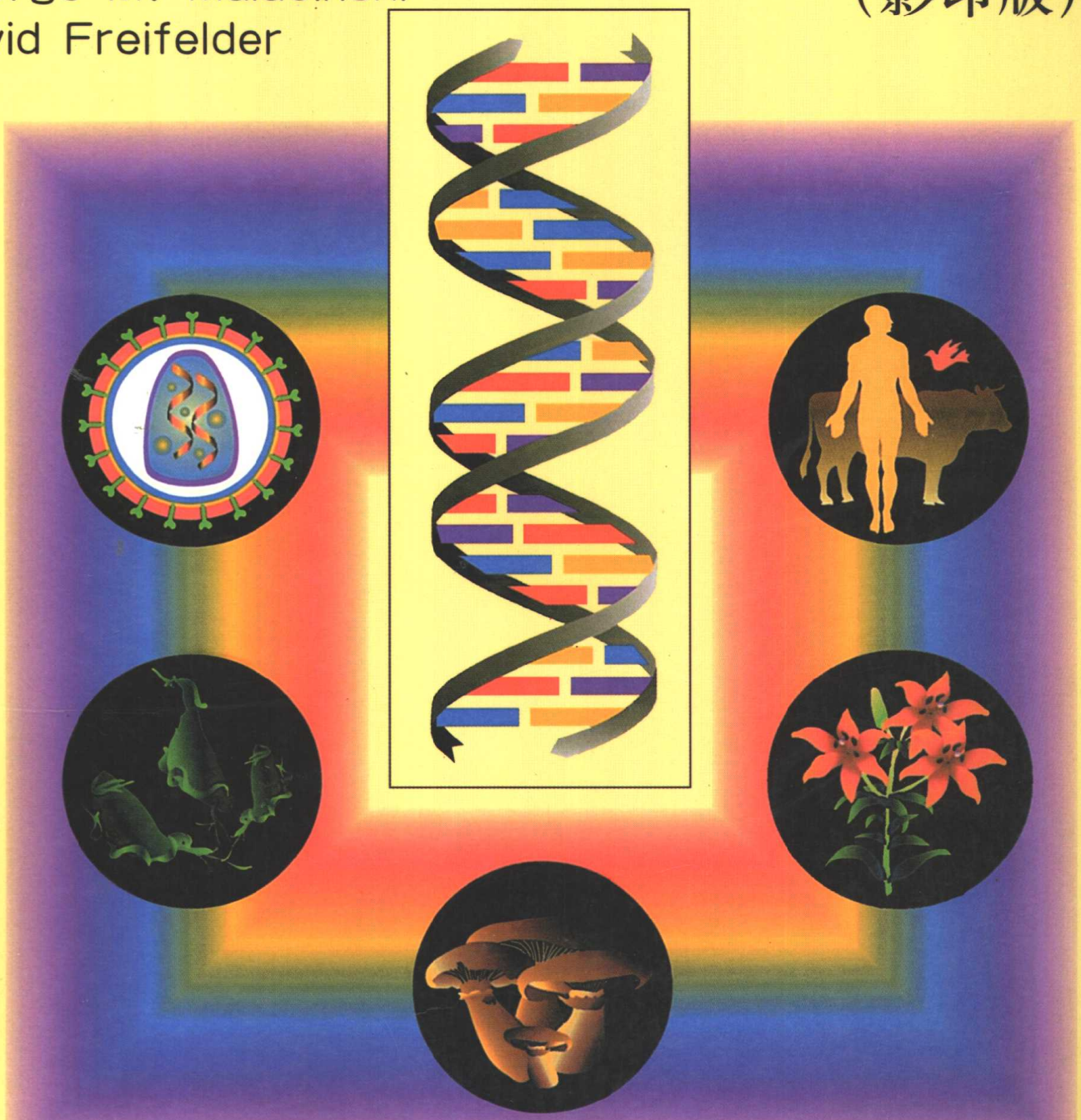
国 外 优 秀 教 材

Essentials of Molecular Biology

分子生物学精要

George M. Malacinski
David Freifelder

(影印版)



科 学 出 版 社
JONES AND BARTLETT PUBLISHERS

分子生物学精要

（第三版　影印版）

Essentials of Molecular Biology

(Third Edition)

George M. Malacinski
David Freifelder

科学出版社

2002

内 容 简 介

本书深入浅出地阐明了蛋白质和核酸等生物大分子的结构、功能、协调和实验操作。

书中简明扼要、图文并茂地提炼了日新月异的分子生物学进展，着重培养学生分析数据、解决问题和实验设计能力。书中还精选分子生物学家传略，附章前提示和章末小结、各类习题和解答、名词概念解释、参考文献及主题索引。适用于高等院校生物学专业师生。

图字：01-2002-0539

Original English Language Edition Published by

Jones and Bartlett Publishers, Inc.

One Exert Plaza

Boston, MA 02116

Copyright 1998

All Rights Reserved

图书在版编目（CIP）数据

分子生物学精要 = Essentials of Molecular Biology/（美）马拉辛斯基（Malacinski, G. M.），（美）弗赖费尔德（Freifelder, D.）著 .—影印版 .—北京：科学出版社，2002

（国外优秀教材）

ISBN 7-03-010312-2

Ⅰ. 分… Ⅱ. ①马… ②弗… Ⅲ. 分子生物学 Ⅳ. Q7

中国版本图书馆 CIP 数据核字（2002）第 018566 号

科学出版社 出版

北京东黄城根北街16号

邮政编码：100717

http://www.sciencep.com

新蕾印刷厂 印刷

科学出版社发行 各地新华书店经销

*

2002 年 4 月第 一 版 开本：850×1168 1/16

2002 年 4 月第一次印刷 印张：35

印数：1—4 000 字数：788 000

定价：56.00 元

（如有印装质量问题，我社负责调换〈环伟〉）

brief contents

Prologue xv

Preface xvii

Introduction 1

CHAPTER 1 Welcome to Molecular Biology! 3

PART I **The Structure of Proteins, Nucleic Acids, and Macromolecular Complexes** 21

CHAPTER 2 Macromolecules 23

CHAPTER 3 Nucleic Acids 39

CHAPTER 4 The Physical Structure of Protein Molecules 67

CHAPTER 5 Macromolecular Interactions and the Structure of Complex Aggregates 87

PART II **Function of Macromolecules** 107

CHAPTER 6 The Genetic Material 109

CHAPTER 7 DNA Replication 131

CHAPTER 8 Transcription 163

CHAPTER 9 Translation 187

CHAPTER 10 Mutations, Mutagenesis, and DNA Repair 213

PART III **Coordination of Macromolecular Function in Cells** 249

CHAPTER 11 Regulation of Gene Activity in Prokaryotes 251

CHAPTER 12 Bacteriophage 281

CHAPTER 13 Regulation of Gene Activity in Eukaryotes 311

PART IV **Experimental Manipulation of Macromolecules** 349

CHAPTER 14 Plasmids and Transposons 351

CHAPTER 15 Recombinant DNA and Genetic Engineering: Molecular Tailoring of Genes 381

CHAPTER 16 Molecular Biology Is Expanding Its Reach 409

APPENDIX Chemical Principles Important for Understanding Molecular Biology 442

List of Essential Concepts of Molecular Biology 471

Glossary 475

References for Further Reading 491

Answers to Questions and Problems 497

Index 515

Prologue xv
Preface xvii

CHAPTER 1 **Welcome to Molecular Biology!** GEORGE M. MALACINSKI 3
Goals of Molecular Biology 3
The Early Years 4
Model Biological Systems 5
Methodology of Molecular Biology 9
Rapid Progress in Molecular Biology 12
Putting the Details of Molecular Biology in Perspective 14
Concepts of Molecular Biology 16
Progression Diagram 17
Rewards from Studying Molecular Biology 17

CHAPTER 2 **Macromolecules** GEORGE M. MALACINSKI 23
Chemical Structures of the Major Classes of Macromolecules 24

试读结束：需要全本请在线购买： www.ertongbook.com

Noncovalent Interactions that Determine the Three-dimensional Structures of Proteins and Nucleic Acids 28
Macromolecule Isolation and Characterization 31

CHAPTER 3 **Nucleic Acids** ROBERT CEDERGREN 39
Physical and Chemical Structure of DNA 40
Alternate DNA Structures 43
Circular and Superhelical DNA 45
Renaturation 50
Hybridization 53
The Structure of RNA 55
Hydrolysis of Nucleic Acids 56
Sequencing Nucleic Acids 58
Synthesis of DNA 60
A Future Practical Application? 62

CHAPTER 4 **The Physical Structure of Protein Molecules** ALEXANDRA CYNTHIA NEWTON 67
Basic Features of Protein Molecules 68
The Folding of a Polypeptide Chain 68
The α Helix and β Structures 70
Protein Structure 73
Proteins with Subunits 76
Enzymes 79
A Future Application 82

CHAPTER 5 **Macromolecular Interactions and the Structure of Complex Aggregates** GEORGE M. MALACINSKI 87
A Complex DNA Structure: The *E. Coli* Chromosome 88
Chromosomes and Chromatin 91
Interaction of DNA and Proteins that Recognize a Specific Base Sequence 96
Biological Membranes 99
Cytoskeletal Elements 102
A Future Practical Application? 103

PART 2 Function of Macromolecules 107

CHAPTER 6 **The Genetic Material** ROBERT L. SINSHEIMER 109
Early Observations on the Mechanism of Heredity 110
Identification of DNA as the Genetic Material 112
Identification of RNA as the Genetic Material of Certain Viruses 120

Properties of the Genetic Material 121
RNA as the Genetic Material 127

CHAPTER 7 **DNA Replication** KENNETH MARIANS 131
Semiconservative Replication of Double-Stranded DNA 132
Untwisting of Highly Coiled DNA Is Required for DNA Replication 133
Initiation of DNA Replication 136
Unwinding of DNA for Replication 139
Elongation of Newly Synthesized Strands 140
DNA Polymerase III Consists of Multiple Subunits 143
Antiparallel DNA Strands and Discontinuous Replication 145
The Complete DNA Replication System 152
Replication of Eukaryotic Chromosomes 156
A Future Practical Application? 158

CHAPTER 8 **Transcription** JOHN RICHARDSON 163
Enzymatic Synthesis of RNA 164
Transcription Signals 166
Classes of RNA Molecules 171
Transcription in Eukaryotes 174
Means of Studying Intracellular RNA 180
A Future Practical Application? 182

CHAPTER 9 **Translation** JOSEPH ILAN 187
Outline of Translation 188
The Genetic Code 189
The Wobble Hypothesis 194
Polycistronic mRNA 196
Overlapping Genes 196
Polypeptide Synthesis 198
Stages of Polypeptide Synthesis in Prokaryotes 200
Complex Translation Units 204
Antibiotics 208
A Future Practical Application? 208

CHAPTER 10 **Mutations, Mutagenesis, and DNA Repair** PHILIP C. HANAWALT 213
Types of Mutations 214
Biochemical Basis of Mutants 216
Mutagenesis 218

Spontaneous Mutations and Their Repair 220
Induced Mutations 223
Reversion 229
Reversion as a Means of Detecting Mutagens and Carcinogens 234
DNA Repair Mechanisms 236
Repair by Direct Reversal 236
Excision-Repair 237
Recombinational Repair 238
The SOS Response 240
Future Practical Applications? 243

Part III Coordination of Macromolecular Function in Cells 249

CHAPTER 11 Regulation of Gene Activity in Prokaryotes SANKAR L. ADHYA **251**
Principles of Regulation 252
Transcriptional Regulation 253
Post-Transcriptional Control 272
Feedback Inhibition and Allosteric Control 274
A Future Practical Application? 276

CHAPTER 12 Bacteriophage DAVID PARMA AND LARRY GOLD **281**
Stages in the Lytic Life Cycle of a Typical Phage 283
Specific Phage 286
Transducing Phage 304
A Future Practical Application? 307

CHAPTER 13 Regulation of Gene Activity in Eukaryotes HANS-PETER MÜLLER AND WALTER SCHAFFNER **311**
Important Differences in the Genetic Organization of Prokaryotes and Eukaryotes 312
The Regulation of Transcription Initiation 313
The Regulation of RNA Processing 324
Regulation of Nucleocytoplasmic mRNA Transport 330
Regulation of mRNA Stability 331
Regulation of Translation 334
Regulation of Protein Activity 335
Gene Rearrangement: Joining of Coding Sequences in the Immune System 340
A Future Practical Application? 344

PART IV Experimental Manipulation of Macromolecules 349

CHAPTER 14 Plasmids and Transposons BARRY POLISKY 351

Plasmid-Borne Genes 353
Plasmid Transfer 354
Plasmid DNA Replication 361
Transposable Elements 364
Transposable Elements in Eukaryotes 374
A Future Practical Application? 375

CHAPTER 15 Recombinant DNA and Genetic Engineering: Molecular Tailoring of Genes DOROTHY M. SKINNER AND CHRISTIE A. HOLLAND 381

Plasmids Act as Nature's Interlopers 382
Restriction Enzymes Function as Nature's Pinking Shears 382
Genetic Interlopers: Vectors Function as Vehicles for Transferring Genes 392
Detection of Recombinant DNA Molecules 399
Applications of Genetic Engineering 403

CHAPTER 16 Molecular Biology Is Expanding Its Reach PAMELA L. HARMATTY 409

Uses of Recombinant DNA Technology in Research 410
Uses of Recombinant DNA Technology in Medicine 417
Uses of Recombinant DNA Technology in Agriculture 427
Other Commercial and Industrial Applications 430
Molecular Biology: On the Front Line of the Battle Against AIDS 431
Social and Ethical Issues 433

APPENDIX Chemical Principles Important for Understanding Molecular Biology JUDITH A. JAEHNING 443

Structure of the Atom 444
Chemical Bonds 444
The Ionization of Water—The pH Scale 450
Organic Chemistry 453
Concluding Note 469

List of Essential Concepts 471
Glossary 475
References for Further Reading 491
Answers to Questions and Problems 497
Index 515

Introduction

PROFESSOR OF BIOLOGY
Indiana University
Bloomington, Indiana

UNDERGRADUATE DEGREE:
Boston University
Majors: Biology and Chemistry
1962

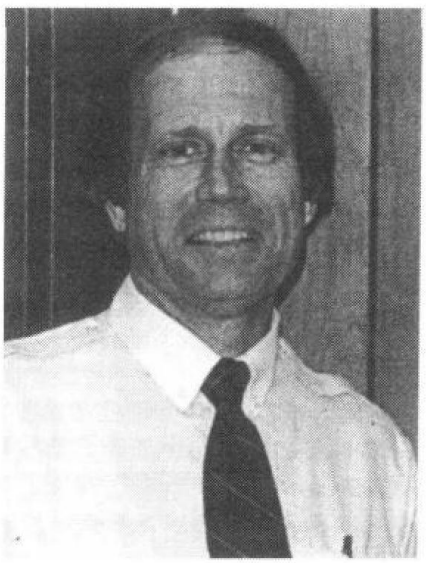
GRADUATE DEGREE:
Indiana University
Ph.D. 1966, Bacteriology and Biochemistry

POSTDOCTORAL TRAINING:
University of Washington
1966–1968, Biochemistry

Skeletal muscle is one of the first tissues to differentiate in early vertebrate embryogenesis. Because muscle is so highly specialized and contains such high concentrations of the contractile proteins actin and myosin, it is an excellent model system for investigating the mechanisms that regulate gene expression. Accordingly, my research program focuses on elucidating the structure, transcription, and translation of the myosin-heavy chain genes. The amphibian embryo provides a convenient model system because of its large size, external development, and ready availability, so it is used as the experimental organism.

Rather than containing a single myosin gene, however, the genome contains a family of up to a dozen or, in some animals, even more numerous closely related myosin genes, each coding for a unique myosin-heavy chain protein. Some of the genes are expressed only in skeletal muscle, while others are expressed in other muscles as well. Several of the genes appear to be expressed only at certain times in development (e.g., embryo, larva, adult).

By isolating and characterizing the genes at the nucleotide sequence level, and using recombinant DNA techniques to generate novel combinations of coding sequence/upstream sequence, my research program seeks to elucidate the mechanisms that act to control when and where individual myosin genes are expressed.



What advice can you offer to undergraduates who want to become scholars of molecular biology?

Develop your analytical thinking skills. Prospective molecular biologists should take every opportunity during their undergraduate training to (1) engage in problem solving exercises; (2) become proficient in analyzing data (e.g., graphs, charts, etc.); and (3) learn to design experiments. So much of the day-to-day "goings on" in contemporary molecular biology is data oriented (versus concept oriented). To be successful, one needs to become highly competent in those aspects of intellectual activity, and come to feel comfortable when engaged in those sorts of endeavors.

试读结束：需要全本请在线购买： www.ertongbook.com

chapter 1

Welcome to Molecular Biology!

Goals of Molecular Biology

THE ULTIMATE GOAL OF MOLECULAR BIOLOGY IS AMBITIOUS: to understand the five basic cell behavior patterns (growth, division, specialization, movement, and interaction) in terms of the various molecules that are responsible for them. That is, molecular biology wants to generate a complete description of the structure, function, and interrelationships of the cell's macromolecules, and thereby to understand why living cells behave the way they do.

This goal might appear overly zealous. Yet the rate at which progress is being made often astonishes even the most optimistic scientists. One might, in fact, consider these years to represent a golden era for biology, with the field of molecular biology providing the main driving force.

Significant discoveries are emerging from research laboratories nearly every day and the front pages of national newspapers frequently

herald exciting announcements of the identification of disease-causing genes, or promising biotechnology products, or new agricultural processes.

A few decades ago the most important discoveries in molecular biology were made using the simplest organisms (e.g., viruses and bacteria). Nowadays, however, equally important findings are regularly reported for both plants and mammals. A few key discoveries and the efforts of a small group of pioneering scientists have set the stage for the present era.

The Early Years

Molecular Biology

The term molecular biology was first used in 1938 by Warren Weaver. As Director of the Natural Sciences Section of the Rockefeller Foundation, he advocated that financial support be given to this "new branch of science—a new biology—**Molecular Biology**." By that time, biochemists began to discover many fundamental intracellular chemical reactions, and to appreciate the importance of specific reactions and of protein structure in defining the numerous properties of cells. However, the development of molecular biology itself could not begin until this realization was reached: The most productive advances would be made by studying "simple" systems such as bacteria and bacteriophages (bacterial viruses). Although bacteria and bacteriophages are still quite complicated, they are far simpler than animal cells. In fact, they enabled scientists to identify DNA as the molecule that contains most, if not all, of the genetic information of a cell.

Although DNA was first described in 1869 by F. Miescher, its significance to cell function and the definitive proof that it is responsible for inherited traits did not come until almost a century later. The experimental evidence that led to the assignment of genes to DNA depended heavily on the use of bacteria and their viruses (described in Chapter 6).

Once it became clear that DNA contains the chemical basis of heredity, it was not long before J. D. Watson and F. H. C. Crick offered a model for the physical structure of DNA. That model (described in Chapter 3) also proposed a mechanism for DNA replication and the spontaneous origin of mutations. Shortly thereafter, RNA was revealed to be an intermediate for the synthesis of enzymes and other proteins.

Following these discoveries, the new field of molecular genetics progressed rapidly in the late 1950s and early 1960s. It provided new concepts at a rate matched only by the development of quantum mechanics in the 1920s. The initial success and the accumulation of an enormous body of information enabled researchers to apply the techniques and powerful logical methods of molecular genetics to a variety of subjects: muscle and nerve function, membrane structure, the mode of action of antibiotics, cellular differentiation and development, immunology, and others. Faith in the basic uniformity of life processes was an important factor in this rapid growth. That is, it was believed that the fundamental biological

principles that govern the activity of simple organisms, such as bacteria and viruses (organisms that lack an organized nucleus), must apply to more complex cells; only the details should vary. This faith has been amply justified by experimental results.

In this book prokaryotes and eukaryotes will be discussed separately and compared and contrasted. Usually prokaryotes will be discussed first, because they are simpler. In keeping with this practice, we begin by briefly reviewing the properties of several model living systems, including bacteria and their viruses.

Model Biological Systems

virus

The simplest living organism is of course the **virus.** As a minimalist life form, it consists of a DNA (or, in some cases, an RNA) inner core surrounded by a protein coat. The key to the virus's simplicity is its parasitic nature. It borrows functions from its host cell. The host is, for some kinds of viruses, a bacterial cell, while for others it is a plant cell, and for yet others it is an animal cell. Of these hosts, the bacterial cell is the simplest. We will review its general features here briefly, then return to viruses.

bacteria

Bacteria are free-living unicellular organisms. They have a single chromosome, which is not enclosed in a nucleus (they are prokaryotes), and, compared to eukaryotes, they are simple in their physical organization. For all practical purposes, a bacterium can be thought of as consisting of several thousand chemicals and a few organized particles, all in liquid solution, enclosed in a rigid cell wall.

Bacteria have many features that make them suitable objects for the study of fundamental biological processes. For example, they can be grown easily and rapidly and, compared to cells in multicellular organisms, they are relatively simple in their needs. The bacterium that has served the field of molecular biology best is *Escherichia coli* (usually referred to as *E. coli*), which divides every 20 minutes at 37°C under optimal conditions. Thus, a single cell becomes 10^9 bacteria in about 20 hours!

Bacteria can be grown in a **liquid growth medium** or on a solid surface. A population growing in a liquid medium is called a bacterial **culture.** If the liquid is a complex extract of biological material, it is called a **broth.** If the growth medium is a simple mixture containing no organic compounds

minimal medium

other than a carbon source, such as a sugar, it is called a **minimal medium.** A typical minimal medium contains each of the ions Na^+, K^+, Mg^{2+}, Ca^{2+}, NH_4^+, Cl^-, HPO_4^{2-}, SO_4^{2-}, and a source of carbon (such as glucose, glycerol, or lactate). If a bacterium can grow in a minimal medium—that is, if it can synthesize *all* necessary organic substances such as amino acids, vitamins, and lipids—the bacterium is said to be a **prototroph.** If any organic

used for growing bacteria was a slice of raw potato. This was eventually replaced by **agar,** a jelling agent obtained from seaweed. It is resistant to the action of bacterial enzymes and hence is considered biologically inert. Figure 1-1 illustrates growth of bacteria on an agar surface.

agar

Metabolism in bacteria is precisely regulated. Thus, bacteria represent the most efficient free-living organisms yet discovered. They rarely synthesize substances that are not needed. For example, the amino acid tryptophan is not formed if tryptophan is present in the growth medium, but when the tryptophan in the medium is used up, the tryptophan-synthesizing enzymatic system will be quickly activated. The systems responsible for utilization of various energy sources are also efficiently regulated. A well-studied example is the metabolism of the sugar lactose as an alternate carbon source to glucose. Control of both tryptophan synthesis and lactose degradation are two examples of **metabolic regulation.** This very general phenomenon will be explored extensively throughout the book, especially in Chapter 11. Both simple and complex regulatory systems will be described, all of which act to determine how much of a particular compound is utilized and how much of each intracellular compound is synthesized at different times and in different circumstances. We will learn about the lengths to which the so-called simple cells go to utilize limited resources efficiently and to optimize their metabolic pathways for efficient growth.

The ease with which bacteria can be grown in the laboratory on agar surfaces or even in liquid growth medium in large, industrial-scale tanks has facilitated rapid progress in the physical and chemical characterization of macromolecules. For example, the original descriptions of nucleic acids (Chapter 3) and proteins (Chapter 4) were largely made with components fractionated and isolated from mass quantities of bacterial cells. And knowledge of metabolic regulation, discussed in Chapters 11 and 13, can be traced back to early studies of bacteria, and more recently to plant and animal cells, grown under conditions similar to those illustrated in Figure 1-1.

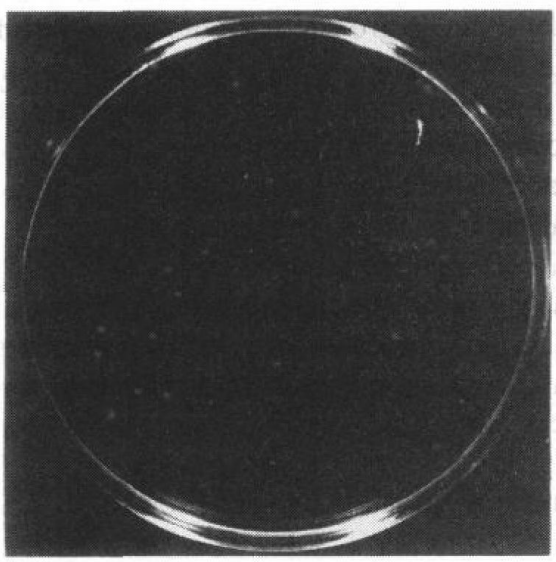


Figure 1-1 A glass dish displaying colonies of *E. coli* grown on the surface of an agar-containing growth medium. Each colony contains a cluster, or clone, of cells that represents the progeny of a single cell that divided many times. For instance, if 100 cells were spread on the agar surface, 100 colonies would appear the next day.

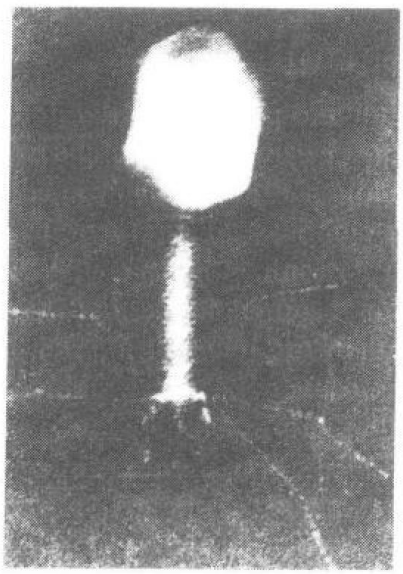


Figure 1-2 An *E. coli* T4 phage. The DNA is contained in the head. Tail fibers come from the pronged plate at the tip of the tail and serve to attach the virus to the host bacterium's surface.

Bacteriophage

bacteriophage
phage

Once the culture conditions for growing bacteria were established and many of the metabolic processes of normal bacterial life were known, bacterial viruses (**bacteriophage,** or the shortened form **phage**) were studied in earnest. Being much simpler than bacteria (unlike bacteria, they are not "free-living"), they could be studied in a relatively straightforward fashion. Since they indeed represent the simplest form of life, as their biochemical features became known, several physicists began to study them in the hopes of discovering new laws or first principles of physics!

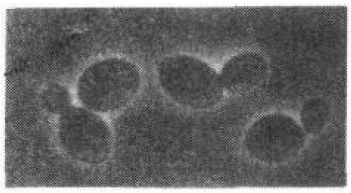
Figure 1-2 illustrates a bacteriophage that is relatively complex. It contains a protein coat, or phage head, to which is attached a tail. Some phages are simpler yet, and lack well-defined tail structures.

Molecular biologists have utilized viruses as simple model systems for many kinds of studies. One of the most significant used the minimalist protein coat/DNA core composition of phage to establish whether protein or DNA carries heredity information. Chapter 6 will explain the life cycle of a typical bacteriophage and review how phage, like the one illustrated in Figure 1-2, were used in pioneering experiments that helped prove that DNA rather than protein contains genetic information.

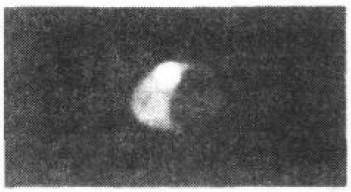
Yeasts

Another favorable model system that shares many of the advantages of bacteria is yeast [Figure 1-3 (a, b)]. They are, however, eukaryotes. Having a true nuclear membrane surrounding their chromosomes, they represent a higher level of organization than bacteria. That level approaches the complexity of animal (e.g., human) cells. Yet being a microorganism, yeast can be grown and manipulated much like *E. coli.*

Yeasts have been used for millennia for producing wine and beer. A great deal of early biochemical research was carried out with yeasts rather



(a)



(b)

Figure 1-3 (a) A light micrograph of the yeast *Saccharomyces cerevisiae*. Many cells are budding by outgrowth from the cell wall of the mother. (Courtesy of Breck Byers.) (b) A fluorescence micrograph of a single cell stained with a fluorescent dye that binds to nucleic acids. The bright spot is the nucleus. The dark region is the vacuole, a liquid-filled sac that is free of nucleic acids.

than bacteria, work stimulated mainly by interest in understanding and improving beer.

In contemporary molecular biology, mutant strains of yeast are often employed to discover genes which control growth, division, and cell behavior patterns. As well, yeasts are presently employed as tools for producing large numbers of copies of human chromosome fragments. So-called "yeast artificial chromosomes" represent miniature chromosomes that contain foreign (e.g., human) DNA. They are propagated within yeast cells, providing the molecular biologist with opportunities for genetic engineering.

Animal Cells (and Embryos)

Many types of animal cells, including several kinds of human cells, can be cultured using methods based on bacteria and yeast culture techniques. **Primary cell cultures** represent normal animal tissue that is usually derived from either skin cells (Figure 1-4) or embryos. They grow well initially, but eventually die off. Tumor cells, however, grow indefinitely, and are

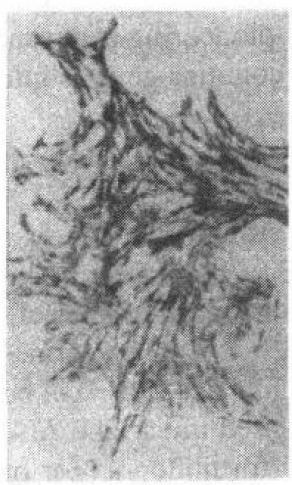


Figure 1-4 A microcolony of Chinese hamster fibroblasts that have been growing for a few days on a glass surface. (Courtesy of Theodore Puck.)

试读结束：需要全本请在线购买： www.ertongbook.com