Preface

Structural glycobiology is a rapidly progressing field of research, where the diverse structural and functional roles of carbohydrates (oligo- and polysaccharides, glycolipids, and glycoproteins) are examined using a wide variety of experimental as well as theoretical (predictive) approaches. Carbohydrates are key molecules in diverse biological processes that include, but are not limited to, metabolic pathways, cell–cell interactions, carbohydrate–protein interactions, host–pathogen interactions, and immunity.

Although there are several well-written and comprehensive textbooks on glycobiology and the chemistry, biochemistry, and microbiology of carbohydrates, no current book focuses on the specific topic of structural glycobiology. We believe that this book fills the gap by bringing together world-recognized authors to contribute chapters that cover their own specialties in the experimental, theoretical, and emerging technologies employed in this field.

In this book, individual chapters are written by expert authors who are active research scientists in the field and are specialists in key techniques that are relevant to modern structural glycobiology. The book provides concise overviews of the application of specialized technologies to the study of carbohydrates in biology, reviews of relevant and current research in the field, and is illustrated throughout by specific examples of how research investigations have yielded key structural and associated biological information on carbohydrates, glycolipids, and glycoproteins.

The topics covered in this book are broadly divided into four sections. Section I covers well-established, but often challenging, experimental approaches for structure determinations of carbohydrate–protein complexes and large glycoprotein assemblies and explores the techniques of x-ray crystallography and small-angle scattering (Chapter 1), nuclear magnetic resonance (NMR) (Chapter 2), and cryoelectron microscopy (Chapter 3). Jeffries, Farrugia, and Ramsland (Chapter 1) discuss two complementary approaches examining the high-resolution three-dimensional structures (x-ray crystallography) and the solution shapes and conformations (small-angle x-ray and neutron scattering) of carbohydrate binding proteins and glycoproteins. They outline the general features of carbohydrate–protein interactions and discuss the importance of multivalent carbohydrate binding and the role of oligomerization in carbohydrate recognition by proteins. Koharudin and Gronenborn (Chapter 2) provide an easily accessible and educational outline of how NMR can be applied to the study of protein–glycan interactions. The power of the different NMR methodologies for investigating carbohydrate binding, bound carbohydrate conformations, and detailed structures of carbohydrate–protein complexes is beautifully illustrated with carbohydrate–lectin systems. The state-of-the-art in cryoelectron microscopy (cryoEM) for studying very large assemblies of glycoproteins is presented by Zeev-Ben-Mordehai and Grünewald (Chapter 3). Recent advances in sample preparation, image collection, and processing are greatly accelerating the use of cryoEM for structural studies of glycoproteins under near native settings (e.g., in viruses, cells, and tissues). They provide stunning examples of where cryoEM, particularly tomographic methods, are providing unprecedented structural information on biological assemblies, such as membrane channels, intracellular junctions, and viral glycoproteins.

Section II covers theoretical, or modeling-based, approaches, such as molecular mechanics, molecular dynamics, and free energy calculations (Chapter 4) and carbohydrate docking (Chapter 5). Sarkar and Pérez (Chapter 4) give an excellent overview of the computational approaches used to study protein–carbohydrate interactions. They complement the description of traditional methods with a brief foray into alternative methods used for the enhancement of conformational sampling, such as molecular robotics. Agostino, Ramsland, and Yuriev (Chapter 5) demonstrate the usefulness of molecular docking in structural glycobiology by considering recent docking validation studies on a range of protein targets. They also describe very recent developments in the modeling of water-mediated carbohydrate–protein interactions.

Section III covers alternative techniques for yielding structural information on carbohydrates from complex biological samples (fluids/secretions, cells, and tissues). Here, the rapid advances in mass spectrometry (Chapter 6) are being complemented with glycan-based arrays (Chapter 7) for the study of carbohydrate specificity and recognition. Kolarich and Packer (Chapter 6) provide a detailed overview of the latest mass spectrometric methods for characterization of complex *N*- and *O*-linked oligosaccharides and how the exciting subfield of glycoproteomics is emerging for studying diverse protein glycoforms that are relevant to health and disease. A brief discussion of the need for uniform collection and reporting standards for glycomics-based mass spectrometric investigations is followed by a useful overview of the bioinformatics resources available to researchers using mass spectrometry in glycobiology. The contribution by Song, Smith, and Cummings (Chapter 7) illustrates glycan array technology, focusing on the Consortium for Functional Glycomics methodologies and also introduces the cutting-edge shotgun glycomics approach, which has enormous potential to accelerate research into carbohydrate-mediated interactions from diverse and complex biological samples.

Section IV deals with carbohydrates in medicine. Although carbohydrates are centrally involved in many physiological, biochemical, and cellular processes, three areas of modern medicine (organ transplantation, cancer immunotherapy, and infection treatment) have been directly impacted by our understanding of the structural role of carbohydrates in immune recognition. Brockhausen and Gao (Chapter 8) focus on a range of cancer-related structural and enzymatic glycoaberrations. Christiansen et al. (Chapter 9) deal with carbohydrate antigens implicated in organ rejection. Specifically, they discuss the biochemical, genetic, and immunological characteristics of these carbohydrates, their origins, and interactions with antibodies. Xu and Wilson (Chapter 10) highlight the role of protein–carbohydrate binding for viral adhesion and invasion. They focus on three paradigm systems of viral proteins that recognize sialic acid in cell surface glycans as receptors for viral attachment. They demonstrate, using high-resolution x-ray structures, the subtle structural variations governing the recognition process; for example, for avian versus human influenza A hemagglutinin. Gandhi and Mancera (Chapter 11) describe molecules designed to mimic the biological activity of glycosaminoglycans (GAGs) through modifications of structure, composition, and sulfation patterns. These new generation GAG-mimetics offer rich potential as therapeutics for treating cancer, inflammation, and infection.

Although each chapter could be a useful stand-alone introduction to a specific technique or area of structural glycobiology, several themes are consistent throughout the book, namely, the role of specific proteins in carbohydrate recognition and function: lectins (Chapters 1, 2, 4, and 5), antibodies (Chapters 1, 4, 5, 9, and 10), and glycosyltransferases (Chapters 4, 5, 8, and 9). From the ligand point of view, the structure and biological roles of two particular types of carbohydrates are of interest in several areas of study: sialic acid and its derivatives (Chapters 1, 8, and 10) and glycosaminoglycans (Chapters 5, 7, 8, 10, and 11).

In summary, this book covers the experimental, theoretical, and alternative technologies that are being applied to the study of the structural basis for the diverse biological roles of carbohydrates. This should be a valuable reference for researchers, graduate students, postdoctoral scientists, and academics with an interest in glycobiology. Researchers from other fields, such as medicinal chemists, biochemists, immunologists, and microbiologists, should also find this a relevant and up-to-date reference and a suitable introduction to the field.