

edited by
Seung-Woo Lee
Toyoki Kunitake

Handbook of
**Molecular
Imprinting**
Advanced Sensor Applications



edited by
Seung-Woo Lee
Toyoki Kunitake

Handbook of
**Molecular
Imprinting**
Advanced Sensor Applications



Published by

Pan Stanford Publishing Pte. Ltd.
Penthouse Level, Suntec Tower 3
8 Temasek Boulevard
Singapore 038988

Email: editorial@panstanford.com

Web: www.panstanford.com

British Library Cataloguing-in-Publication Data

A catalogue record for this book is available from the British Library.

Handbook of Molecular Imprinting: Advanced Sensor Applications

Copyright © 2013 by Pan Stanford Publishing Pte. Ltd.

All rights reserved. This book, or parts thereof, may not be reproduced in any form or by any means, electronic or mechanical, including photocopying, recording or any information storage and retrieval system now known or to be invented, without written permission from the publisher.

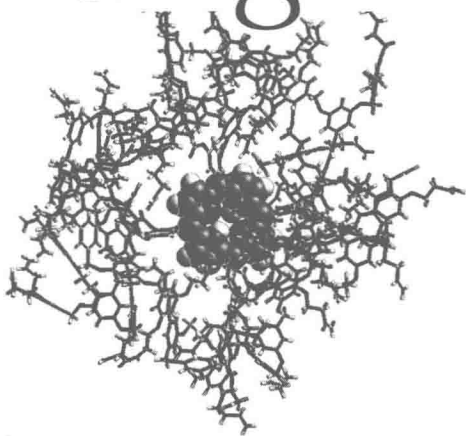
For photocopying of material in this volume, please pay a copying fee through the Copyright Clearance Center, Inc., 222 Rosewood Drive, Danvers, MA 01923, USA. In this case permission to photocopy is not required from the publisher.

ISBN 978-981-4316-65-1 (Hardcover)

ISBN 978-981-4364-32-4 (eBook)

Printed in the USA

Handbook of
Molecular
Imprinting



Preface

Molecular imprinting is now established as an indispensable tool for separation and sensor technologies. The most popular scheme to realize the molecular imprinting concept is probably the cross-linking of linear polymers in the presence of template molecules. Three-dimensional cavities would be created in the polymer network after the removal of template molecules. Unfortunately, the conformational adaptability of linear polymers is limited, and template molecules and the surrounding polymer chains cannot produce best molecular fitting in most cases. Molecular fitting by commonly employed imprinting materials is less than satisfactory compared with polypeptide chains of protein molecules. Superior three-dimensional fit of active sites of enzyme molecules and their specific substrates are truly remarkable.

Some of the inorganic chains are much more flexible than organic chains. For example, rotational and bending motions of metal–oxygen bonds are more facile than those of carbon–carbon bonds. This fact implies that metal oxide gels provide better molecular fitting with template molecules. In fact, the first example of molecular imprinting was reported in 1931 for silica matrix, as mentioned in Chapter 1. The use of inorganic matrices became much expanded in recent years and now occupies a significant fraction of molecular imprinting studies.

This handbook reflects this situation and attempts to survey the recent advances of molecular imprinting in inorganic and organic matrices in a combined form. The functional aspect is more or less focused on sensor applications. Such applications have become increasingly important in relation to environmental and biomedical issues, as summarized as Parts 3 and 4, respectively. The discussion in Chapter 1 will help grasp the pros and cons of inorganic matrices relative to organic matrices, and Part 5 provides a patent-based market analysis of molecular imprinting technology.

We are grateful to Mr. Stanford Chong of Pan Stanford Publishing for his continuous encouragement during the preparation of this handbook. Many thanks also to our wives, who showed splendid perseverance towards the absent (minded) husbands.

Contents

Part 1	Fundamentals of Molecular Imprinting and Sensor Applications	1
1.	Fundamentals and Perspectives of Molecular Imprinting in Sensor Applications	3
	<i>Seung-Woo Lee, Sergiy Korposh, Roman Selyanchyn, and Toyoki Kunitake</i>	
1.1	Introduction	3
1.2	Molecular Imprinting in Organic Matrices	4
1.2.1	Covalent Approach	6
1.2.2	Non-Covalent Approach	7
1.2.3	Other Approaches for Organic MIP Fabrication	9
1.3	Molecular Imprinting in Inorganic Matrices	11
1.3.1	Sol-Gel Approach	12
1.3.2	Liquid Phase Deposition (LPD) Approach	15
1.4	Major Transducers	16
1.4.1	Mass-Sensitive Transducer	17
1.4.2	Electrochemical Transducer	19
1.4.3	Optical Transducer	21
1.5	Applications of Organic MIP Materials in Sensors	26
1.6	Applications of Inorganic MIP Materials in Sensors	31
1.6.1	Silica Based Imprinted Materials	31
1.6.2	Hybrid Imprinted Materials	38
1.6.3	LPD Based Imprinted Materials	40
1.6.4	Strategy for Improved Selectivity	43
1.7	Conclusions	45
2.	Molecularly Imprinted Optical Sensing Receptor	65
	<i>Sing Muk Ng and Ramaier Narayanaswamy</i>	
2.1	Introduction	65
2.2	Chronological Protocols and Procedures	67

2.2.1	Selection of Materials and Ingredients	67
2.2.2	Polymerization Options	72
2.2.2.1	Free-radical initiated polymerization	72
2.2.2.2	Condensation polymerization	73
2.2.2.3	Electropolymerization	74
2.2.3	Configurations of Matrix	75
2.2.3.1	Bulk	75
2.2.3.2	Monoliths	76
2.2.3.3	Membranes	77
2.2.4	Handling and Preparation	78
2.3	Rational Design of Receptors	79
2.3.1	Interaction Study of Pre-Polymerization Ingredients	79
2.3.2	Computational Modeling	81
2.3.3	Thermodynamic Considerations	83
2.3.4	Repeatability and Reproducibility	86
2.3.5	Commercialization	87
2.4	Optical Sensing Schemes and Transduction Systems	89
2.4.1	Direct Monitoring of Analyte	89
2.4.2	Direct Fluorescence	90
2.4.3	Displacement Assay	92
2.4.4	Reflectance and Absorbance	94
2.4.5	Phosphorescence	96
2.4.6	Chemiluminescence	97
2.4.7	Surface Plasmon Resonance	98
2.4.8	Fluorescence Lifetime Decay	100
2.5	Advanced Probe Designs and Sensing Configuration	102
2.5.1	Sensor Arrays	102
2.5.2	Optical MIP Chips	104
2.5.3	Micro- and Nano-sized Sensors	106
2.6	Binding Aspects and Analytical Signals	108
2.6.1	Binding Isotherms and Affinity Distributions	108
2.6.2	Batch Binding Analysis and Binding Models	109

2.6.3 Correlation of Analytical Signal with Binding Isotherms Models	110
2.6.4 Advantage and Limitation	111
2.7 Summary	112
3. Translational Applications of Molecularly Imprinted Polymer-Based Electrochemical Sensors	119
<i>Hung-Yin Lin, James L. Thomas, and Mei-Hwa Lee</i>	
3.1 Introduction	119
3.2 Principle of Molecularly Imprinted Polymers	121
3.2.1 Synthesis of MIPs	121
3.2.2 Characterization of MIPs	123
3.2.3 Morphology of MIPs	124
3.3 Transducers Employed with Molecularly Imprinted Polymers as Sensing Elements	126
3.3.1 Types of Transducers	126
3.3.2 Interface of Transducer and Molecularly Imprinted Polymers	130
3.3.3 Miniature MIPs-Based Sensors	130
3.3.4 Demonstration of MIPs-Based Electrochemical Sensors	134
3.4 Molecularly Imprinted Polymers-Based Sensors for the Real World	135
3.4.1 Source of Real Samples	135
3.4.2 Biomarkers	138
3.4.3 Cross-Talk Interference	138
3.5 Prospective	139
4. Optical Sensors for Monitoring Trace Inorganic Toxins	147
<i>T. Prasada Rao, Dhanya James, and Milja T. Elias</i>	
4.1 Environmental Trace Analysis	148
4.2 Inorganic Toxins	148
4.3 Importance of Sampling in Trace Analysis	152
4.3.1 Sample Handling	152
4.3.2 Sample Pre-Treatment, Homogenization and Sub-Sampling	152
4.3.3 Sample Preparation	152

4.3.3.1	Decomposition of inorganic or organic matrices	153
4.3.3.2	Separation and pre-concentration steps	153
4.4	Trace/Ultra Trace Analytical Techniques	154
4.4.1	Selection of Analytical Technique/Method	157
4.4.2	Essential Features of Analytical Techniques	158
4.4.2.1	Signal processing, data handling and reporting	158
4.4.2.2	Signal integrity	158
4.4.2.3	Data handling	158
4.4.2.4	Good Automated Laboratory Practice (GALP) [1]	159
4.4.2.5	Reporting of results	159
4.5	Chemical Speciation	160
4.6	Sensors	161
4.6.1	Fundamentals of Optical Sensors (Optodes)	163
4.6.2	Optical Sensing of Ionic Analytes	163
4.6.3	Optical Sensing of Neutral Analytes	165
4.7	Molecularly Imprinted Polymers	166
4.7.1	Molecular Imprinting Technology	167
4.7.2	MIPs in Optical Sensing	168
4.8	Optical Sensors vis-a-vis Other Sensor Techniques	174
4.9	Future Outlook	174
5.	MIP Thermistor	181
	<i>Rajagopal Rajkumar, Umporn Athikomrattanakul, Kristian Lettau, Martin Katterle, Bengt Danielsson, Axel Warsinke, Nenad Gajovic-Eichelmann, and Frieder W. Scheller</i>	
5.1	Introduction	181
5.1.1	The MIP Concept	181
5.1.2	MIP Sensors	183
5.1.3	Enzyme Thermistors	184
5.2	Covalently Imprinted Polymers Using Boronic Acid Derivates	188
5.2.1	Synthesis of Template (Fructosyl Valine)	189

5.2.2	Synthesis of Functional Monomer (Vinyl Phenyl Boroxine)	189
5.2.3	Synthesis of N-[β -D-Fructopyranosyl-(1)]-L-Valine _{2,3} ; 4,5-bis-O- ((4-Vinylphenyl) Boronate)	190
5.2.4	Synthesis of MIP and Control Polymers	190
5.2.5	MIP Thermistor Set-Up and Measurements	190
5.2.6	Thermometric MIP Sensor for Fructose	191
5.2.7	Thermometric MIP Sensor for Fructosyl Valine	193
5.2.8	Concentration Dependence of Fru-Val Binding	194
5.2.9	Closed Loop Studies	196
5.3	Non-Covalent MIPs Containing Two Functional Monomers for Carboxyphenyl Aminohydantoin (CPAH) as Analogon of Nitrofurantoin (NFT)	197
5.3.1	Synthesis of an Analogue Template, Carboxyphenyl Aminohydantoin (CPAH)	197
5.3.2	Synthesis of Functional Monomers	198
5.3.3	Preparation of MIPs Based on Two Functional Monomers	199
5.3.4	MIP-Based Thermometric Study	200
5.4	Bi-Functional Esterolytically Active MIP	203
5.4.1	Polymer Preparation	204
5.4.2	Thermometric Characterization of Adsorption and Catalysis	205
5.5	Conclusions	209

Part 2 Potential Materials for Molecular Imprinting 217

6. The Use of a Thermally Reversible Bond for Molecular Imprinting 219

Ji Young Chang

6.1	Introduction	219
6.2	Cross-Linked Vinyl Polymer Matrix	221
6.3	Silica Matrix	226
6.4	Polyimide as Noncross-Linked Matrix	228
6.5	Summary and Outlook	232

7. Molecular-Sieving Silica/Tin Oxide Sensor Prepared by Chemical Vapor Deposition in the Presence of Template Molecule	235
<i>Naonobu Katada and Miki Niwa</i>	
7.1 Introduction	235
7.2 Preparation Method	238
7.3 Selective Chemisorption	241
7.4 Sensing Function	244
7.4.1 Selectivity for Various Molecules	244
7.4.2 Improved Response and Selectivity of Film-Type Sensor	249
7.4.3 Detection of Dialkyl Phthalate	252
7.5 Conclusion	254
8. Environmental Approaches by Molecular Imprinting on Titanium Dioxide	259
<i>Milka Nussbaum and Yaron Paz</i>	
8.1 Introduction	260
8.2 Preparation	269
8.2.1 Preparation of Molecularly Imprinted (MI) Structures	269
8.2.1.1 Sol-gel method using alkoxide chemistry	271
8.2.1.2 "Layer-by-layer" approach using sol-gel method	272
8.2.1.3 Liquid phase deposition/chemical bath deposition	274
8.2.1.4 Titanyl sulfate chemistry	275
8.2.1.5 Titanium tetrachloride chloride chemistry	276
8.2.1.6 Potassium titanyl oxalate chemistry	276
8.2.2 Preparation of Molecularly Imprinted Polymer (MIP) Structures	276
8.2.3 Preparation of Molecularly Imprinted Inorganic (MIIn) Structures	277
8.2.4 Preparation of Molecularly Imprinted Host (MIH) Structures	278
8.3 Characterization	279

8.3.1 Interaction Between Host and Template	279
8.3.2 Assessment of Removal of Template Molecules	281
8.3.3 Concentration and Structure of Sites	282
8.3.4 Surface Area	282
8.3.5 Film Morphology and Particles' Size	283
8.3.6 Film Thickness	283
8.3.7 Crystalline Phase	284
8.4 Applications	284
8.4.1 Sensing	284
8.4.1.1 Quartz crystal microbalance (QCM) sensors	285
8.4.1.2 Electrochemical sensors	286
8.4.1.3 Ion sensitive field effect transistors	288
8.4.1.4 Matrix-assisted laser desorption/ionization (MALDI) mass-spectrometry	290
8.4.1.5 Evaluation of performance of sensors	290
8.4.1.5.1 Sensitivity	291
8.4.1.5.2 Imprinting efficiency ratio	291
8.4.1.5.3 Selectivity	293
8.4.1.5.4 Response time	303
8.4.1.5.5 Repeatability	304
8.4.1.5.6 Stability and reproducibility	304
8.4.2 Photocatalysis	305
8.4.2.1 Introduction	305
8.4.2.2 Performance	307
8.4.2.2.1 Efficiency	308
8.4.2.2.2 Selectivity	310
8.4.2.2.3 Adsorption vs. photocatalytic degradation	313
8.4.2.2.4 Imprinting of pseudo-target molecules	316
8.4.2.2.5 Intermediates and by-products	318

8.4.2.2.6 Stability and repeatability	319
8.4.3 Separation by Selective Filtration	320
8.5 Conclusion	321
Part 3 MIP Sensors for Environmental and Trace Detection	331
9. Molecularly Imprinted Nanocomposites for Highly Sensitive SPR Detection	333
<i>Jun Matsui and Kensuke Akamatsu</i>	
9.1 Introduction	333
9.2 Surface Plasmon Resonance of Metal Nanoparticles	335
9.2.1 Biosensors Utilizing Gold Nanoparticles	337
9.2.2 Synthesis of Surface-Functionalized Gold Nanoparticles	339
9.3 Molecularly Imprinted Nanocomposite	340
9.3.1 Concept	340
9.3.2 Colorimetric Sensing with Molecularly Imprinted Nanocomposite	340
9.3.2.1 Physical properties	342
9.3.2.2 Selectivity	343
9.3.3 SPR Sensor with Molecularly Imprinted Nanocomposite Gel	344
9.3.3.1 Preparation of sensor chip	345
9.3.3.2 SPR measurement	346
9.3.4 SPR Sensing of Atrazine	348
9.3.4.1 Preparation of sensor chip	348
9.3.4.2 Effects of gold nanoparticles on sensitivity	349
9.3.4.3 Effects of molecular imprinting on sensitivity	350
9.3.4.4 Selectivity	352
9.4 Conclusion	353
10. Molecularly Imprinted Room Temperature Phosphorescent Optosensors for Environmental Pollutants	359
<i>He-Fang Wang and Xiu-Ping Yan</i>	
10.1 Introduction	359

10.2	Fabrication of MIPs-Based RTP Optosensors	361
10.2.1	Conventional MIPs with RTP Detection	361
10.2.2	Incorporation of Heavy Atoms into MIPs	364
10.2.3	Surface Imprinting on Phosphorescent Nanoparticles	368
10.3	RTP Detection Modes	374
10.3.1	Static Measurement	374
10.3.2	Flow-Through Assays	377
10.4	Applications	379
10.4.1	RTP Sensing of Nafcillin	379
10.4.2	RTP Sensing of PAHs	381
10.4.3	Sensing of Copper Ions	382
10.4.4	Sensing of Pentachlorophenol	383
10.5	Conclusions	384
11.	Electrochemical Sensing of Nitroaromatic Compounds in Natural Waters and Soil Samples	389
	<i>Taher Alizadeh</i>	
11.1	Introduction	389
11.2	Nitroaromatic Compounds	390
11.3	Different Strategies Developed for Preparation of MIP for Nitroaromatic Compounds	392
11.4	Electrochemistry of Nitroaromatic Compounds	398
11.5	MIP-Based Electrochemical Sensors	400
11.5.1	Polymerization Directly on the Electrode Surface	401
11.5.1.1	Sol-gel and poly TiO ₂ systems	401
11.5.1.2	Electrodes modified with electropolymerized films	405
11.5.2	Coupling of the MIP Particles with Electrochemical Transducers	407
11.5.3	MIP as a Solid Phase Sorbent for Separation and Preconcentration Before Electrochemical Determination	413
12.	Trace Detection Based on Cyclodextrin Anchored Molecularly Imprinted TiO₂ Thin Films	421
	<i>Seung-Woo Lee</i>	
12.1	Introduction	421
12.2	Surface Sol-Gel Process and Molecular Imprinting	423

12.3	Two-Dimensional Imprinting with Juxtaposed CD Hosts on Metal Oxide Surface	426
12.3.1	BPA Sensing Based on Electrochemical Impedance Changes	427
12.3.2	SAM Effects on cSPI Response	429
12.3.3	cSPI Response to BPA on a BPA-Imprinted $\text{TiO}_2/\beta\text{-CD}$ Film	431
12.3.4	Selectivity of the BPA-Imprinted $\text{TiO}_2/\beta\text{-CD}$ Film	433
12.4	Trace Detection of Explosives Using a CD-Anchored Metal Oxide Matrix	435
12.4.1	Surface Modification for 2,4-DNT Recognition	436
12.4.2	cSPI Response and Sensitivity to 2,4-DNT	437
12.5	Imprinting Process Associated with a Gas Phase Sol-Gel Technique	439
12.5.1	Gas-Phase Surface Sol-Gel (GSSG) Process	439
12.5.2	Three-Dimensional Assembly of Templated CDs with TiO_2 Ultrathin Layers	440
12.5.3	BPA Response and Imprinting Effect	441
12.6	Future Prospects	444
13.	Molecularly Imprinted Au Nanoparticle Composites and Their Application for Sensing, Controlled Release, and Photoelectrochemistry	453
	<i>Itamar Willner and Ran Tel-Vered</i>	
13.1	Introduction	453
13.2	Imprinting of Molecular Recognition Sites in Au NP Composites via Donor-Acceptor and/or Electrostatic Interactions	456
13.3	Imprinted Ligand-Functionalized bis-Aniline-Crosslinked Au NP Composites for Sensing	462
13.4	Electrochemically Triggered Imprinted Au NP "Sponges"	467
13.5	Controlling the Wettability of Surfaces by Imprinted Au NP Composites	471
13.6	Imprinted Semiconductor Nanoparticle/Metal Nanoparticle Composites for Enhanced Photoelectrochemistry	474