The action of drugs on plants / by J.C. Bose.

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The Action of Drugs on Plants.

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It was not till recently that we realized how numerous are the difficulties that confront an investigator into the action of drugs upon the human subject. The medical faculty is amazed at the claims made by another body professing faith in science, who are reported to have made astounding cures without the aid of medicine. This body, hailing from the New World, even counts among its votaries citizens of this country. Sceptics explain away these alleged cures by a theory of auto-suggestion. But in the practice of medicine itself auto-suggestion is not excluded; for among the curative factors we have the personality of the physician, the inherited memory of the medicine man and his magical practices, and the pure effect of drugs as such. This will give us some idea of the great intricacy of the problem; and the only way in which we can evade the almost insuperable difficulties that confront us, is by taking for our experimental subject an organism whose psychic power is so undeveloped as to be incapable of reacting to a suggestion. Such a rigorous condition is amply fulfilled by the plant, for no one will impute an emotional exuberance to a turnip. Results of experiments carried out with plants will therefore give us the pure effect of the chemical agent. Therefore we shall be on somewhat safer ground if before hazarding a new drug on a patient we examine its potency on an inarticulate and uncomplaining piece of vegetable.

That such expectations are not purely fanciful will become evident when I cite one of our greatest living authorities, whose work has become classical. In his standard work on medicine, Sir Lauder

Brunton expresses his deliberate conviction that scientific investigations regarding the effects of various drugs on the animal could not be regarded as satisfactory until we succeeded in discovering their effects on living organisms as a whole, including the plant.

It is not necessary here to discant upon the importance of the more universal aspect of the subject as in the investigation by the comparative method. It will, however, be admitted that it is only by the study of the simpler phenomena of irritability in the vegetal organism that we can ever expect to elucidate the more complex physiological reactions in the animal tissues; and in the scientific study of the effect of drugs we should aim to get at the very root of the matter, in discovering the fundamental reactions of drugs on the simplest protoplasmic mechanism of the plant.

Assuming that plant tissues respond to the characteristic action of different drugs, yet the physiological change induced will elude our visual scrutiny. To take an extreme case, we find that it is impossible by mere inspection to distinguish between plant specimens one of which is alive and the other killed. We have then to discover means by which the plant itself is made to reveal its internal condition, and changes in that condition by characteristic signals recorded by it. Our success in devising such a method will enable us to determine whether a given drug causes an excitatory or depressing effect on the plant.

The results obtained with plants might lead us to expect that effects essentially similar would be found in the animal. But this expectation can only be justified if it can be shown that the physiological response of the plants are in the main similar to those of the animal. This inference, however, runs counter to the prevailing opinion. For ordinary plants, unlike animals, maintain an attitude of passivity under a succession of blows. Animal tissues give electrical signs of irritation; ordinary plants, on the other hand, are supposed not to give any such signs of excitement. The animal possesses a wonderful nervous system by which the organism is put into intimate communication with its different parts and with the environment. On the other hand, all authorities are unanimous in declaring that in a plant admittedly so sensitive as *Mimosa* there is no such thing as nervous impulse. And lastly, certain rhythmic tissues of the animal go on beating incessantly without any apparent cause, this spontaneous activity undergoing very characteristic modification under definite physiological changes. No phenomenon corresponding to this had been suspected in the plant.

I shall have occasion to demonstrate that the assumption of such difference between animal and vegetable organisms is not justified. I shall on the contrary show that the phenomena of contractile response in the plant reveal characteristics similar to those of the animal; that even ordinary plants exhibit under excitement a responsive electrical variation of the same sign as in the animal; that excitatory impulses are transmitted through certain conducting tissues of the plant in a manner precisely similar to the nervous impulse in the animal; and that there are rhythmic tissues in the plant which react under various external conditions in a manner just the same as those of the animal.

After demonstrating the similar physiological characteristics in vegetal and animal organisms, I shall next speak of the effects of various stimulating and depressing agents, such as a constant electrical current, various drugs, narcotics and poisons, on the contractile, the conducting and the rhythmic tissues of the plant.

It will further be shown how the normal effect of a drug on the plant is profoundly modified by two other factors. The first of these is the influence of dose or strength of application. The second factor of modification is the change induced in the tissue by the cumulative action of stimulus, in consequence of which the response of the organism undergoes a complete cyclic change. Consideration of these questions will probably throw much light on various anomalies met with in medical practice.

Having now briefly outlined the subject of my discourse, I shall next describe my experimental devices, the methods of investigation, and their results. This somewhat extensive subject I shall treat in the following order:—

(I) PLANT SCRIPT.
    (1) Mechanical response of plant.
    (2) The Resonant Recorder.
    (3) Electrical response of plants.

(II) SIMILARITIES OF MECHANICAL RESPONSE IN PLANT AND ANIMAL.
    (1) Additive effect of stimulus.
    (2) Effect of temperature.
    (3) Work performed by contractile tissue.
    (4) Latent period and its variations.
    (5) Diurnal variation of excitability.
    (6) Death-spasm in plant.

(III) DEMONSTRATION OF NERVOUS IMPULSE IN PLANTS.
  (1) Excitatory impulse in absence of mechanical disturbance.
  (2) Velocity of impulse modified under physiological variation.
  (3) Physiological block of nervous impulse.
  (4) Confirmatory evidence of electrical investigation.

(IV) CONDUCTING POWER OF NERVE AND ITS VARIATION.
  (1) Induction of artificial paralysis and its cure.
  (2) Canalization of conducting path.
  (3) Control of nerve-conduction.

(V) SIMILARITIES BETWEEN RHYTHMIC PULSATIONS IN PLANT AND ANIMAL.
  (1) Refractory period.
  (2) Effect of ligature.
  (3) Effect of temperature.

(VI) EFFECT OF ELECTRICAL CURRENT ON PLANT-RESPONSE.
  (1) Polar reactions on contractile tissue.
  (2) Contrasted effect of anode and kathode on rhythmic pulsation.
  (3) Inhibitory effect of transmitted electric stimulation.

(VII) EFFECT OF CHEMICAL AGENTS ON RESPONSE OF CONTRACTILE TISSUE.

(VIII) EFFECT OF DRUGS ON THE CONDUCTING NERVE.
  (1) Effect of poison in the abolition of conduction.
  (2) The Conductivity Balance.

(IX) EFFECT OF DRUGS ON THE PULSATION OF RHYTHMIC TISSUES.

(X) MODIFYING INFLUENCE OF DOSE.

(XI) THE MOLECULAR CYCLE.

(I) PLANT SCRIPT.

As regards the possibility of revealing internal changes in the plant, the only conceivable way of doing so is by the detection and record of the response of the organism to a definite testing shock. If we can find out in the plant the relation between the stimulus and response, we shall be able to determine its state of vitality at the moment. In an excitable condition the feeblest stimulus will evoke an extraordinarily large response; in a depressed state even a strong stimulus will evoke only a feeble response; and at the onset of death there is an abrupt end of the power to answer at all. Thus by means of testing blows we are able to make the plant itself reveal those invisible internal changes which would otherwise have entirely escaped us.

We may, as we shall see, employ different methods of recording the response of the plant. The most evident is the method in which the answer is given in the form of mechanical movement.

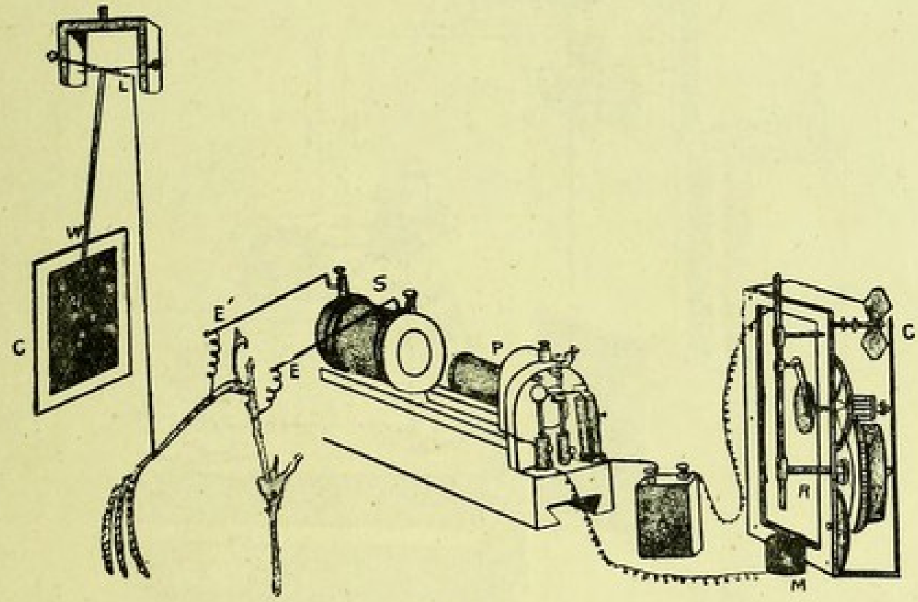

Fig. 1.

Diagrammatic representation of Automatic Plant Recorder. Petiole of *Mimosa*, attached by thread to one arm of lever, L; writing index, W, traces on smoked glass plate, G, the responsive fall and recovery of leaf; P, primary, and S, secondary, of induction coil. Electric shock passes through the plant by electrodes, E, E′; A, accumulator; C, clockwork for regulating duration of tetanizing shock. Primary circuit of coil completed by plunging rod, R, dipping into cup of mercury, M.

(1) *Mechanical Response of Plant.*

At the joint in the leaf of the so-called sensitive plant, *Mimosa*, there is a cushion-like mass of tissue known as the pulvinus. Under excitation the parenchyma in the more excitable lower half of the pulvinus undergoes contraction, in consequence of which there is a fall of the leaf. This sudden movement constitutes the mechanical response of the leaf. By the invention of different types of recorders I have succeeded in making the plant itself write an answering script to a testing stimulus; and in order that the results obtained should not be influenced by any personal factor, arrangements have been made that the plant attached to the recording apparatus should be automatically excited by a stimulus absolutely constant, should make its own responsive record, going through its own period of recovery and repeating the same cycle over again without assistance at any point on the part of the observer (fig. 1).

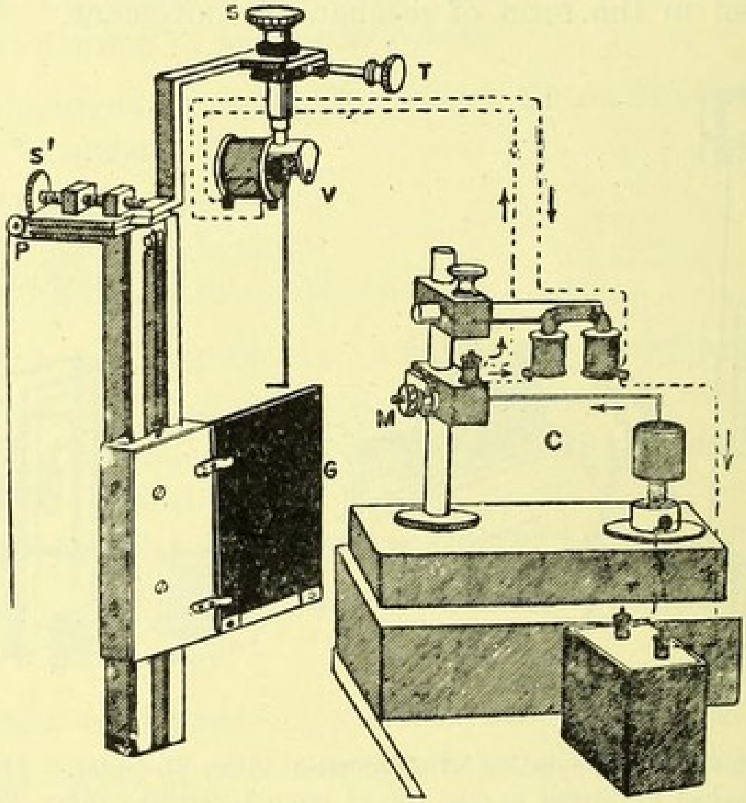

FIG. 2.

Upper part of Resonant Recorder (from a photograph). Thread from clock (not shown) passes over pulley, P, letting down recording plate. S', screw for adjustment of distance of writing-point from recording plate; S, screw for vertical adjustment; T, tangent screw for exact adjustment of plane of movement of recorder, parallel to writing surface; V, axis of writer supported perpendicularly at centre of circular end of magnet; C, reed; M, micrometer screw for adjustment of length of reed.

(2) *The Resonant Recorder.*

In obtaining the actual record of responsive movements in plants we encounter many serious difficulties. In the case of muscle-contraction, the pull exerted is considerable and the friction offered by the recording surface constitutes no essential difficulty. In the case

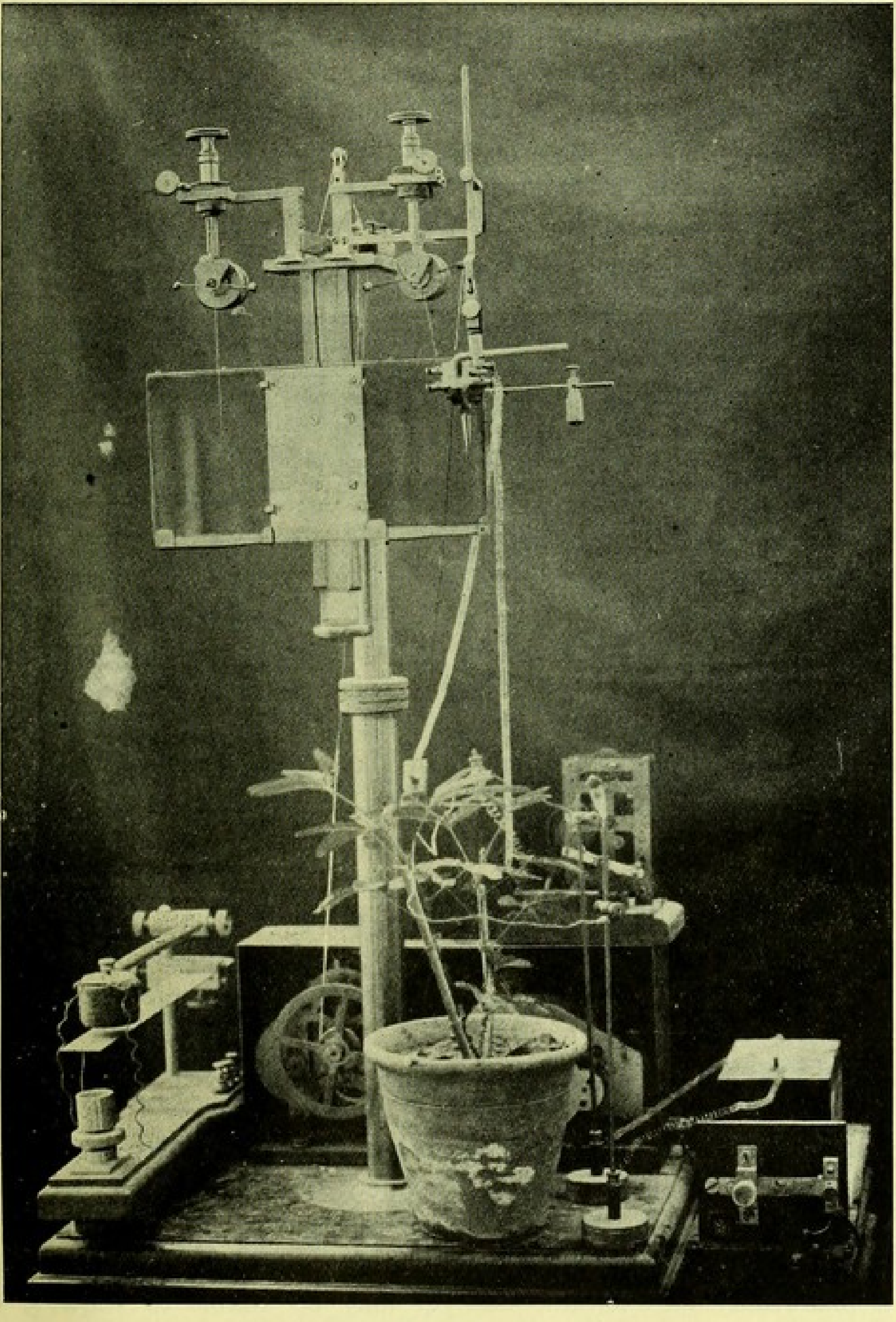

Fig. 3.

Photograph of Duplex Resonant Recorder, with plant and accessories.

of plants, however, the pull exerted by the motile organ is relatively feeble, and in the movement of the very small leaflets of *Desmodium gyrans,* or the telegraph plant, for instance, a weight so small as four-hundredths of a gram is enough to arrest the pulsation of the leaflets. The difficulty could not be removed as long as the writer remained in continuous contact with the writing surface, but I was finally able to overcome it by making an intermittent, instead of a continuous contact. The possibility of this lay in rendering the writer tremulous, this being accomplished by an invention depending on the phenomenon of resonance.

The principle of my Resonant Recorder depends on sympathetic vibration. If the strings of two violins are exactly tuned, then a note sounded on one will cause the other to vibrate in sympathy. We may likewise tune the vibrating writer, V, with a reed, C (fig. 2). Suppose the reed and the writer are both tuned to vibrate a hundred times per second. When the reed is sounded the writer will also begin to vibrate in sympathy. In consequence of this the writer will no longer remain in continuous contact with the recording plate, but will deliver a succession of taps a hundred times in a second. The record will therefore consist of a series of dots, the distance between one dot and the next representing one-hundredth part of a second. With other recorders it is possible to measure still shorter intervals. It will now be understood how, by the device of the Resonant Recorder, we not only get rid of the error due to friction, but make the record itself measure time as short as may be desired. The extreme delicacy of this instrument will be understood when by its means it is possible to record a time-interval as short as the thousandth part of a second. Fig. 3 is a photograph of the entire apparatus with accessories.

(3) *Electrical Response of Plant.*

In *Mimosa* the responsive fall of the leaf is due to greater contraction of the lower half of pulvinus. It is evident that if the upper half had been equally excitable the two excitatory contractions would have balanced each other with no resulting movement. It is thus seen that a plant may be excitable and yet may be unable to show it by external movement.

By electrical methods of investigation I have been able to show that every plant, and each organ of every plant, is sensitive, and exhibits the state of excitement by electromotive variation of galvanometric negativity—that is to say, an electrical change identically the same as that induced in an excited animal tissue.[1] In fig. 4 is shown a series of electrical response in *carrot*, and its gradual arrest under the action of a narcotic.

Thus the two independent methods are at our disposal by which the excitability of a plant tissue and its variations under physiological changes may be detected and accurately recorded.

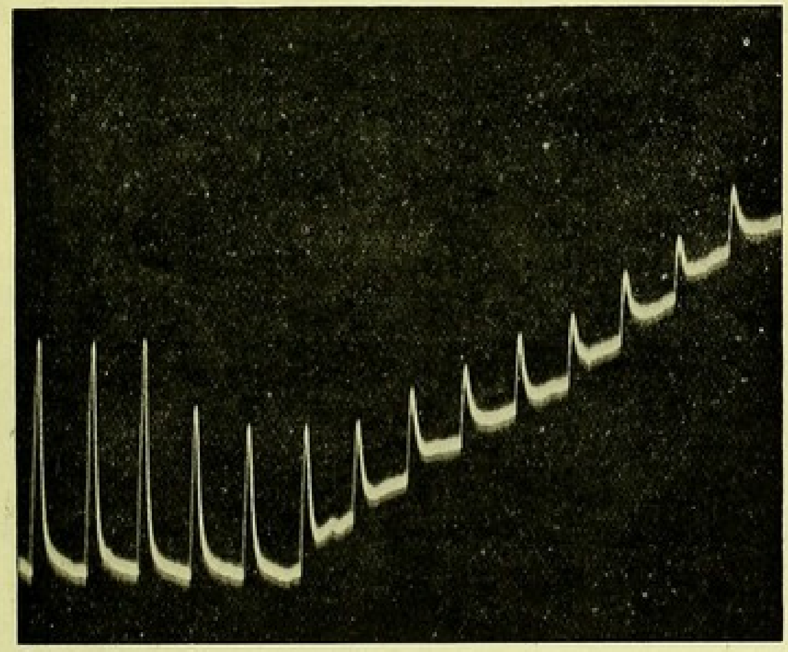

FIG. 4.

Effect of chloroform on electrical responses of carrot. The anæsthetic was applied after the third response.

(II) SIMILARITIES OF MECHANICAL RESPONSE OF PLANT AND ANIMAL.

I shall next describe various characteristics of response of contractile plant tissues, from which their remarkable similarity with corresponding response of animal tissue, will become evident.

(1) *Additive Effect of Stimulus.*

In the response of animal tissue it is found that a single stimulus, by itself ineffective, becomes effective upon repetition. The same is found to be the case in plant tissue. Thus, in a particular experiment,

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[1] Bose : Friday Evening Discourse, Royal Institution, May 10, 1901. Bose : " Comparative Electro-Physiology," 1907 ; Longmans, Green and Co.

while an electrical stimulus of intensity 0·1 was singly ineffective, it became effective after being repeated twenty times. It is found, moreover, that this additive effect is, within limits, strictly quantitative.

(2) *Effect of Temperature.*

As in the case of the animal tissue, so also in *Mimosa*, the response is abolished at a sufficiently low temperature. With rise of temperature the amplitude of response is increased and the period of recovery shortened.

(3) *Work performed by Contractile Tissue.*

The effect of load on the response of *Mimosa* is similar to that on the contractile response of muscle. In both, under increasing load, the height of response undergoes a progressive diminution, with shortening of the period of recovery. Within limits the amount of work performed by the muscle increases with the load. The same is true of the work performed by the pulvinus of *Mimosa*.

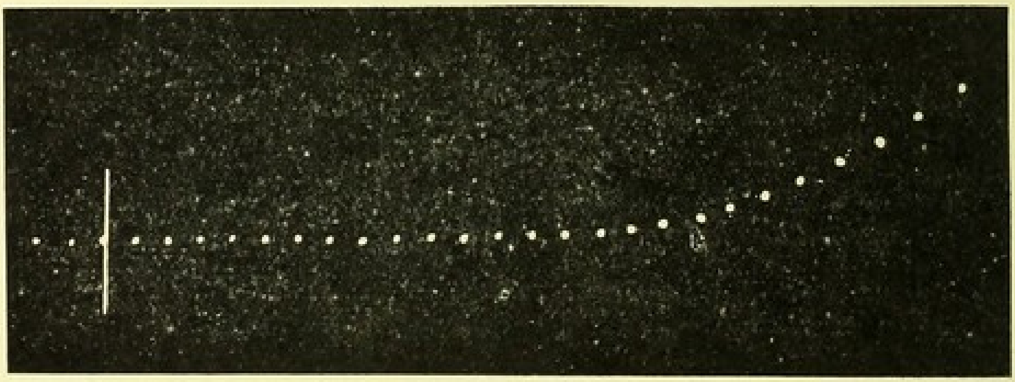

FIG. 5.

Record showing the latent period of *Mimosa*. This recorder vibrates 200 times per second. The time-interval between successive dots is here 0·005 second. Vertical line represents moment of application of stimulus.

(4) *Latent Period and its Variations.*

The latent period is in general shorter under greater intensity of stimulus, the value becoming constant above a maximal stimulus. The shortest value in the pulvinus of *Mimosa* 0·06 second. Fig. 5 is a record giving a value of 0·076 second. A rise of temperature shortens the latent period.

Under fatigue, on the other hand, the latent period is very much prolonged. When excessively tired the plant temporarily loses its power of response. In this condition the plant requires at least half an hour's absolute rest to regain its equanimity. In all these reactions we observe a remarkable parallelism with contraction phenomena in the muscle.

(5) *Diurnal Variation of Excitability in Plants.*

I do not know if any specific investigation has been carried out to ascertain whether the life-activity in the human subject remains uniform during the twenty-four hours, or whether it undergoes any definite periodic variation. I believe it is generally found that vitality is at its lowest ebb in the early hours of the morning. In any case, I find the physiological activity of the plant does not remain uniform, but undergoes a diurnal fluctuation. For carrying out investigations on this subject I made *Mimosa* record its answers to uniform testing shocks repeated every hour of day and night. The amplitude of the answering twitch gave a measure of its activity at each hour. I always found that the excitability of the plant was at its minimum in the early morning, attaining its maximum at noon (fig. 6).

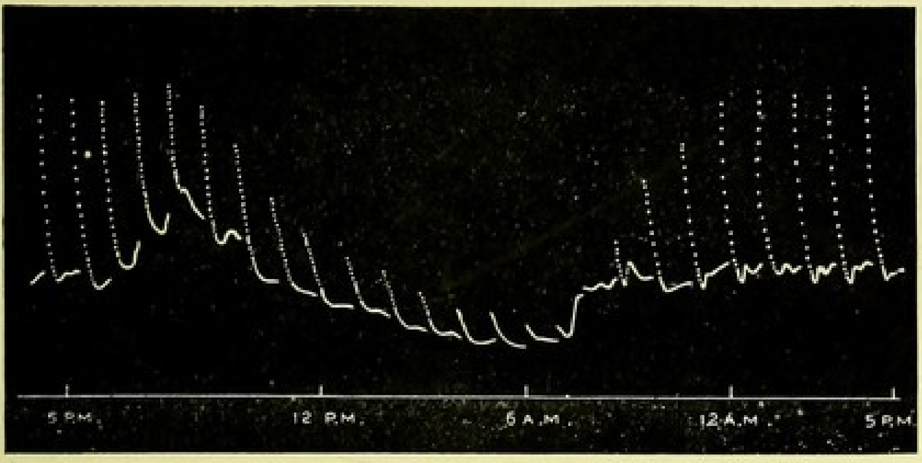

Fig. 6.

Record for twenty-four hours, exhibiting diurnal variation of excitability, commencing at 5 in the afternoon.

(6) *Death Spasm in Plants.*

The electrical response of galvanometric negativity is abolished on the death of the plant. When the plant is subjected for a time to a temperature of 60° C. the electrical response disappears. This temperature is therefore fatal for most plants. In order to determine the exact death point I subjected *Mimosa* and various other plants to a gradual rise of temperature. This is attended by a progressive, expansive, or erectile movement; at the critical temperature of 60° C., however, the movement of expansion is suddenly reversed to a spasmodic excitatory contraction. The reversal takes place under standard conditions at or about 60° C.; after this the response of the plant is permanently abolished. The death-record is a V-shaped curve, the sharp point of inversion being the death-point. After death, repetition of this experiment shows no further inversion.

It may be thought that this spasmodic movement is not physiological, but that the contraction is caused by coagulation of protoplasm. The following facts, however, dispose of that supposition. In the event of the contraction being due to coagulation the resulting movement, brought on by general shortening, would be non-discriminative in direction. But in the case of excitatory movement the direction would be discriminative, i.e., determined by the question of the differential excitabilities of the two sides of the tissue. In *Mimosa* it is the lower half of the pulvinus that is more excitable, hence the excitatory contraction of the more irritable lower half determines the spasmodic down-movement at death. Again, if we take a hollow tubular organ, such as the flower peduncle of dandelion or daffodil, and cut it in the form of a spiral, we get a preparation of which the inner or protected side is the more excitable. Hence at the fatal temperature the death-spasm is here exhibited by a greater contraction of the inner surface, resulting in a *curling* movement or tightening of the spiral. But if instead of this we take a tendril that has twined itself round a support, the inside of the spiral, owing to constant irritation by contact, will have been rendered less excitable through fatigue. In this case it is the outer side of the spiral that is relatively more excitable. The death-spasm of the tendril is shown in this case by a movement of sudden *uncurling* — i.e., a movement exactly the opposite of that exhibited by the cut spiral. The difference in the two cases emphasizes the excitatory character of the phenomenon. Again, if the spasm observed at the fatal temperature be physiological, the extent of the movement will depend on the vigour of the specimen; and in conformity with this we find that the death-spasm in younger specimens is far more violent than in old specimens. Moreover, the sudden contraction, or death rigor, in the plant is followed by a post-mortem relaxation. Hence in a complete death-curve we have first a down-curve indicative of expansion; then a sudden notch or inverted up-curve, exhibiting spasmodic contraction; and finally another down-curve showing post-mortem relaxation, the whole curve being like an inverted **N**. It is found, as stated before, that the size of this notch, indicative of death-throe, depends on the vigour of the plant. With a young specimen it is very large, and becomes smaller and smaller with advancing age. With extreme old age the notch almost vanishes, and life passes imperceptibly into death.

That this spasmodic contraction is a physiological phenomenon is further seen from the fact that the death-point, as determined from the inversion of the curve, is lowered under physiological depression. Thus, fatigue will lower it to an extent depending upon the degree of fatigue. In a certain instance the death-point, owing to the above cause, was lowered from the normal 60° C. to 37° C. Previous administration of dilute poison lowered the death-point in another case by 18° C.

Finally I have shown that all excitatory reactions have as their concomitant a sudden electrical change, of a definite sign; and it is very significant that at the critical temperature of 60° C. there occurs a sudden electrical discharge in the plant, the direction of the current being determined by the differential excitabilities of the tissue.

(III) DEMONSTRATION OF NERVOUS IMPULSE IN PLANTS.

It has been hitherto supposed that in *Mimosa* the impulse caused by irritation is merely hydro-mechanical, and quite different from the nervous impulse in the animal. According to the hydro-mechanical theory, the application of mechanical stimulus is supposed to squeeze the tissue, in consequence of which the water thus forced out delivers a mechanical blow to the motile organ of the plant. This mechanical theory was accepted in view of the anæsthetic experiment of Pfeffer, who, applying chloroform to the *surface* of the stem, found that this did not arrest the impulse. A little reflection will, however, show that under the particular conditions of the experiment the conducting tissue in the interior could not have been affected by the narcotic; the task being, in fact, as difficult as narcotizing a nerve-trunk lying between muscles by application of chloroform to the skin outside.

We may apply several crucial tests to decide the question as to whether the impulse in the plant is mechanical or physiological:—

(1) The impulse could not be mechanical, if excitation can be initiated and propagated without any physical disturbance.

(2) The impulse must be physiological, or of a nervous character, if it can be shown that physiological changes induce appropriate variation in the velocity of transmission of the impulse.

(3) If the impulse is arrested by various physiological blocks, then it must be excitatory or of a nervous character.[1]

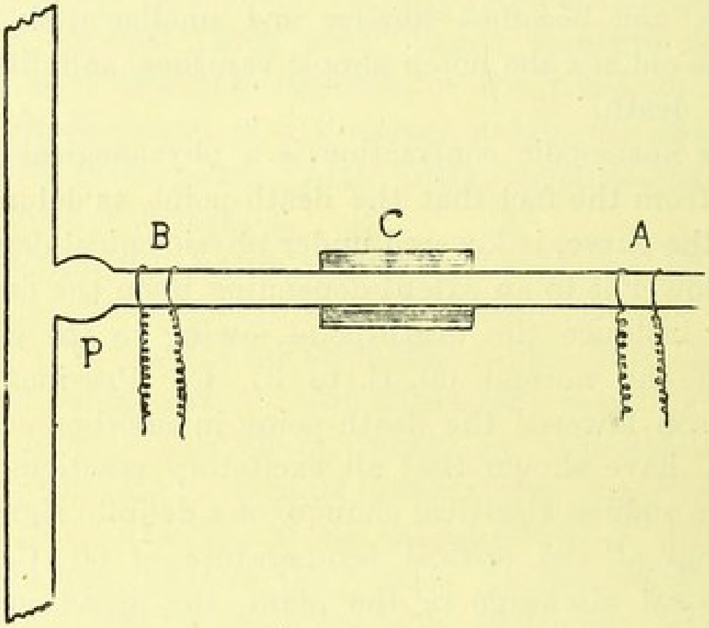

FIG. 7.

Experimental arrangement for determination of velocity of transmission and its variation. Record is first taken when stimulus is applied near the pulvinus at B (latent period) and then at a distant point on the leaf-stalk at A. Difference of two gives time for transmission from A to B. The band of cloth, C, is for local application of warmth, cold, anæsthetics, and poison.

(1) *Excitatory Impulse in Absence of Mechanical Disturbance.*

I have shown elsewhere that excitation takes place in the plant under the polar action of an electrical current, in the complete absence of any mechanical disturbance. This is realized when we find that in certain plants an excitatory impulse is initiated and transmitted by the action of a current which is so feeble as not to be perceived even by the very sensitive human tongue.

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[1] For a more detailed account see: Bose, "An Automatic Method for the Investigation of Velocity of Transmission of Excitation in *Mimosa*," *Phil. Trans. Roy. Soc.*, Series B, cciv; Bose, "Researches on Irritability of Plants" (Longmans, Green and Co., 1913.)

(2) *Velocity of Impulse modified under Physiological Variation.*

The experimental method employed to determine whether any physiological change induces variation in the speed of transmission is seen in fig. 7.

Among the favourable agents which have a marked effect on the nervous impulse of the animal is the influence of temperature. Hence we may devise a decisive experiment to discriminate between the theories of mechanical and nervous transmission in the plant. Temperature has no effect on mechanical propagation, whereas a moderate variation of it profoundly affects nervous transmission. The result given in fig. 8 is quite conclusive as regards the excitatory character of the impulse in plants. It is seen that with rising temperature the time required for transmission through the same distance is continuously reduced. In the present case the velocity is seen to be more than doubled by a rise of temperature through 9° C.

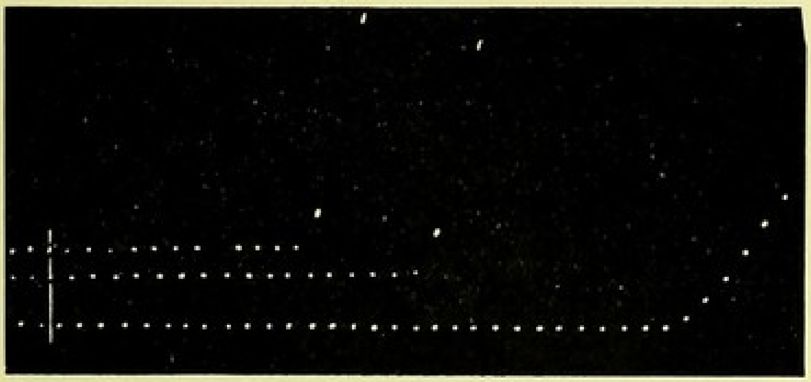

Fig. 8.

Effect of rising temperature in enhancing velocity of transmission. The three records from below upwards are for temperatures 22° C., 28° C., and 31° C. respectively. Successive dots represent intervals of 0·1 second.

The velocity of transmission of 30 mm. per second in *Mimosa* is of the same order as the speed of nervous impulse in some of the lower animals. This is seen in the fact that the velocity in the nerve of the slug is 125 mm. and in *Anodon* only 10 mm. per second.

(3) *Physiological Block of Nervous Impulse.*

As in the case of the animal, so also in the case of the plant, the excitatory impulse may be arrested by the action of an electrotonic block. As long as the current is maintained, so long is the impulse arrested; on the cessation of the blocking current, however, the conducting power is immediately restored. Local application of poison is found to arrest permanently the excitatory impulse through the poisoned tract.

(4) *Confirmatory Evidence of Electrical Investigation.*

Another distinct line of investigation independently supports these conclusions. I have shown that the excitatory change in the plant is accompanied by a concomitant electrical change of galvanometric negativity. Electrical investigation carried on with certain isolated strands of conducting tissue of the plants shows that this excitatory electrical impulse is transmitted to a distance along them.

(IV) CONDUCTING POWER OF NERVE AND ITS VARIATION.

We have seen how the physiological characteristics of the excitatory impulse in the plant are similar to those of nervous impulse in the animal. Under certain conditions the animal nerve undergoes changes leading to paralysis. In such a case a cure may sometimes be effected. The problem here is to impart a better conducting power to an ineffectively conducting tissue. This power of conduction or its absence are ultimately dependent on obscure molecular modifications. Discovery of parallel phenomena in the plant will undoubtedly prove of great importance.

(1) *Induction of Artificial Paralysis and its Cure.*

An interesting experiment relates to the artificial induction of temporary paralysis. When localized cooling is applied to a part of the petiole of *Mimosa*, the conduction of excitation through that portion becomes greatly delayed, till with sufficient cooling there is an actual block to the transmission of excitation. Thus it is possible by applying a fragment of ice to cause local paralysis of the conducting power of the petiole, which persists for over an hour, even after restoration of the tissues to the normal temperature. It is extremely suggestive, that I was able under these conditions to quickly restore the conducting-power by application of electrical shocks of moderate intensity to the paralysed region. Too strong a shock was however found to be highly detrimental.

(2) *Canalization of Conducting Path.*

In plant experiments I find a very significant result as regards the power of stimulus to fashion its own conducting path. Thus a plant carefully protected under glass from the stimulating buffets of the elements looks sleek and flourishing, yet is in reality flabby. Its conducting power is found to be in abeyance, though the motile organ exhibits its normal power of contraction. Anatomically the conducting elements are present, but from want of use they remain functionally inactive. Now in this condition it is very interesting to watch the growth of conducting power under the influence of stimulating blows. There is at first no transmission; after a time excitatory impulse begins to be initiated. Continued stimulation enhances the conducting power to a maximum. The concluding part of this process is illustrated in the records given in fig. 9.

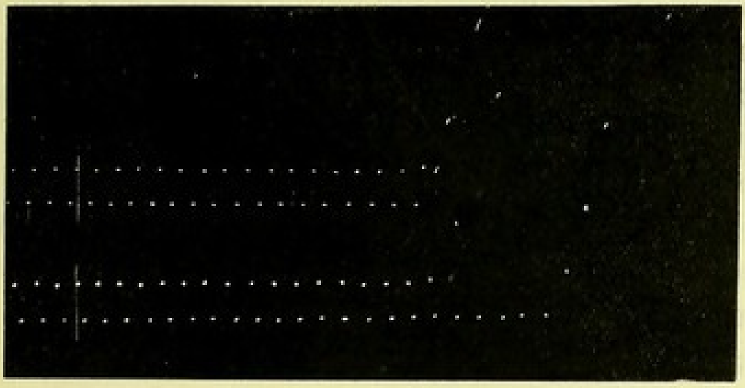

FIG. 9.

Canalization of conducting path by stimulus. Sluggish conducting power seen in lowest record. Next record shows enhancement of conducting power in consequence of previous stimulation. Uppermost record shows attainment of maximum power of conduction.

(3) *Control of Nerve-conduction.*

What is the change of the tissue which brings on paralysis? What is the molecular condition which confers conducting power on a nerve? These are very obscure problems, and any investigation calculated to throw light on the subject will undoubtedly prove of the highest importance not only in theory but also in practice.

The nerve may have been rendered abnormal in two different ways.

In one case it may have become extremely sluggish in transmitting an impulse. In the other case it may have become so hypersensitive as to transmit the feeblest excitation with intolerable intensity. In restoring the nerve to a normal condition, we want to augment the conducting power in one case or arrest it in the other.

A man who constantly uses the telephone has it in his power, by a simple process of switching on and off, to keep the circuit open or closed to the calls he receives, according as the message is pleasant or unpleasant. Can he similarly have the same control over the conducting system which exists within himself? Is it possible for him to augment or inhibit the nervous messages?

The phenomenon of excitation may be regarded as a process of molecular upset caused by stimulus, and the transmission of excitation as the propagation of the molecular disturbance. The phenomenon of molecular upset we may simply picture by means of a row of standing books. A certain intensity of blow applied, say, to the book on the extreme right would cause it to fall to the left, hitting its neighbours and causing them to topple over in succession. If the books have previously been slightly tilted towards the left, a disposition would have been given to them which, by facilitating the fall, would accelerate the speed of transmission. Conversely, an opposite disposition would retard or arrest the movement. Thus by means of a directive or polar force we may induce a molecular predisposition which would enhance or retard the speed of the disturbance according to the directive action, positive or negative, of the polar force. It may thus be possible to discover some polar force which, by inducing characteristic molecular dispositions, would enhance or retard the conduction in a nerve.

So much for theory; its value must be judged by practical results. It may be briefly stated here that, acting on the principle that has been described, I have been successful in inducing at will and by turns two opposite molecular dispositions in the conducting tissue of the plant. When the polar force was maintained in a positive direction, the speed of the excitatory impulse was enhanced in a remarkable manner. The nervous impulse could on the other hand be increasingly retarded, and finally arrested, by reversing the direction of the force and increasing its intensity. These *supra* or *a*-conducting states were maintained as long as the nerve was subjected to the action of the given force.[1]

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[1] The detailed account of this investigation has recently been communicated to the Royal Society of London.

I have referred to the conducting tissue of the plant as a *nerve.* The use of this term has, I think, been justified by the remarkable similarities of reactions between the conducting tissues of the plant and animal under varied conditions. Perhaps the crucial test of a theory may lie in the power which it gives of predicting unknown phenomena, the predictions being afterwards fully verified. Believing in the identity of characteristics of plant and animal nerves, I applied the same polar forces which I found to be so effective in my plant experiments to the nerve of the frog; and it was a matter of intense gratification to me to find that by employing the same methods I could exalt or inhibit at will the conducting power of the experimental nerve. The importance of this investigation must be obvious to all. Its success further proves the importance of physiological investigation on plants in elucidating intricate problems of animal physiology.

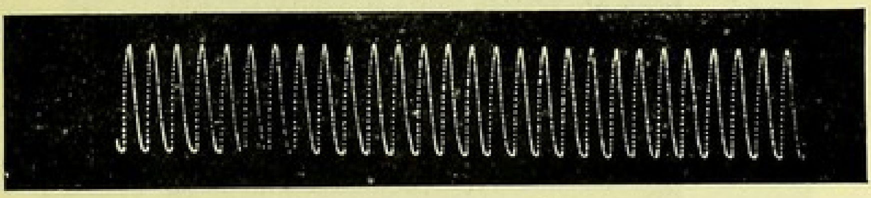

FIG. 10.

Record of automatic pulsations in *Desmodium gyrans.*

(V) SIMILARITIES BETWEEN RHYTHMIC PULSATIONS IN PLANT AND ANIMAL.

In *Desmodium gyrans*, or the telegraph plant, the small lateral leaflets exhibit automatic pulsations. I find that the characteristics of the rhythmic tissues in the plant are surprisingly similar to those of the cardiac tissue in the animal. The down-movement of the leaflet is quicker and corresponds to the systolic movement of the heart. The maximum rate of this down movement is 0·9 mm. per second. The diastolic or up movement is much slower, its maximum rate being 0·56 mm. per second. The pulsating activity of the detached heart of a frog can be maintained for long periods by subjecting it to intercardiac pressure. Similarly the activity of the detached leaflet of *Desmodium* can be renewed by the application of internal hydrostatic pressure, after which the pulsation can be maintained uniform for many hours (fig. 10).

(1) *Refractory Period.*

The cardiac tissue of the animal has a long refractory period. The tissue takes no account of the stimulus which falls within the refractory period. This is also characteristic of the response of the rhythmic tissue of *Desmodium*. Rhythmic tissues, animal and vegetable alike, are incapable of tetanus. The pulsating leaflet of *Desmodium*, like the pulsating heart, is more susceptible to excitation at diastole than at systole. An extra pulsation is induced in both by an induction shock, applied during the diastolic phase.

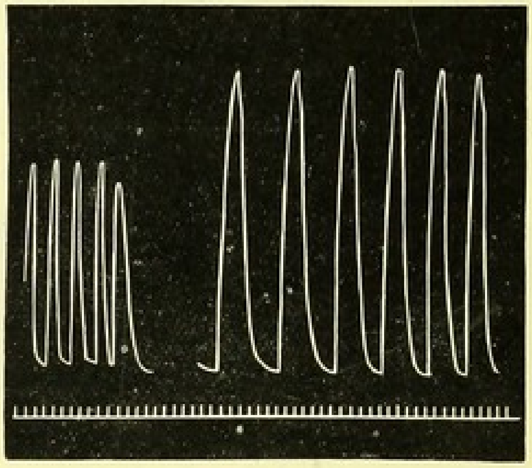

Fig. 11.

Effect of lowering of temperature in producing increase of amplitude and decrease of frequency in pulsation of frog's heart. Record to left, normal pulsations; record to right, effect of lowered temperature (Brodie).

(2) *Effect of Ligature.*

By the application of Stannius' ligature, the pulsation of the heart is arrested at diastole. A similar arrest at diastole is found to take place in the pulsation of *Desmodium* by the application of a ligature immediately below the motile organ. The arrest takes place either at once or after one or two vigorous beats. Similar effects are also obtained by making a cut, after suitably supporting the leaflet. While the leaflet is in the condition of this arrest, it is often possible to renew the pulsation by the stimulus of an electrical shock.

(3) *Effect of Temperature.*

The effect of lowering of temperature on the rhythmic pulsation of *Desmodium* is similar to that on the pulsation of a frog's heart.

Lowering of temperature enhances the amplitude, but reduces the frequency of pulsation of both. A rise of temperature, on the other hand, causes enhanced frequency and diminished amplitude of pulsation (figs. 11, 12).

We have seen the extraordinary similarities of physiological reaction in the contractile, the conducting, and the rhythmic tissues of plant and animal. We shall now take up the reactions of the plant under medical treatment. This latter includes the application of electricity and drugs; we shall therefore consider in some detail the stimulating or depressing effects induced by an electrical current and the stimulating, depressing, narcotic and poisonous effects of various drugs on the plant.

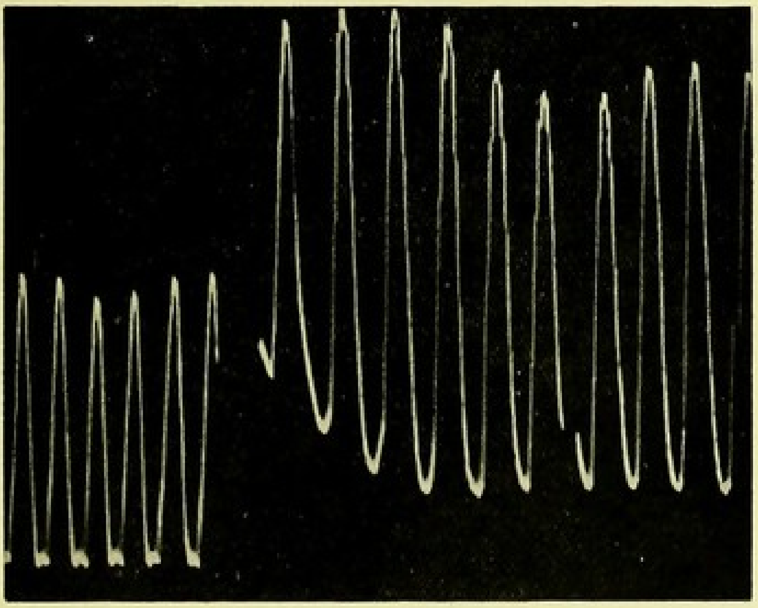

Fig. 12.

Effect of lowering of temperature on pulsation of *Desmodium*. Record to left, normal; record to right, effect of lowered temperature.

(VI) Effect of Electrical Current on Plant-Response.

The sensitiveness of some plants to the stimulus of an electrical current is extraordinarily high. The human tongue is known to be an extremely sensitive detector of an electrical current, the tongue of an average European detecting a current as low as 6 micromperes. But we must bow down to the superior perceptive power of the plant, which in the case of *Biophytum*, for example, is ten times more sensitive than the European!

(1) *Polar Reactions on Contractile Tissue.*

As regards the action of constant current in inducing excitation of the contractile plant-tissue, I find that with feeble current, it is the kathodic point which excites at the make and not at the break of the current; the anode excites at neither make nor break. With current of moderate intensity, the kathode still excites at make and not at break. The anode, however, now induces excitation at the break but not at the make. In all these we have a series of reactions which are identical with those which take place in the contractile animal tissue.

(2) *Contrasted Effect of Anode and Kathode on Pulsating Tissues.*

Taking the case of rhythmic tissues in the animal, the point of application of anode on a beating heart induces an expansion. The effect of the kathode would be the opposite.

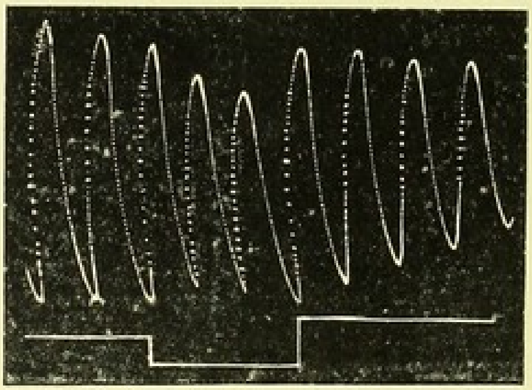

Fig. 13.

Alternate effects of anode and kathode in diminishing systolic contraction and diastolic expansion. Continuous line below record indicates duration of application of current. Line below normal represents application of kathode; line above, application of anode.

Similar effects are also observed in the pulsating leaflets of the telegraph plant. Thus, the application of anode, inducing expansion, tends to oppose the contraction at the systolic phase. The effect is a diminution of contraction. In the record shown in fig. 13 the up-movement represents contraction and the down movement expansion. The diminution of contraction under anode thus appears in the record as progressive diminution of heights of responses. The application of kathode, on the other hand, inducing contraction, opposes the diastolic expansion; the amplitude of pulsations is seen progressively reduced with continuously diminishing relaxations, the base-line being shifted in consequence.

(3) *Inhibitory Effect of Transmitted Electric Stimulation.*

The pulsation of the beating heart may be inhibited by the stimulation of the vagus nerve. The rhythmic pulsation of *Desmodium* leaflets may similarly be inhibited by applying electrical stimulation at some distance from the pulsating organ. This is seen in fig. 14, where the inhibitory effect of transmitted excitation is seen to diminish the normal amplitude of pulsation. On the cessation of excitation the pulsations are seen gradually to regain their normal amplitude.

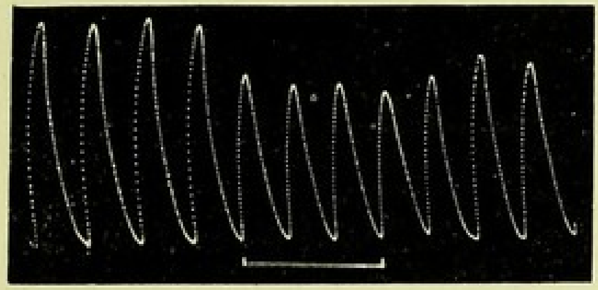

FIG. 14.

Inhibitory effect of transmitted excitation on the pulsation of leaflet of *Desmodium*. Line below indicates duration of transmitted excitation. Note the gradual removal of inhibitory effect on cessation of stimulation.

(VII) EFFECT OF CHEMICAL AGENTS ON THE RESPONSE OF CONTRACTILE TISSUE.

For this investigation a series of uniform responses is first obtained under uniform stimuli. After the application of the given agent, another series of responses is once more obtained under the same stimuli as before. The variation of amplitude of response then gives an indication of the excitatory or depressing action of the agent. The plant is intensely susceptible to the impurities present in the air. The vitiated air of the town has a very depressing effect. According to popular science, what is death to the animal is supposed to be life for the plant; for does it not flourish in the deadly atmosphere of carbonic acid gas? The record (fig. 15) shows that, instead of flourishing, the plant gets suffocated just like a human being. Note the gasp of relief when fresh air is introduced. Only in the presence of sunlight is this effect modified by photosynthesis. In contrast to the effect of carbonic acid, ozone renders the plant highly excitable. Sulphuretted hydrogen, even in small quantities, is fatal to the plant. Chloroform acts as a strong narcotic, inducing a rapid abolition of excitability. The ludicrously unsteady gait of the response of the plant (fig. 16) under alcohol could be effectively exploited in a temperance lecture! The record (fig. 17) is in the nature of an anticlimax, where the plant has drunk (pure water!) not wisely but too well. The gorged plant is seen to have lost all power of movement. I was, however, able to restore the plant to normal condition by extracting the excess of liquid by application of glycerin.

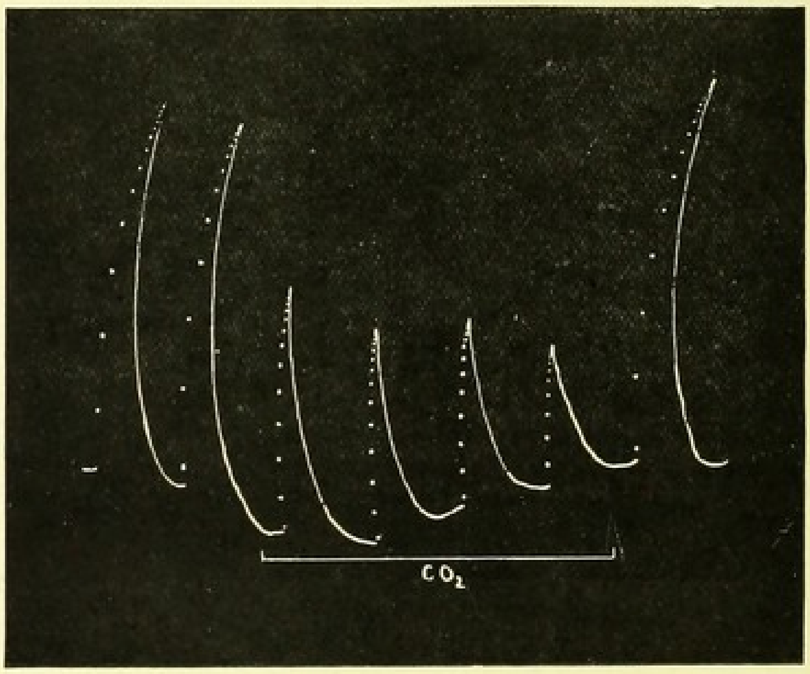

FIG. 15.

Effect of carbonic acid gas.

(VIII) EFFECT OF DRUGS ON THE CONDUCTING NERVE.

I have already described how the variation of conducting power in *Mimosa* is obtained from the automatic records of velocity of transmission of excitation. The arrival of excitation here is signalled by the sudden fall of the leaf. Investigation by method of mechanical response is possible in the case of the so-called sensitive plants. For ordinary plants the motile indicator is not available and an electrical method, to be presently described, has to be employed in such a case.

(1) *Effect of Poison on the Abolition of Conduction.*

Below I give a record which exhibits the effect of poisonous reagents in inducing retardation and subsequent abolition of the conducting

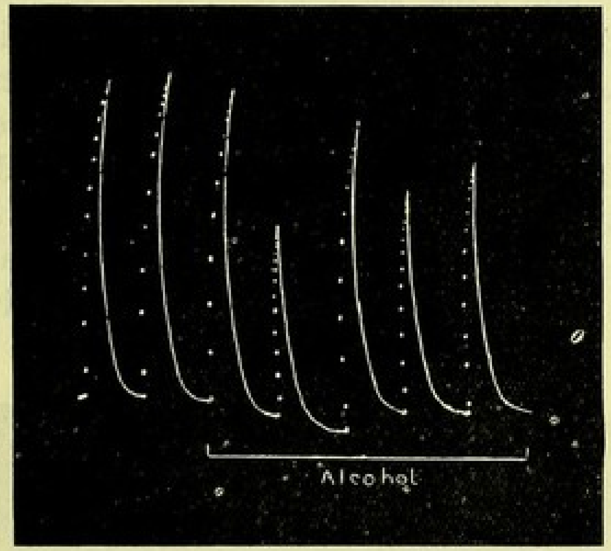

FIG. 16.
Effect of vapour of alcohol.

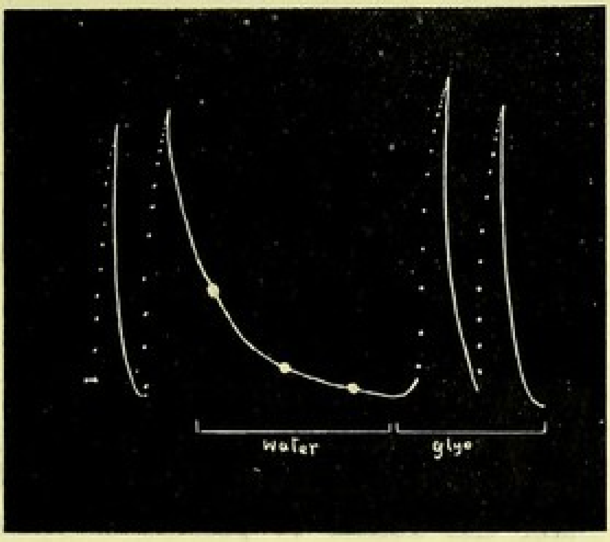

FIG. 17.
Abolition of motile excitability by excessive absorption of water, and subsequent restoration by withdrawal of excess.

power. In the experiments, the record of which is given in fig. 18, copper sulphate solution was applied locally on a portion of conducting petiole, 10 mm. in breadth. It must be remembered that a certain time must elapse before the toxic agents will get access to the conducting tissue in the interior by absorption. The effect of the toxic agent will thus be increasingly effective with time. Record (1) in the figure shows the normal record for transmission of excitation to a distance of 30 mm., the successive dots representing intervals of 0·1 second. Record (2) was taken after twenty minutes' application of the copper sulphate ; the transmission period is seen to be prolonged, indicating growing depression of conductivity. Record (3) was taken forty minutes after the application. The transmitted effect is seen to be completely blocked by the action of the poison. In order to show that the absence of response was due not to the abolition of motile excitability of pulvinus, but to the block of conductivity in the petiole, a fourth record was taken under direct stimulation, which proves that the motile excitability of the leaf had remained unimpaired.

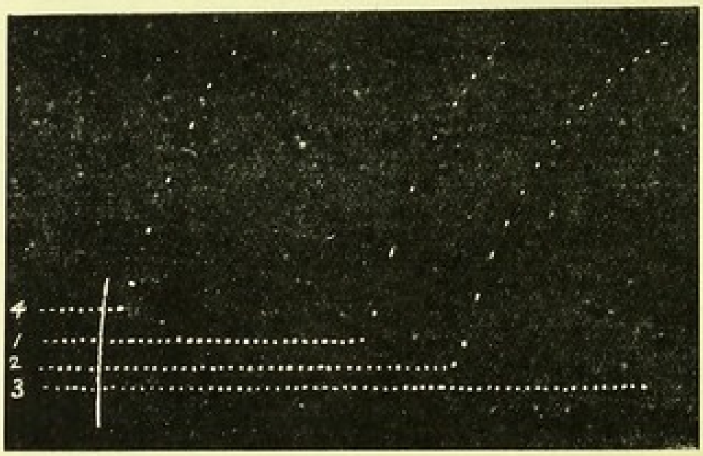

Fig. 18.

Effect of copper sulphate solution in the retardation and final arrest of conduction. 1, normal record ; 2, retardation after twenty minutes' application ; 3, arrest after forty minutes ; 4, record of direct stimulation.

It is interesting to note that the abolition of conducting power takes place quicker under the action of poisons which are more virulent. Thus under the action of potassium cyanide solution the conducting power was abolished in a period of application as short as five minutes.

(2) *The Conductivity Balance.*

For demonstrating the universitality of nervous conduction in plants I have experimented on isolated conducting tissue of ordinary plants, the method of investigation being electrical. And for this purpose I have devised a new method of extreme delicacy, known as the Method of Conductivity Balance. An isolated conducting strand of the plant is taken and stimulus applied about the middle. Excitatory waves travel along both arms of the balance through the conducting regions R to the right, L to the left, and induce excitatory electro-motive effects at the two responsive points, E and E′. The excitatory electrical effects at E and E′ are opposed, and when these are equal they balance one another, the resulting galvanometric indication being reduced to zero. Exact balance is produced by bringing the stimulator nearer one of the two points E or E′. In order to study the influence of an agent on conductivity, we first take a balanced record, and then apply the given reagent on a short length of the conducting arm, say, to the right R.

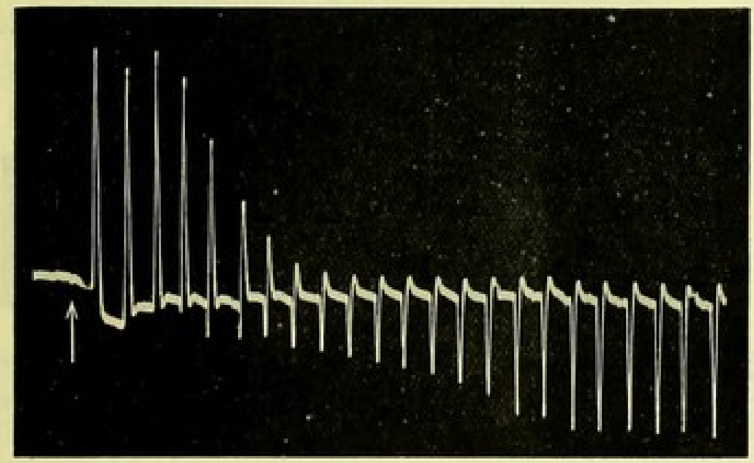

FIG. 19.

Record of effect of dilute solution of Na_2CO_3 on variation of conductivity. Record commenced with exact balance; reagent applied on right arm at moment marked by arrow. Note immediate enhancement of conductivity giving rise to up-curves, followed by depression exhibited by down-curves.

If the effect of the agent be to induce an enhanced conducting power the excitation transmitted to the right will be greater, there will be *overbalance* to the right, and the response caused by the upsetting of the balance will be upward. But if the agent had caused a depression of conduction there would be an *underbalance* and the resulting response would be downwards. In this way we can study the accelerating and retarding effects of various drugs on conduction of excitation (fig. 19). Again, we can compare the relative effects in conductivity-variation brought about by different agents, which are applied simultaneously, the record giving us a continuous graphic illustration of the relative and varying effects of the two, one on the arm R, the other on L.

We may similarly compare the conductivity and excitability changes induced by the same reagent.

(IX) Effect of Drugs on the Pulsation of Rhythmic Tissue.

In studying the effect of chemical agents in the form of gases and liquids, automatic records of pulsation are first taken under normal conditions, and the gases and vapours subsequently introduced into the plant chamber, or the liquid agent applied internally or externally. Internal application may be secured by forcing in the solution at the cut end of the petiole by means of hydrostatic pressure.

As regards the action of ether, the effect of very diluted vapour is generally to induce a transient exaltation, followed by depression and arrest of pulsation. If the leaflet be subjected to strong vapour and if the application be prolonged the arrest is apt to be permanent. But if diluted vapour be employed and fresh air substituted immediately after the arrest, then there is a slow revival of pulsation (fig. 20). The effect of chloroform is similar to that of ether, its reaction, however, being far more toxic; a slight excess in the application is attended by a permanent arrest of pulsation.

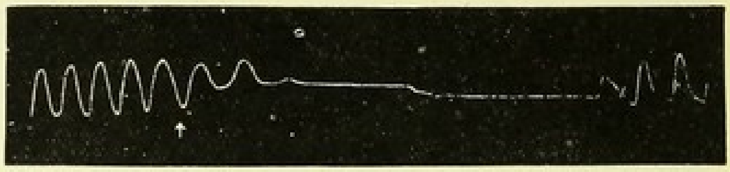

Fig. 20.

Arrest of pulsation of *Desmodium* under ether; restoration of pulsation on blowing off ether. The arrow indicates the time of application.

This and numerous other reactions exhibit the remarkable similarity in the effect of various chemical agents on the animal and vegetable tissues. A very striking characteristic is the antagonistic reaction of acid and alkali on the animal heart. Application of very dilute acid induces in the heart an atonic reaction, in consequence of which there is brought about an arrest of pulsation in the relaxed or diastolic condition. The action of dilute alkaline solution is the very reverse of this—namely, a tonic contraction and arrest in systole (figs. 21 and 23). I find these effects repeated in an astonishing manner in the pulsation of

FIG. 21.

Arrest of pulsation of the heart of frog in diastole by the action of dilute lactic acid (Gaskell). Record to be read from right to left in this and following figures.

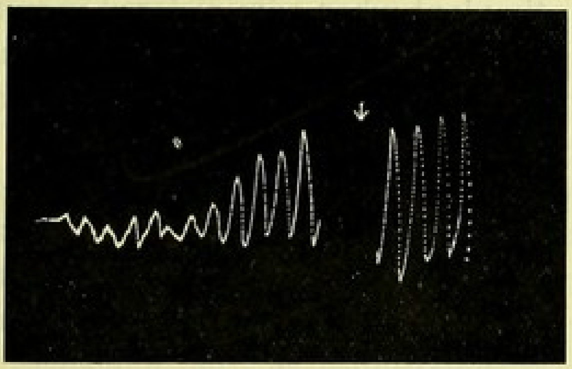

FIG. 22.

Arrest of pulsation in *Desmodium* in diastole by the action of dilute lactic acid.

FIG. 23.

Arrest of pulsation of heart in systole by the action of dilute NaHO (Gaskell).

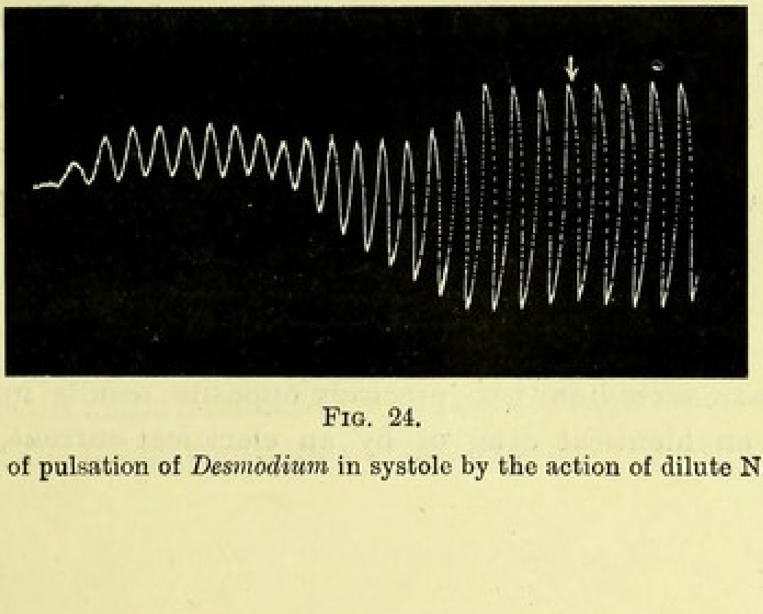

FIG. 24.

Arrest of pulsation of *Desmodium* in systole by the action of dilute NaHO.

Desmodium. The internal application of dilute solution of lactic acid is seen to induce an arrest in a state of diastolic relaxation (fig. 22). The application of dilute NaHO solution on the other hand induces exactly the opposite effect—i.e., an arrest at systole (fig. 24).

(X) EFFECT OF DOSE.

Another striking result that came out in my investigations on plant reactions is the modification of effect brought on by the strength of the dose. Thus, a poisonous reagent which caused depression or death was found to act as a stimulant when administered in minute quantities.

As regards application of electrical current in medical practice, it is assumed that Pflüger's law, that it is the kathode that excites and anode that causes depression, is universally applicable. I find, however, that here too the strength of the current is a very important determining factor. Though the application of the anode causes depression with moderate currents, the reaction is completely reversed when the intensity of current exceeds a certain limiting value.

The very great importance of the influence of intensity on the character of reaction was exhibited in a still more striking manner in my investigation on enhancement or depression of nervous conduction. The application of positive polar force induced, as we have seen, an enhancement, and the negative force a depression, in the conducting power, culminating in its complete arrest. But the result was subject to great modification dependent upon the intensity of the force. When the positive force was gradually increased, the conducting power was also increased till it reached a critical point; beyond this there was produced a complete reversal. The force which had hitherto caused an enhancement now caused a profound depression when carried beyond the critical point and finally brought about arrest of conducting power. The application of a negative force also led to a similar cycle of change. The increasing intensity caused enhanced depression; beyond a critical point the effect was reversed into increased conductivity above the normal. It will thus be seen that want of knowledge of the critical factor may bring about a result exactly the opposite of what was intended.

(XI) THE MOLECULAR CYCLE.

We have seen how two precisely opposite results may be brought about by an identical drug or by an electrical current, owing to the varied strength of application. There is, however, still another obscure factor which creates great perplexity. A given agent may cause a certain effect on one individual and an altogether different effect on another—"what is one man's meat is another man's poison." This difference is considered in some mysterious manner to be due to the varied constitutions of the individuals. As a concrete example I may cite the different reactions given by three batches of seedlings primarily similar. These were kept for some time under three distinct conditions and afterwards subjected to the action of a given dose of dilute poison. The first batch succumbed to the poison immediately; the second struggled for a time against it, recovered and exhibited a moderate rate of growth afterwards. But the third batch was actually stimulated by the poison and demonstrated this by invigorated growth!

Why should we find this difference? We must remember that the living tissue is not merely a mass of inert matter, but is a complexus of matter and energy held latent. The tissue may thus exist under widely different conditions, according as to whether it has been rendered active by the stimulating influence of its environment, or reduced to a state of lethargy through being deprived of this. The source of stimulus here referred to includes every cause, internal or external, which brings about excitation. From the normal state of vigour the condition of the tissue may, according to circumstances, be carried to two opposite extremes—the state of inanition through lack of stimulation, and the state of exhaustion through excess of stimulation. Between these two extremes are numerous gradations of tonic condition in the living tissue, these being determined by its past history; and it is impossible to predict what the answering reaction of the organism will be unless we know the exact position of the tissue in the scale of tonicity.

How then are we to obtain some measure of this obscure internal condition? There are two conceivable ways in which this could be attempted. One, by the study of outward posture or appearance of the organism; and second, by the character of its answers to testing shocks.

A trained observer may be able to draw his inferences more or less accurately from outward appearances, but with plants we can depend on something more definite than this rule-of-thumb procedure. In the most favourable tonic condition of *Mimosa*, for example, the leaf is held out at a certain angle determined by the tonic contraction of the tissue. When the plant is kept completely isolated from all sources of stimulation it grows atonic, the tissue becomes relaxed, this being outwardly exhibited by the abnormally erect posture of the leaf. The plant is brought once more to a normal condition when subjected to the action of stimulus, the leaf once more occupying its normal outspread position. Under further stimulation the contractile movement reaches a limit, and when stimulation is carried to excess, the contractile movement of fall is reversed into erectile movement of relaxation. If we had attached a recording lever we should have found a complete curve traced, something like this:—

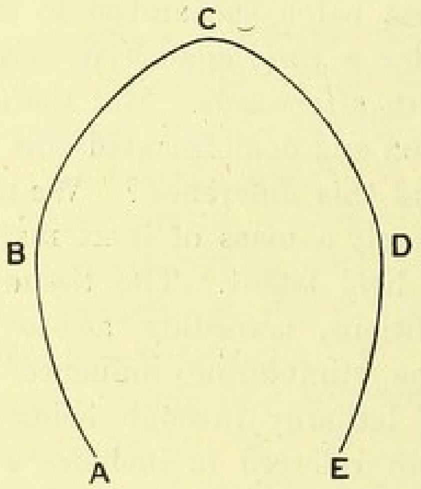

FIG. 25.

Characteristic cyclic curve showing growing contraction brought about by increasing stimulus from atonic **A** to **C** through subtonic **B**; subsequent reversal under over-stimulus; **D** moderate, **E** excessive fatigue.

In the study of this curve it should be remembered that, on account of the method of record employed, the up-movement of the leaf is shown by the descent of the curve and vice versa. These outward manifestations are the expressions of internal molecular change of a physico-chemical character, and the cyclic curve representing the varied conditions of the tissue I shall refer to as the *Cyclic Molecular Curve.*

It will be seen from the diagram that a point in the ascending has a corresponding point in the descending curve. From this we can see how liable we are to draw a wrong inference from exclusive reliance on outward appearance or posture; for example, the parallel relaxed positions of **A** and **E** may have been brought on by two diametrically opposite conditions—i.e., extreme atonicity as at **A**, over-fatigue as at **E**. In order to restore the tissue to the normal, the aim should be to bring it to the optimum condition **C**. For this, diametrically opposed treatments are necessary, depending on the question of whether the tissue is at **A** or **E** condition. If it be at **A** stimulation is necessary, if at **E** rest or sedative treatment. But if we mistook **E** for **A** and applied further stimulation, the case would have ended fatally through extreme exhaustion, while the other mistake would have been equally unfortunate for the plant, which would have met an untimely end through excessive inanition.

Turning next to the second method by which the changing condition of the tissue may be found from the progressive modification of replies to a testing stimulus, it is extremely interesting to find that corresponding to the molecular cycle which has been referred to, there is a concomitant cyclic variation of response. In fig. 26 I have given the characteristic responses of the tissue under varying molecular conditions typical of **A**, **B**, **C**, **D** and **E**. I may say here that these results have been verified by experimenting on various kinds of tissues, the methods of investigation employed being so different as the electrical and the mechanical.

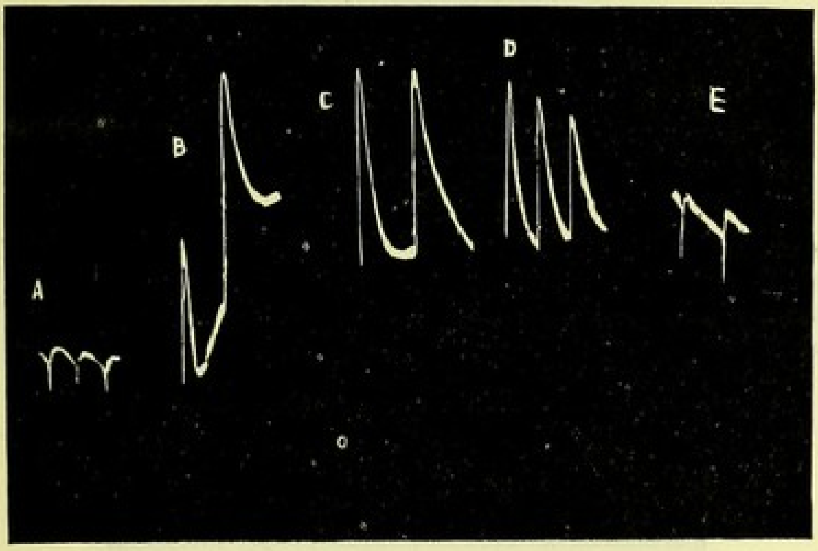

FIG. 26.

Typical responses under different molecular conditions, **A**, **B**, **C**, **D**, and **E**.

In describing the changes of response corresponding to changes in the molecular condition of the tissue, I shall for the sake of simplicity designate all normal response by contraction or by galvanometric negativity, as the *negative* response; its converse—i.e., response by relaxation or galvanometric positivity—will be termed *positive* response. Beginning with the case of extreme sub-tonicity corresponding to the point **A** in the cyclic curve, we find a maximum variation from the normal, the response being abnormally *positive.* Continued stimulation improves the general tone from a condition of relaxation to a growing tonic condition and converts abnormal positive to normal negative.

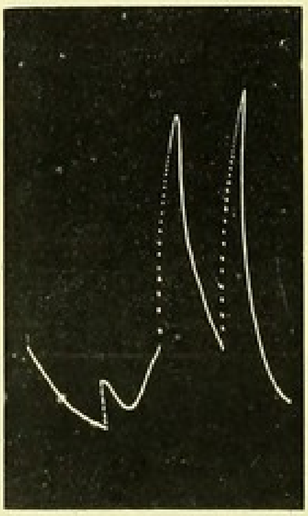

Fig. 27.

Record showing effect of stimulus modifying tonicity. Growing relaxation or atonicity arrested by stimulus at thick dot. After-effect of this induced moderate contraction. Subsequent stimuli gave rise to staircase increase in response.

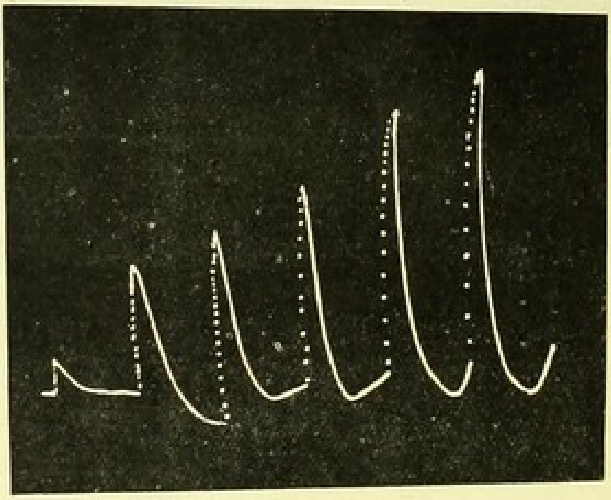

Fig. 28.

Staircase increase of response in **B** stage.

In fig. 27 stimulus applied at the thick dot is seen to arrest growing relaxation in an atonic specimen of *Mimosa*. After this, successive stimuli give rise to staircase response. At the phase corresponding to **B**, the condition of sub-tonicity is moderate; stimulus removes the inertness and confers on it an increasingly better tone. Hence the characteristic response at this stage is a staircase enhancement (fig. 28) culminating in the optimum condition **C** (fig. 29). The highest point of the molecular cycle is thus reached. Further stimulation, strong and long continued, completes the other half of

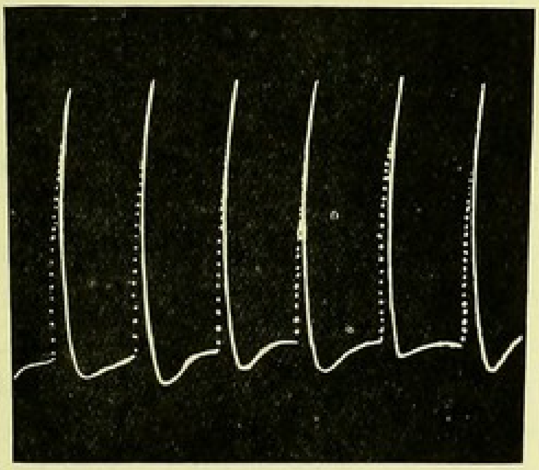

FIG. 29.

Uniform response in **C** condition.

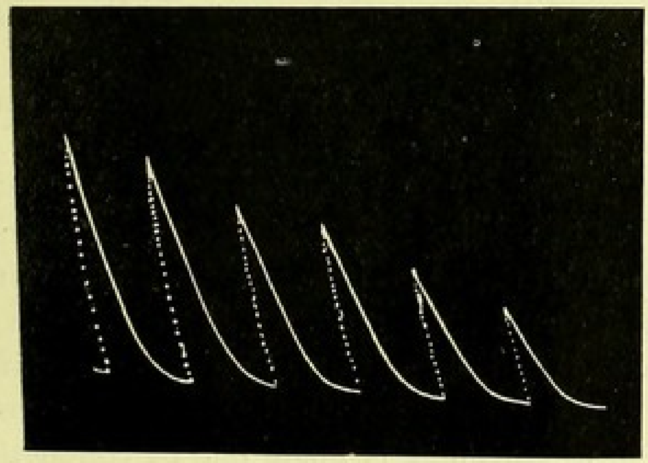

FIG. 30.

Exhibition of fatigue in the **D** stage.

the cycle, now of descent. During this descent the response at first undergoes a change from negative to less negative; that is to say, there is an appearance of fatigue (fig. 30). Again, under excessive stimulation the response may decline to zero, or even undergo a reversal to abnormal *positive*. As in the characteristic curve so also in the series of responses, the two halves of the cycle are strangely alike, one being as it were the reflection of the other. The cycle begins with extreme sub-tonicity due to lack of stimulation and ends with exhaustion brought on by excessive stimulation. The starting point of the one may be supposed to meet the end of the other in a common fatality. But though the one half thus mimics the other there is as it were a polar difference between the two, by reason of the difference in their past histories, necessitating treatment which must be diametrically opposite according as the tissue happens to occupy the beginning or end of the cycle.

Thus it is clear that the progress of medicine may be greatly facilitated when the attention of investigators is drawn to the importance of the molecular aspects of the phenomena with which they have to deal. Thus in examining the action of drugs a threefold question is seen to rise. It must first be determined what is the nature of the reaction induced by the given agent under normal conditions. The second matter of inquiry is what is the critical dose above and below which opposite effects are brought about? And finally, as the nature of the response is profoundly influenced by the position which the tissue then occupies in the curve of molecular cycle, it follows that the most important element in the application of a curative agent will be in the determination of the place of the tissue in the cyclic curve.

I have given, this evening, accounts of various experiments which seem to bring the plant much nearer to us than we ever thought. We find that it is not a mere mass of vegetative growth, but that its every fibre is instinct with sensibility. We find it answering to outside stimuli, the responsive twitches increasing with the strength of the blow that impinges on it. We are able to record the throbbings of its pulsating life, and find these wax and wane according to the life-conditions of the plant, and cease with the death of the organism. We have seen how the whole plant is made one by conducting threads, so that the tremor of excitation initiated in one place courses through the whole; and how this nervous impulse, as in man, can be accelerated or arrested under the several actions of drugs and poisons. In these and many other ways the life-reactions in plant and man are alike: and thus, through the experience of the plant, it may be possible to alleviate the sufferings of man.

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