Second Edition

THE CELL

DON W. FAWCETT. M.D.
Hersey Professor of Anatomy
Harvard Medical School

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CONTRIBUTORS OF ELECTRON MICROGRAPHS

Dr. John Albright
Dr. David Albertini
Dr. Nancy Alexander
Dr. Winston Anderson
Dr. Jacques Aubert
Dr. Baccio Baccetti
Dr. Michael Barrett
Dr. Dorothy Bainton
Dr. David Begg
Dr. Olaf Behnke
Dr. Michael Berns
Dr. Lester Binder
Dr. K. Blinzinger
Dr. Gunter Blöbel
Dr. Robert Bolender
Dr. Aiden Breathnach
Dr. Susan Brown
Dr. Ruth Bulger
Dr. Breck Byers
Dr. Hektor Chemes
Dr. Kent Christensen
Dr. Eugene Copeland
Dr. Romano Dallai
Dr. Jacob Davidowitz
Dr. Walter Davis
Dr. Igor Dawid
Dr. Martin Dym
Dr. Edward Eddy
Dr. Peter Elias
Dr. A. C. Faberge
Dr. Dariush Fahimi
Dr. Wolf Fahrenbach

Dr. Marilyn Farquhar
Dr. Don Fawcett
Dr. Richard Folliot
Dr. Michael Forbes
Dr. Werner Franke
Dr. Daniel Friend
Dr. Keigi Fujiwara
Dr. Penelope Gaddum-Rosse
Dr. Joseph Gall
Dr. Lawrence Gerace
Dr. Ian Gibbon
Dr. Norton Gilula
Dr. Jean Gouranton
Dr. Kiyoshi Hama
Dr. Joseph Harb
Dr. Etienne de Harven
Dr. Elizabeth Hay
Dr. Paul Heidger
Dr. Arthur Hertig
Dr. Marian Hicks
Dr. Dixon Hingson
Dr. Anita Hoffer
Dr. Bessie Huang
Dr. Barbara Hull
Dr. Richard Hynes
Dr. Atsushi Ichikawa
Dr. Susumu Ito
Dr. Roy Jones
Dr. Arvi Kahri
Dr. Vitauts Kalnins
Dr. Marvin Kult
Dr. Taku Kanaseki

Dr. Shuichi Karasaki
Dr. Morris Karnovsky
Dr. Richard Kessel
Dr. Toichiro Kuwabara
Dr. Ulrich Laemmli
Dr. Nancy Lane
Dr. Elias Lazarides
Dr. Gordon Leedale
Dr. Arthur Like
Dr. Richard Linck
Dr. John Long
Dr. Linda Malick
Dr. William Massover
Dr. A. Gideon Matoltsy
Dr. Scott McNutt
Dr. Oscar Miller
Dr. Mark Moosiker
Dr. Enrico Mognini
Dr. Toichiro Nagano
Dr. Marian Neutra
Dr. Eldon Newcomb
Dr. Ada Olins
Dr. Gary Olson
Dr. Jan Orenstein
Dr. George Palade
Dr. Sanford Palay
Dr. James Paulson
Dr. Lee Peachey
Dr. David Phillips
Dr. Dorothy Pitelka
Dr. Thomas Pollard
Dr. Keith Porter

CONTRIBUTORS OF PHOTOMICROGRAPHS

Dr. Jeffrey Pudney
Dr. Elio Raviola
Dr. Giuseppina Raviola
Dr. Janardan Reddy
Dr. Thomas Reese
Dr. Jean Revel
Dr. Hans Ris
Dr. Joel Rosenbaum
Dr. Evans Roth
Dr. Thomas Roth
Dr. Yoko Saito
Dr. Peter Satir

Dr. Manfred Schliwa
Dr. Nicholas Severs
Dr. Emma Shelton
Dr. Nicolai Simionescu
Dr. David Smith
Dr. Andrew Somlyo
Dr. Sergei Sorokin
Dr. Robert Specian
Dr. Andrew Staelen
Dr. Fumi Suzuki
Dr. Hewson Swift
Dr. George Szabo

Dr. John Tersakis
Dr. Guy de Thé
Dr. Lewis Tilney
Dr. Greta Tyson
Dr. Wayne Vogl
Dr. Fred Warner
Dr. Melvyn Weinstock
Dr. Richard Wood
Dr. Raymond Wuerker
Dr. Eichi Yamada
PREFACE

The history of morphological science is in large measure a chronicle of the discovery of new preparative techniques and the development of more powerful optical instruments. In the middle of the 19th century, improvements in the correction of lenses for the light microscope and the introduction of aniline dyes for selective staining of tissue components ushered in a period of rapid discovery that laid the foundations of modern histology and histopathology. The decade around the turn of this century was a golden period in the history of microscopic anatomy, with the leading laboratories using a great variety of fixatives and combinations of dyes to produce histological preparations of exceptional quality. The literature of that period abounds in classical descriptions of tissue structure illustrated by exquisite line drawings. In the decades that followed, the tempo of discovery with the light microscope slackened; interest in innovation in microtechnique declined, and specimen preparation narrowed to a monotonous routine of paraffin sections stained with hematoxylin and eosin.

In the middle of the 20th century, the introduction of the electron microscope suddenly provided access to a vast area of biological structure that had previously been beyond the reach of the compound microscope. Entirely new methods of specimen preparation were required to exploit the resolving power of this new instrument. Once again improvement of fixation, staining, and microtomy commanded the attention of the leading laboratories. Study of the substructure of cells was eagerly pursued with the same excitement and anticipation that attend the geographical exploration of a new continent. Every organ examined yielded a rich reward of new structural information. Unfamiliar cell organelles and inclusions and new macromolecular components of protoplasm were rapidly described and their function almost as quickly established.

This plentiful harvest of new structural information brought about an unprecedented convergence of interests of morphologists, physiologists, and biochemists; this convergence has culminated in the unified new field of science called cell biology.

The first edition of this book (1966) appeared in a period of generous support of science, when scores of laboratories were acquiring electron microscopes and hundreds of investigators were eagerly turning to this instrument to extend their research to the subcellular level. At that time, an extensive text in this rapidly advancing field would have been premature, but there did seem to be a need for an atlas of the ultrastructure of cells to establish acceptable technical standards of electron microscopy and to define and illustrate the cell organelles in a manner that would help novices in the field to interpret their own micrographs. There is reason to believe that the first edition of The Cell: An Atlas of Fine Structure fulfilled this limited objective.

In the 14 years since its publication, dramatic progress has been made in both the morphological and functional aspects of cell biology. The scanning electron microscope and the freeze-fracturing technique have been added to the armamentarium of the microscopist, and it seems timely to update the book to incorporate examples of the application of these newer methods, and to correct earlier interpretations that have not withstood the test of time. The text has been completely rewritten and considerably expanded. Drawings and diagrams have been added as text figures. A few of the original transmission electron micrographs to which I have a sentimental attachment have been retained, but the great majority of the micrographs in this edition are new. These changes have inevitably added considerably to the length of the book and therefore to its price, but I hope these will be offset to some extent by its greater information content.

Twenty years ago, the electron microscope was a solo instrument played by a few virtuosos. Now it is but one among many valuable research tools, and it is most profit-

ably used in combination with biochemical, biophysical, and immunocytochemical techniques. Its use has become routine and one begins to detect a decline in the number and quality of published micrographs as other analytical methods increasingly capture the interest of investigators. Although purely descriptive electron microscopic studies now yield diminishing returns, a detailed knowledge of the structural organization of cells continues to be an indispensable foundation for research on cell biology. In undertaking this second edition I have been motivated by a desire to assemble and make easily accessible to students and investigators the best of the many informative and aesthetically pleasing transmission and scanning electron micrographs that form the basis of our present understanding of cell structure.

The historical approach employed in the text may not be welcomed by all. In the competitive arena of biological research today investigators tend to be interested only in the current state of knowledge and care little about the steps by which we have arrived at our present position. But to those of us who for the past 25 years have been primarily concerned with the development of electron microscopy as an independent and self-sustaining field of research, the history of morphology, the young seem to be entering the theater in the middle of an absorbing motion picture without knowing what has gone before. Therefore, in the introduction to each organelle, I have tried to identify, in temporal sequence, a few of the major contributors to our present understanding of its structure and function. In venturing to do this I am cognizant of the hazards inherent in making judgments of priority and significance while many of the dramatis personae are still living. My apologies to any who may feel slighted; in such cases I have striven to provide a useful introduction to the architecture of cells and for teachers of cell biology a guide to the literature and a convenient source of illustrative material. The sectional bibliographies include references to many reviews and research papers that are not cited in the text. It is believed that these will prove useful to those readers who wish to go into the subject more deeply.

It is my hope that for students and young investigators entering the field, this book will provide a useful introduction to the architecture of cells and for teachers of cell biology a guide to the literature and a convenient source of illustrative material. The sectional bibliographies include references to many reviews and research papers that are not cited in the text. It is believed that these will prove useful to those readers who wish to go into the subject more deeply.

Some of the magnifications for each of the micrographs will no doubt draw some criticism. Their inclusion was impractical since the original negatives often remained in the hands of the contributing microscopists and micrographs submitted were cropped or copies enlarged to achieve pleasing composition and to focus the reader's attention upon the particular organelle under discussion. Absence was considered preferable to inaccuracy in stated magnification. The majority of readers, I believe, will be interested in form rather than measurement and will not miss this datum. Among these micrographs illustrating the remarkable order and functional design in the structure of cells has been a satisfying experience. I am indebted to more than a hundred cell biologists in this country and abroad who have generously responded to my requests for exceptional micrographs. It is a source of pride that nearly half of the contributors were students, fellows or colleagues in the Department of Anatomy at Harvard Medical School at some time in the past 20 years. I am grateful for their stimulation and for their generosity in sharing prints and negatives. It is a pleasure to express my appreciation for the forbearance of my wife who has had to communicate with me through the door of the darkroom for much of the year while I printed the several hundred micrographs; and for the patience of Helen Déacon who has typed and retyped the manuscript; for the skill of Peter Ley, who has made many copy negatives to gain contrast with minimal loss of detail; and for the artistry of Sylvia Collard Keene whose drawings embellish the text. Special thanks go to Elio and Giuseppina Ravio who read the manuscript and offered many constructive suggestions and to Albert Meier and the editorial and production staff of the W. B. Saunders Company, the publishers.

And finally I express my gratitude to the Simon Guggenheim Foundation whose commendable policy of encouraging the creativity of the young was relaxed to support my efforts during the later stages of preparation of this work.

PREFACE

Don W. Fawcett
Boston, Massachusetts
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The cells of many organs contain brown cytoplasmic inclusions that classical histologists described as *lipochrome pigment*, or *lipofuscin*. These coarse granules exhibit a golden brown fluorescence in ultraviolet light; they stain lightly with lipid-soluble dyes; they give a positive staining reaction for carbohydrates; they are insoluble in acid and alkali and in most lipid solvents. Lipofuscin deposits are rare or absent in the cells of young animals but increase in number with advancing age. They were formerly referred to as "wear-and-tear pigment" in the belief that they represented breakdown products of cell components. Weak acid phosphatase and esterase activities can be demonstrated in some of these pigment granules.

Since the discovery of lysosomes and their characterization as an intracellular digestive system capable of degrading damaged or excess organelles, lipofuscin pigment granules have come to be regarded as end-stages of lysosomal autophagic activity. Accordingly, they are now believed to be accumulations of the metabolically inert residues of cellular material that could not be completely degraded by the lysosomal hydrolases.
Lipofuscin deposits are frequently seen in the brains of older animals and humans and are one of the few available cytological manifestations of the aging process. The granules vary in size and shape. They are limited by a membrane and their content is, for the most part, very dense and coarsely granular, but homogeneous spherical bodies with little natural density or osmiophilia are often present (see at the arrows).

Figure 291. Lipofuscin pigment in a neuron of rat brain. (Micrograph courtesy of Enrico Mugnaini.)
Long-lived cells, such as the Sertoli cells of the testes, which are normally engaged in phagocytosis and degradation of the residual cytoplasm of spermatids, often accumulate conspicuous deposits of lipochrome pigment as illustrated in the accompanying micrograph.

Steroid secreting endocrine glands are also especially prone to develop large amounts of pigment. Massive accumulation of such pigment in the inner part of the adrenal cortex and in the interstitial cells of the ovary of old mice was formerly described by light microscopists as "brown degeneration." Evidently, cells can accommodate a very large burden of lipochrome pigment without seriously jeopardizing their function but ultimately reach a point at which they are no longer viable.

Figure 292. Lipofuscin pigment in a cultured Sertoli cell. (Micrograph courtesy of Wayne Vogl.)
A common site of accumulation of lipofuscin pigment is in the cells of the myocardium. Pigment granules are typically located in the conical zones of sarcoplasm at the poles of the nucleus. With advancing age, they become increasingly abundant and may come to represent as much as 30 per cent of the total solids of human heart muscle fibers.

The accompanying micrographs of cardiac muscle cells from an old cat show lipofuscin pigment bodies and numerous mitochondria in a sarcoplasm that is rich in small dense particles of glycogen.

Figures 293 and 294. Lipofuscin pigment in right ventricular papillary muscle of an old cat.
Lipochrome Pigment


