ON RESPONSE IN A NERVE MEMBRANE OWING TO A TIME-DEPENDENT STIMULUS

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In this paper the linear spread of nerve potential owing to suitable time-dependent excitation has been determined. The results have been discussed and illustrated by tables and graphs.

INTRODUCTION

A number of studies have been made on the dynamics of nerve membranes on account of their relevance to problems of physiology. It is an important problem in nerve dynamics to investigate the generation of impulses arising out of excitation of tissues. The celebrated papers by Hodgkin and Rushton (1946) and Hodgkin and Huxley (1952) bear testimony to this. Hodgkin and Rushton (1946) considered the problem of linear spread of nerve potential. The object of the present paper is to extend the analysis of Hodgkin and Rushton (1946) to a suitable time-dependent excitation. It has been shown in this paper that there exist some marked distinguishing features of the results on spatial and temporal voltage distributions on the axon in response to current impulse and these have been discussed and illustrated by tables and graphs. The case for break has also been considered and compared with the other situations.

STATEMENT OF THE PROBLEM, FUNDAMENTAL EQUATIONS AND BOUNDARY CONDITIONS

We consider a membrane of a nervous system. Our problem is to investigate the response in respect of electrical voltage due to time dependent stimulus to which the membrane is subjected. The analysis presented here proceeds on the lines shown by Hodgkin and Rushton (1946).

In this analysis, we have made the following assumptions :—

(1) The axon has a uniform cable-like structure with a conducting core, and an external conducting path and a surface membrane with resistance and capacity.

(2) The axon is sufficiently thin and the membrane resistance is sufficiently high for the flow of currents in core and interstitial fluid to be strictly parallel. We can say alternatively that, throughout the external fluid the potential is constant at any given distance along the nerve.

(3) The axoplasm and external fluid behave as pure Ohmic resistances.

(4) When the current density throughout the membrane is small, then the membrane resistance is constant.

(5) The membrane capacity behaves like a pure dielectric with no loss.

On account of these assumptions, we can write the differential equations for current or, potential.

Let X be the distance along axon, T be the time i_1 be the current flowing through the external fluid and i_2 be the current flowing through the axoplasm, and I be the impressed current. Let $I = i_1 + i_2, \ldots, i_m$ be the current penetrating the surface membrane at any point. Let V_1 be the potential of the external fluid w.r.t. distant point, so that

$$V_1 = -\int_{-\infty}^{x} r_1 i_1 \, dx \quad \text{and}$$

V_2 be the potential of the internal fluid w.r.t. a distant point.

$$\therefore \; V_2 = -\int_{-\infty}^{x} r_2 i_2 \, dx$$

Let V_m be the change in potential difference across the surface membrane which results from the flow of current, so that $V_m = V_1 - V_2$, C be the capacitance per unit length of the surface membrane in axon, 'A' be the area and 'd' be the thickness, λ be the characteristic length which is equal to $\sqrt{(r_4/r_1 + r_2)}$, where r_4 is the resistance $\times$ unit length of the surface membrane in the axon, i.e.,

$r_4 = \dfrac{R_4}{2\pi a}$, R_4 being the resistance $\times$ unit area of the surface membrane and r_2 is the resistance per unit length of the axoplasm, i.e., $r_2 = \dfrac{R_2}{\pi a^2}$, and r_1 is the resistance per unit length of the external fluid. We have,

$$Y = \frac{m\lambda r_1}{2r_2} = \frac{r_1^2 \lambda}{2(r_1 + r_2)}.$$

Let $\tau = r_4 C = R_4 C_M$, which is the time constant of the surface membrane, and C_M be the capacity per unit area of the surface membrane.

We have,

$$\frac{\partial V_1}{\partial x} = - r_1 i_1 \qquad \ldots (1)$$

$$\frac{\partial V_2}{\partial x} = - r_2 i_2 \qquad \ldots (2)$$

$$\frac{\partial V_m}{\partial x} = (r_1 + r_2) i_2 - I r_1. \qquad \ldots (3)$$

The total current through the membrane can be obtained in two ways

$$i_m = \frac{\partial i_2}{\partial x} \qquad \text{.. (4)}$$

and

$$i_m = \frac{V_m}{r_4} + C\frac{\partial V_m}{\partial t} \qquad \text{... (5)}$$

where r_4 and C are the membrane elements.

From (3) we have,

$$\frac{\partial i_2}{\partial x} = \frac{1}{r_1 + r_2}\frac{\partial^2 V_m}{\partial x^2} + \frac{r_1}{r_1 + r_2}\frac{\partial I}{\partial x} \qquad \text{... (6)}$$

Hence

$$-\lambda^2\frac{\partial^2 V_m}{\partial x^2} + \tau\frac{\partial V_m}{\partial t} + V_m = r_1\lambda^2\frac{\partial I}{\partial x}$$ at electrode, and $= 0$, away from electrode ... (7)

Changing the variables of (7),

$$X = \frac{x}{\lambda},\ T = \frac{t}{\tau},\quad U = V_m e^T$$

We have

$$-\frac{\partial^2 U(X, T)}{\partial X^2} + \frac{\partial U(X, T)}{\partial T} = 0 \qquad \text{... (8)}$$

except at electrode

3. Solution of the Problem

Taking the Laplace transform of parameter S, with suitable initial conditions, we find,

$$\frac{d^2U(X, S)}{d X^2} = S\,U(X, S) \qquad \text{... (9)}$$

The solution of this is given by

$$U(X, S) = A\,e^{-|X|\sqrt{S}} \qquad \text{... (10)}$$

where $|X| \equiv$ absolute value, and A is a parameter. On account of symmetry at $V = 0$ as $|X| \to \infty$, we obtain only one constant A for this double integration.

To evaluate A, we consider the derivatives at the boundary region of the electrode, of width $\pm\,\delta$. The change of slope at the electrode is,

$$\Delta'' V_m = T\left[\frac{\partial V_m}{\partial x}\Big|_{x=\delta} - \frac{\partial V_m}{\partial x}\Big|_{x=-\delta}\right],$$

which we can write as

$$\Delta'' \ V_m = T(r_1 + r_2)\left[i_2 \Big|_{x=\delta} - i_2 \Big|_{x=-\delta} \right] - r_1 \left[I \Big|_{x=\delta} - I \Big|_{x=-\delta} \right]$$

Changing from V to U,

$$\triangle'' \ U = \ - \ \frac{r_1 \ I_0 \ \lambda}{(s-1)^2}$$

by taking the Laplace transform

$$\triangle'' \ U = \frac{\partial U}{\partial X} \Bigg|_{x=\Delta/\lambda} - \frac{\partial U}{\partial X} \Bigg|_{x=-\Delta/\lambda}$$

Now, since

$$U(X, S) = A \ e^{-|x|\sqrt{s}}$$

$$A = \frac{r_1 I_0 \lambda}{2} \cdot \frac{1}{\sqrt{S} \ (S-1)^2} \cdot \qquad \ldots (11)$$

Therefore, we have from (10),

$$U(X, S) = \frac{r_1 I_0 \lambda}{2}\left[\tfrac{1}{4} \cdot \frac{e^{-|X|\sqrt{S}}}{S(\sqrt{S}-1)^2} - \tfrac{1}{4} \cdot \frac{e^{-|X|\sqrt{S}}}{S(\sqrt{S}+1)^2} \right]. \qquad \ldots (12)$$

The inverse Laplace transform is obtained as follows :

$$L^{-1}\{p^{-1}(p^{1/2}+\beta)^{-2} e^{-ap^{1/2}}\}, \ \mathrm{Re}\,(a^2) > O$$

$$= \beta^{-2} \ Erfc \left(\tfrac{1}{2} \ a \ T^{-1/2}\right) - 2\pi^{-1/2} \beta^{-1} \ T^{1/2} \ e^{-1/4 \ a^2 T}$$

$$+ \ (2T + a\beta^{-1} - \beta^{-2}) \ e^{\,a\beta + \beta^2 T} \ Erfc \left(\tfrac{1}{2} \ aT^{-1/2} + \beta T^{1/2}\right),$$

where $Erf \ Z = \dfrac{2}{\sqrt{\pi}} \displaystyle\int_0^Z e^{-w^2} \, dw$ *and* $Erfc = 1 - Erf.$

Since, $V_m(x, t) = U_m \, e^{-T}$, we obtain the membrane potential explicitly as given by,

$$V_m(x, t) = e^{-T} \ \frac{r_1 I_0 \lambda}{8}\Bigg[\frac{4\sqrt{T}}{\sqrt{\pi}} \ e^{-\frac{X^2}{4T}} + (2T - X - 1)e^{-X+T} \left\{ 1 - Erf\left(\frac{X}{2\sqrt{T}} - \sqrt{T}\right)\right\} - (2T + X - 1) \ e^{X+T} \left\{ 1 - Erf\left(\frac{X}{2\sqrt{T}} + \sqrt{T}\right)\right\}\Bigg]$$

The values for V_m are tabulated in Tables I and II.

TABLE I

T \ X	—3	—2.8	—2.5	—2.2	—2	—1.8	—1.5	—1.2	—1	—0.5
0	1047	767	478	288	201	136.5	72	34.1	19.009	2.2
1	2074	1610	1100	749	576	441	294	193.5	146	70.6
2	3100	2454	1720	1200	953	749	501	362	281.6	150

T \ X	0	0.5	1	1.2	1.5	1.8	2	2.2	2.5	2.8	3
0	Undefined	0	0	0	0	0	0	0	0	0	0
1	21.65	14.6	5.95	4.13	2.7	1.27	0.85	0.563	0.473	0.142	.0865
2	73.4	40.8	21.8	15.5	10.02	6.46	4.85	3.74	2.35	1.46	1.168

TABLE II

X \ T	0	1	2	2.3	2.7	3.2	4	5	6	7
—2	201	576	953	1069	1213	1410	1675	2083	2498	2814
—1	19	146	281.6	323.5	376	452	548	694	845	974
1	0	5.95	21.8	29.1	33.8	42.4	56.2	74.6	94.6	112
2	0	0.85	4.85	8.77	10.02	12.1	17.3	24.3	31.6	37.7

The solution for the case when the applied current is maintained for a long time and then broken suddenly at $T = 0$ can be written down at once using the superposition theorem. They are

$$V_m = e^{-T} \frac{r_1 I_0 \lambda}{8}\left[\frac{4\sqrt{T}}{\sqrt{\pi}} e^{-\frac{x^2}{4T}} - (2T - X - 1)\, e^{-X+T} \left\{1 - Erf\left(\frac{X}{2\sqrt{T}} - \sqrt{T}\right)\right\} - (2T + X - 1)\, e^{X+T} \left\{1 + Erf\left(\frac{X}{2\sqrt{T}} + \sqrt{T}\right)\right\}\right] \text{ for } -\infty < X < O$$

and

$$V_m = e^{-T} \frac{r_1 I_0 \lambda}{8}\left[\frac{4\sqrt{T}}{\sqrt{\pi}} e^{-\frac{x^2}{4T}} + (2T - X - 1)\, e^{-X+T} \left\{1 + Erf\left(\frac{X}{2\sqrt{T}} - \sqrt{T}\right)\right\} + (2T + X - 1)\, e^{X+T} \left\{1 - Erf\left(\frac{X}{2\sqrt{T}} + \sqrt{T}\right)\right\}\right] \text{ for } O < X < \infty$$

4. DISCUSSIONS

Let us now discuss the results on membrane potentials both for make and break of current. These results are illustrated by Tables I—IV and Figs 1—4.

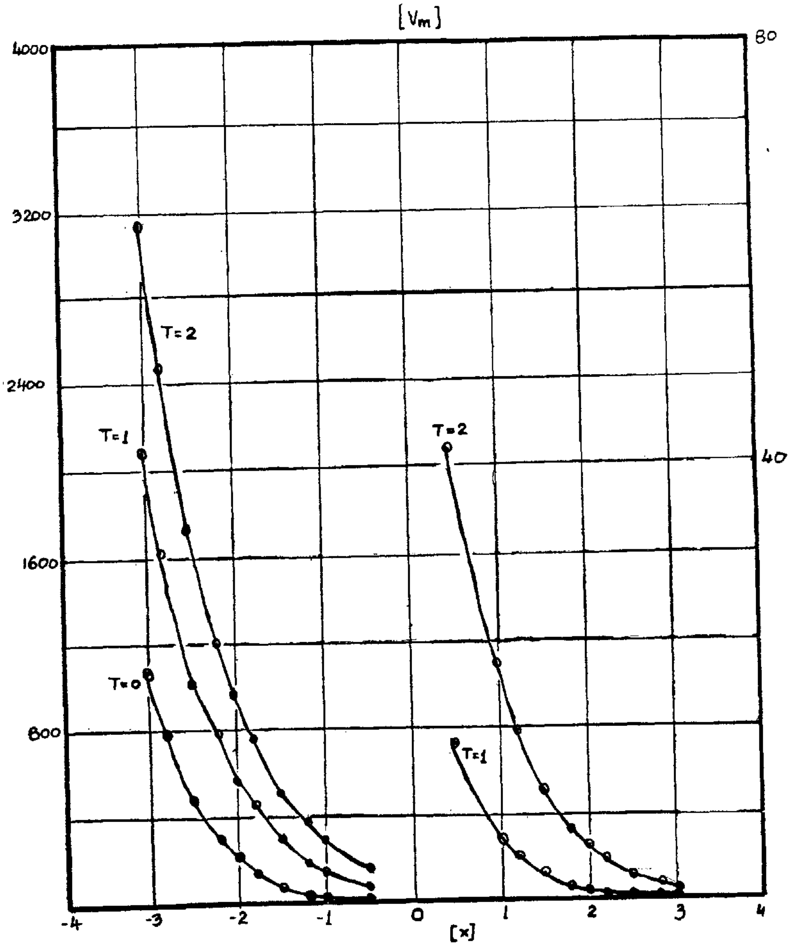

FIG. 1

TABLE III

T \ X	—3	—2.8	—2.5	—2.2	—2	—1.8	—1.5	—1.2	—1	—0.5	—0.2
0	—2065	—758	—471	—278	—189.9	—124.2	—57.6	—17.1	0	21.2	25.15
1	—2070	—1610	—1091	—738	—566	—430	—280	—178	—130	—58.2	—40
2	—3080	—2455	—1718	—1198	—945	—753	—519	—363.5	—290.5	—178	—150

T \ X	0.2	0.5	1	1.2	1.5	1.8	2	2.2	2.5	2.8	3
0	—25.3	—23.4	—18.9	—17	—14.32	—11.9	—10.4	—9.14	—7.38	—2.99	—5.09
1	14.57	13.3	10.72	9.25	6.64	4.81	3.53	2.4	0.854	0.0426	—0.407
2	9.14	5.36	7.53	7.78	7.02	5.54	5.32	4.59	3.75	2.84	2.42

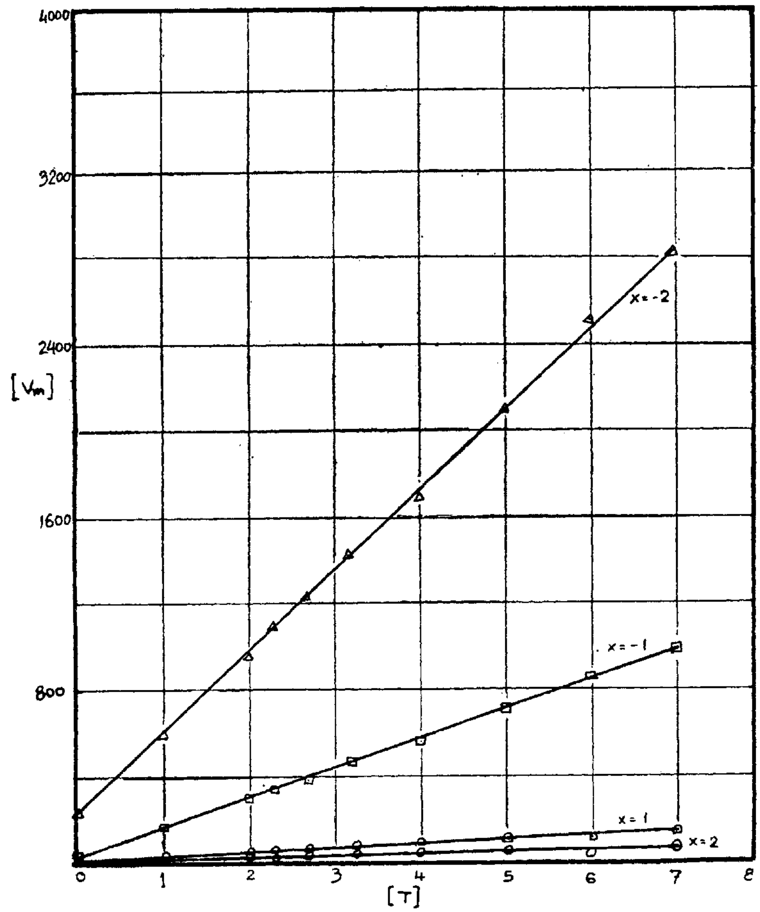

FIG. 2

TABLE IV

T \ X	0	1	2	3	4	5	6
—2	—189.9	—566	—945	—1350	—1690	—2104	—2410
—1	0	—130	—290.5	—458	—604	—768	—907
1	— 18.9	10.72	7.53	2.4	0.968	0.733	0.272
2	— 10.4	3.53	5.32	3.05	0.74	0.494	0.266

As for the make of current the disturbance-profiles represent the spatial and temporal voltage distribution on HR-axon corresponding to a current pulse stimulus. Both the tables of the corresponding V_m show some distinguishing features unlike, those observed by Hodgkin-Rushton (1946). For instance, V_m becomes imperceptible after a certain interval. While it shows a marked and rapid dimunition in values for other ranges of time, the response continues to be indeterminate at

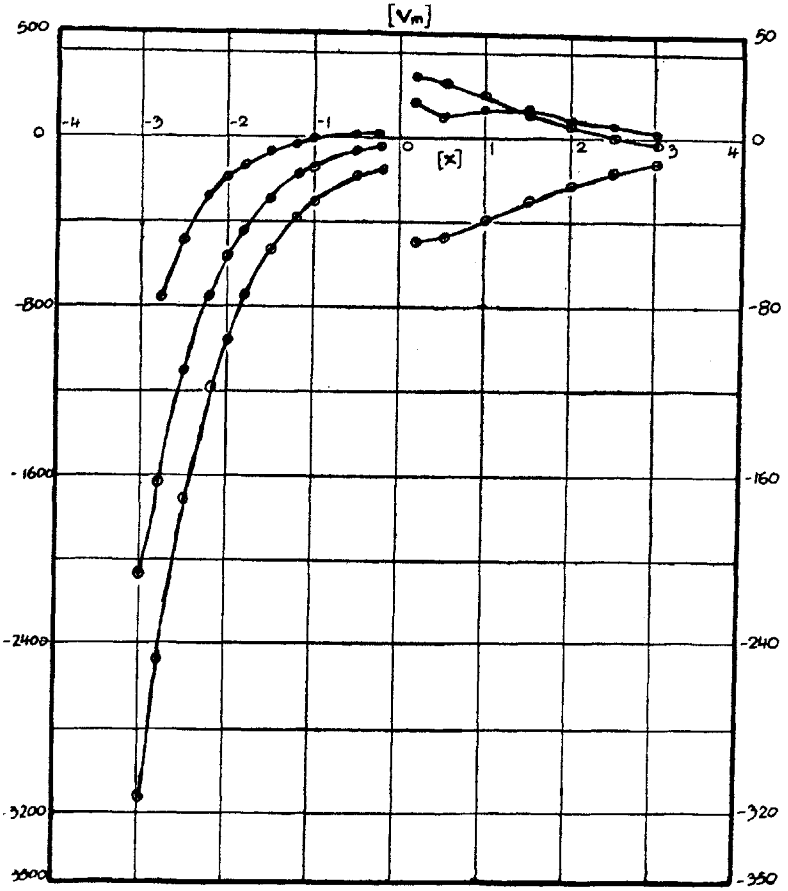

FIG. 3

$X = 0$ and for $T = 0$, as in Hodgkin and Rushton (1946). The graph shows that as we move along the axon towards the origin, the voltage distribution shows an increase. The voltage distribution preserves this property for the present kind of disturbance. Further, the rate of change of voltage distribution for lower ranges of values of time is much slower than that for higher ranges of time. With the onset of the current, the transmembrane potential shows a linear increase with time and the voltage potential shows a discontinuity after a long period without breaking the source, while it is otherwise in the case of linear spread of nerve potential, *vide*, Hodgkin and Rushton (1946).

We now turn to the case corresponding to the break of current. As the tables show, the value corresponding to $X = 0$ has not been taken into account. The responses in respect to voltage distribution are all perceptible, unlike the previous situation. Unlike the previous situation, the curves representing the voltage distribution are closely spaced. As a matter of fact the curve corresponding

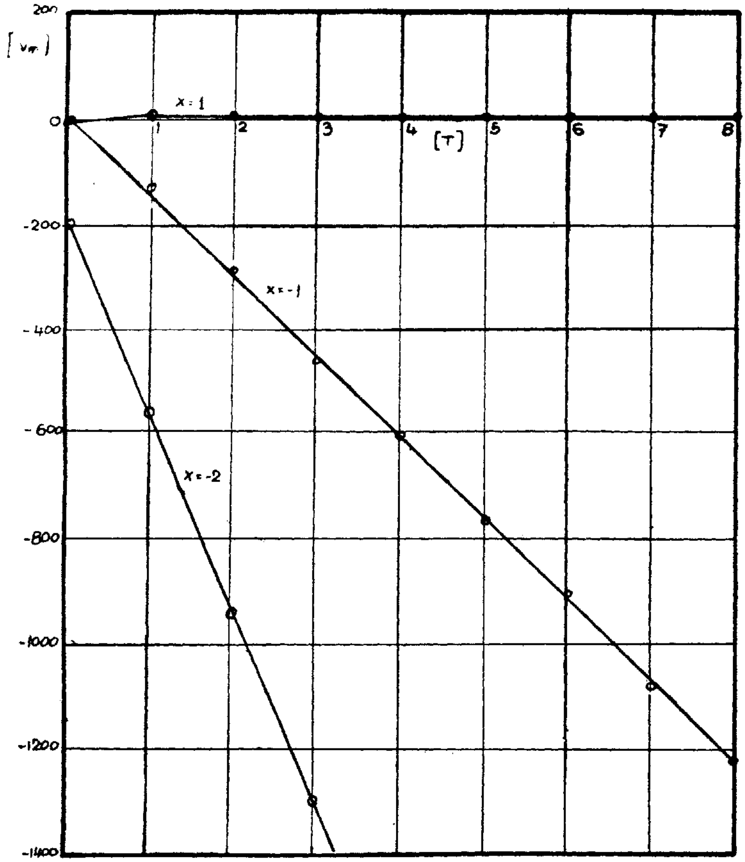

FIG. 4

to $T = 1$ and $T = 2$ intersect each other which is not the case in the previous situation. The voltage distribution decreases as we move along the axon towards the origin, for all possible forms of $\Delta''U$. For infinitely large time, the voltage distribution suffers a discontinuity, as in the previous situation, while for similar situations they tend to zero as in Hodgkin and Rushton (1946).

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