GENOMES 4

T. A. BROWN



CONTENTS

CHAPTER 1 GENOMES, TRANSCRIPTOMES,		End-modification enzymes	38
AND PROTEOMES	1	2.2 THE POLYMERASE CHAIN REACTION Carrying out a PCR	38 39
1.1 DNA Genes are made of DNA	2 3	The rate of product formation can be followed during a PCR	40
DNA is a polymer of nucleotides The double helix is stabilized by base pairing	4	PCR has many and diverse applications	41
and base stacking The double helix has structural flexibility	8 9	2.3 DNA CLONING Why is gene cloning important?	41 41
1.2 RNA AND THE TRANSCRIPTOME	11	The simplest cloning vectors are based on <i>E. coli</i> plasmids	
RNA is a second type of polynucleotide	12	Bacteriophages can also be used as cloning	43
The RNA content of the cell	12	vectors	44
Many RNAs are synthesized as precursor molecules	13	Vectors for longer pieces of DNA	47
There are different definitions of the transcriptome	15	DNA can be cloned in organisms other than <i>E. coli</i>	48
1.3 PROTEINS AND THE PROTEOME	16	CHAMAADV	
There are four hierarchical levels of protein structure Amino acid diversity underlies protein diversity	e 16 17	SUMMARY	50
The link between the transcriptome and the		SHORT ANSWER QUESTIONS	51
proteome The constituted is not universal.	19	IN-DEPTH PROBLEMS	51
The genetic code is not universal The link between the proteome and the biochemistry of the cell	20 22	FURTHER READING	52
SUMMARY	23	CHAPTER 3	
		MAPPING GENOMES	55
SHORT ANSWER QUESTIONS	24	MINIT IN G GENONIES	,,,
IN-DEPTH PROBLEMS	24	3.1 WHY A GENOME MAP IS IMPORTANT	55
FURTHER READING	25	Genome maps are needed in order to sequence	
CHARTER		the more complex genomes Genome maps are not just sequencing aids	55 57
CHAPTER 2		denome maps are not just sequencing alus	37
STUDYING DNA	27	3.2 MARKERS FOR GENETIC MAPPING Genes were the first markers to be used	58 58
2.1 ENZYMES FOR DNA MANIPULATION The mode of action of a template-dependent DNA	28	RFLPs and SSLPs are examples of DNA markers	59
polymerase	28	Single-nucleotide polymorphisms are the most useful type of DNA marker	61
The types of DNA polymerase used in research Restriction endonucleases enable DNA molecules	30	2 2 THE DAKIS TO CENETIC MARRING	
to be cut at defined positions	32	3.3 THE BASIS TO GENETIC MAPPING The principles of inheritance and the discovery	63
Gel electrophoresis is used to examine the results of a restriction digest	34	of linkage Partial linkage is explained by the behavior of	63
Interesting DNA fragments can be identified by Southern hybridization	35	chromosomes during meiosis From partial linkage to genetic mapping	65 68

3.4 LINKAGE ANALYSIS WITH DIFFERENT TYPES OF ORGANISMS	69	Shotgun sequencing of eukaryotic genomes requires sophisticated assembly programs	102
Linkage analysis when planned breeding experiments are possible	69	More complex genomes can be sequenced by a hierarchical shotgun approach	104
Gene mapping by human pedigree analysis	71	What is a genome sequence and do we always	
Genetic mapping in bacteria	73	need one?	107
The limitations of linkage analysis	74	A A SUDVEY OF FULL DVOTIC CENOME	
3.5 PHYSICAL MAPPING BY DIRECT		4.4 A SURVEY OF EUKARYOTIC GENOME SEQUENCING PROJECTS	109
EXAMINATION OF DNA MOLECULES Conventional restriction mapping is applicable	75	The Human Genome Project: genome sequencing in the heroic age	109
only to small DNA molecules Optical mapping can locate restriction sites in	75	The Neanderthal genome: assembly of an extinct genome by use of the human sequence as a	
longer DNA molecules	77	reference	110
Optical mapping can be used to map other features in a DNA molecule	79	The giant panda genome: shotgun sequencing based entirely on next-generation data	111
3.6 PHYSICAL MAPPING BY ASSIGNING		The barley genome: the concept of gene space	113
MARKERS TO DNA FRAGMENTS	81	SUMMARY	115
Any unique sequence can be used as an STS	81	SHORT ANSWER QUESTIONS	115
DNA fragments for STS mapping can be obtained as radiation hybrids	82	IN-DEPTH PROBLEMS	116
A clone library can be used as the mapping reagent	83	FURTHER READING	117
SUMMARY	84		
SHORT ANSWER QUESTIONS	85	CHAPTER 5	
IN-DEPTH PROBLEMS	85	GENOME ANNOTATION	119
FURTHER READING	86	5.1 GENOME ANNOTATION BY COMPUTER ANALYSIS OF THE DNA SEQUENCE	119
CHAPTER 4		The coding regions of genes are open reading frames	119
SEQUENCING GENOMES	87	Simple ORF scans are less effective with genomes of higher eukaryotes	120
4.1 CHAIN-TERMINATION SEQUENCING	87	•	
Chain-termination sequencing in outline		Locating genes for noncoding RNA	122
Not all DNA polymorasos can be used for	87	Locating genes for noncoding RNA Homology searches and comparative genomics	122
Not all DNA polymerases can be used for	87	Locating genes for noncoding RNA Homology searches and comparative genomics give an extra dimension to gene prediction	122 123
sequencing	87 89	Homology searches and comparative genomics give an extra dimension to gene prediction	
sequencing Chain-termination sequencing with <i>Taq</i> polymerase Strengths and limitations of chain-termination	87 89 90	Homology searches and comparative genomics give an extra dimension to gene prediction 5.2 GENOME ANNOTATION BY ANALYSIS OF GENE TRANSCRIPTS	
sequencing Chain-termination sequencing with <i>Taq</i> polymerase Strengths and limitations of chain-termination sequencing	87 89 90 91	Homology searches and comparative genomics give an extra dimension to gene prediction 5.2 GENOME ANNOTATION BY ANALYSIS OF GENE TRANSCRIPTS Hybridization tests can determine if a fragment contains transcribed sequences	123
sequencing Chain-termination sequencing with <i>Taq</i> polymerase Strengths and limitations of chain-termination sequencing 4.2 NEXT-GENERATION SEQUENCING Preparation of a sequencing library is the common	87 89 90 91 92	Homology searches and comparative genomics give an extra dimension to gene prediction 5.2 GENOME ANNOTATION BY ANALYSIS OF GENE TRANSCRIPTS Hybridization tests can determine if a fragment contains transcribed sequences Methods are available for precise mapping of the ends of transcripts	123 124
sequencing Chain-termination sequencing with <i>Taq</i> polymerase Strengths and limitations of chain-termination sequencing 4.2 NEXT-GENERATION SEQUENCING	87 89 90 91 92 93	Homology searches and comparative genomics give an extra dimension to gene prediction 5.2 GENOME ANNOTATION BY ANALYSIS OF GENE TRANSCRIPTS Hybridization tests can determine if a fragment contains transcribed sequences Methods are available for precise mapping of the	123 124 125
sequencing Chain-termination sequencing with <i>Taq</i> polymerase Strengths and limitations of chain-termination sequencing 4.2 NEXT-GENERATION SEQUENCING Preparation of a sequencing library is the common feature of next-generation methods Various next-generation sequencing methods have been devised Third- and fourth-generation methods enable	87899091929395	Homology searches and comparative genomics give an extra dimension to gene prediction 5.2 GENOME ANNOTATION BY ANALYSIS OF GENE TRANSCRIPTS Hybridization tests can determine if a fragment contains transcribed sequences Methods are available for precise mapping of the ends of transcripts Exon–intron boundaries can also be located with precision 5.3 ANNOTATION BY GENOMEWIDE RNA	123 124 125 126 126
sequencing Chain-termination sequencing with <i>Taq</i> polymerase Strengths and limitations of chain-termination sequencing 4.2 NEXT-GENERATION SEQUENCING Preparation of a sequencing library is the common feature of next-generation methods Various next-generation sequencing methods have been devised Third- and fourth-generation methods enable sequencing in real time	87 89 90 91 92 93	Homology searches and comparative genomics give an extra dimension to gene prediction 5.2 GENOME ANNOTATION BY ANALYSIS OF GENE TRANSCRIPTS Hybridization tests can determine if a fragment contains transcribed sequences Methods are available for precise mapping of the ends of transcripts Exon–intron boundaries can also be located with precision 5.3 ANNOTATION BY GENOMEWIDE RNA MAPPING	123 124 125 126
Sequencing Chain-termination sequencing with <i>Taq</i> polymerase Strengths and limitations of chain-termination sequencing 4.2 NEXT-GENERATION SEQUENCING Preparation of a sequencing library is the common feature of next-generation methods Various next-generation sequencing methods have been devised Third- and fourth-generation methods enable sequencing in real time 4.3 HOW TO SEQUENCE A GENOME The potential of the shotgun method was proven	87 89 90 91 92 93 95 97	Homology searches and comparative genomics give an extra dimension to gene prediction 5.2 GENOME ANNOTATION BY ANALYSIS OF GENE TRANSCRIPTS Hybridization tests can determine if a fragment contains transcribed sequences Methods are available for precise mapping of the ends of transcripts Exon-intron boundaries can also be located with precision 5.3 ANNOTATION BY GENOMEWIDE RNA MAPPING Tiling arrays enable transcripts to be mapped onto chromosomes or entire genomes	123 124 125 126 126
Sequencing Chain-termination sequencing with <i>Taq</i> polymerase Strengths and limitations of chain-termination sequencing 4.2 NEXT-GENERATION SEQUENCING Preparation of a sequencing library is the common feature of next-generation methods Various next-generation sequencing methods have been devised Third- and fourth-generation methods enable sequencing in real time 4.3 HOW TO SEQUENCE A GENOME	8789909192939597	Homology searches and comparative genomics give an extra dimension to gene prediction 5.2 GENOME ANNOTATION BY ANALYSIS OF GENE TRANSCRIPTS Hybridization tests can determine if a fragment contains transcribed sequences Methods are available for precise mapping of the ends of transcripts Exon–intron boundaries can also be located with precision 5.3 ANNOTATION BY GENOMEWIDE RNA MAPPING Tiling arrays enable transcripts to be mapped onto	123 124 125 126 126

SUMMARY	132	CHAPTER 7	
SHORT ANSWER QUESTIONS	132	EUKARYOTIC NUCLEAR	
IN-DEPTH PROBLEMS	133	GENOMES	155
FURTHER READING	133	7.1 NUCLEAR GENOMES ARE CONTAINED IN CHROMOSOMES Chromosomes are much shorter than the DNA	155
CHAPTER 6		molecules they contain	155
IDENTIFYING GENE FUNCTIONS	135	Special features of metaphase chromosomes DNA-protein interactions in centromeres	157
6.1 COMPUTER ANALYSIS OF GENE FUNCTION Homology reflects evolutionary relationships	135 135	and telomeres 7.2 HOW ARE THE GENES ARRANGED IN A	159
Homology analysis can provide information on the function of a gene	136	NUCLEAR GENOME? Genes are not evenly distributed within a genome	161 161
Identification of protein domains can help to assign function to an unknown gene	137	A segment of the human genome The yeast genome is very compact	162 164
Annotation of gene function requires a common terminology	138	Gene organization in other eukaryotes	165
6.2 ASSIGNING FUNCTION BY GENE INACTIVATION AND	.50	7.3 HOW MANY GENES ARE THERE AND WHAT ARE THEIR FUNCTIONS? Gene numbers can be misleading	167 168
OVEREXPRESSION Functional analysis by gene inactivation	139 140	Gene catalogs reveal the distinctive features of different organisms	169
Individual genes can be inactivated by homologous recombination	140	Families of genes Pseudogenes and other evolutionary relics	172 174
Gene inactivation without homologous recombination Gene overexpression can also be used to	142	7.4 THE REPETITIVE DNA CONTENT OF EUKARYOTIC NUCLEAR GENOMES	176
assess function The phenotypic effect of gene inactivation or overexpression may be difficult to discern	144 145	Tandemly repeated DNA is found at centromeres and elsewhere in eukaryotic chromosomes Minisatellites and microsatellites	176 176
6.3 UNDERSTANDING GENE FUNCTION	. 13	Interspersed repeats	177
BY STUDIES OF EXPRESSION PATTERN AND PROTEIN PRODUCT	146	SUMMARY	178
Reporter genes and immunocytochemistry can be used to locate where and when genes	146	SHORT ANSWER QUESTIONS	178
are expressed	146	IN-DEPTH PROBLEMS	179
Directed mutagenesis can be used to probe gene function in detail	147	FURTHER READING	179
6.4 USING CONVENTIONAL GENETIC ANALYSIS TO IDENTIFY GENE		CHAPTER 8 GENOMES OF PROKARYOTES	
FUNCTION Identification of human genes responsible for inherited diseases	149	A LIPS WILLIAM DATE OF THE STATE OF THE STAT	181
Genomewide association studies can also identify genes for diseases and other traits	150 151	8.1 PHYSICAL FEATURES OF PROKARYOTIC GENOMES	181
SUMMARY	152	The traditional view of the prokaryotic chromosome	181
SHORT ANSWER QUESTIONS	153	Some bacteria have linear or multipartite genomes	183
N-DEPTH PROBLEMS	153	8.2 GENETIC FEATURES OF PROKARYOTIC	
FURTHER READING	154	GENOMES Gene organization in the F coli K12 genome	186

xiii

Operons are characteristic features of prokaryotic genomes Prokaryotic genome sizes and numbers of genes	188	CHAPTER 10 ACCESSING THE GENOME	219
vary according to biological complexity Genome sizes and numbers of genes vary within	189	10.1 INSIDE THE NUCLEUS The nucleus has an ordered internal	219
individual species Distinctions between prokaryotic species are	190	structure The DNA content of a nondividing nucleus	220
further blurred by lateral gene transfer Metagenomes describe the members of a	192	displays different degrees of packaging The nuclear matrix is thought to provide	221
community	194	attachment points for chromosomal DNA	222
8.3 EUKARYOTIC ORGANELLAR GENOMES	195	Each chromosome has its own territory within the nucleus	223
The endosymbiont theory explains the origin of organellar genomes	195	Each chromosome comprises a series of topologically associated domains	224
Most organellar genomes are circular The gene catalogs of organellar genomes	196 197	Insulators mark the boundaries of topologically associated domains	226
SUMMARY	198	10.2 NUCLEOSOME MODIFICATIONS AND GENOME EXPRESSION	228
SHORT ANSWER QUESTIONS	200	Acetylation of histones influences many nuclear	228
IN-DEPTH PROBLEMS	201	activities including genome expression Histone deacetylation represses active regions	
FURTHER READING	201	of the genome Acetylation is not the only type of histone modification	229 230
CHAPTER 9		Nucleosome repositioning also influences gene expression	231
VIRAL GENOMES AND MOBILE GENETIC ELEMENTS	203	10.3 DNA MODIFICATION AND GENOME EXPRESSION	234
9.1 THE GENOMES OF BACTERIOPHAGES AND EUKARYOTIC VIRUSES	203	Genome silencing by DNA methylation Methylation is involved in genomic imprinting and X inactivation	234 235
Bacteriophage genomes have diverse structures and organizations	203	SUMMARY	233
Replication strategies for bacteriophage genomes	205	SHORT ANSWER QUESTIONS	237
Structures and replication strategies for	206	IN-DEPTH PROBLEMS	238
eukaryotic viral genomes Some retroviruses cause cancer	200 207 209	FURTHER READING	238
Genomes at the edge of life 9.2 MOBILE GENETIC ELEMENTS	210	CHAPTER 11	
RNA transposons with long terminal repeats are related to viral retroelements	210	THE ROLE OF DNA-BINDING	
Some RNA transposons lack long terminal repeats	212	PROTEINS IN GENOME EXPRESSION	241
DNA transposons are common in prokaryotic genomes	213	11.1 METHODS FOR STUDYING	2
DNA transposons are less common in eukaryotic genomes	214	DNA-BINDING PROTEINS AND THEIR ATTACHMENT SITES	241
SUMMARY	216	X-ray crystallography provides structural data for any protein that can be crystallized	241
SHORT ANSWER QUESTIONS	216	NMR spectroscopy is used to study the structures	
IN-DEPTH PROBLEMS	217	of small proteins Gel retardation identifies DNA fragments that	243
FURTHER READING	217	bind to proteins	244

Protection assays pinpoint binding sites with greater accuracy Modification interference identifies nucleotides	244	RNA silencing was first identified as a means of destroying invading viral RNA MicroRNAs regulate genome expression by	276
central to protein binding Genomewide scans for protein attachment sites	246 247	causing specific target mRNAs to be degraded 12.4 INFLUENCE OF RNA PROCESSING	278
11.2 THE SPECIAL FEATURES OF		ON THE COMPOSITION OF A	270
DNA-BINDING PROTEINS	249	TRANSCRIPTOME The splicing pathway for eukaryotic pre-mRNA	278
The helix-turn-helix motif is present in prokaryotic and eukaryotic proteins	249	introns	279
Zinc fingers are common in eukaryotic proteins	250	The splicing process must have a high degree of	
Other nucleic acid-binding motifs	251	precision	280
44 2 INTERACTION DETWEEN DNA AND ITS		Enhancer and silencer elements specify alternative splicing pathways	282
11.3 INTERACTION BETWEEN DNA AND ITS BINDING PROTEINS	252		
Direct readout of the nucleotide sequence The nucleotide sequence has a number of indirect	252	12.5 TRANSCRIPTOMES IN RESEARCH Transcriptome analysis as an aid to genome annotation	284 284
effects on helix structure	253	Cancer transcriptomes	286
Contacts between DNA and proteins	253	Transcriptomes and the responses of plants	
SUMMARY	254	to stress	287
SHORT ANSWER QUESTIONS	255	SUMMARY	289
IN-DEPTH PROBLEMS	256	SHORT ANSWER QUESTIONS	289
FURTHER READING	256	IN-DEPTH PROBLEMS	290
		FURTHER READING	290
CHAPTER 12			
CHAPTER 12 TRANSCRIPTOMES	257	CHAPTER 13	
TRANSCRIPTOMES 12.1 COMPONENTS OF THE		CHAPTER 13 PROTEOMES	293
TRANSCRIPTOMES 12.1 COMPONENTS OF THE TRANSCRIPTOME	257 257	PROTEOMES	293
TRANSCRIPTOMES 12.1 COMPONENTS OF THE TRANSCRIPTOME The mRNA fraction of a transcriptome is small	257		293
TRANSCRIPTOMES 12.1 COMPONENTS OF THE TRANSCRIPTOME The mRNA fraction of a transcriptome is small but complex		PROTEOMES 13.1 STUDYING THE COMPOSITION OF A PROTEOME The separation stage of a protein profiling	293
TRANSCRIPTOMES 12.1 COMPONENTS OF THE TRANSCRIPTOME The mRNA fraction of a transcriptome is small	257 257	PROTEOMES 13.1 STUDYING THE COMPOSITION OF A PROTEOME The separation stage of a protein profiling project	
TRANSCRIPTOMES 12.1 COMPONENTS OF THE TRANSCRIPTOME The mRNA fraction of a transcriptome is small but complex Short noncoding RNAs have diverse functions Long noncoding RNAs are enigmatic transcripts Microarray analysis and RNA sequencing are	257 257 259 260	PROTEOMES 13.1 STUDYING THE COMPOSITION OF A PROTEOME The separation stage of a protein profiling project The identification stage of a protein profiling	293 294
TRANSCRIPTOMES 12.1 COMPONENTS OF THE TRANSCRIPTOME The mRNA fraction of a transcriptome is small but complex Short noncoding RNAs have diverse functions Long noncoding RNAs are enigmatic transcripts	257 257 259	PROTEOMES 13.1 STUDYING THE COMPOSITION OF A PROTEOME The separation stage of a protein profiling project The identification stage of a protein profiling project	293
TRANSCRIPTOMES 12.1 COMPONENTS OF THE TRANSCRIPTOME The mRNA fraction of a transcriptome is small but complex Short noncoding RNAs have diverse functions Long noncoding RNAs are enigmatic transcripts Microarray analysis and RNA sequencing are	257 257 259 260	PROTEOMES 13.1 STUDYING THE COMPOSITION OF A PROTEOME The separation stage of a protein profiling project The identification stage of a protein profiling	293 294 297 299
TRANSCRIPTOMES 12.1 COMPONENTS OF THE TRANSCRIPTOME The mRNA fraction of a transcriptome is small but complex Short noncoding RNAs have diverse functions Long noncoding RNAs are enigmatic transcripts Microarray analysis and RNA sequencing are used to study the contents of transcriptomes 12.2 SYNTHESIS OF THE COMPONENTS OF THE TRANSCRIPTOME	257 257 259 260	PROTEOMES 13.1 STUDYING THE COMPOSITION OF A PROTEOME The separation stage of a protein profiling project The identification stage of a protein profiling project Comparing the compositions of two proteomes	293 294 297
TRANSCRIPTOMES 12.1 COMPONENTS OF THE TRANSCRIPTOME The mRNA fraction of a transcriptome is small but complex Short noncoding RNAs have diverse functions Long noncoding RNAs are enigmatic transcripts Microarray analysis and RNA sequencing are used to study the contents of transcriptomes 12.2 SYNTHESIS OF THE COMPONENTS OF THE TRANSCRIPTOME RNA polymerases are molecular machines	257 257 259 260 262	PROTEOMES 13.1 STUDYING THE COMPOSITION OF A PROTEOME The separation stage of a protein profiling project The identification stage of a protein profiling project Comparing the compositions of two proteomes Analytical protein arrays offer an alternative approach to protein profiling	293 294 297 299
TRANSCRIPTOMES 12.1 COMPONENTS OF THE TRANSCRIPTOME The mRNA fraction of a transcriptome is small but complex Short noncoding RNAs have diverse functions Long noncoding RNAs are enigmatic transcripts Microarray analysis and RNA sequencing are used to study the contents of transcriptomes 12.2 SYNTHESIS OF THE COMPONENTS OF THE TRANSCRIPTOME RNA polymerases are molecular machines for making RNA	257 257 259 260 262	PROTEOMES 13.1 STUDYING THE COMPOSITION OF A PROTEOME The separation stage of a protein profiling project The identification stage of a protein profiling project Comparing the compositions of two proteomes Analytical protein arrays offer an alternative	293 294 297 299
TRANSCRIPTOMES 12.1 COMPONENTS OF THE TRANSCRIPTOME The mRNA fraction of a transcriptome is small but complex Short noncoding RNAs have diverse functions Long noncoding RNAs are enigmatic transcripts Microarray analysis and RNA sequencing are used to study the contents of transcriptomes 12.2 SYNTHESIS OF THE COMPONENTS OF THE TRANSCRIPTOME RNA polymerases are molecular machines for making RNA Transcription start points are indicated by	257 257 259 260 262	PROTEOMES 13.1 STUDYING THE COMPOSITION OF A PROTEOME The separation stage of a protein profiling project The identification stage of a protein profiling project Comparing the compositions of two proteomes Analytical protein arrays offer an alternative approach to protein profiling 13.2 IDENTIFYING PROTEINS THAT	293 294 297 299 300
TRANSCRIPTOMES 12.1 COMPONENTS OF THE TRANSCRIPTOME The mRNA fraction of a transcriptome is small but complex Short noncoding RNAs have diverse functions Long noncoding RNAs are enigmatic transcripts Microarray analysis and RNA sequencing are used to study the contents of transcriptomes 12.2 SYNTHESIS OF THE COMPONENTS OF THE TRANSCRIPTOME RNA polymerases are molecular machines for making RNA Transcription start points are indicated by promoter sequences Synthesis of bacterial RNA is regulated by	257 257 259 260 262 263 264	PROTEOMES 13.1 STUDYING THE COMPOSITION OF A PROTEOME The separation stage of a protein profiling project The identification stage of a protein profiling project Comparing the compositions of two proteomes Analytical protein arrays offer an alternative approach to protein profiling 13.2 IDENTIFYING PROTEINS THAT INTERACT WITH ONE ANOTHER Identifying pairs of interacting proteins Identifying the components of multiprotein	293 294 297 299 300 301 301
TRANSCRIPTOMES 12.1 COMPONENTS OF THE TRANSCRIPTOME The mRNA fraction of a transcriptome is small but complex Short noncoding RNAs have diverse functions Long noncoding RNAs are enigmatic transcripts Microarray analysis and RNA sequencing are used to study the contents of transcriptomes 12.2 SYNTHESIS OF THE COMPONENTS OF THE TRANSCRIPTOME RNA polymerases are molecular machines for making RNA Transcription start points are indicated by promoter sequences Synthesis of bacterial RNA is regulated by repressor and activator proteins	257 257 259 260 262 263 264	PROTEOMES 13.1 STUDYING THE COMPOSITION OF A PROTEOME The separation stage of a protein profiling project The identification stage of a protein profiling project Comparing the compositions of two proteomes Analytical protein arrays offer an alternative approach to protein profiling 13.2 IDENTIFYING PROTEINS THAT INTERACT WITH ONE ANOTHER Identifying pairs of interacting proteins Identifying the components of multiprotein complexes	293 294 297 299 300 301 301 304
TRANSCRIPTOMES 12.1 COMPONENTS OF THE TRANSCRIPTOME The mRNA fraction of a transcriptome is small but complex Short noncoding RNAs have diverse functions Long noncoding RNAs are enigmatic transcripts Microarray analysis and RNA sequencing are used to study the contents of transcriptomes 12.2 SYNTHESIS OF THE COMPONENTS OF THE TRANSCRIPTOME RNA polymerases are molecular machines for making RNA Transcription start points are indicated by promoter sequences Synthesis of bacterial RNA is regulated by repressor and activator proteins Synthesis of bacterial RNA is also regulated by	257 257 259 260 262 263 264 266 268	PROTEOMES 13.1 STUDYING THE COMPOSITION OF A PROTEOME The separation stage of a protein profiling project The identification stage of a protein profiling project Comparing the compositions of two proteomes Analytical protein arrays offer an alternative approach to protein profiling 13.2 IDENTIFYING PROTEINS THAT INTERACT WITH ONE ANOTHER Identifying pairs of interacting proteins Identifying the components of multiprotein complexes Identifying proteins with functional interactions	293 294 297 299 300 301 301
TRANSCRIPTOMES 12.1 COMPONENTS OF THE TRANSCRIPTOME The mRNA fraction of a transcriptome is small but complex Short noncoding RNAs have diverse functions Long noncoding RNAs are enigmatic transcripts Microarray analysis and RNA sequencing are used to study the contents of transcriptomes 12.2 SYNTHESIS OF THE COMPONENTS OF THE TRANSCRIPTOME RNA polymerases are molecular machines for making RNA Transcription start points are indicated by promoter sequences Synthesis of bacterial RNA is regulated by repressor and activator proteins Synthesis of bacterial RNA is also regulated by control over transcription termination	257 257 259 260 262 263 264 266	PROTEOMES 13.1 STUDYING THE COMPOSITION OF A PROTEOME The separation stage of a protein profiling project The identification stage of a protein profiling project Comparing the compositions of two proteomes Analytical protein arrays offer an alternative approach to protein profiling 13.2 IDENTIFYING PROTEINS THAT INTERACT WITH ONE ANOTHER Identifying pairs of interacting proteins Identifying the components of multiprotein complexes Identifying proteins with functional interactions Protein interaction maps display the interactions	293 294 297 299 300 301 301 304
TRANSCRIPTOMES 12.1 COMPONENTS OF THE TRANSCRIPTOME The mRNA fraction of a transcriptome is small but complex Short noncoding RNAs have diverse functions Long noncoding RNAs are enigmatic transcripts Microarray analysis and RNA sequencing are used to study the contents of transcriptomes 12.2 SYNTHESIS OF THE COMPONENTS OF THE TRANSCRIPTOME RNA polymerases are molecular machines for making RNA Transcription start points are indicated by promoter sequences Synthesis of bacterial RNA is regulated by repressor and activator proteins Synthesis of bacterial RNA is also regulated by	257 257 259 260 262 263 264 266 268	PROTEOMES 13.1 STUDYING THE COMPOSITION OF A PROTEOME The separation stage of a protein profiling project The identification stage of a protein profiling project Comparing the compositions of two proteomes Analytical protein arrays offer an alternative approach to protein profiling 13.2 IDENTIFYING PROTEINS THAT INTERACT WITH ONE ANOTHER Identifying pairs of interacting proteins Identifying the components of multiprotein complexes Identifying proteins with functional interactions Protein interaction maps display the interactions within a proteome	293 294 297 299 300 301 301 304 305
TRANSCRIPTOMES 12.1 COMPONENTS OF THE TRANSCRIPTOME The mRNA fraction of a transcriptome is small but complex Short noncoding RNAs have diverse functions Long noncoding RNAs are enigmatic transcripts Microarray analysis and RNA sequencing are used to study the contents of transcriptomes 12.2 SYNTHESIS OF THE COMPONENTS OF THE TRANSCRIPTOME RNA polymerases are molecular machines for making RNA Transcription start points are indicated by promoter sequences Synthesis of bacterial RNA is regulated by repressor and activator proteins Synthesis of bacterial RNA is also regulated by control over transcription termination Synthesis of eukaryotic RNA is regulated primarily by activator proteins	257 257 259 260 262 263 264 266 268 271	13.1 STUDYING THE COMPOSITION OF A PROTEOME The separation stage of a protein profiling project The identification stage of a protein profiling project Comparing the compositions of two proteomes Analytical protein arrays offer an alternative approach to protein profiling 13.2 IDENTIFYING PROTEINS THAT INTERACT WITH ONE ANOTHER Identifying pairs of interacting proteins Identifying the components of multiprotein complexes Identifying proteins with functional interactions Protein interaction maps display the interactions within a proteome 13.3 SYNTHESIS AND DEGRADATION	293 294 297 299 300 301 301 304 305
TRANSCRIPTOMES 12.1 COMPONENTS OF THE TRANSCRIPTOME The mRNA fraction of a transcriptome is small but complex Short noncoding RNAs have diverse functions Long noncoding RNAs are enigmatic transcripts Microarray analysis and RNA sequencing are used to study the contents of transcriptomes 12.2 SYNTHESIS OF THE COMPONENTS OF THE TRANSCRIPTOME RNA polymerases are molecular machines for making RNA Transcription start points are indicated by promoter sequences Synthesis of bacterial RNA is regulated by repressor and activator proteins Synthesis of bacterial RNA is also regulated by control over transcription termination Synthesis of eukaryotic RNA is regulated primarily by activator proteins	257 257 259 260 262 263 264 266 268 271 272	13.1 STUDYING THE COMPOSITION OF A PROTEOME The separation stage of a protein profiling project The identification stage of a protein profiling project Comparing the compositions of two proteomes Analytical protein arrays offer an alternative approach to protein profiling 13.2 IDENTIFYING PROTEINS THAT INTERACT WITH ONE ANOTHER Identifying pairs of interacting proteins Identifying the components of multiprotein complexes Identifying proteins with functional interactions Protein interaction maps display the interactions within a proteome 13.3 SYNTHESIS AND DEGRADATION OF THE COMPONENTS OF THE	293 294 297 299 300 301 304 305 306
TRANSCRIPTOMES 12.1 COMPONENTS OF THE TRANSCRIPTOME The mRNA fraction of a transcriptome is small but complex Short noncoding RNAs have diverse functions Long noncoding RNAs are enigmatic transcripts Microarray analysis and RNA sequencing are used to study the contents of transcriptomes 12.2 SYNTHESIS OF THE COMPONENTS OF THE TRANSCRIPTOME RNA polymerases are molecular machines for making RNA Transcription start points are indicated by promoter sequences Synthesis of bacterial RNA is regulated by repressor and activator proteins Synthesis of bacterial RNA is also regulated by control over transcription termination Synthesis of eukaryotic RNA is regulated primarily by activator proteins	257 257 259 260 262 263 264 266 268 271	13.1 STUDYING THE COMPOSITION OF A PROTEOME The separation stage of a protein profiling project The identification stage of a protein profiling project Comparing the compositions of two proteomes Analytical protein arrays offer an alternative approach to protein profiling 13.2 IDENTIFYING PROTEINS THAT INTERACT WITH ONE ANOTHER Identifying pairs of interacting proteins Identifying the components of multiprotein complexes Identifying proteins with functional interactions Protein interaction maps display the interactions within a proteome 13.3 SYNTHESIS AND DEGRADATION	293 294 297 299 300 301 301 304 305

During stress, bacteria inactivate their ribosomes in order to downsize the proteome	311	Yeast mating types are determined by gene conversion events	338
Initiation factors mediate large-scale remodeling of eukaryotic proteomes	312	Genome rearrangements are responsible for immunoglobulin and T-cell receptor	
The translation of individual mRNAs can also be regulated	313	diversity	339
Degradation of the components of the	313	14.3 CHANGES IN GENOME ACTIVITY	
proteome	314	UNDERLYING DEVELOPMENT Bacteriophage λ: a genetic switch enables a	341
13.4 INFLUENCE OF PROTEIN		choice to be made between alternative	242
PROCESSING ON THE COMPOSITION OF THE PROTEOME	215	developmental pathways Bacillus sporulation: coordination of activities in	342
The amino acid sequence contains instructions	315	two distinct cell types	343
for protein folding	315	Caenorhabditis elegans: the genetic basis of positional information and the determination	
Some proteins are activated by proteolytic cleavage	318	of cell fate	346
Important changes in protein activity can be		Fruit flies: conversion of positional information into a segmented body plan	348
brought about by chemical modification	320	Homeotic selector genes are universal features	340
13.5 BEYOND THE PROTEOME	322	of higher eukaryotic development	350
The metabolome is the complete set of metabolites present in a cell	322	Homeotic genes also underlie plant development	352
Systems biology provides an integrated		SUMMARY	252
description of cellular activity	323		352
SUMMARY	326	SHORT ANSWER QUESTIONS	353
SHORT ANSWER QUESTIONS	326	IN-DEPTH PROBLEMS	354
IN-DEPTH PROBLEMS	327	FURTHER READING	354
FURTHER READING	327	CHARTER 45	
		CHAPTER 15	257
CHAPTER 14		GENOME REPLICATION	357
GENOME EXPRESSION		15.1 THE TOPOLOGY OF GENOME	
IN THE CONTEXT OF CELL		REPLICATION The double-helical structure complicates the	357
AND ORGANISM	329	replication process	358
14.1 THE RESPONSE OF THE GENOME		The Meselson–Stahl experiment proved that replication is semiconservative	359
TO EXTERNAL SIGNALS	330	DNA topoisomerases provide a solution to the	
Signal transmission by import of the extracellular signaling compound	330	topological problem Variations on the semiconservative theme	361 363
Receptor proteins transmit signals across cell		variations on the semiconservative theme	303
membranes	222	4	
Some signal transduction pathways have few	332	15.2 THE INITIATION PHASE OF GENOME REPLICATION	364
Some signal transduction pathways have few steps between receptor and genome	332 333	REPLICATION Initiation at the <i>E. coli</i> origin of replication	364 364
steps between receptor and genome Some signal transduction pathways have many	333	REPLICATION Initiation at the <i>E. coli</i> origin of replication Origins of replication have been clearly defined	364
steps between receptor and genome Some signal transduction pathways have many steps between receptor and genome Some signal transduction pathways operate	333 334	REPLICATION Initiation at the <i>E. coli</i> origin of replication Origins of replication have been clearly defined in yeast Origins in higher eukaryotes have been less easy	364 365
steps between receptor and genome Some signal transduction pathways have many steps between receptor and genome	333	REPLICATION Initiation at the <i>E. coli</i> origin of replication Origins of replication have been clearly defined in yeast	364
steps between receptor and genome Some signal transduction pathways have many steps between receptor and genome Some signal transduction pathways operate via second messengers 14.2 CHANGES IN GENOME ACTIVITY	333 334	REPLICATION Initiation at the <i>E. coli</i> origin of replication Origins of replication have been clearly defined in yeast Origins in higher eukaryotes have been less easy to identify 15.3 EVENTS AT THE REPLICATION FORK	364 365
steps between receptor and genome Some signal transduction pathways have many steps between receptor and genome Some signal transduction pathways operate via second messengers 14.2 CHANGES IN GENOME ACTIVITY RESULTING IN CELLULAR	333 334 336	REPLICATION Initiation at the <i>E. coli</i> origin of replication Origins of replication have been clearly defined in yeast Origins in higher eukaryotes have been less easy to identify 15.3 EVENTS AT THE REPLICATION FORK DNA polymerases are molecular machines for	364 365 366 367
steps between receptor and genome Some signal transduction pathways have many steps between receptor and genome Some signal transduction pathways operate via second messengers 14.2 CHANGES IN GENOME ACTIVITY	333 334	REPLICATION Initiation at the <i>E. coli</i> origin of replication Origins of replication have been clearly defined in yeast Origins in higher eukaryotes have been less easy to identify 15.3 EVENTS AT THE REPLICATION FORK	364 365 366

Okazaki fragments must be joined together to complete lagging-strand replication	370	Defects in DNA repair underlie human diseases, including cancers	406
15.4 TERMINATION OF GENOME		SUMMARY	406
REPLICATION	372	SHORT ANSWER QUESTIONS	407
Replication of the <i>E. coli</i> genome terminates within a defined region	373	IN-DEPTH PROBLEMS	407
Little is known about termination of replication in eukaryotes	374	FURTHER READING	408
Telomerase completes replication of chromosomal DNA molecules, at least in some cells	375	CHAPTER 17	
Telomere length is implicated in cell senescence and cancer	378	RECOMBINATION AND	444
<i>Drosophila</i> has a unique solution to the end-shortening problem	379	TRANSPOSITION	411 412
15.5 REGULATION OF EUKARYOTIC GENOME REPLICATION Genome replication must be synchronized	380	17.1 HOMOLOGOUS RECOMBINATION The Holliday and Meselson–Radding models for homologous recombination The double-strand break model for homologous	412
with the cell cycle	380	recombination	414
Origin licensing is the prerequisite for passing the G1-S checkpoint	380	RecBCD is the most important pathway for homologous recombination in bacteria	415
Replication origins do not all fire at the same time The cell has various options if the genome is	382	E. coli can also carry out homologous recombination by the RecFOR pathway	417
damaged	383	Homologous recombination pathways in eukaryotes	417
SUMMARY	384	The primary role of homologous recombination is thought to be DNA repair	418
SHORT ANSWER QUESTIONS	385		
IN-DEPTH PROBLEMS	385	17.2 SITE-SPECIFIC RECOMBINATION Bacteriophage λ uses site-specific recombination	419
FURTHER READING	386	during the lysogenic infection cycle	419
CHAPTER 46		Site-specific recombination is an aid in construction of genetically modified plants	421
CHAPTER 16		17.3 TRANSPOSITION	421
	389	Replicative and conservative transposition of DNA transposons	422
16.1 THE CAUSES OF MUTATIONS Errors in replication are a source of point mutations	389 390	Retroelements transpose replicatively via an RNA intermediate	423
Replication errors can also lead to insertion and deletion mutations	391	SUMMARY	425
Mutations are also caused by chemical and	391	SHORT ANSWER QUESTIONS	426
physical mutagens	394	IN-DEPTH PROBLEMS	427
16.2 REPAIR OF MUTATIONS AND OTHER TYPES OF DNA DAMAGE Direct repair systems fill in nicks and correct	398	FURTHER READING	427
some types of nucleotide modification	398	CHAPTER 18	
Base excision repairs many types of damaged nucleotide	399	HOW GENOMES EVOLVE	429
Nucleotide excision repair is used to correct more extensive types of damage	401	18.1 GENOMES: THE FIRST 10 BILLION YEARS	429
Mismatch repair corrects replication errors	402	The first biochemical systems were centered on RNA	429
Single- and double-strand breaks can be repaired If necessary, DNA damage can be bypassed during	403	The first DNA genomes	432
genome replication	405	How unique is life?	433

18.2 EVOLUTION OF INCREASINGLY	
COMPLEX GENOMES	434
Genome sequences provide extensive evidence	42.4
of past gene duplications	434
A variety of processes could result in gene duplication	438
Whole-genome duplication is also possible	439
Smaller duplications can also be identified in	.55
the human genome and other genomes	442
Both prokaryotes and eukaryotes acquire	
genes from other species	444
Genome evolution also involves rearrangement of existing genes	445
There are competing hypotheses for the origins of	
introns	448
The evolution of the epigenome	449
18.3 GENOMES: THE LAST 6 MILLION	
YEARS	450
The human genome is very similar to that of the	
chimpanzee	451
Paleogenomics is helping us understand the	450
recent evolution of the human genome	452
18.4 GENOMES TODAY: DIVERSITY IN	
POPULATIONS	453
The origins of HIV/AIDS	454
The first migrations of humans out of Africa	455
The diversity of plant genomes is an aid in crop	457
breeding	457
SUMMARY	458
SHORT ANSWER QUESTIONS	459
IN-DEPTH PROBLEMS	460
FURTHER READING	460
FUNTHER READING	400
GLOSSARY	463
INDEX	491
	マシリ