微纳技术著作丛书（影印版）

CMOS技术中的集成化学微传感系统

Integrated Chemical Microsensor Systems in CMOS Technology

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内 容 简 介

本书涵盖了CMOS化学微传感系统的各个领域，详细论述了化学微传感器在CMOS中的集成技术。在做了简要介绍之后，阐述了所有必备的基础知识，介绍了各种化学敏感方法，并介绍了CMOS技术及其在微传感器中的应用，最后对未来的发展作出了展望。

本书内容丰富，涵盖了大量的基础知识及CMOS技术中化学微传感器的相关重要信息，适合希望从事此领域工作的学生、工程技术人员、科学家阅读，对于熟悉本领域的专家也很有参考价值。

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序

科学出版社准备出版一套《微纳技术著作丛书》，包括原创作品和引进作品（影印或翻译）两种形式，并聘请专家组成编委会。这是一件大事，希望能坚持把它办好。

微纳米技术作为21世纪重要的一项技术，已成为国际科学界和工程技术界研究的热点。近年来，微米纳米技术进展迅速，已经发展成为一个包含机械、材料、电子、光学、化学、生物、基因工程、医学等基础学科的综合领域，而不仅仅属于任何单一的科学和技术门类。就其产品而言，也早已超越了人们广为熟悉的微型加速度传感器和纳米碳管等，呈现出向各个科学和技术领域全面渗透的趋势。

由于微纳米技术使得人们除了可以在同一基片上实现包括机械、流体、化学、生物、光学等器件外，也可以将信号处理和传输系统集成在同一基片上用以处理信息，决定计划，控制周围环境，从而大大提高最终产品的综合性能，实现高度智能化。在未来的航空航天、生物医学、环境监控、无线通信、汽车和交通、石油化工、能源、工农业、国家安全、食品和消费的各个领域都将有广泛应用，对国民经济、科学技术、社会发展与国家安全具有重要意义。今后的几十年里，随着微米纳米技术的迅速发展和向现代科学和技术的各个门类渗透，其对我们现代生活的各个方面带来的影响将是长期和深远的。从某种意义上来说，微米纳米技术的发展，可能改变人类的工作和生活方式，乃至基本概念，其潜在的影响有可能和以计算机技术为代表的微电子工业对世界的影响相提并论。

正是由于其诱人的应用前景和巨大的潜在市场，微米纳米技术目前已成为世界各国大力投资进行研究和发展的热点领域，其研究范围包括了材料、器件和系统，涉及的技术包含机理研究、设计分析、计算仿真、制造工艺、系统集成或组装、测控技术和应用研究等。随着微纳米技术的迅猛发展，近年来国外有大量这方面的专业书籍出版。

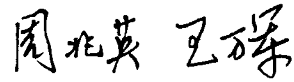
《微纳技术著作丛书》涵盖材料开发、系统设计、检测技术、集成技术、通信网络、传感系统、微加工技术等方面，它们都是本领域的研究热点。这套丛书的出版对促进我国微米纳米技术的发展将有很大的推动作用。

这套丛书中，原创作品收录的都是国内从事微纳技术的一线研究人员在本领域的研究成果与心得，具有很强的独立性、创造性和系统性。引进作品都是与国际知名的出版集团合作，经国内专家的甄别，挑选出能反映国外最新研究成果、对国内读者又有借鉴价值的作品，具有权威性、前瞻性和可读性。因为微纳米技

术是一个交叉学科领域，我们有意识的选择了一些由多人合写的专著。通常这类著作都是由相关领域的知名专家，各自在每一章节涵盖一个专题，既有进行综合性的论述，也有个人的具体独创性研究。这样的书籍，通常能帮助读者既获得某一领域的研究概况，又能从一个具体的应用专题中获得收益。

2007 年初推出的第一批影印版图书，我和王万军教授进行了评读，此套丛书很实用，不少作者在该领域有很高的声望。我们建议致力于微米纳米技术的研究人员，包括研究生、技术人员，能够花些时间阅读。

总之，我们对科学出版社组织出版这套丛书的举措很赞赏，也希望他们能将这一工作认真、长期地做下去。同时，我们也希望国内的专家能够积极、踊跃地加盟，为我国微米纳米技术的推进做出贡献。



2006 年 12 月 7 日

Preface

This book provides a comprehensive treatment of the very interdisciplinary field of CMOS technology-based chemical microsensor systems. It is, on the one hand, targeted at scientists and engineers interested in getting first insights in the field of chemical sensing since all necessary fundamental knowledge is included. On the other hand, it also addresses experts in the field since it provides detailed information on all important issues related to realizing chemical microsensors and, specifically, chemical microsensors in CMOS technology. A large number of sensor and integrated-sensor-system implementations illustrate the current state of the art and help to identify the possibilities for future developments. Since microsensors produce "microsignals", sensor miniaturization without sensor integration is in many cases prone to failure. This book will help to reveal the benefits of using integrated electronics and CMOS-technology for developing chemical microsensor systems and, in particular, the advantages that result from realizing monolithically integrated sensor systems comprising transducers and associated circuitry on a single chip.

After a brief introduction, the fundamentals of chemical sensing are laid out, including a short excursion into the related thermodynamics and kinetics. Fabrication and processing steps that are commonly used in semiconductor industry are then abstracted. These more fundamental sections are followed by a short description of microfabrication techniques and the CMOS substrate and materials. Thereafter, a comprehensive overview of semiconductor-based and CMOS-based transducer structures for chemical sensors is given. The corresponding chemically sensitive materials and the related applications are mentioned in the context of each transducer structure. CMOS-technology is then introduced as platform technology, which allows the fabrication of microtransducers and, moreover, enables the integration of these microtransducers with the necessary driving and signal conditioning circuitry on the same chip. Several examples such as microcapacitors, microcalorimeters, microcantilevers, and microhotplates are described in great detail. In a next step, the development of monolithic multisensor arrays and fully developed microsystems with on-chip sensor control and standard interfaces is depicted. A short section on packaging shows that techniques from the semiconductor industry can also be applied to chemical microsensor packaging. The book concludes with a short outlook to future developments such as developing more complex integrated microsensor systems and interfacing biological materials such as cells with CMOS microelectronics.

As with all interdisciplinary efforts, teamwork plays a central role in being successful. Therefore I am particularly grateful to many colleagues and former students, who contributed much to the work that is the topic of this book. I would like to thank Prof. Henry Baltes for giving me the opportunity and the support to enter in the field of CMOS-based sensors in his laboratory. I very much appreciated his continual interest in discovering new things and exploring new fields of science. I am also very grateful to Prof. Oliver Brand, who was always a valuable source of information on microtechnology and microfabrication. I am very much obliged to several highly motivated and excellent coworkers, whose work is amply cited in this book: Christoph Hagleitner and Kay-Uwe Kirstein, the chief circuit designers, the microhotplate group: Markus Graf, Diego Barrettino, Stefano Taschini, Urs Frey, and Martin Zimmermann, the guys working on cantilevers: Dirk Lange, Cyril Vancura, Yue Li, Jan Lichtenberg, the capacitor freaks: Andreas Koll, Adrian Kummer, the microcalorimeter people: Nicole Kerness and Petra Kurzawski, and, finally, Wan Ho Song, who did the microsensor packaging.

In the outlook some first results on the combination of microelectronics and cells are mentioned. These rely on the work of Flavio Heer, Wendy Franks, Sadik Hafizovic, Robert Sunier, and Frauke Greve. I am very grateful for all their efforts, and I am looking forward to exciting new results in this research area.

I am also indebted to European collaboration partners, Udo Weimar and Nicolae Barsan, University of Tübingen, and to AppliedSensor GmbH, Reutlingen, who provided many of the chemically sensitive materials such as the metal oxides. The fruitful collaboration with Sensirion AG, Zürich, namely Felix Mayer and Mark Hornung, is also gratefully acknowledged.

Financial support for the CMOS chemical-sensor projects came from the European Union (FP5, FP6, IST-program), the Swiss Bundesamt für Bildung und Wissenschaft (BBW), the Swiss Commission for Technology and Innovation (CTI), and the Körber Foundation, Hamburg, Germany.

Zurich, September 2004 *Andreas Hierlemann*

Contents

1 Introduction

The detection of molecules or chemical compounds is a general analytical task in the efforts of chemists to obtain qualitative and/or quantitative time- and spatially resolved information on specific chemical components [1]. Examples of *qualitative information* include the presence or absence of certain odorant, toxic, carcinogenic or hazardous compounds. Examples of *quantitative information* include concentrations, activities, or partial pressures of such specific compounds exceeding, e.g., a certain threshold-limited value (TLV), or the lower explosive limits (LEL) of combustible gases.

All this information can, in principle, be obtained from either a chemical analysis system or alternatively by using chemical sensors. In both cases sampling, sample pretreatment, separation of the components and data treatment are the tasks to be fulfilled. The main components of a state-of-the-art chemical analysis or sensor system are depicted schematically in Fig. 1.1.

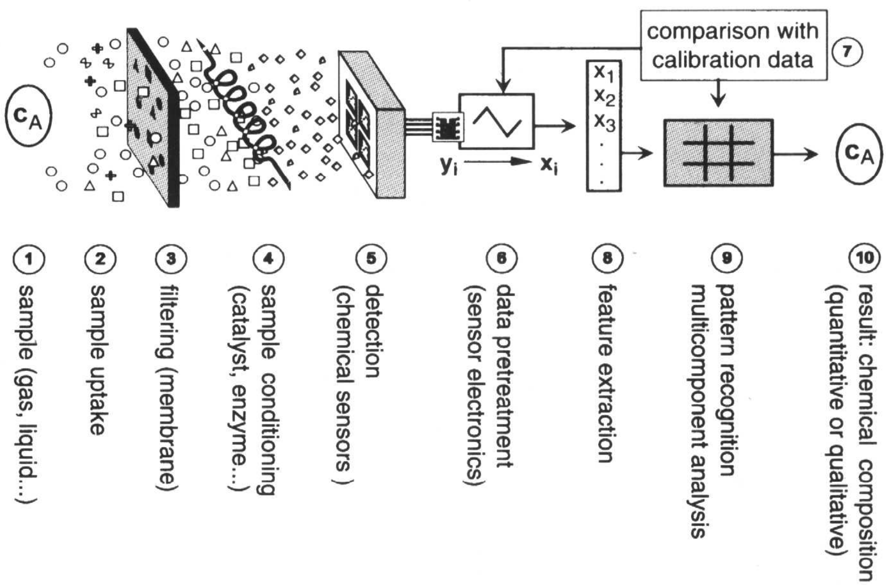


Fig. 1.1. Components of a chemical analysis or sensor system. Adapted from [15]

It is not easy to clearly distinguish between a chemical sensor and a complex analytical system. Integrated or miniaturized chromatographs or spectrometers may be denoted chemical sensors as well. However, a typical chemical sensor is, in most cases, a cheaper, smaller, and less complex device as compared to miniaturized analytical systems. A draft of the IUPAC (International Union of Pure and Applied Chemistry) provides a definition of a chemical sensor [2]: *"A chemical sensor is a device that transforms chemical information, ranging from the concentration of a specific sample component to total composition analysis, into an analytically useful signal"*. This rather wide definition does not require that the sensor is continuously operating and that the sensing process is reversible. But intermittently operating devices exhibiting irreversible characteristics are usually referred to as dosimeters [3]. In this context it is useful to introduce some important keywords used extensively throughout the chemical sensor literature [1,4–11].

Reversibility

Thermodynamic reversibility, strictly speaking, requires that the sensor measurand is related to a thermodynamic state function. This implies that, e.g., a certain sensor response unequivocally corresponds to a certain analyte concentration (analyte here denotes the chemical compound to be monitored). The sensor signal may not depend on the history of previous exposures or how a certain analyte concentration is reached (no memory effects or hysteresis). More details on fundamental thermodynamics of the chemical sensing process will be given in Chap. 2.

Sensitivity and Cross-Sensitivity

Sensitivity usually is defined as the slope of the analytical calibration curve, i.e., how largely the change in the sensor signal depends upon a certain change in the analyte concentration. Cross-sensitivity hence refers to the contributions of compounds other than the desired compound to the overall sensor response.

Selectivity/Specificity

Selectivity or specificity can be defined according to Janata [4] as the ability of a sensor to respond primarily to only one species in the presence of other species (usually denoted as interferants).

Limit of Detection and Limit of Determination

The limit of detection (LOD) corresponds to a signal equal to k-times the standard deviation of the background noise (i.e., k represents the signal-to-noise ratio) with a typical value of $k = 3$. Values above the LOD indicate the presence of an analyte, whereas values below LOD indicate that no analyte is detectable.

The limit of determination implies qualitative information, i.e., that the signal can be attributed to a *specific* analyte. This in turn requires more information and, therefore, the limit of determination is always higher than the limit of detection.

Transducer
Transducer is derived from Latin "*transducere*", which means to "transfer or translate". Therefore, a device that translates energy from one kind of system (e.g., chemical) to another (e.g., physical) is termed a transducer.

Biosensor
Biosensors are usually considered a subset of chemical sensors that make use of biological or living material for their sensing function [10, 11]. Since this book covers mostly chemical sensors, there will not be any further diversification into chemo- and biosensors within this work.

Using the above definitions, chemical sensors usually consist of a sensitive layer or coating and a transducer. Upon interaction with a chemical species (absorption, chemical reaction, charge transfer etc.), the physicochemical properties of the coating, such as its mass, volume, optical properties or resistance, reversibly change (Fig. 1.2).

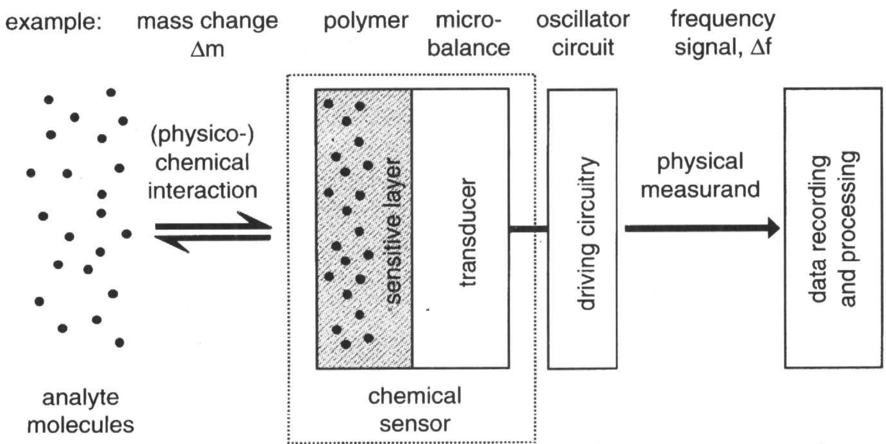


Fig. 1.2. Components of a chemical sensor exemplified for the mass-sensitive principle

These changes in the sensitive layer are detected by the respective transducer and are translated into an electrical signal such as a frequency, current, or voltage, which is then read out and subjected to further data treatment and processing. In Fig. 1.2, this is exemplified for the mass-sensitive principle. Analyte molecules are absorbed into a coating material (polymer) to an extent governed by intermolecular forces. The change in mass of the polymeric coating in turn causes a shift in the resonance frequency of the transducer, e.g., a quartz microbalance. This frequency shift constitutes the electrical signal that is used in subsequent data processing.

To supply the different needs in chemical sensing, a variety of transducers based on different physical principles has been devised. Following the suggestion of Janata [4, 5], chemical sensors can be classified into four principal categories according to their transduction principles:

1. Chemomechanical sensors (e.g., mass changes due to bulk absorption)
2. Thermal sensors (e.g., temperature changes through chemical interaction)
3. Optical sensors (e.g., changes of light intensity by absorption)
4. Electrochemical sensors (e.g., changes of potential or resistance through charge transfer)

Each of those four categories of chemical sensors will be treated in great detail in Chap. 4. An overview of more recent literature on chemical sensors with regard to different transduction principles is given in [5].

Various inorganic and organic materials serve as chemically sensitive layers that can be coated onto the different transducers. Typical inorganic materials include metal oxides like tin dioxide (SnO_2) for monitoring reducing gases such as hydrogen or carbon monoxide, or zirconium dioxide (ZrO_2) to detect oxygen, nitrogen oxide, and ammonia. Organic layers mostly consisting of polymers such as polysiloxanes or polyurethanes are used to monitor hydrocarbons, halogenated compounds and different toxic volatile organics. A survey of typical chemically sensitive materials and their applications is given in Table 1.1. Further information on the coating materials will be provided, e.g., in the context of the different transducers in Chap. 4.

Current research and development work in chemical sensors and sensitive materials evolves in three main directions:

1. *Miniaturization and monolithic integration* of transducers with electronics and, possibly, auxiliary sensors.
2. Search for *highly selective (bio)chemical layer materials* (molecular recognition, key-lock-type interactions).
3. Using *arrays of sensors exhibiting different partial selectivity* (polymers, metal oxides) and developing pattern recognition (odors, aromas) and multicomponent analysis methods (mixtures of gases and liquids).

The latter strategy has grown very popular [12–17], especially since compact sensor arrays can presently be fabricated at low costs, and interferants, which are present in almost any practical application, can be handled.

Chemical sensors meanwhile have also reached the stage of exploratory use in a variety of industrial and environmental applications, some examples being quality control or on-line process monitoring in the food-industry as well as preliminary tests in the areas of medical practice and personal (workplace) safety [18]. In particular in environmental monitoring, there is an urgent need for low-cost sensor systems detecting various pollutants at trace level.

Table 1.1. Typical sensitive materials and applications

Materials	Examples	Applications
metals	Pt, Pd, Ni, Ag, Sb, Rh, ...	inorganic gases like CH_4, H_2, ...
ionic compounds	*electronic conductors* (SnO_2, TiO_2, Ta_2O_5, In_2O_3, $AlVO_4$, ...) *mixed conductors* ($SrTiO_3$, Ga_2O_3, perowskites, ...) *ionic conductors* (ZrO_2, LaF_3, CeO_2, nasicon, ...)	inorganic gases (CO, NO_x, CH_4 ...) exhaust gases, oxygen, ions in water, ...
molecular crystals	phthalocyanines (Pcs): PbPc, $LuPc_2$, ...	nitrogen dioxide, volatile organics
Langmuir-Blodgett films	lipid bilayers, polydiacetylene ...	organic molecules in medical applications, biosensing, ...
cage compounds	zeolites, calixarenes, cyclodextrins, crown ethers, cyclophanes, ...	water analysis (ions), volatile organics, ...
polymers	*nonconducting polymers* polyurethanes, polysiloxanes, ... *conducting polymers* polypyrroles, polythiophenes, nafion, ...	detection of volatile organics, food industry (odor and aroma), environmental monitoring in gas and liquid phase, ...
components of biological entities	*synthetic entities* phospholipids, lipids, HIV-epitopes, ... *natural entities* enzymes, receptors, proteins, cells, membranes, ...	medical applications, biosensing, water and blood analysis, pharmascreening, ...

Key requirements for a successful chemical sensor include:

- High sensitivity and low limit of detection (LOD)
- High selectivity to target analyte and low cross-sensitivity to interferants
- Short recovery and response times
- Large dynamic range
- Reversibility
- Accuracy, precision and reproducibility of the signal
- Long-term stability and reliability (self-calibration)
- Low drift
- Low temperature dependence or temperature compensation mechanisms
- Ruggedness
- Low costs (batch fabrication) and low maintenance
- Ease of use

Semiconductor technology provides excellent means to effectively realize device miniaturization and to meet some of the chemical-sensor key criteria listed above (low cost, batch fabrication). The rapid development of the integrated-circuit (IC) technology during the past decades has initiated many initiatives to fabricate chemical sensors consisting of a chemically sensitive layer on a signal-transducing silicon chip [19,20]. The earliest types of chemical sensors realized in silicon technology were based on field-effect transistors (FETs) [21,22]. Reviews of silicon-based sensors (not only chemical sensors) are given in [23–25]. In this context two more keywords have to be introduced here.

Integrated Sensor
A sensor is denoted an integrated sensor if the chemical sensing operation is based on a direct influence on an electric component (resistor, transistor, capacitor) integrated in silicon or another semiconductor material [11].

Smart or Intelligent Sensor
The combination of interface electronics and an integrated sensor on a single chip results in a so-called "smart sensor". At least some basic signal conditioning is usually carried out on chip. One major advantage of smart sensors is the improved signal-to-noise and electromagnetic interference characteristics [11]. In addition the connectivity problem, which occurs especially in multisensor arrays, can be eased by using on-chip multiplexers and by using bus interfaces. For more details on sensor system integration, see Chap. 5.

The largely planar integrated-circuit (IC) and chemical-sensor structures processed by combining lithographic, thin film, etching, diffusive and oxidative steps have been recently extended into the third dimension using microfabrication technologies (see Chap. 3 in this book). A variety of micromechanical structures including cantilever beams, suspended membranes, freestanding bridges, gears, rotors, and valves have been produced using micromachining technology (***M****icro****E****lectro****M****echanical****S****ystems MEMS*) [26–29]. MEMS technology thus provides a number of key features, which can serve to enhance the functionality of chemical sensor systems [9,11,26,29–34].

Micromechanical structures (MEMS-structures) and microelectronics can be realized on a single chip allowing for on-chip control and monitoring of the mechanical functions as well as for data preprocessing such as signal amplification, signal conditioning, and data reduction [29–34]. ***C****omplementary-****M****etal-****O****xide-****S****emiconductor* or CMOS-technology is the dominant semiconductor IC technology for microprocessors and ***A****pplication-****S****pecific* ***I****ntegrated* ***C****ircuits* (ASICs) and has also been used to fabricate integrated chemical microsensors. The use of CMOS technology entails a limited selection of device materials (see Sect. 3.3) and a predefined fabrication process for the CMOS part. Sensor-specific or transducer-specific materials and fabrication steps have to be introduced in most cases as post-processing after the CMOS fabrication.

In the next chapters the fundamentals of the chemical sensing process itself will be laid out (Chap. 2) followed by a short description of microfabrication techniques and the CMOS substrate (Chap. 3). In Chap. 4, there will be an extensive treatment of the different microtransducers that are commonly used for chemical sensors. This transducer overview will be restricted to *semiconductor-based and CMOS-based* devices and will, for the sake of completeness, also include short abstracts on devices, which are described in much more detail in the subsequent Chap. 5 on the CMOS technology platform for chemical sensors. Chapter 5 will show the evolution from single transducers, which are integrated with the necessary driving and signal conditioning circuitry to monolithic multisensor arrays and fully developed systems with on-chip sensor control and standard interfaces. The concluding Chap. 6 will include a short glance at future developments such as combining cells and CMOS devices to develop biosensors or bioelectric interfaces.