6.1 INTRODUCTION

Many biological processes are governed by complex interactions between biomolecules. Molecular recognition is, therefore, a fundamental feature of life. Antibody-antigen, ligand-receptor and enzyme-substrate interactions are examples of such biorecognition systems, wherein the recognition domain of the protein binds its ligand or substrate through the cumulative action of multiple intermolecular interactions mostly of a noncovalent nature. These natural molecular recognition molecules offer exquisite selectivity and high affinity, and thus are often incorporated into sensors and used in a variety of bioanalytical techniques, such as ligand binding assays and affinity chromatography. However, despite their excellent recognition capabilities, these proteins can lack stability, especially under harsh chemical conditions (e.g. extremes of pH and temperature, organic solvents), can be time-consuming to prepare or costly and difficult to obtain, and their reuse is often limited. For these reasons alternative approaches that use artificial recognition elements with affinities and selectivities similar to their biological counterparts, but with enhanced stability are actively being pursued.

Relatively simple artificial receptors that efficiently and selectively bind certain inorganic ions are currently available. By incorporating a fluorophore into or adjacent to the binding domain of the receptor molecule, fluorescent chemosensors have been developed that undergo selective target-induced changes in fluorescence. Many such compounds are now available, and are popular and powerful tools for investigating the intracellular concentrations and localization of calcium and a variety of other ions in real time.

Preparation of an artificial receptor of high affinity and selectivity for a molecule that is larger and more complex than a simple spherical ion is a more daunting task, as it requires the synthesis of a cleft or cavity that has a size and shape to match the analyte, as well as the correct spatial arrangement of functional groups to interact with
complementary groups on the target molecule. This often involves substantial effort and elaborate organic synthesis. Towards this end, researchers are investigating the technique of molecular imprinting as a means of creating artificial receptors with biological-like binding capabilities (i.e. biomimetic receptors). Molecular imprinting is a process whereby selective recognition sites are created for a target molecule in a polymer by copolymerizing functional and cross-linking monomers in the presence of a template molecule (also referred to as an imprint or print molecule) (Fig. 6.1). The template is normally the target molecule itself, but could also be a close structural analogue. Subsequent removal of the template molecules from the polymer exposes microcavities or imprints with a shape to match the template. These microcavities also contain precisely oriented functional groups complementary to those of the template, held in place through the rigidity of the three-dimensional cross-linked polymer network. Following removal of the template, the molecularly imprinted polymer (MIP) can rebind the target molecule through multipoint attachment to these microcavities, as occurs in enzyme-substrate and receptor-ligand binding, and can exclude other molecules according to the lock-and-key principle originally proposed by Fischer about 100 years ago. This MIP exhibits tailor-made selectivity for the template molecule, and can thus act as an artificial macromolecular receptor.

The concept of molecular imprinting dates back to the 1930’s when Polyakov dried silica gel in the presence of various small aromatic molecules, and found that the silica later preferentially adsorbed the aromatic molecule that had been present during drying. In 1949, Frank Dickey, then a student of Linus Pauling, was inspired by Pauling’s theory for the production of antibodies in vitro, and took the idea of molecular imprinting one step further. He prepared “specific adsorbents” by synthesizing silica gel in the presence of different dye molecules, namely methyl, ethyl, n-propyl and n-butyl orange. The resulting silica, after washing, displayed “maximum adsorption power for the dye used in the preparation of the adsorbent.” However, it wasn’t until the 1970’s with the work of Wulff and coworkers that molecular imprinting, as we know it today, was...