PREFACE

The term 'molecular recognition' refers to the specific interaction between two or more molecules through noncovalent bonding. This book presents research in the study of molecular recognition, including next generation molecular imprinted polymers; applications of molecular imprinting; recent advances in DNA-Ligand molecular recognition and allosteric interactions; the proteomic code and the molecular recognition of odorant-binding proteins in insect olfaction.

Chapter 1 - Synthetic molecules able for efficient and selective binding of carboxylic acids belong to very promising receptor structures. Special focus on hydroxy- and dicarboxylic acids is due to the central role of these molecules in metabolic paths of the living organisms and commercial importance in biotechnology. In addition, wide range of biological and organic molecules contain carboxylic group. For this reasons, great attention is paid to modeling of the synthetic receptors able to specifically bind carboxylic acids or their fragments. This chapter describes the current state-of-the-art in research and development of the methods for development of artificial receptors for carboxylic acids. The focus is on the structural and physical properties of synthetic receptors because the efficiency of interaction between the receptors and acids depends on various factors, i.e. nature of the substituents, their structural accepting characteristics, geometrical complementarity of the binding sites etc. In general, the development of artificial receptors for carboxylic acids has some difficulties and now full understanding of all the principles of molecular recognition of acids is still far from being completed. Due to their unique properties, the synthetic receptor molecules can contribute to solution of these problems. They offer new opportunities for modeling artificial living systems and physiological processes, designing therapeutic agents and sensitive elements of (bio)sensors and others diagnostic tools devoted to fast detection of pathogens and pathological stages in medicine. Active search in the area led to development of artificial receptors different in efficiency of recognition toward a number of hydroxy-, amino and dicarboxylic acids. In this chapter, general approaches to the design of synthetic receptor, their classification and performance in recognition of various substrates are considered.

Chapter 2 - Molecular imprinted polymers (MIPs) have been studied for a few decades. They enable the specific recognition of the molecule for which they have been prepared. They have been thoroughly studied in organic solvents and this showed that a good recognition was observed only when a crosslinking ratio above 70% was used. In this case, however, the capacity of the MIP was limited owing to a poor accessibility of the imprinted cavities. In the ongoing research on this subject, many teams assess the possibility of controlling the

recognition process and that of using the MIPs in aqueous systems. They present here their experience in liquid crystal MIPs as tunable systems and hydrogel-MIPs for the recognition of proteins.

In the first case, the MIP is composed of a liquid crystal elastomer which is built around the template. The difference from regular MIPs lies in the percentage of crosslinker agent, which is in the 5-10% range. This low range becomes possible owing to replacing a large part of the chemical crosslinking by a physical one, coming from the interactions between liquid crystal moieties attached to the material. This brings up a recognition ability similar to the regular MIPs, but with an increased accessibility to the cavities. Thus, the mass capacity of this LC-MIP is tremendously increased. Furthermore, since liquid crystal elastomers exhibit an organized/disorganized transition temperature and have a shape memory capacity, the LC-MIP can be controlled with external parameters, such as temperature or solvents. By this method, different types of materials have been examined and are presented here: MIPs able to specifically interact with an enantiomer, catalytic MIPs acting as artificial enzymes or MIPs able to interact with pesticides.

The second part of the manuscript describes the state of the art as well as the author's preliminary experiments aiming at developing MIPs made of hydrogels which will be able to selectively recognize a protein in solution. The goal is to fix the hydrogel MIP to a detection device for a future application in diagnostics. Due to this, a severe constraint exists for process: temperature and pH limits, process in less than 30minutes, porosity slightly lower than the size of the protein. Indeed, since proteins are large molecules, recognition at the surface of the MIP is sought. Several monomer formulations have been studied and the technological problems have been examined.

Chapter 3 - The concept of molecular recognition in supramolecules with different types of intermolecular interactions and in some biological processes is discussed. The features and manifestations of hydrogen bonding as one of the most important types of interactions participating in the molecular recognition are presented in geometric, spectroscopic and natural bond orbitals terms. Molecular recognition in co-crystals and polymorphs is object of discussion in order to give a general view of this matter in different technologies, particularly in the pharmaceutical one. The role of molecular conformation and association in solution in predicting crystalline structures is investigated. Attention is also given to the molecular recognition in solid/solution interfaces in some important processes of crystal growth.

Chapter 4 - Molecular recognition can be defined as recognition of molecules, i.e. polar molecules by other polar molecules, or recognition of chiral molecules by other chiral molecules. These molecules can interact together, for instance, by creating hydrogen bonding. This review shows using of microscopy, spectroscopy and other methods to investigate of chiral recognition (i.e. chiral surfaces).

The term of chiral surface can be defined as surface of metal (i.e Cu, Au) or non–metal (i.e graphite) covered by chiral molecules. The covering ratio of surfaces can be different, and it depends of method specification used in appropriate experiment. In this review the author want to show, so chiral molecule (i.e. α–amino acids) adsorbed on surface (i.e. metal) can recognize another chiral molecule also adsorbed on surface. The useful methods discussed in this paper are: STM (scanning tunneling microscopy), AFM (atomic force microscopy), electrochemistry and vibrational spectroscopy – infrared and Raman, including SERS effect (surface–enhanced Raman scattering) and others. Molecular recognition can be investigated, for instance, when molecules create i.e. the SAMs or Langmuir–Blodgett films.

The most sensitive methods are STM, AFM and Raman spectroscopy (SERS), because the most interesting results were obtained using these methods. The author would like to underline, so every method has its own limitation and specification, and results are strong depended from using method. Structural information obtained using various techniques for chiral surfaces can be useful in understanding of key of interaction of adsorbed chiral molecules.

Chapter 5 - Molecular imprinting has been widely studied and applied in the last two decades as an innovative tool for various technological and scientific fields. The first approach to molecular imprinting was not well known until 1949 when Dicky and his coworkers succeeded to create complementary molecular cavities for certain dye molecules. Dickey's silicates could be considered as the first molecularly imprinted material [1and2].

In general, molecular imprinting process involves the formation of molecular cavities inside the polymer matrix being imprinted which are of complementary structural, functional group orientation and geometrical features with respect to the molecule being imprinted. Specifically, the molecular cavities are created by the incorporation of the template molecule during the polymerization process in such a way that a three dimensional network is formed around the molecule being imprinted. Upon extraction of the molecular moiety (template) from the polymer matrix, molecular cavities with specific shape, size and electrostatic features, remain in the cross-linked host material [3-5].

Because of its unique properties, molecularly imprinted materials have been widely utilized for a lot of applications and in various fields. They were applied in high performance liquid chromatography [6], food analysis [7], capillary chromatography, solid phase extraction [8] and drug delivery techniques [9].

One of the most important applications of the imprinting technique is the molecular recognition. Sensors prepared by imprinting methods could introduce good solution for the recognition of a variety of biologically active molecules. Recognition mechanism of the molecules is largely similar to what happens in living organisms. In their bodies, there are a large number of different molecules, and cells, without which they cannot survive, which are able to work cooperatively in such a way that certain function are carried out very precisely and accurately. For example, the receptors on the surface of cell membranes bind hormones specifically and selectively. When the receptor binds a hormone, its conformation is changed and a message of the hormone is transferred in terms of a conformational change and as a result of that a specific function of that hormone is fulfilled. In molecular recognition, the molecules being imprinted can rebind to their molecular cavities with very high degree of selectivity and specificity, so that these materials may be named as artificial antibodies.

Chapter 6 - It is generally recognized that elucidating the molecular basis for recognition of specific sequences in target DNA by proteins and small synthetic molecules vitally underpins research on the modulation of gene expression. In this review they discuss the fundamental basis of DNA sequence recognition by small molecules at the atomic bonding level based on recent X-ray diffraction results together with circular dichroism spectra and footprinting experiments on DNA-small ligand binding. Monodentate (single) interactions, intrastrand bidentate interactions and interstrand bidentate interactions are considered not only central to the capabilities of small ligands and proteins to recognize DNA sequences, but also provide the means for allosteric communication between multiple DNA binding loci. Thermodynamic, kinetic and allosteric features of molecular recognition by drugs and small ligands within the minor groove of DNA are reviewed. Allosteric interactions between small

synthetic peptides and multiple DNA binding sites are discussed, and hypothetical models are proposed to interpret the complex allosteric communication process. In contrast to protein-protein interaction networks which have been extensively investigated, studies on small ligand-DNA interaction networks have only recently been commenced. In this review, three different types of novel allosteric interaction networks between peptides and DNA are considered, together with hypothetical models featuring monodentate interactions and interstrand bidentate interactions. The new concept of DNA-small ligand interaction networks illuminates some basic chemical rules of DNA-small ligand allostery and may find applications in future drug design as well as structural biology research.

Chapter 7 - Like other animals, insects sense chemicals evoke their behaviors, such as aggregation, mating, feeding and migration behaviors, through their olfactory and taste recognition systems. The olfactory molecules, in the air out of insect body, diffuse into sensillum lymph through the cuticle pores and at first step interact with the small soluble odorant-binding proteins (OBPs). The odor specificity of a given olfactory neuron is determined by expressed olfactory receptor (OR) genes along with other accessory proteins. The signals accepted by ORs then are sent to higher processing centers in the brain to elicit distinct behavioral outputs.

So far over 100 OBPs have been identified from more than 40 species of insects. However, only a few have been studied for their recognition with ligands during binding activity. Although OBPs certainly show binding ability to hydrophobic odorants, their physiological roles are still in controversy. There are three unclear points which people are very interested in. Firstly, whether or not insect OBPs have binding specificity and how do they perform such binding specificity? Secondly, how do the proteins recognize the odorants, and which binding sites are involved in recognition? Thirdly, how do OBPs interact with odorant receptors? To reveal mechanisms of OBPs molecular recognition is helpful in understanding their physiological functions and in designing interfering molecules to ruin normal recognition and control insect pests. Therefore this field is attracting more and more scientists' passions and interests.

Recently some interesting experiments on insect OBPs had been conducted to partly address these questions with the combination of three dimensional structure analysis, binding experiments, site-directed mutagenesis, and simulation and docking experiments. Here the authors discuss insect OBPs molecules recognition and review the progress in the field. It has been found that the conformational change of OBPs can be induced either by pH value alteration or by ligand binding. Some hydrophilic amino acids at the entrance of OBPs binding pocket, as well as the hydrophobic amino acids in the pocket, are involved in ligand binding and may contribute to the recognition specificity of OBPs.

Chapter 8 - The Proteomic Code is a set of rules by which information in genetic material is transferred into the physico-chemical properties of amino acids and determines how individual amino acids interact with each other during folding and in specific protein–protein interactions. The Proteomic Code is part of the redundant Genetic Code. The 25-year-old history of this concept is reviewed from the first independent suggestions by Biro and Mekler, through the works of Blalock, Root-Bernstein, Siemion, Miller and others, followed by the discovery of a Common Periodic Table of Codons and Nucleic Acids in 2003 and culminating in the recent conceptualization of partial complementary coding of interacting amino acids as well as the theory of the nucleic acid-assisted protein folding. A novel cloning method for the design and production of specific and with high affinity reacting proteins

(SHARP) is presented. This method is based on the concept of proteomic codes and is suitable for large-scale, industrial production of specifically interacting peptides.

Chapter 9 - The 'on/off'-switched molecular recognition by a smart imprinted polymer (MIP-T) was presented in this chapter. The smart MIP-T was prepared using PNIPA as the thermosensitive element and 2-aminopurine as the template. The thermal phase transition of PNIPA induced a self-switching ability in the prepared polymer. At a relatively low temperature (such as 20 °C), the MIP-T was capable of highly specifically recognizing the imprint species, i.e., 2-aminopurine. However, above the transition temperature, the MIP-T did not demonstrate significant resolution for 2-aminopurine compared with its analogue 2-amino-6-methylpurine. Such temperature-responsive recognition, in nature, was comparable to an on/off-switched process, which allows an efficient self-regulation in the molecular recognition behavior.