Preface

Protein–carbohydrate interactions are ubiquitous in nature. Though sometimes underappreciated, they play pivotal roles in countless and diverse biological processes ranging from mediating leukocyte rolling during the course of inflammation, gamete–gamete interactions that initiate fertilization, and recognition by and attachment to host cells by pathogenic organisms. During the past two decades, great strides have been made toward better understanding the chemical and molecular basis for protein–carbohydrate interactions and how they manifest in biology. In concert with many elegant biological studies, much of this progress can be attributed to advances in synthetic, organic, or carbohydrate chemistry; in the development of powerful tools that allow for robust, rapid, and diverse screening of protein–carbohydrate interactions such as carbohydrate and protein microarrays; in instrumentation used to make biophysical measurements such as isothermal titration calorimetry and surface plasmon resonance; in the development of carbohydrate-based conjugate vaccines; and in high-resolution structural analyses by X-ray crystallography and NMR. Perhaps the well-studied aspect of protein–carbohydrate interactions in biology pertains to their involvement in infectious diseases. Indeed, the outer surfaces of all cells of most pathogens are decorated with a distinct set of complex carbohydrate structures, usually in the context of glycolipids or glycoproteins; distinct carbohydrate-binding proteins (typically lectins or toxins) that recognize with specificity particular carbohydrate structures; or both. Consequently, the initial contact between two cells or a cell and pathogen almost certainly boils down to protein–carbohydrate interactions. Depending on the biological system, this initial event is one and the same with cellular recognition, attachment, adhesion, or a combination of the three. Given the interdisciplinary nature of the fields of carbohydrate chemistry and glycobiology, the study of protein–carbohydrate interactions in infectious diseases presents a field that is wide open for exploration.

A number of truly outstanding text and reference books giving comprehensive coverage to individual areas such as organic or enzymatic synthesis of carbohydrates, saccharide biosynthesis, and glycobiology, to name a few, are available. It is my hope that collectively, the set of chapters presented here, will educate and inform graduate students, postdoctoral fellows, and non-specialist readers alike, on the central role that protein–carbohydrate interactions play in mediating and initiating most infectious diseases; and the indispensable roles that chemistry and structural and cell biology play in studying these interactions. An introductory chapter outlining the atomic features behind carbohydrate recognition is presented by Sharon. Blaauw and Appelmelk describe carbohydrate structures displayed from glycolipids that are unique to mycobacterial species and account for virulence, while Imberty *et al.* and Sharon and Ofek describe co-crystal structures and biological studies that reveal the basis for carbohydrate recognition by surface lectins of *Pseudomonas aeruginosa* and diverse enterobacterial species such as *Escherichia coli*, *Klebsiella pneumoniae* and *Salmonellae* species, and introduce the notion of anti-adhesive therapies. Using high-resolution NMR techniques, Bernardi, Podlipnik, and Jiménez-Barbero describe the structural basis for bacterial enterotoxins binding to gangliosides as well as synthetic multivalent GM-1 mimetics. Chapters by Lehrer and van Kooyk and colleagues provide an opposing view of carbohydrate recognition, that is from the host cell's side, and review the defensive and immunologic roles of primate and human lectins known as theta defensins and C-type lectins, respectively. In a chapter covering sialic acid metabolism, Vimr and Steenbergen review the prevalence of sialic acid in microbial cell walls and touch on a topic on everyone's mind, namely that of targeting carbohydrate structures and metabolism, or alternatively carbohydrate receptors for chemotherapy. Chapters by Hölemann and Seeberger, and Kováč on carbohydrate-based conjugate vaccines for malaria and cholera, respectively, fill two essential aspects of the book's subject matter, namely elegant synthetic routes to assemble complex and homogeneous carbohydrate structures and protein conjugates on a fairly large scale, and current progress on the efficacy of carbohydrate-based vaccines. In the spirit of the 'omics' revolution, the final chapter by Shin describes the construction and use of carbohydrate or glycan microarrays that can provide initial information on carbohydrate specificity of lectins, toxins, enzymes, or whole cells. For those seeking more information, the book contains nearly 1000 references to the chemistry and glycobiology literature, and will hopefully give the reader an overall view of how carbohydrates and their protein partners mediate infection.