A TEXTBOOK OF GENERAL PHYSIOLOGY

by
HUGH DAVSON

A TEXTBOOK OF
GENERAL PHYSIOLOGY

by
HUGH DAVSON
D.Sc. (Lond.)
Scientific Staff, Medical Research Council; Honorary Research Associate and Fellow of University College London

THIRD EDITION

With 573 illustrations including 50 plates

J. & A. CHURCHILL LTD.
104 GLOUCESTER PLACE, LONDON, W.1
1964

To

SIR CHARLES LOVATT EVANS, F.R.S.
Emeritus Professor of Physiology in the University of London

First Edition . . .	1951
,, ,, *reprinted* . .	1952
,, ,, ,, . .	1954
Japanese translation . .	1955
Second Edition . . .	1959
,, ,, *reprinted* .	1960
Third Edition . . .	1964

Printed in Great Britain

PREFACE TO THE THIRD EDITION

ONCE again I must apologize for an increase in size, which has occurred in spite of a vigorous pruning of what had already been written. The tasks of preparing this and the previous edition were so severe that I was frequently tempted to say "Never again", and to exchange the author's stool for the editor's chair. I trust very much that I shall not succumb to this temptation, however, so that if a fourth edition should be called for I shall once again be able to summon the energy to execute, albeit inadequately, a task that, as the years go by, approaches asymptotically the impossible.

Whilst this edition has been going through the press, I have been on leave from University College London as visiting professor at the University of Louisville and the University of California in Los Angeles; it is a pleasure to acknowledge here the hospitality of these two universities and, at the risk of being invidious, to thank especially Professor Victor E. Hall for providing a quiet refuge in his department where the most onerous task of all, the revision of the index, could be carried out in peace, interrupted, however, by stimulating conversations with him and his colleagues.

HUGH DAVSON

University of Louisville, Kentucky
University of California, Los Angeles.

EXTRACT FROM THE PREFACE TO THE SECOND EDITION

WERE it not the custom, with new editions, to leave the preface to the first edition unaltered, as a record of the author's original intentions, I should alter the definition of general physiology I presented there. It served as a useful practical guide in the selection of subjects for study but, as a definition, it is too naïve and might be replaced by "the study of those features of life that appear to be common to all forms". The features common to a variety of manifestations of a given process are clearly the most fundamental, just as the most common features of a series of books are the individual letters and words rather than sentences. The general physiologist therefore carries his investigations to the point where they are susceptible of a fundamental interpretation, i.e. in terms of physics and chemistry, so that we shall never be far wrong if we use, as a practical guide, the definition presented in the first edition, namely, the "study of those aspects of living material that show some immediate prospect of being described in terms of the known laws of physics and chemistry".

PREFACE TO THE FIRST EDITION

IN the 'twenties of this century, two great textbooks, both published from University College London, occupied a prominent position in the physiological literature, and graced the shelves of most teachers and students of physiology; I need hardly say that their titles were *Principles of Human Physiology* and *Principles of General Physiology* by Starling and Bayliss respectively. To-day, Starling's *Physiology* still occupies its dignified station, thanks to the labours of Lovatt Evans. Bayliss' *General Physiology* has had a less fortunate history;* in 1924 a revised edition was brought out by a group of Bayliss' colleagues, but since then it has remained out of print and become progressively out of date. In speculating on possible causes for the different fates of these books, it has occurred to me that a factor is the growing tendency to drop the distinction between mammalian or human physiology, on the one hand, and general physiology, on the other. Claude Bernard, who first introduced the term, described "general physiology" as "the study of phenomena common to animals and plants", whilst Bayliss, in the introduction to his *Principles*, adopted the definition of his teacher, Burdon-Sanderson, namely, "the study of the endowments of living material"; and, although this definition is so wide as to include all biological research within its compass, in practice it has meant, so far as I have gathered from the scope of his *Principles*, the study of those aspects of living material that show some immediate prospect of being described in terms of the known laws of physics and chemistry.

The behaviour of living matter in its highest development, namely in mammals, is so complex that the general physiologist has usually turned to other forms for study, leaving the elucidation of those phenomena depending on the *organization* of living material—rather than its "endowments"—to others, who have therefore been commonly described as "mammalian physiologists", since these organizational, or integrative, characteristics have been most commonly studied in this class. Nevertheless, the distinction between the two types of physiologist is not based on a difference of experimental material; the difference between them is essentially one of attitude. The general physiologist, because he has had a thorough training in mathematics, physics, or chemistry, seeks to provide explanations in terms of concepts already familiar to him; consequently, if nervous activity interests him, he will be concerned in interpreting the origin of the resting and action potentials, and the special problems involved in synaptic transmission; in his search for suitable material he may range widely over the animal and vegetable kingdoms; and it has frequently happened, as the following pages will testify, that the most revealing experimental material has been from cold-blooded and invertebrate sources. The mammalian physiologist, with a primarily biological training, will accept the action potential at its face value and utilize the power of recording it to elucidate the more complex aspects of animal behaviour; he, also, should be liberal in his choice of experimental material, and the wide use of the mammal has been occasioned more by the accident of its close relationship to man, and the desire of so many physiologists to relate

* That is, up to the moment of writing (June, 1951); my colleague, Dr. L. E. Bayliss, tells me that he is busy preparing a new edition of his father's book—a courageous enterprise, in the execution of which all general physiologists will wish him God speed.

their work to human pathology, than by its greater value as an experimental object.

With the progress of the science, the fields of the general and mammalian physiologists have tended to overlap, and nowhere is this better illustrated than in the study of synaptic function, so that in many instances it would be hard and profitless to distinguish the contributors to this branch of the physiological literature in terms of their attitude to the problem. In this field, therefore, the mammalian physiologist, by simplifying his concepts, and the general physiologist, by extending the application of physico-chemical principles, have met on common ground; and ultimately it is the hope of all physiologists that such a state of affairs will pertain over the whole field of biological research.

A rigid segregation of general and mammalian physiologists, whereby they tended to work in different departments and to belong to different learned societies, would be a harmful development; and it might, therefore, be considered that the publication of a new textbook of general physiology would be a retrograde step, emphasizing as it does the existence of a distinction that must eventually, with the growth of the science, vanish. This would be a just consideration, if it were not for a very important point, namely that, in Britain the teaching of physiology, and to a very large extent the research work, are becoming progressively restricted to the field covered by the mammalian physiologist. So long as the learning of anatomy occupies the lion's share of the medical student's time, it is only reasonable that the teaching of physiology to these students be confined to those aspects that have a fairly immediate bearing on medicine, and that general physiology, with its more remote usefulness and greater difficulty in understanding, should be squeezed out of the curricula. As a result of this tendency, a number of fields of physiological research are slipping beyond the ken of the mammalian physiologist, and the very meaning of the word "physiology", as currently used in this country, is contracting rather than expanding.

In the present book, therefore, I have attempted to gather together the results of modern research carried out by workers with the viewpoint of the general physiologist, namely that of the investigator who attempts to explain living phenomena in terms of concepts familiar in the basic sciences of physics and chemistry. Regarding the distinction between the two forms of physiology as one of outlook rather than of subject for investigation, I have roamed a wide field and have necessarily covered a great deal of ground regularly trodden by the mammalian physiologist; in these regions of overlap the more detailed treatment provided in this book may amplify, and make more intelligible, the sometimes scanty treatments of the same subjects afforded by the ordinary physiological texts.

This, then, is my justification to potential readers in this country for writing a new textbook of general physiology. In the United States of America, the flourishing of the *Journal of General Physiology* alongside the *American Journal of Physiology*, the existence in some of the large universities of chairs of both mammalian and general physiology, and the currency of several textbooks of general physiology, relieve me of the duty of apologizing for writing this book; furthermore, the fact that it is an intruder, competing with others of established worth, needs no special apology or justification in a field where viewpoints change rapidly and where the selection of material gives such scope for individuality.

In writing this book I have been guided by the requirements of several types of reader. First, there is the degree student in physiology and related subjects—

zoology, botany, etc.—for whom the ordinary textbooks of physiology are generally inadequate; such a student requires, besides a lucid explanation of a given subject, references to the literature that will permit him to dig deeper; generally, references to monographs and review articles are sufficient for his purpose. Secondly, there is the medical student who is genuinely fond of physiology, and who is willing to absorb rather more than the quantum considered necessary for a medical education. Such a student will be well advised not to attempt a systematic reading, but to browse and to skip with agility when the going becomes heavy. With some diffidence, I have considered the research worker in physiology and related fields; generally, for the specific purposes of his research, a textbook, however well documented, is unnecessary to the experienced research worker. To the beginner, on the other hand, still uncertain as to the real direction in which his interests lie, I feel that a textbook of this character can be of real value, and to that end I have made every effort, consistent with the difficulties of publishing in this country, to make my accounts up to date, and to document them with reasonable care. At the same time I have desired to avoid prolixity, and the overburdening of the text with names and dates, that are the necessary corollaries of exhaustiveness; prolixity has been partly avoided by the generous use of footnotes, whilst the text has been relieved of dates by the simple expedient of quoting the titles of the published papers and monographs in the bibliographies. Since, with few exceptions, I have only quoted the papers that I have read, the number of references at the end of any chapter is not so large as to make it inconvenient, where necessary, to read through them in search of the required title. The progress of physiology depends on the recruitment of adequate numbers of research workers who have already qualified in one of the more exact sciences; bearing these in mind, too, I have been at pains to make the matter intelligible to readers without a biological training. Finally, there is the mammalian physiologist who wishes to understand what his general physiologist colleagues are doing, both for his own interest and for the purposes of teaching. To such a reader I can offer this book with some confidence that it will be useful, however much it may fall short of its great predecessor in this country, Bayliss' *Principles*. One serious defect, which will be evident at a glance, is the restricted scope of the book; this, however, is a failing occasioned by the necessity to keep its size within bounds imposed by the extraordinary increase in publishing costs since the war. In spite of the generous allowance of space that Messrs. Churchill have made me, chapters on electrical activity in smooth muscle, on the aqueous humour and synovial fluid, and on phototropic phenomena, which I had already written, had to be removed before going to press, and a chapter on the comparative physiology of respiration and circulation died at conception.

Most, if not all, textbooks of general physiology begin with a synopsis of the principles of physical chemistry which may be as long as the part devoted to physiology. It has always seemed to me that this is a wrong procedure, for several reasons which I need not detail; and in writing the present book I have assumed that the reader has some knowledge of the principles of physics and chemistry, so that I have only introduced simple accounts of the more advanced aspects in the contexts to which they are appropriate.

In writing a textbook covering a wide field, a modern author must necessarily expound matters with which he, himself, has had no first-hand experience; in doing so, he is in continual danger of committing solecisms occasioned by his ignorance or defective comprehension; this book doubtless contains many such errors, but far fewer than would have been the case had I not been fortunate enough to have three such critical proof-readers as my colleagues Dr. R. D. Harkness, Dr. E. J. Harris, and Dr. Bernhard Katz; I am sincerely grateful to them for the conscientious manner in which they carried out what must have been a tiresome—but not a thankless—task.

When its need has to be proved by experience, the production of a new book is an uncertain venture for a publisher, and I must therefore take this opportunity of thanking Mr. J. Rivers, the managing director of Messrs. J. & A. Churchill Ltd., for taking up my suggestion of writing this book, and for accepting a manuscript very much longer than he had been led to anticipate.

In dedicating this book to my former chief, Sir Charles Lovatt Evans, F.R.S., I wish to express something more than my appreciation for help and encouragement, manifested in numerous ways since I first entered his department at University College, I wish to emphasize also, on the occasion of his retirement from the Jodrell chair, the great contribution to the progress of physiology that his enlightened direction of the department has made. From his successor, Sir Lindor Brown, F.R.S., I have already acquired a heavy, but pleasing, burden of indebtedness; especially for the hospitality that has permitted me to return to what I must be permitted to call my true academic home, the Department of Physiology, University College London. I must also express my thanks to my employers, the Medical Research Council—personified for me by two courteous gentlemen, Sir Harold Himsworth and Sir Landsborough Thomson, who have silently acquiesced in the theft of so many hours, devoted to this book, which might, perhaps, have been better employed in original research.

This partial recital of my indebtedness—the account is completed on page x—would oppress me with my inability to repay it, were I not able, like Don Quixote, to lay the flattering unction to my soul, that "if I have not been able to repay the good deeds I receive with other deeds, I put in their place the desire to do them, and if that be not sufficient, I make them public; for he that tells and proclaims the kindnesses he receives would repay them if he could."

HUGH DAVSON.

University College London.
June, 1951.

ACKNOWLEDGMENTS

I HAVE to thank my secretaries, Miss Mollie Kirk and Miss Linda Mills, and the Thane Librarian of University College, Mr. C. F. A. Marmoy, for their great help, whilst Mr. C. A. Evans and Mr. L. J. Shaw were most valuable with their photographic skill in enabling me to reproduce diagrams from the original literature. Mr. C. A. Purvis is responsible for many of the original line-drawings. To the Managing Director of Messrs. J. & A. Churchill, Mr. J. Rivers, and his assistant, Mr. A. Knightley, I owe a great deal; to Mr. Rivers for permitting the increase in scope of the book and to Mr. Knightley for his unfailing help in all the manifold technical matters that arose during the actual production of the book.

In a work of this kind an author has to rely largely upon published material, and this is naturally reflected to a great extent in the collection of suitable illustrations. The present author is under a great debt to the writers of scientific books and papers, all of whom have readily given their consent to the reproduction of illustrations from their work.

The granting of permission to reproduce illustrations, by author and publisher, is a courtesy so universally extended as to be taken as a matter of course and acknowledged perfunctorily; on the other hand, the provision of original micro-photographs is more than a courtesy—it is an act of kindness for which an author must be sincerely grateful; on this account, therefore, my thanks are due to W. T. Astbury, R. Barer, H. W. Beams, P. W. Brandt, F. Carlsen, T. Caspersson, A. Claude, A. I. Cohen, A. Couceiro, A. J. Dalton, E. De Robertis, M. W. Dewey, P. Doty, G. A. Edwards, D. W. Fawcett, Sir Howard Florey, S. Gibbs, S. Granick, W. Grassmann, J. Gross, C. E. Hall, H. K. Hartline, H. F. Helander, J. Hillier, A. J. Hodge, U. Hofmann, R. W. Horne, A. L. Houwink, H. E. Huxley, B. Katz, D. Lacy, A. W. Linnane, V. T. Marchesi, A. Mauro, E. H. Mercer, K. Mühlethaler, A. R. Muir, G. E. Palade, S. L. Palay, G. D. Pappas, D. C. Pease, the late F. J. Pittock, R. J. Przybylski, T. A. Quilliam, J. Rhodin, K. C. Richardson, J. D. Robertson, M. A. Rudzinska, F. O. Schmitt, G. Schramm, F. S. Sjöstrand, W. Stoeckenius, J. H. Taylor, J. C. Thaemert, H. H. Ussing, and R. W. G. Wyckoff.

Whilst it is indeed hoped that the credits given individually in the captions to borrowed illustrations are both exhaustive and correct, it is a pleasure to acknowledge the co-operation of the editors, publishers and official bodies similarly concerned in making available copyright illustrations. The method of identification adopted in the text has been to cite author and original source after the caption. The source is then listed more fully in the References at the end of the appropriate chapter. I am thus indebted to the following extensive list: Academic Press Ltd.; *Acta Physiologica Scandinavica;* American Association for the Advancement of Science (*Science*); American Heart Association (*Circulation*); *American Journal of Anatomy; American Journal of Botany; American Journal of Medicine; American Journal of Ophthalmology;* American Physiological Society (*American Journal of Physiology; Journal of Applied Physiology; Journal of Neurophysiology* and *Physiological Reviews*); *Anatomical Record; Annali di Ottalmologia e Clinica Oculista; Annals of the New York Academy of Sciences; Archiv für mikroskopische Anatomie; Archives internationales de Physiologie et Biochimie; Archives of Biochemistry and Biophysics; Arkiv* *för Botanik; Australian Journal of Experimental Biology and Medical Science;* J. S. Barth, Leipzig; Biochemical Society (*Journal and Symposia*)*; Biological Bulletin; Biological Reviews; Biological Symposia; Botanical Gazette; Biophysical Journal; British Journal of Ophthalmology; British Medical Bulletin; British Science News;* Butterworth Scientific Publications Ltd.; Butterworth-Springer & Co.; Cambridge University Press; Carnegie Institute, Washington; *Chronica Botanica;* Clarendon Press, Oxford; *Cold Spring Harbour Symposia;* Elsevier Publishing Co. (*Biochimica et Biophysica Acta*)*; Enzymologia; Experientia; Experimental Cell Research; Experimental Cytology; Federation Proceedings; Gastroenterology;* Grune & Stratton Inc.; Walter de Gruyter & Co. (*Hoppe-Seyler's Zeit für Physiologische Chemie*)*;* Herman, Paris; Jacques Cattell Press; Johns Hopkins Press, Baltimore (*Symposium on Light and Life*)*; Journal of Bacteriology; Journal of Biophysical and Biochemical Cytology; Journal of Clinical Investigation; Journal of Experimental Biology; Journal of Experimental Zoology; Journal of the Franklin Institute; Journal of Histochemistry and Cytochemistry; Journal of the Optical Society of America; Journal of Physiology; Lancet;* H. K. Lewis & Co. Ltd.; E. & S. Livingstone Ltd. (*Quarterly Journal of Experimental Physiology*)*;* Longmans Green & Co. Ltd.; Macmillan & Co. Ltd. (*Nature, London*)*;* Macmillan Co., New York; Methuen & Co.; National Academy of Sciences, Washington (*Proceedings*); Noordhoff, Groningen; W. W. Norton & Co. Inc.; Oxford University Press; *Pflügers Archiv für die gesamte Physiologie; Physiologia Plantarum;* Pitman Medical Publishing Co. Ltd.; Ronald Press, New York; Springer Verlag, Heidelberg (*Ergebnisse der Physiologie, biologischen Chemie und experimentellen Pharmakologie*)*;* Pergamon Press Ltd.; *Protoplasma;* The Rockefeller Institute Press (*Journal of Biophysical and Biochemical Cytology* and *Journal of General Physiology*)*;* The Royal Society (*Proceedings*); Society of Dyers and Colourists (*Symposium on Fibrous Proteins*)*; Soil Science; Symposia of the Society for Experimental Biology;* C. C. Thomas (*Harvey Lectures*)*;* University of Chicago Press; University of Illinois Press; University of Pennsylvania Press; Wistar Institute of Anatomy and Biology (*various periodicals*)*; Zeitsch. für Naturforschung; Zeitsch. für vergleichende Physiologie.*

PLATES

As most of the plates contain more than one figure, not always numbered consecutively, it may help the reader to consult the following list.

CONTENTS

1. The Structural Basis of Living Matter

2. Transformation of Energy in Living Systems

3. The Transport of Water and Solutes

PAGE

4. Characteristics of Excitable Tissue

5. The Mechanism of Contraction of Muscle

6. Light: Its Effect on, and its Emission by, the Organism

I. The Structural Basis of Living Matter

CHAPTER I

THE INDIVIDUAL CELL

ALTHOUGH all the cells of a given organism are ultimately derived from a single fertilized ovum, such specialization to meet particular needs has taken place during development that, when we contemplate the erythrocyte, the long fibre-like cells of nerve and muscle, and the syncytial cells of the heart, it is indeed difficult to conceive of a "typical" cell. In the following discussion, therefore, it must be borne clearly in mind that the characteristics that are being described are essentially those of the given cell in which they are observed. In view, however, of the common origin of the cells of an organism, it is very likely that any given feature of a cell has an analogue in other and functionally remote cells. For example, the power of conduction of an impulse is associated in our minds primarily with the nerve cell, yet there is reason to believe that numerous other cells likewise possess this feature though not in so highly developed a form; in fact, the propagation of a disturbance from one part of a cell surface to another may be a universal characteristic of all living cells, however primitive or specialized.

Experimental studies on single living cells from the complex organism are by no means easy; and, although the comparatively recent development of the technique of tissue culture has provided useful information on the behaviour of certain types of cell, we are still largely dependent, for information regarding the essential characteristics of the cell, on the results of researches on protozoa such as *Amœba*, the eggs of certain marine animals such as the sea-urchin, *Arbacia punctulata*, and various plant cells; it is therefore useful to employ these as our reference point.

Experimental Methods

Light-Microscope. Before entering into a detailed description of the cell, we may review some of the modes of study available to the modern cytologist. The classical light-microscope depends for its power of exhibiting structural detail on a difference in absorption of light between the parts to be differentiated. Most cells reveal little detail when viewed in the living state through the light-microscope; and this is due mainly to the absence of sufficiently great differences in absorption of light by the structural components; it is also due to the fact that many of these elements are too small to be resolved by the microscope. Thus true images of particles smaller than the wavelength of the light employed cannot be formed, a limitation that excludes particles of less than about 0.4 μ (4,000A); by the use of ultra-violet light and photographing the image, even greater magnification is possible, but even here the limit is in the region of 1,000A. With differential staining techniques, the presence of various elements in the cell, previously unsuspected, can be made evident; these techniques generally involve the killing of the cell by "fixation" procedures which coagulate the protoplasm, so that for a long time the real existence in the living cell of many of the structures brought to light by the classical staining methods was called into question.

Histochemistry

The use of differential staining techniques, as a result of which certain structures in the cell take up dye-stuffs preferentially, is still largely empirical, but under the form of *histochemistry* the rationale is rapidly becoming clearer; histochemical techniques rely on the production of certain chemical reactions in localized regions of the cell; thus if a cell is known to decompose organic phosphate, incubation of the cell with a solution of glycerophosphate and calcium should result in the deposition of insoluble calcium phosphate in those regions where the reaction occurred. By subsequent treatment of the cell with a cobaltous salt and ammonium sulphide a black precipitate is formed where the calcium was deposited. As we shall see, the Golgi apparatus of the cell was for long considered an artefact, but by treating the cell in the above manner a black structure appears, identical in situation and general contour with the bodies originally identified by ordinary staining techniques. In this example the histochemical technique has exhibited a structure by virtue of its power of catalysing a chemical reaction (*i.e.*, by virtue of the presence of the enzyme *phosphatase*); simple staining reactions, on the other hand, rely on a chemical reaction between the dye and the structure to be stained; thus the common stains fall into two main classes, acidic and basic, and the structures in the cell are classed as *acidophilic* or *basophilic* in accordance with their power of combining with an acid or basic dye. The main chemical reaction resulting in staining is thus a simple salt formation; for example, the marked power of the cell nucleus to take up basic stains is due to the presence in it of nucleic acid which, even though it is itself probably united to protein, retains sufficient acidity to combine with basic dyes. The observation, moreover, that the nature of a staining reaction frequently depends on the technique of fixation is consistent with this explanation, since certain fixing reagents, such as the heavy metals, by combining with the acidic groups of proteins, tend to make the latter more basic and so favour their combination with acid dyes; formic acid, on the other hand, makes a structure basophilic. The presence of fatty materials is generally demonstrated by their power of behaving as reducing agents; thus osmic acid, which may be applied as a vapour, is reduced to give a black precipitate by fatty structures; the value of osmic acid is further increased by its power of fixing the tissue at the same time as it behaves as a stain. To return to the more recent developments of histochemistry, we may note that the presence of certain materials within a cell may be verified frequently by the simple process of removing them by appropriate reagents which either decompose them or dissolve them out. Various enzymes, which specifically attack certain substances, have been applied to thin sections of tissues, and the consequent disappearance of structures has been observed; for example, the nucleic acids associated with certain particles in the cytoplasm may be removed with the enzyme *ribonuclease*, with the result that the particles lose their basophilia; again, by simply soaking the section in various concentrations of NaCl, Bensley & Hoerr were able to dissolve out different structures from the cell one by one.

Radioautography

The technique of *radioautography* may be regarded as a development of histochemistry. If an animal is injected with the radioactive isotope (p. 280) of iodine, for example, the material will accumulate in the cells of the thyroid gland; and it may be exactly localized by covering a histological section with a