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A. Hierlemann

Integrated Chemical Microsensor Systems in CMOS Technology

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Integrated Chemical Microsensor Systems in CMOS Technology

With 125 Figures

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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.

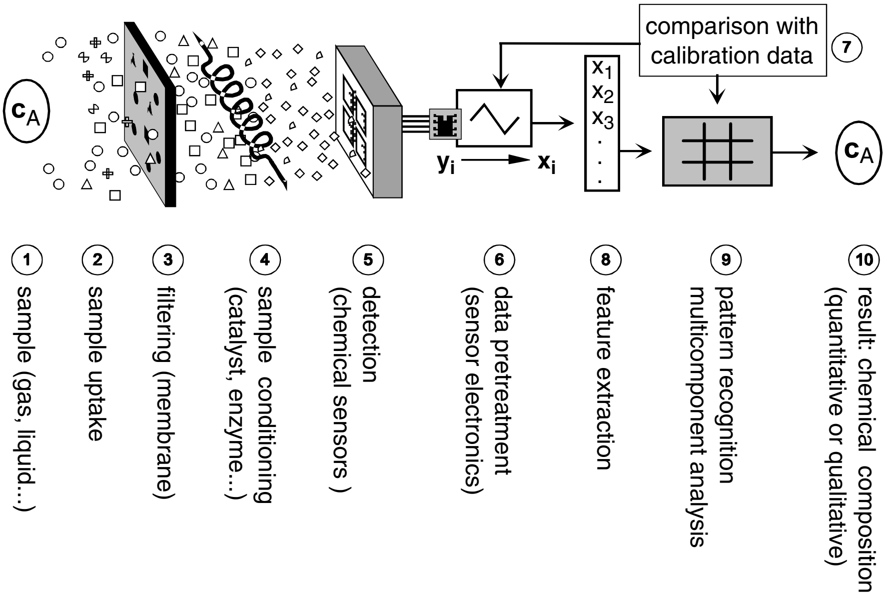

Fig. 1.1. Components of a chemical analysis or sensor system. Adapted from [15]

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).

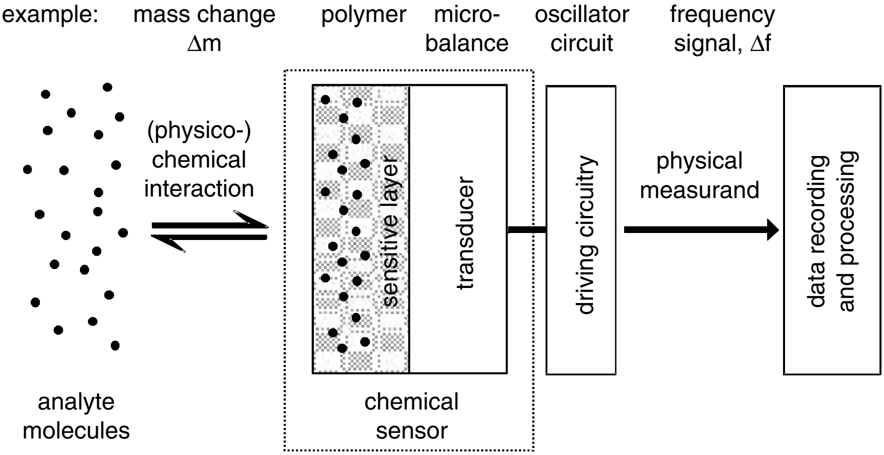

Fig. 1.2. Components of a chemical sensor exemplified for the mass-sensitive principle

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.

2 Fundamentals of Chemical Sensing

The interaction of a chemical species with a chemical sensor can either be confined to the surface of the sensing layer, or it can take place in the whole volume of the sensitive coating. Surface interaction implies that the species of interest is *adsorbed* at the surface or interface (gas/solid or liquid/solid) only, whereas volume interaction requires the *absorption* of the species and a *partitioning* between sample phase and the bulk of the sensitive material. The different types of chemical interactions involved in a sensing process range from very weak *physisorption* through rather strong *chemisorption* to charge transfer and chemical reactions.

Physisorption in this context implies that the compound is only physically ab/adsorbed (London or Van-der-Waals dispersion forces) with an interaction energy of 0–30 kJ/mol, whereas in the case of the much stronger chemisorption (interaction energy >120 kJ/mol), the particles stick to the surface by forming a chemical (usually covalent) bond. Charge transfer and chemical reactions involve, in most cases, interaction energies comparable to those of chemisorption and higher. Some of the most common interaction mechanisms and associated energies are listed in Table 2.1, for further details, see [35].

Table 2.1. Typical intermolecular interactions and energies

Interaction type	Typical energy [kJ/mol]	Comment
covalent bond	120–800	chemical reaction
ion-ion	250	only between ions
coordination, complexation, charge-transfer bonding	8–200	weak "chemical" interaction
ion-dipole	15	
hydrogen bond	20	hydrogen bond: A–H···B
dipole-dipole	0.3–2	between polar molecules
London dispersion (induced dipole-induced dipole)	0.1–2	physical interaction between any molecules

High chemical selectivity and rapid reversibility place contradictory constraints on desired interactions between chemical sensor coating materials and analytes. Low-energy, perfectly reversible (physisorptive) interactions generally lack high selectivity, while chemisorptive processes, the strongest of which result in the formation of new chemical bonds, offer selectivity, but are inherently less reversible. A practicable compromise has to be achieved with due regard to the specific application. In this context it should be noted that the commonly accepted limit of reversibility up to 20 kJ/mol refers to room temperature and will not apply to the case of, e.g., tin-dioxide–coated semiconductor sensors operated at 300°C to 400°C. On the other hand, spontaneous chemical reactions occurring at room temperature often require a tedious regeneration of, e.g., biological recognition units (enzymes).

Any interaction between a coating material and an analyte is governed by chemical thermodynamics and kinetics. Thus, a fundamental thermodynamic function, the Gibbs free energy, G [J], is the most important descriptor in all chemical sensing processes: The direction of spontaneous reactions is always towards lower values of G (minimization of the Gibbs energy). The Gibbs free energy is a *state function* in the thermodynamic sense, i.e., its value depends only on the current state of the system and is independent of how that state has been prepared. This implies that any chemical (sensing) process described by a Gibbs energy function moves towards a dynamic equilibrium ($\Delta G = 0, G$ minimal), in which both reactants and products are present but have no tendency to undergo net change. This equilibrium is reversible, i.e., an infinitesimal change in the conditions in opposite directions results in opposite changes in its state. The interaction equilibrium of an analyte, A, with a sensor coating, S, can thus be represented by:

$$A + S \underset{\overleftarrow{k}}{\overset{\overrightarrow{k}}{\Leftrightarrow}} A \cdots S \,. \tag{2.1}$$

Here, $\overrightarrow{k}$ and $\overleftarrow{k}$ denote the rate constants of the forward reaction and the reverse reaction, which will be detailed below. Such equilibrium can be described by an equilibrium constant, K, which relates the activity, a, of reaction products (A$\cdots$S) to those of the reactants (A and S). This constant is thus a characteristic value for the progression of the reaction ($K \leq 1$: no reaction takes place), its numerical value depends on the system temperature.

$$K = \frac{a_{A \cdots S}}{a_A \cdot a_S} \quad \text{and in general:} \quad K = \prod_i a_i^{n_i} \,. \tag{2.2}$$

The index i denotes the chemical substance, n_i are the corresponding stoichiometric numbers in the chemical equation. This expression signifies that each activity (or fugacity) is raised to the power equal to its stoichiometric number, and, then, all such terms are multiplied together. Stoichiometric numbers of the products are positive and those of the reactants are negative, i.e., reactants appear as the denominator and reaction products as the numerator. The activity[1], a_i (fugacity, f_i, for gases), which denotes the *effective quantity* of compound i participating in, e.g., a chemical reaction, is related to the mole fraction, x_i, (partial pressure, p, for gases) of a species via: $a_A = \gamma_A \cdot x_A$ with $\gamma_I \leq 1$. The activity coefficient, γ_i, measures the degree of departure of a components behavior from ideal or ideally dilute behavior.

The equilibrium constant, K, is also related to kinetics. For the simple reaction in (2.1), two kinetic constants can be defined: $\overrightarrow{k}$ for the reaction leading to the product A$\cdots$S, and $\overleftarrow{k}$ for the reaction in the opposite direction.

$$\frac{da_A}{dt} = -\overrightarrow{k}\; a_A a_S + \overleftarrow{k}\; a_{S\cdots A}\;. \tag{2.3}$$

K then represents the ratio of those two kinetic constants in equilibrium state.

$$K = \frac{\overrightarrow{k}}{\overleftarrow{k}}\;. \tag{2.4}$$

Both, thermodynamics and kinetics hence affect the progress of any chemical process or reaction. Thermodynamics, namely the Gibbs free energy (minimum) or the equilibrium constant, can tell us the direction of spontaneous change and the composition at the equilibrium state, whereas kinetics tell us, whether a kinetically viable pathway exists for that change to occur, and how fast an equilibrium state will be achieved. Kinetics are important in the context of chemical sensors, since there exist chemical processes, the activation barrier of which is too high to get a reaction going, although the Gibbs free energy of the products would be below that of the reactants. Such effects can be used to advantage in tuning the selectivity of, e.g., catalytic chemical sensors (see, e.g., Sect. 4.4.3.1.2).

A *chemical potential* has been introduced in thermodynamics. The chemical potential shows how the Gibbs energy of a system changes when a portion of a specific chemical compound is added to it or removed from it. The chemical potential of the *i-th* component, μ_i, is defined as:

$$\mu_i = \left(\frac{\partial G}{\partial n_i}\right)_{p,T} \quad \text{and} \quad \Delta G = \sum_i \mu_i\, dn_i\;. \tag{2.5}$$

---

[1] The activities and activity coefficients used throughout this book are related to mole fractions for simplicity reasons. The standard states include (a) a pure compound or (b) infinite dilution. There exist also activities and activity coefficients that are related to molalities (mol/kg) or concentrations (mol/m^3). The standard state of molality is 1 mol/kg, that of concentration is 1 mol/liter. The values of the activity coefficients related to molalities or concentrations are significantly different from those for molar fractions. A detailed discussion of this issue can be found, e.g., in Levine, I., Physical Chemistry, 2nd edition, McGraw-Hill 1983, New York, pp. 249–258.

Here n_i denotes the stoichiometric number or the amount of substance in moles. Again, the stoichiometric numbers of the products are positive and those of the reactants negative. The pressure, p, and the temperature, T, are kept constant. The chemical potential can be expressed in terms of mole fractions, x_i, or activities, a_i, in liquids, and partial pressures, p_i, or fugacities, f_i, in the gas phase [35]:

$$\mu_i = \mu_i^0\,(p,T) + RT\,\ln a_i \quad \text{or} \quad \mu_i = \mu_i^0\,(p,T) + RT\,\ln f_i\ . \tag{2.6}$$

$\mu_i^0\,(p,T)$ here denotes the chemical potential of an appropriately defined standard state such as, e.g., "infinite dilution" or a "pure compound"; R is the molar gas constant (8.314 J/Kmol) and T denotes the temperature in [K]. So there are two terms in (2.6), a reference term and an activity-dependent term. Plugging the terms of (2.6) into (2.5), the reference terms (μ_i^0) can be subsumed into ΔG^0 as shown in the following equation:

$$\Delta G = \sum_i n_i \mu_i^0\,(p,T) + RT \sum_i n_i \ln a_i = \Delta G^0\,(p,T) + RT\,\ln \prod_i a_i^{n_i}\ . \tag{2.7}$$

Both, ΔG and K are characteristic descriptors for the direction of a chemical reaction. In comparing (2.2) with (2.7), it is evident that in a thermodynamic equilibrium state $(\Delta G = 0)\,\Delta G^0$ and K are interrelated via the following equation (for details, see [35]):

$$\ln K = -\frac{\Delta G^0}{RT}\ . \tag{2.8}$$

The more negative ΔG^0, the larger is K, or in other words, the higher the chemical potential of the reactants with regard to the products, the larger is the reaction extent, and the more spontaneous will the reaction occur in case that (already discussed) kinetic factors will not upset such predictions. According to the Gibbs fundamental equation, ΔG^0 is composed of an enthalpy term, ΔH^0, representing the reaction heat at constant pressure, and an entropy term, ΔS^0, representing the degree of "disorder" or, thermodynamically more precise, the number of different ways in which the energy of a system can be achieved by rearranging the atoms or molecules among the states available to them (for details, see [35]):

$$\Delta G^0 = \Delta H^0 - T\Delta S^0\ . \tag{2.9}$$

For spontaneous reactions (ΔG^0 negative), the entropy increases and/or the enthalpy term is negative, i.e., heat is released during the chemical reaction.

In the following, the thermodynamics of three prototype reactions of chemical sensors will be briefly discussed.

Simple Adsorption/Absorption

At thermodynamic equilibrium state, the free species and the ad/absorbed species are in dynamic equilibrium, i.e., the chemical potentials of a certain compound A in gaseous and polymeric phase are identical: $\mu_A^{\text{gas}}(p,T) = \mu_A^{\text{polymer}}(p,T)$ (2.6). Absorbing all the constant terms (μ_i^0, R, T) into a sorption constant, K_{sorption}, or so-called partition coefficient, the equilibrium state can be described by:

$$K_{\text{sorption}} = \frac{a_A^{\text{sorbed}}}{a_A^{\text{free}}} \,. \tag{2.10}$$

The partition coefficient is a dimensionless "enrichment factor" relating, e.g., the activity of a compound in the sensing layer (a_A^{sorbed}) to that in the probed gas or liquid phase (a_A^{free}) and also represents a thermodynamic equilibrium constant, which is related to ΔG^0 via (2.8).

For surface adsorption, it is more common to relate the fractional coverage of the surface, θ, to the concentration of the analyte in the probed phase and to use different types of adsorption isotherm like Langmuir-, Freundlich-, or BET-(Brunauer-Emett-Teller) isotherms [35].

Chemical Reaction

In this case, (2.2) can be applied in principle. It has to be modified with regard to the respective reaction mechanism occurring. For a simple reaction like $n_A A + n_B B \leftrightarrow n_C C + n_D D$, the equilibrium constant is given in analogy to (2.2):

$$K = \prod_i a_i^{n_i} \quad \text{and in particular:} \quad K = \frac{a_C^{n_C} \cdot a_D^{n_D}}{a_A^{n_A} \cdot a_B^{n_B}} \,. \tag{2.11}$$

The chemical potentials as defined in (2.6) can be used, and (2.8) holds. As already mentioned, the interaction leading to a true chemical reaction may be too strong to be reversible.

Charge Transfer and Electrochemical Reaction

For a reaction of type $A^+ + e^- \leftrightarrow A$, an electrochemical potential has to be introduced. The contribution of an electrical potential to the chemical potential is calculated by noting that the electrical work, W_e, of adding a charge, $z \cdot e$ (z denotes the number of elementary charges, e), to a region where the potential is ϕ (ϕ denotes the *Galvani* potential, which represents the bulk-to-bulk inner contact potential of two materials and is defined as the difference of the Fermi levels of these two materials), is:

$$\begin{aligned} W_e &= z \cdot e \cdot \phi \; ; \text{ hence, the work per mole is:} \\ W_e &= z \cdot F \cdot \phi \end{aligned} \tag{2.12}$$

F here denotes the Faraday constant, 96485 C/mol, which is equivalent to one mole of elementary charges. Consequently, the electrochemical potential is (compare 2.6):

$$\mu_i = \mu_i^0(p,T) + RT \ln a_i + zF\phi \,. \tag{2.13}$$

When $z = 0$ (neutral species), the electrochemical potential is equal to the chemical potential (2.6). Rewriting (2.7) for the electrochemical potentials leads to:

$$\Delta G = \Delta G^0 \left(p, T\right) + RT \ln \prod_i a_i^{n_i} + zF \cdot \Delta\phi \; . \tag{2.14}$$

In the equilibrium state ($\Delta G = 0$), (2.13) can be expressed in terms of K (2.2). By replacing E, the "electromotive force", for $\Delta\phi$ and by replacing E^0, the standard cell potential, for $-\Delta G^0/zF$ (a positive voltage per convention always corresponds to a negative ΔG: spontaneous reaction), the so-called "Nernst-equation" results:

$$E = E_0 - \frac{RT}{zF} \ln K \; . \tag{2.15}$$

The Nernst equation now can be used to derive an expression for the potential of any electrochemical cell or, in our case, electrochemical sensor. Electrochemical reactions can be triggered by applying currents or voltages via electrodes to a sensing layer.

After this short excursion into thermodynamics and kinetics, the different microfabrication techniques and the fundamentals of CMOS-devices will be detailed in Chap. 3.

3 Microtechnology for Chemical Sensors

Microtechnology and microfabrication processes are used to produce devices with dimensions in the micrometer to millimeter range. Microfabrication processes can be effectively applied to yield a single device or thousands of devices. The so-called "batch processing", i.e., the fabrication of many devices in parallel, does not only lead to a tremendous cost reduction, but also enables the production of array structures or large device series with minute fabrication tolerances. Microfabrication processes hence significantly differ from conventional machining processes, such as drilling or milling with mechanical tools. Integrated circuit (IC) fabrication processes are the most important microfabrication processes [36–38]. The success of CMOS-technology, which is one of the enabling technologies of the information age, clearly demonstrates the efficiency of microfabrication technologies.

Standard processing steps originating from semiconductor technology can be used in combination with dedicated micromachining steps to fabricate three-dimensional mechanical structures, which form the basis for the chemical microsensors detailed in Chap. 4. Key advantages of microfabricated chemical sensors include small device size and sampling volume, the possibility of batch processing, and the reproducibility of transducer/sensor characteristics due to the precise geometric control in the fabrication steps. Microfabrication techniques also can be used to either significantly improve sensor characteristics in comparison to conventionally fabricated devices, or to develop devices with new functionality that cannot be realized in conventional fabrication technology. Microsensor success stories, such as micromachined pressure sensors and accelerometers, show that microfabrication techniques are especially suitable for high-volume applications in, e.g., automotive industry. In high-volume production, the advantage of batch processing is paramount, and the high development and setup costs amortize.

This chapter is organized in the following way: Microsystem substrate materials and standard processing steps originating from semiconductor technology are detailed in the first sections, followed by a short introduction to CMOS technology and a description of micromachining and layer-deposition processes that are specific to chemical microsensors and -systems.