ANALYSIS AND MODELLING OF NEURAL SYSTEM

A DISSERTATION

submitted in partial fulfilment of
the requirements for the award of the degree
of
MASTER OF ENGINEERING
in
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CERTIFICATE

Certified that the dissertation entitled "Analysis and Modelling of Neural Cycles" which is being submitted by (Mr.) Ranjan Mukherjee in partial fulfilment for the award of the degree of MASTER OF TECHNOLOGY in "MANAGEMENT AND SYSTEMS" of University of Roorkee is a record of student's own work carried out by him under our guidance. The matter embodied in this dissertation has not been submitted for the award of any other degree or diploma.

He is further certified that he has worked for a period of 6 months from February 1977 to July 1977 for preparing dissertation for Master of Engineering Degree of this University.

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Contents

ABSTRACT

Nerve cells and their processes called neuron are considered to be the basic functional unit of the nervous system. Many types of models of varying complexities have been developed in the last three decades for getting the slow, excitatory and complex phenomena of neural neuron and its processes. In the present work, the neuron, its processes and also its important electrical characteristics are critically analysed and studied. The existing important electronic models of neuron are briefly examined. A new electronic model of neuron is developed which is having following merits :

(i) Linear integrated circuits are used for handling the physiological data more accurately and conveniently.

(ii) Use of IC's gives a very simple mathematical relationship between inputs and outputs.

(iii) Rational use of IC's has facilitated in the development of reliable, accurate, compact size, simple and inexpensive model of neuron.

(iv) The excitation and inhibition phenomena have been included.

(v) Several such type models can be used after interconnection to study the role of interconnected neuron.

(vi) It is possible to examine and observe electrical potential for various types of input and other conditions at every stage using IC's or recorders.

CHAPTER - I

INTRODUCTION

1.1 IMPORTANCE OF NEURAL MODELLING

The development of the models of biological systems are universal in the search of a consistent and instructive picture of nature. The models are in general synonymous analogs which are similar in functions but differ in structure and origin from the actual system.

When the governing emphasis being placed on the information processing aspect of nervous system, theoretical studies assume increasing importance. The use of models to help elucidate behaviour of the nervous system has expanded rapidly during the last two decades. The advances so far obtained in this field suggest that neural system modelling may be expected to exert increasing influence on the course of neurophysiological research. The utility of a model lies in its ability to focus disparate evidence and interpretations into one coherent view, parsimony of explanation often leads to revealing unity. Models are valuable to the extent that they raise new questions, suggest new relationships and lead to new experiments that might not otherwise have been considered. In most of the cases the models are predictive and new relevant properties are deducible from them. Model also suggests constraints existing in the system being modelled. Thus the model reveals, computes, extrapolates and predicts the new facts which accelerates the process of learning about the actual nervous system.

There are two distinct philosophies in the selection of parameter in neural modelling. In one, a very large number of neural properties of actual neurons are represented with high accuracy. In the other type, a more restricted set of properties is used, but the restrictions have been made on the basis of only a small set of assumptions as to the significant ones. Both types are having some advantages and disadvantages. Models of first type are more complex but more difficult to realize and are more costly. Models of the second type are more amenable to analysis but are in great danger of important omissions.

Once a model of neural system has been realized, there are three types of actions which are to be taken. The first, which is necessary, consists of preliminary validation by testing normal whole accuracy. This is done by matching the model behavior with actual physiological parameters of the neural system. Successive refinements of the model may then lead to convergence to an accurate and workable abstraction. Beyond the validity is tentatively established, one should attempt to discover new properties of the model, i.e. the operations not explicitly considered in the original design. Although, such "discovered" properties are implicit owing to the choice of parameters, it is not unlikely that all of them will have been foreseen. The third kind of valid consists of testing hypothesis and exploring their consequences more fully and essentially the first physiological experiment on the actual neural model.

Neural models have variety of forms, ranging from informal verbal models to highly abstract physical and mathematical constructs. Most of the neural models have been developed in the last three decades. All these modelling techniques have their advantages and disadvantages and their selection depends upon the requirement and objectives.

1.2 <u>BRIEF REVIEW OF THE PRESENT WORK</u>

The work reported in this dissertation deals with the analysis and modelling of neural system. The neural neural system is analysed for its important electrical characteristics. An electronic model has been developed using these electrical properties.

Chapter - II of the dissertation deals with the analysis of the nerve cell or neuron which is the basic functional unit of the nervous system. The anatomy of the neuron is given followed by the analysis of the processes occurring inside the cell. All the important electrical characteristics of the neuron are analysed and discussed which form the basis for the development of the model.

The IIIrd chapter deals with the existing models of the system. The models are critically examined.

Chapter IV deals with a new model of the neuron which has been developed by the author. The advantages of this model over the other existing ones are also given. The model has been constructed and tested for all the important electrical characteristics of the neuron. The potentials are examined and studied at

all the important points of the model. The model is tested for steady state and transient conditions. The results are reasonably good and shows the models behaviour very near to the physiological observations.

In the next chapter, the general conclusions are drawn about the existing models and also about new developed model. The influence of this study on the course of study of the neuro-physiologists and the bioengineers is also discussed. Some suggestions are given for the further work in this area.

In brief, it can be said that the actual neuron and its process are analysed and a new model is developed which is superior than the other existing ones and has some unique features. This work gives a positive influence in the modelling field of neurons.

CHAPTER - XI

ANALYSIS OF NERVOUS TISSUE

THE NERVE CELL

1. Structure : The basic structural element of the nervous system is the nerve cell or neuron [1] . The typical structure of a neuron can be :-

(1) Reception of stimulation

(2) Conduction of nerve impulses

(3) Transmission of nerve impulses to other cells.

Neurons vary greatly in size and structure. Some are 4 to 6 μ and others (e.g. cells of the cerebral cortex) are as large as 100 μ . The shape of neurons also varies. The most complex neurons are found in the cells of the cerebral cortex and cerebellum. This complexity of structure is attributed to the complexity of functions performed by these parts of the brain. The nerve cell and its various parts are shown in Fig.(2) [1] .

Each neuron consists of :-

(1) Dendrons and Dendrites

(2) Cell body or soma.

(3) Axon - Nissl's & Axon (or nerve fibre).

Synapse and Conduction in the Nervous System [2,3] : It has been discovered that there is a protoplasmic continuity between the nerve cells of the CNS or that they are structurally joined from each other. It has now been established that protoplasmic continuity between the processes of nerve cells

exists only in lower invertebrates in which the CNS has a neuropil structure.

In the higher invertebrates and in all vertebrates the nerve cells of the CNS are connected with one another only through synapses.

The axon of each neuron, in approaching other nerve cells, ramifies and forms numerous endings in the bodies of these cells and their dendrites. The dendrites are having numerous processes and their functions are the reception of impulses coming from other neuron at synapses and their conduction to the cell body of its own neuron. In the body and dendrites of a large motor nerve cell there are thousands of nerve endings (synapses) formed by the nerve processes of many other neurons. One nerve fibre can form as many as 10,000 synapses in many nerve cells [1] .

Synapses located on the body (soma) of a neuron are called axosomatic and those on the dendrites axodendritic. A synapse in the CNS, consists of three principal elements [2] :-

(i) Presynaptic membrane
(ii) Post-synaptic membrane
(iii) Synaptic cleft.

These elements are shown in Fig.(2).

(i) <u>Presynaptic membrane</u> : It is the membrane covering the nerve ending. The nerve ending is a peculiar neurosecretory apparatus, which secretes the mediator that produces a stimulating (excitatory) or inhibitory effect on the innervated cell. The mediators are highly active chemical compounds.

(ii) Postsynaptic membrane : The portion of the membrane of the innervated cell directly adjoining the nerve ending known as the postsynaptic membrane. The postsynaptic membrane differs in its properties from the membrane covering the remainder of the cell, the chief difference being that it possesses very high chemical sensitivity to the mediator and is insensitive to an electric current.

(iii) Synaptic cleft : This divides the presynaptic and postsynaptic membranes. This fissure is between 150 and 200 Å wide and is filled with intercellular fluid of a salinity close to that of blood plasma.

(B) Cell body or soma : The neuron soma is contained within a thin wall similar to that of an unmyelinated fibre. It receives the input from the dendritic network.

The motoneuron somas are physically located in the spinal cord, topologically opposed to the muscles they direct. Soma responds to the algebraic summation of incoming messages [8].

The soma performs a trophic function as regards their processes i.e. they regulate their metabolism and nutrition. As a result the separation of an axon from the body of the nerve cell leads to degeneration of its processes.

(C) Axon and Axon-Hillock : Axon is a long process whose function is to convey impulses from the cell-body to other cells or to peripheral organs. It is a feature that only one such process extends from the cell-body. The place where it projects from the body of the nerve cell is called the axon-hillock. Over the

first 50 to 100 microns of its length the axon has no medullary sheath, and that portion with the hillock at which it starts is called the <u>initial segment</u>. The special feature of this segment is its high excitability. Its stimulus threshold is one-third of that of other parts of the neuron [1].

The body and processes of the neuron are covered with a membrane that is selectively permeable <u>at rest to</u> K^+ ions and during excitation to Na^+ ions.

The membrane resting potential is approximately - 70 mV and its action potential about 110 mV with respect to the resting potential [1]. In warm blooded animals, action potential duration is 1 to 3 ms [1].

In a state of rest there is a difference in potential of the order of 60-80 mV between the outer surface of the cell and its protoplasm. This potential difference is commonly called the resting membrane potential. Its origin has been explained (theoretically as well as experimentally) by Hodgkin and Huxley (1952) [1]. According to their theory the bio-electric potentials are caused by unequal concentrations of K^+, Na^+ & Cl^- ions within the cell and outside it, and by the variable permeability of the surface of the membrane to them. The protoplasm of nerve and muscle cells contains between 30 and 50 times as many K^+ ions, 8 to 10 times fewer Na^+ ions and 50 times fewer Cl^- ions as does the extracellular fluid [1]. Quick levelling of the difference of concentration is hampered by the extremely thin plasmatic membrane covering living cells (100 Å).

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The body and processes of the neuron are covered with a membrane that is selectively permeable _at rest to_ K^+ ions and during excitation to Na^+ ions.

The membrane resting potential is approximately - 70 mV and its action potential about 120 mV with respect to the resting potential [1]. In warm blooded animals, action potential duration is 1 to 3 ms [2].

In a state of rest there is a difference in potential of the order of 60-90 mV between the outer surface of the cell and its protoplasm. This potential difference is commonly called the resting membrane potential. Its origin has been explained (theoretically as well as experimentally) by Hodgkin and Huxley (1952) [2]. According to their theory the bio-electric potentials are caused by unequal concentrations of K^+, Na^+ & Cl^- ions within the cell and outside it, and by the variable permeability of the surface of the membrane to them. The protoplasm of nerve and muscle cells contains between 20 and 50 times as many K^+ ions, 5 to 10 times fewer Na^+ ions and 50 times fewer Cl^- ions as does the extracellular fluid [1]. Quick levelling of the difference of concentration is hampered by the extremely thin plasmatic membrane covering living cells (100 A°).

The structure of this membrane is based on data obtained by electron microscopy, X-ray diffraction, and chemical analysis. It consists of a double layer of phospholipid molecules lined on the inside and on the outside with a layer of molecules of compound carbohydrates — mucopoly-saccharides. The structure is shown in Fig.(2). In the cell membrane there are minute channels or pores, a few A° in dia, through which molecules of water, ions and other substances pass in and out of the cell.

In the membrane are found various ions which lend a particular electric charge to the walls of its pores, thereby impeding or facilitating the passage of other ions.

It's supposed that the presence of dissociated phosphate and carboxyl groups is the reason why the membrane of nerve fibre is much less permeable to anions than to cations.

Permeability to different cations also varies and changes regularly in the different functional conditions of the tissue. At rest, the permeability of nerve fibre membrane to K^+ ions is between 20 and 100 times that to Na^+, whereas in the excited state, the ratio is reversed.

In a state of physiological rest the diffusion of positively charged K^+ ions from protoplasm to the external fluid lends a positive charge to the outer surface of the membrane and a negative charge to the inner one. Experiments have shown that the concentration gradient of K^+ ions is really the principal factor determining the value of the resting potential of the neuron [1].

Actually resting potential is 60 or 70 mV, but by Nernst's formula (Mathematical treatment) resting potential should be 90 mV. The reason is attributed to the Na^+ ions diffusing into protoplasm from the extracellular fluid giving rise to a resting potential. The diffusion is hampered by the low permeability of membrane to Na^+ at rest. Even then, in diffusing the membrane Na^+ ions transfer their positive charges into the protoplasm, which reduces the value of the resting potential produced by the diffusion of K^+ ions out of the cell.

2.1.2 <u>Action Potential</u> : If a sufficiently strong stimulus (for instance an electric shock) is applied to part of a nerve or muscle fibre, it will give rise to excitation, the main manifestations of which is a rapid variation of the membrane potential, which is known as the <u>action potential</u> [1]. It has been verified experimentally that the amplitude of the action - potential exceeds the value of the resting potential by 40 to 60 milli volts, as occurs due to the fact that the resting potential does not simply disappear with excitation, but that the potential difference is reversed, so that the outer surface of the membrane receives a charge which is electrically negative in relation to its inner side.

Fig. 4 shows an action potential registered in a skeletal muscle fibre by means of an intracellular electrode. In this case the difference in potential across the membrane at rest was 88 mV (i.e. the charge on the inner side was 88 mV).

Under the influence of an isolated stimulus (the moment of its application is indicated by the arrow) the difference in

potential on the membrane began to fall sharply, and was reduced to zero, after which it reappeared but with the opposite sign ; the inner side of the membrane became electrically positive in relation to its outer one. When the reversal of potential had reached 30 mV, a restorative process began by which the membrane potential reverted to its initial level.

Ascending and descending phases are distinguished on the curve of the action potential. Since the initial polarization of the membrane disappears in the ascending phase (a) its called the depolarization phase; corresponding the descending phase during which the membrane polarization reverts to the resting level, is known as the repolarization phase (b). The length of the action potential in nerve and skeletal muscle fibres varies between 0.1 and 5.0 milliseconds, during which repolarization phase is always longer than the depolarization [1]. Cooling of the fibre by 10°C makes the action potential approximately three times longer, especially its descending phase.

2.2.3 <u>After Potentials</u> : The action potential is followed by after potentials. After potentials may be negative or positive. The amplitude of either does not exceed several millivolts, while their duration varies between a few milliseconds and a hundred or more milliseconds [1]. After potentials of two types :-

(a) Negative after-potential.

(b) Positive after-potential.

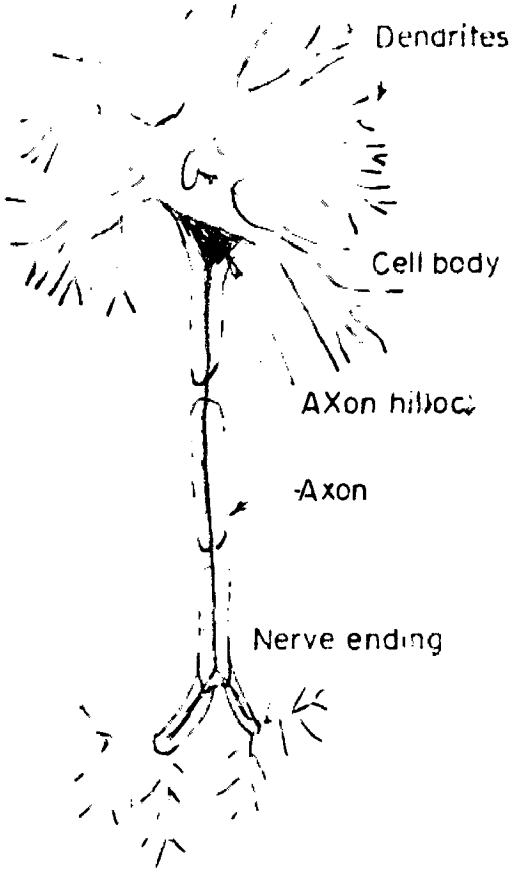


FIG.1 NEURON TREE.

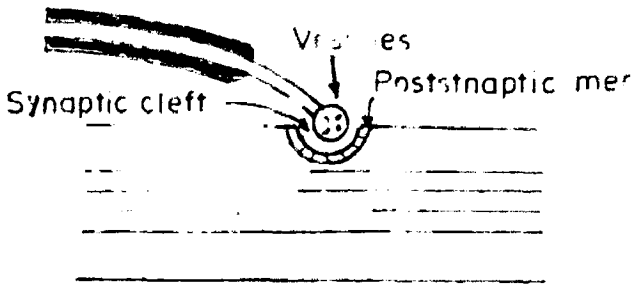


FIG.2

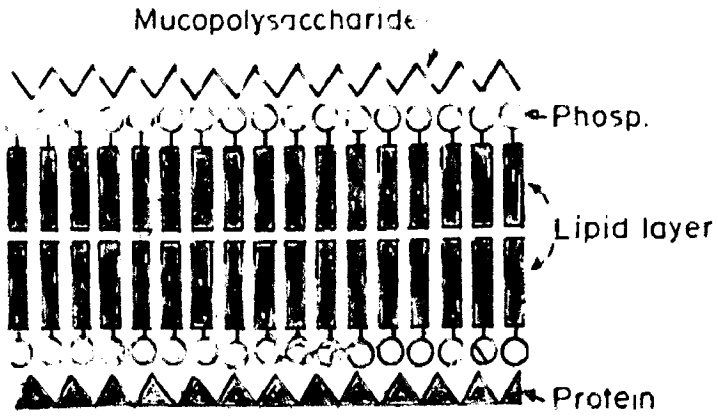


FIG.3 MOLECULAR STRUCTURE OF MEMBRAN.

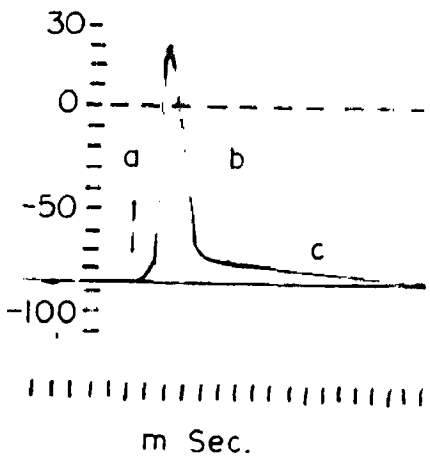


FIG.4 ACTION POTENTIAL OF A SKELTON MUSCLE FIBER

(a) <u>Relationship between action potential and negative after potential</u> :

This is illustrated by the example of the action potential of a skeletal muscle fibre which is shown in Fig.6 [8]. The repolarisation phase is divided into two parts of unequal duration. At first repolarisation of the membrane proceeds quickly, then slackens and stops and it is that moment that corresponds to the beginning of the negative after-potential (a). The membrane remains partly depolarised for a certain time and complete restoration to the initial potential of 90 mV occurs after approximately 15 milliseconds. Negative after potential is often called after depolarisation of the membrane.

(b) <u>Relationship between action potential and positive after potential</u> :

This is observed in unmyelinated giant axon of the squid. These fibres are chiefly found in the sympathetic nervous system. A myelinated fibre consists of an axis cylinder enclosed in a myelin sheath and a sheath of Schwann. The axis cylinder is covered with a plasma membrane, and contains axoplasm pierced by extremely thin neurofibrils (100 to 400 A° in diameter) between which lies a large number of mitochondria and microsomes. The diameter of nerve fibres varies between 0.5 and 20 micron (μ).

The myelin sheath and neurilemma, taken together, are approximately as thick as the axis cylinder itself. At intervals of 1.0 to 2.0 mm the myelin sheath is interrupted by annular constrictions ; the portions of the axis cylinder not covered by

the sheath (of a width not exceeding 2.0 μ) are known as Ranvier's nodes. Non-medullated nerve fibres have neither a myelin sheath nor nodes of Ranvier. Their axis-cylinder is covered only by a sheath of Schwann. Refer Fig.5.

The descending phase, refer Fig.6, of the action potential is transformed directly into a positive after potential whose amplitude reaches approximately 15 mV; only then does the membrane potential revert to the initial resting level.

In myelinated nerve fibres after changes of potential are more complex in character; a negative after potential is often replaced by a positive after potential.

(c) <u>Explanation of the action potentials and after-action potentials</u>:

The reason for the appearance of an action potential in nerve and muscle fibres is a change in the ion permeability of the membrane.

As has been said earlier, membrane permeability to potassium in a state of rest exceeds that to sodium. As a consequence the flow of positively charged potassium ions from the protoplasm to the surrounding fluid exceeds the contrary flow of sodium cations from the outside into the cell, so that at rest the outer side of the membrane is electrically positive to the inner one. Under the effect of a stimulus on the cell, membrane permeability to Na^+ ions increases markedly to a point where it is approximately ten times that to K^+ ions. The flow of positive sodium ions from the surrounding fluid into the

protoplasm increases begins to exceed the outflow of K^+ ions osmotically, which reverses the sign of the membrane charge, the outer surface becoming electrically negative to the inner surface. The charge is reflected as a dip of the action potential curve (repolarization phase).

The increase in the permeability to Na^+ ions continues for only a very short time and is followed by the appearance of a refractive process in the cell that leads to a new decrease in membrane permeability to Na^+ ions and an increase in that to K^+ ions.

The process leading to a fall in the cell permeability of the membrane is called inactivation by Hodgkin [1]. As a result of inactivation, the flow of positive Na^+ ions into the protoplasm is sharply reduced, while a simultaneous increase in K^+ permeability increases the flow of positive K^+ ions out of the protoplasm into the surrounding medium. As the process nears its completion, the outer surface again acquires a positive charge and the inner surface a negative one. The charge is reflected as a descending part of the action potential curve (repolarization phase).

After potential and ion kinetics the changes in membrane permeability to Na^+ and K^+ ions. For example the positive after-potential is due to the fact that membrane permeability to K^+ ions remains heightened for a time after termination of the action potential as compared with the initial level. On the other hand, an increase in the flow of K^+ ions

from the protoplasm leads to an increase in membrane potential i.e. to an after-hyperpolarisation of the membrane. Negative after-potential is clearly due to membrane permeability to Na^+ ions remaining increased for a time after termination of the action potential as compared with the initial level.

2.14 <u>Synaptic potentials</u> : The mechanism of synaptic transmission of impulses is based on the interaction of the mediator and the post-synaptic membrane.

<u>At rest</u> the mediator is contained in the synaptic vesicles which are distinctly seen in electron photomicrographs of nerve endings.

<u>During depolarisation</u> : of the presynaptic membrane these vesicles burst, releasing the mediator which flow through the membrane into the synaptic cleft.

The presence of a chemical link in the mechanism helps us to understand the two common properties of synapses :-

(i) The one way transmission of impulses across the synapse (in contrast to two way transmission in nerve fibres).

(ii) Synaptic delay.

<u>One-way transmission</u> is linked with the fact that the mediator secreted by the nerve ending stimulates the post-synaptic membrane of the muscle fibre but the action potential that arises in the muscle fibre, cannot stimulate the nerve endings and nerve fibres because of the presence of the synaptic cleft.

Synaptic delay is the delay in the transfer of impulses across a synapse. This is determined mainly by the time it takes the mediator to diffuse from the membrane of the nerve ending to that of the nerve fibre. In a myoneural jn synaptic delay lasts between 1 - 3 ms [1]. Synapses are distinguished as excitatory or inhibitory acc. to the effect produced [1].

Excitatory post synaptic potential (EPSP).

The mediator produced in the nerve endings of these synapses is freed from its bound state through the action of an incoming nerve impulse and is secreted into the synaptic cleft. Since the latter is very narrow (about 200 Å), the mediator quickly (within about 0.5 ms) diffuses to the post synaptic membrane and interacts with its structural components i.e. with definite protein lipoid compounds. This results in a considerable increase in the permeability of the post synaptic membrane to sodium & potassium ions, which is followed by its depolarization and the appearance of what is called the EPSP. As soon as this potential reaches the critical value a wave of excitation (an action potential or spike) arises in the cell. Since the membrane of the initial segment of the axon has the lowest critical level of depolarization, the action potential is generated first in that part of the neuron and spreads from there to both to the cell body and along the axon.

The nature of the excitatory mediators in the CNS is still uncertain. As regards certain excitatory synapses in the brain

and spinal cord it has been established that the mediator in them is acetylcholine. It is also known that the level of certain other highly active compounds (noradrenaline, serotonine) which are possibly also mediators, is increased in the tissues of the brain and spinal cord during intense excitation. The EPSP potential waveform is shown in Fig.7.

Inhibitory Postsynaptic Potentials (IPSP) :

It is now established that there are inhibitory neurons in the spinal cord and in different parts of the brain, in addition to excitatory neurons. The axons of these neurons form nerve endings in the bodies and dendrites of the excitatory cells, secreting a special inhibitory mediator whose nature is still uncertain (in the opinion of some researchers it is gamma aminobutyric acid). The nerve impulses generated by stimulation of inhibitory neurons do not differ from the action potentials of ordinary neurons, but an impulse arriving at the nerve ending of the former along the axon causes the secretion of a mediator which does not depolarise the postsynaptic membrane, but on the contrary hyper-polarises it. The hyper-polarisation is registered in the form of an electrically positive wave described as the IPSP as shown in Fig.8. The IPSP too can be summated spatially or in time, so that an increase in the strength of the stimuli inhibiting nerve centres leads to a rise in the inhibitory potential.

Interaction of EPSP & IPSP : In each nerve cell there are numerous excitatory and inhibitory synapses in close proximity to one another

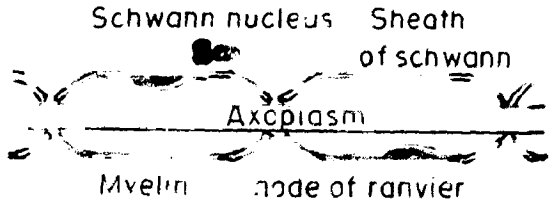


FIG. 5 MODULATED NERVE FIBER.

a – Positive after potential

FIG. 6

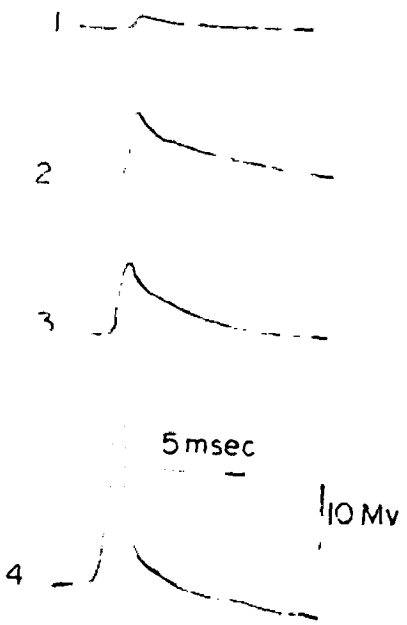
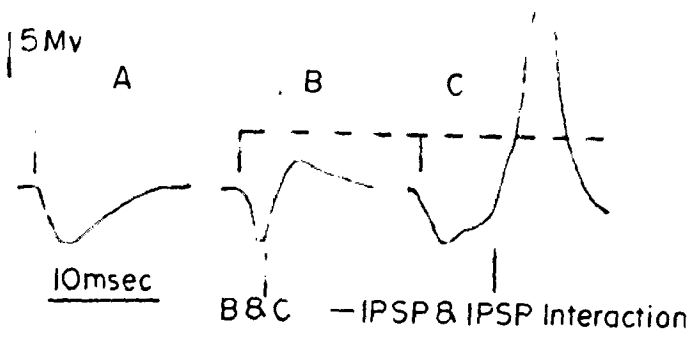


FIG. 7 GENERATION OF ACTION POTENTIAL WITH EPSP



A. IPSP

B. No action potential

C " "

FIG. 8

which provides favourable conditions for their interaction.

The IPSP weakens the EPSP and prevents the attainment of the critical level of depolarization required to trigger spreading excitation.

When IPSP is ahead EPSP in time , an action potential will not arise in the cell.

When IPSP is applied after EPSP has begun i.e. in the presence of rythmic discharges of impulses, then the impulses will come less frequently or will be terminated completely.

The degree of inhibition of a cell depends on the ratio of the magnitudes of the EPSP and IPSP and on the no. of synapses of both types involved in the reaction. If the EPSP is of suprathreshold value, while IPSP is low, then despite the weakening of the critical depolarization the action potential arises. With an increased IPSP, critical depolarization under the influence of EPSP is impossible.

2.2 ELECTRICAL CHARACTERISTICS OF NEURON

Till now the discussion was about the anatomy and physiology of the neuron. Some important electrical characteristics of the neuron are analysed in this section which are required to be included in the analog of the actual neuron.

2.2.1 Laws of Stimulation : Any agent that increases the Na^+ permeability of a membrane stimulates excitable tissue.

Neurons can be stimulated by electric current, mechanical action (pinching, striking or cutting), sudden chilling or heating, or by various acids, alkalis and concentrated salt solutions etc. [1].

Study of the action of electrical stimulation on excitable tissue is of great interest to physiologists because excitation is transmitted through the nerves and muscles by local current arising between the excited and resting portion of tissue. Also, stimulation by electric current has the full advantages :

(1) It can easily and accurately be dosed in strength, duration and steepness of increase.

(2) It does not damage living tissue while its action is quickly and completely reversible when it is strong enough to cause excitation.

To excite the neurons, electrical stimuli of various kinds is employed; rectangular, sinusoidal, linearly, and exponentially increasing currents, induction shocks, condenser discharges etc. as shown in Fig.9.

The mechanism by which electricity stimulates is identical in principle for all types of stimuli, but is most distinctly seen when direct current of rectangular waveform is used.

For a stimulus to cause excitation it must have sufficient strength, duration and steepness of increase.

2.2.3 Stimulus Threshold : The lowest strength of stimulation required to give rise to an action potential in the excitable tissue is called the threshold of stimulation. Stimuli below threshold strength are known as subthreshold, while those above are called

supra-threshold stimuli. When an electric current is used as a stimulus the threshold is expressed in units of current strength or voltage.

2.1.3 Utilization Time : The minimum time during which an electric current must act upon tissue to cause a wave of excitation is inversely proportional to its voltage and strength. If this minimum time (for eg., a [illegible] impulse) is plotted in ms along the abscissa the current voltage or strength along the ordinate, a strength - duration curve is obtained as shown in Fig.10 [1]. This curve has been studied by Lapicque. Study of the curve shows that a current below a definite minimum strength or voltage does not cause excitation, however long its excitation. Lapicque called the minimum strength (or voltage) of a current capable of producing and excitation the rheobase (the OA ordinate).

The minimum time (OB segment) that a current equal to the rheobase must act to induce an action Potential is designated by the term utilization time. The utilization time implies that further prolongation of the effect of current has no value or is useless in generating action potential. Intensification of the current leads to a shortening of the minimum time of stimulation, but not without limits. As can be seen from the graph, for a short duration stimuli, the strength duration curve becomes parallel to the axis of the ordinate, which means that they produce no excitation, however strong they may be. In practice its difficult to determine the utilization time (OB segment) as

the value of the rheobase undergoes continuous slight variation. Hence, Lapicque proposed measuring another conventional value, called Chronaxie. Chronaxie is the least time required for a current equal to double the rheobase (R) to produce excitation in a tissue. Utilization time and Chronaxie characterize the rate at which a stimulus causes excitation.

1.2.4 Accommodation and Adaptation [2] : The level of the threshold of nerve or muscle excitability depends not only on stimuli strength and duration but also on the steepness of its increase. The stimulus threshold is at its lowest value with rectangular current impulses characterized by maximum rapidity of increase in strength. If, stimuli increasing linearly or exponentially are used, then thresholds prove to increase in inverse proportion to the rate of increase in current strength.

When the steepness of the rise is reduced below a certain minimum, no action potential appears, no matter how great the final strength of the current. This is because of the fact that during the period of increase in stimulus strength, active changes occur in the tissue raising the threshold and interfering with stimulation. This phenomenon of adaptation of excitable tissue to a slowly increasing stimulus is known as accommodation. The higher the rate of accommodation, the more steeply the stimulus must increase so as not to lose its effect.

Accommodation develops not only during stimulation of neurons with an electric current but also during the application of mechanical and thermal stimuli, etc. For e.g., quick tapping of

a nerve with a rod causes excitation, whereas pressure slowly applied to the nerve does not. As nerve can be stimulated by very rapid chilling, whereas gradual chilling evokes no response.

In the lab., linearly or exponentially increasing currents are used to measure accommodation, the index of the rate of accommodation being the minimum rate of increase of the current (known as the minimum gradient or critical slope) at which the stimulus retains its capacity to evoke an action potential. Fig.11 gives the accommodation curves of a nerve fibre, measured by means of linearly increasing currents [1].

The inclination of the time lines to the abscissa corresponds to the rate of increase of the stimuli.

The rate of accommodation of various excitable formation varies widely. The highest is that of the motor neurons of warm blooded animals. Sensory fibres have a lower rate, while that of the fibres of heart muscle & of the smooth muscles of the intestines, stomach etc.(i.e. of formations tending to automatic activity) is very low.

2.2.6 <u>Membrane Potential and Membrane Pore Constant</u> : When an electric current is passed through a nerve or muscle fibre, there is a change in the membrane charge. In the region where positive pole (anode) is applied to the surface of the tissue the positive charge on the outside of the membrane increases i.e. hyperpolarisation takes place. When negative, the pole (cathode) is applied to the surface, the charge is reduced ie, depolarisation occurs.

The membrane potential of the nerve fibre rises and ceases gradually rather than instantaneously describing an exponential curve. This is because the surface membrane of a living cell has the properties of an electrical condenser (Chagovets) .

The plate of this tissue 'condenser' are the outer and inner surfaces of the membrane, while the dielectric is the layer of lipoids, which posses considerable resistance. Because of the presence of pores in the membrane, through which ions can pass, the resistance of this layer is not infinite, as it is in an ideal condenser. The surface of membrane of the cell is therefore similar to a condenser with a resistor connected in p parallel, through which leakage of charges can occur as shown in Fig. 11.

The rate at which the membrane potential changes when current is switched on off depends on the capacitance (c) and resistance (R) of the membrane. The product of RC is known as the membrane time constant. The lower the RC product quicker is the rise of potential at a given current strength, conversely a lower rate of potential increase corresponds to a larger value of RC. Changes in membrane potential not only occur directly at the points where the direct current cathode and anode are applied to the nerve fibre, but are also observed at a certain distance from the poles, though their value gradually diminishes the further the point is from cathode or anode. Such changes of potential near the poles are called electrotonic. Catelectrotonic changes around the cathode and anelectrotonic changes around the anode are distinguished. These changes in membrane potential have no connection with the active response of an excitable formation

to the current applied. They are of purely physical nature, and are therefore usually considered to be passive charges of potential. Active charges => active depolarization and hyperpolarization of the membrane occuring during conduction and caused by changes in the permeability to sodium and K^+ ions. Hence, a rise in membrane potential of the axon (passive hyperpolarization) is not accompanied with any change in the ion permeability of the membrane even when a steady current is applied. Hence when a depolarizing current is passed an excitation occurs at the axon. A fall in membrane potential at the cathode (passive depolarization) results in an increase in permeability to Na^+ ions and then a slow increase in permeability to K^+ ions as shown in Fig.29 [1].

The first sign of a slight increase in sodium permeability are noted with a current strength used so to say of the threshold value. As the current increases in strength and approaches the threshold, sodium permeability rises further. But as positively charged sodium ions begin to enter the protoplasm under the influence of this charge, depolarization of the membrane increases, which leads to another considerable rise in permeability to sodium and consequently to further depolarization, which in turn again increases sodium permeability etc.

This ever growing cycle process is called regenerative depolarization and can be represented as follows.

One of the most acceptable reasons for the increase in Na^+ permeability during depolarization is that the pores through

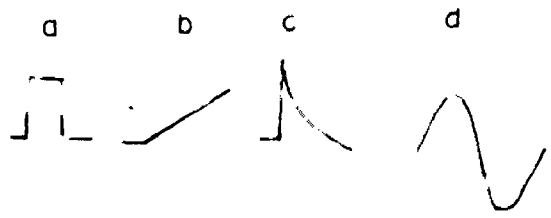


FIG.9 ELECT STIMULI OF VARIOUS SHAPE.

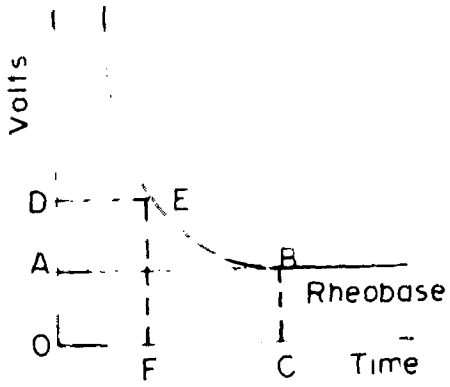


FIG.10 A STRENGTH DURATION CURVE.

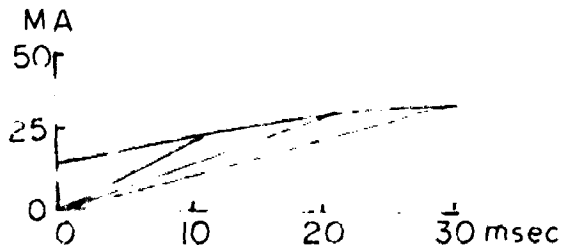


FIG.11 Accomodation curve of a nerve fiber.

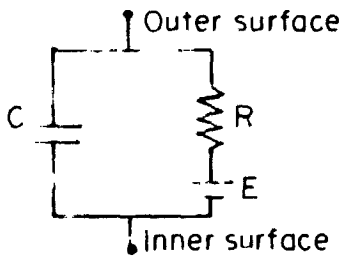


FIG.12 Membrane representation.

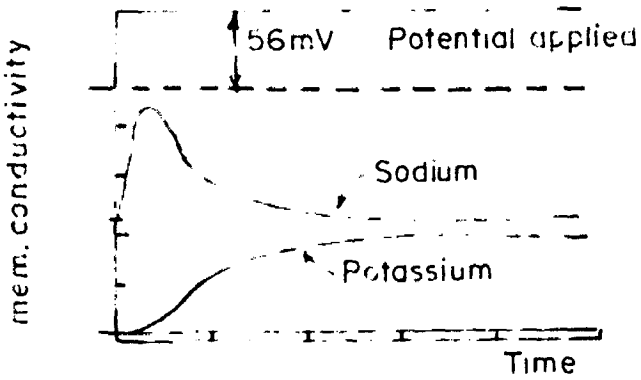


FIG.13 Change in sodium and potassium permeability.

which radial ions can diffuse into the cell are closed (blocked) in a state of rest by larger cation ions, while the difference in potential across the membrane (resting potential) retains the ions in the pores. Like a chemical depolarization the membrane, the Ca° ions pass out of the pores and so make way for Na° ions.

The increased Na° permeability lasts for only tenths of a millisecond. If the neuron can again be polarized again by increasing depolarization, because of the development of a positively active process in the membrane known as inactivation. Inactivation of Na° permeability leads to suppression of depolarization and begins off repolarization during conduction [2] .

The increase in potassium permeability during depolarization occurs with a longer latent period than that Na° permeability, potassium permeability grows parallel with the inactivation of the latter, thus promoting repolarization of the membrane. Registration of changes in the membrane potential of nerve fibre at the cathode has shown that an action potential arises at the moment that depolarization reaches a critical level, which depends not on the character of the stimulus applied, as the period of the electrical one. but on the properties of the membrane itself Fig.24. shows curves of the changes in membrane potential of a nerve fibre under the influence of (1) prolonged (A) (11) short (B) and (C) stimuli of variable strength .

The action potential arises in all cases at the moment the resting potential drops from 70 mV to the critical level of 50 mV. The difference lies in the rate at which the depolarization

takes place. With a weak current, depolarization of the membrane develops slowly and for the action potential to appear the stimulus has to be of longer duration. With a rise in current strength, the rate of depolarization increases and the minimum time of stimulus action correspondingly shortens. From this, it follows that the minimum stimulation time is the period required and sufficient for depolarization of the membrane at the cathode to reach the critical level. The faster the rate of depolarization at a given current the shorter the utilization time and vice versa. The rate, however, depends, first on the membrane time constant, RC and second on the rate of increase in sodium permeability.

Hence the utilization ~~time of stimulation is determined~~ both by the passive electrical properties of the membrane its capacitance and resistance and by the active properties of the mechanism of change in its ion permeability [2].

[illegible] <u>Local Response</u> : An action potential capable of spreading along a nerve or muscle fibre is not the only form of response to stimulation. A local, unspreading response can be had, in any excitable formation, by application of stimuli of near-threshold strength. The passage of an electric current through an excitable tissue primarily causes a change in membrane potential. With a weak sub threshold current, the changes of potential at the cathode are brought about by purely physical (passive) changes in the polarization of the membrane.

As current strength increases and approaches the threshold, to passive depolarization at the cathode there is added an

cells exhausted depolarisation in the form of a so-called local response. The local response varies in its properties from the cell potential as follows:-

(1) It has no distinct threshold.

(2) It is not governed by the all-or-none law.

(3) The amplitude of the local response depends on the strength of the current applied. On stronger the stimulus, the greater is the local response.

(4) During local response, there conductivity is increased.

The local response is brought by an increase in the cell permeability of the membrane. With the appearance of a local response the increase in cell permeability is slight and increase does not proceed to cell potential. It is not until the critical level of depolarisation is reached that the local response grows into an cell potential. So run to the chain of phenomena is as follows :-

Passive depolarisation of the membrane ⟶ increase in cell permeability ⟶ increase in the flow of cell ions across the membrane into the fibre ⟶ active depolarisation of the membrane (local response and cell potential). Refer fig (15)

S.S.7 All or None Law :- This law was established as a result of study of the relationship of stimulation effects to stimulus strength. According to this law individual stimulation produces no contraction while threshold stimuli gradually produces maximum contraction magnified by a further increase in stimulus strength. When a nerve fibre is subject to small doses of caffeine, procaine,

Urethane, there is not only a reduction in the amplitude of the action potential but also a breach of the all-or-none law which is expressed in the sharp response to stimulation being a function intermediate between a local response and a normal action potential.

Thus, it's concluded that the all-or-none law should be regarded merely as a rule characterizing the feature peculiar to the type of an action potential set by an axon as an electric conductor.

2.2.0 Excitability (Refractory period) [2] :

Excitability is the capacity of tissue to respond to stimulation and consequently to generate an action potential. The threshold strength or voltage of a stimulating current is usually taken as its measure. The lower the stimulus threshold the higher is the excitability of a tissue and vice-versa. The appearance of an action potential is accompanied with a sudden change in the excitability of the tissue. To discuss this, consider the above electrical circuit applied to a nerve of cortex to intervals and the action potential is registered as shown in Fig.2 [1]. The curves obtained have revealed important facts.

2.3.0 The Refractory period :

The period in which the spike appears and develops corresponds to the complete lack of excitability known as the absolute refractory state when another spike cannot be aroused

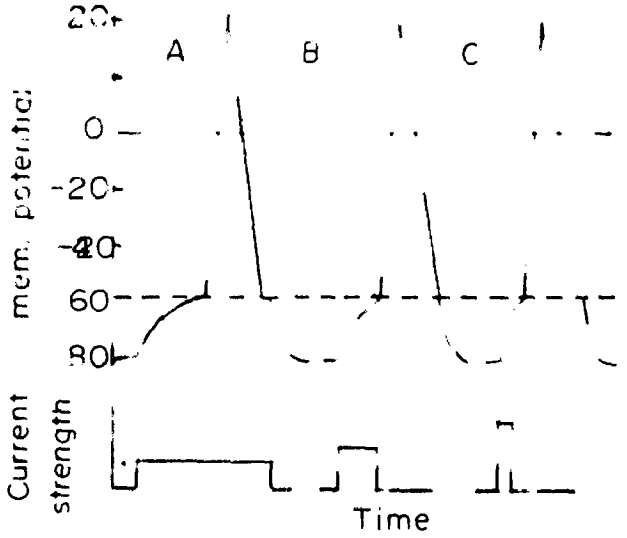


FIG.14 Change in the membrane potential.

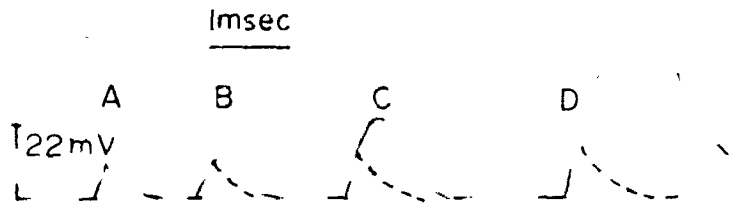


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FIG. Local response of nerve fiber.

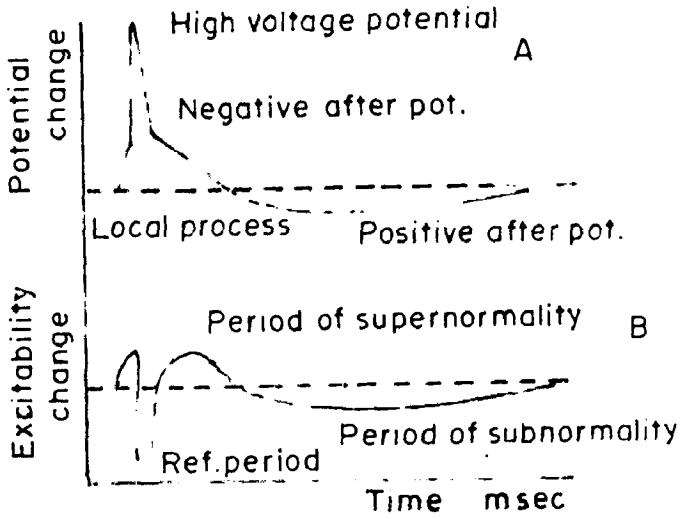


FIG.16 Change in excitability of nerve fiber

by a second stimulus, however strong. The duration of absolute refractory period varies within wide limits with various excitable tissues. In the quick-conducting nerve fibres of warm blooded animals it lasts about 0.5 ms. In the fibres of heart muscle characterized by a very long plate-shaped action potential the refractory phase continues for some 200 to 300 ms. [2].

3.3 <u>Relative Refractory Period</u> : The absolute refractory phase is followed by relative refractory phase which lasts for four to eight ms in nerve fibres during which time excitability gradually reverts to the initial level prevailing before the first stimulation. In the relative refractory period the fibre is capable of responding to a strong stimulus but the amplitude of the action potential is much reduced. The amplitude of the spike induced by the second stimulus increases only when the interval between consecutive stimuli is lengthened.

Acc. to Hodgkin & Huxley's ion-theory [1], the abs. refractory state is effected by changes in membrane properties. The membrane loses its capacity to react to a stimulus with an increase in sodium permeability and at the same time its permeability to potassium ions is heightened. Both processes interfere with the appearance of an action potential in response to a new stimulation. This refractory phase is very prolonged when fibres are cooled and hence its supposed that chemical processes of some kind underlie these changes in the ion permeability of the membrane. The relative refractory phase is replaced by one of supernormality i.e. of increased excitability, the moment of development of which

coincides in time with the period of after depolarization (negative after-potential) following the spike potential. The after-discharge is followed by a phase of subnormal excitability corresponding to a positive after-potential [2].

2.2.3 Spatial Summation : This was first described by Lorente (1933) [2]. It occurs in that a combination of two or more stimulations of peripheral receptors or afferent nerves excites a motor, whereas each taken separately is not sufficient to elicit the reaction. The types of summation are known as

(a) Spatial (successive)

(b) Central.

(a) Spatial Summation : In the interval of impulses arising in a nerve cell after another of these intervals along the same afferent nerve fibre.

It can be induced easily by applying a series of rhythmic stimuli to an afferent nerve or to the receptive field of a reflex.

If each of the stimuli is strong enough to elicit a reflex, then rhythmic application will increase it. If the strength of the stimulus is calculated as not to cause a reflex. Like acting alone, the reflex can be elicited by a succession of them. Some reflexes can never be triggered by a single stimulus, however strong, acting on the receptors.

(b) Central Summation occurs when two or more stimuli are acting simultaneously on different receptors belonging to the same receptive field. For eg, the scratching reflex in a dog can be had by simultaneous application of two sub-threshold stimuli to

two areas of the skin lying 10 cm apart but within the limits of the receptive fil of the reflex [1]. Either of these stimuli acting alone will not induce the scratching reflex, but in combination they do.

The summation of excitation in nerve centre occurs as follows. An action potential arises in a neuron when depolarization of the postsynaptic membrane of the nerve cell reaches a definite critical level and is brought about by the influence of the exciting mediator secreted by the nerve ending. The portion of mediator released by each nerve ending in response to an impulse, however is very small, so that the EPSP arising in a synapse is only between 1/20 or 1/8 of the threshold value [1].

The critical depolarization required to give rise to a spreading excitation is possible either upon simultaneous stimulation of many synapses located in the same cell or upon the arrival at one synapse of a series of impulses following one another at short intervals. In either case post synaptic potentials are added. The difference is that with simultaneous excitation of several neighbouring synapses the potentials are summed up spatially whereas with consecutive stimulation they are summed up in time.

2.3.3 <u>The Response of the Neuron</u>: The neuron operates with a threshold of about −70 mV. When the inside at any pt becomes more than this value the breakdown is triggered. The membrane becomes permeable to sodium ions for 1 msec. typically (for some neurons its also 2-3 m sec); as the ions + enter the fibre, the voltage

increases to approx + 30 V. After the 1 m sec. interval there is an additional 1 m sec. (this value too varies) refractory interval during which the membrane becomes and relatively good insulator again. Because the disturbance is 2 m sec. wide, the maximum possible pulse frequency is 500 Hz [2] .

CHAPTER - III

REVIEW OF MATHEMATICAL MODELLING

3.1 INTRODUCTION

Human knowledge is the basis of the entire analytical understanding of the central nervous system. In this knowledge the single nerve cells and their process together into a network are considered as the basic functional unit involved in the functioning of the nervous system. Many models of mathematical and electronic or electrical types of varying complexities have been developed in the past for understanding the process of neuron [3-11]

Mathematical models are based on the concept of variables or states which specify the state of the system and which mathematically are dependent variables of a set of differential equations. In most of them the non-linear differential equations are used which cannot be solved analytically but requires the use of numerical methods of computation. Also some simulations are done. So the mathematical models have utility in limited domain. Many mathematical models have been developed but these models do not develop an insight into the nerve cells mechanism.

Electronic models can simulate continuous-variable non-linear operations very accurately and economically. Providing real time signals that may be observed while experimental conditions are manipulated, they permit a rapid and efficient kind of observer control and interaction not followed by other techniques. There are

considerable advantages of direct observations of wave forms, phase relationship, modulation and time-dependent interaction while stimuli and model parameters are changed. Analog computer models have advantages similar to those of electronic models, but tend to be slow and cumbersome. Both have advantage over mathematical models as they do not compel the over simplifications of the actual system.

3.2 ELECTRONIC MODELS OF NEURON

A good number of the electrical and electronic models have been devised in the past. The following important models are critically examined:-

3.2.1 Hodgkin - Huxley's model
3.2.2 Neuronal membrane model by Lewis.
3.2.3 NEUROMIME analog by G. Roy
3.2.4 R-C and R-L-C analog model's of nerve fibre.
3.2.5 Lewis's model using [illegible] networks.
3.2.6 Neural model based upon double energy storage system.
3.2.7 Model's based upon high-pass and low-pass networks.
3.2.8 Electronic model by Harmon.
3.2.9 Flexible analog by French and Stein.
3.2.10 Dendritic compartment model of neuron.
3.2.11 Electronic model for impulse transmission by Choudhury et.al.

3.2.1 Hodgkin - Huxley model [3-5] : Hodgkin and Huxley proposed a mathematical model for squid nerve to meet the experimental results

of voltage. According to this model, the membrane current could be separated into ionic currents with conductance parameters which are both functions of time and voltage. The model is shown in Fig.(17)..

Here g_{Na} and g_K are the conductances of sodium and potassium and dependent on membrane voltage and time, g_L is the leakage conductance and independent of voltage and time. These three ionic components are in parallel. C_M is the membrane capacitance, E_K, E_L and E_{Na} are the constant voltages. Total membrane current, I, consists of capacitive and ion current and is given as

$$I = C_M \frac{dV}{dt} + I_i$$

where I_i = ionic current

V = displacement of membrane potential from its resting value.

t = time

Ionic current is given as

$$I_i = I_{Na} + I_K + I_L$$

where I_{Na} = Sodium ionic current

I_K = Potassium ionic current

I_L = Leak current.

The values of individual ionic currents are given as,

$$I_{Na} = g_{Na} (E - E_{Na})$$

$$I_K = g_K (E - E_K)$$

$$I_L = g_L (E - E_L)$$

where E_{Na} = Equilibrium potential for sodium.

E_K = Equilibrium potential for potassium.

E = The potential at which leakage current due to chloride and ions is zero.

g_K is given by Hodgkin and Huxley as $g_K = \bar{g}_K n^4$

where n = dimensional variable having a value between 0 and 1.

$\bar{g}_K$ = constant.

The sodium conductance, g_{Na}, is

$$g_{Na} = m^3 h \bar{g}_{Na}$$

$$\frac{dm}{dt} = \alpha_m (1 - m) - \beta_m m$$

$$\frac{dh}{dt} = \alpha_h (1 - h) - \beta_h h$$

where $\bar{g}_{Na}$ is a constant.

α, β are functions of voltage but not of time.

From this model we can gather the foll features :-

(1) Permeability appears to depend on membrane potential and not on membrane current.

(2) At fixed depolarisation of sodium current follows a time course whose form is independent of current through membrane.

(3) If Na concentration is such that $E_{Na} < E$, Na current is inward. If $E > E_{Na}$, the current changes in sign but follows same time course.

3.2.8 <u>Neuronal membrane model by Lewis</u> [4]: Lewis's model consists of seven parallel circuits and includes the synaptic membrane analogs. The entire model may be considered to be a composite of a patch of electrically excitable membrane contiguous with a patch of subsynaptic membrane. Five conductances out of six are constant and they undergo transient change owing to either to change in synaptic inputs or to change in transmembrane potential (V_m). The current through each conductance is product of time varying conductance itself and the time-varying voltage across it. Fig.(23) illustrates the operation of simulated synaptic conductance. In case of synaptic conductance, Fig.23(b) a presynaptic spike is transformed into a decaying exponential by means of a RC filter. The exponential represents the time course of synaptic conductances. The multiplier circuit produces a current proportional to product of conductance and net voltage ($V_m - V_r$) across it.

3.2.9 <u>A simple electronic analog of the squid axon membrane — The NEUROFET</u>:

In this paper a simple electronic circuit is proposed as an analog of the excitable membrane. It is based on the H-H model. The simulated potassium and sodium conductances are reproduced satisfactorily and the electronic action potentials are very similar to the experimentally recorded ones. Since this electric analog contains only a few electronic elements, it is small and inexpensive to build. The simplicity of the ckt makes it an ideal unit to build complex neuron networks.

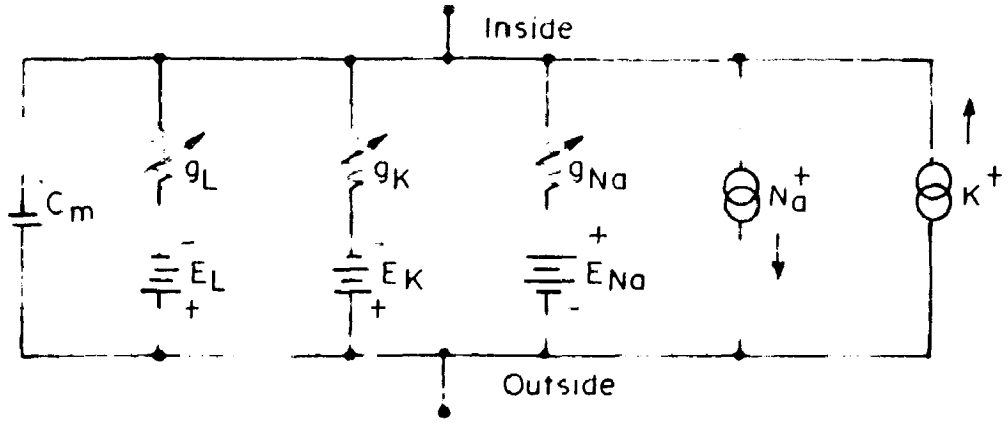
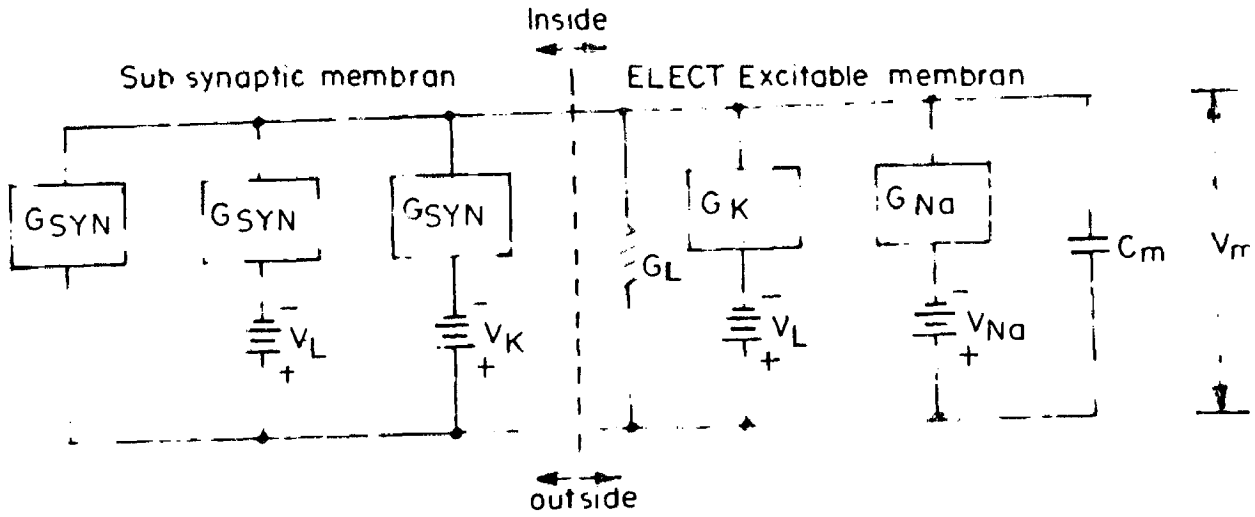


FIG.17 HODGKIN AND HUXLEY'S MODEL.



(a) 6 PARALLEL ELECTRONICS CKT. SIMULATED BOTH BY SYNAPTIC & ELECTRICALLY EXCITABLE MEMBRANE

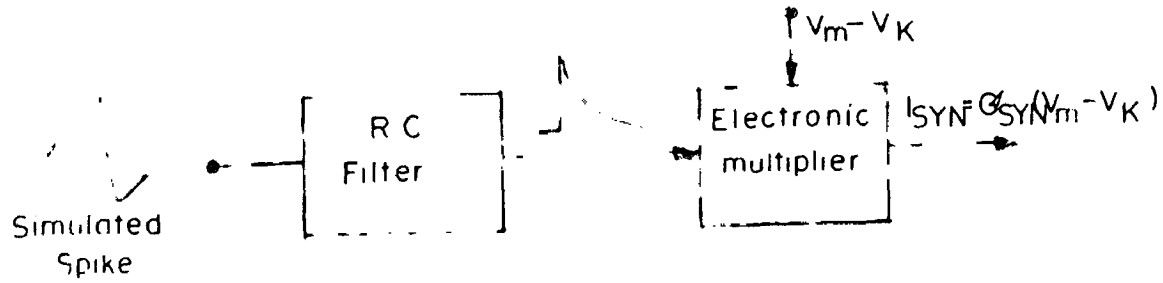
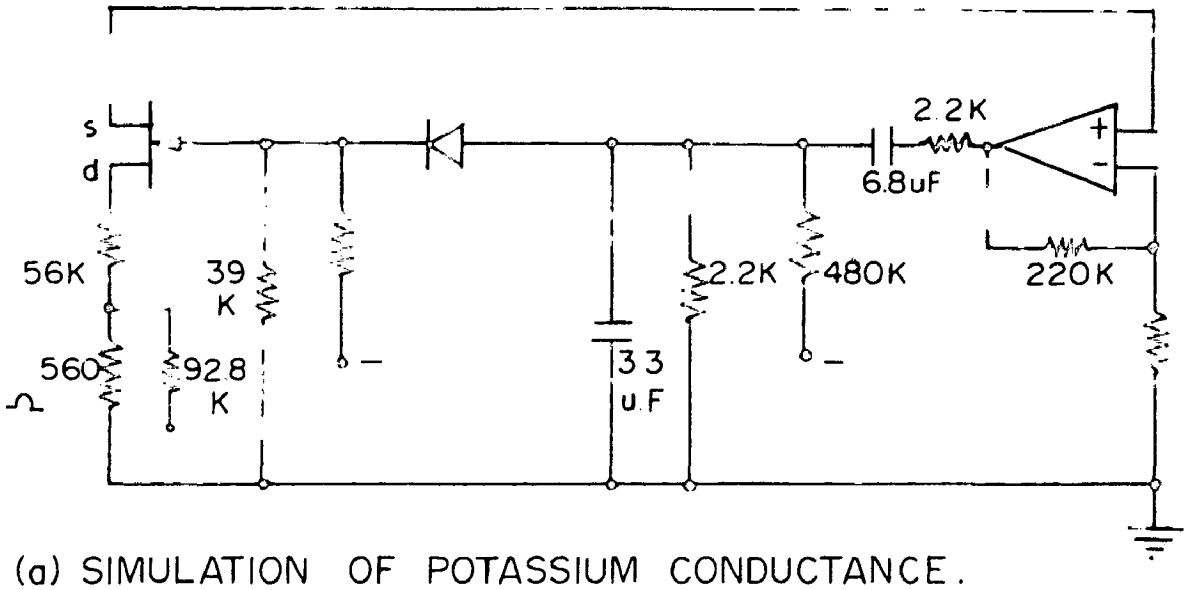


FIG 18(b) NEURONAL MEMBRANE MODEL

O. Roy (19) found that FET is the ideal electronic element to simulate the axon membrane conductances. The experimental data of H-H show that sodium and potassium conductances have very low values in their resting state. When an external potential is applied across the membrane, both conductances are increased; when the applied potential is sufficiently large, they reach a saturation value beyond which they remain constant. Also, the conductances have a slow time dependence.

In order to simulate the characteristics of these conductances, the foll. equivalences are introduced: the transconductance g_{ds} represents either g_{Na} or g_K. One FET is used for g_K and one for g_{Na}. The voltage across the axon membrane is represented by the drain-source voltage V_{ds} and the membrane current is represented by the drain-source current I_{ds}. At first, a negative bias on the gate of each FET was established to bring g_{ds} to a low value corresponding to that of g_K and g_{Na} in their resting state. Afterwards, the drain-source voltage V_{ds} is fed back via an intervening ckt to the gate, in order to provide an appropriate voltage dependence of the conductance g_{ds}. This feedback ckt will modify the value of the conductances g_{ds} when a voltage V_{ds} is applied and their change is made time-dependent with the introduction of an RC ckt in the feedback path. An amplifier is used to isolate the FET from the ckt determining the time-dependence of g_{ds}. This amplifier is also used at the same time to increase the low V_{ds} voltage to a larger value in order to obtain the required change in g_{ds}. The basic ckt to simulate potassium and sodium conductances is below.



(a) SIMULATION OF POTASSIUM CONDUCTANCE.

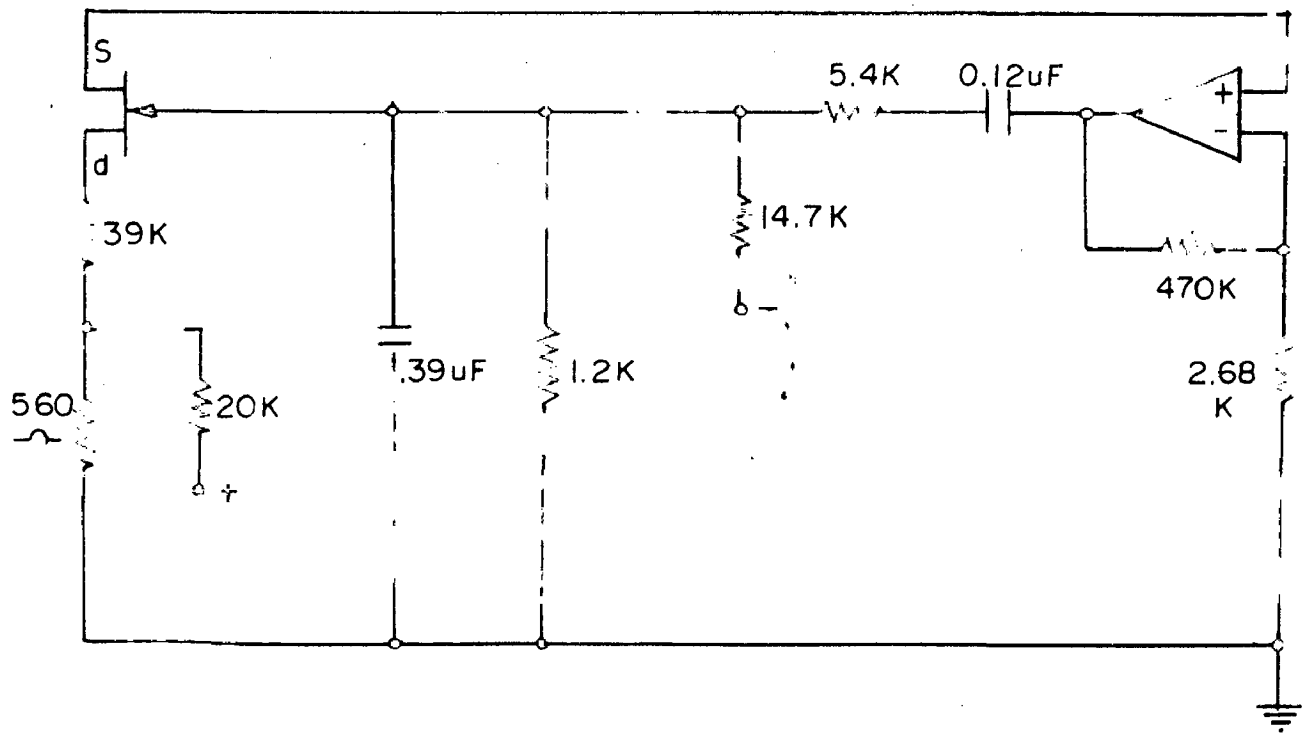


FIG.19(b) SIMULATION OF SODIUM CONDUCTANCE.

The -ve biases are adjusted so that the diode is non-conducting when $V_{in} = 0$. When a source voltage V_{in} is applied, the voltage on the capacitor (2.5 µF) becomes less negative. This makes the diode conducting and brings a delayed rise in the gate voltage. This delay can be adjusted by varying the two -ve biases on the diode. A coupling capacitor 0.5 µF was added to cut the dc biases from the source terminal of the FET. It has the effect of bringing the conductance back to its initial value when a step-voltage V_{in} is maintained too long. This is called a slow-inactivation of the K^{+} conductance.

To reproduce the Na^{+} conductance, a similar ckt is used but the diode is removed because the initial delay is negligible on the expt. curves for the Na^{+} conductances. The time constant for the rise of gds is made more rapid and coupling cap (0.12 µF) is much smaller in order to provide a faster inactivation for the Na^{+} conductance in accordance with the expt. data.

1.2.4 R-C and R-L-C models of fibres : [2,6]

This type of models represents the equivalent of axons ~~represents the equivalent~~ of axon or nerve fibres by R-C or R-L-C network. The equivalent R-C analog of axon is shown in Fig.(23). These models are like the transmission line equivalent of power system. The resistance and capacitance parameters are taken distributed along the length. The voltages at the different points of equivalent model are calculated by writing the voltage

and current differential equations and then by finding out their solutions by using transforms. The fibre section is assumed to uniform throughout. The R-L-C model is claimed to be superior than R-C model due to :-

(1) The actual phenomena is considered.

(2) The realistic waveform may be considered.

.2.5 Lewis's Model's Using Ballistic Potentials [4,8]:

Lewis gave a new approach to the study of neural systems. The approach is based on the fact that the neuron is functionally much more complex than as thought of in the classical view where the synaptic region was considered to be coupled directly to a spike or impulse-generating region.

The input to a synapse is an impulse or series of impulses originating in presynaptic neuron. These impulses are transmitted intercellularly. They induce a change in the potential across the synaptic membrane of post synaptic neuron. The presynaptic potential has a duration of 1 ms and the post-synaptic potential has duration of 40 ms or more. Thus, a single, sharp, presynaptic spike induces a slowly varying, long lasting post-synaptic potential. This potential is often called ballistic potential and its formation is not completely understood.

In simulating the ballistic response Lewis assumes 3 parameters :-

(a) Rise time

(b) Fall time

(c) Maximum amplitude.

A unilateral network is required for independently-controllable rise and fall time. A single R-C realisation of a ballistic network is shown in Fig.21(a).

The functional power of neurons lies not in their ability to integrate many incoming spikes from an axon but from many axons. Thus, the neuron should respond to a group of series of spikes. It is a well established fact that a single neuron responds differently to different input frequencies, and it is quite possible that it can also differentiate between varied pulse patterns. Two mechanisms are thus important in this respect.

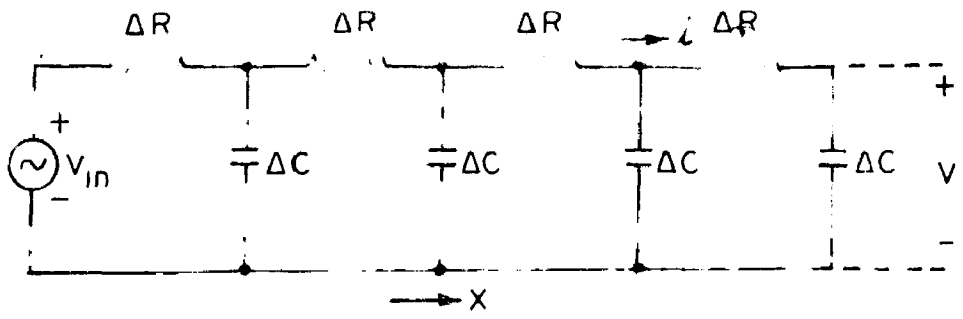
(1) Facilitation

(2) Antifacilitation

<u>Facilitation</u> : Refer Fig.21(b). The first impulse conditions the synapse in such a way as to enhance or facilitate subsequent responses.

<u>Antifacilitation</u> : Refer Fig.21(c). The first spike reduces or antifacilitates the response.

<u>Facilitating network</u> : Refer Fig.21(d). The input pulse is applied simultaneously to base and collector circuits of the transistor Q. Initially, the voltage at collector is V_c. At the first pulse, a positive going pulse of amplitude V_c appears at the collector. This is applied to the output network and results in a ballistic potential whose amplitude is proportional to V_c. The first pulse also leave a residual voltage in the collector-bias network which adds to V_c. Depending on the compt. values in the network, the



(a) RC CABLE MODEL

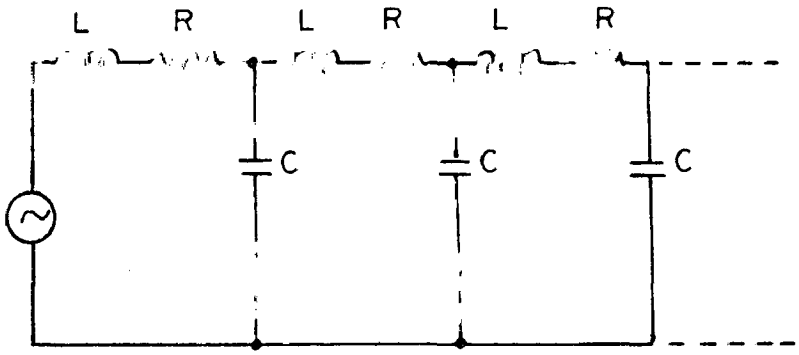
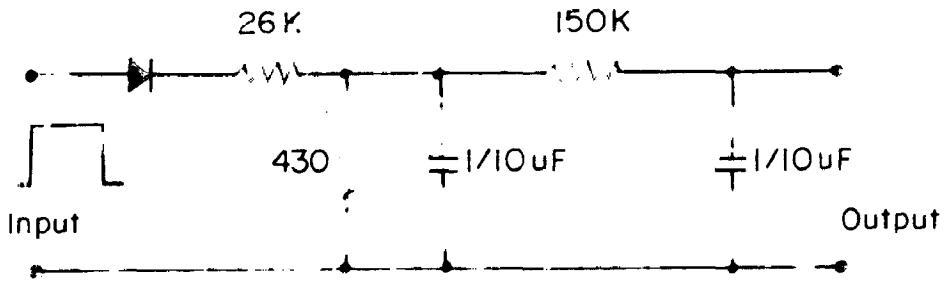


FIG.20(b) RLC NETWORK.



(a) SIMPLE RC BALLISTIC NETWORK.

(b) FACILITATION.

FIG.21(c) ANTI FACILITATION.

added bias may develop rapidly (in a few u s) or slowly(upto 100 ms). It cannot decay more rapidly than it develops.

Analysis : Let $\Delta V(t)$ = residual added collector bias. For subsequent input pulse, the amplitude of the pulse applied to the network is = $V_o + \Delta V(t)$ subsequent ballistic potential is proportional to $[V_o + \Delta V(t)]$. The rise and fall times of this ballistic potential are completely independent of collector and bias network.

The rise time of the added bias is determined by R_1 and C_3 and $(R_1 + R_2)$ and the fall time is determined by C_1 & C_2 in series with R_3. After first pulse the collector bias V_c is ;

$$V_c = V_{in} (1 - e^{-t/\tau 1}) (e^{-t/\tau 2}) + V_o.$$

where V_{in} = amplitude of input pulse.

and $\tau_1 = R_1 C_1$ and $\tau_2 = R_3 (C_1 + C_2)$.

Antiparalyzing network : Refer Fig.11(c).

In the absence of an input pulse the voltage at point 1,(V_1) is zero. During applied pulse, V_1 is expressed as ;

$$V_1 = (V_{in} - V_{ext}) e^{-t/\tau 1} = (V_{in} - V_c) e^{-t/\tau 1}$$

where V_{in} = input pulse amplitude

V_{ext} = V_c = residual voltage across C_1 and

τ_1 = $R_1 C$.

Thus, a +ve pulse at input results in a +ve pulse at pt (1) of amplitude V_1 where

$$V_1 \propto V_{in} \quad \text{and}$$

V_{in} is diminished by antifacilitating voltage V_{C_1}. The time course of V_{C_1} is thus the time course of antifacilitatio may be written :

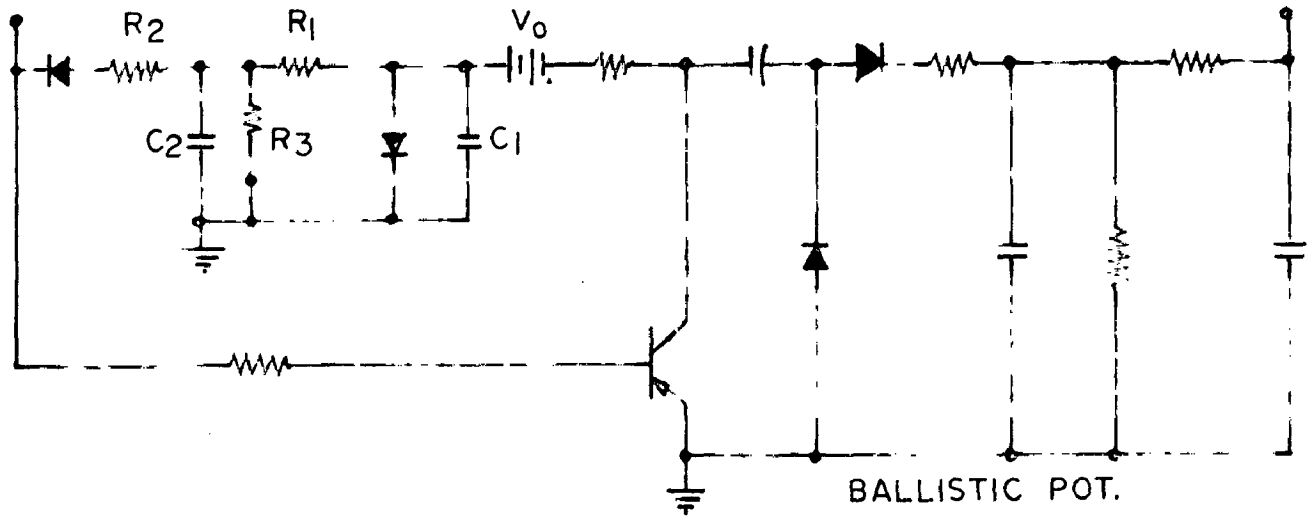
$$V_{C_1} = V_1 (1 - e^{-t/\Gamma_1}) e^{-t/\Gamma_2} \quad \text{where}$$

$$\Gamma_1 = R_2 C_1 \quad \text{and} \quad \Gamma_2 = R_1 C_1$$

In the network Γ_1 & Γ_2 are varied independently of each other Emitter follower can be used to isolate the final output from any moderate load. In complete cone analog, the outputs from these networks will represent positive (inhibiting) and negative (excitatory) excursions in the cone-membrane potential. It is applied either directly or through a local response locus to the spike initiator.

<u>After effects</u> :<u>Rebound and Decreased excitability</u> :-

Many neurons exhibit after effects of several forms. Rebound effects An inhibited neurons when inhibiting stimulus was ceased, was found to fire spontaneously. This implide that there was a rebound or negative, after effects. It may cease firing and go into a state of subnormal and in fact, it may oscillate back and forth between supernormal and sub-normal states for several cycles.



(d) FACILITATION NETWORK.

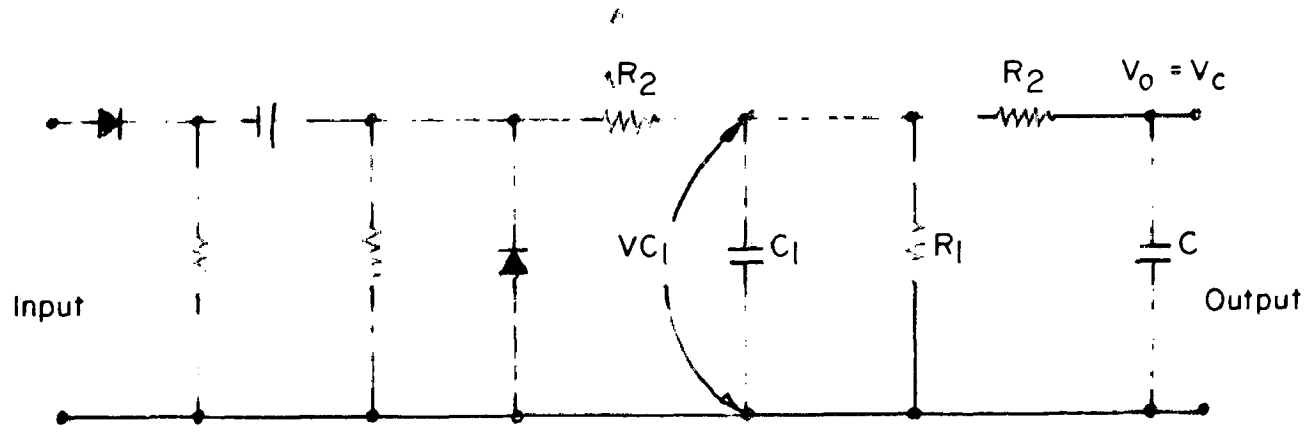


FIG. 21(e) ANTI FACILITATION NETWORK.

<u>Depressed excitability effect</u> :

In a similar manner as excited neuron, an excitation of prolonged excitation may go through a period of depressed excitability.

The origin of rebound phenomenon is not well established, it may be represented by rebound in either the synaptic region or all over same region. The networks of ~~Fig.(6) and Fig.(7) exhibit,~~ this type of behaviour current are obtained.

5) <u>Model based on double energy storage element system</u> :

Circuits containing two energy storage elements have poles separated widely enough so that the transient response can be approximated by treating them as two isolated single-energy circuits. Its essential that the continuity across the boundary between two individual response curve and they must satisfy the original system.

The system response into two time regions depends upon the physical characteristics of the energy storage elements. Refer Fig.11(a). Let a voltage step of height V_1 be applied. The output is constrained in its rate of rise by C_1. For full charging current flow after the excitation is applied is determined by input capacity C_1. The same charge is accumulated in C_0. Since $C_0 >> C_1$, the voltage across C_0 will change slightly, while C_1 charges fully. Thus coupling capacitor C_0 can be assumed to be short circuited during this entire interval. The eqvt. ckt is now reduced to a ckt containing a single-energy storage element. Refer Fig.11(b).

By taking the Thevenin theorem equt. across C_1, the final steady state output and the ckt. time constant are found thus;

$$V_{oo_1} = \frac{(R_1 \parallel R_3)}{(R_0 + R_1 \parallel R_3)} V_1$$

$$= \frac{C_1}{(R_3 \parallel R_1 \parallel R_0)}$$

Hence the eqn. defining the initial portion of output response is

$$V_{o_1} = V_{oo_1} (1-e^{-t/\tau_1}) \quad \ldots \quad \ldots \quad (1)$$

In four time constants, the output rise to 98% of the steady state value of V_{oo_1} and initial rise may be assumed complete.

During this whole interval, C_0 is charging, though very slowly. The relative large current required (because of the large value of C_0) will control the output voltage and wipe out any contribution from the discharge of C_1. Thus we are justified in ignoring C_1 and removing it from the ckt. If the initial value of the output across R_1 upon the sudden excitation of the system is calculated, its also found to be V_{oo_1}. As C_0 discharge with new time constant, the output

$$\tau_2 = C_0 (R_0 + R_1 \quad R_3)$$

Thus, eqn. defining the final portion of the response may be written by inspection,

$$V_o(t) = V_{oo_1} e^{-t/\tau_2} \quad \ldots \quad \ldots \quad (2)$$

A question yet to be answered is that at what time will decay take over from initial rise. When equations (1) and (2) are compared

its observed that both the capacity and resistance term of Γ_2 are much larger than Γ_1. Since decay time constant is so very much larger, error introduced by starting the decay anywhere in the vicinity of zero will be negligible.

3.27 [illegible] OF HIGH PASS LOW PASS [illegible].

Spike potential can be obtained by interconnecting two high pass and low pass networks to meet the required experimental results.

The combination of one low-pass and high-pass network is shown in Fig.23(a) we assume that successive network do not react i.e. do not load each other. The transient response can be approximated by treating them as two isolated single energy units. The response can be separated into two regions, both the regions depend upon the individual characteristics of energy storage element.

In first energy-storage unit on successively rapid rise depends upon the rate of charging of C_1 capacitor charges to the d.c level of input with circuit time constant - The solution of equation in general form is

$$\tau \frac{dv}{dt} + V = 0 \qquad (1)$$

$$V(t) = V_0 e^{-t/\tau_1} + V_\infty(1 - e^{-t/\tau_1}) \qquad (2)$$

where $\tau = R_1C_1$

The step transient is reduced to a rising curve $V_0 = 0$. The final value V_∞ is same as of the input V_1. Hence equation (2) becomes

$$V_2(t) = V_1(1 - e^{-t/\tau_1}) \qquad (3)$$

In second energy storage unit, a series circuit have output

~~and~~ to derivative across the resistor. The major portion of the circuit voltage drops across C, when the time constant is small. With a sufficient small time constant, an exact output wave shape is reasonably close, except at discontinuities.

The output has no d.c compt. after infinite time $V_o = 0$ From eqn.(1)

$$V_2(t) = V_2 e^{-t/\tau_2} \qquad (4)$$

where $V_o = V_2$, the output of first low pass network.

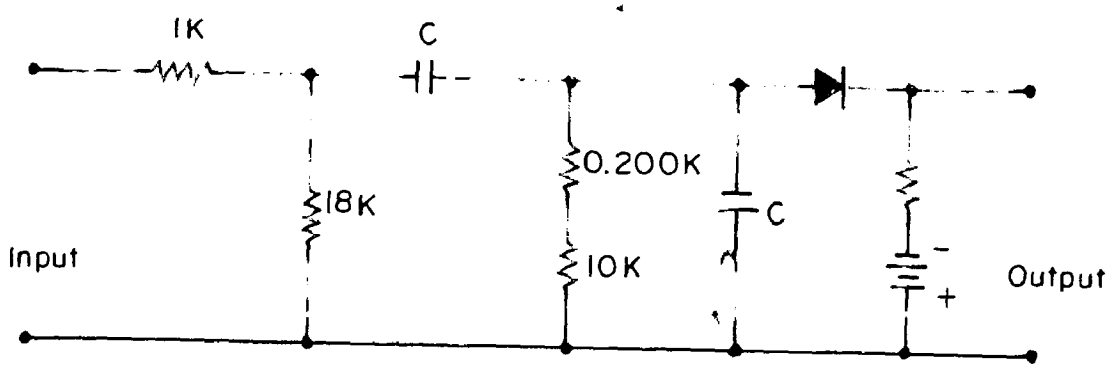
$V_2(t)$ = Output of second high pass network

$\tau_2 = R_2C_2$, time constant.

The eqn.(4) shows the characteristics of the exponential decay with time constant R_2C_2. By changing these value of capacitor C_2 or R_2, time constant can be varied. If τ_2 is high, then fall will be sharp. If τ_2 is low, decay takes a long time. In this circuit, value of capacitor C_2 is varied, to get different decaying characteristic of the output wave form when step input is applied.

Battery V_B is used to have steady state condition. The minimum firing potential for squid axon is 6 12mV.

Block diag. of neuron Fig.2(b) It consists of a threshold unit and pulse generating unit. A step input is applied to any of four input terminals. This input is differentiated with R=22K



(a) ELECTRONIC MODEL OF NEURON

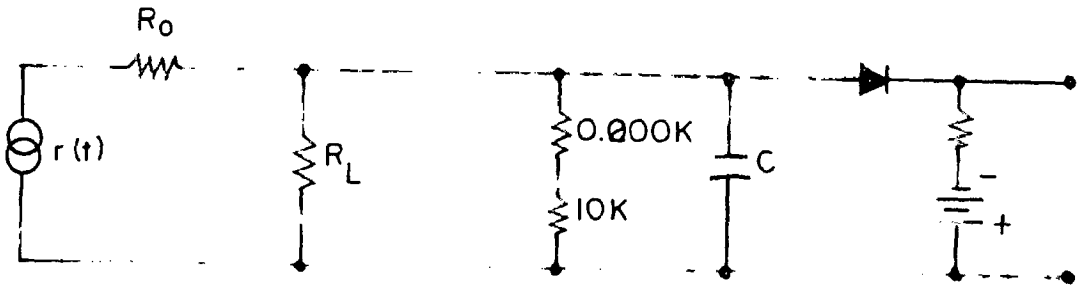
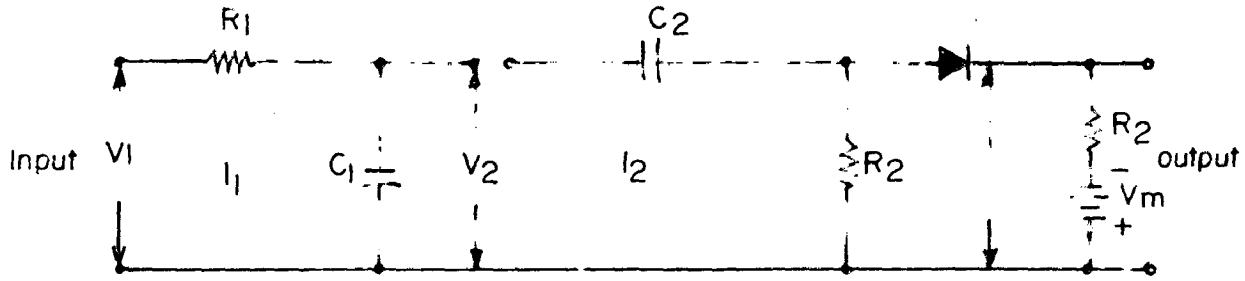


FIG.22(b) EQUIVALENT CIRCUIT OF E.M.



(a) ELECTRONIC MODEL OF NEURON

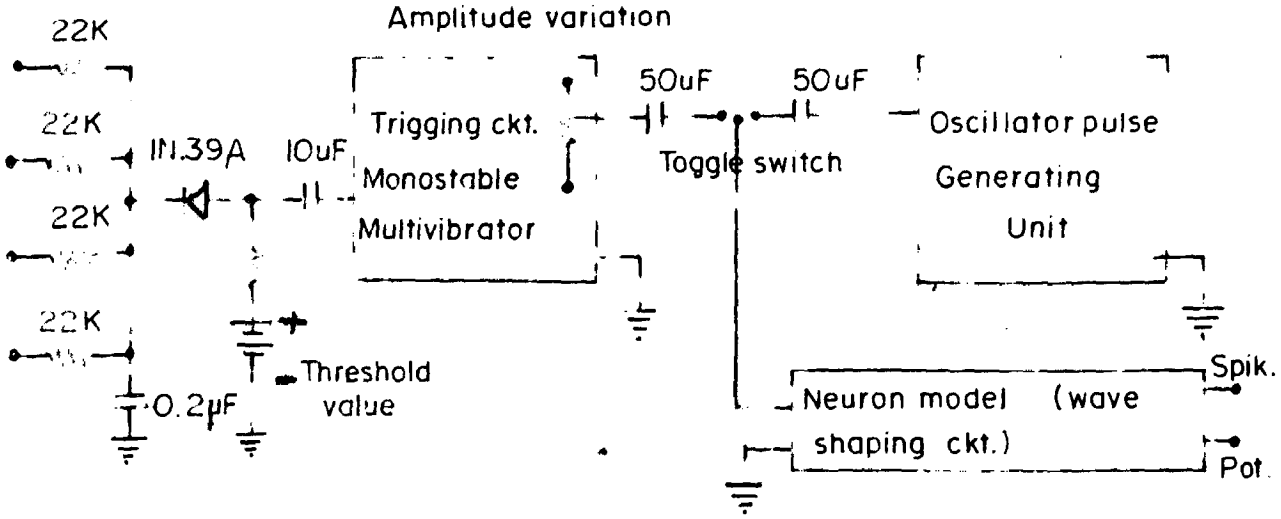


FIG.23(b) SCHEMATIC DIAGRAM OF ELECTRONIC MODEL OF NEURON.

and C = 0.02μF. This differentiated wave works as input to threshold unit, consisting of limited circuit. In this diode D_1 is connected in forward bias,and the threshold value for wave can be adjusted from the battery V_2 connected. If the differentiator output is sufficient or greater than V_2, the diode will be in forward bias, then this differentiated pulse can pass through the diode and capacitor of 10μF to trigger the next unit. By varying the battery voltage V_2 a particular voltage level can be set for input differentiated pulse, i.e. if input is greater than V_2, then this pulse trigger the unit. If input differentiated pulse amplitude is smaller than the battery voltage V_2, then the diode would not conduct. The battery voltage V_2 in the circuit works as threshold unit.

The differentiated pulse(amplitude greater than threshold value) triggers the monostable multivibrator and causing a delay of 0.69 RC and output is pulse . The amplitude of this pulse can be varied by using the potentiometer. This pulse output is fed to neuron model, which converts the pulse into spike potential, satisfying the steady state and transient conditions.

.28 ELECTRONIC MODEL[4]
BY HARTO

Horton used a non parameter electronic model(the neuristor) to examine the theoretical input-output properties of a single neuron. The basic circuit is shown in Fig.24.

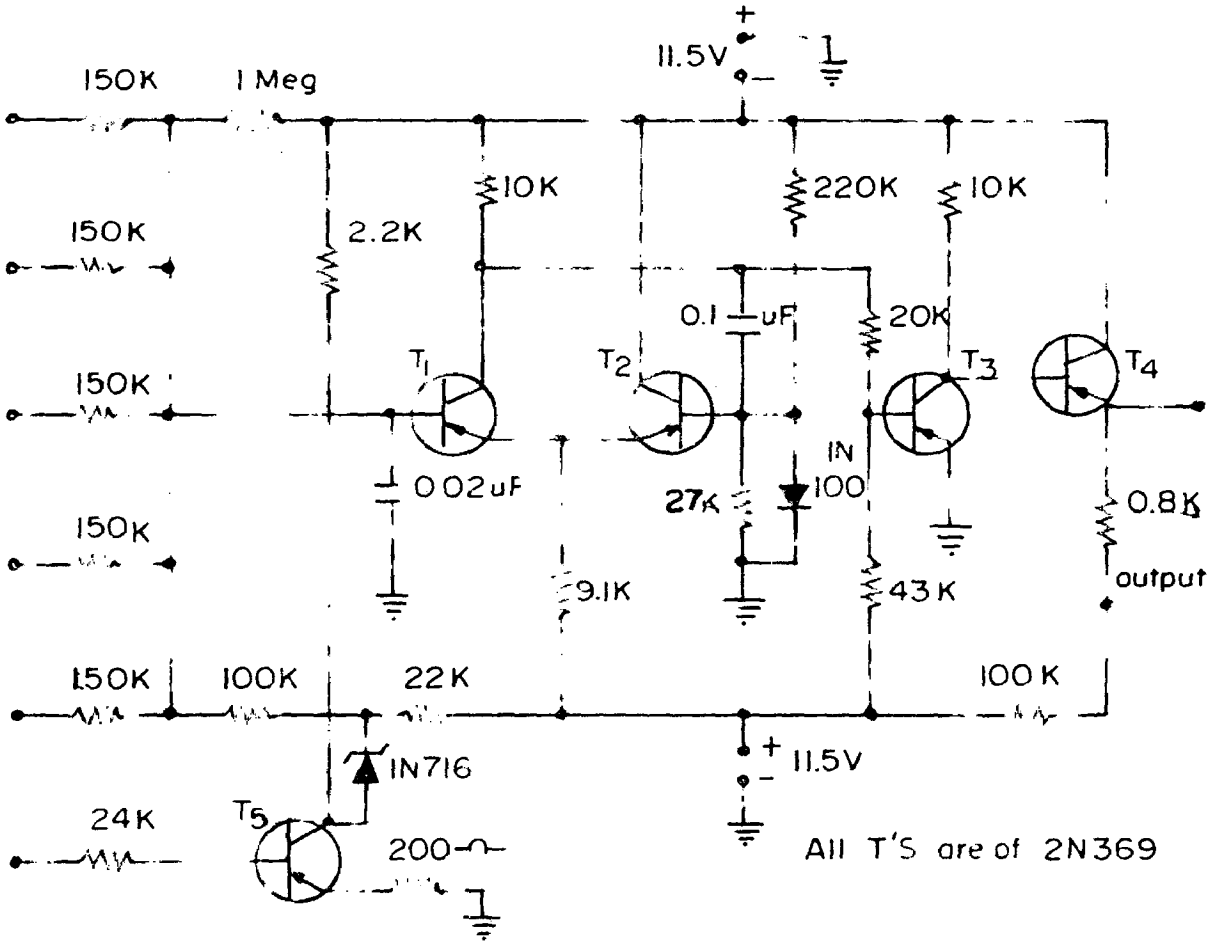

11.5V
150K
1 Meg
10K
220K
10K
150K
2.2K
0.1 uF
20K
T1
T2
T3
T4
150K
0.02uF
IN
100
27K
0.8K
150K
9.1K
43K
output
150K
100K
22K
100K
IN716
11.5V
24K
T5
200
All T'S are of 2N369

FIG. 24

The model provides

(a) Spatial and temporal summation

(b) All or nonepulse

(c) Abs. refractory periods

(d) Created inhibitation

The all or none law is satisfied as follows - when the excitatory inputs exceed the threshold value, only then will there be action potential for only then will the monostable fire.

The absolute refractory period is fixed by the time constant of the monostable multivibrator.

9.29. A FLEXIBLE NEURAL ANALOG USING IC[15]

The basic block diagram of the neural analog is shown in Fig 29.. A leaky integrator sums the inputs from a number of sources over a period determined by its time constant τ_1. This time constant represents the membrane time constant. The integrated voltage is continually compared to a threshold voltage V_0 and when this is exceeded, a pulse is generated at the output. Sub-threshold voltages are fed forward to increase the threshold level with a second time constant τ_2, so that the analog shows accomodation to slowly rising inputs. Each output pulse resets the integrator and holds it at its initial value until the end of the pulse. The pulse duration t_0 determines the absolute refractory period of the analog, i.e. the period during which a second pulse cannot be generated. Each pulse also

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increases the threshold by an amount ΔV_0 and the effect decays with the time constant τ_2. If τ_2 is short compared to the normal interval between pulses, it determines a 'relative refractory period in which a second pulse is readily elicited.

Thus, this model of French and Stein incorporates - (1) Variable absolute and refractory periods (2) two time constants (3) separate control of the accommodations to sub-threshold voltage changes.

3.30 A DENDRITIC COMPARTMENT MODEL NEURON[14]

An electronic model is described which features a multiple input compartmental system analogous to a dendritic net and a simulated action potential. The input to the model are rectangular voltage pulses which initiate excitatory/ or inhibitory changes in the dendritic compartments. The outputs are the simulated action potential.

The membrane potential at each compartment and the depolarizing and hyper-polarizing conductances can be easily monitored. The simulated action potential is generated electronically.

The model is constructed from standard electronic components so as to minimize size and cost. A block diagram of the basic 5-compartment model is given Figure 26. Field effect transistors(FET's) are employed to gate rectangular input conductance pulses to the simulated dendritic resistance-capacitance

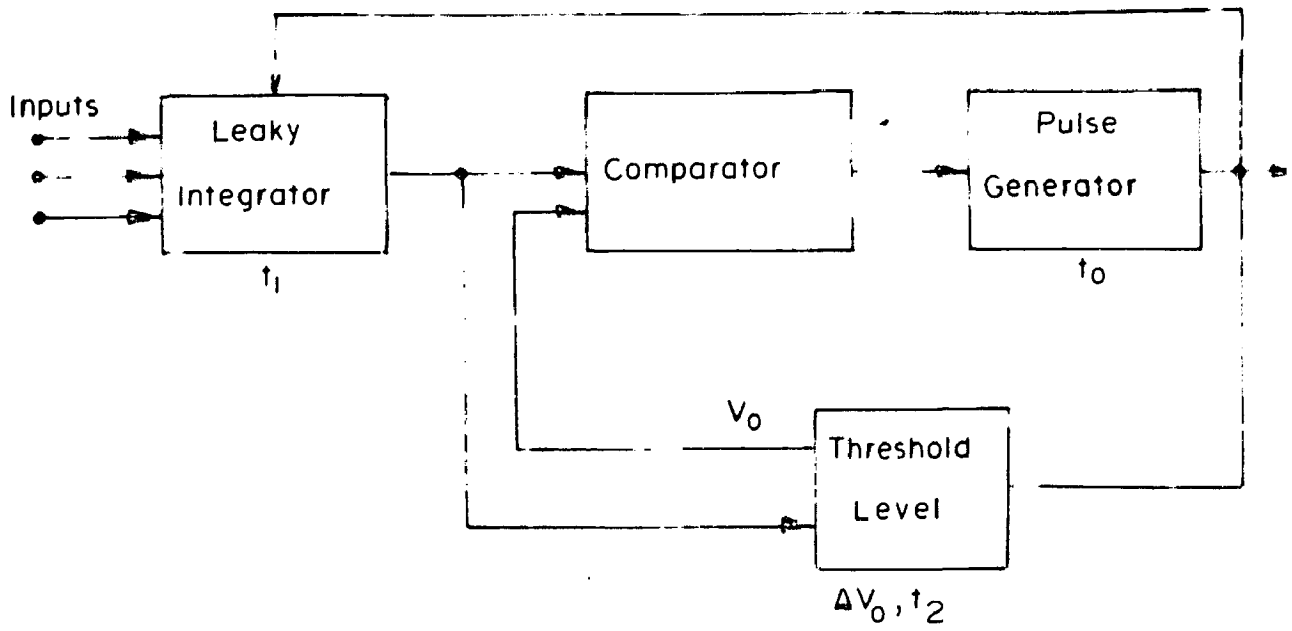

FIG.25 BLOCK DIAGRAM.

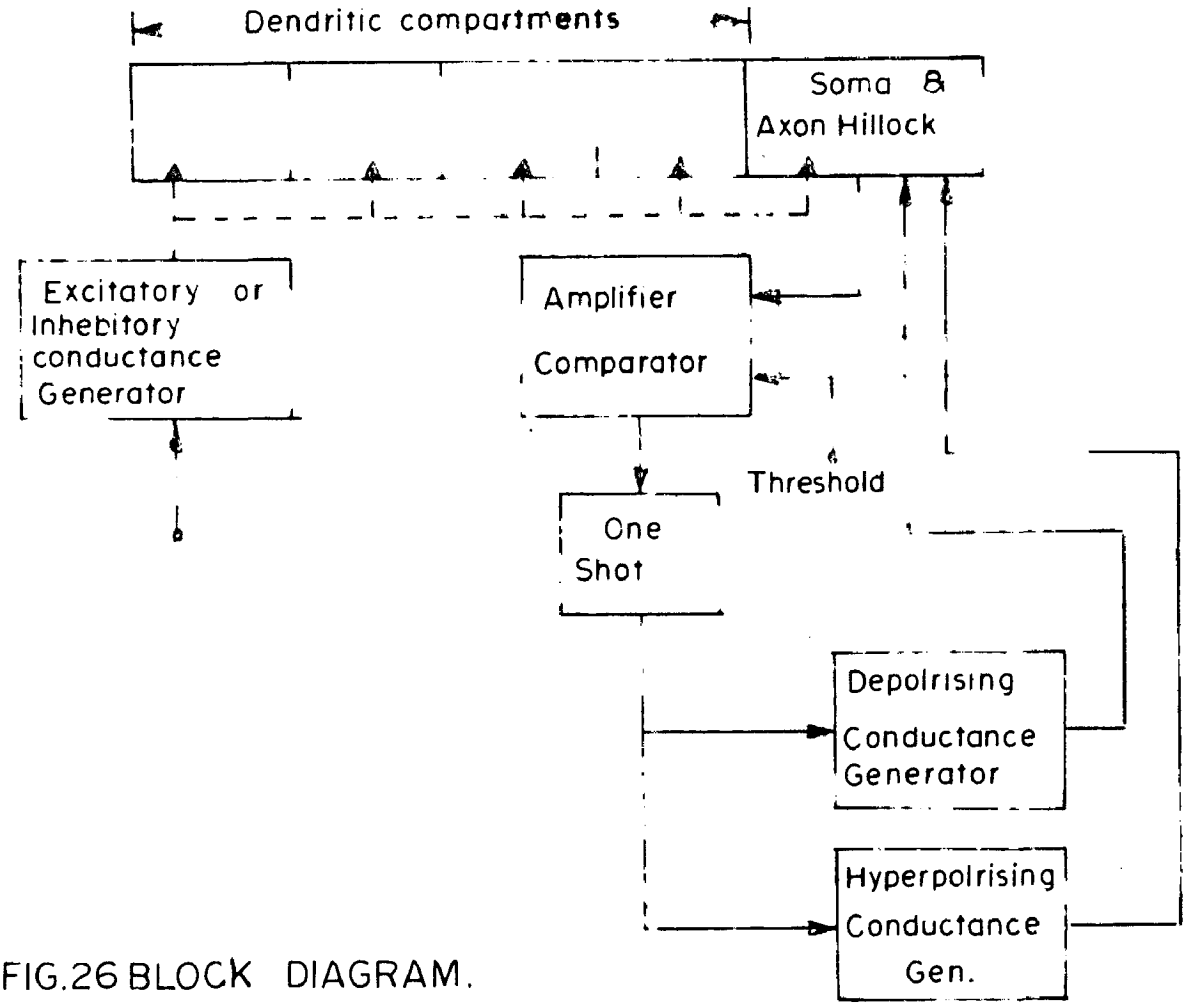

FIG.26 BLOCK DIAGRAM.

compartments. The simulated action potential is generated by varying the output conductances of two FET's which are used as the actual hyperpolarising and depolarising conductances. The detailed process of spike generation is as follows.

The simulated membrane potential of the trigger region is continuously amplified and compared to a reference potential. When this signal exceeds threshold, a Schmitt Trigger is fired which in turn triggers a one-shot. the output from the one-shot is fed to both hyperpolarising and depolarising conductance waveform generators. The output voltages from these two wave-shaping circuits are then applied to the gates of the hyper-polarising and depolarising FET's.

This model gives insight into:

(1) The manner in which an action potential can modify the shape and duration of postsynaptic.

(2) It can be used to study the spatial temporal interactions among post synaptic potentials or between post synaptic potentials and action potentials.

(3) It's possible to investigate the interdependence between input conductance changes and the period of after hyperpolarisation.

3.31 AN ELECTRONIC MODEL FOR NEURAL TRANSMISSION OF INFORMATION

This model successfully illustrates two basic types of transmission of neural signals, namely (i) the conduction of information along a nerve fibre. (ii) the transmission of

information at synapsis, refer fig.2?[15].

For simulating the threshold phenomenon an Op. Amp(I) is used with summing resistors for multiple inputs. The 5.7V Zener(Z_1) at the non-inverting input of the Op-Amp(I) indicates the threshold voltage. For the purpose of illustrating the all-or non-law a numbers of inputs are connected at the inverting point of the Op-Amp(I). When the summing point voltage is less than the threshold voltage, diode D_1 blocks the negative pulses at the output of the Op. Amp(I). The output of Op-Amp(I) is connected to a monostable multivibrator with an integrating capacitance C_1. The output of the monostable multivitrator is differentiated by Op-Amp(II). The time constant C_2R_2 accounts for the refractory period.

The models suggested by the various workers can be classified under two categories:

(1) Models simulating the membrane parameters and the membrane potential levels.

(2) Models simulating the membrane characteristics.

The models of Hodgkin and Huxley[4,5], Lewis[4] and G. Roy[12] come under the first category. The rest of the models come under the second category. In the first type of models, the effect of various model parameter individually or collectively can be seen on the individual sections or on the over all model. Here every parameter represents some equivalent parameter of physiological system and the model parameter

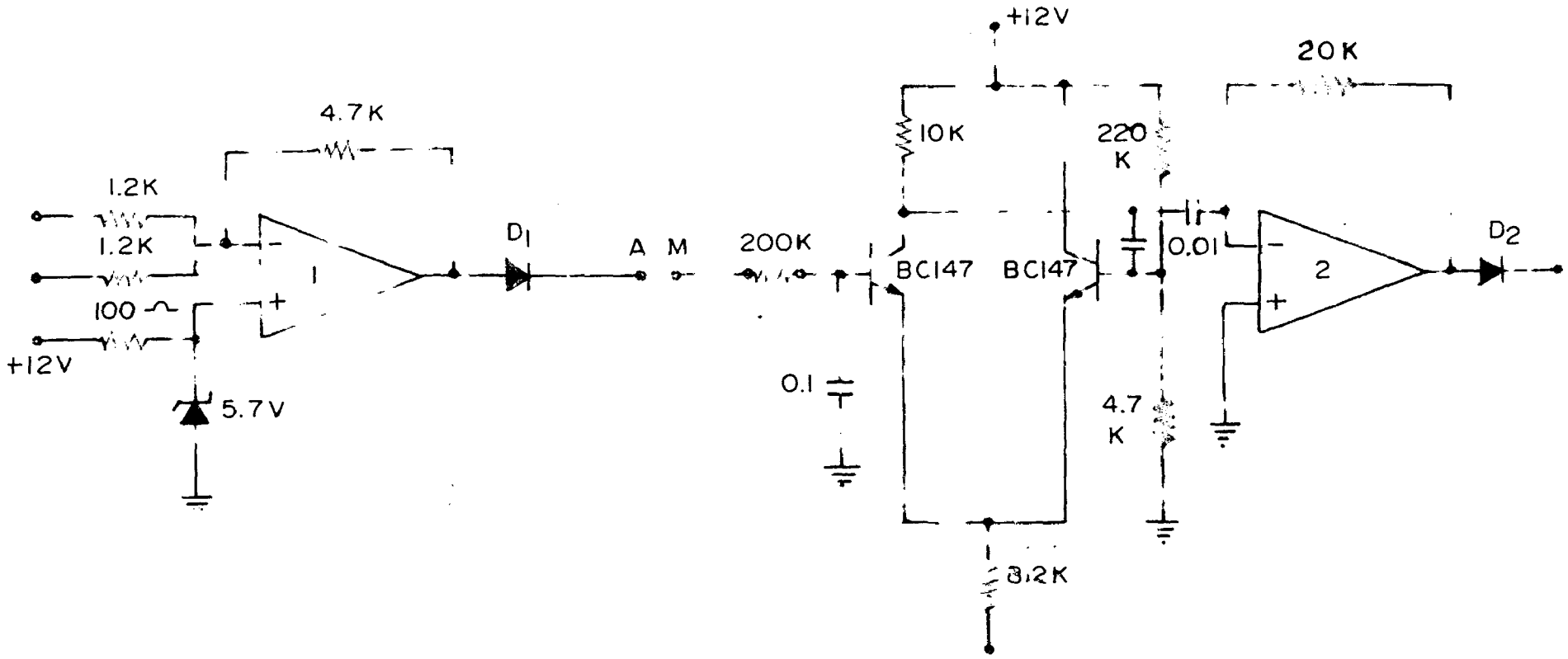
4.7K
1.2K
1.2K
100
+12V
5.7V
1
D1
A M
+12V
10K
220
K
20K
200K
BC147
BC147
0.01
2
D2
0.1
4.7
K
3.2K

FIG. 27

values are in proportion to them only. In the second type of models, the characteristics of the physiological system are simulated and there is no concern with the individual element of the model to the actual system parameters.

CHAPTER - IV

A NEW PROPOSED PLASTIC MODEL OF NEURON

4.1 INTRODUCTION

This chapter deals with an electronic model of neural system which has been developed by the author. Number of electronic models have been developed in the past which has also been reviewed in the earlier chapter, but the present model has some distinct advantages and gives an accurate functional representation of the neural system activities. Some points in favour of this model are:

(i) Linear IC's have been used to handle the physiological data of neuron more conveniently and accurately. They also give simple mathematical relationship between input-output at various stages.

(ii) The IC's are used in economical way which has facilitated in the development of a reliable, compact, inexpensive model of neuron.

(iii) This model includes all the important electrical characteristics of actual neuron. The accomodation and adaptation phenomenon of the neuron have also been included.

(iv) As this model is compact and inexpensive, several such type of models can be used to study the interconnection among neurons.

(v) The changes in various electrical characteristics

at every stage can be observed simultaneously by putting the oscilloscope at the points of interest. It is possible to determine the effect of EPSP and IPSP potentials, intracellular and extracellular potentials at every point, firing pattern of neuron with and without accomodation and adaptation, interaction between firing and postsynaptic potentials and some other interesting characteristics.

4.2 BLOCK DIAGRAM OF NEURON MODEL

The block diagram of the model that incorporates all the important features of an actual neuron is shown in Fig.(20). It has excitatory and inhibitory inputs, cell body, axon-hillock and axon. The excitatory and inhibitory inputs are generated by producing positive and negative pulses of known width and duration by differentiating circuits. The cell body is represented by an integrator, half-wave rectifier, adaptive threshold gate and a comparator. The axon-hillock is modelled by a repeatable multivibrator, differentiator and pulse-stretcher. The axon is represented by a resistance-capacitance combinational transmission line. This axon-model line is triggered by a switch through repeatable multivibrator and generates action potential which travels down along the line.

The time constant of the integrator represents the membrane time constant. It is usually of the order of 1 millisecond. The accomodation and adaptation phenomenon is simulated by the half wave rectifier and a adaptive threshold gate. The

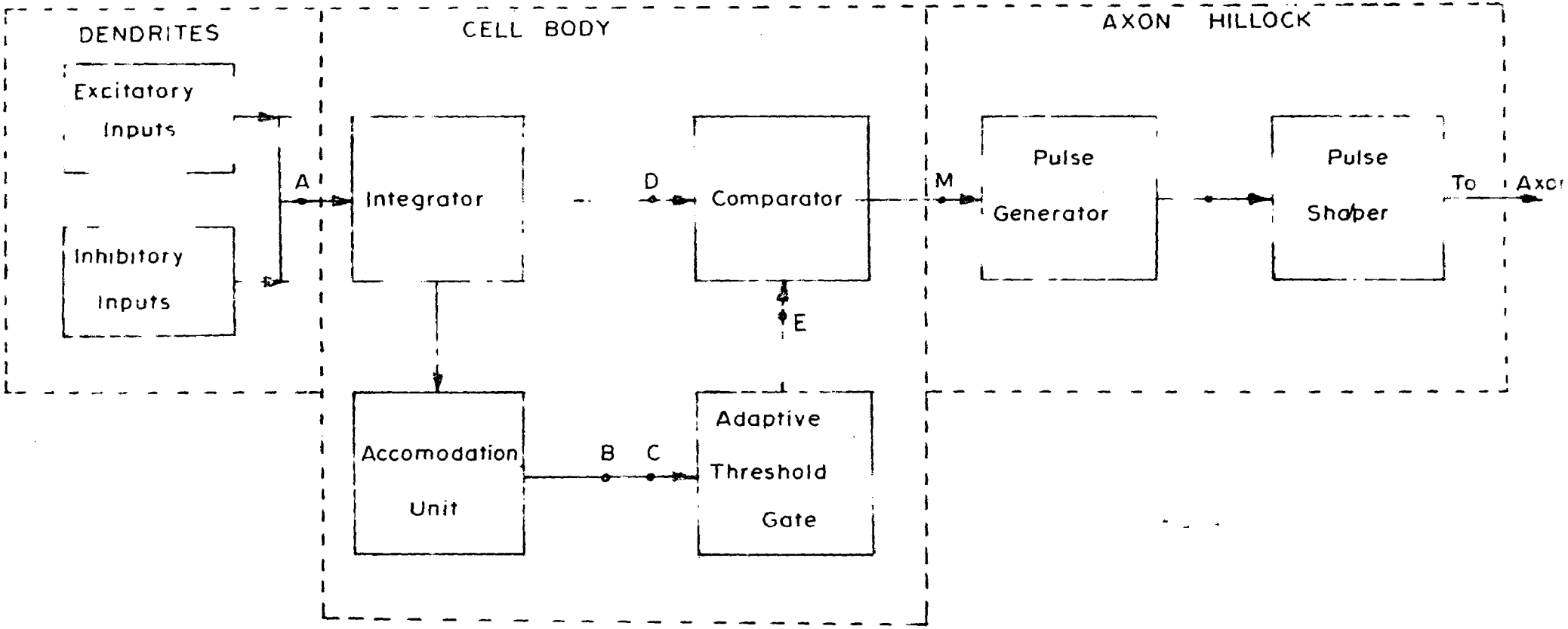

FIG.28 BLOCK DIAGRAM OF NEURON MODEL

relative refractory period is decided by the time constant of the adaptive threshold gate. The outputs of the integrator and the adaptive threshold gate are compared by a comparator. The output of the comparator is connected to a monostable multivibrator which triggers only when all the conditions are satisfied in the cell body units. The time constant of the monostable multivibrator decides the absolute refractory period of neuron model. The output pulse of the multivibrator generates the action potential through differentiator and pulse shaper which travels down on the axon analog.

4.3 ELECTRONIC CIRCUIT DETAILS OF THE MODEL

The detailed electronic circuit of the neuron model is shown in Fig 29. The inputs to the model are electrical pulses. The excitatory inputs are given in the form of positive potential pulses and inhibitory inputs are in the form of negative potential pulses. In the model, five EPSP inputs and two IPSP inputs are used. The sharp pulses of positive and negative nature are generated by a RC differentiator. The diode in EPSP input line allows only positive pulse to pass towards cell body analog and the negative pulse is blocked and grounded through resistance. The diode in IPSP input line blocks the positive pulse and allows only negative pulse to cell body analog. The differentiator time constant is taken as 1 millisecond by selecting the resistance of 10 K Ohms and capacitance 0.1μF. The SR204 diode is used for blocking

or passing the pulses corresponding to EPSP and IPSP inputs in both the modes. The dendrite distances and lengths are represented by the resistances. A variable resistance of 10 K Ohms is used which can be adjusted. Its minimum value indicates that the dendrite concerned is very near to cell body and maximum value of presynaptic potential is contributed to the cell body analog input. Its maximum value indicates that the dendrite concerned is at the far most distance from cell body and minimum value of presynaptic potential is contributed. All these inputs are added up at a point 'A' and given to the integrator unit of cell body. The potential at point 'A' is the summation of all EPSP and IPSP inputs. The value of this summed up potential is responsible for the further actions in the next stages of the system. The parallel combination of resistance capacitance in the feedback path of integrator provides the membrane time constant. A typical value of 10 millisecond using 100 K Ohms resistance and 0.1 μF capacitance is taken for this model. The other capacitances 1μF and 10μF are also provided for getting some other values of membrane time constant for study purposes. For more critical examination some other capacitance and resistance combinations can be incorporated in the model. The output of the integrator is the inverted potential of point 'A'. The output of the integrator is given to half wave rectifier unit and also to the comparator unit. The half wave rectifier is used for getting the accomodation phenomenon. The output at the point 'B' is observed only for EPSP inputs and not for IPSP inputs, just like the actual neuron. When there is positive potential at the output

of integrator (i.e. the IPSP inputs are more than EPSP inputs), the negative potential is observed at point 0 of half rectifier which conducts diode D_1 and does not allow to conduct diode D_2 because its reversed biasing. The output is not available at point D in this case; So the next stages of adaptive threshold gate does not work. When the negative potential is observed at the output of integrator (i.e. the EPSP potentials are more than IPSP potentials) and the positive potential is observed at point 0 which conducts diode D_2 and reverse biase diode D_1. Now output is observed at point 'B' which is fed to adaptive threshold gate. The output of the rectifier is connected at point 'C' to threshold gate. The threshold is provided by giving a fixed positive potential at the non-inverting input terminal of IC by using a potential divider. This threshold can be adjusted by changing the potential divider setting. The parallel combination of the resistance capacitance in the feedback path of the threshold gate decides the relative refractory period. A typical value of 10 millisecond is taken in this model. The capacitance of 1 μF and 10 μF are also shown in parallel to this combination which can be connected by a switch in place of capacitance .1μF for setting, the values of relative refractory period as 100m sec. and 1 sec. When there is no output at point 'B'.of half wave rectifier, the fixed potential of point 'C' due to potential divider arrangement is observed at the output of threshold gate and it does not adapt to any change. When an output is observed at point 'B', that potential of point 'D' is added up with the

potential of point 'C' and a varying output corresponding to changes at 'D' is observed at the output of adaptive threshold gate that means it adopts to the changes. It increases the threshold of the comparator for integrator output. The outputs of the integrator and the threshold gate are continuously compared by the IC comparator unit. When the total sum of the inputs (EPSP's and IPSP's) is more than the threshold value of the neuron, the output of the integrator unit connected at terminal 'D' of comparator becomes more than the threshold unit output connected at point 'E' and the output of the comparator changes at point 'H' from positive value to negative value which triggers monostable multivibrator. The monostable multivibrator is connected after comparator and the time period of this multivibrator for 220K Ohms resistance and .01 μF capacitance is equal to the absolute refractory period of the model which is taken 1 millisecond in this model. The capacitance of .1 μF and 1 μF are connected here to get the other combinations of absolute refractory period. Transistor T_1 is normally 'off' and T_2 normally 'on'. The transistor T_3 is used as a switch when the multivibrator is in reset state and no command signal is coming from the earlier stage, the switch transistor T_3 remains off owing to positive biasing at its base. The biasing is adjusted at its base by using the potential divider arrangement as shown in figure (29) When the multivibrator changes its state on command from the cell-body making the base of T_3 becomes sufficient negative

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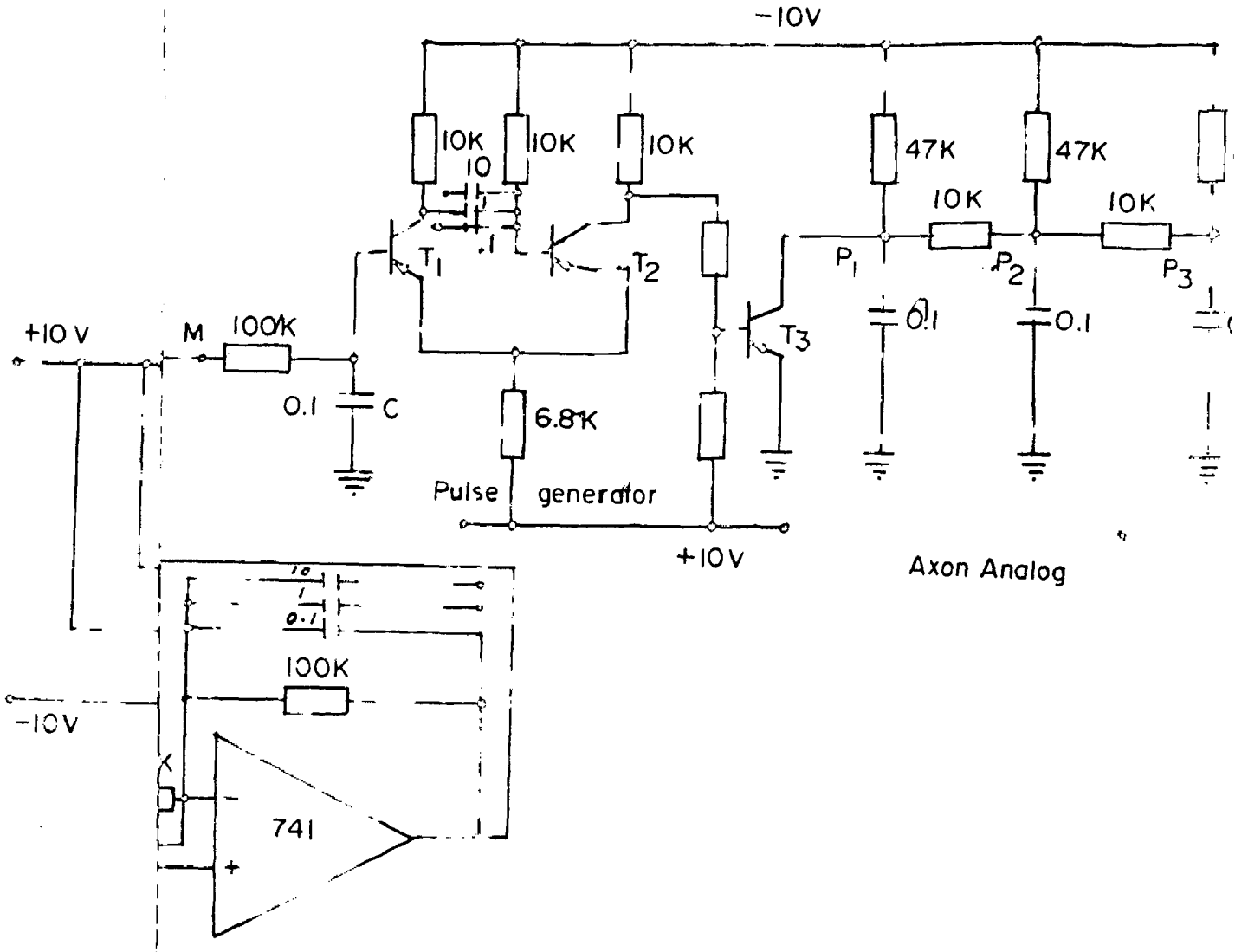

Adoptive threshold gate

ALOG.

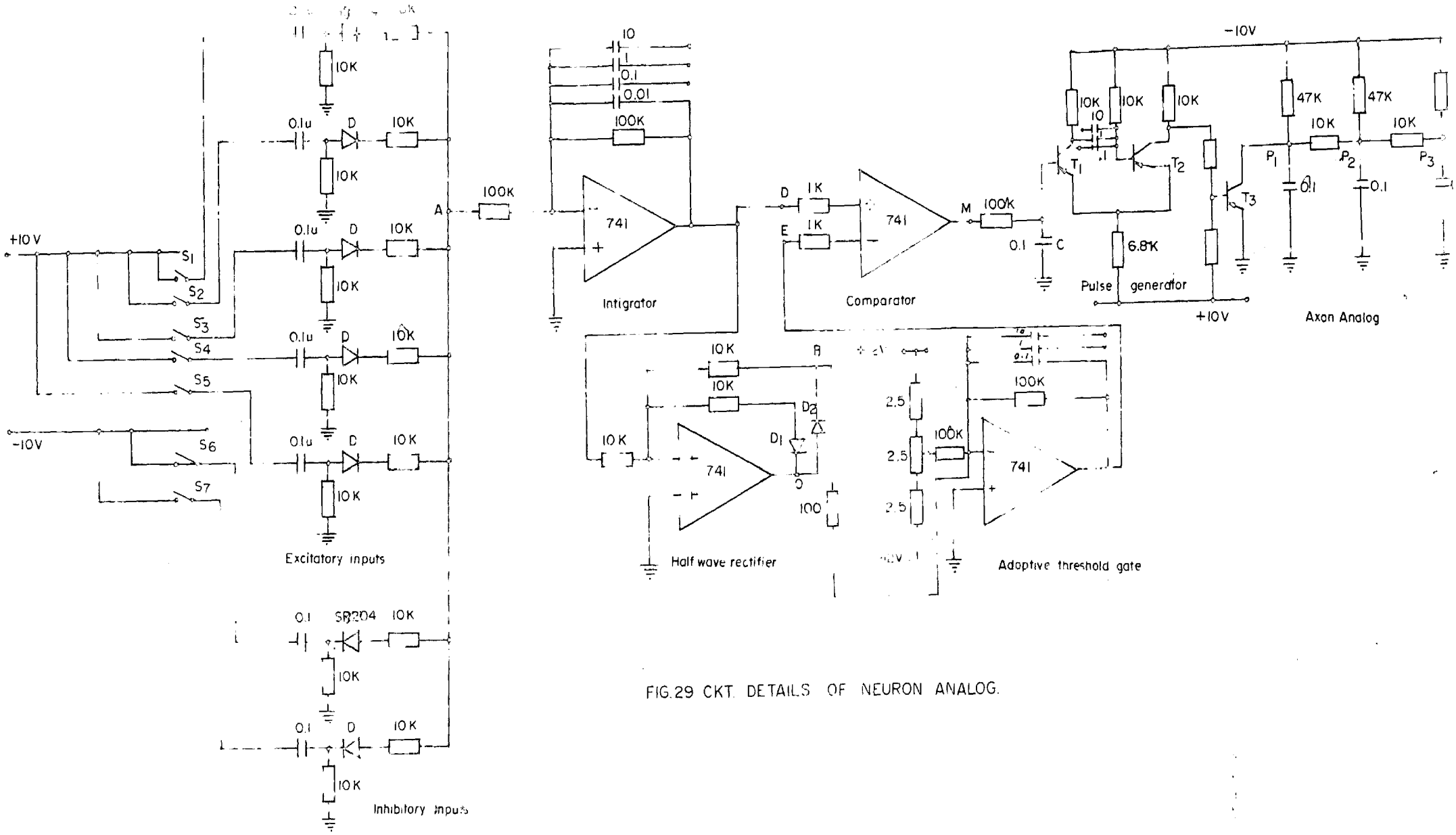

FIG.29 CKT. DETAILS OF NEURON ANALOG.

to drive this transistor in fully saturation state. Now T_3 earths the point 'P_1' of the axon analog capacitive-resistive network. Normally the point P's are at some negative potential (in the model at - 10 Volts) which corresponds the steady state condition of the nerve fibre. When switch T_3 earths P_1, all the capacitances discharges through this saturated transistor and spike potential is produced at the point. The amplitude of this action potential is maximum at point P_1 and minimum at the last. Also the spike at P_1 is sharp as compared to spikes at other points later on the analog line.

4.4 EXPERIMENTAL RESULTS

The electronic circuit shown in Fig.29 was fabricated and tested for the various electrical characteristics of neuron as discussed below.

(i) There is a particular threshold value for an input to cause excitation. When the output signal exceeds this threshold value, the action-potential output is observed. Table-1 shows the amplitude of the output response for different values of the step input (observed at point H) for various values of threshold settings.

(ii) The effect of accomodation and adaptation of the model has been observed in the model. When the total value of EPSP potentials is more than total IPSP potentials and the summed potential at point 'D' in the model is negative i.e. corresponding to excitation state, the potential of point 'B' changed the value

of the output of adaptive threshold state after some time (which is required for adaptation) and the unit stopped giving action potential. So, the output action potential is available only upto the period for which the accomodation unit and the adaptive threshold gate takes to adjust to this new value. After this period the pulse generator stops giving any output pulse. It is just the same as that in actual neuron. This adaptation time can be capacitance combination in the feedback path of the threshold gate. It will also change relative refractory period of the model.

(iii) The output frequency of the neuron model for the several values of the input signals when they are applied just before the multivibrator at point 'T' is shown in Fig.30. This is the steady state frequency response of the model produced by steady d.c input in the absence of accomodation and adaptation properties. If the accomodation unit and adaptive threshold gate is also connected in the circuit, then the output is observed only to the time which these units takes to adapt to this new value. After this adaptation time, the reference input at the comparator at point 'E' becomes more than the input at point 'D' and the output of the comparator unit at point 'F' changes from negative value to positive value and the monostable multivibrator stops responding to input signals. This adaptation time increases by increasing the capacitance value in parallel with resistance in the feedback path of adaptive threshold gate.

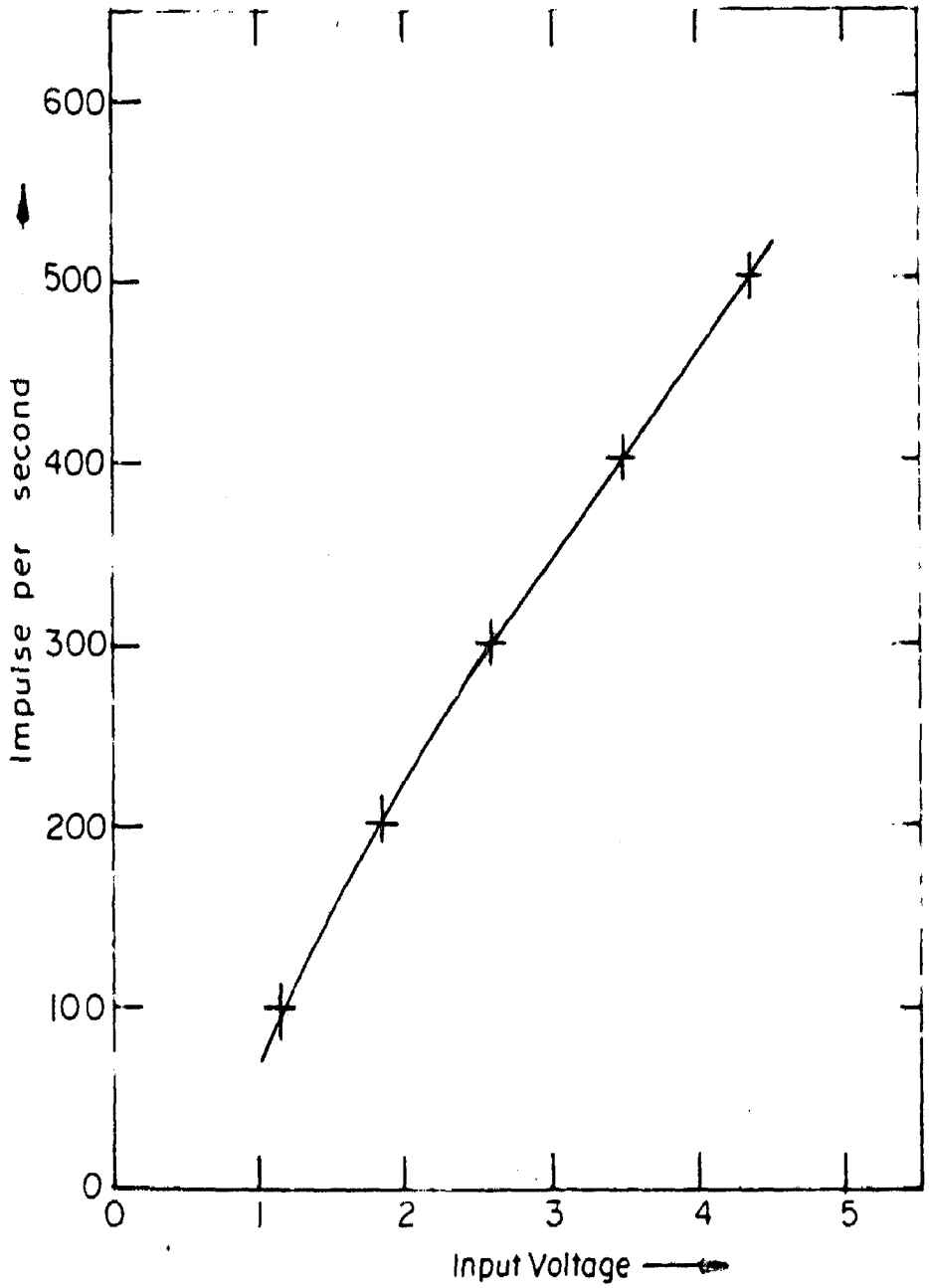

FIG.30 OUTPUT FREQUENCY OF NEURON MODEL AS A FUNCTION OF INPUT VOLTAGE.

(iv) Various combinations of the EPSP and IPSP type of inputs have been tested on the model. It is observed that when the sum of the total value of the inputs becomes more than the threshold, only at that time the neuron model gives action potentials. Table-I shows the behaviour of the model for different threshold values.

(v) Experimental observations showing the refractory period phenomenon are shown in Table II. This response data is for an input pulse of constant amplitude (3V), duration (5ms) and of variable frequency which is applied at the input of neuron. The output signal is observed only upto the time which satisfies the condition for absolute refractory period. Table II shows the response for an absolute refractory period of 9 m sec. When the frequency exceeds the limit, the output action potential is not observed. The tests were also conducted for the other values of absolute refractory period by increasing the value of capacitance of the monostable multivibrator circuit. Increase in absolute refractory period decreases the frequency range of neuron model and the model becomes slow i.e. it represents an actual slow responding neuron.

All the experimental results of this model are similar to those which have been observed by many Scientists and bio-engineers on actual neuron. It is possible to simulate the characteristics of the fast medium and slow responding neurons by this model.

Table - I

Threshold Phenomenon for Step Inputs

Threshold value = 2 volts		Threshold value = 3 volts		Threshold value = 4 volts	
Input Signal Amplitude (Volts)	Output Signal Amplitude (Volts)	Input Signal Amplitude (Volts)	Output Signal Amplitude (Volts)	Input Signal Amplitude (Volts)	Output Signal Amplitude (Volts)
0.0	NIL	0.0	NIL	0.0	NIL
1.0	NIL	1.0	NIL	1.0	NIL
2.0	NIL	2.0	NIL	2.0	NIL
2.5	10.0	3.0	NIL	3.0	NIL
3.0	10.0	3.5	10.0	4.0	NIL
3.5	10.0	4.0	10.0	4.5	10.0
4.0	10.0	4.5	10.0	5.0	10.0
5.0	10.0	5.0	10.0	6.0	10.0

Table-II

Absolute Refractory Period for Applied Inputs at point "A" just before the Axon Hillock Analog Input pulse = 2 volts

Input Pulse Frequency (Hz)	Output Response Amplitude (Volts)
50	10
100	10
150	10
200	10
250	10
300	10
350	10
400	10
450	10
500	10
550	Absent
600	Absent
700	Absent
800	Absent

.5 DISCUSSION

The electronic model discussed is a very convenient means for studying the several electrical characteristics of the actual neuron. It is possible to study the effect of each individual parameter, which is analogous to some part of actual neuron, or some sub-section of the model or on overall neuron model performance. Several such type of models after interconnection can be used to study the behaviour of interneurons. This model proves to be a very good aid to bioengineers and neuro-physiologists for explaining and studying the various important functional characteristics of the neuron. A very clear concept about the electrical characteristics of the neuron will help in the diagnostic purposes. If it becomes possible to construct a very small microstructure model, then it will be a very good replacement of the neuron which has stopped functioning in some part of the body. It may be helpful in the treatment of some paralysis cases where only a small segment has stopped working and because of that some major part of body has stopped functioning as the information from the brain to that part or vice-versa is not flowing.

CHAPTER V

CONCLUSIONS AND RECOMMENDATIONS FOR FUTURE WORK

In this dissertation, the actual neural system is critically analysed for getting the useful data for developing the neural system model. The existing models have been reviewed. Also, a new model of neuron has been developed which incorporates all the important electrical characteristics of the actual neuron. This model has been successfully fabricated and tested.

In the further work, more details can be incorporated in the dendrite system and in the axon system. Each of these may be considered either myelinated or unmyelinated fibres. A detailed analysis of the actual neural system and consequently a more exact electrical analogous representation could be done. After interconnecting several such type of neural analogous models, the combined behaviour of the overall system can be studied in detail.

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