BIOLOGICAL SYMPOSIA

VOLUME III

Muscle

Edited by

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Biological Symposia

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Edited by

JAQUES CATTELL

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PREFACE

This volume grew out of a symposium on muscle organized by the editor at the request of the American Physiological Society for its annual meeting at New Orleans in April, 1940. It was stipulated by the Society that the subject of muscle chemistry should be eliminated from the program.

In order to limit the field still further the subject of myoneural transmission was later excluded by the editor because it seemed to be in less need of further discussion than some other aspects of the subject more immediately related to the contractile mechanism. With these considerations in mind the following program was arranged.

1. Emil Bozler, Ohio State University.
   Action potentials and conduction of excitation in muscle.
   Discussion by A. S. Gilson, Jr., Washington University.
2. R. W. Ramsey, University of Rochester.
   Muscle function as studied in the single isolated muscle fiber.
   Discussion by F. H. Pratt, Boston University.
3. Dugald E. S. Brown, New York University.
   Heat production and the process of shortening.
   Discussion by A. C. Young, University of Pennsylvania.
4. Ernst Fischer, Medical College of Virginia, Richmond.
   Changes during muscle contraction as related to the crystalline pattern.
   Discussion by F. O. Schmitt, Washington University.

We are much indebted to the Jaques Cattell Press for undertaking the publication of this symposium. In order to do so, however, it was necessary to expand the symposium by the collection of additional manuscripts. This was willingly undertaken because of a conviction that a source-book of modern information on this complicated subject would be a valuable contribution for both teachers and investigators. At that time, however, it appeared probable that the Europeon war would not interfere too seriously with the solicitations of manuscripts from many of the non-belligerent European countries. Since then the situation has become so much worse that almost all help from abroad has become impossible. Indeed the only paper from Europe is that written by Professor Meyerhof under very difficult circumstances. The scope of this volume is accordingly much more limited than had been anticipated, and it has become impossible to cover the whole field of muscle physiology in a systematic way. Many aspects of the subject have had to be omitted which would otherwise have been covered by experts of distinction. Thanks to the energetic cooperation of many authors, however it has been possible to complete the volume with some sacrifice of quantity but no sacrifice of quality. It will be observed that muscle chemistry has not been excluded from this collection as it was from the original symposium. Articles on various other subjects not represented, have been solicited in vain. The scope of the volume has been expanded to include myoneural transmission. Had this not been excluded from the original tentative plan other authors could doubtless have been induced to contribute, thus amplifying in particular the material relative to the chemical theory of transmission.

The original four papers are published herewith in the order in which they were presented but grouped with each of them are the other papers on closely related subjects which have been contributed subsequently. Papers on subjects not originally represented on the symposium program are grouped together at the end of the collection. Dr. Ramsey's paper is now published, as it should be, with his wife as co-author and the discussion of the paper by Dr. Pratt has been expanded into a separate contribution. The discussion of Dr. Bozler's paper by Dr. Gilson and that of Dr. Fischer's paper by Dr. Schmitt are also included. Dr. Young's discussion of Dr. Brown's paper was omitted by request.

In a few short papers or even in a volume like the present one, it is hopeless to attempt to do justice to a subject embracing so many subordinate fields each one of which is large enough to require a whole symposium of its own for an adequate presentation. One can only express regret that so many other experts who could have made equally valuable contributions were not in a position to do so and offer thanks to the many contributors to this collection who have thus placed their special experience at our disposal.

THE EDITOR.

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INTRODUCTION TO MUSCLE PHYSIOLOGY

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PROBABLY no living cell has been so intensively studied from so many points of view as the muscle cell. If this statement is challenged there are no data to support it. But one may properly ask what other cell offers so many points of interest for the curious and so many points of attack for the investigator?

While at rest the muscle is a very ordinary looking bit of translucent jelly. It is composed of fibers containing potassium surrounded by extracellular space and connective tissue containing chloride. The fibers contain a viscid sticky jelly and are surrounded by a tough elastic membrane. The fibers have an appearance under the microscope of more than ordinary interest with alternating light and dark bands. The polarizing microscope and the x-ray diffraction pattern reveal the fact that the orderly structure extends even to the molecules themselves which are arranged in parallel chains. The fibers are composed largely of a remarkable protein, myosin, with elastic properties closely resembling those of rubber. Like rubber and unlike most solids it shortens when heated, is highly extensible and gives off heat when stretched. It shortens when exposed to high pressures and decreases just perceptibly in volume when it shortens and thereby disturbs the orderly arrangement of its molecules. It shows double refraction and might be properly described as a liquid crystal.

Like other cells the fiber is surrounded by a membrane which is permeable to some ions and impermeable to others and is in consequence electrically polarized, thus providing probably the necessary machinery for excitation and conduction. It has a respiratory metabolism of great complexity which varies remarkably in magnitude with variation in the condition of the muscle. Thus even at rest the muscle fiber possesses some outstanding peculiarities.

Unlike other cells, however, the muscle cell can be conveniently stimulated to contraction, thereby bringing about an almost instantaneous transformation of its shape and its cytology, its mechanical and electrical state, its temperature, chemical composition and rate of respiration. Thus at the desire of the experimenter a whole series of new chemical reactions can be thrown into activity in an orderly and reproducible manner. This sudden transformation so produced may properly be described as an explosion. The muscle is a self-cocking explosive machine with a convenient trigger. The explosion turns chemical potential energy into mechanical energy. Thus the machine is useful. We can use it to heave rocks, sew on buttons or for the still more delicate task of dissecting another muscle from the leg of a fly. It has a highly orderly structure of both microscopic and sub-microscopic dimensions. Many refined optical methods are available for the examination of this structure and the changes incident to the contraction. The forces developed in a muscle "explosion" are of amazing magnitude. Some of our tendons transmit forces of the order of half a ton. Single fibers of the muscle can also be isolated in Ringer's solution by painstaking dissection, and the resulting threads of muscle contract vigorously for days and exert relatively large forces.

Along with the development of mechanical energy there is a development of electrical energy. In the muscle as in the nerve this provides a mechanism for conduction of a contraction wave from one end of the muscle to the other. We are just beginning to appreciate that this electrical change can be resolved into various parts comparable to the spike and the after potentials of nerve and to learn what other processes are associated with these potentials. Of particular significance are the newly discovered potentials associated with activity of the myoneural junctions. Several times in the course of evolution the "discovery" has been made independently that this electrical charge could be turned into a weapon useful for both offense and defense. Thus electric organs were made out of many different muscles, sometimes a tail muscle, sometimes an eye muscle, a back muscle, or one of the jaw muscles. The largest potentials developed by such organs amount to well over 100 volts.

The contraction of a muscle offers almost innumerable opportunities for exact observation. The tension is measured, the course of the heat production is followed, the action potential is photographed, optical changes of transparency, microscopical appearance, double refraction and x-ray diffraction spectrum are followed. Changes in volume, water content and chemical composition, repiratory rate and many other functions are measured, all as a function of time, temperature, load, length of muscle, duration and frequency of stimulation, or composition of the medium. Chiefly because of the contraction process, therefore, the muscle offers a far greater variety of methods and opportunities for investigation than any other tissue. In this respect a muscle is to any other tissue as a game of chess is to a game of checkers.

The muscle is a machine which goes. It can be made to "run" at will. As a gadget which works it has an obvious fascination for any boy or girl. It has a similar fascination for physiologists, the what-makes-it-go boys of biology. It is a lasting fascination and formidable challenge, for as yet we have no adequate comprehension of its machinery.

Care has been taken to have represented in this volume one aspect of muscle physiology which has gone out of fashion in this country and has been almost totally neglected until recent years. One of the earliest volumes on muscle was that of Borelli on animal mechanics. The subject developed in later years as fast and as far as the principles of mechanics were developed by the physicists, and like physics it finally reached a stage where apparently everything important was already known and further investigation was not warranted and treated with scorn. Only by German and to a lesser extent French physiologists and anatomists was any serious effort made to advance our knowledge of the behavior of muscles in the body. In the English language there is scarcely anything written on the subject and the German works are not often read. More recently there has been a revival of interest in the mechanics of walking, running and other bodily movements, and in the hands of Dr. Elftman the subject has been notably advanced by his calculation of the forces manifested about the various axes of rotation during both running and walking. His analysis of the two joint muscles is of particular interest. Most of the principles of muscle physiology which are usually taught in the class room by fussy experiments on moribund frog muscles are better exemplified by experiments on man. Here we see muscles exerting greater tension at greater frequencies of stimulation, greater tension at greater lengths, greater tension at lower velocities of shortening, mucles shortening more or less isometrically, and in addition muscles contracting while being stretched (an unusual class room phenomenon but common in normal life); we see contraction alternating with relaxation in rapid succession, acceleration and positive work alternating with deceleration and negative work. The medical student at least, should learn muscle physiology from his own body. Fortunately the muscle diseases are relatively rare and unimportant clinically and unfortunately they are not very well understood as yet. For this reason presumably the medical student does not need to remember much about muscles, and the most extensive physiology text now used by medical students in this country refers to muscle only incidentally in other connections and contains no chapter on muscle per se. From the point of view of physiology, however, muscles are important because they can be and have been investigated in so many different ways and because our relatively detailed knowledge concerning them throws important light on the physiology of other cells.

The writer feels impelled to draw special attention to one problem in muscle physiology in which recent advance has been made which is not available in the text books. It is discussed in this volume by Dr. Brown and is largely the result of work by A. V. Hill.

It is a familiar fact that a small weight can be lifted more rapidly than a large one. Conversely a muscle can exert a larger force when shortening slowly than when shortening rapidly. Because of our subjective familiarity with the behavior of our own muscles this result seems so obvious at first glance that the average man would never suspect how many physiologist-hours had been expended in trying to find the reason for this simple phenomenon. In fact the phenomenon is not simple and its explanation, so far as it is now known, penetrates deeply into the fundamental mechanism of the muscle contraction. If this interesting problem is mentioned at all in text books it is attributed to muscle viscosity. The writer has long believed that it was due instead to the extra energy which must be liberated for shortening. The faster the muscle shortens the greater the drain upon its energy supply for purposes of shortening and the less the energy available for maintaining tension. This indeed is the essence of the new theory proposed by Hill.

If we ask how much more rapidly a muscle shortens with a small load than with a large load the curve relating force to velocity can be shown. The writer found an exponential equation to fit this curve empirically, but Hill has interpreted it as a rectangular hyperbola with negative asymptotes at a and b. Thus from a force-velocity curve for any muscle the values of these two constants may be determined. Now the same muscle may be put upon a thermopile and made to contract against varying loads. The rate of heat production at different speeds of shortening can be measured and is found to be proportional to the difference between the isometric tension and the load. The proportionality constant is identical with b and the extra heat liberated for unit shortening is the constant a. It is impressive that the same constants can be derived from two entirely separate sets of data. The velocity of shortening is limited by the rate of energy liberation. This theory therefore, relates the mechanical changes and the energy changes for the active muscle just as the theory of the thermoelastic effect relates heat production and length changes for the resting muscle. Whether or not this theory is correct, it is certain to have a very stimulating effect upon future research in this field. In its present form it can be properly described as a very elegant theory in need of further experimental support.

There may be some legitimate doubt as to whether muscle physiology has as yet made sufficient progress to justify calling it a science in the strict sense of the term. Most parts of the subject are still in the stage of mere qualitative description. There is as yet little in the way of mathematical orderliness to the phenomena. In the field of electrical excitability, however, many lengthy descriptions may now be replaced by a single equation applicable to both muscle and nerve. Substantial progress has been made in the study of energy metabolism and in the submicroscopic description of muscle structure. One can just begin to visualize an inclusive theory which will be based rationally on the ultramicroscopic configuration of the fiber and will relate the energy changes to the mechanical changes in truly scientific fashion. Such a theory will be an explanation of how a muscle contracts and many lines of investigation are now converging to this end.

Among the less advanced and more purely descriptive aspects of muscle physiology may be mentioned; (1) comparative muscle physiology and smooth muscle; (2) end plate physiology and the effects of acetylcholine and other drugs; (3) muscle electrolytes. Articles in this volume testify to the differences of opinion which may arise regarding the interpretation of the behavior of various types of smooth muscle. The relation between the various types of muscles and muscle fibers with their various types of unitary or multiple innervations will be better understood when the facts have been better described. Our own muscles represent only one type among many.

End plate physiology is still divided between the electrical and the chemical theories. The field would seem to be ripe for a compromise theory which will combine the essential features of both, for it seems that both theories contain features which cannot properly be discarded. The whole question is also intimately bound up with the effects of various drugs and electrolytes on the behavior of muscle. Further study promises also to shed important light upon the causes of some or all of the various muscle diseases. The reverse is also true and it is because muscle pathology offers such important lessons for normal muscle physiology that an article on muscle diseases was solicited for this volume.

The subject of muscle electrolytes still needs more routine observations of a purely descriptive nature. The data are already sufficient to make possible some tentative efforts to formulate a mathematical theory. The article on this subject in this volume will indicate what success has been met with in this direction. The reader will undoubtedly be greatly dissatisfied with a theory which would explain the electrolyte equilibrium in muscle by postulating a "pump" of unknown nature which continuously displaces the equilibrium in one direction by pumping sodium out of the fiber, but it is no small recommendation for a theory if it describes precisely what the "pump" actually does.

This introduction should properly be terminated by an attempt to make some prediction about future developments in the field of muscle physiology. Those who are eagerly pulling the muscle machine to pieces to see how it works must always feel that they are on the verge of discovering the secret principle which is involved. Pre-