Molecular imprinting for selective chemical sensing of hazardous compounds and drugs of abuse

Piyush Sindhu Sharma, Francis D'Souza, Wlodzimierz Kutner

Environmental and health safety requires thorough determination of hazardous compounds and drugs of abuse. In determinations of these analytes, traditional instrumental analytical techniques often suffer from tedious assay procedures.

Biosensors are simpler to construct and faster in use, so they can better meet the analytical demands in determination of these biohazards. However, their stability and reproducibility when operating under harsh conditions are poor, so artificial recognition units have become attractive as replacements for natural receptors in sensing applications.

Molecular imprinting is one of the most powerful tools for preparing materials that can bind analytes reversibly and selectively in the presence of their interferents.

This review critically evaluates the development of chemical sensing of biohazards and drugs of abuse using the molecular-imprinting approach to recognition in combination with different ways of analytical signal transduction.

We compile analytical parameters of the molecularly-imprinted receptors, identify difficulties in the determinations encountered and highlight proposed solutions to problems.

Keywords: Analytical parameter; Biohazard; Chemical sensing; Drug of abuse; Electronically-conducting polymer; Herbicide; Insecticide; Molecular imprinting; Molecularly-imprinted polymer (MIP); Pesticide

Abbreviations: AA, Ascorbic acid; AChE, Acetylcholine esterase; ACN, Acetonitrile; AgNP, Silver nanoparticle; AIBN, Azobisisobutyronitrile; AMPSA, 2-acrylamido-2-methyl-1-propanesulfonic acid; 2-APh, 2-aminophenol; 2-AThPh, 2-aminothiophenol; 4-AThPh, 4-aminothiophenol; ATRS, Attenuated total reflectance spectroscopy; AuNP, Gold nanoparticle; BTEB, Bis(trimethoxysilylethyl)benzene; BR, Britton-Robinson (buffer); CV, Cyclic voltammetry; DEAEM, 2-(diethylamino)ethyl methacrylate; DHA, Dihydrobenzoic acid; Diglyme, 1-diethylene glycol dimethyl ether; DMF, *N,N*-dimethylformamide; DPV, Differential pulse voltammetry; EBPh, 4,4′-ethylenebisphenol; ECP, Electronically-conducting polymer; EDA, 4,4′-ethylenedianiline; EDOT, Ethylenedioxythiophene; EGDMA, Ethylene glycol dimethacrylate; EIS, Electrochemical impedance spectroscopy; GCE, Glassy carbon electrode; IA, Itaconic acid; ISE, Ion-selective electrode; ISFET, Ion-selective field effect transistor; ITO, Indium-tin oxide; LOD, Limit of detection; LSV, Linear sweep voltammetry; MA, Methacrylic acid; MBA, *N,N*′-methylenediacrylamide; MBI, 2-mercaptobenzimidazol; MIECP, Molecularly-imprinted, electronically-conducting polymer; MIP, Molecularly-imprinted polymer; MIPEDOT, Molecularly-imprinted polyethylenedioxythiophene; MIPPy, Molecularly-imprinted polypyrrole; MP, Methyl parathion; MPS, 3-methacryloxypropyl trimethoxysilane; NBD, 7-nitrobenz-2-oxa-1,3-diazole; NIP, Non-imprinted polymer; OPP, Organophosphorous pesticide; PBS, Phosphate buffer saline; PD, Phenylenediamine; PEDOT, Polyethylenedioxythiophene; PM, Piezoelectric microgravimetry; PPy, Polypyrrole; PPV, Poly(4-phenylene vinylene); PVC, Poly(vinyl chloride); Py, Pyrrole; QCM, Quartz-crystal microbalance; RIfS, Reflectometric interference spectroscopy; SA, Salicylic acid; SAM, Self-assembled monolayer; SCE, Saturated calomel electrode; SEM, Scanning electron microscopy; SPR, Surface-plasmon resonance; SWV, Square-wave voltammetry; 3-TAA, 3-thiophene acetic acid; TFMAA, 2-(trifluoromethyl)acrylic acid; THF, Tetrahydrofurane; ZnPP, Zinc(II)protoporphyrin

Symbols: C, Concentration; C_0, Capacitance; *f*, Resonance frequency of a quartz resonator; *I*, Current; K_{MIP-A}, Stability constant of a complex of the analyte A and the molecular cavity of MIP; *R*, Dynamic resistance

Piyush Sindhu Sharma, Wlodzimierz Kutner*
Department of Physical Chemistry of Supramolecular Complexes, Institute of Physical Chemistry, Polish Academy of Sciences, Kasprzaka 44/52, 01-224 Warsaw, Poland
Francis D'Souza*
Department of Chemistry, University of North Texas, Denton, 1155, Union Circle, #305070, TX 76203-5017, USA
Wlodzimierz Kutner*
Faculty of Mathematics and Natural Sciences, School of Science, Cardinal Stefan Wyszynski University in Warsaw, Wóycickiego 1/3, 01-815 Warsaw, Poland

*Corresponding authors. Fax: +940 565 4318 (FD), +48 22 34 33333 (WK).;
E-mail: Francis.Dsouza@unt.edu, wkutner@ichf.edu.pl

0165-9936/$ - see front matter © 2012 Elsevier Ltd. All rights reserved. doi:10.1016/j.trac.2011.11.005

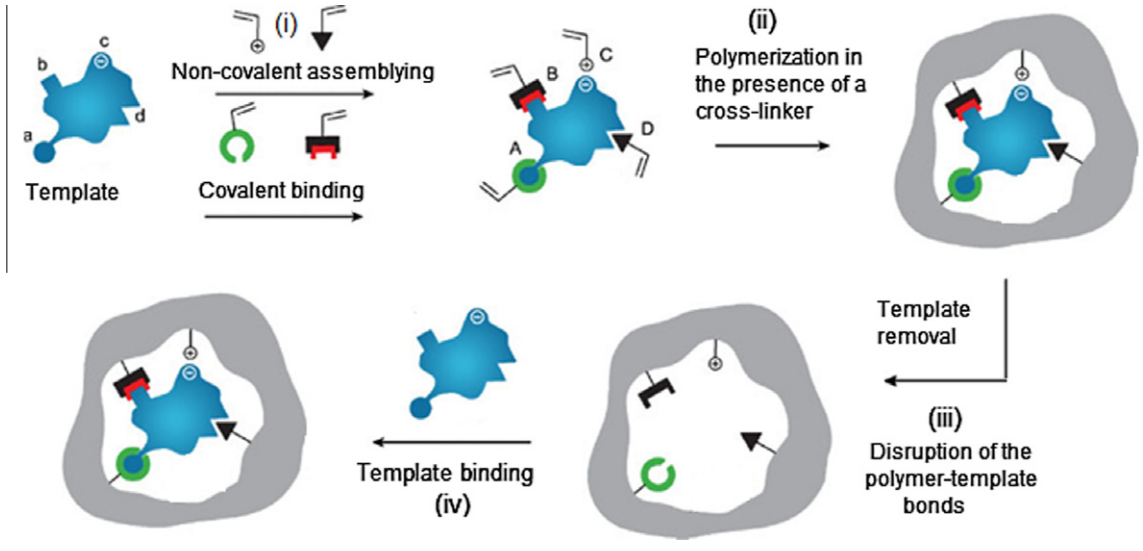
1. Introduction

Most physiological processes in living organisms are mediated by molecular recognition (e.g., enzymes specifically recognize their substrates and antibodies their antigens, hormones bind to an individual set of cell-surface receptors, and cells communicate and interact with each other only after recognition of certain cell-surface markers). These biological recognition units are widely used in biosensors, in order to detect one particular species, the analyte in a complex physiological matrix.

One approach to build such a biosensor is to isolate a biological receptor from its natural environment and to integrate it with a transducer that is capable of indicating analyte binding by alteration of a measured physical quantity. However, this procedure of biosensor preparation suffers one major deficiency (i.e., bioreceptors often comprise several sub-units, which degrade during immobilization under conditions different from their natural environment). Other drawbacks include limited stability (because of poor tolerance of extreme solution acidity or basicity, temperature, some organic solvents, and exposure to external fields, like the electromagnetic or ultrasonic field), short lifetime, low availability, and high cost (because of the necessity of tedious purification and inadequate reproducibility). As a result, the same enzyme, from the same manufacturer but a different batch, may reveal different activity.

An alternative approach is to use a synthetic recognition unit in a sensing system instead of a fragile biological receptor. Nowadays, the design and the synthesis of synthetic recognition units capable of binding a target analyte with affinity and selectivity similar to those of a bioreceptor are of interest to researchers. For that, one technique increasingly explored is molecular imprinting [1,2], in which functional and cross-linking monomers are co-polymerized in solution in the presence of a template and a porogenic medium. The analyte itself or its close structural analogue is used as the template, and different organic solvents and ionic liquids serve as porogens. The functional monomers initially form a complex with the template. Polymerization of the complex in the presence of a cross-linking monomer holds recognition sites of the functional monomers in position. Subsequent removal of the template generates molecular cavities that are complementary in size and shape to the analyte. Moreover, orientation of the recognition sites of these cavities is dictated by the binding sites of the template molecules. In effect, recognition of the resulting molecularly-imprinted polymer (MIP) synthetic receptor imitates the receptor-ligand, antibody-antigen, or enzyme-substrate biorecognition.

Besides the near antibody-like selectivity, other major advantages of MIPs, compared to their biological counterparts, include physical robustness, resistance to elevated temperatures and pressures, inertness to acids, bases and aggressive organic solvents, and low cost and



Scheme 1. Molecular imprinting. (i) Formation of reversible interactions between the template and the functional monomer may involve one or more of the following reciprocal actions: (A) reversible covalent binding; (B) covalent attachment of polymerizable binding groups that are activated for non-covalent interactions by template cleavage; (C) electrostatic interactions; and, (D) hydrophobic or van der Waals interactions – each formed with complementary functional groups or structural elements of the template (a–d), respectively. (ii) A subsequent polymerization in the presence of a cross-linking monomer, a cross-linking reaction or another process results in formation of an insoluble matrix (which itself can contribute to recognition through steric, van der Waals and even electrostatic interactions), in which the template molecules reside. (iii) Template removal from the polymer through disruption of polymer-template bonds and extraction from the matrix. (iv) The analyte, or analogues thereof, selectively binding in the cavities vacated by the template. While vinyl polymerization is presented here by way of example, the same basic scheme can equally well be applied elsewhere (e.g., sol-gel polycondensation, and electropolymerization) (Adapted from [3]).