

Contents

Part I Chemistry of Saccharides

Vol. 1 Chemical Synthesis of Glycosides and Glycomimetics

	List of Contributors	LV
	Abbreviations Used in Volumes 1 and 2	LXIII
I	Chemical Synthesis of Glycosides	1
1	Introduction to Volumes 1 and 2	3
2	Trichloroacetimidates	5
	<i>Richard R. Schmidt and Karl-Heinz Jung</i>	
2.1	Introduction.....	5
2.2	Methods.....	6
2.3	O-Glycosides.....	7
2.3.1	Synthesis of Oligosaccharides	7
	β -Glucosides, β -Galactosides, α -Rhamnosides, <i>etc.</i>	7
	Aminosugar Trichloroacetimidates.....	8
	β -Mannosides	13
	2-Deoxyglycosides	13
	Miscellaneous Compounds	14
	Complex Oligosaccharides.....	14
2.3.2	Inositol Glycosides.....	36
2.3.3	Glycosylation of Sphingosine Derivatives and Mimics	38
2.3.4	Glycosylation of Amino Acids	40
2.3.5	Polycyclic and Macrocyclic Glycosides	42

2.3.6	Glycosides of Phosphoric and Carboxylic Acids	44
2.3.7	Solid-Phase Synthesis	45
2.4	S-Glycosides	49
2.5	N- and P-Glycosides	51
2.6	C-Glycosides	51
2.7	Conclusion and Outlook	53
	References	53
3	Iterative Assembly of Glycals and Glycal Derivatives: The Synthesis of Glycosylated Natural Products and Complex Oligosaccharides...	61
	<i>Lawrence J. Williams, Robert M. Garbaccio, and Samuel J. Danishefsky</i>	
3.1	Introduction	61
3.2	Ciclamycin 0	64
3.3	Allosamidin	66
3.4	KS-502 and Rebeccamycin	69
3.5	Extension to Thioethyl Donors	74
3.6	Lewis ^y	76
3.7	Globo H	82
3.8	KH-1	86
3.9	Concluding Remarks	90
	Acknowledgments	90
	References	90
4	Thioglycosides	93
	<i>Stefan Oscarson</i>	
4.1	Introduction	93
4.2	Synthesis of Thioglycosides	94
4.2.1	From Anomeric Acetates	94
4.2.2	From Glycosyl Halides	95
4.2.3	Protecting Group Manipulations in Thioglycosides	96
4.3	Glycosylations with Thioglycoside Donors	97
4.3.1	A Two-Step Procedure: Transformation of Thioglycosides into Other Types of Glycosyl Donors	97
4.3.2	Direct Activation of Thioglycoside Donors	99
	Heavy Metal Salt Promoters	99
	Halonium, sulfonium and carbonium type promoters	100
	Single-Electron Activation	106
	Other Types of Donors With an Anomeric Sulfur	108
4.4	Applications of Thioglycosides	110
4.4.1	Block Syntheses, Orthogonal Glycosylations	110
	Thioglycosides as Acceptors	110
	Thioglycosides as Both Donors and Acceptors	111
4.4.2	Intramolecular Glycosidations	112
4.4.3	Solid Phase Synthesis	113
	References	113

5	Glycosylation Methods: Use of Phosphites	117
	<i>Zhiyuan Zhang and Chi-Huey Wong</i>	
5.1	Introduction.....	117
5.2	Preparation of Glycosyl Phosphites	118
5.3	Glycosylation using Glycosyl Phosphites	119
5.3.1	Mechanism.....	119
5.3.2	Low Temperature-Dependent Stereoselectivity	121
5.3.3	Glycosylation of Sialyl Phosphites	122
5.3.4	Glycosylation of C-2-Acylated Glycosyl Phosphites.....	123
5.3.5	Glycosylation with C-2- <i>O</i> -Benzylated Glycosyl Phosphites	124
	Glycosylation using Glucosyl Phosphites with a Benzyl Group at C-2	124
	Glycosylation using Galactosyl and Fucosyl Phosphites with a Benzyl Group at C-2.....	125
	Glycosylation using other Glycosyl Phosphites with a Benzyl Group at C-2.....	126
5.3.6	Glycosylation with 2-Deoxy Glycosyl Phosphites	127
5.4	Other Applications of Glycosyl Phosphites	128
5.4.1	Synthesis of CMP–NeuAc.....	129
5.4.2	Synthesis of GDP–Fucose.....	129
5.4.3	Formation of Glycosyl Phosphonate.....	131
5.4.4	Transformation to other Types of Glycosyl Donor.....	131
	Phosphate	131
	Phosphorimidate	131
	References.....	132
6	Glycosylation Methods: Use of <i>n</i>-Pentenyl Glycosides	135
	<i>Bert Fraser-Reid, G. Anilkumar, Mark R. Gilbert, Subodh Joshi, and Ralf Kraehmer</i>	
6.1	Introduction.....	135
6.2	Fundamental Reactions	135
6.3	Determination of Relative Reactivities.....	138
6.4	<i>n</i> -Pentenyl Orthoesters as Glycosyl Donors.....	141
6.5	<i>n</i> -Pentenyl Orthoesters as Latent C2 Esters.....	144
6.6	Protecting Groups	146
6.7	Solid-Phase Iterative Couple–Deprotect–Couple Strategy	146
	References.....	153
7	Glycosylidene Diazirines	155
	<i>Andrea Vasella, Bruno Bernet, Martin Weber, and Wolfgang Wenger</i>	
7.1	Introduction.....	155
7.2	Synthesis of Glycosylidene Diazirines	155
7.3	Stability of the Glycosylidene Diazirines.....	158
7.4	Glycosidation by Glycosylidene Diazirines	158
7.4.1	General Aspects.....	158

7.4.2	Glycosidation of Strongly Acidic Hydroxy Compounds	162
	Glycosidation of Phenols	162
	Glycosidation of Fluorinated Alcohols	163
7.4.3	Glycosylation of Weakly Acidic Hydroxy Compounds	163
	Glycosidation of Monovalent Alcohols	163
	Glycosidation of Diols and Triols	164
7.5	Synthesis of Spirocyclopropanes	168
7.6	Addition to Aldehydes and Ketones	170
7.7	Exploratory Use of Diazirines: Formation of Glycosyl Phosphines, Stannanes, <i>N</i> -Sulfonylamines, Esters, Boranes, and Alanes, and of 1,1-Difluorides	171
	Acknowledgments	174
	References	174
8	Glycosylation Methods: Alkylations of Reducing Sugars	177
	<i>Jun-ichi Tamura</i>	
8.1	Introduction	177
8.2	Anomeric O-Alkylation	177
8.2.1	Anomeric O-Alkylation of Ribofuranose with Primary Triflates: Effect of the Protecting Group at O-5 of Ribofuranose	178
8.2.2	Anomeric O-Alkylation of Mannofuranose with Primary Triflates: The Crown Ether Effect	179
8.2.3	Anomeric O-Alkylation of Gluco- and Galactopyranoses with Primary Triflates: High β -Selectivity as a Result of the Reactive Anomeric β -Anion	180
8.2.4	Anomeric O-Alkylation of Acyl-Protected Nucleophiles with Primary Triflates	181
8.2.5	Anomeric O-Alkylation of Mannopyranose with Primary Triflates: Possibility of Intramolecular Complexation of the Nucleophile	184
8.2.6	Anomeric O-Alkylation of KDO with Primary Triflates	185
8.2.7	Anomeric O-Alkylation of Some Protected Aldoses with Primary Triflate	186
8.2.8	Anomeric O-Alkylation of Unprotected Aldoses with Primary Triflate, Bromides, and Cyclic Sulfates	187
8.2.9	Anomeric O-Alkylation with Secondary Triflates and Nonaflate ...	188
8.3	Glycosylation <i>via</i> the Locked Anomeric Configuration	189
8.3.1	Synthesis of Methyl, Allyl, and Benzyl Glycosides <i>via</i> Stannylene Acetals	189
8.3.2	Epimerization at C-2 by the Locked Anomeric Configuration Method	189
8.3.3	The Locked Anomeric Configuration Method for Rhamnosyl Stannylene Acetal	190
8.3.4	The Locked Anomeric Configuration Method for Mannosyl Stannylene Acetal: Isomerization of Acetal [25, 26]	190
8.3.5	The Locked Anomeric Configuration Method for Stannylene Acetal with the Glucose Configuration [25, 26]	191

8.4	Conclusion	192
	References.....	193
9	Other Methods of Glycosylation.....	195
	<i>Luigi Panza and Luigi Lay</i>	
	Introduction and Summary.....	195
	Highlights	195
9.1	Enol Ethers	197
9.1.1	Endo-Enol Ethers.....	198
9.1.2	Exo-Enol Ethers.....	201
9.1.3	Endo-Glycals.....	202
9.1.4	Exo-Glycals	204
9.1.5	Vinyl Glycosides	206
9.2	1-Hydroxy Sugars.....	209
9.2.1	Acidic Activation	210
	Acidic Activation With Additional Reagents	211
9.2.2	Dehydrative Glycosylation	212
	In the Presence of the Acceptor From the Beginning.....	213
9.2.3	Mitsunobu Glycosylation.....	214
9.2.4	1-O-Silyl Glycosides	215
9.3	Esters and Related Derivatives.....	216
9.3.1	Esters.....	216
9.3.2	Sugar Carbonates and Derivatives	221
9.3.3	Orthoesters and Oxazolines.....	223
9.3.4	Phosphorus and Sulfur Derivatives	229
	References.....	233
10	Polymer-Supported Synthesis of Oligosaccharides.....	239
	<i>Jiri J. Krepsky and Stephen P. Douglas</i>	
10.1	Introduction.....	239
10.2	General Reflections	240
10.3	Polymer Supports.....	246
10.4	One-Phase Systems (Syntheses in Solution).....	247
	Polyethyleneglycol _ω -monomethylether (MPEG).....	248
	Linear Polystyrene	249
10.4.1	Linkers	250
	Succinoyl Diester	250
	Dioxyxylyl Diether (DOX).....	252
10.4.2	Chemistry Investigations	254
10.5	Two-Phase Systems (Syntheses on Solid Supports)	255
	Controlled Pore Glass	256
	Cross-Linked Polystyrene.....	256
	Polyethylene Grafts on Cross-Linked Polystyrene.....	256
10.5.1	Linkers	259
	Dialkyl- or Diaryl-Silyl	259
	Thioglycoside Linkers	259

	Linkers Cleavable by Photolysis	260
10.6	Examples of Syntheses	260
10.7	Combinatorial Libraries	261
10.8	Capping	262
10.9	Concluding Remarks	262
	References	262
11	Glycopeptide Synthesis in Solution and on the Solid Phase	267
	<i>Horst Kunz and Michael Schultz</i>	
11.1	Introduction	267
11.1.1	Which Protecting Groups are Suitable for Carbohydrates (Table 2)?	269
11.1.2	Which Glycosylation Methods are Useful for the Formation of Glycopeptides?	271
	Formation of Asparagine <i>N</i> -Glycosides	271
	α -Fucosylation	271
	Formation of the β -Lactosamine Linkage	272
	α -Sialylation	272
11.1.3	Glycopeptides Containing Particularly Sensitive Linkages	272
	Acid Sensitivity	273
	Base Sensitivity	273
11.2	Synthesis of Glycopeptides in Solution	274
11.2.1	<i>O</i> -Glycopeptides	274
	Glycopeptides Carrying <i>N</i> -Acetylgalactosamine (Tn-Antigen)	274
	Glycopeptides Carrying the T-Antigen (Gal-GalNAc)	276
	Glycopeptides Carrying the Sialyl T Antigen (NeuAc α 2,6[Gal β 1,3]GalNAc)	278
	Glycopeptides Carrying <i>O</i> -GlcNAc	279
11.2.2	<i>N</i> -Glycopeptides	280
	<i>N</i> -Glycopeptides Carrying Natural Saccharide Side-Chains	280
	<i>N</i> -Glycopeptides with Lewis-Type Saccharide Side-Chains	285
11.3	Glycopeptide Synthesis on the Solid Phase	286
11.3.1	<i>O</i> -Glycopeptides	287
	Glycopeptides Carrying <i>N</i> -Acetylgalactosamine (Tn-Antigen)	287
	<i>O</i> -Glycopeptides Carrying the T Antigen (Gal-GalNAc)	290
	<i>O</i> -Glycopeptides Carrying the Sialyl Tn Antigen (NeuNAc- α 2,6- GalNAc)	291
	<i>O</i> -Glycopeptides Carrying the 2,3-Sialyl T Antigen	293
	<i>O</i> -Glycopeptides Carrying <i>O</i> -GlcNAc Side-Chains	294
	<i>O</i> -Glycopeptides Carrying <i>O</i> -Linked Fucose	295
	<i>O</i> -Glycopeptides Carrying a Sialyl Lewis Antigen Structure	296
11.3.2	<i>N</i> -Glycopeptides	297
	The Construction of <i>N</i> -Glycopeptide Libraries on the Solid Phase	298
	Sequential <i>N</i> -Glycopeptide Synthesis on the Solid Phase with Oligosaccharides from Natural Sources	299

11.4	Conclusion	300
	References.....	300
12	Glycolipid Synthesis.....	305
	<i>Hideharu Ishida</i>	
12.1	Introduction.....	305
12.2	Synthesis of Ganglio-Series Gangliosides	305
12.2.1	Retrosynthetic Analysis of Ganglioside GD1a	305
12.2.2	Preparation of Sialylgalactose Donor as Building Block	306
12.2.3	Construction of Oligosaccharide	308
12.2.4	Transformation of Oligosaccharide into Glycolipid	310
12.3	Synthesis of Polysialo Ganglio-Series Gangliosides.....	311
12.3.1	Retrosynthetic Analysis of GQ1b	313
12.3.2	Preparation of Building Block.....	313
12.3.3	Construction of Oligosaccharide	314
12.4	Conclusion	315
	References.....	316
13	Stereoselective Synthesis of β-Mannosides	319
	<i>Vince Pozsgay</i>	
13.1	Introduction.....	319
13.2	Chemical Methods.....	320
13.2.1	Glycosylation with Mannosyl Donors	320
	Mannosylation using Insoluble Promoters.....	320
	The Sulfonate Approach.....	322
	Intramolecular Mannosylation	324
	Other Mannosyl Donor-Based Methods	327
13.2.2	Epimerization of β -Glucopyranosides at C-2	329
	The Oxidation–Reduction Approach	329
	Direct Inversion.....	329
13.2.3	The 2-Ulosyl Donor Method	331
13.2.4	Anomeric <i>O</i> -alkylation	332
	Alkylation of 1- <i>O</i> -Metal Complexes	332
	The Stannylene Acetal Method	332
13.2.5	Miscellaneous Methods.....	333
	Radical Inversion of the Anomeric Chirality of α -D-Mannopyranosides.....	333
	Reductive Cleavage of Cyclic Orthoesters	334
	<i>De novo</i> Syntheses	334
13.2.6	2-Acetamido-2-deoxy- β -D-mannopyranosides	335
13.2.7	Aryl β -D-mannopyranosides	336
13.2.8	1-Thio- β -D-mannopyranosides	336
13.2.9	β -D-Mannopyranosylamines	337
13.3	Enzymatic Synthesis	337
13.4	Conclusions	338
	References.....	338

14	Special Problems in Glycosylation Reactions: Sialidations.....	345
	<i>Makoto Kiso, Hideharu Ishida and Hiromi Ito</i>	
14.1	Introduction	345
14.2	Sialidation by the Koenigs–Knorr Method.....	345
14.3	Sialidation Using an Auxiliary Group at C-3	347
14.4	Sialidation Using 2-Thioglycosides, Xanthates, or Phosphites of Sialic Acids in Acetonitrile	349
14.4.1	Thioglycosides	349
14.4.2	Xanthates and Phosphites	356
14.4.3	Reaction Mechanism	359
14.5	Further Solutions to the Problem	359
14.5.1	Combination of C-3 Auxiliary and Sterically less Hindered Sugar Acceptors	359
14.5.2	Combination of C-3 Auxiliary and Specific Activation of the Anomeric Center C-2.....	360
14.5.3	Thioglycoside of <i>N,N</i> -Diacetylneuraminic Acid and Combination with C-3 Auxiliary.....	363
	References	364
15	Special Problems in Glycosylation Reactions: 2-Deoxy Sugars	367
	<i>Alain Veyrières</i>	
15.1	Introduction	367
15.2	Electrophilic Additions to Glycals: Mechanistic Aspects and Applications to the Synthesis of 2-Deoxyglycosides.....	368
15.2.1	Protonation of Glycals	369
15.2.2	Enzyme-Catalyzed Additions to Glycals.....	370
15.2.3	Halogenation of Glycals	370
15.2.4	Bromo- and Iodoalkoxylation of Glycals.....	372
15.2.5	Epoxidation of Glycals.....	377
15.2.6	Addition of Sulfur Based Electrophiles to Glycals	379
15.2.7	Addition of Selenium Based Electrophiles to Glycals	382
15.3	The Cycloaddition Way to Glycosyl Transfer	384
15.4	Fluoroglycosylation of Glycals.....	385
15.5	Glycosyl Donors with a C-2 Heteroatom.....	386
15.5.1	2-Bromo-2-deoxyglycosyl bromides.....	386
15.5.2	2-Deoxy-2-(thiophenyl)-glycosyl fluorides	387
15.5.3	2,6-Anhydro-2-Thio-Glycosyl Donors	388
15.5.4	1,2-Di- <i>O</i> -Acetyl- β -Hexopyranoses and <i>N</i> -Formylglucosamine Derivatives.....	392
15.6	2-Deoxyglycosyl Donors	393
15.6.1	2-Deoxy-Hexopyranoses	394
15.6.2	Tert-Butyldimethylsilyl 2-Deoxyglycosides	394
15.6.3	1- <i>O</i> -Acyl- and Acetimidyl-2-Deoxy-Hexopyranoses.....	394
15.6.4	2-Deoxyglycosyl Bromides and Fluorides	395
15.6.5	<i>S</i> -(2-Deoxyglycosyl)phosphorodithioates	396

15.6.6	2-Deoxyglycosyl Phosphates, Phosphoramidites and Phosphites....	397
15.6.7	2-Deoxy Thioglycosides	398
15.6.8	2-Deoxyglycosyl Sulfoxides.....	399
15.7	Other Approaches to 2-Deoxyglycosides.....	400
15.7.1	Cyclization of Acyclic Sugars	401
15.7.2	Use of Alkoxy-Substituted Anomeric Radicals	402
	References.....	403
16	Orthogonal Strategy in Oligosaccharide Synthesis	407
	<i>Osamu Kanie</i>	
16.1	Introduction.....	407
16.2	Analysis of the Strategic Aspects of Oligosaccharide Synthesis	408
16.2.1	General Aspects.....	408
16.2.2	The Pursuit of Efficiency in Oligosaccharide Synthesis.....	408
16.3	The Introduction of the Orthogonal Glycosylation Strategy	410
16.3.1	Limitation of Current Concepts.....	410
16.3.2	The Orthogonal Coupling Concept	412
16.3.3	What is Orthogonality Anyway?	413
16.3.4	Orthogonal Glycosylation and Solid-Phase Oligosaccharide Synthesis	414
16.4	The Orthogonal Glycosylation Strategy	414
16.4.1	Orthogonal Chain Elongation of Homo-Oligosaccharides: Synthesis of Chito-Oligosaccharides [19].....	414
16.4.2	Orthogonal Coupling for Hetero-Oligomer Synthesis [22].....	418
16.4.3	Application to Polymer-Supported Synthesis [26]	420
16.5	Conclusions and Prospects	421
	Acknowledgments	424
	References.....	424
17	Protecting Groups: Effects on Reactivity, Glycosylation Stereoselectivity, and Coupling Efficiency	427
	<i>Luke G. Green and Steven V. Ley</i>	
17.1	Introduction.....	427
17.2	Glycosidic Mechanism.....	428
17.3	Electronic and Torsional Effects	430
17.4	Influence of Protecting Group on Donor Reactivity.....	431
17.5	Stereoselectivity	436
17.5.1	Neighboring-Group Participation.....	436
17.5.2	Reactivity Control	437
17.6	Influence of the Protecting Group on the Acceptor	441
17.7	Steric Effects on Glycosylation.....	443
17.8	Conclusions	444
	Acknowledgments	445
	References.....	446

18	Intramolecular Glycosidation Reactions	449
	<i>Jacob Madsen and Mikael Bols</i>	
18.1	Introduction	449
18.2	Reactions in which the Tether Participates in the Reaction.....	450
18.2.1	Tethering to the Glycosyl Donor	450
	Carbon Tethers	450
	Silicon Tethers	454
18.2.2	Tethering to the Leaving Group	459
18.3	Reactions in which the Tether does not Participate in the Reaction	459
18.4	Conclusion.....	464
	References	465
19	Classics In Total Synthesis of Oligosaccharides and Glycoconjugates	467
	<i>Jean-Maurice Mallet and Pierre Sinay</i>	
19.1	Introduction	467
19.2	Syntheses of Nod factors	467
19.2.1	Introduction	467
19.2.2	The K. C. Nicolaou Synthesis (1992) [3].....	468
19.2.3	The J.-M. Beau Synthesis (1994) [12]	471
19.2.4	The T. Ogawa Synthesis (1994) [16]	475
19.2.5	The Y. Z. Hui Synthesis (1992) [18]	477
19.2.6	Conclusion	480
19.3	Synthesis of the Antithrombin-Binding Pentasaccharide Sequence in Heparin (1984) [19, 20].....	480
19.3.1	Introduction	480
19.3.2	An Overview of the Synthesis of the Protected Pentasaccharide 73	481
19.3.3	Synthesis of the Disaccharidic Bromide Donor 68	483
19.3.4	Synthesis of the Disaccharidic Acceptor 69.....	484
19.3.5	Synthesis of the Protected Pentasaccharide 73.....	484
19.3.6	Synthesis of the Active Site of Heparin	485
19.4	Total Synthesis of VIM-2 Ganglioside [31]	485
19.4.1	Introduction	485
19.4.2	The Total Synthesis of VIM-2—a General Strategy	486
19.4.3	Preparation of the Key Protected Octasaccharide 87.....	487
19.5	Epilogue	490
	References	491
II	Synthesis of Oligosaccharide Mimics	493
20	Synthesis of C-Oligosaccharides	495
	<i>Troels Skrydstrup, Boris Vauzeilles, and Jean-Marie Beau</i>	
20.1	Introduction	495
20.2	The Anionic Approach.....	496
20.2.1	C5-Alkynyl Anions	496

20.2.2	C1-Glycal Carbanions	500
20.2.3	Anomeric Samarium Species	502
20.2.4	C-Branched Carbanions	506
20.2.5	C6-Phosphoranes	508
20.3	The Radical Approach	511
20.3.1	Intermolecular Anomeric Radical Addition	511
20.3.3	Intramolecular Anomeric Radical Addition	513
20.4	The Partial <i>de Novo</i> Approach	518
20.5	The Cycloaddition and Rearrangement Approach	527
	References.....	528
21	Synthesis of Oligosaccharide Mimics: S-Analogs.....	531
	<i>Jon K. Fairweather and Hugues Driguez</i>	
21.1	Introduction.....	531
21.2	General Synthesis	532
21.2.1	Preparation of Thioglycoses	532
	1-Thioglycoses	532
	2-, 3-, 4-, 5-, or 6-Thioglycoses	532
	Selective S-Deprotection of Thioglycoses	533
	Glycosylation Methods	534
21.3	Establishment of 1,6-Thio Linkages.....	534
21.3.1	6-Thiodisaccharides.....	534
21.3.2	6-Thiooligosaccharides	538
21.3.3	Branched Thiocyclodextrins	538
21.4	Establishment of 1,4-Thio Linkages.....	541
21.4.1	1,4-Thiodisaccharides.....	541
	General Approaches	541
	S _N 2-Displacement on Triflates	541
21.4.2	1,4-Thiooligosaccharides	546
	Conventional Approaches	546
	Chemoenzymatic Approaches	548
	Michael Addition to Unsaturated Acceptors	549
	Solid-Support Synthesis.....	550
21.5	Establishment of 1,3-Thio Linkages.....	551
21.5.1	1,3-Thiodisaccharides	551
	Conventional Methods	551
	Cyclic Sulfamidate and Aziridine	551
21.5.2	1,3-Thiooligosaccharides	552
21.6	Establishment of 1,2-Thio Linkages.....	553
21.6.1	1,2-Thiodisaccharides	553
	Conventional Methods	554
	Other Approaches	555
21.7	Establishment of 1,1-Thio Linkages.....	557
21.8	Establishment of Mixed Thio linkages	558
21.9	Thiooligosaccharides and Proteins	558
21.9.1	The Conformation of Thiooligosaccharides in Solution.....	558

21.9.2	Enzyme–Substrate Interactions	560
	α -Glucan-Active Enzymes	560
	β -Glucan-Active Enzymes	561
21.9.3	Lectin–Ligand Interactions	562
21.10	Conclusion	562
	Acknowledgments	562
	References	562
22	Saccharide–Peptide Hybrids	565
	<i>Hans Peter Wessel</i>	
22.1	Introduction	565
22.2	Carbohydrate Amino Acids	566
22.2.1	Natural Carbohydrate Amino Acids	566
22.2.2	Synthetic Carbohydrate Amino Acids	567
22.3	Amide-Linked Carbohydrate Polymers	572
22.4	Amide-Linked Carbohydrate Oligomers	574
22.4.1	Solution Synthesis	574
22.4.2	Solid-Phase Synthesis	578
22.4.3	Biological Activity	579
22.4.4	Conformational Properties	582
	References	583
	Index	I 1

Part I Chemistry of Saccharides

Vol. 2 Enzymatic Synthesis of Glycosides and Carbohydrate-Receptor Interaction

III	Enzymatic Synthesis of Glycosides	587
23	On the Origin of Oligosaccharide Species—Glycosyltransferases in Action	589
	<i>Dirk H. van den Eijnden</i>	
23.1	Introduction	589
23.2	Protein <i>N</i> -Glycosylation: Pre-assembly of Oligosaccharide–PP–Dolichol and en bloc Transfer	591
23.3	Trimming of the Polypeptide-Bound Oligosaccharide	592
23.4	Folding and Quality Control	593
23.5	Committed Steps in the Formation of Complex-Type Oligosaccharide Chains and Branching	594
23.6	Topology of the Reaction Catalyzed by a Typical GlcNAcT	596
23.7	Elongation and Termination Reactions in the <i>trans</i> -Golgi	596
23.8	Activity with Branched Substrates	598

23.9	Branch Specificity	600
23.10	Essential Requirements for Activity with LacNAc	601
23.11	Further Terminal Reactions in Complex-Type Oligosaccharide Synthesis	602
23.12	Specific Modifications of Polylactosaminoglycans	603
23.13	The Invariable Core of N-linked Oligosaccharide Chains, and Site- and Protein-Specific Processing	606
23.14	Comparison of the Synthesis of Type 1 (Gal(β1-3)GlcNAcβ-R) and Type 2 (Gal(β1-4)GlcNAcβ-R) Chains	607
23.15	The LacdiNAc Pathway of Complex-Type Oligosaccharide Synthesis	607
23.16	Protein O-Glycosylation	608
23.17	Glycosyltransferase Families	608
23.18	Sialyltransferase Family	610
23.19	α2-Fucosyltransferase Family	611
23.20	α3/4-Fucosyltransferase Family	612
23.21	α3-Galactosyl/N-Acetylgalactosaminyltransferase (Histo-Blood Group ABO) Family	613
23.22	β6-N-Acetylglucosaminyltransferase Family	613
23.23	Polypeptide N-Acetylgalactosaminyltransferase Family	614
23.24	β4-N-Acetylgalactosaminyltransferase Family	615
23.25	β4-Galactosyltransferase Family	615
23.26	β3-Galactosyltransferase Family	617
23.27	β3-Glucuronyltransferase Family	617
23.28	Glycosyltransferases Standing Alone	617
23.29	Concluding Remarks	618
	References	618
24	Synthesis of Sugar Nucleotides	625
	<i>Reinhold Öhrlein</i>	
24.1	Introduction	625
24.2	Synthesis of Sugar Nucleotides	626
24.2.1	Chemical Synthesis	626
	UDP-Activated Donors	626
	CMP-Activated Sugars	629
	GDP-Activated Donors	632
	Comments	634
24.2.2	Chemo-Enzymatic Synthesis	635
	Uridine Diphosphate-Activated Donor Sugars	635
	CMP-Activated Sugars	637
	GDP-activated sugars	639
	Comments	640
24.3	In situ Generation of Sugar Nucleotides	641
	Comments	641
24.4	Outlook	644
	References	644

25	Enzymatic Glycosylations with Glycosyltransferases.....	647
	<i>Ossi Renkonen</i>	
25.1	Introduction	647
25.2	<i>In vitro</i> Synthesis of the Core Region of <i>O</i> -Glycans.....	648
25.2.1	Initialization of <i>O</i> -Glycan Biosynthesis.....	648
25.2.2	Synthesis of Core 1	648
25.2.3	Synthesis of Core 2	649
25.2.4	Synthesis of Core 3 and Core 4	650
25.2.5	<i>In vitro</i> Extension of Core 1 Glycans	650
25.2.6	<i>In vitro</i> Extension of Core 2 Glycans	651
25.2.7	Extension of Core 3 and Core 4 Glycans	651
25.3	Enzymatic <i>in vitro</i> Synthesis of Polylactosamine Backbones.....	651
25.3.1	Enzymatic Synthesis of the Primary Chains of Blood Group i-Type	652
25.3.2	Distal Branching of i-Type Polylactosamine Backbones	653
25.3.3	Central Branching of i-Type Polylactosamine Backbones.....	654
25.3.4	β 4-Galactosylation in Polylactosamine Backbones.....	656
25.4	α 3-Sialylation of <i>N</i> -Acetylactosaminoglycans at the Terminal Gal	656
25.5	α 3-Fucosylation of Lactosamine Saccharides.....	657
	References	659
 26	 Recycling of Sugar Nucleotides in Enzymatic Glycosylation.....	 663
	<i>Kathryn M. Koeller and Chi-Huey Wong</i>	
26.1	Introduction	663
26.2	Glycosyltransferases of the Leloir Pathway and their Sugar Nucleotide Substrates	663
26.3	Design of Regeneration Systems	665
26.4	Practical Regeneration Systems	666
26.4.1	UDP-Galactose	666
26.4.2	Other UDP-Sugars.....	669
26.4.3	CMP-NeuAc	671
26.4.4	GDP-Sugars.....	676
26.4.5	Other Carbohydrate-Based Regeneration Systems	680
26.5	Conclusion	682
	References	683
 27	 Enzymatic Glycosylations with Non-Natural Donors and Acceptors.....	 685
	<i>Xiangping Qian, Keiko Sujino, and Monica M. Palcic</i>	
27.1	Introduction	685
27.2	Enzymatic Glycosylations.....	686
27.2.1	Galactosylations.....	686
	β 1,4-Galactosyltransferase	686
	α 1,3-Galactosyltransferase	688

27.2.2	Fucosylations	690
	Human Milk α 1,3/4-Fucosyltransferase.....	690
	FucT III and VI	692
	FucT V.....	692
27.2.3	Sialylations.....	692
	α 2,3-Sialyltransferase and α 2,6-Sialyltransferase.....	692
27.2.4	<i>N</i> -Acetylglucosaminylation.....	696
	<i>N</i> -Acetylglucosaminyltransferase I, II, and III.....	696
	<i>N</i> -Acetylglucosaminyltransferase V	698
27.3	Summary.....	700
	Acknowledgments	700
	References.....	700
28	Solid-Phase Synthesis with Glycosyltransferases	705
	<i>Claudine Augé, Christine Le Narvor, and André Lubineau</i>	
28.1	Introduction.....	705
28.2	General Aspects.....	705
28.3	Enzymatic Synthesis on Insoluble Supports.....	707
28.3.1	Enzymatic Synthesis of Oligosaccharides	707
	Use of an Amino-Functionalized Water-Compatible Polyacrylamide Gel.....	707
	Use of a Sepharose Matrix	708
	Use of Controlled-Pore Glass	711
28.3.2	Enzymatic Synthesis of Glycopeptides	712
	Use of Controlled-Pore Glass	712
	Use of Polyethylene Glycol Polyacrylamide (PEGA).....	715
28.4	Enzymatic Synthesis of Oligosaccharides and Glycoconjugates on Soluble Supports.....	715
28.4.1	Enzymatic Synthesis of Oligosaccharides	715
	Use of Water-Soluble Amino-Substituted Poly(vinyl alcohol)	715
	Use of Water-Soluble Glycopolymer Synthesized by Polymerization	717
28.4.2	Enzymatic Synthesis of Glycolipids on Water-Soluble Polyacrylamide–Poly(<i>N</i> -acryloxysuccinimide) (PAN)	718
	References.....	722
29	Glycosidase-Catalysed Oligosaccharide Synthesis	723
	<i>David J. Vocadlo and Stephen G. Withers</i>	
29.1	Introduction.....	723
29.2	Background on Glycosidases	723
29.3	Basic Mechanisms	724
29.4	Synthesis by the ‘Thermodynamic’ Approach	724
29.5	The Kinetic Approach.....	728
29.6	Recent Developments and New Directions	732
	References.....	838

30	Production of Heterologous Oligosaccharides by Recombinant Bacteria (Recombinant Oligosaccharides)	845
	<i>Roberto A. Geremia and Eric Samain</i>	
30.1	Introduction	845
30.2	Concept and Methodology of Heterologous ('Recombinant') Oligosaccharide Production in <i>E. coli</i>	847
30.2.1	Biosynthesis of Nod Factors	847
30.2.2	Expression Systems and Cloning Strategy	849
30.2.3	High Cell-Density Cultivation	851
30.2.4	Purification of Recombinant Oligosaccharides	852
30.3	Examples of Recombinant Oligosaccharides	852
30.3.1	Production of Chitin Oligosaccharides in <i>E. coli</i> Expressing NodC	852
30.3.2	Production of Nod Factor Precursors	853
30.3.3	Production of Derivatives of <i>N</i> -Acetylactosamine	855
30.4	Conclusions and Future Perspectives	856
30.4.1	Production of Labeled Chitin Oligosaccharides to Study Their Interactions with Proteins	856
30.4.2	Improvement of Oligosaccharide Production, and Metabolic Engineering	858
30.4.3	Production of More Complex Oligosaccharides	858
	Acknowledgments	859
	References	859
IV	Carbohydrate–Protein Interactions	861
31	Protein–Carbohydrate Interaction: Fundamental Considerations ...	863
	<i>Nikki F. Burkhalter, Sarah M. Dimick, and Eric J. Toone</i>	
31.1	Introduction	863
31.2	Association in Aqueous Solution	864
31.2.1	Gas Phase Non Covalent Interactions	864
	Dipole–Dipole Interactions	864
	Dipole–Induced Dipole	866
	Dispersive Interactions	867
	Specific Forces: Hydrogen Bonding and n - σ Bonding.....	868
31.2.2	The Effect of Water on Intermolecular Interactions.....	869
	Coulombic Stabilization.....	870
	Hydrogen Bonding	871
	Dispersive Interactions	872
31.2.3	'Hydrophobic' Interactions.....	872
31.3	The Evaluation of Protein–Carbohydrate Binding.....	876
31.3.1	Precipitin Assays.....	877
31.3.2	Enzyme-Linked Lectin Assay (ELLA).....	878
31.3.3	Isothermal Titration Microcalorimetry	878
31.4	The Interpretation of Calorimetric Data.....	882

31.4.1	Solvation/Desolvation	882
	Solvation Entropy	883
	Translational/Rotational Entropy.....	884
31.4.2	Other Contributions to Thermodynamics of Association	885
	Proton Transfer	885
	Salt Effects/Binding Site Reorganization	885
31.4.3	van't Hoff versus Calorimetric Enthalpies	886
31.5	The Thermodynamics of Protein–Carbohydrate Interaction.....	887
31.6	The Role of Multivalency in Protein–Carbohydrate Interaction...	901
31.6.1	Phenomenology	901
31.6.2	The Energetic Consequence of Ligand Linkage	905
	Enthalpic Contributions to ΔG_i	906
	Entropic Contributions to ΔG_i	907
31.6.3	A Molecular Basis for the Cluster Glycoside Effect	910
	Acknowledgments	911
	References.....	911
32	Structural Analysis of Oligosaccharides: FAB-MS, ES-MS and MALDI-MS	915
	<i>Anne Dell, Howard R. Morris, Richard Easton, Stuart Haslam, Maria Panico, Mark Sutton-Smith, Andrew J. Reason, and Kay-Hooi Khoo</i>	
32.1	Introduction.....	915
32.2	Fast Atom Bombardment-Mass Spectrometry (FAB-MS).....	915
32.3	Matrix Assisted Laser Desorption Ionization-Time of Flight-Mass Spectrometry (MALDI-TOF-MS)	917
32.4	Electrospray-Mass Spectrometry (ES-MS).....	918
32.5	Appearance of Mass Spectra Obtained in FAB-MS, MALDI-MS and ES-MS Experiments	919
32.6	Assignment of Mass Values	921
32.7	Derivatisation.....	921
32.8	Fragmentation Pathways	922
32.9	Protocols for MS Analysis.....	924
32.9.1	Protocol 1—Sample Loading for FAB-MS Analysis.....	924
32.9.2	Protocol 2—Sample Loading for NanoES-MS and MS-MS Analysis on the Q-TOF.....	925
32.9.3	Protocol 3—Sample Loading for LC-ES-MS and LC-ES-MS-MS on the Q-TOF.....	925
32.9.4	Protocol 4—Sample Loading for MALDI-MS Analysis	925
32.10	Applications of FAB-MS, MALDI-MS and ES-MS in Glycobiology.....	926
32.10.1	Case Study 1—Molecular Weight Profiling of Polysaccharides by MALDI-MS	926
32.10.2	Case Study 2—Analysis of Glycoproteins by LC-ES-MS and FAB-MS	927

32.10.3	Case Study 3—Characterization of a Novel <i>N</i> -Glycan by FAB-MS and FAB-MS-MS.....	930
32.10.4	Case Study 4—High Sensitivity Sequencing of a Novel Glycopeptide by Q-TOF ES-MS-MS and MALDI-MS.....	933
32.10.5	Case Study 5—FAB-MS Screening of Biological Samples for Glycan Content.....	935
32.10.6	Case Study 6—MS Analysis of Mycobacterial Glycoconjugates ..	942
32.11	Concluding Remarks	944
	References	945
33	Conformational Analysis in Solution by NMR	947
	<i>S. W. Homans</i>	
33.1	Introduction	947
33.2	Solution Conformations of Oligosaccharides	947
33.2.1	The NMR Technique.....	947
33.2.2	Conformational Parameters in Oligosaccharides	948
33.2.3	Conformational Restraints	949
33.2.4	¹³ C Isotopic Enrichment	949
33.2.5	Additional Conformational Restraints.....	950
	Exchangeable Protons	950
	Heteronuclear Overhauser Effects.....	952
	¹³ C– ¹³ C Coupling-Constants	953
	Dipolar Couplings.....	954
33.3	Experimental Restraints in Conformational Analysis	955
33.3.1	Restraining Protocol.....	955
	Biharmonic Restraints.....	955
	Time-Dependent Restraints	957
33.3.2	Dynamical Simulated Annealing.....	957
33.4	Analysis of Oligosaccharide Dynamics	958
33.4.1	Monte-Carlo Simulations	959
33.4.2	Molecular Dynamics Simulations.....	959
33.5	A Case Study on Neu5Aca2-3Galβ1-4Glc	959
33.5.1	Resonance Assignments in Neu5Aca2-3Galβ1-4Glc	960
33.5.2	ROE Connectivities	960
33.5.3	‘Global Minimum’ Conformation of Neu5Aca2-3Galβ1-4Glc	961
33.5.4	Conformational Dynamics of Neu5Aca2-3Galβ1-4Glc	962
33.5.5	Short-range vs Long-range Restraints	963
33.6	Conclusions	966
	References	966
34	Oligosaccharide Conformations by Diffraction Methods.....	969
	<i>Serge Pérez, Catherine Gautier, and Anne Imberty</i>	
34.1	Introduction	969
34.2	General Analysis	970
34.3	Crystalline Conformations of Disaccharide Moieties	973
34.3.1	The Disaccharides	973

34.3.2	The Analogs (S, C, N, ...)	985
34.4	Hydrogen Bonding in Crystalline Oligosaccharides	987
34.5	Packing Features	988
34.6	Selected Examples	990
34.7	Crystalline Conformations of Oligosaccharides Complexed with Lectins	992
34.8	Concluding Remarks	996
	References	998
35	Transfer NOE Experiments for the Study of Carbohydrate-Protein Interactions	1003
	<i>Thomas Peters</i>	
35.1	Introduction	1003
35.2	The Transfer NOE Experiment	1004
35.3	Measurement of trNOEs	1006
35.4	Bioactive Conformations of Carbohydrate Ligands From trNOE Experiments	1008
35.5	Spin Diffusion may Generate Misleading Distance Constraints	1009
35.6	The Conformation of Sialyl Lewis ^x Bound to E-selectin	1011
35.7	Interaction of Bacterial Lipopolysaccharide Fragments with Monoclonal Antibodies	1016
35.8	Conclusions and Future Directions	1019
	References	1021
36	Carbohydrate-Protein Interactions: Use of the Laser Photo Chemically Induced Dynamic Nuclear Polarization(CIDNP)-NMR Technique	1025
	<i>Hans-Christian Siebert and Johannes F. G. Vliegenthart</i>	
36.1	Introduction	1025
36.2	The CIDNP Method	1026
36.3	CIDNP-related Molecular Modelling	1027
36.4	Applications	1027
36.5	Hevein-like Lectins	1029
36.6	Galactoside-binding Lectins from Plant and Animal Origin	1032
36.7	Sialidase from <i>Clostridium Perfringens</i> (Wild Type and Mutants)	1037
36.8	CIDNP Analysis of Glycoproteins	1039
36.9	Conclusions	1040
	Acknowledgments	1041
	References	1042
37	Biacore	1045
	<i>Wolfgang Jäger</i>	
37.1	Introduction	1045
37.1.1	Real-time Analysis by Surface Plasmon Resonance	1045
37.1.2	Information in a Sensorgram	1047
37.2	Experimental Procedures	1048

37.2.1	Immobilization of Biomolecules at the Sensor Surface.....	1048
37.2.2	Surface Regeneration.....	1050
37.2.3	Interaction Analysis and Controls	1051
37.2.4	Determination of Kinetic Rate Constants	1052
37.2.5	Affinity Determination	1053
37.3	Application Areas	1054
37.3.1	Selectin Binding to a Glycoprotein Ligand	1054
37.3.2	Oligosaccharide Characterization	1055
37.3.3	<i>In situ</i> Modification of Immobilized Carbohydrates.....	1056
	References	1056
V	Carbohydrate–Carbohydrate Interactions	1059
38	Carbohydrate–Carbohydrate Interactions	1061
	<i>Dorothe Spillmann and Max M. Burger</i>	
38.1	Introduction	1061
38.2	From Structural Components to Cell Recognition.....	1063
38.2.1	Carbohydrate–Carbohydrate Interactions as Part of Structural Components	1063
	Extracellular Matrix of Seaweeds—Agarose, Carrageenan and Alginate.....	1063
	Cell Walls.....	1064
	Mammalian Extracellular Matrix Components	1066
38.2.2	Carbohydrate–Carbohydrate Interactions as Part of Recognition Keys?.....	1068
	Carbohydrate Interactions in Invertebrates—The Marine Sponge <i>Microciona prolifera</i> as a Model System.....	1069
	Carbohydrate Interactions in Vertebrates—Embryonal and Tumor Cells.....	1071
	Repulsive Carbohydrate–Carbohydrate Interactions.....	1072
38.3	Molecular Aspects of Carbohydrate Interactions.....	1074
38.3.1	Polyvalence to Inforce Weak Interactions	1074
38.3.2	Arrangement of Motifs and the Possibility to Control Specificity .	1075
38.3.3	Molecular Basis of Carbohydrate–Carbohydrate Interactions.....	1076
38.4	Experimental Approaches.....	1078
38.4.1	General Considerations	1078
38.4.2	Affinity Interactions	1079
	Cell Binding Studies	1079
	Aggregation of <i>de novo</i> Complexes	1081
	Affinity Chromatography	1082
	Distribution between Compartments	1082
38.4.3	Microscopy	1083
	Electron Microscopy	1083
	Atomic Force Microscopy	1083
38.4.4	Crystallography.....	1084

38.4.5	Mass Spectrometry	1085
38.4.6	Nuclear Magnetic Resonance	1085
38.4.7	Molecular Modelling	1086
38.4.8	Tools	1086
	Synthetic Oligosaccharides	1086
	Antibodies against Carbohydrate Motifs	1087
	Cells	1088
	References.....	1088

VI Carbohydrate–Nucleic Acid Interactions 1093

39 Carbohydrate–Nucleic Acid Interactions 1095

Heinz E. Moser

39.1	Introduction.....	1095
39.2	Carbohydrates Binding to DNA	1096
39.2.1	Ene-Diyne Antibiotics and Antitumor Agents.....	1096
	Esperamicins	1096
	Calicheamicins	1100
39.2.2	Anthracyclins	1106
39.2.3	Pluramycins and Aureolic Acids	1111
39.3	Carbohydrates Binding to RNA	1112
39.3.1	Aminoglycosides	1113
	References.....	1120

Index I 1

Part II Biology of Saccharides

Vol. 3 Biosynthesis and Degradation of Glycoconjugates

Introduction to Volumes 3 and 4..... V

Abbreviations Used in Volumes 3 and 4 LV

I Biosynthesis of Glycoconjugates 1

1 Metabolism of Sugars and Sugar Nucleotides 3

Hudson H. Freeze

1.1	Introduction.....	3
1.2	Basic Principles	3
1.3	Transporters Deliver Monosaccharides to Cells	4
1.4	Intracellular Sources of Sugars	5
1.4.1	Salvage	5

1.4.2	Activation and Interconversion of Monosaccharides.....	6
	Glycogen.....	6
	Glucose	7
	Glucuronic acid.....	8
	Iduronic acid.....	8
	Xylose.....	8
	Mannose	8
	Fucose	9
	Galactose	10
	<i>N</i> -Acetylglucosamine	10
	<i>N</i> -Acetylgalactosamine	10
	Sialic acids	11
1.5	Sugar Nucleotide Transporters.....	11
1.6	Control of Sugar Nucleotide Levels	13
1.7	Possible Future Directions	13
	References	14
2	Nucleotide Sugar Transporters	19
	<i>Rita Gerardy-Schahn and Matthias Eckhardt</i>	
2.1	Introduction	19
2.2	General Considerations	20
2.3	The Requirement for Nucleotide Sugar Transporters and Their Mechanism of Function: A Comprehensive Overview of the Last 20 Years	20
2.4	Molecular Cloning of Nucleotide Sugar Transporters	22
2.5	The Structure of Nucleotide Sugar Transporters	25
2.6	The Subcellular Distribution of Nucleotide Sugar Transporters.....	27
2.7	Molecular Defects that Cause Inactive UDP-Galactose and CMP-Sialic Acid Transporters	28
2.8	Association Between Defects in Nucleotide Sugar Transporters and Diseases.....	29
2.9	Involvement of Nucleotide Sugar Transporters in the Regulation of Glycosylation	29
2.10	Future Perspectives	30
	Acknowledgements	31
	References	32
3	Biosynthesis of Oligosaccharyl Dolichol.....	37
	<i>Sharon S. Krag</i>	
3.1	General Overview	37
3.2	Oligosaccharyl Dolichol.....	38
3.3	Key Enzymatic Steps in the Assembly Process	39
3.4	Topology of the Assembly Process.....	42
3.5	Utilization of Oligosaccharyl Dolichol	42
	Acknowledgment	43
	References	43

4	Biochemistry and Molecular Biology of the <i>N</i>-Oligosaccharyl-transferase Complex.....	45
	<i>Roland Knauer and Ludwig Lehle</i>	
4.1	Introduction.....	45
4.2	Biochemistry of OST	46
4.2.1	Lipid–Saccharide Donor	47
4.2.2	Acceptor Specificity of OST	48
4.2.3	Catalytic Mechanism of OST	49
4.2.4	Regulation of OST Activity	51
4.3	Isolation of OST Complexes from Different Sources	51
4.4	Molecular Biology of OST	52
4.4.1	WBP1/OST48.....	54
4.4.2	SWP1/Ribophorin II	54
4.4.3	OST1/Ribophorin I.....	55
4.4.4	OST3/OST6.....	55
4.4.5	OST5	56
4.4.6	OST4	56
4.4.7	OST2/DAD1.....	57
4.4.8	STT3	58
4.5	Structural Organization of the OST Complex	59
	Acknowledgments	60
	References.....	60
5	Processing Enzymes Involved in the Deglucosylation of <i>N</i>-Linked Oligosaccharides of Glycoproteins: Glucosidases I and II and Endomannosidase	65
	<i>Robert G. Spiro</i>	
5.1	Introduction.....	65
5.2	Glucosidase I.....	66
5.3	Glucosidase II.....	68
5.4	Endo- α -mannosidase.....	70
5.5	Concerted Action of Deglucosylation Enzymes.....	72
5.6	Mutants	74
5.7	Role of Monoglucosylated <i>N</i> -Linked Oligosaccharides and Glucose Trimming Enzymes in Regulating Quality Control of Glycoproteins	75
5.8	Effect of Glucosidase Inhibitors on Viral Proliferation.....	77
	Acknowledgments	78
	References.....	78
6	α-Mannosidases in Asparagine-linked Oligosaccharide Processing and Catabolism.....	81
	<i>Kelley W. Moremen</i>	
6.1	Overview	81
6.2	Introduction.....	82

6.2.1	Roles of <i>N</i> - and <i>O</i> -Linked Glycans and Compartmentalization of Biosynthetic and Catabolic Reactions	82
6.2.2	Processing of Asn-Linked Oligosaccharides	82
6.2.3	Early Trimming Events: importance for quality control glyco-protein degradation and anterograde transport	85
6.2.4	Glycoprotein Catabolism: multiple routes for glycoprotein breakdown	87
6.2.5	Consequences of Genetic Defects in Oligosaccharide Biosynthesis and Catabolism	88
6.3	Mannosidases in Glycoprotein Processing and Catabolism	89
6.3.1	Classification of Mannosidases	89
6.3.2	Class 1 Mannosidases: enzymes of the ER and Golgi	93
	ER mannosidase I subfamily	93
	Golgi mannosidase I sub-family	95
	Fungal secreted mannosidases	97
	New genes with unknown functions	98
6.3.3	Class 2 Mannosidases: enzymes of the cytosol, ER, Golgi, and Lysosomes	98
	Golgi mannosidase II	99
	Lysosomal mannosidase	101
	Epididymal/sperm mannosidase	103
	Heterogeneous cluster of mannosidase homologs among eukarya, eubacteria, and archaea	104
6.4	Conclusions and Future Prospects	106
	Acknowledgments	107
	References	107
7	The Role of UDP-Glycglycoprotein Glucosyltransferase as a Sensor of Glycoprotein Conformations	119
	<i>Armando J. Parodi</i>	
7.1	Introduction	119
7.2	General Properties	120
7.3	GT Recognizes Glycoprotein Conformations	121
7.4	The Primary Structure of the UDP-Glycglycoprotein Glucosyltransferase	122
7.5	The Role of Monoglucosylated Oligosaccharides in Glycoprotein Folding	123
	Acknowledgments	126
	References	127
8	Mannosyltransferases	129
	<i>Peter Orlean</i>	
8.1	Introduction	129
8.2	Occurrence of Covalently-linked Mannose	130

8.2.1	Eukaryotic Secretory Glycoproteins	130
8.2.2	Glycophospholipids.....	130
8.2.3	Eubacterial and Archaeal Mannose-containing Molecules.....	130
8.2.4	C-linked Mannose	130
8.3	Biochemistry of Mannosyl Transfer.....	131
8.3.1	Many Linkages, Two Donors	131
8.3.2	Donor Specificity	131
8.3.3	Acceptor Specificity.....	132
8.3.4	Structural Features of Man-T	132
8.4	Man-T Families and the Pathways They Participate in	133
8.4.1	Man-Ts of the ER [1–5]	134
	Alg1p.....	134
	Alg2p/Alg11p.....	134
	Dpm1p.....	135
	Alg3p.....	135
	Alg9p/PIG-Bp family.....	135
	Pmt1p family.....	136
8.4.2	Golgi Man-Ts and Fungal Mannan Synthesis.....	136
	Och1p family.....	137
	Mnn9p family.....	137
	Mnn10p/Mnn11p family	138
	Mnn1p family.....	138
	Ktr1p family	138
8.4.3	“Missing” Eukaryotic Man-T.....	138
8.4.4	Eubacterial and Archaeal Man-T	139
8.5	Coordinating Man Transfer with the Cell Cycle and Morphogenesis.....	139
8.6	Concluding Remarks	140
	Acknowledgments	140
	References.....	140
9	Branching of <i>N</i>-Glycans: <i>N</i>-Acetylglucosaminyltransferases	145
	<i>Harry Schachter</i>	
9.1	Introduction.....	145
9.2	Processing of <i>N</i> -Glycans within the Endomembrane Assembly Line	146
9.3	General Properties of the <i>N</i> -Acetylglucosaminyltransferases.....	148
9.3.1	Domain Structure.....	148
9.3.2	Targeting to the Golgi Apparatus.....	150
9.4	UDP-GlcNAc:Man α 1-3R [GlcNAc to Man α 1-3] β -1,2- <i>N</i> - Acetylglucosaminyltransferase I (GnT I, EC 2.4.1.101)	150
9.5	UDP-GlcNAc:Man α 1-6R [GlcNAc to Man α 1-6] β -1,2- <i>N</i> - Acetylglucosaminyltransferase II (GnT II, E.C. 2.4.1.143).....	152
9.6	The Role of GnT I and II in Mammalian Development	153

9.7	UDP-GlcNAc:R ₁ -Man α 1-6[GlcNAc β 1-2Man α 1-3]Man β 1-4R ₂ [GlcNAc to Man β 1-4] β -1,4- <i>N</i> -Acetylglucosaminyltransferase III (GnT III, E.C. 2.4.1.144).....	155
9.7.1	Overexpression of GnT III Activity.....	156
9.7.2	GnT III Activity and Cancer.....	157
9.8	UDP-GlcNAc:R ₁ Man α 1-3R ₂ [GlcNAc to Man α 1-3] β -1,4- <i>N</i> - Acetylglucosaminyltransferase IV (GnT IV, E.C. 2.4.1.145).....	157
9.9	UDP-GlcNAc:R ₁ Man α 1-6R ₂ [GlcNAc to Man α 1-6] β -1,6- <i>N</i> - Acetylglucosaminyltransferase V (GnT V, E.C.2.4.1.155)	158
9.9.1	GnT V Activity and Cancer.....	159
9.10	UDP-GlcNAc:R ₁ (R ₂)Man α 1-6R ₃ [GlcNAc to Man α 1-6] β -1,4- <i>N</i> -Acetylglucosaminyltransferase VI (GnT VI)	161
9.11	GnT VII and GnT VIII	161
	References	162
10	The Galactosyltransferases	175
	<i>Nancy L. Shaper, Martin Charron, Neng-Wen Lo, Jane R. Scoocca, and Joel H. Shaper</i>	
10.1	Introduction	175
10.2	Using the Databanks to Obtain Information on the Galactosyltransferases	177
10.2.1	Nomenclature.....	177
10.3	The Dual Role of β 4-Galactosyltransferase-I (β 4GalT-I) in Oligosaccharide and Lactose Biosynthesis: The Early Days	178
10.3.1	β 4GalT-I: Isolation and Characterization of cDNA Clones	181
10.3.2	The Murine β 4GalT-I Gene: Genomic Organization and Structure of the 5'-End.....	181
10.3.3	β 4GalT-I and Lactose Biosynthesis	182
10.3.4	β 4GalT-I and the Vertebrate β 4GalT Gene Family	182
10.3.5	Evolution of the β 4-Galactosyltransferase Gene Family	184
10.4	The Vertebrate β 3Galactosyltransferase (β 3GalT) Gene Family ..	185
10.4.1	General Characteristics of the β 3-Galactosyltransferase Gene Family Members	186
10.4.2	β 3GalT-IV: UDP-galactose:GM1 β 3-galactosyltransferase (GM1 Synthase; GalT-3)	187
10.4.3	Other Vertebrate β -Galactosyltransferase Activities.....	187
10.4.4	UDP-Galactose:Ceramide β -Galactosyltransferase (CGalT; EC 2.4.1.45).....	187
10.5	The Vertebrate α 3-Galactosyltransferase Gene Family	188
10.5.1	α 3-Galactosyltransferase (α 3GalT: UDP-Gal:Gal β 4GlcNAc α 3- Galactosyltransferase; EC 2.4.1.87)	188
10.5.2	The Blood Group B α 3-Galactosyltransferase (EC 2.4.1.37).....	190
10.5.3	The Forssman Glycolipid Synthetase (EC 2.4.1.88).....	191
10.5.4	Evolution of the α 3GalT Gene Family	191

10.6	A UDP-Gal:Gal β 3GalNAc α 4Galactosyltransferase Activity	192
	Acknowledgments	192
	References.....	192
11	Fucosyltransferases	197
	<i>Ernesto T. A. Marques, Jr.</i>	
11.1	Introduction.....	197
11.2	General Characteristics	198
11.2.1	Nomenclature	198
11.2.2	Gene Structure	199
11.2.3	Sequence Peptide Motifs.....	199
11.2.4	Specificity	199
11.2.5	Protein Structure and Topology.....	200
11.2.6	Enzymatic Reaction Mechanism	201
11.2.7	Inhibitors.....	203
11.3	Specific Fucosyltransferases	203
11.3.1	GDP-Fucose: Fucal(Fuca1,2Fuc) α 2-fucosyltransferase.....	204
11.3.2	GDP-Fucose: Gal β 1(Fuca1,2Gal) α 2-fucosyltransferase.....	204
11.3.3	GDP-Fucose: Gal β 1,4/3GlcNAc(Fuca1,3/4GlcNAc) α 3/4-fucosyltransferases	204
	Blood group Lewis: FucT III, V and VI.....	204
	Myeloid enzyme: FucT IV.....	205
	Leukocyte enzyme: FucT VII	206
	Neuronal enzyme: FucT IX	206
11.3.4	GDP-Fucose: Gal β 1,3GlcNAc(Fuca1,3GlcNAc) bacterial (<i>Helicobacter pylori</i>) α 3-fucosyltransferase	207
11.3.5	GDP-Fucose: GlcNAc-N(Fuca1,6GlcNAc) α 6fucosyltransferases ..	207
11.3.6	GDP-Fucose: O-Ser(Fuca1-O-Ser)GlcNAc polypeptide fucosyltransferases	207
11.3.7	Unconventional Types of Fucosylation: Fuc β 1-P-Ser and cytoplasmic Fucal,2-Gal β 1,3-GlcNAc-Pro (<i>Dictyostelium discoideum</i>)	207
	Fuc β 1-P-Ser	207
	Fuca1,2-Gal β 1,3-GlcNAc-Pro	208
	Acknowledgments	208
	References.....	208
12	Sialyltransferases	213
	<i>Joseph T. Y. Lau and Sherry A. Wuensch</i>	
12.1	Introduction.....	213
12.2	General Features of Sialyltransferases	213
12.3	Cloning and Identification Strategies for Sialyltransferases	215
12.4	Sialyltransferase Classification and Nomenclature.....	216
12.5	The α 2,3-ST Family	216
12.6	The α 2,6-ST Family	217
12.7	The α 2,8-ST Family	218

12.8	Regulation and Functionality of Sialyltransferases.....	219
	References	221
13	Biochemistry of Sialic Acid Diversity	227
	<i>Roland Schauer</i>	
13.1	Introduction	227
13.2	Occurrence and Biosynthesis	227
13.3	General Biological Functions	229
13.4	<i>N</i> -Glycolylneuraminic Acid	231
13.5	<i>O</i> -Acetylated Sialic Acids	234
13.6	<i>O</i> -Methylated and <i>O</i> -Sulfated Sialic Acids	238
	Acknowledgments	239
	References	239
14	Carbohydrate Sulfotransferases	245
	<i>Steven D. Rosen, Annette Bistrup, and Stefan Hemmerich</i>	
14.1	Introduction	245
14.2	Basic Features of Sulfotransferase Reactions.....	245
14.3	Tyrosine Sulfation	246
14.4	Diversity of Carbohydrate Sulfation.....	246
14.5	Biochemical Demonstration of Carbohydrate Sulfotransferases ...	249
14.6	Molecular Cloning of Carbohydrate Sulfotransferases.....	250
14.7	Primary Structures of Carbohydrate Sulfotransferases.....	252
	Acknowledgments	256
	References	256
15	Novel Variant Pathways in Complex-type Oligosaccharide Synthesis	261
	<i>Dirk H. van den Eijnden</i>	
15.1	Introduction	261
15.2	The lacNAc Pathway of Complex-type Oligosaccharide Synthesis	261
15.3	Occurrence and Biology of lacdiNAc-based Complex-type Oligosaccharides.....	262
15.4	Biosynthesis of lacdiNAc Backbone Units.....	263
15.5	The lacdiNAc Pathway of Complex-type Oligosaccharide Synthesis	264
15.6	Other Shared Properties of β 4-GalT and β 4-GalNAcT	266
15.7	Cloning of a snail UDP-GlcNAc:GlcNAc β -R β 4- <i>N</i> -acetylglucosaminyltransferase	266
15.8	The Chitobio Pathway of Complex-type Oligosaccharide Synthesis	267
15.9	Competition Between Pathways.....	267
15.10	Concluding Remarks	269
	References	269

16	Control of Mucin-Type <i>O</i>-Glycosylation: <i>O</i>-Glycan Occupancy is Directed by Substrate Specificities of Polypeptide GalNAc-Transferases	273
	<i>Helle Hassan, Eric P. Bennett, Ulla Mandel, Michael A. Hollingsworth, and Henrik Clausen</i>	
16.1	Introduction.....	273
16.2	The Mammalian UDP-GalNAc: Polypeptide GalNAc-Transferase Gene Family	274
16.3	The GalNAc-Transferase Gene Family is Evolutionarily Old	276
16.4	The Kinetic Properties of GalNAc-Transferase Isoforms are Different.....	278
16.4.1	Lessons from in vivo Analysis of GalNAc-transferase Substrate Specificities.....	279
16.4.2	Lessons from in vitro Analysis of the Acceptor Substrate Specificities of GalNAc-transferase Isoforms	280
	Isoforms may have distinct acceptor substrate specificities	281
	Isoforms may have overlapping substrate specificities.....	283
	Isoforms may act in different order on substrates with multiple acceptor sites.....	283
	Isoforms may require prior (GalNAc) glycosylation	283
16.5	Expression of the GalNAc-Transferase Genes are Differentially Regulated	285
16.6	Predictive Value of in vitro <i>O</i> -glycosylation?	288
16.7	Conclusions and Future Perspectives.....	288
	References.....	289
17	Glycosyltransferase Inhibitors	293
	<i>Xiangping Qian and Monica M. Palcic</i>	
17.1	Introduction.....	293
17.2	Inhibitors of Glycosyltransferases.....	296
17.2.1	Inhibitors of Galactosyltransferases.....	296
	Inhibitors of β 1,4-galactosyltransferase	296
	Inhibitors of α 1,3-galactosyltransferase	297
17.2.2	Inhibitors of Fucosyltransferases	298
	Inhibitors of α 1,2-fucosyltransferases	300
	Inhibitors of α 1,3-fucosyltransferases	300
17.2.3	Inhibitors of Sialyltransferases	301
	Inhibitors of α 2,6-sialyltransferase	302
	Inhibitors of α 2,3-sialyltransferase	304
17.2.4	Inhibitors of <i>N</i> -Acetylglucosaminyltransferases	305
17.2.5	Inhibitors of Human Blood Group A and B Glycosyltransferases	306
17.3	Summary	309
	Acknowledgments	309
	References.....	309

18	Biosynthesis of the <i>O</i>-Glycan Chains of Mucins and Mucin Type Glycoproteins	313
	<i>Inka Brockhausen</i>	
18.1	Summary.....	313
18.2	Introduction	313
18.3	Structures of <i>O</i> -Glycans.....	314
18.4	Functions of Mucin Type <i>O</i> -Glycans.....	314
18.5	Primary <i>O</i> -Glycosylation.....	315
18.6	Synthesis of <i>O</i> -Glycan Core 1.....	315
18.7	Synthesis of <i>O</i> -Glycan Core 2.....	317
18.8	Synthesis of <i>O</i> -Glycan Core 3.....	319
18.9	Synthesis of <i>O</i> -Glycan Core 4.....	319
18.10	Synthesis of <i>O</i> -Glycan Cores 5–8	319
18.11	Elongation and Branching Reactions.....	320
18.12	Synthesis of Terminal Structures.....	321
	Acknowledgments	324
	References	324
19	Glycosyltransferases in Glycosphingolipid Biosynthesis	329
	<i>Subhash Basu, Kamal Das, and Manju Basu</i>	
19.1	Introduction	329
19.2	Fucosyltransferases in Glycolipid Biosynthesis	329
19.3	Galactosyltransferases in Glycolipid Biosynthesis	332
19.4	<i>N</i> -Acetylgalactosaminyltransferases in Glycolipid Biosynthesis....	334
19.5	<i>N</i> -Acetylglucosaminyltransferases in Glycolipid Biosynthesis.....	336
19.6	Sialyltransferases in Glycolipid Biosynthesis	337
19.7	Glucuronyltransferases in Glycolipid Biosynthesis	340
	Acknowledgments	342
	References	342
20	Biosynthesis of Glycogen	349
	<i>Peter J. Roach</i>	
20.1	Summary.....	349
20.2	Introduction	350
20.3	Glycogenin and the Initiation of Glycogen Synthesis	351
20.3.1	History	351
20.3.2	Properties	351
20.3.3	Reaction Mechanism	352
20.3.4	Domain Structure	352
20.3.5	Function	354
20.4	Glycogen Synthase and the Bulk Synthesis of Glycogen.....	354
20.4.1	Properties	354
20.4.2	Structure of Glycogen Synthase.....	355
20.4.3	Branching Enzyme	356
20.5	Intermediates in the Biosynthesis of Glycogen	357

20.6	Conclusion	358
	Acknowledgments	359
	References.....	359
21	Biosynthesis of Hyaluronan	363
	<i>Paraskevi Heldin and Torvard C. Laurent</i>	
21.1	Introduction.....	363
21.2	Site of Biosynthesis	364
21.3	Biosynthetic Precursors	364
21.4	Hyaluronan Synthases	365
21.4.1	Microbial Enzymes	365
21.4.2	Vertebrate Synthases.....	366
21.5	Mechanism of Synthesis	367
21.5.1	Chain Elongation	368
21.5.2	Translocation	369
21.5.3	Shedding	369
21.6	Regulation of HA Synthesis	370
21.7	Concluding Remarks	371
	Acknowledgments	372
	References.....	372
22	Biosynthesis of Chondroitin Sulfate and Dermatan Sulfate	
	Proteoglycans	375
	<i>Geetha Sugumaran and Barbara M. Vertel</i>	
22.1	Introduction.....	375
22.2	Proteoglycan Structure	379
22.2.1	Proteoglycans and Their Core Proteins	379
22.2.2	What Initiates GAG Chain Addition?	381
22.2.3	The Linkage Region	381
22.2.4	CS and DS Chains	382
22.3	Biosynthesis of CS and DS Proteoglycans	383
22.3.1	Biosynthesis of the Core Protein	383
22.3.2	Origin of Sugar and Sulfate Precursors	384
22.3.3	Addition of the Linkage Oligosaccharides	385
	Xylosylation.....	385
	Galactosylation	386
	Addition of GlcA and completion of the common tetrasaccharide linkage region	387
	Initiation of CS/DS chains by addition of the first GalNAc	388
22.3.4	Formation of the CS/DS Chains	388
	Addition of the repeating disaccharides.....	388
	Epimerization of GlcA to IdoA to form DS.....	389
	Sulfation of GalNAc.....	390
	Sulfation of uronic acid.....	391

22.4	Concluding Remarks/Perspectives	391
	Acknowledgments	392
	References	392
23	Biosynthesis of Heparin and Heparan Sulfate Proteoglycans	395
	<i>Lena Kjellén and Ulf Lindahl</i>	
23.1	Introduction	395
23.2	The Proteoglycans: Structure, Location and Functions	396
23.3	Biosynthesis of the Polysaccharide Backbone	396
23.4	Outline of Polymer-Modification Reactions	397
23.4.1	The <i>N</i> -Deacetylase/ <i>N</i> -Sulfotransferases	399
23.4.2	The C5-Epimerase	399
23.4.3	The 2- <i>O</i> -Sulfotransferase	399
23.4.4	The 6- <i>O</i> -Sulfotransferases	400
23.4.5	The 3- <i>O</i> Sulfotransferases	400
23.5	The Products, Heparin and Heparan Sulfate	400
23.6	Interactions with Proteins	401
23.7	Regulation of HS Biosynthesis	402
	References	403
24	Biosynthesis of Proteoglycans with Keratan Sulfates	407
	<i>James L. Funderburgh</i>	
24.1	Introduction: Keratan Sulfate Renaissance	407
24.2	Keratan Sulfate Structure and Distribution	407
24.2.1	Corneal KS	408
24.2.2	Non-corneal KSI	409
24.2.3	KSII	409
24.2.4	KSIII	410
24.3	Keratan Sulfate Proteoglycans	410
24.3.1	SLRPs	410
24.3.2	Aggrecan	411
24.3.3	Cell-Associated KS	411
24.3.4	Brain	412
24.4	Enzymatic Reactions of KS Biosynthesis	412
24.5	Metabolic Control of KS Synthesis	413
	Acknowledgments	414
	References	414
25	The Biosynthesis of GPI Anchors	417
	<i>Yasu S. Morita, Alvaro Acosta-Serrano, and Paul T. Englund</i>	
25.1	Introduction	417
25.2	Structure of GPI Anchors	417
25.2.1	Glycan Core Modifications	417

25.2.2	Variations in Anchor Lipid Structure	419
25.3	GPI Precursor Synthesis	419
25.3.1	GlcNAc-PI Synthesis	420
25.3.2	GlcNAc-PI Deacetylation	421
25.3.3	Inositol Acylation.....	421
25.3.4	GPI Mannosylation.....	422
25.3.5	Transfer of EtN-P	423
25.3.6	Lipid Remodeling.....	423
25.3.7	Addition of Carbohydrate Side Chains	424
25.3.8	Topology of Biosynthetic Pathways.....	424
25.4	Attachment of the GPI Precursor to a Protein	425
25.4.1	Basic Features	425
25.4.2	Protein Machinery for GPI Addition	426
25.4.3	Signal Sequence for GPI Addition	426
25.5	Evolution of GPI Biosynthesis	426
25.6	Future Studies	427
	Acknowledgments	427
	References.....	427
26	<i>Escherichia coli</i> Lipid A: A Potent Activator of Innate Immunity ...	435
	<i>Teresa A. Garrett and Christian R. H. Raetz</i>	
26.1	Introduction.....	435
26.2	Structure of Lipopolysaccharide.....	435
26.3	Lipid A Biosynthesis in <i>E. coli</i>	437
26.3.1	Acylation of UDP-GlcNAc	439
26.3.2	Disaccharide Formation.....	440
26.3.3	Phosphorylation by the Lipid A 4' Kinase.....	440
26.3.4	Kdo Addition and the Late Acyltransferases	441
26.3.5	Other Acyltransferases.....	442
26.3.6	Transport of Lipid A and the Role of MsbA	442
26.4	Lipid A Activation of Signal Transduction in Animal Cells	444
26.5	Summary.....	447
	Acknowledgments	447
	References.....	447
II	Glycosidases.....	453
27	Lysosomal Degradation of Glycolipids.....	455
	<i>Thomas Kolter and Konrad Sandhoff</i>	
27.1	Summary.....	455
27.2	Introduction.....	455
27.3	Mechanisms of Lysosomal Glycolipid Degradation	456
27.3.1	Glycosidases	456

27.3.2	Topology of Endocytosis and Lysosomal Glycolipid Degradation	457
27.3.3	Sphingolipid Activator Proteins.....	458
	The GM2-activator and its role in lysosomal digestion	459
	SAP-A to SAP-D	460
27.3.4	Lateral Pressure.....	460
27.3.5	Lipid Composition	461
27.3.6	Membrane Curvature	462
27.4	Degradation of Selected Lipids	462
27.4.1	Ganglioside GM2	462
27.4.2	Lactosylceramide	464
27.4.3	Glucosylceramide.....	464
27.4.4	Ceramide.....	465
27.4.5	Sphingomyelin.....	465
27.4.6	Sulfatide	465
27.4.7	Galactosylceramide.....	466
27.5	Pathobiochemistry	466
27.5.1	Animal Models for Sphingolipidoses	467
27.5.2	Therapy	469
27.6	Future Directions.....	470
	References	470
28	Lysosomal Degradation of Glycoproteins	473
	<i>Nathan N. Aronson, Jr.</i>	
28.1	Summary.....	473
28.2	Introduction	473
28.3	Roles of Lysosomes	474
28.4	Lysosomal Degradation of <i>N</i> -Linked Glycoproteins.....	475
28.4.1	General Features	475
28.4.2	Carbohydrate Digestion	476
28.4.3	Protein and Linkage Hydrolysis	476
28.5	Formation of Thyroid Hormone via Lysosomal Degradation of Thyroglobulin	477
28.5.1	Synthesis of Thyroid Hormone	477
28.5.2	Carbohydrate Degradation.....	478
28.5.3	Proteolysis	479
28.6	Degradation of Free Polymannose-Type Oligosaccharides Derived from <i>N</i> -Linked Glycoproteins During Biosynthesis	479
	References	481
29	Sialidases.....	485
	<i>Garry Taylor, Susan Crennell, Carl Thompson, and Marina Chuenkova</i>	
29.1	Abstract.....	485
29.2	Introduction	485

29.3	Influenza Virus Neuraminidase.....	486
29.4	Paramyxovirus Hemagglutinin-Neuraminidase (HN)	487
29.5	Non-Viral Sialidases	487
29.6	Small Sialidases	490
29.7	Large Sialidases	491
29.8	<i>T. cruzi</i> Trans-Sialidase (TS)	491
29.9	Conclusion	493
	Acknowledgments	494
	References.....	494
30	Microbial Glycosidases.....	497
	<i>Kenji Yamamoto, Su-Chen Li, and Yu-Teh Li</i>	
30.1	Exo-Glycosidases	497
30.1.1	α -Glucosidase	497
30.1.2	β -Glucosidase	498
30.1.3	α -Galactosidase	498
30.1.4	β -Galactosidase	499
30.1.5	α -Mannosidase.....	500
30.1.6	β -Mannosidase.....	500
30.1.7	β - <i>N</i> -Acetylhexosaminidase	501
30.1.8	α - <i>N</i> -Acetylgalactosaminidase.....	501
30.1.9	α -L-Fucosidase	502
30.1.10	β -D-Fucosidase.....	503
30.1.11	Sialidase.....	503
30.1.12	KDNase.....	504
30.1.13	α -L-Rhamnosidase	504
30.1.14	β -Xylosidase	505
30.2	Endo-Glycosidases.....	505
30.2.1	Endo- β - <i>N</i> -acetylglucosaminidase.....	505
30.2.2	Peptide-N-glycanase F.....	506
30.2.3	Endo- α - <i>N</i> -acetylgalactosaminidase.....	506
30.2.4	Endo- β -galactosidase	507
30.2.5	Endoglycoceramidase.....	507
	References.....	508
31	Glycoprotein Processing Inhibitors.....	513
	<i>Magid Osseer and Alan D. Elbein</i>	
31.1	Introduction.....	513
31.2	Structural Classification	515
31.3	Distribution of Glycosidase Inhibitors in the Plant Kingdom.....	515
31.4	Isolation and Structural Determination	516
31.5	Glycosidase Inhibitory Activity	517
31.6	Structure-Activity Relationships	518
31.7	<i>N</i> -Linked Oligosaccharide Processing.....	519
31.8	Inhibitors of <i>N</i> -Linked Oligosaccharide Processing.....	522

31.8.1	Glucosidase Inhibitors.....	522
31.8.2	Mannosidase Inhibitors	525
31.9	Summary and Future Prospects.....	528
	References	529

Index	I I
--------------------	------------

Part II Biology of Saccharides

Vol. 4 Lectins and Saccharides Biology

III	Lectins	533
32	Plant Lectins.....	535
	<i>Marilynn E. Etzler</i>	
32.1	Summary.....	535
32.2	Introduction	535
32.3	Carbohydrate Specificity	536
32.4	Other Activities.....	539
32.5	Structure	540
32.6	Biological Roles	543
	Acknowledgments	546
	References	547
33	Interactions of Oligosaccharides and Glycopeptides with Hepatic Carbohydrate Receptors	549
	<i>Yuan C. Lee and Reiko T. Lee</i>	
33.1	Summary.....	549
33.2	Introduction	550
33.3	Molecular Characteristics of Hepatic Lectins	551
33.4	Cellular Aspects of HL.....	552
33.5	Binding Specificity	553
33.6	Photoaffinity Labeling.....	557
33.7	Subunit Organization on Rat Hepatocyte Surface	558
33.8	Applications	559
	References	560
34	P-Type Lectins and Lysosomal Enzyme Trafficking	563
	<i>Patricia G. Marron-Terada and Nancy M. Dahms</i>	
34.1	Introduction	563
34.2	Intracellular Trafficking of the MPRs	564
34.3	Primary Structure and Biosynthesis of the MPRs	566

34.3.1	CI-MPR.....	566
34.3.2	CD-MPR.....	567
34.4	Lysosomal Enzyme Recognition by the MPRs.....	569
34.5	Structural Determinants of Man-6-P Recognition.....	571
34.5.1	Expression of Mutant Forms of the MPRs.....	571
34.5.2	Crystal Structure of the CD-MPR.....	572
34.6	Conclusions.....	574
	Acknowledgments.....	574
	References.....	575
35	The Siglec Family of I-Type Lectins.....	579
	<i>Paul R. Crocker and Soerge Kelm</i>	
35.1	Introduction.....	579
35.2	The Immunoglobulin Superfamily and Carbohydrate Recognition.....	579
35.3	Siglecs as a Family of Sialic Acid Binding Proteins.....	580
35.4	Biology of Siglecs.....	581
35.5	Sialic Acids in Cellular Recognition.....	583
35.6	Mode of Carbohydrate Recognition by Siglecs.....	584
35.7	Importance of Multivalent Binding.....	588
35.8	Sialic Acid Recognition by the Immunoglobulin Fold— Evolutionary Considerations.....	588
35.9	Role of <i>eis</i> Interactions in Modulating Adhesion to Other Cells in <i>trans</i>	589
35.10	Sialoadhesin as a Macrophage Adhesion Molecule.....	590
35.11	Signalling Versus Adhesion Mediated by Siglecs.....	591
35.12	Conclusions.....	592
	Acknowledgments.....	592
	References.....	592
36	C-Type Lectins and Collectins.....	597
	<i>Russell Wallis</i>	
36.1	Summary.....	597
36.2	Structure and Function of C-Type Animal Lectins.....	598
36.2.1	The Carbohydrate-Recognition Domain.....	599
36.2.2	Ligand Binding.....	600
36.3	Mannose-Binding Protein and Collectins.....	601
36.3.1	Domain Organization.....	601
36.3.2	MBPs as Prototype Collectins.....	603
36.3.3	Ligand Binding by Serum MBP.....	603
36.3.4	MBP and Innate Immunity.....	604
36.3.5	Liver MBP.....	607
36.3.6	Pulmonary Surfactant Proteins.....	608
36.3.7	Conglutinin and CL-43.....	608
36.4	Conclusions.....	609

	Acknowledgments	609
	References	609
37	Selectins	613
	<i>Rodger P. McEver</i>	
37.1	Introduction	613
37.2	Structure of Selectins	613
37.3	Selectin Ligands	614
37.4	Requirements for Selectins to Mediate Tethering and Rolling of Leukocytes under Hydrodynamic Flow	619
37.5	Functions of Selectins and their Ligands in vivo	621
37.6	Conclusions	621
	References	622
38	Galectins	625
	<i>Douglas N.W. Cooper and Samuel H. Barondes</i>	
38.1	Introduction	625
38.2	Galectin Structure	626
38.3	Novel Candidate Galectins.....	631
38.4	Unorthodox Subcellular Targeting.....	635
38.5	Regulation of Galectin Expression.....	637
38.6	Galectin Binding Specificity and Identified Ligands.....	639
38.7	Physiological Functions	640
38.8	Summary.....	642
	References	642
IV	Saccharide Biology	649
39	Structures and Functions of Nuclear and Cytoplasmic Glycoproteins	651
	<i>Robert S. Haltiwanger</i>	
39.1	Introduction	651
39.2	O-Linked <i>N</i> -Acetylglucosamine (O-GlcNAc).....	652
39.2.1	O-GlcNAc Appears to be a Regulatory Modification much like Phosphorylation	653
39.2.2	Modulation of Protein Stability and Function by O-GlcNAc	655
39.3	Other Forms of Nuclear and Cytoplasmic Glycosylation.....	658
39.3.1	Unique Cytoplasmic Forms of Glycosylation	658
39.3.2	Conventional Forms of Glycosylation in the Nucleus and Cytoplasm	660
39.3.3	Nuclear and Cytoplasmic Lectins.....	661
39.4	Conclusions.....	662
	Acknowledgments	662
	References	662

40	Structure and Functions of Mucins	669
	<i>Joyce Taylor-Papadimitriou and Joy M. Burchell</i>	
40.1	Classification of Mucins	669
40.2	The Epithelial Mucins	670
40.3	Mucin Type <i>O</i> -Glycosylation Pathways	670
40.3.1	Initiation of <i>O</i> -Glycosylation.....	671
40.3.2	Chain Extension	671
40.3.3	Chain Termination.....	671
40.4	Expression of Epithelial Mucins.....	672
40.5	The Complex Gel-Forming Mucins: Processing and Function.....	672
40.6	Epithelial Membrane Mucins	674
40.7	Studies Related to the MUC1 Mucin	675
40.7.1	Changes in the Patterns of <i>O</i> -Glycosylation of MUC1 in Breast Cancer.....	675
	Differences in sites of glycosylation	675
	Changes in the composition of <i>O</i> -glycans added to MUC1 in Breast Cancer	676
	Correlation in changes of Glycosyltransferase activities with changes in <i>O</i> -glycan structure in Breast Cancer	676
40.7.2	Changes in Glycosylation of MUC1 in other Cancers	677
40.7.3	Effects of MUC1 Expression on the Behavioral Properties of Cancer Cells.....	677
	Effects on cell interactions and tumourogenicity.....	677
40.7.4	MUC1 Expression and Immune Responses.....	678
40.7.5	Active Specific Immunotherapy Based on MUC1	679
	Animal models.....	679
	Clinical studies.....	680
40.8	Comments.....	681
	References.....	681
 41	 Biological Roles of Hyaluronan	 685
	<i>Bryan P. Toole</i>	
41.1	Introduction.....	685
41.2	Hyaluronan is a Biopolymer with Unusual Physical Properties....	685
41.3	Hyaluronan Binds to Several Types of Proteins (Hyaladherins) ...	687
41.3.1	General Properties of Hyaladherins.....	687
41.3.2	Structural Hyaluronan-Binding Proteins.....	688
41.3.3	Hyaluronan Receptors.....	688
41.3.4	Intracellular Hyaluronan-Binding Proteins	689
41.3.5	Inter- α -Trypsin Inhibitor	689
41.4	Hyaluronan-Dependent Pericellular Matrices Assemble Around Several Cell Types	690
41.4.1	Hyaluronan-Dependent Cellular "Coats"	690
41.4.2	Assembly of Chondrocyte Pericellular Matrix	691

41.4.3	Tethering of Cell Surface Hyaluronan to Hyaluronan Synthase...	691
41.5	Hyaluronan Influences Cell Behavior During Morphogenesis and Tissue Remodeling	693
41.5.1	Migratory and Proliferating Cells are Surrounded by Hyaluronan-enriched Matrices.....	693
41.5.2	Hydrated Pericellular Milieux Provide Cellular Pathways	693
41.5.3	Receptors Mediate Effects of Hyaluronan.....	693
41.5.4	Hyaluronan-Cell Interactions in Limb Development.....	694
41.5.5	Hyaluronan-Cell Interactions in Other Physiological and Developmental Systems	695
41.6	Hyaluronan Plays a Crucial Role in Cancer.....	696
	References	696
42	Biological Roles of Heparan Sulfate Proteoglycans.....	701
	<i>Ofer Reizes, Pyong Woo Park, and Merton Bernfield</i>	
42.1	Introduction	701
42.2	Heparan Sulfate Biosynthesis	701
42.3	Functions of Heparan Sulfate.....	702
42.4	Proteoglycans.....	703
42.5	Intracellular Proteoglycans.....	703
42.5.1	Serglycin and Heparin.....	704
42.6	Cell Surface Heparan Sulfate Proteoglycans.....	705
42.6.1	Syndecans.....	705
42.6.2	Glypicans	706
42.7	Part-time Cell Surface Heparan Sulfate Proteoglycans.....	707
42.7.1	Betaglycan	707
42.7.2	CD44.....	708
42.8	Functions of Cell Surface Heparan Sulfate Proteoglycans	708
42.8.1	Ligand Receptors.....	708
42.8.2	Ligand Coreceptors.....	709
42.8.3	Shed Effectors	709
42.9	Extracellular Matrix Heparan Sulfate Proteoglycans and Their Functions	710
42.9.1	Perlecan.....	710
42.9.2	Agrin.....	712
42.9.3	Other Extracellular HSPGs	713
42.10	Conclusions.....	713
	References	713
43	Biological Roles of Keratan Sulfate Proteoglycans.....	717
	<i>Gary W. Conrad</i>	
43.1	Introduction	717
43.2	Corneal Transparency	718

43.3	Nerve Growth Cone Guidance.....	719
43.4	Cell Adhesion.....	721
43.5	Other Possible Roles of KSPGs.....	722
	Acknowledgment	723
	References.....	723
44	Developmental and Aging Changes of Chondroitin/Dermatan Sulfate Proteoglycans	729
	<i>J. Michael Sorrell, David A. Carrino, and Arnold I. Caplan</i>	
44.1	Proteoglycans	729
44.2	Glycosaminoglycans	729
44.3	Core Proteins	731
44.3.1	Hyalectans	731
44.3.2	Small Leucine-rich Proteoglycans	733
44.4	Chondroitin/Dermatan Sulfate Proteoglycans in Development and Aging.....	735
44.4.1	Core Proteins in Development, Aging, and Pathologies.....	735
44.4.2	Chondroitin/Dermatan Sulfate Glycosaminoglycan Chains in Development, Aging, and Pathologies	736
44.5	Summary	740
	References.....	740
45	Proteoglycans and Hyaluronan in Vascular Disease.....	743
	<i>Thomas N. Wight</i>	
45.1	Introduction.....	743
45.2	Proteoglycans and Hyaluronan.....	744
45.3	Versican (CSPGs).....	745
45.4	Hyaluronan	747
45.5	Decorin/Biglycan (DSPGs).....	748
45.6	Perlecan/Syndecans (HSPGs).....	749
45.7	Summary	750
	Acknowledgments	750
	References.....	750
46	Functions of Glycosyl Phosphatidylinositols	757
	<i>Nikola A. Baumann, Anant K. Menon, and David M. Rancour</i>	
46.1	Introduction.....	757
46.2	Parasite Coats: Extreme GPI-Anchoring.....	758
46.3	Yeast GPIs and the Cell Wall.....	758
46.4	Paroxysmal Nocturnal Hemoglobinuria (PNH): Disease and Defects in GPI-Anchoring of Proteins	759
46.5	GPIs in the Secretory and Endocytic Pathways.....	760
46.6	Organization of GPI Proteins in the Plasma Membrane	762

46.7	Association of GPI-Anchored Proteins with Caveolae.....	764
46.8	Detergent Insolubility and Signaling via GPI-Proteins.....	764
46.9	Membrane Release of GPI-Anchored Proteins.....	765
46.10	GPIs as Second Messenger Signaling Molecules.....	766
46.11	Summary.....	767
	Acknowledgments.....	767
	References.....	768
 47	 Glycosphingolipid Microdomains in Signal Transduction, Cancer, and Development	 771
	<i>Sen-itiroh Hakomori and Kazuko Handa</i>	
47.1	Clustered GSLs as Functional Units.....	771
47.2	GSL Clusters, Associated with Signal Transducers, are Functional Units Separable from Caveolae.....	772
47.3	Cell Adhesion Coupled with Signal Transduction Initiated by GSL Microdomain: Concept of Glycosignaling Domain (GSD).....	773
47.4	Role of GSLs in Control of Growth Factor and Hormone Receptors: Possible Relationship with GSL Microdomain.....	774
47.5	Functional Role of Developmentally-Regulated and Tumor-Associated GSLs.....	776
	References.....	778
 48	 The Primary Cell Walls of Higher Plants	 783
	<i>Jocelyn K. C. Rose, Malcolm A. O'Neill, Peter Albersheim, and Alan Darvill</i>	
48.1	Introduction (What is a Cell Wall?).....	783
48.2	Purification of Cell Walls and Isolation of Wall Components.....	784
48.3	The Structural Components of the Primary Cell Wall.....	786
48.3.1	Cell Walls and the Diversity of Flowering Plants.....	786
48.3.2	The Structural Components of the Primary Wall.....	786
48.4	Biosynthesis of Wall Components.....	791
48.5	Organization of the Plant Primary Cell Wall.....	793
48.6	Cellulose-Xyloglucan Interactions.....	793
48.7	Interactions Between Pectins and Other Cell Wall Components... ..	794
48.8	Glycoproteins in the Cell Wall.....	796
48.9	Heterogeneity in the Primary Cell Wall.....	797
48.10	Function and Metabolism of Plant Primary Cell Walls.....	798
48.10.1	Mechanical Support.....	798
48.10.2	Regulation of Cell Expansion.....	798
48.10.3	Morphogenesis and Differentiation.....	800
48.10.4	Plant Cell Wall Oligosaccharides in Defense and Cell Signalling..	801
48.11	Intercellular Transport and Storage.....	803
48.12	Biotechnology and Future Directions in the Commercial Applications of Plant Primary Cell Walls.....	803

	Acknowledgment	804
	References.....	804
49	Glycolipids and Bacterial Pathogenesis	809
	<i>Clifford A. Lingwood</i>	
49.1	Introduction.....	809
49.2	Modulation of Glycolipid Receptor Function	810
49.3	Stress Response and Glycolipid Receptors.....	812
49.4	Subcellular Gb ₃ Trafficking	813
49.5	Model for Lipid Sorting Based on Chain Length.....	815
49.6	Glycosphingolipids and Signal Transduction	815
	Acknowledgments	817
	References.....	817
50	Glycobiology of Viruses.....	821
	<i>Hildegard Geyer and Rudolf Geyer</i>	
50.1	Summary.....	821
50.2	General Aspects.....	821
50.2.1	Functions of Viral Surface Glycoproteins.....	825
50.2.2	Biosynthesis	826
50.2.3	Function of Carbohydrate Substituents.....	826
50.2.4	Oligosaccharide Diversity	827
50.3	Examples.....	830
50.3.1	Friend Murine Leukemia Virus Complex.....	830
50.3.2	Marburg Virus (MBGV)	832
50.3.3	Hepatitis B Virus (HBV)	833
	Acknowledgments	836
	References.....	836
51	The Glycobiology of Influenza Viruses.....	839
	<i>Stephen J. Stray and Gillian M. Air</i>	
51.1	Introduction.....	839
51.2	Receptor Binding Proteins: Influenza A HA _g and Influenza C HEF.....	840
51.2.1	Structure of Receptor Binding Domain and Mechanism of Sialic Acid Recognition.....	843
51.2.2	HEF Esterase Domain and Mechanism of Cleavage.....	844
51.3	Influenza NA _m (types A and B)	844
51.3.1	Mechanism of Sialic Acid Cleavage.....	845
51.4	Function of Viral Receptor Destroying Enzymes.....	847
	Acknowledgments	847
	References.....	848

52	Glycobiology of Aids.....	851
	<i>Ten Feizi</i>	
52.1	Abstract.....	851
52.2	Introduction	851
52.3	The Repertoire of <i>N</i> -Glycans on the Envelope Glycoprotein of HIV of Human Immunodeficiency Virus Produced in Different Cell Types.....	853
52.4	Evidence for the Occurrence of <i>O</i> -Glycans on the Envelope Glycoproteins of HIV-1 Produced in Certain Cell Lines.....	854
52.5	Oligosaccharides of gp 120 and gp 41 at <i>N</i> -Glycosylation Sites and Their Possible Influence on Viral Infectivity	855
52.6	gp 120 Glycosylation Can Influence Antigenicity and Immunogenicity	856
52.7	Saccharides Recognized by Carbohydrate-binding Proteins and Antibodies as Potential Neutralization Epitopes on the Envelope Glycoprotein of HIV-1	857
52.7.1	Lectins and Antibodies with Mannose-related Specificities	857
52.7.2	Antibodies to <i>O</i> -Glycan Sequences	858
52.7.3	Antibodies to Blood Group A	858
52.7.4	Xeno-antibodies to Gal α 1-3Gal Sequence	859
52.7.5	Potential Medical Relevance	859
52.8	Does Viral Oligosaccharide Display Influence Tissue Tropism? ...	860
52.9	Concluding Remarks	862
	Acknowledgment	862
	References	863
 53	 Glycobiology of Protozoan and Helminthic Parasites.....	 867
	<i>Richard D. Cummings, and A. Kwame Nyame</i>	
53.1	Introduction	867
53.2	General Classification of Parasites.....	867
53.3	The Major Protozoan Parasites.....	868
53.3.1	Malaria	868
53.3.2	Trypanosomiasis.....	873
53.3.3	Leishmaniasis.....	874
53.4	Other Protozoan Parasites.....	878
53.4.1	<i>Entamoeba histolytica</i>	878
53.4.2	<i>Acanthamoeba</i>	878
53.4.3	<i>Giardia lamblia</i>	878
53.4.4	<i>Cryptosporidium parvum</i>	878
53.4.5	<i>Sarcocystis</i> spp.....	879
53.4.6	<i>Toxoplasma gondii</i>	879
53.4.7	<i>Pneumocystis carinii</i>	879
53.5	Helminthic Parasites.....	879
53.6	Carbohydrate-Binding Proteins in Parasitic Helminths	883

53.7	Unusual Glycans in Other Helminthic Parasites.....	883
53.8	Future Directions.....	885
	Acknowledgments.....	885
	References.....	886
54	The Involvement of the Oligosaccharide Chains of Glycoproteins in Gamete Interactions at Fertilization	895
	<i>Noritaka Hirohashi and William J. Lennarz</i>	
54.1	Introduction.....	895
54.2	Advantages of Marine Invertebrates as an Experimental System ..	895
54.3	Induction of the Acrosome Reaction.....	896
54.3.1	Studies in Sea Urchins.....	896
54.3.2	Studies in Starfish.....	899
54.4	Sperm–Egg Coat Binding	899
54.4.1	Studies in Mammals	900
54.4.2	Studies in Frog.....	900
54.4.3	Studies in Ascidians.....	902
54.4.4	Studies in Sea Urchins.....	904
54.5	Carbohydrate as a Species-Specific Determinant	906
	References.....	907
55	Glycosylation and Development.....	909
	<i>Michèle Aubery and Christian Derappe</i>	
55.1	Summary.....	909
55.2	Introduction.....	911
55.3	Lectins as Tools to Analyze Changes in Cell-surface Glycoconjugates During Development.....	911
55.4	Cell-adhesion Molecules.....	912
55.4.1	Neural Cell-adhesion Molecule.....	912
55.4.2	The Adhesion Molecule L1.....	914
55.5	Glycosyltransferases	914
55.6	Altered Expression of Endogenous Lectins During Development ..	915
55.6.1	Galectins	915
55.6.2	Selectins	917
55.6.3	Other Endogenous Lectins	917
55.7	Conclusion	918
	References.....	918
56	Protein Glycosylation and Cancer	923
	<i>James W. Dennis and Maria Granovsky</i>	
56.1	Introduction.....	923
56.2	Protein Glycosylation Generates Molecular Diversity.....	923
56.3	Cancer Initiation and Progression.....	926

56.4	Tumor Cell Proliferation	927
56.5	Cell Migration	930
56.6	Sialylation and Metastasis	933
56.7	Endogenous Lectins and Tumor Cell Adhesion	934
56.8	Carbohydrate Processing Inhibitors as Anti-Cancer Agents	935
56.9	Other Considerations	936
	Acknowledgments	937
	References	937
57	Lysosomal Storage Diseases	945
	<i>Nathan N. Aronson, Jr.</i>	
57.1	Summary	945
57.2	Introduction	946
57.3	Animal Models	947
57.4	Mucopolysaccharidoses	947
57.5	Cathepsin K Deficiency and Pycnodysostosis	949
57.6	Mouse Models for Tay-Sachs and Sandhoff Diseases	951
57.7	Impact of Lysosomal Diseases and Their Study	953
	References	954
58	Genetic Diseases of Glycosylation	959
	<i>Tomoya Akama and Michiko N. Fukuda</i>	
58.1	Introduction	959
58.2	CDGS	959
58.2.1	CDGS Type I	959
58.2.2	CDGS Type II	961
58.3	HEMPAS	963
	References	964
59	Glycobiology of <i>Helicobacter pylori</i> and Gastric Disease	967
	<i>Karl-Anders Karlsson</i>	
59.1	Introduction	967
59.2	The Bacterial Surface and Molecular Mimicry	968
59.3	Host Surfaces and <i>H. pylori</i> Recognition of Glycoconjugates: Unique Complexity	968
59.3.1	Sialic Acid	969
59.3.2	Sulfatide	970
59.3.3	Heparan Sulfate	970
59.3.4	Fucose-Dependent Binding (H-1 and Lewis b)	971
59.3.5	Gangliotetraosylceramide	971
59.3.6	Lactosylceramide	972
59.4	The Meaning of Multiple Binding Specificities	972
59.5	Aspects for the Future	973
	References	973

60	Immunoglobulin G Glycosylation and Galactosyltransferase Changes in Rheumatoid Arthritis	977
	<i>John S. Axford</i>	
60.1	Introduction.....	977
60.2	Oligosaccharide Synthesis	977
60.3	Galactosyltransferase	978
60.4	Immunoglobulin G	978
60.5	Rheumatoid Arthritis.....	979
60.6	Quantification of IgG sugars in RAr.....	979
60.7	RAr and Pregnancy.....	980
60.7.1	Galactosylation of IgG	980
60.7.2	α 3-Fucosylation of α 1-Acid Glycoprotein	981
60.8	Agalactosyl-IgG and Rheumatoid Factor Binding	982
60.9	Tissue-specific Galactosyltransferase Abnormalities in an Experimental Model of Rheumatoid Arthritis.....	983
60.10	Glycosylation Homeostasis within RAr Lymphocytes is Abnormal	985
60.11	Are the Rheumatoid Arthritis Associated Glycosylation Abnormalities Unique?	986
60.12	Sugar Printing Rheumatic Disease is Possible	990
60.13	Rapid Profiling of IgG N-Glycans by Fluorophore-coupled Oligosaccharide Electrophoresis has the Potential of Differentiating Rheumatic Diseases.....	992
60.14	In What Way could GTase Enzymatic Control be Abnormal?	992
60.15	Conclusion	993
	References.....	994
 61	 Calnexin, Calreticulin and Glycoprotein Folding Within the Endoplasmic Reticulum	 997
	<i>Michael R. Leach and David B. Williams</i>	
61.1	Structure and Properties of Calnexin and Calreticulin	997
61.2	Biological Functions	1000
61.3	Mechanism of Action.....	1002
61.4	Functional Relationship Between Calnexin and Calreticulin.....	1005
61.5	Relationship with other ER Chaperones and Folding Catalysts .	1007
	References.....	1008
 62	 Glycobiology of The Nervous System	 1013
	<i>Ronald L. Schnaar</i>	
62.1	Introduction.....	1013
62.2	Nervous System Glycoconjugates—Overview	1013
62.3	Nervous System Glycolipids.....	1014
62.3.1	Galactosylceramides	1014

62.3.2	Gangliosides and Related Anionic Glycosphingolipids	1016
62.4	Nervous System Glycoproteins.....	1019
62.4.1	Polysialic Acid	1020
62.4.2	The HNK-1 Determinant	1020
62.5	Nervous System Glycosaminoglycans	1020
62.6	Lectins in the Brain.....	1021
62.6.1	Myelin-Associated Glycoprotein.....	1021
62.6.2	Other Nervous System Lectins	1022
62.7	Concluding Remarks	1023
	References	1023
 63	 Glycobiology of the Immune System	 1029
	<i>Elizabeth F. Hounsell</i>	
63.1	Infection and Pathogenesis	1029
63.2	Control of the Immune Response.....	1033
63.3	Bacterial and Tumor Antigens, Mucins and Mucin-like Molecules	1034
63.4	Immunoglobulins and Pathology	1036
	References	1038
 64	 Metabolic Engineering Glycosylation: Biotechnology's Challenge to the Glycobiologist in the Next Millennium	 1043
	<i>Thomas G. Warner</i>	
64.1	Introduction	1043
64.2	Recent Developments in Carbohydrate Biosynthesis.....	1044
64.2.1	Optimizing Sialylation of Recombinant Proteins by Metabolic Engineering Sialic Acid Biosynthesis.....	1044
64.2.2	Optimizing Galactosylation of Recombinant Proteins by Metabolically Engineering Galactose Biosynthesis.....	1049
64.2.3	Mannose Biosynthesis and Mannosylation of Recombinant Proteins	1052
64.3	Glycosylation Engineering Alternate Expression Hosts For Recombinant Protein Therapeutic Production	1053
64.3.1	Engineering Glycosylation of Recombinant Proteins Expressed in Baculovirus-Insect Cells	1053
	Genes needed to supplement glycosylation of recombinant proteins in insect cells	1054
	Deleterious genes may need to be deleted or inhibited to enhance recombinant glycoprotein biosynthesis in insect cells.....	1054
64.3.2	Engineering Glycosylation of Recombinant Proteins Expressed in Plants.....	1056
	Genetic addition and supplementation needed to improve plant recombinant protein glycosylation	1058
	Inhibition or deletion of plant glycosylation genes	1059

64.4	Summary	1059
	Acknowledgments	1060
	References.....	1060
	Index	I 1