ON THE THEORY OF NERVOUS CONDUCTION

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Although we know as yet very little about the actual mechanism of the propagation of the nervous impulse, it is however generally recognized that this propagation is based on the excitation caused by the action current of the nerve itself.¹ When a nerve is stimulated by an electric current, the excitation occurs in that region, in which the current flows from the nerve, and the excited region becomes electronegative with respect to the rest of the nerve. This electronegativity of the region $E$ (Fig. 1) generates local bioelectric currents, which at $E$ flow into the nerve, but in the adjacent regions, $A$ and $B$, flow from the nerve (Fig. 1). It is assumed that this causes an excitation at $A$ and $B$ and the excitation will thus spread from $E$ in both directions.²

The tacit assumption is usually made, that this spread of the excitation occurs with constant velocity. However, to our best knowledge, no one has yet established the exact equations which should govern this process and thus justify the assumption. The mathematical treatment of this problem is the purpose of this communication.

In order to establish the desired equations we must possess a mathematical description of the laws of excitation by electric currents. This mathematical description must account for the two fundamental facts, namely:

1. For suddenly established constant currents the relation between the intensity of the current and the time which the current must act in order to cause excitation, is represented by a curve like that shown in Fig. 2; $i_0$ corresponds to the threshold value of the current, below which no excitation will occur at all.

2. If the current increases from zero sufficiently slowly, it may exceed the threshold value many times without the excitation taking place.
We shall consider two mathematical expressions, both describing these two facts. One is the formula of Hoorweg, which we shall discuss mainly because of its historical importance, and the other is a more recent expression, proposed by L. Lapique. This latter is quite arbitrary, but presents some interesting features.

According to Hoorweg, the exciting current causes the increase of a
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certain quantity \( e \), whose physical nature is not specified, and which is called "elementary excitation" (Elementarerregung). The actual excitation occurs when \( e \) reaches a certain value \( e_0 > 0 \). Hoorweg assumes:

\[
\frac{de}{dt} = i(t)e^{-\beta t}
\]  

(1)

where \( i(t) \) denotes the current, which is some function of time \( t \), and \( \beta \) is a constant. Hence:

\[
e(t) = \int_0^t i(t)e^{-\beta t} dt
\]

(2)

Formula (2) represents, at least quantitatively, the above two facts. For a current which is suddenly established at \( t = 0 \) and kept at a constant value \( i \), we have \( i(t) = i \), hence:

\[
e(t) = i \int_0^t e^{-\beta t} dt = \frac{i}{\beta} \left( 1 - e^{-\beta t} \right)
\]

(3)

Equating the right hand side of (3) to \( e_0 \) we obtain for the \( i - t \) curve the equation:

\[
i = \frac{\beta e_0}{1 - e^{-\beta i}}
\]

(4)

which is of the desired type, with \( i_o = \beta e_0 \).

For a slow linear increase of the current we have \( i = \lambda t \), which gives:

\[
e(t) = \lambda \int_0^t te^{-\beta t} dt = \frac{\lambda}{\beta} \left[ \frac{1}{\beta} \left( 1 + \frac{1}{\beta} \right) e^{-\beta t} \right]
\]

(5)

With increasing \( t \), \( e(t) \) tends asymptotically to the value \( \frac{\lambda}{\beta^2} \) and never exceeds this value. If therefore \( \lambda < \beta e_0 \) then \( e(t) \) will never reach \( e_0 \).

Now we shall establish the equations for the velocity of propagation of the nervous impulse assuming that Hoorweg's law holds for the excitation. The distribution of the currents around an excited region \( E \) (Fig. 1) will not be uniform. The current flowing from the nerve at
any point will be the weaker, the farther the considered point is away from \( E \). As to the actual distribution of the current, it will depend on the constitution of the nerve fiber and on the electrical conductivities of various parts of it. Some more or less simplifying hypothesis is therefore unavoidable. If we make the usual assumption, that the nerve consists of a comparatively better conducting core and of a worse conducting sheath, it can easily be shown that the distribution of the current around an excited region \( E \) will be exponential. That is, if \( s \) denotes the distance of a point along the nerve from \( E \) the current caused at this point by the electronegativity of \( E \) and flowing from the nerve, will be given by:

\[
i(s) = Ie^{-\alpha s}
\]

where \( \alpha \) is a constant depending on the conductivities of the sheath and the core and \( I \) is the current in the immediate neighborhood of \( E \), which also is a constant for a given nerve. If the "internal" resistance of the excited region \( E \) is small as compared with the resistance of the rest of the nerve, \( \alpha \) and \( I \) will also be independent of the size of the region \( E \) and \( s \) must be counted from its "edge" \( e \) (Fig. 3).

Let the excitation at \( E \), caused by an external exciting current, have occurred at the time \( t = 0 \). That is, the current distribution described by (6) is established at that time. In order that this bioelectric current should cause an excitation in the immediate surroundings of \( E \), \( I \) must exceed the value of \( i_0 = \beta \alpha s \). And even then it requires a finite time until the excitation in the neighborhood of \( E \) will occur. This time is found from equation (4) by putting \( i = I \). It is equal to

\[
t_1 = -\frac{1}{\beta} \log \left( 1 - \frac{\beta \alpha s}{I} \right)
\]

(\( t_1 \) is positive because the log is negative).

Hence only after this time has past from the moment of establishment of the excitation in \( E \) will this excitation begin to spread in both directions from \( E \). Since the whole phenomenon is symmetrical with respect to the original position of \( E \), we shall consider only the propagation in one direction. We shall take as origin of coordinates the point \( E \) at which the nerve is originally stimulated.
Consider any other point along the nerve, \( x_0 \). At the moment \( t = 0 \) a current

\[
i(x_0) = I_0 e^{-\alpha x_0}
\]

is established at that point (Fig. 3). But as soon as the excitation begins to spread from \( E \), the current at \( x_0 \) begins to increase, because the distance \( s \) from this point to the excited region decreases.

Let the velocity of propagation of the nervous impulse, in other words the velocity of this spread of excitation, be in general some function of time, which we shall denote by \( v(t) \). It is the shape of this function \( v(t) \) that we wish to determine.

\[
FIG. 3
\]

Since the propagation begins only at the moment \( t = t_1 \), the distance \( s \) of the point \( x_0 \) from the edge of the excited region at any time \( t > t_1 \) is given by:

\[
s = x_0 - \int_{t_1}^{t} v(t) dt = x_0 - u(t).
\]  

(8)

Hence between \( t = 0 \) and \( t = t_1 \) the current at \( x_0 \) is constant and has the value

\[
I_0 e^{-\alpha x_0},
\]  

(9)

whereas after \( t = t_1 \) the current at \( x_0 \) varies with time according to the expression:

\[
I_0 e^{-\alpha x_0 + \alpha v(t)}.
\]  

(10)
Hence the elementary excitation is given, according to (2) by:

\[ \varepsilon(t) = I e^{-\alpha x_0} \int_0^t e^{-\beta t'} dt' + I e^{-\alpha x_0} \int_0^t e^{\alpha u(t') - \beta t'} dt', \]  

(11)
or otherwise:

\[ \varepsilon(t) = I e^{-\alpha x_0} \left( K + \int_0^t e^{\alpha u(t') - \beta t'} dt' \right), \]  

(12)

where \( K \) denotes the constant quantity

\[ \int_0^t e^{-\beta t} dt = \frac{1}{\beta} (1 - e^{-\beta t}). \]  

(13)

The excitation at \( x_0 \) happens at that moment when at this point \( \varepsilon(t) \) reaches the value \( \varepsilon_0 \). Hence the equation:

\[ I e^{-\alpha x_0} \left( K + \int_0^t e^{\alpha u(t') - \beta t'} dt' \right) = \varepsilon_0, \]  

(14)

which can also be written:

\[ \frac{\varepsilon_0}{I} e^{\alpha x_0} = K + \int_0^t e^{\alpha u(t') - \beta t'} dt', \]  

(15)

will give us, when resolved with respect to \( t \), the time at which the excitation will reach the point \( x_0 \). Since we have taken the point \( x_0 \) along the nerve quite arbitrary, this means that equation (15) gives for each point the corresponding time, at which the excitation reaches that point. But this in its turn means, that if resolved with respect to \( x_0 \), equation (15) will give us the distance travelled during the time \( t \) by the excitation from the point \( x = 0 \), at which it started. But this distance is equal to:

\[ \int_0^t u(t') dt' = u(t). \]  

(16)

Hence the unknown function \( u(t) \) must be of such a form, that when the equation (15) is resolved with respect to \( x_0 \), the expression of \( x_0 \) as a function of \( t \), thus found, must be again of the form \( u(t) \). In order
to determine \( u(t) \) we must therefore substitute in (15) \( u(t) \) for \( x_0 \) and thus obtain a functional equation:

\[
\frac{e_0}{I} e^{\alpha u(t)} = K + \int_{t_0}^{t} e^{\alpha u(t') - \beta t'} dt'.
\]  

(17)

Differentiating this we have:

\[
\frac{e_0}{I} e^{\alpha u(t)} \frac{du}{dt} = e^{\alpha u(t) - \beta t}
\]

(18)

or:

\[
\frac{du}{dt} = \frac{I}{e^{\alpha t}} e^{-\beta t}
\]

(18)

with the initial condition:

\[
u(t_0) = 0.
\]

(19)

Hence:

\[
u(t) = \frac{I}{\alpha e_0} (e^{-\beta t} - e^{-\beta t_0})
\]

(20)

and, according to (16):

\[
v(t) = \frac{I}{\alpha e_0} e^{-\beta t}.
\]

(21)

We thus see that the velocity of propagation gradually drops to zero and that the distance travelled by the excitation approaches asymptotically the value

\[
\frac{I}{\alpha e_0} e^{-\beta t_0}
\]

(22)

without ever reaching this point. The physical reason for this is obvious: The farther a point is situated from the point \( x = 0 \) of the original excitation the slower will the action current at this point increase up to the necessary threshold value, because the more time will be required for the excited region to come close enough to the point in question. Therefore, according to the second fundamental fact mentioned on page 517, the excitation at such a point will never occur.
L. Lapique has however criticised Hoorweg's formula (2) and has proposed another one. Lapique imagined a hydraulic model which represents some phenomena of excitation better than Hoorweg's formula. This model is governed by a system of two differential equations.

We shall investigate now, to what conclusions about the velocity of propagation we will be led by applying Lapique's equations to our problem in a purely formal way. The question as to whether these equations can be interpreted physically will be left open. But the remarkable properties of Lapique's model make the following investigation desirable.

We now must consider two quantities, $h$ and $h'$, whose variations are governed by the following equations:

\[
\frac{dh}{dt} = -k(h - h') + i(t) \quad (23)
\]

\[
\frac{dh'}{dt} = k(h - h') \quad (24)
\]

where $k$ denotes a constant and $i(t)$ is again the exciting current.

Excitation occurs when the following equation becomes satisfied:

\[
a(p + h) = b(p + h') \quad (25)
\]

where $a$, $b$, and $p$ are other constants.

Lapique shows that for $i(t) = \text{constant}$, and with the initial condition $h = h' = 0$ for $t = 0$, equations (23) and (24) also lead to a curve of a general type represented in Fig. 2. The only difference is that now the curve actually touches the line $i = i_0$, without however intersecting it, as shown on Fig. 2 by the dotted line. He shows also that for $i = \lambda t$ no excitation occurs at all if $\lambda$ is sufficiently small.

We shall now apply equations (23), (24), and (25) to our problem. From (23) and (24) it follows:

\[
\frac{d(h + h')}{dt} = i(t) \quad (26)
\]

hence:

\[
h' = \int_0^t i(t) dt - h \quad (27)
\]
Similarly to the previous case we have here also a constant retardation time \( t_1 \). Due to the transcendency of the equations involved in the integrals of (23) and (24), \( t_1 \) cannot however be expressed in a simple form like (7) in terms of the constants \( k, a, b \) and \( \rho \). But equations (9) and (10) remain valid also in this case, so that we have:

\[
\int_0^t \theta'(t) \, dt = I e^{-a \theta_0} + I e^{-a \theta_0} e^{a \gamma(t)} \, dt =
\]

This, introduced in (28), gives:

\[
\frac{dh}{dt} + 2kh \left( 2h - \int_0^t \theta(t) \, dt \right) = i(t) = 0.
\]  

(28)

Hence, if \( C \) denotes a constant of integration:

\[
h = Ce^{-2kt} + e^{-2kt} \int_0^t I e^{-a \theta_0} \left( t_1 + \int_0^t e^{a \gamma(t)} \, dt \right) \, dt.
\]  

(31)

The function \( \theta(t) \) has the form (9) for \( t < t_1 \) and the form (10) for \( t > t_1 \). Hence the expression in the square brackets has also different forms for \( t < t_1 \) and \( t > t_1 \). If we denote these correspondingly by \( [ ]_1 \) and \( [ ]_2 \) we may write: (\( [ ]_1 \) denoting the expression in the square brackets in general)

\[
\int_0^t [ ]_1 \, dt = \int_0^{t_1} [ ]_1 \, dt + \int_{t_1}^t [ ]_1 \, dt = K_1 + \int_{t_1}^t [ ]_1 \, dt
\]

(32)

with

\[
K_1 = \int_0^{t_1} [ ]_1 \, dt \quad \text{and} \quad K_2 = K_1 - \int_0^{t_1} [ ]_1 \, dt.
\]

Since we are interested only in what happens at times \( t > t_1 \), we may take zero as lower limit in the integral in the round brackets in (31),
since this will result only in the addition of a constant to the final result and will not affect the shape of the function \( u(t) \) which we seek. Hence:

\[
h = C e^{-2kt} + e^{-2kt} \int_0^t \left[ k \left( t_2 + \int_0^t e^{\alpha u(t)} dt \right) + e^{\alpha u(t)} \right] e^{2kt} dt
\]

with

\[
t_2 = t_1 - \int_0^t e^{\alpha u(t)} dt.
\]

Transforming in a similar manner the integral in (27) we obtain for \( h' \):

\[
h' = I e^{-\alpha x_0} \int_0^t e^{\alpha u(t)} dt - C e^{-2kt} - e^{-2kt} I e^{-\alpha x_0} \times
\]

\[
\times \int_0^t \left[ k \left( t_2 + \int_0^t e^{\alpha u(t)} dt \right) + e^{\alpha u(t)} \right] e^{2kt} dt + K_3
\]

where \( K_3 \) denotes another constant.

If we now introduce (31) and (35) into (25) we obtain after some rearrangement:

\[
e^{\alpha x_0} + P \int_0^t \left[ k \left( t_2 + \int_0^t e^{\alpha u(t)} dt \right) + e^{\alpha u(t)} \right] e^{2kt} dt - Q e^{2kt} \int_0^t e^{\alpha u(t)} dt = K e^{2kt}
\]

with

\[
P = \frac{1}{C}, \quad Q = \frac{I_b}{(a + b)C}
\]

and \( K_4 \) another constant, which is algebraically expressed in terms of \( t_2 \) and \( K_3 \).

Equation (36), resolved with respect to \( x_0 \), gives now the distance travelled by the excitation as a function of time. Hence for the determination of \( u(t) \) we must again put in (36) \( u(t) \) for \( x_0 \) and thus obtain:

\[
e^{\alpha u(t)} + P \int_0^t \left[ k \left( t_2 + \int_0^t e^{\alpha u(t)} dt \right) + e^{\alpha u(t)} \right] e^{2kt} dt -
\]

\[
Q e^{2kt} \int_0^t e^{\alpha u(t)} dt = K e^{2kt}.
\]
Introducing now a new variable:

$$y(t) = e^{\alpha u(t)} \quad (39)$$

and differentiating (38) we obtain:

$$\frac{dy}{dt} + P \left[ k \left( h + \int_0^t y \, dt \right) + y \right] e^{2kt} - Q \left( y + 2k \int_0^t y \, dt \right) e^{2kt} = R e^{2kt} \quad (40)$$

with

$$R = 2kK.$$  

If we now put:

$$\int_0^t y \, dt = z, \quad y = \frac{dz}{dt}, \quad (42)$$

we obtain after some calculations:

$$\frac{d^2 z}{dt^2} + \left( P - Q \right) e^{2kt} \frac{dz}{dt} + k(P - 2Q)e^{2kt} z = \left( R - P k t_0 \right) e^{2kt}. \quad (43)$$

When $z$ is determined from (43) then we obtain also $u(t)$ from (42) and (39), and all the arbitrary constants involved will be determined by the requirement that for $t = 0$ at all points of the nerve we must have $h = h_1 = 0.$

Although the general integral of (43) is not known, we see that for very large $t$ (43) reduces to

$$\frac{dz}{dt} + Az = B \quad (44)$$

with

$$A = k \frac{P - 2Q}{P - Q}; \quad B = \frac{R - P k t_0}{P - Q}. \quad (45)$$

Since Lapicque assumes that always $b > a$, we see that $A < 0$. Hence the solution of (44) for very large $t$ has the form:

$$z = \text{Const}. \cdot e^{\xi t}, \quad \xi = A. \quad (46)$$

This gives for $u(t)$:

$$u(t) = \text{Const}. + \xi t, \quad (47)$$
and for the velocity of propagation $v(t)$:

$$v = \epsilon t.$$

We thus see that in this case the velocity tends asymptotically to the constant value $\epsilon^2$. How rapidly, or in other words, how far from the point of initial stimulation this asymptotic value will be sufficiently closely approached depends upon the values of the constants in Lapique's equations.

**SUMMARY**

Assuming that the propagation of the nervous impulse consists in the excitation of adjacent regions of the nerve by the action current of the already excited region, exact equations for the velocity of such a propagation are established and integrated. The result depends on the assumptions which we make about the laws of excitation. If Hoorweg's law is accepted, it is found that the velocity of propagation decreases exponentially with time, and that there is a limiting distance which the impulse will travel and which cannot be exceeded. If however a set of equations proposed by L. Lapique is assumed to govern the process of excitation, we find that the velocity of propagation asymptotically reaches a constant value.

**CITATIONS**