Preface

Synthetic Receptors: Design Versus Evolution

Despite the considerable progress achieved to date in the application of enzymes, antibodies, and biological receptors to diagnostics and in separations, the last two decades have witnessed the emergence of a clutch of alternative technologies based on their synthetic analogues. Research and development in this area is expanding, as can be seen from a steady increase in the number of relevant publications (Fig. 1). The move to the use of artificial receptors in place of natural molecules has been driven by practical considerations, in particular the need for stable, sterilizable, and non-immunogenic materials. Novel diagnostics based on synthetic receptors are not only suitable for clinical applications but have the potential to fill niches in, e.g., online monitoring of industrial (pharmaceutical manufacturing) processes or continuous environmental monitoring, where the technology can benefit from materials that combine excellent specificity and affinity with durability at low cost.

Most publications in this area, however, are related to fundamental aspects of materials design with only a small proportion being concerned with practical applications of the technology.

The challenges facing the adoption of synthetic receptors in "real life" applications are substantial and stem from two reasons: The first is related to the fact that tremendous progress has already been achieved in improving the performance of biological molecules through, e.g., site-directed mutagenesis and by combinatorial chemistry. The second reason is the difficulty of translating the fundamental knowledge of molecular recognition mechanisms gleaned from biological systems into designs for the creation of synthetic receptors. Basically it is easier to develop completely new synthetic recognition systems than to mimic the corresponding biological analogue. Synthetic receptor molecules prepared by design do not, however, always possess superior characteristics that can justify their use in, e.g., biosensors. Thus the important questions are whether there is a real need to develop a new generation of synthetic

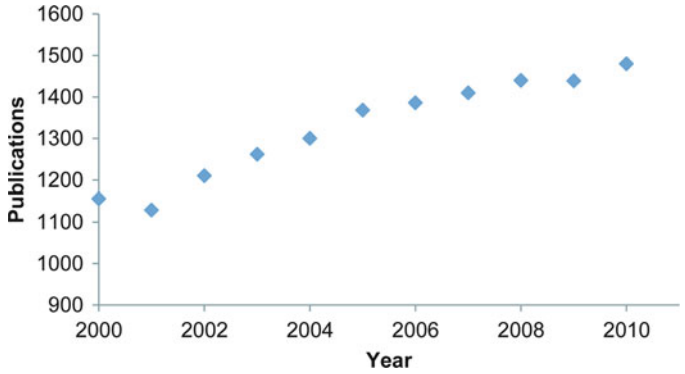

Fig. 1 Number of publications dedicated to synthesis and investigation of synthetic receptors (calculations made from the analysis of information available at ISI Web of Knowledge)

receptors which can successfully compete with biological molecules in diagnostics, and how this can be achieved? The answer to the first question is firmly positive. Enzymes, antibodies, and receptors are products of natural evolution and consequently are relatively unstable under non-physiological conditions. They also tend to be expensive and difficult to integrate with the device using standard manufacturing tools and protocols such as photolithography. There is a fundamental limit, imposed by nature, to what can be achieved by modification of biological molecules to suit their practical applications. Synthetic chemistry, however, is not limited to 20 or so amino acids and 4 or 5 nucleotides (the building blocks of peptides, proteins, and aptamers) and can be used to construct its products from a huge range of functional motifs and chemical entities. Bespoke molecules can be designed with particular functional characteristics for complex and diverse applications such as diagnostics.

The present book intends to answer the second question – how synthetic receptors can be designed with characteristics that make them attractive alternatives to biological molecules. To start with we would like to suggest a definition of synthetic receptors: these can be considered to be: *synthetic, semisynthetic, or rationally designed biological molecules created with the purpose of selectively binding a single compound or group of structurally similar compounds*. Although the structural and chemical diversity of chemical entities which might have affinity for a particular compound or groups of compounds is very large, the most prominent groups of synthetic receptors include the following (Fig. 2):

- Synthetic peptides with receptor properties
- Macrocycles
- Molecularly imprinted polymers (MIPs)
- Aptamers
- Combinatorially selected compounds
- Supramolecular receptors

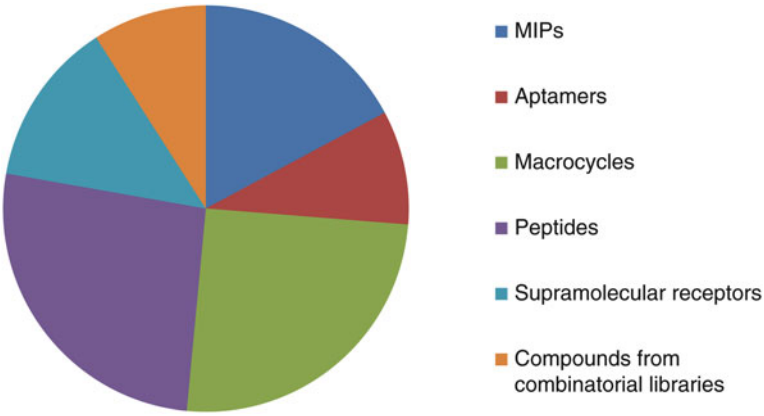

Fig. 2 The relative share of research publications dedicated to various groups of synthetic receptors (calculations made from the analysis of information available at Web of Knowledge)

For this collection we have invited contributions from top experts in the area of synthetic receptors whose work is relevant to diagnostic applications. The particular focus of all chapters is on practical aspects, either in the development process or on the applications of the synthesized materials. We hope this will differentiate our book from other, recently published volumes and make it an interesting and important reference work for business leaders and technology experts in the sensors and diagnostics sectors. In conclusion, we would like to express our deepest gratitude to our colleagues who found the time in their busy schedules to share their results, thoughts, and visions with you, the reader.

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