ON STUDIES IN INJECTED CURRENT LEADING TO SOME TIME-DEPENDENT MEMBRANE POTENTIAL

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(Received on 14. 10. 77)

ABSTRACT

The present paper is an attempt to investigate possible forms of injected current leading to some plausible membrane potential in electrical activities of a nervous system. The results have been discussed with the help of tables and graphs.

1. *Introduction*

In studies of nerve dynamics Hodgkin-Huxley equations play an important role in describing the behaviour, particularly the electrical properties. There have been some studies on the excitation and propagation of axon potentials under a wide range of experimental conditions vide, Holden.[1] The present author, Ghosh[2] has also studied time-dependent membrane potential responses of a non-myelinated fibre due to a step-type injected current. The experimental findings vide, Holden[1] suggests the spontaneous activity of a class of neural models in which the threshold is an explicit function of time. The present paper is an attempt to consider some characteristic features of injected current leading to a variety of time-dependent membrane potential. While the choice of the first two time-dependent forms are experimentally realistic, it has been explored whether the third form is physically plausible or, otherwise. The physiological implications have also been mentioned.

2. *Statement of the problem, Fundamental equations, Initial and Boundary conditions*

Our problem is to investigate the characteristics of injected current through a non-myelinated fibre where the membrane potential is in the form of known function of time.

Let us consider a non-myelinated axon in which a current I is to be injected so that the responses owing to a membrane potential which decays after an action potential at time $t=0$, with a time-course given by,

$$V_m(x,\, t)=K\ exp\left(\frac{X}{T}\right)......(A)$$

and so $V_m \rightarrow K$ as $t \rightarrow \infty$, where K is a constant and V_m is the membrane potential and the axon is thought of as being cut into cylindrical segments x and $X=\frac{x}{\lambda}$, λ is the axonal space constant, $T=\frac{t}{\lambda}$. The model proposed in (A) is akin to the kind of threshold which Hagiwara[3] proposes so as to account for amphibian muscle spindle discharge and also to its subsequent modifications by Ten Hoopen.[4]

The second type of response owing to membrane potential decreases hyperbolically with time in the form given by,

$$V_m(x,\, t)=\frac{KX}{T}......(B)$$

where K, X, T represent the same parameters as mentioned above. One may however easily obtain (B) by expanding (A) with the value of x sufficiently small. This model is in keeping with a model proposed by Buller, Nicholly and Storm.[5]

Further in earlier communication Ghosh[2], an attempt has been made to investigate time-dependent membrane potential responses of a non-myelinated fibre owing to a step-type injected current and it has been found that the membrane potential does not exhibit a linear profile but the steadiness (in increase) in the behaviour of potential is maintained and it was also found that even in the small range of time-intervals, one can distinguish a perceptible growth beyond initial point and an almost uniform pattern at the other end. In this present paper, we consider an opposite situation in which an injected current increases quite uniformly and this steadiness (in increase) is maintained throughout the interval of time under consideration resulting in a membrane potential in the form of a Gamma function given by,

$$V_m(x,\, t)=\frac{K^{\mu}}{\mu}\ \frac{T^{k-1}\, exp\left(-\frac{KT}{\mu}\right)}{\Gamma(K)}$$

where

$$\Gamma(K)=\int_0^{\infty} x^{k-1} exp(-x)dx\ \ ,\ \ k>0$$

with an order $K=2$ and also $\frac{K}{\mu}$ is set to unity.

In particular, when $K=1$, the Gamma distribution gives a Poisson distribution and when K is large then Gamma distribution tends to a Gaussian distribution. Further, it may be pointed out that the Poisson distribution arises when the probability of an impulse occuring in a short time is constant, vide Holden.[1] The models generating Gamma distribution and Gaussian distribution are discussed by Holden.[1] From this point of view it is quite worthwhile to investigate the nature of the current so as to get a membrane potential of the form of Gamma distribution.

Let the current along the interior cell is j_i, through the membrane j_m and the current in the extracellular fluid be j_0. The axon is thought of as being cut into cylindrical segments of length x.

We can write the differential equations for current and potential as $\frac{\partial v_0}{\partial x} = -r_0 j_0$ .... (1), where v_0 is the exterior potential, r_0 is the ECF resistance/unit length, and $\frac{\partial v_i}{\partial x} = -r_i j_i$ ...... (2), i denotes the interior variable. The total current flow is $j=j_0+j_i$ and the membrane potential is $v_m=v_1-v_0$.

By continuity of current (Kirchoff's law), the membrane current j_m (per unit length of axon) is, given by,

$$j_m = -\frac{\partial j_i}{\partial x} = \frac{\partial j_0}{\partial x} \qquad \text{... (3)}$$

Substracting (1) from (2), we get

$$\begin{aligned} \frac{\partial v_i}{\partial x} - \frac{\partial v_0}{\partial x} = \frac{\partial v_m}{\partial x} &= -r_i j_i + r_0 j_0 \\ &= -(r_0+r_i) j_i + r_0 (j_0 + j_i) \\ &= -(r_i + r_0) j_i + r_0 j \qquad \text{... (4)} \end{aligned}$$

Differentiating (4) and using the fact that $\frac{\partial j}{\partial x}=0$ we get,

$$\frac{\partial^2 v_m}{\partial x^2} = -(r_i+r_0)\frac{\partial j_i}{\partial x}$$

or, by equation (3),

$$\frac{\partial^2 v_m}{\partial x^2} = (r_i+r_0) j_m \qquad \text{... (5)}$$

The membrane current has two components, one is the displacement current $j_D = C_m\left(\frac{\partial v_m}{\partial t}\right)$ that charges the membrane capacitor and the second is the ionic current $j_{ion} = \frac{(V_m - V_R)}{r_m}$, where V_R is the resting potential. Thus we have, $j_m = C_m \frac{\partial V_m}{\partial t} + \frac{V_m - V_R}{r_m}$ ... (6)

Equations (5) and (6) may be combined into one equation for

$$\frac{\partial^2 V_m}{\partial x^2} = C_m(r_i + r_0)\frac{\partial V_m}{\partial t} + \left(\frac{r_i + r_0}{r_m}\right)(V_m - V_R) \quad \text{... (7)}$$

The axonal space constant is defined by $\lambda^2 = \frac{r_m}{(r_0 + r_i)}$ where r_m is the nodal resistance. The membrane time constant is $\tau_m = r_m C_m = R_m C_m$ where R_m is the specific nodal resistance and C_m is the nodal capacity. The deviation of $V_m(x, t)$ from V_R is $\overline{V_m}(x, i) = V_m(x, t) - V_R$. So equation (7) may be rewritten as,

$$\lambda^2 \frac{\partial^2 V_m}{\partial x^2} - \overline{V}_m = \tau_m \frac{\partial V_m}{\partial t} \quad \text{... (8)}$$

3. *Solution*

In steady state, the current supplied axon via microelectrode has been on for a sufficiently long time, as $\overline{V_m}$ has reached a steady value. Thus, taking $\left(\frac{\partial \overline{V}_m}{\partial t}\right) = 0$, which will be true when the membrane capacity is charged and no displacement current is flowing. Equation (8) becomes, with $\underset{t \to \infty}{Lt}\ \overline{V_m}(x, t) = \overline{V}_{mss}$

$$\lambda^2 \frac{d^2 \overline{V}_{mss}}{dx^2} = \overline{V}_{mss} \quad \text{... (9)}$$

which has the general solution given by,

$$\overline{V}_{mss} = A_1 exp\left(\frac{x}{\lambda}\right) + A_2 exp\left(-\frac{x}{\lambda}\right) \quad \text{... (10)}$$

The determination of constants in equation (10) requires the specification of boundary conditions on $\overline{V}_{mss}(x)$. For this particular problem as $x \to \pm\infty$, $\overline{V}_{mss}$ must remain finite. It is further required that $\overline{V}_{mss}$ be continuous at $x=0$. These criteria applied to equation (10) give with $A_1 = A_2 = A$,

$$\overline{V_{mss}} = A exp\left(-\frac{|x|}{\lambda}\right) \quad \text{... (11)}$$

The constant A in equation (11) is to be determined.

We know that, current $I=\int_{-\infty}^{\infty} j_m(x)dx=2\int_{0}^{\infty} j_m(x)dx$, by definition and symmetry.

From equations (5) and (11), $I=\dfrac{2}{r_0+r_i}\displaystyle\int_{0}^{\infty}\frac{\partial^2 \overline{V}_m}{\partial x^2}\,dx=\frac{2A}{\lambda(r_0+r_i)}$

Therefore, $A=\dfrac{I\lambda(r_0+r_i)}{2}$ ... (13)

So, $\overline{V}_{mss}(x)=\dfrac{(r_0+r_i)\lambda I}{2}\ exp\left(-\dfrac{|x|}{\lambda}\right)$ ... (14)

Thus equation (14) may be rewritten as,

$$V_{mss}(x)=IR_c\ exp\left(-\frac{|x|}{\lambda}\right) \quad \text{... (15)}$$

which is a form of Ohm's law.

To determine the injected current I when the potential V_m is either an exponential function or, a hyperbolic function or, a Gamma distribution function of x and t.

We make two transformations of the independent variables in equation (8).

First we define two new dimensionless independent variables by $X=\dfrac{x}{\lambda}$ and $T=\dfrac{t}{\lambda}$. With these new variables, equation (8) may be written as,

$$\frac{\partial^2 \overline{V}_m}{\partial x^2}-\overline{V}_m=\frac{\partial \overline{V}_m}{\partial T} \quad \text{... (16)}$$

Secondly, we transform the dependent variable by,

$$U=\overline{V}_m\ exp\ (T)$$

Thus, $\overline{V}_m=U\ exp\ (-T)$, $\dfrac{\partial^2 \overline{V}_m}{\partial x^2}=\dfrac{\partial^2 U}{\partial x^2}\ exp\ (-T)$ and

$$\frac{\partial \overline{V}_m}{\partial T}=\left[\left(\frac{\partial U}{\partial T}\right)-U\right] exp\,(-T) \quad \text{... (17)}$$

So equation (16) becomes,

$$\frac{\partial^2 U}{\partial x^2}=\frac{\partial U}{\partial T} \quad \text{... (18)}$$

To solve equation (16) or equation (18), boundary, initial and continuity conditions must be specified. These are

$\lim_{x \to \infty} \overline{V}_m(x, t) = 0$: $\overline{V}_m(x, t) = 0$ for $-\infty < t < 0$ and $\overline{V}_m(x, t)$ is continuous at $x = 0$ respectively.

Taking Laplace transform of equation (18) w.r.t. T, we get,

$$\frac{d^2 U}{dx^2} = SU - U(T=0) = SU \qquad \ldots (19)$$

where

$$L[U(X, T)] = U(X, S)$$

The solution of equation (19) may be written as,

$$U(X, S) = \begin{cases} A_1 exp(\sqrt{sx}) + A_2 exp(-\sqrt{sx}), & x \leqslant 0 \\ B_1 exp(\sqrt{sx}) + B_2 exp(-\sqrt{sx}) & x \geqslant 0 \end{cases} \qquad \ldots (20)$$

The boundary conditions imply that $A_2 = B_1 = 0$ while the continuity conditions imply $A_1 = B_2 = A$.

Thus equation (20) reduces to

$$U(x,s) = A exp(-\sqrt{sx}) \qquad \ldots (21)$$

To determine the constant A, proceeding as before, we use

$$I = \frac{2}{\lambda(r_0 + r_i)} \int_0^\infty \frac{\partial^2 \overline{V}_m}{\partial x^2} dx \qquad \ldots (22)$$

$$\text{or,} \quad I exp(T) = \frac{2}{\lambda(r_0 + r_i)} \int_0^\infty \frac{\partial^2 U}{\partial x^2} dx \qquad \ldots (23)$$

Taking Laplace transform of equation (23) we get,

$$I = \frac{2A\sqrt{s}(s-1)}{\lambda(r_0 + r_i)}$$

Therefore, $A = \dfrac{I\lambda(r_0 + r_i)}{2\sqrt{s}(s-1)}$

So, $U(x, s) = \dfrac{\lambda I(r_0 + r_i)}{2} exp(-\sqrt{sx}) \left[\frac{1}{2}\left\{ \dfrac{1}{\sqrt{s}-1} + \dfrac{1}{\sqrt{s}+1} \right\} - \dfrac{1}{\sqrt{s}} \right]$

Again, $V_m(x, t) = U(x, t) e^{-T}$

To obtain the inverse transform, we know that,

$$L^{-1}\left\{\frac{exp(-\sqrt{s}x)}{\sqrt{s}\mp 1}\right\}=\frac{exp\left(-\frac{x^2}{4T}\right)}{\sqrt{\pi T}}+\left\{1-erf\left(\frac{x}{2\sqrt{T}}\mp\sqrt{T}\right)\right\}exp(T\mp x)$$

and $$L^{-1}\left\{\frac{exp(-\sqrt{s}x)}{\sqrt{s}}\right\}=\frac{1}{\sqrt{\pi T}}exp\left(-\frac{x^2}{4T}\right)$$

where the error function $erf(z)$ is defined by,

$$erf z=\frac{2}{\sqrt{\pi}}\int_0^z exp(-\omega^2)d\omega$$

Taking Inverse Laplace transform we get,

$$U(x,\ T)=\frac{\lambda I(r_0+r_i)}{2}\left[\left\{1-erf\left(\frac{x}{2\sqrt{T}}-\sqrt{T}\right)\right\}exp(T-x)\right.$$

$$\left.-\left\{1-erf\left(\frac{x}{2\sqrt{T}}+\sqrt{T}\right)\right\}exp(T+x)\right.$$

We know that, $U=V_m\ exp\ (T)$

Therefore, $$V_m(x,\ t)=\frac{I\lambda(r_0+r_i)}{2}\left[\left\{1-erf\left(\frac{x}{2\sqrt{T}}-\sqrt{T}\right)\right\}exp\ (-x)\right.$$

$$\left.-\left\{1-erf\left(\frac{x}{2\sqrt{T}}+\sqrt{T}\right)\right\}exp\ (x)\right] \quad \ldots (24)$$

Case 1: Let us consider the responses owing to a membrane potential which is of the from $V_m(x,\ t)=k\ exp\left(\frac{X}{T}\right)$ ... (A)

and so $V_m\to K$ as $t\to\infty$, where K is a constant.

Substituting (A) in equation (24) we get,

$$K\ exp\left(\frac{X}{T}\right)=\frac{I\lambda(r_0+r_i)}{2}\left[\left\{1-erf\left(\frac{X}{2\sqrt{T}}-\sqrt{T}\right)\right\}exp\ (-x)\right.$$

$$\left.-\left\{1-erf\left(\frac{X}{2\sqrt{T}}+\sqrt{T}\right)\right\}exp\ (X)\right]$$

Therefore, $$I=\frac{2K\ exp\ (X/T)}{\lambda(r_0+r_i)}\left[\left\{1-erf\left(\frac{X}{2\sqrt{T}}-\sqrt{T}\right)\right\}exp\ (-x)\right.$$

$$\left.-\left\{1-erf\left(\frac{X}{2\sqrt{T}}+\sqrt{T}\right)\right\}exp\ (x)\right]^{-1} \quad \ldots (I)$$

Case II: We consider responses owing to a membrane potential given by,

$$V_m(x, t)=\frac{KX}{T} \qquad \dots \text{(B)}$$

Substituting (B) in equation (24) we get,

$$\frac{KX}{T}=\frac{I\lambda(r_0+r_i)}{2}\left[\left\{1-erf\left(\frac{X}{2\sqrt{T}}-\sqrt{T}\right)\right\} exp\,(-x)\right.$$
$$\left.-\left\{1-erf\left(\frac{X}{2\sqrt{T}}+\sqrt{T}\right)\right\} exp\,(x)\right]$$

Therefore, $I=\dfrac{2KX}{T\lambda(r_0+r_i)}\left[\left\{1-erf\left(\dfrac{X}{2\sqrt{T}}-\sqrt{T}\right)\right\} exp\,(-x)\right.$

$$\left.-\left\{1-erf\left(\frac{X}{2\sqrt{T}}+\sqrt{T}\right)\right\}exp\,(x)\right] \qquad \dots \text{(II)}$$

Let us suppose that the membrane potential defined by equation (C), as given below, with an order $K=2$ and $\frac{K}{\mu}$ of equation (C) are set to unity.

$$V_m(x, t)=\frac{K}{\mu}\,\frac{T^{k-1}exp\left(-\frac{KT}{\mu}\right)}{\Gamma(k)} \qquad \dots \text{(C)}$$

where $\qquad \Gamma(K)=\displaystyle\int_0^\infty X^{k-1}\,exp\,(-x)dx, \quad K>0$

To discuss the form of injected current for this model, we substitute (C) in equation (24).

$$\frac{K}{\mu}\,\frac{T^{k-1}exp\left(-\frac{KT}{\mu}\right)}{\Gamma(K)}=\frac{I\lambda(r_0+r_i)}{2}\left[\left\{1-erf\left(\frac{x}{2\sqrt{T}}-\sqrt{T}\right)\right\}exp(-x)\right.$$
$$\left.-\left\{1-erf\left(\frac{x}{2\sqrt{T}}+\sqrt{T}\right)\right\}exp(x)\right]$$

Therefore,

$$I=\frac{2K}{\mu}\,\frac{T^{k-1}exp\left(-\frac{KT}{\mu}\right)}{\Gamma(K)\lambda(r_0+r_i)}\left[\left\{1-erf\left(\frac{x}{2\sqrt{T}}-\sqrt{T}\right)exp(-x)\right.\right.$$
$$\left.-\left\{1-erf\left(\frac{x}{2\sqrt{T}}+\sqrt{T}\right)\right\}exp(x)\right]^{-1} \qquad \dots \text{(III)}$$

4. *Discussions*

We can now turn to discuss on the results arrived in the foregoing sections. To get at the interpretation, we use tables and graphs based on the data applied to the above results. The tables with $x=0{\cdot}1$ for the three cases are given below :

Table for case I :

t	0·1	0·2	0·3	0·4	0·5	0·6	0·7	0·8	0·9	1·0	1·1	1·2
$I \propto t$	5·35	2·75	2·30	2·23	2·235	2·36	2·52	2·88	3·24	3·75	4·32	5·29

Table for case II :

t	0·1	0·2	0·3	0·4	0·5	0·6	0·7	0·8	0·9	1·0	1·1	1·2
$I \propto t$	1·97	·834	·55	·43	·37	·33	·31	·32	·323	·34	·36	·41

Table for equation (III) :

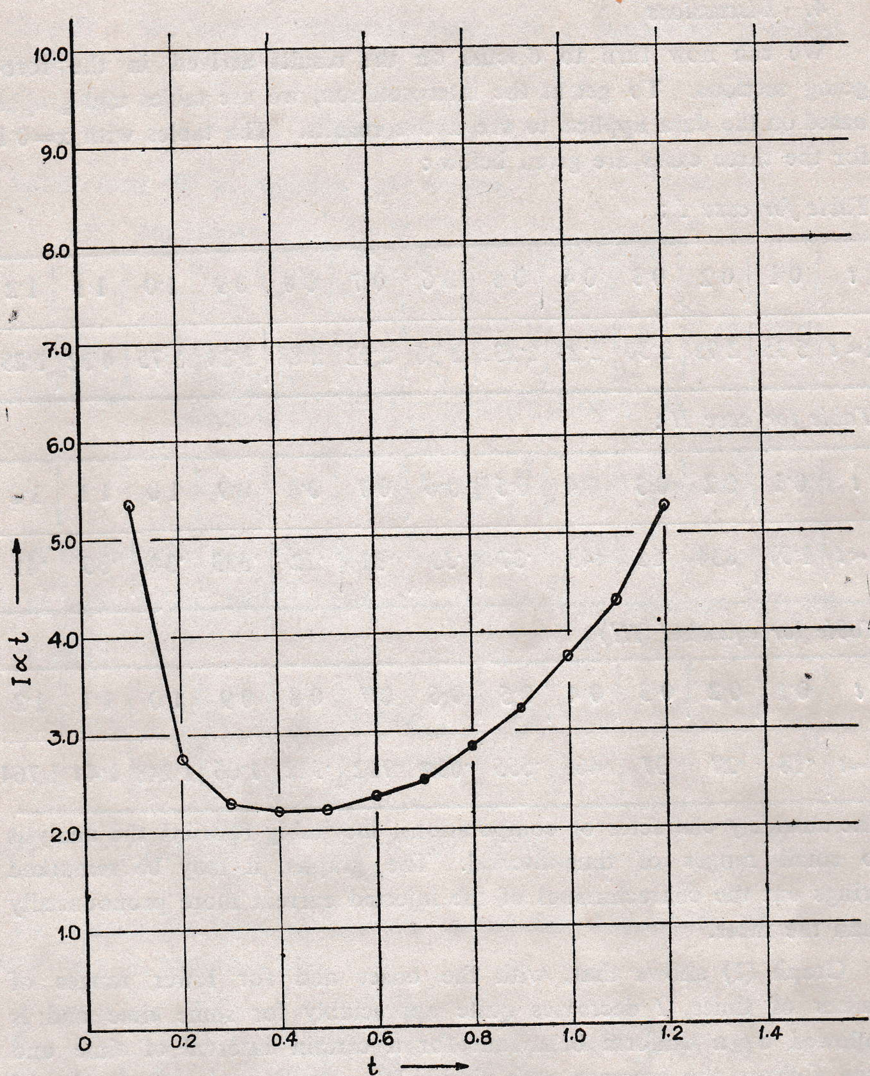
t	0·1	0·2	0·3	0·4	0·5	0·6	0·7	0·8	0·9	1·0	1·1	1·2
$I \propto t$	·18	·27	·37	·465	·555	·659	·762	·912	1·06	1·248	1·44	1·764

The unwidely character of computations, inevitably restricts the analysis to small ranges of time-interval. The graphs, it may be remarked brings out the characteristics of the injected current more pronouncedly than the table.

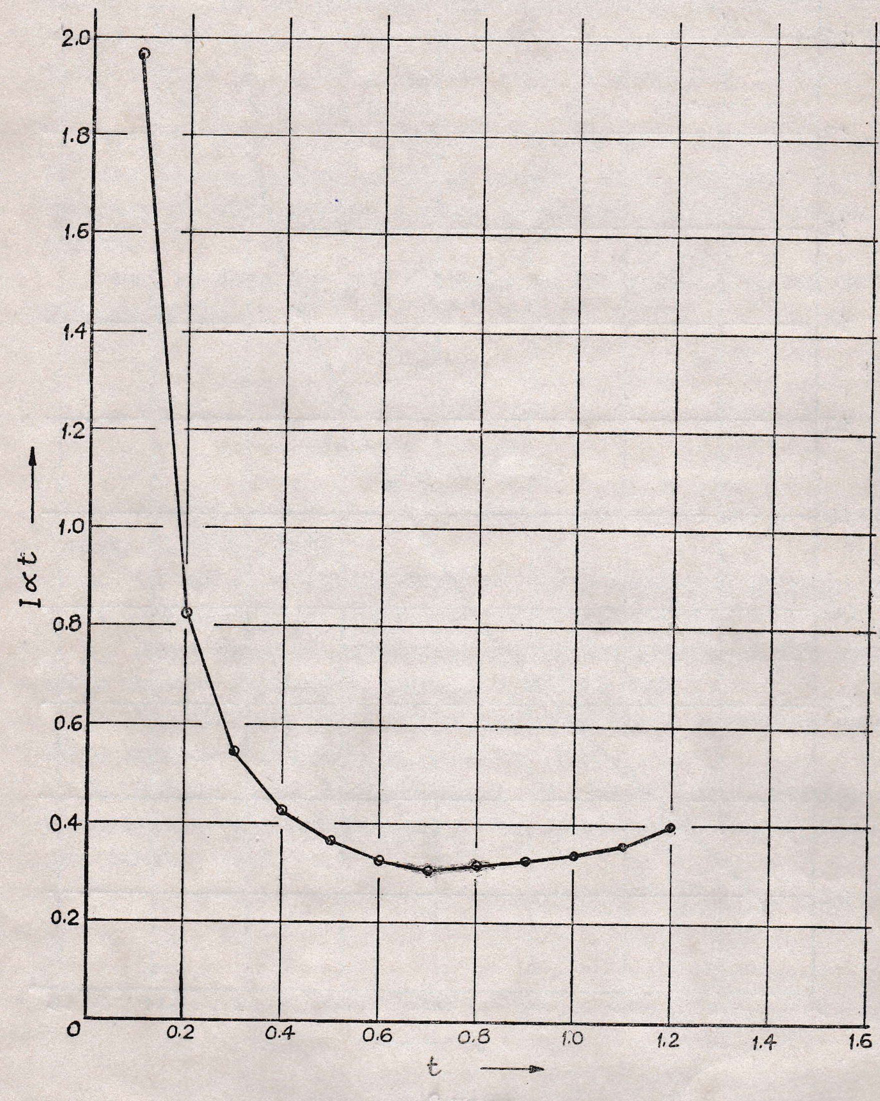
Graph (1) shows that, with the onset and for lower ranges of values of times, I decreases quite appreciably for some time and is followed by a uniform behaviour for a certain interval of time and then follows the increase with time. It must be pointed out that, I decreases more rapidly than that increases for higher range of values of t.

Graph (2) shows that while I decreases for lower range of values of t, it soon becomes almost uniform.

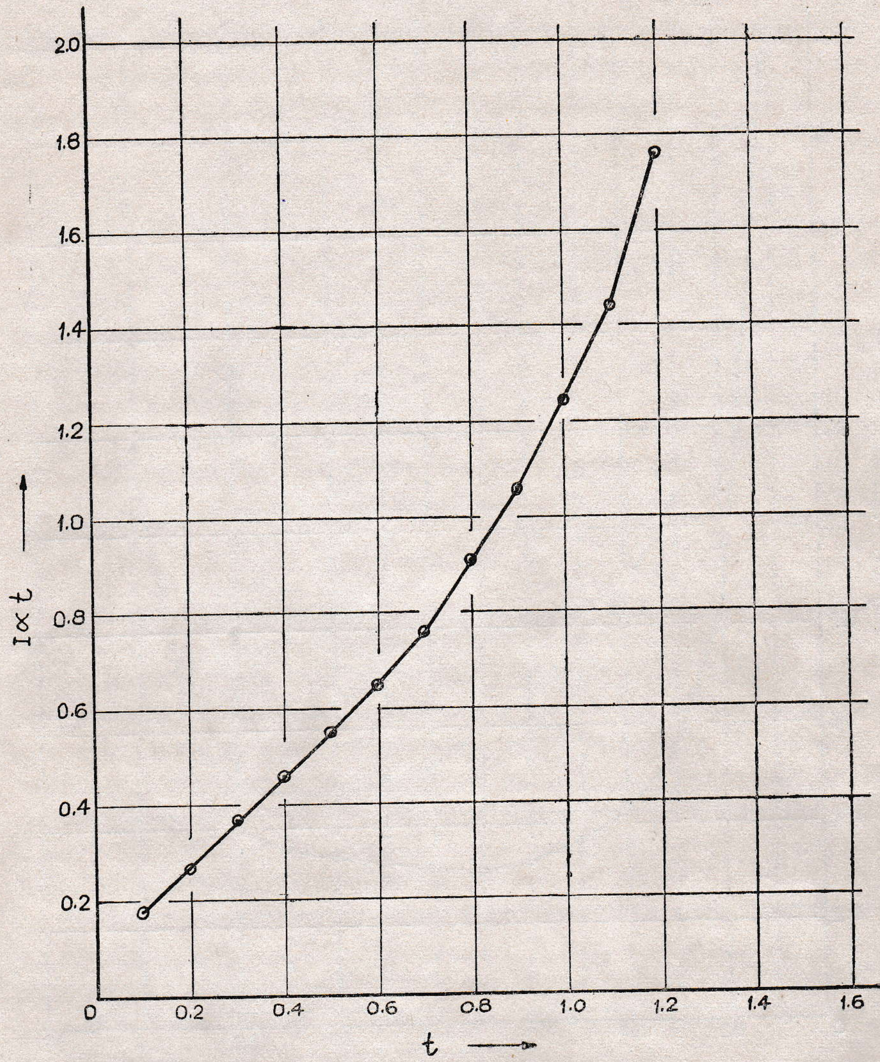
The third graph, contrary to the above two graphs, shows a steady rate of increase of I with time. Thus in order to have a distribution of injected current which shows a steady increase, one may have the distribution of the membrane potential in the form of a Gamma



GRAPH 1



GRAPH 2



GRAPH 3

distribution. In the particular and limiting cases the Gamma distribution being reduced to Poission or Gaussian distribution. It is likely that a discrete or, a fairly random form of membrane potential may result out of an injected current with the above characteristics.

From the physiological standpoint the first two models may account for the bio-mechanical behaviour resulting from dynamical processes involving electrical activity in which membrane potential responses are emitted.

I wish to thank Dr. D. K. Sinha of Jadavpur University for his valuable advice.

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