

CROONIAN LECTURE.—“On the Relation of Motion in Animals and Plants to the Electrical Phenomena which are associated with it.” By J. BURDON-SANDERSON, M.A., M.D., F.R.S. Received March 2,—Read March 16, 1899.

In a Croonian Lecture which I delivered to the Royal Society in 1867—more than thirty years ago—I exhibited a number of diagrams of graphic records, in evidence of the mechanical relations which I then sought to establish between the movements of the heart and those of respiration in the higher animals.

I have to-day to bring before you results which have also been obtained by a graphic method, which however differs from the other in that the records are written by light, and not by pen on paper; that the time taken in recording is measured in thousandths of seconds, not tenths; and finally, that the events recorded are not the movements of the chest or heart, but the electrical changes which, as will be shown, are found to associate themselves with all manifestations of functional activity in living organisms, whenever these take place under conditions which admit of their being investigated.

Our purpose is to consider the relation of two coincident and concurrent processes, with reference to which we make at the outset the assumption that one is functional, the other concomitant, using the word “function” in the biological sense to imply the doing by an organ of the work for which it is adapted. In the observations which I have made from time to time during the last twenty years relating to the electrical phenomena of plants and animals, it has always been my endeavour to regard them exclusively in relation to the functional activity of the structures in which they manifest themselves. In investigating the function of a living organ or organism, you have to do with a machine that you cannot take to pieces, and it is often the best way to observe how, after its action has been arrested, it goes on again. To do this under experimental conditions is one of the most frequently used methods of the physiologist. The possibility of employing it depends on the circumstance that all animal organisms, and certain parts of plants, possess the faculty of being awakened from a state of rest to normal activity.

Even under the most favourable conditions, the observation of this transition is attended with difficulties which arise from the complexity of the chemical and mechanical changes, and the shortness of the time spent in their accomplishment. It is this crowding together of chemical, thermal, and electrical phenomena into a very brief period which determines the method for their elucidation, a method consisting to a large extent of a determination of *time-relations*, *i.e.*, of the order of

succession of phenomena; for it is evident that when you have to do with a number of events which appear to be simultaneous, the most effectual way to determine their causal relations is to ascertain the order of their occurrence. For, inasmuch as one event which follows another cannot be its cause, the proof of their sequence which accurate time-measurement affords may be of infinite value in indicating where the starting point in a complex series of changes is to be sought for.

The inquiry as to the relation between functional activity and the electrical phenomena accompanying it, can only be entered upon by finding instances in which both processes can be observed together. Amongst these, those are to be preferred in which the question presents itself in its simplest form, the experimental conditions can be most easily controlled, and the observations can be made with the greatest exactitude.

It might at first sight seem desirable to begin by describing the electrical manifestations of functional activity in the simplest organisms and organs. There are, however, important reasons for following the reverse order. To do so is in conformity with the general rule that a problem can be most easily solved when it presents itself in its simplest form. In the lowest organisms the relation of function to structure, so far from being simple, is necessarily very complex, for functions of the most varied kind have to be discharged by one and the same mechanism, and often in default of any mechanism at all that we can discover; whereas in the higher plants and animals we find for the most part that every kind of work has its instrument, every action its agent. It is in the highest organisms therefore that elementary physiological questions must be studied, and it is in them that they have been most studied.

Of the elementary vital functions, *motion* was the one fixed upon as the subject of this lecture by its founder. Its fitness for our purpose is pre-eminent. Motion, in the physiological sense, is simple, controllable, measurable. It is, moreover, a function of paramount importance as the means by which the animal organism maintains its relation to the external world. In the higher animals, *muscle* is the instrument of motion, and therefore claims our consideration. It has, in addition, the advantage of being a structure of which the chemical, thermal, and mechanical properties are better known than those of any other. This advantage applies particularly to the muscles of the *frog*, which on that account, as well as on the grounds which have been the occasion of their being most studied, are to be preferred for our present investigation. What we have first to do therefore this afternoon is to determine the relation between the *electrical* concomitants of muscular action and muscular action itself; but before entering upon it, I must occupy you for a few minutes in stating what is at present most certainly known as to the nature of that action.

When a muscle is roused to activity by the presence of an exciting cause, its mechanical properties suddenly change. It shortens and, if the shortening is resisted, becomes tight. If the resistance is such as cannot be overcome, it tightens without shortening. With reference to this mechanical change, we know that it is dependent on chemical change, and that that change is oxidation. Admitting these propositions, we must necessarily believe that the oxidation is sudden, *i.e.*, explosive, because its mechanical effect (the tension or tautness I have mentioned) attains its maximum at a very short period after the moment at which the process begins.

At ordinary temperature we find that in a whole muscle the tension which is induced by an excitation attains its maximum in about 3/100 second. But if we fix our attention on a single muscular element, *i.e.*, on one of the infinite number of molecular mechanisms by the cooperation of which the mechanical change consequent on excitation is brought about, it can be shown that in each taken separately a much shorter duration than 3/100 second must be assigned to the process of transition. According to Bernstein, less than 1/100 second must be assigned to the chemical process which takes place in a muscular element in response to a single stimulus.\*

This chemical process of extreme suddenness is followed without measurable loss of time by the conversion of the chemical energy of the oxidisable material into mechanical energy, which immediately manifests itself either in shortening or in the effort to shorten. The way in which this transference takes place must for the present be left an open question, for, as Professor Engelmann explained in the Croonian Lecture for 1895, the transformation of chemical into mechanical energy consequent on excitation of muscle, though by no means an insoluble, is still an unsolved physical problem. We know how much chemical energy is liberated, we know how much work is done, and how much heat is wasted, but we cannot explain how it happens; it being difficult to suppose that the temperature required for such transformation can exist in living muscle.

The absence of a sufficient physical theory of the origin of muscular force does not, however, deprive the mechanical manifestations of the process of their value as simple, measurable, and controllable indications of functional activity. Whether we take the case in which a

\* See Pflüger's 'Archiv,' vol. 67, p. 211, 1897, where Bernstein describes his method of measuring the period of latency. As in the method described by me in the 'Journal of Physiology' in 1895, a magnified image of the moving surface of a muscle excited directly is received on a slit, behind which a sensitive plate passes. From the curve so obtained, Bernstein determines the moment at which the rate of expansion increases most rapidly, and regards this as the moment at which the moving force is at its maximum. This conclusion, of course, applies to the part of the muscle immediately excited.

muscle strives against a resistance which it cannot overcome, or shortens without resistance, or does both simultaneously, the change of tension in the one case, of form in the other, or of both, are measurable processes of which the time-relations can be ascertained with great accuracy. We are on safe ground therefore in using either change of tension or change of form as a means of estimating the vital activity of muscle, and in fact both are required.

For every investigation in which muscular function is in question, three points come prominently forward: (1) The moment at which mechanical energy comes into play; (2) the maximum energy displayed; and (3) the time at which that display culminates. As regards the first point, the time occupied before the mechanical response begins was, for many years, believed to be  $1/100$  second. This estimate was accepted as though on the authority of Helmholtz, but was really based on a misunderstanding of his experimental data. But we now know that the change of form resulting from the action of a single instantaneous stimulus begins in the muscle *element* not later than  $4/1000$  second after the moment of excitation, and I may be permitted to show you how this result can be arrived at with absolute certainty by the photographic method. (Photograph shown.)

As regards the second and third points, we find it better to measure contractile activity by change of tension rather than by change of form, firstly, because the method of measuring tension is less liable to error, and, secondly, because the process of development of tension is more rapid than the development of change of form. For, although with the exquisite methods we now possess of getting rid of inertia in our recording apparatus, it is possible to measure the shortening with great exactitude, yet it is easier to guard against errors of observation when the other (isometric) method is used.

Having seen how functional activity can be measured, we may advert to the question that principally concerns us this afternoon—the question, namely, whether the electrical phenomena may also be regarded as expressions of functional activity. Assuming for the moment the question to be answered in the affirmative, with what part of our tension curve should we expect the electrical concomitant to coincide? Assuredly with the first and second hundredths of a second after excitation, *i.e.*, with the period of greatest activity of the unknown process by which chemical is replaced by mechanical energy, and, for a reason which I will at once explain, with the very beginning of that process. For, as I have already indicated, the transition does not occur at the same moment everywhere, and inasmuch as the method which we use for the investigation of electrical change takes cognisance only of what happens within an area of a couple of millimetres, we should expect it to occur not at a moment corresponding to the maximum development of tension in the whole muscle, but at

the moment at which the transition process is going on with the greatest rapidity in the elements immediately concerned within that limited area. Assuming for the moment that this rapidity is expressible as a measurable electromotive force, we should expect the appearance and disappearance of that electromotive force to be represented, not by a curve resembling the tension curve, but by a curve of the form indicated in the diagram. (Curve P' in Diagram 4.)

Before losing sight of the mechanical changes which have for the last few minutes been occupying our attention, there are two other points which must be shortly adverted to on account of their bearing on what follows. The one is the terminableness and the cyclical character of the mechanical process. The muscle returns to its *status quo* at a certain time after it has been disturbed, a time strictly dependent on temperature and other well ascertained physiological conditions. We do not know as yet *how* it relaxes, whether it is merely a physical reaction, or whether it is by the intervention of a new chemical process. This is a *questio vexata* which for the present must remain open.

The second point is that although the mechanical process is limited in time it is not limited in space. If it were possible to imagine a *continuum* of contractile protoplasm, an excitation once started would go on for ever, *i.e.*, it would be propagated from element to element—in every direction if it were of the nature of cardiac muscle, in two directions only if it were of the nature of skeletal muscle. For this process to take place we suppose that each element excites its neighbour. In each transmission the time lost is almost infinitesimal, yet by summation it acquires a definite value, so that the relation between distance travelled and time occupied can, when the temperature and other conditions are known, be foretold. In so far as each element transmits its state of change to its neighbour without loss it resembles the propagation of light and sound, but the velocity of propagation is of so different an order that the comparison must not be carried too far.

### *Method of Observation.*

We are now in a position to enter on the inquiry which more immediately concerns us. Having the order of the mechanical changes which constitute muscular action before us, it will be our purpose to compare with this order that of its concomitant electrical phenomena. Before I proceed with this comparison it is desirable to say that it should be understood that no reference will be made to electrical theory. We merely derive our modes of observation and of measurement from the exact sciences, and aim at the utmost attainable precision; but the phenomena have their chief interest as outward and visible signs of intimate vital processes, of which they afford us the only knowledge that is within our reach.

We choose as our subject of observation a muscle of nearly symmetrical form—a band of parallel fibres. We explore its electrical state, by a conducting arch containing a galvanoscope, the ends of the arch being in contact with its surface. If the muscle is no longer living, the galvanoscope gives no evidence of current. If it is living, there is again no current, provided that the two surfaces are in the same physiological state. If one is *less* living than the other the fact is indicated by a difference of potential between them, a current *flowing through the galvanoscope from the more living to the less living*. Vitality is, therefore, here indicated by difference of potential. By vitality we mean nothing more than the *capacity for discharging function*. This capacity diminishes by discharge, *i.e.*, by activity. Accordingly we find that when, for any reason, the muscular substance at one part becomes more active than the muscular substance at another, the former becomes negative to the latter.

Every observation of the electrical phenomena of muscle (or of any other excitable structure) relates either to the state of capacity for action (called in physiology “rest”), or to the state of action or discharge. In either case it consists in comparing the states of two contacts,\* *i.e.*, of two parts to which electrodes of a galvanoscope are applied. It is obviously desirable for the investigation of the changes at either, that those which take place at the other should be annulled during the period of observation. On this consideration a rule is based, to the mode of carrying out of which I will advert presently.

Most of the results which I shall place before you were obtained with the aid of the capillary electrometer, of the use of which as an aid to electrophysiological investigations I brought before the Royal Society some instances nearly twenty years ago. Its application has since been studied with great completeness by Mr. Burch, to whose skill I am indebted for the instruments which I have used for my work during the last ten years, and more particularly for the one which has enabled me to submit to you the photographic results I am now about to exhibit. These photographs, I need scarcely explain, express the excursions of the meniscus of the mercury column as a sensitive plate moves rapidly past the slit on which it is projected, each upward movement of the image indicating that the surface of contact connected with the mercury has become at that moment positive to the other.

I do not propose to give this afternoon even the shortest description of the instrument, and I should not occupy time in explaining why it answers my purpose so perfectly, were it not that with the exception of Professor Einthoven and Dr. R. du Bois-Reymond the leading authorities on the other side of the Channel, and particularly Professor

\* It may be well to note that the contacts referred to here and elsewhere are made by means of non-polarisable electrodes of the kind originally devised by du Bois-Reymond and always used in physiological work.

Hermann, have condemned it as an instrument of which the defects are essential and irremediable. As I have answered these criticisms elsewhere, I need only say here that for the investigation of the order and duration of a rapid succession of electrical changes, such as those with which we are now concerned, the instrument surpasses all others ; and that by means of it my colleague, Professor Gotch, has with Mr. Burch's aid, successfully photographed phenomena in nerve, of which the very existence could not be demonstrated a few years ago.\*

The purposes to which we apply it are (1) for the measurement of intervals of time between electrical changes which succeed each other with great rapidity, and (2) the obtaining an estimate of their relative intensities. The properties which make it so invaluable to us are (1) that it responds to the action of a current promptly, beginning when the current is closed, and indicating every change in its strength or direction without measurable loss of time ; (2) that *cet. par.*, the rate of ascent is proportional to the electromotive force of the current which produces it ; and (3) that the instrument can be graduated, and its graduation verified by comparison with instruments of greater precision, and thus used for the measurement of differences of potential of longer duration.

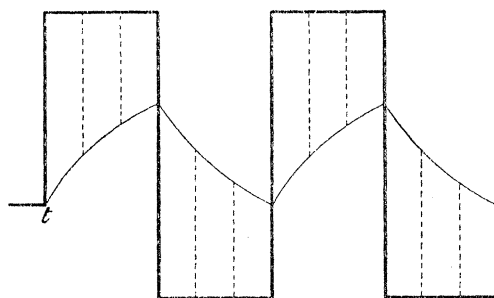
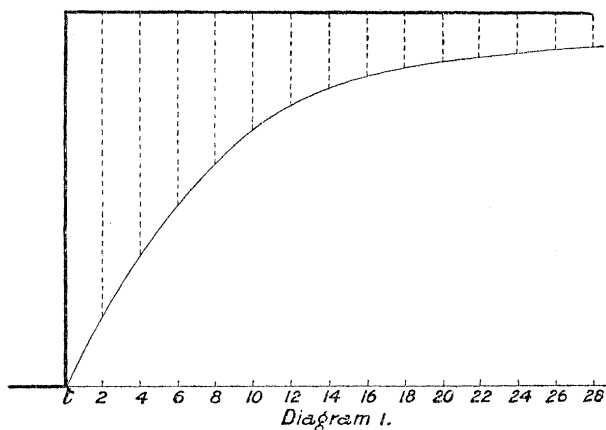
The diagrams 1, 2, and 4 illustrate the bearing of these three properties on the cases we have to investigate. As we shall see, a muscle can be brought into action either by an instantaneous stimulus, by a series of stimuli, or by continuous stimulation. Each of these has its mechanical and its electrical response. I will anticipate so far as to say that the three forms of electrical response correspond to the three forms of mechanical. They correspond to the changes indicated by the black lines in the three diagrams. I will further premise that all known excitatory responses—all *electrical changes which are concomitants of action*—may be compared with one of these types.

*Case 1.*—Response to a continuous stimulation. A difference of potential comes into existence at the contacts at the time  $t$ , and persists long enough to produce its full effect on the column. (Diagram 1.)

*Case 2.*—Series of short continuous stimulations. The column moves in alternately opposite directions. (Diagram 2.)

*Case 3.*—Response to a single instantaneous stimulation. A differ-

\* Full information relating to the instrument will be found in Mr. Burch's work 'The Capillary Electrometer in Theory and Practice,' and his papers in the 'Proceedings' (vol. 48, 1890) and 'Transactions' (A, vol. 183, 1892) of the Royal Society. A very perfect method of recording the excursions of the electrometer photographically and of interpreting the curves was described by Prof. Einthoven in Pflüger's 'Archiv' in 1894, and applied by him to the investigation of the electromotive phenomena of the human heart. It need scarcely be added that the two methods are the same in principle. An important paper has also recently been published by Dr. R. du Bois-Reymond in the 'Archiv f. An. u. Physiol.,' 1898, p. 516.



ence of potential comes into existence abruptly, and subsides abruptly at first, afterwards less rapidly. ( $P'$  in Diagram 4.)

Now I have found that in the study of my experimental results it is of great advantage to proceed *a priori*. Let us assume that there are three types of stimulation, and that each has its form of response. We can best begin by inquiring to which of these three forms the observed variation belongs, and then determine in what respects it conforms with, or differs from, the type.

In the diagrams, I have shown the types of photographic curves which correspond to the three forms of response to stimulation I have indicated. The faint lines represent photographic curves; the strong, variations of potential-difference. In each diagram the strong and the faint lines have been drawn in their true mathematical relation to each other, *i.e.*, so that the vertical distance apart of strong from faint is everywhere proportional to the gradient or slope of the photographic curve, the proportion being such that if the E.M.F. of the current acting on the electro-

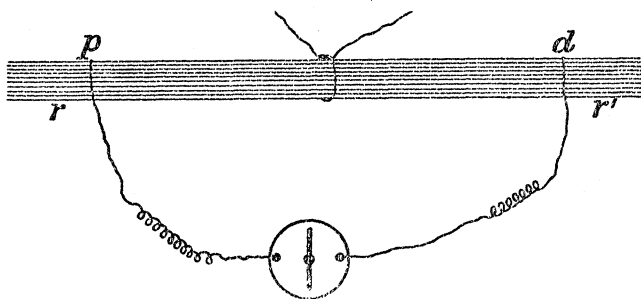
meter varied according to the strong line, the movement of the head of the mercury column would be expressed by the faint line. We shall see as we proceed that one or other of the three forms of photographic curve, which correspond to the three forms of electrical change, just designated as typical, presents itself in every excitatory response we have to investigate, provided that, as I mentioned just now, the changes under one contact only are recorded.

To ensure this, the exploring contacts must be so arranged, and the muscle itself so prepared, as to enable us to separate the part of the surface we desire to investigate from the rest, so far as concerns its effect on the instrument we are using as indicator. It is obvious that when we apply our leading-off electrodes to two parts of the surface, both of which are at the same time undergoing change, there must always be a difficulty in determining how far the effect is due to changes at the one or at the other contact. It is therefore essential for the correct observation of an electrical change at one of them, that the other should be protected from disturbing influences.

### *The First Fundamental Experiment.*

An experiment will show how this may be accomplished. It will also bring us face to face with a phenomenon which is, perhaps, the most fundamental of those which at present concern us, the phenomenon of the wave of excitation, or, to use the designation given to it by its discoverer, the *Reizwelle*. The nature of the experiment is illustrated by Diagram 3, in which the band of parallel fibres represents the sartorius muscle. It is excited (instantaneously) at *r*. A change

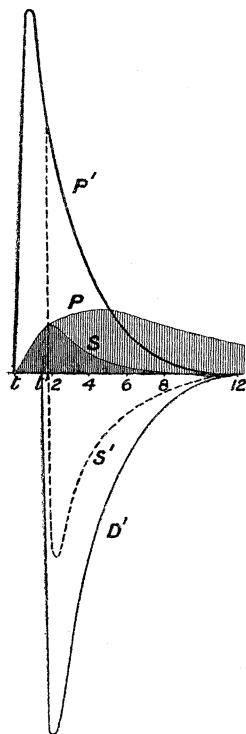
Diagram 3.



occurs there which is propagated first to the proximal contact *p*, and then onwards to the distal contact *d*, at a rate which in our preparation may be 150 cm. per second. This change is essentially a vital one, but it is attended by a mechanical change represented by the muscle

curve, and an electrical change, which we record photographically. Diagram 4 will serve to explain what (as will be immediately seen)

Diagram 4.



*Explanation of Diagram 4.*—The horizontal line is that of equipotentiality of the two surfaces of contact  $p$  and  $d$ . The curve  $P'$  expresses the relative negativity (negative difference of potential) of the surface  $p$ ; the curve  $D'$  the corresponding relative negativity of the surface  $d$ .  $S$  is a curve of which the ordinates are the algebraic sums of the corresponding ordinates of  $P'$  and  $D'$ .  $S$  is the photographic curve which expresses  $S'$ ;  $P'$  is the photographic curve which expresses  $P$ . The numbers under the horizontal line indicate hundredths of a second. The distance  $t t'$  expresses the time taken by the wave in its progress from  $p$  to  $d$ .

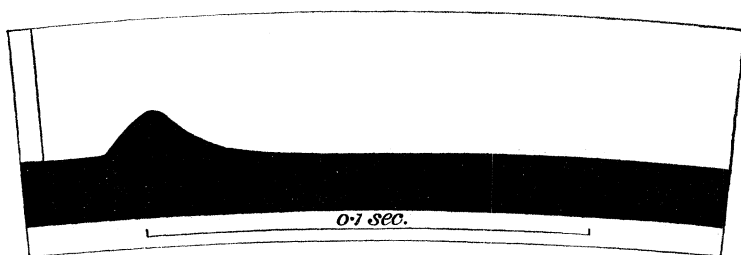
actually happens at the moment the wave passes under  $p$ . It means that a current suddenly appears there, of which the direction is from  $p$  to  $d$ . When the wave reaches  $d$ , a second effect of the same kind ( $D'$ ) occurs, of which the direction is opposed to the first. What the galvanoscopic effect of this must be is easily understood from Diagram 4, in which the two curves  $P'$  and  $D'$  are placed in a relative position to each other which expresses their time-relation. The two effects sum together. In the diagram the curve  $S'$  expresses the result of that summation, *i.e.*, the actual variations of difference of potential between the contacts which occurred while the wave was passing from  $p$  to  $d$ . It will be seen at once why we call this effect the *diphasic variation*.

I explained before, that in accordance with the fundamental properties of our instrument the curve  $P'$  would have as its photographic expression the curve  $P$ . Similarly the combination-curve  $S'$ , would

have for its photographic counterpart the curve  $S$ . May I emphasize the point that if you have the curve  $P'$  of a parallel-fibred muscle, you can calculate from it  $S''$  and consequently  $S$ , but that from  $S$  alone you cannot deduce the others. In other words, if you know the form of  $P'$ , you know everything as to the form of the electrical response—the *Reizwelle*.

Let us now take the actual result. As before stated, the two contacts are at  $p$  and  $d$ , and the muscle is excited at  $r$ . The wave affects the muscle first at  $p$  then at  $d$ , and the consequent movement of the column is photographed (Photo. 1).

Photograph 1.\*

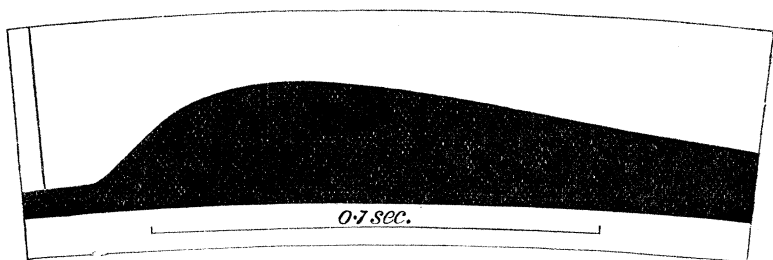


You recognise that it is the counterpart of the deduced curve  $S$ . In other words it is the expression of the effects of two similar processes having their seats at the two contacts. Our aim must now be, as I have explained, to annul or suspend the effect of one of them, leaving the other intact. The method is simple. After having obtained the record I have shown you, I tie a fine thread round the muscle between  $p$  and  $d$ . I tighten the ligature so as to constrict the muscle and again record the variation. There is no change of effect, for the wave is still able to pass the constriction. I tighten again: it still passes. I then draw the ends of the ligature hard, and again photograph. I find the photographic curve is no longer  $S$  but  $P$ , *i.e.*, it has assumed the characteristic form of the *monophasic* electrometer curve (Photo. 2).

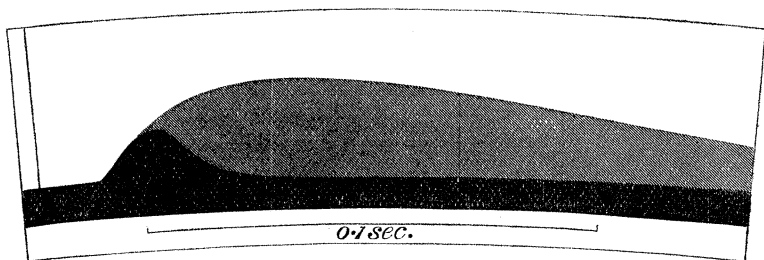
What has the ligature effected? It has exercised no influence on either contact, but it has arrested the progress of the excitatory wave, so that its effect at  $p$  only is manifested, and not that at  $d$ . The relation between the two curves ( $P$  and  $S$ ) is obvious enough when they are seen in succession. It will be still more obvious if I place them on the screen together, in such a way that they are in synchronic relation to each other (Photo. 3).

\* Photographs 1, 2, and 3.—Curarised Sartorius kept for about twenty-four hours in 0.6 per cent. solution of chloride of sodium. Temperature during observation 9° C. Contacts, &c., as in Diagram 5, but  $p$  much nearer to  $d$ .

Photograph 2.\*



Photograph 3.\*



The experiment may be further varied by altering the seat of excitation from  $r$  to  $r'$ . You thus obtain a photographic record which represents what happened at  $d$  in the unligatured muscle. If the muscle is in a normal state, this is an exact reversed counterpart of photograph 2.

If instead of placing the ligature half way between  $p$  and  $d$ , we place it close to the distal electrode  $d$ , the proximal may then be placed in a succession of experiments at different distances from the seat of excitation without altering the form of the recorded variation; the time at which it begins depends in each case on the distance of the proximal contact from the seat of excitation.†

In all of these instances the ligature acts as a *block*. Without interfering with the condition of any other parts it kills the part which it grasps and makes it incapable of transmitting the excited

\* *Photographs 1, 2, and 3.*—Curarised Sartorius kept for about twenty-four hours in 0.6 per cent. solution of chloride of sodium. Temperature during observation  $9^{\circ}$  C. Contacts, &c., as in Diagram 5, but  $p$  much nearer to  $d$ .

† An experiment of this kind is by far the most exact method which we possess of measuring the conduction-rate in muscle. This rate is most correctly expressed by the quotient  $\frac{\text{Difference between the distances}}{\text{Difference between the times}}$  as measured in two experiments in which the distances are different.

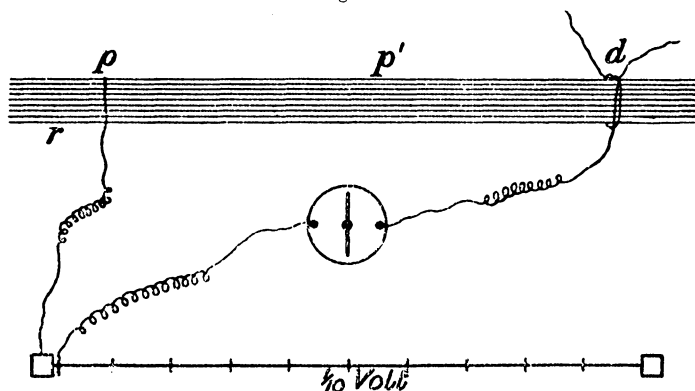
state from the living structural elements on one side to those on the other ; but if we compare the condition of the unexcited preparation immediately before and after the application of the ligature, we find evidence that breach of continuity of function is not the only effect produced by it. If the one contact is placed *on* the ligatured part it is found that, irrespectively of any excitation, there exists a large difference of potential between the contacts, which may amount to four or six hundredths of a volt.

### *The Muscle Current.*

Now it is easy to prove that this difference is not due to breach of continuity, for if you shove the electrode away from the ligature in either direction it disappears. The phenomenon which is thus brought to light is that to which the great founder of animal electricity, du Bois-Reymond, applied the term "muscle-current," and when the method I have described is employed, it presents itself in its utmost simplicity—for by the act of tightening the ligature previously applied under an electrode, you at once bring into existence a state of things in which the constricted part is negative to the living parts on either side.

What happens in this case ? What is the difference between the state of the surface of contact immediately before and immediately after the tightening of the ligature ? Nothing more can be said than that a certain process which was going on there and which provisionally we call "life," being ignorant of its nature, has been annulled. What we actually observe may be represented diagrammatically thus :—

Diagram 5.



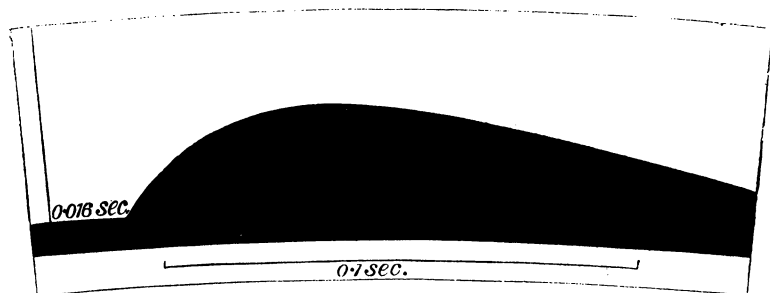
The divided line represents the graduated wire of a potentiometer ; at *d* is a ligature as yet not tightened round a muscle ; *p* and *d* are equipotential. The galvanometer is at zero and the slider of the potentiometer is up to the block. The ligature is tightened ; at once the needle indicates a current directed from *d* to *p*, but can be brought by the slider again to zero.

The contacts are as shown in the diagram. Before tightening the ligature between them they are equipotential, because they both rest on muscle in the same physiological state. I represent the electrical concomitant of that state by an arrow, by which I mean nothing more than that if it were possible to connect  $p$  with some other part of the muscle, without passing through another electromotive surface, there would be a current in that circuit from  $p$  to the galvanometer. But inasmuch as the actual circuit passes through  $d$  where the same conditions exist as at  $p$ , but opposed in direction, there is no current. If by tightening the ligature I annul the effect of  $d$ , the effect of  $p$  comes into evidence. This statement is simple, and seems to arise naturally from the observed facts; but cannot be received without question, for it suggests that what we call the "demarcation current" has its seat, not at the surface of demarcation, but at the living surface, so that we should have to consider the state of "*Stromlosigkeit*" not as a state of electrical inaction, but as a state of balance.

A similar question would arise as regards the response to excitation. For when, as we have seen, the *Reizwelle* passes under the proximal contact (Exp. 1), what happens there (during the 100th of a second that it is passing) is analogous to what I have just described as the effect of suddenly tightening a ligature at that spot. The moment before excitation a state of balance existed between  $p$  and  $d$ . As the wave passes under  $p$  it upsets that balance by annulling the outgoing current, then pursues its course until it is extinguished by the ligature. From the moment that the tail of the wave has left the edge of the surface of contact behind, it has no action whatever on the indicating instrument. We have evidence of this in the curve of variation itself, for the form of the curve is the same whether the wave is blocked by the ligature at one centimetre from the point of observation, or at three, which could not be the case if, as I once imagined, something happened at the moment of extinction.

The complete proof that this is so, is however obtained by another form of experiment in which the seat of excitation ( $r$ ) is shifted from the proximal side of  $p$  to the proximal side of  $d$ . The unligatured and therefore equipotential muscle is excited in the two positions successively. The results show (1) that the excitation wave is propagated in both directions, and (2) that the form of the curve varies according to the order in which the electrodes are reached. This having been determined, the progress of the wave is stopped by a ligature under the distal contact  $d$ , and the excitations in the two positions repeated. It is now seen that the form of the wave is the same whatever the direction from which it approaches the point of observation  $p$ . When the excitation is proximal to  $d$ , it is not now anticipated by a variation at  $d$ , and there is consequently a long delay (see Photograph 4) during which the electrometer is unaffected. The experiment affords direct

Photograph 4.\*



evidence that, although the whole muscle is in circuit, the presence of the wave cannot reveal itself until it is *under the electrode*. As regards the action-current therefore, the electromotive source is always the surface of contact of the leading-off electrode with living substance, not the surface of contact between dead and living.

We may now resume our consideration of the form of the propagated monophasic variation, or excitatory wave. It would be easy to prove by the exhibition of numerous photographs of the monophasic variation relating to different muscles, that all have the same characteristic features, indicating that in each muscular element the electrical change culminates from two to six thousandths of a second after excitation, according to the physiological state of the muscle and the time it has been kept, subsiding at first abruptly, afterwards more gradually, so that its whole duration (*i.e.*, to the summit of the electrometer curve) amounts to from two to six hundredths of a second.

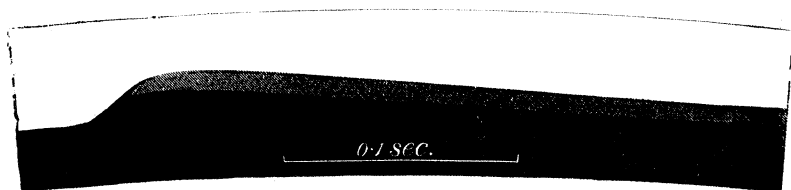
The discoverer of the *Reizwelle*, Professor Bernstein, assigned to it a very different duration. "In every element of muscular structure, the variation lasts between  $1/250$  and  $1/300$  second, and coincides with the period of latent stimulation." At first sight this statement seems irreconcilable with fact, but it is much less so than it appears to be. We have only to assume that Bernstein's method of estimating a small and transitory difference of potential between two surfaces, was not sufficiently delicate to enable him to appreciate those which exist during the period of decline, and that what he regarded as the duration of the whole variation, was in reality the duration of its summit only. However this may be, it is clear that we may divide the period of variation into two parts, which we may call respectively the initial rise and the decline, of which the latter lasts eight to ten times as long as the former; and that we may regard the first as a period of upset, the second as a period of restoration. Taking *the period of upset* as equivalent to

\* Curarised Sartorius kept for twenty-four hours. Seat of excitation between the leading off contacts, 4 mm. from *d*, 20 mm. from *p*.

Bernstein's "*negative Schwankung*," we can accept all he says as to its coincidence in time with the moment of greatest intensity of the process by which chemical is transformed into mechanical energy—the moment in the shortening of an unloaded muscle at which *its rate of change increases most rapidly*. As regards the period of decline, it might suggest itself that the return of each element to its previous state is in every instance the expression of an anabolic process, not merely a result of the cessation of the opposite process. The facts we are considering, however, lead us for the present to regard the whole variation as the concomitant of one and the same chemical process, and we are confirmed in this view by the observation that, as we shall see immediately, the modifications which the monophasic variation undergoes under external or accidental conditions affect both stages equally.

Of these conditions one of the most important is temperature, particularly when muscles which have been kept for some time in physiological salt solution are used.\* We have hitherto had in view the Sartorius which has been kept for some twenty-four hours, and is at the temperature of about 10° C. By placing it in a cooled chamber at a temperature some 6° C. lower, and allowing it to remain there until it has acquired the temperature of its environment, its mode of responding is not changed, but only in its relation to time. In shortening, it takes a longer time to attain its minimum length, and if its con-

Photograph 5.



traction is resisted, its period of effort is of longer duration. Consequently it is able to do more external work in a *single* effort than before, although it is not able to support a heavier weight or maintain a greater tension in a *continuous* effort. Now all these modifications depend, so far as I have been able to ascertain, on diminution of the rate of propagation of the excitatory wave. As has been already stated, we are able to measure this rate with great facility and accuracy. By alternately cooling and warming our chamber we can determine in any number of instances the change of rate which a difference of 2°, 4°, or 6° C. produces, and compare the data so obtained with the effects of the same changes on the duration of the monophasic variation and on that of the mechanical effort which it accompanies.

\* 'Journ. of Physiol.,' vol. 23, p. 332.

Up to this point the phenomena we have had under consideration have been associated with the response of a muscle to a single instantaneous excitation, *i.e.*, the monophasic variation and the momentary contraction which it ushers in. We must now pass on to the consideration of the electrical concomitants of those forms of contraction which more obviously resemble the natural action of muscles.

Physiologists have for half a century taught that natural muscular action, whether reflex or voluntary, is made up of single contractions of definite duration, such as those we have been considering, *i.e.*, of a rhythmical series of such contractions of definite frequency. This doctrine—that voluntary motion is a well organised system of twitches—is now commonly expressed by calling it a *tetanus*, a word which was some fifty years ago diverted from its medical signification to be adopted as a technical term in physiology, but not precisely in its present sense. What is now meant by it is that every contraction, however continuous it may appear to be, is in reality discontinuous. This conclusion was arrived at by a method which, though sometimes of great value to the physiologist, does not always lead to the discovery of truth—the method which consists in first imitating a natural process, and then mentally transferring the characteristics of the imitation process to the natural process which it represents. In the present instance the study of artificial tetanus has taught us a large proportion of what we know as to the properties of muscle, but not much about voluntary contraction. In assuming the identity of the latter with experimental tetanus, physiologists have perhaps minimised certain fundamental difficulties and assigned undue value to certain analogies.

Of the difficulties, the most obvious one is that discontinuity could not, if it existed, be of any advantage. For if we regard the muscular system as the mere instrument of the central nervous system, and every muscular fibre as the instrument of the motor cell which governs it, it is difficult to see how subjecting that muscular fibre to a rhythm of its own could have any other effect than to interfere with its efficiency. Of the analogies the chief are, first, that just as when you listen to a muscle in artificial tetanus you hear a musical sound of which the frequency of vibration corresponds to that of the stimuli, so a muscle when contracting voluntarily gives out the *quasi*-musical sound, which Wollaston compared to the rumble of wheels over pavement. The other analogy relates to the reflex spasm of strychnine, which is not only rhythmical in itself, but is accompanied by a series of electrical changes which are as rhythmical as if they were evoked by a series of stimuli. The discussion of the muscle sound lies outside of our present inquiry: the spasm of strychnine will be considered after we have examined the electrical concomitants of artificial tetanus.

*Second Fundamental Experiment.*

The point to which I have first to draw your attention is the form of photographic curve which is obtained when the Sartorius, injured under one electrode by a ligature, is excited by a series of stimuli of which the frequency is about 60 per second. The photograph shows that

Photograph 6.\*



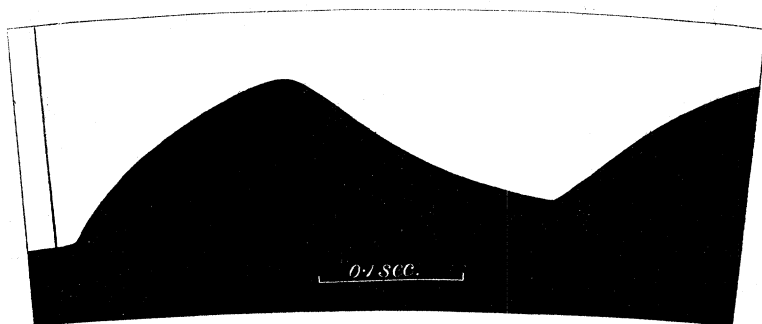
the column rises at first abruptly, but afterwards in such a way that the rate at which it rises is at any moment proportional to its distance from the point to which it will eventually arrive, *i.e.*, to the distance between the corresponding point of the curve and its asymptote. The electrical state, therefore, which comes into existence when a muscle is tetanised (*i.e.*, subjected to a frequent series of excitations) corresponds to diagram 1. In other words, the electrometer is acted on by the same difference of potential between its terminals throughout, with the exception that the effect of the first, or first couple, of excitations is often greater than that of the succeeding ones. Although this hardly needs proof, it can be easily verified by direct experiment. With this view our circuit is so arranged that we can, without altering the resistance, project on to a second photographic plate the effect of allowing a constant difference of potential to act on the mercury column just as the plate is passing behind the slit. On comparing this curve with the tetanus curve they are found to be nearly identical.

Let us now take the case in which a muscle is tetanised in the same way as in the last instance for a succession of periods of one-fifth second, alternating with equal periods of rest (Photo. 7). The complete correspondence of the photographic curve with that represented in

\* Sartorius not curarised. Indirect excitation. The undulations on the line of ascent indicate the frequency of the stimuli—60 per second. The radial line indicates here, not the moment of stimulation but that at which the short circuit of the secondary coil was opened.

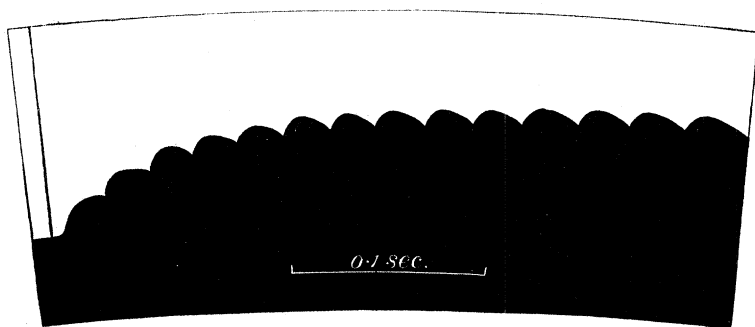
diagram 2 indicates that the conditions correspond with those which are there theoretically represented. During each period of excitation (tetanus) the movement upwards of the meniscus is determined by the difference of potential. During the intervals it follows in its fall the similar curve of depolarisation.

Photograph 7.\*



From this we may now proceed to other forms of experimental tetanus in which the excitations are less frequent. Provided that the frequency is not much less than 40 per second, the general contour of the curve resembles the other one, with the exception that the effect of each excitation is seen separately (Photo. 8). If the frequency is diminished to 20 per second the undulations are more ample, while the

Photograph 8.†



curve rises to a lower level, the reason obviously being that the electrometer is acted on by a smaller number of excitations in a given time.

\* Frequency of excitation as in Photo. 6. The original shows similar undulations in the ascents, which the copy by inadvertence does not show.

† The first four undulations have been imperfectly copied.

Photograph 9.



Diminishing the frequency still further (to 14 per second) we obtain a curve (Photo. 9) of which the character is that of a series of equal and similar monophasic variations.

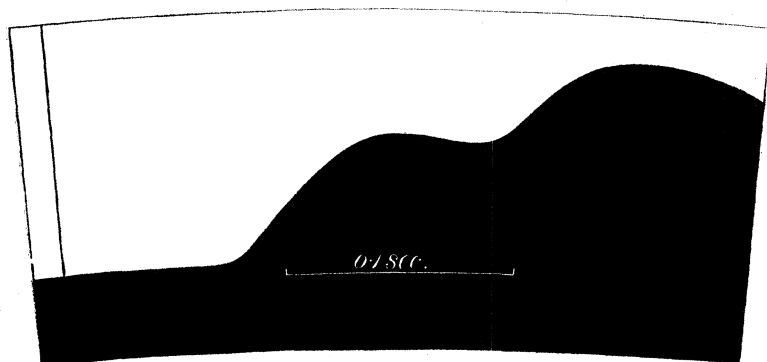
#### *The Reflex Electrical Response.*

We now go on to compare the variation-curve of artificial tetanus with the nearest approach to a normal contraction we can obtain for investigation, viz., the reflex response of the motor apparatus of the spinal cord to an instantaneous stimulation of the cutaneous surface. A ligature is applied as before to the tibial end of the Sartorius under the distal contact; but inasmuch as the muscle must now be excited through its nerve, the proximal leading-off contact is on the hilus. The mode of excitation is the same as before, but in this case the effect has first to be communicated to the motor cells of the spinal cord through the sensory apparatus, a process which occupies a relatively considerable length of time. The motor cells then deal with it automatically, responding to it in their own way, and inducing in the muscles under their control an action which is the faithful and exact expression of the changes going on in themselves.

As is well known, it is not possible in a normal preparation to obtain an unflinching response to an instantaneous stimulus applied to the cutaneous surface, but the previous injection of a trace of a strychnine salt (*e.g.*, 1/30 milligram of the sulphate) is sufficient to give to the motor apparatus of the cord the required degree of excitability. A single induction current applied to the skin then evokes in the Sartorius and other muscles, first a twitch which resembles the response of the same muscle to a similar stimulus applied to its nerve; a little later, this twitch is replaced by a short, sometimes thrilling, spasm resembling a short tetanus. What I have to show you is that,

although the reflex spasm resembles a short artificial tetanus as regards the way in which the muscle contracts, the contractions are shown by their electrical concomitants to be of a different nature. The strychnine spasm, as it is rightly called, is seen not to be a tetanus, *i.e.*, not to consist of a series of single twitches, but to be a succession of continuous contractions, the rhythm of which depends on the spinal cord, not on the muscle.

Photograph 10.\*



The grounds on which this conclusion is founded appear to me to be unequivocal. The observation is a simple one. The automatic mechanism, which carries the photographic plate, liberates as before, at the beginning of the period of exposure, an induction current which pricks the skin of the preparation. After an interval which may be about a tenth of a second (during which a *quasi*-psychological process is going on in the spinal cord) the muscle responds. A curve is drawn simultaneously by the writing lever to which the end of the muscle is attached, which indicates that it is in spasm;† but it is the photographic curve which tells us the nature of that spasm. Each ascent of the meniscus is seen to be the response, not to a single instantaneous, but to a short continuous, stimulation, of which the duration can be easily deduced by measuring the time interval between the beginning and the culmination of an excursion. By subjecting the muscle artificially to series of excitations of similar duration with corresponding intervals of inactivity, one can produce an imitation of the strychnine spasm which, both in its mechanical and electrical characters, resembles the natural one (see Photo. 7).

\* Freshly prepared Sartorius attached to pelvis and connected to spinal cord by its nerve. Leading off electrodes on hilus and tibial end. Exciting electrodes applied close together to skin of flank of decapitated preparation.

† The curve is often toothed, the teeth corresponding in frequency with the electrical undulations.

Before leaving the subject of the strychnine reflex, I must refer very briefly to such previous observations as bear on our present inquiry. The phenomenon is of interest as being one which could not have been discovered had we not possessed the capillary electrometer. Its discovery was, indeed, the outcome of the first attempt made by Professor C. Lovén to use that instrument for the investigation of the electrical properties of muscle just twenty years ago. He was good enough to make for me the electrometer which was used in some of my own earliest experiments. Shortly afterwards, Mr. Page devised the method of obtaining photographic records of our own results and, amongst others, of those of Lovén relating to the strychnine spasm. Lovén's observation has served ever since as a support for the doctrine of discontinuity. No one would be more willing than he would, if he were with us this afternoon, to recognise its true meaning.

The conclusion to which all the facts we have had before us up to this moment lead, is that normal muscular action is the manifestation of what happens in the motor nervous system. If this motor impulse is so short that we are obliged to call it *instantaneous*, the response is correspondingly brief; if it lasts longer, we call it *continuous*, recognising that the difference between the two is merely one of duration. In either case it is of the essence of the response that it is terminable. There is no difficulty in understanding on teleological grounds why a muscle *must* relax; but of the mechanism by which it is brought about we know little, excepting that it is localised in the muscular structure. Each element—each tagma—returns to its *status quo* in the same way in a curarised muscle, as in a normal one; but whether this power of recovery is a process by itself, as some physiologists hold, is a question which is at this moment much debated, but by no means settled. It is only in so far as it relates to the electrical concomitants that it here concerns us. Without prejudice to the question whether, as Fick and Gad maintain, the relaxation of a muscle is dependent on a special chemical process or not, it falls within our present scope to inquire whether by comparing with a normal muscle, one which not only does not relax but has been deprived of the faculty of relaxing, we can arrive at any electrical indication of such a process. Fortunately we have within reach a means by which this experiment can be made.

#### *The Continuous Response of a Veratrinised Muscle.*

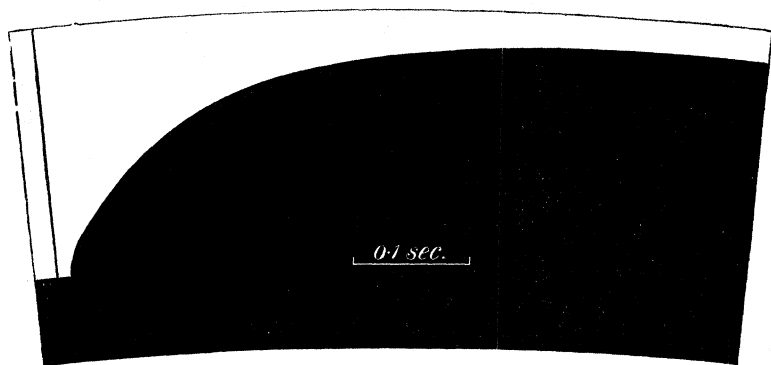
The alkaloid veratrine\* is an agent by which a muscle excited by an instantaneous stimulus is deprived of its power of recovering itself. The quantity of the alkaloid required to produce the effect is extremely small. The addition of one part in a million of veratrine to the

\* The veratrine used was kindly prepared by my friend Professor Dunstan, F.R.S.

physiological salt solution in which a muscle has been kept for several hours, is sufficient to give it this property or, as it may be expressed, to "veratrinise" it thoroughly. The alteration of the properties of a muscle by veratrine in such a way that it *must* continue an effort once begun, has been long known. It is an example of perfectly continuous contraction. Normal muscular contraction being regarded, as I have said, as discontinuous, the relation between it and the continuous contraction of veratrinised muscle has not been sufficiently considered. When therefore we set to work to measure the maximum contractile effect of a "veratrine spasm," I was both surprised and gratified to discover that the tension of a veratrinised muscle, when excited by a single instantaneous stimulus, was as great as that of a similar but unveratrinised muscle when subjected to a succession of stimuli, *i.e.*, when artificially tetanised. It can also lift as great a load and hold it up for several (10—20) seconds at as great a height. (Tracings shown.)

We then proceeded to investigate the electrical concomitant of the veratrine "tetanus," if I may so call it (Photo. 11) and found it to be identical with that of an artificial tetanus produced by a succession of stimuli of sufficient frequency. Its true character can be best judged of by comparing it with Photo. 12, which was obtained by

Photograph 11.\*

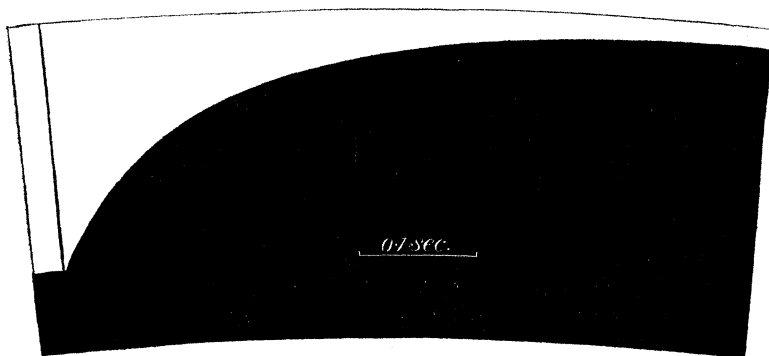


introducing into the unchanged circuit a constant difference of potential in the way before explained (p. 54).

The fact that the veratrine spasm has the mechanical and electrical character of a continuous contraction is of value, not from its bearing

\* Electrical response of curarised and veratrinised Sartorius to an instantaneous stimulation. Leading off contacts at middle and tibial end, exciting electrodes near pelvic end. The initial rise of the curve is steeper than that of the comparison curve (Photo. 12).

Photograph 12.\*



on the mode of action of a particular chemical substance, but from the evidence it affords that discontinuity is not essential to energetic display of contractile force. In this respect it would be wholly irrelevant to object that the data derived from experiments on a poisoned muscle cannot be applied to a normal one. All that it is required to prove is that it is possible for a spasm which is not discontinuous to be as effectual for the doing of external work as a normal contraction. It can hardly be disputed that the contraction of a veratrised muscle is continuous. It is, therefore, no longer possible to assert that discontinuity is essential to functional capacity.

That our results differ from those of other observers is to be attributed to the mode of using the alkaloid, and to the homœopathic minuteness of the dose. We estimate the quantity of veratrine which actually enters the muscle not to exceed 1/10,000 milligram.

### *The Heart.*

We now turn from the skeletal muscles to the organ by the rhythmical contractions of which the circulation is maintained. The mechanical response of cardiac, like that of skeletal, muscle can be evoked either directly or indirectly, but the heart has this peculiarity that each part of it has attributes which we are accustomed to regard as nervous rather than muscular. It has above all the property which belongs, as we have seen from our experiments with strychnine, to the motor cells of the spinal cord—that of discharging itself rhythmically when in a state of continuous excitation. It is characteristic of heart-muscle that it exhibits alternating periods of rest and activity, and we have now the clearest evidence that it is not in virtue of its possessing

\* Comparison curve obtained by leading off from the compensator a current of E.M.F. equal to that of the "action current"; leaving the unexcited muscle in circuit.

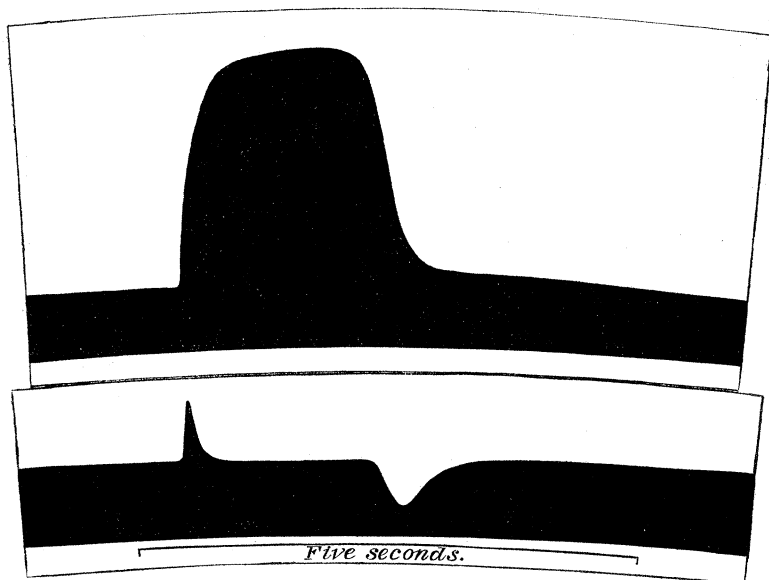
an intrinsic nervous system that it has this property. In another important respect it resembles the motor apparatus of the cord, namely, that its relations to stimuli are governed by what has been called the "all or not at all" principle. It either does not respond or, if at all, responds completely. In these respects, therefore, the action of the heart is comparable neither with that of muscle acting independently, nor even with that of the muscle nerve preparation, but rather with that of muscle acting under the direction of the motor *neuron* which governs it.

I began the investigation of the electrical phenomena of the heart's beat in 1881 with Mr. Page. We made out two new facts, namely, that the electrical change which is evoked by excitation of the surface is propagated, at a rate dependent on temperature, not in one direction only but in all, as Engelmann had already shown to be the case with regard to the wave of contraction; and secondly, that the monophasic variation is not, as had been supposed by previous observers, an instantaneous change, but lasts during the whole period of energetic systole. But neither Mr. Page nor I understood then the nature of the initial "spike," which is so striking a feature in the photographic record of the variation in the *uninjured* heart. For its explanation I am indebted to Mr. Burch, whose investigations on the use of the capillary electrometer for measuring the electromotive force of currents of short duration have been of so much value to physiologists. The moment it was understood that the spike indicated a diphasic variation analogous to that of the muscle, I felt that I had the key to the complete understanding of my own previous observations. I was, moreover, able to bring these into complete harmony with those of Professor Engelmann made about the same time with the rheotome and galvanometer.

Let me ask your attention to the photographic curves of the diphasic and monophasic variations which I have placed one above the other in synchronic relation to each other. It is to be noticed that the movement of the recording surface is very slow, about a centimetre a second only. To obtain the monophasic curve you have to place the distal electrode on a spot which has been devitalised by scorching, and which is consequently physiologically inactive, the proximal electrode on the living surface near the junction between auricle and ventricle. The instantaneous stimulation is applied to the auricle some couple of millimetres distant from the proximal leading-off electrode. The *Reizwelle* is propagated from the auricle to the base of the ventricle and then on to the devitalised spot, so that before it arrives at the contact it is extinguished.\* Consequently the change which is expressed by the electrometer-curve takes place exclusively at the proximal contact-surface. It differs only from the monophasic variation of skeletal

\* This mode of observation corresponds to the first fundamental experiment in muscle (see p. 45).

Photographs 13 and 14.\*



muscle in the longer duration of the period which intervenes between culmination and decline, and consequently bears a greater resemblance to the effect of a short continuous excitation of muscle than to that of an instantaneous one.

Turning to the diphasic variation obtained when the surface underlying the distal contact is not devitalised, we see that during the whole intervening period just referred to, the two contact surfaces are approximately equipotential. This of course does not mean that both are physiologically inactive, but simply that the influence of the one exactly balances that of the other. This meaning of the diphasic variation is (with the exception of the initial spike) that which was assigned to it in 1882. It results from the mutual interference of two monophasic variations, the dip of the curve at the end indicating that the effect of the distal contact overlasts that at the proximal.

The general result of these observations is that, just as from the mechanical point of view the systole of the ventricle has lately been shown to be entirely analogous to the response of a muscle to an instantaneous stimulus, provided that we substitute volume for length and lateral pressure for tension,† so as regards the electrical phenomena

\* Ventricle of heart of *R. esculenta* arrested by Stannius' ligature. Exciting electrodes on auricle. Leading off contacts at base and apex. In 13, apex surface devitalised by heat; in 14, both surfaces uninjured.

† O. Frank, "Zur Dynamik des Herzmuskels," 'Zeits. f. Biol.,' vol. 32, p. 370.

there is a complete analogy between the monophasic and diphasic variation of the heart and of muscle, respectively, provided that we bear in mind that the one is a response to a short continuous stimulation, the other to an instantaneous one.

*Dionæa.*

My last example of motion and its accompanying electrical phenomena I will take from the plant. As everyone knows, there are certain parts of some of the higher plants which respond to stimulation like the motor organs of animals. These instances have been regarded as indications of the close relationship which exists between plants and animals as regards their elementary physiology. The subject attracted the attention of Mr. Darwin in relation to certain insectivorous plants, and it was at his suggestion that the observations to which I am now about briefly to refer, were made. The electrical changes can be most easily studied and appear in the most striking way in the leaf of *Dionæa*. The leading-off contacts are applied to the opposite surfaces of one lobe of the leaf. In the resting state the one surface is found to be positive to the other. At a certain moment, a hair on one lobe some 10 or 12 millimetres away from the place under investigation, is touched by a camel-hair pencil or excited by an induction current. The surface which was before positive becomes less so, and the curve described resembles, as you see, the monophasic heart curve.

It is not necessary on the present occasion to do more than refer to this typical experiment, by which it was shown for the first time that the migration of liquid, and consequent sudden closure of the lobes on excitation, is accompanied by an electrical change analogous to that in contracting muscle, and that in the leaf this is propagated at a rate varying with temperature. Although the experiment is one of extreme simplicity the method of investigation has not, so far as I know, been pursued by any plant physiologist. The criticisms which were bestowed on it by animal physiologists I was able to answer in my second communication to the Royal Society, and have now the satisfaction to find that the experimental data set forth in that paper are given in full in Biedermann's important treatise on 'Electro-Physiology.'

I have now, though in a very incomplete way, described the phenomena bearing on my subject so far as I have been able to observe them. May I be permitted to submit to you the indications which they seem to me to afford?

In striated muscle the primary effect of every excitation is a process of oxidation having its seat at the excited part. It may be surmised that this consists of two stages, namely, liberation of previously intramolecular oxygen, and actual oxidation. In a single element of

muscular structure the duration of this process, when induced by an instantaneous stimulus, must be exceedingly short, and corresponds with that of the excitatory variation; but in the whole organ may last until the development of tension has reached its maximum.

We have further learned that the monophasic variation is a phenomenon of great regularity, and may be taken as the type from which all other forms of response to stimulation may be derived, either by repetition, prolongation, or interference.

Although no attempt has been made to settle the question whether the natural contraction of muscle is discontinuous, it has been shown that the electrical phenomena of reflex contraction afford no ground for supposing that it is so. The efficiency of the veratrine spasm seems, at least, to justify us in doubting whether discontinuity is an essential quality of muscular contraction.

Finally, reasons have been given for thinking that the phenomena known as the "muscle current" and the "demarcation current" are manifestations of processes which have their seat at the surface of contact between electrode and living muscle.

*April 20, 1899.*

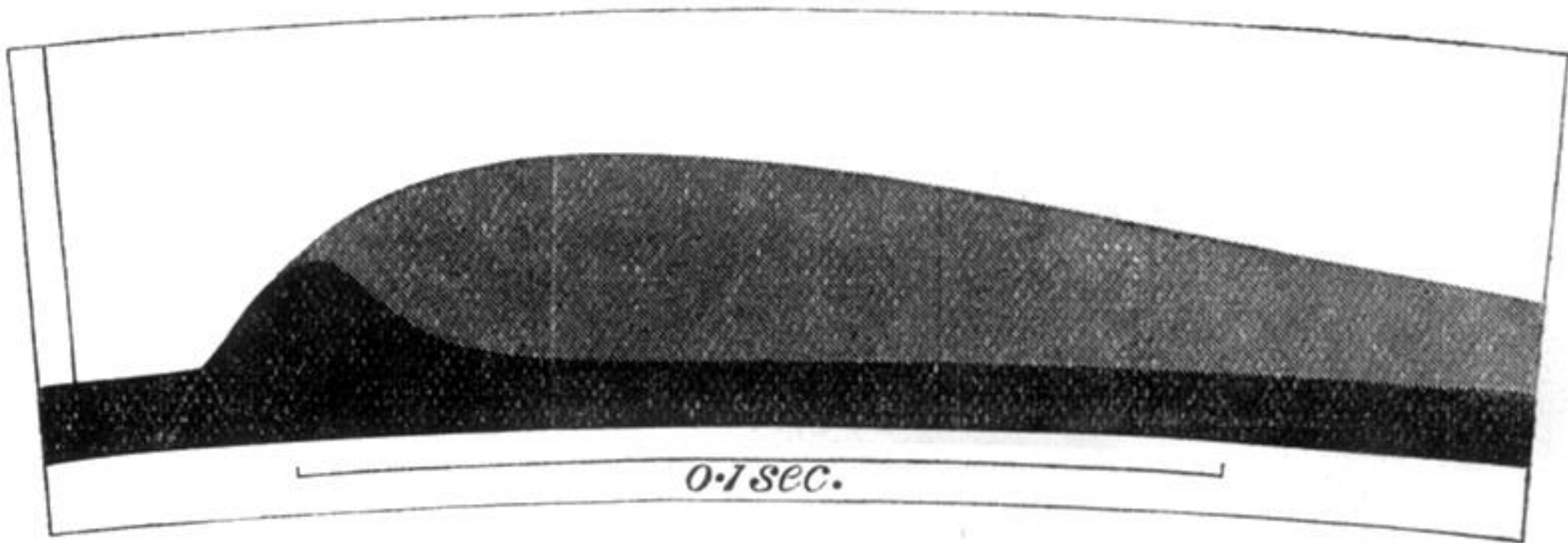
The LORD LISTER, F.R.C.S., D.C.L., President, in the Chair.

A List of the Presents received was laid on the table, and thanks ordered for them.

The following Papers were read:—

- I. "The Physiological Action of Choline and Neurine." By Dr. MOTT, F.R.S., and Dr. HALLIBURTON, F.R.S.
  - II. "On Intestinal Absorption, especially on the Absorption of Serum, Peptone, and Glucose." By Professor E. WAYMOUTH REID, F.R.S.
  - III. "Studies in the Morphology of Spore-producing Members. IV. The Leptosporangiate Ferns." By Professor F. O. BOWER, F.R.S.
  - IV. "Note on the Fertility of different Breeds of Sheep, with Remarks on the Prevalence of Abortion and Barrenness therein." By W. HEAPE, M.A. Communicated by Professor WELDON, F.R.S.
  - V. "Some further Remarks on Red-water or Texas Fever." By A. EDINGTON, M.B. Communicated by Dr. GILL, F.R.S.
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Photograph 3.\*



Photograph 5.

