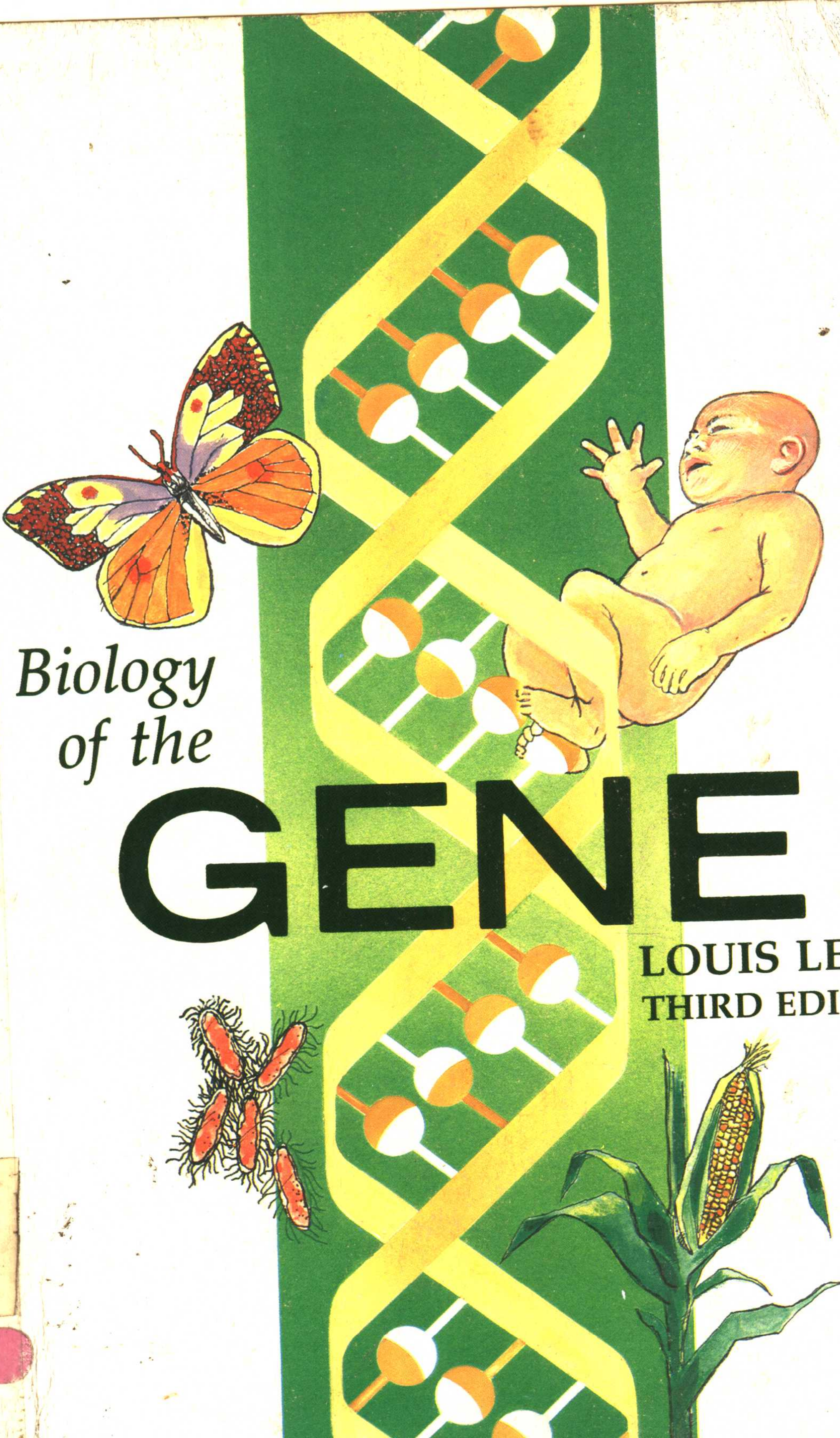

Biology of the GENE

LOUIS LEVINE

THIRD EDITION

Biology of the gene

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To my professors of genetics who
inspired as they taught

Theodosius Dobzhansky
L. C. Dunn
Howard Levene
Francis J. Ryan

Preface

This book is written for an undergraduate course in genetics. Two factors influence its content and organization. The first factor is the central and unifying position of genetics in the biological sciences, which requires consideration of such diverse areas as biochemistry, physiology, cytology, development, behavior, and evolution. The second factor is a desire to present, wherever possible, the experimental procedures and data that have led to our present concepts in genetics. This manner of presentation is an outgrowth of my firm conviction that education should not result solely in the accumulation of a body of information but must also include an understanding of the methodology used in the discipline studied and of the limitations in our knowledge about the subject.

It has been traditional to begin textbooks in genetics with a consideration of the work of Mendel and the principles of inheritance that his findings elucidated. However, discoveries on the nature of the genetic material and the manner in which it operates have shed light on the chemical bases of many previously known genetic phenomena. In order that the student may benefit from this information in the study of inheritance patterns, the first topics considered are the nature and functions of hereditary material, the genetic code, and the physical basis of inheritance. Discussions then follow of gene interactions, multiple-factor inheritance, sex linkage and sex determination, chromosome numbers, chromosome mapping, chromosomal rearrangements, and extrachromosomal inheritance. In all these discussions, the insight provided by recent findings on the nature and functions of the genetic material is stressed. Next follows an analysis of the nature of the gene as seen in mutation, recombination, and complementation. This consideration of the different aspects of the gene leads into a study of the regulation of gene action and the control that genes have over metabolism, development, and behavior. The final topics discussed are the genetic composition of populations of organisms and the fate of genes in succeeding generations of a given population. Other subjects included in these latter discussions are the roles of mutation, selection, migration, and genetic drift in determining the genetic composition of different populations of a species and the permanent establishment of genetically diverse populations through species formation. The importance of investigations in ecological genetics for an understanding of the evolutionary process is stressed. The book closes with a discussion of a laboratory experiment designed to demonstrate evolution on the molecular level.

Wherever possible, the relationship of genetic phenomena to human beings has been stressed. This is done not only to increase the student's interest in the material being discussed but also because human genetics has become one of the very active fields in modern research. The present explosive period of genetic research and publication has added a tremendous body of information to an already considerable amount available from the older literature. Because of the necessity of limiting the various discussions in the book to workable dimensions, a list of further readings is provided at the end of each chapter. Some of these references are designed to give the student historical background for topics covered within the chapter, while others are provided to afford the student a wider acquaintance with modern research efforts in the field.

It has been 7 years since the second edition of this book was published. In that time, the field of genetics has continued its explosive contribution to virtually every aspect of biology and medicine. The current edition has been revised with this recent material in mind. New topics have been added, and a number of original discussions have been rewritten in the light of new information. It is hoped that these additions and revisions will help present the material of genetics as the exciting body of information it is.

Since its publication, this book has been used by many genetics classes both in the United States and abroad. I am deeply grateful to those instructors and students who have written either to the publisher or directly to me and have made suggestions for the book's improvement. I would specifically like to acknowledge the efforts of Dr. Brian K. Davis (Virginia Polytechnic Institute) and Dr. Frank H. Wilcox, Jr. (Indiana State University), who wrote at length covering all aspects of the book. Their recommendations have received careful study during the preparation of the present edition. I am especially indebted to two of my own students, Ms. Harriet Laine and Ms. Linda Rubenstein, who have given me the advantage of the student's point of view. The present effort has been guided by and has benefited a great deal from all of the above. I sincerely hope that those who use this book will continue to advise me of their reactions to it.

This edition of the book has benefited from the efforts of many persons. I am especially indebted to the following associates for their helpful discussions and collegiality: Dr. Thaddeus A. Bargiello, Dr. Sharon D. Cosloy, Dr. Joseph Grossfield, Dr. Max Hamburgh, and Dr. Robert F. Rockwell. Any shortcomings of the book, however, are my responsibility alone. Finally, I wish to express my appreciation to Mr. Joseph T. Fevoli for preparing the illustrations and to Mrs. Mary Lou Thompson for performing the arduous task of typing the manuscript. Credits for tables and figures from other publications are given in the legends according to the wishes of the author or publisher. I am indebted to the literary executor of the late Sir Ronald A. Fisher, F.R.S.; to Dr. Frank Yates, F.R.S.; and to Oliver & Boyd, Ltd., Edinburgh, for permission to reprint Tables 3 and 4 from their book *Statistical Tables for Biological, Agricultural and Medical Research.*

Louis Levine

Contents

1

Nature and functions of hereditary material

Genetics is the branch of biology that deals with heredity and variation. This definition would appear to limit the area of study to the transmission of characteristics from parents to offspring and to the study of the variability in traits that may occur from one generation to the next. However, the field of genetics is in reality very broad, for within its scope lie such topics as (1) identification of the hereditary material and the nature of its chemical and structural properties; (2) study of the organization of the genes into chromosomes and the transmission of the chromosomes from parents to progeny either in asexual or sexual reproduction; (3) analysis of the interactions of the different genes and the role of environment in producing the characteristics of the individual; (4) study of the different types of genetic diversity that can occur and the consequences of this diversity to the individual and to the population. Genetic studies may attempt to gather information on such differing subjects as the origin of living material from nonliving matter and the future of the human species.

It is obvious that our knowledge concerning many of these topics is incomplete. In our discussions the limits of our information on a particular subject will be stated, and whenever possible, the areas in which future research might bring meaningful answers to questions will be indicated. Let us begin our study of genetics with a review of our knowledge of the nature and functions of the hereditary material.

IDENTIFICATION OF GENETIC MATERIAL

Prime goals in the study of genetics have been the identification and analysis of the actual genetic material. As it turned out, we had acquired much information about the modes of inheritance and about the relationships of genes to one another before we were able to demonstrate which of the many chemical compounds of the cell is the genetic material. Furthermore, much of the chemistry of the genetic material was known long before its significance in genetics achieved wide understanding and acceptance.

As long ago as 1807 the distinction between inorganic and organic compounds was made. By 1820 it had become customary to think of the organic compounds as falling into one or another of three broad groups: the carbohydrates, the lipids, and the proteins. By the mid-nineteenth century it seemed clear that, of the three organic compounds, *proteins* were the most complicated in structure and the most important in cell function. However, in 1871 a chemist named F. Miescher reported that he had isolated from the nuclei of pus cells a substance that turned out not to be carbohydrate, lipid, or protein. Since he had obtained the new substance from nuclei, Miescher named it *nuclein*. Later the substance was discovered to have acid properties, and it was renamed *nucleic acid*.

Transformation in bacteria

The identification of the genetic material became a point of dispute between investigators who thought the material resided in the protein of the nucleus and those who believed it to be in the nucleic acids. A resolution of the problem did not come until 1944 when Avery, MacLeod, and McCarty reported their work on *transformation* in pneumococci. In human beings, pneumonia is sometimes caused by the bacterium *Diplococcus pneumoniae*, commonly known as *pneumococcus*. There are two types of pneumococcal cells. In one type of cell a considerable amount of polysaccharide material is secreted by the cell, and a large capsule forms around the cell. The colony produced by these cells has a glistening appearance and is called "smooth" (S). In the other type of cell no polysaccharide slime layer is secreted by the cell. The colony formed by such cells has an irregular appearance and is termed "rough" (R). Smooth (S) cells are virulent and can cause pneumonia, but rough (R) cells are nonvirulent.

Investigations of the S form of *pneumococcus* revealed the existence of many kinds of capsules, each distinguishable on the basis of differences in the chemical composition of its polysaccharide. The S pneumococci were classified as type I-S, type II-S, type III-S, etc. Each type, when it divides, produces cells of the same type as the parental cell. Occasionally an S bacterium will change to an R bacterium (1 per 10^6 or 10^7 cells). The reverse change, R to S, almost never occurs. When the R cells divide, they always give rise to more R cells. Avery and co-workers disrupted encapsulated cells of type III-S. They then fractionated the debris from the disrupted cells into its various chemical components (carbohydrates, lipids, etc.). After this they took R cells that had been derived from type I-S cells and separately mixed different samples of them with each of the cell components from the type III-S cells. Only the DNA fraction of the type III-S cells was found capable of transforming some of the unencapsulated (R) cells to encapsulated (S) cells. The transformed encapsulated cells were type III-S, the same type as the cell from which the DNA was obtained (Table 1-1).

Table 1-1. Experiment demonstrating that the genetic property for pneumococcus capsule formation resides only in DNA of cell

Colonies cultured	Colonies recovered
R derived from type I-S	R
Type III-S	Type III-S
Heat-killed type III-S	None
R derived from type I-S and heat-killed type III-S	R and type III-S
R derived from type I-S and carbohydrates from type III-S	R
R derived from type I-S and lipids from type III-S	R
R derived from type I-S and proteins from type III-S	R
R derived from type I-S and DNA from type III-S	R and type III-S

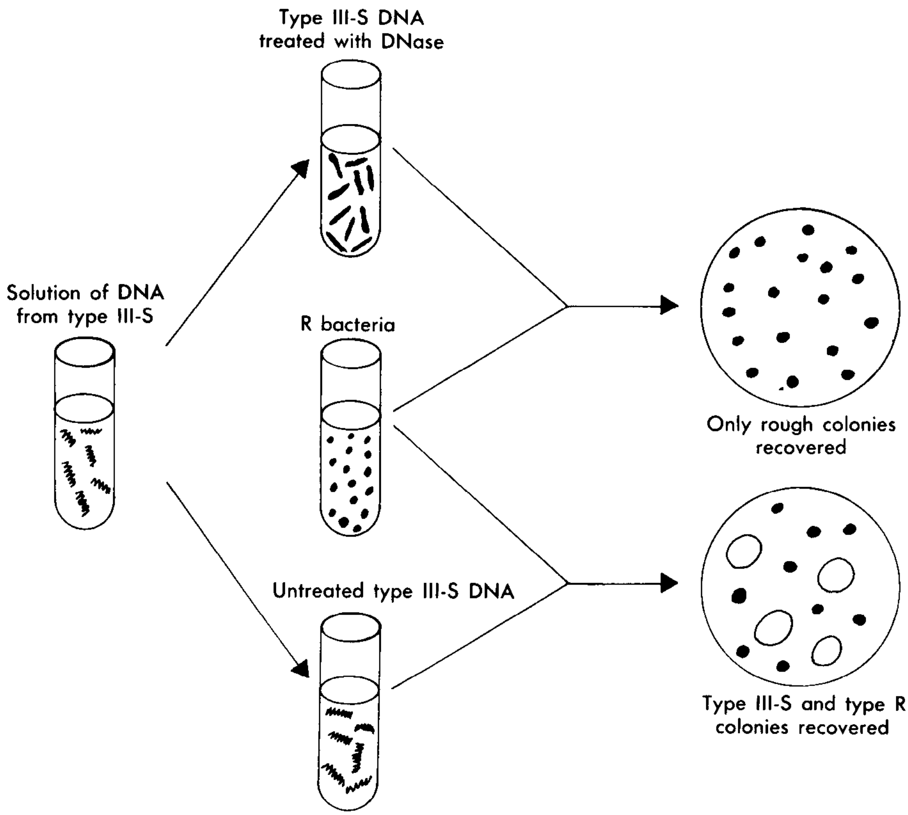

Fig. 1-1. Transformation of pneumococcus, using DNA extracted from heat-killed smooth cells. DNase is an enzyme that breaks down DNA.