ELECTRONIC REPRESENTATION AND ANALYSIS OF NEURAL TRANSMISSION PROCESS

A DISSERTATION

Submitted in partial fulfilment of the
requirements for the award of the degree
of
MASTER OF ENGINEERING
in
ELECTRICAL ENGINEERING
(Measurement & Instrumentation)

By

ANIL KUMAR GARG

DEPARTMENT OF ELECTRICAL ENGINEERING
UNIVERSITY OF ROORKEE
ROORKEE-247 667 (INDIA)

December, 1985

DEDICATED TO
MY PARENTS

CANDIDATE'S DECLARATION

I hereby certify that the work which is being presented in the thesis entitled, "Electronic Representation and Analysis of Neural Transmission Process", in partial fulfilment of the requirement for the award of the Degree of Master of Engineering in Electrical Engineering (MEASUREMENT & INSTRUMENTATION), submitted in the Department of Electrical Engineering of the University is an autbentic record of my own work carried out during a period from August, 1984 to November, 1985 under the supervision of Dr D S Chittore.

The matter embodied in this thesis has not been submitted by me for the award of any other degree.

Candidate Signature
(ANIL KUMAR GARG)

This is to certify that the above statement made by the candidate is correct to the best of my knowledge.

7/12/85

Dr.D. S. Chittore
Reader
Electrical Engineering Department
University of Roorkee
Roorkee

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ROORKEE

(ANIL KUMAR GARG)

DEC. 6 , 1985.

C O N T E N T S

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CHAPTER - I

INTRODUCTION

Modelling of biological systems help in getting a clear and consistent picture of its working and various processes. It can be used to verify experimentally known relationships and to establish new relationships. The models are similar in function but different in structure from the original biological systems.

In most of the cases the models are predictive and it is possible to deduce some some characteristics of the system. Model also suggests the 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.

Models could be of various types such as mathematical, chemical, electrical, electronics etc. [1] Every type of modelling techniques has some advantages and disadvantages and their selection depends upon requirements and objectives. Biological systems usually require complex equations for representations in mathematical format. Chemical models require large space, more cost and also are not convenient in varying its parameters for observing their effects on overall systems or a part of the system. The electrical/electronic models are small in size, less costly and convenient in handling. Any type of nonlinearity can be included with reasonable accuracy.

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Interest in the clinical application of peripheral and central electrical stimulation of nerves is growing rapidly. Thousands of patients are now being treated for chronic pain.

Using both superficial and implanted electrode Glenn (4) have developed an electropnremic respirator which have been implanted in nearly thousands of the patients with inadequate or no respiratory function. Waters have reported (5) on a series of stroke victims in which paralysed muscles of the leg are activated electrically during ambulation to improve walking. Experimental work is under way (5) to develop neuroelectric prostheses for the deaf and blind. As these clinical efforts multiply, it becomes imperative that an electrical model of nerve system is made available to provide an analytical and experimental foundation for the study of electrical signal propagation and nerve excitation.

Many physical systems are linked to nerve system and therefore many attempts have been made to model the nerve characteristics from last two centuries. (2) Neural system modelling may be expected to exert increasing influence on the course of neurophysiological research.

The selection of parameters in neural modelling has two distinct philosophies.

(a) A very large number of neural properties of actual neuron are reproduced with high accuracies.

(b) A more restricted set of properties is used but the restrictions have been made on the basis of a priori set of assumptions with regard to the significant one.

Models of first type are more complete but more difficult to realise and are more costly. Models of second type are more amenable to analysis but are in great danger of important ommissions.

Once a model of neural system has been realised, there are three types of actions which are to be taken. The first, which is mandatory consists of preliminary validation by testing neural models performance with actual physiological behveriour of the neural system. Successive refinements of the model may then lend to convergence to an accurate and revealing abstraction. Second, after the validity is tentatively established it could be attempted to discover new propertiesof 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 of the circuit, it is likely that all of them will have been foreseen. Another use of the model is tat it can test hypothesis and explore then direct physiological measurement on the actual neuron.

1.1 ORGANISATION OF PRESENT WORK:- This work deals with analysis and modelling of actual neural system for its important electrical characteristics. An electronic model of neuron with a local feed back has been developed which has capacity to show equivalent electrical properties.

The second chapter deals with the discussion on anatomical and physiological aspects of the neuron. It deals

the analysis of the nerve cell or neuron which is the basic functional unit of the nervous system. Anatomy of neuron is followed by the analysis of the processes occuring inside this unit. All the important electrical characteristics of the neurons are analysed and discussed which form the basis for the development of the neuron model.

The third chapter presents uptodate review of the existing models of the neural system and the research work in this field.

The fourth chapter deals with a new model of the neuron with a local feed back which has been developed by the another. The improvement in this model over existing models are also given. The model is constructed and tested for all the important electrical characteristic of the neuron. The model is tested for steady state and transient conditions.

The fifth chapter summerizes general conclusions about the existing models and also about the new model. Some suggestions are also given for the further work in this field.

CHAPTER 2

ANATOMY AND PHYSIOLOGY OF NEURAL SYSTEM

2.1 INTRODUCTION:

The nervous system of multicellular organism is typically composed of neurons or nerve cells [2]. Neuron is an elementary unit of nervous system which serves to sense and transmit the information in an electrical form from central nervous system to different parts of the body and vice-versa. These may be arranged in a simple or in complex arrays. When a particular part of body is excited the information is carried in either direction with characteristic velocity [1, 4] e.g. if a finger is suddenly exposed to thermal shock, the information reaches to the brain through the neural network and reaction of the brain is transmitted back through the neurons to the finger muscles for further necessary action (say to remove the finger from the source of heat). There is nothing inherrent in neurons which governs the direction of information in it; that is, the same neuron work as sensory as well as motoneuron [1].

The information flow is essentially an electrical phenomenon as has been evidenced by experimental facts [2]. There are some 10^{10} neurons [2] in the human Central Nervous System (CNS) consisting of brain and spinal cord.

The Central Nervous System is most important part of the human transmission system. It consists of the following parts [34]:-

1. Nerve cells
2. Glial cells
3. Blood vessels
4. Cerebraspinal fluid

2.2 ANATOMY OF NEURONS:

The human Central Nervous System contains a complicated network of perhaps ten billion highly specialised cells called neurons, or nerve cells [2]. Although no two neurons have exactly the same structure, fortunately they do share certain features [2] that are significant for the neurophsiologist. Like other cells, the neuron is supported by a thin membrane (the plasma membrane) and has a cell body or equivalent soma. Projecting from the soma are a number of extensions of the cell known as the dendrites and the axon. Figure 2.1 shows the important parts of the cell. Generally a single axon arises from the soma, but, as shown in the figure, this axon may give off side branches and characteristically divide into a number of smaller branches, just before terminating. Several dendrites arise from the cell body and then branch again and again to form a complicated tree like structure known as the dendritic tree. Two neurons are interconnected through a Renshaw Cell. The dimensions of a neuron vary greatly from one to the next. Generally the cell body is roughly 30 micron across (1 micron = 10^{-6} meter), and dendrite

so much so that the somatic and dendritic membranes are literally encrusted with synaptic endings [2], on the other hand, a synapse between two axons is less frequently observed [2] although such axo-axonal synapses do occur.

The synapse is of such central importance that it will be useful to have a more detailed picture of structural features shared by the more common types of synapse. Figure 2.2 shows a schematic cross section through a segment of dendrites and several of the numerous axon terminals which make contact with the dendrites. A narrow space about 200 to 300°A wide ($1°A=10^{10}$ meter or 10^{14} micron) [3, 4] separates the presynaptic membrane (the axon terminal adjacent to the dendrites) from the post-synaptic membrane (dendritic part of the synapse); this space is known as the synaptic cleft. On the presynaptic side are found a number of mitochondria, indicating that the region is metabolically active. Although mitochondria are found in cells of all types, there is a conspicuous structre which is characteristic of synapses, the synaptic vesael. Synaptic vehhel as seen with the electron microscope are circular in cross section, 300 to 600°A in diameter, and are nearly always found in numbers adjacent to the presynaptic membrane.

A neuron receives informations through synapses located on its dendrites and soma, integrates this information in its soma, and finally transmit the information over its axon to other cells. The accuracy of the CNS control over the activity of the various organs is due to the existance of a two way circular connection between nerve centres & the peripheral organs [4].

are 200 to 300 micron long. It is the length of the axon which is subjected to the greatest variation from one nerve cell to the next, for axons may be from perhaps 50 micron to several meters long [2].

Nerve cells are not isolated but rather are inter connected in a very characteristic way. A bundle of nerves is called a trunk. A trunk includes a wide range of axon sizes. Diameter of fibres ranges between 0.5 to 1.5 micron [2]. The conduction speed for typical fibers is 1.73×10^6 diameter/sec [2, 3] indicating the speed between 0.5 and 2.3 m/sec [2]. The same trunk carries afferant (toward the brain) fibers from sensory receptors and efferent (away from the brain) fibers to muscles. The largest fibers are myelinated. Myelinated sheath is a relatively thick layer of fatty substances, myelin etc. The walls of the unmyelinated fibers also consists of fatty molecules but these are not visible because they are very thin (100°A wide) [2, 4]. Special points of contact between neurons called synapses, are of particular importance, for it is at the synapse that information flows from one nerve cell to the next. Typically, the axon of one nerve cell forms a synapse with (or synapses with) either the cell body or dendrites of other neurons. Thus there are two principle types of synapses, axo-dendritic (axon with dendrite) and axo-somatic (axon with cell body). In fact, it has been discovered in recent years that virtually all of the surface of a neurons soma and dendrites are provided with axon terminals,

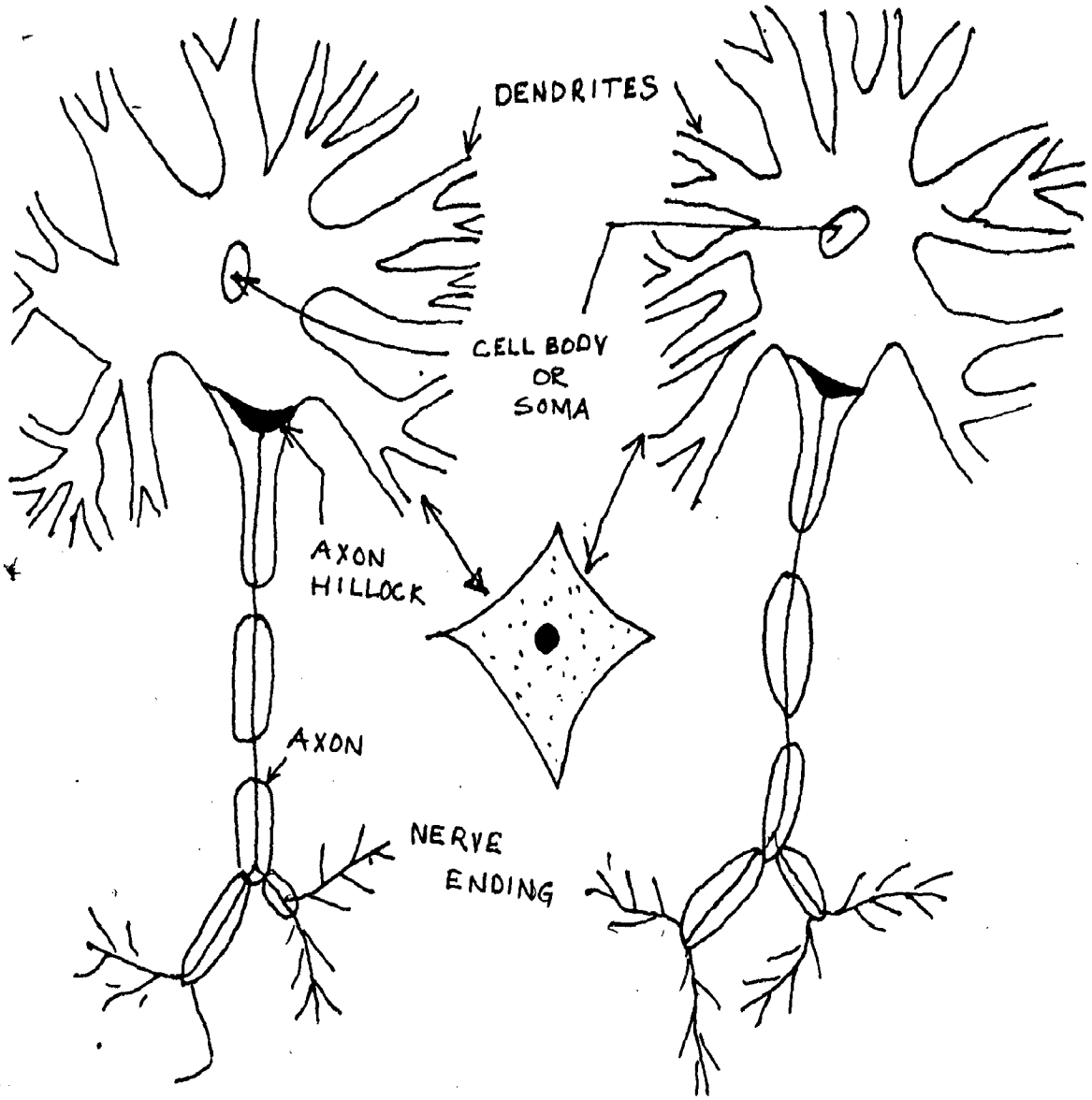


FIG 2.1. IMPORTANT PARTS OF NEURON WITH FEED BACK

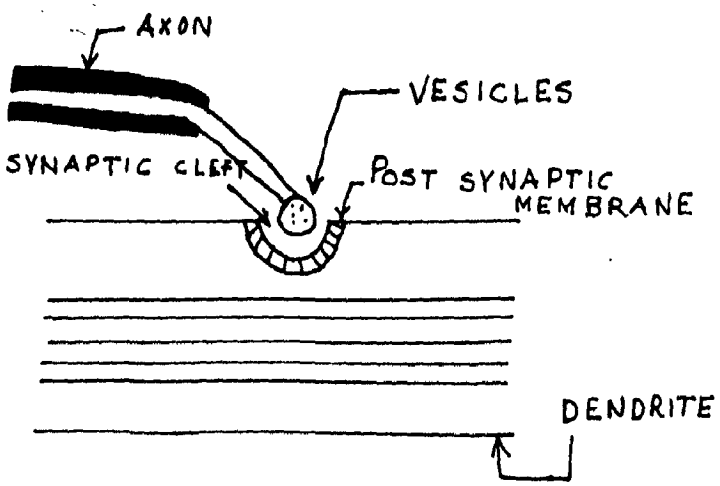


FIG 2.2. SYNAPTIC CONNECTION OF NERVE

Because neurons have synaptic connections with one another, they form neural circuits, and it is the property of these circuits that determine the behaviour of the nervous system and thus of the organism.

Although the brain is complicated, fortunately it is not chaotic despite individual variations. In general, it is possible to distinguish particular brain areas where cell bodies and dendritic trees are concentrated (such areas are called nuclei) and other regions which consists primarily of axons running from one group of neurons to another. In these later region large numbers of closely packed axons run in parallel to form structures called tracts (or fibre tracts) fiber here refers to axon or nerve fibre. Similar tracts also run outside of the brain (for example, to muscles), in which case they are referred to as nerves. Cell bodies are grouped to form nuclei. A single nucleus might contains thousands of neuron cell bodies.

Thus the neuron consists of —

(i) Cell body or soma

(ii) Processes

(a) Dendrites

(b) Axon-Hillock & Axon

2.2.1 <u>CELL BODY OR SOMA:</u>

The cell bodies of neurons are concentrated in the grey matter of the cerebral hemispheres, the subcortical formations, the brain stem, cerebellum and spiral cord. The cell body of a

neuron contains a well defined nucleus and nucleons. Within the cytoplasm are small masses of a deep standing material called Nissl substance. This

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 spiral cord, topologically opposite the muscles they direct. Soma responds to the algebraic summation of incoming message [2].

The soma 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. Cell bodies vary considerably in size, roughly from 5 to 50 microns in diameter. They are a vital part of the neuron. If, as a result of mechanical injury or disease, the cell body is unable to survive, then the processes also die and are unable to carry nervous impulses. Paralysis of muscles follows if injury to neurons prevents nervous impulses from reaching the muscles.

2.2.2 DENDRITES:

The projected part from cell body is known dendrites. Each dendrite branches again and again to form complicated tree like structure as shown in Figure 2.1. The dendrites have certain properties which specialise them for receiving the information transmitted along the axon; similar to the one which originally generated the axonal nerve impulses. The dendrites integrate the information contained in arriving nerve impulses.

After a nerve impulse arrives at an axon terminal, there is a brief delay of about a half millisecond known as synaptic delay followed by a characteristic fluctuation of the dendritic membrane potential. This fluctuation is known as the post-synaptic potential or PSP. The typical PSP has a rapid rise to a peak followed by a much longer (approx. exponential) return to the resting potential.

There are two differences [2] between PSPs and action potentials.

(i) PSPs time duration is larger than an action potential.

(ii) Much smaller in amplitude.

The arriving nerve impulse causes the release of a small quantity of a chemical, generally known as a transmitter substance, which diffuse across synaptic cleft and results in the dendritic electrical response.

There are two important properties of dendrites.

I. GRADED RESPONSIVENESS:- It refers to the fact that the size of a PSP is proportional to the amount of transmitter released and is to be contrasted with the threshold and all or none behaviour characteristic of the axon Figure 2.6.

II. TEMPORAL SUMMATION:

Dendrites, in contrast to the axon, shows no refractory period, "period during which second spike can not arise till the response of the first impulse is not completed". Figure 2.7 shows

that two PSP occuring in rapid succession are seen to sum. This important property, that a new PSP simply adds to what remains of all proceedings PSPs is referred to a temporal summation, if at a particular synapse, nerve impulse begin to arrive with a constant frequency, each resulting PSP will add to the reminder of all preceeding an an increasing depolarisation will occur as the PSPs sum. Rather than increasing indefinitely, the depolarisation will level off at an average value proportional to the frequency at which the nerve impulses are arriving as shown in Figure 2.8.

Since the depolarisation of the neuron results in the production of nerve impulses, the depolarising PSP is termed as excitatory post-synaptic potential (EPSP).

The hyperpolarising PSP is known as an inhibitory post-synaptic potential (or IPSP) because it opposes the action of EPSPs and tends to prevent the generation of action potentials.

The period in which the spike appears and develops correspond to the complete lack of excitability. It is known as the absolute refractory period [4] when another spikes cannot be evolved by a second stimulus, however strong i.e. the minimum period during which it is impossible to evoke a second action potential is known as absolute refractory period. In the quick conducting fibres of warm blooded animals its value is about 0.5 milli-second.

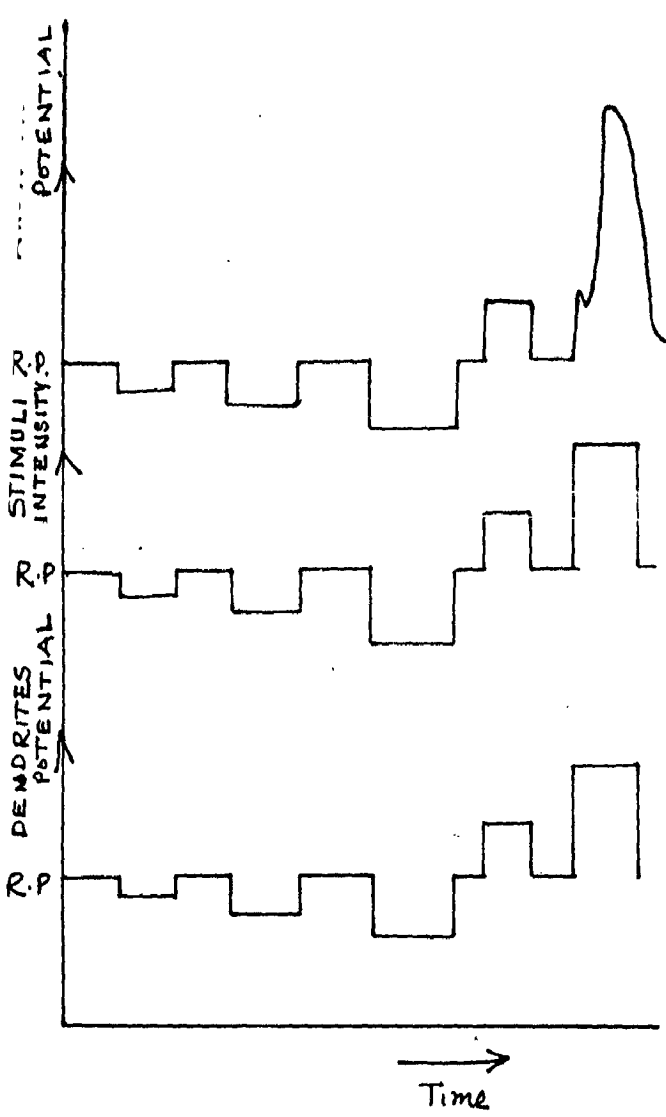


FIG 2.4 RESPONSE OF DENDRITE & AXON WITH AMPLITUDE OF INPUT PULSE

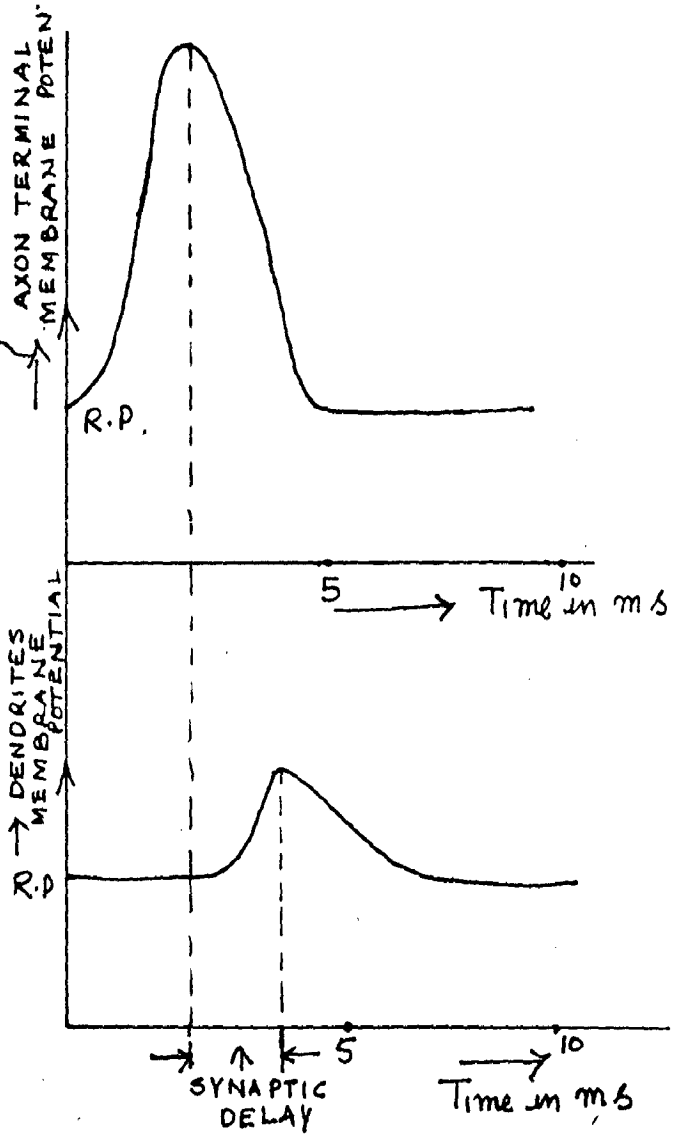


FIG 2.5. RESPONSE WITH ABOVE THRESHOLD STIMULI

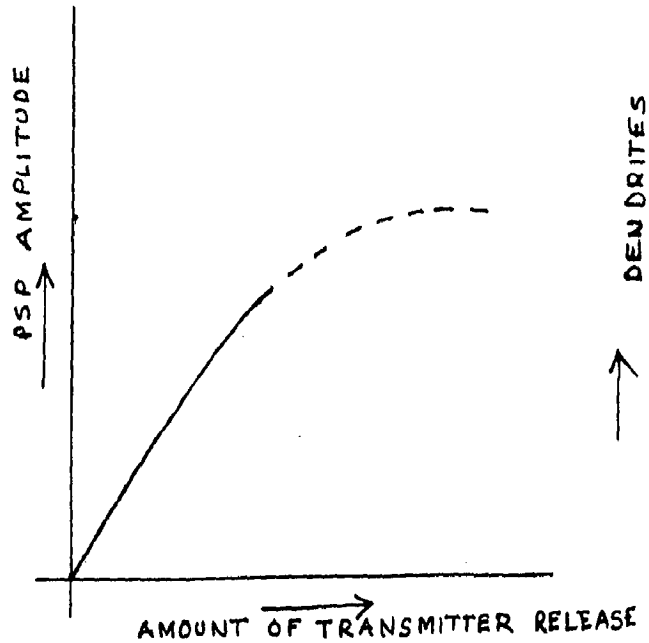
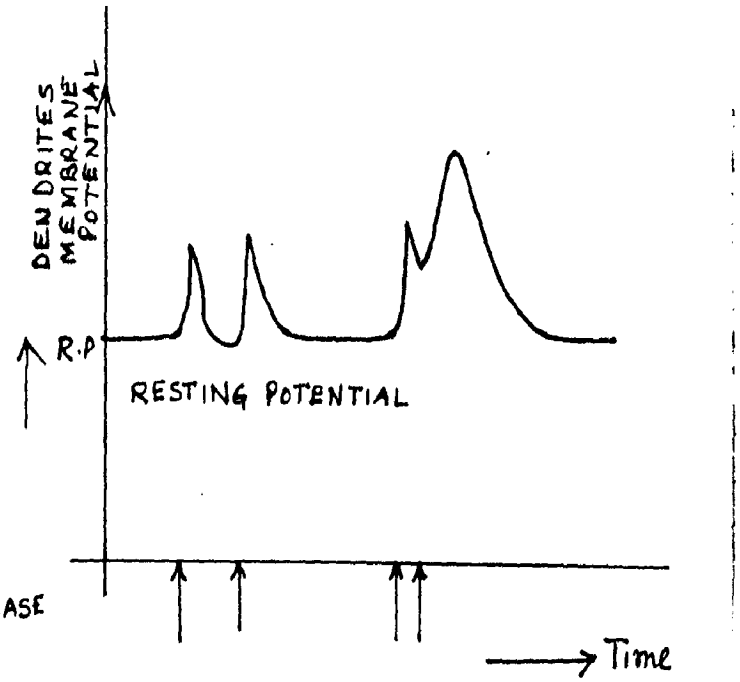


FIG 2·6 GRADED RESPONSE



FIG·2·7 RESPONSE OF DENDRITE

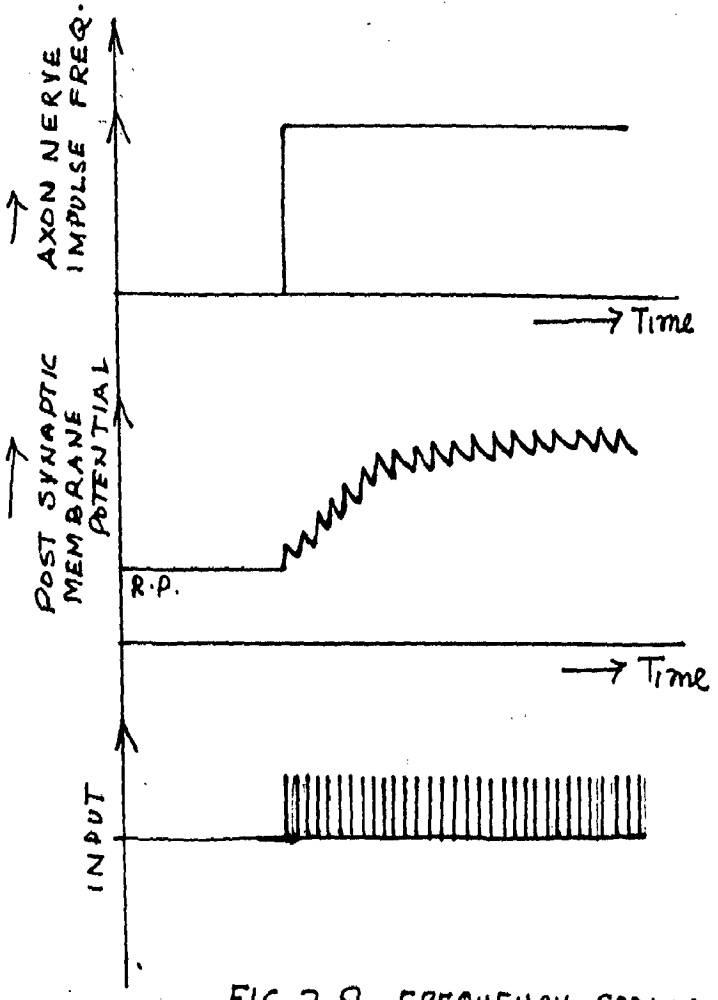


FIG 2·8 FREQUENCY CODING

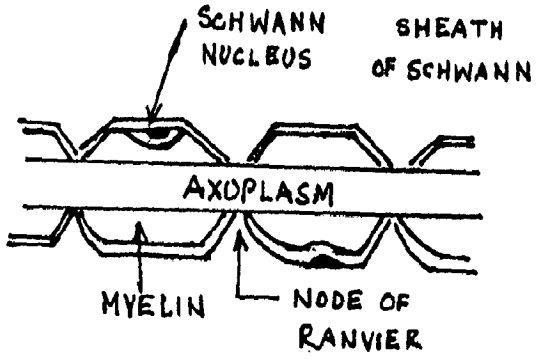


FIG 2·9A MYELINATED NERVE FIBRE

The absolute refractory period is followed by relative refractory phase which lasts for 4 to 8 milli-second [4] in nerve fibres during which the excitability gradually reverts to the initial level prevailing before the first stimulation. In the refractory period which fibre is capable to respond to a strong stimulus but the amplitude of the action potential is much reduced. The amplitude of spike induced by second stimulus increases only when the interval between consecutive stimuli lengthened.

2.2.3 AXON AND AXON-HILLOCK:

The axon is a process that conducts an impulse away from the cell body to other cells or to peripheral organs, it is extended from cell body. The area of the cell from which the axon arises is 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 before the axon becomes covered by the myelin sheath is the initial segment. The special features of this segment is its high excitability. Its stimulus threshold is one-third of that of other parts of the neuron [1, 2]. The axon of the neuron may be very short, as in association neurons (Golgi type II) or it may be two or three feet long, such as those extending from the grey matter to the spinal cord to the muscles of the fingers or toes. Axons terminate in fine branches called terminal filaments or telodendria. The tips of these terminal branches appear to be highly specialised to

provide the transmission of the nerve impulse to succeeding neurons or to a muscle effector. The difference between axon and dendrite is based primarily not on minor differences in structure but on difference in function. The nerve impulse conducted over a series of neurons passes from the axon and terminal filament of on neuron by synaptic transmission to the dendrites and cell body of the succeeding neuron.

The information is transmitted in the form of frequency or the number of impulses per second travelling along the axon. There are two properties of axons which give rise to nerve impulse and to the coding of information [2].

The inside-outside voltage difference across the axon's membrane is referred to as a membrane potential. In the new terminology, the presence of nerve impulse is signalled by a fluctuation in membrane potential. The value of the membrane potential when the axon is at rest, that is, when no nerve impulses are occuring is known as resting membrane potential or simply resting potential. The value of resting potential is same at different locations of the axon. Typical value of resting potential is -60 m.V, so resting potential provide a reference point.

Whenever the membrane potential is more positive than the resting potential, that is, whenever the inside-outside voltage difference is less than -60 mV, the axon is said to be depolarized. If however, the membrane potential is below

the resting value (i.e. about -80 mV), that is more negative than -60 mV, the axon is said to be hyper-polarized. Finally any change which decreases the inside-outside potential difference is known as a depolarisation whereas an increase in the membrane potential is called as hyper polarisation. Axon is normally polarised, that is, has a resting potential and alteration in membrane potential which diminish this resting polarisation are depolarisations, whereas those acting to increase the polarisation are hyper polarisations.

The dendrites, like all parts of the nerve cell including the axon has a resting potential of approximately -60 mV, this resting potential is constant over the length of dendrites and, indeed, over the entire neuron. The dendrites and axons have the same response to hyperpolarising stimuli. In both cases, the response mirrors the stimuli with a slight distortion. The axon response to small depolarisation is passive being always a mirror image of the response to hyperpolarisation of similar magnitude. The property is also shared by dendrites. In summary, dendrites have all of the passive electrical properties of axons as shown in Figure 2.4.

The distinctive property of the axon is its active response to above threshold depolarisation known as the action potential. But the dendrites do not respond to depolarisation, as do axons, by producing action potentials, but rather show only passive responses to both depolarizing and hyperpolarising stimuli of all magnitude as shown in Figure 2.5.

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The magnitude of dendritic depolarisation is approximately proportional to transmitter concentration. When a nerve impulse arrives at the synapse, a small amount of transmitter is released and diffuse across the 200°A or 300°A synaptic cleft to the dendritic membrane. The transmitter concentration at the dendritic membrane increases very rapidly to a peak. Thus dendritic depolarisation increases very rapidly and returns slowly to the resting potential, thus producing the PSP.

2.2.4 SYNAPSES IN THE CNS:

Special points of contact between neurons, called synapses, are of particular importance, for it is at the synapse that information flows from one nerve cell to the next. Synapses located on the body (Soma) of a neuron are called axo somatic and those on the dendrites are called axo dendritic. As pointed out earlier a synapse in the CNS, consists of three principal elements [1, 2] as shown in Figure 2.2.

(i) Presynaptic membrane

(ii) Post-synaptic membrane

(iii) Synaptic cleft

(i) PRE-SYNAPTIC MEMBRANE:

Nerve ending in the CNS vary in shape, generally looking like knobs; each synaptic knob is covered with a membrane, the so called pre-synaptic membrane [1, 2]. It is the axon terminal adjacent to the dendrite. Nerve cells are not isolated rather

inter-connected in a very characteristic way. Pre-synaptic membrane covers the nerve ending. The nerve ending is a peculiar neuro-secretary apparatus, which secrete the mediator that produces a stimulating excitatory or inhibitory effect on the innervated Cell. [4]. The mediatrons are highly active chemical compounds.

(ii) POST-SYNAPTIC MEMBRANE:

It is the dendritic part of the synapse. The portion of the membrane of the innervated cell directly adjoining the nerve ending is known as the post synaptic membrane. The post synaptic 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 [1, 2].

(iii) SYNAPTIC CLEFT:

A narrow space about 200 to 300°A wide ($1°A = 10^{10}$ metre) separates the pre-synaptic membrane (the axon terminal adjacent to the dendrite) from the post synaptic membrane (dendritic part of the synapse); this space is known as the synaptic cleft.

Because neurons have synaptic connections with one another, they form neural circuits, and it is the properties of these circuits that determine the behaviour of the nervous system and thus of organism.

2.2.5 UNMYELINATED AXON:

It resembles a tube that is filled with a weak solution mostly of potassium ions (K^+). The fibre is surrounded by the interstitial fluid of the body essential a Na^+ Cl^- solution.

Total internal and external concentrations are about the same. The diameter of the fibres ranges between 0.3 and 1.3 micron [1]. The conduction speed for typical fibres is 1.73×10^6 times diameter per second indicating speed between 0.5 and 2.3 m/sec [1].

The difference between internal and external concentration and temperature are maintained by metabolic activity. The inside of the fibre at rest displays a potential of $v = -70$ mV with respect to the outside. This corresponds to an electric field within the membrane of 70 mV/100°A = 70000 V/Cm. By way of comparison the dielectric strength of insulating oil is about 10000 V/Cm [1]. It turn out that the fibre signal is a spike that is accompanied by break-down of the membrane. This break-down, in fact, regenerates the signal. The fibre operates with a threshold of about -50mV, when the inside at any point becomes more positive than this value, the break down is triggered. The membrane becomes permeable to sodium ions for about 2 milli second, as the ions enter the fibre, the voltage increases to approximately +30mV. After about 2 milli second internal, there is an additional 2 milli second refractory period (interval) during which the membrane becomes a relatively good insulator again. Because the disturbance is 4 milli second wide, the maximum possible frequency is 250 Hz. The excess sodium ions that leaked in are slowly and more or less continuously pumped out with energy supplied by the metabolic activity. The -70mV resting membrane potential [1] may be regarded as a d.c. component that is super-imposed on the 100 mV peak spike known as an action potential that actually constitutes the axon signal.

In unmyelinated axon the action potential sweeps continuously along the axon, the action potential from one small segment of axon spreads passively to the adjacent segment where it acts as a stimulus to produce another action potential. This process is repeated for entire length of axon [2].

2.2.6 MYELINATED AXON:

The myelin sheath at a regular interval of 1 to 2.5mm is periodically interruped by the nodes of Ranivier [1, 4] as shown in Figure 2.9. It is at these modes that the action potential is regenerated in the usual way by an inward diffusion of sodium ions between one node and the next. The fibre behaves like a passive RC cable that is if a 100 mV spike originate at a particular node [4], it will appear at the next node with increased width and reduced height. The height is normally sufficient to overcome the threshold requirement of 20 mV peak, so that regeneration takes place. Fibre external diameter range from 1 to 22 microns [2]. In contrast to the unmyelinated structure in which the membrane thickness remains constant of 100°A. The myelin thickness if approximately proportional to fibre diameter. The conduction speed is about 10 times (i.e. 120 m/sec) than that of unmyelinated axon [2].

Large nerve fibres are characterised by the fact that they are surrounded by a myelin sheath of mainly lipoid material as shown in Figure 2.9A. The myelin sheath in turn is surrounded by a specialised tube of cell called the Schwann Cell. According to present concepts, the myelin sheath actually consists of many

layers of schwann cell membrane which were left behind as the cell body rotated around the axon during growth. The nodal region is characterised by its low electrical resistance. This geometry imparts certain constraints on conduction in myelinated axons.

The plasma membrane surrounding a neuron can be investigated by using electron microscopy and X.ray differaction methods. Additional information on the properties of the membrane has been deducted from permeability, electrical conductivity and surface tension measurements.

The presence of myelin sheath around large axons tend to alter the mode of propagation in this type of fibre [1].

To sheath which may be composed of a considerable number of tight turns of 120°A thick lamina [1, 2] has low electrical conductivity and functions much as insulating material on a metallic wire. The node of ranvier is covered only by schwann cell cytoplasm and form a functional point of view, the axon plasma membrane is bare at the node. Activation in the myelinated axons, therefore, occurs at a nodal region and produces a local circuit current which completes the closed loop via adjacent nodes. As current flow is constrained primarily to nodal area, current density is relatively high at these circumscribed sites. For this reason, the activation jumps from node to node, and this phenomenna is called saltatory conduction. Myelinated portion of the axon does not give action potential when depolarised. Thus the action potential moves along the axon by passive spread in the myelinated regions and by the occurence

of action potentials at the nodes [2].

2.2.7 RENSHAW CELL:

Impulses arriving at central nervous system do not only produce excitation in a given neuron or nerve centre but also in other neurons or nerve centres. This spread of excitation is known as irradiation. It is due to the numerous branching of the dendrites and axons and also due to chains of inter neurons connected to various nerve centres. This phenomenon of irradiation is obstructed by the inhibitory inputs at various nerve centres. An important role is played in limiting this irradiation by Renshaw Cell. It has inhibitory synapses with neurons. Renshaw Cell gives inhibitory inputs to neurons and its output frequency dependent upon level of excitation. Renshaw Cell acts as a protective device against excessive excitation. It forms a local negative feed back loop in the neuron and also with nearby neurons [3].

In Figure 2.4 (a) the antagonistic inhibition suppress excitatory events without influencing the excitatory process by which it was generated. Therefore, there is no feed back to the source of excitation [7]. On the other hand, the inhibitory interneuron in Figure 2.9 (b) act back as the cells by which they themselves were activated. In this case there is a negative feed back and this inhibition is termed as feed back inhibition. As Figure 2.9 (b) shows the motoaxons give off collaterals to

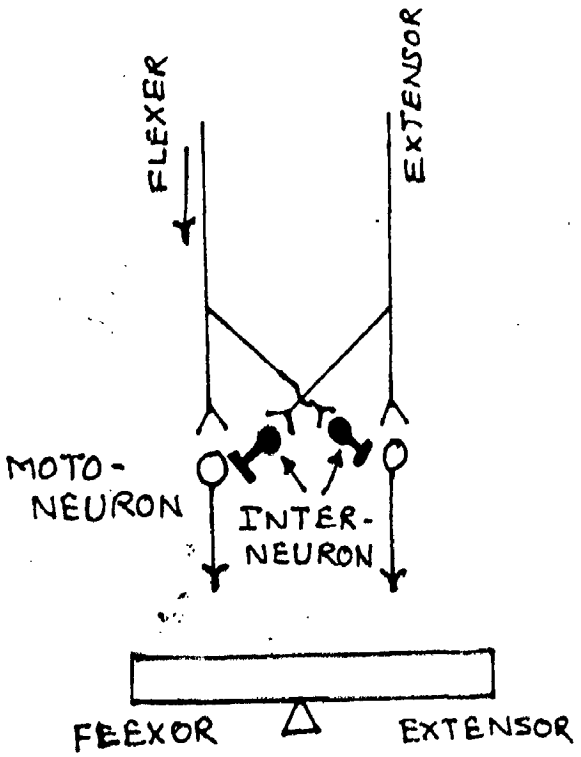


FIG 2.9(a)

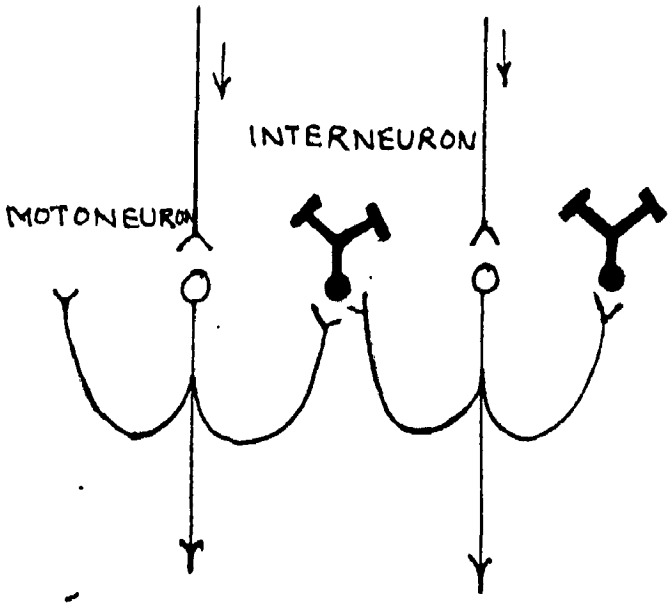
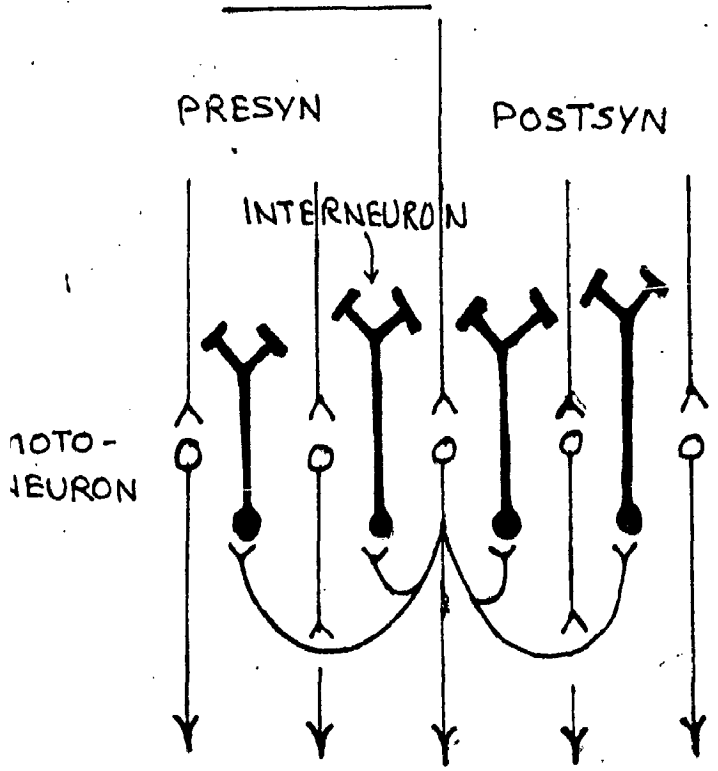


FIG 2.9 (b)



TO CENTER

FIG 2.9(c)

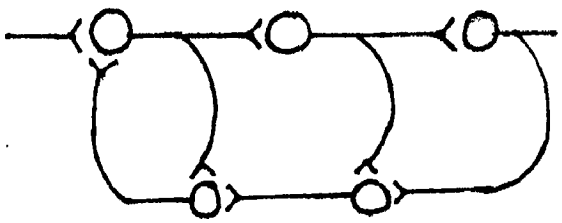


FIG 2.9 (d)

FIG 2.9 B

FIG 2.9 (a) ANTAGONISTIC INHIBITION

FIG 2.9 (b) NEGATIVE FEEDBACK INHIBITION (RENSHAW INHIBITION)

FIG 2.9(c) LATERAL INHIBITION (SURROUNDING INHIBITION)

FIG 2.9 (d) EXCITATORY FEEDBACK

inhibitory interneurons whose axons in turn form inhibitory synapse on motoneurons [7]. This inhibitory inter neurons are called Renshaw Cells. As the moto neurons becomes more excited, the Renshaw Cells also become more excited, resulting in greater inhibition as the moto neurons after a short latent period (one inter neuron). This guarantees that weak moto neurons activity is transmitted undisturbed to the muscles while the excessive activity is damped to prevent hyperactivity of the muscles. The inhibitory inter neurons shown in dark in Figure 2.4.

A similar form of inhibitory feed back circuit frequently encountered in the CNS as shown in Figure 2.6 (c). The inhibitory inter neurons are connected in such a way that they act not only back on the excited cell itself (arrow) but also on neighbouring cells with the same function and in such a manner that these cells are particularly strongly inhibited. This type of inhibition is called lateral inhibition because it ensures that an inhibited zone is generated lateral to the excited zone. Excitation is thus surrounding from all sides by an inhibited field, therefore, the phenomenon is also referred to as surrounding inhibition.

The CNS also contains positive feed back circuit which by feeding back excitation to already excited cells, would cause the excitation to move in a circle (reverberating excitation). An excitatory feed back circuit of this type is shown in

...23...

Figure 2.3 (d). It could serve to maintain an induced activity for a long period. Many people say [7] that short term memory is due to the reverberating of excitation in such positive feed back circuits, yet there is almost no experimental evidence to support this [7].

2.2.8 SOURCE OF THE NERVE IMPULSE:

The impulse that travels along a nerve was once thought to be an electric current. In myelinated nerves of animals it travels at about the same speed as a bullet from a revaluer, the maximum velocity being about 90 to 120 metre/second. The speed of the nerve impulse is much slower in cold blooded animal. In the frog, at room temperature, the maximum velocity is about 30 metre/second. Conduction rates vary with the temperature, the kind of animal invalued, the diameter of fibre and the nature of the fibre covering, that is, whether or not the fibre is myelinated. In general, the largest fibres record the highest conduction rates and greatest spike potential and vice versa.

The nerve impulse is an action potential in the nerve fibre membrane that progresses along the nerve fibre, jumping from one node to another, and deriving its energy from metabolic sources within the neuron as seen earlier. This action is called the saltatory conduction. The action potential is self propagating and represents a progressive depolarisation of the membrane. The nervous excitation is a series of ionic changes

resulting in a change of electrical sign, as the membrane excitation becomes much more permeable to sodium ions and at rest it is permeable to Potassium ions (K^+).

The membrane resting potential is approximately -70mV (to the outside) 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].

2.2.9 SOURCE OF RESTING MEMBRANE POTENTIAL:

The potential difference in rest state between the outer surface and its protoplasm is called resting membrane potential, which is of the order of -60 to -90 mV. Its origin has been explained theoretically as well as experimentally by Hodgkin and Huxley in 1952 [1]. According to their theory the bio-electric potentials are caused by unequal concentrations of K^+, Na^+ and 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 contain 30 to 50 times as many K^+ ions, 8 to 10 times fewer Na^+ ions and 50 times fewer Cl^- ions as does the extra cellular 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 with the help of electron microscopy, X-Ray differaction and chemical analysis. It consists of a double layer of phospholipid

It is postulated that in the resting neuron, so called 'Sodium pump' continually forces sodium ions outward through the membrane against an electro-chemical gradient. At the same time the potassium ions are able to move into the fibre. To maintain a ratio of 30:1, however, there must be some sort of active transport for potassium ions also. The energy for this active transport must come from the Cell's own metabolism. Chloride ions are able to diffuse through the cell membrane in either direction at equal rates. Actually chloride ions, being negative Cl^- tends to be repelled by the negative charge inside the fibre and are forced outward through the membrane. The initial negativety also tends to keep them outside. The interstitial fluid on the outside of the axon membrane is composed largely of sodium and chlorides ions, which represents about 90% of the ionic consentration, where ever such ions represent less than 10% of the total concentration inside the fibre. Membrane potential can be get from Nernst's equation [33]

$$V = \pm \frac{RT}{F} \ln \frac{C_e}{C_i}$$

R = Gas constant

T = Absolute temperature

F = Faraday constant

C_e = External concentration

C_i = Internal concentration

...27...

molecules lines on the inside and on the outside with a layer of molecules of compound carbohydrates mucopoly-saccharides. In the cell membrane there are minute channels or pores a few °A in diameter, through which molecules of water, ions and other substances pass in and out of the cell as shown in Figure 2.10.

It is supposed that the presence of dissociated phosphate and carboxyle groups is the reason why the membrane of nerve fibre is much less permeable to anion than that the cations. Permeability of 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 to 100 times that to Na^+ ions, 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 external fluid gives 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].

In the resting neuron, the sodium ions, which are positive, are in excess outside the membrane in the ratio of about 10:1. Potassium ions, also positive, are in excess within the fibre, the ratio being 30:1. It is obvious that these ratios represent a high degree of ionic unbalance.

2.2.10 SOURCE OF ACTION POTENTIAL:

The reason for the appearance of an action potential in the nerve and a muscle fibre is a change in the ion permeability of the membrane. The membrane permeability to potassium in a state of rest, exceeds that of the 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 cell body membrane is electrically positive to the inner one [2].

Under the effect of a stimulus on the cell, membrane permeability of sodium ions increases remarkably to a point where it is approximately 10 times that of potassium ions. The flow of Na^{+} ions from the surrounding fluid into the protoplasm therefore begins to exceed the outflow of potassium ions considerably, which reverses the sign of the membrane charge, its outer surface becomes electrically negative to its inner surface. The change is registered as a rise of the action potential curve (depolarisation phase) Figure 2.11A & 2.11B.

The increase in permeability to sodium ions continue in nerve fibres for only a very short time, and is followed by the appearance of restorative process in the cell that lead to new decrease in membrane permeability to sodium ions and an increases in that to potassium ions.

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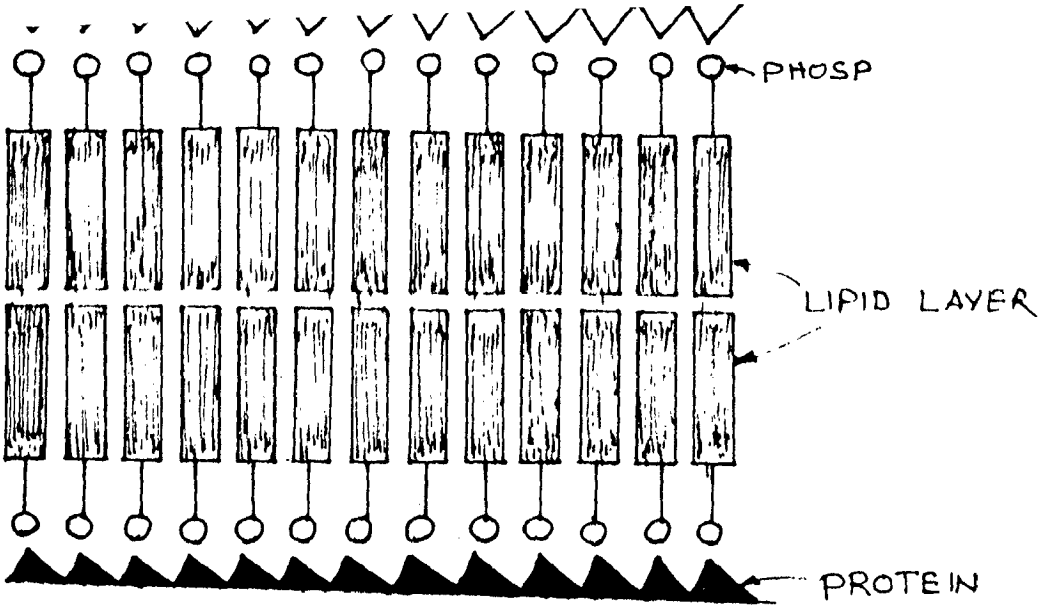

FIG 2.10 MOLECULAR STRUCTURE OF MEMBRANE

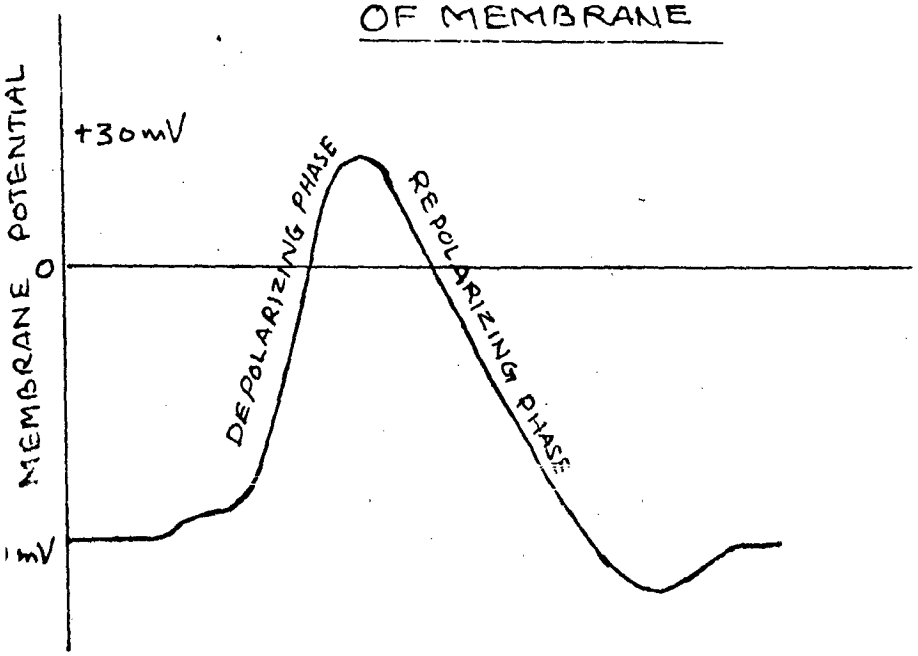

FIG 3.11(a) ACTION POTENTIAL

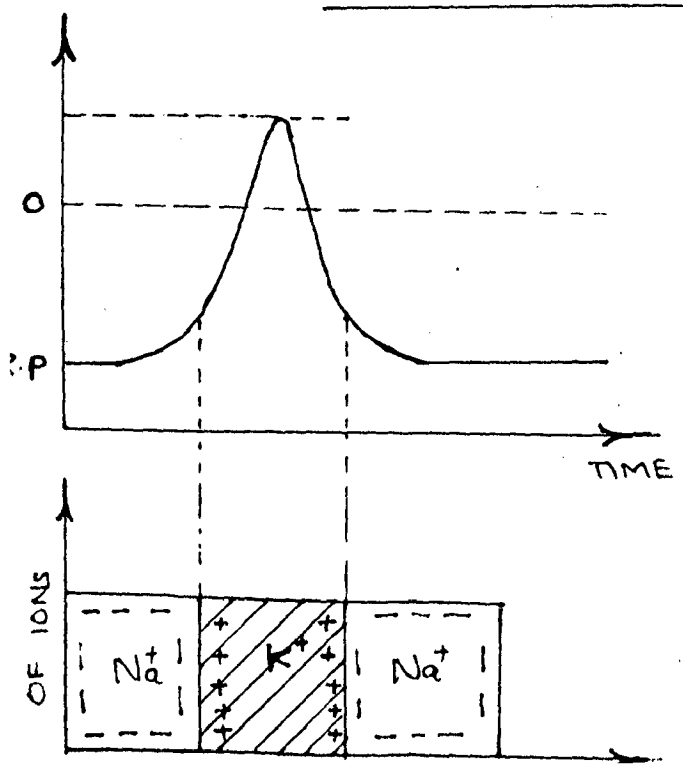

FIG 3.11(b) MEMBRANE POTENTIAL Vs CONCENTRATION

→ EXCESS OF K^+ IONS

→ EXCESS OF Na^+ IONS

The process leading to a fall in the sodium permeability of the membrane is called inactivation by Hodgkin. As a result of inactivation the flow of positive Na^+ ions into the protoplasm is sharply reduced, while a simultaneously increase in potassium permeability intensifies the flow of positive K^+ ions out of the protoplasm into the surrounding medium. The two processes results in repolarisation of the membrane, its outer surface again acquires a positive charge and the inner surface a negative one. The change is registered as a descending part of the action potential curve (repolarisation phase) as shown in Figure 2.11.

The electrical model of the nerve cell is as shown in Figure 2.12.

The current flows

$$i = C\frac{dv}{dt} + G_{Na}(V - V_{Na}) + G_K(V - V_K)$$

Current flows through G_L is very small as compared to others, where

G_{Na} = Sodium permeability conductance

G_K = Potassium permeability conductance

G_L = Chloride permeability conductance

<u>At steady state:</u>

$$i = \frac{dv}{dt} = 0$$

$$V = \frac{G_{Na}V_{Na} + G_K V_K}{G_{Na} + G_K}$$

Here V_K V V_{Na}

At resting state:

g_k is larger than g_{Na} and so V is nearer to V_k than to V_{Na}.

NEGATIVE AFTER POTENTIAL:

The repolarisation phase of the action potential is divided into two parts of unequal duration. At first depolarisation of the membrane proceeds quickly, then there is a slackness and finally stops, and it is at this moment the beginning of the negative after potential starts. The membrane remains partly depolarised for a certain time and complete restoration to the initial potential of -85 mV occurs after approximately 15 millisecond [1] Figure 2.13. Negative after potential is often called after depolarisation of the membrane. This is apparently due to membrane permeability to sodium ions remaining increased for a specifiedtime after termination of the action potential as compared with initial level.

POSITIVE AFTER POTENTIAL:

Positive after potential occurs before the depolarising phase start and it is well seen in unmyelinated nerve fibre Figure 2.14 [4]. The positive action potential is due to the fact that membrane permeability to K^+ ions remains heightened for a time of termination of the action potential as compared with the initial level. An increase in the flow of potassium ions

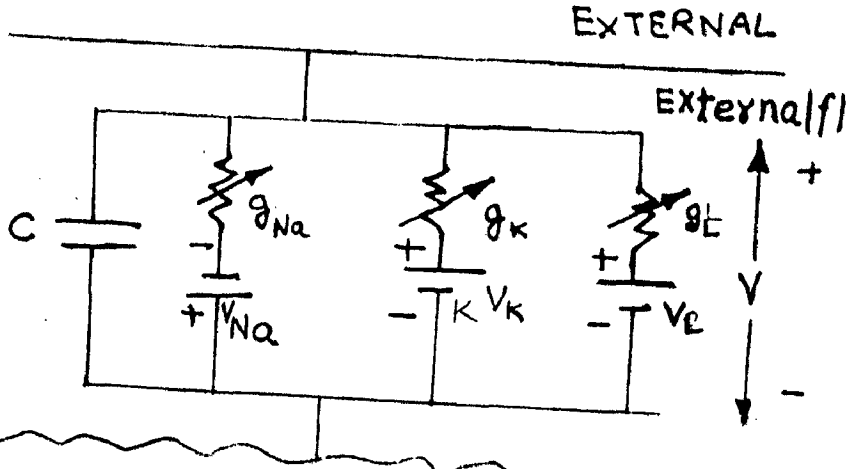

FIG 2.12 ELECTRICAL MODEL OF NERVE CELL

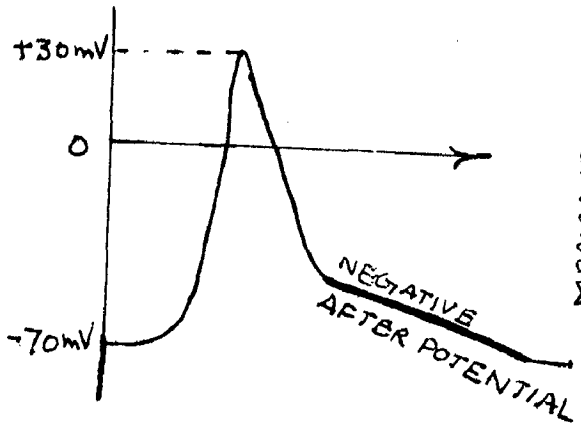

FIG 2.13 NEGATIVE AFTER POTENTIAL

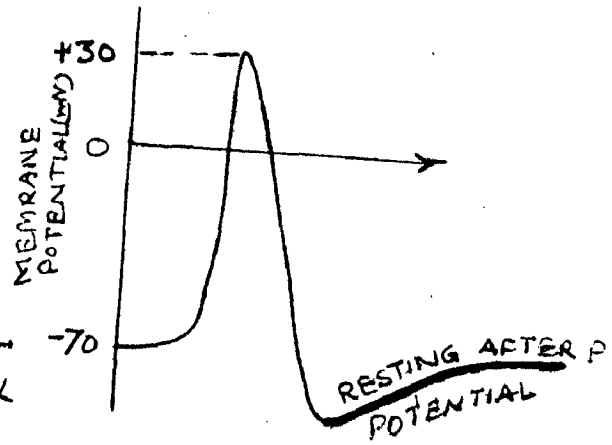

FIG 2.14 POSITIVE AFTER POTENTIAL

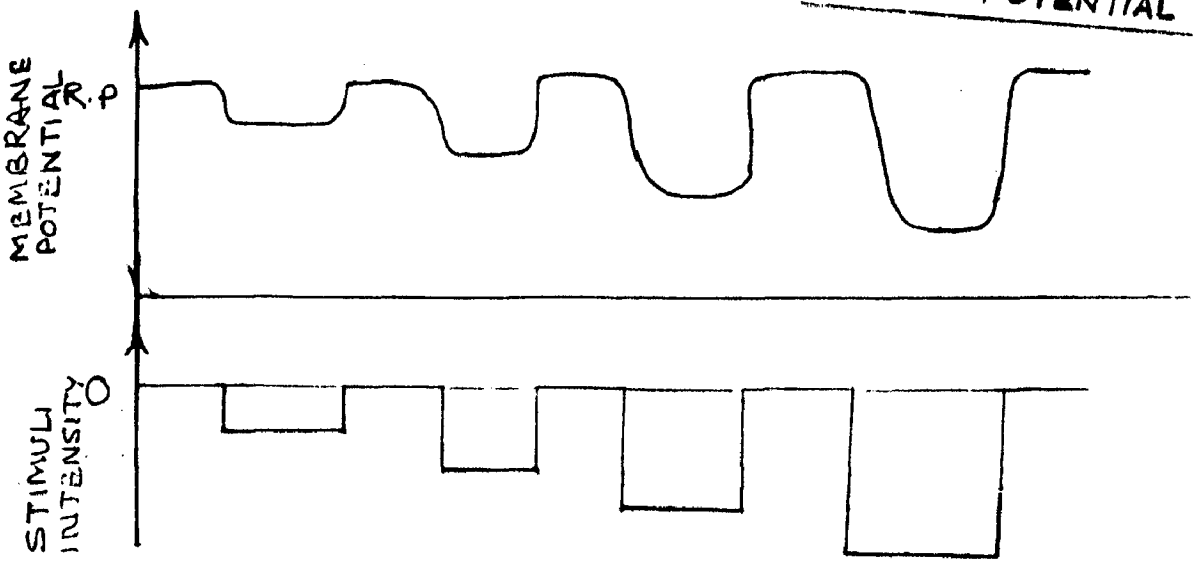

FIG 2.15 RESPONSE OF HYPERPOLARIZING STIMULI

from the protoplasm leads to an increase in membrane potential i.e. to an after hyper polarisation of the membrane.

2.2.11 THE ACTION POTENTIAL AND FREQUENCY CODING:

Any voltage applied to the electrode, which is inserted into the axon acts as stimulus. If a brief stimulus is applied to the axon (a stimulus resulting in a perhaps 15 mV depolarization) the response of axon is an action potential. This action potential consists of a brief (approximately 0.5 milli second) fluctuation in membrane potential with a characteristic configuration; the membrane potential undergoes a large, rapid depolarisation followed by a slightly less rapid return to the resting potential (Fig. 2.11). The peak depolarisation makes axon positive on the inside briefly, that is, the depolarisation is so large at the peak of the action potential that the sign of inside-outside potential differences actually reverse from negative to positive (+30 mV). It is called ascending phase. During the descending phase the membrane polarisation reverts to the resting level is known as repolarisation phase. The length of the action potential in nerve and skeltal muscle fibres varies from 0.1 to 5 mS during which repolarisation phase is always larger than the depolarisation. Cooling of the fibres by 10°C makes the action potential approximately three times larger [2], specially its descending phase.

When hyperpolarising stimulus (negative) is applied through the electrode, no action potential results, but rather the membrane potential simply follows the stimulus with slight distortion, as in the case of dendrites, shown in Figure 2.15.

Because the axon's response to the hyperpolarisation is simply a reflection of the stimulus, it can be said that hypder-polarising stimuli result in a passive response, while depolarizing stimuli result in an active response i.e. action potential.

For a very small depolarizing stimuli, only a passive response results the response simply mirrors the stimulus with slight distortion. This passive response is identical to the one seen with hyper-polarising stimuli, except, of course, that the direction is reversed to mirror the depolarizing stimuli applied as shown in Figure 2.16.

As the intensity of the stimulus is gradually increased, the magnitude of the passive response increases proportionally. With still further increase in stimulus strength a new active component of the stimulus is removed, a small bump is seen on the falling phase of the passive response (Figure 2.17).

As the stimulus magnitude is made still large, this bump grows in size. Finally, when the stimulus intensity is increased beyond threshold value, an action potential generated. Further increase in the stimulus intensity produce no further increases in the size of axon's response, all action potentials are of same size irrespective of the stimulus magnitude as shown in Figure 2.18.

Thus, whenever stimulus beyond threshold value is available, action potential is generated whereas no response results if stimulus is less than threshold. This property of axon is known as 'all or none law".

The interval between the onset of the stimulus and the peak of the action potential is known as latency. It decreases systematically as stimulus magnitude increased. Thus stronger the stimulus, the shorter the latency. A graph of latency as a function of stimulus strength (Figure 2.19) is known as a strength latency curve, it has approximately the same shape for different types of axons although the range of latencies observed may be very different.

The phenomenon of frequency coding is a consequence of several properties of the action potential. Frequency coding means, the coding of the information in terms of the impulse frequency [2].

If a long duration sub-threshold stimulus is used, it will simply produce depolarisation lasting for the period of time that the stimulus was applied. However, if a long lasting above threshold stimulus is used, action potential will generate. Immediately after the first action potential the situation is complicated by the presence of a stimulus during the absolute refractory period when another action potential is not possible. In one type of axon the threshold returns from its high value to the resting level and eventually reaches a point at which the

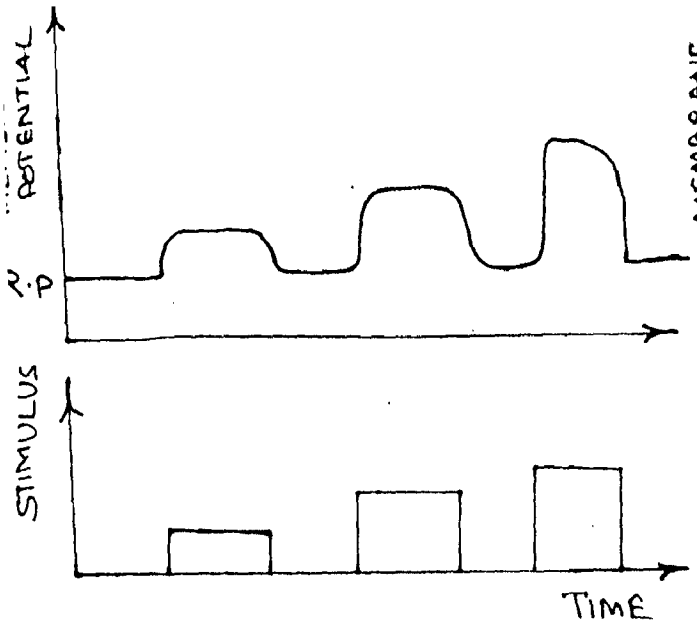

FIG 2.16
PASSIVE RESPONSE OF NERVE

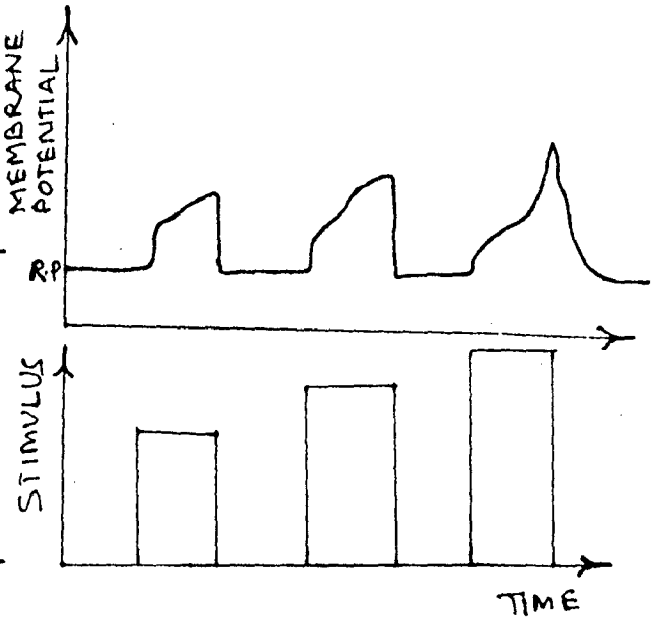

FIG 2.17
PASSIVE RESPONSE OF NERVE OF DEPOLARIZING STIMULI

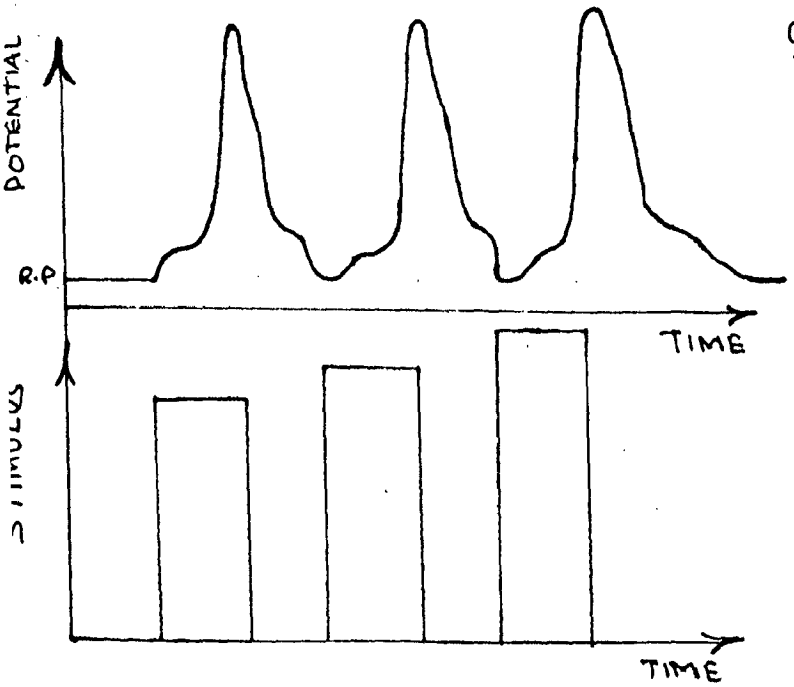

FIG 2.18 : ACTIVE RESPONSE OF NERVE

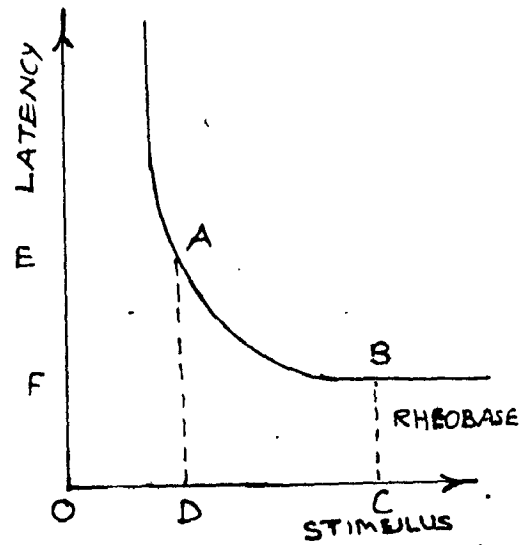

FIG 2.19 : STRENGTH -Vs LATENCY CURVE

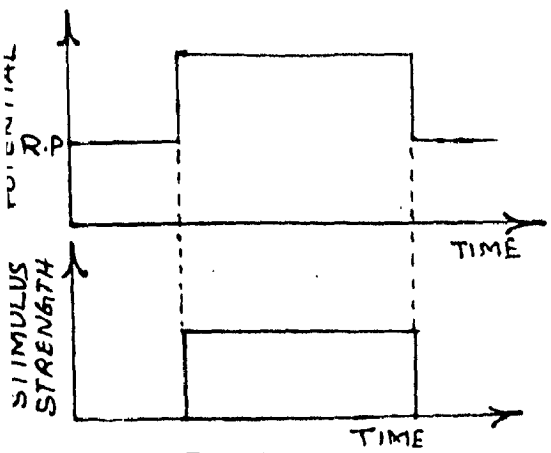

FIG 220 (a)

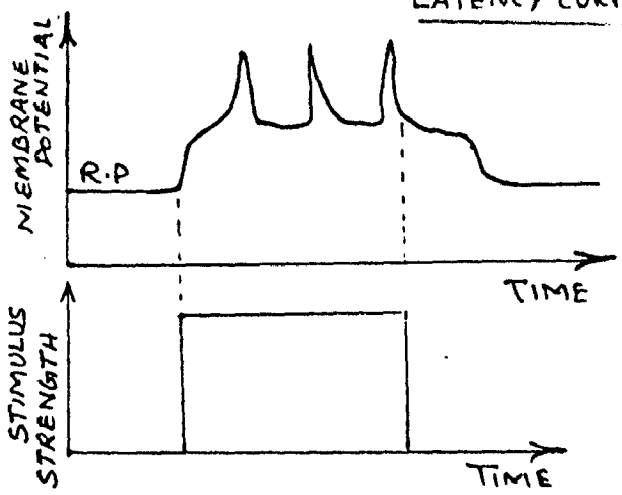

FIG 220 (b)

IG 2.20 - MEMBRANE POTENTIAL Vs STIMULUS INTENSITY
(a) BELOW THRESHOLD (b) ABOVE THRESHOLD

maintained stimulus is effective in causing a second action potential. The same process will re-occur again and again as long as the stimulus is maintained, repeatedly, giving rise to action potential as shown in Figure 2.20.

By similar reasoning it is possible to deduce the relationship between nerve impulse frequency and stimulus intensity for the type of neuron which is considered.

The repetative occurence of nerve impulses in response to maintained depolarisation was predicted on the basis of the refractory period; after one action potential has occured, a certain amount of time is necessary for the threshold to return to a level where the maintained stimulus is again able to evoke a second action potential. If the stronger stimulus was used, however, there would be a shorter interval between successive impulses since the threshold would not have to return to as low level for the larger stimulus to be effective. Thus nerve impulse frequency would increase as the magnitude of a maintained depolarisation increased.

The strength - latency relationship provides a second reason why increasing stimulus-strength produces a higher nerve impulse frequency.

The all or none law, which states that the size of an action potential is independent of the magnitude of the stimulus which produces its means that information about stimulus intensity

must be carried some way other than response magnitude. An alternate means of coding information is provided by the properties of refractory period and strength-latency relationship; information about stimulus intensity is contained in the number of nerve impulses occuring per second. The relationship is shown in Figure 2.21.

Some axons do not produce action potentials repeatively when it is subjected to a constant depolarization, but rather produces only one or several action potential at the onset of the stimulus and then becomes silent inspite of the continuing depolarisation. This phenomenon is usually called accommodation. Usually only the initial segments near the cell body translate depolarisation into nerve impulse frequency.

Excitation of some neurons depends not only on stimuli strength and duration but also on the steepness of its increase. When the steepness of the rise is reduced below a certain minimum value, 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 tissues raising the threshold and interfering with stimulation. This phenomenon is known as adaptation. The phenomenon of adaptation of excitable tissue to a slowly increasing stimulus is known as accommodation.

EXCITATORY POST-SYNAPTIC POTENTIAL (EPSP):

Since the synaptic cleft is very narrow (about 200Å) the mediator quickly (0.5 milli second) diffuse to the post-synaptic membrane and interact with its structural components when impulse is applied. This results in considerably increase in permeability of the post-synaptic membrane to sodium and potassium ions which is followed by its depolarisation and the EPSP appears [4].

INHIBITORY POST-SYNAPTIC POTENTIAL (IPSP):

The impulse generated by inhibitory neurons, which are present in the spinal cord and in brains, is arrived at the nerve ending along the axons cause secretion of a mediator which does not depolarise the post-synaptic membrane, but on the contrast, hyper-polarises it. The hyperpolarisation is registered in the form of an electrical positive wave described as IPSP.

2.2.12 THE EFFECTS OF TEMPERATURE ON NEURONAL EXCITABILITY:

The effect of temperature over the range of 30°C to 37°C, on the membrane was studied by Mac Ever [22].

The experiment was conducted to carry out the effect of temperature. It was shown that the inter-cellular electrode diffusion potential and tip resistance varied considerably with temperature. The following results were made.

I. DEPOLARISATION:

Resting membrane potential depolarised from -82.5 ± 0.5mV

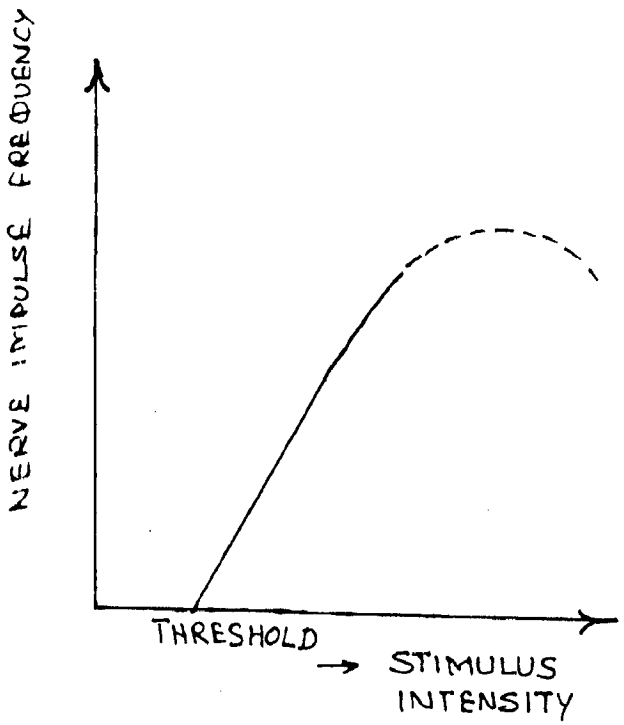

FIG. 3.21

NERVE IMPULSE FREQUENCY Vs STIMULUS INTENSITY

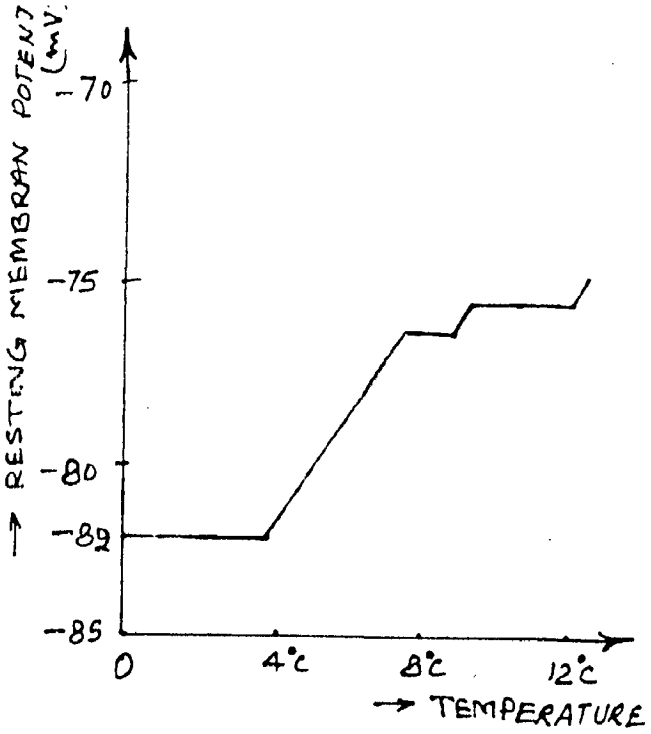

FIG 2.23(a)

RESTING MEMBRANE POTENTIAL OVER TEMP. RANGE 5-15°C

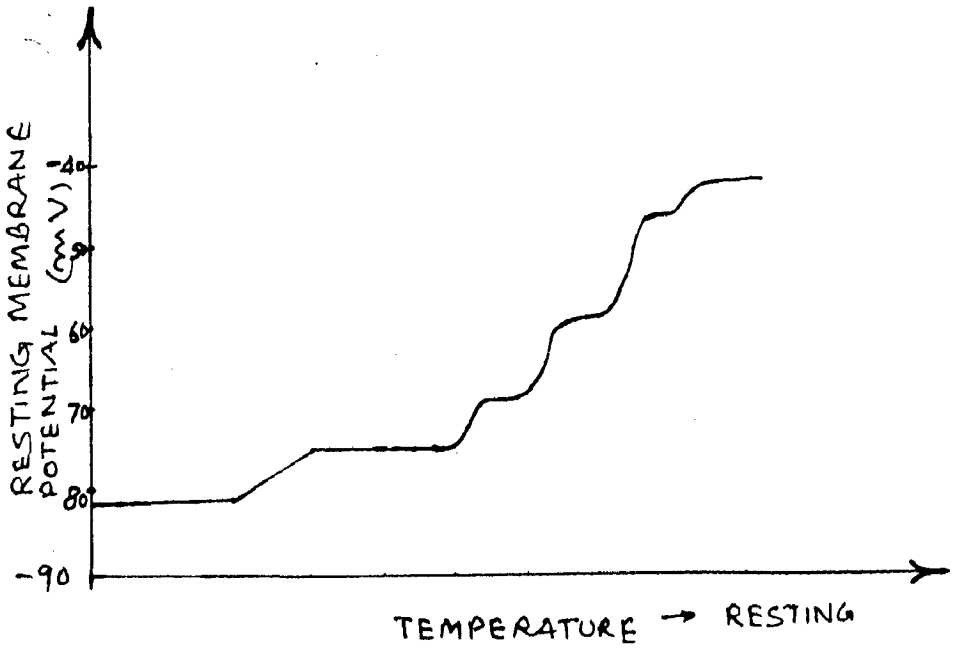

FIG 2.22

RESTING MEMBRANE POTENTIAL Vs TEMP. OVER 3°C - 37°C

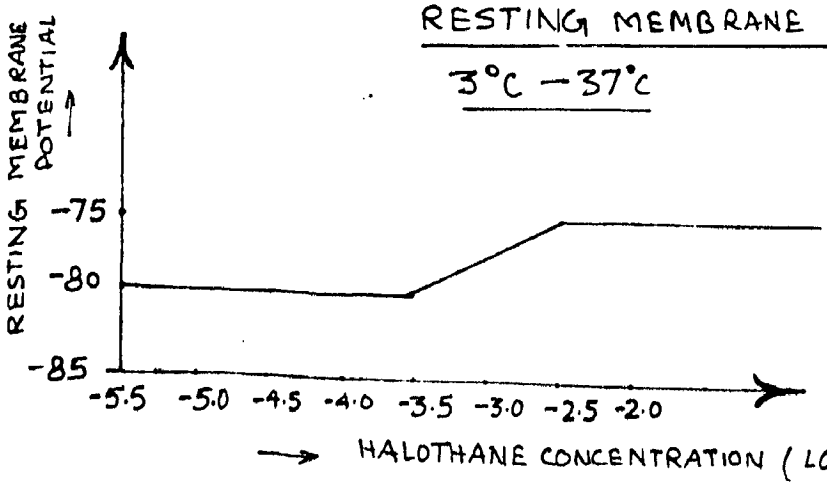

FIG 2.23(b)

FIG 2.23(b)

RESTING MEMBRANE POTENTIAL Vs HALOTHANE CONCENTRATION OF SENSORY NEURON

at 3°C to -47 ± 0.5 at 37°C. The rate of change was not linear figure 2.22. The change in potential as the function of temperature occured in a step like manner, which may reflect transition changes of the membrane at critical temperature.

II. MEMBRANE RESISTANCE:

The membrane resistance was reduced from 4.1 Mohms at 3°C to 1.2 Mohms at 37°C. The relationship between membrane resistance and temperature is non-linear, and occured in a step like manner similar to the effects observed with resting potential. The break point for both relationship 2.23 (a) & (b) occured at similar temperature.

Halothane produce depolarisation Figure 2.23 (b).

III. ACTION POTENTIAL:

The amplitude of action potential decreased by 80 to 90 mV as temperature was increased (Figure 2). At 3°C the antidromic spike amplitude was 110 mV (average) and at 37°C the amplitude had decreased to 20mV. The spike duration decreased and conduction velocity increased as temperature was raised.

The amount of depolarisation current required to produce a spike via the intra-cellular electrode decreased as temperature was raised i.e. the threshold for spike initiation decreased Figure 2.24.

At temperature beyond 28°C, spontaneous discharge activity was observed (Figure 2.24 (d). This may reflect the high level of depolarisation produced at these temperature. The normal discharge pattern of single action potential was also altered at temperature of 28°C or greater, such that multiple spikes or bursts were produced in response to a single stimulus input (Figure 2.25 (e).

SYNAPTIC TRANSMISSION: The IPSP duration decreased as temperature was increased. Complete depression occured at approximately 20°C.

All the effects observed were reversible over the temperature range from 5°C to 37°C. The temperature above or below this range usually produced cell death. In few cells hystresis was observed when the temperature was raised and subsequently lowered back to previous level.

The observed decreases of membrane resistance, spike threshold and action potential, amplitude were consistent with the depolarisation of the resting membrane potential produced by higher temperatures.

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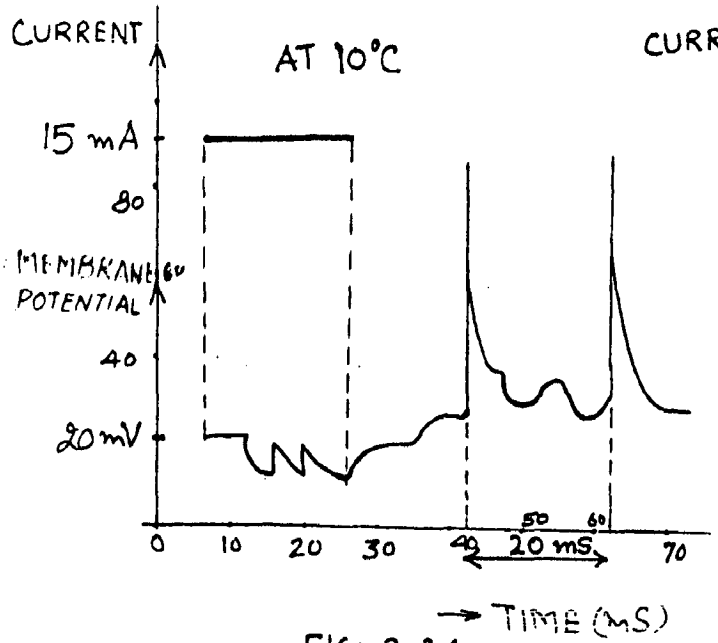

FIG 2.24 (a)

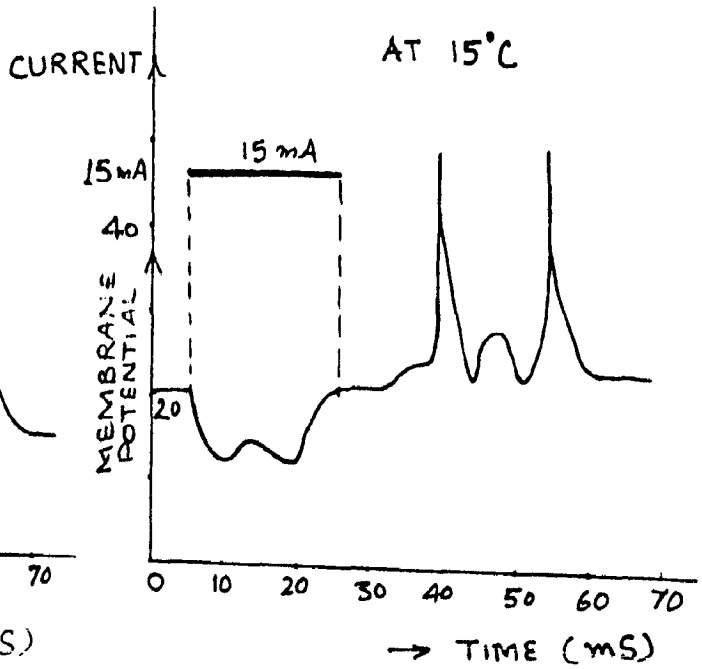

FIG. 2.24 (b)

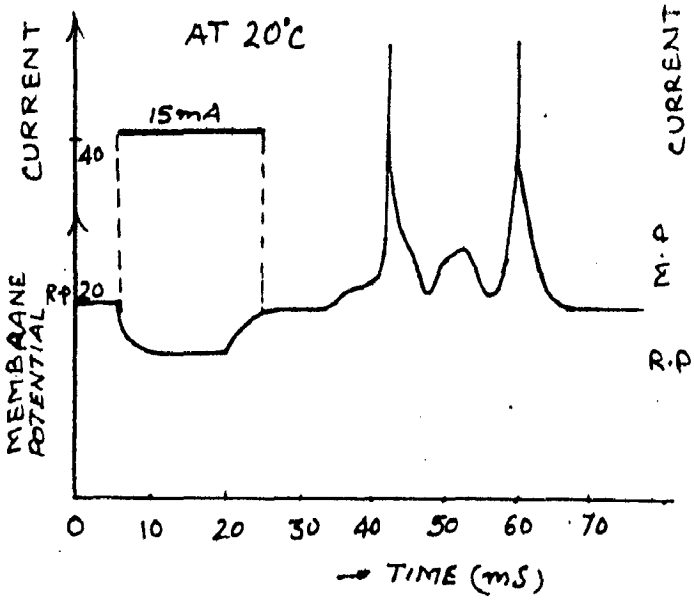

FIG 2.24 (c)

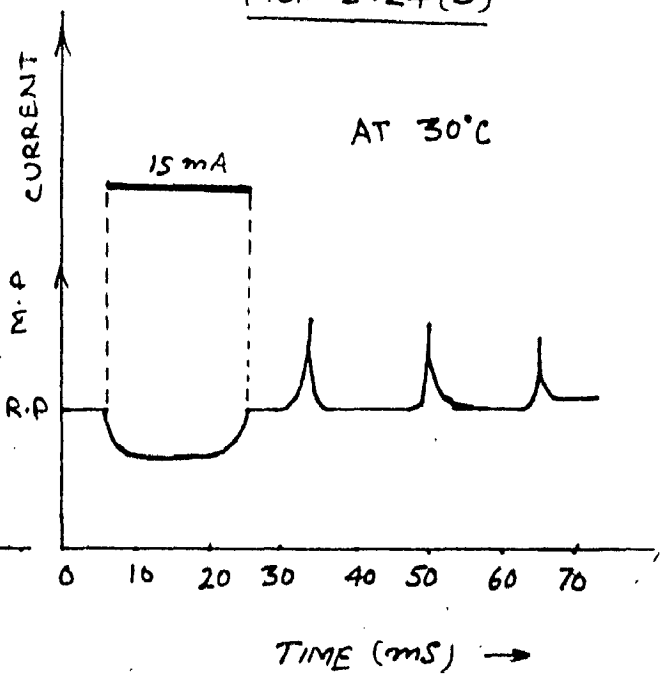

FIG 2.24 (d)

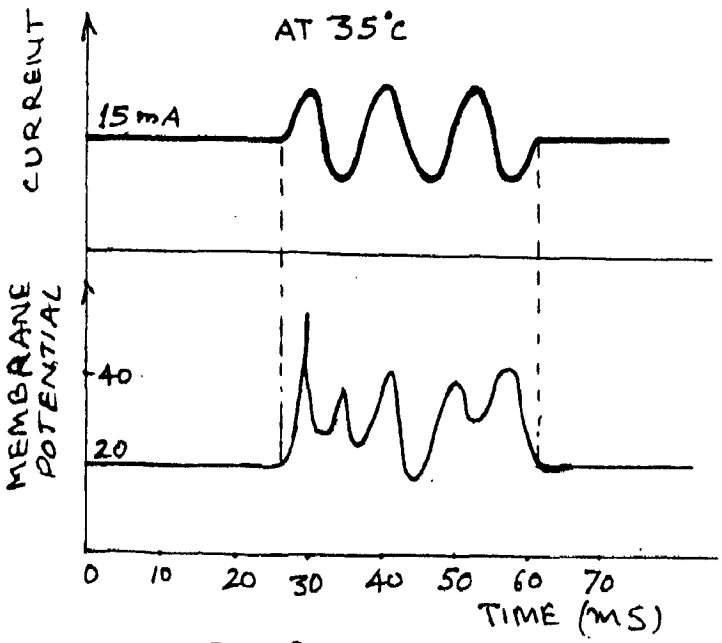

FIG 2.24 (e)

FIG 2.24 (a)-(d) : CURRENT Vs MEMBRANE POTENTIAL IN RESPONSE TO THE STIMULUS SEQUENCE

FIG 2.24 (e) : EXTRACELULAR (UPPER) & INTRACELLULAR (LOWER) RECORDING

CHAPTER - 3

REVIEW OF NEURAL MODELLING

3.0 INTRODUCTION:

The history of the neural modelling is one of many false starts, dead ends, and continual grouping. Progress has seldom been rapid and has often been frustrating. The advances, nonetheless, is measurable. The advances has, in fact, been substantial.

Neural analogs take a variety of forms, ranging from informal, verbal models to highly elaborate physical and mathematical constructs. Most models that have appeard[1] during the last half century or so have taken the form of chemical systems, electronic circuits, mathematical formulation, or computer simulations.

Considerable advantages and serious short-comings are found in each, although for a given modelling problem there is generally little difficult in selecting the most appropriate technique. Since mathematical, electrical, electronic and computer simulation models comprise the majority of contemporary analogs, it is of interest to examine some of their intrinsic merits and deficiencies.

Mathematical models have great utility in limited domains. They are invaluable in cases where the number of variables is reasonably limited and non-linearities do not present

severe analytical difficulties. An outstanding application of this type of model is found in the analysis of membrane biophysics. Formal mathematical description, however, is simply unable in its present state of development to deal adequately with the multivariable non-linear non-linear complexities of entire neurons, complete net-work analysis is even more formidable.

In certain special cases, however, mathematical models of net-work behaving are extremely well qualified. This is particularly true for statical treatment of large ensembles and for the analysis of large scale electrical activity such as wave formation and propagation.

Electronic models can simulate continuously variable and non-linear operations accurately and economically. Providing real time signals that may be observed while experimental conditions are manipulated, they permit a rapid and effective kind of observer model interaction not easily achieved by other techniques. There is considerable advantage of direct observation of wave forms, phase relationship, modulations, and time dependent inter-actions while stimuli and model parameters are changed. Such advantage is most effective for the modelling of one or few inter-connected units. For large net-works, however, both observation and manipulation of parameters and connections becomes very difficult.

Analog computers have advantages similar to these of electronics models, but tend to be slow and cumbersome. Both have the advantages over mathematical models that they do not tend to compel over simplification.

The growing speed and storage capabilities of digital computers carry great promise for flexible, realistic modelling.

In this review the author has discussed electrical and electronic model of the neuron. This review is representative rather than exhaustive. The author attempts to delineate the main stream of activity in neural modelling and to emphasize what seem to be important directions and achievements.

In this review the author restrict to models of fixed properties of membrane, single unit and relatively small net-works only. There has been no attempt was made to include mathematical models, chemical models and models of information storage i.e. analogs of memory, conditioning or learning. Emphasis throughout is on the dynamic information-processing aspects of nervous systems.

The following electrical and electronic models are critically examined:-

1. Hodgkin-Huxley's Model of Neuron
2. Lewis model of Neuron
3. G. Roy's Model of Squaid Axon membrane
4. R.C. Model of nerve fibre
5. RLC model of nerve fibre

6. Lewis model using Ballastic Net-works

7. Model based on double energy element system

8. Ionic transistor model of neuron

9. Neural model based on low-pass & high-pass net-works

10. Harmann's model of neuron

11. French & Stein's model of neuron

12. Dendritic compartment model of neuron

13. Model of neuron by Nagumo

14. Electronic model of Neuron with feed back through Renshaw Cell

15. Biophysical model to explain Nerve Impulses

3.1 HODGKIN-HUXLEY'S MODEL:

In this model electro-chemical effect is taken into account for the modelling of neural system. Hodgkin and Huxley proposed a mathematical model [3, 12] for squid nerve to meet the experimental results.

The general equation for the action potential for model shown in Figure 3.1.

$$\frac{1}{R_{ax}} \frac{\partial E_m(y,t)}{\partial y^2} = C_m \frac{\partial E_m(y,t)}{\partial t} + g_{Na}(E_m(y,t) - E_{Na}) + g_k(E_m(y,t) - E_k)$$

where g_{Na} and g_k represent the unknown conductance functions; conductance will be functions (at least) of membrane potential and time.

$g_{Na} = g_{Na}(E_m, t)$ and $g_k = g_k(E_m, t)$

The above equation is very complicated.

The membrane current is exactly whatever current is applied from external sources.

$$I_{membrane} = i_{app} = i_m = C_m \frac{\partial E_m}{\partial t} + g_{Na}(E_m - E_{Na}) + g_k(E_m - E_k) + g_l(E_m - E_l)$$

Here g_{Na} = conductance of sodium dependent on the membrane voltage & time
g_k = condutance of Potassium dependent on the membrane voltage and time
g_L = leakage conductance which is independent of voltage and time

These three ionic components are in parallel.

C_m = membrane capacitance.

E_k, E_L and E_{Na} are the constant voltage

E_m = membrane voltage

V = Displacement of membrane potential from its resting value

$$g_{Na}(E_m - E_{Na}) + g_k(E_m - E_k) + g_L(E_m - E_L)$$

$= I_{Na} + I_k + I_L$ where I_L = leakage current

E_m is the potential at which leakage current due to chloride and ions is zero. The Na conductance increased when the axon was depolarised, and then decreased again in the presence of steady depolarisation is called sodium inactivation. The decrease

in sodium conductance with maintained depolarization is termed sodium inactivation, and the conductance increases are called potassium and sodium activation. Hodgkin and Huxley found emperical equations describing these functions. The pair of equation describing the potassium conductance are —

$$g_k = \bar{g}_k n^4$$

$$\frac{dn}{dt} = \alpha_n (1 - n) - \beta_n \cdot n$$

where $\alpha_n = \frac{0.01 (V + 10)}{e^{(V+10)/10} - 1}$

$$\beta_n = 0.125 \; e^{V/80}$$

$\bar{g}_k$ = Maximum potassium conductance (a constant)

are functions of voltage but not of time

n = Dimensional variable having a value between 0 and 1.

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

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

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

$$\alpha_m = \frac{0.1 (V + 25)}{e^{(V + 25)/10} - 1}$$

$$\beta_m = 4 \; e^{V/18}$$

$$\alpha_h = 0.07 \; e^{V/20}$$

$$\beta_h = \frac{1}{e^{(V+30)/10} + 1}$$

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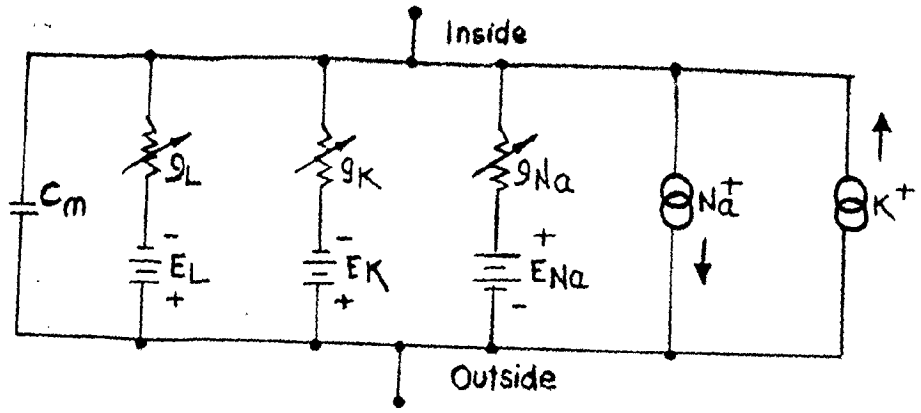


FIG.34 HODGKIN AND HUXLEY'S MODEL.

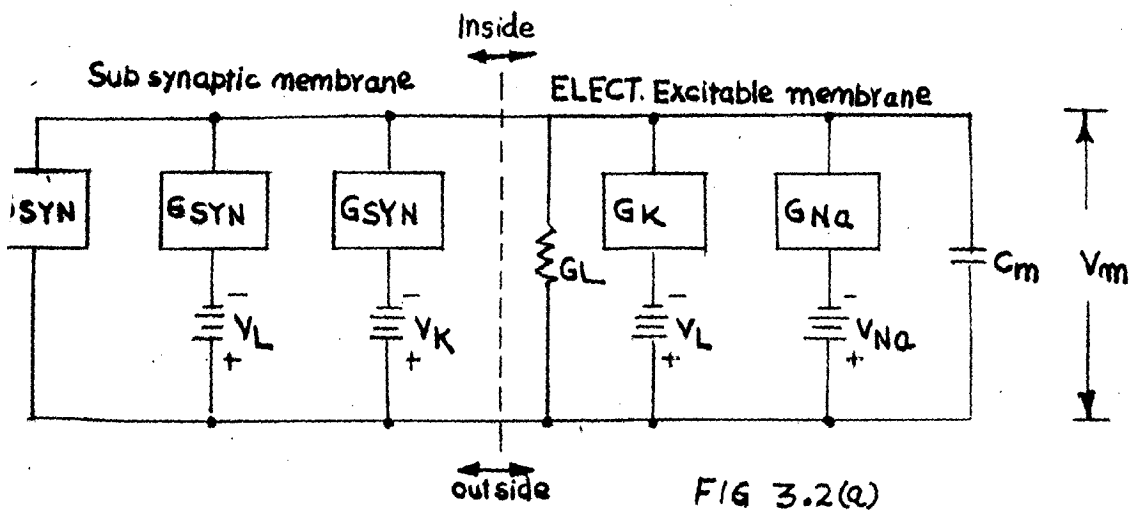


FIG 3.2(a)

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

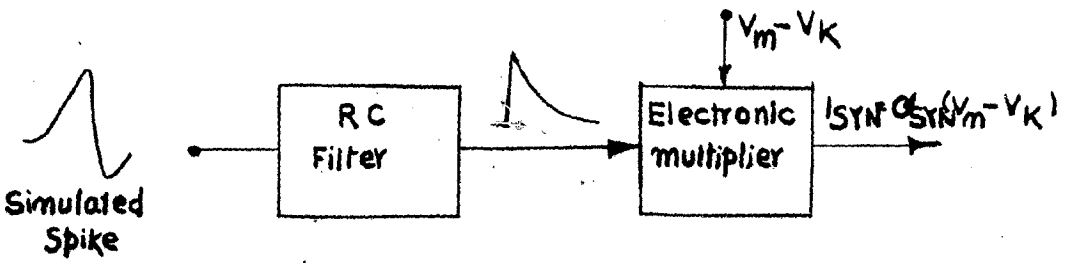


FIG.32(b) NEURONAL MEMBRANE MODEL BY LEWIS

From this we gathered —

1. Permeability appears to depends on membrane potential and not on membrane current.

2. If Na concentration is such that E_{Na} E, Na current is onward. If E_{Na} E, the current changes in sign but follows same time course.

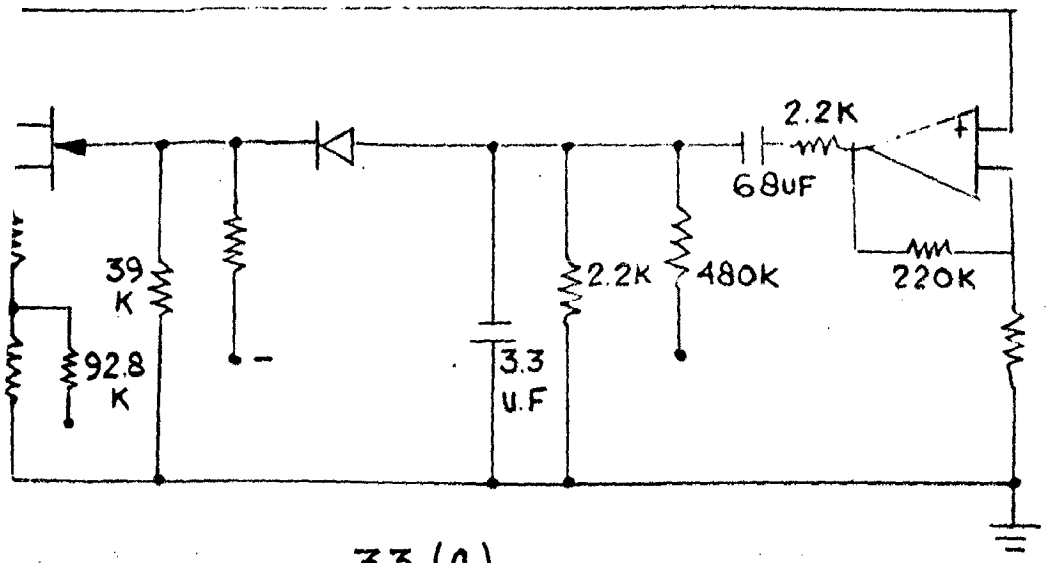
3. At fixed depolarisation of sodium current follows a time course whose form is independent of current through membrane.

3.2 LEWIS MODELS:

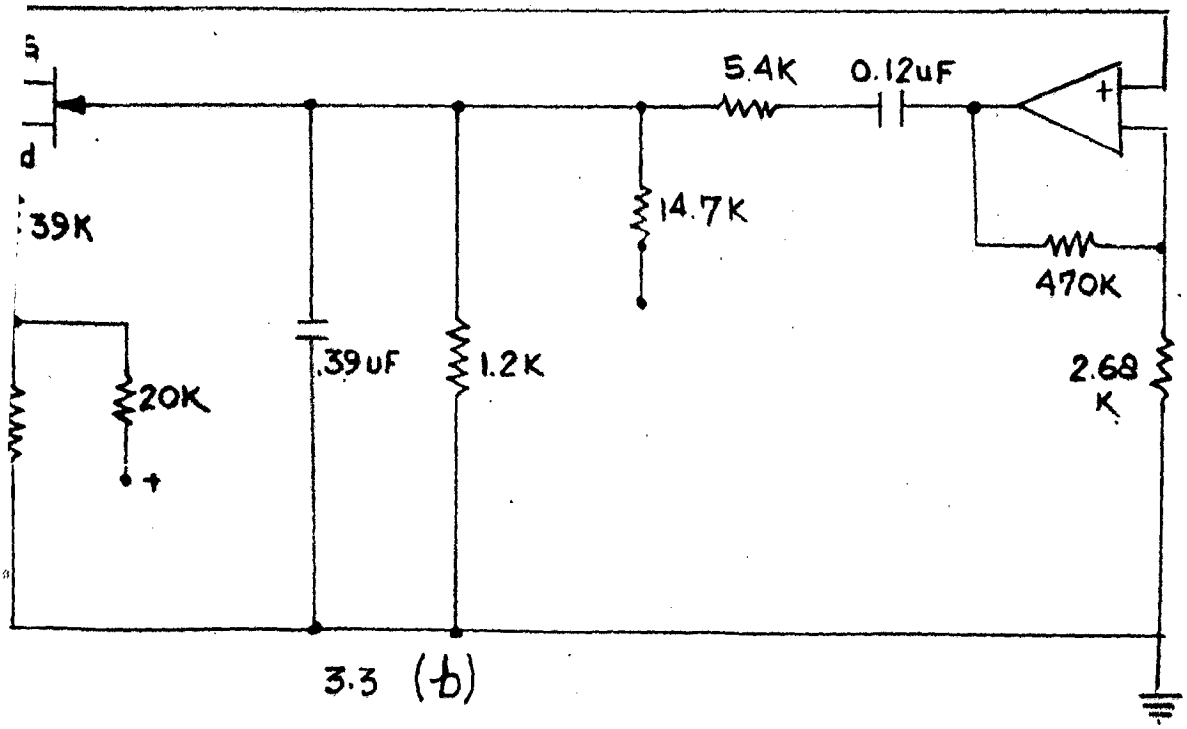
The model [1] consists of seven parallel circuits and includes the synaptic membrane analoge. Five conductance out of six are constant and they undergo transient change owing to either to change in synaptic inputs or to change in trans-membrane potential (V_m). The current through each conductance is the product of time varying conductance itself and the time varying voltage across it. Figure 3.2 illustrates the operation of simulated synaptic conductance. In case of synaptic conductance, Figure 3.2 (b) a pre-synaptic strike is transferred into a decaying exponential by means of a RC filter. The exponential represents the time course of synaptic conductance. The multiplier circuit produces a current proportional to product of condutance and voltage (Vm - Vk) across it.

3.3 G. RAY'S MODEL OF SQUID AXON MEMBRANE:

The electronic model proposed by G. Ray is based on the H-H model. According to H-H theory, sodium and potassium



3.3 (a)



3.3 (b)

FIG 3.3 G·ROY MODEL

(a) SIMULATION OF POTASSIUM CONDUCTANCE

(b) SIMULATION OF SODIUM CONDUCTANCE

condutanses have very low values in their resting state. When an external voltage is applied across membrane, the conductances of both are increased, when the applied potential is large, they reach a saturation value beyond which they remain constant. G. Ray [17] found that FET is the ideal electronic element to simulate the axon membrane condutances.

One FET is used for g_k and one for g_{Na}. The voltage across axon membrane is represented by drain-source voltage (Vds) and current by the drain-source current Ids. Negative bias is on the gate of FET for resting state. As the Vds is feed back via an intervening circuit to the gate for providing voltage with dependence of condutance g_{ds}. The g_{ds} becomes time-dependent with the introduction of RC in the feed back circuit. An amp. is used to amplify the Vds and to isolate the FET from the circuit determining the time dependemde of g_{ds}. The -Ve biases are adjusted so that the diode is non conducting when Vds = 0. The coupling capacitor is much smaller in order to provide faster inactivation for the Na^+ conductance.

3.4 RC MODEL OF NERVE FIBRE:

The equivalent RC analog of axon [3, 12] is shown in Figure-14. These models are like the transmission line of power system. The resistance and capacitance are distributed along the length. The number of Resistances (R) and Capacitances (C) parameters depends upon the length. The voltage & current can be calculated from the differential equation at any point of model.

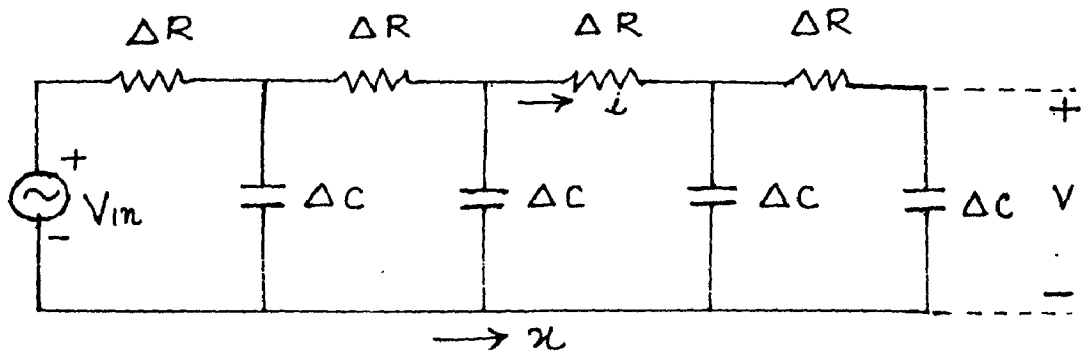


FIG 3.4 R·C. MODEL OF NERVE FIBRE

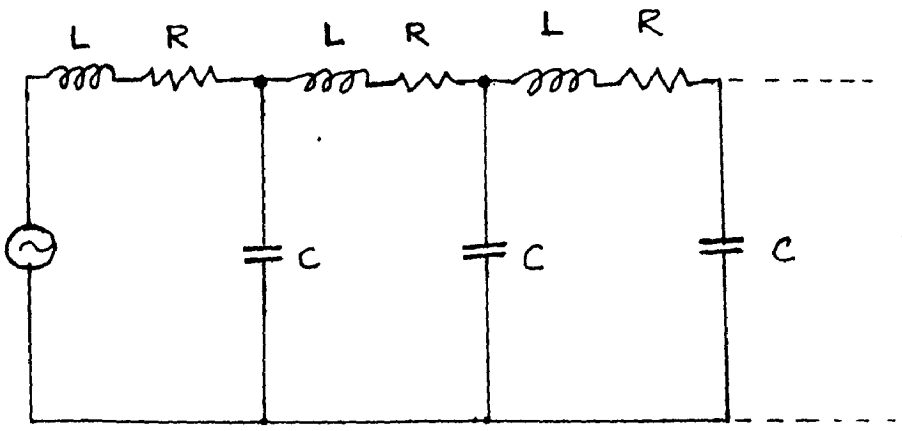


FIG. 3.5. RLC MODEL OF NERVE FIBRE

3.5 RLC MODEL OF NERVE FIBRE:

It is equivalent to the long transmission line [3, 12]. The R, L and C parameters are distributed all along the length of the fibre length. The value of current and voltage can be got by solving the differential equation of the net-work. The fibre section is assumed to uniform throughout.

The RLC model (Figure 3.5) is assumed superior than RC model due to following reasons:-

1. The actual phenomenon is considered

2. The realistic wave form may be considered

3.6 LEWIS MODEL USING BALLASTIC NET-WORKS:

The Lewis model [1, 12] 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. A simple RC realisation of a ballistic net-work is shown in Figure 3.6 (a). In simulating the ballistic responses Lewis assumes three parameters.

1. Rise time which is determined by $R_2\ C_2$

2. Fall time is determined by $(C_1 \,//\, C_2).R_2$

3. Maximum amplitude

The impulses originating in pre-synaptic neuron, transmitted through inter-cellularly, induce a charge in the synaptic

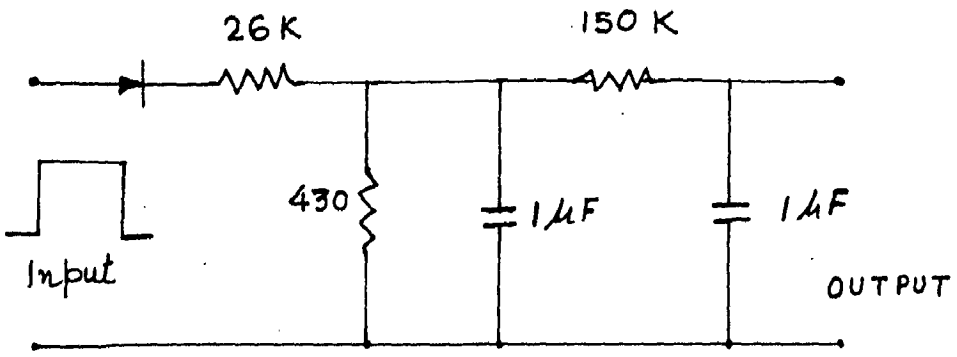


FIG 3.6 (a)

FIG 3.6.(b)

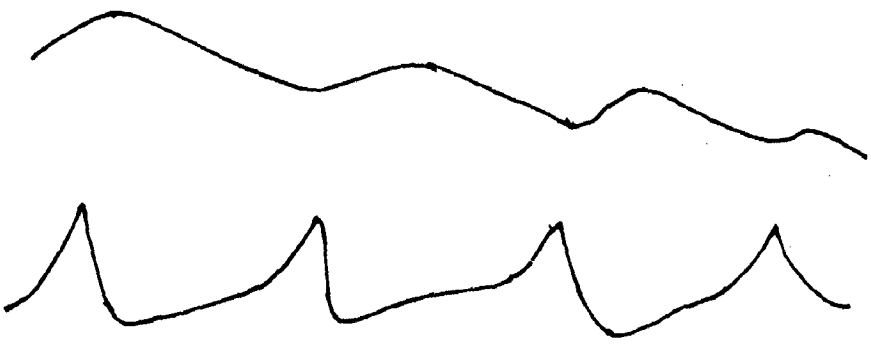


FIG 3.6(c)

FIG 3.6(a) LEWIS MODEL USING BALLASTIC NETWORK

FIG 3.6(b) FACILITATION

FIG 3.6(c) ANTI FACILITATION

membrane of post-synaptic neuron. Thus, a single pre-synaptic spike induces a slowly varying, long lasting post-synaptic potential known as ballistic potential. And the formation is not completely understood.

There are two important mechanisms —

FACILITATION:- The first impulse conditions the synapse in such a way as to enhance or facilitate subsequent responses, Figure 3.6 (b).

ANTI-FACILITATION:- The first spike reduce or anti-facilitates the response, Figure 3.6 (c).

An inhibited neuron, when inhibiting stimulus was ceased, was found to fire spontaneously. This implied that there was a rebound or negative after effect. In a similar manner an excited neuron, on cessation of prolonged excitation may go through a period of depressed excitability.

3.7 MODEL BASED ON DOUBLE ENERGY ELEMENT SYSTEM:

The system responses depends upon the physical characteristics of the energy storage element, Figure 3.7 (a). Circuits containing the energy storage elements have pales seperately widely enough so that the transient response can be approximated by treating them as two isolated single energy circuits.[16]

Let a step voltage V_i is applied. For full charging current which flows after the excitation is applied, is determined by the input capacity C_g. The same change is accumulated in C_o.

Since C_c C_g, the voltage changed across C_c will be very small, which C_g charged fully. Thus C_c can be assumed short circuited during the entire interval. The equivalent circuit is now reduced to a circuit containing a single energy storage Figure 3.7 (b).

Now we can get the following relationships from the circuits:-

$$V_{01} = V_{SS1} (1 - e^{-t/\quad 1})$$

$$1 = C_g (R_g // R_L // R_0)$$

C_c discharge through

$$2 = C_c (R_g + R_L // R_0)$$

The final response equation.

$$V_0 (t) = V_{SS1} e^{-t/\ 2}$$

Since decay time is very large, error introducing by starting the decay anywhere in the vicinity of ZERO will be negligible.

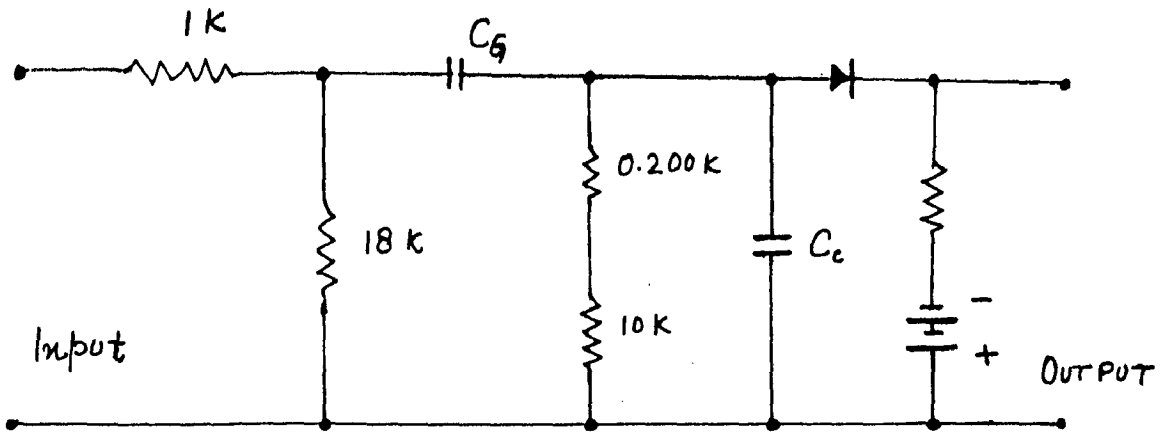


FIG 3.7 (a)

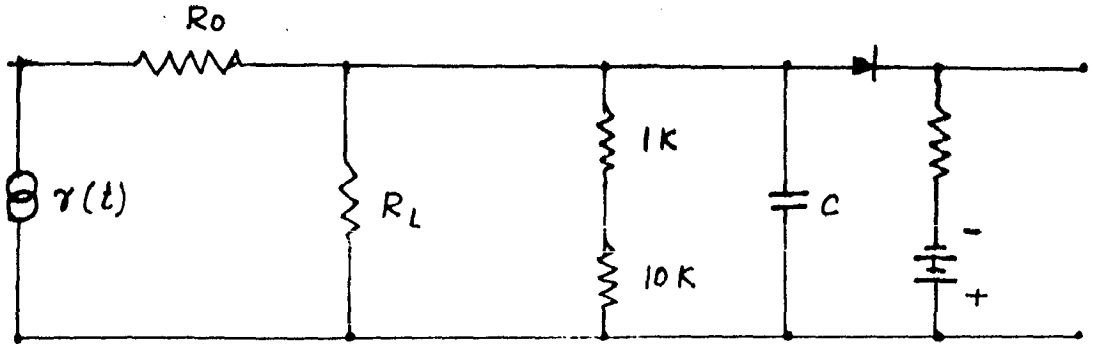


FIG 3.7 (b)

FIG 3.7(a) MODEL BASED ON DOUBLE ENERGY ELEMENT

FIG 3.7 (b) EQUIVALENT CIRCUIT OF E.M. SYSTEM

3.8 IONIC TRANSISTOR MODEL:

An equivalent circuit of transistor model is given in Figure 3.8 (a).

A voltage step is applied. The behaviour of ionic currents are studied by the method of Laplace transform techniques. Concept of membrane conductivity modulation is used to calculate the various parameters of ionic transistor.

Where

r_b = Membrane resistance

C_M = Membrane capacitance

r_e = Junction resistance between membrane and external solution

r_c = Junction resistance between internal solution and membrane

Since the external solution is usually at or referred to as the ground potential, a nerve has so called grounded emitter configuration. A stimulating potential is applied between external

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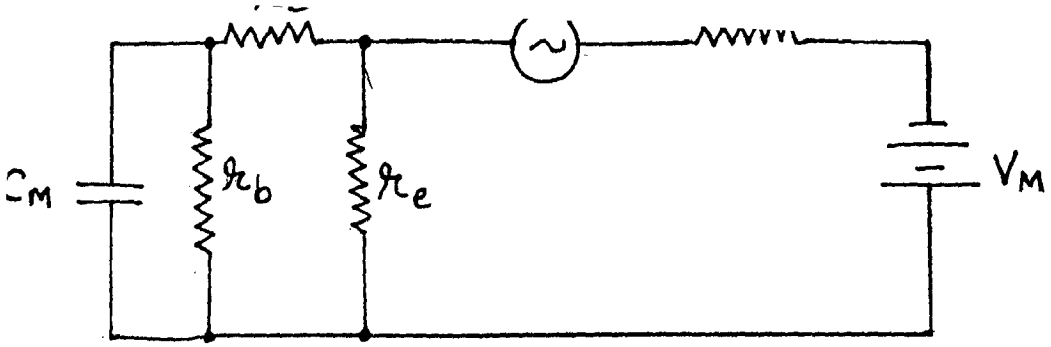

FIG 3·8 (a)

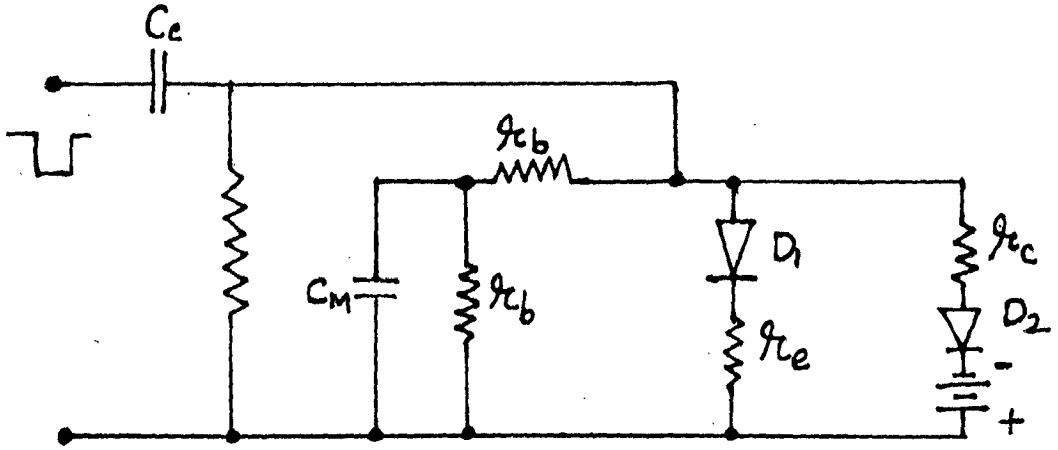

FIG 3·8 (b)

FIG. 3.8(a) EQUIVALENT CIRCUIT OF IONIC TRANSISTOR MODEL

FIG 3.8 (b) EQUIVALENT ELECTRONIC MODEL OF NEURON

solution and axoplasm. Part of the potential will appear across the outer junction, and the rest across membrane. Due to this applied voltage, current start flowing.

When applied step voltage is greater then the voltage providing at reserve bias across the diode D_1 show in Figure 3.8(a) the membrane capacitance C_M discharges through the diode D_1 with time constant equivalent to

$$\left(\frac{r_b\,(r_b + r_e)}{r_b + r_b + r_e}\right) C_M$$

Once capacitance C_M is discharged it starts getting charged up with time constant of $(R_o + R_b)\, C_M$. During the discharge period of C_M sodium currents flows, and during the charging phase of C_M, sodium current decreases while K^+ current increase to saturation value. Using an equivalent circuit of ionic transistor, and applying Laplace transform technique, the expressions for sodium and potassium currents are obtained.

Applying a Laplace transform for the step voltage excitation, and writing loop equation for mesh one and two in Figure 3.8(b) The expression for sodium and potassium currents can be obtained. It is seen seen step voltage excitation is applied between intra-cellular and extra-cellular solution. Most of this applied step voltage occurs across membrane region, as the resistivity of these solutions are negligible compared to the membrane. The expression for time constant

$$T_{Na} = \frac{r_b\,(r_b + r_e)\,C}{(2\,r_b + r_e)\left(1 - \dfrac{2 r_b\, r_o\, \alpha_N}{2\,r_b\,(r_o + r_e) + r_e\, r_o}\right)}$$

And similarly $T = T_k$ for the rise of potassium currents by adjusting different parameters as R_c, R_b and R_a. The different shapes of the wave form can be obtained required for the action potential. It is also satisfying the steady state conditions.

3.9 NEURAL MODEL BASED ON LOW PASS & HIGH PASS NET-WORK:

In this model [12], there is one low pass and one high pass net-work, connected in cadcade as shown in Figure 3.9 (a). The successive net-works do not load each other. The response can be separated into two regions, both the regions depends upon the individual characteristics of energy storage element.

V_1 = Input voltage

V_2 = O/P of low pass = I/O of High Pass

V_3 = O/P of High Pass

So, V_m = Membrane Resting Potential

$V_2(t) = V_1(1 - e^{-t/\tau_1})$ where $\tau_1 = R_1 C_1$

$V_3(t) = V_2 \cdot e^{-t/\tau_2}$ where $\tau_2 = R_2 C_2$

The block diagram shown in Figure 3.9 (b) consists of threshold unit and pulse generating unit and wave shaping circuit. The differentiated input is applied to threshold circuit. If input is greater than threshold level, the multi-vibrater triggers. This pulse output is fed to the wave shaping circuit which converts the pulse into spikes to satisfy the steady state and transient conditions.

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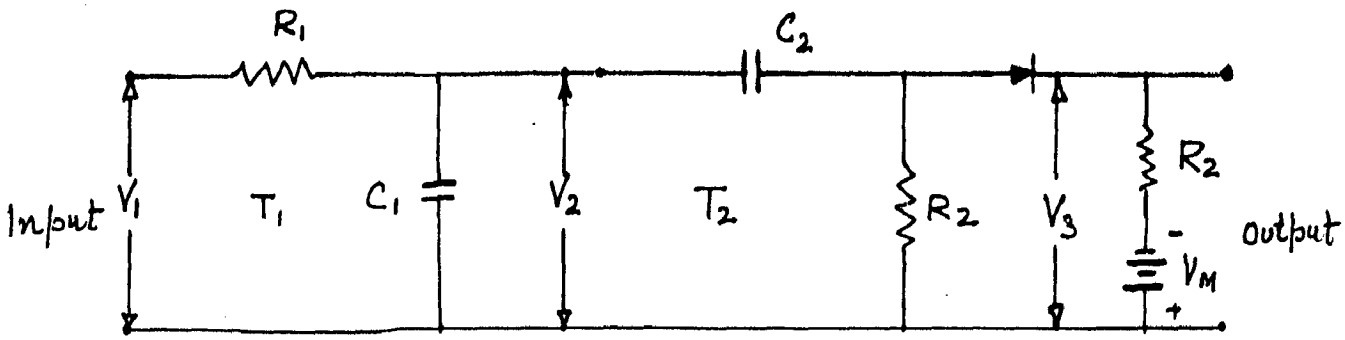

FIG 3.9 (a)

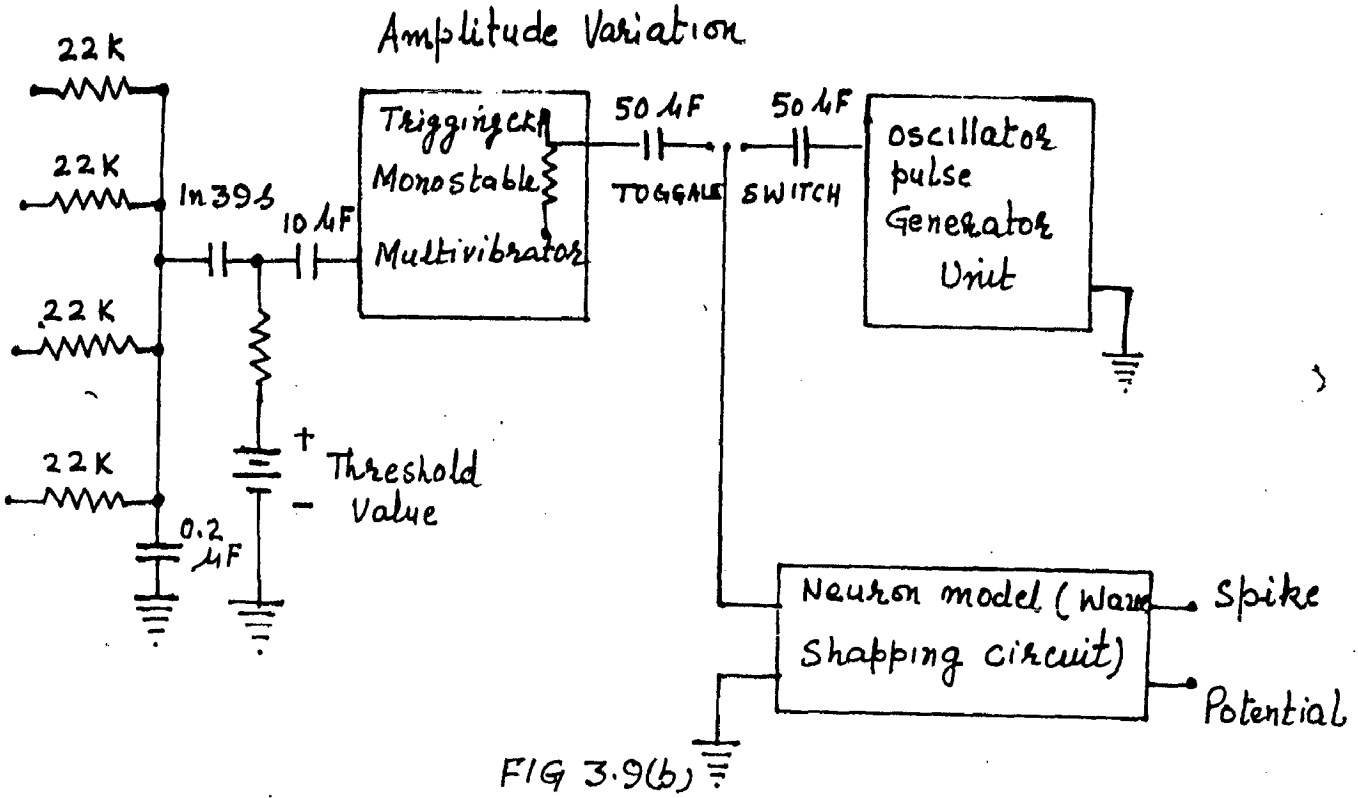

FIG 3.9(b)

FIG 3.9(a) MODEL BASED ON LOW PASS AND HIGH PASS NETWORK

FIG 3.9(b) BLOCK DIAGRAM. OF NEURON

3.10 HARMON'S MODEL:

Harmon [1] proposed an electronic model of Neuron by using the transistors, as shown in Figure 3.10, to show the input output properties of neuron. In this model following four basic properties of neuron are provided:-

a) Spatial and temporal summation

b) All or none law

c) Absolute refractory period, and

d) Graded inhibitations

The time constant of monostable multi-vibrator shows the absolute refractory period.

3.11 FRENCH AND STEIN'S ANALOG MODEL:

The block diagram of the model [18] is shown in Figure The model consists a leaky integrator, threshold level Comparator and pulse generator. Leaky integrator sums the various input over a period determined by the constant γ_1 of the integrator. As the integrated voltage exceeds the threshold level, the comparator send a signal to the pulse generator which gives pulses at the output. The pulse duration determines the absolute refractory period which we can adjust by charging the passive parameters of the pulse generator.

Subthreshold voltages are fed to increase the threshold level with a second time constant γ_2, so that the analog show accommodation to slowly rising inputs. Each output pulse resets

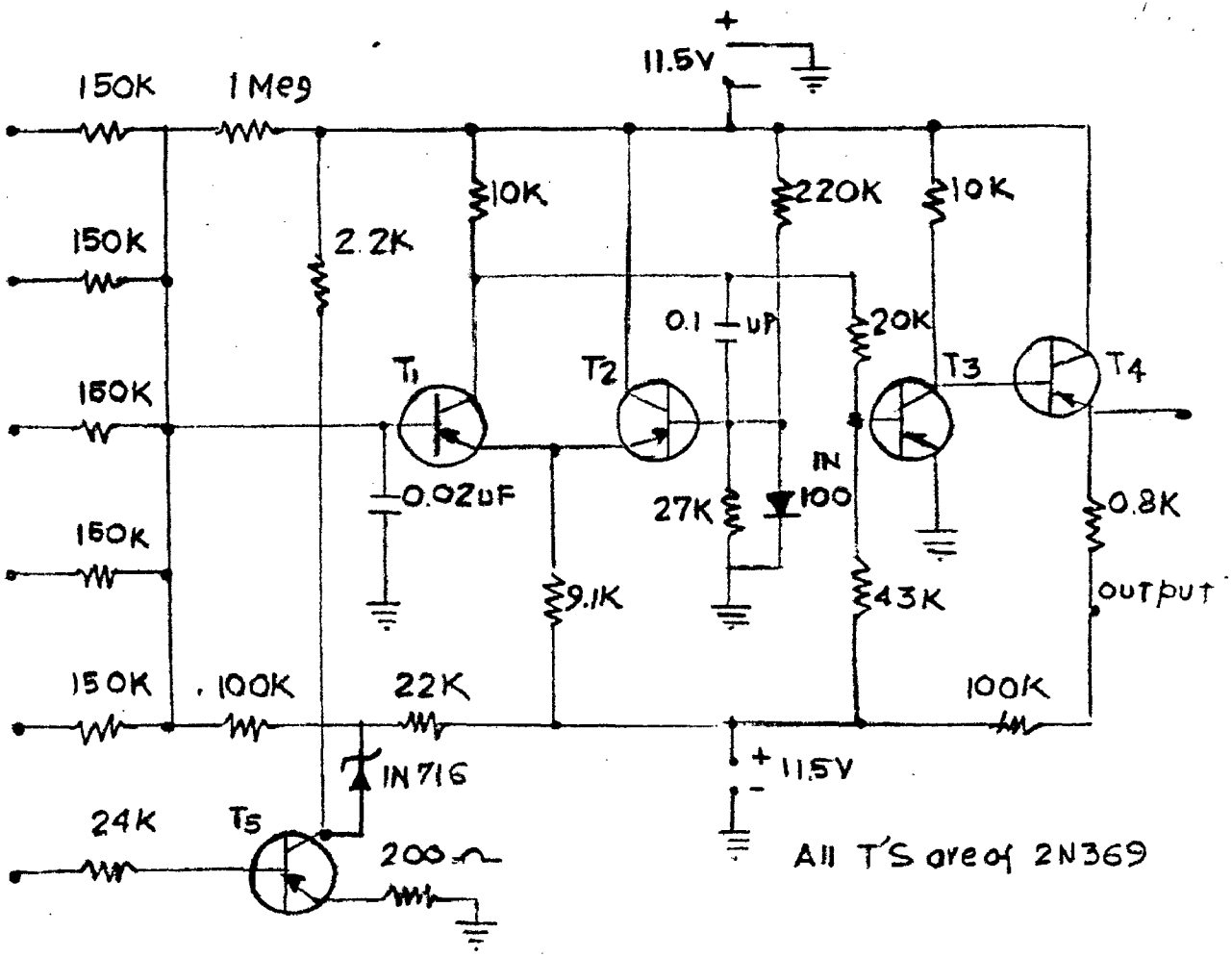

FIG 3·10 HARMON MODEL

the integrator and hold at at its initial value until the end of the pulse. Each pulse also increases the threshold by an amount V0 and effects decays with the constant T_2. If T_2 is small compared to the normal intervals between pulses, it determines a relative refractory period in which a second pulse is readily elicited.

This model of French and Stein incorporate -

1) Variable absolute & refractory period

2) Two time constant

3) Seperate control of the accommodation to sub threshold voltage changes

3.12 A DENDRITIC COMPARTMENT MODEL OF NEURON:

In this model [19] multiple input compartmental system analogous to a dendritic net is used. The model described a simulated action potential. The input to the model is voltage pulses and O/P is simulated action potential.

A block diagram of the basic 5 compartment model is given in Figure 3.12. In this model FET's are used. The simulated membrane potential as the trigger region is continuously amplified compared to a reference potential. When this signal exceeds threshold, a Schmitt Trigger is fixed which in turn triggers a one-shot multivibrator. The O/P of the one-shot multi-vibrator is fed to both hyperpolarising and depolarising conductance wave from generators. The O/P voltages from these two wave shaping circuits are then applied to the gates of the hyperpolarising and depolarising FET's.

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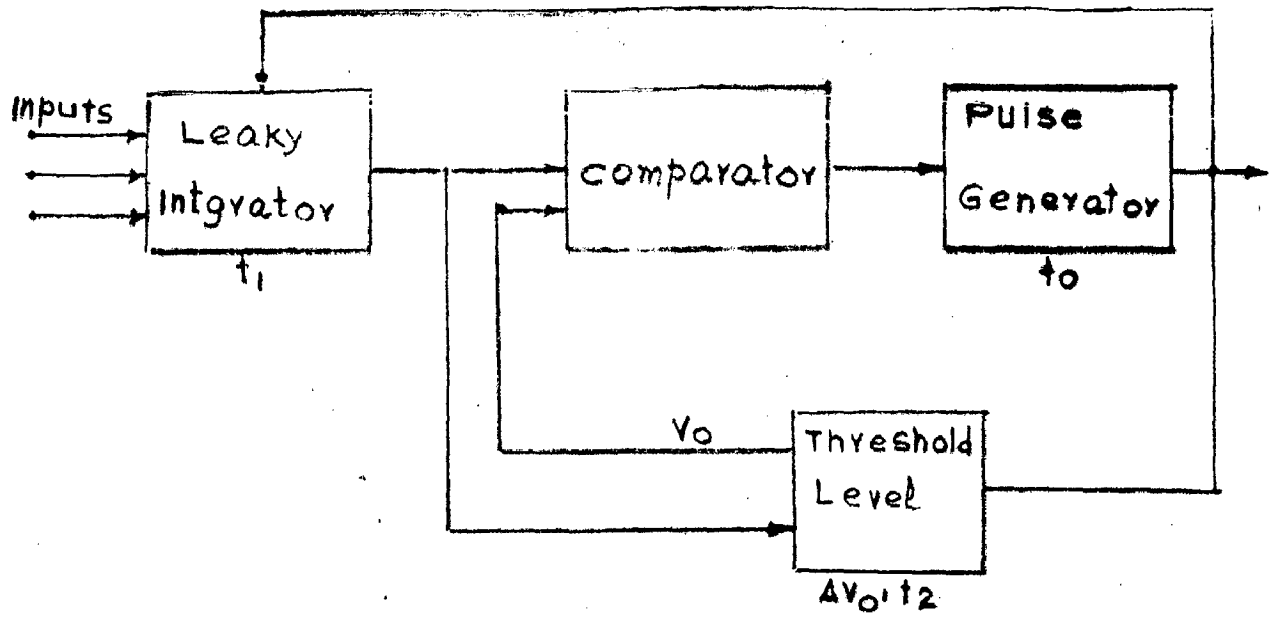

FIG.3.11 BLOCK DIAGRAM OF FRENCH & STEIN'S MODEL

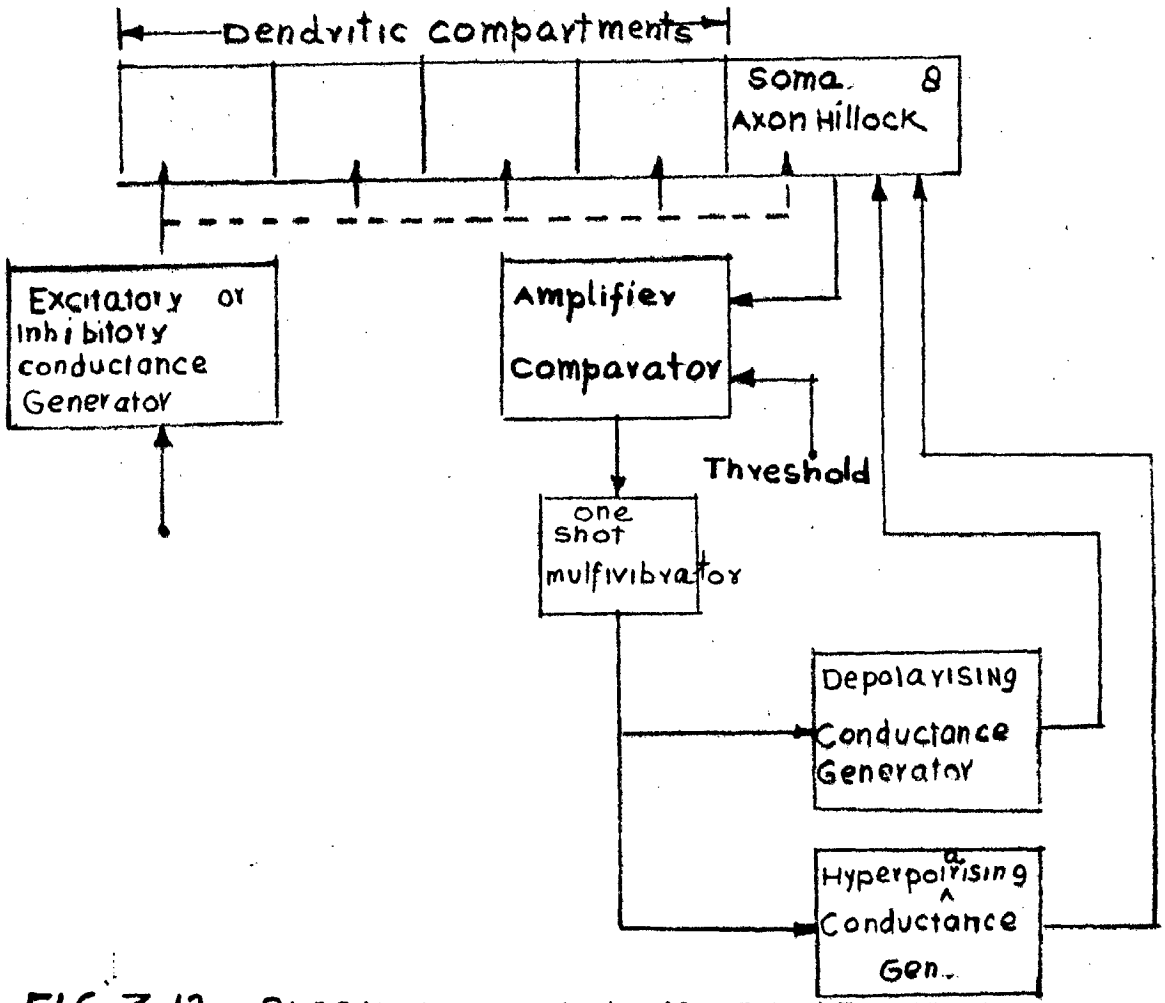

FIG 3.12 BLOCK DIAGRAM OF DENDRITIC COMPARTMENT MODEL

3.13 MODEL BY NAGUMO:

It is simplified model of the Hodgkin-Huxley nerve equation. The neuron model [23] proposed by Naguma is the circuit shown in Figure 3.13 where TD indicates a tunnel diode whole voltage-current characteristic (V Vs $F_1(V)$ is shown in Figure 3.14 and e (s) represents the voltage applied by the voltage pulse generator at time S.

The differential equation of the circuit was given by

$$\frac{dv}{ds} = \frac{1}{c}(I - f_1(V)$$

$$\frac{dI}{ds} = \frac{1}{L}(E + e(s) - V - RI)$$

The response characteristic of an electric neuron model proposed by Naguma was theoretically investigated. In the degenerate case the behaviour of this neuron model is governed by a non-linear differential equation of the first order and two jump conditions. It was shown that the relation between the pulse width (or amplitude) of the stimulating pulse sequence with a fixed frequency and the firing rate of the nruon model takes the form of an extended cantor function.

3.14 ELECTRONIC MODEL OF NEURON BY SAXENA:

In this model [34] proposed (Figure 3.15) the cell body of the neuron is represented by an integrator, the half wave rectifier, adaptive threshold gate and a comparator. The axon-hillock is modelled by a monostable multi-vibrator, differentiator

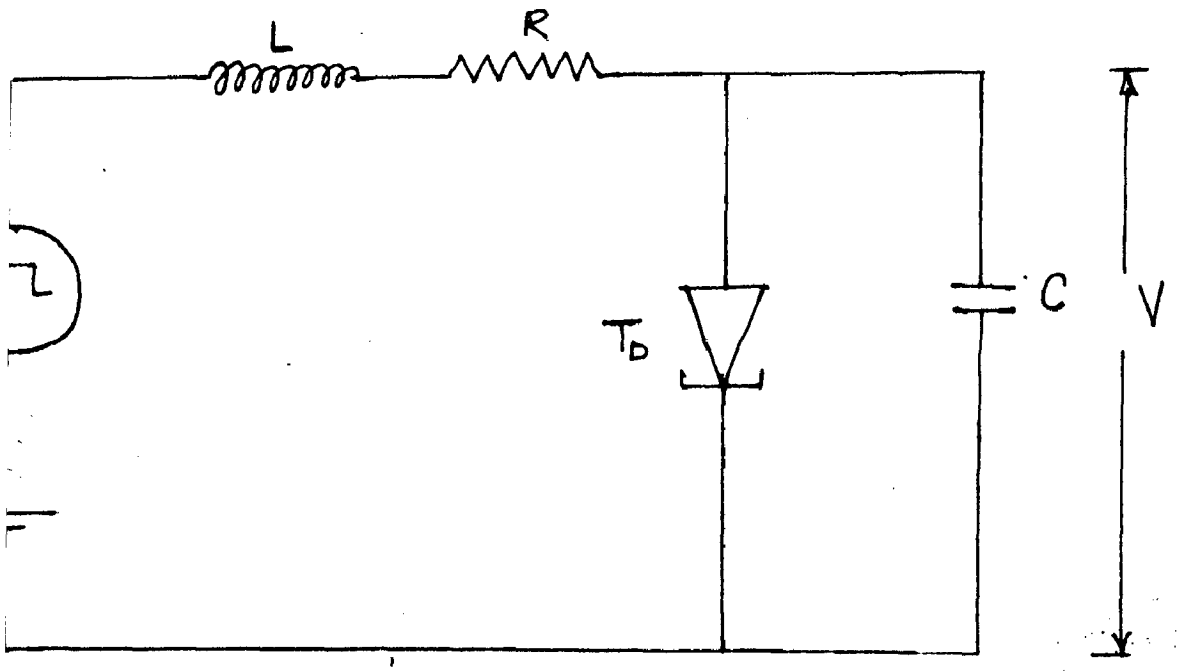

FIG 3.13
NEURON MODEL PROPOSED BY NAGUMO

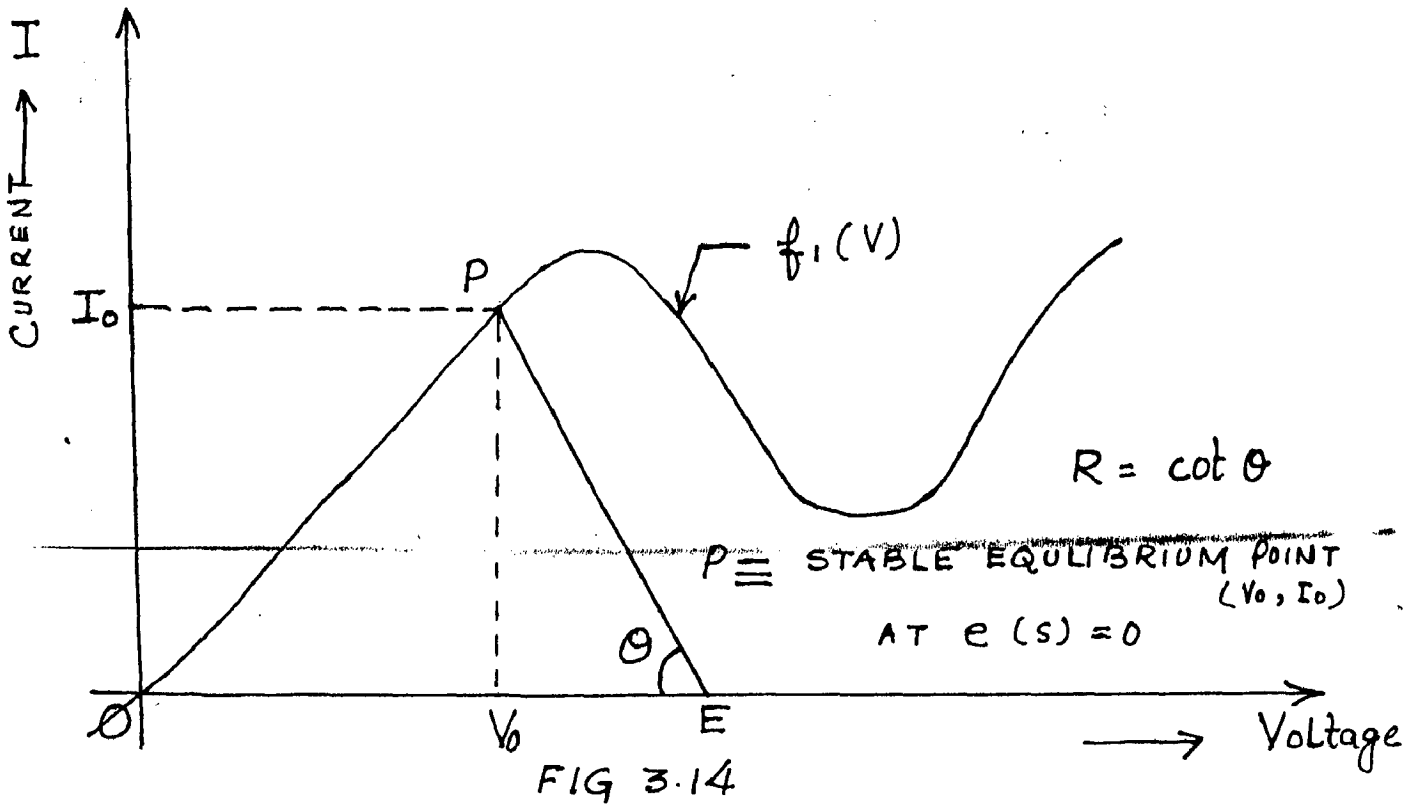

FIG 3.14

VOLTAGE - CURRENT CHARACTERSTIC

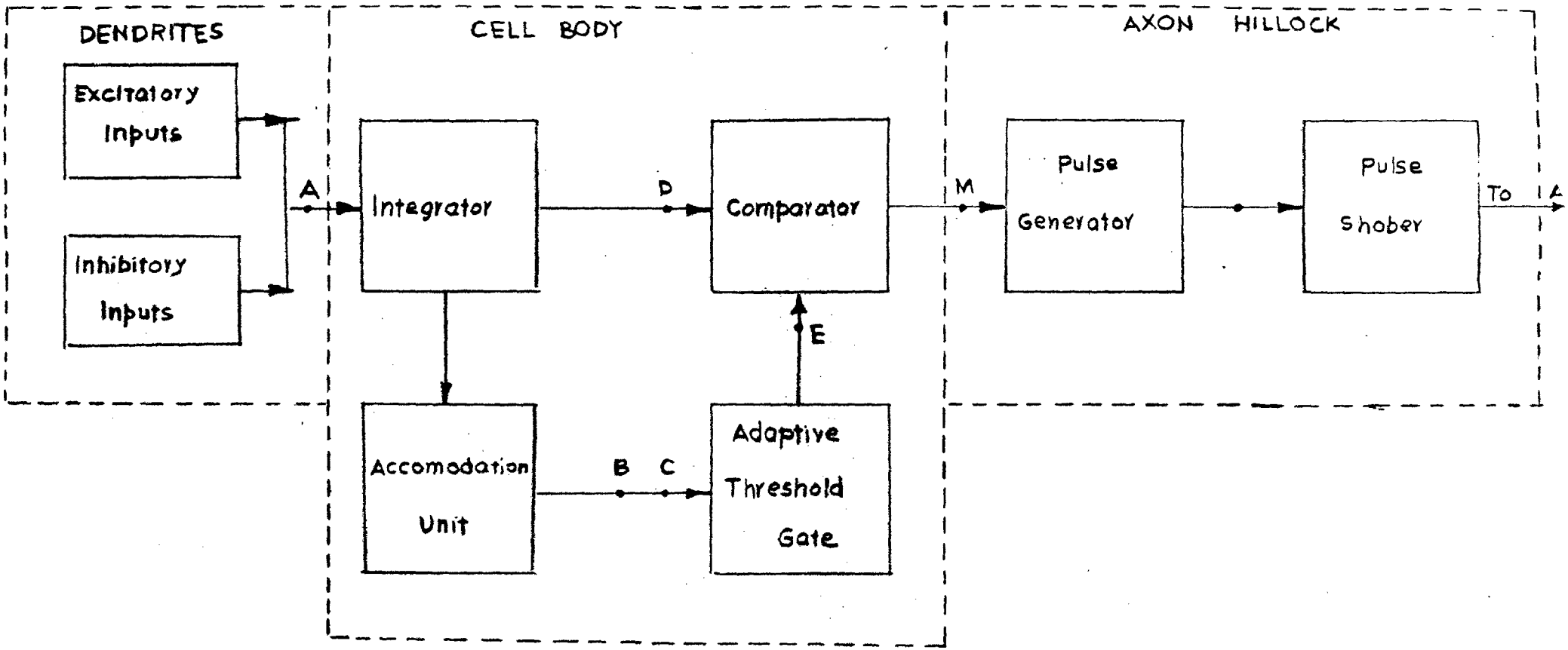

FIG-3-15 BLOCK DIAGRAM OF NEURON MODEL.

and pulse-stretcher. The axon is represented by a resistance capacitance combinational transmission line. This axon analog line is triggered by a switch through mono-stable multivibrator and generates action potential which travels down along the line.

The time constant of the integrator represents the membrane time constant (= τ_m). The accommodation and adaptation phenomenon is simulated by half wave rectifier and an adaptive threshold gate. The relative refractory period is decided by the time constant of the adaptive threshold gate. The O/P of the integrator and the adaptive threshold gate are compared by a comparator. The output of comparator is connected to a mono-stable 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 multi-vibrator generates the action potential through differentiater and pulse shaper which travels down on the axon analog.

The model [26] proposed by Saxena simulates the transmission of information in the dendrites, cell body, axon hillock, axon and inhibitory feed back through Renshaw Cell. Renshaw Cell works as protective device against excessive excitation and generation of action potential. In this Model shown in Figure 3.16, most of the electrical characteristics of

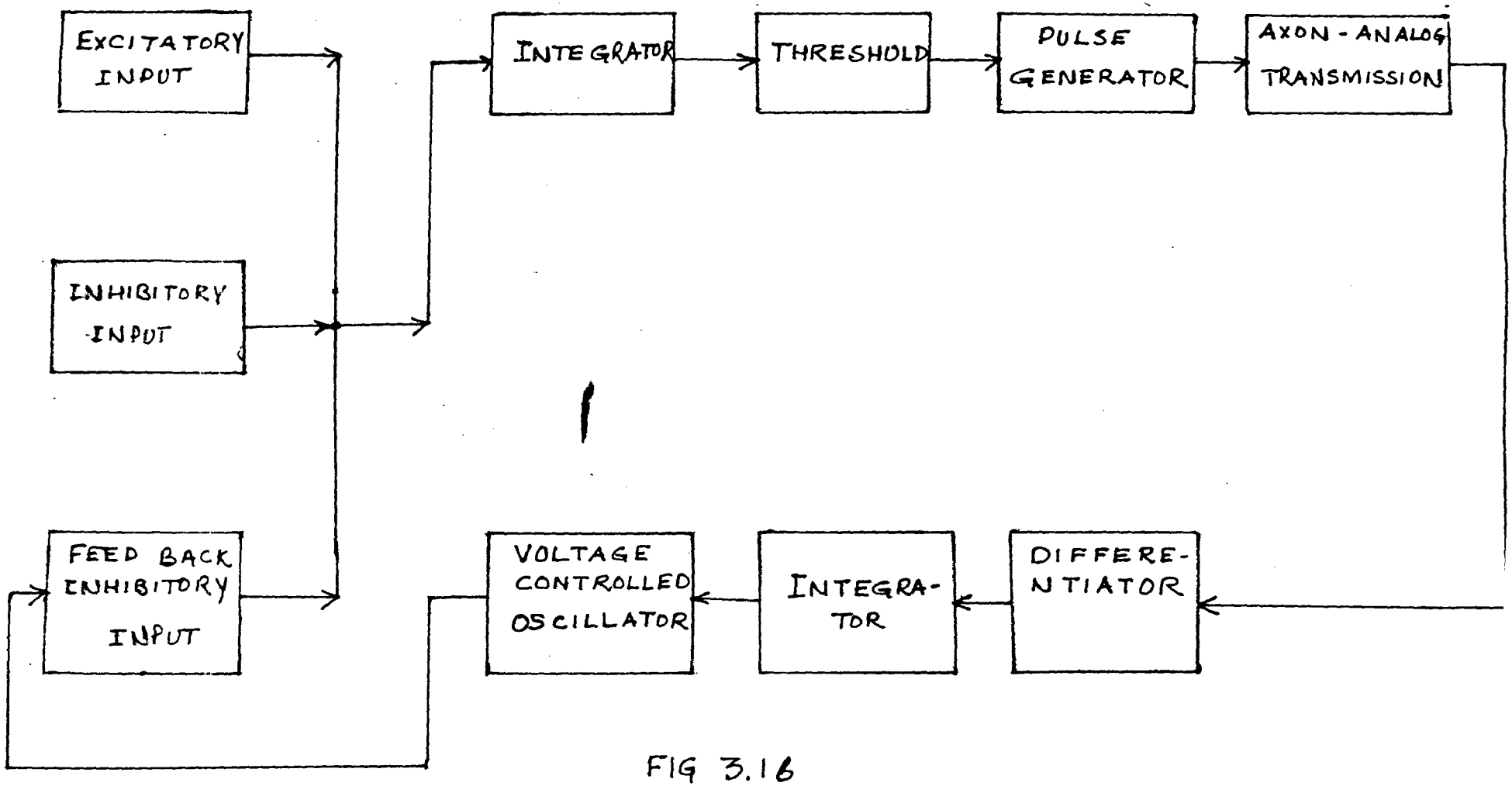

FIG 3.16

BLOCK DIAGRAM OF ELECTRONIC MODEL BY SAXENA

neuron along with its feed back loop through Renshaw Cell. The summation and integration of EPSP and IPSP inputs, integration phenomenon in cell body membrane, threshold and sub-threshold phenomenon, refractory period, inhibitory input from Renshaw Cell etc. can be easily studied by the bio-engineers. In this case threshold is taken arbitary value.

3.15 BIO-PHYSICAL MODEL TO EXPLAIN NERVE IMPULSES:

The classical theory [24] of function in the nervous system postulates that the nerve impulse is the result of a sequential reversal as the membrane potential due to an increased permeability of the membrane, first to sodium ions, then to Potassium ions. The new theory presents a bio-physical model which depicts the nerve impulse as an event involving the motions of the electrons and waves, and their inter-actions with sodium and potassium atoms and ions. The velocity of thenerve impulse (the most important parameter of the nerve function) is determined by the products of two constants ; C = the speed of light, which is a constant for all nerves;

k = a constant for each nerve and is believed to be a specific property of nerve matter related in same way to the atomic process.

The theory proposes that —

1. Function in the nerve axon is dublistic; it involves three significant aspects; electrons and waves in motion and their inter-action with atoms and ions.

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2. The dualistic nature accounts for the most fundamental characteristics of conduction of the nerve impulse:

a) Periodicity: Conduction of nerve impulse over long distances with constant velocity and form.

b) Non-summing: (two nerve impulses can not be the same at the same)time).

c) Quantum nature of each nerve: The unit message of the nerve impulse is an indivisible unit.

The explanation for this offered by the classifical theory (the ironic hypothesis of nerve conduction) is that nerve axons have an 'absolute refractory period'. During this period a second nerve impulse can not be generated. According to new theory, the nerve impulse is an event during which two very different but inter-related phenomenon are not 'mixable' since one can not occur unless the other has completed its function. Thus, each component of the dualistic phenomenon remains discrete.

3. The velocity of the nerve impulse is dependent upon the product of the two constants: C, the universal constant - the speed of light and K, a product of two "Constants" factors: the speed of the atomic process, a_p, and the fibre configuration, t_g, as a rate constant.

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4. Function in the axon is regarded as being mathematical. The mathematics arise as a result of the fusion (inter-action, union, combinations) of energy and matter as depicted in the schematics and the quantum theoretical equations.

5. The notions of time, distance, velocity, etc. are formulated in synaptic region where "brain function" actually takes place. The axon is regarded mainly as a transporting system transporting numbers it receives from the synaptic region to another synaptic region. To correctly express this belief, it is postulated, there is a synaptic function, such that

$$V_{n.i} \xrightarrow{f} x$$

Where x is a constant number for every nerve impulse in a specific axon, the f is the synaptic function.

6. Therefore, the nerve impulse in the axon is regarded both as a wave and a number.

EXPERIMENTAL OBSERVATIONS ON WHICH THE THEORY IS BASED:

1. The resting membrane potential of various axons vary from 0.05 to 0.01 volts.

2. The nerve impulse is a two-time sequantial reversal of the r.p.m.

(a) From negative inside and positive outside, to positive inside and negative outside. This corresponds to the ascending limbs of the nerve impulse;

(b) From positive inside and negative outside, to negative inside and positive outside. This corresponds to the descending limp of the nerve impulse and the restoration of the r.p.m.

3. The process described in (2) repeats itself spontaneously all along the axon with constant velocity and from regardless of its length.

4. Nerve axons under constant conditions conduct a nerve impulse with a velocity and from that is specific and constant for that axon.

5. The velocity of the nerve impulse is an unmyelinated nerve is approximately 1/10 of the velocity in myelinated nerve.

6. In a myelinated nerve, the resistance to current flow in nerve envelope (nerve membrane and myelin sheat) is so high, ions (sodium, potassium, chloride) cannot move across the nerve envelope. The current is made to flow between the gaps in the myelin sheath. These gaps are called the nodes of Ranvier. Thus, the nerve impulse is said to 'jump' from node to node 'skipping' considerable sections of nerve, thus accounting for the higher velocities in myelinated nerves. This form of conduction in a myelinated nerve is called 'Saltatory Conduction'.

7. Conduction velocity is generally dependent upon fiber diameter. In myelinated nerves the velocity also depends upon the thickness of the myelin sheath relative to axon diameter, and on the distance between nodes (0.5 to 2.0mm) collectively, these parameters will be referred to in the theory as fiber geometry with the symbol (F_g).

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8. The node of Ranvier - the distance between adjacent Schwann Cells is approximately 1 micro meter ($1x10^{-6}$ Meter). This is the only section of a myelinated nerve where the axon membrane is in free communication with the extra-cellular fluid. This section of the nerve the node of Ranvier plys a most critical role in formation of the nerve impulse, and in nerve conduction because resting and action potentials are generated only at nodes, inter-nodal regions are unexcitable.

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CHAPTER - 4

ELECTRONIC MODEL PROPOSED BY THE AUTHOR FOR NEURON FOR QUALITATIVE ANALYSIS

The author developed an electronic model of neuron which exhibits all electrical properties of actual neuron. This electronic model of neuron has a local feed back path as is existing in actual system. This proposed model has following advantages over other models developed in the past.

i) The model is compact, reliable and inexpensive.

ii) The physiological data has been handled with reasonable accuracy.

iii) The model includes the local inhibitory feed back through Renshaw Cell as reported by Robert F. Schmidt [7].

iv) The model includes the effects of temperature on neural excitability as reported by M.B. Maciver and S.H. Rath [22].

v) The model includes protective device Renshaw cells against excessive excitation and generation of action potential.

vi) The model includes all the important electrical characteristics such as summation, all or none law, threshold, refractory period, etc. [34].

vii) Linear IC's have been used to handle the physiological data of neuron for convenience.

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viii) Resting potential in actual neuron is taken into consideration to decide threshold level.

Taking into consideration the above points, it is thought that the proposed model might be of use to understand and demonstrate the functions of the neuron.

4.1 BLOCK DIAGRAM OF THE PROPOSED MODEL OF NEURON:

The block diagram of the neuron model proposed by the author takes into considerations all the features of an actual neuron. The block diagram shown in Figure 4.1 shows the different blocks of the neuron model. The neuron and its feed back loop is divided into dendrites, cell body or soma, axon hillock, axon or nerve fibre, and Renshaw Cell. Dendrites sense the information from adjoining cells at synaptic junctions and pass it on to cell body. In actual system number of dendrites can be as few as one and as many as thousands [2]. The cell body processes the information received from dendrites. The axon-hillock is the next section where action potential is initiated which finally travels down along axon. This output signal is feed back through Renshaw Cell.

The dendrites receiving excitatory, inhibitory inputs from other cells and an inhibitory input whose frequency depends upon the level of excitation from its axon through Renshaw Cell. The excitatory and inhibitory inputs of actual system are simulated in the form of positive and negative pulses by differentiating

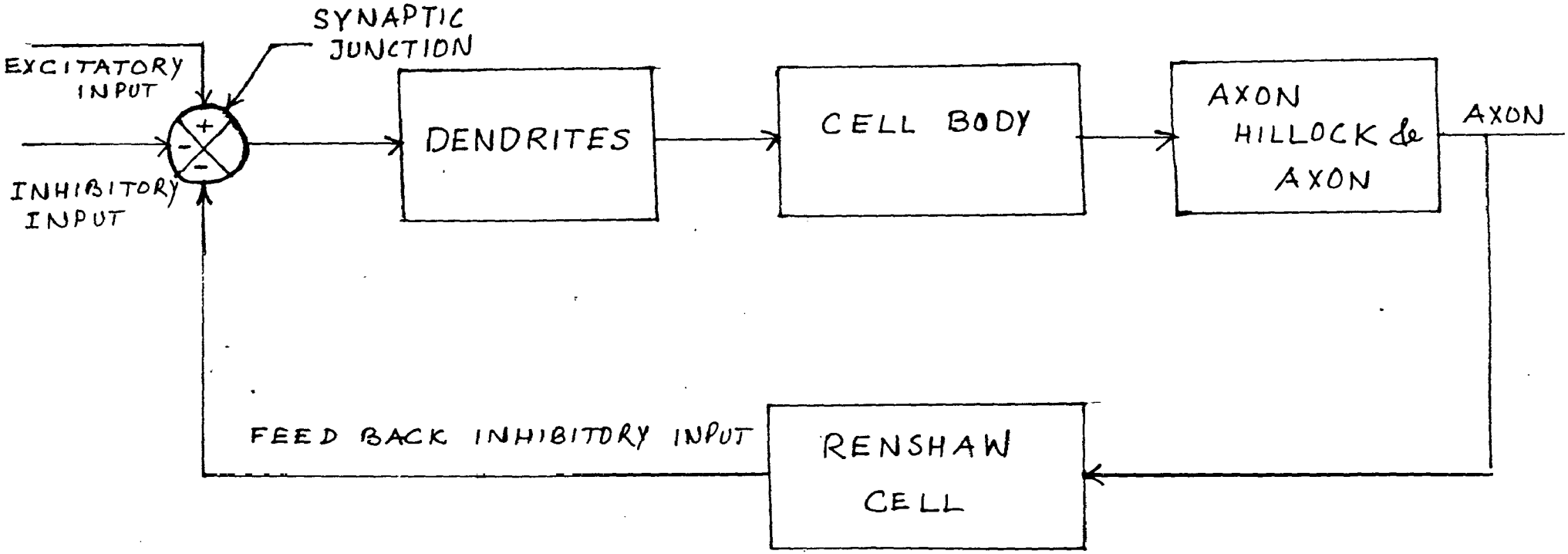

FIG 4.1

BLOCK DIAGRAM OF PROPOSED NEURON MODEL

circuit. The frequency of pulses can be raised upto 500 Hz [2]. The cell body representation consists of an integratory, threshold gate and temperature dependent threshold level. As the temperature changes the value of threshold changes because resting potential of the neuron changes as temperature changes in actual system. The axon hillock is represented by a pulse generator (mono-stable multivibrator). The transmission line analogy is given to axon. The axon consists resistance - capacitance combinational transmission line. The Renshaw Cell consists of wave shaping circuit and a voltage controlled oscillator. The wave shaping circuit furhher consists an differentiator and integrator. The output of the Renshaw Cell is feed back to the cell body of the neuron. So it forms a local negative feed back loop with nearby neurons. In this way the Renshaw Cells acts as protective device against excessive excitation.

The absolute refractory period is equal to the time period of the multivibrator (i.e. = 1 milli second) and the time constant of the integrator is equal to membrane time constant of cell body and is of the order of 1 milli second. The relative refractory period is decided by the time period of threshold gate.

4.2 DETAILS OF ELECTRONIC MODEL OF NEURON:

The complete circuit details of the electronic model of the neuron is shown in Figure 4.2. There are two types of input are fed to the model one is excitatory input equivalent to EPSP

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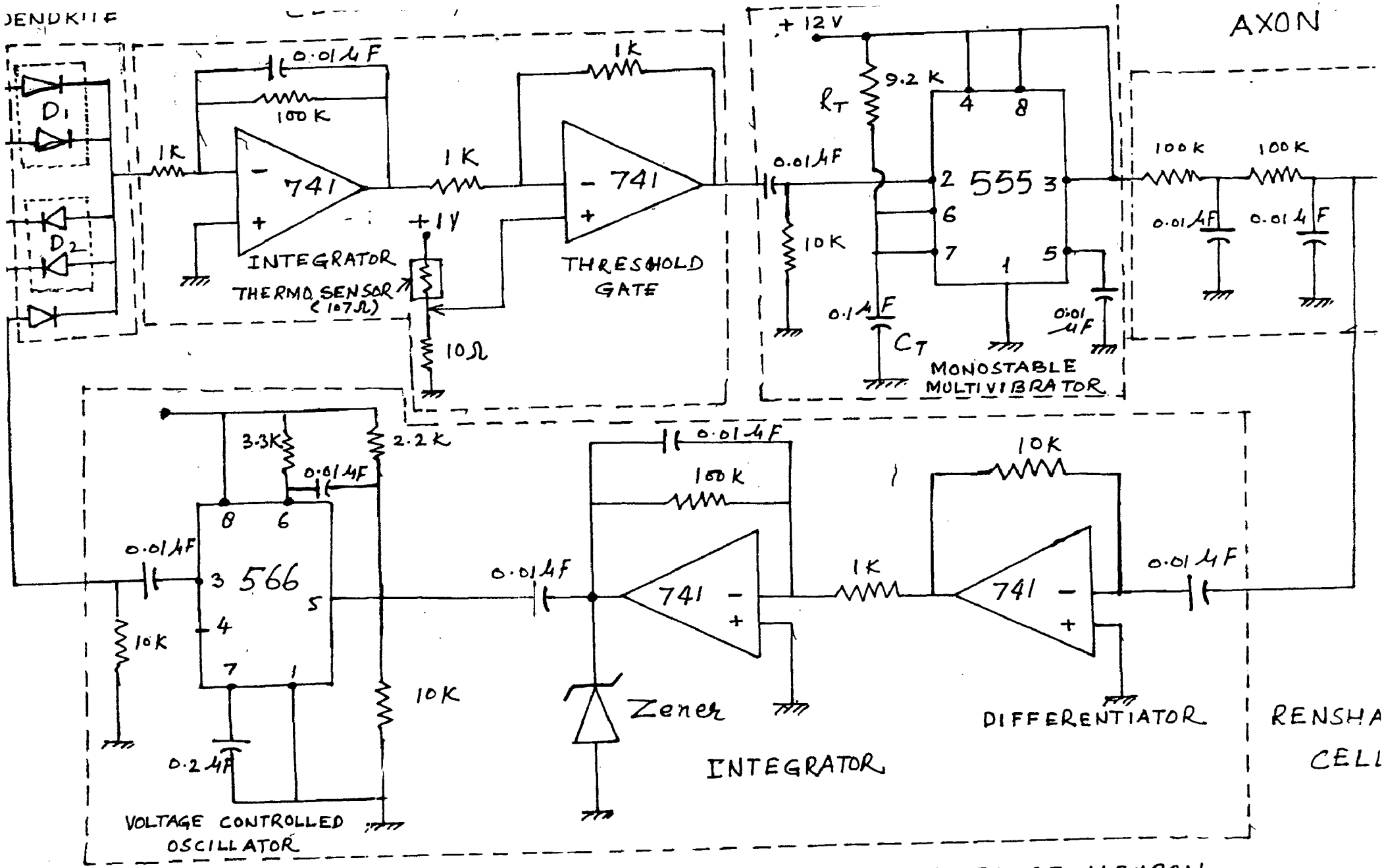

FIG 4.2. CIRCUIT DETAILS OF ELECTRONIC MODEL OF NEURON

and other is inhibitory input equivalent to IPSP. The excitatory input is given in the form of positive potential pulses and inhibitory inputs are in the form of negative potential pulses. Input pulses are differentiated with the help of RC differentiator to get the sharp pulses. The diodes D_1 are used in the EPSP input allows only positive pulses. It blocks the negative pulses. Similarly diodes D_2 are used in IPSP input allows only negative pulses. It blocks positive pulses. That means that the same line cannot be used for passing on both EPSP and IPSP input differentiating time constant of 1 milli second has been selected with C = 0.01 micro farade and R = 100 kohm.

The length of dendrites i.e. the distance between synaptic junctions and the cell body is represented by a resistance. The larger value of resistance shows that the synaptic junction is far away from cell body and the smaller value of resistance indicates that the synaptic junction is very close to cell body. For this purpose a variable resistance of 100 kohm which can be adjusted as per the requirement is thought to be the acceptable representation.

The input of the Renshaw Cell and the EPSP and IPSP inputs are differentiated before applying at dendrites. All the inputs EPSP, IPSP and feed back through Renshaw Cell are connected to an integrator where integration of inputs takes place. The time constant of the ingrator which is decided by the parallel combination of resistance and capacitance is adjusted to be equal to actual membrane time constant. There are many experimental result available [2] to show the membrane time constant is of the

order of 1 milli second. To provide the 1 milli second value of the membrane time constant a 100 kohm resistance and 0.01 micro farade capacitance has been used in this model. The other value of capacitance (i.e. 0.1 micro farade, 1.0 micro farade) may be used in the same model for getting the large value of membrane time constant for further study of neuron model. The output of the integrator is inverted sum of the signals received by it.

The output of the integrator is given to the threshold for its comparison against the reference level. When the integrator output exceeds reference level (threshold) the threshold gate changes its state and provide a signal for further processing in the model. If theingrator output is below the reference level then threshold gives no response. This show the all or none law.

The threshold gate excite only when there is negative potential at the output of integrator i.e. the value of EPSP inputs are more than the value of IPSP inputs. If IPSP inputs value is more than EPSP's inputs value then the output at the integrator is positive and then threshold will not be crossed. Resting potential of about +80 mV [2] of actual neuron system provides for this reference. Thus the threshold gate has been designed to have reference of +80 mV. In this model the effects of temperature on the exhitability of neuron as given by MacIver and Roth [22] has also been considered. For this purpose a thermosensor has been used so that its characteristic match with the requirement

For this purpose a thermosensor of 107 OHM which exhibited the required characteristics is used. The resistance of thermosensor for different value of temperature is also shown in the Table-1.

For the working of electronic model, it is assumed that the resting membrane potential of the neuron is -80mV at 19°C. This assumption is valid since this figure of -80mV has been found by many investigator. As the temperature changes to the 40°C the value of resting membrane potential changes from -80mV to -72mV. If the resting potential decreases to a value of -60mV then the action potential is generated even there is no input at that instant [2]. To get the above value of the resting potential we used a resistance of 10 ohm and a thermosensor of 109 ohm in the threshold gate circuit.

So as the temperature changes the resting membrane potential changes, so the threshold value changes. So the output of the threshold will not only depends on the input excitation signal put on temperature also. At high temperature the input signal of comparatively low amplitude can excite the threshold gate and generate a signal. This output signal of the threshold gate triggers the pulse generator which is a monostable multivibrator. The time period of the multi-vibrator is 1 milli second which is equal to the absolute refractory period.

In the present model, IC 555 is used as mono-stable multivibrator. The external timing capacitor C_T is held initially discharged. Upon application of a negative pulse to pin 2, the flipflop is set which releases the short circuit across the external

capacitor. Now rise exponentially with the time constant $R_T C_T$, this time constant $R_T C_T$ is equivalent to the absolute refractory period. When the voltage across the capacitor equal 2/3 Vcc the threshold comparator rests the flipflop which in turn, discharge the capacitor rapidly and desired the output to its low state. The circuit triggers on a negative going input signal, when the level reaches 1/3 Vcc. Once triggered the circuit will remain in this state until the set time is elapsed, even if it is triggered again during this interval. The time that the output is in high state Vs 1.1 $R_T C_T$. Applying a negative pulse simultaneously to reset terminal (Pin 4) and trigger terminal (Pin 2) during the timing cycle discharge the external capacitor C_T and cause the cycle to start over again. The output pulse is square wave which can be get at (Pin 3).

The output generated by the monostable multivibrator travels down on resistance-capacitance analog of axon. As the length of axon increases the number of resistance-capacitance groups also increases. It is assumed as a long transmission line which is uniformly distributed over entire length. No action takes place in the axon-analog it only shows the elapse to transmit the signal in the axon.

These output pulses are transmitted to the central nervous system for further necessary control processing.

The shape of the outout pulses are distorted due to the transmission of pulses along the entire length of the axon analog

which is the combination of resistance and capacitance. To over come this difficulty, the axon is connected to the differentiator unit whose output depends upon the number of action potential travelling along the axon not on the shape of action potential. For this purpose an operational amplifier IC 741 is used as a differentiator unit. The time constant of the differentiator unit is decided by the resistance and capacitance connected to its terminals and this is of the order of 1 milli second. With selecting the value of R = 100 K and C = 0.01 microF. The output of the differentiator is a train of spikes. FIG 4.4.

The differentiator output is connected to an integrator which integfates the train of spikes. The integrator controls the frequency of voltage controlled oscillator (VCO). The frequency of the output pulses of the integrater depends upon the time constant of the integrator which is decided by the resistance and capactiance connected to the operational amplifier IC 741. The time constant (RC) of the integrator is taken 1 milli second by choosing R=100 K and C=0.01 microF. During the time constant RC if there is any spike arrives than it will not excite the integrator. So output of the integrator is a train of pulses of square pulses. Theim time of integration is 1 milli second.

The output of the integrater is connected to a voltage controller oscillator. In this electric circuit IC-566 is used as a voltage controlled oscillator. The SMC 566 function generator is a general purpose voltage controlled oscillator designed for

highly linear frequency modulation. The control terminal (Pin 5) is biased externally with a voltage (Vc) in the range of

$$\frac{3}{4} V^+ \quad V_c \quad V^+$$

where Vcc is the total supply voltage. The control voltage Vc is sent by the voltage divider formed with R_2 and R_3. The modulating signal is then ac coupled with the capacitor C_2. The modulating signal can be directly connected as well, if the appropriate dc bias voltage is applied to the control terminal. The frequency is given approximately by

$$F_0 = \frac{2 (V^+ - V_c)}{R_1 C_1 V^+}$$

and R_1 should be in the range 2 K R_1 20 K. A small capacitor typically 0.001 micronF should be connected between Pins 5 & 6 to eliminate possible oscillation in the control current source.

The output of VCO is connected as an inhibitory input to dendrites through a differentiator i.e. a combination of Resistance and Capacitance. The VCO output increase with increase in excitation. So this acts as protection device against excessive excitation. As the excitation increase from a certain level the input of the VCO is also large. So output of VCO also increase proportionately but VCO output is connected as inhibitory input to dendrites, it decrease the summing of all EPSP and IPSPs inputs. So far high excitation the output at the axon is not effected to much so the signal transmitted to the CNS is of regularised nature. The increase of the output frequency of VCO ultimately decreased the excitation input of neuron.

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4.3 EXPERIMENTAL RESULTS:

The electronic model of neuron proposed by the author was fabricated and has been tested for its various characteristics and processes. It shows all the electrical characteristics of neuron.

1. There is a particular threshold value for an input below which there is no excitation (there is no output). All the threshold or above threshold input the neural system is excited and output is observed and action potential generated. Output amplitude response for different values of the step input for different values of threshold is shown in Table-1.

Table-1

Threshold value = 1 V		Threshold value = 2V		Threshold value=3V	
Input	Output	Input	Output	Input	Output
0.0	NIL	0	NIL	0	NIL
0.5	NIL	0.5	NIL	0.5	NIL
1.0	NIL	1.0	NIL	1.0	NIL
1.5	10	1.5	NIL	1.5	NIL
2.0	10	2.0	NIL	2.0	NIL
4.0	10	2.5	10	2.5	NIL
5.0	10	3.0	10	3.0	NIL
		4.0	10	4.0	10
		5.0	10	5.0	10

2. (ii) The different values of the EPSP and IPSP inputs are applied as input to the proposed model. The action potential is generated only when the sum of the EPSPs and IPSPs inputs is above threshold level.

3. When a pulse of constant amplitude above the threshold level and variable frequency is applied at the input of theneurons; the output signal is observed only for the time which satisfies the condition for absolute refractory period. When the frequency exceeds the limit, the output action potential is absent. In the proposed model the absolute refractory period is 1 milli second i.e. equal to the time constant of the monostable multivibrator.

The frequency range of neuron model and therefore the model becomes slow. This is similar to an actual neuron. Table-2 shows the frequency response for the absolute refractory period of 1 milli second.

Table-2

Input Pulse Frequency	Output Response
50	Present
100	Present
150	Present
200	Present
250	Present
300	Present
350	Present
400	Present
450	Present
500	Absent
550	Absent
600	Absent

4v) The output frequency response of the neuron model is shown in Figure 4.3 for the several values of the input signal, which is a steady state d.c. voltage, when they are applied just before the multi-vibrator. It is within the range as in the actual neuron.

5. When the sum of EPSPs and IPSPs inputs are less than the threshold value then there is no action potential generated and when the sum is more than threshold level then action potential is generated. Above threshold level it does not depend upon the amplitude of the input. So it show all or none law. As in the actual neuron i.e. for sub-threshold stimulus produces no excitation, while threshold and above threshold produces excitation as shown in Table-1.

6. In the present work the effect of temperature is also considered. A thermo-sensor is used in the threshold level-gate. As the temperature increases threshold level decreases, so the threshold gate triggered at sub-threshold level.

7. The membrane resting potential is used for threshold level, which changes as the temperature changes. As temperature increase resting membrane potential increases so the threshold level decreases.

8. The waveshapes at different terminal are shown in FIG 4.4.

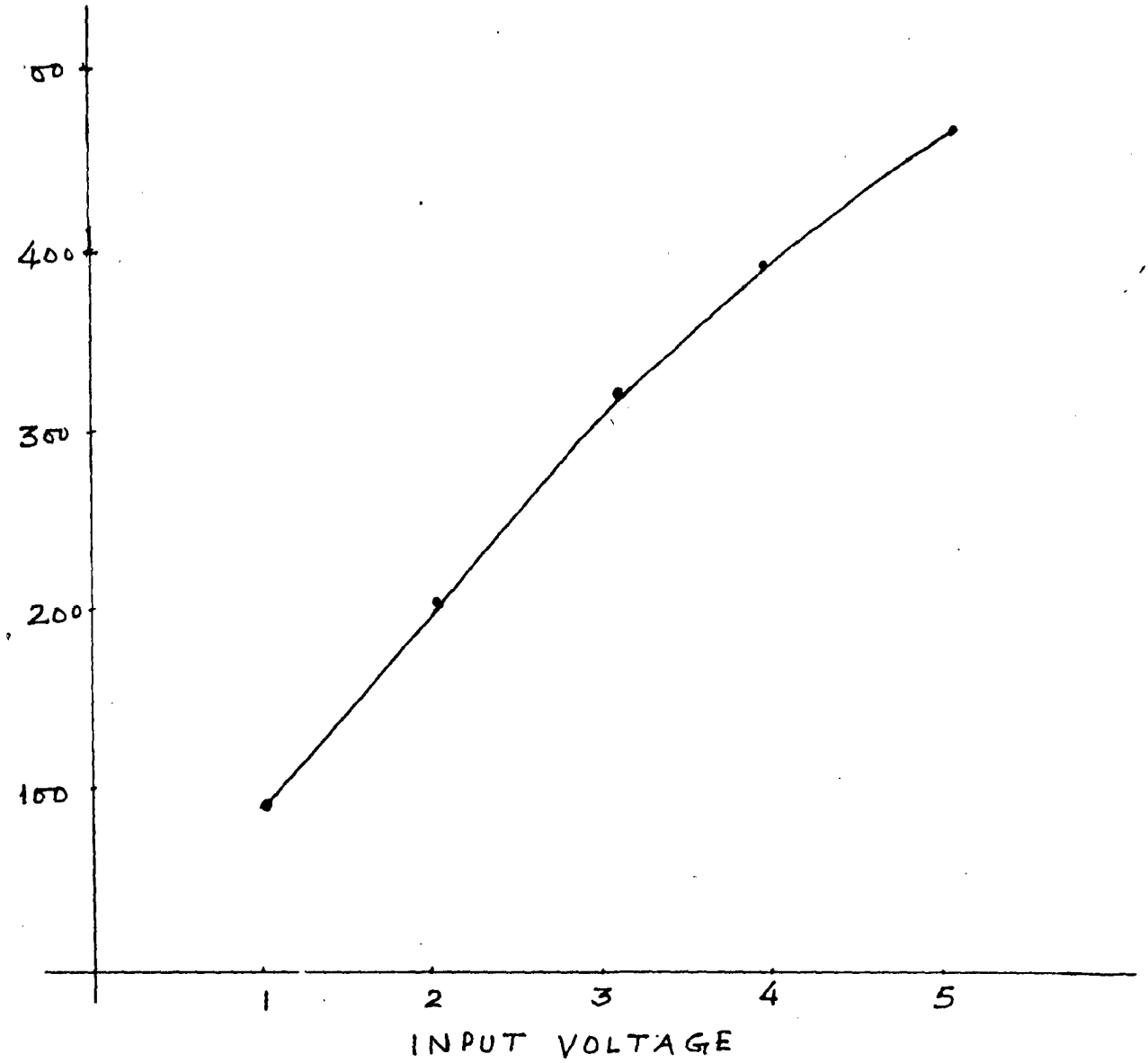

FIG 4.3 OUTPUT FREQUENCY V/S INPUT VOLTAGE

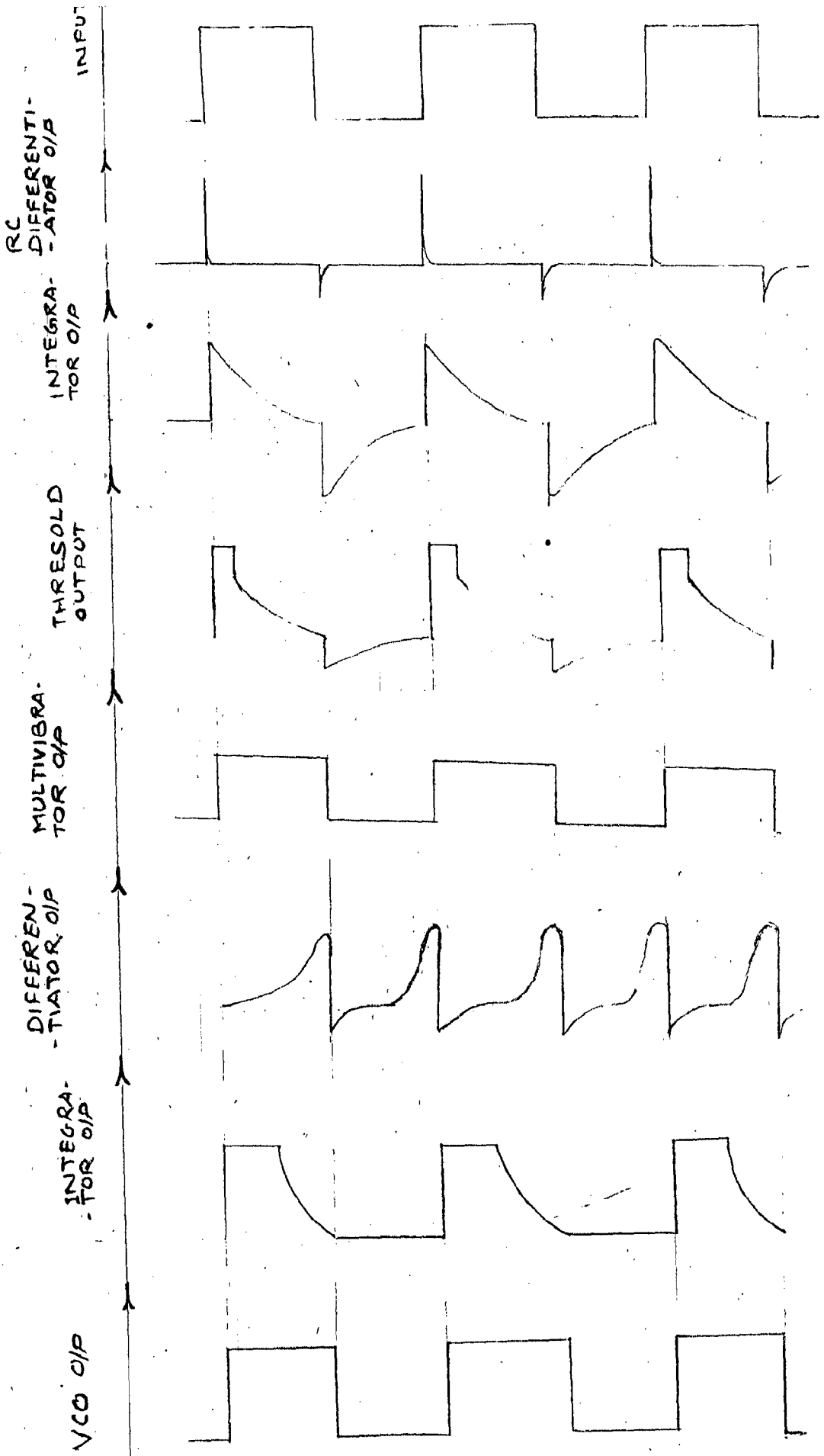

FIG 4.4 WAVESHAPES AT DIFFERENT TERMINALS OF NEURON MODEL

The model proposed by the author shows all the electrical properties of an actual neuron. The experimental results observed are similar to the results which have been observed by the many bio-engineers and scientist in past.

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CHAPTER - 5

CONCLUSION AND DISCUSSION:

The dissertation deals with an electronic model of neuron processes and its feed back loop through Renshaw Cell. It simulates the transmission of information in the dendrites, cell body, axon Hillock, axon and inhibitory feed back through Renshaw Cell. Renshaw Cell works as protective device against excessive excitation and generation of action potential. The existing models are reviewed in the present work.

The model described in this dissertion includes most of the electrical characteristics of neuron. The effect of the temperature on the resting membrane potential which acts as the threshold of the proposed neurle model is also taken into account. The summation and integration of EPSPs and IPSPs inputs, integration phenomenon in cell body membrane, threshold and sub-threshold phenomenon, refructory period, inhibitory input from Renshaw cell etc. can be easily studied by the bio-engineers and neurophysiologists for explaining the neurnn processes. The model is compact, reliable and inexperience and several such models can be inter-connected to study the behaviour of inter-neurons, nerve cent-res and other complex processes. It also proves to be a good aid to diagnostic and prosthetic purposes. If it becomes possible to construct a very small micro-structure model than it may be helpful in treatment of some paralysis cases, where a small segment has stopped working.

by replacing it with artificial built micro-structure model of neuron.

This model has the advantage that it is very flexible in its principal of operation and studies can be carried out on the properties of different kinds of nerve cells by the simple process of changing several parameters of the circuit. Integrated circuit chips have been used in the present model so as to minaturize the set up.

The above model could be perfected by including gradually discovered physiological aspects of the neural structure.

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