed by a second in the opposite direction. If the excitation was at the base, the order of succession was reversed." See also our former paper *loc. cit.* p. 414.

If the above interpretation of the phenomena is correct, it is evident that in each individual element of the ventricular substance the state of excitation, as indicated by electrical change, does not, as has been supposed, coincide with the "period of latent stimulation" of the ventricle, but must have a duration limited on one side by the beginning of the initial phase, on the other by the beginning of the terminal phase. Accordingly, assuming the facts stated on p. 397 to be correct, each muscular element of the ventricle must at 12° C. be in a state of excitation for about 1''·8. Now it is well known that in all excitable parts, the state of excitation is characterized by a diminution or absence of excitability; in other words, that in whatever degree the state of excitation exists in any such structure, its susceptibility to a second excitation is correspondingly diminished. This being so, we should expect that in the ventricle the period of non-excitability would correspond in duration to that of excitation (1''·8 at 12° C.), and further that it would be similarly abbreviated by increase of temperature.

Period of non-excitability. In experiments published by M. Marey in 1876[1], the relative excitability of the ventricle was tested in the rhythmically contracting heart at various periods of the cardiac revolution, the mode of excitation employed being the passage of opening induction shocks through the heart. It was found that when the excitation was produced by opening the primary current at the moment that the contraction of the ventricle was seen, no second contraction followed; and the same absence of response was observed whenever the second excitation occurred "during the commencement of the systole of the ventricle" (termed by Marey the "refractory period") even when the induction shocks were stronger than were required to evoke a contraction of the resting heart. During the remainder of the systole "the heart responds to strong excitations but does not respond to weak ones." It was further observed that heat shortens and may even suppress the "refractory period," and that cold lengthens it, but no measurements are given either of the temperature or of the duration of the systole. Another important result was that with excitations occurring during systole, the response, if it occurred at all, was delayed, the duration of the delay being the greater the sooner the excitation happened after the close of the "refractory period." It can scarcely be doubted that this shortening of the delay in the later stage of the systole indicates a gradual increase of excitability.

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[1] "Des excitations artificielles du cœur," *Physiologie expérimentale*, II., 1876, p. 85.

The observations of M. Marey as to the "refractory period" are unavailable for the purpose of determining the duration of the period of diminished excitability for two reasons, viz., (1) that no time measurements are given, and (2) that while the observations show that the period varies with the strength of the induction shock used, the strength is not stated.

It is obvious that the only way in which this can be accomplished is by employing minimal excitations, *i.e.* induction shocks of just sufficient strength to evoke a response in the resting state, and by ascertaining how soon after a first minimal excitation the ventricle has so far recovered its excitability as to respond to a second of equal strength; in other words, to determine the shortest period of time which must intervene between two equal and minimal excitations in order to produce two contractions.

For this purpose the rheotome was found to be well adapted. It was introduced into the primary circuit of the induction apparatus in such a way that one pole of the battery was connected with the coil by two wires, of which one passed through the inner pools, the closing shock being cut off as before by the electromagnetic key. In this way an opening shock passed through the preparation whenever the circuit was momentarily closed, whether through *b*, *b'*, or *g*, *g'*.[1]

We have found it necessary in order to obtain satisfactory results, to depart from the principle above laid down in so far as to substitute for "minimal" excitations in the strict sense, induction shocks which were just strong enough to be responded to without fail in at least six successive excitations, occurring at sufficient intervals of time.

Experiments made in this way showed that in the ventricles of winter frogs (*R. esculenta*) at the temperature 12° C. two seconds is the limit of the period of diminished excitability, and that by increasing the temperature to 22° or 24° it can be shortened to one second. If this is done gradually, as in the experiment of which the results are given in the following Table, it is strikingly seen that the duration of the "refractory" state is as strictly dependent on temperature as that of the variation, and secondly that the two periods are in general coincident.

[7] Stannius' preparation, of which the temperature was raised by 3° C. at a time, from 12° to 21°. The period of diminished excitability was measured at each temperature. After testing the condition of the preparation by

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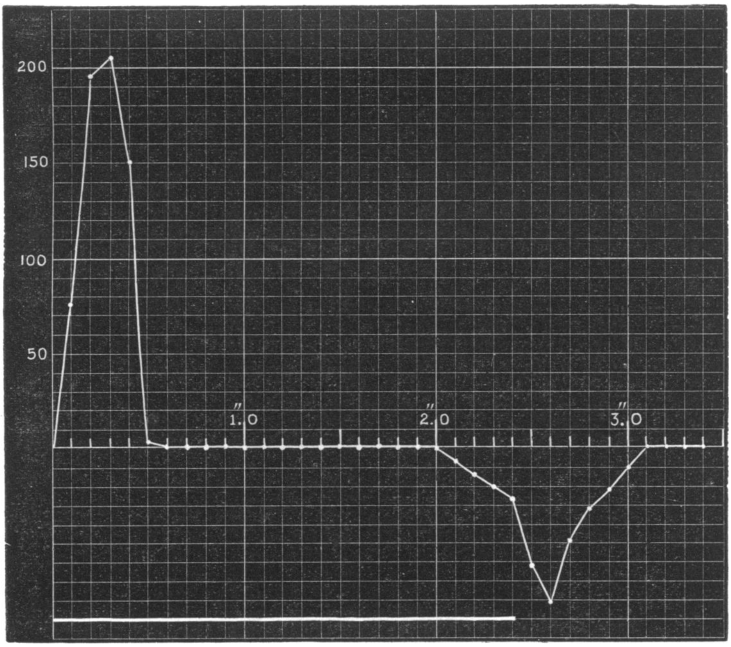
[1] See the description of the rheotome in the Appendix to this paper.

reducing the temperature to 12°, it was again raised successively to 24° and 27°.

Temperature	12°	15°	18°	21°	12°	24°	27°
Period of diminished excitability	2″·0	1″·8	1″·5	1″·2	2″·0	0″·9	0″·8

With reference to their coincidence in particular cases, we have made numerous experiments which we hope to embody in a future communication. At present it is sufficient to state that the heart remains unexcitable to stimuli which are of just sufficient strength to evoke a certain response, up to the culmination of the terminal phase, as is shown in the following graphic record of the variation of the ventricle preparation of the heart of the tortoise at 20° C. The horizontal line below the tracing represents the duration of the period of diminished excitability.



For the purpose of examining the other fact observed by M. Marey, viz., that when the strength of the stimulus employed is increased the refractory period is diminished, we have found the heart of the tortoise more advantageous than that of the frog, on account of the longer duration of the excitatory state. The method consists in first determining the outer limit of the period of diminished excitability, i.e., the period which must intervene between two infallibly adequate excitations, in order that the second may be effectual, and then repeating the experiment with induction currents of which the strength has a definite relation to that of the shocks first employed, for which purpose the du Bois' induction apparatus must be graduated in the usual way. By this method we found that in the ventricle apex preparation of the tortoise at 25° it was necessary to double the strength of the excitation in order to shorten the period of diminished excitability from 2″·5 to 2″·0.

Duration and character of the initial phase. In a series of experiments made at the beginning of our inquiry, rheotome observations were made of the first phase of the variation. In these, the duration of closure of the galvanometer circuit was usually 0″·06. The preparation was excited at the apex and led off at apex (*m*) and base (*f*). The exciting contact was at a very short distance from *m*. The observations were made at temperatures from 15° to 17° C. for we were at the time not aware of the importance of slight differences of temperature. The results are given in the following Table.

[8]

	Time after excitation of			Distance of *m* from *x* in millims.	Duration.	Largest deflection.
	First appearance of negative deflection.	Maximum.	Last deflection observed.			
I.	0″·078	0″·100	0″·172	1½	0″·094	16 scale
II.	0·042	0·114	0·160	very near	0·120	32 „
III.	0·034	0·049	0·099	„	0·065	30 „
IV.	0·045	0·082	0·104	1½	0·059	16 „
V.	0·045	0·130	0·150	less than 1	0·105	22 „
VI.	0·102	0·112	0·150	3	0·048	23 „
VII.	0·028	0·055	0·166	less than 1	0·138	24 „
VIII.	0·090	0·146	0·180	3	0·089	25 „

From these observations we were at first led to accept the statement of Engelmann that the duration of the initial phase was about $\frac{9}{100}$ of a second, and this appeared to be confirmed by subsequent experiments in which the rheotome observations were taken at regular time-intervals. Thus in a series of nine Stannius' preparations examined in December last we had in five preparations the following results, the numbers at the heads of the columns indicating the times at which the galvanometer circuit was opened :—

[9]

	0″·04	0″·06	0″·08	0″·10	0″·12	0″·14	0″·16	0″·18	0″·20	0″·22	0″·24	0″·26	0″·28	0″·30
I.	0	0	− 9	− 20	− 40	− 68	− 70	− 72	− 70	− 55	− 40	− 11	0	0
II.	− 1	− 12	− 31	− 42	− 46	− 40	− 32	− 12	− 7	− 4	0	0	0	0
III.	0	− 2	− 29	− 40	− 61	− 85	− 99	− 90	− 70	− 49	− 30	− 11	− 2	0
IV.	− 2	− 20	− 30	− 40	− 39	− 34	− 15	− 3	− 2	− 2	− 2	0	0	0
V.	0	− 7	− 28	− 40	− 48	− 45	− 31	− 20	− 8	− 2	0	0	0	0
Means	0·6	8·0	25·4	36·4	46·8	54·4	49·4	39·4	33·4	22·4	14·4	4·4	0·4	0

From the means it is apparent that in these preparations the initial phase lasted from 0″·06 after excitation to 0″·14 or even later, but in the remaining four it was evidently of much shorter duration :—

[10]

	0·04	0·06	0·08	0·10	0·12	0·14	0·16	0·18	0·20	0·22	0·24	0·26
I.	0	− 2	− 30	− 20	− 9	0	0	0	0	0	0	0
II.	0	− 3	− 13	− 20	− 19	− 10	0	0	0	0	0	0
III.	0	0	− 13	− 22	− 27	− 25	− 16	− 5	0	0	0	0
IV.	0	− 7	− 30	− 40	− 32	− 15	− 2	0	0	0	0	0
Means		3·0	21·5	25·5	21·7	12·5	4·5	1·2	0	0	0	0

In four ventricle apex preparations observed for another purpose, we had :—

[11]

	0″·02	0″·04	0″·08	0″·12	0″·16	0″·20	0″·24	0″·28
I.	0	− 4	− 32	− 29	− 7	− 1	− 1	− 1
II.	0	− 5	− 50	− 50	− 19	0	0	0
III.	0	− 12	− 66	− 60	− 33	0	0	0
IV.	0	0	− 36	− 47	− 42	− 11	− 9	− 9
Means	0	5·2	46	46·5	25·2	3	2·5	2·5

Bearing in mind that in this, as in the two other preceding experiments the closing time lasted $\frac{1}{10}$ of a second, we see that the strong part of the initial phase could not in any case have lasted beyond 0″·08 after excitation. We may therefore conclude that so long as the distance between the leading-off electrodes does not exceed two and a half millims., the duration of the strong part of the initial phase is not more than 0″·03, and we are confirmed in this conclusion by the following observations, in which the period of closure was shortened to 0″·033 by trebling the rate of revolution of the rheotome :—

[12]

	0″·02	0″·04	0″·06	0″·08	0″·10	0″·12	0″·14	0″·16	0″·18	0″·20
I.	0	– 30	– 72	– 51	– 10	0	0	0	0	0
II.	0	– 41	– 72	– 52	– 20	– 5	– 3	0	0	0
III.	0	– 25	– 70	– 43	– 30	– 21	– 18	– 18	– 18	– 18
IV.	0	– 30	– 36	– 12	0	0	0	0	0	0
V.	0	– 4	– 32	– 37	– 9	0	0	0	0	0
VI.	0	– 2	– 26	– 40	– 20	– 2	0	+ 5	+ 5	+ 10

The numbers indicate that the initial phase began in these six preparations about 0″·03 after excitation (the distance between *x* and *m* being always about one millim.) and very rapidly culminated, not later than 0″·06, and was virtually over by 0″·07 or 0″·08.

For the purpose of determining the earliest moment after excitation at which an electrical change can be observed, we in two experiments passed the insulated platinum wires which were used as exciting electrodes through the leading-off electrode *m*, in such a manner as to render the seat of excitation as nearly as possible identical with the point by which the surface was led off. Notwithstanding this arrangement the closure of the galvanometer circuit at the moment of excitation was without effect on the needle. Ventricle-apex preparations were used and the period of closure was in each instance 0″·03. The first deflections were observed in one case 0″·035, in the other 0″·023 after excitation.

It has been already stated that Engelmann found the duration of the first part of the negative phase (Stadium steigender Negativität) to be 0″·09, but in some of his observations it was very much shorter, for it was observable only at three successive positions of the rheotome, which corresponded to intervals of time of 0″·03. In other words it was already inappreciable 0″·03 after it was first seen.

As regards the total duration of the negative part of the variation, Engelmann found that when the distance between the leading-off contacts (*f* to *m*) was from three to three and a-half millimeters, and the distance of the seat of excitation from them was two millims., the closing time being 0″·57, the initial phase began at 0″·07 after excitation, reaching its maximum at 0″·165 and ending at 0″·26. When the distance *f* to *m* was five to six millims. and the distance of the seat of excitation was one millim., the closing time being 0″·05, the negative phase began at 0″·01, culminated at 0″·096, and ended at 0″·192. These numbers are taken from the curves (Pflüger's *Archiv*, Vol. XVII. p. 136) representing the means of 43 observations, of which 33 were made with the exciting electrodes at the longer distance, the remainder at the shorter. In the first set, the period during which negative deflections were observed was 0″·26 – 0″·07 = 0″·19. Deducting from 0·19 the duration of the closing time (0″·06) we have 0″·13 as the duration of the initial phase. In the second set it was also 0″·13.[1]

Engelmann's "positive Schwankung." Engelmann found that in 47 out of 77 cases, the variation presented the character of what he calls a *Doppelschwankung*, i.e. that the initial phase is followed immediately or after a short interval by an opposite electrical condition (*positive Schwankung*) which lasted from about 0″·20 after excitation to 0″·35, when the distance between *x* and *m* was very short, and from 0″·26 to 0″·56 when it was longer. The existence of this phase was indicated by deflections of which the maximum extent was from one third to one half of that of the negative deflections of the initial phase.

As our method resembles that employed by Prof. Engelmann in so far that in both, the proximal leading-off contact (*m*) is between the seat of excitation (*x*) and the distal contact (*f*), and that *x*, *m* and *f* are in the same line, the only difference being that in our observations Stannius' preparations were used instead of ventricle apex preparations, it is clear that if during the period succeeding the initial phase (the second fifth of the first second) the distal contact *f* becomes, in the uninjured inhibited ventricle, for a very short period positive to the proximal *m*, the fact could not escape observation. Although at the beginning of our investigations our attention was not specially directed to this period, a

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[1] Engelmann estimates the total duration of the negative part of the variation (örtliche Dauer der negativ electromotorischen Wirksamkeit) as 0·2, but the careful scrutiny of his results seems scarcely to justify this statement.

great number of our rheotome investigations covered it, it being in all uninjured hearts included in the period of equipotentiality.

In ventricle apex preparations we have also failed in observing any indication of the existence of a temporary state of positivity during the first half second. Thus in the experiments to which Table [12] relates the state of equipotentiality, which began in preparations II. and III. at $0''\cdot2$ after excitation, continued without change up to $0''\cdot5$. In IV., *m* was negative to *f* during the whole of this period, an effect which, as will be subsequently shown, is always observed when a sufficient time has not been allowed to elapse after the severance of the ventricle. A trace of a similar condition was observed in I.

We are therefore compelled to confess our inability to confirm Prof. Engelmann's observations in respect of the "Doppelschwankung." As we find it impossible to doubt their accuracy, we must suppose that the conditions under which they were made were, in some unknown respects, different.

Electromotive force of the initial phase. Our determinations of the electromotive force of the initial phase at its acme, i.e. of the electrical difference between *m* and *f* at the maximum, lead us to the conclusion that it exceeds the estimate of Engelmann. He says that the maximal excitatory deflection is never as large as that given when a current derived from the compensator of which the electromotive force is 0·03 Daniell is sent through the galvanometer circuit, with all conditions (closing time, resistance, and sensibility of the needle) unaltered. And having found that the "latente Kraft" of the ventricle (i.e. the greatest difference observable between the freshly-cut surface and the uninjured surface) was 0·03 Daniell, he concludes that the excitatory electromotive force is "mit hoher Wahrscheinlichkeit" inferior to the "latente Kraft." Using the same method as that indicated by Engelmann we have obtained higher values. Thus in the preparation to which Table [13] refers, we found that the largest deflection corresponded to an electromotive force of 0·04 Daniell, the mean of the six experiments being 0·033 Daniell. If, as seems certain, the excitatory force rises to and falls from its acme very abruptly, it is clear that it must have considerably exceeded this value, for the closing time ($0''\cdot033$) was long enough to cover a great part of the periods of increasing and of diminishing negativity[1].

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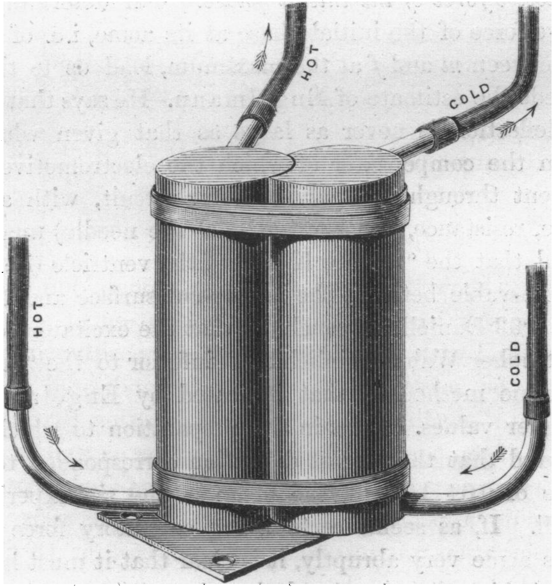
[1] For this reason any curve, such as that given in fig. 4, representing graphically the course of the initial phase, is higher and much narrower than the graphic record of the corresponding rheotome deflections. For it represents the record that would be obtained

II. INFLUENCE OF INEQUALITIES OF TEMPERATURE ON THE EXCITATORY VARIATION.

We have next to show that the characters we have stated to be those of the normal variation of the ventricle in the uninjured heart, depend for their manifestation on equality of temperature between the surfaces of the ventricle with which the leading-off electrodes *m* and *f* are in contact.

For this purpose it is necessary to observe in what way the normal characters of the variation are modified when the temperatures of *m* and *f* are unequal. With this view the cylindrical water-box on which the preparation is supported is modified in such a way that while the base of the ventricle and the auricles rest on a surface at a temperature we have for convenience taken as normal, viz. 12° C., the apex is in contact with a colder or warmer surface. The sketch represents the instrument in its altered form.



It is seen that the upper end presents two surfaces, of which one is crescent-shaped, the other circular, the base of the ventricle being on the former, the apex on the latter. These are the ends of two cylinders,

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if the sensibility of the galvanometer and the frequency of the observations had been increased and the period of closure diminished to the utmost.

one of which is crescentic in section. Each cylinder receives its supply of water from a separate source, so that the temperature of the two surfaces can be regulated as required.

By means of this contrivance the terminal phase of the variation was observed galvanometrically with the aid of the rheotome, under three conditions, viz., (1) with the apex at the same temperature with the base, (2) with the apex 3° C. cooler, and (3) with the apex 2°·5 C. warmer, each observation of the second and third kind being followed and preceded by an observation at equal temperatures.

[13] A Stannius' preparation of a large Hungarian specimen of R. esculenta was used. It was led off in the same way as those previously described, and the arrangements for exciting were similar. Difference $m - f$ + 0·0002 D. On excitation at apex deflection of − 20 followed by + 70 galv. scale. On exciting at base + 20 followed after a pause by + 35. Distance between *m* and *f* 4 millims., both on ventral meridian. Apex and base at same temperature, viz. 13° C.

Time after excitation of opening of circuit	0″·04	0″·08	0″·12	0″·16	0″·20	0″·22 to 1″·40	1″·5
Excitation at *x*	− 3	− 7	− 39	− 40	− 12	0	+ 20
Excitation at *x′*	0	+ 10	+ 38	+ 23	+ 3	0	0

Time after excitation of opening of circuit	1″·6	1″·7	1″·8	1″·9	2″·0	2″·1
Excitation at *x*	+ 10	+ 20	+ 40	+ 8	0	0
Excitation at *x′*	0	0	+ 15	+ 4	0	0

The readings show that the variation, although due care was taken in preparation, was irregular, for with excitation at *x* the end phase was excessive, and with excitation at *x′* it was positive instead of negative. As will be subsequently shown, this indicated that at *m* the "excitatory state" declined after a shorter duration than at *f*, the effect of diminution of temperature being to lengthen as well as to strengthen the excitatory state; it was therefore anticipated that the normal characters would appear on slightly cooling the apex. Accordingly when the observation was repeated with the base at 13° C., the apex at 10° C., the end phase was as follows:—

Time after excitation of opening of circuit	0″·40 to 1″·4	1″·6	1″·7	1″·8	1″·9	2″·0	2″·1	2″·2
Excitation at *x*	0	0	+ 1	+ 4	+ 18	+ 12	0	0
Excitation at *x′*	0	− 5	− 9	− 9	− 10	0	0	0

The heart was now brought back to its former condition as regards temperature, and the observation repeated. It was observed that when x was excited, the positive phase was exaggerated, and that when x' was excited, what was before negative became positive.

The next step was to raise the temperature of the apex to 16° C., the base remaining at 13°·5.

On exciting at x, a deflection of -60 followed by $+80$: on exciting at x', a deflection of $+20$ followed by $+80$. Difference $m - f = +0{\cdot}8$.

Time after excitation of opening of circuit	0″·4 to 1″·3	1″·4	1″·5	1″·6	1″·7	1″·8	1″·9
Excitation at x	0	+ 3	+ 6	+ 27	+ 30	+ 6	0
Excitation at x'	0	0	+ 1	+ 5	+ 18	+ 2	0

The heart was finally brought back to equality of temperature, water at 13°·5 passing through both chambers.

The result was as follows:—

Time after excitation of opening of circuit	0″·4 to 1″·3	1″·4	1″·5	1″·6	1″·7	1″·8	1″·9
Excitation at x	0	+ 3	+ 9	+ 14	+ 18	+ 2	0
Excitation at x'	0	− 1	0	+ 2	+ 9	+ 1	0

When the difference of temperature was greater, similar but larger effects were observed, and the after effect which followed the restoration of equality of temperature between the two contacts was much more considerable. This was shown in the following experiment:—

[14] Difference $m - f = +0{\cdot}0004$. On excitation at $x - 40$: on excitation at $x' + 20$ followed by -80. Apex and base at 12° C.

Time after excitation of opening of galvanometer circuit	0″·04	0″·06	0″·08	0″·10	0″·12	0″·14	0″·16	0″·18
Excitation at x	− 2	− 20	− 30	− 40	− 39	− 34	− 15	− 3
Excitation at x'	0	+ 3	+ 10	+ 24	+ 29	+ 25	+ 16	+ 7

Time after excitation of opening of galvanometer circuit	0″·2	0″·3 to 1″·6	1″·8	2″·0	2″·2	2″·3	2″·4	2″·5	2″·6
Excitation at x	− 2	− trace	tr.	− 2	− 3	0	+ 2	+ 2	0
Excitation at x'	0	− trace	− 9	− 7	− 9	− 10	− 5	− 5	0

It is to be noted that in the first line the terminal phase was nearly absent when the seat of excitation was at the base. The apex was now warmed to 30° C.

On excitation at x, a deflection of − 10 followed by + 105 : on excitation at x' + 10 followed by + 105.

Time after excitation of opening of galvanometer circuit	0″·04	0″·08	0″·12	0″·16	0″·20	0″·3 to 0″·7	0″·8	1″·0	1″·2	1″·4	1″·6	1″·8	2″·0
Excitation at apex	− 1	− 29	− 29	− 11	0	0	+ 2	+ 3	+ 10	+ 32	+ 50	+ 2	0
Excitation at base	+ 1	+ 12	+ 25	+ 14	0	0	0	+ 2	+ 17	+ 20	+ 45	+ 2	0

The above observation was taken about ten minutes after the temperature of the cylinder had been raised. The apex was then cooled to 12°, so that base and apex were now at equal temperatures.

Time after excitation of opening of galvanometer circuit	0″·04	0″·08	0″·12	0″·16	0″·20	0″·30 to 0″·80	1″·0	1″·2	1″·6	1″·8	2″·0	2″·2	2″·4
Excitation at x	− 2	− 31	− 45	− 25	− 4	0	− 3	− 5	− 5	− 10	− 20	− 4	0
Excitation at x'	+ 2	+ 14	+ 27	+ 17	0	0	− 3	− 5	− 5	− 15	− 26	− 7	0

Here it was seen that the ventricle, of which the apex had been warmed to 30° C. for a period of 25 minutes, was no longer normal, notwithstanding that the equality of temperature had been restored. The abnormality consists in this, that the preparation behaves as if the part which had been heated were at a lower temperature, the phenomena corresponding closely with those observed when the apex has been cooled in a normal preparation. This being so, we should expect that by slightly raising the temperature of the apex, it would be possible to compensate the abnormal negativity of the terminal phase. The temperature of the apex was therefore raised to 18°, and it was found that the galvanometer deflections were nearly normal; and with the rheotome the highest negative deflections of the terminal phase were, when x was excited − 2 at 2″·2, when x' was excited − 6 at 2″·0. No doubt if a slightly higher temperature had been employed the variation would have been completely normal. It is to be noted that after warming the apex the duration of the whole variation is diminished.

The record of another experiment of the same kind may be usefully introduced for the purpose of showing that the physiological effect produced by the inequality of temperature subsides rapidly, even though the difference of temperature remains unaltered. The mode of observation was the same, the ventricle however being excited only at the apex. It having been first ascertained that when the apex was at 12° C. the variation was normal as regards both its phases, the temperature of the apex was raised to 30°, a rheotome observation was made of the second part of the variation as rapidly as possible, repeated at intervals of five seconds. The apex was then brought back to 12° C. when, as before, it was observed that the terminal phase was negative. In this experiment as in the last the duration of closure of the galvanometer circuit was 0″·09. The preparations used in this and in all the preceding experiments were from Hungarian frogs.

[15]

Time after excitation of opening of galvanometer circuit	0″·5	0″·8	1″·2	1″·6	2″·0	2″·2	2″·4	2″·5	2″·6	2″·7	2″·8	2″·9
Temperature of base and of apex, 12° C.	0	0	0	0	0	+ tr.	+ 6	+ 11	+ 30	+ 37	+ 11	0
Temperature of apex raised to 30°												
immediately after	0	+ 4	+ 19	+ 100	+ 70	+ 4	0	0				
five minutes after	0	0	+ 9	+ 70	+ 10	0	0	0				
ten minutes after	0	0	+ 3	+ 20	0	0	0	0				
Temperature of base and apex again equal, 12° C.	0	0	− 2	− 12	0	0	0	0				

In the next observation the apex instead of being warmed was cooled to 4° C. the base remaining at 14° C.

Difference $m - f = 0$. On excitation at x, deflection − 50 followed by + 20 : on excitation at x', − 30. Temperature at base and apex 14°.

Time after excitation of opening of galvanometer circuit	0″·06	0″·08	0″·10	0″·12	0″·14	0″·16	0″·18	0″·20	0″·22	0″·24 to 1″·20	1″·4	1″·6	1″·7	1″·8	1″·9
Excitation at x	− 7	− 28	− 40	− 48	− 45	− 31	− 20	− 8	− 2	0	0	+ 6	+ 15	+ 10	0
Excitation at x'	+ tr.	+ 7	+ 20	+ 40	+ 41	+ 39	+ 30	+ 15	+ 4	0	− 8	− 9	− 12	+ 3	0

The apex was now cooled to 4° C.

On excitation at x, deflection of − 60 followed by a further deflection of − 140 : at x', + 12, followed by − 200.

Time after excitation of opening of galvanometer circuit	0″·06	0″·08	0″·20	0″·24	0″·28	0″·3 to 0″·6	0″·8	1″·2	1″·6	2″·0	2″·2	2″·4
Excitation at x	− 3	− 13	− 9	− 2	− 2	− 2	− 6	− 6	− 10	− 36	− 3	0
Excitation at x'	0	+ 9	+ 18	0	− 2	− 2	− 6	− 6	− 20	− 46	− 8	0

The temperature of the apex was now raised to 14° C. so that the two contacts were at the same temperature.

On excitation at x, deflection of − 80 followed by + 20: at x', + 10 followed by − 60.

Time after excitation of opening of galvanometer circuit	0″·06	0″·08	0″·12	0″·16	0″·20	0″·3 to 0″·8	1″·2
Excitation at x	− 12	− 30	− 49	− 35	− 2	− 2	0
Excitation at x'	+ 6	+ 7	+ 48	+ 34	+ 2	− 2	− 5

Time after excitation of opening of galvanometer circuit	1″·5	1″·6	1″·7	1″·8	2″·0
Excitation at x	+ 2	+ 10	+ 11	+ 4	0
Excitation at x'	− 7	− 9	+ 9	+ 4	0

In this case the restoration of equality of temperature was accompanied by restoration of the normal characters of the variation.

[16] The following experiment with the capillary electrometer affords further illustration of what has been stated.

The ventricle of a Stannius' heart was led off as usual at apex and base, and excited at apex. The excitation took place at intervals of one minute, the ventricle resting by its apex on one cylinder, by its base on the other. The temperatures of the cylinders in successive observations were as follows:—

			Scale reading of	
			initial phase.	terminal phase.
I.	base 13	apex 13	− 10	+ 6
II.	„ 13	„ 14	− 10	+ 7
III.	„ 13	„ 15	− 10	+ 10
IV.	„ 13	„ 16	− 10	+ 11
V.	„ 13	„ 18	− 10	+ 13

In the last three cases the apex electrode (m) was positive during the whole of the interval between the initial and terminal phases. The value of a division of the electrometer scale was about 0·0015 D.

The observations showed that the increase of temperature of the apex was without effect as regards the initial change, but increased the terminal.

In the preceding experiments it has been seen that very slight differences of the temperature to which the apex and base respectively of the Stannius' heart preparation are exposed, are sufficient to alter the character of the variation, the change being such that in case the preparation is led off at apex and base, and the apex is warmed, its positivity is increased in the terminal phase; and further that when the difference is considerable, the effect diminishes notwithstanding that the warming continues. It has also been seen that if under these circumstances the equality of temperature is restored, the heart is not entirely in the same condition as before.

The method employed in these experiments is open to two objections — that the effect produced, although admitting of accurate graduation and measurement in respect of its intensity, is not confined within sufficiently narrow limits either of extent or duration. In these respects another mode of observation, which was first employed by us in the experiments of which we published the results in 1878, was preferable, though from its nature the difference in temperature scarcely admitted of accurate measurement. That method consisted in arranging a loop of platinum wire at a fixed distance (usually three millims.) from the surface of the heart in such a position as to be as nearly as possible opposite to the contact *m*. The ends of the platinum wire having been connected with a battery of two grove-cells, the circuit was closed for measured periods of several seconds duration, at the expiration of which the preparation was excited in the usual way. The general result of this experiment was described in our former paper[1], that description being founded on a large number of exploratory observations made with the capillary electrometer.

We now proceed to give an account of experiments in which the same phenomena were investigated with the aid of the rheotome and galvanometer. The mode of observation was as follows: the rheotome was arranged so that the Stannius' preparation, which as before was led off at base (*f*), and apex (*m*), was excited in the neighbourhood of *m* at each revolution. The rate of revolution was slow—one revolution in twelve seconds.

The platinum loop having been placed in position, its circuit was closed for a definite period which ended immediately before an excitation. The effect of this temporary warming of the surface was investigated by the comparison in each case of ten series of rheotome measurements. In the first series the rheotome was set so as to close the galvanometer circuit for a period of one-fifth of a second, ending

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[1] *Proceedings of the Royal Society*, Vol. XXVII. p. 110, Par. 12 and 13.

0″·1 after excitation: in the second series the closure terminated at 0″·2; in the third at 0″·4, and so on.

At the first revolution of the rheotome in the first series, the normal galvanometrical effect corresponding to the period of closure was observed and recorded. In the meantime the heating circuit was closed as above described, so that at the second revolution the immediate effect of the heating could be observed. The observation was repeated at each succeeding revolution, *i. e.* at intervals of 12″, until the effect of the single heating to which the preparation had been exposed disappeared. This having been accomplished, the rheotome was set so as to close the circuit 0″·1 later, and the process repeated, and so on to the end of the variation.

[17] Stannius' preparation led off at base (*f*) and apex (*m*). Variation by electrometer normal, *i. e.* − 6 scale, followed by + 1. Duration of closure of warming circuit 5″. Distance of wire 2½ millims. Temperature 12° C.

The results of the observation are given in the following table:

	0″·1	0″·2	0″·4	0″·6	0″·8	1″·0	1″·2	1″·4	1″·6	1″·8	2″·0
Preliminary observation	− 30	− 30	0	0	0	0	+ 5	+ 23	+ 20	+ 5	0
At end of period of warming	− 30	− 24	+ 17	+ 30	+ 71	+ 95	+ 99	+ 63	+ 9	+ 5	0
12″ later	− 30	− 25	+ 5	+ 2	+ 9	+ 24	+ 55	+ 52	+ 6	+ 2	0
24″ later		− 29	0	0	0	+ 6	+ 14	+ 50	+ 9	+ 2	0
38″ later			0	0	0	+ 2	+ 7	+ 34	+ 14	+ 5	0
48″ later			0	0	0	0	+ 5	+ 24	+ 16	0	0

During the whole progress of the observation the electrical condition of the led off surfaces underwent very little change. The difference which was at first + 0·0006, varied to − 0·0002. The immediate effect of the warming was to produce a temporary disturbance in which the warmed part became positive. The amount of this change, which was indicated by a deflection of + 7 divisions of the galvanometer scale, was about 0·00003 Daniell.

The rheotome readings show that notwithstanding the repeated warmings of the apex, the preparation preserved its normal condition to the end of the experiment, which lasted about twenty-five minutes, as seen in the perfectly normal character of the deflections recorded in the upper line of the table, and particularly by its isoelectrical state during the interval between the two phases. It is further seen from the deflections recorded in the second line, which were observed a second after the warming had terminated, that as regards the first phase warming is without effect, but that from the 2nd tenth of a second after excitation the variation was altered in character, the apex contact being positive during the whole of the remainder of the variation, and the positivity greatest when the period of closure terminated 1″·2 after the excitation.

As, with the preparation and rheotome in circuit, it was found that a deflection of 93 galvanometer scale was observed with an electromotive force of 0·01 Daniell, it may be concluded that at the period of maximum positivity the difference between the two contacts slightly exceeded this amount. The third line shows that the effect at first produced quickly diminishes, the negative phase still remaining unaltered. In the succeeding lines is seen the gradual reinstatement of the normal condition.

[18] The two following experiments resemble the last:—

Stannius' preparation, led off as above. Variation by electrometer – 4 scale followed by – 1. Difference 0·0, varying during progress of observation to – 0·0008. Distance of wire 4 millims. Duration of warming 8″. Temp. 12° C. Warming was followed as before by a transitory positivity of the warmed contact. The variations observed before warming differed slightly from the normal in this respect, that the terminal phase was indistinguishable.

It is to be observed that the effect in this case is much smaller than in the last, the distance being twice as great. A previous tentative observation had been made with the wire at a greater distance, when the effect was still smaller.

	0″·1	0″·2	0″·4	0·″6	0″·8	1″·0	1″·2	1″·4	1″·6
Before warming	– 9	– 10	– 2	– 2	– 2	– 1	0	0	0
At end of period of warming	– 9	– 10	– 2	0	0	+ 7	+ 15	+ 6	0
12″ later	– 9	– 10	– 2	0	0	+ 2	+ 10	+ 2	0
24″ later	– 9	– 10	– 2	0	0	0	+ 5	+ 1	0

Stannius' preparation led off in the same way. Variation by electrometer – 2 followed by + 1. Difference 0·0002, varying during observation to – 0·001. Distance of warming loop, 3 millims. Duration 5″. The immediate effect of warming on the difference was expressed by a deflection of 10° corresponding to an E. M. F. of 0·00009 Dan. The maximum effect of warming on the variation was observed during the 2nd fifth of the 2nd second. It amounted to 0·008 Daniell.

	0″·1	0″·2	0″·4	0″·6	0″·8	1″·0	1″·2	1″·4	1″·6	1″·8	2″·0
Before warming	− 11	− 12	− 2	0	0	0	0	0	+ 1	0	0
At end of period of warming	− 11	− 11	− 2	0	0	+ 10	+ 23	+ 26	+ 12	0	0
12″ later				0	0	+ 2	+ 8	+ 13	+ 6	0	0
24″ later				0	0	0	1	4	6	0	0
36″ later				0	0	0	0	1	4	0	0

[19] In the following instance a heart was employed in which the led off contacts exhibited a slight unexplained inequality.

Stannius' heart, led off as before. Variation by electrometer − 1 followed by + 0. Difference + 0·0012, slightly varying during observation. Distance of wire 2½ millims. Duration 5″. Temp. 12° C. The usual transitory effect of warming was observed: it amounted to 0·0007 Daniell. The first observation was made at 3.20 p.m., the second at 4.15, each lasting about half an hour. The maximum effect of warming on the variation (0·009 Daniell) was observed during the 2nd fifth of the 2nd second. The subsequent readings at 1″·6 were + 7, + 2, 0, − 2; − 2, − 3, − 5, &c.

	0″·1	0″·2	0″·4	0″·6	0″·8	1″·0	1″·2	1″·4	1″·6	1″·8
Before warming	− 19	− 20	− 10	− 5	− 6	− 6	− 7	− 8	− 10	0
At end of period of warming	− 21	− 20	− 6	+ 2	+ 22	+ 43	+ 86	+ 90	+ 15	0
12″ later	− 19	− 20	− 9	− 4	0	+ 2	+ 26	+ 60	+ 9	0
24″ later	− 19		− 10	− 6	− 5	− 2	+ 4	+ 24	+ 14	0
36″ later	− 19			− 7	− 7	− 5	− 1	+ 3	+ 10	0

III. INFLUENCE OF INJURY OF THE SURFACE OF THE VENTRICLE ON THE EXCITATORY VARIATION.

In the paper communicated in May, 1878, to the Royal Society the following statements, founded on observations with the capillary electrometer, were made as to the effect of localized injury of the surface of the ventricle on the characters of the variation. They related both to the rhythmically contracting entire heart and to the ventricle preparation. (1) When the rhythmically contracting heart is led off at base and apex, *m* being at the apex, and the surface of the ventricle near the base is injured, the "second phase" is intensified. (2) If the apex is similarly injured "the second phase is abolished, the variation being indicated by a single large excursion in the direction of the first phase." (3) When the rhythmically contracting "ventricle preparation" is led off in the same way, the characters of the variation are similar so long as the injury is recent. After a time the second phase diminishes in extent and duration, and finally the characters of the normal variation reappear. In the Stannius' preparation, injury of the apex produces a modification of the excitatory variation which corresponds to that above described in the rhythmically contracting ventricle.

These phenomena have been re-examined with the aid of the rheotome both in the Stannius' preparation and in the ventricle apex preparation. The accuracy of the statements previously made has been confirmed in every particular.

In the rhythmically contracting ventricle, when led off in the manner stated in (1), the second phase, which we now prefer to call the terminal phase, has a definite direction in relation to the heart itself, that is, it is always such that the apex becomes negative to the base. In the Stannius' heart, as has been shown in a previous section, its direction is determined by the seat of excitation, that is, it is such that the contact nearest the seat of excitation becomes positive. Accordingly the phraseology used in (1) and (2) can be applied to the Stannius' heart only when the seat of excitation is at the base, and both of these statements can be included in the following more general proposition:—In the inhibited ventricle, if either of the leading-off contacts is injured the terminal phase disappears, and the initial phase is followed by an electrical condition in which the injured surface is more positive, or less negative relatively to the uninjured surface; this condition lasts during the whole of the isoelectrical period and extends beyond it. In the following experiment the seat of injury was near the base.

[20] Stannius' heart, led off at apex (*m*) and base (*f*), and excited at apex at 2 millims. distance from *m*. Before injury the contacts were isoelectrical. After injury by touching the surface instantaneously with a platinum wire heated by the passage of a voltaic current, the difference was + 0·0128 D. During the observation it diminished to + 0·0078 D. The electrometer variation before injury was – 6 followed by + 4, after, – 35. The galvanometric circuit was closed every tenth of a second after excitation, the period of closure being 0″·18.

Time after excitation	0″·2	0″·3	0″·4	0″·5	0″·6	0″·7	0″·8	0″·9	1″·0
Uninjured	– 20	– 20	– 6	– 5	– 5	– 5	0	0	0
Injured	– 80	– 110	– 120	– 128	– 118	– 110	– 110	–100	– 100

Time after excitation	1″·1	1″·2	1″·3	1″·4	1″·5	1″·6	1″·7	1″·8	1″·9	2″·0	2″·1	2″·2
Uninjured	0	0	0	0	0	+ 2	+ 6	+ 15	+ 10?	+ 27	+ 10	0
Injured	– 98	– 90	– 85	– 80	– 80	– 74	– 65	– 60	– 30	– 20	– 15	0

In the uninjured state the preparation presented the typical characters of the normal variation, the isoelectrical period lasting from the middle of the 1st second to the middle of the 2nd. In the injured state the condition of the preparation was nearly the same from the 2nd tenth to the end of the first second, after which period the deflections show a gradual diminution to the end of the 2nd second. It is particularly to be noticed that the effect of injury manifested itself as early as the 1st fifth, but, as judged by the deflection, was only half as great as during the 2nd fifth. It need scarcely be stated that the difference of potential which during the observation diminished rapidly, was compensated before each observation.

In the next two experiments the seat of injury was in the first at the apex, in the second at the base.

[21] Stannius' hearts led off and excited as above. In the first experiment the apex contact before injury was slightly negative (– 0·0012). After injury it was – 0·0076 D. and declined to – 0·0028 D. during the observation.

(1)

Time after excitation	0″·1	0″·2	0″·3	0″·4	0″·5	0″·6	0″·7	0″·8	0″·9
Uninjured	– 12	– 12	– 6	0	0	0	0	0	0
Injured	+ 30	+ 70	+ 95	+ 80	+ 78	– 78	+ 78	+ 76	+ 72

Time after excitation	1″·0	1″·1	1″·2	1″·3	1″·4	1″·5	1″·6	1″·7	1″·8
Uninjured	0	0	0	0	0	0	0	0	+ 3
Injured	+ 70	+ 60	+ 60	+ 60	+ 54	+ 50	+ 39	+ 15	+ 10

Time after excitation	1″·9	2″·0	2″·1	2″·2	2″·3
Uninjured	+ 4	+ 12	+ 30	+ 50	0
Injured	+ 20	0			

(2)

Time after excitation	0″·1	0″·2	0″·3	0″·4	0″·5	0″·6	0″·7	0″·8	0″·9
Uninjured	- 12	- 30	- 23	0	0	0	0	0	0
Injured	- 20	- 40	- 40	- 30	- 38	- 40	- 22	- 20	- 18

Time after excitation	1″·0	1″·1	1″·2	1″·3	1″·4	1″·5	1″·6	1″·7	1″·8
Uninjured	0	0	0	0	+ 6	+ 10	+ 10	+ 10	+ 10
Injured	- 15	- 19	- 19	- 19	- 15	- 12	- 10	0	+ 20

Time after excitation	1″·9	2″·0	2″·1	2″·2	2″·3	2″·4
Uninjured	+ 12	+ 32	+ 35	+ 12	0	
Injured	+ 17	+ 6	0	0		

In experiment (2) the effect of the injury was slighter, for the largest deflections which were obtained during the middle fifth of the 1st second were found to correspond to a difference of potential of only 0·0066 D. Accordingly, towards the end of the 2nd second the difference declined to zero, the subsequent deflections in the opposite direction having the same meaning as in the normal variation.

[22] Ventricle apex preparation, led off and excited as above described. The observation was not begun until the effect of cutting off the ventricle had so far subsided that the difference between the contacts *m* and *f* had diminished to - 0·0006 D. The variation as observed with the electrometer was - 5 followed by + 5. Two minutes after injury of the surface at *m*, the difference was - 0·0076 D., and the electrometer readings of the variation, + 13 scale. The difference subsided rapidly during the observation to 0·0022 D. The duration of closure was the same as in the other experiments, viz. 0″·18, but the periods terminated at every fifth of a second instead of at every tenth.

Time after excitation	0″·1	0″·2	0″·4	0″·6	0″·8	1″·0	1″·2
Before injury	- 40	- 46	0	0	+ 4	+ 6	+ 9
After injury	+ 10	+ 63	+ 102	+ 83	+ 72	+ 65	+ 60

Time after excitation	1″·4	1″·6	1″·8	2″·0	2″·2	2″·4
Before injury	+ 14	+ 14	+ 15	+ 27	+ 58	0
After injury	+ 50	+ 45	+ 32	0	0	0

The readings show that the greatest effect of injury was observed in the first half of the 1st second, after which it declined, at first gradually then rapidly. During the period ending 0″·2 after excitation, the difference between the state of the preparation before and after injury, as indicated by the deflections −46 and +63, amounted to 0·0177 Daniell.

In another series of experiments, the influence of injury was studied by comparing the condition of the injured part successively with the sound surface on either side of it, the purpose being to show that the effect of injury is strictly limited to the injured spot. The following is an example.

[23] A Stannius' preparation was led off by contacts *f* and *m* on opposite sides of the ventricle (*f* on the right side and *m* on the left side) about half-way between base and apex, the seat of excitation being at *m*. After a series of observations had been taken, the surface was injured between the two contacts, the distance of which from each other was 3·5 millims. After as well as before the injury the led off surfaces were sensibly equipotential (0·0002 D. to 0·0006 D.). The readings were as follows:—

Time after excitation	0″·1	0″·2	0″·4	0″·6	0″·8	1″·0	1″·2
Before injury	−35	−85	0	0	+1	+3	+8
After injury	−42	−73	−15	−10	−6	0	0

Time after excitation	1″·4	1″·6	1″·8	2″·0	2″·2
Before injury	+14	+50	+29	0	0
After injury	+3	+15	+30	+4	0

The position of the contact *m* was then shifted to the injured surface and two sets of observations were taken, first with *f* in its original position, and secondly with *f* in the position originally occupied by *m*. The readings were:—

Time after excitation	0″·1	0″·2	0″·4	0″·6	0″·8	1″·0	1″·2
f on the left side	+5	+38	+92	+96	+96	+88	+80
f on the right side	+20	+61	+80	+79	+76	+72	+65

Time after excitation	1″·4	1″·6	1″·8	2″·0
f on the left side	+54	+11	0	0
f on the right side	+48	+6	−4	−2

In these, as in all the preceding cases, the largest deflections were observed during the 1st second after excitation. Each of the numbers is the mean of two observations. Between the first and second observation in each case the injury was renewed by retouching the surface with the hot wire. The deflections 96 and 80, the highest observed in the two sets of experiments, correspond respectively to the electromotive forces 0·0132 D. and 0·011 D. The difference between the two contacts in the unexcited state, in the observation recorded in the first line varied from 0·0067 D. to 0·0043 D.; as regards those in the second line from 0·0048 D. to 0·0032 D.

Relation between the effects of injury and those of the temporary application of heat. The effects described in the preceding pages as produced by the destruction of the part of the surface of the ventricle to which the electrode *m* is applied, correspond in the main with those observed when the same part is temporarily exposed to a temperature higher than that of the rest of the ventricle. There are, however, differences which cannot fail to excite attention as suggesting the question whether or not the two actions are of the same nature. The chief of these differences relates to the time after excitation at which the largest positive deflections of the needle are observed. In the case of the injured ventricle the positive maximum occurs at about the middle of the 1st second; in that of the temporarily warmed preparation it occurs later. So long as the effect lasts it may be described by saying that the terminal phase begins and culminates earlier, so as to encroach on the period of equipotentiality, and that the extent of its deflection is much greater.

It seemed to us probable from the comparison of the results produced by slight injuries, of which the effects are very transitory, with those above referred to, that this difference was not fundamental, and was in great measure dependent on the nature of the injury inflicted. For this reason it was thought desirable to investigate other modes of acting on the surface of the heart and in particular those of chemical excitants. The object we had in view was to bring about a very slight alteration of the surface of the ventricle in the neighbourhood of the leading-off electrode *m*, and then gradually to increase it until an effect corresponding with that of mechanical injury presented itself. This we hoped to accomplish by gradually increasing the strength of the solution of salt with which the tip of *m* was moistened. It is well known that the 0·75 per cent. solution which is ordinarily used is without action. We had found that strong solutions (e.g., 40 per cent.) when applied to the surface of the ventricle act in the same way as mechanical injury. It might therefore be expected that by using solutions of intermediate strength, intermediate results might be obtained.

We therefore acted on the surface of the ventricle in a series of Stannius' preparations led off and excited in the usual way, by first dipping a camel-hair pencil in 20 per cent. solution of salt, then draining it with filtering paper and applying it to the beak of the electrode *m*. In this way the reagent reached the surface very gradually. Its advent was always indicated by a motion of the needle which slowly swung in a direction indicating that the surface affected had become positive. This subsided after about a minute. It was then observed with the aid of the capillary electrometer that the variation had altered its character. The nature of the alteration differed according to the strength of the solution used. When 10 per cent. solution was applied very sparingly, it usually happened that the deflections of the initial phase were increased and those of the terminal phase diminished, but on repeating the process (the effect of which was, of course, to strengthen the solution of salt at the surface of contact) the terminal positive was increased and showed itself earlier, so as to encroach on the isoelectrical period. In this stage the effect produced corresponded closely with the temporary effect of warming. If the application was repeated with a stronger solution, the isoelectrical period became shorter and shorter, and the positive deflections larger and larger, until finally the variation assumed the characters which are observed when *m* is applied to an injured surface. From these facts it is apparent that the characters of the variation which severally present themselves when the surface of the ventricle at *m* is temporarily warmed and when it is more permanently injured, although they are distinguishable, may pass into each other by a continuous series of gradations.

IV. RATE OF PROPAGATION OF THE EXCITATORY STATE.

The rate of propagation of the electrical change which serves as the sign of the excitatory state, admits of being determined by two methods. The first consists in measuring directly with the rheotome, the time after excitation at which the first indications of electrical change are appreciable, and the distance from the seat of excitation at which the observation is made. The second depends on the assumption that the culmination of the initial phase, *i.e.* the sudden return from negativity of the nearer of the two leading-off contacts towards equipotentiality, is dependent on the arrival of the excitation-wave to the more distant contact. Both of these methods have been used by Engelmann and have led in his hands to the conclusion that the rate of propagation is less than 50 millims. per second. With reference to the first method, we found that correct results cannot be obtained by comparing the distance between the seat of excitation and any point in its progress, with the time at which its arrival at that point is indicated galvanometrically, for the reason that, neither the time nor the place of starting can be determined with certainty. When an induction current passes through a tissue, its excitatory influence extends over an undefined area which surrounds the contacts. The excitation-wave starts from the edge of this area, and consequently at an unknown distance from the electrodes. The uncertainty of time appears to affect the result much more seriously. It is not yet known how long is required for the development of the excitatory electromotive force at any excited point. All that can be said is that it is a very short time. No statement can be made either as to its duration or its constancy. This being so, the only satisfactory way of measuring the rate of transmission is to compare the difference between the times at which the excitation-wave attains two points in a straight line emanating from the seat of excitation, with the distance between these points.

In order to carry out this method the ventricle is as usual excited at the apex (x) and led off by one contact (f) at the base and by one of two contacts (m and m') which occupy different distances between x and f. If a large specimen of *Rana esculenta* is used, a distance of 7 millimeters may be interposed between x and m' and a distance of 3 millimeters between x and m. m and m' must be so connected by means of a switch that the preparation can be led off either by f and m or by f and m'. In the first case the excitatory-wave has to travel from x to m, in the second from x to m', consequently the difference between the times after excitation at which the first effect appears corresponds to the distance between m and m'.

[24] In an experiment of this kind, made at the temperature of 12° C., it was found that when the preparation was perfectly fresh, the first effect appeared at m at 39 divisions of the scale of the rheotome, at m' at 50 divisions, the distance between m and m' being 4 millims. As 10 divisions correspond to $0''{\cdot}0291$, this result gives as the rate of propagation 125 millims. per second. In another preparation observed in the same way the number of divisions was 12, the temperature being the same. In a third, at a lower temperature (7° C.) it was also 12. In each instance the measurements were twice, and in one instance three times repeated before any notable lengthening of the time-interval took place, but in all this happened sooner or later, indicating that the rate gradually diminished from 125 per second to 100 or 90.

The second method appears to us, when rightly used, to be equally reliable; it yields results which agree with those above stated. It consists simply in measuring the time-interval between the beginning and the culmination of the initial phase. We have already seen that the interval does not exceed three-hundredths of a second when the distance between the two leading-off electrodes is three millimeters. In the heart of the tortoise, when the leading-off electrodes are 15 millimeters apart, and the temperature is 20° C., we found it to be $0''{\cdot}15$.

We venture to think that Engelmann's application of this method is open to objection. According to Engelmann the propagation rate $V=\frac{i}{\Delta t}$, Δt being the time-interval between the negative and positive maxima of the "Doppelschwankung" and i the distance between the electrodes. V was found to be 37·4 millims. Substituting for Δt the duration of the "Stadium steigender Negativität" as it is shown in Plate XI. Fig. 1 of Prof. Engelmann's paper, *viz.* $0''{\cdot}06$, and for i the mean distance between the leading-off contacts in the ten experiments which the curve represents, we have $V=\frac{6}{0{\cdot}06}=100$. Engelmann's own curves seem therefore, unless it can be shown that our mode of interpreting them is wrong, to afford evidence that in his preparations the rate of propagation did not fall far short of the estimate given above.

V. CONCLUSION.

In explanation of the phenomena described in the preceding paragraphs the only assumptions which are necessary are the following: 1. Every excited part of the surface of the ventricle is during the excitatory state *negative* to every unexcited part. 2. The excitatory state is propagated in all directions. The rate of propagation (in the direction from apex towards base) is about 125 millimeters per second. (It is probably the same in all directions.) 3. The duration of the excitatory state is in winter frogs from $1''{\cdot}6$ to $1''{\cdot}8$

at the temperature of 12° C. 4. The duration of the state of diminished excitability is the same.

Analogous propositions to these have been recognized and experimentally proved as regards voluntary muscle by Bernstein in his discussion of the theory of the excitatory process[1]. For their application to the ventricle of the frog heart we are answerable. As regards the duration of the excitatory state and its rate of propagation, our conclusions differ from those of Engelmann with whom in other respects we agree. With reference to the duration of the state of diminished excitability, we have endeavoured to extend the observations of M. Marey.

The rate of propagation being as above stated 125 millimeters per second and the local duration of the excitatory state $1''\cdot 7$ at the temperature 12° C., the variation as observed in the normal heart led off by two electrodes at four millimeters distance from each other is represented by the following diagram in which the continuous line expresses the duration and degree of the negativity (Reizwelle) at the near electrode *m* and the broken line the negativity of the more remote electrode *f*. This being so the *differences* between the ordinates of the two curves express the negativity of the contact *m* when the ordinates of the curve *m* exceed those of the curve *f* and *vice versâ*. Transferring these differences to another axis from which the negative ordinates stretch upwards, those of opposite sign downwards, we have the curve *V* as the theoretical curve of the excitatory variation. It need scarcely be pointed out how entirely it agrees with that yielded by observation.

The effect of partially warming the surface of the ventricle at *m* is to shorten the local duration of the excitatory state at the part warmed. In *V′* the modification which this would produce is shown. Above are inscribed the curves *m* and *f*, of which *V′* is the difference. The initial phase is unaltered, but the terminal phase begins earlier and is strengthened.

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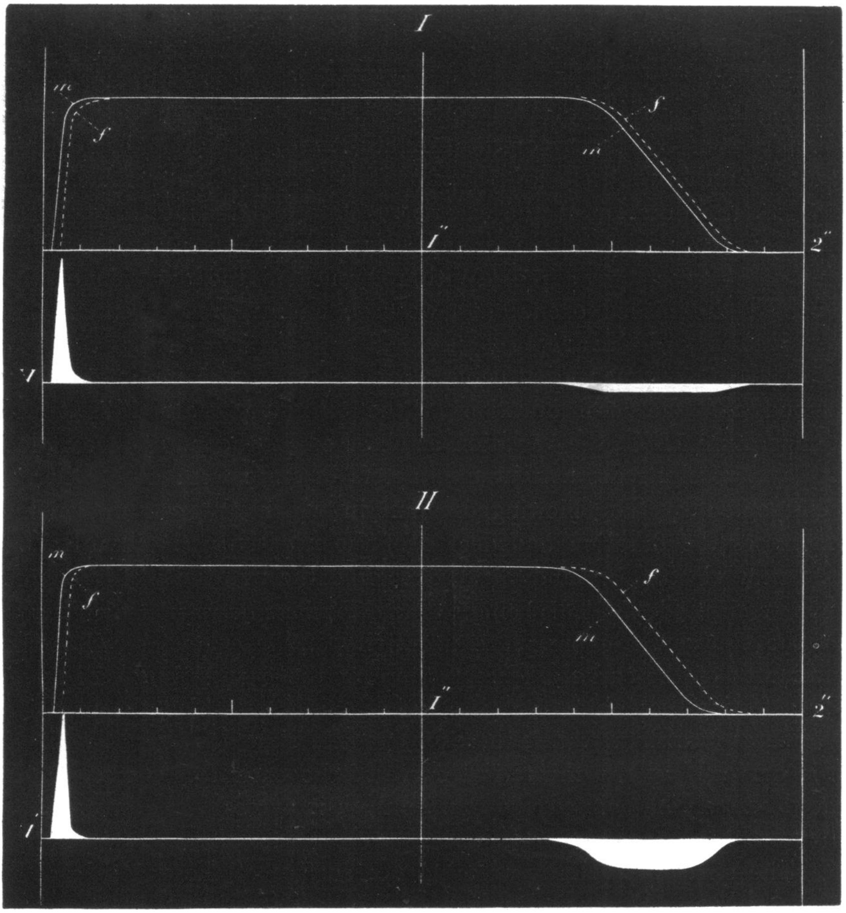
[1] *Untersuchungen über den Erregungsvorgang*, Heidelberg, 1871. The following passages may be referred to: as regards proposition 1, "Eine Stelle des Langschnitts, innerhalb der Reizwelle ist negativ gegen eine Stelle ausserhalb derselben" (p. 63); as regards 2 and 3, the whole of p. 56 (loc. cit.); as regards 4, "Die Intensität der Erregung nimmt ab sobald die Zahl der Reize in der Secunde so gross geworden ist, dass das Interval zwischen zweien kleiner geworden ist, als die Dauer einer Reizwelle" (p. 140), the propagation rate being about 3 metres per second. In the ventricle the duration is about 300 times greater, and the rate of propagation diminished in nearly corresponding proportion. According to Bernstein the "Dauer einer Reizwelle" is $\frac{4}{1000}$ sec.



The upper figure is intended to exhibit the time-relations of the normal variation, the lower the same relations as modified when the temperature of *m* exceeds that of *f*. Of the three vertical lines, the one to the left marks the moment of excitation, the other two the ends of the 1st and of the 2nd second. The curves *m* and *f* (in I) express respectively the electrical changes which take place during these two periods, *m* being the curve of negativity of the contact *m*, and *f* the curve of negativity of the contact *f*. Accordingly the distance, measured horizontally, between the ascending parts of *m* and *f* expresses the time occupied in the propagation of the negative wave from the contact *m* to the contact *f*. The distance between the two contacts in the case represented is three millims. and the time about 0″·025. It being assumed that the duration of the excitatory state (the state of negativity) is the same at *m* as it is at *f*, the descents of the curves are as far apart as their ascents.

The *differences* of potential which exist during the period represented between the two contacts are expressed by the corresponding *distances* between the two curves measured vertically. These distances are set off on the horizontal line *V*. During the greater part of the excitatory period the two contacts are equipotential; and accordingly the broken and continuous lines are coincident. The relative negativity of *m* to *f* during the initial phase is expressed by the white space above the line *V* and the relative positivity of *m* to *f* during the terminal phase by the white space below the same line, the vertical measurements of these spaces being equal to those of the corresponding distances of the curves *m* and *f*.

In comparing the theoretical form of the first phase of the variation, as exhibited in that of the white space which represents it, with the curve which is obtained when the successive deflections of a rheotome observation are set off as ordinates on a time-axis, it is seen that the latter is wider and at the same time less peaked. The reason of this difference has been explained in the text. It is the more considerable the longer the period of closure of the rheotome. For example, an initial phase of the duration indicated in the diagram (which, although obtained deductively, agrees closely with the results of experiment) would, in case the closing time of the rheotome were one-tenth of a second, express itself by negative deflections which would cover a period of not less than 0″·17 (whereas the actual duration of the period of negativity is not more than 0″·08), and would be nearly maximal for about 0″·05. If on the other hand the period of closure were shortened to one hundredth of a second, the curve obtained would very accurately represent the true form of the variation. The same considerations of course apply to the terminal phase.

The effect of injury of the surface at *m* is to diminish or weaken the excitatory state (Reizwelle) at the injured part. Consequently the equilibrium which normally exists between all parts of the surface during the "isoelectric interval" is destroyed. The initial phase is diminished in extent and is immediately followed by a positive phase which lasts to the end of the variation.

The time relations which are expressed by the curves *V* and *V′* help us to understand most of the irregularities which occasionally present themselves in our rheotome readings. Thus for example we have seen that the initial phase is sometimes followed by a transitory phase of opposite sign giving rise to Engelmann's "Doppelschwankung." This must inevitably happen if the rise of the excitatory wave is more gradual than it usually is at *m* or more abrupt at *f*. There is however one anomaly which for the present we must leave unexplained; it is the apparent shortening of the total duration of the period of variation which happens after injury of which indications are to be found in almost all of the observations recorded in Section III.

APPENDIX I.

Electrical condition of the external surface of the resting ventricle.

On the condition of the resting ventricle, when all parts of it are at equal temperature, we have nothing to add to the account already given by Prof. Engelmann.

Throughout our observations we have met with no exception to his statement that the surface of the ventricle is in every case equipotential. When, however, the surface is unequally heated this equality is disturbed. This disturbance may be temporary or permanent.

Temporary effect. When the surface of the ventricle is led off at two points (*f* and *m*) and one of them is warmed by the approach of a heated loop of platinum wire for a period of two seconds or more, the warmed contact becomes positive to the other, as in the following experiment:—

[25] A Stannius' heart was led off at base (*f*) and apex (*m*). The wire loop was placed at a distance of three millimeters from *m*. About one second after closing the current the needle began to move in a direction indicating that the spot warmed became positive. By four seconds this movement had attained its maximum. If the heating was now discontinued, the effect subsided, *i. e.* the needle returned to zero. If at this moment the ventricle was excited by a single induction shock at the base, a deflection took place indicating that the apex became positive, the extent of this deflection being three or four times as great as the normal excitatory variation in the same direction. Thus before warming, the surface being equipotential, the excitatory deflection was 59. After warming for three seconds the warmed contact became positive (12 galv. scale), and on excitation the deflection was 177, after which the needle returned to zero. When the heating was prolonged or the distance of the loop from *m* was diminished, the warmed surface became for a moment positive, then permanently negative.

Another Stannius' heart was led off and warmed in the same way. The excitatory deflection before warming was 56. After warming for 10 seconds, the warmed contact became positive (15 galv. scale), but immediately afterwards negative (– 130 galv. scale), and on excitation the needle swung to + 210, returning to its previous negative position. In a precisely similar experiment in another heart the positive movement of the needle began at 4″, the negative at 9″ after the closure of the warming current. Similar observations made at the same time yielded results which corresponded in every respect with those above given, showing that after a slight local increase of temperature the warmed spot becomes temporarily positive, speedily returning to its normal state of equipotentiality after the warming has ceased, and that if the warming is continued, the difference of potential changes sign. It will be seen subsequently that this negativity is the first sign of a permanent impairment of the physiological properties of the surface.

Permanent effect. In the following experiments the effect of warming the surface of the heart at the same spot repeatedly was observed. At first the effect resembled that which has been already described. Gradually, however, it was observed that the surface which had been warmed became slightly negative to the unwarmed; *i.e.* the positive effect which was the immediate consequence of each successive warming, was followed by a permanent and gradually increasing change in the opposite direction, the total amount of which, however, even in those experiments in which the warming was repeated ten or more times, never amounted to so much as a thousandth of a Daniell.

[26] I. Stannius' heart, warmed by wire at 2 millims. distance, for 8″ at a time, and at intervals of two minutes. Before warming, + 0·002 D.; after three warmings, the difference was + 0·0014; after five warmings, + 0·0012; after ten warmings, − 0·0008; after seven additional warmings, − 0·0012. Immediately after each of these warmings the variation exhibited the characters previously described.

II. Stannius' heart, warmed by wire at 3 millims. distance. Before warming, − 0·0004 D. After repeated warming for 5 seconds at a time at intervals of two minutes, − 0·0006. When with the rheotome the galvanometer circuit was closed during a period of 0″·18, ending 1″·4 after excitation, the deflection was, before warming, + 5 : after warming, + 37. As the value of this deflection in E. M. F. was about 0·006 D., it was about 30 times as great as the difference in the negative direction produced by warming.

III. Stannius' heart. Warmed by wire at two and a half millims. Before warming, + 0·0012 D.; after warming ten times for 5″, + 0·0004. The deflection during the rheotome period ending 1″·4 was, before warming, − 8 scale; after warming + 90, = about 0·009—that is, about eleven times as great as the difference due to injury.

In a second observation on the same heart the results were:—Before warming, + 0·0004; after warming six times as before, 0·0. The deflection during the rheotome period ending at 1″·0 after excitation, before warming, + 1; after warming, + 95, &c.

IV. Stannius' heart warmed at two millims. Before warming, + 0·0006; after warming 12 times, 0·0. The deflection during the rheotome period ending 1″·4 was before warming, + 12; after warming. + 76. E. M. F. value of + 76, + 0·007 D.

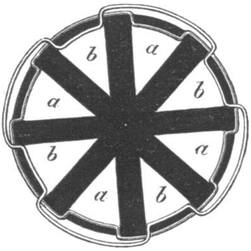
It cannot be doubted that the change of the surface of the heart produced in the mode of experiment above described is of the same kind with the larger effects which manifest themselves when it is visibly destroyed or injured, whether mechanically or chemically, in which case, as was before stated, a difference of potential may exist immediately after the injury amounting to 0·03 D, that is some twenty or thirty times as great as that described above. The application of heat by the methods used in the preceding experiments thus affords a means of producing in the part acted on a local change or impairment, of which the extent can be graduated with the utmost nicety.

APPENDIX II.

Description of the Rheotome used in the preceding investigation[1].

From a circular iron plate, supported on levelling screws, spring two strong brass pillars, each 6 centims. in height, on the summits of which rests a horizontal bar. In the middle of the bar is a screw, which ends below in a steel point. A similar steel point rises from the centre of the iron plate. On these centres works a vertical axis about 5 centims.

Fig. 1.



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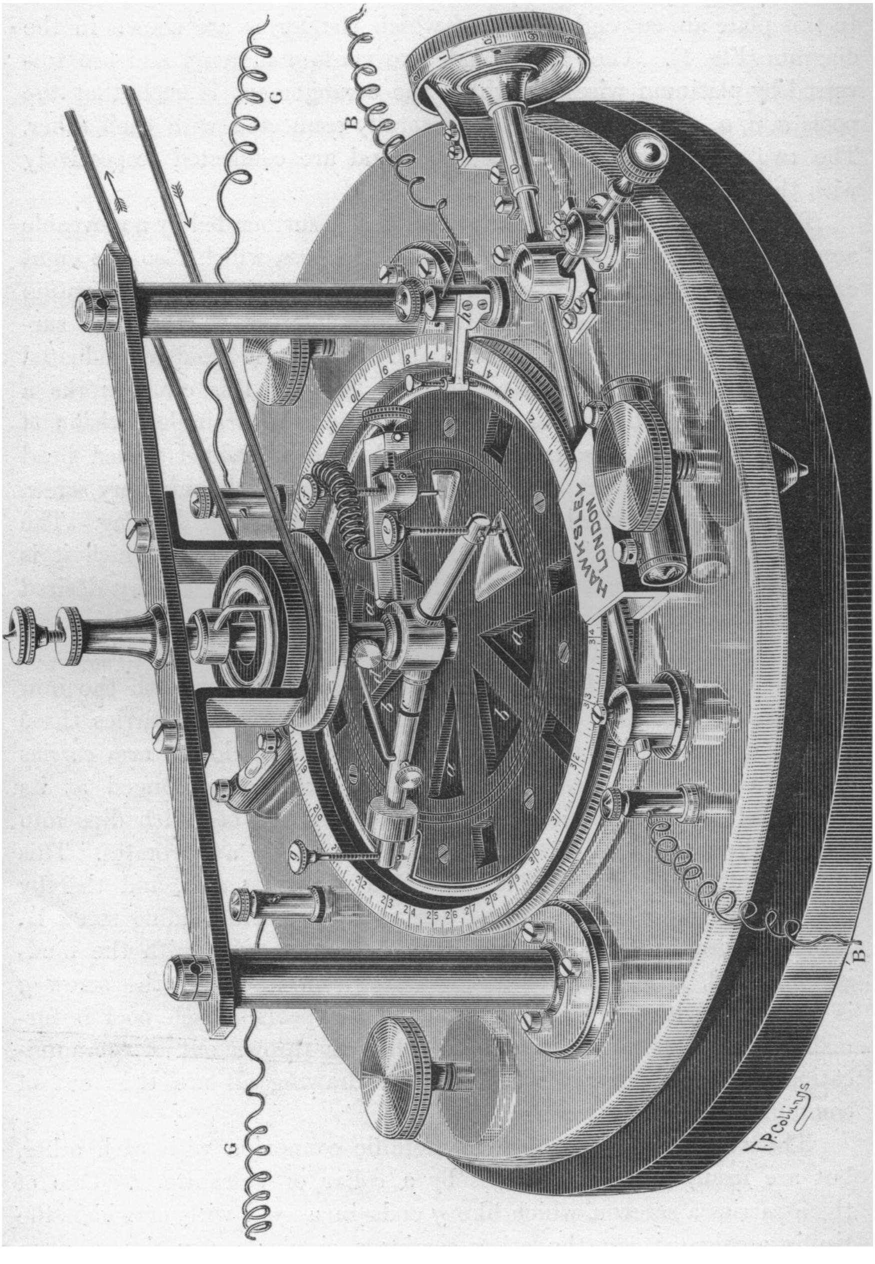
[1] From a paper, "On a New Rheotome," recently communicated to the Royal Society by J. Burdon-Sanderson. See Fig. on the next page.

in length. The steel point on which the lower end of the axis works is surrounded by a circular plate of vulcanite about 0·5 centim. thick. In this plate are cut eight pools, of which the forms are shown in the diagram (Fig. 1). They are intended to contain mercury and are traversed by platinum wires, of which the arrangement is such that the pools *a, a, a, a,* and *b, b, b, b,* are severally connected with each other. The two rings of wire are insulated and are connected respectively with the binding-screws G and G.

The fixed circular plate above described is surrounded by a moveable annular plate of the same material and thickness, which also has eight excavations or pools, all of which can be brought into communication by means of an annular trough of mercury by which they are surrounded. To the outer edge of the annular plate is fixed a graduated circle of brass, which revolves with it. Against this circle works a tangent screw, each turn of which corresponds to a single division of the graduation; this screw is furnished with a divided milled head and can be thrown out of gear when necessary by the auxiliary screw, in a manner which will be readily understood from the drawing. The vertical axis carries at its upper end a pulley, by means of which it is connected with a motor, and can be made to revolve at any desired rate. Above the pulley is a platinum wire, the end of which is bent downwards so as to dip into an annular pool of mercury, which is in metallic connexion with the horizontal bar, and thereby with the iron plate and the binding screw B′. The vertical axis also carries three arms, of which one is longer than the other two; the longer arm carries at its end the vertical screw *g*; this screw is prolonged at its lower end by an amalgamated gold wire, the end of which dips into the mercury contained in the external pool, as the axis rotates. This arm is insulated at *c*, but is connected with the axis, and thereby through the annular pool above described with the binding screw B′. As the external pools are connected through the arm *h* with the binding screw B, B and B′ are in communication whenever the screw *g* is in contact with the mercury in any of the pools. Each pool is furnished with a vulcanite stop, by which it is thrown out of communication with the external pool. In the drawing all are thus out of communication excepting one.

The two shorter arms are in metallic connexion with each other, but are insulated from the axis by a collar of vulcanite *d*. One of them carries a screw *e*, which like *g* ends in a gold wire, of which the tip is amalgamated; the other carries a similar screw *f*, and is so

Fig. 2.



constructed that the screw *f* can be moved radially (*i.e.* in a vertical plane which contains the axis of rotation) to any required distance from the axis. The two arms meet each other at an angle of 45°.

From the form and arrangement of the internal pools (see Fig. 1) it is evident that whenever the screw *e* is in contact with any of the pools *b, b, b, b,* the screw *f* must be in contact with the pools *a, a, a, a* (see Fig. 2), and further inasmuch as *f* is nearer the axis than *e*, the times at which *e* makes and breaks contact with the pool *b* must respectively precede and follow those at which contact with the pool *a* is made and broken by *f*. Consequently the time during which both are in contact (*i.e.* during which the circuit G G is closed) is determined solely by the duration of the immersion of *f*, and can be varied by altering its distance from the centre.

When it is desired to use the rheotome for investigating the effects of series of excitations recurring at short intervals (tetanus of muscle or nerve), all the pools are equally filled with mercury.

Their equality must be tested by interpolating each set of pools in the circuit of a Grove's cell, which also includes a recording chronograph; if the chronographic record shows that the durations of the contacts are not perfectly equal, the error must be corrected by adding or subtracting mercury. For investigating the effects of single excitations, only one of the external and one couple of the internal pools are used.

The drawing (Fig. 2) shows the arrangement of the apparatus as used in the investigation of the electrical phenomena of the ventricle of the heart of the frog. The instrument is set so that the external contact *g* is broken at a moment which immediately precedes the immersion of *f*: consequently the galvanometer circuit G G is open at the moment of excitation, but closed immediately after, remaining closed so long as *f* is immersed. By means of the tangent screw, the interval between the opening of the exciting circuit B B′, and the closing of the galvanometer circuit G G, can be varied at will.