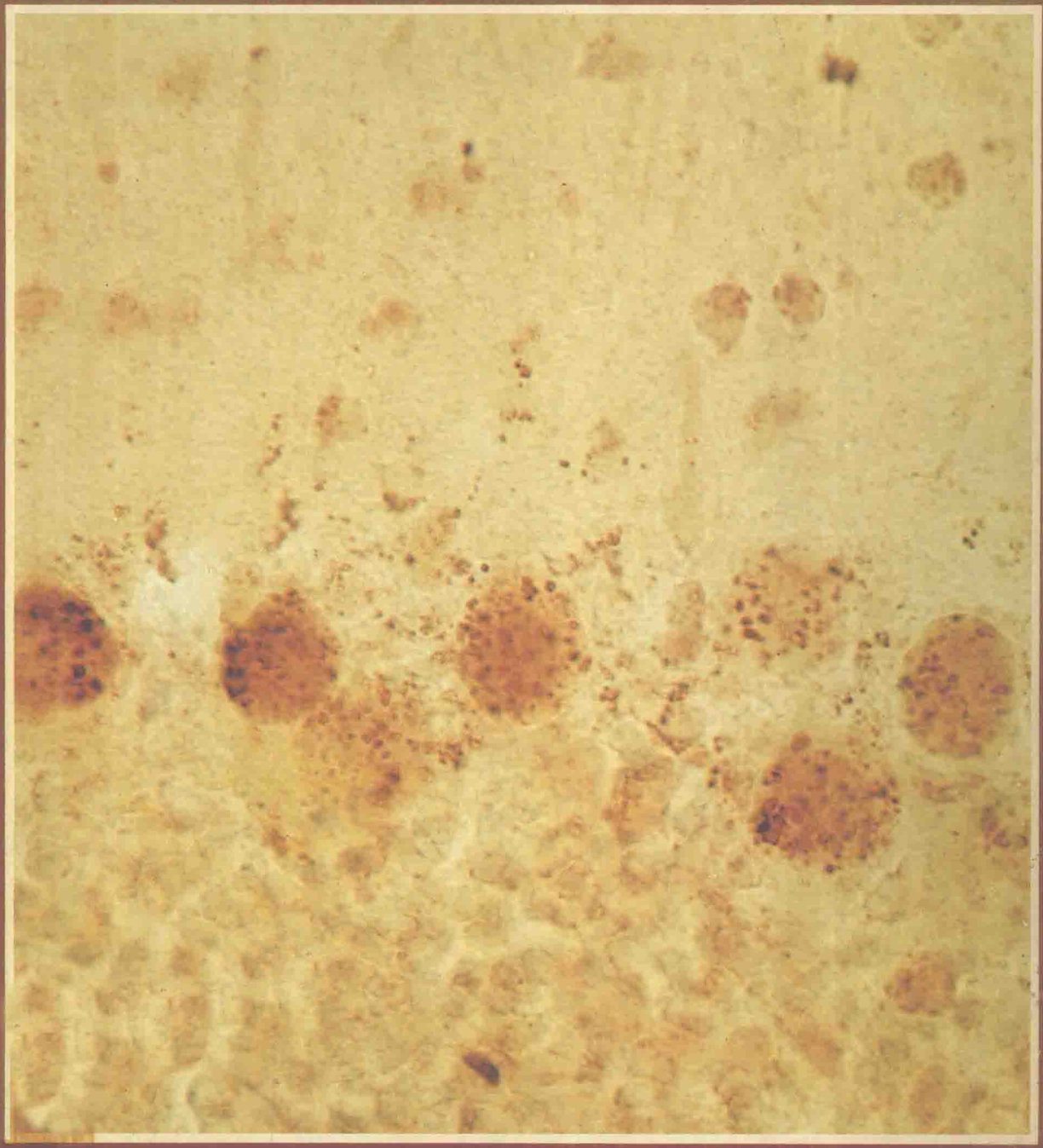
Cells & Organelles

THIRD EDITION

Holtzman & Novikoff



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Preface to the Third Edition

The past few years have been eventful ones in cell biology. We have revised our text to take into account the many conceptual and technical advances that have occurred. Our general approach remains the same as in the previous editions: We have integrated structural, molecular, biochemical, and physiological information and have tried to provide a view of the experimental and observational groundwork on which current concepts rest. We think it important also to give students a feeling for present uncertainties and for the thrust of current research. Thus, we continue to point out loose ends and inadequacies in present information.

In addition to integrating structural and biochemical approaches, we have updated and expanded our summaries of *background* biochemistry and molecular biology. Our experience, however, indicates that biology students are being exposed to such material at increasingly earlier stages of their education and that the attempt both to incorporate an introduction to basic chemistry and to provide a comprehensive introduction to cell biology within a single book would lead either to too long a book or to problems with level, scope, or depth of treatment. Consequently, we have retained the focus implied by our book's title.

A number of organizational infelicities present in the last edition have been eliminated in the present one through reordering of the sequence of treatment of several topics. We are grateful to the students and colleagues who called our attention to these and other features of the book that needed improving.

Many colleagues and friends have contributed to this revision. Those who provided micrographs are acknowledged in the corresponding legends. Arthur Karlin read the manuscript in its entirety and made numerous valuable suggestions and criticisms. So did Catherine Fussell, Andrew Hamilton, and Joseph Scott. Sherman Beychok, Larry Chasin, Bill Cohen, Art Forer, Jack Harding, John Hildebrand, Nancy Lane, Myron Ledbetter, Alberto Mancinelli, Jim Manley, Sandra Masur, Debby Mowshowitz, Bob Pollack, Diane Robins, Dave Soifer, Cathy Squires, Alex Tzagoloff, and Maurice Zauderer commented helpfully on long segments of the manuscript.

Note also that many of the figure legends accompanying diagrams indicate the names of the principal contributors to the research summarized in the diagrams.

New York, N.Y. *E. H.*
June 1983 *A. B. N.*

Preface to the Second Edition

Little need be added to what we have written above, regarding either the sense of excitement among students of the cell, or our general approach to presenting the material.

Note should be made that the 1974 Nobel Prize for Physiology or Medicine was awarded to three cell biologists "for their discoveries concerning the structural and functional organization of the cell": Albert Claude, Christian de Duve, and George E. Palade. Their contributions to cell fractionation procedures and the techniques of electron microscopy permitted them, and others, to lay the basis for much of the cell biology of today.

In planning the second edition we gave serious consideration to the suggestion from a number of teachers and students that we include references for the statements we make in the book. We resisted the temptation chiefly for two reasons: We did not wish to overly enlarge the book's size, or diminish its readability. The book is being utilized for courses at quite a variety of levels, and reference lists suitable for all would be unwieldy. In addition, in our experience as teachers we find reference lists to go out of date very rapidly. Even to support an "old" point, one tends to refer to newly appearing review articles and research reports in which recently appreciated nuances are covered. We do intend our Further Reading lists to provide access to the background literature, and we have revised and updated them accordingly.

We take this occasion to thank most sincerely those who read and reviewed our book in manuscript form, and those who have troubled to write us their views since publication of the first edition.

New York, N.Y. *A. B. N.*
February 1976 *E. H.*

Preface to the First Edition

Cytologists study cells, all cells, and by many techniques. Because of their dependence on the microscope, they tend to analyze living systems in terms of visible structure, but in recent years cytologists have become increasingly concerned with biochemistry. *Cell biologists* start with a bias toward viewing cells in terms of molecules. Recently they have been much concerned with nucleic acids and proteins, the macromolecules which molecular biology has revealed to play primary roles in heredity. However, as studies progress, it is becoming more and more difficult to make a sharp differentiation among the various approaches to the cell—structural (classical cytology), physiological (biochemistry and biophysics), and molecular (cell biology). As distinctions between cell biology and cytology have become blurred, and perhaps outmoded, this book is about cytology and cell biology.

The book is divided into five parts. The first part introduces the major features of cells and the methods by which they are currently studied. In the second, we consider each of the organelles in turn, presenting structural and functional information. Then, in the third part, we discuss the diversity of cell types constructed from the same organelles and macromolecules. The fourth part presents major mechanisms by which cells reproduce, develop, and evolve. The final part is a brief look at the progress and the future of cell study.

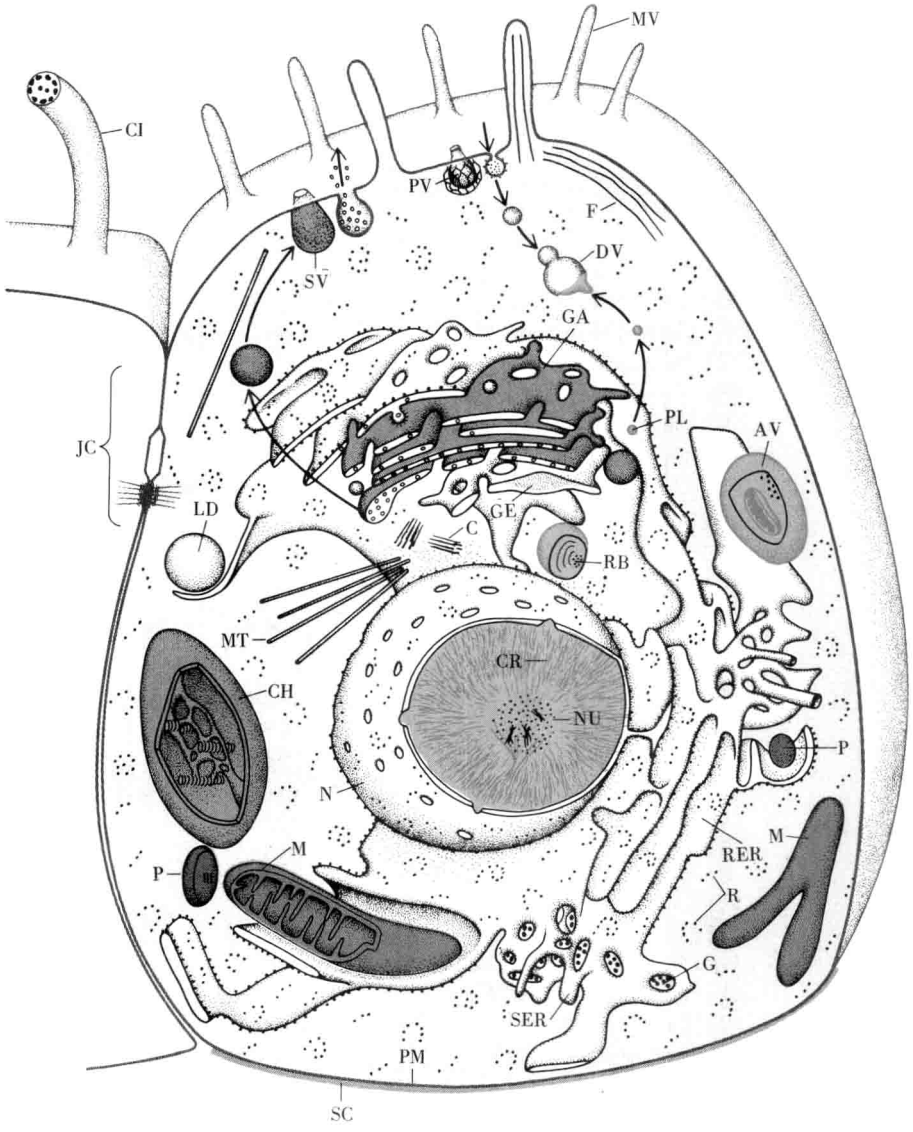
Many of the cells used to illustrate the principles we discuss are from higher animals. This is not only because the authors have had more direct experience with such cells. It also reflects the historical development of cytology; the cells of higher animals have been best analyzed from the viewpoint of correlated structure and function. However, increasing attention is being focused on protozoa, higher plants, and bacteria and related cells. Wherever possible we have referred to studies of such organisms.

We begin the book and each of the parts with introductions outlining the major themes of the chapters that follow and commenting upon some topics that do not fit conveniently into one chapter. In the chapters we combine descriptive and experimental information to provide key portions of the evidence on which contemporary concepts are based. The illustrations have been obtained from leading students of the cell. The figure legends and suggested

reading lists will familiarize the reader with the names of some of those who have contributed to the progress of cytology and cell biology.

We hope that we convey some of the excitement felt today by students of the cell. In addition, we hope that not only past achievements, but important problems awaiting future solution become evident to the reader.

New York, N.Y. *A. B. N.*
January 1970 *E. H.*



Schematic diagram of a cell and its organelles drawn to reveal their three-dimensional structure.

AV, **autophagic vacuole;** ***C,*** **centriole;** ***CH,*** **chloroplast;** ***CI,*** **cilium;** ***CR,*** **chromatin;** ***DV,*** **digestion vacuole;** ***F,*** **filaments;** ***G,*** **glycogen;** ***GA,*** **Golgi apparatus;** ***GE,*** **GERL;** ***JC,*** **junctional complex;** ***LD,*** **lipid droplet;** ***M,*** **mitochondrion;** ***MT,*** **microtubules;** ***MV,*** **microvillus;** ***N,*** **nucleus;** ***NU,*** **nucleolus;** ***P,*** **peroxisome;** ***PL,*** **primary lysosome;** ***PM,*** **plasma membrane;** ***PV,*** **pinocytic vesicle;** ***R,*** **ribosomes and polysomes;** ***RB,*** **residual body;** ***RER,*** **rough endoplasmic reticulum;** ***SC,*** **extracellular coat (as drawn, "basal lamina");** ***SER,*** **smooth endoplasmic reticulum;** ***SV,*** **secretion vacuole.**

The organelles have been drawn only roughly to scale. Also, the sizes and relative amounts of different organelles can vary considerably from one cell type to another. For example, only plant cells show chloroplasts. A detailed enumeration of the organelle content of one cell type is presented in Chapter 2.12.

Contents

Introduction

The analogy between cells and atoms is a familiar one, and like many familiar comparisons it is both useful and limited. Cells and atoms are units. Each is composed of simpler components which are integrated into a whole that exhibits special properties not found in any of the parts or in random mixtures of the parts. Both exhibit considerable variation in properties, based on different arrangements of components; the number of variations far exceeds the number of major components. Both serve as basic building blocks for more complex structures.

However, the analogy cannot be pressed too far; cells can reproduce themselves, whereas atoms cannot. The ability to utilize the nonliving environment to make living matter is probably the most fundamental property of life, and cells are the simplest self-duplicating units. Duplication is based on DNA (deoxyribonucleic acid), which can be *replicated* to form perfect copies of itself. Thus the genetic information encoded in DNA is perpetuated from one cell generation to the next, sometimes without significant variation over vast periods of time. DNA is unique among macromolecules in its replication. Only in certain viruses has another macromolecule (RNA, ribonucleic acid) been shown to replace DNA in its central hereditary role; the replication of RNA in these viruses is based on the same principles as that of DNA.

Genetic information is expressed in cells by the mechanisms of *transcription* and *translation*. Transcription transfers the DNA-coded information to RNA molecules. Translation results in the formation of specific proteins whose properties are determined by the information carried by these RNA molecules. Among the proteins are *enzymes*, catalytic molecules that control most of the chemical reactions of cells. Enzymes differ in the kinds of molecules they affect (their *substrates*) and in the kinds of reactions they catalyze. Many are involved in the synthesis of the other cellular macromolecules, the nucleic acids (DNA and RNA), the lipids (fats and related compounds), and the polysaccharides (polymers made of linked sugar molecules). Through this chain of transcription, translation, and enzymatic activities, DNA directs its own replication and controls as well the rest of *metabolism*, the sum total of all the chemical reactions that take place in cells. The chain is universal, and thus all cells are made of the same classes of macromolecules (nucleic acids, proteins, lipids, polysaccharides) and smaller components such as water and salts. Duplication, and the presence in different cells of similar molecular and structural materials and

mechanisms, are features of *cellular constancy,* one of the main themes of this book.

A second theme of the book is *cell diversity.* Cells may be classified into a large number of categories. *Eucaryotic* cells are distinguished from *procaryotic* cells, plant cells from animal cells, and muscle cells from gland cells. These distinctions derive from differences in morphology and metabolism. Eucaryotes differ from procaryotes in complexity of cellular organization. The unicellular protozoa, most algae, and the cells of multicellular plants and animals fall in the eucaryote category. In these cells, different specialized functions (such as respiration, photosynthesis, and DNA replication and transcription) are segregated into discrete cell structures, many of which are delimited from the rest of the cell by membranes. The cell's *organelles* reflect this segregation; they are subcellular structures of distinctive morphology and function. The most familiar of the organelles is the *nucleus,* which contains most of the DNA of the cell and enzymes involved in replication and transcription. The nucleus is separated by a surrounding membrane system from the rest of the cell, the cytoplasm. The cytoplasm contains many organelles including the *mitochondria,* the chief intracellular sites of respiratory enzymes; in plants, the cytoplasm contains *chloroplasts* in which are present the enzymes of *photosynthesis,* a metabolic process unique to plant cells. The mitochondria, chloroplasts, and a number of other cytoplasmic organelles are also delimited as discrete structures by surrounding membranes.

The procaryotes include the bacteria, the blue-green algae, and some other organisms. In contrast to the eucaryotes, they have relatively few membranes dividing the cell into separate compartments. This is not to say that all components are mixed together in a random fashion. The DNA, for example, does occupy a more or less separate nuclear region, but this is not delimited by a surrounding membrane. In fact, the traditional distinguishing feature of procaryotes is the absence of a membrane-enclosed nucleus (the suffix *caryote*—or *karyote,* as it is often spelled—refers to the nucleus). Respiratory and photosynthetic enzymes are not segregated into discrete mitochondria or chloroplasts, although, as will be seen, the enzymes are held in ordered arrangements within the cell.

The diversity of cell types owes its origin to evolution. By comparison with other macromolecules, DNA is remarkably stable. But *mutations* and other changes do occur at an appreciable, though low, frequency. Mutations alter the genetic information that is encoded in DNA and passed by a cell to its progeny; thus they can produce inherited changes in metabolism. Some result in a *selective advantage:* Roughly speaking, organisms with such alterations produce relatively more viable offspring and therefore will increase in relative frequency in the population. This can take place more or less rapidly in different circumstances. In the final analysis, however, the pattern of spread of a genetic change in a population depends on reproduction and therefore, ultimately, on division of cells.

Usually the daughter cells resulting from division of *unicellular organisms* are essentially similar to the parent cells; the daughters contain replicates of the

parent cells' DNA, and the DNA establishes the range of potential responses to the environment by specifying the available range of metabolic possibilities. Given a similar environment, there is little difference between parent and daughter. If the environment changes, parents and daughters will change in similar fashion and within genetically imposed limits. Diversity of cell types rests upon mutation and attendant evolutionary phenomena.

In *multicellular organisms,* diversification of cell type without mutation is a regular feature of development. Most multicellular animals and plants start life as a single cell, a *zygote,* with a nucleus formed by the fusion of two parental nuclei. (Usually this results from fusion of sperm and egg or the equivalent.) The cell divides to produce daughter cells with identical DNA, but these *differentiate* into specialized cell types with different morphology and metabolism (for example, gland cells producing digestive enzymes or muscle cells rich in specially organized contractile proteins). In different cell types, different portions of the DNA are used in the transcription that underlies macromolecule synthesis. For a given cell type only a particular part of the total genetic information is responsible for the cell's characteristics. Thus constancy in DNA coexists with diversity in metabolism and morphology of the cells carrying that DNA.

Differentiation implies that cells are not mere aggregates of independent molecules or structures each "doing its own thing," and that DNA molecules are not autonomous rulers of subservient collections of other molecules. The expression of genetic information in a given cell depends largely on the interactions of DNA with other molecules—especially proteins—which control the production of RNA. Interactions among cells are key factors in determining the patterns of molecular interplay governing differential gene expression in a developing organism. The immediate environment of a given cell is strongly influenced by other cells, both neighboring and more distant; this environment can have major impact on the directions and timing of a cell's differentiation.

As in development, the normal functioning of adult multicellular organisms also depends upon the interaction of neighboring cells and upon long-range cell-to-cell interactions mediated, for example, by hormones or nerve impulses. Cells are integrated into tissues, tissues into organs, and organs into an organism. Similarly, cells are themselves highly organized: Molecules are built into structures in which they function in a coordinated and interrelated manner; they often show properties not found in a collection of the same molecules free in solution. The products of one organelle may be essential to the operation of another. Cell functions depend upon mutual interaction of parts. These interactions are elements of a network of mechanisms that regulate metabolism. *Cell organization* and the implications of organization for function are a third theme of the book. A fourth is the system of *regulatory* mechanisms by which cells—individually, and through their interactions—control the rates and directions of their activities: the timing of events; the nature and amounts of materials to be synthesized, broken down, or taken up from the outside; and cell shape and movement.

Reproduction and constancy, evolutionary and developmental diversity, the integration of cellular components into a functional whole—all are subjects

for investigation in modern cell biology. The fifth theme of the book is the dependence of major biological findings upon the development of *new methods of study* and upon the *choice of the best organism* for the problem at hand. We shall illustrate the kinds of experiments and approaches currently used in cell biology. The microscope is a central tool, but (as outlined in the first Preface) microscopic, biochemical, and physiological approaches increasingly are interwoven: Present-day cell biologists merge the structural focus of classical "cytology" and the molecular focus with which "cell biology" originally developed. Similarly, descriptive and experimental approaches supplement each other. The great diversity of cells and organisms presents opportunity for choice of cell types especially well suited for analyses of new problems. Investigations of pathological material and of cells experimentally stressed by abnormal conditions provide valuable clues to normal functioning.

Study of the cell is progressing rapidly, and the solution of many problems presently unsolved may be anticipated with confidence. Some of the unsolved problems are of practical importance. As our understanding of cells increases, so does our ability to control and modify them. This ability is crucial for medicine and agriculture. It also raises important ethical and social questions.

PART 1

Cytology and Cell Biology of Today

About 60 years ago, the last edition of E. B. Wilson's great book, *The Cell in Development and Heredity,* was published. It was a summation and synthesis of a vast cytological literature. The work reflects the extraordinary ingenuity of early experimenters and the great excitement over what was then a recent appreciation of the roles of chromosomes in heredity. It is concerned mainly with eucaryotic cells. The nucleus had been extensively studied; some of the cytoplasmic organelles had been identified although clarification of their functions was only beginning. Biochemical analysis of cells was in its infancy.

Since that time, and especially in the last 25 years, there has been a remarkable development of techniques applied to the study of cells. The electron microscope has extended the cytologists' investigation of structure down to the level of macromolecules. Biochemists have separated and analyzed cell molecules and organelles and determined their metabolic functions. Cytology and biochemistry have been combined to the extent that modern cytology is often referred to as *biochemical cytology.*

To illustrate current views of cell *organization,* we will begin with the rat *hepatocyte,* the major cell type of the liver. This cell type has many important functions, ranging from the secretion of blood proteins and the storage of carbohydrates to the destruction of toxic material produced elsewhere in the body. This variety of physiological functions is one reason that hepatocytes are widely studied by biochemists. Biochemical study is facilitated by the relative homogeneity of the organ; hepatocytes constitute over 60 percent of the cells and 90 percent of the weight of the liver in the rat. (The remainder consists of cells of blood vessels, ducts, and supporting tissues and specialized *phagocytes,* cells that engulf and remove from the blood a variety of materials such as some damaged or aged red blood cells.) Thus, constituents isolated from the liver

come primarily from one cell type, the hepatocyte. Rats are readily available, and they have large livers (almost 12 grams in an adult rat) from which relatively great quantities of cell constituents may be obtained. The hepatocytes are easily disrupted, to provide isolated organelles that can be studied by biochemical techniques. In addition, the liver is relatively easy to prepare for both light microscopy and electron microscopy.

To illustrate current views of *cellular metabolism,* we have chosen the metabolic pathway responsible for the formation of most of the ATP (*adeno-*

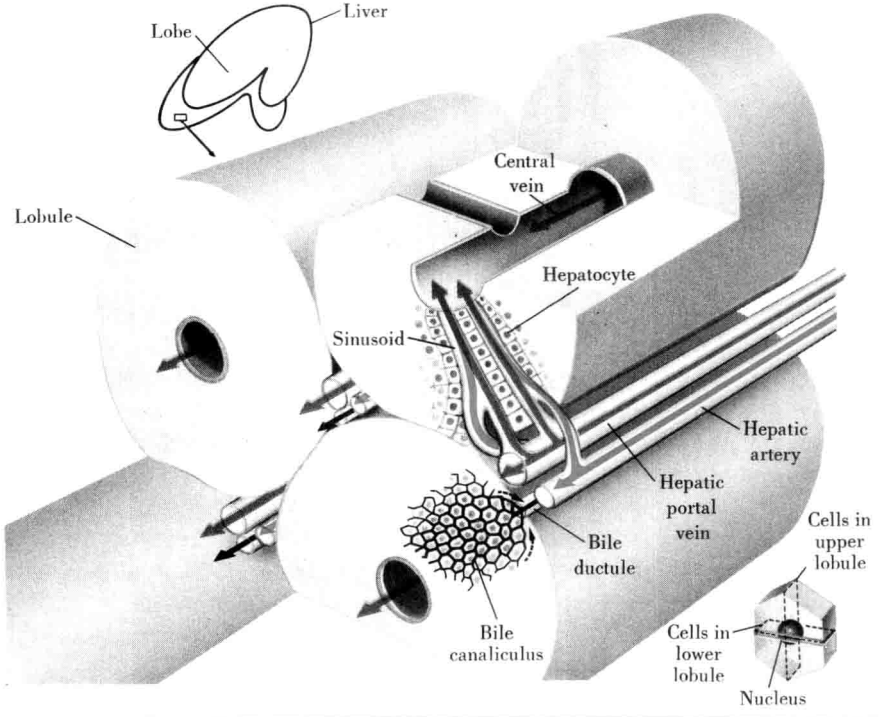


Figure I–1 ***Diagram of hepatic lobules*** **(rat liver). The lobule at the upper right illustrates the relations of the liver cells (hepatocytes) to the blood; that at the lower right illustrates hepatocyte relations with the channels (bile canaliculi) into which the cells secrete bile. The two lobules diagram different views of the same cells as indicated by the dashed boxes at the lower right (these illustrate the planes along which the cells would be cut—Figure I–10—to generate the views shown). Nutrient-rich blood, carried from the intestine by the hepatic portal vein and oxygen-rich blood from the hepatic artery enter the sinusoids (modified capillaries) within each lobule. After exchanges have occurred with the hepatocytes arranged along the sinusoids, the blood enters the central veins of the lobules and is carried out of the liver.**