

Genetics

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 *To my son, the writer*



Preface

Historically, the science of genetics has developed along two tracks, the classical and the molecular. Classical genetics originated in the 1870s with Mendel, whose work led to the establishment of the basic laws of the inheritance of alleles. Continuous developments have occurred along the classical track up to the present time. Molecular genetics, by contrast, arose only in the 1940s. It began with the hypothesis that there is a one-to-one correlation between genes and proteins, and with the demonstration that nucleic acid is the chemical basis of heredity. During the 1950s and the 1960s, molecular genetics made rapid strides in the study of prokaryotes and viruses. Coincidentally, great advances were being made in our understanding of DNA, RNA, and protein synthesis. After gene manipulation techniques were developed, in the 1970s, even the most complex eukaryotes became accessible to molecular genetic analysis.

In order to comprehend what has been accomplished in genetics, as well as what is being done in the field today, a student must be acquainted with a broad range of principles and techniques relating to both classical and molecular genetics. Unfortunately for the student, however, there is a tendency to categorize classical and molecular genetics as distinct subjects presented in separate chapters or separate lectures. The division of genetics along these lines is, of course, artificial and does not accurately reflect genetic processes in nature. One of the main goals of this text is to provide instructors and students with an alternative, by supplying a unified treatment of both classical and molecular genetics.

In addition to presenting such a unified view, the emphasis in this text is on clarifying principles through the presentation of critical experiments.

For this purpose I have found it pedagogically effective to focus on a limited number of organisms. This approach allows the reader to view each organism fairly extensively and from several vantage points. More important, it ensures that the emphasis is always on genetic principles and not on the general biological characteristics of many organisms.

The organisms selected for attention include *E. coli* and lambda bacteriophage, from the prokaryotic world; the yeast *Saccharomyces cerevisiae* and the fungus *Neurospora crassa*, from the eukaryotic protists; the fruit fly *Drosophila melanogaster*, mice, and humans, from the animal world; and peas and corn, from the plant world. All have been the subjects of extensive genetic research and therefore serve my purpose well. Nevertheless, I have included references to other systems whenever an especially interesting genetic principle could not otherwise be demonstrated.

The internal logic of genetics gives it an intellectual beauty unsurpassed among the biological sciences. Consistent with the uniquely logical relationship between genetic principles and genetic facts, the progression of major discoveries in genetics has also assumed a logical course. By presenting key observations in the order of their discovery, that is, by using the historical approach, it is possible to illustrate this logical consistency in a most interesting manner. Indeed, the history of genetics consists of one adventure after another, and the entire subject may be presented as one exciting story. I have found, therefore, that within any given chapter, the historical approach increases student interest in the subject, as well as most closely depicting reality. On the other hand, the order from chapter to chapter is not strictly historical because another pedagogical principle takes precedence. That principle is to proceed carefully from fundamental concepts to more complex phenomena and techniques of study.

• ORGANIZATION

The first seven chapters (Parts 1 and 2) are intended to present basic principles. Chapters 1 and 2 encompass the fundamental rules that govern inheritance patterns and chromosomal behavior. Chapters 3 and 4 deal with the chemical nature of the gene. The biochemical basis of gene expression is explained in Chapters 5–7. The content and presentation are appropriate for a student's first exposure to the subject, and will enable one to understand the molecular relationship between genotype and phenotype. Chapters 8–11 (Part 3) describe different ways in which genes may be altered through mutation or recombination and the effects these changes have on gene expression. This subject is presented before considering the arrangement of genes because mutation and recombination are the basic tools used to determine gene arrangement. Chapters 12–15 (Part 4) discuss the arrangement of genes in a select group of organisms. Examples have been carefully chosen to illustrate the broad array of techniques used by geneticists to determine gene arrangement. The reader who has

completed Chapter 15 should have a good grasp of the basic principles and techniques of genetics.

At this point in the text, attention turns to some of the more interesting questions in modern genetics—those related to the different mechanisms of regulating gene expression. Chapters 16–18 (Part 5) describe some relatively well understood examples of gene regulation among microorganisms before presenting more complex examples involving higher organisms.

The concluding portion of the book, Chapters 19–22 (Part 6), covers several very important contemporary genetic concerns. Chapter 19 can be regarded as an extension of Part 5, on gene expression. It deals with the regulation of gene expression at the level of a multicellular developing organism that ultimately contains an array of differentiated cell types. Chapter 20, on evolution and population genetics, can be considered an extension of Part 3; it treats the problems of inheritance at the level of populations rather than at the level of individual organisms or individual mating pairs. The dynamics of mutagenesis and selection can be properly appreciated only by considering whole populations. The same is true of most evolutionary phenomena, and that is why I consider it important to treat population and evolutionary considerations in the same chapter. Chapter 21, on the function of mobile genetic elements, could also be regarded as an extension of Part 3, as it deals with the question of nonhomologous recombination, a topic that was introduced in Chapter 10. The final chapter discusses animal viruses, with the emphasis on a few animal viruses that cause cancer. Our knowledge of cancer has dramatically increased because of detailed observations of these viruses and of the genes in the viruses which are related to carcinogenesis. These studies are leading to a picture of cancer as a state where the normal factors controlling growth have been altered and become deregulated.

There are many possible ways to organize a course in genetics, and thus a textbook in genetics. I have chosen an organization that facilitates my goal of unifying the presentation of classical and molecular genetics. At the same time, however, I have sought the input of many instructors and have tried to produce a text that will be effective for other, diverse course goals.

● SUGGESTIONS FOR READING ASSIGNMENTS

The text was written so that, in theory, it could be read from cover to cover. However, there are practical limitations to the amount of material that can be covered in a given term. I do not expect the entire text to be used in any given classroom. Some instructors may choose to spend most of their course time on the parts that cover the fundamental concepts of genetics; others will prefer to save substantial amounts of classroom time for examining later material, such as the regulation of gene expression.



In many cases a decision to delete or add material caused me great discomfort as I evaluated conflicting opinions. On the whole I have chosen to maintain comprehensive coverage throughout. This choice results, again, from my awareness that different instructors will have different goals, even as no two students will have the same preparation or interests upon entering the course. Because the text is written with a variety of users in mind, it should support whatever emphasis an instructor may prefer.

In the table of contents I have indicated sections within each chapter that I consider most essential to understanding the general subject of a chapter. Those sections, which can be used as core material, are preceded by an asterisk. Other sections contain added examples. In addition, many chapters are constructed with basic concepts at the beginning and more elaborate details towards the end. This structure should allow for use in a wide selection of course outlines. Material that is clearly supplementary appears in boxes located near the relevant text. Instructors who would like any help in devising a sequence that fits their course objectives should feel free to contact me. I would also be interested in hearing about alternative course organizations that have worked well in use.

● ADDITIONAL FEATURES

In addition to being organized in a manner that promotes flexibility, the text has other significant features. Each chapter has been written with several levels of explanatory subheads. Their purpose is to provide students with a framework for learning and to enhance the volume's usefulness for review and later reference. The figure captions are sufficiently detailed to support the illustrations without the need for continual referral to text discussion. Each chapter ends with a summary of key points, additional reading sources, and problems. A complete solutions manual is available for purchase at the instructor's discretion.

● DEVELOPMENT OF THIS TEXT

Now that I have explained how this text can be used, I would like to briefly explain how it was written. Even after thirty years of living genetics day and night, I found that there were significant gaps in my knowledge of the subject. Fortunately, I was able to entice some of my colleagues to write sections of the text in the areas where I did not feel that I had sufficient expertise. Many additional colleagues were consulted during the process of writing and review. Indeed, every chapter was reviewed at three levels: First, each chapter was reviewed for accuracy and appropriate content by authorities in that area. Second, the book was reviewed for style, level, and explanation by instructors at a variety of schools, a process that resulted in revisions until there was uniform satisfaction among the reviewers. Third and finally, the entire manuscript was intensively reviewed for readability and general pedagogy by Ruth Melnick, a professional development editor.



As a result of her criticisms large sections of text were substantially rewritten. Throughout this process chapters were revised by me personally to give the text a uniform flow and consistency of style without duplications or omissions. Much thought and care also went into the illustrations that accompany the text, and James Funston was an enormous help to me there. But perhaps my greatest debt is to Bruce Spatz, my editor at Addison-Wesley, who oversaw this work most of the way. He shared my perception of how the material should be presented, and his shrewdness and support were a major factor in bringing the text to a much higher standard than would otherwise have been achieved.

Many readers may imagine that once an author has delivered a final manuscript to the publisher, the show is over. This is certainly not the case. The people involved in the production of a printed text are extremely important in assuring its readability, accuracy, and attractive appearance. I was extremely fortunate in having the most skilled professionals involved in the production of this text. My thanks go foremost to Sherry Berg, who managed the overall production and picked the others to be involved. Joe Vetere managed the illustrations, Emily Arulpragasam was responsible for the copy editing, and Lorraine Hodsdon did the page arrangement. Finally, Vanessa Piñeiro was in charge of design. Their contributions, like those of all who have helped along the way, are deeply appreciated.

New York

G.Z.

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