

ON THE PROPAGATION OF EXCITATION IN AN ELECTROCHEMICAL DIFFUSION MODEL OF A NERVE

(O RASPROSTRANENII IMPUL'SA VOZBUZHDENIIA V
ELEKTROKHEMICHESKOI DIFFUZIONNOI MODELI NERVA)

PMM Vol.29, № 6, 1965, pp.977-992

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(Received July 21, 1965)

The problem of propagation of excitation along a nerve is of considerable interest and has drawn the attention of many investigators. The difficulties in the treatment of this problem arise mainly from the indefiniteness and unclear nature of physico-chemical processes which accompany and stipulate these phenomena.

A detailed presentation of the current state of knowledge of this subject can be found in a recent book of Hodzhkin [1].

As a certain model of the process for the propagation of an impulse along a nerve, Ostvald and later Bonhoeffer [2 and 3] suggested a simple electrochemical system.

In the present paper the above-mentioned system is used to develop a mathematical investigation of the impulse propagation process. The mathematical scheme of this phenomenon is based on ideas introduced by Bonhoeffer and his school concerning electrochemical processes which ensure the propagation of an impulse.

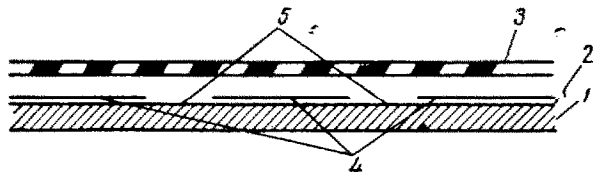


Fig. 1

The system under consideration consists of a ferris string (1) placed in a capillary (3) filled with concentrated nitric acid (2), Fig.1. Two processes result from the interaction of nitric acid and iron. These are dissolution of iron manifesting in the departure of

ions to the solution and oxidation of iron which results in forming a dense film of ferric oxide (4) on the string surface. If the concentration of nitric acid is sufficiently strong the latter process becomes predominant. Since the oxide film prevents the process of dissolution from continuing, a state of equilibrium is set up in which processes of dissolution and oxidation practically cease. The oxide film is spread over the entire surface of iron and the potential difference between the iron and solution assumes a constant value.

This state of iron is called a "passive" state and the process of transition into this state is termed "passivation". If the potential difference is artificially decreased to a certain limiting value, then the oxide film will be destroyed and iron will pass to the active state characterized by the vigorous oxidation process. Simultaneously nitric acid is generated

with an essential influence on the run of the process. In the equilibrium state the whole iron surface is covered by oxide film.

Let us assume that the film has been artificially destroyed over a certain region of the string. Since the oxide film has a high electrical resistance, the current flows into the destroyed surface. Consequently, the difference between the potentials of the iron and the solution diminishes. If the dimensions of the destroyed area are sufficiently large, the drop in the potential difference will be so pronounced that even on the string surface still covered by oxide film, the potential difference reaches its limiting value. This in turn will cause vanishing of the oxide film in the vicinity of the initially destroyed area and the front of the disturbance starts to move in both directions along the string surface. However, during an active state of the surface, the string will not be completely dissolved mainly because of the and increase of concentration of nitric acid. The newly created oxide coating will eventually lead to the passivation process, hence the passivation front propagates in both directions behind the activation front. In this way two disturbances propagate in opposite directions along the string surface (sections 5 in Fig.1).

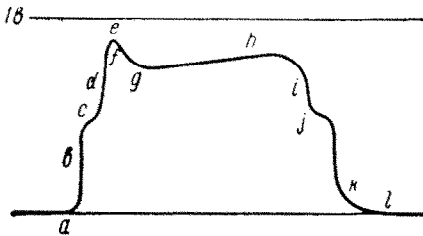


Fig. 2

The pulse advancing is recorded by measuring the differences in potentials ϕ between the solution and iron. A typical plot of the dependence of ϕ upon time t is shown in Fig.2, taken from the paper [4].

Experiments [2 and 3] have proved that the pulse becomes stationary and propagates with constant velocity without distortion in a short time after the initiation of the process. In the following the theory of propagation of the stationary pulse associated with

generation and absorption of energy will be considered.

1. Statement of the problem and basic equations. 1°. According to the assumption of Bonhoeffer and his school, the following processes take place on the boundary between iron and solution:

- 1) Dissolution of iron on the active surface.
- 2a) Formation of an oxide coating transferring the active surface into the passive.
- 2b) Disintegration of the oxide coating transferring the passive surface into the active.
- 3a) Generation of nitric acid on the active surface.
- 3b) Generation of nitric acid on the passive surface.

Each of these processes is characterized by the density of electric current j (positive or negative), which is proportional to the amount of conveyed substance. This amount depends upon the local value of the potential difference ϕ between the iron and the solution. The above-mentioned relationship is shown in the diagram, the original version of which, [4], differs slightly from the presented here in Fig.3. The difference in potentials is measured with reference to the equilibrium state corresponding to the entirely passive state (the unity on the current axis corresponds to 0.65 A/cm^2 and the currents j_{3a} and j_{3b} are displayed out of scale). The generation process of nitric acid is autocatalytic, i.e. its rate depends on the poten-

tial difference φ as well as on the concentration c of nitric acid within the boundary layer. For sufficiently weak concentrations the latter dependence can be assumed as a linear function. Therefore the current density, shown in Fig.3, corresponds to the unit concentration. The true value of current density is obtained from curves j_{3a} and j_{3b} (Fig.2), through a multiplication by a local value of boundary layer concentration of nitric acid.

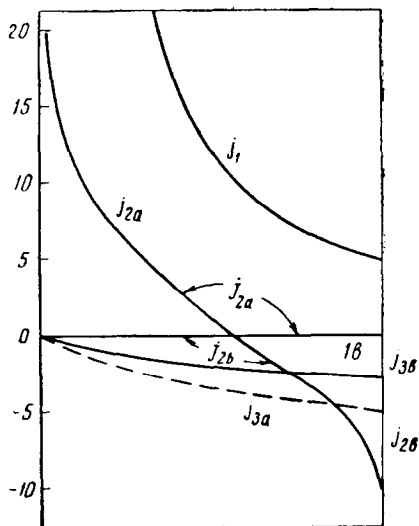


Fig. 3

During the interchange of active and passive processes intermediate states are also possible where the string surface is partly covered by oxide coating. There are indications that the oxide film is generated or destroyed at once through its entire thickness [3].

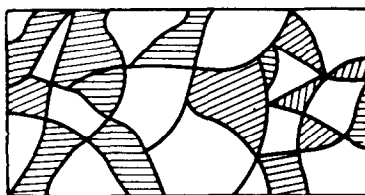


Fig. 4

Assuming this as a hypothesis, the complete description of the state of the surface at a given string point can be obtained in terms of a rate of activation α which is a relative area of activation regions. (It is assumed that a physically infinitesimal element of the surface involves a sufficiently large number of active and passive regions, as shown in Fig.4 by white and shaded areas).

The rate of transport of substance on the surface in the course of any reaction is proportional to the corresponding current density. Therefore, in a unit time, the fraction of surface $K\alpha j_{2a}$, is converted from the active to the passive and the fraction $K(1 - \alpha)|j_{2b}|$ from the passive state to the active. The rate of increase in the share of active surface can thus be expressed [4] as

$$\frac{\partial \alpha}{\partial t} = -K[\alpha j_{2a} + (1 - \alpha)j_{2b}] \tag{1.1}$$

Since the current can flow into the string surface solely from the solution, therefore, assuming the electric conductivity σ as a constant, we have for the total density the following expression:

$$-\sigma \left(\frac{\partial \varphi}{\partial r} \right)_{r=r_0} = \alpha(j_1 + j_{2a}) + (1 - \alpha)j_{2b} + [\alpha j_{3a} + (1 - \alpha)j_{3b}]c \tag{1.2}$$

where r_0 denotes the string radius in the cylindrical coordinate system (r, φ, z) and the z -axis coincides with the axis of capillary, r is the distance from the latter.

The nitric acid produced in the course of reactions diffuses into the solution. The rate of generation of acid is proportional to the total density of current $j_3 = [\alpha j_{3a} + (1 - \alpha) j_{3b}] c$. Thus, the expression for the flux of nitric acid on the string surface has a form

$$D \left(\frac{\partial c}{\partial r} \right)_{r=r_0} = \beta c [\alpha j_{3a} + (1 - \alpha) j_{3b}]_{r=r_0} \quad (1.3)$$

where D stands for the coefficient of diffusion, and β denotes a proportionality coefficient.

In order to obtain a full system of equations, it remains to write down equations for the distribution of potential φ and concentration of nitric acid C in the solution as well as the boundary conditions on the capillary wall. The distribution of potential φ satisfies the Laplace equation, which in view of axial symmetry of the problem, has the form

$$\frac{\partial^2 \varphi}{\partial r^2} + \frac{1}{r} \frac{\partial \varphi}{\partial r} + \frac{\partial^2 \varphi}{\partial z^2} = 0 \quad (1.4)$$

For distribution of concentration $C(r, z, t)$ is described by the equation of diffusion

$$\frac{\partial C}{\partial t} = D \left(\frac{\partial^2 C}{\partial r^2} + \frac{1}{r} \frac{\partial C}{\partial r} + \frac{\partial^2 C}{\partial z^2} \right) + q(C) \quad (1.5)$$

where $q(C)$ denotes the rate of absorption of nitric acid in the volume of solution in the course of certain auxiliary reactions. The significance of these reactions consists in the supporting of concentration on a specified level c_0 in the absence of impulse. Hence, the function $q(C)$ should satisfy the following conditions:

$$q(c_0) = 0, \quad q(C) < 0 \quad \text{for } C > c_0, \quad q(C) > 0 \quad \text{for } C < c_0$$

In practice, the above mentioned reactions are accomplished by adding to the solution a definite amount of urea.

Assuming the capillary wall as impermeable and electrically insulated, the boundary conditions on the wall take the form

$$\frac{\partial \varphi}{\partial r} = 0, \quad \frac{\partial C}{\partial r} = 0 \quad \text{for } r = R \quad (1.6)$$

where R is the capillary radius.

Thus, the solution for potential φ and nitric acid concentration C can be determined by considering Equations (1.4) and (1.5), boundary conditions on the capillary wall (1.6) and also Formulas (1.1) to (1.3) which after elimination of α yield two differential conditions relating values of φ and $C = c$ on the string surface. It should be mentioned that these boundary values of φ and c are of particular interest in the problem under consideration.

2°. In the following, we shall consider the solution of the derived equations, corresponding to the condition of uniform steady propagation of a single pulse of excitation. For a pulse travelling to the left with constant velocity w this means that quantities φ , α and C depend upon the argument $\zeta = z + wt$, but not upon z and t , separately

$$\varphi = \varphi(\zeta, r), \quad C = C(\zeta, r), \quad c = c(\zeta), \quad \alpha = \alpha(\zeta) \quad (1.7)$$

Ahead and behind the impulse, the surface undergoes a passive state, hence, $\alpha(\pm \infty) = 0$. Since the excitation propagates along the undisturbed, passive state of string, the following relation holds:

$$\varphi(-\infty, r) = 0, \quad C(-\infty, r) = c_0 \quad (1.8)$$

The mathematical problem formulated in this way is overdetermined, and for arbitrary value of w does not have in general a nontrivial solution. The requirement of the existence of nontrivial solution provides the condition for the determination of pulse velocity w , which is found as an independent result in the course of solution of the problem. This situation is also characteristic for the theory of propagation of gene of Kolmogorov, Petrovskii and Piskunov [5], and for the theory of flame propagation of Zel'dovich [6]. There exists a deep internal relation between these problems and that considered in the present paper, as will be shown later.

3°. For the complete solution of the problem, it would be necessary to determine the range of parameters in which the required form of the solution exists (this corresponds to the known "range problem" in the theory of flame propagation). That complicated problem is beyond the scope of the present paper.

2. Uniform propagation of impulse. In view of (1.7), the basic system of Equations (1.1) to (1.6) and (1.8) describing a uniform propagation of pulse to the left, with velocity w , take the form

$$w \frac{d\alpha}{d\zeta} = -K [\alpha j_{2a} + (1 - \alpha) j_{2b}] \quad (2.1)$$

$$-\sigma \left(\frac{\partial \varphi}{\partial r} \right)_{r=r_0} = \alpha (j_1 + j_{2a}) + (1 - \alpha) j_{2b} + [\alpha j_{3a} + (1 - \alpha) j_{3b}] c \quad (2.2)$$

$$D \left(\frac{\partial C}{\partial r} \right)_{r=r_0} = \beta c [\alpha j_{3a} + (1 - \alpha) j_{3b}] \quad (2.3)$$

$$\frac{\partial^2 \varphi}{\partial \zeta^2} + \frac{\partial^2 \varphi}{\partial r^2} + \frac{1}{r} \frac{\partial \varphi}{\partial r} = 0 \quad (2.4)$$

$$w \frac{\partial C}{\partial \zeta} = D \left(\frac{\partial^2 C}{\partial \zeta^2} + \frac{\partial^2 C}{\partial r^2} + \frac{1}{r} \frac{\partial C}{\partial r} \right) \quad (2.5)$$

$$\frac{\partial \varphi}{\partial r} = 0, \quad \frac{\partial C}{\partial r} = 0 \quad \text{for } r = R \quad (2.6)$$

$$\varphi(-\infty, r) = 0, \quad C(-\infty, r) = c_0, \quad \alpha(\pm \infty) = 0 \quad (2.7)$$

Let us assume that the clearance δ between the string and capillary wall is sufficiently small so that the change in the potential over the clearance thickness can be neglected. The value of the potential on the string boundary can thus be replaced by the mean value of the potential over the clearance surface.

This assumption together with (2.2) yields

$$-\sigma\delta \frac{d^2\varphi}{d\zeta^2} = \alpha(j_1 + j_{2a}) + (1 - \alpha)j_{2b} + [\alpha j_{3a} + (1 - \alpha)j_{3b}]c \quad (2.8)$$

where the previous notation for φ is maintained. Thus, the problem of uniform propagation of pulse has been reduced to the solution of Equations (2.1), (2.8) and (2.5) with the boundary conditions (2.3) and (2.7) and the second condition (2.6), (recall $c(r_0, \zeta) = c(\zeta)$).

In the following, we shall be concerned with the problem of existence of the solution, which satisfies all conditions listed above, and has the form of a uniformly propagated pulse. In the present paper, the qualitative analysis of characteristic singularities in the potential distribution will be also given.

3. Propagation of the activation front and conditions of impulse existence. 1°. Qualitative investigation of the governing system. Finiteness of activation front velocity. We shall start with the proof that the velocity of activation front is always finite. At the pulse front $\zeta = 0$, the potential φ reaches the limiting value, whereas for all points ahead the front of excitation $\alpha = 0$. Indeed, for $\zeta \rightarrow -\infty$, we have $\varphi \rightarrow 0$ and $\alpha \rightarrow 0$, according to the boundary condition (2.7). Consequently, for sufficiently large absolute value of ζ , the following inequality should hold $\frac{d\alpha}{d\zeta} \geq 0$. At the same time $\varphi < \varphi_*$ and, hence, $j_{2b} = 0$, whereas $j_{2a} > 0$. Therefore, Equation (2.1) can be satisfied only if $\alpha \equiv 0$. The activation ratio α becomes variable for all $\zeta > 0$, i.e. everywhere to the right of the limiting point φ_* .

2°. The second boundary condition for the potential. According to boundary condition, the surface activation ratio should drop to zero for $\zeta \rightarrow +\infty$. It follows from Equation (2.1), that in this case the current density j_{2b} vanishes, what implies the condition \sim . It can be shown that under the natural requirements of finiteness of the potential, φ tends to zero with $\zeta \rightarrow +\infty$. Indeed, if $\zeta \rightarrow \infty$, by virtue of (2.8) φ cannot continue to exceed certain fixed, arbitrary small value, since this would imply the unboundedness of φ . Among the integral curves of (2.8) passing through the region of sufficiently small φ , there is one curve passing through the origin $\varphi = 0$, (see [7]), Chapter XIII, Section 4, Theorem 4.1). Finally, the curves passing through the region of small φ will never return back to that region according to Equation (2.8) and condition $\alpha \rightarrow 0$. Therefore, the second boundary condition for the distribution of potential has been derived from the single assumption concerning the boundedness of potential φ

$$\varphi(+\infty) = 0 \quad (3.1)$$

3°. Basic equation for the potential in the case of slowly variable nitric acid concentration. Eliminating α from (2.1) and (2.8),

we obtain

$$\sigma\delta(A + A_1)\varphi'' - \frac{wB}{K}\varphi' - \frac{w\sigma\delta E}{K}\varphi''\varphi' = X - \frac{w\sigma\delta}{KJ}\varphi''' + \frac{w}{K}S\frac{dc}{d\zeta} \quad (3.2)$$

where

$$A = \frac{j_{2a} - j_{2b}}{J} > 0, \quad B = -\frac{J_b J - J' J_b}{J^2} > 0, \quad E = \frac{J'}{J^2} < 0$$

$$X = j_{2b} - AJ_b, \quad J = j_1 + j_{2a} - j_{2b} + (j_{3a} - j_{3b})c, \quad J_b = j_{2b} + j_{3b}c \quad (3.3)$$

$$S = -\frac{j_{3b}J - (j_{3a} - j_{3b})J_b}{J^2}, \quad A_1 = -\frac{w}{K}(j_{3a} - j_{3b})\frac{dc}{d\zeta}$$

and a dot denotes differentiation with respect to φ for constant c . As it is seen from Equation (2.3), for small values of $\kappa = \beta/D$, the rate of change of nitric acid concentration is small. Thus, the term with $dc/d\zeta$ in (3.2) can be neglected, to give

$$\sigma\delta A\varphi'' - \frac{wB}{K}\varphi' - \frac{w\sigma\delta E}{K}\varphi''\varphi' = X - \frac{w\sigma\delta}{KJ}\varphi''' \quad (3.4)$$

It should be emphasized that the latter equation does not become self-contained in the case $\kappa \neq 0$. The coefficients in this equation depend on ζ through the slowly variable function $c(\zeta)$. The full system of governing equations involves Equation (3.4), appropriate equation describing the concentration of nitric acid together with corresponding boundary conditions. In the following, considerable attention will be given to Equation (3.4) which is the basic equation for all further results. The reason why Equation (3.4) can be considered independently is that under a slow change in nitric acid concentration, the character of this change is not important.

4°. Necessity for the account of the production of nitric acid. Nevertheless the change in nitric acid concentration cannot be entirely neglected (by assuming $\kappa = \beta/D = 0$). It will be shown that if the concentration is assumed to be constant, no impulse-type solution exists.

In the case of $\kappa = 0$ and $\zeta < 0$ the problem reduces to the solution of the following equation:

$$-\sigma\delta\frac{d^2\varphi}{d\zeta^2} = j_{3b}c, \quad c = c_0 \equiv \text{const} \quad (3.5)$$

with boundary conditions

$$\varphi(-\infty) = 0, \quad \varphi(0) = \varphi_k \quad (3.6)$$

(Equation (3.5) has been derived from (2.8) by putting $\alpha \equiv 0$ and $j_{2b} = 0$ for $\varphi < \varphi_k$). The existence and uniqueness of the solution of the latter problem can be proved by means of direct integration.

For $\zeta > 0$ Equation (3.4) is an exact equation and its coefficients do not depend on ζ . The boundary conditions for Equation (3.4) can be obtained from the requirements of continuity of φ and α for $\zeta = 0$, they are:

$$\varphi(+0) = \varphi(-0) = \varphi_k, \quad \varphi'(+0) = \varphi'(-0), \quad \varphi''(+0) = \varphi''(-0) \quad (3.7)$$

where $\varphi'(-0)$ and $\varphi''(-0)$ are independent on w and are determined from the solution of problem (3.5) and (3.6).

The problem described by (3.4), (3.1) and (3.7) is overdetermined since there are four conditions for the third order differential equation. This circumstance gives a possibility to determine the unknown velocity of pulse propagation.

It will be shown that the range of possible velocities of pulse propagation is bounded. Assume the converse. In the course of the process of pulse propagation, the value of potential φ necessarily attains the maximum. Consider an inflection point ζ^* on the extreme left of the diagram $\varphi(\zeta)$ where $\zeta > 0$. According to the definition, $\varphi = \varphi_x$ for $\zeta = 0$, whereas within the range $0 < \zeta < \zeta^*$, the function φ , together with its first derivative φ' , increase and the second derivative φ'' tends simultaneously to zero. Finally, the value $\varphi'(0)$ is independent on velocity w . These statements are in contradiction with Equation (3.4) written down at the point of inflection.

Since the range of admissible pulse velocities is bounded, it is always possible to find such a relation between parameters that the coefficient of third derivative term in Equation (3.4) is small for all velocities from the considered range.

Let us show that under the latter assumption, the problem (3.4), (3.1) and (3.7) has no solution (i.e. the pulse does not exist) if the mechanism of production of the nitric acid is off.

Since the coefficient of the third derivative term has been assumed to be small, Equation (3.4) becomes in some sense a second order equation. It is convenient to change variables $p = d\varphi / d\xi$ and $\xi = \zeta / \sqrt{\sigma\delta}$ and consider behavior of integral-curves on the plane (p, ξ) . Equation (3.4) in new variables takes the form

$$p \frac{dp}{d\varphi} (A - \omega E p) = X + \omega B p - \lambda p \frac{d}{d\varphi} \left(p \frac{dp}{d\varphi} \right) \quad (\omega = w / K \sqrt{\sigma\delta}, \lambda = \omega / J) \tag{3.8}$$

Consider first a simplified equation without the second term in the right-hand side of Equation (3.8). This is a first order equation and the phase diagram for that equation is shown in Fig.5.

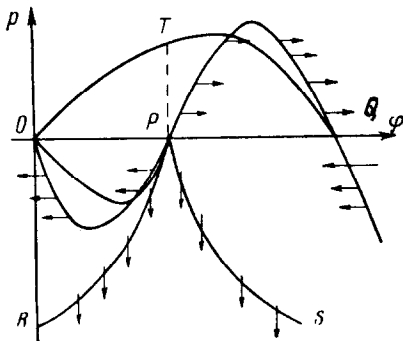


Fig. 5

The point T on the phase diagram corresponds to $\xi = 0$ and its position does not depend on w . (The curve OT relates to the solution of the problem (3.5), (3.6)). The curve representing a desired solution should follow the directional field on the path from T to O . It is seen from Fig.5 that in the case of simplified equation, this cannot occur. The situation will not be changed if an account is made for the small, disregarded third derivative term, i.e. if a full equation (3.8) is considered.

Indeed, the sought trajectory of the considered point should necessarily intersect the φ -axis within a defined distance right of the point P . This follows from the fact that the trajectory passing through T has a positive slope and, as can be shown, the tangent of trajectory is vertical nowhere except on the φ -axis. (The last statement is true for arbitrary trajectory corresponding to the full equation). It is easy to see that the representative point after having intersected the φ -axis should necessarily depart from this axis by a finite distance, (otherwise the second derivative term can be neglected in (3.8) which is not consistent with the behavior of curves describing the solution of simplified equation).

The zero isoclinic of the simplified equation is given by Formula

$$p = -\frac{1}{\omega B} X \quad (3.9)$$

Above this line, trajectories of the full equation cannot have a maximum and below this line a minimum. Indeed, the condition for a maximum requires $p' = 0$ and $p'' \leq 0$, whereas Equation (3.8), written down for example at a point above the line (3.9), gives the converse.

Thus, if the sought integral curve intersects the segment PQ (including also point Q), it should also intersect the line PS within a defined distance from the point P . This is true since the point P cannot be approached by the trajectory at an arbitrary small distance. However, if the representative point approaches the point of intersection with the isoclinic of infinity, the slope of trajectory increases until the term with second order derivative becomes significant, preventing the slope of the trajectory to be vertical.

On the line PS , the slope of the trajectory assumes a large positive value if the coefficient of the second derivative term in (3.8) is sufficiently small. Furthermore, the trajectory can approach the line PR only from below of the point of intersection with PS since otherwise there would be a minimum between PR and PS but this cannot occur. Finally, there exists such a strip enclosing the line PR that its width tends to zero with the second derivative of (3.8). Inside the strip, the trajectory has a large negative slope. Indeed, as previously, the trajectory cannot surpass a finite distance within the strip. Consequently, the trajectory is advanced within the strip by the distance of the order of strip width.

Inside the strip Equation (3.8) simplifies to give

$$\frac{\omega}{2J} \frac{d^2(p^2)}{d\varphi^2} = \frac{X + \omega B p}{p} + \dots \quad (3.10)$$

where the right-hand side can now be regarded as constant. Taking into account that the coefficient of the second derivative term is small, we come to the desired result.

Thus, the trajectory intersecting lines PS and PR should have a large positive slope near PS and large negative slope near PR . However, this is not possible since below the line (3.9) the trajectory cannot attain a

minimum.

We shall prove now that an integral curve corresponding to the impulse cannot meet the φ -axis to the right of the point O . Indeed, suppose the φ -axis has been intersected to the left of the point Q . It is now possible for the representative point to follow the directional field of the simplified equation after having passed through the narrow strip surrounding φ -axis. This would be no longer possible in the case when the location of intersection point is to the left of the point Q . Now, the directional field is pointed opposite to the motion of the representative point, thus preventing the trajectory from leaving the narrow strip surrounding the φ -axis where the second derivative is essential. The arguments advanced imply that the sought integral curve cannot remain within the strip all the time.

This completes a proof that no pulse of excitation is possible for $\kappa = 0$.

4. Construction and qualitative analysis of the impulse-type solution.

1°. General considerations. The proof given above not only provides a confirmation of nonexistence of the pulse excitation in the case when the mechanism of change in nitric acid concentration is absent, but also indicates the nature of this mechanism.

Let us assume that κ is small, although not zero. Then concentration c of nitric acid becomes variable, Equation (3.4) is no longer self-contained and the phase diagram, Fig.5, loses its stationary character and changes slowly.

In particular, the saddle point O moves to the left until it reaches the point P (*). This makes possible that the trajectory returns to the origin.

Since the change in the concentration of nitric acid is slow, the derived results, concerning the trajectories of the representative point, remain valid everywhere except the small neighborhood of singular points P and Q . The motion of the representative point is slowed down so that the velocity of the saddle O , resulting from the variation in concentration c , becomes comparable with the velocity of the representative point. In order to return to the origin, the representative point should fall within a small neighborhood of the moving saddle and then together with the neighborhood of O approach the singular point P . This is possible solely in the case of non-constant concentration of nitric acid.

Besides the small parameter κ determining the rate of change of concentration of the nitric acid, there is another small parameter λ . This is the coefficient in the term with the highest derivative in Equation (3.8).

*) For sufficiently slow absorption intensity q and diffusion coefficient, the increasing concentration c will exceed this value for which Q coincides with P .

Equation (3.8) in the immediate neighborhood of an arbitrary regular point (φ_1, p_1) , on the plane φ, p , can be written in the form

$$\lambda_1 z' + \left(\frac{A_1}{p_1} - \omega E_1 \right) z = \omega B_1 + \frac{X_1}{p_1}, \quad z = p \frac{dp}{d\varphi} \quad (4.1)$$

where the subscript 1 denotes the value of corresponding coefficient at the point $\varphi = \varphi_1$ and $p = p_1$.

The solution of Equation (4.1) is expressed as

$$z = \frac{X_1 + p_1 B_1 \omega}{A_1 - p_1 E_1 \omega} + C \exp \left[- \frac{(A_1 - \omega p_1 E_1)}{\omega p_1} J_1(\varphi - \varphi_1) \right] \quad (4.2)$$

where C is a constant of integration. The first term in Formula (4.2) corresponds to the solution of simplified equation with $\lambda = 0$, whereas the second term represents a correction which may increase or decay exponentially depending upon the sign of coefficient

$$(A_1 - \omega p_1 E_1) / \omega p_1 \quad (4.3)$$

and the direction of change in φ .

2°. Construction of the solution. The solution of the problem (3.5), (3.6) is independent of the value ω over the part OT of the trajectory. Since the concentration of nitric acid varies slowly, the quantity σ can be regarded as constant and equal to σ_0 . Now, the problem is to separate one trajectory which corresponds to all prescribed conditions of impulse propagation. Assuming variable concentration of nitric acid, let us examine a possible motion of the representative point along the part of the trajectory, behind the point T . Inside the quadrant TPQ the quantity (4.3) is positive. Simultaneously φ increases and the correction for the trajectory, resulting from the consideration of full equation (second term in Equation (4.2)), tends to zero. Hence, the further motion follows the trajectory of simplified equation corresponding to $\lambda = 0$. This property remains valid even after the intersection of this trajectory with the φ -axis, since simultaneously coefficient (4.3) changes its sign and the direction of change of φ becomes reversed. Thus, the preliminary construction of impulse trajectory can be based upon the simplified equation.

Since the rate of change of concentration, and consequently the velocity of saddle Q are small, there exists such an interval of ω that all trajectories passing through T intersect the φ -axis left of the point Q . Each value of ω uniquely determines the distribution of concentration $\sigma(\zeta, \omega)$. The computation of the nitric acid distribution can be simplified by the replacement of function J_0 by the finite function, vanishing for $|\varphi| > N$, where N is a sufficiently large number. Clearly, the latter assumption will distort only those trajectories which do not correspond to the impulse.

Let us denote by $\zeta_*(\omega)$ the value of ζ , corresponding to the first intersection of trajectory with the φ -axis under given ω . The sought solution of the boundary value problem, for the simplified equation (3.4), should conform to conditions

$$\varphi(\infty) = \varphi_k, \quad \varphi'(\zeta_*) = 0 \quad (4.4)$$

The coefficients in Equation (3.4) can be determined using the appropriate distribution of $\sigma(\zeta, \omega)$. In the limiting case $\kappa \rightarrow 0$ the solution of the formulated boundary value problem should approach the function $\varphi = \varphi_0(\zeta)$, where φ_0 denotes the coordinate of saddle Q . The condition of smoothness implies that for small positive κ the solution should close to the value $\varphi_0(\zeta)$. Thus, the simplified equations and corresponding boundary conditions can be written in the form

$$A\psi'' - B\omega\psi' - X_1\psi = O(\varphi_0', \varphi_0'') + o(\psi, \psi', \psi'') \quad (\psi = \varphi - \varphi_0) \quad (4.5)$$

$$\psi(\infty) = 0, \quad \psi'(\zeta_*) = -\varphi_0'(\zeta_*) \quad (4.6)$$

According to the assumptions concerning the finiteness of J_3 , the derivatives φ_0' and φ_0'' uniformly tend to zero with $\kappa \rightarrow 0$, and the first term in the right-hand side of Equation (4.5), (a forcing term), can be made arbitrarily small. The characteristic equation corresponding to Equation (4.5) has always one positive and one negative root. Neither of them vanish as ζ varies. This implies that the simplified equation (4.5) without the source term has always a solution ψ_0 , which uniformly tends to zero with $\zeta \rightarrow \infty$. (This statement is a generalization of corresponding theorem proved in [7], Chapter 13, for the case of constant coefficients).

The solution of Equation (4.5), satisfying condition (4.6), can be expressed in terms of the Green function which decays exponentially at infinity.

From the exponential decay of the Green function, it follows that the quantity ψ should tend uniformly to zero with diminishing amount of disturbance, i.e. with deceleration of increase in the concentration of nitric acid.

An additional consideration of nonlinear terms with respect to ψ in the right-hand side of Equation (4.5) will not introduce any essential corrections.

The solution of boundary value problem (4.4) for fixed $\zeta = \zeta_*$ can be written as

$$\varphi_* = \varphi_0(\zeta_*) + \psi(\zeta_*)$$

In this way, two points on the φ -axis can be associated with any value of the parameter ω from a certain defined interval: the point $\varphi^*(\omega)$, corresponding to the first intersection of a trajectory passing through T with φ -axis and the point $\varphi_*(\omega)$, determined by the solution of the considered boundary value problem.

If κ and ζ_* are sufficiently small, the point φ_* will fall to the left of the saddle Q ($\varphi_* < \varphi_0$). Moreover, the quantity $\psi(\zeta_*)$ is so small that $\varphi_* < \varphi^*$.

With increasing ζ_* the quantity φ_* does not decrease and the saddle Q moves to the left, towards the point P . Therefore, there exists such a value of ζ that both Q and φ^* will be on the left-hand side of the point φ_* at a small distance apart. In view of continuity condition, points φ_*

and φ^* will coincide for a certain intermediate value of ζ_* . The corresponding value of parameter $\omega = \omega^*$ determines the sought trajectory of the simplified equation which passes through T and P .

On the other hand there is a fan of curves going out from the point P . Each of these curves corresponds to a different value of ω . One integral curve should necessarily fall into the point O . The value of parameter ω , corresponding to that particular curve uniquely determines the value of impulse

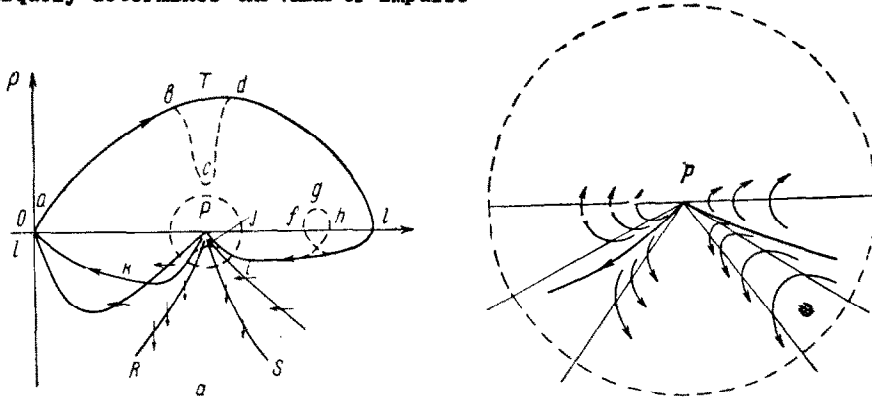


Fig. 6 a and b

propagation velocity. It was shown before that such a value exists.

The above considerations, concluding the construction of an impulse-type solution (see the phase diagram in Fig. 6 a), have been based on the simplified equation. Such an assumption is admissible as long as the solution of full and simplified equations differ by the exponentially decaying factor. It is easy to see that this is true over the entire length of trajectory, except in the immediate neighborhood of the point P , where the exponent of the additional term vanishes.

The curve, corresponding to the impulse-type solution, separates two regions of different behavior, Fig. 6 b. Above this curve, the trajectories of simplified equations, turn round smoothly and intersect the φ -axis. Below this curve the trajectories undergo an abrupt turn and proceed downward, after having intersected the zero and infinity isoclinic of the simplified equation.

Approaching the point P , the curvature of trajectories increases, becoming infinite in the limiting case.

The above analysis provides an explanation why, irrespective of the smallness of λ , the second derivative term in Equation (3.8) cannot be neglected. The latter remark relates to the curves of the second type passing sufficiently close to the point P , including also the sought curve passing through the point P .

The performed analysis of the influence of the second derivative term indicates that the solution of an exact equation does not deviate much from the trajectory of the simplified equation. This is true everywhere except in a small neighborhood of the point P , where instead of a corner point, there is a smooth round off.

This remark is of particular importance since the point P represents a state of unstable equilibrium. The solution based on the simplified equation without a correction term would lead to an infinitely long duration time of transition through the point P , whereas the time of motion along the smooth trajectory is finite.

All considerations, concerning the final phase of impulse propagation (the vicinity of the point O) relate to the constant value of nitric acid concentration. However, the velocity of motion, along the found trajectory is bounded from below. Thus, for small values of κ , this velocity will far exceed the rate of change of concentration. Therefore, the integral curves on the phase diagram will undergo only a slight distortion. This situation will continue until the representative point reaches the point O , where the velocity becomes arbitrarily small. In that case, the change in the nitric acid concentration should be taken into account, and it can be shown that there exists a curve passing through points P and O .

5. Qualitative comparison with experimental data. Conclusion. 1°. We shall now turn to a more detailed consideration of a typical curve (Fig.2), describing the change in potential with time at a given distance as the impulse proceeds. The process can be essentially divided into three stages:

1. A rapid rise in potential to the value in excess of φ_k , part *abcde*
2. A slow decrease of potential to the value φ_k , part *efghij*
3. Final part *jkl*, where the potential falls rapidly to the zero initial value.

Such a distinction of three stages immediately follows from the considered theoretical scheme even in the simplest case of an infinitely slow change in the concentration of nitric acid. In the limiting case ($\kappa \rightarrow 0$) the trajectory on the phase diagram of impulse follows the line $OTQPO$ (Fig.5).

The physical sense of the existence of three stages in the process investigated corresponds to the basic scheme of Bonhoeffer. Initially, there is a transition from the stable, passive state to the stable active state (part OP). Then the value of potential, in the stable active state, diminishes as a result of a change in concentration. This stage (QP) will continue until the equilibrium in the active state becomes unstable, (the moment of coincidence of P and Q). Finally, there is a sudden drop in the potential and the process returns to the passive state (part PO).

In the limiting case considered, the velocity of impulse propagation is determined by taking into account exclusively the first stage of the process

(on the phase diagram, the trajectory passing through the point O should intersect the φ -axis at the saddle O). There is a full analogy in the mathematical description of the first stage of the process and the problem of flame propagation [5].

2°. The description of impulse propagation in the considered limiting case $\kappa \rightarrow 0$ is not sufficiently accurate. During the first stage of the process, the experimental value of impulse amplitude is lower than that predicted by the theory under a constant nitric acid concentration at $\kappa \rightarrow 0$. The discrepancy between theory and experiments is connected with the finiteness in the value of κ , as can be expected from the fact that the length of intermediate stages, although far exceeding the duration of the first stages, in fact differs only by one order of magnitude.

If κ is small, but not zero, i.e. if the rate of change in concentration is not infinitesimally small, the impulse trajectory intersects the φ -axis to the left of the initial position of the saddle O , according to the results derived in Section 4. This is equivalent to the drop in the impulse amplitude (see Fig. 6a where the dotted line denotes the phase diagram of an observed impulse and a full line relates to the present solution).

During the last stage of the process, the experimental curve exhibits a sharp delay in the potential drop (point j in Fig. 2). This is again attributed to the finiteness of the quantity κ . At that instant, the curve representative for the impulse-type solution would approach the φ -axis (Fig. 6a), i.e. in the vicinity of P the derivative $p = d\varphi / d\xi$ would diminish.

During the intermediate stages of the process, slight oscillations in the value of potential are observed (loop fnh in Fig. 6a). This phenomenon cannot be explained within a theory based on the simplified equation. Since the directional field of the simplified equation is directed downward over the entire segment PQ , the curve corresponding to the impulse cannot pass from the lower half-plane to the upper half-plane. Consideration of a full Equation (3.8) provides again a full explanation of the observed oscillations but a more detailed analysis is required to solve completely the problem considered. It can be shown that a consideration of the higher derivative term does not introduce any major correction which is in agreement with experimental results.

According to the results of paper [8], the excitation travels along the string with velocity $w = 42.4$ cm/sec. The string and capillary radii are $r_0 = 0.62$ mm and $R = 0.98$ mm, respectively, and the electric conductivity of the solution is $\sigma = 0.52$ 1/ohm cm. The approximate duration time of the initial stage of the process equals 35 ms, whereas the duration time of the entire impulse is approximately one order of magnitude longer. The change in potential during the first stage is approximately 1V. The limiting value of φ_k is of an order 0.5V and the initial value of a concentration of nitric acid is such that the current $C_0 j_{3b}(\varphi_k)$ equals 10 mA/cm². In the course of pulse advancing, this value of current increases some one

hundred times because of a rise in the concentration of nitric acid, and approaches the value 10A/cm^2 which is representative for the current j_1 . The value of current j_3 , by several times exceeds the value of j_{3b} . The order of magnitude of quantity K can be determined from

$$\tau \sim \frac{1}{K j_{2a}}$$

where τ denotes the duration time of the initial phase of impulse corresponding to the full activation of surface.

Introduce the dimensionless independent variables

$$\eta = \zeta / Z, \quad \Theta = \varphi / \Phi \quad (5.1)$$

where Z and Φ denote characteristic scale of a distance and potential difference, respectively, Equation (3.4) takes the form

$$A\Theta'' - \omega BZ\Theta' - \frac{\omega E\Phi}{Z}\Theta'\Theta'' = \frac{XZ^2}{\Phi} - \frac{\omega}{JZ}\Theta''' \quad (5.2)$$

The scales Z and Φ should be so chosen that within the considered range, the values of all derivatives be of order of unity.

Considering the first and third stage of the phase diagram and taking as a characteristic linear element $Z = \omega\tau$ the following orders for the non-dimensional parameters in Equation (5.2) are obtained

$$A \sim 10^{-1} - 10^0, \quad \omega BZ \sim 10^1 - 10^2, \quad \omega E\Phi / Z \sim 10^{-1} - 10^0 \\ XZ^2 / \Phi \sim 10^2 - 10^3, \quad \omega / JZ \sim 10^{-1} - 10^0 \quad (5.3)$$

These estimates indicate that an "inertial" effect caused by the higher derivative term in (5.2) is displayed only locally since the corresponding coefficient is small.

During the intermediate stage, the characteristic dimension Z becomes one order larger. Therefore, the term XZ^2/Φ is now comparable with the remaining terms only if the quantity X is small. Thus, over a considerable part of the intermediate stage, the potential should remain close to the value $\varphi = \varphi_0$, corresponding to $X = 0$. This provides a full confirmation of the previous result that the representative point approaches the point P on the phase diagram following the moving saddle.

During the first stage of the process, one can distinguish a portion of a sharp delay in the potential increase (point α in Fig.2). The occurrence of this portion cannot be explained within the considered theoretical scheme and apparently has no connection with any part of the present theory.

The analysis of an experimental technique employed and the results of tests used for the comparison give indications that the considered portion is caused by the influence of residual external current applied to indicate the excitation. The latter current reaches several mA/cm^2 . This value is comparable with the proper current generated during the first stage.

3°. The system of governing equations is fairly complicated and therefore the performed analysis involves solely the investigation of qualitative

properties of uniformly propagated excitation. A full treatment of the propagation of self-supporting impulses would require consideration of a whole collection of problems, the major part of which have a direct connection with the theory of combustion.

In the first place, the problem of uniqueness of a uniformly propagating impulse should be investigated. The proof presented in Section 4 does not say anything about the possible number of solutions. The difficulties arise here from the fact that in contrast to the theory of combustion, the solution does not depend monotonously upon the unknown velocity of impulse propagation.

Two further problems are of particular interest. These are the investigation of stability of a stationary impulse with respect to small disturbances, and also the more general problem concerning the development of a random initial distribution of active and passive regions. It is clear that from a certain initial distribution of passive and active regions may develop either a uniformly propagating impulse or a uniform passive state of a surface. It is important to notice that in contrast to the combustion process the above listed unsolved problems do not exhaust all possible cases. It may happen under suitable initial conditions that a series of consecutive impulses propagate down the string. An important feature of the present model is the possibility of the occurrence of periodical behavior. A simple example of such periodical behavior is an interchange of active and passive states where an external current is transmitted.

All remarks mentioned above concern not only an electrochemical model of nerve, but to a large extent also a nerve itself. A quantitative comparison of experimental results and theoretical predictions can be performed using numerical analysis. This would also permit solution of an inverse problem, i.e. to determine parameters of the system from experimental data as functions of the potential.

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Translated by T.W.