H. R. Downes

THE CHEMISTRY OF Living Cells

SECOND EDITION

THE CHEMISTRY OF

Living Cells

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Second Edition

LONGMANS

Preface to the First Edition

THIS BOOK is the outgrowth of a course in biochemistry which has been given at Barnard College for the past twenty years. The students have been senior majors in chemistry or in one of the biological sciences. The subject matter included in the book has been chosen not only to provide the material for a course in the fundamentals of biochemistry, but also to serve as a simple reference book for students whose primary interest is in zoology or botany or related fields. In practice it has always been found necessary to review the laws of solutions and the chemistry of the foodstuffs before attempting to deal with the complex transformations which take place in the cell.

The historical approach has been used where it seemed suitable in the belief that students should be introduced to the outstanding scientists in their field and encouraged to give them "a local habitation and a name." In this way students may begin to sense the nature of the great intellectual adventure which we call science, to understand how it progresses, and to appreciate the qualities which go toward the making of a scientist. Above all they may be led to meditate upon a truth which T. H. Huxley stated long ago: "... anyone who is practically acquainted with scientific work is aware that those who refuse to go beyond fact, rarely get as far as fact; and anyone who has studied the history of science knows that almost every great step therein has been made by ... the invention of hypotheses, which, though verifiable, often had very little foundation to start with; and, not infrequently, in spite of a long career of usefulness, turned out to be wholly erroneous in the long run."

As far as possible, the subject matter has been presented in conjunction

with specific experimental data, but since this is an introductory textbook, no attempt has been made to cite individual authorities for each statement. The references given at the ends of the chapters have been chosen with a view to helping the inexperienced student find his way into the subject. Recent review articles have been included not only for their full bibliographies, but also because a logical and coherent summary of a mass of experimental data is often of great assistance to a beginner. The references given to original papers have been chosen either to emphasize work which has been of special significance or to bring the bibliographies up to date with respect to the main topics discussed in the text. The majority of the papers cited are in English; when references are given to German or French sources, the titles have been given in translation.

I am, as the figures in the book bear witness, greatly indebted to a number of people who not only have allowed me to reproduce material from their books and papers, but have couched their permissions in terms of friendliness and encouragement that went far beyond the call of duty. To all of these and to their publishers in England, Switzerland, Germany, Sweden, and here at home I tender my grateful thanks.

To two colleagues on the Barnard College faculty I owe special debts of gratitude. Professor Victor Larsen of the Botany Department has done his best to save me from the consequences of my own ignorance of his science, and Professor Ingrith Deyrup of the Zoology Department, in the performance of a like service, not only has read and criticized portions of the manuscript but has taken time for many helpful discussions. The extent to which the book is sound zoologically and botanically is a result of the friendly efforts of my colleagues; its shortcomings, alas, are my own.

I count myself especially fortunate in having had during the writing of this book the encouragement and wise advice of my former teacher, Professor Emeritus Marie Reimer of the Barnard Chemistry Department. She has read a large part of the manuscript and has made many valuable suggestions as to its organization and presentation. This present occasion for expressing my gratitude to her is but one in a long series, dating back to my own student days when her contagious enthusiasm first inspired in me the desire to become a chemist.

In such a book as this I have inevitably attempted to simplify and summarize material which is far outside the field of my own major interest. I shall therefore be especially grateful if readers will point out mistakes of fact or of interpretation.

HELEN R. DOWNES

New York
September, 1954

Preface to the Second Edition

IN THE SEVEN YEARS SINCE THIS BOOK WAS PUBLISHED, so much new material has appeared that the text has had to be very nearly completely rewritten, with the exception of the purely historical and the purely structural parts. The plan is, in general, that followed in the first edition, except that the chapter on oxidation and the one which surveys broadly the field of biosynthesis now appear before instead of after the chapters concerned with metabolism. It is hoped that this change will make the development of the subject more unified and complete at each stage.

As in the earlier edition, references have been omitted from the body of the text. In compiling the references at the ends of the chapters an attempt has been made to include any papers of special historical interest, and beyond that to use summarizing articles wherever possible or to give only a late reference or two. Only in this way could the list be kept manageable, and both types of papers always carry adequate references for those who want more detail. In citing references I have reluctantly omitted all except one author's name if the joint authorship included more than two names. This is hard on both the young coauthors for whom the paper may be a unique claim to fame and the senior authors whose names often appear last. To both groups I offer my apologies and regrets, but the citing of every author when a paper may carry eight or ten names has become too unwieldy a job. It seemed more important from the point of view of the student to make room for the titles of articles, or for some indication of their subject matter. The latter has been done when the title was so general that a student might miss its significance.

I am happy to acknowledge my indebtedness to many colleagues and

friends. Again Professor Ingrith Deyrup has contributed much to the accuracy of certain chapters, both through informal discussions and through critical reading of several sections of the book. The members of the Barnard College Chemistry Department have been incredibly patient about my raids upon their library, and both Professor Edward J. King and Professor Emma D. Stecher have been generous beyond the call of duty in putting at my disposal their special knowledge of physical and organic chemistry. A special word of thanks goes to Paul Stecher, editor of the *Merck Index*, who has provided me with several recent structural formulas. Thanks are also due the biochemists at Michigan State University for several very helpful critical discussions. I am especially indebted to Professor John C. Speck for suggestions in the field of carbohydrate chemistry and nomenclature and to Professor James L. Fairley who read and criticized three long chapters. Finally I offer sincere thanks to the many people who have permitted me to reproduce their tables and figures. I am especially indebted to Dr. George E. Palade and to Dr. A. E. Vatter for their beautiful electron micrographs and to Dr. M. F. H. Wilkins for the unpublished photograph of his nucleic acid model.

If it was pertinent to acknowledge six years ago that I had had to write about material well outside the field of my own special interests, it is doubly so today. I shall be most grateful if readers will point out errors of fact or interpretation.

HELEN R. DOWNES

Yorktown Heights, N. Y.
January, 1962

Abbreviations

Acta Chem. Scand.	Acta Chemica Scandinavica
Advances in Carbohydrate Chem.	Advances in Carbohydrate Chemistry
Advances in Enzymol.	Advances in Enzymology
Advances in Protein Chem.	Advances in Protein Chemistry
Am. J. Physiol.	American Journal of Physiology
Anal. Biochem.	Analytical Biochemistry
Anal. Chem.	Until 1947 Industrial and Engineering Chemistry, Analytical Edition
Ann.	Annalen der Chemie (Justus Liebig's)
Ann. chim. phys.	Annales de chimie et de physique
Ann. Rev. Biochem.	Annual Review of Biochemistry
Ann. Rev. Plant Physiol.	Annual Review of Plant Physiology
Arch. Biochem. Biophys.[1]	Archives of Biochemistry and Biophysics
Arch. ges. Physiol.	Archiv für gesamte Physiologie
Beitr. chem. Physiol. u. Pathol.	Beiträge zur chemischen Physiologie und Pathologie
Ber.	Berichte der deutschen chemischen Gesellschaft

[1] Up to 1955 was simply the Archives of Biochemistry.

Biochem. J.[2]	Biochemical Journal (London)
Biochem. Z.	Biochemische Zeitschrift
Biochim. et Biophys. Acta	Biochimica et Biophysica Acta
Bull. soc. chim. France	Bulletin de la société chimique de France
Chem. Eng. News	Chemical and Engineering News
Chem. Revs.	Chemical Reviews
Compt. rend.	Comptes rendus hebdomadaires des séances de l'académie des sciences, Paris
Federation Proc.	Proceedings of the Federation of American Societies for Experimental Biology
Helv. Chim. Acta	Helvetica Chimica Acta
J. Am. Chem. Soc.	Journal of the American Chemical Society
J. Biochem. (Tokyo)	Journal of Biochemistry (Tokyo)
J. Biol. Chem.[3]	Journal of Biological Chemistry
J. Chem. Soc.[4]	Journal of the Chemical Society (London)
J. Colloid Sci.	Journal of Colloid Science
J. Chromatog.	Journal of Chromatography
J. Gen. Physiol.	Journal of General Physiology
J. Lipid Research	Journal of Lipid Research
J. Physiol. (London)	Journal of Physiology (London)
Nature	Nature
Naturwiss.	Naturwissenschaften
Physiol. Revs.	Physiological Reviews
Proc. Natl. Acad. Sci. U. S.	Proceedings of the National Academy of Sciences of the United States of America
Proc. Roy. Soc. (London)	Proceedings of the Royal Society (London) Series A: Mathematical and Physical Series B: Biological
Proc. Soc. Exptl. Biol. Med.	Proceedings of the Society for Experimental Biology and Medicine

[2] Summaries of papers presented at meetings of the Society are printed together from time to time at the back of the Journal with independent paging, and the references carry the letter P before the page number.

[3] Preliminary communications are segregated in a special section at the back of some numbers and given independent paging. References carry the letters P.C. before the page numbers.

[4] Recent numbers carry no volume number. The year of publication is given in parentheses.

Trans. Faraday Soc.	Transactions of the Faraday Society
Z. physikal. Chem. (Leipzig)	Zeitschrift für physikalische Chemie (Leipzig)
Z. physiol. Chem.	Zeitschrift für physiologische Chemie (Hoppe-Seyler's)

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Part I

SOME PRELIMINARY CONSIDERATIONS

But this is certain; by how much one man has more experience
of things past, than another; by so much also
he is more Prudent and his expectations the seldomer faile him.

THOMAS HOBBES: *Leviathan* (1651)

Biochemical history and literature 1

BIOCHEMISTRY IS THAT BRANCH OF SCIENCE which is concerned with the chemical events which take place in living tissues. It has existed as a separate discipline for less than one hundred years, but it is rooted in that distant past, almost lost in the mists of prehistory, in which men first began to observe the world about them. Thus Babylonia contributed to science the beginnings of astronomy and of mensuration, and the Egyptians' skill in embalming bears witness to their knowledge of anatomy. Although these earliest-known civilizations have left few records of their own, it is clear from the writings of the early Greeks that the knowledge which they had accumulated was disseminated by traders and travelers throughout the eastern Mediterranean lands and became part of the Hellenic heritage. This heritage had been growing in a haphazard, empirical, and often accidental way for several millenia. But in the course of comparatively few years it was to be transmuted by the Greeks into a new way of living and thinking. It is not easy to define even superficially the Greek contribution. It was partly a sturdy independence and a respect for the rights of the individual which are not matched elsewhere until comparatively modern times. It was partly a rare clarity of mind, coupled with a wide ranging intellectual curiosity. It was partly the first stirrings of the experimental method. But chiefly it was an attitude toward life and a belief in the fundamental importance of truth and beauty which worked together in the social structure of that small nation to foster a freedom of the human mind and spirit which is unique.

ATHENIAN SCIENCE

The story of civilization in Greece and on the islands and mainland of Asia Minor can be traced back beyond 1500 B.C., but the earliest records of Greek biological science date from about the sixth century before Christ. By this time the great colonizing period was over, and people of the Greek race were established in city-states not only on the Greek mainland, but in southern France, in Italy and Sicily, around the Aegean and on its islands, and even on the shores of the Black Sea. Thus it happened that the two outstanding figures in Greek biological science although closely associated with Athens were neither of them born in Greece itself. The physician Hippocrates[1] was born on the island of Cos and Aristotle's home was the colonial city of Stagira on the shore of Thrace.

Hippocrates, who was born about 460 B.C., lived for nearly one hundred years, traveling about the regions bordering the Aegean, teaching and practicing medicine. His ideas were not only far in advance of his own time but also of any intervening time until very recent ones. He taught first-hand observation of disease and patient checking of facts, and expressed clearly for the first time the fundamental faith on which all progress in science still depends, namely belief in an orderly universe in which effects follow inevitably from natural causes. For example, in the Hippocratic work dealing with the plague we find, "As for this disease called divine, surely it has its nature and causes as have other diseases." This was a far cry from the attitude toward disease which is characteristic of primitive people, that it results from the anger of the gods and can be cured by magic and incantation. It is of course impossible at this distance in time to know how many of the writings of the so-called Hippocratic Collection are truly the work of the great physician himself. But what is certain is that the medical learning which he collected and systematized was treasured by generations of students in what were called schools of Greek medicine though many of them were founded long after the fall of Greece. And although the learning of these schools crystallized into a stifling dogma during the Dark Ages, yet the spirit of modern medicine can be traced back in almost unbroken continuity to that springtime of learning in which Hippocrates lived and taught.

Aristotle (384–322 B.C.) as a young man was sent from his provincial home to study under Plato in Athens. Some years later he acted for six years as tutor to the young Prince Alexander of Macedon, returning to Athens when his famous pupil set out on his brief career of conquest. There he founded the famous Peripatetic School, so-called because of Aristotle's habit of walking

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[1] Not to be confused with the mathematician, Hippocrates of Chios, who was a contemporary of the physician.

back and forth as he taught. The doctrines which originated with the Peripatetics were destined to exert a great and lasting influence upon the development of both science and philosophy. That this influence proved to be partly bad arose from the fact that Aristotle's writings, which covered the whole field of learning, were of two sorts. His earliest studies were biological, and in this area he was a scientist of erudition and originality. He observed and recorded and classified a wide range of biological forms and phenomena, and when he was thus in immediate contact with his material he wrote in the true scientific vein.

But Aristotle had in full measure that "exuberant genius for speculation" which characterized his nation. Given a few observations he was impelled to build them into a coherent philosophical system, and his speculations soon outran his data. Indeed in his later writings he made statements which could easily have been put to the test of experiment, but which he never tested. Thus undeterred by inconvenient facts he outlined a system of terrestrial mechanics and fitted a small number of data into a richly imaginative astronomical system in which he assumed that celestial motion is regulated by quite different laws from those which are operative on the earth. In thus allowing free play to his fancy Aristotle was not only disobeying his own behests but also was all unwittingly forging chains which were to bind and inhibit western thought for hundreds of years.

THE HELLENISTIC ERA

Biological science came as a relatively late development in Greece. Hippocrates lived in that Age of Pericles when classical Greek learning centered in Athens had already reached its brilliant culmination. Before his death the long Peloponnesian War had been fought to its costly conclusion. Technically it was won by Sparta, but actually all the Greek city-states including Sparta were the losers. They were left at the end (404 B.C.) torn with dissension and jealousy and weakened by twenty-seven years of intermittent fighting during which not only armies but whole communities had been destroyed. Thus the survivors fell an easy prey when in 338 B.C. Alexander's father, Philip of Macedon, struck from the north. He quickly made himself master of Greece, and by the time Aristotle returned to Athens in 336 B.C. the day of the old independent city-states was past.

Although this conquest spelled the end of that first, unique expression of the Greek genius in its own homeland, it was also the beginning of a new period, known to history as the Hellenistic Age, in which the culture of Greece was preeminent throughout the ancient world. In the course of about nine years Philip's son Alexander swept triumphantly with his armies through Asia Minor, Egypt, Syria, Mesopotamia, and Persia, and even penetrated into India.