THEORETICAL ANALYSIS OF MECHANISMS OF NERVE IMPULSE CONDUCTION ALONG MYELINATED FIBER AFTER A FUNCTIONAL CHANGE IN THE PROPERTIES OF INDIVIDUAL NODES

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It is shown in a mathematical model of a myelinated nerve fiber that the development of a local response in an inexcitable node plays an important role in the mechanism of the "jumping" of an action potential (AP) across the inexcitable node. In the absence of such a response (for example, in the case of a 1000-fold decrease in the maximum sodium permeability, $P_{Na}$) in fibers with normal relations between the length of the internodal segment (L) and its diameter (D) ($L/D > 100$), the conduction is blocked. It is possible only in fibers with relatively short internodal segments ($L/D < 90$). With a decrease in the $P_{Na}$ in several nodes, the transmission of excitation from the first to the second altered node is of critical importance for propagation of the impulse. The conduction of an AP becomes decremental if in each of the altered nodes the AP acquires a gradual character, for example, in the case of acceleration of sodium inactivation through the rate constant $\beta_h$.

INTRODUCTION

In investigations carried out on a mathematical model of a giant axon of the squid [5-7], we studied the mechanisms of the conduction of nerve impulse (single and series) along a geometrically and functionally nonuniform pulpless nerve fiber. The use of a model made it possible to investigate in considerably more detail than is possible in an experiment on a living subject the changes in the AP at different points of the fiber (in 100 simultaneously) and to analyze the kinetics of the ionic conductances and currents underlying these changes.

During the study a number of data were obtained which escaped the experimenters’ attention (the retrograde depolarization wave, the changes in the AP as it approached the area of alteration, etc.), but which are of great importance for an understanding of such phenomena as Venkebach's periodicities [1], Vvedenski's pessimal inhibition [2] in the nerve, etc. It was natural to go on to determine to what degree the principles established in the model of a pulpless fiber are applicable to myelinated nerve fibers. However, before studying this question, it was necessary to analyze the conduction of a single wave of excitation along a nonuniform myelinated fiber. This was the purpose of our investigation. The mathematical model of a myelinated nerve fiber which we used in our work is a set of equations which describe the electrical behavior of the membrane of the nodes of Ranvier and the cable characteristics of the internodal segments [9,10,11]. We studied on this model the role of ionic and local currents in the development of a spreading AP; the mechanism of the "jumping" of the AP across an inexcitable node; the conduction of the AP across several nodes with decreased excitability or an increased rate of sodium inactivation.

METHOD

The formal assumptions are similar to those which were made by FitzHugh and Goldman and Albus [9,11]. An equivalent diagram of a myelinated fiber is presented in Fig.1,A. A system of equations, suggested by Frankenhaeuser and Huxley [10], was used to describe the changes in the membrane potential in j-th node. The internodal segment is considered as a segment of a uniform cable.
Equation (1) describes the distribution of the potential in the internodal segment of the fiber ("cable equation"), Eq. (2) the change in potential in the node. Equations (3)-(7) represent the boundary and initial conditions for Eqs. (1) and (2). The axon is considered as symmetrical relative to the zero node to which the stimulating current $I_0(t)$ is applied. In the last node the potential is fixed at the level of the potential at rest, Eq. (6), in order to avoid complications in the calculations connected with the spread of the depolarization from the cut end of the fiber (see [8, 5]). Since in this case some disturbances in the impulse occur when it approaches the end of the fiber, the computed AP in the five last nodes (from the 11th through the 15th) were not used for analysis. The relation $I_0(t)$ can be assigned by any method. In examining the conduction of a single impulse we used the function $I_0(t) = I_0$ at $0 \leq t \leq \tau$.

The values of the ionic currents, $I_{Na}$, $I_K$, $I_P$, and $I_I$ were computed in accordance with the equations presented by Frankenhaeuser and Huxley [10].

The method of integration which we used consists in the following:

1. The internodal section is divided into segments with length $L/4$, assuming that the potential throughout each of them is the same. Each node is considered as uniform, since the length of the node is very small, of the order of $2.5 \mu$ [11].

2. We replaced $\partial V/\partial x$ and $\partial^2 V/\partial x^2$ by their difference approximations.

3. We solved the equations obtained for $dV/dt$.

4. We integrated the system of equations solved for $dV/dt$ by the Runge–Kutta method. The integration step $\Delta x = 0.375$ mm, $\Delta t = 10^{-4}$ msec. Integration with a larger $\Delta t$ step is impossible since in this case the method becomes unstable and the approximate solution diverges. Since a further decrease in the