

Contents

List of abbreviations			
List of applications	XXV	Chapter 2 Enzymes	2
Part 1 Introduction to the		Enzyme catalysis	2
		The nature of enzyme catalysis	2
chemical reactions of the co	ell	The induced fit mechanism of enzyme catalysis	2
		Enzyme kinetics	2
		 Hyperbolic kinetics of a 'classical' enzyme 	2
hapter 1 Chemistry, energy, and metabolism	3	Allosteric enzymes	2
What determines whether a chemical reaction is possible?	3	General properties of enzymes	2
Reversible and irreversible reactions and ΔG values	4	Nomenclature of enzymes	2
The importance of irreversible reactions in the strategy of metabolism	_	• Isozymes	2
	5	Enzyme cofactors and activators	2
Why is this metabolic strategy used in the cell? How are ΔG values obtained?	5	Effect of pH on enzymes	2
Standard free energy values and equilibrium constants	6 6	Effect of temperature on enzymes	2
	0	Effect of inhibitors on enzymes	2
©Given that a reaction has a negative ∆G value, what determines whether it actually takes place at a		Reversible inhibitors	2
perceptible rate in the cell?	6	Competitive and noncompetitive inhibitors	2
w is food breakdown in cells coupled to drive		Further reading	2
nergy-requiring reactions in the cell?	7	Problems	2
The high-energy phosphate compound	8		
What is a 'high-energy phosphate compound'?	8	Part 2 Structure of proteins	_
What are the structural features of high-energy			5
phosphate compounds?	8	and membranes	
What transports the — ® around the cell?	11		
How does ATP perform chemical work?	11	•	
How does ATP drive other types of work?	12		
A note on the relationship between AMP, ADP, and ATP	12	Chapter 3 The structure of proteins	3:
teak bonds and free-energy changes	13	The primary structure of proteins	3
What causes weak bond formation and breakage?	14	What is a native protein?	3
The vital role of weak bonds in molecular recognition	15	What are the basic considerations which determine the three-dimensional structure of a protein?	_
The state of the s	.,	three-dimensional structure of a protein? • Structures of the 20 amino acids	3
ppendix: Buffers and pK, values	15	Hydrophobic amino acids	3
		Hydrophilic amino acids	3
urther reading	17	Amino acids for special purposes	3
		lonization of amino acids	3
ablems	18	Symbols for amino acids	

The different levels of protein structure — primary,		
cocondons toutland and access	8 Chapter 4 The cell membrane: a structure	
• Secondary structure of proteins	g depending only on weak forces	67
The α helix	An overview of cellular membranes	67
The β-pleated sheet	Why are cell membranes needed?	68
Connecting loops	1 The lipid bilayer	70
• Tertiary structure of proteins 4	• What are the polar lipid constituents of cell membranes?	70
How are proteins made up from the three motifs—the α helix, the β -pleated sheet, and connecting loops?	What are the polar groups attached to the phosphatidic	
14th at Course to 14 st. and	acid: A note on membrane lipid nomenclature	71
Where do the disulfide or S-S covalent bonds come into protein	Why are there so many different types of membrane lipids?	74 74
Quaternary structure of proteins 4	What are the fatty acid components of membrane lipids?	75
Membrane proteins 4	and a second sec	75 75
• Conjugated proteins 4		76
What are protein modules or domains? 4		76 76
Why should domains be of interest?	·	70
• The problem of protein folding 4	Menorane biorents and memoratie design	77
What are the structural features of enzyme proteins that	what holds integral proteins in the lipid bilayer?	77
confer catalytic activity on them?	Anchoring of peripheral membrane proteins to membranes	78
A special note	 Glycoproteins or membrane proteins with sugars attached on the exterior surface 	79
Mechanism of the chymotrypsin reaction 4	7	1,7
The catalytic triad of the active centre		80
The reactions at the catalytic centre of chymotrypsin	Transport of substances in and out of the cell	80
What is the function of the aspartate residue of the	Active transport	80
catalytic triad?	Mechanism of the Na ⁺ /K ⁺ pump	80
Other serine proteases 53		82
A brief description of other types of proteases 53		82
Extracellular matrix proteins 5:	Uniport systems	82
Structure of collagens 52	Passive transport or facilitated diffusion	82
Genetic diseases of collagen	Gated ion channels	83
Structure of elastin 54	Nerve impulse transmission	83
Structure of proteoglycans 54	The acetylcholine-gated Na ⁺ /K ⁺ channel or acetylcholine receptor	84
Adhesion proteins of the extracellular matrix 56	now does acetylcholine binding to a membrane receptor result in a	
Experimental handling and separation of proteins 57		84
o Column day of the column day	Machanism of control of the voltage and divided the	86 88
• CDC notine and and all all all all all all all all all al	Why doesn't the Na ⁺ /K ⁺ nump conflict with the proposition of action	00
Mathada of protein assurantes	potentials?	89
Methods of protein sequencing 60	Signal transduction—a brief preliminary note	89
 Deduction of a protein sequence from the nucleotide structure of its gene 	 Role of the cell membrane in maintaining the shape of the cell and in cell mobility 	90
Protein databases and proteomics 61	and gap junctions	
• A note on where we are at this point in the book 62	and cellular adhesive proteins	90
Further reading 62	Further reading	91
Problems 63	Problems	92

112

112

Overall control of the logistics of food distribution in the

body by hormones

• Post-absorptive phase



Part 3 Metabolism

		Fasting condition	113
		 Prolonged fasting or starvation 	113
hapter 5 Digestion and absorption of food	97	The situation in diabetes	113
hemistry of foodstuffs		 The emergency situation—fight or flight 	113
gestion and absorption	97	Problems	114
, - :	97		
Anatomy of the digestive tract	97	Charter 7 Discharged at 1 and	
What are the energy considerations in digestion and absorption?	98	Chapter 7 Biochemical mechanisms involved in food transport, storage, and mobilization	117
A major problem in digestion—why doesn't the body digest itself?	98	Glucose traffic in the body	117
Zymogen or proenzyme production	99	Mechanism of glycogen synthesis	117
Protection of intestinal epithelial cells by mucus	99	How is energy injected into the process?	118
Digestion of proteins	99	How does the liver release glucose?	120
HCl production in the stomach	99	 Why does liver have glucokinase and the other tissues hexokinase? 	
Pepsin, the proteolytic enzyme of the stomach	99		122
Completion of protein digestion in the small intestine	100	 What happens to other sugars absorbed from the intestine? 	122
Activation of the pancreatic proenzymes	100	Amino acid traffic in the body (in terms of fuel logistics)	124
Absorption of amino acids into the bloodstream	101	Fat and cholesterol traffic in the body	-
Digestion of carbohydrates	101	•	125
Digestion of starch	101	Uptake of fat from chylomicrons into cells	125
Digestion and absorption of fat	103	Logistics of fat and cholesterol movement in the body	125
What happens to the fatty acids and monoacylglycerol absorbed into the intestinal brush border cells?	104	An overviewUtilization of cholesterol in the body	125 126
Resynthesis of neutral fat in the absorptive cell	104	Lipoproteins involved in fat and cholesterol movement in	
What are chylomicrons?	105	the body	127
Digestion of other components of food	106	Apolipoproteins	127
		Mechanism of TAG and cholesterol transport from the	
urther reading	106	liver and the reverse cholesterol transport in the body	127
roblems	106	How do cells get rid of cholesterol?	127
		How does cholesterol exit cells to be picked up by HDL?	129
hapter 6 Preliminary outline of fuel		Cholesterol homeostasis in cells Inhibitors of cholesterol synthesis	130
Istribution and utilization by the different			130
ssues of the body	109	How is fat released from adipose cells?	130
urposes of metabolism	109	How are free fatty acids carried in the blood?	131
prage of food in the body	109	Further reading	132
How are the different foods stored in cells?		Problems	132
	109		
Glucose storage as glycogen Storage of fat in the body	109	Chapter 8 Energy release fromn foodstuffs—a	···········
Storage of fat in the body Are amino acids stored by the body?	110 110	preliminary overview	135
•	110	Energy release from glucose	
haracteristics of different tissues in terms of energy etabolism			135
LE CONTROLLE	111	The main phases of glucose oxidation	135

xvi CONTENTS

Biological oxidation and hydrogen transfer systems	135	Mechanisms of the citric acid cycle reactions	15
NAD+—an important electron carrier	136	The synthesis of citrate	157
FAD—another important electron carrier	137	Conversion of citrate to α-ketoglutarate	15
FAD, FMN, and their reduction	137	• The C ₄ part of the cycle	158
 Stages in the release of energy from glucose—first glycolysis 	137	Generation of GTP coupled to splitting of succinyl-CoA	159
Stage 2 of glucose oxidation—the citric acid cycle	138	Conversion of succinate to oxaloacetate	159
How is pyruvate fed into the citric acid cycle?	- '	 What determines the direction of the citric acid cycle? 	160
What is coenzyme A?	138 139	Stoichiometry of the cycle	160
Oxidative decarboxylation of pyruvate	139	Topping up the citric acid cycle	161
Stage 3 of glucose oxidation—electron transport to oxygen	139	Stage 3—the electron transport chain that conveys electrons from NADH and $FADH_2$ to oxygen	162
The electron transport chain—a hierarchy of electron		The electron transport chain	162
carriers	140	Where does it take place?	162
Energy generation from oxidation of fat and amino acids	140	Nature of the electron carriers in the chain	162
The interconvertibility of fuels	142	Arrangement of the electron carriers	163
A survey of vitamins Further reading	142	How is the free energy released by electron transport	164
Problems	143	used to form ATP?	
10000113	145	 How are protons ejected? How does the proton gradient drive ATP synthesis? —ATP synthase 	166
Chapter 9 Glycolysis, the citric acid cycle, and the electron transport system: reactions involved in these pathways	4.5	Components of the F, unit and their roles in the conversion of ADP $+P$, to ATP	167 169
•	147	Activities of the enzyme catalytic centres on the F ₁ subunit	169
Stage 1—glycolysis	147	How is the energy of proton flow through the F _o utilized for ATP synthesis by the F ₁ ?	170
Glucose or glycogen?	147	What is the role of the F _o unit?	170
Why use ATP here at the beginning of glycolysis?	147	Transport of ADP into mitochondria and ATP out	172
 Why is glucose-6-phosphate converted to fructose-6- phosphate? 	147	The balance sheet of ATP production by electron transport	173
• A note on the ΔG^{or} and ΔG values for the aldolase reaction	149	Yield of ATP from the oxidation of a molecule of glucose	***
 Interconversion of dihydroxyacetone phosphate and glyceraldehyde-3-phosphate 	150	to CO ₂ and H ₂ O	173
Gyceraidehyde-3-phosphate dehydrogenase—a step generating a high-energy-phosphoryl compound		 Is ATP production the only use that is made of the potential energy in the proton-motive force? 	174
The final steps in glycolysis	150 151	Further reading	174
The ATP balance sheet from glycolysis	153	Problems	
Reoxidation of cytoplasmic NADH by electron shuttle systems	153	Todiçina	175
Transport of pyruvate into the mitochondria	154	Chapter 10 Energy release from fat	179
Stage 2—the citric acid cycle	154	Mechanism of acetyl-CoA formation from fatty acids	180
 Conversion of pyruvate to acetyl-CoA-a preliminary step before the cycle 	154	'Activation' of fatty acids by formation of fatty acyl-CoA derivatives	180
Components involved in the pyruvate dehydrogenase		Transport of fatty acyl-CoA derivatives into mitochondria	180
reaction	155	Conversion of fatty acyl-CoA to acetyl-CoA molecules	100
• The citric acid cycle as a water-splitting machine	156	inside the mitochondrion	181
A simplified version of the citric acid cycle	156	Energy yield from fatty acid oxidation	181

		CONTENTS	XVII
xidation of unsaturated fat	181	Synthesis of glucose from glycerol	204
the acetyl-CoA derived from fat breakdown always rectly fed into the citric acid cycle?	182	Synthesis of glucose via the glyoxylate cycle	204
How is acetoacetate made from acetyl-CoA?	182	Further reading Problems	205 206
xidation of odd-numbered carbon chain fatty acids	183	Figureins	200
	183		
Peroxisomal oxidation of fatty acids	165	Chapter 13 Strategies for metabolic control	
urther reading	184	and their application to carbohydrate and	
roblems	184	fat metabolism	20
		Why are controls necessary?	20
		 The potential danger of futile cycles in metabolism 	21
hapter 11 A switch from catabolic to		How are enzyme activities controlled?	21
nabolic metabolism—first, the synthesis of fat		Metabolic control by varying the amounts of enzymes	21
nd related compounds in the body	187	 Metabolic control by regulation of the activities of 	
lechanism of fat synthesis	187	enzymes in the cell	21
General principles of the process	187	Which enzymes in metabolic pathways are regulated?	21
The acyl carrier protein (ACP) and the eta -ketoacyl synthase	188	The nature of regulatory enzymes	21
Mechanism of fatty acyl-CoA synthesis	188	Allosteric control of enzymes	21
Organization of the fatty acid synthesis process	188	The mechanism of allosteric control of enzymes	21
The reductive steps in fatty acid synthesis	189	What causes the sigmoidal response of reaction velocity to	
What is NADP+?	189	substrate concentration?	21
Where does fatty acid synthesis take place?	190	Reversibility of allosteric control	21
huthade of impativated faths acids	191	 Allosteric control is a tremendously powerful metabolic concept 	21
Synthesis of unsaturated fatty acids Synthesis of triacylglycerol and membrane lipids from	171	Control of enzyme activity by phosphorylation	2:
atty acids	192		_
Synthesis of glycerophospholipids	193	 The two classes of controls—intracellular mechanisms and those dependent on extracellular signals 	21
Site of membrane lipid synthesis	194	Hormonal control of metabolism	2:
lynthesis of prostaglandins and related compounds	195	How do glucagon, epinephrine, and insulin, work?	21
The prostaglandins and thromboxanes	195	 What is a second messenger? 	2:
Leukotrienes	196	What is the second messenger for glucagon and	_
Synthesis of cholesterol	196	epinephrine?	2:
	4.5-	Control of carbohydrate metabolism	2
Further reading	197	Control of glucose uptake into cells	2:
roblems	197	 Control of glycogen metabolism Activation of muscle phosphorylase by cAMP 	2:
		Reversal of phosphorylase activation	2:
hapter 12 Synthesis of glucose		Control of glycogen breakdown in the liver	2:
fluconeogenesis)	201	Control of glycogen synthase	2:
	201	How does insulin inactivate GSK3?	2:
Mechanism of glucose synthesis from pyruvate What are the sources of pyruvate used by the liver for	4 01	Control of glycolysis and gluconeogenesis	2:
gluconeogenesis?	202	Allosteric controls	2:
Effects of ethanol metabolism on gluconeogenesis	203	Hormonal control of glycolysis and gluconeogenesis	2
Effects of ethanol metabolism on the NAD/NADH ratio in the liver cell	203	How does cAMP control PFK?	2:

XVIII CONTENTS

Control of gluconeogenesis	226	Further reading	
Control of pyruvate dehydrogenase, the citric acid cycle,		Problems	24
and oxidative phosphorylation	227		-
 Regulation of the cellular ATP level by AMP-activated protein kinase 	228	Chapter 16 Amino acid metabolica	
Controls of fatty acid oxidation and synthesis	228	Chapter 16 Amino acid metabolism	25
Nonhormonal controls		Nitrogen balance of the body	25
Hormonal controls on fat metabolism	228 229	General metabolism of amino acids	25
Insulin and diabetes	229	Aspects of amino acid metabolism	25
A concluding note: metabolic control analysis	230	Deamination of amino acids	25
Further reading		Mechanism of transamination reactions	256
Problems	231	Special deamination mechanisms	250
Trosteria	231	 Fate of the keto acid or carbon skeletons of deaminated amino acids) 257
Chapter 14 Why should there be an alternative		Phenylalanine metabolism has special interest	25
pathway of glucose oxidation—the pentose		 Methionine and transfer of methyl groups 	258
phosphate pathway?	235	Where are the methyl groups transferred to?	259
The oxidative steps	235	Synthesis of amino acids	259
The nonoxidative section and its purpose	235	Synthesis of glutamic acid	259
 Reactions involved in the conversion of ribose-5- 	-33	Synthesis of aspartic acid and alanine	259
phosphate to glucose-6-phosphate	237	Synthesis of serine	259
 Where does the complete oxidation of glucose come into all of this? 		Synthesis of glycine	259
Why do red blood cells have the pentose phosphate	238	Synthesis of other molecules from amino acids	260
pathway?	238	What happens to the amino groups when they are removed from amino acids? —the urea cycle	261
Further reading	239	Mechanism of arginine synthesis	262
Problems	239	Conversion of citrulline to arginine	262
		How is the amino nitrogen transported from extrahepatic	-01
Chapter 15 Raising electrons of water back up		tissues to the liver to be converted into urea?	263
the energy scale—photosynthesis	241	Transport of ammonia in the blood as glutamine	263
Overview	241	Transport of amino nitrogen in the blood as alanine	263
Site of photosynthesis—the chloroplast	241	Further reading	264
The photosynthetic apparatus and its organization in the	241	Problems	264
thylakoid membrane	242		
What is chlorophyll? Machanism of Parks Pa	243	Chapter 17 Cellular disposal of unwanted	
Mechanism of light-dependent reduction of NADP+	244	molecules	267
The water-splitting centre of PSII	244	Lysosomes	267
How is ATP generated?	245	Mechanism of receptor-mediated endocytosis	268
An explanatory note	246	Lysosomal storage diseases	269
 How is CO₂ converted to carbohydrate? 	246	Peroxisomes	
Where does the 3-phosphoglycerate come from?	246	Proteasomes	270
Where does the ribulose-i:5-bisphosphate come from?	247	What are the problems to be solved by the cell to	270
Has evolution slipped up a bit?	247	selectively destroy proteins?	271
• The C ₄ pathway	248	The structure of proteasomes	271

314

314

		CONTENTS	XIX
Relection of proteins for destruction by proteasomes—the		The one-carbon transfer reaction in purine nucleotide	
ubiquitination system	272	synthesis	290
What determines which proteins are ubiquitinated?	273	Where does the formyl group in formyl FH_4 come from? How are ATP and GTP produced from AMP and GMP?	293 294
The role of proteasomes in the immune system	273		
ither reading	273	The purine salvage pathway	294
blems	274	What is the physiological role of the purine salvage pathway?	294
		Formation of uric acid from purines	295
		Control of purine nucleotide synthesis Control of purine title and to the synthesis	295
hapter 18 Enzymic protective mechanisms in		Synthesis of pyrimidine nucleotides How are decrywisher unless tides formed?	296
e body	277	How are deoxyribonucleotides formed?	296
bod clotting	277	Conversion of dUMP to dTMP	297
What are the signals that clot formation is needed?	277	 Tetrahydrofolate, vitamin B₁₂, and pernicious anemia 	298
How does thrombin cause thrombus (clot) formation?	278	Further reading	299
Keeping clotting in check	279	Problems	299
Rat poison, blood clotting, and vitamin K	279		
otection against ingested foreign chemicals	280		
Cytochrome P450	280	Part 4 Information storage	
Secondary modification—addition of a polar group to products of the P450 attack	281	and utilization	
The response of the liver to the ingestion of foreign			
chemicals	281	Chantay 20 DNA its structure and	
Multidrug resistance	281	Chapter 20 DNA—its structure and arrangement in cells	303
otection of the body against its own proteases	282	·	303
otection against reactive oxygen species	282	What are nucleic acids?	303
Mopping up oxygen free radicals with vitamins C and E	283	The primary structure of DNA	303
Enzymic destruction of superoxide by superoxide dismutase	283	What are the bases in DNA?	304
The glutathione peroxidase-glutathione reductase	26)	Attachment of the bases to deoxyribose	304
strategy	283	 What are the physical properties of the polynucleotide components? 	304
irther reading	284	Structure of the polynucleotide of DNA	304
roblems	28 5	Why deoxyribose? Why not ribose?	305
		The DNA double helix	306
		DNA chains are antiparallel; what does this mean?	308
hapter 19 Nucleotide metabolism	287	How large are DNA molecules?	310
tructure and nomenclature of nucleotides	287	How is the DNA packed into a nucleus?	310
The sugar component of nucleotides	287	How does the described structure of DNA correlate with the compact subspect of shromesomes wights in the light	
The base component of nucleotides	288	the compact eukaryotic chromosomes visible in the light microscope?	312
Nomenciature	288	What is a gene in molecular terms?	312
Structure of the bases	288	Some variations on the 'standard' gene	313
Attachment of the bases in nucleotides	288	Repetitive DNA	313
ynthesis of purine and pyrimidine nucleotides	289	Where are we now?	314

289

289

Further reading

Problems

Purine nucleotides

PRPP—the ribotidation agent

		The structure of RNA	
Chapter 21 DNA synthesis and repair	317	How is mRNA synthesized?	• •
Overall principle of DNA replication	317	Some general properties of mRNA	,
Control of initiation of DNA replication in E. coli	318	Some essential terminology	
Initiation and regulation of DNA replication in eukaryotes	318	A note on where we go from here	
Unwinding the DNA double helix and supercoiling	319	Gene transcription in <i>E. coli</i>	
 How are positive supercoils removed ahead of the replicative fork? 	320	 What is specified by the term 'gene' in prokaryotes? What do we mean by the 5' end of a gene? 	
What are the biological implications of topoisomerases? What is SSB? The alternation on the second secon	321 322	Phases of gene transcription Initiation of transcription in E. coli	
The situation so far The basic enzymic reaction catalysed by DNA polymerases	323 323	Untwisting the DNA Termination of transcription The rate of gene transcription initiation in prokaryotes	
Problems in DNA synthesis	324	Control of transcription by different sigma factors	
How does a new strand get started? The polarity problem in DNA replication	324 324	 How are individual E. coli genes regulated in a variable fashion? The lac operon 	
Mechanism of Okazaki fragment synthesis	325	Structure of the E. coli lac operon Control of transcription by extension	
• Enzyme complex at the replicative fork in E. coli The DNA sliding clamp and the clamp loading mechanism	325 326	 Control of transcription by attenuation The structure of DNA binding proteins 	
What happens to the Okazaki fragments?	327	Helix-turn-helix proteins	
Proofreading by polymerase III	328	Leucine zipper proteins	
Methyl-directed mismatch repair	329	Zinc finger proteins	
Repair of DNA damage in <i>E. coli</i>	330	Further reading	
The machinery in the eukaryotic replicative fork	333	Problems	
 The problem of replicating the ends of eukaryotic chromosomes 	333	Chanter 22 Eukanotic construction	
How is telomeric DNA synthesized?	334	Chapter 23 Eukaryotic gene transcription and control	
DNA damage repair in eukaryotes	335		
s the mechanism described above the only way in		The basic processes involved in eukaryotic mRNA production	
which DNA is synthesized?	335	Capping the RNA transcribed by RNA polymerase II	
Fransposons or jumping genes	335	What are split genes?	
lomologous recombination	336	Mechanism of splicing	
 Mechanism of homologous recombination in E. coli 	336		
Formation of cross-over junctions by single-strand invasion Separation of the duplexes	338 338	 What is the biological status of introns? What is the origin of split genes? 	
Recombination in eukaryotes	339	Alternative splicing or two (or more) proteins for the price of one	
urther reading	340	gene	
Problems	341	Mechanism of initiation of eukaryotic gene transcription and its control	
		 Unpacking of the DNA for transcription 	
Chapter 22 Gene transcription—the first step n the mechanism by which genes direct		 A general overview of the differences in the initiation and control of gene transcription in prokaryotes and eukaryotes 	
protein synthesis	343	Types of eukaryotic genes and their controlling regions	
Messenger RNA	343	Type II eukaryotic gene promoters	

Enhancers and their mechanism of gene control: alternative models	362	What is a polysome?	392
Transcription factors	364	How does protein synthesis differ in eukaryotes?	39
How do activators promote transcriptional initiation?	364	Protein synthesis in mitochondria	39
The role of chromatin in eukaryotic gene control	364	Effects of antibiotics and toxins on protein synthesis	39
How do transcription factors open up gene promoters?	366	How does the polypeptide chain synthesized on the	
How is transcription initiated on the opened promoter?	367	ribosome fold up?	39
What is the mechanism by which transcription rates are controlled		Chaperones (heat shock proteins)	39
by the multiple transcription factors?	368	Mechanism of action of molecular chaperones	39
How are activated genes switched off?	368	Enzymes involved in protein folding	39
Synthesis of the messenger RNA	369		
• Termination of transcription in eukaryotes	369	Prion diseases and protein folding	39
nRNA stability and the control of gene expression	369	A note on where we are in the book	39
Determinants of mRNA stability and their role in gene		Further reading	39
expression control	370	Problems	39
Role of the polyA tail	370		
Structural stability determinants of mRNAs	370		
Sene transcription in mitochondria	371	Chapter 25 How are newly synthesized proteins	
Senes that do not code for proteins	372	delivered to their correct destinations?—protein targeting	40
Ribozymes and self-splicing of RNA	372		40
 Self-cleaving in small circular RNA pathogens 	373	A preliminary overview of the field	40
The hammerhead ribozyme mechanism of self-cleavage	374	 Structure and function of the ER and Golgi apparatus 	40
• The concept of gene shears	374	The important role of the GTP/GDP switch mechanism in	
Ribozymes and hypotheses about the origin of life	375	protein targeting	40
Further reading	376	How are proteins secreted through the ER membrane?	40
Problems	378	 Mechanism of cotranslational transport through the ER 	
		membrane	40
		Folding of the polypeptides inside the ER	40
Chapter 24 Protein synthesis	381	 Glycosylation of proteins in the ER lumen and Golgi apparatus 	40
Essential basis of the process of protein synthesis	381	• •	40
The genetic code	381	How are proteins sorted, packaged, and despatched by the Golgi apparatus?	40
How are the codons translated?	382	Proteins to be returned to the ER	
Transfer RNA	382	Proteins to be returned to the EK Proteins destined for lysosomes	40 40
The wobble mechanism	383	Proteins to be secreted from the cell	40
How are amino acids attached to tRNA molecules?	384	How are transport vesicles budded off from the Golgi	
Ribosomes	385	membranes?	40
initiation of translation	386	 How does the vesicle find the correct target membrane? 	41
• Initiation of translation in E. coli	386	 How are membrane integral proteins inserted? 	41
Once initiation is achieved, elongation is the next step	388	How is the membrane protein given the correct orientation?	41
Cytoplasmic elongation factors	388	Posttranslational transport of proteins into organelles	41
Mechanism of elongation	389	Transport of proteins into mitochondria	41
How is fidelity of translation achieved?	390	Targeting peroxisomal proteins	41
Termination of protein synthesis	391	Nuclear-cytoplasmic traffic	41
Shurical structure of the ribecome	204	18/hr. abassid Abasa ba a sasada as sasada as sasada a	

xxii CONTENTS

The nuclear pore complex	414	Vision: a process dependent on a G-protein-coupled	
Nuclear localization signals	415	receptor	441
 Mechanism of nuclear-cytoplasmic transport and the role of guanine nucleotide binding proteins 	416	Transduction of the light signal	442
Regulation of nuclear transport by cell signals and its role in gene control	417	Signal transduction pathways using cGMP as second messenger	443
•		Activation of a guanylate cyclase by nitric oxide	444
Further reading	418	Further reading	445
Problems	420	Problems	443
Chapter 26 Cell signalling	423		· · · · · ·
What are the signalling molecules?	424	Chapter 27 The immune system	451
Neurotransmitters	424	The cells involved in the immune system	451
Endocrine hormones	425	There are two immune protective systems	452
Cytokines and growth factors	426	Where is the immune system located in the body?	452
Growth factors and the cell cycle	426	Antibody-based or humoral immunity	452
Vitamin D ₃ and retinoic acid	426	Structure of antibodies	452
Vitaliiii D ₃ and retirioic acid	420	What are the functions of antibodies?	452
Intracellular receptor-mediated responses	427	What are the different classes of antibodies?	453
Membrane receptor-mediated signalling systems	428	Generation of antibody diversity	453
An overview	428	Activation of B cells to produce antibodies	455
Tyrosine kinase-associated receptors	430	Deletion of potentially self-reacting B cells in the bone	
The Ras pathway	430	marrow	455
Mechanism of the Ras signalling pathway	430	The theory of clonal selection	455
The Ras GTP/GDP switch mechanism	431	What is the mechanism by which B cells are activated to	
The protein kinase cascade of the Ras pathway	431	secrete antibody?	455
Nomenclature of the protein kinases of the Ras pathway	432	Role of helper T cells	456
Inactivation and modulation of the Ras pathway	432	Activation of helper T cells	456
Multiplicity of MAP kinase pathways	433	Activation of B cells by activated helper T cells	456
The phosphatidylinositide 3 (PI3)-kinase pathway and		Affinity maturation of antibodies	457
însulin signalling	433	Memory cells	457
The JAK/STAT pathways; direct intracellular signalling		T cells and cell-mediated immunity	458
pathways from receptor to nucleus	434	 Activation of cytotoxic T cells 	458
The G-protein-coupled receptors	436	 Mechanism of action of cytotoxic cells 	459
Overview	436	Why does the human immune system so fiercely reject	
Structure of G protein receptors	436	foreign human cells?	460
• Epinephrine signalling—a G protein pathway mediated by		Monoclonal antibodies	461
cAMP as second messenger	436	Further reading	461
Control of cAMP levels in cells	437	Problems	462
Different types of epinephrine receptors	438		<u> </u>
How does cAMP control gene activities?	438	Chapter 28 Viruses and viroids	465
Desensitization of the G protein receptors	439	•	
G-protein-coupled receptors which work via a different second messenger; the phosphatidylinositol cascade	439	The life cycle of a virus Types of genetic material in different viruses	465 466
Other control roles of calcium	440	How are viruses released from cells?	467
			,

xxiii

XXIV CONTENTS

Effect of pH on oxygen binding to hemoglobin	517	Control of smooth muscle contractions	F 24
• Role of pH changes in oxygen and CO ₂ transport	517	How does Ca** control smooth muscle contraction?	532
pH buffering in the blood	518		532
Sickle cell anemia	518	Further reading Problems	533 533
Further reading	518		
Problems	519	Chapter 33 The cytoskeleton, molecular motors, and intracellular transport	535
		An overview	53!
Part 6 Mechanical work		The role of actin and myosin in nonmuscle cells	530
by cells		Structural role of actin and its involvement in cell movement	536
Chapter 32 Muscle contraction		 The role of actin and myosin in intracellular transport of vesicles 	537
•	523	Microtubules, cell movement, and intracellular transport	538
A reminder of conformational changes in proteins	523	What are microtubules?	
Types of muscle cells and their energy supply	523		538
Structure of skeletal striated muscle	524	What protects the positive (+) ends of microtubules?	538
Structure of the myofibril	524	 Functions of microtubules 	539
How does the sarcomere shorten?	524	Molecular motors: kinesins and dyneins	539
Structure and action of thick and thin filaments	525	Role of microtubules in cell movement	539
 How does the myosin head convert the energy of ATP hydrolysis into mechanical force on the actin filament? 	526	Role of microtubules in vesicle transport inside the cell Role of microtubules in mitosis	540 540
Mechanism of the conformational changes in the myosin head	526	Intermediate filaments	540
How is contraction in voluntary striated muscle controlled?	530	Further reading Problems	541 542
How does Ca ²⁺ trigger contraction?	530		
Release and uptake of Ca ²⁺ in the muscle	530	Answers to problems	555
How does smooth muscle differ in structure and control		Figure acknowledgements	571
from striated muscle?	531	index	573