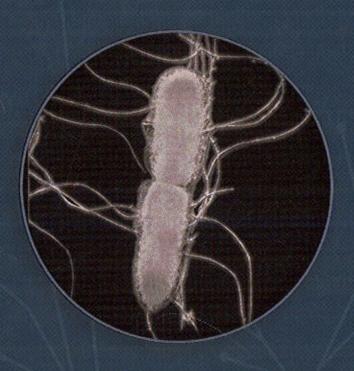
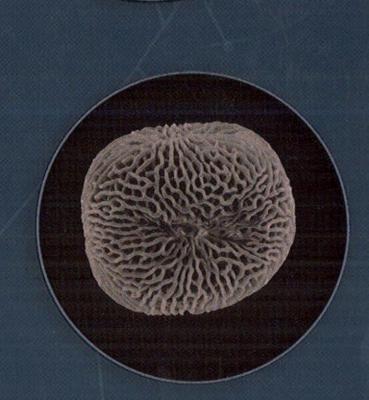
CEL



EDITORS

Benjamin Lewin
Lynne Cassimeris
Vishwanath R. Lingappa
George Plopper



Contents

1.17 Protein folding and unfolding is an essential feature of
all cells 23
1.18 The shape of a eukaryotic cell is determined by its cytoskeleton 24
1.19 Localization of cell structures is important 25
1.20 Signal transduction pathways execute predefined responses 26
 1.21 All organisms have cells that can grow and divide 27 1.22 Differentiation creates specialized cell types, including terminally differentiated cells 28
References 29
Part 2 Membranes and
transport mechanisms 30
2 Transport of ions and small
molecules across membranes, 3 Stephan E. Lehnart and Andrew R. Marks
2.1 Introduction 32
2.2 Channels and carriers are the main types of membrane transport proteins 33
2.3 Hydration of ions influences their flux through transmembrane pores 35
2.4 Electrochemical gradients across the cell membrane generate the membrane potential 36
2.5 K+ channels catalyze selective and rapid ion permeation 38
2.6 Different K+ channels use a similar gate coupled to
different activating or inactivating mechanisms 42 2.7 Voltage-dependent Na+ channels are activated by
membrane depolarization and translate electrical
signals 44
2.8 Epithelial Na+ channels regulate Na+ homeostasis 47
Plasma membrane Ca ²⁺ channels activate intracellular functions 50
2.10 Cl ⁻ channels serve diverse biological functions 52

2.11	Selective water transport occurs through aquaporin channels 56	3.8 Some proteins target and translocate posttranslationally 110
2.12	Action potentials are electrical signals that depend on	3.9 ATP hydrolysis drives translocation 111
2.13	several types of ion channels 58 Cardiac and skeletal muscles are activated by excitation-	3.10 Transmembrane proteins move out of the translocation channel and into the lipid bilayer 113
	contraction coupling 60	3.11 The orientation of transmembrane proteins is determined
2.14	Some glucose transporters are uniporters 63	as they are integrated into the membrane 115
2.15	Symporters and antiporters mediate coupled transport 65	3.12 Signal sequences are removed by signal peptidase 1183.13 The lipid GPI is added to some translocated
2.16	The transmembrane Na+ gradient is essential for the function of many transporters 67	proteins 118
2.17	Some Na+ transporters regulate cytosolic or extracellular pH 70	3.14 Sugars are added to many translocating proteins 1203.15 Chaperones assist folding of newly translocated proteins 121
2.18	The Ca ² +-ATPase pumps Ca ² + into intracellular storage compartments 73	3.16 Protein disulfide isomerase ensures the formation of the correct disulfide bonds as proteins fold 122
2.19	The Na+/K+-ATPase maintains the plasma membrane Na+ and K+ gradients 75	3.17 The calnexin/calreticulin chaperoning system recognizes carbohydrate modifications 123
2.20	The F ₁ F ₀ -ATP synthase couples H+ movement to ATP synthesis or hydrolysis 78	3.18 The assembly of proteins into complexes is monitored 124
2.21	H+-ATPases transport protons out of the cytosol 79 What's next? 82	3.19 Terminally misfolded proteins in the ER are returned to the cytosol for degradation 125
2.23 2.24	Summary 82 Supplement: Derivation and application of the Nernst	3.20 Communication between the ER and nucleus prevents th accumulation of unfolded proteins in the lumen 128
2.25	equation 83 Supplement: Most K+ channels undergo rectification 85	3.21 The ER synthesizes the major cellular phospholipids 130
2.26	Supplement: Mutations in an anion channel cause cystic fibrosis 86	3.22 Lipids must be moved from the ER to the membranes of other organelles 132
	References 88	3.23 The two leaflets of a membrane often differ in lipid composition 133
***	Membrane targeting of	3.24 The ER is morphologically and functionally subdivided 133
	proteins97	3.25 The ER is a dynamic organelle 135
3.1	D. Thomas Rutkowski and Vishwanath R. Lingappa Introduction 98	3.26 Signal sequences are also used to target proteins to other organelles 138
3.2	Proteins enter the secretory pathway by translocation across the ER membrane (an overview) 100	3.27 Import into mitochondria begins with signal sequence recognition at the outer membrane 138
3.3	Proteins use signal sequences to target to the ER for translocation 102	3.28 Complexes in the inner and outer membranes cooperate in mitochondrial protein import 139
3.4	Signal sequences are recognized by the signal recognition particle (SRP) 103	3.29 Proteins imported into chloroplasts must also cross two membranes 141
3.5	An interaction between SRP and its receptor allows proteins to dock at the ER membrane 104	3.30 Proteins fold before they are imported into peroxisomes 142
3.6	The translocon is an aqueous channel that conducts	3.31 What's next? 144
	proteins 105	3.32 Summary 144
3.7	Translation is coupled to translocation for most eukaryotic secretory and transmembrane proteins 108	References 146

2	Protein trafficking between	Part	3 The nucleus	204
	membranes 153			
	Graham Warren and Ira Mellman	5	Nuclear structure and transp	ort 20!
4.1	Introduction 154	C	Charles N. Cole and Pamela A. Silver	
4.2	Overview of the exocytic	5.1 I	ntroduction 206	
	pathway 156	5.2	Nuclei vary in appearance according to cell t	type and
4.3	Overview of the endocytic pathway 159	C	organism 207	
4.4	Concepts in vesicle-mediated protein	5.3	Chromosomes occupy distinct territories 2	209
4.5	transport 162 The concepts of signal-mediated and bulk flow protein		he nucleus contains subcompartments that nembrane-bounded 210	are not
	transport 164	5.5	Some processes occur at distinct nuclear site	es and may
4.6	COPII-coated vesicles mediate transport from the ER to	r	eflect an underlying structure 212	
	the Golgi apparatus 166		he nucleus is bounded by the nuclear envel	•
4.7	Resident proteins that escape from the ER are retrieved 168		he nuclear lamina underlies the nuclear env	
4.8	COPI-coated vesicles mediate retrograde transport from the Golgi apparatus to the ER 169		arge molecules are actively transported bet nucleus and cytoplasm 216	ween the
4.9	There are two popular models for forward transport		Nuclear pore complexes are symmetrical cha	nnels 217
	through the Golgi apparatus 171		Nuclear pore complexes are constructed from nucleoporins 220	n
4.10	Retention of proteins in the Golgi apparatus depends on the membrane-spanning domain 172		Proteins are selectively transported into the Chrough nuclear pores 222	nucleus
4.11	Rab GTPases and tethers are two types of proteins that regulate vesicle targeting 174	5.12	Nuclear localization sequences target proteinucleus 224	ns to the
4.12	SNARE proteins likely mediate fusion of vesicles with target membranes 176	5.13	Cytoplasmic NLS receptors mediate nuclear p mport 224	orotein
4.13	Endocytosis is often mediated by clathrin-coated vesicles 179	5.14	Export 224 Export of proteins from the nucleus is also renember 226	eceptor-
4.14	Adaptor complexes link clathrin and transmembrane cargo proteins 182		neulated 226 The Ran GTPase controls the direction of nuc	clear
4.15	Some receptors recycle from early endosomes whereas		ransport 228	
	others are degraded in lysosomes 185		Multiple models have been proposed for the of nuclear transport 230	mechanism
4.16	Early endosomes become late endosomes and lysosomes by maturation 187	5.17	Nuclear transport can be regulated 232	
4.17	Sorting of lysosomal proteins occurs in the <i>trans</i> -Golgi network 189		Multiple classes of RNA are exported from th nucleus 233	ne
4.18	Polarized epithelial cells transport proteins to apical and basolateral membranes 192		Ribosomal subunits are assembled in the nu exported by exportin 1 235	cleolus and
4.19	Some cells store proteins for later	5.20 t	RNAs are exported by a dedicated exportin	236
	secretion 194		Messenger RNAs are exported from the nucle protein complexes 237	eus as RNA
4.20	What's next? 195		nnRNPs move from sites of processing to NP	Cs 239
4.21	Summary 196		mRNA export requires several novel factors	
	References 196	5.24	J snRNAs are exported, modified, assembled complexes, and imported 241	
			Precursors to microRNAs are exported from t	the nucleus
			and processed in the cytoplasm 242	ane mucicus

5.26	What's next? 242	6.28 Chromatin remodeling is an active process 292
5.27	Summary 245	6.29 Histone acetylation is associated with genetic
-	References 246	activity 296
_		6.30 Heterochromatin propagates from a nucleation event 299
6	Chromatin and chromosomes 253 Benjamin Lewin	6.31 Heterochromatin depends on interactions with histones 300
6.1	Introduction 254	6.32 X chromosomes undergo global changes 302
6.2	Chromatin is divided into euchromatin and heterochromatin 255	6.33 Chromosome condensation is caused by condensins 304
6.3	Chromosomes have banding patterns 256	6.34 What's next? 306
6.4	Eukaryotic DNA has loops and domains attached to a	6.35 Summary 307
	scaffold 258	References 309
6.5	Specific sequences attach DNA to an interphase	•
6.6	matrix 259 The centromere is essential for	Part 4 The cytoskeleton 316
6.6	segregation 260	
6.7	Centromeres have short DNA sequences in	7 Microtubules 317
	S. cerevisiae 262	Lynne Cassimeris
6.8	The centromere binds a protein complex 263	7.1 Introduction 318
6.9	Centromeres may contain repetitious DNA 263	7.2 General functions of microtubules 320
6.10	Telomeres are replicated by a special	7.3 Microtubules are polar polymers of α - and
	mechanism 264	β-tubulin 323
6.11	Telomeres seal the chromosome ends 265	7.4 Purified tubulin subunits assemble into
6.12	Lampbrush chromosomes are extended 266	microtubules 325
6.13 6.14	Polytone chromosomes form bands 267	7.5 Microtubule assembly and disassembly proceed by a
0.14	Polytene chromosomes expand at sites of gene expression 268	unique process termed dynamic instability 327 7.6 A cap of GTP-tubulin subunits regulates the transitions of
6.15	The nucleosome is the subunit of all	7.6 A cap of GTP-tubulin subunits regulates the transitions of dynamic instability 329
	chromatin 269	7.7 Cells use microtubule-organizing centers to nucleate
6.16	DNA is coiled in arrays of nucleosomes 271	microtubule assembly 331
6.17	Nucleosomes have a common structure 272	7.8 Microtubule dynamics in cells 333
6.18	DNA structure varies on the nucleosomal surface 274	7.9 Why do cells have dynamic microtubules? 336
6.19	Organization of the histone octamer 276	7.10 Cells use several classes of proteins to regulate the
6.20	The path of nucleosomes in the chromatin fiber 278	stability of their microtubules 339
6.21	Reproduction of chromatin requires assembly of nucleosomes 279	7.11 Introduction to microtubule-based motor proteins 342
6.22	***************************************	7.12 How motor proteins work 346
6.23	Do nucleosomes lie at specific positions? 282	7.13 How cargoes are loaded onto the right motor 349
6.24	Domains define regions that contain active genes 285 Are transcribed genes organized in nucleosomes? 287	7.14 Microtubule dynamics and motors combine to generate the asymmetric organization of cells 350
6.25	Histone octamers are displaced by transcription 288	7.15 Interactions between microtubules and
6.26	Nucleosome displacement and reassembly require special	actin filaments 354
	factors 290	7.16 Cilia and flagella are motile structures 356
6.27	DNAase hypersensitive sites change chromatin	7.17 What's next? 361
	structure 290	7.18 Summary 362

7.19 7.20	Supplement: What if tubulin didn't hydrolyze GTP? 363 Supplement: Fluorescence recovery after	8.23 Summary 404 8.24 Supplement: Two models for how pol	umer assembly can
	photobleaching 364	generate force 404	ymer assembly can
7.21	Supplement: Tubulin synthesis and modification 365	References 405	
7.22	Supplement: Motility assays for microtubule-based motor		
	proteins 366 References 368	9 Intermediate filaments E. Birgitte Lane	411
8	Actin	9.1 Introduction 412	
•	Enrique M. De La Cruz and E. Michael Ostap	9.2 The six intermediate filament protein structure but different expression	ı groups have similar 413
8.1 8.2	Introduction 372 Actin is a ubiquitously expressed cytoskeletal	9.3 The two largest intermediate filamen and type II keratins 415	t groups are type I
	protein 373	9.4 Mutations in keratins cause epithelia	l cell fragility 418
8.3	Actin monomers bind ATP and ADP 373	9.5 Intermediate filaments of nerve, mus	scle, and connective
8.4	Actin filaments are structurally polarized polymers 374	tissue often show overlapping expres	
8.5	Actin polymerization is a multistep and dynamic process 375	9.6 Lamin intermediate filaments reinfor envelope 422	
8.6	Actin subunits hydrolyze ATP after polymerization 378	9.7 Even the divergent lens filament pro- in evolution 424	teins are conserved
8.7	Actin-binding proteins regulate actin polymerization and organization 380	9.8 Intermediate filament subunits asser	
8.8	Actin monomer-binding proteins influence polymerization 381	affinity into strain-resistant structur 9.9 Posttranslational modifications regul	late the
8.9	Nucleating proteins control cellular actin polymerization 382	configuration of intermediate filame 9.10 Proteins that associate with interme	diate filaments are
8.10	Capping proteins regulate the length of actin filaments 383	9.11 Intermediate filament genes are pres	29 ent throughout
8.11	Severing and depolymerizing proteins regulate actin filament dynamics 384	metazoan evolution 430 9.12 What's next? 432	
8.12	Crosslinking proteins organize actin filaments into bundles and orthogonal networks 385	9.13 Summary 433 References 434	
8.13	Actin and actin-binding proteins work together to drive cell migration 386		
8.14	Small G proteins regulate actin polymerization 388	Part 5 Cell division,	
8.15	Myosins are actin-based molecular motors with essential roles in many cellular processes 389	apoptosis, and can	cer 438
8.16	Myosins have three structural domains 392	10 Mitosis	//30
8.17	ATP hydrolysis by myosin is a multistep reaction 394	Conly Rieder	
8.18	Myosin motors have kinetic properties suited for their	10.1 Introduction 440	
0 10	cellular roles 396	10.2 Mitosis is divided into stages 443 10.3 Mitosis requires the formation of a n	a a
8.19	Myosins take nanometer steps and generate piconewton forces 396	the spindle 445	
8.20	Myosins are regulated by multiple mechanisms 398 Myosin-II functions in muscle contraction 399	10.4 Spindle formation and function depe behavior of microtubules and their a proteins 447	
8.22	What's next? 403	proteins 447 10.5 Centrosomes are microtubule organiz	ring centers 450

are regulated in several I reenter the cell cycle 501 d S phase is tightly
es the ordered assembly of protein
by several protein kinases 507
anges occur
ondensation and segregation and cohesin 512
res more than cyclin
ordinate different cell
NA damage checkpoints monitor blism 518
checkpoint monitors defects in ule attachment 522
can lead to cancer 524
53
poptosis by cleaving specific
are activated by cleavage, whereas activated by dimerization 537
otosis proteins (IAPs) block
unctions in inflammation 539
thway of apoptosis transmits
y TNFR1 is complex 541
hway of apoptosis 543
mediate and regulate MOMP and
2 proteins Bax and Bak are require

12.12	Cytochrome c, released upon MOMP, induces caspase activation 547	13.13 Access to vital supplies is provided by angiogenesis 582
12.13	Some proteins released upon MOMP block IAPs 548	13.14 Cancer cells may invade new locations in the body 583
12.14	The death receptor pathway of apoptosis can engage	13.15 What's next? 584
	MOMP through the cleavage of the BH3-only	13.16 Summary 585
4045	protein Bid 548	References 585
12.15	MOMP can cause "caspase-independent" cell death 550	
12.16	The mitochondrial permeability transition can cause MOMP 550	Part 6 Cell
12.17	Many discoveries about apoptosis were made in nematodes 551	communication 587
12.18	Apoptosis in insects has features distinct from mammals and nematodes 552	14 Principles of cell signaling 589
12.19	The clearance of apoptotic cells requires cellular interaction 553	Melanie H. Cobb and Elliott M. Ross
12.20	Apoptosis plays a role in diseases such as viral infection	14.1 Introduction 590
	and cancer 554	14.2 Cellular signaling is primarily chemical 591
12.21	Apoptotic cells are gone but not forgotten 555	14.3 Receptors sense diverse stimuli but initiate a limited repertoire of cellular signals 592
12,22	What's next? 556	14.4 Receptors are catalysts and amplifiers 593
12.23	Summary 557	14.5 Ligand binding changes receptor conformation 593
	References 557	14.6 Signals are sorted and integrated in signaling pathways and networks 595
13	Cancer—Principles and	14.7 Cellular signaling pathways can be thought of as
	overview 561	biochemical logic circuits 597
	Robert A. Weinberg	14.8 Scaffolds increase signaling efficiency and enhance spatial organization of signaling 598
13.1	Tumors are masses of cells derived from a single cell 562	14.9 Independent, modular domains specify protein-protein interactions 600
13.2	Cancer cells have a number of phenotypic	14.10 Cellular signaling is remarkably adaptive 602
13.3	characteristics 563 Cancer cells arise after DNA damage 566	14.11 Signaling proteins are frequently expressed as multiple species 604
13.4	Cancer cells are created when certain genes are mutated 567	14.12 Activating and deactivating reactions are separate and independently controlled 605
13.5	Cellular genomes harbor a number of proto-oncogenes 569	14.13 Cellular signaling uses both allostery and covalent modification 606
13.6	Elimination of tumor suppressor activity requires two mutations 570	14.14 Second messengers provide readily diffusible pathways for information transfer 606
13.7	The genesis of tumors is a complex process 572	14.15 Ca ²⁺ signaling serves diverse purposes in all eukaryotic
13.8	Cell growth and proliferation are activated by growth factors 575	cells 608 14.16 Lipids and lipid-derived compounds are signaling
13.9	Cells are subject to growth inhibition and may exit from the cell cycle 577	molecules 609
13.10	Tumor suppressors block inappropriate entry into the cell	14.17 PI 3-kinase regulates both cell shape and the activation of essential growth and metabolic functions 612
13.11	cycle 579 Mutation of DNA repair and maintenance genes can	14.18 Signaling through ion channel receptors is very fast 612
	increase the overall mutation rate 580	14.19 Nuclear receptors regulate transcription 614
13.12	Cancer cells may achieve immortality 581	

14.20	G protein signaling modules are widely used and highly adaptable 615	15.7	Vitronectin facilitates targeted cell adhesion during blood clotting 658
14.21	Heterotrimeric G proteins regulate a wide variety of	15.8	Proteoglycans provide hydration to tissues 659
14.22	effectors 618 Heterotrimeric G proteins are controlled by a regulatory	15.9	Hyaluronan is a glycosaminoglycan enriched in connective tissues 662
14.23	GTPase cycle 618 Small, monomeric GTP-binding proteins are multiuse	[15.10]	Heparan sulfate proteoglycans are cell surface coreceptors 664
	switches 620	15.11	The basal lamina is a specialized extracellular
14.24	Protein phosphorylation/dephosphorylation is a major regulatory mechanism in the cell 621	15.12	matrix 666 Proteases degrade extracellular matrix
14.25	Two-component protein phosphorylation systems are signaling relays 624	15.13	components 667
14.26	Pharmacological inhibitors of protein kinases may be		Most integrins are receptors for extracellular matrix proteins 670
	used to understand and treat disease 625	15.14	Integrin receptors participate in cell signaling 672
14.27	Phosphoprotein phosphatases reverse the actions of kinases and are independently regulated 625	15.15	Integrins and extracellular matrix molecules play key roles in development 676
14.28	Covalent modification by ubiquitin and ubiquitin-like proteins is another way of regulating protein function 626	15.16	Tight junctions form selectively permeable barriers between cells 677
14.29	The Wnt pathway regulates cell fate during development and other processes in the adult 628	15.17	Septate junctions in invertebrates are similar to tight junctions 680
14.30	Diverse signaling mechanisms are regulated by protein	15.18	Adherens junctions link adjacent cells 682
	tyrosine kinases 628	15.19	Desmosomes are intermediate filament-based cell adhesion complexes 684
14.31	Src family protein kinases cooperate with receptor protein tyrosine kinases 630	15.20	Hemidesmosomes attach epithelial cells to the basal lamina 686
14.32	MAPKs are central to many signaling pathways 631	15.21	Gap junctions allow direct transfer of molecules between
14.33	Cyclin-dependent protein kinases control the cell cycle 632		adjacent cells 688
14.34	Diverse receptors recruit protein tyrosine kinases to the	15.22	Calcium-dependent cadherins mediate adhesion between cells 690
14.35	plasma membrane 633 What's next? 637	15.23	Calcium-independent NCAMs mediate adhesion between neural cells 692
14.36	Summary 637	15.24	Selectins control adhesion of circulating
	References 637	4500	immune cells 694
3 1	The system collection markets and self	15.25	What's next? 696
	The extracellular matrix and cell	15.26	Summary 696 References 697
	adhesion 645 George Plopper		
15.1	Introduction 646	Parl	7 Prokaryotic and
15.2	A brief history of research on the extracellular matrix 648		lant cells 703
15.3	Collagen provides structural support to tissues 649		Prokaryotic cell biology 705
15.4 15.5	Fibronectins connect cells to collagenous matrices 652 Elastic fibers impart flexibility to		Jeff Errington, Matthew Chapman, Scott J. Hultgren, and Michael Caparon
1602	tissues 654	16.1	Introduction 706
15.6	Laminins provide an adhesive substrate for cells 656	16.2	Molecular phylogeny techniques are used to understand microbial evolution 708

16.3	Prokaryotic lifestyles are diverse 709	17.2	How plants grow 765
16.4	Archaea are prokaryotes with similarities to eukaryotic cells 711	17.3	The meristem provides new growth modules in a repetitive manner 766
16.5	Most prokaryotes produce a polysaccharide-rich layer called the capsule 713	17.4	The plane in which a cell divides is important for tissue organization 768
16.6	The bacterial cell wall contains a crosslinked meshwork of peptidoglycan 716	17.5	Cytoplasmic structures predict the plane of cell division before mitosis begins 770
16.7	The cell envelope of Gram-positive bacteria has unique	17.6	Plant mitosis occurs without centrosomes 772
16.0	features 720	17.7	The cytokinetic apparatus builds a new wall in the plane anticipated by the preprophase band 774
16.8	Gram-negative bacteria have an outer membrane and a periplasmic space 722	17.8	Secretion during cytokinesis forms the cell plate 776
16.9	The cytoplasmic membrane is a selective barrier for secretion 725	17.9	Plasmodesmata are intercellular channels that connect plant cells 777
16.10	Prokaryotes have several secretion pathways 726	17.10	Cell expansion is driven by swelling of the vacuole 779
16.11	Pili and flagella are appendages on the cell surface of most prokaryotes 728	17.11	The large forces of turgor pressure are resisted by the strength of cellulose microfibrils in the cell wall 780
16.12	Prokaryotic genomes contain chromosomes and mobile DNA elements 731	17.12	The cell wall must be loosened and reorganized to allow growth 782
16.13	The bacterial nucleoid and cytoplasm are highly ordered 733	17.13	Cellulose is synthesized at the plasma membrane, not preassembled and secreted like other wall
16.14	Bacterial chromosomes are replicated in specialized replication factories 735	17.14	components 784 Cortical microtubules are thought to organize
16.15	Prokaryotic chromosome segregation occurs in the		components in the cell wall 785
222	absence of a mitotic spindle 737	17.15	Cortical microtubules are highly dynamic and can change their orientation 787
16.16	Prokaryotic cell division involves formation of a complex cytokinetic ring 739	17.16	A dispersed Golgi system delivers vesicles to the cell
16.17	Prokaryotes respond to stress with complex	17.10	surface for growth 790
16.18	developmental changes 742 Some prokaryotic life cycles include obligatory	17.17	Actin filaments form a network for delivering materials around the cell 791
10110	developmental changes 746	17.18	Differentiation of xylem cells requires extensive
16.19	Some prokaryotes and eukaryotes have endosymbiotic		specialization 793
	relationships 747	17.19	Tip growth allows plant cells to extend processes 795
16.20	Prokaryotes can colonize and cause disease in higher organisms 749		Plants contain unique organelles called plastids 797
16.21	Biofilms are highly organized communities of	[17.21]	Chloroplasts manufacture food from atmospheric CO ₂ 799
	microbes 751	17.22	What's next? 801
16.22	What's next? 754	17.23	Summary 801
16.23	Summary 754		References 803
	References 755	Glossa	n. 907
a==	Diant cell history		ry 807
17	Plant cell biology763	Protei	n database index 825
	Clive Lloyd	Index	827
17.1	Introduction 764		