A METHOD FOR THE REMOTE CONTROL OF ELECTRICAL STIMULATION OF THE NERVOUS SYSTEM*

E. LEON CHAFFEE AND RICHARD U. LIGHT

I. The History of Electrical Excitation

In his studies of function the physiologist has been greatly dependent on the basic sciences, not only in the attempt to identify the separate processes, but also in the interpretation of their actions. Particularly has this been true of investigations of the neuromuscular system, where electrophysics has paved the way to many important discoveries. It may even be said that the history of neurophysiology has been decided in large part by the development of electric-recording instruments on the one hand, and by the increasingly effective use of electric currents for stimulating on the other. As Adrian has written: "It would be hard to think of any other method which has done so much to show us how the body works, for it gives us a means of throwing a muscle or a nerve into activity at will by an agency which does no damage and can be precisely controlled."[1]

The early developments of these two sciences went forward hand in hand, since many of the discoveries in electricity were due to the tell-tale sensations and spasms caused by the passage of a current; in the absence of precise instruments for measuring electrical currents, the unique susceptibility of the neuromuscular system to electrical excitation made it an indispensable detector. Thus it was that in 1746 a group of scientists in Leyden encountered unexpectedly the "capacity" of an electrified glass of water, because of the sudden shock which accompanied its discharge. The sensation was described vividly by one of the group: "Mr. Muschenbroeck, who tried the experiment with a very thin glass bowl, says, in a letter to Mr. Réaumur, which he wrote soon after the experiment,

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* From the Cruft Laboratory of Physics and Engineering, Harvard University, and the Department of Surgery, Yale University School of Medicine. A preliminary report of this method was published in Science, March 30, 1934, Vol. 79, pp. 299-300.

that he felt himself struck in his arms, shoulders and breast, so that he lost his breath, and was two days before he recovered from the effects of the blow and the terror. He adds, that he would not take a second shock for the kingdom of France."[24] In such manner began the history of electrical excitation, together with the recognition of the first known reservoir of electrical energy, the famed Leyden jar.

Medicine, in its traditional weakness, promptly embraced the new spark phenomenon as a therapeutic agent, and applied it with little hesitancy to human ailments. During the years which followed the announcement of the "Leyden Phial" there was a wave of new cures. Most of these hinged on the fantastic belief that if odoriferous medicines were confined in glass vessels, and the vessels were excited electrically, the medicinal virtues would transpire through the glass to be absorbed by the patients in whose hands the containers were placed![25] The fallacy of these ill-judged methods was soon to be exposed by the Abbé Nollet,[26] but the procedure of electrification meanwhile had been transferred directly to the patient, and numerous cures of paralyses were being recorded. Among the most optimistic of the "electrotherapists" was John Wesley the divine who, although possessing neither medical nor scientific degrees, yet organized dispensaries for the treatment of disease, and used "this unparalleled remedy" as one of his principal therapeutic agents. His book,[31] published in 1759, is replete with miracles which tested the patience of men of stricter scientific discipline. The remedy fell into better hands when Jean Paul Marat adopted it in his lucrative medical practice, but he too wrote with an enthusiasm which exceeded the evident results.[21] In the hands of charlatans it was an ideal tool, and the notorious Graham,[29] who exploited the English public unmercifully, was the first of a never-ending succession of quacks who have used the mysterious nature of electricity to further their deceptions.

The interest of Benjamin Franklin in electrotherapy appeared at an early date, for in the early fifties he had gathered a number of paralyzed patients from eastern Pennsylvania for systematic daily treatment in his laboratory, by application of a series of condenser discharges of fairly high capacity. His battery of jars yielded sparks great enough to produce local hyperthermia, petechiae, and paræsthesias. Occasionally the treatments resulted in some increase of voluntary motion, and he wrote to a friend: "These appearances gave great spirits to the patients, and made them hope a perfect cure; but I do not remember, that I ever saw any amendment after the fifth day; which the patients perceiving, and finding the shocks pretty severe, they became discouraged, went home, and a short time relapsed; so that in palsies, I never knew any advantage from electricity, that was permanent. And how far the temporary advantage might arise from the exercise of the patient's journey, and coming daily to my house, or from the spirits, given by the hope of success, enabling them to exert more strength in moving their limbs, I shall not pretend to say."[10] Sagacious Franklin! He recognized the effectiveness of this measure in the treatment of psychiatric disorders, but he held little belief in the wildly hailed specificity of its action.

It was logical that electric sparks should one day be applied to exposed nerves and muscles, and to Galvani and his coworkers belongs the credit for this crucial experiment, which resulted in the discovery of the electrical excitability of nerves (1780-83).[12] It was an important finding, for not only did it open up new methods in the study of neurology, but it provided a detector of electric currents far better than tactile sensation, and thus paved the way for Galvani's second great contribution, the discovery of chemically generated electric current (1789).[13] The quantity of electricity necessary to evoke a convulsion in the freshly killed frog's leg is exceedingly minute, and Volta[30] found it to be 50 to 60 times less than that which could be detected by the most sensitive electrometer of the day, so that for 30 years the nerve-muscle preparation (called by Volta "the animal electrometer") occupied a unique position in the physicist's laboratory.

The rapidly growing science of electricity was soon to demand instruments of greater precision, however, and the epochal work of Oersted[23] (1820) in linking the two forces of galvanism and magnetism provided a basis for the detection of a current by its magnetic effect. The instrument constructed on this principle was called a "galvanometer", and the appellation is proper not only for its descriptive force, but because the device marked the first advance over Galvani's other "meter", the animal electrometer.

At this time Magendie (1822), while utilizing the galvanic current to supplement his studies of the spinal roots, demonstrated that stimulation of the anterior roots causes muscular contraction and that of posterior roots sensation.[20] His studies were of fundamental importance to an understanding of the neurological structure, and they gave rise to a type of experiment which since has been steadily repeated: first, to reduce the activity of an organ through *nerve section*, and second, to increase its activity (or certain phases thereof) through *nerve stimulation*. This method has been at the root of much of our present knowledge of neurology, but it lacks a certain balance in that the results which follow division of a nerve are virtually permanent, whereas those attendant upon stimulation are of the briefest duration,—for the current can be applied only during the course of a surgical exposure.

It had not escaped the attention of Galvani that muscular contraction occurs at the beginning and at the end of current flow, while the muscle remains quiescent during the period of steady flow. This characteristic made possible a series of repeated stimuli from a source of interrupted current, and in 1845 DuBois-Reymond[6] began to apply the methods for generating alternating currents recently uncovered by Faraday to the uses of physiology. His device, an induction coil with a magnetically driven breaker in the primary circuit, produced a series of closely spaced stimuli as the current went through its cycles. The frequency of the current pulses was varied in a rough way through adjustments of the spring tension, and the amount of current could be controlled by changes in the degree of magnetic coupling. This mechanism, simple and effective, is still to be found in every physiological laboratory today. It has, however, three disadvantages: it operates at unknown frequencies, except when regulated by tuning forks; the precise current developed is unknown; and the wave-form used for stimulation is irregular and varies in shape from one coil to another and with varying conditions of use. The latter characteristic has come into much prominence of recent years, largely through the demonstrations by Lapicque[17] and Keith Lucas[19] of the quantity called "chronaxie", but even the careful studies of such men as Erlanger and Garrey[7] have not succeeded in stabilizing the output characteristics of the DuBois-Reymond (or "Harvard") coils. It is to be hoped, therefore, that the venerable induction coil will soon be supplanted by low-frequency oscillators employing thermionic vacuum tubes, so that investigations carried on in widely separated laboratories may be reported in terms of the common units of electrophysics and thus be understandable to all.

Electrical stimulation of peripheral nerves has revealed the functions of many tissues, through the exaggerated activity of the parts to which they lead. However, nerves are merely conduction paths, and the controlling action is known to lie deeper, in the spinal cord or the brain. For many years, attempts had been made to elicit responses from the application of currents directly to the surface of the brain, but these resulted in failure until Fritsch and Hitzig[11] (1870) announced that electrical excitation of certain small areas of the cerebral cortex of the dog would give rise to muscular movements in the opposite side of the body. Much interest attaches to this finding, as it has led to the modern views of localization of cerebral function in the hands of Ferrier,[8] Beevor and Horsley,[2] Sherrington,[27] and the host of modern investigators, who have added definition to the picture of cerebral activity by the use of this method. The studies have not been confined to animals alone, however, for as early as 1909 Cushing[5] pointed to the results of electrical stimulation of the postcentral gyrus during the course of surgical removal of intracranial tumors.

As soon as one considers the use of stimulating currents in physiological investigations, he must choose between the employment of two closely spaced electrodes (bipolar) and the method of grounding the body to a large indifferent plate, leaving only one wire as an active electrode (monopolar). The relative efficacy of the two systems has been the cause of much controversy, although so far as the brain is concerned, it appears that properly constructed electrodes are as satisfactory in pairs as in a grounded circuit.[28] In peripheral nerve studies, however, an important distinction exists, for it must not be forgotten that Galvani's original experiments were made with monopolar stimulation, and that Volta's successful argument against "animal electricity" hinged on the application of both electrodes to the nerve, thus showing that a nervous impulse and not a conducted current traversed the remaining nerve trunk to set the muscle into contraction.

Until very recent years physiologists have been content to observe the effects produced by direct electrical excitation during the short period of a crucial experiment in the decorticate animal, or in one under general anæsthesia. With the growing recognition of the immense duties of the central nervous system in the regulation of autonomic functions, it has become apparent that no method of study can succeed in revealing these central controlling mechanisms, that does not permit the student to reproduce artificially a controlling force which is similar to the function under investigation. This conception is best examined by a comparative consideration of the motor apparatus, for in this system the activities are directive, precise, and capable of attaining full accomplishment in a few moments. They respond to individual electric stimuli, even under anæsthesia, and the shocks may be given with fair rapidity since the cycle of activity can be completed many times in the course of a second. Cerebral autonomic centers, on the other hand, are invested with the regulation of the ceaseless mechanism of internal life, in which changes are of degree and not of the fundamental act, and ebb and flow succeed each other at a comparatively leisurely pace. The very existence of higher autonomic centers has only been suggested, largely as the result of accident or disease, and they have proved extraordinarily refractory to experimental demonstration. It is quite possible that the difficulty rests with the investigative method employed, for not only does it lack the continuing character of automatism, but it is usually applied together with a general anæsthesia, the depressing action of which is exerted on the very region under consideration.

Several efforts have been made to simulate more nearly the functional character of these processes, as well as to reach the other neurological systems during their normal phases of activity. In 1915 Keeton and Becht,[15] during an experimental study of the pituitary body in dogs, implanted some iron filings directly into the gland. The dogs were allowed to recover, and were then brought within the range of an electromagnet in the hope that local stimulation might occur at the site of the implanted iron. The experiment failed to demonstrate any resulting change and this was attributed to the weak magnetic fields available,[16] although in any case there would have resulted only a movement of the filings (mechanical stimulation) and not an induced electric current. In Zürich, Hess[14] has developed a technic for bringing conducting wires out through the skin to form a direct electrical circuit, and his patience and thoroughness in handling this difficult method are an inspiration to those who visit his laboratory. In this country Mussen,[22] Bradford Cannon,[8] and others have adopted similar means. These workers have succeeded in prolonging the duration of the experiment from a few hours at the time of the operation, to a period of several days after recovery. The drawback to the method lies in the wires and clamps used, which project through the skin, and are therefore susceptible to accident and facilitate infection, so that it is seldom that the experiment can be continued longer than two or three weeks. Furthermore, the arrangement requires the constant watch and restraint of the animal during the time that wires are connected to the source of current, so that the subject does not enjoy real freedom, nor can the experiment be adjusted to the changing phases of physiology.

The germ of a new bio-electric relationship seems to have been demonstrated by Feser,[9] who reports the successful transmission of radio waves to an exposed nerve-muscle preparation, without the use of any receiving "pick-up" mechanism other than the nerve itself, which he believes acts as a dipole antenna. His experiments, which deserve more thorough substantiation, may prove useful to analytical studies of the nervous impulse.

The development toward which all of these experiments point is the complete separation of the animal from restraint. The complications of the sterile surgical field, and the time limit set by the operative procedure, must be avoided. Anæsthesia, which suppresses many functions, should not be used during the investigation of the nervous system, yet the animal must not be led into awareness of the experiment through pain or restraint. Under the best conditions, the animal would be allowed to lead a normal life throughout the duration of the experiment, without interference of eating and drinking, sleeping, or exercising. The actual excitation should be confined to the small area of the nervous system under consideration and be applied without fear of current spreading. Since the degree of stimulation depends in part upon the current density in the excited tissue, and also on the manner in which the current varies with time,[4] these factors must be under ready control of the operator. Because, too, the character of the response is often dependent on the number of times per minute or per second that the stimulus is repeated, provision must be made for accurate and rapid adjustments of the rate of stimulation.

With these difficult requirements in mind, the junior author enlisted the aid of Professor Chaffee in designing a circuit which would be simple, effective, and durable and which would incorporate the precision methods of electrophysics, so that subsequent physiological analyses might rest on ground as secure as possible. Professor Chaffee has taken keen interest in the problem, and gives in the next section his development of the circuits employed.*

II. Design and Operation of the Apparatus

In order to produce electrical stimulation a current of electricity is caused to flow through the tissue to be excited, the degree of stimulation being dependent upon the maximum current density and the way the current varies with time. The exciting current is caused to flow between two electrodes applied to the tissue by connecting the electrodes to some source of electrical energy, such as a battery, an induction coil, or a source of alternating current. If the nerve or muscle being excited is excised or is a part of an anæsthetized animal, the connecting wires from the preparation to the electrical source cause little or no interference or inconvenience. If, however, it is desired to study the effect of stimulating definite portions of the brain or nervous system of an animal in its normal state and perhaps over extended periods of time, connecting wires cannot be employed. The method to be described permits stimulation through an electromagnetic connection instead of by a physical connection, and hence eliminates the undesirable features of previous methods.

An important feature of the method to be described in this paper is that fairly exact knowledge of and control of the intensity and wave form of the stimulating current are possible.

Principle of the Method. The bare principle of operation of the method is briefly as follows: A large condenser, charged from a source of direct current, is periodically discharged through a few

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* The apparatus requires the use of a small secondary coil, implanted in the animal during a preliminary surgical operation. It is of interest that during the past year two other groups have also come independently to the use of buried collodion-coated coils for this purpose. Loucks,[18] in Baltimore, during an attempt to test the effect of repeated cerebral stimuli in creating conditioned reflexes, implanted small coils beneath the cervical skin of dogs, which received current through inductive coupling to a primary coil tied to the dog's neck. Fender and Scott (Rochester, New York) have informed us of tests conducted with an apparatus in which a primary coil of several hundred turns surrounds a small box, while the terminals of the imbedded secondary coil are led to a vasomotor nerve.

turns of a primary coil three or more feet in diameter. This discharge is very intense, amounting to about a thousand amperes, although of short duration. The resulting intense magnetic field produced by this discharge induces an electromotive force in a sterile secondary coil of many turns of fine wire implanted beneath the skin of the animal located within the large primary coil. One terminal of the secondary coil is connected to a silver plate imbedded anywhere in the moist tissue of the animal. This electrode is inert with respect to stimulation effects. The other terminal of the coil is led by a fine insulated wire to a spot to be stimulated. Only a small area approximately equal to the cross section of this wire makes

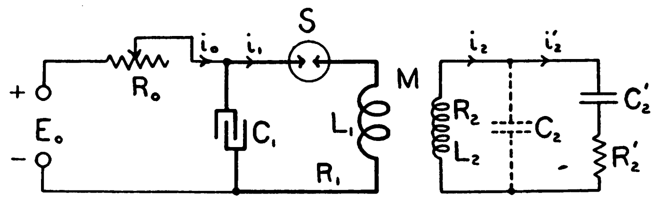

FIG. 1. Schematic Circuit Diagram.

contact with the tissue. The potential induced in the secondary coil causes current impulses to flow between the two electrodes. The current density is maximum at the exposed surface of the fine wire electrode and hence, if the current is not too great, stimulation is confined to a very small volume of tissue at the end of the stimulating electrode.

The two coils described above are actually the primary and secondary coils of an induction coil, the secondary coil being entirely imbedded inside the animal. In order, however, that sufficient potentials be produced in the secondary coil the electrical elements must have quite different characteristics from those of the ordinary induction coil.

A simplified wiring diagram of the essential elements of the system is shown in Fig. 1. Letters L_1 and R_1 indicate the inductance and resistance of the large primary coil.* C_1 is a large condenser charged from a source of power of voltage E_0 through the variable resistance R_0. The condenser C_1 is discharged periodically through

* In the mathematical analysis to follow L_1 and R_1 stand for the inductance and resistance of the entire primary circuit.

L_1 by means of a contacting device S which closes and opens the circuit at an adjustable frequency. The secondary coil has inductance indicated by L_2 and resistance indicated by R_2. The coil and wires have a certain distributed capacitance represented by the dotted condenser C_2. The conduction path through the tissue being stimulated has a resistance R'_2, and an equivalent series capacitance C'_2 which is due to the electrolytic polarization at the terminals.

The various elements of the circuits are chosen so as to produce the greatest current density at the stimulating terminal. The choice of sizes of elements to attain the maximum stimulation can be made only by analysing mathematically the system. This analysis is given later, but to assist better in visualizing the actual system, the sizes of the various elements as used in a particular experimental system are now given.

Sizes of various Elements of the Circuit. Condenser C_1 consists of a bank of paper condensers, the total capacitance of which is 73.8 microfarads. These condensers are grouped in four parallel blocks so that four values of capacitance can be inserted in the circuit. The condensers are capable of withstanding a peak potential of 600 volts and of operating at 100 cycles with an effective alternating potential of 500 volts. The connections from the condenser to the coil L_1 are heavy copper strips about 0.5 inch wide arranged to be as close together as possible to reduce inductance.

The primary coil L_1 is composed of five turns of one-inch copper ribbon wound in a circular form 36 inches in diameter. Taps are brought out from each turn so that any number of turns up to five can be used. The inductance of the primary coil for various numbers of turns is given in Table I. The inductance of the connections from the condenser to the interrupter and primary coil is 1.5 microhenries.

TABLE I

INDUCTANCE OF PRIMARY COIL

Diameter = 36 inches

Turns	*Inductance* microhenries
1	3.3
2	12.
3	23.
4	38.
5	56.

The resistance of the primary circuit varies with the number of turns in the primary coil and also with the frequency because of increasing skin effect with increasing frequency. The resistance of the entire primary circuit, exclusive of the interrupter S, was measured by means of a resonance bridge at the resonance frequency of the circuit. The results are given in Table II.

TABLE II

RESISTANCE AND FREQUENCY OF PRIMARY CIRCUIT

$C_1 = 73.8\mu f$

Primary coil 36 inches diameter.

Turns	*Frequency in cycles per second*	*Resistance of circuit*
2	5030	0.011 ohms
3	3740	0.015
4	2950	0.021
5	2445	0.028

The strength of field varies with position inside the primary coil, but as shown later the variation is most rapid near the periphery. The variation of field was found not to be excessive within a cubic cage 20 inches on a side placed within a coil 36 inches in diameter. Monkeys and small baboons can live comfortably in such a cage. With this experimental arrangement voltages as high as 110 volts could be obtained in the secondary coil, which indicate that a considerably larger primary coil can to advantage be used, permitting either a larger cage or a smaller variation of field within the same cage.

The interrupter S was first a mechanically operated contact between large silver-tipped terminals. Sparking rapidly spoils such a contact. For this reason and also to eliminate the noise of the contactor, a special mercury-pool vacuum tube was used with circuits to be described later. This tube, type FG 158, is a new development of the General Electric Company and at the request of the company details of construction cannot be given at this time. The characteristics of the tube are as follows: When the tube is not conducting its resistance is very great. Conduction through the tube is initiated by impressing a high potential from an induction coil between the mercury pool and an outside band of metal surrounding the tube just above the mercury. The resistance of the tube rapidly drops to a very low value as the current attains values of the order of a thousand amperes. The resistance of the tube varies with the current but the voltage drop across the tube is approximately constant at about 14 volts during conduction.

Resistance R_0 is variable from a minimum of about 50 ohms to a maximum of about 30,000 ohms. This resistance is made up of several units, and each unit must have adequate current-carrying capacity because practically all of the power supplied by the generator E_0 is lost in this resistance. The low values of resistance can carry up to 10 amperes and dissipate five kilowatts of power.

Fig. 2. Secondary coil.

The source of power E_0 is capable of delivering up to 5 kilowatts at 500 volts.

The design of the secondary coil to be implanted in the subject depends upon many factors. The physical dimensions are limited on the one hand by the size and shape that can conveniently be implanted, while on the other hand the magnitude of electrical potential produced for stimulation depends in part upon the area of the coil and the cross section of the winding space. The coil adopted for implanting in a circular hole cut in the skull of a small monkey has an outside diameter of 1½ inches and a thickness of ⅛ inch, with a winding depth in a radial direction of ¼ inch. Such a coil is shown in Fig. 2.

The number of turns of wire with which the secondary coil should be wound to give the best results is best determined by mathematical analysis to be given later, and depends upon the frequency used and the resistance R'_2 of the tissue between the terminals. The standard coil adopted for most of the experiments has 2000 turns of No. 40 (B & S gauge) enamelled copper wire. Such a coil has an inductance of 0.17 henries and a resistance of 700 ohms. For the same winding space the inductance and resistance are practically proportional to the square of the number of turns.

The ends of the coil are soldered to short lengths of No. 32 platinum wire; the joint and inner ends of the platinum wire are securely bound to the coil with silk thread; and then the coil is impregnated and coated with collodion. The platinum-wire leads previously enamelled are also covered with a fairly thick insulating coat of collodion. One platinum wire is cut to a length of approximately 1¼ inches and soldered to a plate of silver ½ inch square. The other platinum-wire terminal is approximately 2½ inches long and is coated throughout its length, the only area exposed being the cross section of the wire at the perpendicularly cut end. This area is 49.7×10^{-6} sq. inches, or 3.21×10^{-4} sq. cms.

The distributed capacitance of the secondary coil in air is approximately 12 micro-micro-farads ($\mu\mu f$), but when the coil and its wire terminals are immersed in a 1/10 normal KCl solution to simulate the tissue in which the coil is implanted, the distributed capacitance represented by C_2 of Fig. 1 is about $100\mu\mu f$. Each inch added to the length of the pair of terminal wires adds approximately $5\mu\mu f$ to the distributed capacitance.

The electrical path through the tissue between the terminals of the secondary coil possesses resistance and capacitance. The capacitance is partly polarization capacitance at the interface between the tissue and the stimulating electrode, and undoubtedly partly capacitance due to the cell walls in the tissue. The capacitance and resistance vary with the potential applied across the tissue path and to some extent with the frequency. At a single frequency we can approximately represent the electrical characteristics of the tissue by a resistance R'_2 in series with a capacitance C'_2 as indicated in Fig. 1.

A number of measurements were made by means of a bridge of the resistance R'_2 and the capacitance C'_2 between copper wires of various sizes and a plate, the wires and plate being imbedded in various locations in the brain of an anæsthetized monkey. The values of R'_2 and C'_2 found varied considerably for the same size wire, due probably to varying amounts of moisture at the end of the wire electrode. Average values for R'_2 and C'_2 for a No. 32 B & S wire are 10,000 ohms and 0.05 μf. If R'_2 is larger C'_2 is less, their product being approximately constant. Since a knowledge of the values of these two quantities is essential to determining the intensity of stimulation, a method will be given later of measuring R'_2 and C'_2 *in situ*.

Single-circuit Diagram. The circuit shown in Fig. 1 is merely diagrammatic and will not operate without some device to start the discharge through S. The complete circuit for a single primary coil is shown in Fig. 3. L_1, C_1, and R_0 have the same significance as in Fig. 1. C_0 is a large condenser of about 50 μf which serves as a reservoir of charge to supply the sudden rushes of current called for by condenser C_1 when it charges. S represents the mercury-pool tube, the discharge through which is started by a high potential

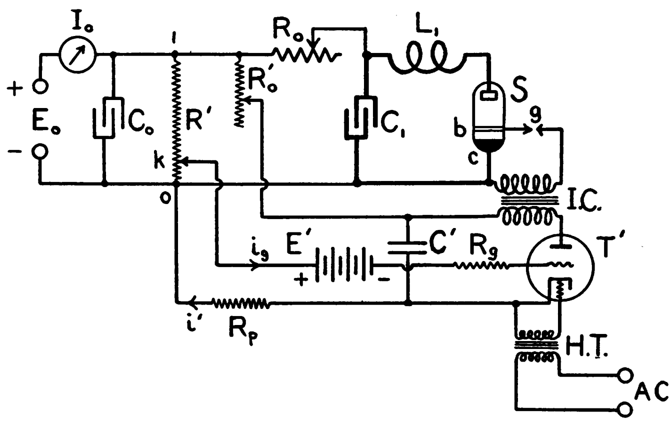

FIG. 3. Diagram of Connections for Single Primary Coil.

impressed between cathode *c* and the external band *b*. This initiating high potential is supplied from the ignition coil I.C., which is a transformer or induction coil capable of giving a potential of the order of 10,000 volts. A small spark gap *g* aids the ignition, probably by causing high frequency surges which are superimposed on the potential impulse.

The time of ignition of S, and the consequent discharge of C_1, is controlled by the auxiliary circuit containing thyratron T', condenser C', resistances R', R_p, R_g, and R'_0, and battery E'. This timing circuit works independently of the main discharge circuit, and its operation depends upon the properties of the thyratron T'. The tube used is a General Electric Type 57 Thyratron. Thyratron T' passes no current so long as the potential between grid and cathode is less than a certain value corresponding to each value of potential between the plate and cathode. At this certain value of grid potential, called the break-down or ignition potential, the tube glows and its resistance drops to a very low value. The relation between grid and plate potentials for ignition depends upon the vapor pressure

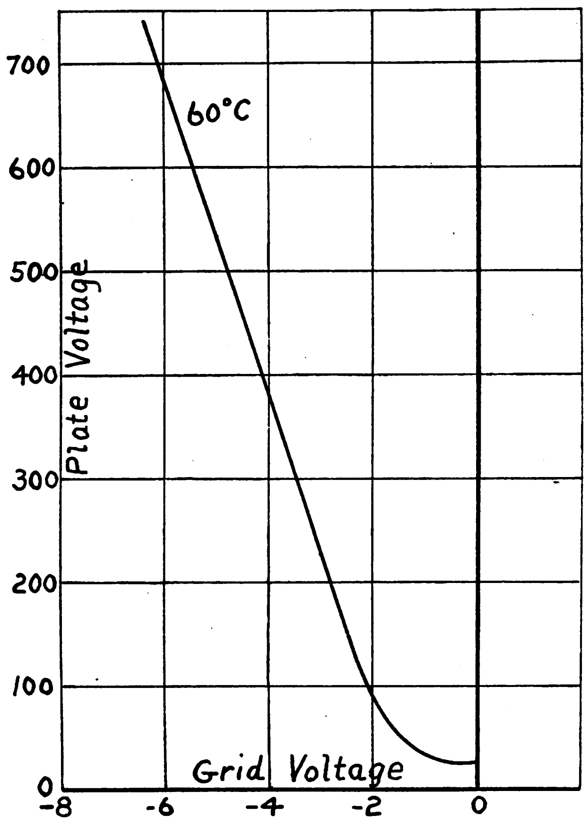

FIG. 4. Break-down Potential of Thyratron Type 57.

of the mercury inside the tube and hence upon the temperature of the tube. Fig. 4 gives the ignition potentials for a temperature of 60°C. The curve moves to the left as the temperature rises. For all points to the right of the curve the tube conducts. After the tube is made to conduct, the current flowing through the tube is unaffected by the grid potential and will cease only if the plate potential is reduced to zero or made negative. The region to the left of the ignition curve is a region in which conduction will not start.

Referring now to Fig. 3, the potential of the grid with respect to the cathode of T′ is

$$e_g = kE_0 - i_g R_g - i' R_p - E' \tag{1}$$

where k may have any value between 0 and 1 according to the setting of the slider on R′. Before the tube T′ conducts, i_g is practically zero so that e_g changes only because of the changes in i′. As condenser C′ charges i′ decreases until e_g attains the ignition value as given by the curve of Fig. 4. Condenser C′ then discharges and e_g immediately becomes highly negative because of the voltage drop through R_p as C′ starts to charge. The inductance of the primary winding of transformer I.C. causes the discharge current to continue until C′ is reversed in potential, at which point conduction through T′ ceases because current can flow through the tube only in one direction. Thus the plate potential of T′ with respect to the cathode is also negative at the end of discharge and remains negative for a sufficient time to allow the vapor in T′ to de-ionize. Condenser C′ again charges at a rate determined by the resistances R'_0 and R_p.

It is instructive to determine the way in which e_p and e_g change while C′ is charging. Eq. (1) gives e_g. The plate potential is

$$e_p = \frac{q'}{C'} \tag{2}$$

where q′ is the charge on C′.

It is easy to show that

$$e_g = \frac{R_p}{R_p + R'_0} e_p + \left(k - \frac{R_p}{R_p + R'_0}\right) E_0 - E' \tag{3}$$

The fraction $\frac{R_p}{R_p + R'_0}$ varies from 1 to zero as R'_0 is increased from zero to infinity. Call this fraction β. Then

$$e_g = \beta e_p + (k - \beta) E_0 - E' \tag{4}$$

Refer now to Fig. 5 in which the ignition curve of Fig. 4 is replotted to a much larger scale of grid voltage. The battery voltage E′ is laid off, and from a point kE_0 volts above E′, a line is drawn sloping downward, as shown, so as to intersect on the vertical and horizontal lines distances from E′ which represent the same number of volts. This line locates E″ which is equal to $-E' + kE_0$. At

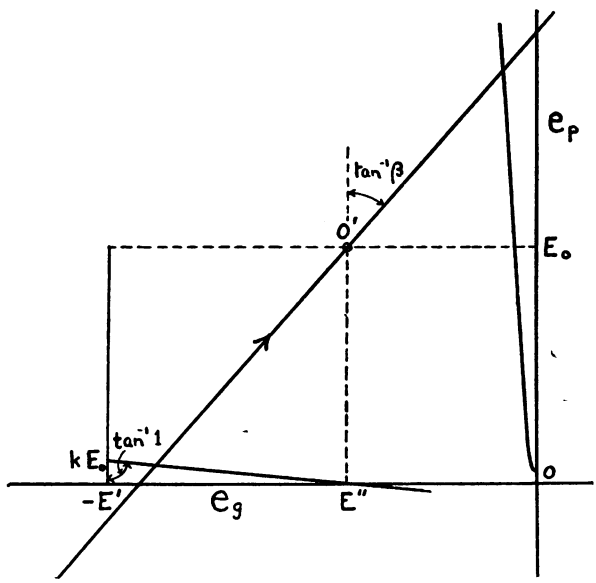

FIG. 5. Path of $e_p - e_g$ Point during Charging.

a point E_0 volts above E″, a line is drawn making an angle whose tangent as determined by scales is equal to β. This line is a plot of Eq. (4) and gives the path of the point representing simultaneous values of e_p and e_g as C′ charges. Obviously this line as drawn in Fig. 5 does not intersect the ignition line at any voltage available, and hence the tube T′ would not break-down. By moving E″ to the right by increasing k, the path can be made to intersect the ignition line at any desired break-down voltage such as 400 volts. This voltage of discharge must be sufficiently great to give a discharge intense enough to start S. If we assume the discharge voltage to be 0.8 of E_0 and that C′ is reversed to a potential of $-0.8\ E_0$

by the discharge, the time required for each charging is 2.2 $C'(R'_0 + R_p)$, approximately. If C' is 1μf, R'_0 is zero, and R_p is 5000 ohms, the frequency of discharge is 91 per second. When R'_0 is zero, β is unity. As R'_0 is increased the frequency of discharge decreases. When R'_0 is 200,000 ohms, the frequency is about 2.2 per second and β is 0.0245. It is obvious that point 0′ in Fig. 5 must always be to the right of the ignition curve by an amount such that the path line passes through the ignition curve at an adequate discharge voltage. Hence as β is varied, E'' must also be varied slightly, that is, as R'_0 is increased to give a lower frequency of discharge, β decreases and E'' must be moved to the left by decreasing k.

Since E'' is merely a polarizing potential which should be variable, let us say, from —10 to +10 volts, it can be supplied in any convenient way. As already stated R_p may be 5000 ohms and R'_0 variable from 0 to a megohm or more if very low frequencies are desired. R_g is merely a protective resistance and should be about 10,000 ohms. Condenser C' may have a capacity of 0.5 or 1μf. R' is a 200,000-ohm potential divider.

The *frequency* of discharge of C' depends only upon the timing circuit associated with T'. The *voltage* at which C_1 discharges is determined by the rate at which C_1 charges and hence depends upon the frequency of discharge and the value of R_0. For a given frequency of discharge, the voltage of discharge of C_1 can be controlled by varying R_0. If we assume that C_1 when it discharges reverses to an equal potential, and that the control circuit discharges as assumed above at 0.8 E_0, then it can easily be shown that the voltage at which C_1 discharges is given by the following expression

$$e_1 = E_0\left(1 - 2\epsilon^{-2.2\frac{C'(R'_0+R_p)}{C_1R_0}}\right) \tag{5}$$

A few results derived from Eq. (5) are given in Table III.

TABLE III

$\frac{e_1}{E_0}$	$\frac{T'}{T} = \frac{C'(R'_0 + R_p)}{C_1R_0}$
0	0.315
0.34	0.5
0.72	1.0
0.975	2.0

It should be noted that tube S, like thyratron T′, allows current to flow in one direction only, and hence the discharge of C_1 consists

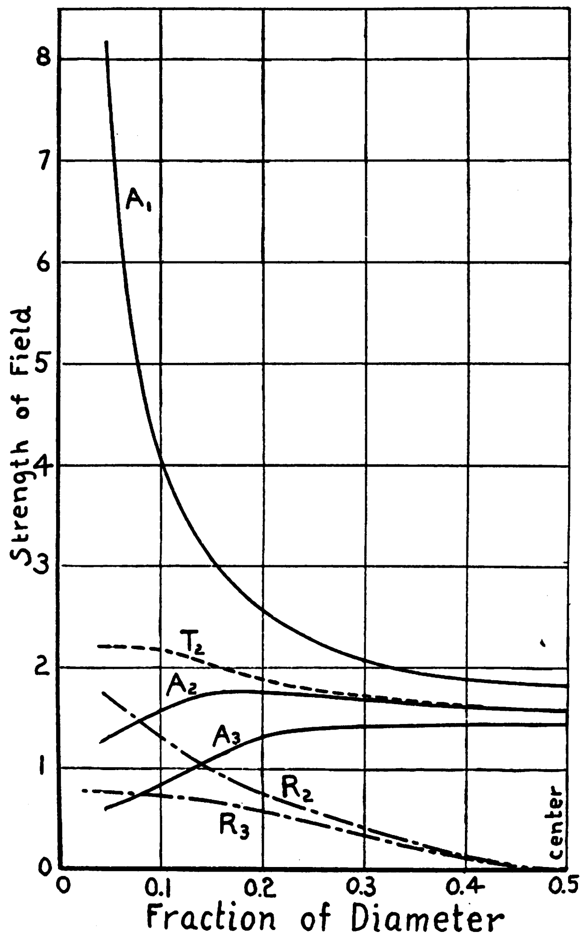

FIG. 6. Field about Primary Coil.

A ———— Field in axial direction.
B — - — - Field in radial direction.
T - - - - - Total Field $= \sqrt{A^2 + R^2}$.

Subscript 1 In plane of coil.
Subscript 2 0.15 of diameter from coil.
Subscript 3 0.32 of diameter from coil.

of a simple rise and fall of current of approximately sinusoidal form. It is the first loop of a damped oscillatory discharge, as explained later and shown in Fig. 8.

Variation of Field about Primary Coil. The primary coil L_1 is made large in order to obtain a more nearly constant field in a cage placed within the coil. Fig. 6 shows the variation of the field about the coil. Curve A_1 gives the potential in arbitrary units induced in a small coil located in the same plane as that of the primary coil for various radial distances and hence gives relative values of the field in the axial direction. Curves A_2 and A_3 give the potentials on the same scale for the small coil placed parallel but at 0.15 and 0.315 of the diameter from the plane of the primary coil. Curves R_2 and R_3 give the radial components of the field in these planes. The dotted curve T_2 gives the total field in one of the planes, where $T = \sqrt{A^2 + R^2}$.

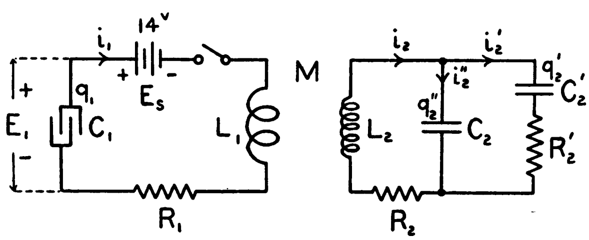

FIG. 7. Schematic Circuit Diagram for Mathematical Analysis.

These curves show that if the secondary coil remains parallel to the primary coil, there is about 40 per cent variation in stimulating potential if the secondary coil is confined within a central circle 0.6 of the diameter of the coil, or 13 per cent for a central circle 0.4 of the diameter of the coil. These variations with position are much less if the secondary coil is in a parallel plane at from 0.1 to 0.3 of the diameter of the primary coil from the plane of the coil.

Electrical Theory of Stimulating Impulse. Observations on the behavior of various animal subjects under electrical stimulation by the method described above would be of little value without a knowledge of the wave-form and intensity of the stimulating impulse. Such knowledge can be had by developing the theory of the electrical discharge in the secondary coil together with certain measurements to be described later. In this section the mathematical theory of operation of the system is presented.

Referring to Fig. 1, let i_1 and i_2 be the instantaneous currents in L_1 and L_2, respectively. Since the discharge tube S during discharge has an approximately constant voltage across it, we can for purposes of analysis represent the primary circuit as in Fig. 7. Resistance R_1 represents the total resistance of the primary circuit, E_1 represents the potential across the primary condenser C_1 at the moment discharge starts, and is numerically equal to e_1* of Fig. 4.

The exact mathematical solution of the circuits shown in Fig. 7 is practically impossible, but fortunately certain assumptions can be made which greatly simplify the analysis without materially affecting the accuracy of the result. For example, the first assumption is that, since the mutual inductance M is small, the current in the secondary circuit reacts a wholly negligible amount upon the primary circuit. Consequently, the discharge in the primary circuit can be calculated independently as follows:

The differential equation for the primary circuit alone is

$$L_1 \frac{di_1}{dt} + R_1 i_1 - \frac{q_1}{C_1} = -E_s \tag{6}$$

where $i_1 = -\frac{dq_1}{dt}$ and $E_s = 14$ volts.

Differentiating Eq. (6) gives

$$L_1 \frac{d^2 i_1}{dt^2} + R_1 \frac{di_1}{dt} + \frac{i_1}{C_1} = 0 \tag{7}$$

The solution of this equation is well known, and is

$$i_1 = A_1 \epsilon^{-\frac{R_1 t}{2L_1}} \sin \omega_1 t \tag{8}$$

* The change in notation is made because during the charging of the primary condenser its potential varies and, since varying quantities are commonly represented by small letters, e_1 was used to indicate the instantaneous potential across C_1. The time taken for a complete discharge is, however, so short in comparison with the time for charging that in the discussion of discharge the initial voltage of the primary condenser is considered a constant quantity.

where A_1 is an arbitrary constant, and

$$\omega_1 = \sqrt{\frac{1}{L_1C_1} - \frac{R_1^2}{4L_1^2}} \tag{9}$$

The constant A_1 is determined by the initial conditions, which are as follows:

When $t = o$, $i_1 = o$, $q_1 = E_1C_1$, and from Eq. (6)

$$\frac{di_1}{dt} = \frac{E_1 - E_s}{L_1}$$

The value of A_1 is, therefore $\frac{E_1 - E_s}{L_1 \omega_1}$, and hence the complete expression for the primary current is

$$i_1 = \frac{E_1 - E_s}{L_1 \omega_1} \epsilon^{-\frac{R_1 t}{2L_1}} \sin \omega_1 t \tag{10}$$

It must be noted, however, that the primary current is zero after the first half-cycle of discharge because tube S passes current only in one direction and loses its conductivity as soon as current ceases to flow. Filling in numerical values of the constants of Eq. (10), which apply to the experimental circuit described above, and assuming that E_1 is 500 volts, we have

$$i_1 = 840\, \epsilon^{-306t} \sin 23{,}600\, t \quad \text{(3 turns)}$$
$$i_1 = 664\, \epsilon^{-266t} \sin 18{,}560\, t \quad \text{(4 turns)}$$
$$i_1 = 550\, \epsilon^{-243t} \sin 15{,}370\, t \quad \text{(5 turns)}$$

These three current forms are shown plotted in Fig. 8.

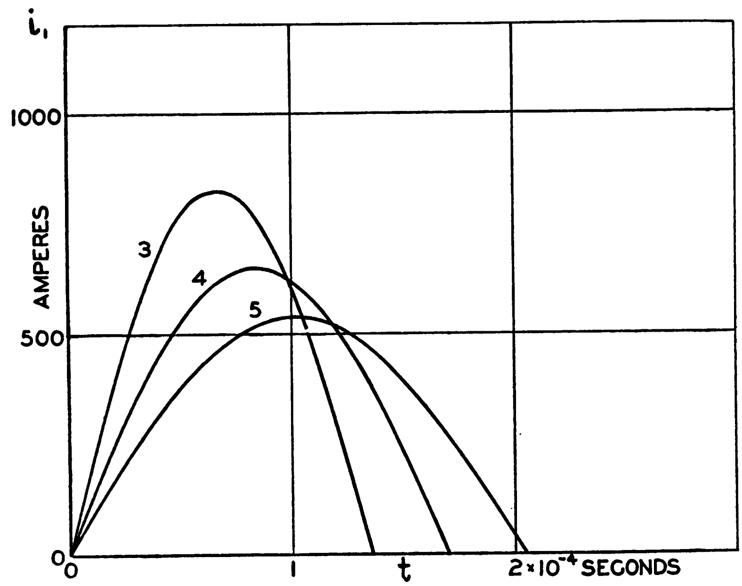

FIG. 8. Wave Form of Primary Current for 3, 4, and 5 Turns of the Primary Coil.

We now pass to the calculation of the secondary current through R'_2, i.e., i'_2. Referring to Fig. 7, the differential equations below express the conditions in the secondary circuit

$$\left.\begin{aligned} &L_2\frac{di_2}{dt}+R_2i_2+\frac{q''_2}{C_2}=M\frac{di_1}{dt}\\ &R'_2i'_2+\frac{q'_2}{C'_2}-\frac{q''_2}{C_2}=0\\ &i'_2+i''_2=i_2\,,\quad i'_2=\frac{dq'_2}{dt}\,,\quad i''_2=\frac{dq''_2}{dt}\end{aligned}\right\}\qquad(11)$$

Eliminating all dependent variables except i'_2, gives

$$\frac{d^2i'_2}{dt^2}+\left(\frac{1}{R'_2C_0}+\frac{R_2}{L_2}\right)\frac{di'_2}{dt}+\left(\frac{1}{L_2C_2}+\frac{R_2}{R'_2L_2C_0}\right)i'_2+\frac{q'_2}{L_2C_2C'_2R'_2}=\frac{M}{L_2C_2R'_2}\frac{di_1}{dt}\qquad(12)$$

In this equation $C_0=\dfrac{C_2C'_2}{C_2+C'_2}$. The solution of this equation comprises two parts, one the forced current pulse due to the primary current, and the other, a transient oscillation set up in the secondary circuit because of the sudden disturbance.

The forced oscillation is of the same form as that of the primary current which produces it. We may write the primary current given in Eq. (8) in the form

$$i_1 = \text{i.p.}\left\{A_1 \epsilon^{(-\alpha_1+j\omega_1)t}\right\} \tag{13}$$

where i.p. indicates that we are to take only the imaginary part of the expression (13). The letter j stands for $\sqrt{-1}$, and $\alpha_1 = \frac{R_1}{2L_1}$. We shall let i'_{2f} indicate the forced part of the final solution, and since it must be of the same form as i_1, we may express it in the form

$$i'_{2f} = \text{i.p.}\left\{A_2 \epsilon^{(-\alpha_1+j\omega_1)t}\right\} \tag{14}$$

It is then only necessary to determine A_2. This can be done by substituting in Eq. (12) expression $A_1\epsilon^{(-\alpha_1+j\omega_1)t}$ for i_1, $A_2\epsilon^{(-\alpha_1+j\omega_1)t}$ for i'_2, and the expression $\frac{A_2}{-\alpha_1+j\omega_1}\epsilon^{(-\alpha_1+j\omega_1)t}$ for q'_2. The result is

$$A_2 = \frac{A_1 M \epsilon^{-j\varphi}}{\sqrt{L_1C_1}\; L_2C_2R'_2\omega_1^2\sqrt{D^2+F^2}} \tag{15}$$

where $D = \frac{\alpha_1^2}{\omega_1^2} - 1 - \frac{\alpha_1}{\omega_1}\left(\frac{1}{R'_2C_0\omega_1} + \frac{R_2}{L_2\omega_1} + \frac{L_1C_1}{L_2C_2C'_2\omega_1R'_2}\right) + \frac{1}{L_2C_2\omega_1^2} + \frac{R_2}{R'_2L_2C_0\omega_1^2}$

and $F = \frac{R_2}{L_2\omega_1} + \frac{1}{R'_2C_0\omega_1} - 2\frac{\alpha_1}{\omega_1} - \frac{L_1C_1}{L_2C_2C'_2\omega_1R'_2}$

and $\varphi = \tan^{-1}\frac{F}{D} - \tan^{-1}\frac{\omega_1}{-\alpha_1} = \tan^{-1}\frac{F}{D} + \tan^{-1}\frac{\omega_1}{\alpha_1} - \pi$

Therefore, the forced part of the secondary current through R'_2 is

$$i'_{2f} = \frac{M(E_1 - E_s)\epsilon^{-\alpha_1 t}}{L_1L_2\sqrt{L_1C_1}\; R'_2C_2\omega_1^3\sqrt{D^2+F^2}}\sin(\omega_1 t - \varphi) \tag{16}$$

The transient part of the solution of Eq. (12) would be obtained by solving the equation with the second member equal to zero. This, however, leads to a third order differential equation which cannot be solved except with numerical coefficients. The approximation will be made for this part of the solution that C'_2 is infinite. This assumption is justifiable because the frequency of the transient oscillation is so high that the reactance of C'_2 is negligible compared with R'_2. The differential equation then becomes

$$\frac{d^2 i'_2}{dt^2} + \left(\frac{1}{R'_2 C_2} + \frac{R_2}{L_2}\right)\frac{di'_2}{dt} + \frac{1}{L_2 C_2}\left(1 + \frac{R_2}{R'_2}\right) i'_2 = 0 \qquad (17)$$

The solution of Eq. (17) is

$$i'_{2t} = B_1 \epsilon^{(-\alpha_2 + \omega_2)t} + B_2 \epsilon^{(-\alpha_2 - \omega_2)t} \qquad (18)$$

where $$\alpha_2 = \frac{1}{2R'_2 C_2} + \frac{R_2}{2L_2}$$

and $$\omega_2 = \sqrt{\alpha_2^2 - \frac{1}{L_2 C_2}\left(1 + \frac{R_2}{R'_2}\right)}$$

The quantities B_1 and B_2 are constants to be determined from the boundary conditions.

The complete expression for i'_2 is $i'_{2f} + i'_{2t}$ which can be written

$$i'_2 = I'_2 \epsilon^{-\alpha_1 t} \sin(\omega_1 t - \varphi) + B_1 \epsilon^{(-\alpha_2 + \omega_2)t} + B_2 \epsilon^{(-\alpha_2 - \omega_2)t} \qquad (19)$$

where

$$I'_2 = \frac{M(E_1 - E_s)}{L_1 L_2 R'_2 C_2 \omega_1^3 \sqrt{L_1 C_1}\sqrt{D^2 + F^2}} \qquad (20)$$

The boundary conditions are that when $t = 0$, $i'_2 = 0$ and $q'_2 = 0$. From these conditions the values of B_1 and B_2 are as follows:

$$B_1 = -I'_2 \frac{\alpha_2^2 - \omega_2^2}{2\omega_2}\left[\frac{\omega_1 \cos\varphi - \alpha_1 \sin\varphi}{\alpha_1^2 + \omega_1^2} + \frac{\sin\varphi}{\alpha_2 + \omega_2}\right] \qquad (21)$$

$$B_2 = I'_2 \frac{\alpha_2^2 - \omega_2^2}{2\omega_2}\left[\frac{\omega_1 \cos\varphi - \alpha_1 \sin\varphi}{\alpha_1^2 + \omega_1^2} + \frac{\sin\varphi}{\alpha_2 - \omega_2}\right] \qquad (22)$$

The only remaining quantity to be expressed in a form suitable for calculation is the mutual inductance M between the secondary and primary coils. This is a geometric quantity and depends upon the position of the secondary coil with relation to the primary coil. The value of M when the secondary coil is in the center of the primary coil and in the same plane with it, is given by the expression:

$$M = \frac{2\pi^2 N_1 N_2 (r_{2o}^2 + r_{2o} r_{2i} + r_{2i}^2)}{3 \times 10^9 r_1} \text{ henries} \tag{23}$$

where N_1 and N_2 are the numbers of turns in the primary and secondary coils, r_1 is the radius in centimeters of the primary coil, and r_{2o} and r_{2i} are the radii of the outside and inside of the secondary coil. For a 36-inch primary coil and a 2000 turn secondary coil of the form described above, the value of M is given in Table IV.

TABLE IV

Turns in Primary Coil	*M* microhenries
2	4.41
3	6.61
4	8.82
5	11.02
6	13.22

Equation (19) gives the secondary current i'_2 only while the primary current is flowing. After the primary current ceases the secondary current falls to zero in accordance with Eq. (18) but with different values of constants B_1 and B_2 because of the different initial conditions applicable to this part of the problem. The new constants B'_1 and B'_2 are determined so that the transient current after the primary current ceases starts off at the value that i'_2 has at the instant i_1 becomes zero. If we consider the calculation of this secondary current a separate problem and place the origin of time at the instant i_1 becomes zero, the secondary current i'_2 is

$$i'_2 = B'_1 \epsilon^{(-\alpha_2 + \omega_2)t} + B'_2 \epsilon^{(-\alpha_2 - \omega_2)t} \tag{24}$$

where

$$B'_1 = \frac{\omega_1}{2\omega_2}\sqrt{I_2'^2 \epsilon^{-2\alpha_1 T} - I^2} + \left(1 + \frac{\alpha_2}{\omega_2} - \frac{\alpha_1}{\omega_1}\right)\frac{I}{2} \tag{25}$$

$$B'_2 = I - B'_1 \tag{26}$$

In these equations I'_2 is given by Eq. (20), I is the value of i'_2 when i_1 becomes zero, and T is the time during which i_1 flows.

We are now finally prepared to calculate the current pulse through the tissue by using Eqs. (19) and (24). This has been done for the standard secondary coil, for $R'_2 = 10{,}000$ ohms, and C'_2

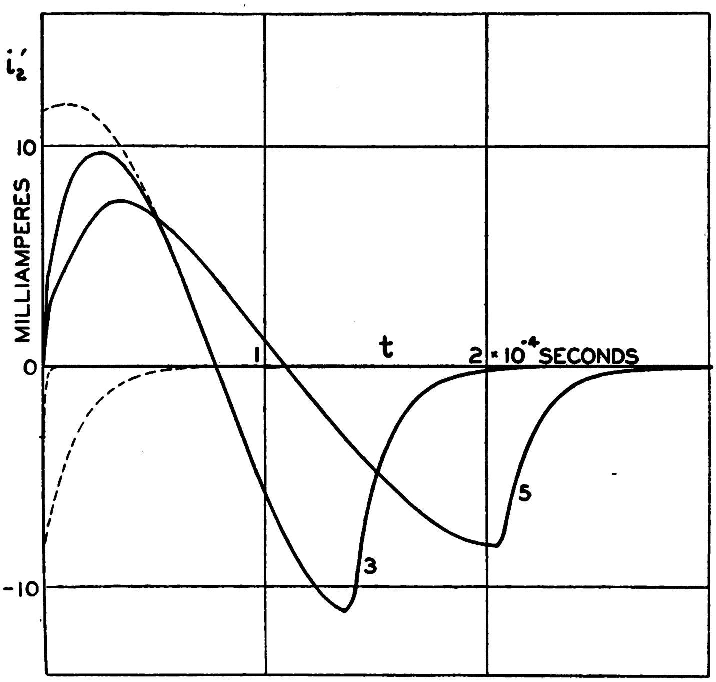

Fig. 9. Secondary Current i'_2 for 3 and 5 Turns in the Primary Coil.

$= 0.05\mu f$, and for 3 and 5 turns in the primary coil. The results are shown in Fig. 9. The dotted curves in Fig. 9 show the contributions from the three terms of Eq. (19), for the case of 3 turns in the primary coil. The upper dotted curve is the first term or the forced current i'_{2f}. The lower dotted curve is the second term, a part of the transient current. The middle or rapidly varying dotted curve is the third term of Eq. (19). It has little effect except for a brief time at the beginning of the current pulse.

Examination of the current pulses shows that they consist of a positive and a negative loop which theoretically enclose, with the time axis, equal areas. This means that the quantity of electricity transferred through the tissue is equal in the two directions and hence each complete pulse causes no net transfer of electricity. The maximum values of the current in the two directions is roughly the same and can be calculated from Eq. (19) but it is much easier to measure these maxima by a method given in the next section. The maximum voltage developed across the tissue can be found by multiplying the maximum current by the value of R'_2. For the 3-turn case this peak voltage amounts to 110 volts. This is of course excessive but can easily be reduced by lowering E_0, by increasing the distance between the two coils, or by using a smaller secondary coil. However, when the electrical constants are changed the shape and duration of the current pulse are altered. It might be of interest, therefore, to state in general terms the effects of varying the sizes of the various electrical elements. In order to make easier this study we shall obtain an approximate but simpler expression for the current pulse.

The second peak of the current pulse is practically equal to I'_2 given in Eq. (20). If we retain only the terms in Eq. (20) which are important in determining the magnitude of I'_2, the values of the various elements being of the order given for the particular experimental system described above, we have the following as an approximate expression for I'_2.

$$I'_2 = \frac{M(E_1 - E_s)}{R'_2 L_1 \sqrt{\left(1+\frac{R_2}{R'_2}\right)^2 + \left(\frac{L_2\omega_1}{R'_2}\right)^2 \left(1 - \frac{L_1 C_1}{L_2 C'_2}\right)^2}} \text{ (approx)} \qquad (27)$$

Since M varies with L_2 and with L_1, we may substitute for M its equal $\tau\sqrt{L_1 L_2}$, where τ is the coefficient of coupling between the primary and secondary coils and depends only upon their sizes and their relative positions. Then

$$I'_2 = \frac{\tau(E_1 - E_s)\sqrt{\frac{L_2}{L_1}}}{R'_2 \sqrt{\left(1+\frac{R_2}{R'_2}\right)^2 + \left(\frac{L_2\omega_1}{R'_2}\right)^2 \left(1 - \frac{L_1 C_1}{L_2 C'_2}\right)^2}} \text{ (approx)} \qquad (28)$$

Changing τ or E_1-E_s results in a proportional change in the height of the secondary current pulse without changing in any way its shape or duration. The strength of stimulation is therefore preferably varied by changing one or both of these factors. E_1 can be conveniently varied without affecting any other factor by changing resistance R_0.

The shape, duration, and magnitude of the secondary current pulse is unaffected by varying the frequency of discharge of the timing circuit *provided* E_1 remains the same. It should be noted, as previously explained, that increasing the frequency of discharge by decreasing R'_0 gives less time for C_1 to charge and hence results in a decrease in E_1 unless R_0 is also reduced. As shown by Eq. (5), E_1 or e_1 remains the same if R_0 and $R'_0 + R_p$ are varied proportionately so that their ratio is constant.

The effect of changing L_1 is shown in Figs. 8 and 9. Roughly, increasing L_1 increases the duration of the pulse and decreases its peak value, leaving the shape approximately the same. On the other hand, increasing C_1 increases the duration of the pulse without materially affecting the peak value. A change in R_1 has little effect unless it is greatly increased.

Changing the values of the constants of the secondary circuit has no effect upon the primary current pulse as illustrated in Fig. 8, but does affect the magnitude of the secondary current pulse and the shape of the transient current at the beginning and end of the current pulse. Decreasing the size of the secondary coil using the same wire size reduces τ, L_2, and R_2. A reduction in τ alone affects the peak value of the current pulse. A change in the value of R_2 either by changing the size of coil or the size of wire has but little effect upon the peak value as shown by Eq. (28) and also but little effect upon α_2 and ω_2 as shown by the expressions following Eq. (18), all provided R_2 is small compared with R'_2. A change in L_2 does, however, affect the peak value of the pulse as shown by Eq. (28). If we assume a fixed coil size we can determine what value of L_2, as determined by the number of turns, gives the maximum peak of the current pulse, by differentiating Eq. (28) with respect to L_2. The approximate value of L_2 thus found which gives maximum I'_2 is given by the following expression

$$\left(\frac{L_2\omega_1}{R'_2}\right)^2 = \left(1 + \frac{R_2}{R'_2}\right)^2 + \frac{L_1 C_1}{C_1'^2 R_2'^2} \tag{29}$$

Changing L_2 also affects to some extent the values of α_2 and ω_2 and hence the shape of the transient current.

The value of R'_2 has a very large effect upon the magnitude of the current pulse as shown by Eq. (28), an increase in R'_2 resulting in a decrease in I'_2. The value of R'_2 has also a very great effect upon the shape of the transient current. If R'_2 is increased α_2 and ω_2 become less, and ω_2 may become imaginary resulting in oscillations which may persist for some time after the primary current ceases. If R'_2 is decreased α_2 and ω_2 become greater and the current through R'_2 is decreased because R'_2 occurs in the denominator of Eq. (20). Along with this decrease in the current, the transient term changes less rapidly with time.

Method of Measuring the Maxima of Current Through the Tissue. The measurement of the maximum values of the current peaks requires that the value of R'_2 be known, and to a lesser degree of accuracy C'_2. A method of measuring these quantities is given in the next section; for the purpose of this section they will be considered as known.

The method of measuring the current maxima briefly consists in measuring the maxima of potential in the two directions across a resistance R'_2 connected in an external secondary circuit having the same electrical constants as those of the implanted circuit and placed in the same position with reference to the primary coil.

The external secondary coil consists of a coil exactly similar to the one implanted. This coil is conveniently bound on a thin piece of wood possessing a handle by means of which the coil can be held in any position desired. The terminals of the coil are connected to bolts through the wood, to which are also connected the two wires of a twisted lamp cord of sufficient length to lead to the voltmeter for measuring the potential. The capacitance of this lamp cord should be measured and enough added capacitance should be connected across the terminals of the coil so that the total capacitance including that of the voltmeter is 100 micro-micro-farads, the value of the distributed capacitance of the implanted coil and leads. The far end of the lamp cord is connected to a voltmeter in parallel with which is connected a variable resistance and variable capacitance in series to simulate R'_2 and C'_2. These are adjusted to the experimentally determined values of R'_2 and C'_2 determined for the implanted coil.

The voltmeter is a vacuum-tube peak voltmeter, shown diagramatically in Fig. 10. The circuit to the left of the circles marked 'terminals' is the external secondary circuit just described. The voltmeter consists of a small thyratron or grid-glow tube (Raytheon VG27 is satisfactory) which passes plate current whenever the grid voltage exceeds a certain critical value. The plate current is indicated by a 25-milliampere instrument connected in the plate circuit or sometimes more sensitively by the glow of the tube. A plate

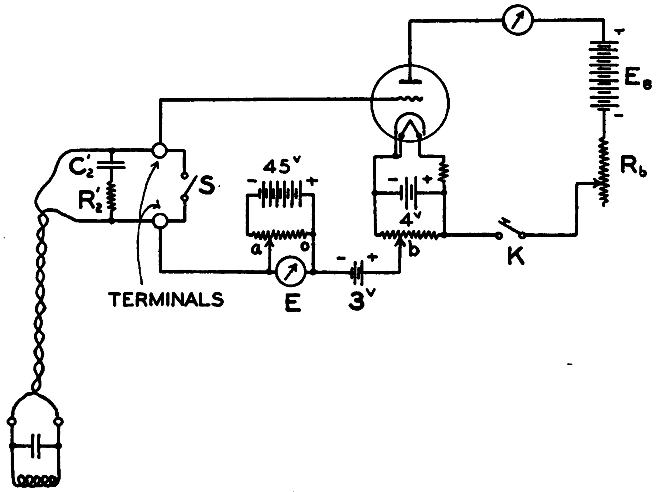

FIG. 10. Voltmeter.

voltage of from 45 to 90 volts should be used, and a series adjustable resistance R_b of about 5000 ohms is included in the circuit to limit the plate current. A key K is also included to interrupt the plate circuit.

The grid circuit includes a portion of a potential divider of about 200 ohms connected across the 4-volt heating battery, a 3-volt polarizing battery, and a portion of a 5000-ohm potential divider connected across a 45-volt battery. A d. c. voltmeter having a 5 and a 50-volt scale gives the voltage introduced in the circuit by this potential divider. A switch S is provided for short circuiting the pick-up coil.

The method of use is as follows. First R_b is set at its maximum value and slider *a* is set to zero. S and K are closed and slider *b* is adjusted at the point where plate current is on the point of starting. After the plate current is started it can be stopped only by opening K. After this zero adjustment is completed, switch S is opened and slider *a* moved until the flow of plate current just ceases. The sensitivity may be increased by decreasing R_b. E gives the peak value of the pulse in the direction which tends to make the grid positive.

Turning the external secondary coil over and repeating the above process gives the maximum of the impulse in the opposite direction. Knowing the direction of winding in the two secondary coils gives sufficient information to tell whether the stimulating electrode is positive or negative during the first loop of current. The polarity of the stimulating electrode can, of course, be changed by turning over the primary coil.

The maximum value of the current density at the stimulating electrode is the peak potential divided by R'_2 and by the cross sectional area of the wire electrode. For example, if the peak potential is 10 volts and R'_2 is 10,000 ohms, the peak current density is 3.12 amperes per sq. cm.

Method of Measuring R'_2 *and* C'_2. A knowledge of the values of R'_2 and C'_2 is essential in order to be able to measure and to specify the magnitude of the stimulating impulse. These quantities vary greatly according to how and where the stimulating electrode is inserted into the tissue, and they also vary with time.

The method of measuring R'_2 and C'_2 consists, briefly, in measuring by an alternating-current bridge the impedance of a small primary coil alone and then placed so as to have as close a coupling as possible with the implanted coil. From these measurements, and certain others to determine C'_2, the value of R'_2 can be calculated. The accuracy of determination of R'_2 is generally not better than 5 per cent, and to obtain this accuracy the bridge measurements must be accurate to better than 0.1 per cent. Such accuracy in the bridge measurements requires the use of a high-grade impedance bridge.* The bridge used is shown diagrammatically in Fig. 11a.

The primary coil is a coil similar to the implanted coil. This primary coil is mounted with permanent terminal wires on a thin board so that it can conveniently be held concentric and close to the

* The bridge used is a General Radio Universal Bridge and a variable frequency audio oscillator made by the same company.

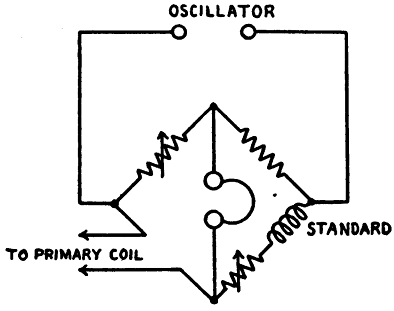

FIG. 11a. Bridge Circuit.

implanted coil. Let L_1 and R_1 represent the inductance and resistance of this coil as measured when M, the mutual inductance to the secondary coil, is zero (see Fig. 11b).

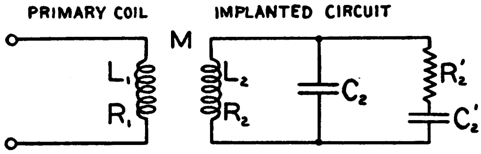

FIG. 11b.

When the primary coil is coupled to the secondary coil, the apparent resistance R_{12} and reactance X_{12} of the primary coil are

$$R_{12} = R_1 + \frac{M^2\omega^2\bar{R}_2}{\bar{R}_2^2+\bar{X}_2^2}, \tag{30}$$

$$X_{12} = L_1\omega - \frac{M^2\omega^2\bar{X}_2}{\bar{R}_2^2+\bar{X}_2^2}, \tag{31}$$

where
$$\bar{R}_2 = R_2 + R_2' \frac{C_0^2}{C_2^2(R_2'^2C_0^2\omega^2+1)}, \tag{32}$$

$$\bar{X}_2 = L_2\omega - \frac{C_0}{C_2}\cdot\frac{R_2'^2C_0\omega+\frac{1}{C_2'\omega}}{R_2'^2C_0^2\omega^2+1}, \tag{33}$$

$$C_0 = \frac{C_2C_2'}{C_2+C_2'}, \tag{34}$$

and ω is 2π times the frequency at which the measurements are made. If the frequency is 5000 cycles per second, $R'^2_2 C_0^2 \omega^2$ is about 0.001 and hence for frequencies below about 5000 this term can be neglected in comparison with unity. Furthermore, C_0 is equal to C_2 within an accuracy of about 0.2 per cent. We can, therefore, write the ratio of the increase in reactance to the increase in resistance in the form

$$\frac{\Delta X}{\Delta R} = \frac{X_{12}-X_1}{R_{12}-R_1} = \frac{\frac{1}{C'_2\omega} + R'^2_2 C_2\omega - L_2\omega}{R_2+R'_2} \qquad (35)$$

First we find an angular velocity $\omega_0 = 2\pi n_0$ for which there is no change in reactance when the primary coil is coupled to the implanted secondary coil. For this frequency $\Delta X = 0$ or

$$\frac{1}{C'_2\omega_0} = \omega_0(L_2 - R'_2C_2) \qquad (36)$$

The factor R'_2C_2 is small in comparison with L_2 and may be taken as 0.01 henry as calculated from the approximate constants of the secondary circuit, i.e., for $R'_2 = 10,000$ ohms and $C_2 = 100$ $\mu\mu$f. From Eq. (36) C'_2 can be calculated.

Substituting this value of C'_2 in Eq. (35) gives

$$\frac{\Delta X}{\Delta R} = \frac{(L_2 - R'_2C_2)(\frac{\omega_0^2}{\omega^2} - 1)\omega}{R_2+R'_2} \qquad (37)$$

The next measurement consists in determining a value of $\frac{\Delta X}{\Delta R}$ for an angular velocity ω which gives values of ΔX and ΔR sufficiently large to be measured accurately. A frequency of 3000 cycles per second has been found satisfactory for this frequency. Then since $\Delta X = \Delta L\omega$ we have

$$R'_2 = \frac{\Delta R}{\Delta L}(L_2 - R'_2C_2)(\frac{n_0^2}{n^2} - 1) - R_2 \qquad (38)$$

where n_0 is the frequency at which no change in reactance was observed, and n is the frequency used in the determination of ΔL and ΔR.

As pointed out before, the accuracy of the determination of R'_2 is usually of the order of from 5 to 10 per cent. Examination of Eq. (38) shows that the percentage error in R'_2 due to error in ΔR is equal to the percentage error in ΔR; the percentage error in R'_2 due to error in ΔL is equal to the percentage error in ΔL; and the percentage error in R'_2 due to error in n_0 is $\dfrac{2}{1-\left(\dfrac{n}{n_0}\right)^2}$ times the percentage error in n_0. The percentage error in ΔL is the greatest, being of the order of 50 times the percentage error in the determination of L, although this factor depends upon the closeness of coupling and to a less degree upon the value of R'_2. Usually ΔR can be determined to an accuracy of about a per cent. The percentage error caused by an error in n_0 is of the order of 4 or 5 times the percentage error in n_0. Consequently extreme care should be taken in the measurement of ΔL, the next important factor being n_0.

Error in the determination of R'_2 is also caused by the fact that R'_2 and C'_2 vary with time, frequency, and voltage. Tests on a coil immersed in 1/10 normal KCl solution indicate that R'_2 and C'_2 are reasonably constant for a frequency range of from 2000 to 5000 cycles, which is the range used in the measurements. It was found, however, that the value of C'_2 and hence n_0 changes if the potential used across the primary coil exceeds about 3 volts. It is desirable, therefore, in making the measurements of R'_2 and C'_2, to allow the voltage across the bridge not to exceed about 5 volts.

Determination of Frequency of Discharge. The frequency of discharge can be obtained by a stroboscopic method, allowing the light flashes from the discharge tube S to illuminate a revolving sectored disk.

A more convenient method of measuring the frequency of discharge is by means of the vacuum-tube counting circuit* shown diagrammatically in Fig. 12. T_1 is a gas-content glow tube, type UX 874, which has practically a constant voltage drop of 90 volts for currents from 10 to 50 milliamperes. R_1 and R_2 are resistances of 3000 and 1000 ohms, respectively. Tube T_2 is a mercury-vapor rectifier, Type 83, the filament of which is heated from a transformer operated on 110-volts alternating current. Tube T_3 is a

*This circuit was suggested by the Vacuum Tube Engineering Department of the General Electric Company, Schenectady, N. Y.

thyratron, Type 57, heated from the same transformer as heats the filament of T_2. L is an inductance consisting of about 100 turns of No. 16 B & S wire wound on a diameter of about 2.5 inches, and C is a 1μf condenser. A is a heavily damped d.c. milliammeter.

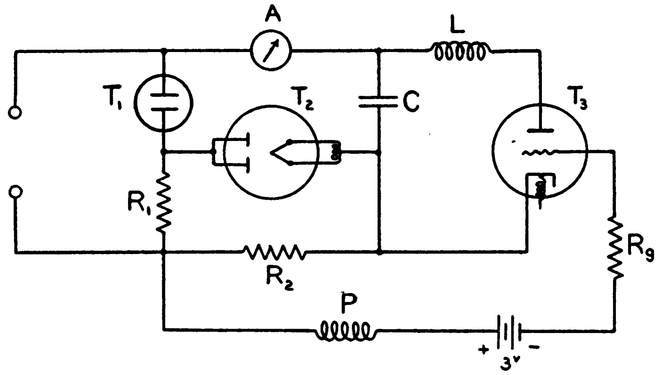

FIG. 12. Frequency Indicator.

The pick-up coil P, connected to the grid of T_3 through a 10,000-ohm protective resistance R_g, is any small coil of one or two thousand turns which is coupled to the large primary coil of Fig. 3. An impulse induced in P initiates a discharge of C through L, leaving C charged in the reverse direction for a sufficient time to allow T_3 to de-ionize. Charging then takes place through the milliammeter A and resistance R_2. The drop through R_2 maintains the grid of T_3 strongly negative during charge. Condenser C tends to charge to a potential of 125 volts, but as soon as its potential rises slightly above 90 volts, conduction takes place through T_2 and the potential of C is prevented from rising above 90 volts. Condenser C is therefore charged each time to the same voltage, and hence the average current through A is directly proportional to the number of discharges of C per second. The instrument A can be calibrated by a stroboscope, or by some other method, to read directly the frequency of discharge.

The Triple Discharge Circuit. The single-circuit system described above possesses the fault that the intensity of stimulation varies with the cosine of the angle between the planes of the primary and secondary coils, and becomes zero when the plane of the secondary coil is at right angles with that of the primary coil. A subject, moving about a cage within a primary coil, can receive impulses

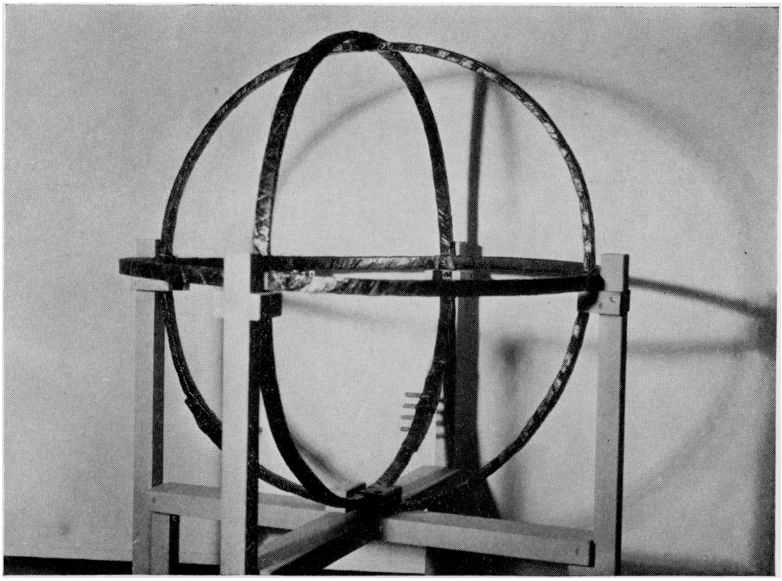

FIG. 13. Three Primary Coils.

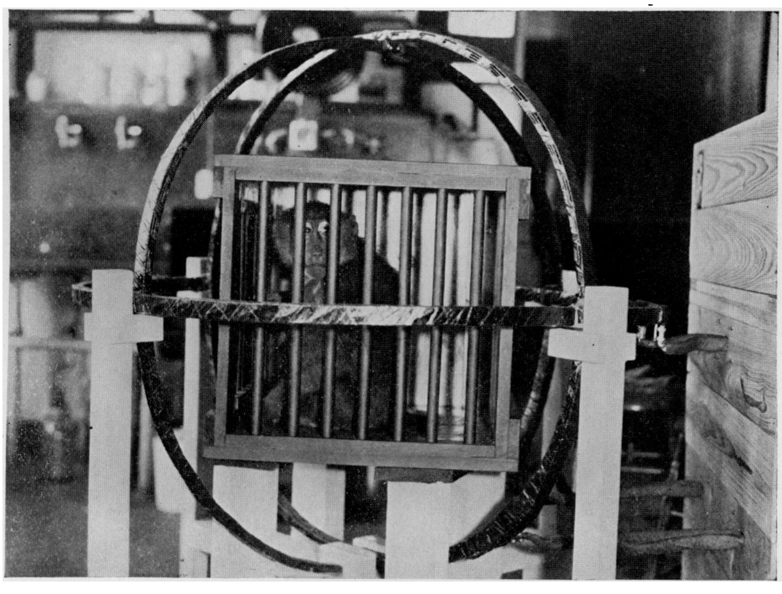

FIG. 14. Cage Inside Primary Coils.

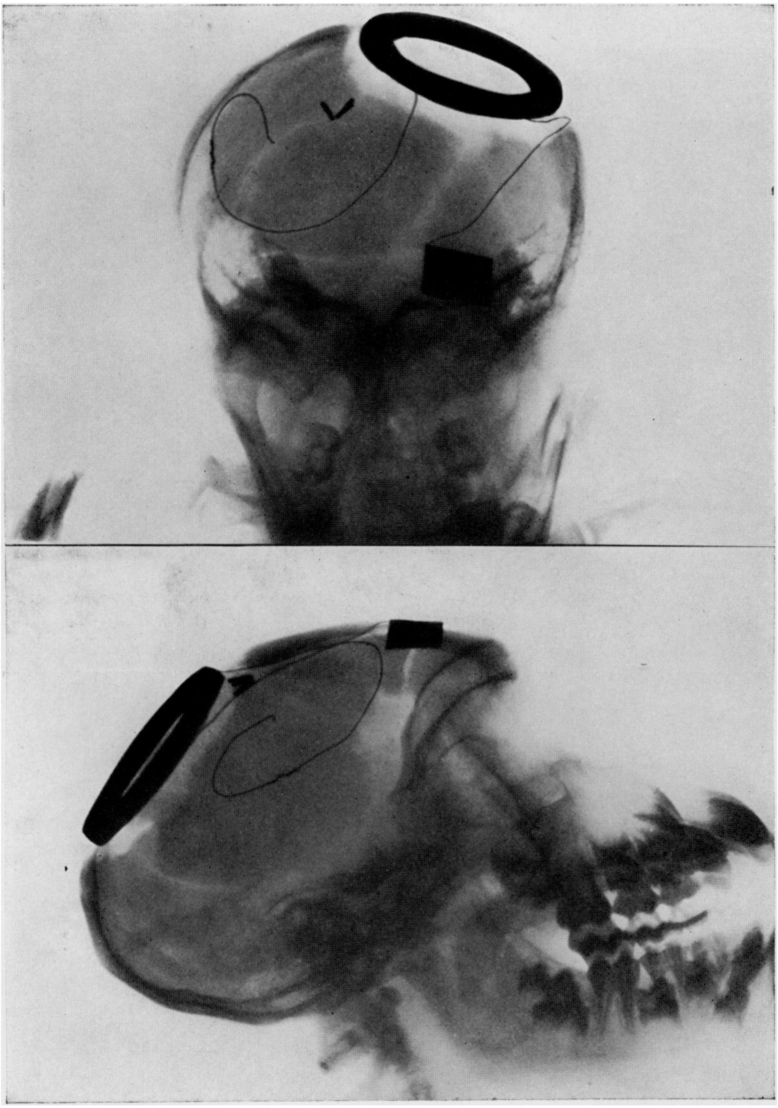

FIG. 16. X-ray film of a coil implanted in a young baboon. The coil occupies a space in the left occipital region from which a circular area of bone has been removed. The silver plate lies beneath the scalp, and the platinum wire terminal, insulated except at its tip, is resting in the hand area of the right motor cortex.

varying widely in intensity according to the angular position of the secondary coil.

To overcome this difficulty three primary coils may be used, arranged in three mutually perpendicular planes. These three coils are excited by three discharge circuits so interlocked that they discharge in rotation. Fig. 13 shows the three primary coils and Fig. 14 the coils with a cage and subject within the coils. With the three coils, the minimum stimulating current is never less than 0.7 of the maximum value.

Various arrangements have been devised to cause discharges to pass through the three primary coils in rotation. Fig. 15 shows

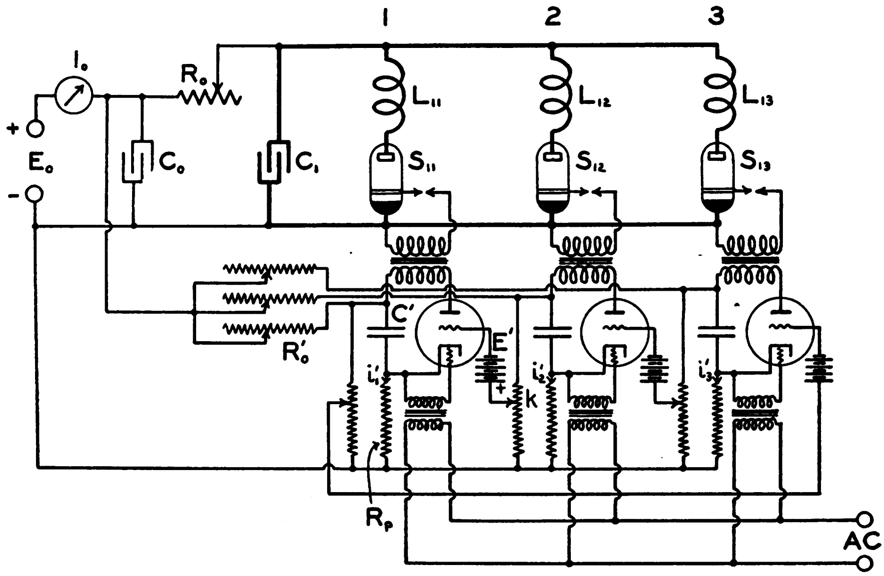

Fig. 15. Triple Circuit Diagram.

one arrangement having one primary condenser and three primary coils, L_{11}, L_{12}, and L_{13} in series with three discharge tubes S_{11}, S_{12}, and S_{13}. These tubes are controlled by a triple timing circuit. Each circuit is similar in most respects to the single timing circuit of Fig. 3, except that the three circuits are tied together through their grid circuits so that they discharge in rotation in the order 1, 2, and 3.

The way in which this coupling works can be understood by examining the expressions for the three grid voltages.

$$\left.\begin{aligned} e_{g1} &= kE_0 - E' - ki'_2R'_0 - i'_1R_p \\ e_{g2} &= kE_0 - E' - ki'_3R'_0 - i'_2R_p \\ e_{g3} &= kE_0 - E' - ki'_1R'_0 - i'_3R_p \end{aligned}\right\} \qquad (39)$$

If we assume that circuit No. 1 has just discharged, then i'_2 is small because C'_2 has been charging for two whole time intervals between discharges of C_1. Current i'_1 is, however, large because C_1 has just discharged and is charging at a high but decreasing rate. This large i_1 makes both e_{g1} and e_{g3} negative as shown by Eqs. (39). Hence the first and third tubes cannot discharge. Current i_3 is intermediate in value between that of i'_1 and i'_2 and as soon as i'_3 and i'_2 drop to a value such that e_{g2} attains the break-down value, tube No. 2 discharges.

The adjustment of k is made much as for the single circuit. E′ should be rather large, that is, of the order of 135 volts. R_p may be 3000 ohms or more, and the potential divider has about 200,000 ohms resistance. The frequency of discharge can be controlled by the three resistances, each of which has the value of R'_0. The sliders on these resistances as well as the sliders on the potential dividers are ganged so that all three move together. If R'_0 is reduced too far some controlling action is lost as shown by Eqs. (39), hence to obtain the highest frequencies it may be necessary to reduce C′.

It is necessary to shield each of the three control circuits because otherwise the spark which occurs at the gap may produce induced potentials in the grid circuits of sufficient magnitude to cause all three timing tubes to discharge simultaneously.

III. Experiences with the Apparatus in Use

The examples which follow indicate something of the practical use of the method, although many of the tests were made early in its development. Experiments with motor and sensory nerves gave evidence that the mechanism was operating as planned, and also afforded an excellent check on the surgical technic. A cerebral implantation was then carried out with the coil inserted in place of a circular area of cranium, as shown in Fig. 16, and the active terminal was laid on the motor cortex. Again the result was definite, with the appearance of an unexpected relationship between the frequency of impulses and the character of the response, to be described in the third protocol. One example is given of implantation in a "silent" center, and another shows the effects of vagal excitation, but thus far attention has been directed chiefly toward the development of a system which would prove easy to control in the situations in which the result was predictable.

Experiences with these animals have made it plain that the experimenter must be able not only to control the various factors of his circuit, but must have accurate indicators for these during the progress of the experiment. It follows from Professor Chaffee's description that the *duration of the stimulus* depends upon the resonance frequency of the primary circuit, a factor which can be found either by calculation or by bridge measurements. *The frequency of repetition of the stimulus* can now be measured directly on an ammeter and the cumbersome stroboscopic unit has been discarded except for calibration of the ammeter dial. The *voltage of stimulation* from the buried coil is measured by feeding the current pickup from a duplicate coil into a vacuum-tube voltmeter, but the determination is complicated somewhat by the *changes of resistance between the buried electrodes*, which must first be determined on an impedance bridge. From a knowledge of these elements the *current density* can be computed.

In spite of the fact that the central autonomic system was our first goal, the apparatus cannot be considered to have any one special field of usefulness. The dramatic duplication of the picture of epilepsy during remotely controlled stimulation of the cerebral cortex has thrown emphasis to the possibilities of restudying other neurological functions. Most localization studies have been carried out under the handicaps of the older methods, and it is probable that not only in the case of the motor cortex, but in the spinal cord and peripheral nerves as well, new characteristics may be brought out by properly regulated stimulation given during the course of the ordinary day's living.

Protocols

1. *Excitation of a pure motor nerve (hypoglossal) in a dog by induction of current into a secondary coil implanted in the neck.* On November 3,

1933, a medium-sized dog was operated on under nembutal anæsthesia and the right hypoglossal nerve was exposed and stimulated for identification with the ordinary close-coupled inductor. A small secondary coil was inserted into a recess in the subcutaneous tissue and the platinum electrode was brought to rest just within the nerve sheath. The indifferent electrode, which consisted of a silver plate ½ inch square, was laid beneath the subcutaneous tissue. The coil and its wires were fastened in place by silk sutures and the wound was closed.

Before outlining the results obtained with this implanted coil, it is worth while to describe the apparatus in use at the time. The primary coil consisted of two turns and its diameter was one foot. The discharge mechanism was operated by a small electric motor driving through two cams. When one of these raised a tappet the line current (220 v.) was connected with the condensers (80 mf.). After the condensers were charged the charging current was disconnected by opening this contact, and the second cam came into position and joined the capacitors with the primary coil through which the discharge then occurred. With this arrangement (and three pairs of interchangeable gears interposed between the electric motor and the cam assembly) it was possible to vary the frequency of discharge from individual impulses spaced three or four seconds apart, up to a frequency of about 20 discharges per second. At these higher speeds the mechanism was noisy and much heat was generated at the contacts, although these were constructed of ½ inch silver discs. Continued operation of 10 or 15 minutes at this speed resulted in the disintegration of the contacts and it was required that they be renewed during the experiment. A commutating mechanism of this type was therefore wholly inadequate for voltages which were used subsequently (450 v.) and for operating speeds of 50-100 per second, and the mechanism was discarded in favor of a vacuum-tube design.

However difficult was the manipulation and maintenance of this apparatus, it still served to demonstrate that the principle could be successfully applied. Stimulation experiments were carried out in this animal both at the conclusion of the operation (with anæsthesia still present) and on the following day. The results differed little, except for the opportunity for observing the animal's own reaction to the unexpected muscular movements of the tongue. The primary coil was brought to a position parallel with the implanted coil and separated from it by about 12 inches. It was found that the right half of the tongue responded to individual discharges as slowly as they might be given. As the frequency of discharge* was increased the muscle still gave individual contractions for each impulse given, until the rate

* "Frequency of discharge" refers to the number of times per second that the condensers are charged and discharged;—not to the self-tuned frequency of the circuit, which is of the order of 3000 cycles.

reached 15 per second. Above this rate the response appeared to be tetanic in nature. During the tests made on the day after operation, the animal stood quietly and was not disturbed by the experience. He made no attempt to draw away from the primary coil and was not alarmed by the unusual motion of the tongue.

2. *Stimulation of the vagus nerve (thoracic portion) of a dog with simultaneous collection of the gastric juice.* On November 9, 1933, an operation was performed under sodium amytal anæsthesia on a dog of medium size to expose the lower portion of the esophagus through a transthoracic approach. The intercostal muscles were divided between the 6th and 7th ribs in the right axillary line and the ribs were separated. The pleura was opened and lobes of the right lung held back with gauze packs. The vagus nerves were identified on the lower esophagus, where they consist of anterior and posterior trunks. A small secondary coil was implanted outside the chest wall just posterior to the incision and the indifferent electrode was placed in the subcutaneous tissue. The active terminal was brought between the ribs and made to lie along the posterior border of the thorax where its tip was sutured so as to be in contact with the posterior branch of the vagus nerve after a small incision was made in the nerve sheath. The electrode lay about 1½ inches above the diaphragm. Careful closure was carried out.

On the following day the dog was awake and moving around actively. The wound was dry, and the buried coil there was not evident except on palpation through the skin. A stomach tube was passed and a fasting specimen of gastric juice was obtained. This was of small amount (2.5 cc.) and showed no free acid but contained a total acidity of 70°. Stimulation was then begun (10:15 A.M.) at a rate of 15 impulses per second for an uninterrupted period of 5 minutes. No abdominal or diaphragmatic muscle spasm was seen and the dog apparently was not aware of the act of stimulation. Two minutes after the stimulation was started gastric juice began to flow from the tube and for fifteen minutes the flow continued intermittently, without the necessity for application of negative pressure to the tube. Stimulation was halted at 10:20 and at 10:30 forty cubic centimeters of light-brown, watery gastric juice had been collected, which was found to be devoid of free acid, but with total acidity of 120°. At 10:50 a third specimen was withdrawn (26 cc.) without free acid, and with 115° total acid. A second period of stimulation was carried out from 10:50 to 10:55 at a rate of 18 impulses per second. On this occasion it was noted that violent peristalsis began two minutes after stimulation was started and continued for 20 minutes. This was so active that not only could it be heard through the stethoscope, but it was visible over the entire surface of the abdomen. No bowel movements occurred, nor was there diarrhea following the experiment. At 11:05, 21 cc. of gastric juice had been collected and showed total acidity of 115°.

The last specimen was taken at 11: 20 and amounted to 13 cc. with free acid of 10° and total acid 105°.

It was recognized at the time of operation that the respiratory movements of the esophagus and diaphragm were of such magnitude that the tiny wire which was sutured to the vagus nerve on the esophagus would not remain in place long without being broken, and an attempt at stimulation on the fifth postoperative day bore out this prediction. The use of fine wire-stranded cable has been suggested by F. A. Fender, to permit mobility without breakage, but it is probably true that an experiment of long duration can be carried out best with this system when the coil and its terminals are implanted in rigid locations such as the skull, the posterior portion of the thorax, and the pelvis. In the case of the vagus, the nerve should be partially transplanted to a retropleural position. This form of study of the action of the vagus and the splanchnic nerves should yield important information concerning the nature of digestion, for it thus provides the means whereby stimulation can be applied in the conscious vegetating animal during the actual time that the various digestive phases are under way. It should also prove of value in identifying the effects of long-continued excessive vagus and splanchnic activity in relation to the problem of peptic ulcer, and perhaps to other disease processes within the abdomen.

3. *Stimulation of the motor cortex of a Macacus rhesus.* On April 27, 1934, operation was performed on an immature monkey under sodium amytal anæsthesia. A left fronto-parietal flap was lifted back, and a coil was implanted in a second opening made by removing a circular area of bone in the right occipital region. The broad plate terminal was laid outside the dura, and the left motor cortex was explored with the active electrode. The operative procedure had been simplified by constructing a special wooden operating table on the under surface of which was fastened the primary coil of the discharge mechanism. The magnetic field extended well above the level of the animal's head, so that with the mechanism in operation currents were generated in the small coil without the necessity of bringing wires into the sterile field. The platinum terminal was laid in the hand region of area 4.

Two weeks later recovery was complete, and the first tests were made. The machine was set to give impulses at 14 per second. So soon as the circuit was thrown into operation, the animal's right arm went into adduction and extension, and the reaction was so pronounced that the current was stopped after only two seconds of stimulation had been received. The right arm continued spastic, and developed a tremor which spread in Jacksonian style to involve the entire right side of the body. The seizure lasted nearly a minute, but recovery was fairly prompt.

After a short rest, stimulation was repeated at the same rate, for a period of 30 seconds. The response in the right hand began immediately, and within 3 or 4 seconds the entire right side was in clonic motion. Very quickly he collapsed to the floor of the cage, and a rhythmical motion (3 or 4 twitches per second) appeared in both arms and both legs. To all appearances he was unconscious, and was breathing noisily, while the face bore a deep cyanotic appearance. In his convulsive motions he struck the back of the head against the cage, and drew a little blood. The seizure subsided gradually over a period of two minutes; he lay quietly for a moment, and then awakened and rose. He was very unsteady on his feet for 15 or 20 seconds and fell down several times, looking as if bewildered. A minute later he was completely normal again.

Although it is impossible here to give a full description of the experiences with stimulation of the motor cortex in conscious animals, it is worth noting that the *rate of stimulation* affects the type of response. So long as the rate is kept below 12 or 13 impulses per second, the response from area 4 consists of discrete muscular contractions which appear coincident with the firing of the tube. When the rate of discharge rises above this level, the response affects more distant areas, and may be either a unilateral or a completely bilateral seizure. Furthermore, the rhythm of shaking becomes about 3 movements per second, instead of small fibrillary twitches in time with the succession of electrical stimuli. This sharp change in response, which occurs while the voltage, current density, and duration of stimulus are kept constant, but when the rate of stimulation is increased, suggests strongly the importance of investigating the counteractive effects of drugs commonly used to reduce or prevent epileptic attacks, while maintaining careful control of the electrical constants of the circuit.

4. *Investigation of the left premotor area of cortex in a Macacus rhesus* (3.5 kg.). The coil was implanted in this animal on May 7, 1934, under light ether anæsthesia. A left boneflap was made, as well as a circular craniotomy on the right for the coil, and the premotor area was identified with a platinum electrode before finally suturing it in place. When the stimulus was applied to area 4 (Brodmann's classification), the response was immediate, in the form of jerky motions of the opposite side synchronous with the current surges from the condensers. As the electrode was moved forward into area 6 the response in the opposite arm became more delayed, like a slowly twisting

cramp, with a distinct tendency to continue after the current had ceased. The terminal was placed upon the premotor hand area, a centimeter rostral to the edge of area 4.

The animal recovered from the operation without incident, and on May 24th was first studied with the stimulation device, before a gathering of the Halsted Club. The reactions are described in the words of Dr. William Mahoney, who conducted the experiment: The animal was placed within the magnetic field and a rate of stimulation of 12 impulses per second was given. Almost immediately there began a series of chewing and tongue-wagging motions. Nothing else happened for a time, but after a minute or perhaps longer the right hand began to assume the position shown in such pictures as are usually presented in text-books for "cerebellar hand," that is, extension of the hand combined with flexion at the wrist. Shortly afterward there appeared clonic motions of the arm, and the animal whirled about on its ischial protuberances and fell to its right side. The clonic jerks then extended into the right leg. The stimulus was stopped after about two minutes, but the seizure persisted for a minute longer, and involved the left side of the body as well as the right side. Then for a time he lay on the left side with the left arm and leg extended, and the right arm and leg flexed. There was no deviation of the eyes, nor anisocoria, and adversive movements of the head were not noticed. Gradually he relaxed, and arose to a sitting posture, but he appeared dazed. The face was flushed, and for a few minutes the right hand hung limply as he moved about. He had voided at the beginning of stimulation.

5. *Experiments with a monkey in which an electrode was inserted in the hypothalamus.* On Nov. 17, 1933, an adult male *Macacus rhesus* weighing 6.5 kg. was operated on under sodium amytal anæsthesia, and a coil was placed in a circular opening in the calvarium. The indifferent electrode was laid beneath the scalp, and the active platinum electrode was brought forward over the surface of the frontal lobe, which was elevated to permit insertion of the wires into the tissue just anterior to the optic chiasm. The tip of the wire was pushed backwards about 1 cm. from this point into the hypothalamus.

Ten days later wound healing was complete, and the animal was stimulated for a period of ten minutes at 10 impulses per second. At first he was restless and moved about the cage, then he became quiet, and yawned several times. There was no urination, pupillary change, nor bowel movements. He remained quiet until the end of the period. Two minutes after stimulation ceased the animal became drowsy, and his head drooped. It was difficult to arouse him with a stick, although five minutes later he woke up for a short time and took interest in his surroundings. His head was soon down again, and for 5 minutes he appeared to be asleep. He was finally aroused by a noise, but not until 30 minutes after the stimulation did he become bright and active.

On a second period of stimulation the same results followed, but we noticed also that there was a general vasodilatation over the entire skin which faded out as the current was stopped, and started when it was recommenced.

In summary a method is presented for the study of excitable regions in the nervous system during the normal life of an animal. It employs two coils which are actually the primary and secondary elements of an induction coil. The secondary coil is entirely imbedded inside the animal and the primary coil is of large size and carries currents of high peak value. The animal is permitted to live comfortably within a cage through which passes the magnetic field from the primary coil. Stimulation occurs at one of the terminals of the secondary coil which can be placed in any portion of the central or peripheral nervous system. A description is given of the electrical circuits employed and several examples are cited to indicate the range of usefulness of the apparatus.

Bibliography

1 Adrian, E. D.: The Mechanism of Nervous Action. Philadelphia, Univ. of Penn. Press, 1932, p. 3.

2 Beevor, A. and Horsley, V.: A minute analysis (experimental) of the various movements produced by stimulating in the monkey different regions of the cortical center for the upper limb, as defined by Professor Ferrier. Phil. Trans. Roy. Soc., London, 1887, *178 B*, 153-67.

3 Cannon, B.: A method of stimulating autonomic nerves in the unanæsthetized cat with observations on the motor and sensory effects. Am. J. Physiol., 1933, *105*, 366-72.

4 Cole, K. S.: Electric excitation in nerve. Cold Spring Harbor Symposia on Quantitative Biology, 1933, *1*, 1-13.

5 Cushing, H.: Faradic stimulation of postcentral gyrus in conscious patients. Brain, 1909, *32*, 44-53.

6 DuBois-Reymond, E.: Untersuchungen über thierische Elektricität. Berlin, 1848.

7 Erlanger, J. and Garrey, W. E.: Faradic stimuli: A physical and physiological study. Am. J. Physiol., 1914, *35*, 377-473.

8 Ferrier, D.: The Functions of the Brain. G. P. Putnam's Sons, N. Y., 1880.

9 Feser, J.: Drahtlose Reizung der Froschnerven mittels elektrischer Wellen. Deut. tierärtz. Wchschr., 1930, *38*, 23-4.

10 Franklin, B., in a letter to Dr. Pringle, read before the Royal Society, Jan. 12, 1758. Quoted in part in (2), pp. 412-13. Reprinted in full in The American Museum: or Repository of Ancient and Modern Fugitive Pieces, etc., Prose and Poetical. 1789, *6*, 53-4.

11 Fritsch, G. and Hitzig, E.: Ueber die elektrische Erregbarkeit des Grosshirns. Archiv. f. Anat., Physiol. u. wissen. Med., Leipzig, 1870, p. 300.

12 Galvani, Luigi: Collezione delle Opera, Bologna, 1841, pp. 17-27. [See also:] Dalton, J. C.: The Experimental Method in Medical Science. Lecture I. Galvani and Galvanism in the Study of the Nervous System. N. Y., G. P. Putnam's Sons, 1882.

13 Galvani, Luigi: De viribus electricitatis in motu musculari, Commentarius. Bologna, 1791.

14 Hess, W. R.: Beiträge zur Physiologie des Hirnstammes. I. Teil. Die Methodik der lokalisierten Reizung und Ausschaltung subkortikaler Hinabschnitte. Leipzig, 1932.

15 Keeton, R. W. and Becht, F. C.: The stimulation of the hypophysis in dogs. Amer. J. Physiol., 1915, *39*, 109-22.

16 Keeton, R. W.: Personal communication to Dr. William Mahoney, April, 1934.

17 Lapicque, L., and Lapicque, Mme. L.: Sur la forme de la loi d'excitation électrique exprimée par la quantité. Réponse à M. Hoorweg. Compt. rend. Soc. de biol., 1905, *58*, 668-70.

18 Loucks, R. B.: Preliminary report of a technique for stimulation or destruction of tissues beneath the integument and the establishing of conditioned reactions with faradization of the cerebral cortex. J. Comp. Psychol., 1933, *16*, 439-44.

19 Lucas, K.: The conduction of the nervous impulse. London, 1917.

20 Magendie, F.: Expériences sur les fonctions des racines des nerfs rachidiens. J. de Physiol. Expér. et Path., 1822, t. ii, p. 276.

21 Marat, J. P.: Mémoire sur l'électricité médicale. Paris, Méquignon, 1784.

22 Mussen, A. T.: Cerebellum and Red Nucleus: A preliminary report on a new method of physiologic investigation. Arch. Neurol. & Psychiat., 1934, *31*, 110-26.

23 Oersted, H. C.: Experimenta circa effectum conflictus electrici in acum magneticam. Copenhagen, 1820.

24 Priestley, J.: The History and Present State of Electricity, with Original Experiments. London, 1767, p. 83.

25 Ibid., p. 146-7.

26 Ibid., p. 152.

27 Sherrington, C. S.: The integrative action of the nervous system. New Haven, Yale Univ. Press, 1906.

28 Smith, W. K.: Motor cortex of the bear (Ursus americanus). Arch. Neurol. & Psychiat., 1933, *30*, 14-39.

29 Turrell, W. J.: Three Electrotherapists of the Eighteenth Century. Ann. Med. Hist., 1921, *3*, 361-67.

30 Volta, A.: An account of some discoveries made by M. Galvani, with experiments and observations on them. London, Phil. Trans. Roy. Soc., 1793.

31 Wesley, J.: The Desideratum: or, Electricity made Plain and Useful. By a Lover of Mankind and of Common Sense. London, 1759.