CHEMICAL SENSORS AND BIOSENSORS

Brian R. Eggins
University of Ulster at Jordanstown
Northern Ireland, UK

JOHN WILEY & SONS, LTD

CHEMICAL SENSORS AND BIOSENSORS

Analytical Techniques in the Sciences (AnTS)

Series Editor: David J. Ando, Consultant, Dartford, Kent, UK

A series of open learning/distance learning books which covers all of the major analytical techniques and their application in the most important areas of physical, life and materials science.

Titles Available in the Series

Analytical Instrumentation: Performance Characteristics and Quality
Graham Currell, University of the West of England, Bristol, UK

Fundamentals of Electroanalytical Chemistry
Paul M. S. Monk, Manchester Metropolitan University, Manchester, UK

Introduction to Environmental Analysis
Roger N. Reeve, University of Sunderland, UK

Polymer Analysis
Barbara H. Stuart, University of Technology, Sydney, Australia

Chemical Sensors and Biosensors
Brian R. Eggins, University of Ulster at Jordanstown, Northern Ireland, UK

Forthcoming Titles

Analysis of Controlled Substances
Michael D. Cole, Anglia Polytechnic University, Cambridge, UK

Liquid Chromatography–Mass Spectrometry: An Introduction
Robert E. Ardrey, University of Huddersfield, UK

CHEMICAL SENSORS AND BIOSENSORS

Brian R. Eggins
University of Ulster at Jordanstown
Northern Ireland, UK

JOHN WILEY & SONS, LTD

Telephone (+44) 1243 779777

Email (for orders and customer service enquiries): cs-books@wiley.co.uk
Visit our Home Page on www.wileyeurope.com or www.wiley.co.uk

Reprinted June 2003, February 2004

Other Wiley Editorial Offices

John Wiley & Sons Inc., 111 River Street, Hoboken, NJ 07030, USA

Jossey-Bass, 989 Market Street, San Francisco, CA 94103-1741, USA

Wiley-VCH Verlag GmbH, Boschstr. 12, D-69469 Weinheim, Germany

John Wiley & Sons Australia Ltd, 33 Park Road, Milton, Queensland 4064, Australia

John Wiley & Sons (Asia) Pte Ltd, 2 Clementi Loop #02-01, Jin Xing Distripark, Singapore 129809

John Wiley & Sons Canada Ltd, 22 Worcester Road, Etobicoke, Ontario, Canada M9W 1L1

British Library Cataloguing in Publication Data

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

ISBN 0 471 89913 5 (cloth)
0 471 89914 3 (paperback)

Typeset in 10/12pt Times by Laserwords Private Limited, Chennai, India
Printed and bound in Great Britain by Antony Rowe Ltd, Chippenham, Wiltshire
This book is printed on acid-free paper responsibly manufactured from sustainable forestry in which at least two trees are planted for each one used for paper production.

To Chrissie and Rosanne

Contents

Series Preface

There has been a rapid expansion in the provision of further education in recent years, which has brought with it the need to provide more flexible methods of teaching in order to satisfy the requirements of an increasingly more diverse type of student. In this respect, the *open learning* approach has proved to be a valuable and effective teaching method, in particular for those students who for a variety of reasons cannot pursue full-time traditional courses. As a result, John Wiley & Sons Ltd first published the Analytical Chemistry by Open Learning (ACOL) series of textbooks in the late 1980s. This series, which covers all of the major analytical techniques, rapidly established itself as a valuable teaching resource, providing a convenient and flexible means of studying for those people who, on account of their individual circumstances, were not able to take advantage of more conventional methods of education in this particular subject area.

Following upon the success of the ACOL series, which by its very name is predominately concerned with Analytical *Chemistry*, the *Analytical Techniques in the Sciences* (AnTS) series of open learning texts has now been introduced with the aim of providing a broader coverage of the many areas of science in which analytical techniques and methods are now increasingly applied. With this in mind, the AnTS series seeks to provide a range of books which will cover not only the actual techniques themselves, but *also* those scientific disciplines which have a necessary requirement for analytical characterization methods.

Analytical instrumentation continues to increase in sophistication, and as a consequence, the range of materials that can now be almost routinely analysed has increased accordingly. Books in this series which are concerned with the *techniques* themselves will reflect such advances in analytical instrumentation, while at the same time providing full and detailed discussions of the fundamental concepts and theories of the particular analytical method being considered. Such books will cover a variety of techniques, including general instrumental analysis, spectroscopy, chromatography, electrophoresis, tandem techniques, electroanalytical methods, X-ray analysis and other significant topics. In addition, books in the series will include the *application* of analytical techniques in areas such as environmental science, the life sciences, clinical analysis, food science, forensic analysis, pharmaceutical science, conservation and archaeology, polymer science and general solid-state materials science.

Written by experts in their own particular fields, the books are presented in an easy-to-read, user-friendly style, with each chapter including both learning objectives and summaries of the subject matter being covered. The progress of the reader can be assessed by the use of frequent self-assessment questions (SAQs) and discussion questions (DQs), along with their corresponding reinforcing or remedial responses, which appear regularly throughout the texts. The books are thus eminently suitable both for self-study applications and for forming the basis of industrial company in-house training schemes. Each text also contains a large amount of supplementary material, including bibliographies, lists of acronyms and abbreviations, and tables of SI Units and important physical constants, plus where appropriate, glossaries and references to original literature sources.

It is therefore hoped that this present series of textbooks will prove to be a useful and valuable source of teaching material, both for individual students and for teachers of various science courses.

Dave Ando
Dartford, UK

Preface

This book is derived partly from the author's earlier book, *Biosensors: An Introduction*, originally published in 1996. Much of the same material is used here, although now it is set in the style of an open learning book, following the presentation of the Analytical Chemistry by Open Learning (ACOL) Series and now set in the style of the new Analytical Techniques in the Sciences (AnTS) Series. The scope of the previous book is broadened to cover chemical sensors as well as biosensors.

The original *Biosensors* book evolved out of a lecture course in biosensors (given at the University of Ulster), as there were very few suitable textbooks available at that time. A number of part-time students were unable to attend the formal lectures, but used the *Biosensors* textbook in open learning mode, helped by informal tutorials. These students, on average, performed at least as well in the examinations as the corresponding full-time students.

After an introductory chapter which describes the general idea of sensors, Chapter 2 discusses in some detail different transduction elements, both electrochemical and photometric. Chapter 3 then describes the various sensing elements used to select particular analytes, while Chapter 4 discusses performance factors such as selectivity, sensitivity, range, lifetimes, etc. Chapter 5 next describes in more detail the applications of electrochemistry in sensors and biosensors. Photometric sensors are described in Chapter 6, with mass-sensitive and thermal-sensitive sensors being discussed in Chapter 7. Finally, Chapter 8 gives five case studies of particular applications in more detail.

I would like to thank my colleagues at the University of Ulster in the Biomedical Environmental Sensor Technology (BEST) Centre for their help and encouragement, Professor John Anderson, Professor Jim McLaughlin, Dr Tony Byrne and Dr Eric McAdams (at UU Jordanstown), Professors Dermot Diamond, Johannes Vos and Malcolm Smyth (at Dublin City University), and from The J Fourier University in Grenoble, France, Drs Pascal Mailley and Serge Cosnier.

I would like to acknowledge the indirect inspiration I have received through the work and contacts with Professor George Guillbault at University College, Cork, Professor Anthony Turner at Cranfield University, and not least, Professor Allen Hill of Oxford University, whose lecture inspired my first interest in writing books on biosensors. I must also mention, through the 'Eirelec Conferences', Professor Joe Wang from the University of New Mexico, and Professor Allen Bard from the University of Texas at Austin. I would also like to acknowledge the contributions of some of my former students, namely Dr Edward Cummings, Dr Min Zhou, Mr Shane McFadden, Ms Catriona Hickey and Mr Stephen Toft.

I wish particularly to thank David Ando, the Managing Editor of the AnTS Series, for his great help and encouragement in advising and editing the manuscript.

Above all, I thank my wife Chrissie, without whose dedicated support, encouragement and domestic provisions I would never have completed this book.

Brian R. Eggins
University of Ulster at Jordanstown

Acronyms, Abbreviations and Symbols

A	analyte
A*	analyte analogue
Ab	antibody
AC	alternating current
Ag	antigen
AMP	adenosine 5′-monophosphate
AP	acid phosphatase; action potential
ATP	adenosine triphosphate
ATR	attenuated total reflectance
BOD	biological oxygen demand
C	coulomb
CHEMFET	field-effect transistor, with chemically sensing gate
Cp	cyclopentadiene
CPE	carbon paste electrode
CV	cyclic voltammetry
DAC	*p*-dimethylaminocinnamaldeyde
DC	direct current
DEAE	diethylaminoethyl
DNA	deoxyribonucleic acid
DVM	digital voltmeter
ECQM	electrochemical quartz crystal microbalance
emf	electromotive force
ENFET	field-effect transistor, with enzyme gate system
EW	evanescent wave
FAD	flavin–adenine dinucleotide
Fc	ferrocene

FET	field-effect transistor
FIA	flow-injection analysis
FITC	fluorescein isothiocyanate
FMH	flavin mononucleotide
GC	gas chromatography
GDH	glucose dehydrogenase
GOD	glucose oxidase
HMDE	hanging-mercury-drop electrode
HPLC	high performance liquid chromatography
id	internal diameter
IGFET	insulated-gate field-effect transistor
IR	infrared
IRE	internal reflection element
ISA	ionic-strength adjuster
ISE	ion-selective electrode
ISFET	ion-selective field-effect transistor
IUPAC	International Union of Pure and Applied Chemistry
J	joule
LDH	lactate dehydrogenase
LDV	laser Doppler velocimetry
LED	light-emitting diode
LMO	lactate monooxidase
LOD	lactate oxidase
LSV	linear-sweep voltammetry
M	molarity (mol dm^{-3})
MIS	metal–insulator–semiconductor
mM	millimolar (10^{-3} mol dm^{-3})
MS	mass spectrometry
NAD	nicotinamide–adenine dinucleotide
NAD^+	nicotinamide–adenine dinucleotide (oxidized form)
NADH	nicotinamide–adenine dinucleotide (reduced form)
NMP	*N*-methylphenothiazine
Ox	oxidized species
PCS	phase correlation spectroscopy
PO	peroxidase
ppm	parts per million
PPY	polypyrrole
QCM	quartz crystal microbalance
QELS	quasi-elastic light scattering spectroscopy
R	reduced species
RF	radiofrequency
RNA	ribonucleic acid
SAW	surface acoustic wave

SCE	saturated-calomel electrode
SHE	standard hydrogen electrode
SI (units)	Système International (d'Unitès) (International System of Units)
SPE	screen-printed electrode
SPR	surface plasmon resonance
TCNQ	tetracyanoquinodimethane
TIRF	total internal reflection fluorescence
TISAB	total-ionic-strength adjustment buffer
TNT	trinitrotoluene
TTF	tetrathiofulvalene
UV	ultraviolet
V	volt
vis	visible
A	absorbance
C	concentration; capacitance
f	frequency
I	electric current; intensity (of light)
L	conductance
m	mass
R	resistance; molar gas constant
t	time
T	thermodynamic temperature
V	electric potential
ε	extinction coefficient
λ	wavelength
ν	frequency (of radiation)

About the Author

Brian Eggins

The author was educated at King Edward's (Five Ways) School, Birmingham, and at Gonville and Caius College, Cambridge University (B.A. and M.A.). He then obtained an M.Sc. degree at The University of Manchester Institute of Science and Technology (UMIST), followed by a Ph.D. at Warwick University. He was then a Research Associate at Colorado University, USA for two years. After a brief period in industry and teaching experience at Grimsby College of Technology, he moved to Ulster Polytechnic (now The University of Ulster).

He is now a Reader in Physical and Analytical Chemistry at the University of Ulster. His research interests include electrochemistry and photo-electrochemistry, as well as biosensors. He has supervised 15 research students and is currently involved in three EU-funded research projects involving groups from four European countries, as well as from Israel. He has lectured in Canada, the USA and Europe. He has published over 100 original research papers, plus is author of *Chemical Structure and Reactivity,* published by Macmillan, *Estructura Quimica y Reactividad*, published by Ediciones Bellaterra, SA, and *Biosensors: An Introduction,* published jointly by John Wiley and Sons, Ltd and B.G. Teubner. He is a Fellow of The Royal Society of Chemistry.

Chapter 1

Introduction

Learning Objectives

- To define different types of sensors.
- To list recognition elements.
- To list the transducers used in sensors.
- To learn the methods of attaching recognition elements to transducers.
- To understand the most important performance factors.
- To know three main areas of application.

1.1 Introduction to Sensors

1.1.1 What are Sensors?

DQ 1.1

What is a sensor?

Answer

We have at least five of these, i.e. our noses, our tongues, our ears, our eyes and our fingers. They represent the main types of sensor. In the laboratory, one of the best known types of sensor is the litmus paper test for acids and alkalis, which gives a qualitative indication, by means of a colour reaction, of the presence or absence of an acid. A more precise method of indicating the degree of acidity is the measurement of pH, either by the more extended use of colour reactions in special indicator solutions, or even by simple pH papers. However, the best method *of measuring acidity is the use of the pH meter, which is an electrochemical device giving an electrical response which can be read by a needle moving on a scale or on a digital read-out device or input to a microprocessor.*

In such methods, the *sensor* that responds to the degree of acidity is either a chemical – the dye litmus, or a more complex mixture of chemical dyes in pH indicator solutions – or the glass membrane electrode in the pH meter.

The chemical or electrical response then has to be converted into a signal that we can observe, usually with our eyes. With litmus, this is easy. A colour change is observed, because of the change in the absorbance of visible light by the chemical itself, which is immediately detected by our eyes in a lightened room. In the case of the pH meter, the electrical response (a voltage change) has to be converted, i.e. *transduced* (= led through), into an observable response – movement of a meter needle or a digital display. The part of the device which carries out this conversion is called a *transducer.*

We can divide sensors into three types, namely (a) physical sensors for measuring distance, mass, temperature, pressure, etc. (which will not concern us here), (b) chemical sensors which measure chemical substances by chemical or physical responses, and (c) biosensors which measure chemical substances by using a biological sensing element. All of these devices have to be connected to a transducer of some sort, so that a visibly observable response occurs. Chemical sensors and biosensors are generally concerned with sensing and measuring particular chemicals which may or may not be biological themselves. We shall usually refer to such a material as the *substrate*, although the more general term *analyte* is sometimes used. Figure 1.1 shows schematically the general arrangement of a sensor.

SAQ 1.1

Draw a labelled diagram of a chemical sensor.

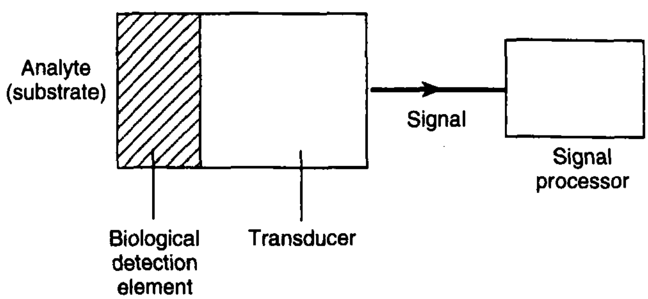

Figure 1.1 Schematic layout of a (bio)sensor. From Eggins, B. R., *Biosensors: An Introduction*, Copyright 1996. © John Wiley & Sons Limited. Reproduced with permission.

1.1.2 The Nose as a Sensor

One might consider the ears, eyes and fingers to be physical sensors as they detect physical sensations of sound, light and heat, etc., respectively. What we detect with the nose – smells – are in fact small quantities of chemicals. The nose is an extremely sensitive and selective instrument which is very difficult to emulate artificially. It can distinguish between many different chemical substances qualitatively and can give a general idea of 'quantity' down to very low detection limits. The chemicals to be detected pass through the olfactory membrane to the olfactory bulbs, which contain biological receptors that sense the substrate. The response is an electrical signal which is transmitted to the brain via the olfactory nerves. The brain then transduces this response into the sensation we know as smell. The tongue operates in a similar way.

Figure 1.2 shows a schematic diagram of the nasal olfactory system, illustrating the comparison with our generalized sensor. The nostrils collect the 'smell sample', which is then sensed by the olfactory membrane, i.e. the sensing element. The responses of the olfactory receptors are then converted by the olfactory nerve cell, which is the equivalent of the transducer, into electrical

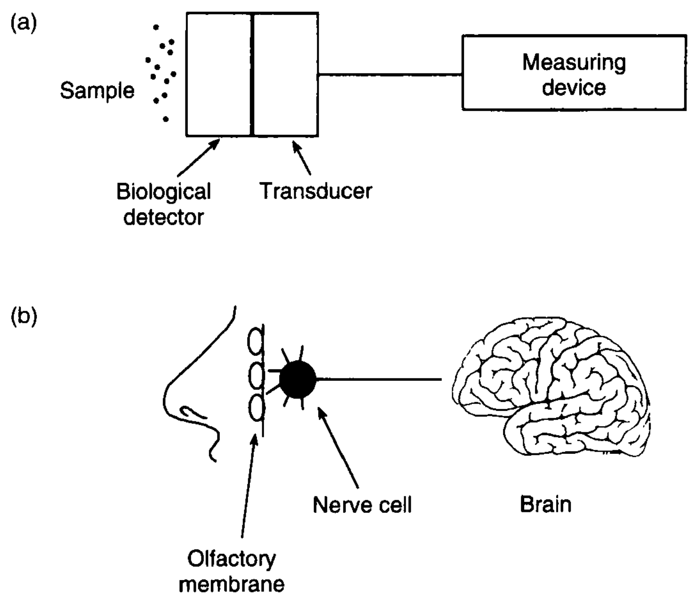

Figure 1.2 (a) Schematic of a sensor, showing the component parts, i.e. analyte, recognition element, transducer, actuator and measuring device. (b) Analogy with the nose as a sensor (actually a biosensor), in which the olfactory membrane is the biological recognition element, the nerve cell is the transducer, the nerve fibre is the actuator and the brain is the measuring element. From Eggins, B. R., *Biosensors: An Introduction*, Copyright 1996. © John Wiley & Sons Limited. Reproduced with permission.

signals which pass along the nerve fibre to the brain for interpretation. Thus, the brain acts as a microprocessor, turning the signal into a sensation which we call smell.

1.2 Sensors and Biosensors – Definitions

There are sometimes differences of usage for the terms *sensors, transducers, biosensors and actuators*, so it is necessary for us to define how they will be used in this book:

- We will use the term *sensor* to describe the whole device, following the Oxford English Dictionary definition, i.e. *a sensor is a device that detects or measures a physical property and records, indicates or otherwise responds to it.* (This is in contrast to the definition in Chambers Dictionary, quoted by Usher and Keating in their book 'Sensors and Transducers'.)
- We will define a *transducer* as *a device that converts an observed change (physical or chemical) into a measurable signal.* In chemical sensors, the latter is usually an electronic signal whose magnitude is proportional to the concentration of a specific chemical or set of chemicals.
- The term *actuator* i.e. *put into action,* is sometimes encountered. This is the part of the device which produces the display.

We can think of three types of sensor, i.e. physical, chemical and biosensors.

DQ 1.2

Distinguish between chemical sensors, physical sensors and biosensors.

Answer

Physical sensors are concerned with measuring physical quantities such as length, weight, temperature, pressure, and electricity – for their own sakes. This present book is not concerned with these as such except that the response of a sensor is usually in the form of a physical response. The book by Usher and Keating (see the Bibliography) is actually entirely concerned with physical sensors.

A chemical sensor is defined in R. W. Catterall's book (see the Bibliography) as **a device which responds to a particular analyte in a selective way through a chemical reaction and can be used for the qualitative or quantitative determination of the analyte.** *Such a sensor is concerned with detecting and measuring a specific chemical substance or set of chemicals.*

Biosensors are really a sub-set of chemical sensors, but are often treated as a topic in their own right. A biosensor can be defined as **a**