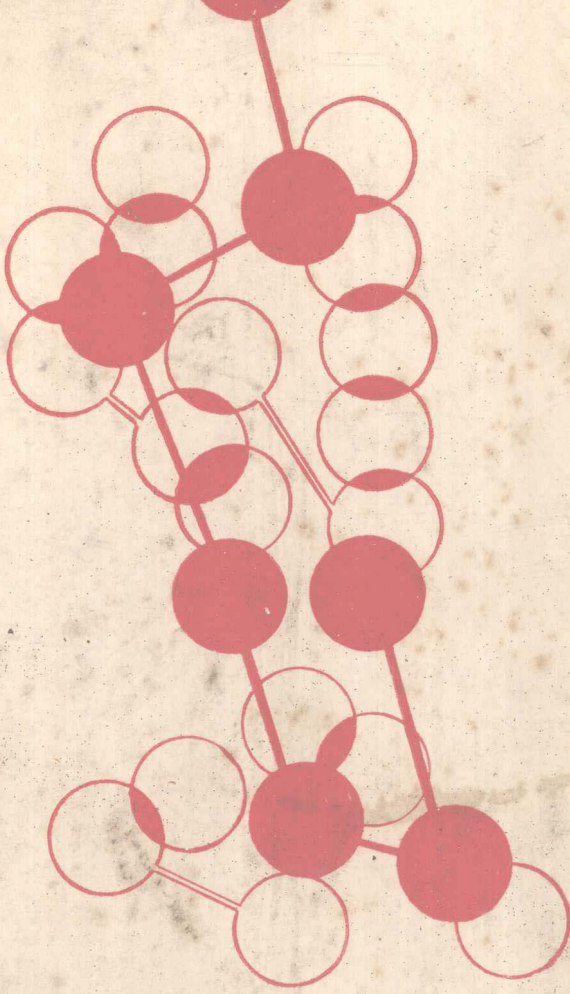
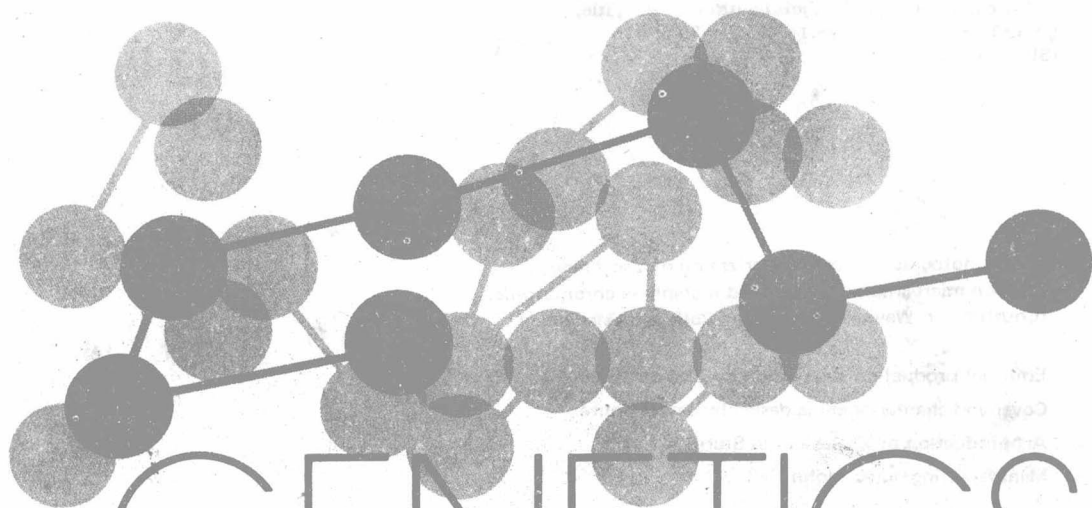


HELEN MARCUS-ROBERTS



GENETICS

Its Concepts and Implications



GENETICS

Its Concepts and Implications

ANNA C. PAI

Department of Biology

HELEN MARCUS-ROBERTS

Department of Mathematics and Computer Science

Montclair State College

PRENTICE-HALL, INC., Englewood Cliffs, New Jersey 07632

Library of Congress Cataloging in Publication Data

Pai, Anna C (date)

Genetics, its concepts and implications.

Includes bibliographies and index.

1. Genetics. 2. Genetics—Social aspects.

I. Marcus-Roberts, Helen, joint author. II. Title.

QH430.P35 575.1 80-39616

ISBN 0-13-351007-7

Cover photograph: A color solarization of a scanning electron micrograph of an isolated metaphase chromosome. (Courtesy Dr. Wayne Wray, Baylor College of Medicine.)

Editorial/production supervision by Zita de Schauensee

Cover and chapter-opening design by Jayne Conte

Art production by Diane Doran Sturm

Manufacturing buyer: John Hall

© 1981 by Prentice-Hall, Inc., Englewood Cliffs, N.J. 07632

All rights reserved. No part of this book may be reproduced in any form or by any means without permission in writing from the publisher.

Printed in the United States of America

10 9 8 7 6 5 4 3 2 1

Prentice-Hall International, Inc., *London*

Prentice-Hall of Australia Pty. Limited, *Sydney*

Prentice-Hall of Canada, Ltd., *Toronto*

Prentice-Hall of India Private Limited, *New Delhi*

Prentice-Hall of Japan, Inc., *Tokyo*

Prentice-Hall of Southeast Asia Pte. Ltd., *Singapore*

Whitehall Books Limited, *Wellington, New Zealand*

Preface

An organism is judged by biologists to be living if it is capable of (1) self-reproduction, (2) metabolism, and (3) mutation. All these phenomena which distinguish living from nonliving matter are now known to involve genes and gene action. Therefore, central as the gene is to life processes, so the science of genetics, the study of the gene and gene action, has become central to the training of a biologist. Furthermore, important as genetic concepts are to biologists, these concepts have also achieved a unique degree of interest in the eyes of the general public as a result of growing public awareness of the relevance of genetic studies to every living organism including humans.

Historically, there has existed a sometimes considerable gap of communication and/or interest between the laboratory sciences and a society which more often than not felt only remotely affected by the activity within the laboratories. More than any other science in modern times, genetics has bridged this gap. Geneticists recognize that their work has bearing on many aspects of the natural world and human society. By informing the nonscientific community about the potential of genetic research, geneticists themselves have encouraged a broadening of communication between scientists and the public which is both necessary and desirable. A geneticist today must not only be knowledgeable but also able to relate his knowledge to the community at large.

In this textbook, the authors aim to present the concepts of genetics as a

aspects of material covered in the text. Answers to some of the problems and an extensive glossary are included in the appendixes.

We hope that students who use this textbook will share both in our excitement over developments in a fascinating and rapidly moving science, and in our concern that the new knowledge will be used with wisdom.

We wish to acknowledge the persuasive encouragement of Mary Ann Richter, who was directly responsible for the initiation of this project. Her untimely death cut short a promising career in publishing and removed a bright spot from the lives of all who knew her.

We further wish to thank the staff of Prentice-Hall and reviewers for their helpful comments. We would like to express our appreciation to the following reviewers: Audrey Barnett, C. William Birky, Jr., Allyn A. Bregman, Loy V. Crowder, Robert G. Fowler, Stephen L. Goldman, David Knauff, Paul A. Roberts, Howard Rosen, and R. C. Vrijenhoek. Thanks also to Marie Hromin for verifying the calculations in Chapter 16; to Sue Rowley, Victoria Berutti, Jane Freund, and Roger Korey for their help in preparing the manuscript; and not least, to my (ACP) students who used the manuscript and contributed constructive suggestions.

We are grateful to the Literary Executor of the late Sir Ronald A. Fisher, F.R.S., to Dr. Frank Yates, F.R.S., and to Longman Group Ltd., London, for permission to reprint portions of Table IV from their book *Statistical Tables for Biological, Agricultural and Medical Research*. (Sixth edition, 1974.)

In addition, Anna Pai acknowledges the moral support of her family and Dina Campos, which was invaluable. Helen Marcus-Roberts wishes to acknowledge the encouragement of her parents and friends. In particular she wishes to acknowledge the love, encouragement, and help of her husband, Fred, and the love of her daughter, Sarah.

Livingston, New Jersey
Westfield, New Jersey

Anna C. Pai
Helen Marcus-Roberts

focal topic in biology to students who may advance to specialize in one of its many subdivisions. The first seven chapters deal with various aspects of heredity, such as the roles of mitosis and meiosis, patterns of transmission, chromosome structure and mapping, and gene interaction. A thorough but simply presented discussion of the application of probability and statistics to the analysis of heredity (as in genetic counseling) is also included. Students are introduced to current techniques being used in these areas, such as somatic cell fusion in mapping human chromosomes.

With a firm understanding of the basic concepts of heredity after study of these first chapters, we turn our attention to the physical structure of genes, and how they function. Historically, the Age of Molecular Genetics began with the discovery that microorganisms such as bacteria and viruses can be used in genetic studies, and accordingly, we begin our chapters on molecular genetics with a discussion of the genetics of bacteria and viruses. From there we proceed to the ingenious experiments which gave us the structure of the double helix of DNA, and the relationship between protein synthesis and gene function.

More recently, much attention has been focused on the manner in which gene activity is regulated, because we are now aware that many biological phenomena, both normal and abnormal, are due to aspects of gene regulation. For example, immune phenomena and the transformation of normal cells into malignant cells in the development of cancer all reflect enormous complexity of regulative processes, and the results when regulation becomes abnormal. Therefore, we include these and other topics in our text, even though they are topics heretofore seldom found in genetics texts.

The controversy which has recently arisen in both the scientific and lay communities over the implications of certain experiments in genetic engineering will be considered at length. With our ever-increasing understanding of life processes, the debate on genetic engineering clearly illustrates the concerns of many as we approach the point where we may be able to control those processes.

We center our attention in the last few chapters on various aspects of mutation: its molecular basis, natural repair processes, agents that cause mutations, and tests for mutagens. Fluctuation in the frequencies of mutations and genes in populations leads from a consideration of population genetics to the genetic basis of evolutionary change.

It is our feeling that a discussion of our evolutionary origins is important for a better understanding of the human species and its part in the natural world. We hope that including a discussion of the genetic basis to race formation and IQ in this context will bring to light misconceptions which have caused so much unnecessary grief to our society. Our concern for the societal implications of genetics carries into the final chapter which explores the promises and perils of genetic research and methodology in the near future.

To present genetic concepts and their implications and yet have a textbook which can be handled within the limits of a one-semester course, we have stressed principles and ideas in the text. Students who desire more details (for example, of experiments) should consult the extensive bibliography listed at the end of each chapter. Central ideas are emphasized by special print within the text. In addition, a number of appendixes have been provided which deal in greater depth with some

Complete Contents

Preface xiX

ONE

Heredity and Cell Division 1

INTRODUCTION 1

History The Chromosomal Basis of Heredity

MEIOSIS 4

*Interphase I Prophase I Metaphase I Anaphase I Telophase I
Division I Interphase II Prophase II Metaphase II Anaphase II
Telophase II Division II*

GAMETOGENESIS 18

Spermatogenesis Oogenesis Genetic Consequences of Aging in Ova

MITOSIS 22

*Interphase Prophase Metaphase Anaphase Telophase Division
The Cell Cycle Twinning*

PROBLEMS 29

REFERENCES 30

TWO

The Transmission of Traits. Simple Mendelian Inheritance 32

MENDELIAN GENETICS 32

Homozygosity and Heterozygosity Law of Segregation

Dominance and Recessiveness The Testcross The Monohybrid Cross

The Dihybrid Cross Law of Random Assortment

Forked-line Method (Method of Tree Diagrams)

Multiplication Rule Mendel's Contributions to Genetics

PEDIGREE ANALYSIS 48

Pedigree Symbols Pattern of Transmission of a Dominant Trait

Pattern of Transmission of a Recessive Trait

The Pedigree as a Tool for Prediction

Limitations on the Usefulness of Pedigree Analysis

PROBLEMS 54

REFERENCES 58

THREE

Probability and Statistics in Genetics 59

INTRODUCTION 59

STEPS IN MODELING 59

PROBABILITY IN GENETIC ANALYSIS 60

The Probability of Combinations of Events

The Probability of Mutually Exclusive Events

USE OF THE BINOMIAL DISTRIBUTION IN GENETICS 66

THE CHI SQUARE GOODNESS OF FIT TEST 73

USE OF THE CHI SQUARE TEST IN GENETICS 83

PROBLEMS 86

REFERENCES 88

FOUR

The Interaction of Genes 89

INTRODUCTION 89

INTERACTION BETWEEN ALLELES 90

Incomplete Dominance Codominance Lethal Genes

Segregation Distortion

INTERACTION BETWEEN NONALLELIC PAIRS OF GENES 98

Pleiotropy Alteration of Phenotype Modification of Phenotype

POLYGENIC TRAITS AND QUANTITATIVE INHERITANCE 105

PROBLEMS 116

REFERENCES 118

Summary Contents

COMPLETE CONTENTS	ix
PREFACE	xix
ONE	Heredity and Cell Division 1
TWO	The Transmission of Traits: Simple Mendelian Inheritance 32
THREE	Probability and Statistics in Genetics 59
FOUR	The Interaction of Genes 89
FIVE	Sex Chromosomes and Sex Determination 120
SIX	Cytogenetics 153
SEVEN	Linkage and Chromosome Mapping 186
EIGHT	The Genetics of Bacteria and Viruses 231
NINE	Molecular Genetics I: Gene Structure, Replication, and Recombination 263
TEN	Molecular Genetics II: Protein Synthesis and the Genetic Code 303
ELEVEN	Regulation of Gene Action in Prokaryotes 342
TWELVE	Gene Regulation in Eukaryotes 369
THIRTEEN	Extranuclear Inheritance and Extrachromosomal Genetic Elements 413
FOURTEEN	Recombinant DNA and Gene Manipulation 439
FIFTEEN	Mutation, Mutagenesis, and Repair 473
SIXTEEN	Population Genetics 499
SEVENTEEN	The Genetics of Evolution 560
EIGHTEEN	Genetics, Behavior, and IQ 590
NINETEEN	Genetics and Society 623
GLOSSARY	645
APPENDIXES	657
ANSWERS TO PROBLEMS	663
INDEX	687

FIVE

Sex Chromosomes and Sex Determination 120

INTRODUCTION 120

SEX CHROMOSOMES 120

TRANSMISSION OF SEX-LINKED TRAITS 121

X-Linkage in Drosophila X-Linkage in Humans

X-Linkage in Pedigrees Y-Linkage

THE X CHROMOSOME AND SEX DETERMINATION 131

The Balance System in Drosophila Drosophila Gynandromorphs

THE Y CHROMOSOME AND SEX DETERMINATION 134

Role of the Y Chromosome in Mammals

The Y Chromosome in Development Testicular Feminization

Sex-influenced and Sex-limited Traits

Genetic Mosaicism in Humans

THE BARR BODY AND X INACTIVATION 143

The Barr Body in Human Cells The Lyon Hypothesis

The Barr Body, Transsexuals, and Athletics

SEX-DETERMINING GENES 146

OTHER SYSTEMS OF SEX DETERMINATION 147

In Chickens and Amphibians In Hymenoptera In Plants

SOME FURTHER THOUGHTS 148

PROBLEMS 149

REFERENCES 151

SIX

Cytogenetics 153

INTRODUCTION 153

THE BIOCHEMISTRY OF CHROMOSOMES 154

Nucleic Acids Proteins

GROSS STRUCTURE OF CHROMOSOMES 160

Giant Chromosomes of Drosophila Human Chromosomes

CHROMOSOME ABNORMALITIES 169

Changes in Chromosome Numbers

Changes in Chromosome Structure

PROBLEMS 183

REFERENCES 184

SEVEN

Linkage and Chromosome Mapping 186

LINKAGE 186

Coupling and Repulsion The Detection of Linkage

Detection of Linkage in Humans

CHROMOSOME MAPPING 198

*Crossing-Over Two-point Crosses Three-point Crosses
Tetrad Analysis*

CHROMOSOME MAPS 221

SIGNIFICANCE OF LINKAGE AND CROSSING-OVER 225

PROBLEMS 225

REFERENCES 229

EIGHT

The Genetics of Bacteria and Viruses 231

INTRODUCTION 231

PROKARYOTES IN GENETICS 232

Some Basic Facts About Bacteria

Some Basic Facts About Viruses

SEXUAL REPRODUCTION IN BACTERIA 236

Transformation Conjugation

GENETICS OF BACTERIOPHAGE 249

*Recombination in Bacteriophages The Genetic Material of Viruses
Transduction*

SEXDUCTION 257

CONTRIBUTIONS OF MICROBIAL GENETICS 258

PROBLEMS 259

REFERENCES 261

NINE

**Molecular Genetics I. Gene Structure, Replication,
and Recombination 263**

INTRODUCTION 263

Pseudoalleles Position Effect

MOLECULAR STRUCTURE OF DNA 265

Biochemical Studies Biophysical Studies

The Watson-Crick Double Helix The Double Helix

DNA and Chromosomes

BIOLOGICAL PHENOMENA REVISITED: REPLICATION 276

Semiconservative Replication In Vitro Synthesis of DNA

Other Aspects of Replication

Enzymes and Proteins in Replication

The Rolling Circle Model of Replication

Replication in RNA Phages

MOLECULAR BASIS OF RECOMBINATION 291

Models of Recombination Rec⁻Mutants in Bacteria

Site-Specific Recombination Recombinant DNA Research

PROBLEMS 299

REFERENCES 300

TEN

Molecular Genetics II: Protein Synthesis and the Genetic Code 303

INTRODUCTION 303

Genes and Metabolism in Humans Genes and Metabolism in Insects

Genes and Enzymes in Fungi

GENES AND PROTEINS 307

Transcription The Genetic Code

TRANSLATION 323

Ribosomes Transfer RNA Protein Synthesis

THE COMPLEXITY OF GENE-DIRECTED CELLULAR PROCESSES 336

PROBLEMS 337

REFERENCES 338

ELEVEN

Regulation of Gene Action in Prokaryotes 342

INTRODUCTION 342

THE LAC OPERON 343

Structural Genes Regulatory Genes and Regions

The Operon Concept Isolation of the Lac Operon DNA

THE ARABINOSE OPERON 352

Genes of the Ara Operon Regulation of Ara Genes

Interaction of Ara Promoters

OPERATOR-ATTENUATOR SYSTEMS OF REGULATION 355

The Tryptophan Operon Novel Features of the Trp Operon

THE HISTIDINE OPERON IN SALMONELLA 358

Possible Role of the Attenuator

REGULATION IN LAMBDA BACTERIOPHAGE 360

Bacteriophage Lambda Genes Involved in Lysis

Genes Involved in Lysogeny Lysis vs. Lysogeny

SIMILARITIES AND DIFFERENCES IN PROKARYOTIC SYSTEMS 364

PROBLEMS 365

REFERENCES 366

TWELVE

Gene Regulation in Eukaryotes 369

INTRODUCTION 369

GENE REGULATION IN DEVELOPMENT 370

Determination in Development Regulative vs. Mosaic Development

Gene Activity in Oogenesis

Evidence of Selective Gene Activity During Development

Regulation of Protein Synthesis in Development

Reversibility of Regulation in Development

GENE REGULATION IN IMMUNE REACTIONS 386

Basic Characteristics of Immune Reactions

Genetic Basis of Immune Reactions

GENE REGULATION IN CANCER 395

General Characteristics of Cancer Cells

Causal Factors in Transformation to Malignancy

FACTORS IN GENE REGULATION 405

DNA and Chromosome Structure in Regulation

Different Levels of Regulation in Eukaryotes

New Approaches to the Study of Gene Regulation

PROBLEMS 409

REFERENCES 410

THIRTEEN

Extranuclear Inheritance and Extrachromosomal
Genetic Elements **413**

INTRODUCTION 413

**MATERNAL EFFECTS AND CYTOPLASMIC INHERITANCE
IN EUKARYOTES 413**

Maternal Effect in Snails Streptomycin Resistance in Chlamydomonas

Mitochondrial Mutations in Yeast Male Sterility in Plants

Kappa Particles of Paramecium

Other Systems of Infective Inheritance

**EXTRACHROMOSOMAL GENETIC ELEMENTS
IN PROKARYOTES 422**

The F Particle and Conjugation in Bacteria

Antibiotic Resistance Factors in Bacteria

Colicin Factors in Bacteria Insertion Elements

POSSIBLE RELATIONSHIPS BETWEEN ECE's 434

INSERTION ELEMENTS IN EUKARYOTES 434

PROBLEMS 436

REFERENCES 436

FOURTEEN

Recombinant DNA and Gene Manipulation **439**

INTRODUCTION 439

RECOMBINANT DNA 440

Restriction Endonucleases

Use of RE-induced Fragments as Tools for the Study of Genes

TRANSMISSION OF RECOMBINANT DNA 446

Transformation in E. coli Use of RTF Plasmids as Vectors

Other Vectors for Recombinant DNA

NEW DIRECTIONS FOR MOLECULAR GENETICS 451

Restriction Mapping Nucleotide Sequencing

<i>The Study of Gene Function with Recombinant DNA</i>	
<i>The Cloning of Eukaryotic Genes</i>	
THE GREAT DEBATE	462
<i>Pros and Cons of Recombinant DNA Research</i>	
<i>NIH Guidelines for Recombinant Research</i>	
<i>Development of Safe Hosts and Vectors</i>	
RECOMBINANT DNA IN PROSPECTIVE	468
REFERENCES	469

FIFTEEN

Mutation, Mutagenesis, and Repair	473
-----------------------------------	------------

INTRODUCTION	473
CLASSIFICATION OF MUTATIONS	474
POINT, OR INTRAGENIC, MUTATIONS	474
<i>Cistrons, Recons, and Mutons</i>	<i>Rearrangements of Base Pairs</i>
<i>Randomness of Mutations</i>	
FACTORS THAT CAUSE MUTATIONS	480
<i>Radiation as Mutagen</i>	<i>Chemicals as Mutagens</i>
<i>Tests to Identify Mutagens</i>	<i>Potentiation</i>
REPAIR MECHANISMS	489
<i>Photoreactivation</i>	<i>Excision Repair</i>
<i>Postreplication Recombination Repair</i>	<i>Repair in Human Diseases</i>
<i>Repair in Aging</i>	
PROBLEMS	496
REFERENCES	497

SIXTEEN

Population Genetics	499
---------------------	------------

INTRODUCTION	499
GENETIC EQUILIBRIUM AND RANDOM MATING	500
THE HARDY-WEINBERG LAW	501
<i>Underlying Assumptions of the Hardy-Weinberg Law</i>	
<i>Verification of the Hardy-Weinberg Law</i>	
<i>Applications of the Hardy-Weinberg Law</i>	<i>Sex-linked Alleles</i>
<i>Multiple Alleles</i>	
NONRANDOM MATING	513
<i>Inbreeding</i>	<i>Self-fertilization</i>
<i>Sibs and More Distant Relatives</i>	
<i>Coefficient of Inbreeding: Summary</i>	<i>Assortative Mating</i>
FACTORS THAT CHANGE GENE FREQUENCIES	524
<i>Mutation</i>	<i>Selection</i>
<i>Interaction of Mutation and Selection</i>	
<i>Genetic Drift</i>	<i>Founder Principle</i>
<i>Genetic Drift and Selection</i>	
<i>Migration</i>	
PROBLEMS	555
REFERENCES	558

SEVENTEEN

The Genetics of Evolution 560

INTRODUCTION 560

A HISTORICAL PERSPECTIVE 560

Lamarckism Darwin and Natural Selection

NEO-DARWINISM 564

Sources of Variability in Populations

Evolutionary Advantages of Variability in Populations Speciation

EVIDENCE FOR NEO-DARWINIAN EVOLUTION 567

Chromosomal Evidence for Genetic Divergence

Evidence for Natural Selection

NEW DIRECTIONS: MOLECULAR EVOLUTION 581

Protein Sequences and Evolution Multigene Families in Eukaryotes

Evolution and Regulatory Genes

WHAT LIES AHEAD 588

PROBLEMS 588

REFERENCES 589

EIGHTEEN

Genetics, Behavior, and IQ 590

INTRODUCTION 590

SINGLE GENES AND BEHAVIOR 591

COMPLEX TRAITS 593

MODELS 594

Variance

HERITABILITY 596

Data for Estimation of Heritability

IQ (INTELLIGENCE) 603

IQ Scores Heritability of IQ (Intelligence)

Environmental Factors and IQ Socioeconomic Class and IQ

Race and IQ Estimation of Heritability in Blacks

PROBLEMS 618

REFERENCES 618

NINETEEN

Genetics and Society 623

INTRODUCTION 623

EUPHENICS 624

Euphenics Today Euphenics in the Future

Genetic Consequences of Advances in Euphenics

Societal Consequences