EFFECT OF MAGNETIC FIELDS ON ANIMAL NERVOUS SYSTEMS

by

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STATEMENT BY AUTHOR

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ABSTRACT

Stimulation of a sciatic-gastrocnemius preparation of the Rana pipens is achieved by the application of a varying magnetic field. Necessary "neuron theory" is developed and explained in terms of an electric analog. Development and design of the magnetic field generator used is indicated. Various measurement techniques are specifically outlined and experimental apparatus is explicitly defined. Physiograph records indicate the results of stimulation under varying experimental conditions. Several hypotheses are advanced to explain the effects observed, and a general outline of further experimentation to either prove or disprove the hypotheses is provided.

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Chapter 1

INTRODUCTION

1.1 STATEMENT OF THE PROBLEM

It has long been known that a nerve can be stimulated by means of an electric shock. This shock can be applied either as a voltage stimulus by means of external electrodes, or as a current stimulus by means of an external-internal electrode arrangement. In both of the above cases there exist definite strength-duration relationships which determine whether or not the stimulus is sufficient to activate the nerve.

In order to achieve stimulation by means of magnetic induction, it is presumed that the induced voltage must conform to the above strength-duration relationship for a voltage stimulus. Since this voltage is proportional to the time derivative of the flux, the magnetic field generator must provide a changing field such that its derivative conforms to the requirements of the strength-duration relationship. Shape of the field producing current pulse is thus an important factor to generator design.

Three parameters describe the required output of the pulsed magnetic field generator. It is the purpose of this thesis to determine certain quantitative aspects of these parameters, apply them to the design and construction of a generator, and test the ability of this generator to stimulate nerve fibers.

1.2 NEED FOR MAGNETIC INDUCTION AS A MEANS OF NERVE STIMULATION

Present methods for electrical stimulation of nerves require the placement of probes in, or in contact with, active nerves. Although these methods achieve the stimulation required, the presence of probes usually results in nerve damage. At least three groups desire a means of "non-contact" nerve stimulation: Biological Scientists, Medical Doctors, and Bio-Medical Electronics Engineers. The biological scientist needs it as a new experimental technique, to further explore the complex physiology of the nerve. The medical doctor needs it as a new diagnostic tool and perhaps even a therapeutic means in the field of neurological disorders. To the bio-medical electronics engineer, it represents a step forward in the field of "non-contact" measurement of electrical activity in the nerve.

In all of these applications, a magnetically induced stimulus will suffice, although the requirements for physical apparatus may vary. Since the purpose of this thesis is to indicate the possibility of magnetically inducing a nerve stimulus, the apparatus is not designed for any particular application.

1.3 GENERAL APPROACH TO THE PROBLEM

The initial problem is to ascertain the strength and duration requirements for threshold stimulus of a nerve fiber. Due to "state-of-the-art" limitations in the field of neurology, certain parallelisms between types of nerve fibers will be assumed, and empirical experimental results, rather than generalized formulization, will be utilized. Once these basic parameters are established, output specifications for the

magnetic pulse generator can be determined.

The output specifications for the generator can then be utilized to determine an appropriate circuit which will provide the required output. Design and construction of the generator can then proceed, taking into consideration physical realizability of the circuit values, and availability of components.

An experimental technique can then be evolved, based upon a comparison between the known result evoked by a standard contact electrode type stimulus, and the unknown result of the magnetically induced stimulus. Selection of the experimental technique must also consider the types of specimens and measurement equipment available. Experimentation can then follow, with the prime object being to prove plausibility of magnetic stimulation. After this has been accomplished, the conditions under which such stimulation can take place, and the results of this stimulation can be measured and recorded.

Finally, conclusions can be made, based on experimental results, which indicate the validity of the original assumption, and summate information for further study.

1.4 REVIEW OF LITERATURE AVAILABLE ON THE SUBJECT

Although as early as 1896 the elicitation of "phosphenes"[1] by a varying electromagnetic field was recorded by d'Arsonval, a review of the literature does not indicate any attempts to utilize varying magnetic fields for the direct stimulation of nerves. However, some of the biological effects of magnetic fields which are recorded in the literature lend credence to the possibility of magnetically induced nerve stimulation;

the more important of these references are discussed here.

In 1947, Barlow, Kohn and Walsh,[1] updated the earlier "phosphene" work of d'Arsonval and others, in the American Journal of Physiology. Of note here is the recorded strength of the fields used in the "phosphene" experiments, which varied from 760 to 1000 Gauss, at 60 cycles per second. If this field strength is broken down as "rate of change" of field, the maximum value is 286,500 to 377,000 gauss/second. Barlow, Kohn, and Walsh interestingly state: "The phosphenes differ in only one respect, namely that shutting the eye raises the threshold for electric stimulation but not for magnetic. In view of these similarities we believe that both forms of stimulation probably activate the same neural elements."

In 1960, Barnothy, in reporting on the "Biological Effects of Magnetic Fields,"[2] referenced the work of Barlow, et al, "indicates that the effect is caused by electric currents induced through the varying magnetic fields." Barlow thence excluded the induced effects of varying magnetic fields from his article and continued with the effects of fixed magnetic fields. From the context of these two articles, it appears evident that a varying magnetic field is capable of exciting some of the visual sensory nerves.

At the "Blood Flowmeter Symposium" in 1959,[3] Spencer and Denison reported on "The Square-Wave Electromagnetic Flowmeter". Although this device utilizes the principle of magnetic "pickup" of current flow, it is of interest here because it demonstrates the effect of an electromagnetic field on body tissue. This effect is noted as the expected induced

voltage caused by a current flow; but of special interest here is the ability of the magnetic field to penetrate the "conductive" wall of the blood vessel.

Chapter 2

ELECTRICAL ACTIVITY IN NERVES

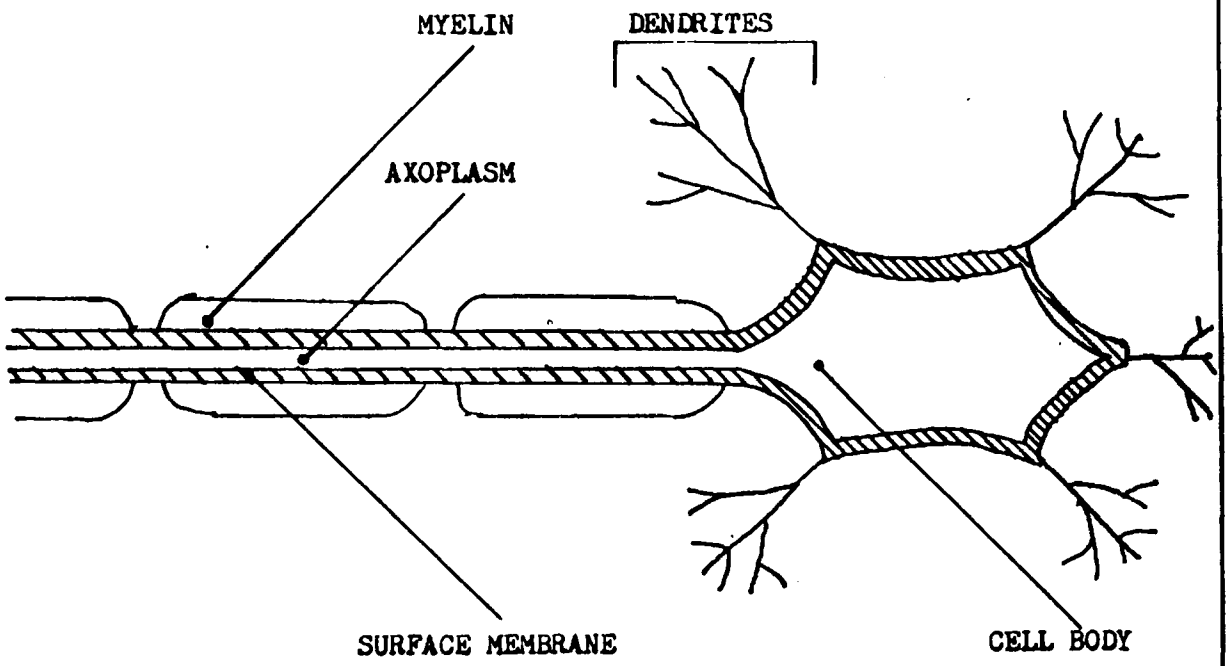
2.1 NEURON PHYSIOLOGY

In 1934, Cajal[4] established the validity of the "neuron-theory" of nervous system composition, which emphasized the importance of the neuron as the basic building block of the nervous system. Since that time, neurophysiologists, with the aid of electron microscopes and electro-physiology techniques, have been compiling information on the content and operation of the neuron. Most of the results of this work still remain in the form of theories or postulates. For purposes of this paper, the neuron will be subdivided into four parts in order to examine their physical dimensions and the part they play in the overall operation of the neuron. Figure 2.1 is a schematic representation of the various portions of the neuron, which are described in detail below.

The cell body is the largest part of the neuron, having a diameter as large as .1mm[5]. It provides the metabolic machinery for the generation of power which is required for neuron operation.

The dendrites are "long, tapering, branching structures"[2] which act as the receptors for the neuron.

The axon is the longest part of the neuron, in some cases reaching lengths of one to two feet[2], and varies in diameter from 1mm (squid) to a few micra. Axons may be further subdivided into "myelinated" and "unmyelinated". Myelinated axons are more complex, possessing a "myelin"



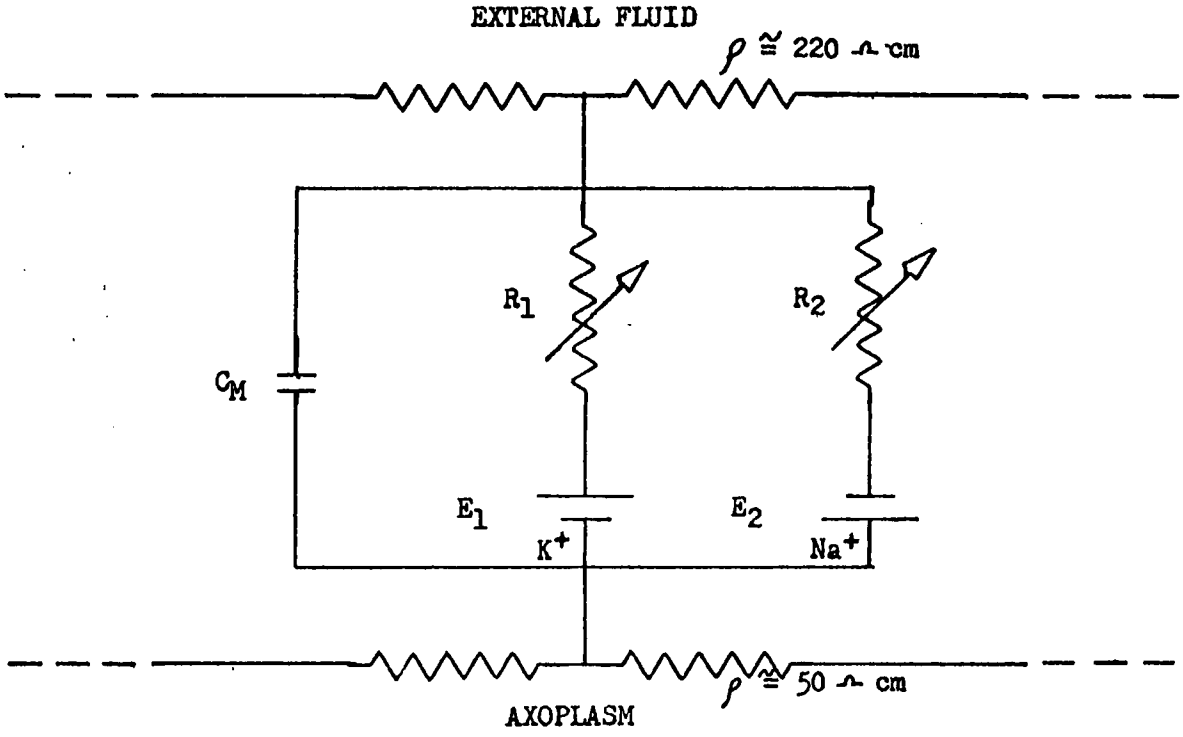
THE NEURON

Figure 2.1

coating and divided into "nodes" and "internodes". The nodes represent breaks in the myelin coating of about 1 micron, and are spaced 1-2 mm apart, by the internodes. The axon is the effector of the neuron, and acts as a transmission line from the cell body to an effector organ, such as a muscle. The action of the "neuromyal" junction is complex, and for the purposes of this paper will be regarded simply as the signal path between the axon and the muscle.

Classically, the most important portion of the neuron from a functional aspect is the surface membrane. This membrane completely covers the neuron, with the exception of the dendrites, as indicated in Fig. 2.1. It has a thickness of approximately 50 $\mathring{A}$, and although a conductor, has a resistivity which varies from 500 to 10,000 ohms/cm^2, depending on the type of neuron[4]. The specific capacitance varies from 1 to 3 uF/cm^2. The functioning of the surface membrane is dependent upon its ability to control the flow of K^+, Cl^-, and Na^+ ions between its outer and inner surfaces, thus affecting a change in internal impedance. A complete explanation of this "ionic hypothesis"[1] is beyond the scope of this paper. However, since it represents a basis for the understanding of nerve impulse propagation, the lumped parameter equivalent of Hodgkin and Juxley[4] will be considered.

This equivalent circuit represents a portion of a squid giant axon, with lumped parameters, as indicated in Fig. 2.2. The resistances, R_1 and R_2 vary as a result of ionic diffusion across the membrane. The batteries, E_1 and E_2 represent the approximate equilibrium potentials for K and Na ions, and the capacitor, C_M represents the membrane capacitance.



C_M _ 1 uF to 3 uF

R_1 - 2×10^3 Ω cm^2 to 25 Ω cm^2

R_2 - 10^5 Ω cm^2 to 10 Ω cm^2

E_1 - 70 mV

E_2 - 40 mV

THE SURFACE MEMBRANE

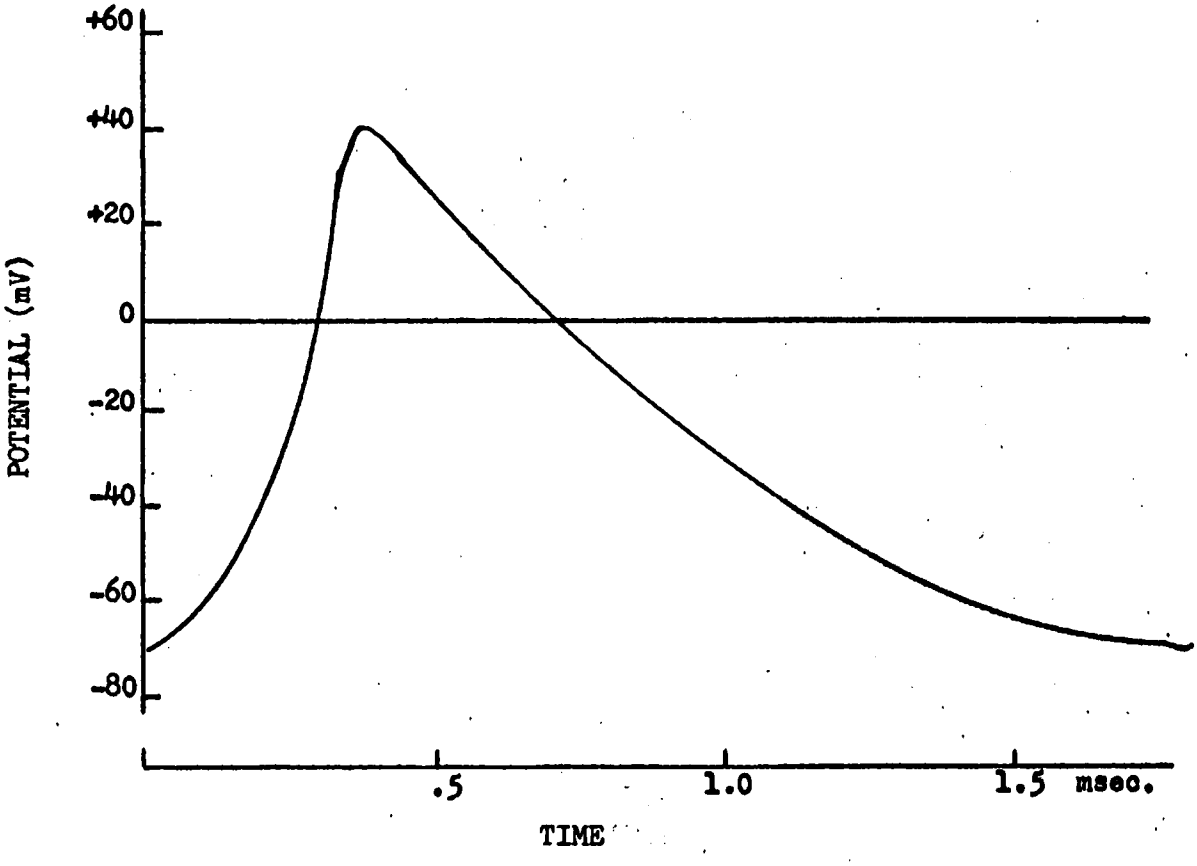
Figure 2.2

2.2 PROPAGATION OF THE NERVE IMPULSE

Although the functioning of the surface membrane in the propagation of the nerve impulse is described by the "ionic hypothesis," a qualitative explanation based on the electronic analogy of the Hodgkin-Huxley circuit is sufficient for present purposes.

The following explanation is the author's interpretation of the analogous circuit of Huxley, as modified by Freyang.[5] With the membrane at rest, R_2 is much greater than R_1, resulting in a potential difference of 70 mV (outside positive) across the membrane. In the analogous circuit, R_1 and R_2 represent voltage sensitive resistances which change from high to low values when the membrane potential changes by a sufficient amount. This amount is approximately 10 mV (inside positive). R_1 also changes to its low value but at a slower rate than R_2 so that, when R_2 has returned to its initial high value, R_1 is still at its low value. At this point, there is an outward flow of current which tends to charge C_M to its original value. As the membrane potential approaches its initial value, R_1 returns to its high value, and the cycle is complete. The voltage transient created by the above cycle is the nerve impulse, or "action potential."

Figure 2.3 represents the action potential, as produced above. Analytical expressions for the curve have been determined by Hodgkins and Huxley[7]. For explanatory purposes only, it may be considered to consist of two exponential functions. The rising function from -70 mV to +40 mV possesses a time constant of R_2C_M, while the decreasing function is determined by R_1C_M. It is noted here that the action potential of a nerve is the discharge of energy "stored" in the membrane as a



ACTION POTENTIAL

Figure 2.3

resting membrane potential, where the storage of this energy depends upon the cell performing metabolic work. Most of this work is performed at the cell body.

Propagation occurs when the outward flow of current at the peak of the action potential flows across the parallel impedances of adjacent generators in the membrane. This flow results in a reduction of the membrane potential in the adjacent generators, triggering them to produce their own action potentials. This process, when continued down the length of an axon, represents propagation of the nerve impulse.

It should be noted here that the generation of the nerve impulse follows the "all-or-none" law in that the membrane is either at rest or propagating an impulse. The thin line that divides the states of the membrane is the "threshold membrane potential," which is defined to be the highest potential level of the membrane which, after the end of the applied stimulating pulse, decays without producing an action potential.

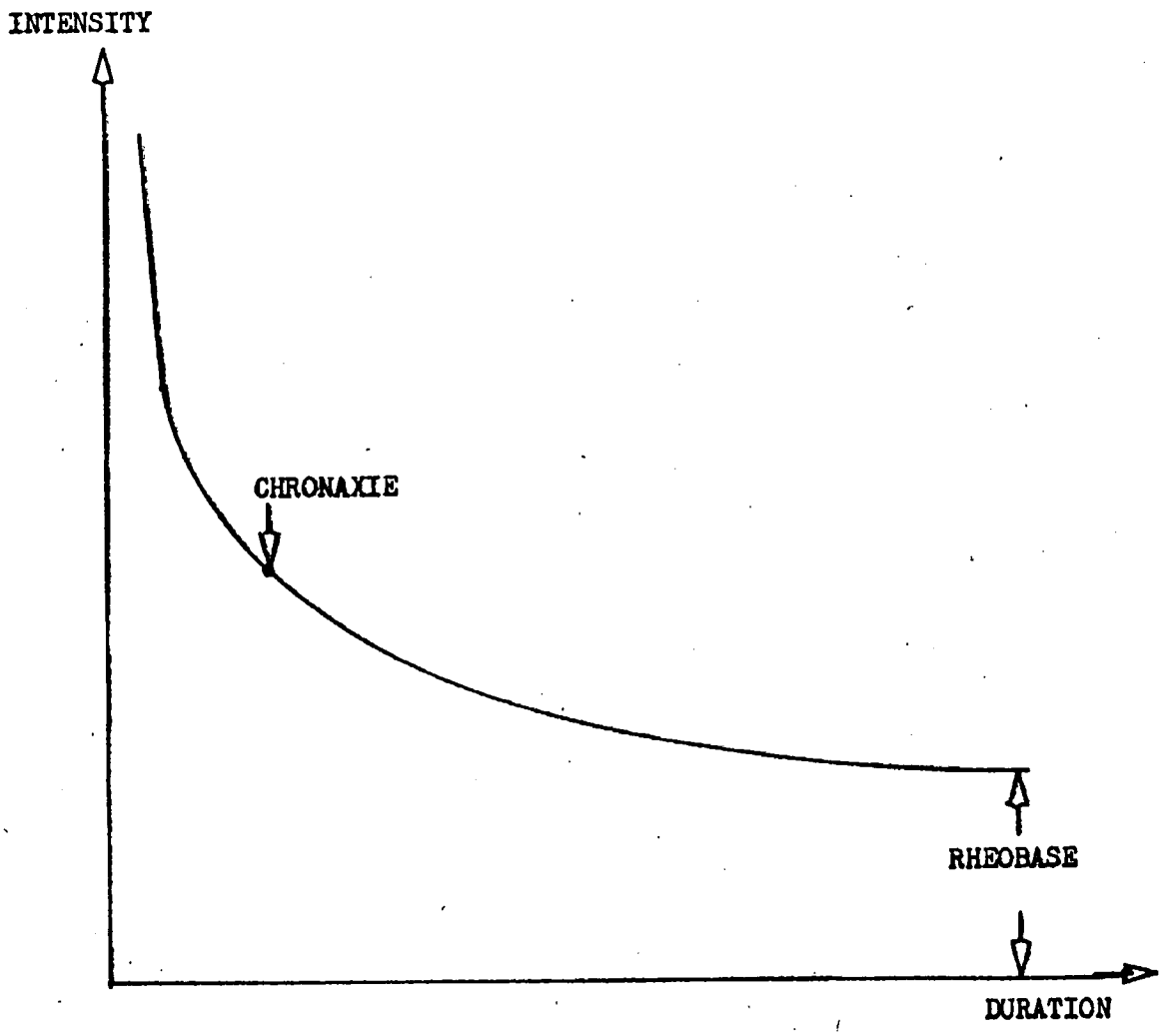
2.3 NERVE STIMULATION

From the definition above, it is evident that stimulation is achieved when the nerve produces an action potential. The means for direct nerve stimulation can be divided into two general classifications: electrical and non-electrical. The non-electrical means include mechanical, thermal, and chemical stimuli, while electrical stimulation can be achieved through either voltage or current pulses. Since the purpose of this paper is to provide a means for stimulation through an induced voltage or current, attention will be focused on electrical excitation of the nerve.

The remainder of the study of nerve stimulation is based on the application of rectangular electrical pulses. Although pulses of varying shape can achieve stimulation[8], the rectangular pulse is used here because of its simple geometry and elementary mathematical description. It also enables a more complete comparison with past experimental results, since most of these experiments used the rectangular pulse as a basis.

It has been found that both the intensity and the duration of the stimulus determine its ability to achieve excitation. This relationship is referred to as the "strength-duration relationship" and is shown graphically in Fig. 2.4. For understanding of this relationship, it is necessary to define two of the terms customarily applied. "Rheobase" is the minimal strength below which no propagating response can be elicited[9]. "Chronaxie" is the time at which stimulation occurs, if the strength is twice rheobase. For optimum stimulation, the pulse should have a strength and a duration such that operation is in the vicinity of chronaxie.

If operation is in the vicinity of chronaxie, the analytical expression, known as "Blair's equation"[10] will apply. This "formal" relationship is expressed as $T = RC \log \frac{I}{I - (V_c/R)}$ where T is the duration of the current pulse, I is the current intensity, RC the time constant of the membrane, and V_c the value of rheobase. This relationship along with certain physical assumptions can be used to determine the output requirements of a pulsed magnetic field generator.



STRENGTH-DURATION RELATIONSHIP

Figure 2.4

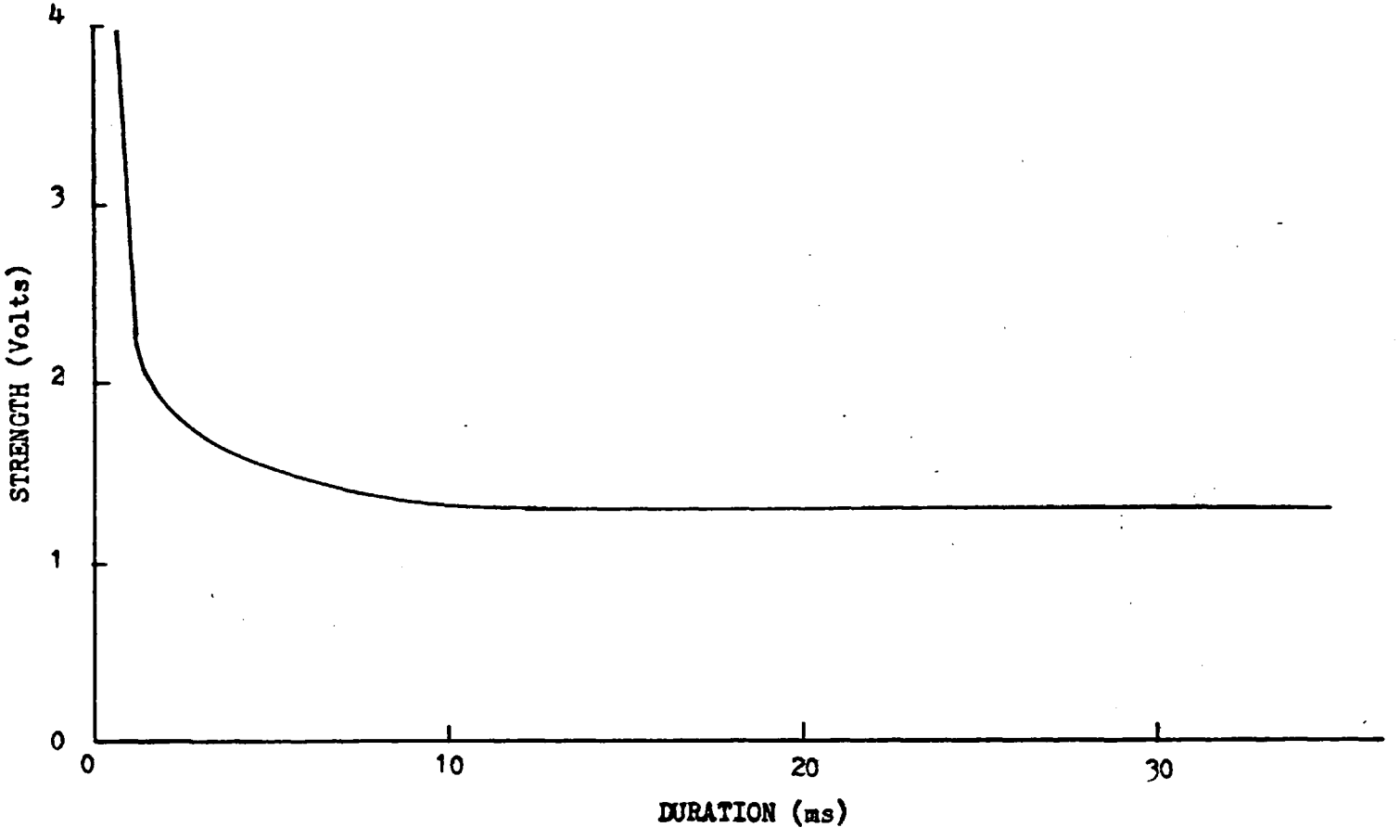
Chapter 3

DEVELOPMENT OF A PULSED MAGNETIC FIELD GENERATOR

3.1 REQUIREMENTS

The determination of the requirements for a pulsed magnetic field generator is based on the premise that a varying magnetic field will induce a voltage or current on or in the surface membrane; and that when this voltage or current reaches a threshold value, as determined by a strength-duration relationship, stimulation of the nerve will result. The time requirement is based on the value of chronaxie obtained from a graphical representation as in Fig. 3.1 of the tabulated experimental data of Blair[10]. This value is approximately 1 milli-second. In order to insure that operation is not in the vicinity of rheobase, a time of .1 milli-second is selected.

The maximum value of rate of change of flux density is determined from the work of Barlow, et al[1], to be in the vicinity of 377,000 gauss/second. To allow a reasonable safety factor in consideration of the difference between a dissected nerve and an eye in its socket, a rate of change of 1,500,000 gauss per second is selected. Since it is convenient to have the voltage induced by this magnetic pulse be of "step" form, the additional requirement of linear rise with time is placed on the magnetic field. The requirements for the generator are therefore a magnetic field rising linearly from 0 to 150 gauss in a time span of .1 milli-seconds.



STRENGTH-DURATION CURVE (FROG SCIATIC)

Figure 3.1

3.2 THEORY OF OPERATION

A cursory examination of Ampere's Law, as applied to an air solenoid

$$B_{axial} = \frac{u_o\, b^2\, NI}{2(b^2 + x^2)^{3/2}}$$

reveals that, in order to meet the requirements stated above, a time varying current with a peak amplitude of 10 to 100 amperes is required. This estimate is based on a solenoid of 1 inch in diameter with from 100 to 700 turns and for x varying between 0 and 1 cm. "X" is the axial distance from the coil to the point where the field is to be measured.

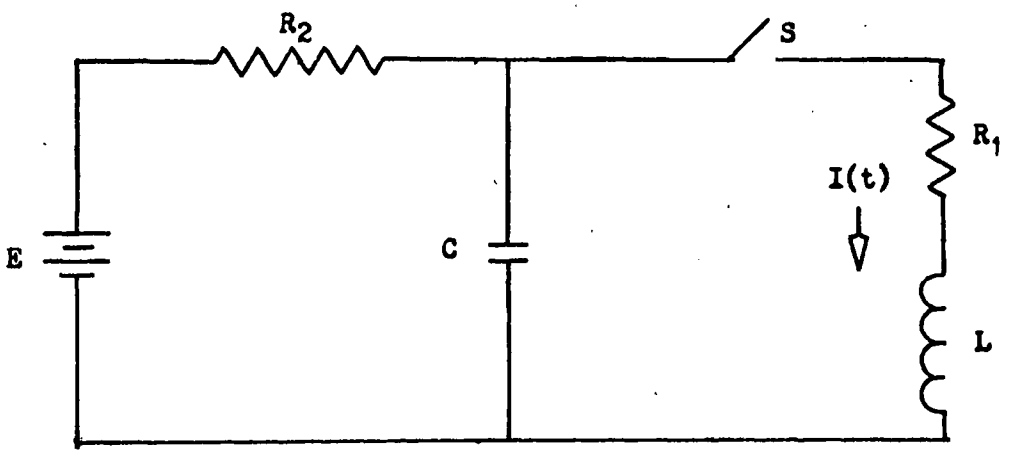
The circuit used for forming a magnetic pulse is similar to those used in radar modulators. It consists of a charged capacitor which discharges through a series R-L circuit as in Fig. 3.2. The switching action is provided by a thyratron, properly selected to meet the time and current magnatude requirements given above. Resistor R_2 is selected such that it is much greater than R_1 in order to protect the power supply from reverse currents subsequent to capacitor discharge.

Since current I(t) is directly proportional to the desired output, it is necessary to know the effect of changes in the various parameters upon this quantity. For this reason, the derivation of I(t) is calculated.

With the aid of the Laplace transformation, we find

$$I(s) = \frac{V(s)}{R + Ls + 1/Cs} = \frac{Vo}{\left(L\, s^2 + \frac{Rs}{L} + \frac{1}{LC}\right)}$$

$$S_{1,2} = -\frac{R}{2L} \pm \sqrt{\left(\frac{R}{2L}\right)^2 - \frac{1}{LC}}$$



BASIC CIRCUIT

Figure 3.2

Where Critical damping: $R = 2\sqrt{\frac{L}{C}}$

Overdamping: $R > 2\sqrt{\frac{L}{C}}$

Underdamping: $R < 2\sqrt{\frac{L}{C}}$

The critically damped case gives t for $I(t)_{max} = \frac{2L}{R}$

and the underdamped case has $I(t) = \frac{V_o}{AL}(e^{-t/T}\ \mathrm{SinAt})$

Where $A = \left|\sqrt{\left(\frac{R}{2L}\right)^2 - \frac{1}{LC}}\right|$ and $T = \frac{2L}{R}$

$I(t)' = \frac{V_o}{AL}\, e^{-t/T}\ (\mathrm{ACosAt} - \frac{R}{2L}\mathrm{SinAt})$

t for $I(t)'_{max} = \frac{1}{A}\mathrm{Tan}^{-1}\ \frac{2LA}{R}$

The underdamped circuit is selected for two reasons. First, dI(t)/dt has a better waveform. Second, of the three cases, the underdamped case is the only one which provides zero current in a finite time, which is desireable for practical reasons associated with a thyratron. Operation of the thyratron is primarily dependent upon two parameters, the plate voltage and the grid voltage. The grid voltage determines the point of firing. However, once the tube has fired, the grid loses control until the plate voltage reaches its "reset" value. Since in most commonly used thyratrons this reset voltage is negative, it is desirable to have a current with a negative swing to insure rapid reset of the thyratron.

Although pulse duration has been determined by physiological requirements placed on the generator, no mention has yet been made of repitition rate. The repetition rate is determined by the ability of the

nerve to recover from one stimulus and prepare itself for the following one. Tasaki states: "The time course of the response of a nerve fiber is not influenced by the rate at which the stimulating shocks are repeated as long as the rate is less than about 10 per sec."[8] The repetition rate of the generator, based on the above, is selected at 1-10 pulses per second.

3.3 DESIGN AND CONSTRUCTION

Since it is assumed that a variety of coils with various L and R values will be used during experimentation, it is desirable to provide the generator with a fixed capacitance C. The value of this capacitance is determined by the energy relationship between stored energy in L and C as

$$\frac{CV^2}{2} = \frac{LI^2}{2}$$

Based on this equation, C = 2uF is selected, using values L = 5mh and I = 20 amperes. The actual capacitor is oil-filled with a rating of 2000V.

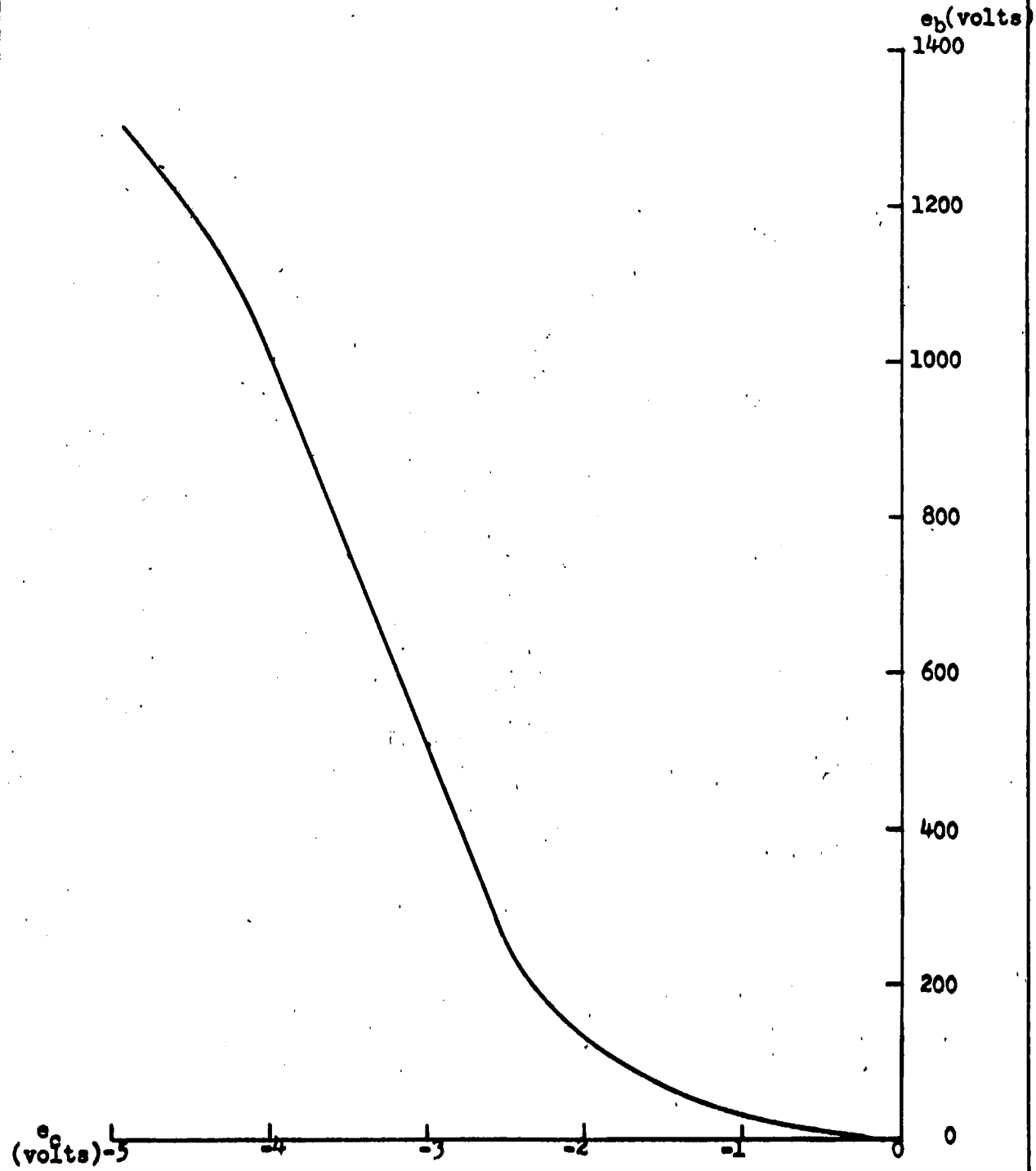
The value of R_2 is determined from constraints as $R_2 \gg R_1$ and $5R_2C < 1/10$ sec. Since R_1 is estimated to be less than 100 ohms, a value of 5000 ohms is selected for R_2. Due to the transient nature of the charging current, the power rating of the resistor is not critical, and a resistor rated at 25 watts is selected as adequate.

The selection of a DC power supply is based on the requirement for 1000V at a current $1000/R_2$ amperes. The current requirement assumes that the capacitor is completely charged to the supply voltage between adjacent pulses. These requirements are met by an available 1250V, 300 ma

supply. Although this supply is not voltage regulated, it is not considered necessary for the accomplishment of its function.

The selection of a thyratron is based on the following criteria: i_b(max) = 100 amperes; v_b(max) = 1250 volts; pulse width(min) = .2ms; pulse width(max) = .5ms; and pulse rate(max) = 10/sec. The pulse requirements are met by most commonly used thyratrons. However, the voltage and particularly the current requirements are difficult to meet in a "standard" size tube. Utilization of the "fault current" rating of the 3C23 thyratron (120 amperes) suggests the use of this tube. The 3C23 also has an adequate volage rating of 1250V.

The determination of the grid voltage supply for the 3C23 is based on the following criteria: firing curve of the tube in use, as in Fig. 3.3; pulse rate of 1 - 10/sec; i_c = 10ma. In accordance with recommended practice a grid resistor of 560 ohms is selected. The trigger source selected is a Hewlett-Packard "Square-Wave Generator," with an external battery which results in a negative-going output. This generator (with battery) is capable of supplying sufficient voltage and current. Its 600 ohm output provides a good impedance match. Although the thyratron ceases conduction when the plate voltage goes negative, it does not extinguish, or "reset" until the grid voltage returns to zero. For this reason, the long negative excursion of the grid pulse is permissable, and allows sufficient time for the capacitor to recharge. Since the only limitation on the length of grid pulse is that it must be longer than the combined charge and discharge times of the capacitor, the trigger source easily achieves the maximum design repetition rate of 10 pulses/sec.



FIRING CURVE - 3C23

Figure 3.3

The determination of R_1 and L is a complex process, based on the following parameters: $I(t)_{max}$; time for rise to $I(t)_{max}$; type of coil construction which is in turn determined by the desired orientation of magnetic field; current handling capabilities of wire used; number of turns required to achieve necessary flux; type of core material used; voltage drop across the thyratron which is included as a portion of R_1 and is a non-linear function of I(t). Due to these many and varying parameters, determination of R_1 and L is accomplished experimentally, constructing the coil first, then noting the results as functions of I(t) and $e_{induced}$. Table 3.1 reflects the electrical and physical dimensions of the coils constructed. Coils #1 and #2 are eliminated from further experimental work due to failure to meet the "time to rise to $I(t)_{max}$" requirement. The remainder of the coils meet this requirement and are held for actual nerve experiments.

The final construction of the generator follows the circuit diagram in Fig. 3.4, with the additional note that a metal shield is required around the thyratron to reduce excessive electrical noise.

COIL CHARACTERISTICS

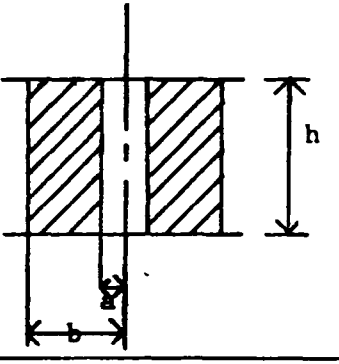
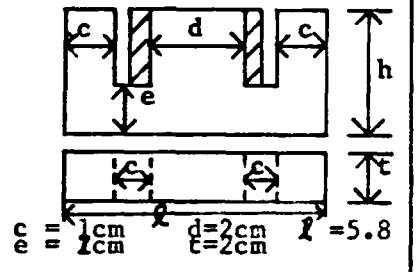
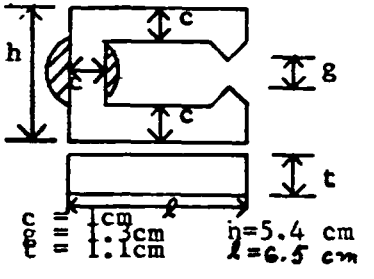
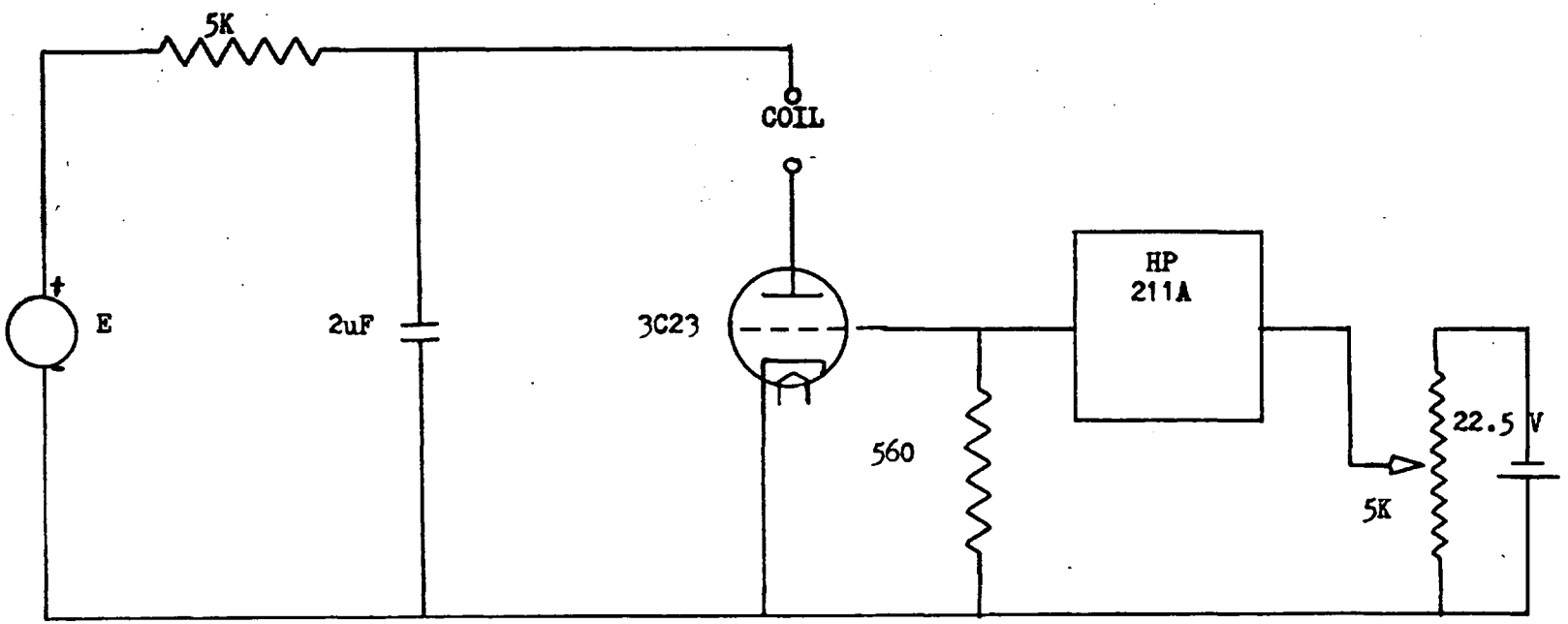
Coil Number	a cm	b cm	h cm	N	Wire Size	R Ohms	L mh	Q	Coil Shape
1	1.25	1.27	5.7	100	18	.005	.14	3.2	
2	1.25	1.28	2.5	260	22	2.0	1.34	6.0	
3	.8	1.35	2.5	527	24	7.3	3.07	5.7	
4	.8	1.6	.9	450	26	28.0	6.8	6.5	
5	1.1	1.75	2.7	750	26	140.0	58.0	28.0	
6				900	26	300.0	80.0	11	

TABLE 3.1



MAGNETIC PULSE GENERATOR

Figure 3.4

Chapter 4

EXPERIMENTAL APPARATUS

4.1 OSCILLOSCOPE

An oscilloscope (Tetronix, 512A) is adequate for important ranges of vertical deflection and sweep time and is used in actual experimentation. Two probes may be employed; one is shielded with an attenuation of 10 and the other is a shielded pair without attenuation.

4.2 ELECTRICAL STIMULATOR

An AC powered "Bio-Stimulator" is available; however, it does not provide the electrical isolation required between the source of electrical stimulus and recording equipment[8]. Although hand-keying of a variable DC supply (battery) meets the isolation criterion, it fails to give a pulse of consistent duration and repetition. Since this consistency determines the clarity of the recorded result, a uniform repetition rate is considered a necessary parameter of an electrical stimulator.

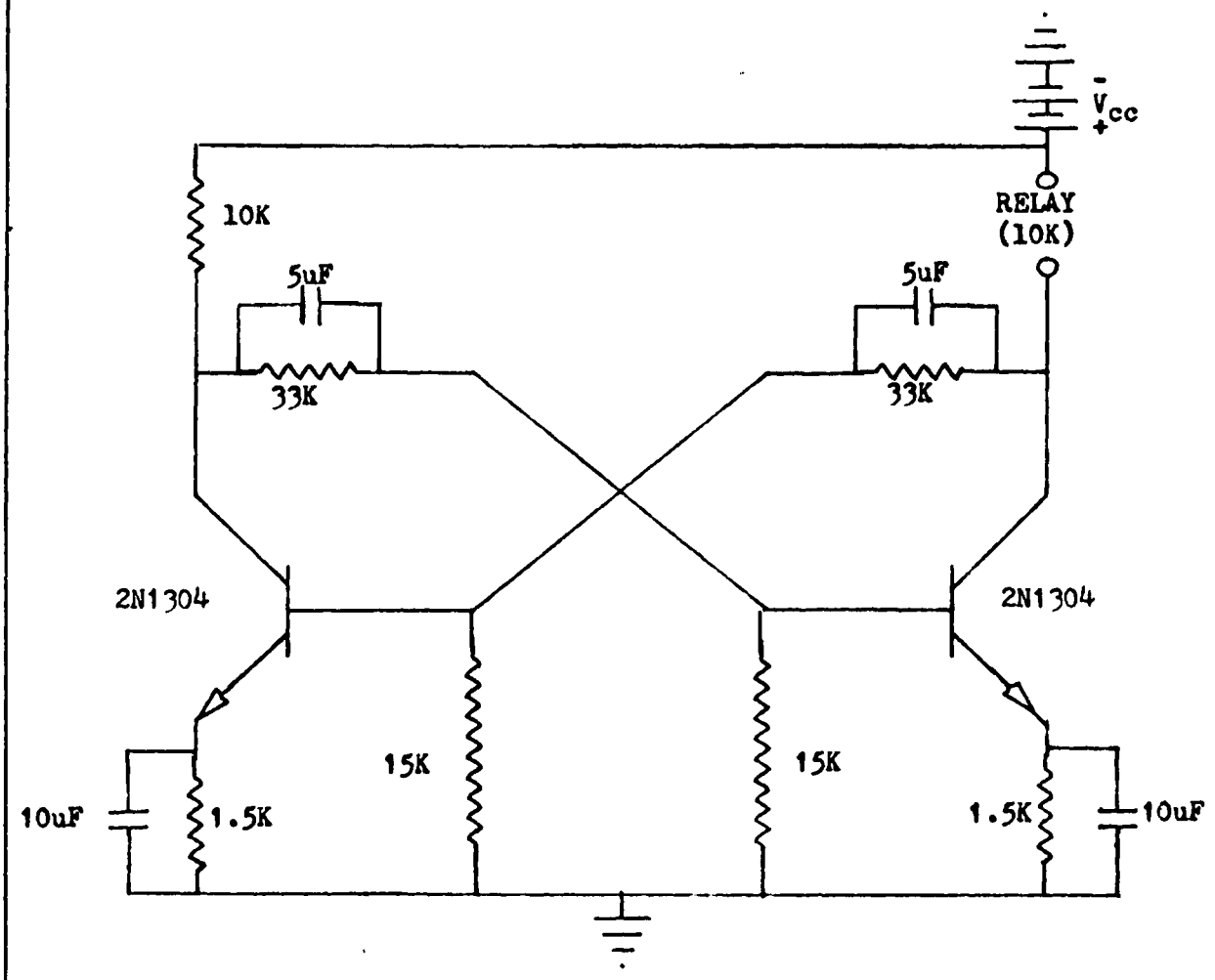
In order to provide a constant pulse repetition rate, an RC coupled, astable multivibrator is designed with a repetition rate of 3 cps, and an output sufficient to key a 10,000 ohm, 1 ma relay. The isolation requirement is met with a transistorized design and self-contained battery supply. The multivibrator periodically keys the relay which is connected in series with a variable DC supply (battery). The output is taken across the relay-battery combination.

The actual design of the multivibrator as in Fig. 4.1 is taken from the design equations presented by Shea[12]. Due to the low repetition rate, the selection of a relay is not critical, and the selection of a Sigma relay (Type 4RJ 10000S-SIL) is based on availability. The DC supply consists of a potentiometer across a 22.5 V battery.

It is realized that the actual output of the multivibrator could be used as the stimulator; however, this involves critical design to insure proper wave shape and is not considered necessary for the purpose of this paper.

4.3 PHYSIOGRAPH

The Physiograph[13] is basically a 3 channel (plus timing pulse) pen recorder. For the purposes of this paper, it derives its usefulness from its ability to provide a permanent record, as well as convenience of operation. This convenience of operation is primarily due to the provision of transducers which are designed for the type of experimentation to be undertaken. Of the many transducers provided, two are described here. The "myograph" is a mechanical transducer for translating mechanical movement into an electrical signal.[13] It is used here to detect muscle contractions. The "cardiac preamplifier MK III" provides amplification of an input potential, resulting in a maximum sensitivity of at least 1 millivolt per centimeter of pen movement[13]. It is used here to amplify muscle potentials for subsequent recording.



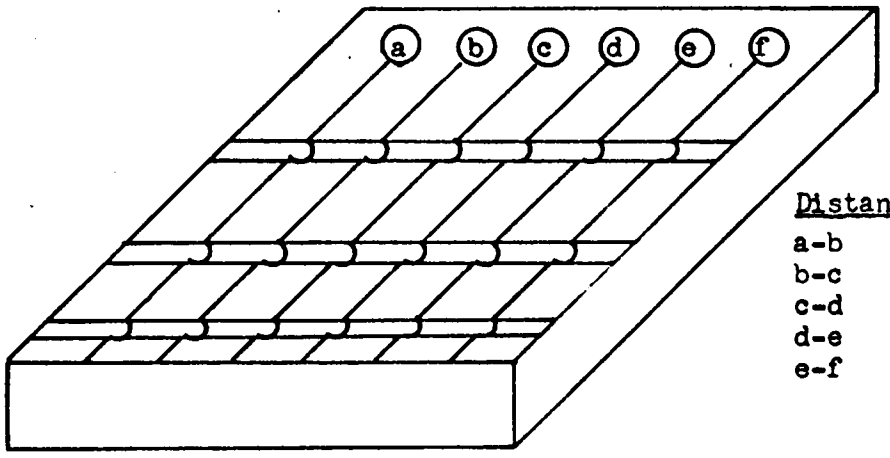
MULTIVIBRATOR FOR DC ELECTRICAL STIMULATOR

Figure 4.1

4.4 NERVE HOLDERS

Two types of nerve holders are described here. The first type is of a molded channel form with surface probes attached to terminals as in Fig. 4.2(a). In operation, the nerve is placed in the channel, and rests on the surface probes. The channel is then filled with the fluid which determines the external environment of the nerve (conducting or non-conducting). The mold is of epoxin resin, and the surface conductors are of #22 AWG solid tinned copper wire. This type of holder is referred to as "Type A", in this paper.

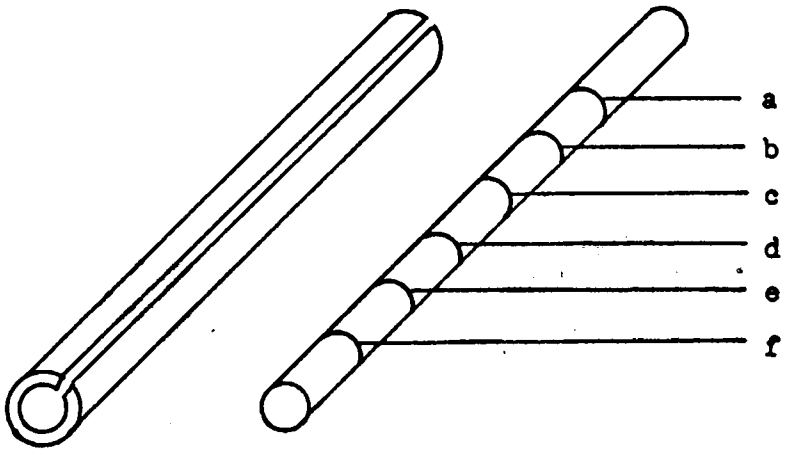
The "Type B" holder is shown in Fig. 4.2(b). It consists of an inner tube of 1/8" "spaghetti", approximately 3 inches in length, with loops of #24 stranded tinned copper wire soldered around the tube at intervals of 5 mm. The outer tube consists of a 3" length of 1/8" (ID) rubber tubing, split lengthwise. In operation, the nerve is placed lengthwise along the inner tube so that it contacts the wire loops; it is held in place with the outer tube placed so that it encloses both the nerve and the inner tube thus insuring good contact between the nerve and the wire loops. Environmental type fluid is inserted between the two tubes by the use of an eye dropper.



Distances(mm)	
a-b	3
b-c	24
c-d	13
d-e	13
e-f	6

Type "A"

(a)



Distances(mm)

	Type "B_1"	Type "B_2"
a-b	5	5
b-c	12	5
c-d	10.5	5
d-e	11.5	5
e-f	11	5

(b)

NERVE HOLDERS

Figure 4.2

Chapter 5

EXPERIMENTAL TECHNIQUE

5.1 GENERAL

The general procedure is one of comparing a known with an unknown. For these experiments, the known is the result of stimulation with an electrical stimulus of known values. The unknown is the effect of the magnetic field. The first question which must be answered is whether or not there is any effect caused by the pulsed magnetic field. Once this is established, this effect is recorded for comparison with the effects of the known stimulus.

5.2 SPECIMEN SELECTION AND PREPARATION

Although the squid giant axon is desirable because it is a single nerve fiber comparable in size to bundles consisting of hundreds of nerve fibers, the procurement of these axons is a lengthy and costly process. Since this experimentation is basic in nature, this sophistication is not considered necessary, and a nerve bundle is sufficient. The particular bundle selected is the sciatic nerve of the Rana pipiens. The selection of this nerve tract is based on availability as well as the fact that much work in the rield of neurophysiology has been done on this particular nerve, thus providing extensive experimental data in the literature.

The removal of the sciatic nerve from the frog follows standard dissection practice with the following conditions. When complete removal of the sciatic is necessary, the nerve is cut at a point before it joins the spinal cord, and at the other end just before it joins the gastrocnemius. When it is desired to observe the effect of stimulation of the nerve on the gastrocnemius, the nerve is severed at a point before it joins the spinal cord, only.

Following removal, the nerve is placed in one of the nerve holders, and fluid is injected into the holder to simulate the required environmental media. The fluid used for a conducting media is amphibian Ringer's solution which consists of the following: 100 cc of .7% NaCl; 1 cc of 1% $CaCl_2$; and .75 cc of 1% KCl. Due to the low humidity conditions at the time of the experiments, it is necessary to apply Ringer's solution liberally to prevent drying of the nerve, or an increase in the critical concentration of salts through evaporation. In addition to providing a conducting media, Ringer's solution is used to maintain normal concentrations of the salts mentioned above. The fluid used for a non-conducting media is General Electric Damping Liquid, D6810A. If muscle reaction is to be observed, there are modifications to the above. The nerve is placed on paper toweling, and Ringer's solution is applied by eye dropper to both the nerve and the muscle.

5.3 DIRECT MEASUREMENT OF ELECTRICAL ACTIVITY IN THE NERVE

This procedure follows that described by Brazier[9] utilizing the oscilloscope as the recording device. The nerve is completely removed and placed in one of the holders. To establish a known situation, an

electrical stimulus is applied to terminals a and b on the nerve holder, and the oscilloscope probe is placed on any pair of the remaining terminals. The distance between terminals will in part determine the shape of the recorded wave. A non-conducting media is normally used with this technique[9]; however, use of Ringer's solution is recorded in the literature.[8] The recorded output is a diphasic action potential, with each phase similar in form to that shown in Fig. 2.3.

After the "normal" response is observed, the electrical stimulator is removed, and a pulsed magnetic field is applied by means of the generator described in Chapter 3. The following parameters are varied: type of coil; distance of coil from nerve; orientation of the coil with respect to the nerve. The results obtained from the above are recorded and compared to the "normal" response.

5.4 INDIRECT MEASUREMENT BY MEANS OF MUSCLE PARAMETERS

One of the oldest means of determining whether or not a nerve is stimulated is by observation of muscular contraction[14]; nerve excitability experiments of Lussier and Rushton establish the fact that the action potential of muscle is an indication of nerve stimulation.[15] A combination of the measurement of these two muscle parameters (contraction and action potential) by means of the Physiograph is thus assumed to constitute a satisfactory method of indirect measurement of nerve stimulation.

The procedure is as follows: The sciatic nerve is separated from all encoutrement along its length, and is severed at is proximal end. The nerve is then laid on paper toweling, perpendicular to the leg. The gastrocnemius is severed at its distal end, and pulled clear of the skeleton. The distal end is then connected by thread to a "myograph"

transducer of the Physiograph. Needle electrodes are inserted in the proximal and distal ends of the gastrocnemius. These electrodes are connected to a "cardiac preamplifier MK III". The "myograph" is connected to channel 3 of the Physiograph, and the preamplifier is connected to channel 2. Standard alignment procedures are carried out in accaordance with the instruction manual.[13] The nerve and muscle are bathed in Ringer's solution by means of an eye dropper. The output of the "electrical stimulator" is applied to the nerve by means of contact electrodes, spaced approximately 5mm. After the "normal" recording has been made, a pulsed magnetic field is applied in the same manner as in Section 5.3. When measurement of the "distance from nerve" parameter is desired, an additional refinement is obtained by connecting the coil to a "myograph" by means of thread, and connecting the transducer to channel 1 of the Physiograph. When properly calibrated, this gives a continuous record of the distance of the coil from the nerve during the experimentation.

Chapter 6

EXPERIMENTAL RESULTS

6.1 COIL SELECTION

The basis for preliminary coil selection is the series of curves in Fig. 6.1. These curves represent approximations to actual oscilloscope traces, with probes across a 1 ohm resistor in series with the coil. On this preliminary basis, coils 1 and 2 are dropped from consideration. Of the remaining coils, 4 and 6 appear to be the most promising, and the maximum values of I(t) for these coils are recorded in Chart 6.1.

6.2 DIRECT MEASUREMENT METHOD

Frog #1: A short section of the left sciatic is cleared, severed at its proximal end, and the distal end allowed to remain attached to the gastrocnemius. A magnetic pulse is applied through coil #3, with the coil situated very close to the nerve. "Muscle twitch" is observed, in exact response to the pulse rate of the generator. Voltage supplied to the generator is 1000V, and the pulse rate is varied from 1 to 10 repetitions per second. The right sciatic is removed from the frog in its entirety, and placed in a type "A" nerve holder, with an environment of Ringer's solution. A 22.5 V battery with output from a potentiometer is placed across terminals a-b and oscilloscope probes are placed across c-d. The battery is keyed manually. No trace on the scope is noted above the noise level.

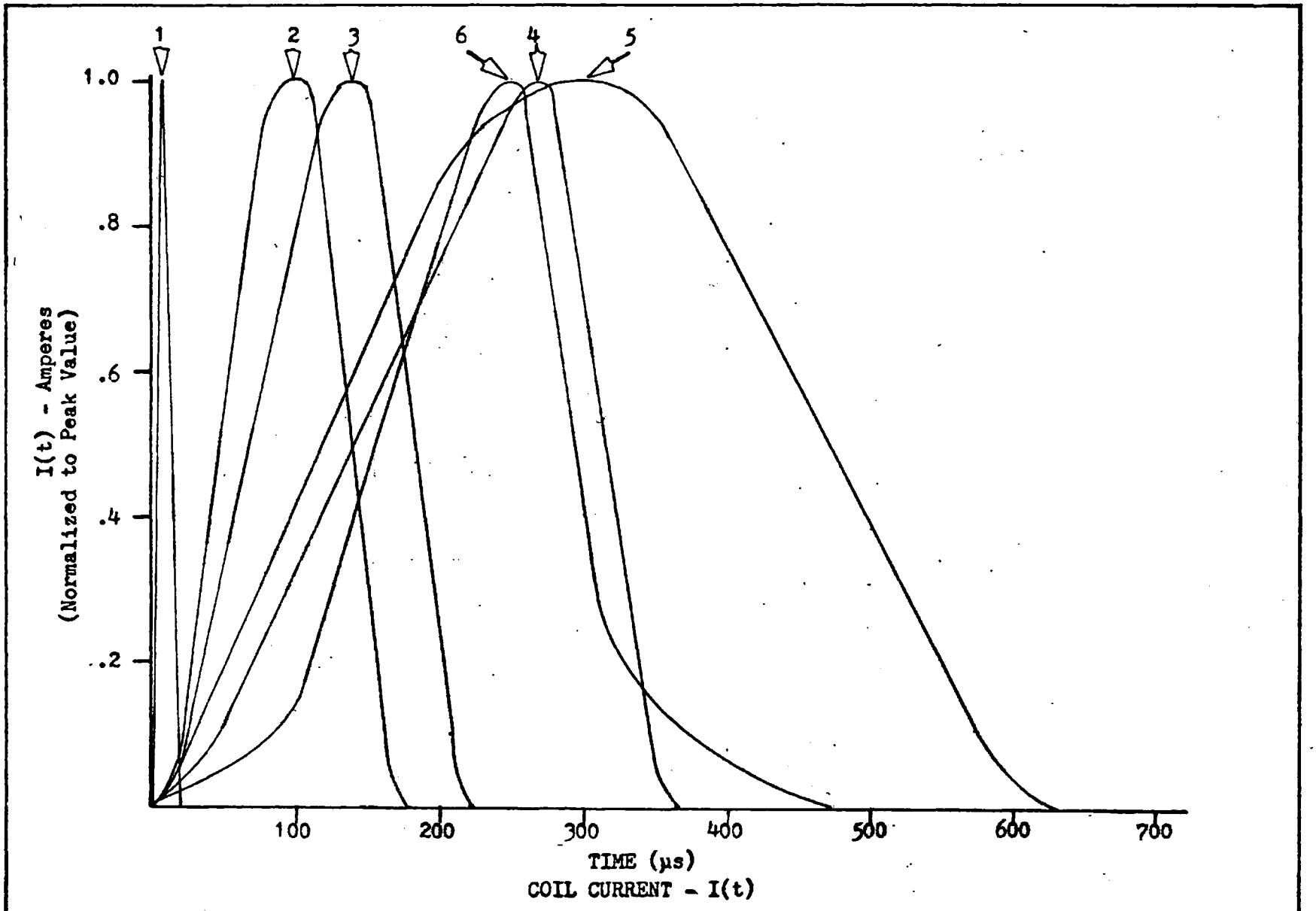

1
2
3
6
4
5
1.0
.8
.6
.4
.2
I(t) - Amperes
(Normalized to Peak Value)
100
200
300
400
500
600
700
TIME (μs)
COIL CURRENT - I(t)

Figure 6.1

E (Volts)	$I(t)_{max}$ (Amps)	
	Coil #4	Coil #6
200	2.5	.94
400	5.0	1.80
600	9.0	5.50
800	12.0	8.00
1000	14.0	12.50
1200	16.0	15.40

COIL CURRENT - MAXIMUM VALUES

Chart 6.1

Frog #2: An attempt is made to record a monophasic action potential[9] rather than the diphasic potential indicated in Section 5.3. To accomplish this, one end of the nerve is crushed prior to placing it in a nerve holder. The crushed end is placed over terminal "e", and the positive scope probe is attached to this terminal. The negative scope probe is attached to terminal "c". All other conditions are similar to those used with frog #1. Stimulation is attempted with both battery and the pulsed magnetic field generator, with no result indicated on the oscilloscope above the noise level.

Frog #3: The same procedure as above is utilized, with no indicated results above the noise level. Before complete removal of the nerve, stimulation is attempted with the magnetic generator (coil #3) which results in muscle twitch.

Frog #4: The same procedure applies as for frog #1 but with special attention directed toward the polarity of the battery stimulus. The battery is connected + to terminal "a" and - to terminal "b". Traces are observed which are of the expected action potential shape, but of a magnitude of 30mV. These traces must be picked out of the noise and are difficult to read.

Frog #5: The same procedure applies as for frog #4 with the exception of the environmental fluid. Non-conducting fluid is used as the external media. There is no discernable evidence of an action potential in the scope trace.

Frog #6: The left sciatic is completely removed and placed in a Type B1 nerve holder. A conducting media is used and the stimulus is applied at terminals a-b by means of manual keying. The stimulus in

this experiment is allowed to vary from 0 to 20 V, whereas in the preceeding experiments it has been held below 2V. A pulse is detected above the noise level, but it is sporadic and difficult to read. The right sciatic is divested of encoutrement, and a Type B_1 nerve holder is attached. Neither end of the nerve is severed. The wave form observed in response to battery stimulus is of the same form as noted for the left sciatic, and muscle twitch is also observed. A magnetic pulse is applied through coil #4 with E set at 1000V. Although the noise level increases, there is evidence of a pulse in response to the stimulus. Muscle twitch is also noted, which follows the pulsing of the generator. It is also noted that stimulation is achieved more readily with the nerve-coil orientation such that the nerve has a maximum field directed along its axis.

Frog #7: The left sciatic is completely removed, and placed in a Type B_2 nerve holder. The use of the rubber tubing to hold the nerve in place is found unsatisfactory; the application of Ringer's solution alone appears to provide a satisfactory contact between the wire loops and the nerve. The experiment is conducted at midnight in an attempt to secure relatively low noise level. The use of an AC "Bio-Stimulator" is attempted during this experiment, but is found unsatisfactory due to the requirement of isolation between stimulus and recording equipment. Physical shielding with a large sheet of aluminum between the specimen and all AC equipment was attempted and found helpful in reducing the already low noise level. The right sciatic is prepared in a similar manner to the left, but stimulus is first applied with a manually keyed battery at approximately 8V. The stimulus is applied (+ to -) to terminals c-d. The scope trace bears close resemblance to the expected diphasic action

potential, although it is difficult to read because of the multiple nature of the pulses. A stimulus is then applied with the pulsed magnetic generator through coil #5 using an E of 500 V. This results in a multiple monophasic pulse of the same approximate shape as observed when battery stimulus is employed. With 500 V applied through coil #5, the distance between the coil and the nerve is so minute that it is difficult to determine whether the magnetic field or the physical vibration of the coil is causing stimulation. Following this experiment, coil #5 is dropped from further experimental work.

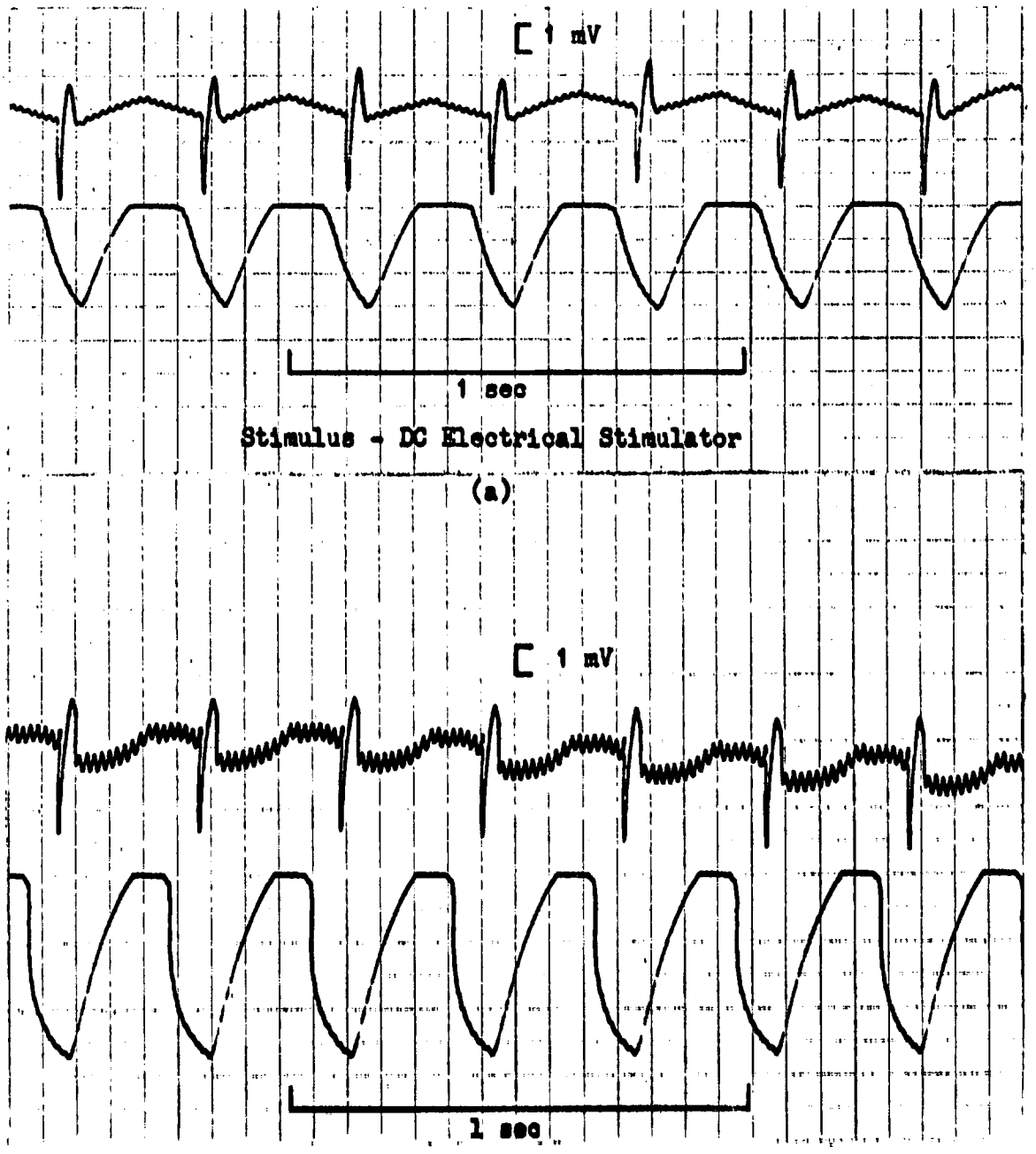
Frog #8: The purpose of this experiment is to verify the results observed in the frog #7 experiment, prior to the utilization of photographic methods of recording oscilloscope traces. Although the experiment is conducted at the same time of day as with frog #7, the noise level is the highest noted during any of the experiments. As a result of the noise level, the only significant data obtained from this experiment are the observations (1) that coil #6 does not cause muscle twitch when the air gap is placed across the nerve at a distance of approximately 4 cm from the severed end; and (2) that with only Ringer's solution in a Type "A" holder, if a magnetic pulse is applied through coil #4, a trace similar to that found in the frog #7 experiment is noted.

Following the experiment with frog #8, it is determined that further experimentation utilizing the direct method is of little use unless sophistication is built into the recording system. Since this sophistication is time consuming and requires equipment that is not readily available, indirect measurement by means of muscle parameters is utilized for the remaining experiments.

6.3 INDIRECT MEASUREMENT METHOD

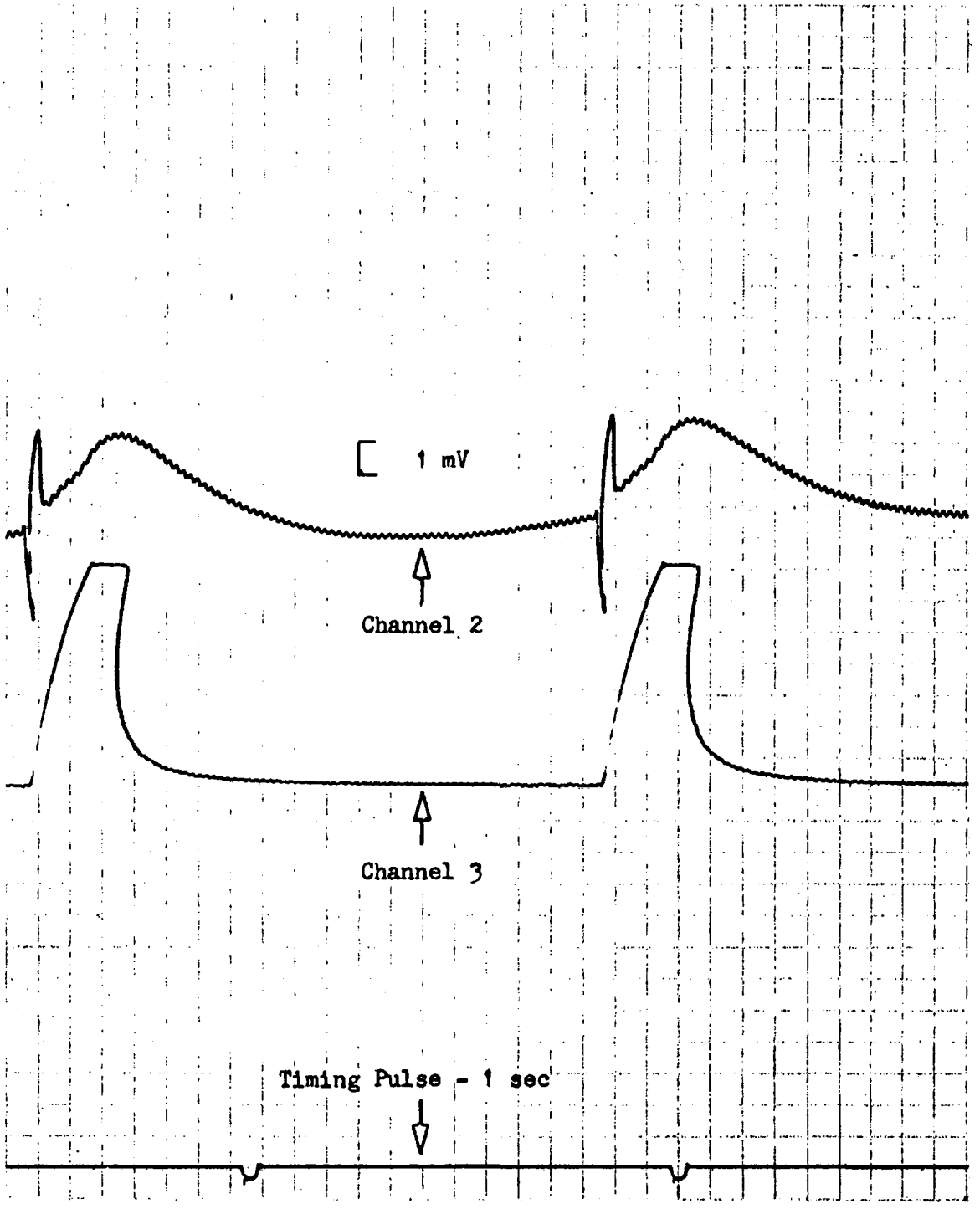
Frog #9: The procedure used here is that described in Section 5.4, except that channel 1 of the Physiograph is not utilized. Fig 6.2 (a) is a record of the muscle action potential (channel 2) and myograph (channel 3) with the stimulus applied by the DC electrical stimulator described in Section 4.2. The strength of the stimulus is set at a threshold of 1.5V, and the repetition rate is 3 per second. Fig. 6.2(b) is made with the same Physiograph connections as above; however, the stimulus is applied by means of the pulsed magnetic generator. E is set at 850 V, and coil #4 is used. The distance between the coil and the nerve is approximately 2 mm. The repetition rate is set at approximately 3 per second in order to implement the comparison of the results of the two types of stimulus. Figure 6.3 indicates a record taken under the same circumstances as Fig. 6.2(b), except that the repetition rate is reduced to approximately 1 per second. The coil is oriented with respect to the nerve as indicated in Fig. 6.4.

Frog #10: The procedure used here is the same as that used for frog #9, except that channel 1 of the Physiograph is utilized to record the distance from the nerve to the coil. Channel 1 is calibrated by the use of a "feeler" gauge at .025" distance between coil face and nerve for a 5mm downward deflection on the Physiograph recording. The actual distance between the coil and the nerve is obtained by adding 1mm thickness of the coil face to the recorded distance. The voltage E is set at predetermined values of 400, 600, 800, and 1000 volts, and the distance is decreased from a maximum value of approximately 1" at each voltage until stimulation is achieved. At an E of 1000V, the distance between the



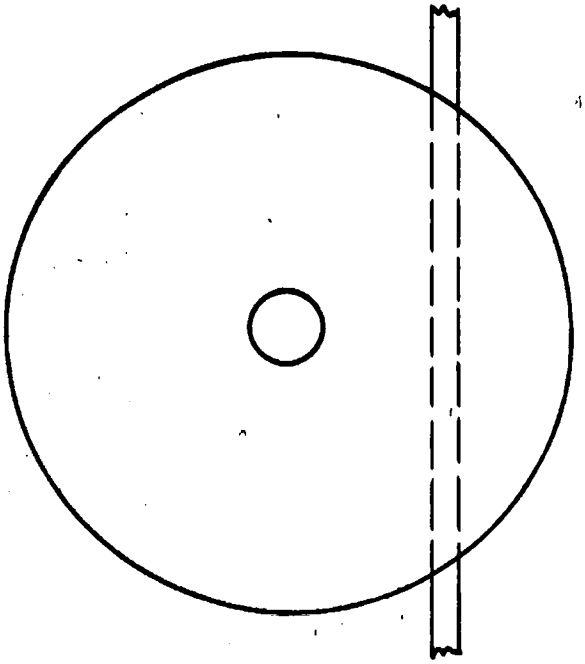
PHYSIOGRAPH RECORD

Figure 6.2



PHYSIOGRAPH RECORD - MAGNETIC STIMULUS (coil #4, E = 800V)

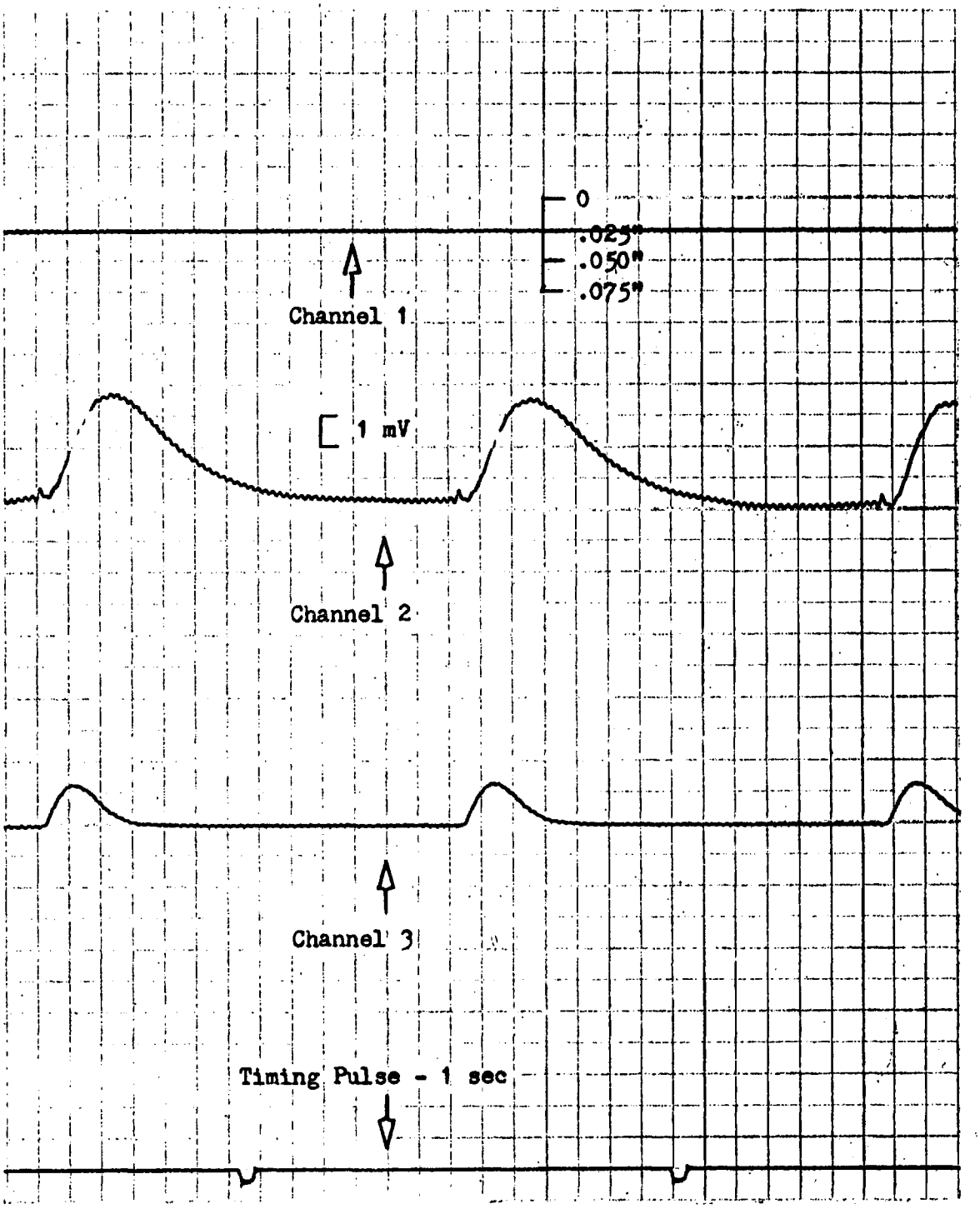
Figure 6.3



COIL-NERVE ORIENTATION (Coil #3)

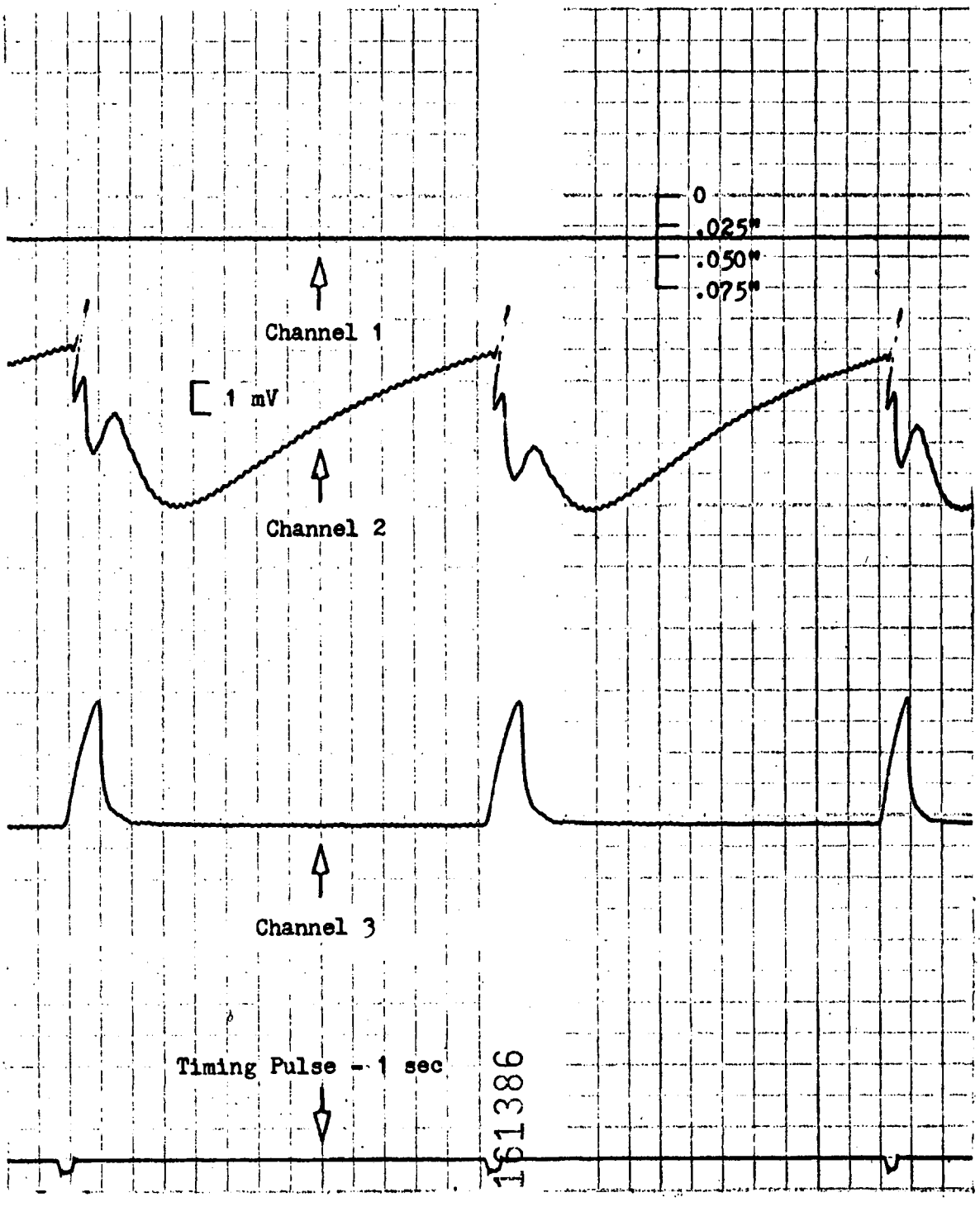
Figure 6.4

coil and the nerve is beyond the calibrated range of the recorder, and is measured at approximately 4mm. The recordings are made with the stimulus pulsed at 1 per second, and the Physiograph is set at maximum paper speed. Figures 6.5 through 6.8 show results. Two additional records are made utilizing coil #6 in which E is set at 750 V and all other parameters remain the same as those used from coil #4. For the first record, as in Fig. 6.9, the orientation of the coil is as indicated in Fig. 6.10(a). All parameters for the second record, as in Fig. 6.11, are the same, with the exception of the coil orientation which is in accordance with that shown in Fig. 6.10(b). It is noted that the air gap of coil #6 is located approximately 1cm from the cut end of the nerve. The trace in the channel 1 position on Fig. 6.11 has no meaning as far as these data are concerned.



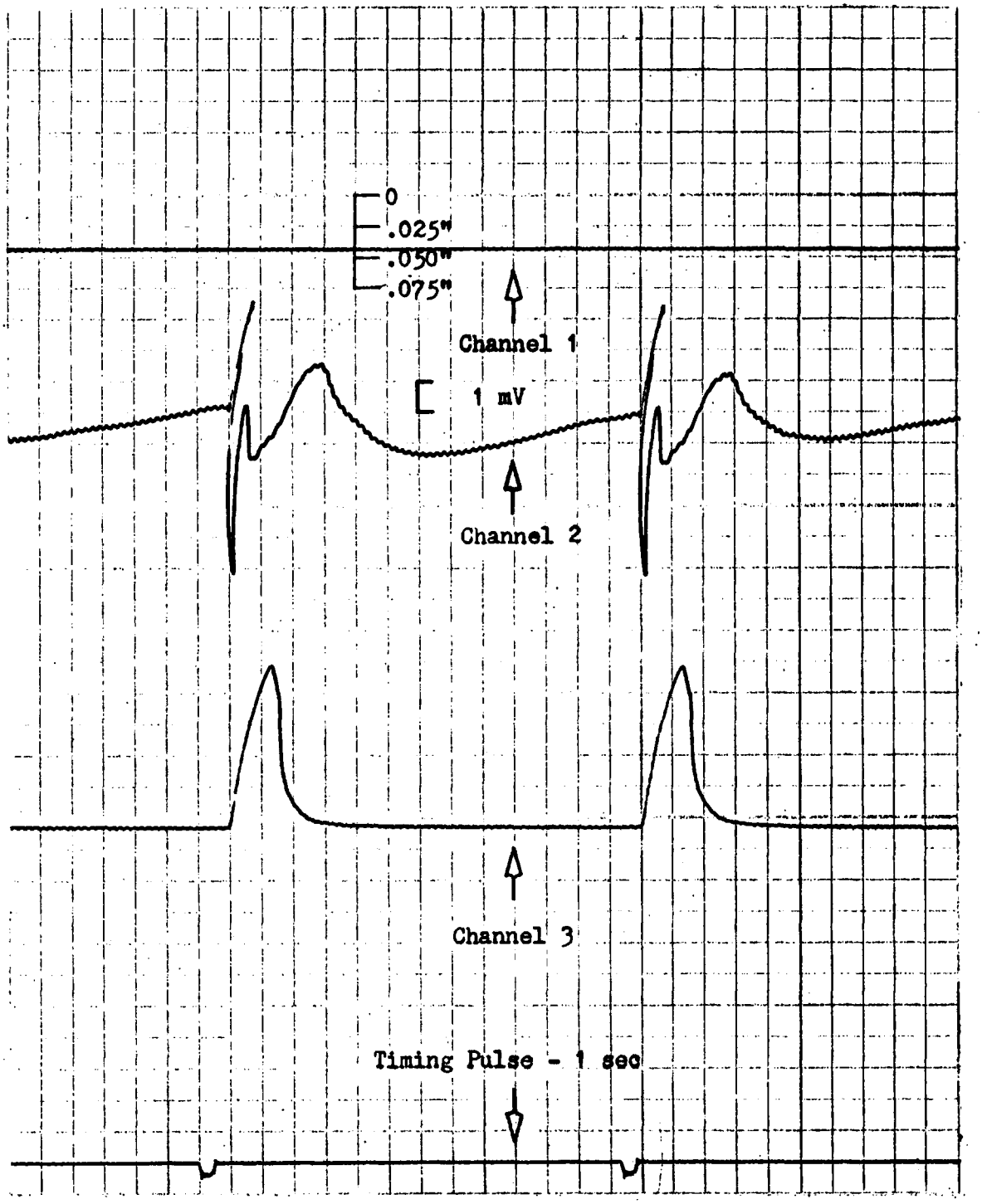
PHYSIOGRAPH RECORD - MAGNETIC STIMULUS (Coil #4, E = 400V)

Figure 6.5



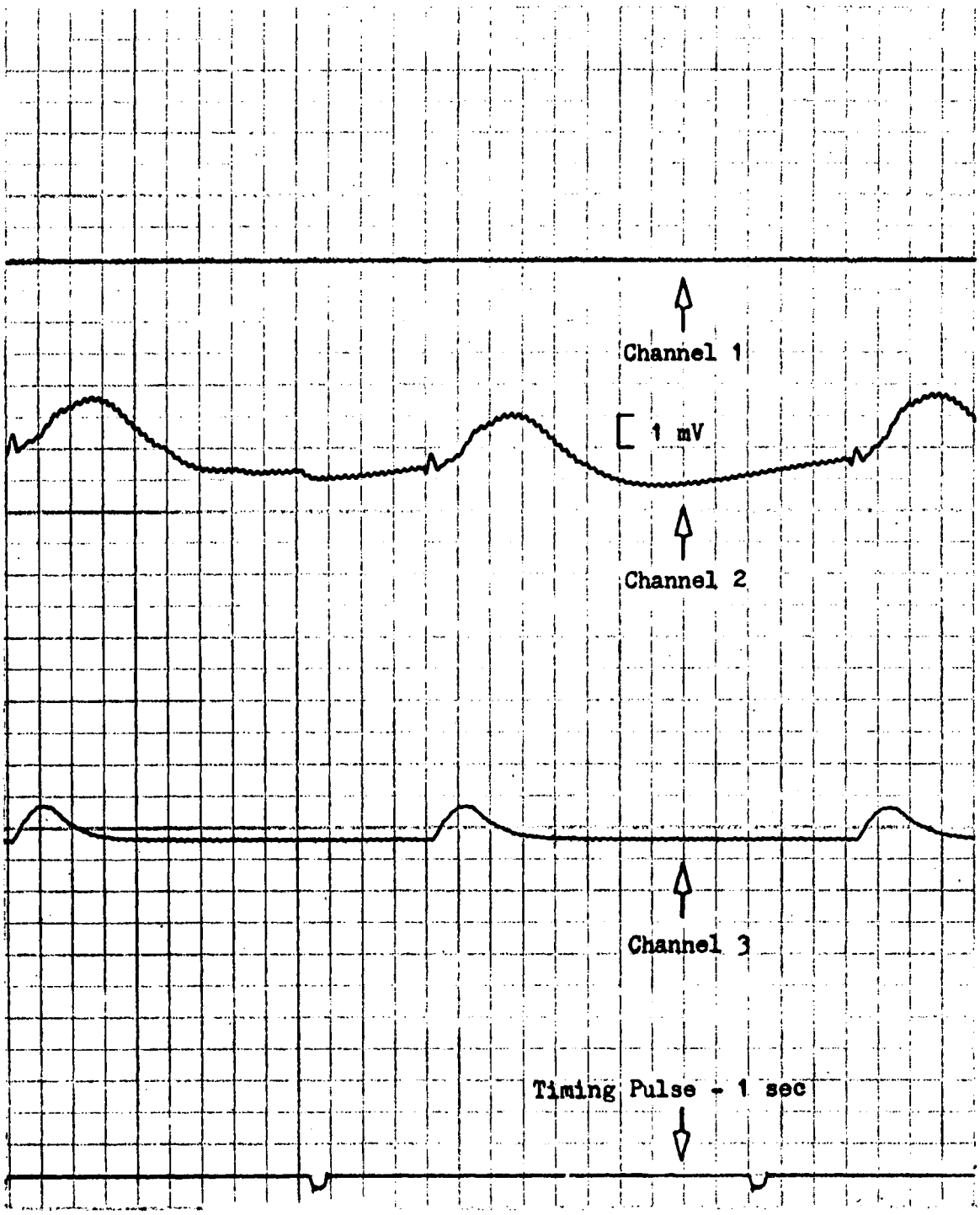
PHYSIOGRAPH RECORD - MAGNETIC STIMULUS (Coil #4, E = 600V)

Figure 6.6



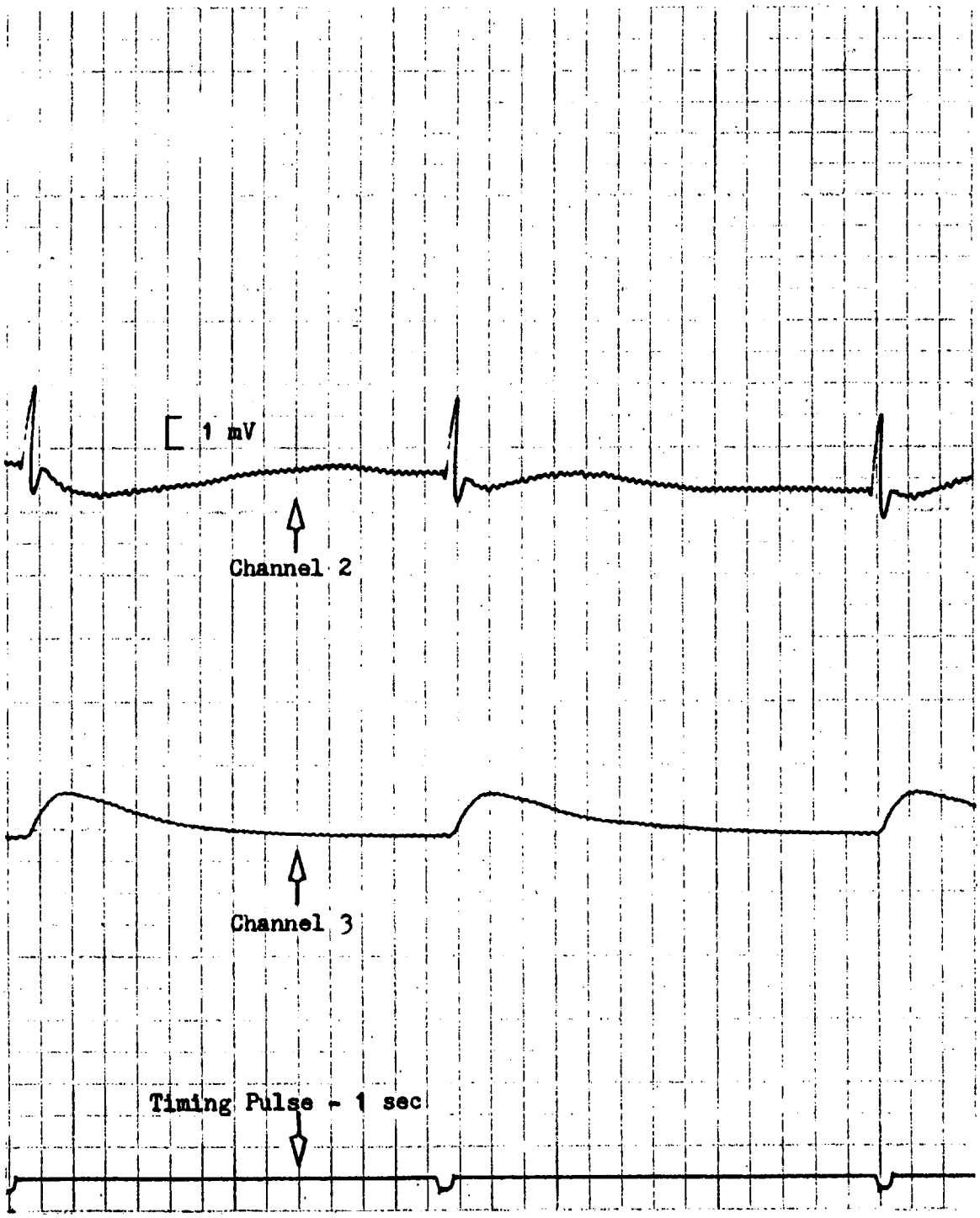
PHYSIOGRAPH RECORD - MAGNETIC STIMULUS (Coil #4, E = 800V)

Figure 6.7



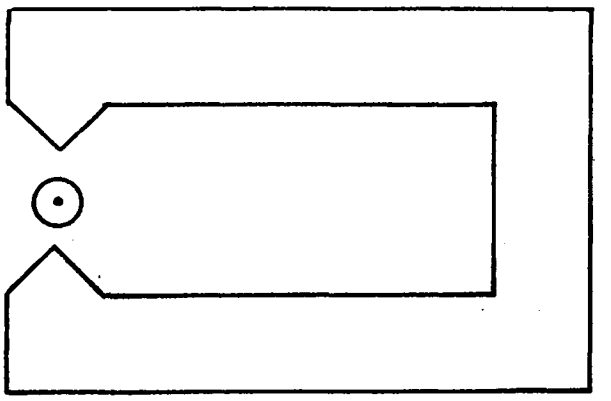
PHYSIOGRAPH RECORD - MAGNETIC STIMULUS (Coil #4, E = 1000V)

Figure 6.8

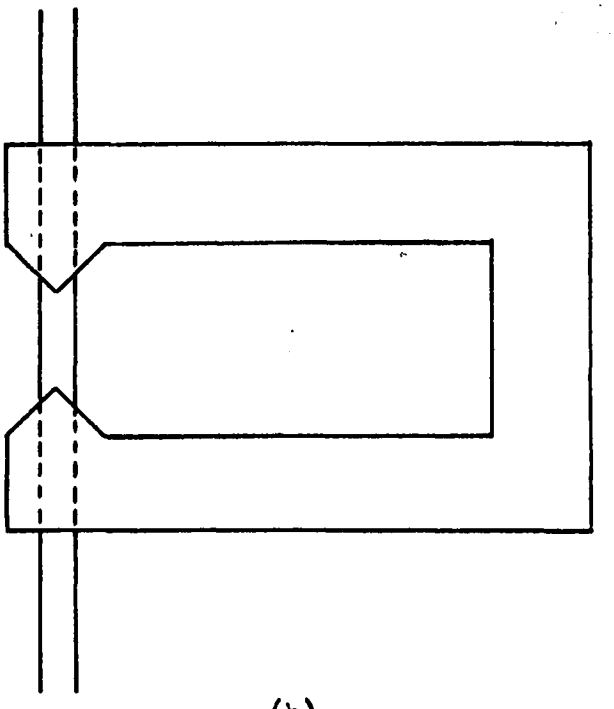


PHYSIOGRAPH RECORD - MAGNETIC STIMULUS (Coil #6, E = 750V)

Figure 6.9



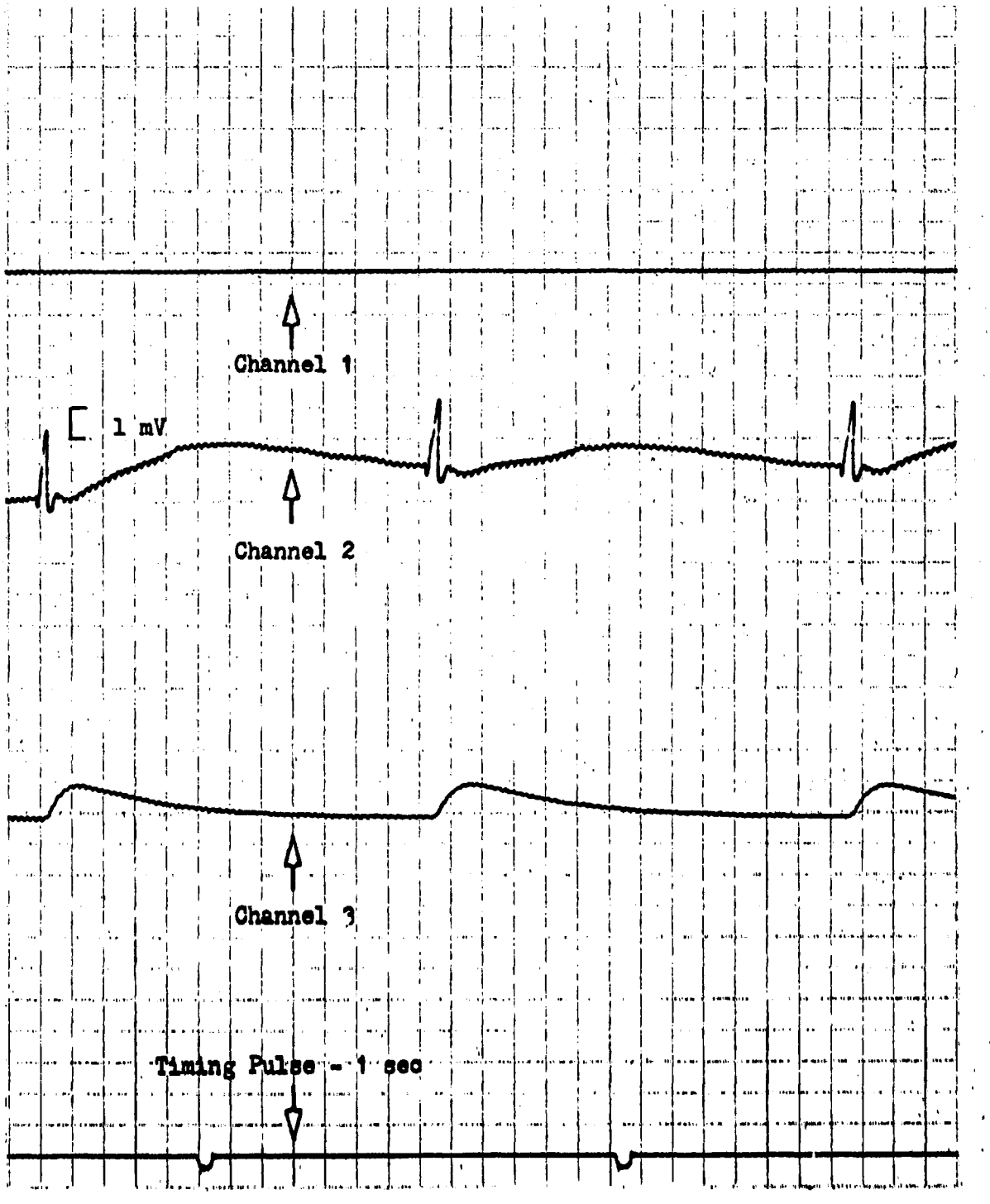
(a)



(b)

COIL-NERVE ORIENTATION (Coil #6)

Figure 6.10



PHYSIOGRAPH RECORD - MAGNETIC STIMULUS (Coil #6, E=750V)

Figure 6.11

Chapter 7

CONCLUSIONS

7.1 GENERAL

Due to the nature of the experimental techniques used, a specific conclusion can be drawn only in reference to the basic question of whether or not a varying magnetic field will stimulate a nerve. The observation of muscle twitch in frogs #1,3,6,8,9 and 10 give support to the general premise, but the Physiograph records of Fig. 6.2 represent the most graphic basis for the general conclusion that a nerve bundle can be stimulated by a pulsed magnetic field. The additional amount of ripple in Fig. 6.2(b) is due to increased 60 cps noise as a result of the proximity of an AC device.

The remainder of the "conclusions" take the form of hypotheses, attempting to explain how the stimulation takes place. These hypotheses are based on known neuron and electromagnetic theory, and are either supported or de-emphasized by experimental data.

The first hypothesis is that the varying magnetic field, normal to the nerve, induces a voltage along the nerve, which is of sufficient strength to achieve stimulation. The experimental evidence tends to disprove this hypothesis. Records indicate that stimulation is most easily achieved when a solenoidal type coil is oriented such that the maximum axial field is effecting the nerve. When the "C" type electromagnet is utilized (coil #6), it does not achieve stimulation when the

nerve is in the gap, unless the cut end of the nerve is in the vicinity of the gap. Rheobase for an electrical "surface electrode" stimulus, with probes separated by approximately 5 mm, is approximately 1.5 V. This voltage is beyond the capabilities of the induced voltage, caused by the magnetic field generator, at the output levels used in the experimentation. However, since paper toweling, soaked in Ringer's solution was utilized in the experiments, it is possible that this increased area, acting as a "target" for a normal magnetic field, could result in an induced voltage of sufficient value to stimulate the nerve. Due to this possibility, the hypothesis is neither proved nor disproved, and further experimental work is required.

The second hypothesis is that the varying magnetic field oriented axially to the nerve, induces a voltage directly across the surface membrane of sufficient magnitude and duration to cause stimulation. This hypothesis is supported in part by the same experimental evidence which tends to disprove the first hypothesis. However, since none of the coils used were designed to elicit a small field, with a specific orientation, the results obtained by the use of these coils cannot be considered conclusive. Although it is believed that a definite correlation exists between the distances and strengths of field as indicated in Figures 6.5 through 6.8, due to the number of assumptions and actual unknowns existing in the electrical analogy of the axon, an analytical evaluation is not feasable with the information available. The problem is further complicated by the fact that the experimental data is based on nerve bundles, rather than a single nerve fiber.

The third hypothesis is that the varying magnetic field induces a voltage across the myelin coating of the axon, effectively charging the capacitance existent in the myelin (5×10^{-9} farad/cm^2)[8], which subsequently discharges through the surface membrane causing stimulation of the nerve. The myelin "time constant" as computed from information supplied by Tasaki[8] is 5×10^{-4} seconds. The method of recording the experimental data does not possess a time scale which is critical enough to either confirm or deny this hypothesis, based on the time factor. It is believed that additional experimentation on unmyelinated nerve fibers would provide conclusive evidence.

The fourth hypothesis is that the varying magnetic field induces a voltage in the myoneural junction, which results in the observed muscle twitch and muscle action potential. Although this hypothesis does not seem probable, due to the unknowns involved in the neuro-muscular junction and the experimental technique used, it is a possibility which is not disproved by experimental data.

7.2 SUGGESTED AREAS FOR FURTHER STUDIES

It is believed that further study should be directed along the lines of either proving or disproving the hypotheses mentioned above by additional experimental work. This experimentation should involve sophisticated measurement equipment and techniques. DC oscilloscopes, DC powered magnetic field generator, and screen room will aid in lowering the noise level. Coils constructed for the purpose of providing a magnetic field over a small area and with specific orientation will overcome the disadvantages of interaction and multi-directional fields

encountered in the experimentation recorded in Chapter 6. Specialized probes used in place of the "surface contact" type will aid in the elimination of interaction between the magnetic stimulus and recording equipment. The use of squid giant axons eliminates the disadvantages found in working with nerve bundles, as well as providing a comparison between myelinated and unmyelinated types of nerve fibers. Separation of a single fibre from the sciatic bundle provides a myelinated fibre for experimentation. Based on the above sophisti cation analytic evaluation can be made, and through the application of electromagnetic theory specific postulates put forth which add to the basic knowledge of neuron operation.

There is a need for a DC Bio-Stimulator, with an internal battery supply. The design and construction of such a device should be based on the specific requirements of electrophysiologists. This device would not only be an asset to physiologists, but would also aid in achieving the sophistication mentioned above.

If the pulsed magnetic field generator is to have any medical application, it must be reduced in size and power requirements. An investigation of various methods of achieving this end is indicated, and should include the possible use of the recently developed "control silicon diode" as a substitute for the thyratron.

REFERENCES

1. H.B. Barlow, H.I. Kohn, and E.G. Walsh, "Visual Sensations Aroused by Magnetic Fields," American Journal of Physiology, Vol. 148 (1947) p.323.

2. J.M. Barnothy, "Biologic Effects of Magnetic Fields," Medical Physics, Vol. 3, Edited by O. Glasser, Year Book Publishers, 1960.

3. M.P. Spencer, and A.B. Denison, "The Square Wave Electromagnetic Flowmeter: Theory of Operation and Design of Magnetic Probes for Clinical and Experimental Application," I.R.E. Transactions Bio-Medical Electronics, Dec. 1959, p. 220.

4. J.C. Eccles, "Neuron Physiology - Introduction," Handbook of Physiology - Neurophysiology I, American Physiological Society, 1959, pp. 59-72.

5. W.H. Freyang, "Some Functions of Nerve Cells in Terms of an Equivalent Network," Proc. I.R.E., Nov. 1959, pp. 1863-1869.

6. J.W. Moore, "Electronic Control of Some Active Biolectric Membranes," Proc. I.R.E., Nov. 1959, p. 1871.

7. A.L. Hodgkin and A.F. Huxley, "A Quantative Description of Membrane Current and Its Application to Conduction and Excitation in Nerves," Journal of Physiology, Vol. 117 (1952), p. 500.

8. I. Tasaki, "Conduction of the Nerve Impulse," Handbook of Physiology - Neurophysiology I, American Physiological Society, 1959, pp. 75-121.

9. M.A.B. Brazier, The Electrical Activity of the Nervous System, 1st Edition, Macmillan Co., 1951.

10. H.A. Blair, "On the Intensity-Time Relations for Stimulation by Electric Currents," Journal of General Physiology, Vol. 15 (1931-32), pp. 709-729.

11. K.S. Cole and A.L. Hodgkin, "Membrane and Protoplasm Resistance in the Squid Giant Axon," Journal of General Physiology, Vol. 22 (1939), p. 671

12. R.F. Shea, Transistor Circuit Engineering, 3rd Edition, John Wiley and Sons, Inc., 1957, pp. 250-255.

13. Physiograph Instruction Manual, B. and M. Instrument Co., Inc., 5815 Sidney Street, Houston 21, Texas, 1959.

14. E. Gardner, Fundamentals of Neurology, 2nd Edition, W.B. Saunders Co., 1952, p. 89.

15. J.J. Lussier and W.A.H. Rushton, "Excitability of Nodes of Ranvier in a Nerve Trunk," Journal of Physiology, Vol. 115, 1951.