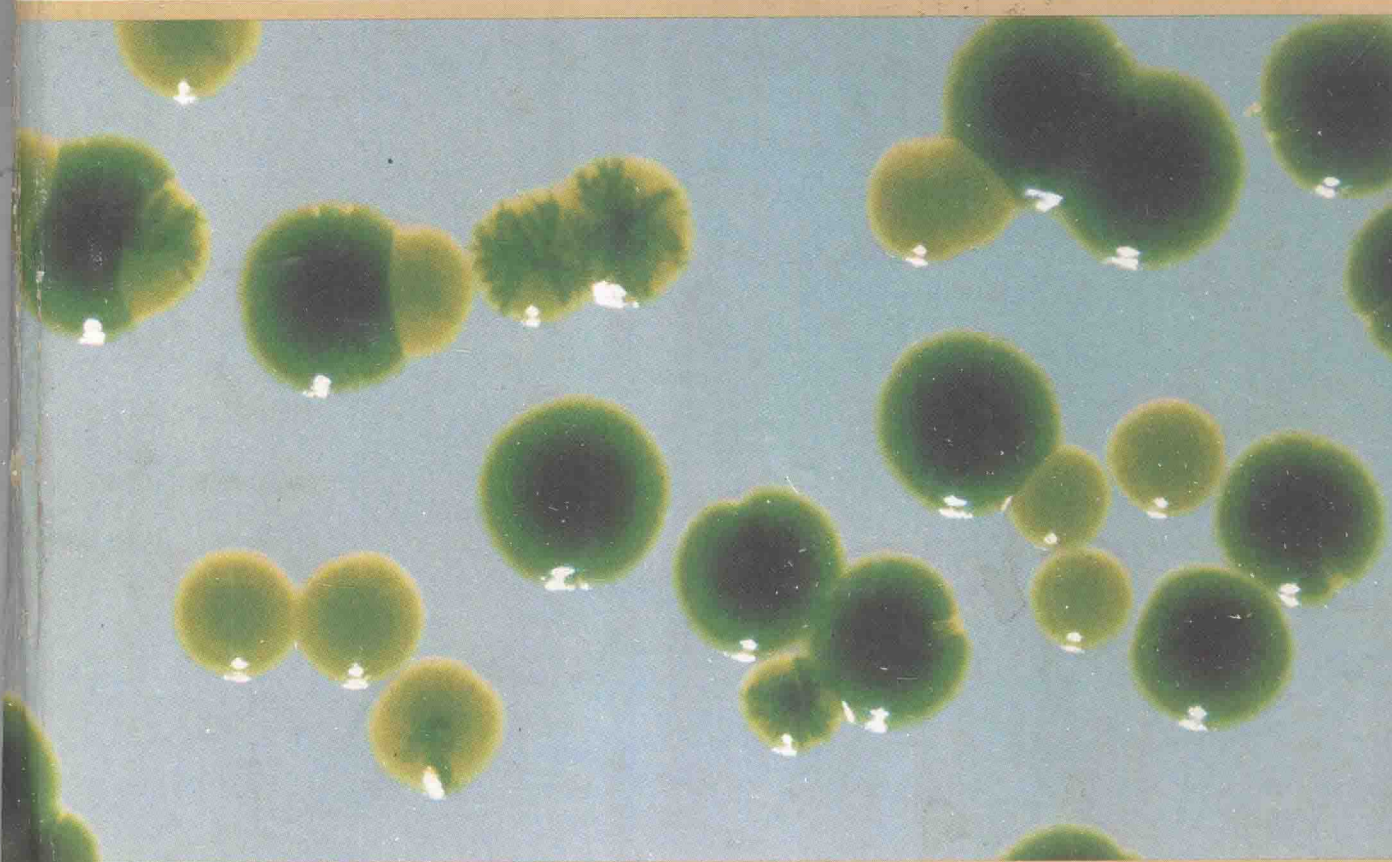


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# GENETICS

THIRD EDITION

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Third Edition

# Genetics

**Ursula Goodenough**

Washington University

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# Preface

Do DNA sequences belong in a genetics textbook? This was the most important question I faced as I undertook writing a third edition of this text in the midst of the cloning/sequencing “revolution.” The DNA sequences prevailed, as a glance through the text will indicate. My reasoning can be summarized as follows.

Genetics seems to have been embroiled in an identity crisis since 1953, when genes began to be actively analyzed as molecular units as well as heritable units of function. Scientists who studied the molecular properties of genes came to call themselves molecular biologists, whereas those who continued to study genes as heritable units of function called themselves geneticists. Pedagogical distinctions soon followed: molecular biology textbooks were devoid of mapping functions and epistasis, whereas genetics textbooks rarely mentioned histone phosphorylation or  $C_0t$  plots. A dichotomy also developed in teaching styles: whereas undergraduate courses in molecular biology were full of the “latest news,” with relatively little attention paid to the development of the field, courses in genetics were usually taught in an historical fashion, with much emphasis placed on the intellectual approaches taken during and since Mendel’s original experiments.

I have written this edition with the conviction that these distinctions are already obsolete in practice and should be made obsolete in the classroom. Molecular biologists, now able to clone genes at will and sequence them in weeks, have come knocking on the doors of geneticists to obtain strains with interesting genetic properties. Geneticists, meanwhile, have come to realize that gene fine structure will never again be productively tackled by the heroic genetic approaches of Benzer, Sherman, or Judd, and they are increasingly receptive to the knocks on the door from their molecular colleagues. Population geneticists are using restriction enzymes to detect polymorphisms; evolutionists are discovering that the genomes of modern organisms contain a rich fossil record of their genetic ancestry;

molecular biologists attend conferences on hybrid dysgenesis in *Drosophila* and the dissociator-activator system in maize. With the old distinctions rapidly blurring in the laboratory, why should they continue to be perpetrated on undergraduates?

I usually hear three answers to this question. One is the notion that the molecular material is "too hard," that students won't understand it. This is certainly true for non-science majors, for whom this text is definitely not written, but biology majors take required chemistry courses that provide ample background for understanding the principles of molecular genetics when they are carefully presented. Indeed, it is my experience that most students are able to understand the implications of a DNA sequence far more readily than a coefficient of coincidence, but perhaps other instructors have a different impression. Then there is the intellectual argument. Once students grasp the construction of a brilliant genetic proof, are they not better trained in science? I strongly agree that they are, and the text includes detailed presentations of many "strictly genetic" experiments. But if these experiments are presented in a molecular vacuum, then the training is incomplete: the student emerges steeped in genetic logic but has not been allowed to combine that logic with a knowledge of how genes are constructed and how they recombine, mutate, and express themselves.

Finally, it is argued that students will learn "that stuff" in another course. I agree that such subjects as DNA replication, renaturation kinetics, and sequencing are rightly considered in considerable depth in biochemistry and molecular biology courses. They are presented quite superficially in this text. It hardly follows, however, that genes should not be the focal subject of a genetics course.

In a field moving as rapidly as genetics, it proves impossible to simply "update" a previous edition. Therefore, this is once again an almost entirely new book. Major changes from the second edition include the following:

1. New chapters have been added on somatic cell genetics, transposable elements, and immunogenetics, three of the most rapidly advancing fields in the past five years.
2. Such topics as mutation, recombination, chromosome structure, and gene structure are each presented in two chapters, the first giving a general overview and the second a more detailed molecular view (see Table of Contents). This should allow instructors more flexibility in determining the "molecular depth" of their assignments.
3. Population and quantitative genetics have been expanded considerably.
4. By popular request, Mendel's experiments are included *per se*.

I have been fortunate to obtain excellent critiques on the previous and current editions. Particular thanks go to Drs. Julian Adams (University of Michigan), Fred Allendorf (University of Montana), Alan Atherly (Iowa



State), C. William Birky (Ohio State), Barbara Brownstein (Temple University), Darrel Falk (Syracuse University), Peter Kuempel (University of Colorado), Gustavo Maroni (University of North Carolina), H. James Price (Texas A & M University), W. Stuart Riggsby (University of Tennessee), Raymond Rodriguez (University of California, Davis), Carol Sibley (University of Washington), Richard Siegal (U.C.L.A.), Edward Simon (Purdue University), Millard Susman (University of Wisconsin), Eric Weinberg (University of Pennsylvania), and Herbert Wiesmeyer (Vanderbilt University) for their overall reviews and to Drs. Douglas Berg (Washington University), Richard Borowsky (New York University), Nam-Hai Chua (Rockefeller University), Jeffrey Davidson (Eleanor Roosevelt Institute, Denver), W. J. Dickinson (University of Utah), John Drake (National Institute of Environmental Health Sciences), Sarah Elgin (Washington University), Nancy Martin (University of Texas, Dallas), Janice Pero and Vicki Sato (Harvard University), and Christopher Woodcock (University of Massachusetts, Amherst) for their individual chapter reviews. Michael Brown, Biology Editor at Saunders, provided important help at many stages in the production process.

This edition was written almost entirely in the serenity of Chilmark, Massachusetts, in the loving presence of my four children—Jason, Mathea, Jessica, and Thomas—and my husband, John Heuser. The book is the product of the peace of mind, and hence the clarity of thought, that they all bring to me.

# Contents

The 20 chapters displayed in black present the “core material” of present-day genetics; the 8 chapters displayed in gray offer detailed presentations of topics in molecular genetics.

Preface    iii

## **1 DNA (and RNA) as the Genetic Material in Chromosomes    1**

---

Introduction	1
The Requirements to Be Met by Genetic Material	2
The Structure of DNA and RNA	4
Relating DNA Structure to Its Genetic Requirements	14
Experiments Indicating DNA and RNA as the Genetic Material	17
<i>Questions and Problems</i>	23

## **2 Cell Cycles, Chromosome Duplication, and Mitosis    25**

---

Introduction	25
The Bacterial Cell Cycle and Chromosome Replication	26
The Eukaryotic Cell and Cell Cycle	34
The Karyotype	48
Atypical Eukaryotic Cell Cycles	57
<i>Questions and Problems</i>	60

---

### **3 Molecular Organization of Chromosomes 62**

---

Introduction	62
Protein Structure	63
Chromosomal Proteins	73
The 10 nm Nucleosome Filament of Chromatin	74
Higher Orders of Chromatin Organization	81
<i>Questions and Problems</i>	92

---

### **4 Molecular Analysis of Chromosomal DNA and Genetic Engineering 93**

---

Introduction	93
Overall Composition of Genomic DNA	94
Reassociation Kinetics ( $C_0T$ Plots) of Genomic DNA	98
The Kinetic Classes of Eukaryotic DNA	102
Restricting, Sequencing, and Cloning DNA	108
<i>Questions and Problems</i>	122

---

### **5 The Meiotic Transmission of Chromosomes 124**

---

Introduction	124
Meiosis	125
Life Cycles of Sexually Reproducing Organisms: Mitosis-Meiosis	
Alternations	137
Meiotic Errors	145
<i>Questions and Problems</i>	153

---

### **6 Mendelian Inheritance of Genes Carried by Autosomes and Sex Chromosomes 153**

---

Introduction	154
Mendel's Experiments	154
Segregation of Alleles	159
Independent Assortment	170
Sex-Linked Inheritance	182
<i>Questions and Problems</i>	196



## **7 Mutation: Induction and Detection of Mutant Organisms and Chromosomes 201**

---

Introduction	201
Screening Procedures	204
Characterizing Mutant Karyotypes	212
Mutagens, Clastogens, and Carcinogens	220
<i>Questions and Problems</i>	227

## **8 DNA Replication and Repair Mechanisms and Their Contribution to Mutagenesis 230**

---

Introduction	230
DNA Replication Mechanisms	231
Direct Mutagenesis Mechanisms	237
Repair and Misrepair Mechanisms	245
<i>Questions and Problems</i>	255

## **9 Genes and Gene Transcripts: General Features 258**

---

Introduction	258
General Features of Transcription	259
Anatomy of Structural Genes	267
"Split Genes" in Eukaryotes	272
Visualizing Structural Gene Transcription	277
<i>Questions and Problems</i>	282

## **10 Genes and Gene Transcripts: Specific Genes 285**

---

Introduction	285
Transfer RNA Genes	286
Ribosomal RNA Genes	294
Structural Eukaryotic Genes	300
<i>Questions and Problems</i>	306

## **11 Structural Gene Expression and the Genetic Code 308**

---

Introduction	308
Protein Synthesis	309
"Cracking" the Genetic Code	317
Nonsense Mutations and Chain Termination	330
Suppressor Mutations	332
<i>Questions and Problems</i>	336

## **12 Mapping Viral Chromosomes 340**

---

Introduction	341
Viral Infection Cycles	341
Complementation Analysis	348
Recombination-Frequency Mapping	352
Deletion Mapping	367
Mapping without Recombination	375
Approaches to Solving Mapping and Complementation Problems	385
<i>Questions and Problems</i>	389

## **13 Mapping Bacterial Chromosomes and Plasmids 399**

---

Introduction	400
Molecular Overview of Bacterial Conjugation	400
Mapping by Bacterial Conjugation	405
Bacterial Transformation	413
Generalized Transduction	417
Specialized Transduction	421
Plasmids	425
Approaches to Solving Mapping Problems	432
<i>Questions and Problems</i>	433

## **14 Mapping Eukaryotic Chromosomes in Sexual Crosses 437**

---

Introduction	438
Classical Studies on Linkage and Recombination	438
Mapping <i>Drosophila</i> in Sexual Crosses	444
Cytological Mapping	450
Linkage Groups and Chromosomes	456

Mapping by Tetrad Analysis	459
Approaches to Solving Mapping Problems in Eukaryotes	472
<i>Questions and Problems</i>	475

## 15 Somatic Cell Genetics 482

---

Introduction	482
The Parasexual Cycle of <i>Aspergillus</i>	483
Genetic Analysis of Cultured Somatic Cells	490
Gene Transfer or Eukaryotic Transformation	498
The Human Chromosome Map	503
<i>Questions and Problems</i>	507

## 16 Extranuclear Genetic Systems 511

---

Introduction	512
Molecular Studies of Mitochondrial Genetic Functions	512
Genetic Analysis of the Yeast Mitochondrial Genome	515
Mitochondrial Genomes of Higher Eukaryotes	523
Chloroplast Genomes	527
Endosymbiosis and the Origins of Organelle Genetic Systems	531
Inheritance of Preformed Structures	533
<i>Questions and Problems</i>	535

## 17 General Recombination Mechanisms 538

---

Introduction	539
Models of General Recombination	539
Enzymes that Mediate General Recombination	547
Formation and Segregations of Physical and Genetic DNA Hybrids during General Recombination	550
Mismatch Repair of Heteroduplex DNA during General Recombination	554
<i>Questions and Problems</i>	565

## 18 Transposition and Mutagenesis by Temperate Viruses and Transposable Elements 569

---

Introduction	569
Integration and Excision by Temperate Bacteriophages	570
Integration and Excision by Transposable Elements	577
<i>Questions and Problems</i>	589

## **19 Related Genes: Alleles, Isoloci, and Gene Families 591**

---

Introduction	591
Traits Controlled by a Single Gene Locus	592
Isozymes Specified by Isoloci	604
Gene Families	606
Distinguishing Alleles, Isoloci, and Gene Families in Genetic Crosses	613
<i>Questions and Problems</i>	615

## **20 Immunogenetics 618**

---

Introduction	619
Properties of the Immunoglobins	619
Construction and Expression of Light-Chain Genes	625
Construction and Expression of Heavy-Chain Genes	634
Somatic Mutation of Antibody Genes, and a Summary of Antibody Diversity Mechanisms	637
<i>Questions and Problems</i>	640

## **21 Genes that Cooperate to Produce Complex Phenotypes and Quantitative Traits 642**

---

Introduction	642
Clustered Genes Specifying One Trait	643
Dispersed Genes Specifying One Trait	652
Biochemical Genetics	654
Polygenes and Continuous Variation	664
<i>Questions and Problems</i>	675

## **22 Control of Gene Expression in Bacteria 681**

---

Introduction	682
General Features of Gene Regulation	682
Regulation of Lactose Utilization	687
Regulation of Tryptophan Biosynthesis	697
Translational Control	704
<i>Questions and Problems</i>	705

## **23 Control of Gene Expression in Bacteriophages and Eukaryotic Viruses 709**

---

Introduction	709
Regulation of Gene Expression by Lytic Bacteriophages	710
Regulation of Gene Expression during Phage $\lambda$ Infection	713
Gene Regulation during SV40 Infection	723
<i>Questions and Problems</i>	726

## **24 Control of Gene Expression in Eukaryotes: Short-Term Regulation 728**

---

Introduction	728
Short-Term Regulation in Fungi	729
Short-Term Regulation in Higher Eukaryotes	733
Mechanisms of Short-Term Regulation in Eukaryotes	739
<i>Questions and Problems</i>	742

## **25 Control of Gene Expression in Eukaryotes: Long-Term Regulation 745**

---

Introduction	746
General Features of Long-Term Differentiation	746
The Differentiation of the Egg and Maternal Influences on Development	753
Development Genetics of <i>Drosophila</i>	760
Developmental Genetics of Vertebrates	774
Differential Expression of Hemoglobin Genes	783
<i>Questions and Problems</i>	788

## **26 Population Genetics I: General Principles and Mendelian Populations 792**

---

Introduction	792
General Principles of Population Genetics	793
Genetic Variability in Populations	797
Mendelian Populations	802
<i>Questions and Problems</i>	814

## **27 Population Genetics II: Evolutionary Agents 819**

---

Introduction	820
Fitness	820
Selection	823
Migration	842
Random Drift in Small Populations	846
The Contributions of Selection and Drift to Polymorphism	851
<i>Questions and Problems</i>	855

## **28 Populations Genetics III: Speciation and Molecular Evolution 858**

---

Introduction	858
Speciation	859
Molecular Evolution	864
<i>Questions and Problems</i>	875

## **Boxed Reference Material**

---

CsCl Gradient Centrifugation	30
Autoradiography	32
Antibodies and Antibody Testing	45
Staining and Banding Chromosomes	53
Chromotography	67
Gel Electrophoresis	69
Properties of Enzymes Relevant to Molecular Genetics	79
DNA Sequencing	114
Sucrose Gradient Centrifugation	273
Southern Blot Hybridization	381

## **Index 879**



# 1

## DNA (and RNA) as the Genetic Material in Chromosomes

- A. Introduction
- B. The Requirements to Be Met By Genetic Material
- C. The Structure of DNA and RNA
  - 1.1 The Polynucleotide
  - 1.2 The Double Helix
- D. Relating DNA Structure to Its Genetic Requirements
  - 1.3 DNA as a Coded Molecule
  - 1.4 DNA Replication
  - 1.5 DNA Expression
  - 1.6 DNA Variation
- E. Experiments Indicating DNA and RNA as the Genetic Material
  - 1.7 Transformation Experiments
  - 1.8 Hershey-Chase Experiments
  - 1.9 Experiments with RNA Viruses
- F. Questions and Problems

### Introduction

Today, when the terms **gene** or **genetics** are mentioned, most biologists immediately think of **DNA**. DNA, or **deoxyribonucleic acid**, is well known as the chemical bearer of genetic information; **RNA (ribonucleic acid)** serves this function in certain viruses.

In the history of genetics as a science, DNA became the center of attention only relatively recently. Focus first centered on **heredity**, on the patterns of inheritance of a given trait (blue eyes, red flower color, short tail) from parent to offspring. It was postulated that these inherited traits were somehow dictated by genes and that genes were linearly arranged along the chromosomes of higher animals and plants. "Maps" of gene order on chromosomes were constructed, and many of the details of gene transmission from generation to generation were worked out well before much was known about what a gene is and how it acts.

As the science of genetics developed, increased attention was given to how genes function, and more experimental use was made of microorganisms, notably bacteria and bacterial viruses. During this period it was proposed, with good evidence, that **the function of most genes is to specify the formation of proteins**. When it was eventually established that most genes are borne within molecules of DNA, primary attention was given to the chemical nature of the gene itself.

In beginning our text with DNA and RNA and in developing a molecular picture of genes and gene function at the same time as we establish patterns of heredity, we are, in one sense, violating the sequence set by scientific history. In another sense, of course, we are more closely following evolutionary history, since genes almost certainly developed their fundamental properties well before the hereditary patterns exhibited by modern organisms were established.

## The Requirements to be Met by Genetic Material

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Certain requirements must be met by any molecules if they are to qualify as the substances that transmit genetic information. These requirements extend directly from what is known about the continuity of species and the process of evolutionary change.

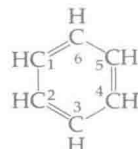

1. **Genetic material must contain biologically useful information that is maintained in a stable form.**
2. **Genetic information must be reproduced and transmitted faithfully** from cell to cell or from generation to generation.
3. **Genetic material must be able to express itself** so that other biological molecules, and ultimately cells and organisms, will be produced and maintained. Implicit in this requirement is that some mechanism be available for decoding, or translating, the information contained in the genetic material into its "productive" form. A narrow, but important, distinction is thus made between a molecule that can generate only its own kind and a molecule that can also generate new kinds of molecules. A salt crystal can "seed" a salt solution so that new salt crystals are formed, but this is the extent of its influence over its surroundings.
4. **Genetic material must be capable of variation.** This requirement is somewhat contradictory to the first requirement, which demanded stability of the genetic material. There is, in fact, no *a priori* reason why genetic material should have built-in provisions for change; one could certainly design a hypothetical genetic system in which information would be rigidly conserved from one generation to another. The dominant theme in the history of life is, however, organic evolution, and

this demands that genetic material be capable of change, if only infrequently.

Two sources of change have been recognized in present-day genetic systems: **mutations** and **recombination**. A mutation changes the nature of the information transmitted from parent to offspring and thus represents a relatively drastic way of bringing about variation. If the change is deleterious (and it usually is), the offspring may be greatly handicapped and may die soon after conception, or else it may introduce a deleterious gene into the population. Recombination is a more moderate way of producing variation. It occurs during the course of some sort of sexual process, and it involves the precise shuffling of parental genetic information such that new combinations of genes are produced. These are then inherited by the offspring.

With these four requirements in mind, we can study the physical and chemical properties of DNA and RNA, putting the molecular facts into a genetic context. Table 1-1 reviews some key definitions from organic chemistry that are relevant to the next few sections of this chapter.

TABLE 1-1 Definitions from Organic Chemistry

 	<p>Benzene ring, with = indicating double bonds where two carbon atoms share four electrons between them. The common abbreviated version of a benzene ring is shown at right.</p>
$-\text{CH}_3$	Methyl group
$-\text{OH}$	Hydroxyl group
$=\text{O}$	Keto group
$\begin{array}{c} \text{H} \\   \\ -\text{C}=\text{O} \end{array}$	Aldehyde group
$\begin{array}{c} \text{O} \\    \\ -\text{C}-\text{OH} \end{array}$	Carboxyl group, characteristically acidic ( $-\text{COO}^-$ )
$-\text{NH}_2$	Amino group, characteristically basic ( $-\text{NH}_3^+$ )
Covalent bond	A strong bond formed when two atoms share a pair of electrons between them.
Hydrogen bond	A weak attractive force between an electronegative (electron-seeking) atom (usually N or O) and a hydrogen atom covalently linked to a second electronegative atom (usually $\text{O}-\text{H}$ or $\text{N}-\text{H}$ ).
Hydrolysis	Breaking a large molecule into two or more smaller molecules by adding water.