

## CONTENTS IN FULL

Foreword	xxi
ACKNOWLEDGMENTS	xxii
Abbreviations	xxv

<b>1 Genomes and the flow of biological information</b>	1
Introduction	1
1.1 The roots of biology	1
1.2 The genome: a working blueprint for life	5
1.3 Bringing genes to life: gene expression	9
1.4 Regulating gene expression	12
1.5 Cellular infrastructure and gene expression	15
1.6 Expression of the genome	18
1.7 Evolution of the genome and the tree of life	21
<b>2 Biological molecules</b>	30
Introduction	30
2.1 Atoms, molecules, and chemical bonds	31
2.2 Life in aqueous solution	35
2.3 Non-covalent interactions	37
2.4 Nucleotides and nucleic acids	40
2.5 The structure of DNA	45
2.6 Chemical properties of RNA	53
2.7 RNA folding and structure	56
2.8 The RNA world and its role in the evolution of modern-day life	58
2.9 Fundamentals of protein structure	61
2.10 Protein folding	65
2.11 Protein folds	70
2.12 Protein–DNA interactions	72
2.13 Sugars and carbohydrates	74
2.14 Lipids	76
2.15 Chemical modification in biological regulation	80
<b>3 The chemical basis of life</b>	86
Introduction	86
3.1 Thermodynamic rules in biological systems	86
3.2 Binding equilibria and kinetics	94
3.3 Binding processes in biology	98
3.4 Enzyme catalysis	104
3.5 Enzyme kinetics	111
<b>4 Chromosome structure and function</b>	117
Introduction	117
4.1 Organization of chromosomes	118
4.2 The cell cycle and chromosome dynamics	120

4.3	Packaging chromosomal DNA	122	6.3	Meiosis: generating haploid gametes from diploid cells	278
4.4	Variation in chromatin structure	129	6.4	Chromosome segregation in bacteria	285
4.5	Covalent modifications of histones	131	7	<b>Transcription</b>	<b>296</b>
4.6	Nucleosome-remodeling complexes	137	7.1	Introduction	296
4.7	DNA methylation	138	7.2	Overview of transcription	296
4.8	The separation of chromatin domains by boundary elements	142	7.3	RNA polymerase core enzyme	299
4.9	Elements required for chromosome function	145	7.4	Promoter recognition in bacteria and eukaryotes	302
4.10	The centromere	146	7.5	Initiation of transcription and transition to an elongating complex	313
4.11	The telomere	151	7.6	Transcription elongation	319
4.12	Chromosome architecture in the nucleus	154	7.7	Transcription termination	324
<b>5</b>	<b>The cell cycle</b>	<b>162</b>	<b>8</b>	<b>Regulation of transcription</b>	<b>330</b>
5.1	Introduction	162	8.1	Introduction	330
5.1	Steps in the eukaryotic cell cycle	162	8.2	Principles of transcription regulation	330
5.2	Cyclins and Cdks	166	8.3	DNA-binding domains in proteins that regulate transcription	335
5.3	Regulation of Cdk activity	171	8.4	Mechanisms for regulating transcription initiation in bacteria	340
5.4	Cell cycle regulation by Cdks	173	8.5	Competition between cl and Cro and control of the fate of bacteriophage lambda	345
5.5	Regulation of proteolysis by Cdks	175	8.6	Regulation of transcription termination in bacteria	351
5.6	Checkpoints: intrinsic pathways that can halt the cell cycle	180	8.7	Regulation of transcription initiation and elongation in eukaryotes	355
5.7	Extrinsic regulators of cell cycle progression	184	8.8	Combinatorial regulation of eukaryotic transcription	360
5.8	The cell cycle and cancer	186	8.9	The role of signaling cascades in the regulation of transcription	363
5.9	The bacterial cell cycle	189	8.10	Gene silencing	365
<b>6</b>	<b>DNA replication</b>	<b>199</b>	<b>9</b>	<b>RNA processing</b>	<b>375</b>
6.1	Introduction	199	9.1	Introduction	375
6.1	Overview of DNA replication	199	9.2	Overview of RNA processing	375
6.2	DNA polymerases: structure and function	207	9.3	tRNA and rRNA processing	378
6.3	DNA polymerases: fidelity and processivity	210	9.4	tRNA and rRNA nucleotide modifications	383
6.4	Specialized polymerases	211	9.5	mRNA capping and polyadenylation	385
6.5	DNA helicases: unwinding of the double helix	213	9.6	RNA splicing	388
6.6	The sliding clamp and clamp loader	218	9.7	Eukaryotic mRNA splicing by the spliceosome	393
6.7	Origins and initiation of DNA replication	221	9.8	Exon definition and alternative splicing	399
6.8	Leading and lagging strand synthesis	224	9.9	RNA editing	405
6.9	The replication fork	227	9.10	Degradation of normal RNAs	410
6.10	Termination of DNA replication	231	9.11	Degradation of foreign and defective RNAs	413
6.11	The end-replication problem and telomerase	233	9.12	RNA-binding domains in proteins	416
6.12	Chromatin replication	235	<b>10</b>	<b>Translation</b>	<b>421</b>
6.13	Regulation of initiation of replication in <i>E. coli</i>	238	10.1	Introduction	421
6.14	Regulation of replication initiation in eukaryotes	241	10.2	Overview of translation	421
<b>7</b>	<b>Chromosome segregation</b>	<b>249</b>	10.3	tRNA and the genetic code	423
7.1	Introduction	249	10.4	Aminoacyl-tRNA synthetases	426
7.2	The stages of mitosis	249	10.5	Structure of the ribosome	431
7.2	Chromosome condensation and cohesion	251	10.6	The translation cycle: the ribosome in action	435
7.3	The mitotic spindle	257	10.7	Protein factors critical to the translation cycle	440
7.4	Prometaphase and metaphase	263	10.8	Translation initiation – shared features in bacteria and eukaryotes	443
7.5	Anaphase: an irreversible step in chromosome segregation	269			
7.6	The completion of mitosis and cytokinesis	276			

11.8 Bacterial translation initiation	444	15.4 Repair of DNA damage by base excision repair	595
11.9 Eukaryotic translation initiation	448	15.5 Nucleotide excision repair of bulky lesions	596
11.10 Translation elongation: decoding, peptide bond formation, and translocation	450	15.6 Translesion DNA synthesis	599
11.11 Translation termination, recycling, and reinitiation	454	15.7 The DNA damage response	601
11.12 Ribosome rescue in bacteria and eukaryotes	460	15.8 The DNA damage response in bacteria	605
11.13 Recoding: programmed stop codon read-through and frameshifting	466	15.9 The DNA damage response in eukaryotes	607
11.14 Antibiotics that target the ribosome	472	15.10 DNA damage and cell death in mammalian cells	618
<b>12 Regulation of translation</b>	<b>479</b>	<b>16 Repair of DNA double-strand breaks and homologous recombination</b>	<b>626</b>
Introduction	479	Introduction	626
12.1 Global regulation of initiation in bacteria and eukaryotes	479	16.1 An overview of DNA double-strand break repair and homologous recombination	626
12.2 Regulation of initiation by <i>cis</i> acting sequences in the 5' untranslated region in bacteria and eukaryotes	482	16.2 Double-strand break repair by NHEJ	628
12.3 Regulation of translation through <i>cis</i> acting sequences in the 3' UTR in eukaryotes	489	16.3 Homology-directed repair of double-strand breaks	631
12.4 Viral corruption of the translational machinery	492	16.4 Generation of single-stranded DNA by helicases and nucleases	632
<b>13 Regulatory RNAs</b>	<b>498</b>	16.5 The mechanism of DNA strand pairing and exchange	637
Introduction	498	16.6 Gene conversion through homology-directed repair	639
13.1 Overview of regulatory RNAs	501	16.7 Repair of damaged replication forks by homology-directed repair	645
13.2 Bacterial base-pairing sRNAs	503	16.8 Homologous recombination	647
13.3 Eukaryotic sRNAs: miRNAs, siRNAs, and rasiRNAs	506	16.9 Chromosome rearrangements during aberrant repair and recombination	659
13.4 Processing of eukaryotic sRNAs	507		
13.5 Loading of Argonaute family proteins with eukaryotic sRNAs	516		
13.6 Gene silencing by small eukaryotic RNAs	519		
13.7 Viral defense role of bacterial, archaeal, and eukaryotic sRNAs	522		
13.8 RNA-mediated regulation in <i>cis</i>	527		
13.9 Protein-binding regulatory RNAs	530		
13.10 Long intergenic non-coding RNAs	532		
<b>14 Protein modification and targeting</b>	<b>539</b>	<b>17 Mobile DNA</b>	<b>668</b>
Introduction	539	Introduction	668
14.1 Chaperone-assisted protein folding	539	17.1 Transposable elements: overview	668
14.2 Targeting of proteins throughout the cell	544	17.2 An overview of DNA-only transposons	675
14.3 Post-translational cleavage of the polypeptide chain	548	17.3 DNA-only cut-and-paste transposition	676
14.4 Lipid modification of proteins	550	17.4 DNA-only nick-and-paste transposition	681
14.5 Glycosylation of proteins	557	17.5 DNA cut-and-paste transposition in adaptive immunity	684
14.6 Protein phosphorylation, acetylation, and methylation	560	17.6 Retrotransposons	688
14.7 Protein modification by nucleotides	567	17.7 LTR retrotransposons	689
14.8 Direct chemical modification of proteins	570	17.8 Non-LTR retrotransposons	693
14.9 Ubiquitination and sumoylation of proteins	572	17.9 Control of transposition	701
14.10 Protein degradation	579	17.10 CSSR: overview	706
<b>15 Cellular responses to DNA damage</b>	<b>587</b>	17.11 CSSR systems that control gene expression	710
Introduction	587	17.12 CSSR conversion of DNA dimers to monomers	713
15.1 Types of DNA damage	588	17.13 Bacteriophage lambda integration and excision	715
15.2 Post-replication mismatch repair	592		
15.3 Repair of DNA damage by direct reversal	594		
<b>18 Genomics and genetic variation</b>	<b>726</b>		
Introduction	726		
18.1 Genome sequences and sequencing projects	727		
18.2 Finding functions in a genome	730		
18.3 Functional genomics	734		
18.4 The ENCODE project	739		
18.5 The evolving genome: evolutionary forces	742		
18.6 The evolving genome: mechanisms of variation	744		
18.7 Gene duplication and divergence of gene function	749		
18.8 Changes in chromosome structure and copy number variation	752		

18.9	Epigenetics and imprinting	754
18.10	Human genetic diseases: finding disease loci	756
18.11	Human genetics: impacts and implications	764

## 19 Tools and techniques in molecular biology

	Introduction	775
19.1	Model organisms	776
19.2	Cultured cells and viruses	784
19.3	Amplification of DNA and RNA sequences	788
19.4	DNA cloning	793
19.5	Genome manipulation	800
19.6	Detection of biological molecules	810
19.7	Separation and isolation of biological molecules	815
19.8	Identifying the composition of biological molecules	824
19.9	Detection of specific DNA sequences	831
19.10	Detection of specific RNA molecules	836
19.11	Detection of specific proteins	842
19.12	Detection of interactions between molecules	845
19.13	Imaging cells and molecules	853
19.14	Molecular structure determination	863
19.15	Obtaining and analyzing a complete genome sequence	866

	Glossary	878
	Index	901

# ABBREVIATIONS

<b>4F5</b>	4F5 monoclonal antibody	640
<b>FISH</b>	fluorescence in situ hybridization	780
<b>FLP</b>	flippase	803
<b>4E-BP</b>	eIF4E-binding protein	970
<b>53BP1</b>	p53 binding protein 1	1040
<b>A</b>	adenine	83
<b>A</b>	adenosine	903
<b>A</b>	aminoacyl	2613
<b>Å</b>	angstrom	1140
<b>AAA+</b>	ATPases associated with a variety of cellular activities	
<b>AAV</b>	adeno-associated virus	874
<b>aCGH</b>	array comparative genomic hybridization	383
<b>acetyl-CoA</b>	acetyl coenzyme A	383
<b>ADAR</b>	adenosine deaminase that acts on RNA	983
<b>ADP</b>	adenosine diphosphate	1043
<b>AFM</b>	atomic force microscopy	8223
<b>AIDS</b>	acquired immunodeficiency syndrome	813
<b>ALT</b>	alternative lengthening of telomeres	973
<b>AMP</b>	adenosine monophosphate	1043
<b>APA</b>	alternative polyadenylation site	901
<b>APC</b>	anaphase-promoting complex	411
<b>ARE</b>	AU-rich element	1940
<b>Asn-tRNA<sup>Asn</sup></b>	asparagine-bound tRNA species	2840
<b>ATM</b>	ataxia telangiectasia mutated	1450
<b>ATP</b>	adenosine triphosphate	4703
<b>ATR</b>	ATM related	
<b>ATRIP</b>	ATR-interacting protein	
<b>attB</b>	attachment site bacteria	
<b>attL</b>	attachment site left	
<b>attP</b>	attachment site phage	
<b>attR</b>	attachment site right	
<b>BAC</b>	bacterial artificial chromosome	170
<b>bHLH</b>	basic region-helix-loop-helix	3
<b>BIR</b>	break-induced replication	1408
<b>BLAST</b>	Basic Local Alignment Sequence Tool	239
<b>bp</b>	base pairs	313
<b>BRCA1</b>	breast cancer type 1 susceptibility protein	363
<b>BRCA2</b>	breast cancer type 2 susceptibility protein	363
<b>BRE</b>	TFIIB recognition element	413
<b>BSA</b>	bovine serum albumin	291
<b>bZIP</b>	basic region-leucine zipper	12M3
<b>C</b>	cytidine	1040
<b>C</b>	cytosine	1043
<b>C</b>	carbon	1403
<b>Ca</b>	calcium	23
<b>Caf1</b>	chromatin assembly factor 1	323
<b>CAK</b>	Cdk-activating kinase	173
<b>cAMP</b>	cyclic adenosine monophosphate	9333
<b>CAP</b>	catabolite activator protein	1043