Physiology and Electrochemistry of Nerve Fibers

ICHIJI TASAKI

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Physiology and Electrochemistry of Nerve Fibers

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Preface

This book is written for students of biology and medicine who are interested in investigating the properties of nerve fibers. A great number of experimental facts known to us at present are described and interpreted on the basis of our present level of understanding of morphology, biochemistry, and physical chemistry of the nerve fiber. Old theories, which were once popular, are also discussed in some detail, for the experimental bases of those theories are still meaningful and ought not to be forgotten. Throughout this volume, effort is made to trace the origins of the concepts that are important in studying the physiology of the nerve fibers.

Historically, evolution of the study of physiology of nerve fibers is linked closely with that of electrochemistry. The foundations were laid by prominent physical chemists: Hermann Helmholtz (1850), Wilhelm Ostwald (1890), Walther Nernst (1899), and others. In addition, many important discoveries in physical chemistry were made by investigators known as biologists or physiologists (see Chapter 13). Thus, great efforts were made in classical physiology to explain properties of nerve fibers in physicochemical terms.

With the advent of the age of electronic engineering, however, the traditionally close tie between physical chemistry and physiology was weakened considerably. Driven by the increasing need for advanced knowledge of various electronic devices employed in their experiments, investigators of physiology started to interpret physiological findings in terms of electronic engineers' concepts, e.g., positive feedback, channels, gates, equivalent circuits, and less emphasis was placed, in recent years, on physicochemical approaches. I have therefore made a conscious effort to "translate" modern electrophysiological terms into physicochemical language.

One of the difficulties encountered in writing this book has been that many students of biology and medicine are not sufficiently familiar with the basic concepts in thermodynamics and electrochemistry. To alleviate this difficulty, an effort has been made to refer to textbooks and papers where the concepts employed to explain electrophysiological data are explained.

This book consists of five general areas of investigation. In Chapter 1, the significant events that led us to the present state of understanding of the behavior of nerve fibers are given in chronological order. In Chapters 2 and 3, the properties of the frog sciatic nerve, known before the advent of the single-fiber technique, are described. An historical account of the discoveries of the action current and conduction velocity and old theories of nerve excitation are presented. Chapters 4 through 7 deal with properties of isolated myelinated nerve fibers. The process of saltatory conduction and experimental facts concerning electrical excitation are explained. In Chapters 8 to 14, old and recent experiments on squid giant axons are discussed. I have focused on experimental results obtained by using the techniques of intracellular perfusion. The experimental results obtained were interpreted on the basis of the theory developed by Jacques Loeb (1900) and Cremer (1906) and combined with the concept of stability of the membrane. In Chapter 15, I have directed the discussion toward the experimental findings obtained by recording nonelectrical signs of nerve excitation. The behavior of dye molecules in and near the axon membrane has yielded useful information about the state of membrane macromolecules during nerve excitation.

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1. Introduction

In this book, a large number of experiments on physiological properties of nerve fibers are described and the results are analyzed from a physicochemical point of view. It is shown that physiology and electrochemistry of nerve fibers have developed to the present level in three, more-or-less discrete, stages. The discovery of the action current and of the conduction velocity of a nerve impulse marked the opening of the first stage. The second stage started when electrophysiological methods for examining properties of individual nerve fibers were devised. The invention of the technique of intracellular perfusion laid the foundation for the third stage. Studies of nonelectrical signs of nervous activity furnished, from time to time, valuable information concerning the physicochemical nature of excitation processes. It is emphasized that every significant achievement in the field has been invariably preceded by advancements in allied sciences.

The significant events that contributed to the development of our present knowledge about the properties of nerve fibers are listed below in chronological sequence.

1746:	Leiden jar was invented; physiological action of electric shocks was widely recognized.
1791–1800:	The Galvani–Volta controversy aroused great interest in studies of electricity; Volta's pile—a continuous source of electricity—was invented.
1808:	Na, K, Ca, Mg, etc., were discovered by electrolysis (Davy).
1822:	Galvanometer was invented (Ampére and Babinet).
1828–1840:	Injury current of the muscle was recognized (Nobili, Matteucci).
1843–1848:	Action current of the muscle and nerve was discovered (du Bois-Reymond).
1850:	The velocity of nerve conduction was determined (Helmholtz).
1855:	Fick's diffusion equation was published.
1871:	The all-or-none property of the cardiac muscle was described (Bowditch).
	Node of Ranvier was discovered (Ranvier).

1879: Cable properties of the nerve were examined and the local current theory was proposed (Hermann).
1880: Effect of K ion on electric properties of the muscle was discovered (Biedermann).
1882–1886: Salt solution for maintaining the normal contractility of the heart muscle was described (Ringer).
1883: Dissociation of electrolytes in water was demonstrated (Arrhenius).
1885: The mobilities of ions were determined (Kohlrausch).
1890: The concept of ionic (charged) membranes, physical and biological, was formulated (Ostwald).
1889–1890: The Nernst–Planck electrodiffusion equations were formulated and the origin of emf's in electrolyte solutions was clarified.
1899–1910: The theory of nerve excitation of Nernst and Hill overshadowed the old theory of du Bois-Reymond.
1899–1912: Attempts were made at explaining bioelectric phenomena on the basis of the Nernst–Planck equations (Nernst, Cremer, Bernstein).
1900–1920: The importance of Ca ion in excitation and contraction was recognized, and the colloid–chemical (macromolecular) theory of nerve excitation was proposed (Loeb, Höber, Bethe).
1911: Donnan's paper on membrane equilibrium was published.
1926–1928: Electric responses of single myelinated nerve fibers were recorded by using electronic amplifiers (Adrian, Zotterman, Bronk).
1934: The importance of Ranvier nodes in excitation and conduction was recognized (Kubo, Ono, Tasaki, Erlanger, Blair).
1934–1939: Intrisic rhythmicity of the nerve fiber was studied (Monnier, Fessard, Arvanitaki).
1935–1936: The Teorell–Meyer–Sievers membrane theory was formulated.
1937–1940: The validity of the local circuit theory was established (Rushton, Hodgkin, Tasaki, Katz, Schmitt).
1939: The fall of the membrane impedance during action potentials was demonstrated (Cole and Curtis).
1939–1941: Intracellular recording of the resting and action potentials was accomplished (Hodgkin, Huxley, Cole, Curtis).
1939–1942: The role of the myelin sheath and the node of Ranvier in nerve excitation and conduction was clarified (Tasaki).

1949:	The importance of extracellular Na ion in nerve excitation was emphasized (Hodgkin and Katz). The method of space clamping of squid giant axons was invented (Marmont).
1952:	The process of nerve excitation was explained on the basis of an equivalent electric circuit (Hodgkin and Huxley).
1961–1962:	The technique of intracellular perfusion was invented (Baker, Hodgkin, Shaw, Tasaki, Watanabe, Takenaka).
1967–1969:	Action potentials were recorded from axons with only a Na-salt solution internally and a Ca-salt solution externally (Watanabe, Tasaki, Lerman). Bistability of the nerve membrane was emphasized (Tasaki).
1967–1971:	Assumption of spatial independence of Na and K channels was popularized by a number of investigators.
1968:	Changes in turbidity and in birefringence during action potentials were discovered (Cohen, Keynes, Hille). Optical signals were recorded from vitally stained nerve fibers (Tasaki, Watanabe, Sandlin, Carnay).
1980:	Swelling of nerve fibers during action potentials was demonstrated (Tasaki and Iwasa).

At present, the field of investigation with which we are concerned is not exactly in a rapidly developing stage. Nevertheless, a number of investigators are making attempts at advancing the frontier of our knowledge. In recent years, electrophysiological properties of "single ion channels" have been pursued on the premise that there are two discrete conformational states in the macromolecular elements of the membrane. Vigorous efforts are being made also toward elucidating the organization of various macromolecular elements in and near the axon membrane by using biochemical, electron microscopic, and immunological techniques.

Currently, a few studies are being conducted indicating that ion channels for different alkali ions in the nerve membrane are not independent. However, it seems unlikely that the proponents of the independence hypothesis will be convinced by the new and the old studies which refute the hypothesis that there is an independent channel for each of Na-, K-, and Ca-ions.

Reflecting on the difficulty of convincing his opponents, Max Planck once remarked that, in physics, a new idea is not usually accepted by convincing one's opponents step by step, but rather, it is accepted when the opponents die out and the new generation accepts the idea from the outset (see p. 267 in "Wege zur physikalischen Erkenntnis," Hirzel, Leipzig, 1933). In the field of physiology and medicine, the factors that determine the acceptability and