NEURAL MODELLING

A DISSERTATION
submitted in partial fulfilment of the
requirements for the degree
of
MASTER OF ENGINEERING
in
ELECTRICAL ENGINEERING
(Measurement & Instrumentation)

By

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CERTIFICATE

Certified that the dissertation entitled "NUERAL MODELLING" which is being submitted by S. JOTINDER SINGH in partial fulfilment for the award of the degree of MASTER OF ENGINEERING in 'MEASUREMENT AND INSTRUMENTATION' of University of Roorkee is a record of students own work carried out by him under our guidance. The matter embodied in this dissertation has not been submitted for the award of any other degree or diploma.

This is further certified that he has worked for a period of 6 months from January 1972 to July 1972 for preparing dissertation for Master of Engineering Degree at the University.

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C O N T E N T S

PAGES

LIST OF SYMBOLS

E	=	electric field across membrane
P	=	No. of ions crossing the membrane
P_{co}	=	Ions density in membrane at infinite time
P_n	=	number ions stored in ionic region
P_{nco}	=	number of ions already present in membrane, in absence of built-in voltage.
P_c	=	number of anions in counter ion layer.
γ_p	=	life time of ions in membrane
D_p	=	Diffusion constant of ions in membrane
V_m	=	membrane voltage
R	=	Universal gas constant
V_p	=	built-in voltage across ionic region
I_p	=	ionic current due to diffusion of ions.
$I_o = I_L$	=	leakage current
J^+	=	charge current density
L_p	=	diffusion length of ion in membrane
J_1	=	Current density due to ions moving into membrane
J_o	=	the outward current due to anions.
σ_m	=	membrane conductivity
$P(0^+)$	=	Ions injected due to step voltage
$P_{ss}(X)$	=	is an ion concentration at steady state
β_R & β_N	=	Reverse and forward amplification factor respectively.
I_m	=	the current due to stored ions in membrane during transient state.
I_{me}	=	anion current from membrane region to interstitial fluid.

I_b = diffusion length of Na^+ ions.

σ_b = conductivity of membrane

σ_e = conductivity of interstitial solution

$q(r,k)$ = density of injected ions in membrane

γ_o = Pore diameter at outer surface of membrane

γ_i = Pore diameter at inner surface of membrane

μ_p = ions mobility in membrane.

CHAPTER - I

INTRODUCTION

The fundamental element of nervous system of a man with which he can sense and transmit any disturbance is neuron. These neurons have two parts viz. axon which is a long process and dendrite, which is terminal part of neuron. When a particular place of body is excited the information is carried to either direction with characteristics velocity. For example, if a finger is suddenly exposed to thermal shock, the information of the brain is again transmitted through the neuron to the finger muscles 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 works as sensory and motor neuron.

The information flow is essentially an electrical phenomenon as has been evidenced by experimental facts and few models are proposed to analyse this complex phenomenon.

The functional unit of nervous system is called neuron. It consists of nerve cell body, small processes called dendrites, and one large process called an axon. Outside of central nervous system are many of the large axons are surrounded by a thick, fatty myelin sheath. The sheath is interrupted somewhat periodically at the node of Ranvier. Along the side of sheath are satellite cell called schwan cells. Some axons are more than a metre long.

The thousand fibers are typically grouped together to form nerves. A bundle of nerve is called a trunk. A trunk includes a wide range of axon sizes. The largest fibers are myelinated; i.e., their insulation is relatively thick layer of a fatty substance, meylin. The walls of unmyelinated fibers also consist of fatty substance molicules. In these fibers, for the model purpose, a tube that filled with a weak solution, mostly K^+ ions, and relatively large organic negative ions. The fiber is surrounded by interstitial fluid of the body essentially Na^+ Cl^- solution. Its concentration is about one ion for 175 water molicules. Diameter of Fibers ranges between 0.3 to 1.3 Micron. The conduction speed for typical fibers is 1.73×10^6 diameters per second, indicating the speed between 0.5 and 2.3 m/sec.

Nervous system is composed of units called neurons which transmit information in form of electrical pulses from one place within the organism to another. Studies of the nerves have shown that they consist of bundles of long processes called axons or nerve fibers. The axon are each a part of an individual neuron. Along the nerve fiber, the information is coded and transmitted in the form of an "all-or-none" or "on-off" electrical pulse called action or spike potential.

During stimulation, the conductive become permeable in addition to potassium, to which membrane becomes most permeable is sodium ions, therefore during, depolarization the sodium ion diffuses from high concentration area of sodium

outside the membrane to low concentration area of sodium inside the membrane. As long as the membrane remains depolarized, the inward flow of sodium increases the number of positive ions outside.

Several theories have been offered to explain the rapid return of normal permeability short after depolarization. It has been suggested that sodium or calcium ions flowing inward through the permeable membrane might react with constituents of the membrane to ions besides Pottasium but at the same time physical changes in the membrane occurs to make it impermeable to further flow of positive ions. Once membrane become impermeable to further inflow of positive ions, the normal outward diffusion creates deficiency of positive ions inside the membrane and causing the membrane to return to resting potential.

CHAPTER - II

R E V I E W

Most models that have appeared during the last two decades, or so have taken the form of electronic systems, chemical systems, mathematical formations, or computer simulation. Mathematical models have great utility in limited domains. Mathematical models, have been developed to simulate behaviour of action potentials, but these models do not provide an insight into membrane mechanism. Models based on physical and chemical assumptions about membrane properties are very few. Mathematical models of network behaviour are extremely well qualified, is particularly true for large - scale electrical-activity such as wave formation and propagation.

Coverage of this review is restricted to models of fixed properties of membrane single units, are relatively small units. There has been no attempt to include the models of information storage, i.e., analogs of memory, conditioning, or learning.

Only a few workers in this field have considered the fundamental molicular mechanism involved in the study of excitable membranes. Cole observed experimentally the steady-state behaviour of nerve, and obtained a negative steady state resistance in membranes.

Goldman and Agin gave theoretical explanation for steady state negative resistance. Goldman explanation based on the polar mechanism, shown in Fig. 8

The state II and state III are reversibly binding to Na^+ and K^+ ions and thus allowing Na and K conductance to increase. These rate constants are assumed to be voltage dependent, driving the reaction through the state II and state III upon depolarization and then, upon repolarization, back to state I. Goldman developed equations shown the similarity of form between his calculation for Na^+ and K conductance observed experimentally. The reduction of potential across the membrane changes the electric field in the vicinity and reducing binding affinity. This would release some of polar heads to move and thus open (or close) a physical channel for the passage of ions. Goldman suggests the radical changes in calcium and absorbility by polar groups can change the energy requirement for ion to enter the lipid. The energy requirements of this hypothesis are as yet unclear.

2.1 HAMEL & ZIMMERMAN'S MODEL :

They assumed a basic membrane model similar to bimolecular leaflet model, this theory has modified in two respects. First, water-lipid partition energy is acting as a barrier for transport across the membrane interface. Second, a configurational transition of the polar portion of molicules and change in voltage across the polar portion, which is function of voltage. It is this change in voltage across polar portions of membrane which produces a negative resistance. A schematic diagram of membrane of Hamel and Zimmerman's model is given in Fig.No. 9

Himel & Zimmerman gave an expression for current J of univalent cation as

$$J = D \left[- \frac{dn}{dx} + \frac{e E_N}{K T} \right]$$

Where

D = Diffusion constant of NPR

E = electric field

K = Boltzman constant

e = electronic charge

T = absolute charge

At I and II region interface

$$J = J_{in} - J_{out}$$

Where

J_{in} = flux into NPR region

J_{out} = flux from NPR to water region.

Hamel & Zimmerman used dipole theory to calculate polar voltage which is given by

$$V_P = \frac{P \overline{\cos \theta}}{A K \epsilon_o} (1 - S)$$

Where

A = Area per dipole in m^2

K = dielectric constant

$\epsilon_o = \frac{10^{-9}}{36\pi}$

$\overline{\cos \theta}$ is the average angle of dipole makes with membrane field.

$$S = \frac{N_1}{N_1 + N_2}$$

Where

N_1 = bound poles (those not free to rotate)

N_2 = free dipole

P = dipole moment

and V_p is the polar voltage.

Some of these data are assumed, and other taken from experimental data, needs eleven basic parameters. But this dipole theory developed so far is not in a position to explain behaviour of excitable membrane under transient condition.

2.2 HH - MODEL, DISCUSSION AND EXPERIMENTAL RESULTS :

Hodgkin and Huxley proposed a mathematical model for squid nerve, to meet the experimental results of voltage. They predicted that membrane current could be separated into ionic currents with conductance parameters which were both function of time and voltage.

The proposed model shown in Fig.No. 10.1 . There are three ionic component are in parallel and a membrane capacitance C_m, in the equivalent circuit. This experiment suggests that gNa and g_c are function of time and membrane voltage, but E_{Na}, E_K, E_l, C_m and g_L may be taken as constants. g_{Na} and g_K are the conductance of sodium and potassium respectively and are voltage sensitive. g_L is leakage conductance of constant quantity.

The influence of membrane potential on permeability can be summerised as first that depolarization cause a transient increase in Na conductance. Secondly, that these changes are graded and that they can be reversed by repolarizing the membrane.

There are two types of currents, one is capacitive current and other is ionic current. Thus

$$I = C_m \times \frac{dv}{dt} + I_i$$

I = Total membrane current density (inward current positive).

I_i = ionic current.

V = displacement of membrane potential from its resting value.

C_m = membrane capacity per unit area

t = time

The ionic current I_i is given as

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

The individual ionic current are given by

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

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

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

Where E_K and E_{Na} is equilibrium potentials for sodium and pottassium ions.

E is the potential at which the 'leakage current' due to chloride and ions is zero.

HH used first order equations whose solutions were raised to powers. For pottassium currents they chose a 4th power, although 6th power fit better. The pottassium conductance g_K was given by the Hodgk and Huxley as

$$g_K = \bar{g}_K \, n^4$$

Where n is dimensionless variable which can vary from 0 to 1.

$\bar{g}_K$ is constant with dimensions conductance/cm^2 and in turn is obtained from

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

Where α_n and β_n are ratio constants, which vary with voltage but not with time and have dimension of $[\text{Time}]^{-1}$

The faster sodium transient was matched with a first order equation whose solution was cubed for the turning on part; while the declining phase was matched by first-order decay with slower time constant.

The sodium conductance is

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

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

$$\frac{dh}{dt} = \alpha_n (1 - h) - \beta_N h$$

Where $\bar{g}_{Na}$ is a constant and α and β are function of voltage but not of time.

First point which emerges is that changes in permeability appear to depend on membrane potential and not on membrane current. At fixed depolarization of sodium current follows a time course whose form is independent of current through membrane. If N_a concentration is such that $E_{Na} < E$, the N_a current is onward. If $E > E_{Na}$ the current changes in sign but follows same time course. After this Fitzhugh did work on digital computer to study the behaviour of HH model.

2.3 NERNST EQUATION :

Empirical mathematical model proposed by Hodgken and Huxley, was not only capable of depen describing the currents observed in a voltage clamp but also could predict the quantities of sodium and pottasium ions which moved across the membrane during transient activity. E_K, E_N , and E_L refer to the equilibrium potentials resulting from concentration gradients. The Nernst equation gives equilibrium potential for the various ions involved, where,

$$E_K = \frac{RT}{F Z_K} \ln \frac{[K]_{out}}{[K]_{in}}$$

$[K]_{out}$ = Pottasium concentration in interstitial fluid

$[K]_{in}$ = Pottasium Concentration in extracellur fluid

Z_K = Valence of pottassium ions.

R = Universal gas constant equal to 8.2 foules per mol-degree abs.

T = absolute temperature.

F = 96500 Coulombs per 1 m of monovalent ions.

There are 6.023×10^{23} molecules in 1 m of any substan

Monovalent ion has a charge of 1 electronic charge

$= 1.6 \times 10^{-19}$ Coulomb

The charge on 1 M monovalent ion is (6.023×10^{23} monovalent ions per 1 m) x (1.6×10^{-19} Coulomb per monovalent ion) = 96500 Coulombs per 1 m of monovalent ion.

or $\frac{RT}{F} \simeq 25$ mV at 300°F

2.4 MODEL OF NEURONAL MEMBRANE BY LEWIS :

HH - model satisfactorily explained the axon spike potential, no coherent view of subthreshold phenomena existed. Lewis postulated that many of the subthreshold effects found in somatic and dendritic regions should be explicable in terms of the same ionic hypothesis used to explain suprathreshold phenomena. This postulate was based on the assumption that since the dendritic and somatic membrane presumably are continuous with the axon membrane, the basic electrical properties of all three should be similar.

The model consists of seven parallel electronic circuits. Four of them are designed to match the squid-axon data of H-H model and thus corresponds to equivalent circuit Fig. 11 a . The other three circuits represent synaptic current pathways so that consequences of synaptic inputs may also be studied. The entire configuration may be considered to be composite of a patch of electrically excitable membrane contiguous with a patch of subsynaptic,

(Chemical excitable) membrane. It can equally well represent a single homogeneous patch of membrane with continuous distribution of electrically excitable and synaptically induced conductance components.

The synaptically controlled conductances, however, operate differently. The presynaptic spikes produce emission of a fixed quantity of simulated transmitter substance. The resulting transmitter concentration is then allowed to decay exponentially, corresponding to a diffusion process. Two synaptic parameters are thus available for analog the quantum of transmitter per presynaptic spike and the transmitter inactivation rate.

Five out of six conductance shown in Fig. 11 a. are not constant; they undergo transient changes owing either to changes in synaptic inputs (presynaptic spikes) or to changes in transmembrane potential (V_m). The current through each conductance is product of time-varying conductance itself and the voltage across it which is also time varying. Two examples shown in Fig. 11(b) one illustrates the operation of simulated synaptic conductance, and other illustrates that for a simulated electrically conductance.

In the case of synaptic conductance, a presynaptic spike is transformed into a decaying exponential by means of a RC filter. This exponential represents the transmitter concentration, or the time course of synaptic conductance. The multiplier circuit produces a current which is proportional to the product of this conductance and net voltage (V_m-V_R) across it.

In the case of electrical excitable conductance (Fig. 11 c.) the input to electronic filter is the transmembrane potential (V_m) rather than presynaptic spike. The filter is considerable more complicated than that of simple passive RC synaptic filter; it is a non-linear, active filter designed to provide the time - and voltage dependencies required to match HH - data. Once multiplier takes the product of conductance thus derived and the driving potential to provide the required current. Several detailed circuit realization of this model are given by Lewis.

2.5 SOLID STATE MODEL :

Guy Roy proposed a solid state model to satisfy the voltage clamp data of squid axon obtained by Hodgkin and Huxley. This model was based on theory of p-n junction of a diode. The steady state value of diode current was similar to pottassium current in its behaviour. They assumed a potential distribution in biological membrane similar to distribution in p - n - junction. From the ratio of current to voltage, they defined a voltage dependent conductance for the diode. The conductance was then used to fit the data for pottassium steady - state conductances and the sodium maximum conductances. They also assumed that the conductances to be self-increasing with time. A first order non-linear equation was formed for pottassium and sodium conductances. To provide inactivation they used first order linear differential equation which started with an initial value and decayed to a voltage dependent steady-state. The product of two solutions gave the transient sodium conductance. The curves were fitted to the

data using integrating computer programme, and least square criteria to determine the value of parameters.

CHAPTER - III

MEMBRANE UNDER STEADY STATE

3.1 INTRODUCTION

The cell electrical membrane probably consists of a few alternating layers of lipids and proteins. These layers are long axes parallel and oriented perpendicular to membrane. The protein layers are bonded to the lipids at their polar ends. Water and water soluble substances can penetrate the membrane in a region where a lipid is closly packed. Membrane is perforated, containing small diameter (about 3 Angstroms) water filled pores. Ions could diffuse through these pores. The membrane is about 100 times more permeable to K^+ ions, than it is to N_a^+ ion. This difference may be due to the pore diameter of 3 Angstroms, and lies between the hydrated diameter of K^+ (2.2 Angstroms) and N_a^+ (3.4 Angstroms).

The boundry between the interacellular and interstitial fluid is considered to be a thin (50 to 100 Angstroms) nonaquous layer, which is called electrical membrane, because its nature has been obtained from different electrical measurements. The sodium and ion concentration is much higher in the interstitial fluid than in the intracellular fluid. Potassium ion concentration is much higher in intercellular fluid. There exists an electrical potential difference between the internal external solution. It is known as rest potential, and is negative inside the cell than to outside.

To study the excitable membrane, the membrane is divided into two regions. One is ionic-region associated with counter ion layer in interstitial fluid and other is non-ionic region. Ions are trapped in membrane from interstitial fluid, in the ionic region. These trapped ions together with CIL adjacent to interstitial solution develop a field or voltage is such that it opposes the entry of ions from interstitial fluid to membrane region.

3.2 THEORY OF MEMBRANE POTENTIAL :

If a membrane is immersed in an electrolytic solution, on one side of this membrane is an excess of Sodium ion, while on other side is an excess of chloride ion. These membrane are so close to each other that electrically balance each other and satisfy the Law of Chemical Composition, that there is one positive ion balancing one negative ion. Consequently the potential will exist at this surface. If on other hand chloride ions and some chloride atoms pass through the membrane to balance remaining Na ions. Then the membrane potential no longer exists.

It is obvious there is greater number of hydrogen ion concentration on inside and outside, the greater tendency for positive hydrogen ions diffuse through membrane. Mathematically the potential measured across the membrane immersed in a electrolytic solution is given by

$$\text{E.M.F.} = 60 \times \log \left(\frac{\text{Concentration I}}{\text{Concentration II}} \right)$$

Where Concentration I is the Concentration of H^+ ions inside the membrane and concentration II is concentration of hydrogen ions outside the membrane.

The resting potential measured across living membranes is in substantial agreement with value calculated from inside and outside the membrane. For calculation work, the Nernst equation can be suitably modified to express the voltage across membrane, given by

$$E = 60/n \log \left(\frac{a_1}{a_2} \right) \quad mV$$

Where n is the number of charges carried on the ions of the salt, and a_1 and a_2 are the effective concentration on opposite sides of membrane.

More generally, when two such salt solutions with activities (effective concentration) a_1 and a_2 about each other, and if diffusion is restricted so that salt cannot flow.

$$E = 2 \frac{RT}{nF} \ln \left(\frac{a_1}{a_2} \right) \quad mV$$

$$E = 2 \times 60 \log \left(\frac{a_1}{a_2} \right) \quad mV$$

Work is potentially available from the concentration ratios of both positive and negative ions, so the factor 2 comes from this fact.

If salt can diffuse, a new factor, t_- the transference number anions, enters, so

$$E = 2\, t_- \times 60 \ln \left(\frac{a_1}{a_2} \right)$$

Here $t_- = \dfrac{\mu_-}{\mu_+ + \mu_-}$

Where μ's are the mobilities or speeds, of the ions in cms per second when the voltage gradient is 1 V/cm. Substituting of the expression for t_- and rearrangement, gives

$$E = 60 \ln \left(\frac{a_1}{a_2} \right) - 60 \frac{\mu_+ - \mu_-}{\mu_+ + \mu_-} \log \left(\frac{a_1}{a_2} \right)$$

The expression gives the potential if cations and anions are not restricted in their motion. When both move with same speed (Kcl in water, e.g.,) $\mu_+ = \mu_-$ (or $t_- = \frac{1}{2}$) and second term is drops out. If motion of one completely restricted, these can no motion of the other if micro-neutrality is to be maintained, and potential is given by first term only. In such a case charged protein ions plus salt water e.g. the values of a_1 and a_2 are the activities of the unrestricted ion.

If an electrode is placed in such a way that it has contact with interior of axon, a negative potential relating to the medium surrounding the axon is detected, this negative potential in normal axon is known as resting potential

which ranges from-400 mV to -120 mV. Diagramically axon can be represented by an insulator shaped in cylindrical cell. The inner and outer faces of the cell are charged, the hollow shell is filled with one conductor medium and immersed in another.

The existance of charges across the extremely thin membrane, indicate the ability of this thin membrane to withstand very high electrical potential. At the surface of many biological cells including neuron, it appears that high field stand of about 10^8 volts/metre occurs whereas the dry air breaks at about 10^6 volts/metre.

3.3 IONIC MODEL :

This model of nerve is similar to Zimmerman's model shownin Fig. No. 12. . It consist of ionic and non-ionic regions. Region I is an interstitial flood or extracellur fluid. Region II is non-ionic region. Region III is intracellular fluid. The liquid-membrane junction has two layers. One is of counter ion of negative charged ions in liquid just adjacent develop surface of membrane. The few cations are trapped with membrane liquid surface. This structure at the outer junction develops a voltage across it, which opposes the flow of ions from interstitial fluid to intercellular solution via membrane.

In rest condition the inner surface of membrane negative w.r.t. outside, thus attracting all the positive

ions. This rest potential does not allow to form ionic region. The inner junction between membrane and intracellular fluid has got a negligible width of ionic and counter-ion-layer because of the polarity developed in the region.

Assumption (i) N.I.R. portion of membrane is free of charged groups. Ion density in N.I.R. region is very small. The electric field could be taken constant. This assumption is not valid for transient condition because large number of ions are present in N.I.R. region.

(ii) The profile of electrostatic potential and ion concentration reach a steady level in a distance small compared to width of each lattice in membrane in moving from solution phase into solid membrane phase.

(iii) Under steady-state condition ion concentration satisfy Maxwell Boltzman's distribution function

For cation $[(N_a^+) \text{ and } K^+]$

$$P(X) = P_{nco} \exp\left[\frac{F (V - V_p)}{RT}\right]$$

V is the membrane voltage

V_p is built in-voltage, and for anions

$$N(X) = N_{Pco} \exp \left[\frac{F (V - V_p)}{RT} \right]$$

$$N(X) = N_{Pco} \exp \left[\frac{F (V - V_p)}{RT} \right]$$

Where $P_{n\infty}$ and $N_{P\infty}$ are ions in the membrane and solution.

P(X) is the number of ions coming into membrane.

(ix) A few cations while entering the membrane are lost due to surface trapping, and in volume of membrane, ions are lost due to forming a bond with anions or lattice of membrane. The section surface and volume recombination are assumed to be negligible.

(v) For mobile ions the continuity equation is valid across the membrane.

The continuity equation (Dennis 'Transistor's) is used for planer geometry. Ion flow for planar geometry is given as

$$\frac{\partial P}{\partial t} = \frac{P_\infty - P}{\tau_p} - \mu_p E \frac{\partial}{\partial x}(P) + D_p \frac{\partial^2 P}{\partial x^2} \quad \text{—(i)}$$

P = no.of ions crossing the membrane

P_∞ = ion density in the membrane with injection of ions in the membrane.

τ_p = life time of ions in membrane.

E = the electric field across the membrane assumed to be constant.

μ_p = Ion mobility in the membrane.

D_p = Diffusion constant of ion

X = Distance in membrane along the direction of flow of ions, the width- of membrane is W.

For steady-state $\frac{\partial P}{\partial t} = 0$

Equation reduces to

$$\frac{P - P_\infty}{P} - \mu_p E \frac{\partial P}{\partial x} + D_p \frac{\partial^2 P}{\partial x^2} = 0 \quad \cdots\cdots (2)$$

The current due to ion flow is combination of diffusion current and drift currents.

The equation is

$$I_p = q \mu_p P E - q D_p \frac{dP}{dx} \quad \cdots (3)$$

The mobility and diffusion constants are related by

$$\frac{D_p}{\mu_p} = \frac{RT}{F} \Big| \text{ For Membrane} \quad \cdots\cdots (4)$$

R = Universal constant

T = absolute temperature

F = 96500 coulomb per 1 M of monovalent ion.

From equation

$$E = \frac{I_p + q D_p \times \frac{dP}{dx}}{q \times \mu_p \times P} \quad \ldots\ldots(5)$$

The voltage across membrane width w is given by

$$V_m = - \int_0^W E \, dx \quad \ldots\ldots(6)$$

Substituting in equation (5) into (6)

$$V_m = - \int_0^W \frac{I_R \, dx}{q \mu_p P} - \frac{q D_p}{q \mu_p} \times \int_0^W \frac{dP}{P}$$

For small injection of ions across the membrane which is a correct assumption under polarised condition, equation reduces to

$$V_m = -\frac{RT}{F} \times \int_0^W \frac{dP}{P} \qquad \ldots\ldots(8)$$

It is assumed that at $x = W$, $P = P_\infty$

and at $x = 0$, $P = P_o + P_\infty$

Equation (8) becomes

$$V_m = \frac{RT}{F} \times \int_{P_\infty}^{P_o+P_\infty} \frac{dP}{P}$$

$$= \frac{RT}{F} \left| \ln P \right|_{P_\infty}^{P_o + P_\infty}$$

$$V_m = \frac{RT}{F} \ln \left[1 + \frac{P_o}{P_\infty} \right] \qquad \ldots\ldots(9)$$

P_o constitutes an injection current I_p whereas ions P_∞ constitutes I_o, a leakage current.

Equation (9) become

$$V_m = \frac{RT}{F} \ln \left[1 + \frac{I_p}{I_\infty} \right] \qquad \ldots\ldots(10)$$

Using equation (10) I-V characteristics's can be plotted provided the built in voltage is also taken care. The built up voltage is subtracted from to get resultant potential.

To estimate built up voltage, a certain amount of energy is required by ions for moving from extracellular fluid region of membrane. Built up-voltage is due to accumulation of ions in this region, which opposes the flow of ions into N.I.R. region of membrane. The built up voltage is estimated from the equation

$$P_n = P_{nco} \exp \left(\frac{F V_p}{RT} \right) \qquad \text{- - - -} \quad (3\cdot3\cdot1a)$$

P_n = No.of ions stored in ionic region.

P_{nco} = No.of ions already present in membrane region.

V_p = built up voltage across ionic region.

From diffusion equation $P_{nco} = \frac{I_o L_p}{q D_p}$ - (3·3·2a)

V_p is estimated from Equation (3·3·1a)

$$V_p = \frac{RT}{F} \ln \left(\frac{P_n}{P_{nco}} \right) \qquad (3\cdot3\cdot3a)$$

Substituting for P_{nco}

$$V_p = \frac{RT}{F} \ln \left[\left(\frac{P_n}{(I_o L_p)/q D_p} \right) \right]$$

Knowing the values of V_m and V_p for 15 percent of ions trapped in ionic region, a curve is plotted between V_m and V_p FIG NO: 15.

The ionic current due to diffusion is given by I_p as follows

$$I_p = \frac{P_o q D_p}{W} \quad \text{per unit area}$$

and $V_m = \frac{RT}{F} \ln \left[1 + \left(\frac{I_P}{I_o} \right) \right]$

As the voltage builds up, built in voltage also builds up across ionic region. This built-up voltage decreases the current flowing into membrane knowing I_p, V_p, and V_m, a V-I characteristics can be plotted. FIG.NO:17 It is seen that membrane voltage reaches near about 50 mV. The current start decreasing thereby giving rise to negative resistance region.

A membrane potential is built-up, as soon as potassium ions start flowing through membrane to intracellular fluid some of the ions cross the membrane, other are used up to built-in voltage V_p. The ionic current $I_p = \frac{P_o \, q \, D_P}{W}$ per unit area, diffuse through membrane due to concentration gradient. Due to the ions flowing into intracellular fluid, the membrane voltage is developed given by $V_m = \frac{RT}{F} \ln \left(1 + \frac{I_P}{I_o}\right)$. As membrane voltage builds up, built-in voltage also builds across ionic region. This built up voltage decreases the current flowing into membrane. Knowing the value if I_p the curve between V_p & V_m. It is seen from curve that after membrane voltage reaches near about 50 mV, the current starts decreasing thereby giving rise to negative resistance region. In steady state condition the injection ions is assumed to be small compared to a transient state condition. Under small injection of ions into membrane, it is assumed that its conductivity does not change. It is also assumed that when ions enter the membrane, they diffuse due to their concentration gradient. This diffusion of ions constitutes a current

membrane under steady state. (26)

STEADY STATE NEGATIVE RESISTANCE:

The built-in voltage is developed due to ions in ionic region. It increases as the no. of ions in ionic region increases. Membrane voltage increases as more and more potassium ions move into intracellular solution from outside of membrane. The polarity of built-in voltage is such as it opposes the incoming ions to intracellular solution. This causes a decrease of inward current. The current start decreasing with increase of membrane voltage at a particular stage. This region is called negative-resistance region. The V-I characteristics pridicted by Hamel and Zimmerman are also plotted. FIG NO. 17.

CHAPTER - IV

MEMBRANE UNDER TRANSIENT STATE

INTRODUCTION:

During stimulation, the conductive become permeable in addition to potassium, to which membrane becomes most permeable is sodium ions, therefore during, depolarization the sodium ion diffuses from high concentration area of sodium outside the membrane to low concentration area of sodium inside the membrane. As long as the membrane remains depolarized, the inward flow of sodium increases the number of positive ions outside.

Basic function of nervous system is to control the whole body. The neuron signals are send in pulses is called spikes. This equivalent to telephony channels at low frequency. In neuron there are two types of signals.

1. Signal which run from Body to C.N.S. is called Afferent.
2. Signal which run from C.N.S. to body is called efferent.

When axon is stimulated the surface potential changes in a characteristics fashion to an action potential or spike potential. Axon may be stimulated by any wide variety, i.e. electrical pulse of various shapes, heat, cold, chemical changes, and mech. pressure all leads to same phenomena. If there is dielectric strength 100 mV/100^{o} A = 10,0000 volts/cm which is in comparison, the dielectric strength of oil is 100,000 volts/

cm. It is turns out that the fiber signal is a 'spike' that is accompanied by the break down of membrane, infact regenerates the signal. The fiber operates with a threshold of about -50 mV. When inside at any point become more positive than this value the break down is treggered. The membrane becomes more permeable to sodium ions for some 2 m sec.; as ions enters the fibers the voltage increases to +30 mV. After 2 m Sec.interval there is another 2 m Sec during which the membrane becomes a relatively good insulator again. Because of disturbance is 4 m Sec wide so its frequency is 250 H_z. The -70 mV resting potential as a d.c. component which is superimposed on 100 mV peak spike, known as action potential. Fig No: 5

The membrane of polarization disappears on reversing the polarity very quickly, then it give rise to series of bumps. This spike travels in both the direction along the axon from the point of stimulation. For a very big stimulus a local response occurs which is similar to smaller than the spike potential as the stimulus increased to certain thrushold is reached when the transmitted spike potential is generated.

The spike potential is an all or None law response. Either there is transmitted spike is present its height and shape is independent of stimulus. The neuron acts in a similar manner to flip flop circuit used in counters and digital circuits. So to say neuron is either conducting or non-conducting state, nothing is transmitted in between.

In Axon, one spike is transmitted at a time or another one can not start. Some time so happens, number of sub-threshold stimuli summed up to give a response at a particular time.

A ionic current start flowing when a step voltage is applied through an electrode to intracellular fluid of nerve. The applied input pulse must have an amplitude greater than threshold value. Here two types of ionic currents flow - The inward current is known as sodium ion currents and outward sodium current is known as pottassium ion currents. The sodium current I_{Na} start flowing first and after certain time delay when N_a^+ ions reaches inside a current due to K^+ ions start flowing. As the value of I_{Na} increases the value of I_K also increases. Thus I_K is dependent on I_{Na}.

The relations between I_{Na} and I_K are their response to a step are very much similar to base and collector current of P - N - P transistor in common emitter configuration. This idea was first suggested by Weid.

DISTRIBUTION OF INJECTED CHARGE :

Assuming, that before the step pulse is applied, the charge existing along membrane is very small or essentially zero. At $t = 0$ let a step voltage ΔV is applied through an electrode in axoplasm. This step voltage forces ions from extracellular solution to enter into membrane toward interstial fluid. Because of this P (0^+) ions step to an appropriate constant value under transient condition. So equation can be reduced to

$$\frac{\partial p}{\partial t} - D_p \frac{\partial^2 p}{\partial x^2} = - \frac{p - p_{\infty}}{\tau_p} \qquad \ldots\ldots(4.1.1)$$

the boundary conditions are

$P(0^+,t) = P(0^+)$, which is constant and $P(W, t) = 0$ as the inside of membrane is negative with respect to outside. After $t = 0$ when all the transient are died away a steady state condition $P_{ss}(x)$ is reached which satisfies

$$D_p \frac{\partial^2 P_{ss}}{\partial x^2} = + \frac{P_{ss}}{\tau_p} \qquad \ldots\ldots(4.1.2)$$

Where τ_p is life time of injected ions in membrane. $P_{ss}(x)$ is an ion concentration at steady-state and is given by

$$P_{ss} = P(0^+) \frac{\text{Sin h}\left[\frac{W-X}{L_p}\right]}{\text{Sin h}\left[W/L_p\right]} \qquad \ldots\ldots(4.1.3)$$

which becomes

$$P_{ss}(X) \simeq P(0^+)\left(1 - \frac{X}{W}\right) \qquad \ldots\ldots(4.1.4)$$

$$L_p \gg W \qquad \ldots\ldots(4.1.5)$$

Where

L_p = diffusion length for ions

W = membrane thickness

The total solution $P(X, t)$ is made up of the steady state and transient solution. Equation (4.1.2) is solved by separation of variable technique and transient solution which is zero at boundaries

$$a_m \sin\left[\frac{mnx}{w}\right] e^{-t/\tau_m} \qquad \text{.....(4.1.6)}$$

a_m is arbitrary constant

$$\tau_m = \frac{P}{1+\left(\frac{mn\, L_p}{w}\right)^2} \qquad \text{.....(4.1.7)}$$

Then a general solution of equation (4.1.2) is

$$P(x,t) = (P(0^+)\ (1-\frac{x}{w}) + \sum_{m=1}^{\infty} a_m \sin\left(\frac{m\pi x}{w}\right)e^{-t/\tau_m}$$

Usually $L_p \gg w$ so $\tau_m = \frac{w^2}{(mn)^2 D_p}$ .....(4.1.8)

Since $L_p^2 = D_p \times \tau_p$

The equation (4.1.8) is independent of τ_p and is related more to steady state transit time. This can roughly from an expression of ion density

$$J = q\ P\ V = -q\ D_p \frac{\partial P}{\partial x} = q\ D_p \times \frac{P(0^+)}{W} \qquad \text{.....(4.1.9)}$$

Where V = velocity ion in membrane

$$V(x) = \frac{D_p\ P\ (0^+)}{W_p} \qquad \text{.....(4.1.10)}$$

Integrating equation (4.1.10) gives sodium ion transit time as

$$t_r = \frac{W^2}{2\ D_p} \qquad \text{.....(4.1.11)}$$

Find solution of equation (4.1.11) is obtained by using initial condition

$$P(X,0) = 0 \qquad \text{for } 0, < X < W$$

This gives co-efficient of a_m in Fourier series of equation (4.1.7), the solution is

$$P(x,t) = P(0^+)\left(1-\frac{x}{w}\right)+2P(0^+)\sum_{m=1}^{\infty}\frac{1}{m\pi}\sin\frac{m\pi x}{w}\, e^{-t/\tau_m}$$

Using data of squid nerve, curves for $P(x,t)$, $\left.\frac{dP}{dx}\right|_{x=w}$ and

$P(x,t)\,dx$ were plotted. These curves gives an idea about the sodium ions in the membrane with time and distance for step voltage excitation.

4.2 ELECTRICAL R-C MODEL :

Now proceeding to investigate the axon in R.C. cable. Fig. No 18 Let applied voltage v and i at any point are the function of both t and distance x. Using capital letters V & I as the point function of both freq. $S = jw = j2nf$ and distance x along cable. If R & C is distributed resistance and capacitance over the line then

$$\Delta V = -IR\,\Delta x \text{ or } \frac{\Delta V}{\Delta x} = -IR \qquad \ldots\ldots(4.2.1)$$

Similarly current loss through shunt capacitance is C.

So $\Delta I = -S\,VC\,\Delta x$

$$\frac{\Delta I}{\Delta x} = -SVC \qquad \ldots\ldots(4.2.2)$$

Eliminate I from both the equation

$$\frac{\partial^2 V}{\partial x^2} = SRCV$$

So the general solution becomes

$$V = C_1 e^{\sqrt{SRC}\,x} + C_2 e^{-\sqrt{SRC}\,x}$$

at $x = \infty$ $\quad V = 0$ $\quad$ So $C_1 = 0$

at $x = 0$ $\quad V = V_{in}$ $\quad C_2 = V_{in}$

This equation becomes

$$V = V_{in} e^{-\sqrt{SRC}\,x} \qquad .....(4.2.3)$$

Now question arises that what should be used for input voltage V_{in}? Studying its action potential which has 2 m sec wide spike. So choosing V_{in} as unit impu which is approx. equivalent to actual spike.

So

$V_{in} = 1$ in Laplace form

So $\quad V = e^{-\sqrt{SRC}\,x} \qquad .....(4.2.4)$

Since $\sqrt{+j} = \text{Cos } \frac{1}{2} \frac{\pi}{2} + j \text{ Sin } \frac{1}{2} \cdot \frac{\pi}{2}$

So $\quad |V(w)| = e^{-\sqrt{wRC}} \text{ x Cos } [\pi/4]$

Magnitude is one at $x = 0$, in agreement with unit impulse and decrease as rapidly as a increases.

Taking Laplace inverse we get (from Laplace Tables)

$$v = \frac{x}{2t} \sqrt{\frac{RC}{\pi t}}\, e^{-x^2 RC/4t} \qquad .....(4.2.5)$$

We can check this answer by using definate integral

$$F(S) = \int_{0}^{\infty} f(t)\, e^{-st}\, dt$$

$$= \int_{0}^{\infty} \frac{1}{t\sqrt{t}}\, e^{-St - \left(\frac{\alpha^2}{4t}\right)}\, dt = \frac{2\sqrt{\pi}}{\alpha}\, e^{-\alpha\sqrt{S}}$$

This describes a wave shape whose width is proportional to x^2 and height is proportional to $x^{\frac{1}{2}}$. It turns out that

$$t = \frac{x^2\, RC\, tv}{4} \qquad \text{and}$$

$$v = \frac{4\, v_n}{x^2\, RC}$$

Where t_n and v_n are normalized time & voltage value

$$\text{Se}\quad V_n = \frac{1}{t_n \sqrt{\pi\, t_n}}\, e^{-1/t_n}$$

The normalized equation is convenient because it is independent of distance. So wave shape is shown in Fig. 19

The area under the curve is unity, after differentiate the equation (4·2·5) w.r.t. $K = \frac{1}{t}$ that peak occurs at time

$$t_p = \frac{x^2\, RC}{6} \qquad \text{or}$$

which corresponds to $t_n = 0.6667$.

This means that x = 2 the width of the impulse response is four times that at x = 1, whereas the height become one fourth as great. It means as x increases, there is rapid attentuation of high frequencies and peak amplitudes. This Axon is useless as a transmitter of a pulse if amplitude of propagating signal. FIG. NO: 19

4.3 R.L.C. MODEL :

The neuron section is thus assumed to have uniform series resistance and inductance and shunt capacitance. FIG NO: 20

Once more considering the drop in voltage and current over a length of Z at a distance Z from the source of excitation, there are

$$-\partial v = (Ri + L \frac{\partial i}{\partial t}) \partial Z \qquad \ldots\ldots(4.3.1)$$

$$-\partial I = C \frac{\partial v}{\partial t} \partial Z \qquad \ldots\ldots(4.3.2)$$

Where R, L and C are parameters per unit length.

From (4.3.1) and (4.3.2)

$$\frac{\partial^2 v}{\partial z^2} = -R \frac{\partial i}{\partial Z} - L \frac{\partial i}{\partial Z \partial t}$$

$$= RC \frac{\partial v}{\partial t} + LC \frac{\partial^2 v}{\partial t^2} \qquad \ldots\ldots(4.3.3)$$

There is no standard form of solution of (4.3.3). Hence a substitution $v = e^{-at} y$ is made in order to simplify this. "a" has been chosen as R/2L because the decrement factor of a lumped R-L-C circuit is $e^{-\frac{R}{2L} t}$

Thus

$$\frac{\partial^2 y}{\partial z^2} = e^{-\frac{R}{2L}t} \frac{\partial^2 y}{\partial z^2}$$

$$\frac{\partial y}{\partial t} = e^{-\frac{R}{2L}t} \left[\frac{\partial y}{\partial t} - \frac{R}{2L} y\right]$$

$$\frac{\partial^2 y}{\partial t^2} = e^{-\frac{R}{2L}t} \left[\frac{\partial^2 y}{\partial t^2} - \frac{R}{L} \frac{\partial y}{\partial t} + \frac{R^2}{2L} y\right]$$

Substituting these in equation (4.3.3), there is,

$$\frac{\partial^2 y}{\partial x^2} = L C \frac{\partial^2 y}{\partial t^2} - \frac{R^2 c}{4 L} y$$

Putting $\gamma^2 = \frac{1}{L c}$, there is,

$$\frac{\partial^2 y}{\partial z^2} = \frac{1}{\gamma^2} \frac{\partial^2 y}{\partial t^2} y - \frac{a^2}{\gamma^2} y \quad \ldots\ldots(4.3.4)$$

This γ may be defined as phase velocity.

Again (4.3.4) is not a standard equation and the independent variable is transformed to obtain a differential equation in terms of one variable only. Several transformations are tried and the one which gives the desired result is shown below.

x is put as $x = a \sqrt{t^2 - \frac{z^2}{\gamma^2}}$

Thus $\frac{\partial y}{\partial z} = \frac{dy}{dx} \cdot \frac{\partial x}{\partial z}$

or $\frac{\partial^2 y}{\partial z^2} = \frac{d^2 y}{dx^2} \left(\frac{\partial x}{\partial z} \right)^2 + \frac{dy}{dx} \frac{\partial^2 x}{\partial z^2}$ .....(4.3.5)

Similarly, $\frac{\partial^2 y}{\partial t^2} = \frac{d^2 y}{dx^2} \left(\frac{\partial x}{\partial t} \right)^2 + \frac{dy}{dx} \frac{\partial^2 x}{\partial t^2}$ ....(4.3.

Now $\frac{\partial x}{\partial z} = a \frac{1}{2} \left(t^2 - \frac{z^2}{\gamma^2}\right)^{-\frac{1}{2}} x \cdot - \frac{2z}{\gamma^2}$

$$= -a \frac{z}{\gamma^2 \left(t^2 - \frac{z^2}{\gamma^2}\right)^{\frac{1}{2}}} \qquad \text{.....(4.3.7)}$$

$$\frac{\partial^2 x}{\partial z^2} = - \frac{a}{\gamma^2} \frac{\left(t^2 - \frac{z^2}{\gamma^2}\right)^{\frac{1}{2}} - z \frac{1}{2} \left(t^2 - \frac{z^2}{\gamma^2}\right)^{-\frac{1}{2}} x - \frac{2z}{\gamma^2}}{\left(t^2 - \frac{z^2}{\gamma^2}\right)}$$

$$= - \frac{a}{\gamma^2} \frac{t^2}{\left(t^2 - \frac{z^2}{\gamma^2}\right)^{3/2}} \qquad \text{.....(4.3.8)}$$

$$\frac{\partial x}{\partial t} = a \frac{1}{2} \left(t^2 - \frac{z^2}{\gamma^2}\right)^{-\frac{1}{2}} 2t$$

$$= \frac{a t}{\left(t^2 - \frac{z^2}{\gamma^2}\right)^{\frac{1}{2}}} \qquad \text{.....(4.3.9)}$$

$$\frac{\partial^2 x}{\partial t^2} = a \frac{\left(t^2 - \frac{z^2}{\gamma^2}\right)^{\frac{1}{2}} - t \frac{1}{2} \left(t^2 - \frac{z^2}{\gamma^2}\right)^{-\frac{1}{2}} 2t}{\left(t^2 - \frac{z^2}{\gamma^2}\right)}$$

$$= a \frac{e^{-\frac{z^2}{\gamma^2}}}{(t^2 - \frac{z^2}{\gamma^2})^{3/2}} \qquad \ldots\ldots(4.3.10)$$

Putting the expressions (4.3.5) to (4.3.40) in (4.3.4) and simplifying, there is,

$$\frac{d^2 y}{dx^2} + \frac{1}{x} \times \frac{dy}{dx} - y = 0 \qquad \ldots\ldots(4.3.11)$$

The above equation is modified Bessel's function of order zero and the solution is,

$$y = A\, I_o(x) + B\, K_o(x) \qquad \ldots\ldots(4.3.12)$$

Assuming a pulse function (rather than an impulse function) as excitation, it may be noted that is not ~~zero~~ infinity even at $t=0, z=0$. Hence B in eq. (4.3.12) must be zero since $K_o(x)$ has logarithmic singularity at the origin.

Thus,

$$v = A\, e^{-at}\, I_o \left(a \Big/ (t^2 - \frac{z^2}{\gamma^2}) \right) \qquad \ldots\ldots(4.3.13)$$

This model is claimed to be superior than R - C model because :

i) the actual phenomenon is considered.

ii) the realistic wave form may be considered.

If the input is a pulse of magnitude V_{in} and of duration T, then the input may be written as,

$$\text{Excitation} = V_{in} = u(t) - u(t - T)$$

Considering the first step function, the solution is,

$$v = A\, e^{-at}\, I_o \left(a \sqrt{(t^2 - \frac{z^2}{\gamma^2})} \right)$$

Now $v = V_{in}$ at $t = 0$, $z = 0$

Hence $A = V_{in}$ as $I_o(0) = 1$

Thus for the first step function which is valid in the region $0 \leq t \leq T$, the solution is,

$$V = V_{in}\, e^{-at}\, I_o \left(a \sqrt{(t^2 - \frac{z^2}{\gamma^2})} \right) \qquad \ldots\ldots(4.3.14)$$

In the range $T \leq t \leq 0$, the response of second step is added.

Hence $$V = V_{in}\, e^{-at}\, I_o\left(a\sqrt{t^2 - \frac{z^2}{\gamma^2}}\right) - e^{-a(t-T)}\, I_o\left(a\sqrt{(t-T)^2 - \frac{z^2}{\gamma^2}}\right)$$

$\ldots\ldots(4.3.15)$

Considering the response due to a step function (4.3.14) the following points are observed :-

(i) At a fixed value of z, the two factors have opposing effects with increase in time t because e^{-at} decreases with t,

and $I_o \left(a \sqrt{(t^2 - \frac{z^2}{\gamma^2})}\right)$ increases with t. However the steady state value is zero as $I_o(\zeta) \rightarrow \frac{e^{\zeta}}{\sqrt{2\pi\zeta}}$ for $S \rightarrow \infty$

Thus

$$e^{-at} I_o \left(a \sqrt{t^2 - \frac{z^2}{2}} \right) = \lim_{t \to \infty} e^{-at} \times \frac{e^{at}}{\sqrt{2\ at}}$$

$$= 0$$

(ii) At a definite time t_1, the signal decreases with increase in distance, because the modulus of I_o decreases with increase in z. When $\frac{z}{\gamma} = t_1$, the magnitude is unity (Say). For values of z larger than t_1, the function I_o is changed to T_o

$\left(a \sqrt{\left(\frac{z^2}{\gamma 2} - t^2\right)}\right.$ and the magnitude is somewhat damped oscillatory with maximum amplitude unity at origin. Thus at very large distances, the signal vanishes in the absence of regeneration.

4.4 IONIC TRANSISTOR MODEL :

When a step voltage (ΔV) (greater than threshold) is applied, ionic current start flowing. First sodium current starts flowing into the membrane from interstitial fluid and after certain time the pottassium current starts flowing out of membrane. Besides this there is also a current due to some other ions present in solutions, such as clorine etc. This is denoted by I_L

So sum of currents is

$$I = I_K + I_{Na} + I_L \qquad \ldots\ldots(4.4.1)$$

$$\frac{d V_m}{dt} = \frac{1}{C_m} (I_K + I_{Na} + I_L) \qquad \ldots\ldots(4.4.2)$$

Assuming here both liquid membrane junctions are included to form an ionic transistor. There are two junctions exists between external solution and membrane and second junction between intracellular fluid and membrane. The two ionic solutions are regarded as p-type semi-conductor materials and membrane as n-type semi-conductor. The ionic transistor is taken, as equivalent to P-N-P semi-conductor transistor in structure. The potential inside the nerve is negative w.r.t. outside under resnt condition, the inner junction is taken as reverse biased and outer junction is taken as forwarded biased. Thus nerve is taken in model form equivalent to P-N-P semi-conductor transistor equivalent model. The ions in nerve axon are like holes in transistor, these ions follows same physical principles.

Amplification factor β_R can be defined in terms of ionic current as the ratio of the change in K^+ current to change in sodium currents, while keeping inside potential constant.

$$\beta_R = \frac{\partial I_K}{\partial I_{Na}}$$

When there is no I_{Na}, then β_R reduces to zero. Since membrane is permeable to only K^+ ions in steady-state, current due to K^+ flow across the membrane.

In absence of electric field, the expression for β_γ can be obtained by solving ion flow continuity equations. In

absence of electric-field, diffusion current dominates and ions injected are also negligible. Under these conditions parameters such as conductivity, mobility, diffusion constant of ions, life time ions are independent of carrier injected.

The continuity equation is given by

$$\frac{\partial P}{\partial t} = - \frac{P - P_{\infty}}{\tau_p} + D_p \nabla^2 p \qquad \ldots\ldots(4.4.3)$$

For steady state

$$D_p \nabla^2 p - \frac{P - P_{\infty}}{\tau_p} = 0$$

For one dimensional case, solving for p(x) and substituting following equations

$$I_{Na} = - q D_p \frac{dP}{dx} \Big/_{x = 0} \qquad \ldots\ldots(4.4.4)$$

$$I_K = - q D_p \alpha \frac{dP}{dx} \Big/_{x=w} \qquad \ldots\ldots(4.4.5)$$

Ratio of I_K to I_{Na} will give amplification factor β_N

EVALUATION OF β_N IN THE PRESENCE OF FIELD :

Various ionic currents flow are shown in Fig. 13 which constitute of

$I_p = N_a^+$ current due entering of N_a^+ ions from interstitial fluid to membrane.

I_m = Injected ions are stored in membrane and they do change with time during transient operation. This current constitutes a surface or volume recombination current.

I_{Ee} = An anion current from membrane region to interstitial fluid. Anions are negligible compared to cations.

Field due to stored charged ionsis developed, under high level of injection. This cause a change in the membrane conductivity.

$$I_m = I_R + I_{Ee} \qquad \text{.....(4.4.6)}$$

$$\frac{\partial I_m}{\partial I_p} = \frac{1}{\beta_N} = \frac{\partial I_R}{\partial I_p} + \frac{\partial I_{Ee}}{\partial I_p} \qquad \text{.....(4.4.7)}$$

I_R & I_{Ee} to be very small because the membrane resistivity is 10^8 tones higher than fluids surrounding it. The amplitude I_K produced is directly proportional to I_p . I_R can be written as combination of surface and volume current.

$$\frac{1}{\beta_N} = \frac{\partial I_{SR}}{\partial I_p} + \frac{\partial I_{VR}}{\partial I_p} + \frac{\partial I_E}{\partial I_p} \qquad \text{.....(4.4.8)}$$

Where SR & VR stands for surface and volume combination. The surface and volume combination current for semi-conductor transistor is given as

$$\frac{\partial I_{VR}}{\partial I_p} = \frac{\partial I_{VR}}{\partial I_p} = \frac{1}{2}\left(\frac{W}{L_p}\right)^2 \qquad \text{.....(4.4.9)}$$

$$\frac{\partial I_{SR}}{\partial I_p} = \frac{I_{SR}}{I_p} = \frac{SW\,A_S}{D_p A} \qquad \text{.....(4.4.10)}$$

$$\frac{\partial I_{EE}}{\partial I_p} = \frac{I_{Ee}}{I_p} = \frac{\sigma_b\, W}{\sigma_e L_e} \qquad \text{.....(4.4.11)}$$

W = thickness of membrane

L_b = diffusion length of Na ions in membrane $=(D_p \tau_p)^{\frac{1}{2}}$

D_p & $_p$ are their diffusion constant and life time.

σ_e = conductivity in interstitial solution.

σ_b = conductivity of membrane.

L_e = diffusion, length of anions in external solution.

S = surface combination velocity.

A = Area of membrane junction per unit length.

A_S = effective area for ion recombination at the interface between the membrane and external solution.

I_p = Inward Na ion current.

Area assumed for surface recombination of ions is nearly the same as area over which ions are entering the membrane. The surface recombination of ions take place along the membrane surface.

The surface recombination current is given by

$$I_{SR} + q\ S\ A_S\ \varphi \qquad \text{.....(4.4.12)}$$

Where

q = charge of ion

S = surface recombination velocity

P = density of ions present near surface.

Most of current is due to diffusion of ions through membrane

$$I_R = \frac{P\ A\ q\ D_p}{W} \qquad \text{.....(4.4.13)}$$

Solving $J_p = \frac{I_p}{A} = - q D_p \text{ grad } P$

Using equation (4.4.12) and (4.4.14)

$$\frac{d I_{SR}}{d I_p} = \frac{S W A_s}{D_p A}$$

The presence of field affects the surface and volume recombination. This field is due to excess of ion density due to high injection. At high currents the diffusion constant of ions through membrane increases and ion lost due to surface and volume recombination, are reduced. The expressions of surface recombination, and volume recombination in presence of field reduces to

$$\frac{\partial I_{SR}}{\partial I_p} = \frac{WS}{D_p} g(Z) \qquad \ldots\ldots (4.4.16)$$

Where

$$g(Z) = \frac{1 + P/N_D}{1 + 2P/N_D} \qquad \ldots\ldots (4.4.17)$$

and $$\frac{\partial I_{VR}}{\partial I_p} = \frac{1}{2} \left(\frac{W}{L_b} \right)^2 (1 + Z) \qquad \ldots\ldots (4.4.18)$$

Where $$Z = \frac{I_p W \mu}{D_p A}$$

Substituting these values in the equation No.(4.4.7) the expression for amplification factor, in the presence of field is given by

$$\frac{1}{\beta_N} = \frac{SW}{D_p} g(Z) + \left[\frac{\tau_b W}{\tau_e L_e} + \frac{1}{2} \left(\frac{W}{L_b} \right)^2 \right] \times (1+Z) \qquad \ldots\ldots 4.4.18)$$

This equation relates the nerve response to physical quantities of nerve axon.

β_N of squid-nerve-axon is obtained by using following data

$W = 50 \times 10^{-18} A^0$ $\mu = 10^{-8}$ cm^2/volt-sec $D_p = 10^{-8}$ cm^2/sec.

$\sigma_b = \frac{1}{1.4 \times 10^9}$ mhos $\sigma_e = \frac{1}{22}$ ohms.

$S = 1 \times 10^{-5}$ to $= x\ 10^{-6}$ mm/cm.

For various values of surface recombination velocity and β_N a curve is plotted shown in Fig. no 15.

It is seen that if surface recombination increases, β_N decreases. So value of β_N or nerve response depends upon how many outer ions reach the inner junction. The transit time crossing the membrane depends upon (a) The number of cations (N_a^+) available in external solution (b) There speed of travelling (c) distance of travel (d) field built-up in membrane due to concentration gradient of density injected ions.

Equation of β. (4·4·10) suggests that it is independent of σ_e, the conductivity of inner solution. This fact was observed experimentally by Cole, which differs from the earlier theories based on ion concentration and potential.

Also it is clear from equation if the width W increases, $_N$ the nerve capability to conduct decreases. ^{B}ecause of increase in the surface and volume recombination increases.

As the conductivity of external solution (σ_e) is reduced (or reduction of N_a^+), the action potential decrease and further the capability of nerve to conduct is decreased, this fact was observed by *wei*.

The I_K starts after a certain delay, while the I_{Na} starts immediately. It is taken as transit time for N_a^+ through membrane. Once they reach inside, I_K starts. So this model does not give any idea about the delay in starting of potassium currents, because one dimensional theory is assumed.

APPLIFICATION FACTOR USING CHARGE - STORAGE MODEL :

In this estimation the cylindrical geometry of nerve, surface recombination of ions at membrane, a life-time of ions in membrane are included. The life time of charged carriers is not same in membrane and in storage charged membrane. To study it, the sodium and potassium ions and a step-voltage appears at junction between membrane and external solution as a forward bias. The continuity equation is applied under this fogward biased condition the carrier-injection into membrane.

$$\frac{\partial (P - P_\alpha)}{\partial t} = - \frac{P - P_\alpha}{\tau_p} + D_p \nabla^2 (P_o - P_\alpha) \quad \text{--- (4.9.19)}$$

Where P_o is injection ion, density in membrane and P_∞ is ion density in membrane at infinite time, D_p is diffusion constant of injected ions, and τ_p is bulk life-time of ions in membrane. Using Laplace technique, the density of injected ions in membrane is given by

$$q(\gamma,k) = \int_0^\infty e^{-st}(P_0 - P_\infty)\,dt \qquad (48)$$

Equation ( ) is reduced to modified Helmoltz partial differential equation -

$$\nabla^2 q(\gamma,k) - K^2 q(\gamma,k) = 0 \qquad \ldots\ldots\ldots (4.4.20)$$

Where

$$k^2 = (1 + s\tau_p)/L^2 \qquad (4.4.21)$$

$$L = \sqrt{D_p \tau_p} \qquad (4.4.22)$$

For finding distribution function $q(\gamma,k)$ following assumptions are made,

(i) ion-density at internal sol. boundry is Q

(ii) ion-density at injection side of membrane - solution boundary is constant, Q_0

(iii) At time $t = 0$, there is no N_a^+ & K^+ ions.

(iv) The surface recombination velocity is proportional to the ion-density of ion free membrane surface.

(v) Ion density in internal and external solution of membrane is in equilibrium.

(vi) Assuming that ion flow through pores. The radii of pores at internal and external membrane surface may be equal or large than other.

(vii) Ions diffuse through pores due to their concentration gradient at one side of membrane.

The Helmholtz equation for cylindrical co-ordinates, and for a symmetry in θ direction ($\frac{\partial}{\partial \theta} = 0$)

$$\frac{\partial^2 u}{\partial \gamma^2} + \frac{1}{\gamma}\frac{\partial u}{\partial \gamma} + \frac{\partial^2 u}{\partial Z^2} - k^2 u = 0 \qquad \text{..... (9.9.23)}$$

By using method of seperation of variable,

$$u = J_o(u\gamma)\ A \text{ Cosh } Z\sqrt{u^2+K^2} + B \text{ Sin h } Z\sqrt{u^2+K^2} \quad \text{.. (9.9.24)}$$

To evaluate constant A & B

At $Z = 0$ $\gamma = \gamma_o$ $Q = Q_o$

$Z = w$ $\gamma = \gamma_i$ $Q = Q_i$

The inward current is given by

$$I = q D_o \iint q(\gamma, k)\ dA \qquad \text{...(9.9.25)}$$

Where dA is the area of pore at outer-surface of membrane in interstitial solution. Substituting for $q(\gamma, k)$ and dA, equation (9.9.25) becomes

$$I = q D_p \int_0^{\theta} \int_0^{\gamma_o} \gamma J_o(u\gamma) \frac{\partial}{\partial Z} \left(A \text{ Cosh } Z\sqrt{u^2+K^2} + B \text{ Sin h } Z\sqrt{u^2+K^2}\right) d\gamma \qquad \text{..... (9.9.26)}$$

A Boundry condition are

$$I = I_{Na} \quad \text{at} \quad Z = 0 \quad \text{and} \quad \gamma = \gamma_o$$

$$I_{Na} = 2\pi q D_p \int_0^{\gamma_o} \gamma J_o(u\gamma)\ B\sqrt{u^2+K^2}\ d\gamma \qquad \text{..... (9.9.27)}$$

Similarly at $Z = w, \omega$ $\gamma = \gamma_i$ and $I = I_K$

$$I_K = 2\pi q D_p \int_0^{\gamma_2} \gamma J_o(u\gamma) \left[A \text{ Sinh } W\sqrt{u^2+K^2} + B \text{ Sinh } W\sqrt{u^2+K^2}\right] \cdot \sqrt{u^2+K^2}\ d\gamma \quad \text{.....}$$

For simplification take $\gamma = \gamma_1 = \gamma_o$ and $Q_1 = Q_o$

Then $B_r = \frac{I_K}{I_{Na}}$ we have

$$B_r = \frac{A \sin h\, W\sqrt{\mu^2+K^2} + B \cosh W \sqrt{\mu^2+K^2}}{B} \qquad \ldots\ldots (4.4.28)$$

On substituting the values of Constants A & B in above equation

$$B_r \simeq 1 \qquad \ldots\ldots (4.4.29)$$

For $\gamma_o \neq \gamma_1$ $B_r \neq 1$

if $\gamma_1 > o$ $B_r > 1$ $\qquad \ldots\ldots (4.4.30)$

It means I_K will be greater than I_{Na} for γ_1 pore diameter at inner surface of membrane is greater than pore diameter at outer-surface of membrane.

4.5 EVALUATION OF B_N &DE-LAY TIME OF K^+CURRENT

There is certain current I_m in the membrane due to surface and volume recombination of ion in membrane.

$$I_m = \frac{\bar{S}\, W}{D_p} I_{Na} + \tfrac{1}{2} \left(\frac{W}{L_p}\right)^2 I_{Na} \qquad \ldots\ldots (4.5.1)$$

Using equation (3.3.4),

$$I_m = I_{Na} \left[\frac{\bar{S}\, W K^2}{\left(S + \frac{1}{\tau_p}\right)} + \tfrac{1}{2} \left(\frac{W}{L_p}\right)^2\right] \qquad \ldots\ldots (4.5.2)$$

$$\frac{1}{B_N} = \frac{I_m}{I_K} = \left[\frac{\bar{S}\, W\, k^2}{\left(S + \frac{1}{\tau_p}\right)} + \tfrac{1}{2} \left(\frac{W}{L_p}\right)\right] \frac{I_{Na}}{I_K} \qquad \ldots\ldots (4.5.3)$$

Since $\frac{I_{Na}}{I_K} = 1$

$$\frac{1}{B_N} = \frac{S W k^2}{\left(S + \frac{1}{\tau_p} \right)} + \frac{1}{2} \left(\frac{W}{L_p} \right)^2 \qquad \text{.....(4.5.4)}$$

$$\therefore \quad B_N \Big/_{S=0} = 1 \Big/ \frac{S W}{L_p \frac{1}{\tau_p}} + \frac{1}{2} \frac{W^2}{L_p}$$

$$= \frac{L_p^2}{S W \tau_p + \frac{1}{2} W^2} \qquad \text{.....(4.5.5)}$$

For Squid $B_{No} \simeq 6$, Rearranging equation (3.3.17)

$$B_N = \frac{\frac{2 L_p}{W^2} \left(S + \frac{1}{\tau_p} \right)}{S + \frac{1}{\tau_p} + \frac{k^2 2 L_p S}{W}} \qquad \text{.....(4.5.6)}$$

I_K as a function of time is obtained by the use of Laplace inversion integral

$$i_k (t) = \sum_{\text{all poles}} \text{residue} \left(e^{St} I_K \right) \qquad \text{.....(4.5.7)}$$

$$i_k(t) = I_{Na} \sum_{\text{all poles}} \text{residue} \frac{e^{-St} \left[2 \frac{L_p^2}{W^2} \left(S + \frac{1}{\tau_p} \right) \right]}{S \left(S + \frac{1}{\tau_1} \right)}$$

.....(4.5.8)

Where $\tau_1 = \frac{\tau_p}{1 + \frac{2 S \tau_p}{W}}$

The dominated poles are located at S = 0 and

$S = -\frac{1}{T_1}$, to find the delay, poles near imaginary axis are considered. So

$$i_k(t) = \Delta i_{Na} \left[\frac{\tau_1}{\tau_p} + \left(1 - \frac{\tau_1}{\tau_p} \right) e^{-t/\tau_1} \right] \qquad \ldots\ldots(4.5.9)$$

Substituting $t = T_0$ and $i_F(t) = 0$, $i_k(t)$ crosses the time axis at time $t = T_D$, and is negative during $t = 0$ to $t = T_D$

$$\therefore \quad T_D = -T_1 \ln \left[\frac{\tau_p - \tau_1}{\tau_1} \right] \qquad \ldots\ldots(4.5.10)$$

T_D is the delay time of starting of potassium current.

CHAPTER - V

ELECTRONIC MODELS OF NEURON

5.1 INTRODUCTION

Electronic models can simulate continuous - variable - non-linear operation 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 achieved by other techniques. There are considerable advantage to direct observations of wave forms, phase relationship, modulation and time dependent interaction while stimuli and model parameters are changed. Such advantage to few interconnected units. For large networks, both observation and manipulation of parameters become very difficult.

Analog computers have advantages similar to those of electronic models, but tend to be slow and combersome. Both have the advantages over mathematical models that they do not tend to compel oversimplifications.

The storage capabilities and growing speed of digital computers carry great promise for flexible, realistic modelling. The large-network simulation are handled more readily by digital computation than other techniques. It seems likely that high-speed digital computers will ultimately provide one of the most satisfactory means for modelling of complex neural systems.

5.2 ANALOG SIMULATION OF NEURON :

Lewis gave a new approach to analog simulation and study of neuron is proposed. This approach is based on recent physiological evidence which indicates that the individual nerve cell is functionally much more complex than the classical view of synaptic region coupled directly to a spike or impulse-generating region.

The ultimate input to a synapse is an impulse or series of impulses which are originated in presynaptic neuron. These impulses are apparently transmitted intercellularly, inducing a change in the potential across the synaptic membrane of post synaptic neuron. While presynaptic potential has duration of 1 m sec, whereas postsynaptic potential has duration of 40 m sec. or more. Thus a single, sharp presynaptic spike induce a slowly varying, long lasting post-synaptic potential , which often called ballistic potential whereas formation of ballistic potential are not completely understood. In simulating the ballistic response it assumes three parameters; the rise time, fall time or decay time, and maximum amplitude. The requirement for independently-controllable rise and fall time implies the need for unilateral network. A simple RC Realization of a ballistic network is shown in Fig.No. 21.

The real functional power of many single neurons lies not in their ability to integrate many incoming spikes

not only from one axon but from many, and thus respond to group of series of spikes. It is known that a single neuron responds differently to different input frequencies, and it is quite possible that it can also differentiate between various pulse patterns. Two mechanism are thus important in this respect are facilitation and antifacilitation. In Fig. 22a the first impulse conditions the synapse in such a way as to enhance or facilitate subsequent responses, Fig. 22.b the first spike reduces or antifacilitates the response. In Fig. 22 , where the second input spike is very close to the first so that antifacilitation is greater. The third spike occurs considerably later and its response is therefore not so greatly facilitated, but the response amplitude is still greater than basic amplitude.

In network Fig. 23 , the input pulse are simultaneously applied to base and collector circuits of the transistor. Prior to first pulse the voltage at collector is V_0. The first pulse thus elicits a positive going pulse of amplitude V_0 at the collector. This is applied to the output network and results in a bullistic potential whose amplitude is proportional to V_0. The first pulse also leaves a residual voltage in the collector-bias network which add to V_0. Depending on the component values in this network, the added bias may develop rapidly (in a few microseconds) or slowly (upto hundred millisecond); it cannot however, decay more rapidly than it develops. For such subsequent input pulse, the amplitude of positive pulse

applied to the network is $V_o + \triangle V(t)$ where $\triangle V(t)$ is residual-added collector - bias. The subsequent ballistic potential are proportional to $V_o + \triangle V(t)$. The rise and fall times for this ballistic potential are completely independent time constants of collector and bias network. The rise time of the added bias is determined by R_2 and C_2; the fall of time is determined by C_1 and C_2 in series with R_2. After first pulse the total collector bias V_C can be approximated by

$$V_C = V_{in} (1-e^{-t/\tau_1}) (e^{-t/\tau_2}) + V_o$$

Where V_{in} is amplitude of input pulse

$\tau_1 = R_2 C_2$ and $\tau_2 = R_3 (C_1 + C_2)$

In Fig. 24 , in the absence of an input pulse, the voltage at point 1, (V_1) is zero. During applied pulse, however, V_1 may be expressed

$$V_1 (V_{in} - V_{out}) e^{-t/\tau_1}$$

Where V_{in} is input pulse amplitude, V_C is residual voltage across C_1 and $\tau_1 = R_2 C_1$. Thus a positive pulse at the input results in a positive pulse at point (1) of amplitude V_1, where V_1 is proportional to V_{in} diminished by antifacilitating voltage V_{C1}. The time course of V_{C1} is thus the time course of antifacilitation and may be written

$$V_{C1} = V_1 \left(1 - e^{-t/\tau_1} \right) e^{-t/\tau_2}$$

Where $\tau_1 = R_2 C_1$ and $\tau_2 = R_1 C_1$

In the network τ_1 and τ_2 are varied independently of each other. Emitter follower can be used to isolate the final output from any moderate load. In complete soma analog the outputs from these networks will represent positive (in Ribitory) negative (excetatory) excursions in the soma-membrane potential, and will be applied either directly or through a loca-response locus to the spike initiator.

Many neurons exhibit after effect which can take any of several forms. An inhibited neurons exhibited neuron, for example, upon cessation of inhibiting stimulus may begin firing spontaneously, thus exhibiting a rebound or negative after effects. It may then cease firing and go into a state of subnormal, and in fact, it may oscillate back and forth between supernormal and sub-normal states for several cycles. Likewise, a neuron on cessation of prolonged excitation may go through a period of depressed excitability. While the origin of rebound phenomena is not well established, it may be represented by rebound in either in the synaptic or the over all some potential. The networks shown in Fig. 25 and Fig. 26 exhibit this type of behaviour and may be useful in simulating this type of synaptic or neural behaviour. Again the outputs from these networks will represent excursions in soma-membrane potential.

5.3 IONIC TRANSISTOR MODEL :

An equivalent circuit of transistor model is given in Fig. [27] [28] A voltage step is applied. The behaviour of ionic currents are studied by the method of Laplace transform technique. 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 solution and axoplasm. Part of the pte 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 reverse bias across the diode D_1 shown in Fig. (27), the membrane capacitance C_M discharges through the diode D_1 with time constant equivalent to

$$\frac{\gamma_b\ (\gamma_b + \gamma_e)}{\gamma_b + \gamma_b + \gamma_e}\ C_M$$

Once capacitance C_M is discharged it starts getting charged up with time constant of $(R_c + R_b)\ C_M$. 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 pottasium currents are obtained.

Applying a Laplace transform for the step voltage excitation, and writing loop equation for mesh one and two in Fig. 28 , the expression for sodium and pottasium currents can be obtained. It is seen that step voltage excitation is applied between intracellular and extracellular 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 is given as

$$T_{Na} = \frac{\gamma_b\ (\gamma_b + \gamma_e)\ C}{(2\gamma_b + \gamma_e)\ \left[\ 1 - \frac{2\gamma_b \gamma_c\ \alpha_N}{2\gamma_b(\gamma_c + \gamma_e) + \gamma_e \gamma_c}\ \right]}$$

and similarly $T = T_K$ for the rise of pottassium currents by adjusting different parameter as R_c, R_b and R_e the different shapes of the wave form can be obtained required for the action potential. It is also satisfying the steady state conditions.

5.4 MODEL BASED ON DOUBLE ENERGY STORAGE ELEMENT SYSTEMS:

Many circuit containing two energy storage elements have poles seperated widely enough so that the transient response can be approximated by treating them as two isolated single-energy circuits. Of course there must be continuity across the boundary between two individual response curve and they must satisfy the original system.

In effecting the separation of the system response into two time regions, we shall have to depend upon the physical characteristics of energy storage elements for clues as to the permissible approximations. FIG No: 29 a.

Considering the application of a voltage step of height V_1. The output is constrained in its time rate of rise primarily by C_g. From the circuit that the full charging current of C_g to-gether with any current through R_g must also flow just after the excitation is applied is essentially determined by uncharged gate input capacity C_g. The same charge is accumulated in C_c. Since $C_c \gg C_g$, the voltage across C_g will change slightly while C_c charges fully. Thus coupling capacitor can be assumed to be short circuited during this entire interval and the equivalent circuit is reduced to one containing a single-energy-storage element in Fig. 29 b.

The final steady-state output and the circuit time constant are found by taking thevnin theorem equivalent across C_g. Then are

$$V_{ss_1} = \frac{(R_L \,/\!/\, R_0)}{(R_s + R_L \,/\!/\, R_0)} V_1 \qquad (5.4.1)$$

$$\tau_1 = \frac{C_0}{(R_0 \,/\!/\, R_L \,/\!/\, R_s)} \qquad \ldots\ldots (5.4.2)$$

We are now in a position to write the equations defining the initial portion of output response

$$V_{o1} = V_{ss_1} \left(1 - e^{-t/\tau_1} \right) \qquad \ldots\ldots (5.4.3)$$

In four time constants, the output rise to 98% of the steady state value of V_{ss_1} and initial rise may be assumed complete.

During this whole interval, C_C is charging, even though it is doing so very slowly. The relatively large current required (because of the large value of C_C) will control the output voltage and swamp any contribution from the discharge of C_0. We are justified in ignoring C_0 and in removing it from the circuit. If the initial value of the output across R_0 upon the sudden excitation of the system is now calculated we also find it to be V_{ss1}.of As C_C discharges, the output delay toward zero, with new time constant.

$$\tau_2 = C_C \left(R_0 + R_L \,/\!/\, R_0 \right) \qquad \ldots\ldots (5.4.4)$$

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

$$v_o(t) = V_{ss_1} e^{-t/\tau_2} \qquad \text{.....} \quad (5.4.5)$$

The only question remaining unanswered is At what time decay will take over from initial rise? If we compare equation (5.4.3) and (5.4.5) we see that both the capacity and resistance term of τ_2 are much larger than τ_1 . Since decay time constant is so very much longer, error introduced by starting the decay any where in the vicinity of zero will be negligible.

5.5 MODEL BASED ON HIGH PASS-LOW PASS NETWORK :

Spike potential can be obtained by interconnecting two high pass and low pass networks, to melt the required experimental results. The combination of one low-pass and one high pass network is shown in Fig. 31 . We shall assume that successive network do not interact i.e. do not load each other. The transient response can be approximated by treating them as two isolated single-energy units. The response can be seperated into two regions, both the regions, both the region depends upon the individual characteristics of energy storage element, assuming that successive network do not interact.

In first energy-storage unit, an excessively rapid rise depends upon the rate of charging of C. Capacitor charges to the d.c. level of input with circuit time constant, and output shift accordingly. The solution of equation in general form

$$\tau \frac{du}{dt} + v = 0 \qquad \ldots\ldots(5.5.1)$$

$$V(t) = V_0 \; e^{-t/T} + V_\infty \left(1 - e^{-t/T_p} \right) \qquad \ldots\ldots(5.5.2)$$

The step transient is reduced to a rising curve, $V_0 = 0$ The final level V_∞ is same as of the input V_1. Hence equation (5.5.2) becomes

$$V_2(t) = V_1 \left(1 - e^{-t/\tau_1} \right) \qquad \ldots\ldots (5.5.3).$$

In second energy - storage unit, a series circuit have output proportional to derivative across the resistor. The major portion of the circuit voltage drop is developed across C, when the time constant are small. With a sufficient small time constants an exact output wave shape is reasonably close, except at discontinuities, assuming a perfect. The output has no dc component after infinite time $V_\infty = 0$.

From equation no. (5.5.1).

$$V_3(t) = V_2 \, e^{-t/\tau_2} \qquad \ldots\ldots(5.5.4)$$

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

$V_3(t)$ = output of second high pass network

$\tau_2 = R_2 C_2$ Time constant.

The equation (5.5.4) shows the characteristics of the exponential decay with time constant $R_2 C_2$. By changing the value of capacitor C_2 or R_2 , time constant can be varied. If τ_2 is high, than full will be sharp and with low value of τ_2, longer delay takes place. In this circuit, value of capacitance C_2 is varied, to get different decaying characteristic of the output wave form when step input is applied.

Battery V_m is used to have steady-state conditions. The membrane resting potential for squid axon is 61 mV, Frog Axon is 86 mV and for Purkinjee fibre of mamlian is 90 mV.

Block diagram of neuron is shown in Fig.No. 30 It consists of thershold unit and pulse generating unit.

A step input is applied to any of four input terminals. This input is differentiated with R = 22 K and C = .02 μF. This differentiated wave works as input to threshold unit, consisting of limiting circuit. In this Diode D_1 is connected in forward bias, and the threshold value for wave can be adjusted from the battery V_T connected. If the differentiater output is sufficient or greater than V_T, the diode will be in forward bias, then this differentiated pulse can pass through the diode and capacitor of 10 μ F to trigger the next unit. By varying the Battery voltage V_T a particular voltage level can be set for input differentiated pulse, i.e. if input is greater than V_T voltage V_T, then this pulse trigger the unit. If input differentiated pulse amplitude is smaller than the battery voltage V_T, then the diode would not conduct. The battery voltage V_T in the circuits works as threshold unit.

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

Photographs attached, shows the output wave forms of fabricated unit at different time constants. For these wave shape, scaling has been done to satisfy required condition. The vertical division is 0.5 volt/div.

CHAPTER - VI

DISCUSSION AND CONCLUSION

Neural modelling has proven valuable in neurophysiology. In review we have studied different models have fulfilled one or more of these goals, contributing concrete knowledge to neurophysiology. Neural models are playing an important role in complementing direct neurophysiological investigation while their accomplishments have been substantial.

Electronic models have been proposed for nerve membrane and ionic theory is used to study the nerve fiber membrane. The study of nerve using electronic models has given much more insight mechanism and structure. Electronic models can simulate continuous variable non-linear operation accurately and economically. Providing real time signals that may be observed while experimental conditions are manipulated, they permit rapid and effective kind of observer-model interaction which can not be achieved by other technique.

The ionic studies help to understand the behaviour of nerve in excitable state. The purpose of modelling was to come to some conclusion that how the nerves behave under transient and steady state condition. The proposed model satisfying the steady state and transient state condition

when it treggered with a pulse. In proposed model the spike potential can be obtained of different wave shapes, the rise and retarding time constant can be varied to get the wave shape of with required Amplitude and time constant. This models give the variation sodium current flowing the membrane but does not give idea about the potassium currents. In electronic modelling, it is restricted to the models of fixed properties of membranes, single units and relatively small networks. There has been no attempt to include models of information storage, i.e. analog of memory, learning, delay time in starting of potassium current. This delay time in starting a potassium current is obtained by using ionic theory, and continuity equation which is solved with proper boundry conditions. It is in the order of 1000 sec.

To study the nerve, a charge-storage model for characterizing the transient behaviour of nerve is taken. Cylindrical geometry of nerve, surface recombination of ions at a membrane surface and life time ions are included. The built-in voltage which is a cause of negative resistance in V-I. Characteristics of membrane is estimated for different membrane voltage. A poisson(s equation is solved to obtain the widths of ionic and counter ionic regions. Various ionic current which flow across the membrane are used to calculate the amplification factor.

There are many questions that still remain open such as generation of inhibitory impulse, interaction of neurons, summation of information, the effect temp., hydrostati c pressure, using ionic theory etc. The increasingly close liason of experimental and theoretical neurophysiology made possible by modelling present intriguing challenge of future.

TABLE - 1 - ELECTRICAL CONSTANTS OF EXCITABLE TISSUES

Tissue	Diameter in micron (μ)	Membrane Rest potential in mV	Length constant in C_j C_m	Membrane Sp.resistance R_m in Ω-Cm^2	Membrane capacitance f%/cm^2	Time constant Tm in milli.sec.	Sp.resistance R_i of intracellular solution Ω- Cm	R Specific resistance of extracellular Ω -Cm
Squid Axon	500	61	0.25	700	1.5	1.0	30	22
Carcinus Axon	30	82	0.21	6.710	1.35	9.0	60	-
Frog Axon	135	86	0.24	4.1	8.0	34.0	250	-
Purkinjee fibre of Mamlian	75	90	1.9	6.0 K	12.4	19.5	105	-
Sepia Axon	200	-	0.6	12.0 K	1.1	13.0	40	-
Lobster	75	-	2.5	2.0 K	1.3	2.0	60	22
Cryfish	100	-	2.8	3.1 K	0.61	1.9	94	-

APPENDIX I

Helmohltz equation for cylindrical co-ordinate and having symmetry in θ direction

$$\frac{\partial^2 u}{\partial r^2} + \frac{1}{r}\frac{\partial u}{\partial r} + \frac{\partial^2 u}{\partial Z^2} - k^2 u = 0 \qquad \ldots\ldots(1)$$

Using method of separation of variable

$$u = R(r)\ Z(z) \qquad \ldots\ldots(2)$$

$$Z\left(\frac{d^2R}{dr^2} + \frac{1}{r}\frac{dR}{dr}\right) + R\left(\frac{d^2Z}{dZ^2} - K^2 Z\right) = 0 \quad \ldots\ldots$$

$$\therefore \quad \frac{1}{R}\left(\frac{d^2R}{dr^2} + \frac{1}{r}\frac{dR}{dr}\right) = \frac{1}{Z}\left(-\frac{d^2Z}{dZ^2} + K^2 Z\right) = \text{Constant}$$

Let const $= -\mu^2$

$$\frac{d^2R}{dr^2} + \frac{1}{r}\frac{dR}{dr} + \mu^2 R = 0 \qquad \ldots\ldots(3)$$

Its solution is $R = J_0(\mu r)$

Where J_0 = Bessel function of zero order

and $Z = A \cosh Z\sqrt{\mu^2 + K^2} + B \sinh Z\sqrt{\mu^2 + K^2}$

$\therefore$ Complete solution is

$$= J_0(\mu r)\left[A \cosh Z\sqrt{\mu^2 + K^2} + B \sinh Z\sqrt{\mu^2 + K^2}\right]$$

APPENDIX II

$$(\gamma_b + \gamma_b)\, i_{na} + \gamma_e (i_{na} + I_{Na}) = 0 \qquad \ldots\ldots(1)$$

$$i_{Na} = - \frac{\gamma_e}{\gamma_b + \gamma_b + \gamma_c} I_{Na} \qquad \ldots\ldots(2)$$

From loop (2)

$$V_m + \alpha_b \gamma_c \; i_{Na} = \gamma_c (1-\alpha_b)\, i_{Na} + \gamma_e (i_{Na} + I_{Na})$$

Where

$$\alpha_b = \frac{\alpha_n \; w_N}{S + w_N}$$

α_n = current gain at zero freq.

w_n = time constant or cutt-off freq.

Rearranging equation no.(3)

$$\frac{V_m}{I_{Na}} = \gamma_c (1 - \alpha_b) + \gamma_e \left[1 + \frac{\gamma_c \gamma_b - \gamma_e}{\gamma_e + 2\gamma_b} \right]$$

The voltage transformer of a step excitation is

$$V_m (S) = \frac{\Delta V_m}{S}$$

or

$$I_{Na}(S) = \frac{\Delta V_m}{S\left[\gamma_c \left(1 - \frac{\alpha_N w_N}{S + w_N}\right) + \gamma_e \left(1 + \frac{(\gamma_c \alpha_N w_N/(S+w_N)] - \gamma_e}{2\gamma_b + \gamma_e}\right)\right]} \qquad \ldots\ldots(6)$$

$$= \frac{(2\gamma_b + \gamma_e)\, \Delta V_m \,(S + w_N)}{S\left[2\alpha_b(\gamma_c + \gamma_e) + \gamma_e \gamma_c\right]\left\{S + w_N - \frac{2\gamma_b \gamma_c \alpha_N w_N}{2\gamma_b(\gamma_c + \gamma_e) + \gamma_e \gamma_c}\right\}}$$

$$= \frac{B\,(S + w_N)}{S\,(S + A)}$$

Where

$$B = \frac{(2\gamma_b + \gamma_e)\,\Delta V_m}{2\gamma_b(\gamma_c + \gamma_e) + \gamma_e\gamma_c}$$

and

$$A = w_N - \frac{2\gamma_b\gamma_c\,\alpha_N\,w_N}{2\gamma_b(\gamma_c + \gamma_e) + \gamma_e\gamma_c}$$

Taking inverse of Laplace transform

$$I_{Na}(t) = \frac{B}{A}\,w_N + \frac{B}{A}\,(A - w_N)\,e^{-At}$$

$$I_{Na}(t) = B/A\ (A\,e^{-At})$$

Substituting for A & B and assuming $\alpha_N \simeq 1$ we get

$$I_{Na}(t) = \frac{\Delta V_m\,(2\gamma_b + \gamma_e)}{\gamma_e\,(2\gamma_b + \gamma_c)}\left\{1 - e^{-t/\tau}\right\} \qquad \ldots\ldots(8)$$

Where

$$\tau = \frac{1}{w_N - \dfrac{2\gamma_b\gamma_c\,\alpha_N\,w_N}{2\gamma_b(\gamma_c + \gamma_e) + \gamma_e\gamma_c}}$$

Putting $w = w_{Na} = \dfrac{(2\gamma_b + \gamma_e)}{\gamma_b\,(\gamma_b + \gamma_e)\,C}$ for rise of sodium current

and $\tau = \tau_{Na}$

$$\tau_{Na} = \frac{\gamma_b\,(\gamma_b + \gamma_e)\,C}{(2\gamma_b + \gamma_e)\left[1 - \dfrac{2\gamma_b\gamma_c\,\alpha_N}{2\gamma_b(\gamma_c + \gamma_e) + \gamma_e\gamma_c}\right]}$$

and similarly $T = T_K$ for rise of Pottassium current

Where

$$T_K = \frac{(\gamma_b + \gamma_c)\ C}{\left[1 - \frac{2\ \gamma_b\ \gamma_c\ \alpha_N}{2\ \gamma_b(\gamma_c + \gamma_e) + \gamma_e \gamma_c}\right]}$$

From equation No.(2)

$$i_{Na}(t) = \frac{e\ (2\gamma_b + \gamma_e)}{(2\gamma_b + \gamma_e)} \cdot \frac{\Delta V_m}{\gamma_e(2\gamma_b + \gamma_e)}\left[1 - e^{-t/T_{Na}}\right]$$

Similarly for rise of pottassium current we have

$$i_k(t) = \frac{\Delta V_m}{(2\gamma_b + \gamma_c)}\left[1 - e^{-t/T_k}\right]$$

The decay of sodium current is given by

$$i_{Na}(t)\ i_{Na}(t)\ \text{decay} = \frac{\Delta V_m}{(2\gamma_b + \gamma_e)} \times e^{-t/T_k}$$

— — ——

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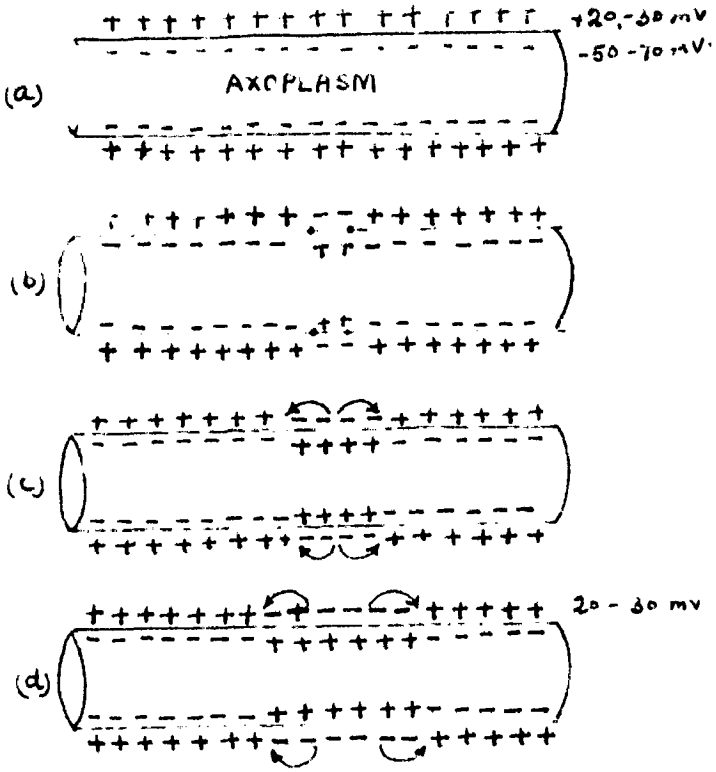
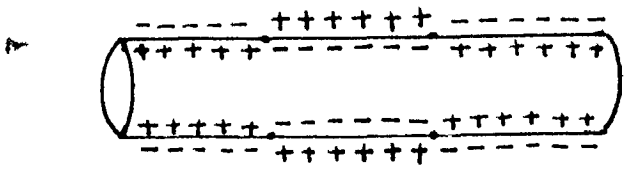


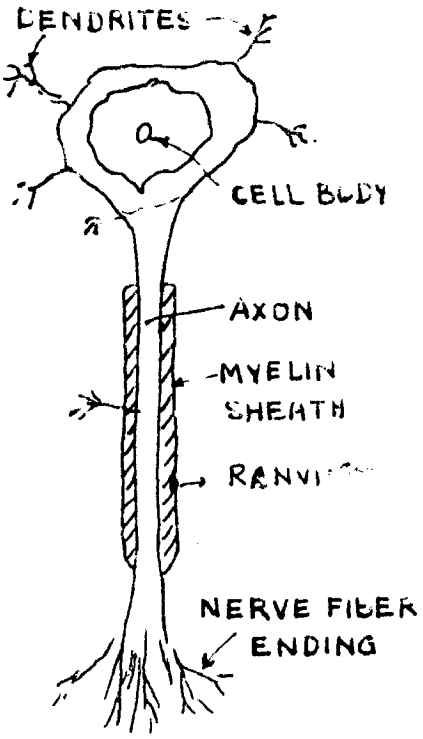
INTIATION AND SPREAD OF DEPOLARIZED WAVE

FIG NO: 2



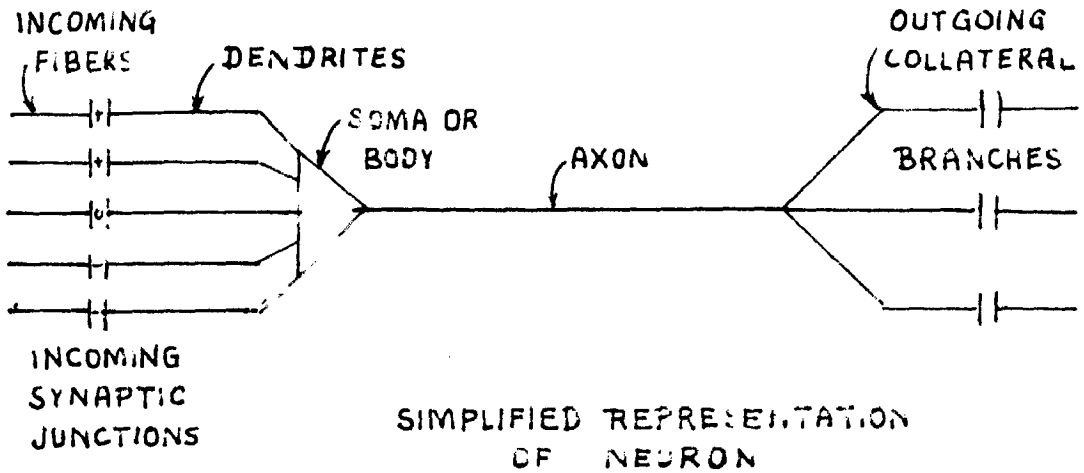
DEPOLARIZATION TO RETURN TO ORIGINAL STATUS

FIG NO: 3



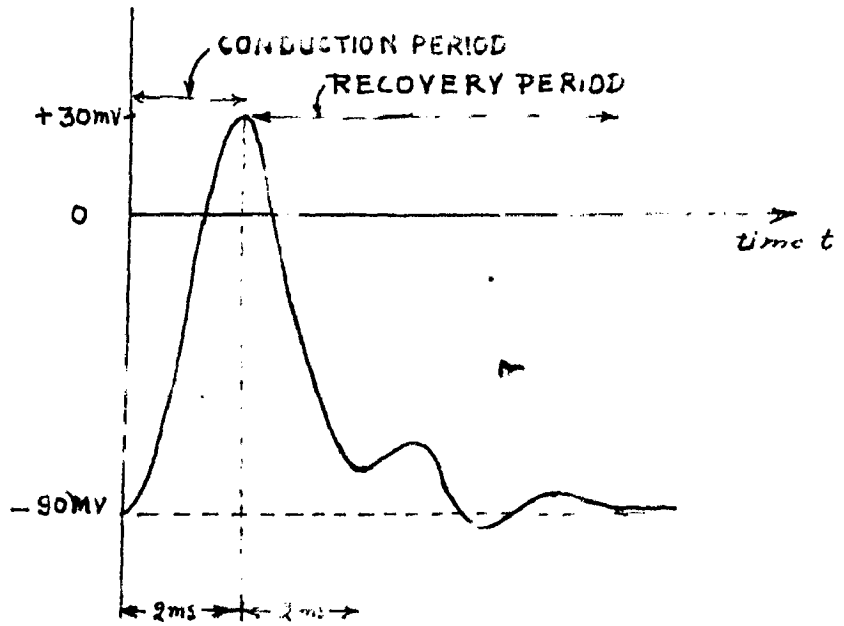
NEURON

FIG NO: 1



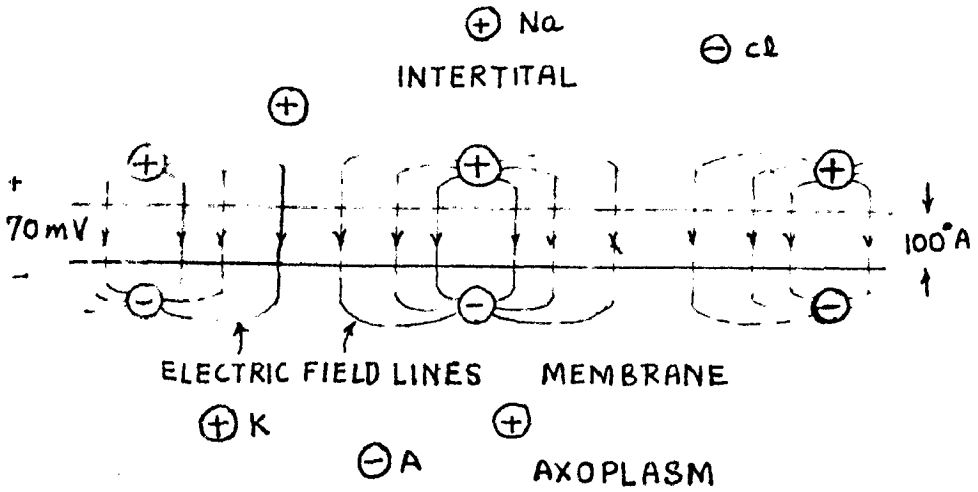
SIMPLIFIED REPRESENTATION
OF NEURON

FIG. NO: 4



SPIKE POTIENTIAL DURING CONDUCTION

FIG. NO: 5



UNMYELINATED FIBER AT REST

FIG. NO: 6

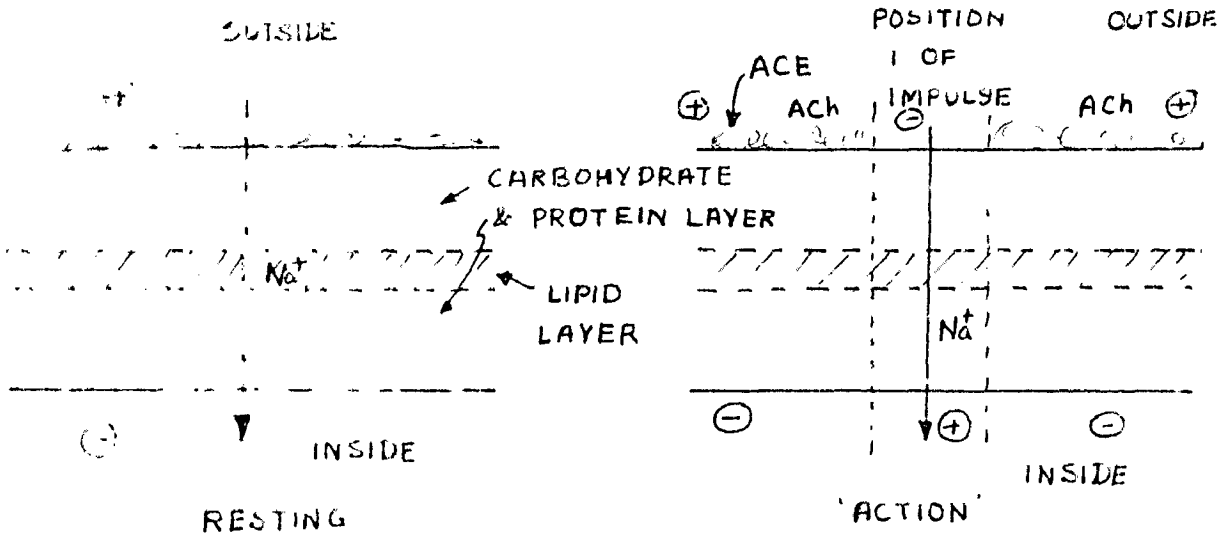
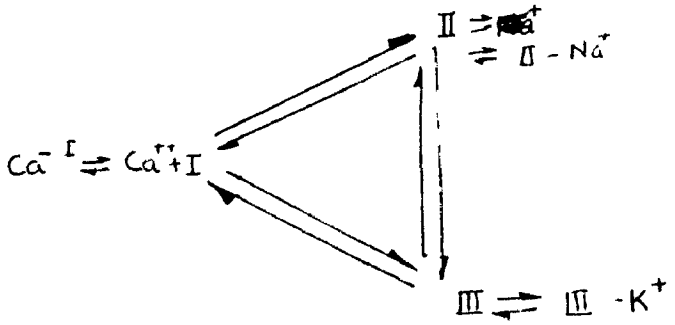
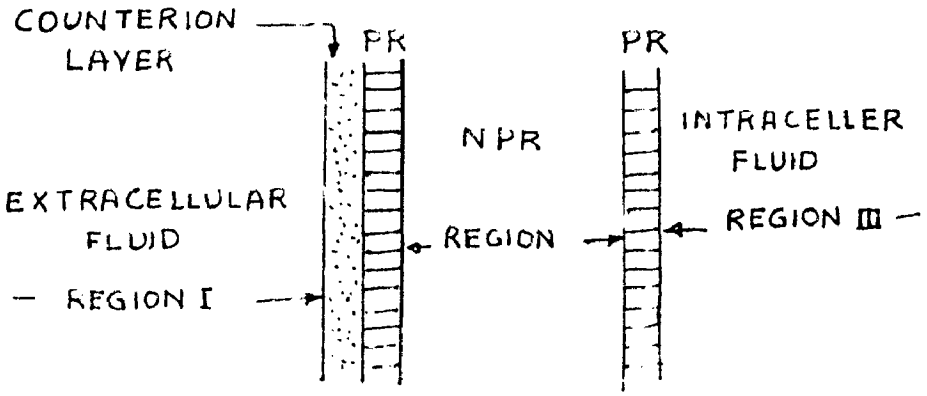


FIG. NO: 7



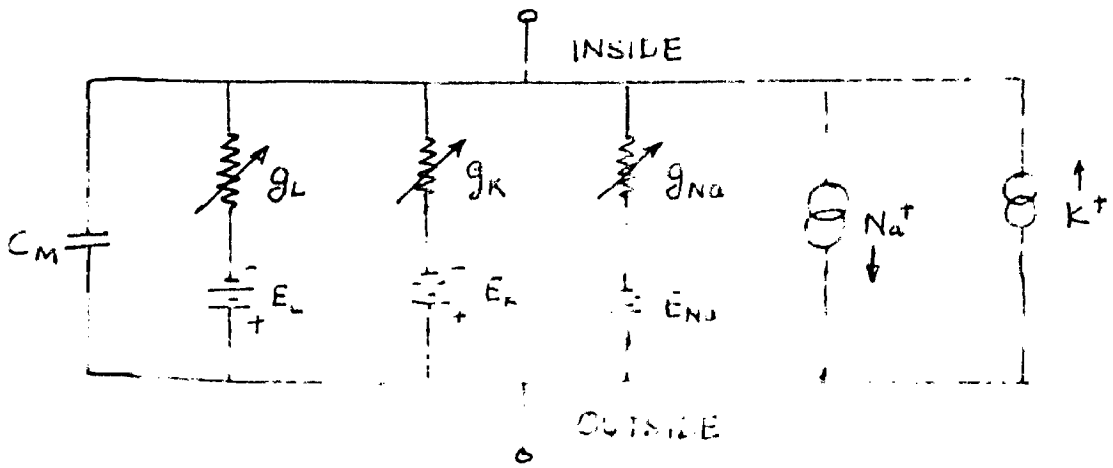
GOLDMAN'S CHEMICAL REACTION MODEL

FIG NO: 8



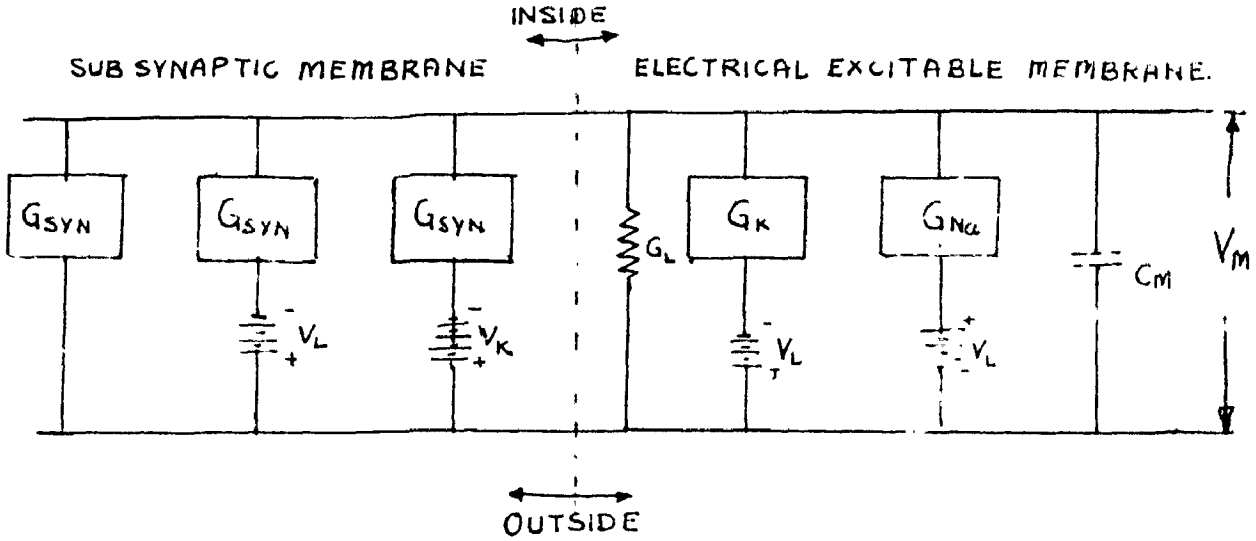
BENARD MODEL.

FIG.NO: 9

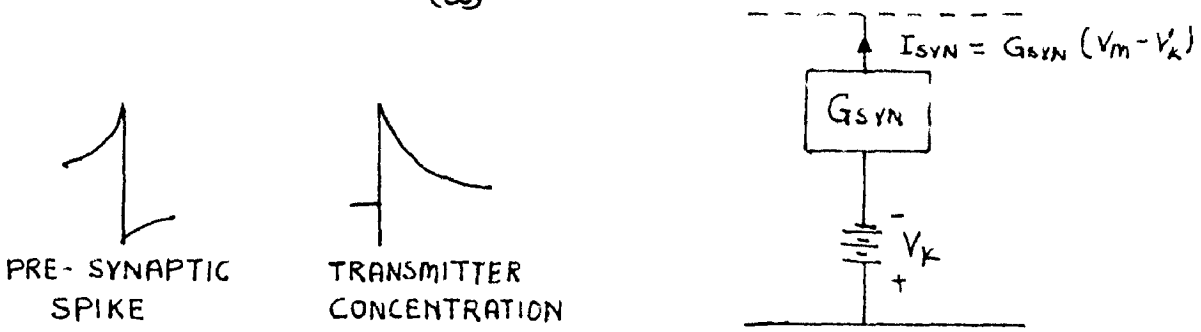


HODGKIN AND HUXLEY'S MODEL

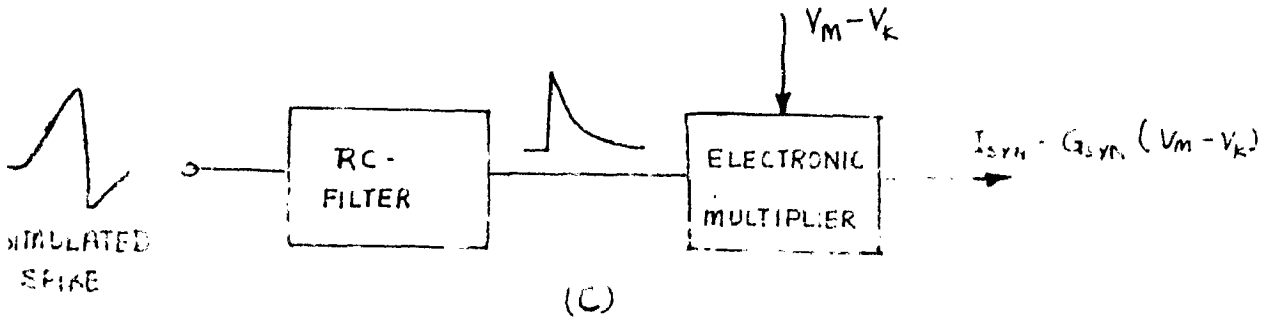
FIG. NO: 10



(a)



(b)



(C)

BLOCK DIAGRAM OF NEURAL MEMBRANE AS MODELLED BY LEWIS.

(a) SIX PARALLEL ELECTRONIC CIRCUITS SIMULATED BOTH BY SYNAPTIC & ELECTRICALLY EXCITABLE MEMBRANE

(b) SYNAPTIC CURRENT AS FUNCTION OF CONDUCTANCE

(c) BLOCK DIAGRAM TO GET SYNAPTIC CURRENT

FIG NO: 11

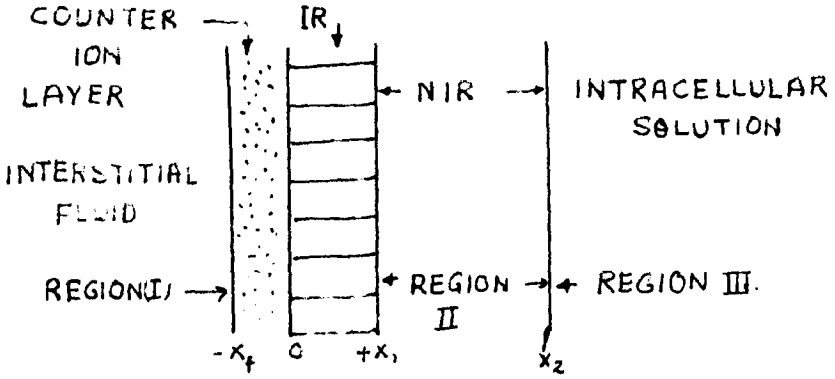


FIG NO: 12

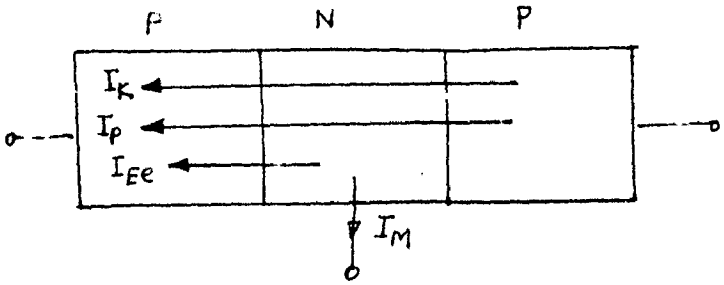


FIG. NO: 13

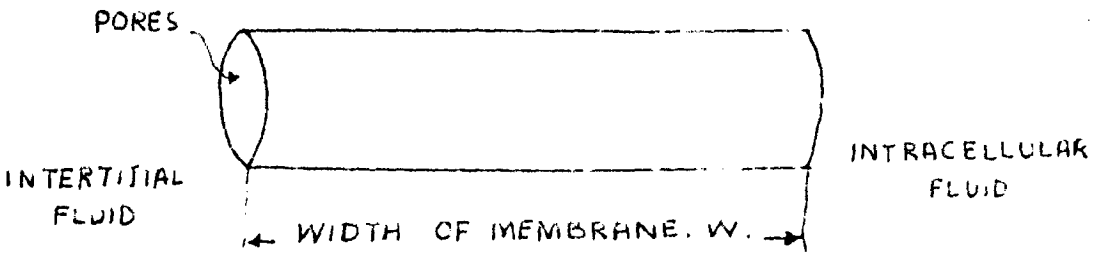


FIG. NO: 14

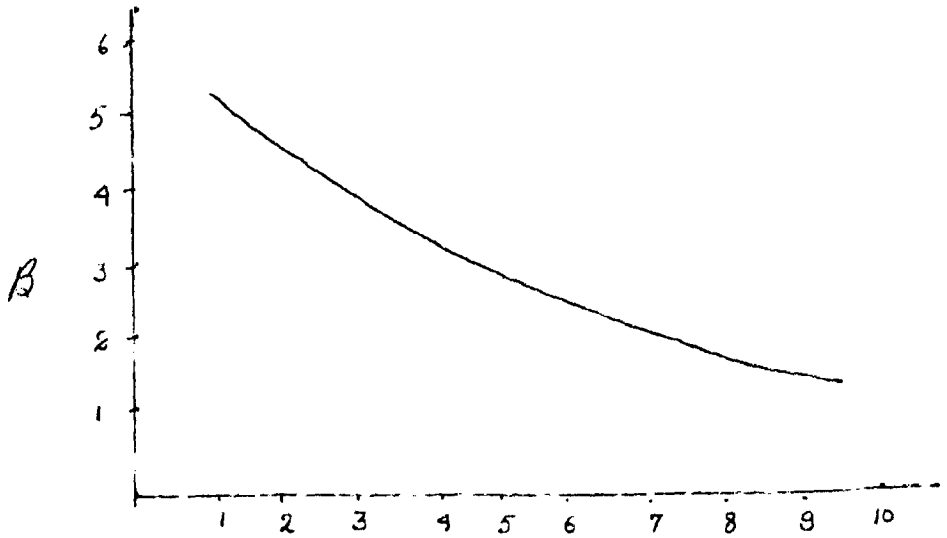


FIG. NO: 15

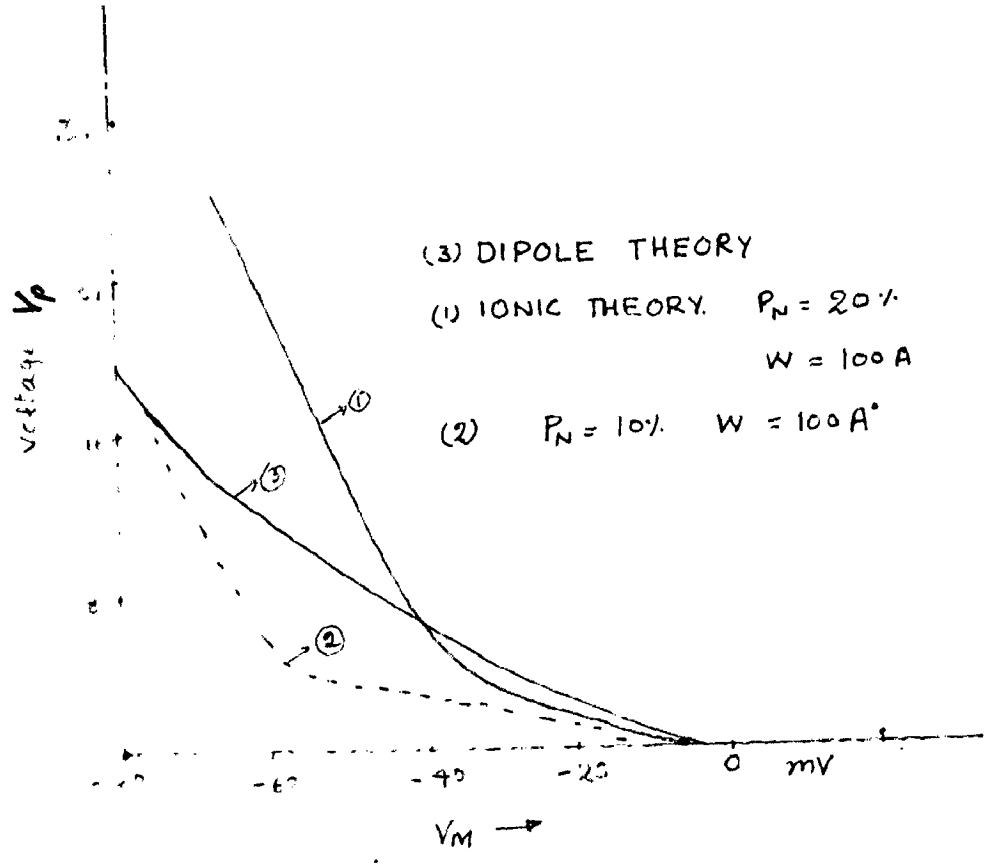


FIG NO: 16

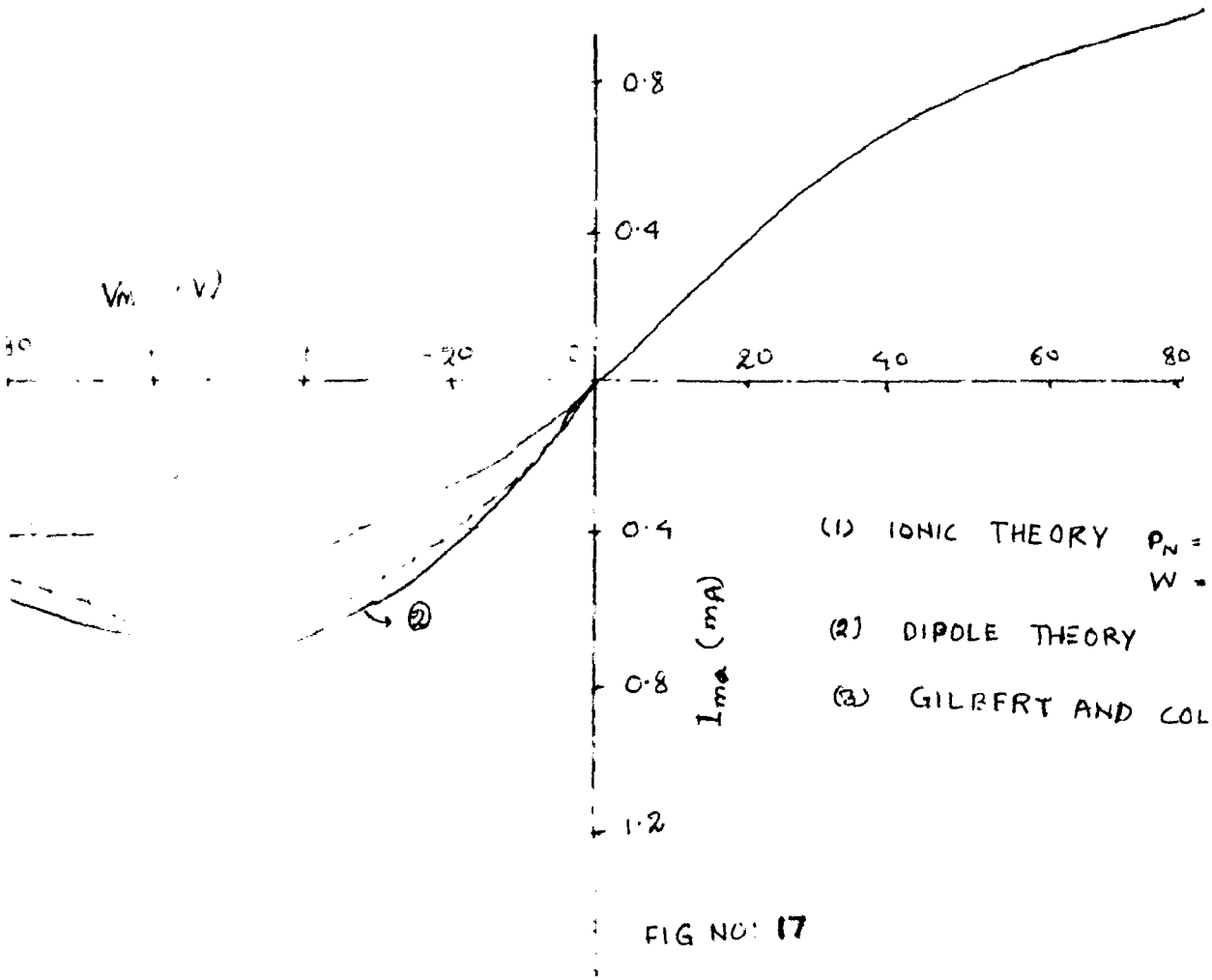
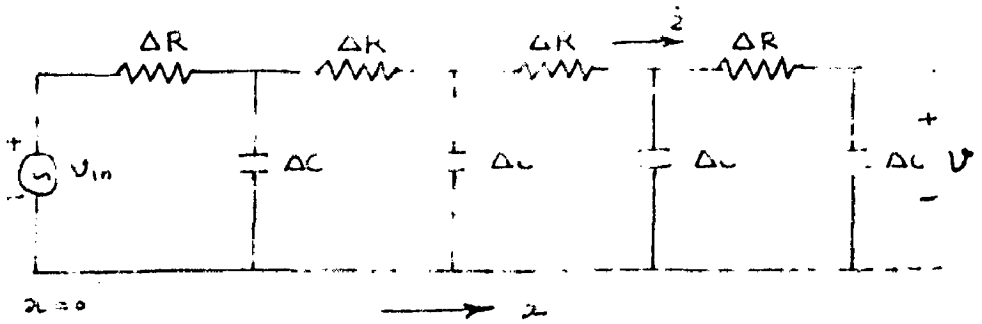


FIG NO: 17



RC CABLE MODEL OF UNMYELINATED FIBER

FIG. NO: 18

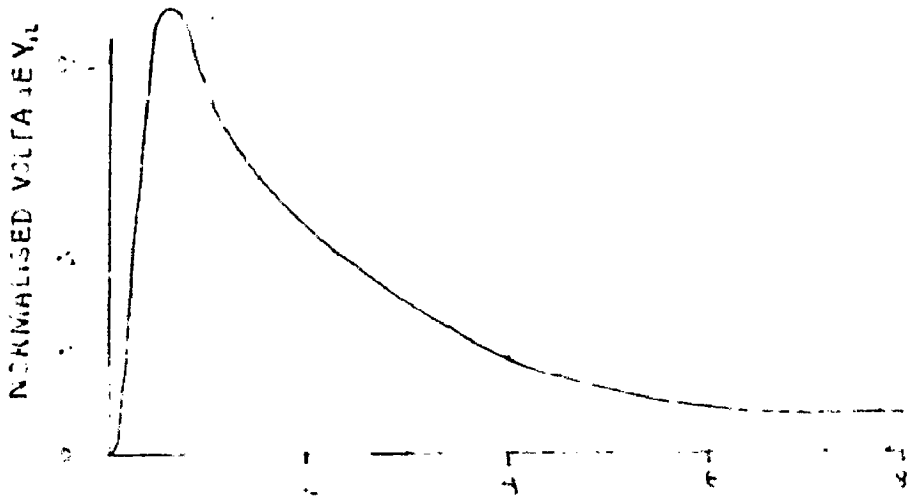
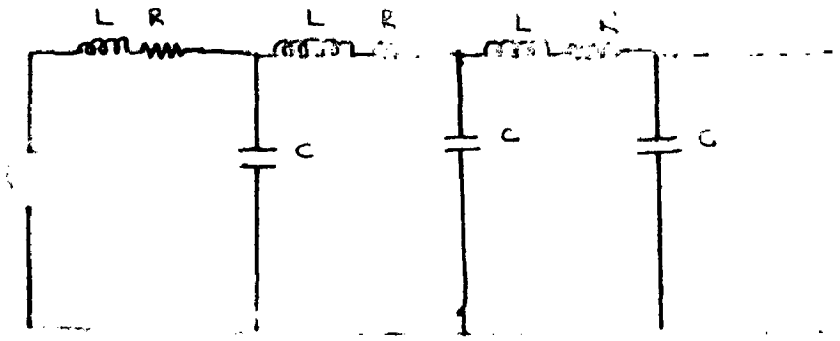


FIG. NO: 19



RLC - NETWORK

FIG. NO: 20

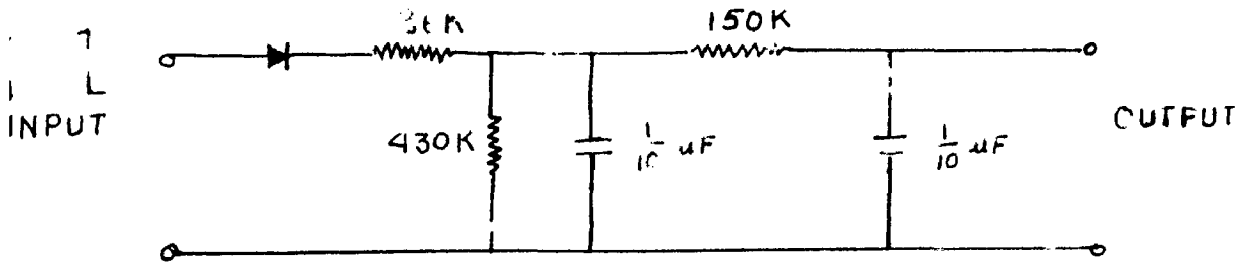
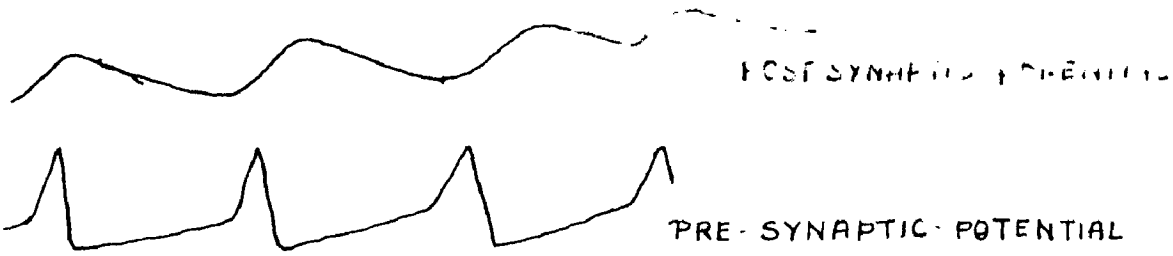


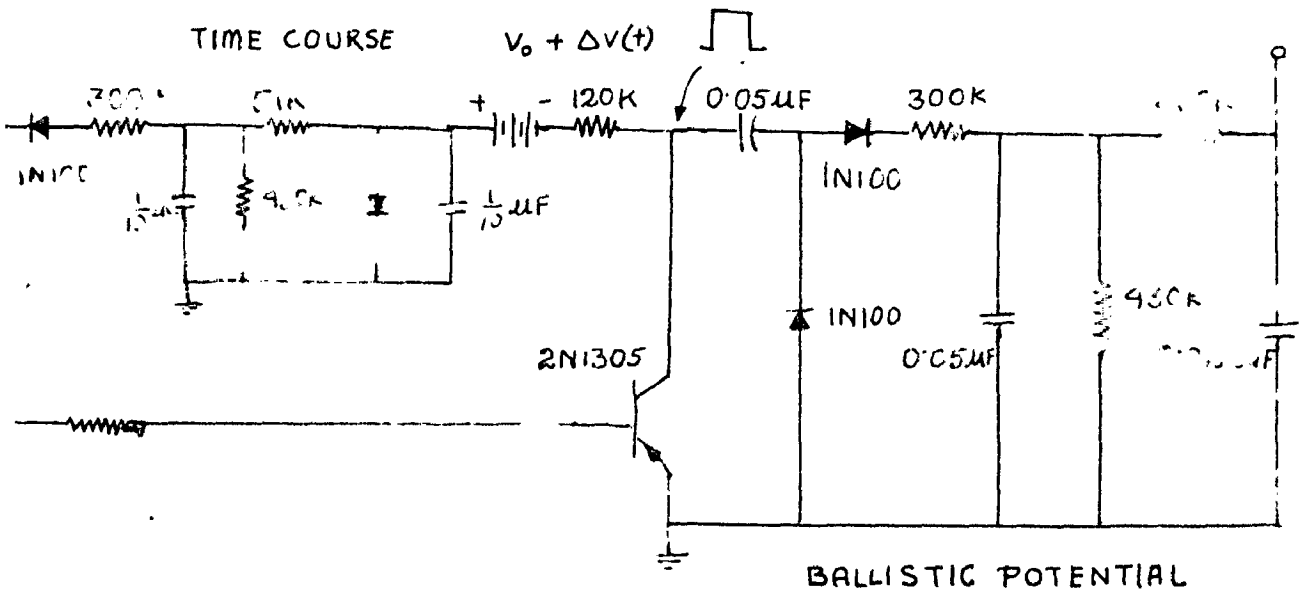
FIG. NO: 21. SIMPLE RC BALLISTIC NETWORK



FACILITATION

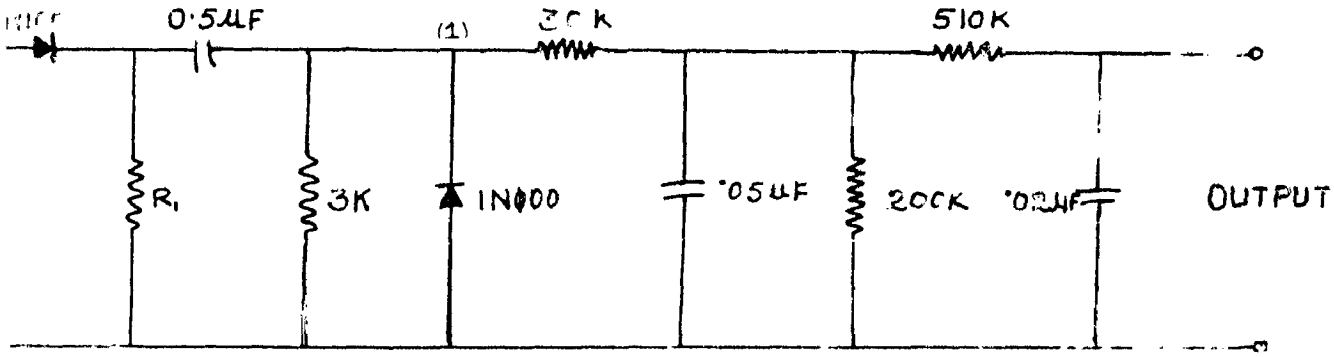
ANTI-FACILITATION

FIG NO: 22.



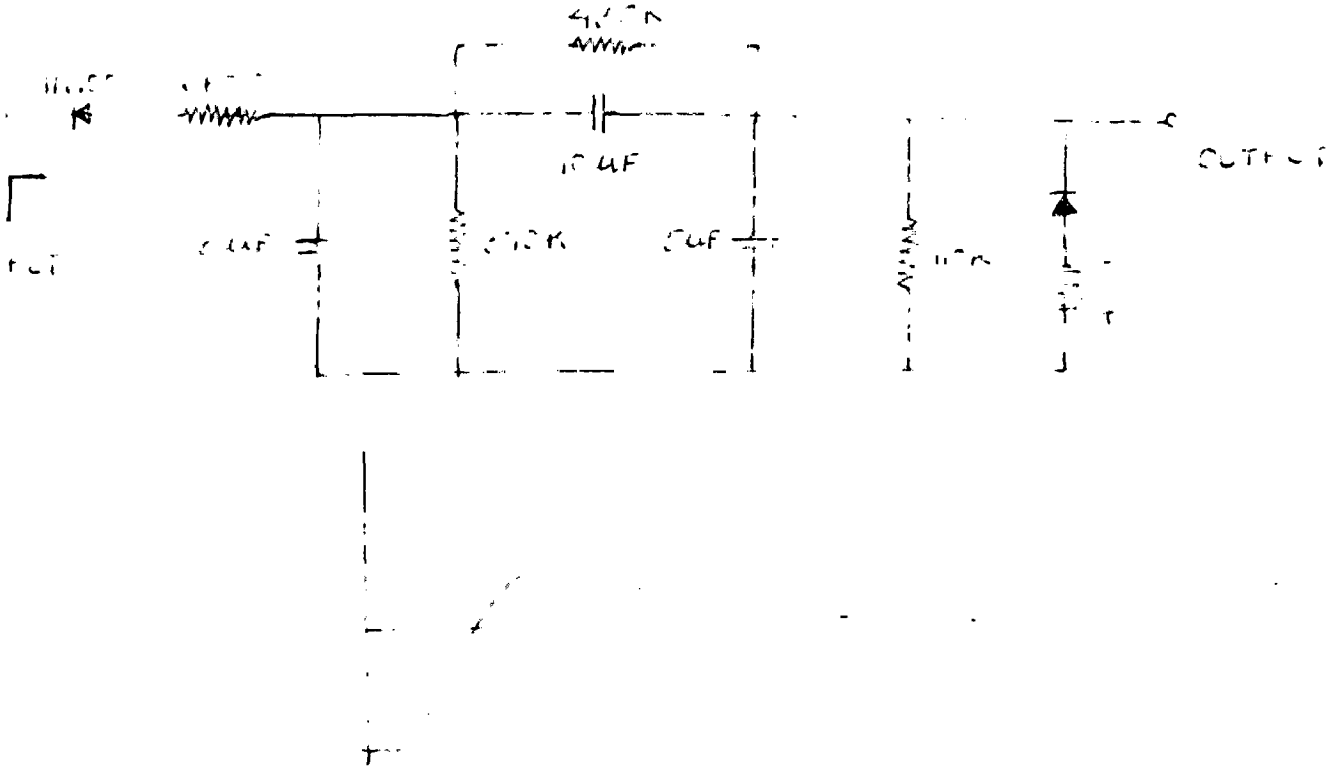
FACILITATING NETWORK

FIG. NO: 23



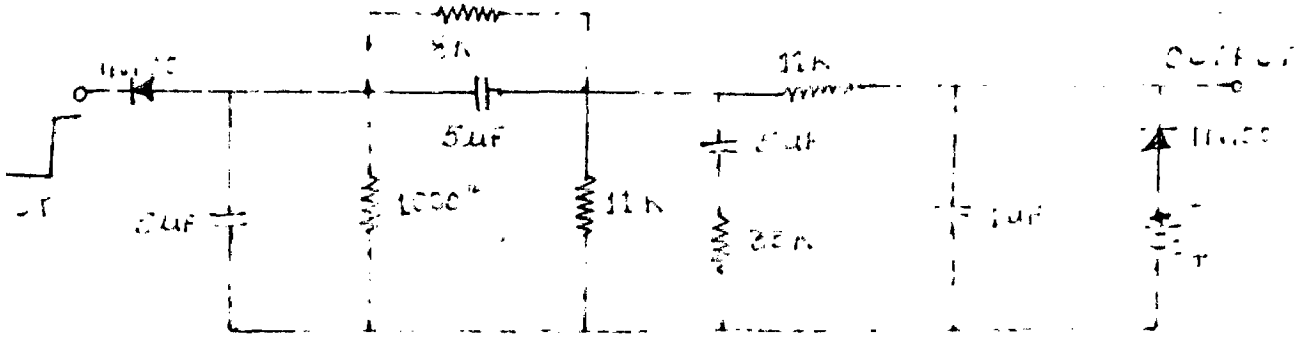
ANTIFACILITATING NETWORK

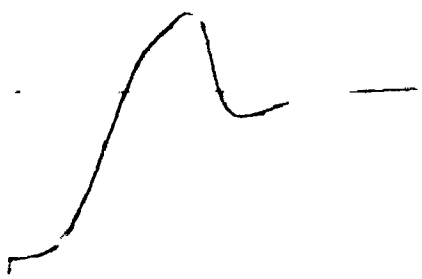
FIG. NO: 24

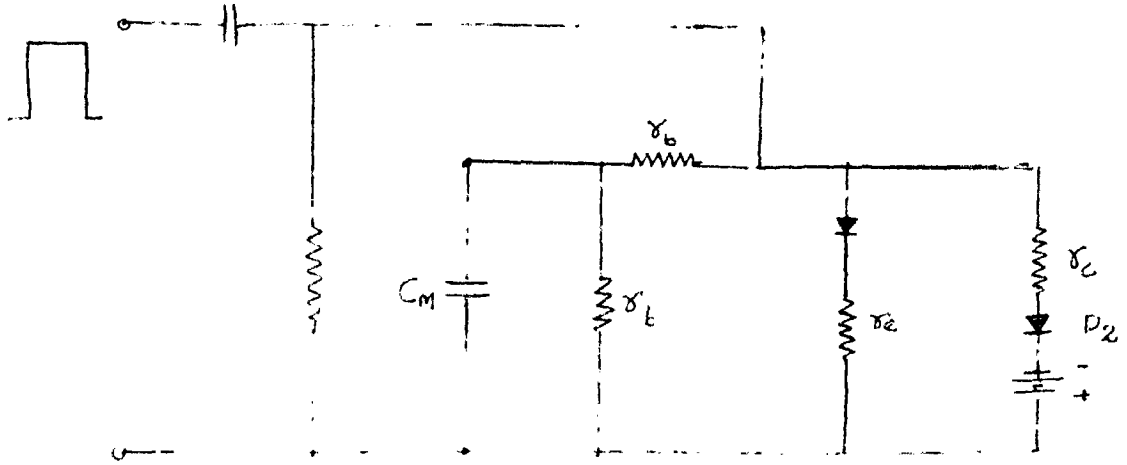


NETWORK EXHIBITING REBOUND & IT'S RESPONSE

FIG NO: 25

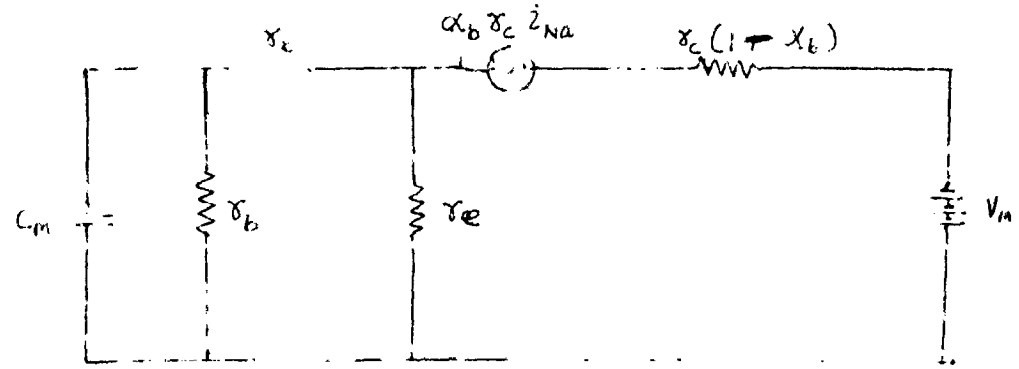






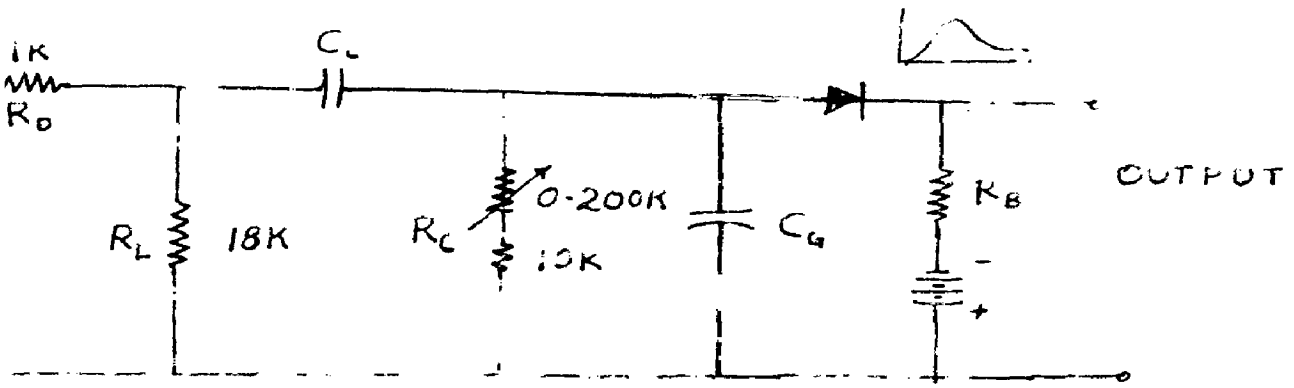
ELECTRONIC MODEL OF NEURON

FIG NO: 27



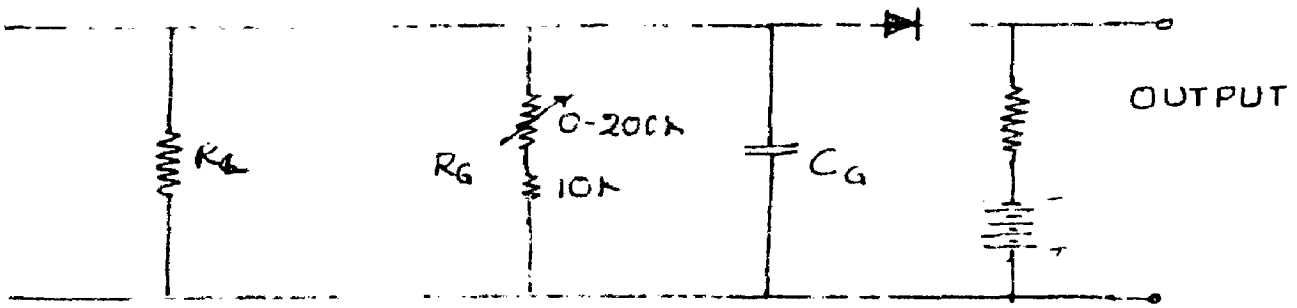
EQUIVALENT CIRCUIT

FIG NO: 28



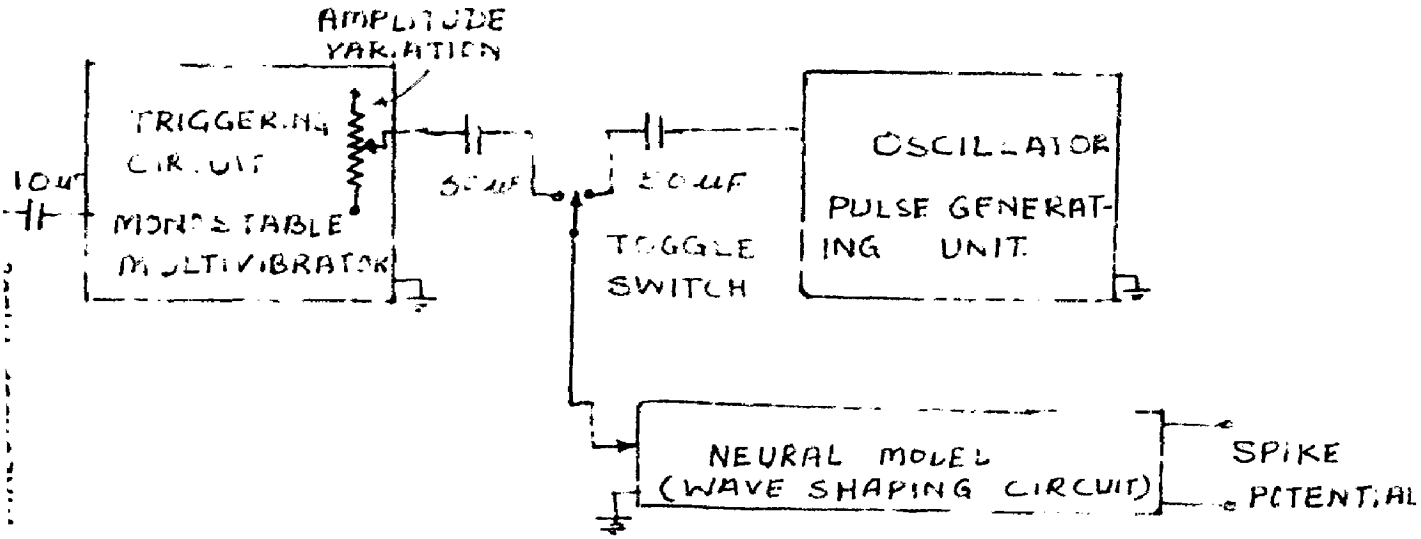
ELECTRONIC MODEL OF NEURON

F. NO: 29(a)



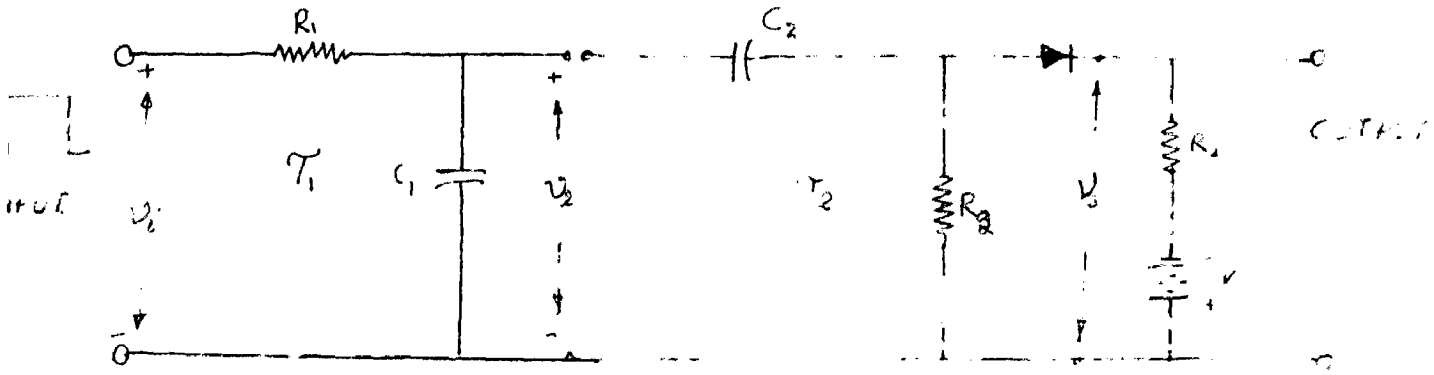
EQUIVALENT CIRCUIT OF ELECTRONIC MODEL DURING RISE CHARACTERISTICS OF SPIKE. ($C_c \gg C_G$)

FIG NO: 29 (b)



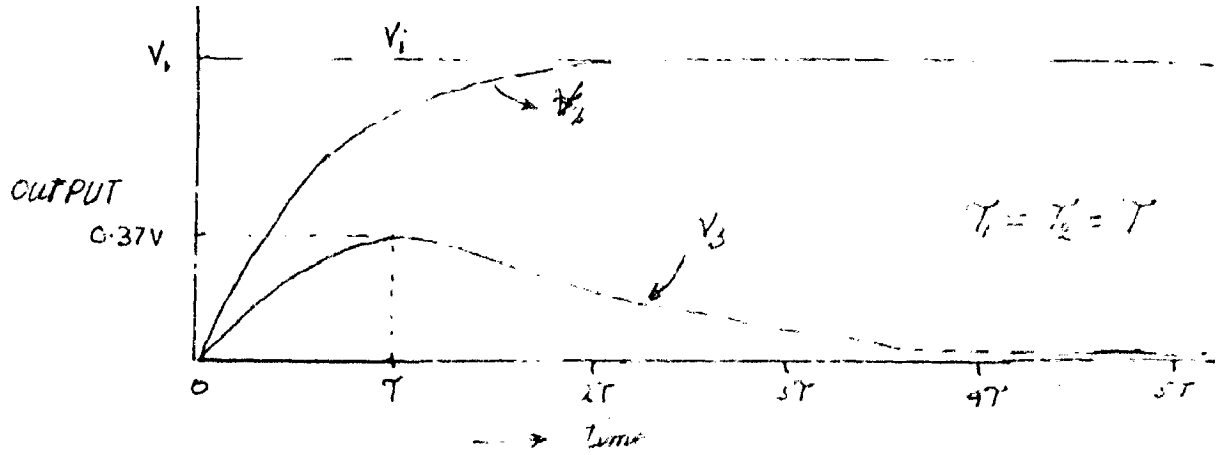
EMATIC DIAGRAM OF ELECTRONIC MODEL OF NEURON

FIG NO: 30



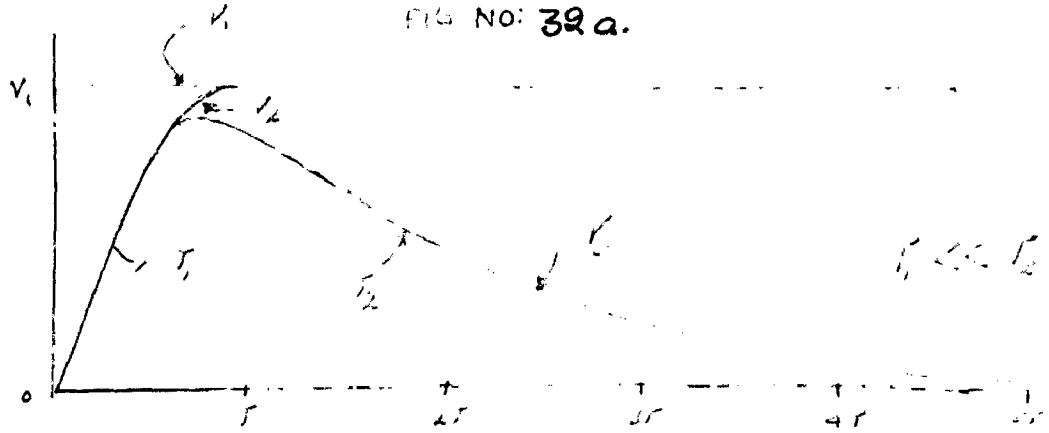
ELECTRONIC MODEL OF NEURON

FIG. NO: 31



RESPONSE OF [illegible] MODEL WITH $T_1 = T_2$

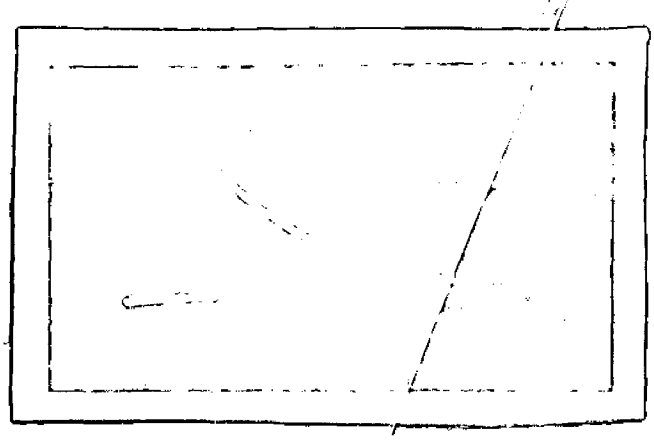
FIG NO: 32 a.

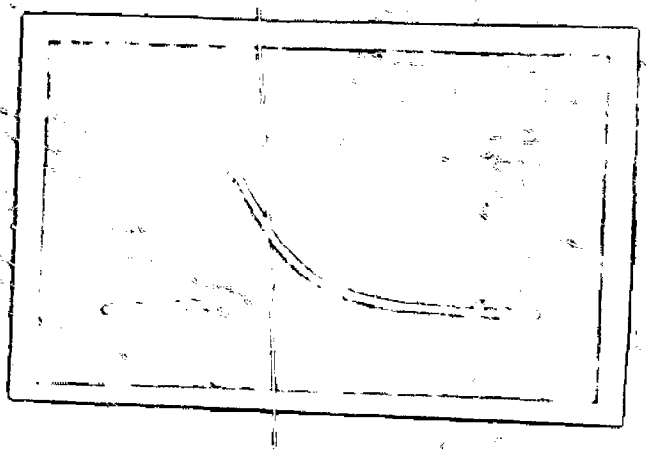


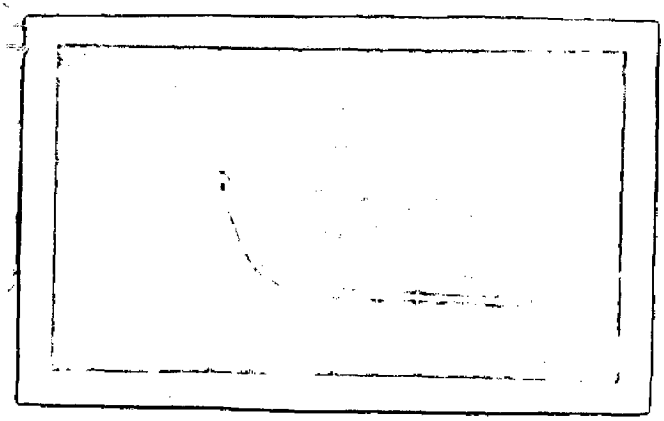
RESPONSE OF ELECTRONIC MODEL

WITH $T_1 > T_2$

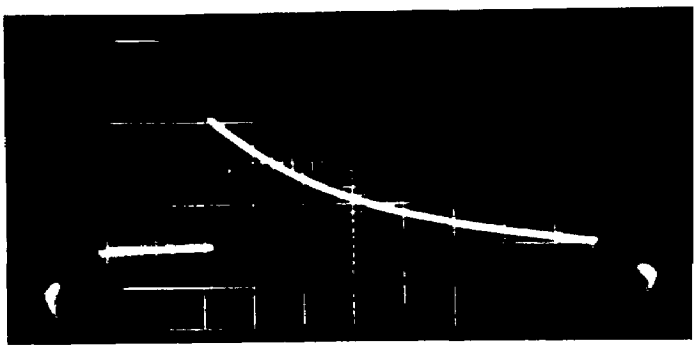
FIG NO: 32 b

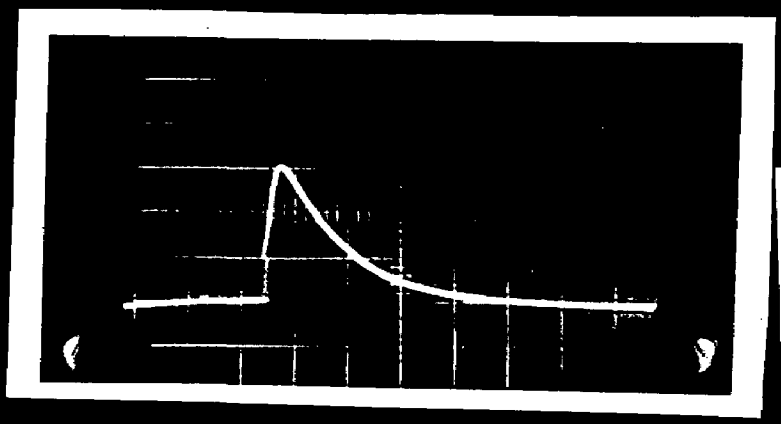






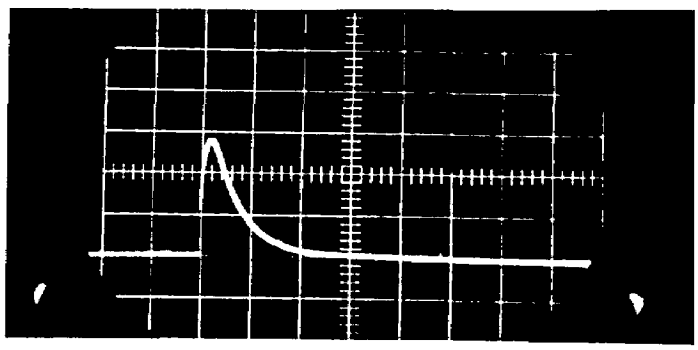
T_R=0.01 -.5 M sec
T_d= 50 m sec
Vertical scale 0.5V/div

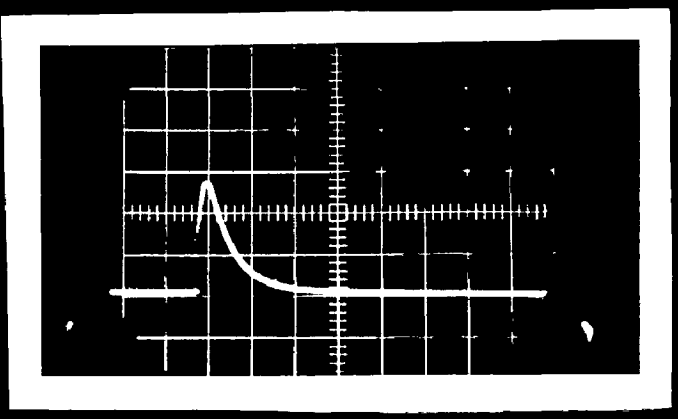




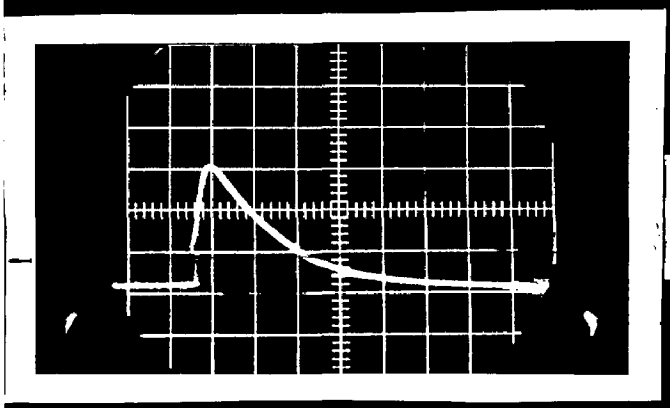
T_R= 1 m sec.
T_d= 20 m sec
Vertical Scale 0.5V/div

T_R=1 m sec T_d= 10 m sec
Vertical Div 0.5V/div

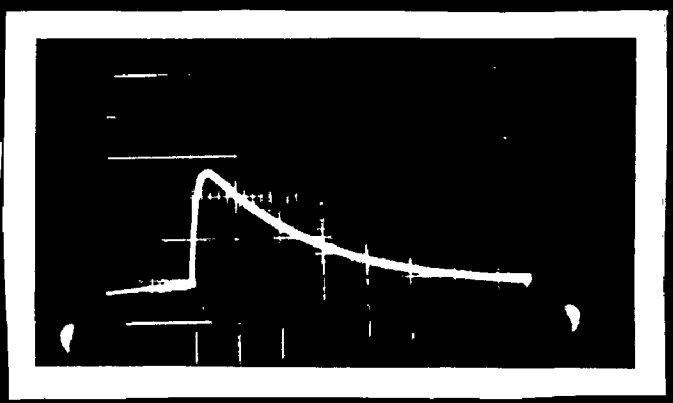




T_R=2 m sec T_d=5 m sec
Vertical Scale=0.5 V/div

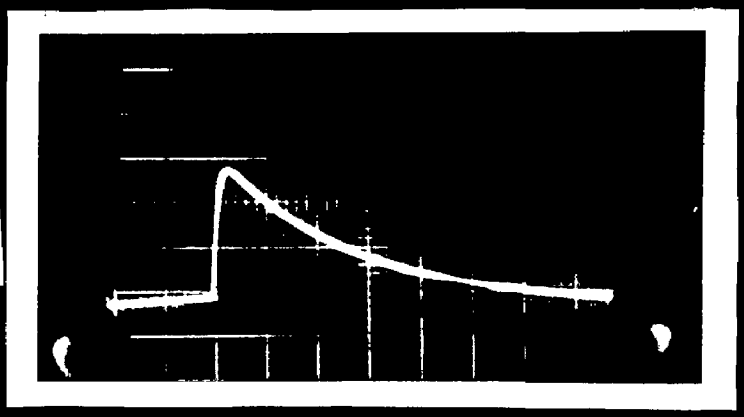


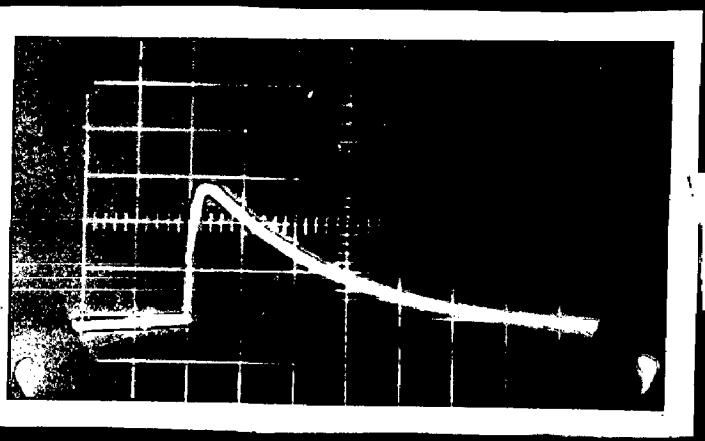
T_R=4 m sec T_d=8 m sec
Vertical scale=0.5 V/div



T_R=2 m sec T_d=40 m sec
Vertical div=0.5V/div

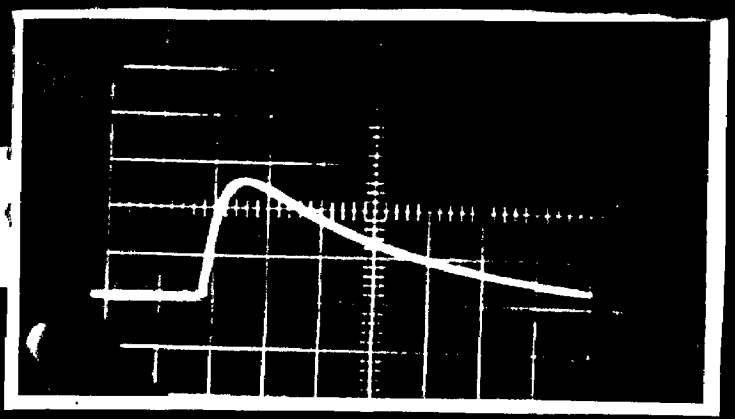
T_R=2 m sec T_d=30 m sec
Vertical scale=0.5V/div



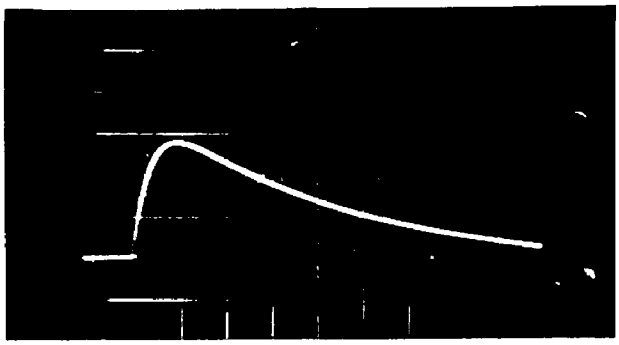


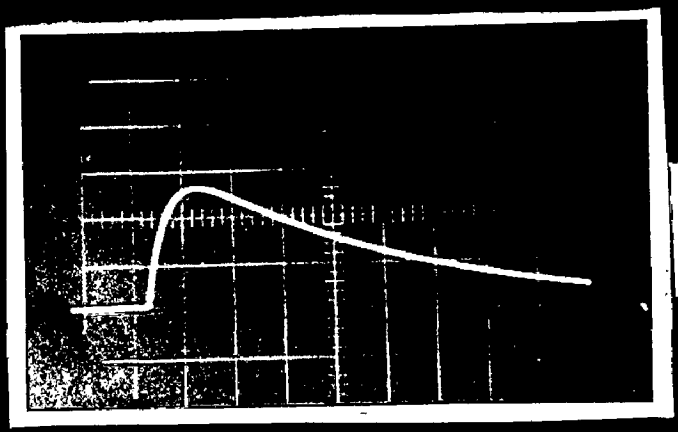
T_R=4 m sec T_d=30 m sec
Vertical scale=0.5V/div

T_R=8 m sec T_d=50 m sec
Vertical div=



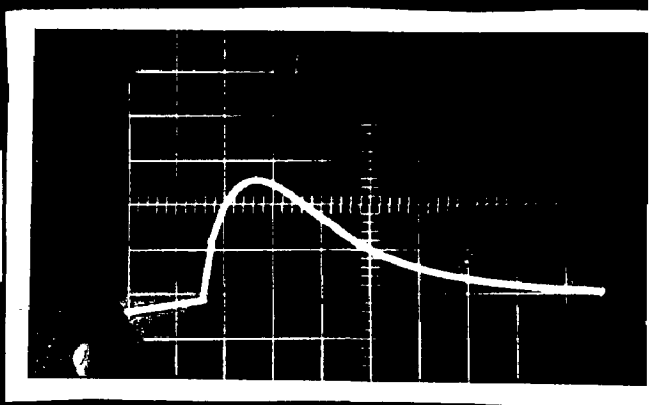
T_R=8 m sec T_d=60 m sec
Vertical Scale=0.5 V/div

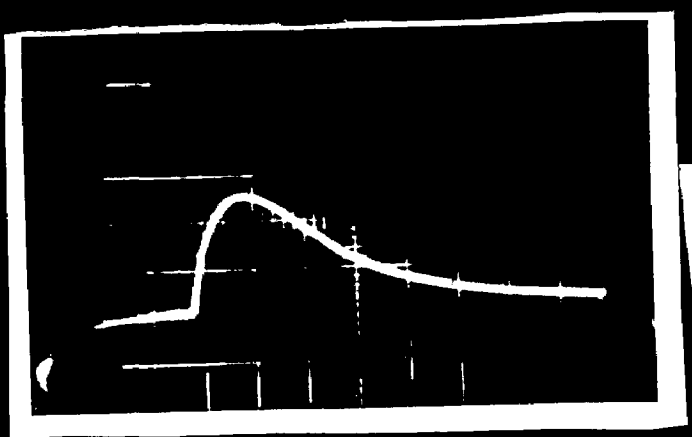




T_R=8 m sec T_d=100 m sec
Vertical scale=0.5V/div

T_R=14 m sec T_d=30m sec
Vertical div=.05V/div





T_R=14 m sec T_d=40 m sec
Vertical scale=0.5V/div.