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Synthetic Receptors for Biomolecules
Design Principles and Applications

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Preface

The field of supramolecular chemistry continues to grow at an accelerated pace, and it is especially active at the interface of chemistry and biology. Pioneering research conducted during the last quarter of the 20th century focused initially on synthetic receptors for structurally simple guests, such as metal cations. As the field expanded, researchers pursued more elaborate synthetic receptors for binding anions and small neutral molecules. The early pioneers recognized the technical advantages that would be gained by developing synthetic mimics of large protein-based receptor systems, such as antibodies, enzymes, and membrane transporters. But time was needed for the field to discover and conceptualize the fundamental physical-organic factors that produce strong and selective binding of biological molecules in aqueous solution. Also required were new synthetic methods and nanoscale fabrication techniques for reliable construction of suitably functionalized synthetic receptors with appropriate geometric arrangement of molecular recognition motifs. These intellectual and technical attributes have now been acquired and merged to create effective receptor design and discovery platforms.

The classic approach to synthetic receptor development is a step-wise process that involves de novo molecular design followed by receptor synthesis and evaluation of supramolecular performance. For some types of research projects, this approach is quite suitable, but for others it is unacceptably slow and inefficient. In response, researchers have developed alternative accelerated discovery processes. One strategy is to prepare libraries of multiple receptor candidates and rapidly screen them for library members that exhibit appropriate binding affinity. A conceptually powerful refinement of this screening approach is to create dynamic combinatorial libraries of receptor building blocks that have been structurally programmed to self-assemble in the presence of a suitable guest template and create a
high-affinity receptor. Using these complementary methods, the field has produced biomolecule-binding systems with functional properties for various applications in complicated biological matrices, including living subjects. These applications are the basis of emerging new nanoscale technologies that will have broad future impact in modern society.

This volume describes the receptor design principles and discovery algorithms, and shows how they have been used to produce synthetic receptors for each major class of biomolecules. A unique feature of the book is the presentation style. To date, virtually all review articles or books on synthetic receptors have been presented in a format that is primarily a list of receptor chemical structures with an ensuing discussion of the various biomolecule guests they bind. This book reverses the format and devotes a chapter to each specific class of biomolecule, with a methodical summary of the different biological and synthetic receptors. The systematic layout allows readers to quickly identify the sections that are relevant to their information needs. The target audience is a broad group of scientists and engineers (academic and industrial) who have a biomolecule targeting problem in mind and want to know what synthetic receptors will likely lead to a solution. What are the unique molecular recognition challenges for each type of biomolecule? What is the best synthetic receptor system for a specific type of biomolecule and a specific type of application? Another large group of readers is the regular community of supramolecular chemists who are developing next-generation synthetic receptors with improved performance. They want an integrated picture of the current state of the art and a sense of future directions and expected challenges.

The opening chapter provides a concise summary of the technical applications that utilize synthetic receptors for biomolecules. The applications are classified broadly into four groups: separations, imaging and sensing, catalysis, and pharmaceutical activity. The various receptor classes are separated into six categories: organic molecules, inorganic molecules, synthetic oligomers, molecular imprinted polymers, dendrimers, and nanoparticles. The chemical and supramolecular attributes of each receptor category are summarized, along with illustrative examples of how the synthetic receptors are employed for each type of application. The second chapter is a tutorial on the fundamental structural and thermodynamic factors that affect biomolecule recognition, and includes the following topics: non-covalent interactions, receptor preorganization and shape complementarity, cooperative binding, solvent effects, and enthalpy–entropy compensation. There is also an informative presentation of the various ways to design and discover new classes of synthetic receptors.

The next eight chapters provide a systematic summary of the best-known receptors for alkali metal cations, organic and inorganic anions, carbohydrates, nucleosides and nucleotides, oligonucleotides and nucleic acids, amino acids and peptides, protein surfaces, and polar lipids. Each chapter follows a similar structural format of: (a) chemical structure and physical properties of the biomolecule; (b) biological recognition of the biomolecule;
(c) synthetic receptors for the biomolecule; and (d) future directions and challenges.

The order of chapters is well suited for instructors who wish to use the book for a graduate-level class on supramolecular chemistry. Alternatively, the book is an excellent source of supplementary information for a range of undergraduate chemistry, biochemistry, health science, and engineering classes. A valuable pedagogical addition is an accompanying series of PowerPoint slides containing graphics from each of the 10 chapters. The PowerPoint files are provided as electronic supplementary information on the Royal Society of Chemistry website (DOI: 10.1039/9781782622062).

I am grateful to the chapter authors for completing their writing tasks in a timely fashion, and for agreeing to follow a consistent presentation format. I warmly acknowledge the wonderful technical assistance of Theresa Bollinger, Kasey Clear, Evan Peck, and the publication staff at the Royal Society of Chemistry. I am grateful for funding and resources from the University of Notre Dame, and the US National Science Foundation (grant: CHE1401783).

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