CMOS-based chemical microsensors
Andreas Hierlemann* and Henry Baltes

Physical Electronics Laboratory, ETH Zurich, Hönggerberg, HPT H 4.2, CH-8093 Zurich, Switzerland. E-mail: hierlema@iqe.phys.ethz.ch; Fax: +41 1 633 1054; Tel: +41 1 633 3494

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1 Introduction

The rapid development of integrated circuit (IC) technology during the past decades has initiated many initiatives to fabricate chemical sensors on silicon or CMOS substrates (CMOS: Complementary Metal Oxide Semiconductor). The largely two-dimensional integrated circuit and chemical sensor structures processed by combining lithographic, thin film, etching, diffusive and oxidative steps have been recently extended into the third dimension using micromachining or MEMS (MEMS: MicroElectro-Mechanical Systems) technologies—a combination of special etchants, etch stops and sacrificial layers. A variety of micromechanical structures including cantilever beams, suspended membranes, freestanding bridges, etc. have been produced. The realization of microelectronics and micromechanics (MEMS-structures) on a single chip allows for on-chip control and monitoring of the mechanical functions as well as for data preprocessing such as signal amplification, signal conditioning, or data reduction.

CMOS- or CMOS-MEMS-technology, therefore, provides excellent means to meet some of the key criteria of chemical sensors such as miniaturization of the devices, low power consumption, rapid sensor response characteristics, or batch fabrication at industrial standards and low costs. Additional advantages come from the possibility of monolithic co-integration of circuitry and transducers. These include improved sensor signal-to-noise characteristics due to on-chip signal processing and analog/digital conversion, or the realization of smart features on the sensor chip. Drawbacks of using CMOS technology encompass a limited selection of materials (see CMOS technology section) and a predefined fabrication process for the CMOS part. Sensor-specific or transducer-specific materials and fabrication steps have to be introduced as post-processing after the CMOS fabrication.

After a short introduction to CMOS and basic micromachining technologies, we will give an overview on different types of chemical sensors fabricated in CMOS and CMOS-MEMS technology.

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2 CMOS technology

CMOS is the dominant semiconductor technology for microprocessors, memories and application-specific integrated circuits (ASICs). CMOS-chips generally consist of a layered structure of aluminum, polysilicon, silicon (doped and undoped), silicon oxide and nitride layers. These structures are fabricated in a defined sequence of material deposition, doping, lithography and etching steps. Semaphore conduct electricity but not enthusiastically. Semiconductors are doped to become conductors of either extra electrons (negative charge, phosphorus-doping) or of positive charge carriers (boron-doping). The denomination ‘complementary’ metal oxide semiconductor is due to the fact that both, n-type and p-type transistors are realized on the same substrate, for example, on a lightly p-doped wafer, that exhibits n-doped areas (n-wells) (Fig. 1). Both n-type (NMOS) and p-type (PMOS) transistors are used to realize logic functions. A CMOS-chip cross-section is shown in Fig. 1. The p-substrate exhibits n-well areas created by implantation. Heavily p-doped structures (p+) in the n-well, and n-doped structures (n+) in the p-substrate form transistor source and drain. The transistor gate is made of polysilicon on top of the gate oxide (SiO2). By applying a voltage to the gate via the polysilicon, electrons or holes are accumulating in the surface area (field effect) below the gate and thus create a conducting n- or p-channel between source and drain. Variation of the gate voltage thus modulates the source drain current; continuously within a certain range in analog circuits, on/off in digital circuits. Several metal layers (Fig. 1: metal 1 and metal 2, aluminum) are used to wire the transistors. Dielectric layer such as field oxide, contact oxide, and intermetal oxide (SiO2) serve as electrical insulation between conducting areas. The silicon nitride on top serves as passivation and provides electrical and mechanical/chemical protection of the circuitry. Silicon nitride and to a lesser extent silicon oxide (or silicon with a native oxide layer) are durable in case of liquid exposure and are biocompatible, which allows for using CMOS chips also with cells or living material. CMOS aluminum is neither stable in liquids (or due to the fact that both, n-type and p-type transistors are realized on the same substrate, for example, on a lightly p-doped wafer, that exhibits n-doped areas (n-wells) (Fig. 1). Both n-type (NMOS) and p-type (PMOS) transistors are used to realize logic functions. A CMOS-chip cross-section is shown in Fig. 1. The p-substrate exhibits n-well areas created by implantation. Heavily p-doped structures (p+) in the n-well, and n-doped structures (n+) in the p-substrate form transistor source and drain. The transistor gate is made of polysilicon on top of the gate oxide (SiO2). By applying a voltage to the gate via the polysilicon, electrons or holes are accumulating in the surface area (field effect) below the gate and thus create a conducting n- or p-channel between source and drain. Variation of the gate voltage thus modulates the source drain current; continuously within a certain range in analog circuits, on/off in digital circuits. Several metal layers (Fig. 1: metal 1 and metal 2, aluminum) are used to wire the transistors. Dielectric layer such as field oxide, contact oxide, and intermetal oxide (SiO2) serve as electrical insulation between conducting areas. The silicon nitride on top serves as passivation and provides electrical and mechanical/chemical protection of the circuitry. Silicon nitride and to a lesser extent silicon oxide (or silicon with a native oxide layer) are durable in case of liquid exposure and are biocompatible, which allows for using CMOS chips also with cells or living material. CMOS aluminum is neither stable in liquids (or in air at higher temperatures) nor is it biocompatible, and, consequently, has to be covered with precious metal coatings such as gold or platinum. More details on semiconductor technology, see, e.g., the standard textbooks of Sze.15,16

3 Micromachining techniques

3.1 Bulk micromachining

One approach to enhance the functionality of IC-based substrates includes micromachining the bulk substrate, in which the transducers are fabricated in a defined sequence of material deposition, doping, lithography and etching steps. Some wet etchants such as nitric acid/hydrofluoric acid lead to isotropic etching (same etch rate in all directions), others like potassium hydroxide lead to anisotropic etching, i.e., preferentially etch away the silicon along certain crystal planes while preserving it in other directions (Fig. 2a). Typical structures obtained by, e.g., anisotropic wet etching through the complete bulk silicon of a CMOS wafer include membranes consisting of the remaining dielectric CMOS layers. The thermal oxide serves as an etch-stop layer. The resulting membrane structures can be used for sensors requiring excellent thermal insulation, such as calorimetric chemical sensors or metal oxide-covered microhotplates.

Another technique is dry etching. Again, there is isotropic etching performed by using, e.g., xenon difluoride or anisotropic etching by reactive-ion-etching (RIE). RIE can be used to release cantilevers or create bridge structures from preformed membranes.

3.2 Surface micromachining

Surface micromachining comprises a number of techniques to produce microstructures from thin films previously deposited onto a substrate and is based on a sacrificial layer method (Fig. 2b). In contrast to bulk micromachining, surface micromachining leaves the substrate intact. A sacrificial layer is deposited and patterned on a substrate. After that, a structural thin film, in most cases polysilicon, is deposited and patterned, which will perform the mechanical or electrical functions in the final device. A selective etchant then removes exclusively the sacrificial layer material. The thickness of the sacrificial layer determines the distance of the structural parts from the substrate surface. Common sacrificial layer materials include silicon oxide etched by hydrogen fluoride and aluminum etched by a mixture of phosphoric, nitric and acetic acid.

Clamped beams, microbridges, or microchannels can be fabricated this way, microrotors and even microgears can be realized by repeated layer deposition and etching.

4 CMOS-based chemical sensors

Chemical sensors usually consist of a sensitive layer or coating and a transducer. Upon interaction with a chemical species (adsorption, chemical reaction, charge transfer etc.), the physicochemical properties of the coating, such as its mass, volume, optical properties or resistance etc. reversibly change. These changes in the sensitive layer are detected by the respective transducer and translated into an electrical signal such as frequency, current, or voltage, which is then read out and subject to further data treatment and processing.

A variety of transducers based on different physical principles have been devised. We will follow a classification scheme

**Fig. 1** Cross-section of a CMOS-chip. The different layers and materials include metals (aluminum), silicon oxides, silicon nitride, and polysilicon on a p-doped silicon wafer with n-well implanted areas.

**Fig. 2** Micromachining techniques: (a) bulk micromachining, anisotropic and isotropic etching, (b) surface micromachining with sacrificial layer, structural layer and a subsequent etch step.
suggested by Janata\textsuperscript{20,21} to give an overview on CMOS-based chemical sensors in the next sections of this review. This scheme includes four principal categories distinguished with regard to the transduction principle:\textsuperscript{20}

1. Chemomechanical or mass-sensitive sensors (\textit{e.g.}, mass changes due to absorption)
2. Thermal sensors (\textit{e.g.}, temperature changes through chemical interaction)
3. Optical sensors (\textit{e.g.}, light intensity change by absorption)
4. Electrochemical sensors (\textit{e.g.}, potential or resistance changes through charge transfer)

We will briefly introduce each of those four sensor categories and then give examples of CMOS-based transducers and devices. Typical chemically sensitive materials and sensor applications will be mentioned in the context of the corresponding transducer structures.

### 4.1 Chemomechanical or mass-sensitive sensors

Chemomechanical or mass-sensitive sensors are in the simplest case gravimetric sensors responding to the mass of species accumulated in a sensing layer.\textsuperscript{26–28} Some of the sensor devices additionally respond to changes in a variety of other mechanical properties of solid or fluid media in contact with their surface such as changes of polymer elastic moduli, liquid density and viscosity,\textsuperscript{26–28} which will not be further discussed here. Chemomechanical sensor, therefore, is a more appropriate denomination. Any species that can be immobilized on the sensor can, in principle, be sensed. As with most of the chemical sensors, the measurements are taken at a thermodynamic equilibrium state.

Mass changes can be monitored by either deflecting a microstructural element due to stress changes or mass-loading (static measurements) or by assessing the frequency changes of a resonating structure or a traveling acoustic wave upon mass loading. Both deflection and resonance frequency change in proportion to stress changes or mass loading on the device.\textsuperscript{26–28}

The most common devices are the thickness shear mode resonator (TSMR) or quartz microbalance (QMB), and the Rayleigh surface acoustic wave (SAW) device, both based on piezoelectric quartz substrates. Both will not be detailed here, since they are not fabricated in CMOS technology. For more details on those devices, see refs. \textsuperscript{26–28}.

In the following, we will describe in more detail two CMOS-technology-based micromechanical structures for mass-sensitive devices, (1) flexural-plate-wave devices (FPWs), and (2) micromachined cantilevers.

#### 4.1.1 Flexural-plate-wave or Lamb-wave devices

The chief advantage of flexural plate wave devices (FPWs) is their high sensitivity to added mass at a low operating frequency (typically 3–10 MHz).\textsuperscript{29} FPW devices feature plates that are only a fraction of an acoustic wavelength thick (typically 2–3 \textmu m). The plates are composite structures (Fig. 3) consisting of a silicon nitride layer, an aluminum ground plane, and a sputtered zinc oxide piezoelectric layer, all of which are supported by a silicon substrate.\textsuperscript{26–32}

The interdigital transducers (IDTs) on these devices generate flexural waves (Lamb waves, Fig. 3) with retrograde elliptical particle motions as in the SAW devices. The Lamb waves give rise to a series of plate modes, one of which has a frequency that is much lower than those of the other possible modes. The velocity of this unique wave decreases with decreasing plate thickness. The entire thickness of the plate is set in motion like a membrane. Deposition on the backside (non-processed side of the wafer) has the advantage, that on-chip-circuitry will not be exposed to chemicals.\textsuperscript{29–32}

Fabrication sequences for monolithic integration of the Lamb device with CMOS electronics are detailed in refs. \textsuperscript{32} and \textsuperscript{33}.

A variant includes a magnetic FPW actuation scheme based on Lorentz forces: A metal meander-line is patterned on the membrane surface, alternating current (AC) is flowing in the meander transducer and interacts with a static in-plane magnetic field to generate time-varying Lorentz forces, which in turn deform the membrane. Magnetic actuation requires an externally applied magnetic field, but eliminates the need for a piezoelectric layer.\textsuperscript{34,35} Such layers frequently contain elements (Zn etc.) that pose contamination problems in IC fabrication.\textsuperscript{34}

Typical FPW applications include the detection of different organic volatiles in the gas phase by using polymeric layers,\textsuperscript{31,35,36} or the use of an FPW-based immunoassay for the detection of breast cancer antigens.\textsuperscript{37}

#### 4.1.2 Resonating cantilevers

A mass-sensitive cantilever usually is a layered structure composed of, \textit{e.g.}, silicon, silicon oxide/nitride, and, eventually, metallizatios. The cantilever base is firmly attached to a silicon support (chip). The free-standing cantilever end is coated with a sensitive layer.

There are two fundamentally different operation methods: (a) \textit{static} mode: measurement of the cantilever deflection upon stress changes or mass loading by means of, \textit{e.g.}, a laser \textit{via} laser light reflection on the cantilever;\textsuperscript{17,41} (b) \textit{dynamic} mode: excitation of the cantilever in its fundamental resonance mode and measurement of the frequency change upon mass loading\textsuperscript{24–28} in analogy to other mass-sensitive transducers. Method (a) requires long and soft cantilevers to achieve large deflections, whereas method (b) requires short and stiff cantilevers to achieve high operation frequencies. Resonators are characterized by their quality factor (\(Q\)-factor), which is defined as the ratio of the resonance frequency and resonator bandwidth: the higher the \(Q\)-factor, the better the frequency stability of the resonator. The dynamic mode (b) is preferable with regard to simplicity of the measurement configuration since there is no need for an optical setup to determine small cantilever deflection by means of, \textit{e.g.}, laser light reflection.\textsuperscript{42–46} Method (a) can also be used in liquid media.\textsuperscript{39,41} The excitation of the resonant cantilever is performed by applying piezoelectric materials (ZnO)\textsuperscript{17} or by relying on Lorentz forces in a magnetic actuation scheme, which is analogous to that already described in the context of the FPWs: one or several conductor loops are patterned along the cantilever edges, AC is flowing in the loops and interacts with a static in-plane magnetic field to generate

The sensitive layer can be deposited on either side of the membrane. Deposition on the backside (non-processed side of the wafer) has the advantage, that on-chip-circuitry will not be exposed to chemicals.\textsuperscript{29–32}

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Typical FPW applications include the detection of different organic volatiles in the gas phase by using polymeric layers,\textsuperscript{31,35,36} or the use of an FPW-based immunoassay for the detection of breast cancer antigens.\textsuperscript{37}

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**Fig. 3** Schematic of a flexural plate wave device. The side view shows the different layers and the membrane movement. Interdigitated electrodes are used for actuation.
time-varying Lorentz forces, which deflect the cantilever.\textsuperscript{48,49} Another actuation variant includes making use of the different temperature coefficients or mechanical stress coefficients of the cantilever layer materials (bimorph effect).\textsuperscript{43–46} The different materials give rise to a cantilever deflection upon heating or applying mechanical forces. Cantilever deflection or resonance frequency changes can be detected by embedding piezoresistors in the cantilever base.\textsuperscript{41–46} The absolute mass resolution of the cantilevers is in the range of a few picograms.\textsuperscript{38–46} This high mass-sensitivity does not necessarily imply an exceptionally high gas sensor sensitivity since the area coated with the sensitive layer (on the order of $100 \times 150\, \mu m$), and hence the overall sorption matrix volume is very small.\textsuperscript{43} The 150 $\mu m$-long cantilever consists of mainly silicon as well as vapor-deposited and thermal oxide. The bimorph effect is used to initiate a cantilever vibration by periodically applying electric pulses to heating resistors embedded at the cantilever base. The cantilever resonates at its fundamental mechanical frequency of 380 kHz with a quality factor of approximately 1000 in air, which is comparable to other acoustic-wave-based devices such as QMB or Rayleigh SAW-device.\textsuperscript{38} The frequency-determining element in a feedback oscillation circuit,\textsuperscript{19,20,57} which is monolithically integrated with feedback electronics,\textsuperscript{43} leads to a better signal-to-noise ratio of the overall system. For more details on the electronics, see refs. 43–46 and 50.

Typical cantilever applications include the detection of organic volatiles or humidity in the gas phase by using polymeric layers,\textsuperscript{41–46,49–55} and biosensing in liquid phase such as the detection of cells,\textsuperscript{39} or complementary strands of oligonucleotides (DNA fragments).\textsuperscript{39}

\subsection*{4.2 Thermal sensors}

Calorimetric or thermal sensors rely on determining the presence or concentration of a chemical by measurement of an enthalpy change produced by the chemical to be detected.\textsuperscript{19,20,57} Any chemical reaction or even absorption/desorption process releases or absorbs from its surroundings a certain quantity of heat. Reactions liberating heat are termed exothermic, reactions abstracting heat are termed endothermic. This thermal effect shows a transient behavior: continuous liberation/abstraction of heat occurs only as long as the reaction proceeds. However, there will be no heat production and hence no measurable signal at thermodynamic equilibrium ($AG = 0$) in contrast to mass-sensitive, optical, or electrochemical sensors (see Fig. 15 later). Conflicting constraints are imposed on the design of a thermal sensor. The sensor has to interact with the chemical species (exchange of matter) and thus constitute a thermodynamically open system, but at the same time the sensing area should be thermally as isolated as possible to achieve maximum sensitivity.

The liberation or abstraction of heat can be conveniently measured as a change in temperature, which then is transduced into an electrical signal. The various types of calorimetric sensors differ in the way that the evolved heat is transduced.\textsuperscript{19,20,57}

The catalytic sensor (often denoted ‘pellistor’\textsuperscript{58}) employs platinum resistance thermometry, while the thermoelectric sensor is based on the Seebeck effect.\textsuperscript{57} Both sensor types benefit from CMOS integration and will be detailed in the following sections.

\subsubsection*{4.2.1 Catalytic thermal sensors (pellistors)}

The development of the catalytic sensor is derived from the need for a hand-held detector for methane to replace the flame safety lamp in coalmines. The catalytic device measures the heat evolved during the controlled combustion of flammable gaseous compounds in ambient air on the surface of a hot catalyst by means of a resistance thermometer in proximity with the catalyst. This method is, therefore, calorimetric. The heated catalyst here permits oxidation of the gas at reduced temperatures and at concentrations below the lower explosive limit (LEL). The term ‘pellistor’ originally refers to a device consisting of a small platinum coil embedded in a ceramic bead, which is impregnated with a noble metal catalyst.\textsuperscript{58}

Fig. 5 shows a surface-micromachined, free-standing, Pt-coated polysilicon micro-filament (10 $\mu m$ wide, 2 $\mu m$ thick) separated from the substrate by a 2 $\mu m$ air gap.\textsuperscript{59,60} Other designs include micromachined membranes.\textsuperscript{61–66} Heat losses to the silicon frame are minimized in both designs. By passing an electric current through the meander, the microfilament is heated to a temperature sufficient for the Pt-surface to catalytically oxidize the combustible mixture; the heat of oxidation is then measured as a resistance variation in the Pt. The combustion of, e.g., methane generates 800 kJ mol$^{-1}$ heat, which translates into a corresponding temperature change.

Detailed processing sequences for microbridges are given in refs. 67 and 68.

Typical applications include monitoring and detection of flammable gas hazards such as methane,\textsuperscript{64,68} hydrogen,\textsuperscript{59–61,64} propane,\textsuperscript{63} or carbon monoxide\textsuperscript{61,65} in industrial, commercial and domestic environments at concentrations below the lower explosive limit (LEL). The LEL is the concentration of gas in air below which it cannot be ignited.

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{figures/cantilever_feedback_circuit.png}
\caption{Micrograph of a 150 $\mu m$-long CMOS-integrated cantilever with on-chip feedback circuitry.}
\end{figure}
4.2.2 Thermoelectric or Seebeck-effect-based sensors. This type of sensor relies on the thermoelectric or Seebeck-effect.\(^{57,69}\) When two different semiconductors or metals are connected at a hot junction and a temperature difference is maintained between this hot junction and a colder point, then an open-circuit voltage is developed between the different leads at the cold point. This thermovoltage is proportional to the difference of the Fermi levels of the two materials at the two temperatures and thus proportional to the temperature difference itself.\(^{57,69}\) This effect can be used to develop a thermal sensor by placing the hot junction on a thermally isolated structure like a membrane, bridge etc., and the cold junction on the bulk chip with the thermally highly conducting silicon underneath.\(^{46,69}\) To achieve a higher thermoelectric voltage, several thermocouples are connected in series to form a thermopile. The membrane structure supporting the hot junctions is covered with a sensitive or chemically active layer liberating or abstracting heat upon interaction with an analyte. The resulting temperature gradient between hot and cold junctions then generates a thermovoltage, which can be measured.

Fig. 6 displays the schematic of a CMOS-based thermopile consisting of a dielectric membrane with polysilicon/aluminum thermocouples (Seebeck coefficient: 111 \(\mu\text{V K}^{-1}\)).\(^{46,72,73}\) CMOS-based thermoelectric sensors are advantageously set up in a sensor/reference configuration. The system includes two membranes, one of which is coated with the gas-sensitive polymer, the uncoated one serves as a reference to compensate for gas-induced temperature fluctuations.\(^{73}\) The sensing and reference thermopiles are connected in parallel to the input stage of a low-noise chopper-stabilized instrumentation amplifier on-chip to record the temperature differences between the two membranes. The thermovoltage can be translated into a digital signal on chip using a Sigma–Delta analog/digital converter.\(^{74}\)

Processing sequences for the integration of thermoelectric sensors with circuitry in a CMOS standard process are detailed in refs. 72 and 75.

Typical applications include the detection of different kinds of organic volatiles in the gas phase by using polymeric layers,\(^{46,72–77}\) and the biosensing of glucose, urea and penicillin in the liquid phase by using suitable enzymes.\(^{71,78–80}\)

4.3 Optical sensors

In comparison to other chemical sensing methods, optical techniques offer a great deal of selectivity already inherent in the various transduction mechanisms. Characteristic properties of the electromagnetic waves such as amplitude, frequency, phase, and/or state of polarization can be used to advantage.\(^{81–83}\) Geometric effects (scattering) can provide additional information. The wavelength of the radiation, \(\text{e.g.,}\), can be tuned to specifically match the energy of a desired analyte-specific resonance or absorption process. In addition, optical sensors like any other chemical sensor can capitalize on all the selectivity effects originating from the use of a sensitive layer.\(^{81–83}\)

If a sample is irradiated with visible light or electromagnetic waves, the radiation can be absorbed (intensity decrease), scattered (direction randomization, possibly frequency changes), refracted or reflected (metallic reflection, internal reflection mediated by evanescent waves) at the interface(s), or can produce phosphorescence/fluorescence (absorption–emission process) and chemiluminescence (conversion of chemical energy into light) effects.\(^{81–83}\)

The generation of light in CMOS or silicon devices is very difficult since there is no first order transition from the valence band to the conduction band without the involvement of a phonon (lattice vibrations).\(^{15}\) However, direct-bandgap semiconductors (III–V–semiconductors) like gallium arsenide (GaAs) or indium phosphide (InP) show first-order radiative electron-hole-recombinations with high quantum efficiency.\(^{15}\) The detection of light is possible with either silicon-based devices (photodiodes) or other semiconducting materials (GaAs, InP). Consequently, integrated optical sensors and systems nowadays mostly are made of III–V–semiconductors, which will not be detailed here, but offer the opportunity for fabrication and integration of lasers, waveguides, phase modulators and detectors on the same chip.\(^{84}\) There is also a wealth of fiber-optical techniques and integrated optical devices, which are realized on silicon substrates without making use of CMOS technology. For details, see review articles.\(^{81–83,85–88}\)

In this article we will exclusively focus on CMOS-based optical sensors, an example of which includes an integrated device making use of bioluminescence.

4.3.1 Bioluminescent bioreporter integrated circuits (BBIC). This technique employs bioluminescent bacteria placed on an application-specific optical integrated circuit (standard CMOS).\(^{89–91}\) The bacteria have been engineered to luminesce, when a target compound such as toluene is metabolized. Chemical reaction between target compound and bacteria leads to an excited state of a participating molecule, which then emits light during transition to the ground state. Chemical energy is thus directly converted into light energy in most cases without additional heat generation (cold luminescence). Such processes take place, \(\text{e.g.,}\) in glowworms.

The integrated circuit detects, processes, and reports the magnitude of the optical signal.\(^{89–91}\) The microluminometer uses the p-diffusion (source and drain diffusions of p-channel MOSFETs, PMOS, Fig. 1) in the n-well as the photodiode. The shallow p-diffusion has a strong response to the 490 nm bioluminescent signal. The entire sensor including all signal processing and communication functions can be realized on a single chip. The integrated circuit contains the devices and circuits to detect the optical signal, to distinguish the signal from noise, to perform analog or digital signal processing, to communicate the results, and to perform auxiliary functions such as temperature assessment or position measurement (Fig. 7).\(^{89–91}\)

Many types of bioluminescent transcriptional gene fusions have been used to develop light-emitting bioreporter bacterial strains to sense the presence, bioavailability, and biodegradation of different kinds of pollutants. The cells here were entrapped on the chip by encapsulation in natural or synthetic polymers providing a nutrient-rich hydrated environment.\(^{89–91}\)

Applications include chemical analysis in gas or liquid phase. Depending on the integration time of the device, trace amounts of toluene and naphthalene were detected in the gas phase using engineered cell colonies of Pseudomonas putida.\(^{89–91}\)

Similar CMOS-based photodiode or phototransistor structures such as CMOS charge-coupled detector (CCD) imagers have been used to develop microspectrometers for biochemical...
and charge transport in the sample are both subject to changes. The resulting charge or current is measured. Electrode reactions in solid or liquid sample phase or transfer reactions, Electrochemical sensors make use of electrochemical or charge-sensitive components. There are methods to prevent polarization. The presence of charge carriers determines the cell potential with small amplitude to a pair of electrodes in order to detect an electrode at equilibrium state, i.e., no current is allowed to flow during the measurement. The measured potential is proportional to the logarithm of the concentration of the electro-active species (Nernst-equation). Conductometric sensors are based on the measurement of a conductance by applying an AC field, which is proportional to the absolute temperature and has a sensitivity of ±2.5 V, can apply voltages from +1 V to −1 V. The reference electrodes in liquid phase are in most cases silver/silver chloride elements. Material consumption due to material in the transducer branch is always electronic.

Electrochemical sensors are usually classified according to their electro-analytical principles. Voltammetric sensors are based on the measurement of the current–voltage relationship. A potential is applied to the sensor, and a current proportional to the concentration of the electro-active species of interest is measured (amperometry is a special case of voltammetry, where the potential is kept constant). Potentiometric sensors are based on the measurement of the potential at an electrode at equilibrium state, i.e., no current is allowed to flow during the measurement. The measured potential is proportional to the logarithm of the concentration of the electro-active species (Nernst-equation). Conductometric sensors are based on the measurement of a conductance by applying an AC potential with small amplitude to a pair of electrodes in order to prevent polarization. The presence of charge carriers determines the sample conductance.

Another method of classification is according to electronic components. There are chemoresistors, chemocapacitors and chemotransistors. We will use the electroanalytical principles as the superordinated scheme and use the component notation within the different sections. We will restrict to CMOS-based systems and omit a wealth of literature on other electrochemical sensor designs, for details of which we refer to literature.

4.4.1 Voltammetric/amperometric sensors. Two different electrode configurations are normally used for voltammetric/amperometric measurements. The two-electrode configuration consists of a reference electrode (RE) and a working electrode (WE). The disadvantage of this method is that the RE carries current and may become polarized if it is less than hundred times the size of the WE. Material consumption due to the current in the RE is another problem. A better approach is hence the use of a three-electrode-system in a potentiostatic configuration. An additional auxiliary electrode (AE, sometimes denoted counter electrode CE) is introduced for current injection in the analyte. The reference electrode is now a true RE with a well-defined potential since no current is flowing through the RE. The potentiostat controls the current at the auxiliary electrode as a function of the applied potential. This is realized in practice with an operational amplifier.

The measured current at any given potential difference depends on the material properties, the composition and geometry of the electrodes, the concentration of the electro-active species (presumably the target analyte) and the mass transport mechanisms in the analyte phase. Among those are migration, the movement of charged particles in an electric field, convection, the movement of material by forced means like stirring or from density or temperature gradients, and diffusion, the movement of material from high-concentration regions to low-concentration regions. The electrochemical reactions at the electrodes are normally fast in comparison to the transport and supply mechanisms. Since convection in the electrode vicinity is avoided, and migration is suppressed by, e.g., a large excess of electro-inactive salts (at the respective potential), diffusion is normally regarded to be the dominant mechanism. There are two components to the measured current, a capacitive component resulting from redistribution of charged and polar particles in the electrode vicinity and a component resulting from the electron exchange between the electrode and the redox species (analyte) termed faradaic current. The faradaic component is the important measurand and is in case of diffusion-limited conditions directly and linearly proportional to the target analyte concentration.

A picture and a schematic of a CMOS-based 3-electrode voltammetric/amperometric sensor is shown in Fig. 8. The monolithic device includes the electrochemical sensor, a temperature sensor, and interface circuitry. The circuit contains an operational amplifier as potentiostat, a switched-capacitor current-to-voltage converter and a clock generator. The circuitry and temperature sensor are realized in 3 μm CMOS technology. The circuit operates at a supply voltage of ±2.5 V, can apply voltages from +1 V to −1 V to the sensor and handles current ranges from 30 nA full scale to 1 μA full scale. The output voltage of the temperature sensor is proportional to the absolute temperature and has a sensitivity of 125 mV K⁻¹. The total sensor dimensions are 0.75 x 5 mm. Sensor processing sequences are given in refs. 97, 100, 101 and 102. The reference electrodes in liquid phase are in most cases silver/silver chloride elements.

Typical applications include chemical analysis in gas or liquid phase. Target analytes in the gas phase include oxygen.
and carbon dioxide using liquid electrolytes. Target analytes in liquid phase comprise dissolved oxygen, glucose, or metal ions. If the target analyte is not an electro-active species like the glucose molecules monitored with the integrated system here, polymer electrolytes or enzymes (glucose oxidase) producing analyte-related ionic species are used in the sensitive electrode coatings.

4.4.2 Potentiometric sensors (chemotransistors). The most important potentiometric sensors are based on the field-effect transistor (FET), and are among the most intensively investigated chemical sensor devices since 1970. Field-effect based transistors, which are the most common electronic components on modern IC logic chips, rely on modulation of the charge carrier density in the semiconductor surface space-charge region through an electric field perpendicular to the device surface: The source-drain current is controlled by an isolated gate-electrode (see Fig. 1 and related text). In the following we will describe the MOSFET (metal-oxide semiconductor-field-effect transistor) for gas sensing applications and the ISFET (ion-selective field-effect transistor) operating in liquid phase.

The MOSFET (metal oxide semiconductor-FET) as used for chemical gas sensing (Fig. 9) has a p-type silicon substrate (bulk) with two n-type diffusion regions (source and drain). The structure is covered with a silicon dioxide insulating layer on top of which a metal gate electrode (electronics: poly-Si gate) is deposited.

When a positive voltage (with respect to the silicon) is applied to the gate electrode, electrons, which are the minority carriers in the substrate, are attracted to the surface of the semiconductor. Consequently, a conducting channel (n-channel) is created between the source and the drain, near the silicon dioxide interface. The conductivity of this channel can be modulated by adjusting the strength of electrical field between the gate electrode and the silicon, perpendicular to the substrate surface.

Palladium-(Pd)-gate FET structures were demonstrated to function as a hydrogen sensor by Lundström et al. Hydrogen molecules readily absorb on the gate metal (platinum, iridium, palladium) and dissociate into hydrogen atoms. These H-atoms can diffuse rapidly through the Pd and absorb at the metal/silicon oxide interface partly on the metal, partly on the oxide surface potential. Typical pH-sensitivities measured with silicon oxide ISFETs are 37–40 mV per pH unit. Gate materials such as silicon nitride, oxynitride, or alumina have better properties than silicon oxide with regard to pH-response, hysteresis and drift. In practice, these layers are deposited on top of the silicon oxide by means of chemical vapor deposition (CVD).

ISFETs can also be covered with organic ion-selective membranes like polyurethane, silicone rubber, polystyrene, and polyacrylates containing ionophores to detect metal ions such as potassium, sodium or silver. Cell metabolism induced pH-changes have been monitored, and glucose has been detected using a proton-producing electrochemical reaction.

The fabrication of CMOS integrated field-effect-based electrochemical sensors with circuitry is described in various publications. An example of an integrated ISFET is shown in Fig. 10a.

The system includes an ISFET amplifier (source and drain follower) and two interdigitated ISFETs realized in a 1.0 μm, two-metal CMOS process (Atmel-ES2, Atmel, France). The pH MOSFET-sensor applications also include the detection of ammonia, amines, and any kind of molecule that gives rise to polarization in a thin metal film (hydrogen sulfide, ethene etc.) or causes changes/dipoles at the insulator surface. In the case of the liquid-phase ISFET (ion-selective field-effect transistor), the gate metal electrode of the MOSFET is replaced by an electrolyte solution, which is contacted by the reference electrode. The gate oxide is directly exposed to the aqueous electrolyte solution (Fig. 9). An external reference electrode is required for a stable operation of an ISFET. The source-drain current is influenced by the potential at the oxide/aqueous solution interface. ISFET amplifiers with feedback keep the source–drain current constant by compensating solution-induced changes in the gate oxide potential by modulation of the gate voltage ($U_g$) that is applied to the reference electrode. The gate-source potential is then determined by the surface potential at the insulator/electrolyte interface. Mechanistic studies of the occurring processes at the solution/gate oxide interface (site binding model) and the oxide semiconductor interface can be found in literature. Theinsulator solution interface is assumed to represent in most cases a polarizable interface, i.e., there will be charge accumulation across the structure but no net charge passing through.

Classic ISFET applications include pH-sensing (acidity or basicity) with an exposed-gate-oxide FET. The surface of the gate oxide contains OH-functionalities, which can be protonated and deprotonated and thus, when the gate oxide contacts an aqueous solution, a change of pH will change the silicon oxide surface potential. Typical pH-sensitivities measured with silicon oxide ISFETs are 37–40 mV per pH unit. Gate materials such as silicon nitride, oxynitride, or alumina have better properties than silicon oxide with regard to pH-response, hysteresis and drift. In practice, these layers are deposited on top of the silicon oxide by means of chemical vapor deposition (CVD).

Fig. 9 Schematic representation of a MOSFET and an ISFET structure. $U_g$ denotes the gate voltage, $U_s$ the source-drain voltage. The ISFET is realized by replacing the metal gate of the MOSFET with an ionic solution and a reference electrode immersed into this solution.

Fig. 10 (a) Micrograph of a CMOS chip hosting two integrated ISFETs and an ISFET amplifier. (b) Schematic and cross-section of the ISFET. For details, see text and ref. 131. Reprinted from ref. 131 with permission.
measurements have been conducted using a Ag/AgCl reference electrode and yielded a sensitivity of 47 mV per pH unit using silicon oxynitride as the pH-sensitive material. To render the fabrication CMOS-compatible, the sensitive oxynitride sits on top of an electrically floating multi-conductor gate structure including the two metal layers and the gate polysilicon, all of which are electrically connected (Fig. 10b). This way, the pH-dependent electrical charge at the surface of the oxynitride in contact with the solution directly affects the silicon surface source–drain current (Fig. 10b).131

4.4.3 Conductometric sensors. Conductometric techniques are a special case of alternating-current (AC) impedance techniques. Instead of the real and imaginary component of the electrode impedance at different frequencies, only the resistive component, related to the sample (sensing material) resistance is of interest. Since complex impedances include capacitive and inductive contributions, chemocapacitors are included here, in the conductometric section. The section on conductometric sensors is hence organized in two subsections, one on chemoresistors and the other subsection on chemocapacitors.

4.4.3.1 Chemoresistors. Chemoresistors rely on changes in the electric conductivity of a film or bulk material upon interaction with an analyte. Chemoresistors are usually arranged in a metal electrode 1/sensitive layer/metal electrode 2 configuration.20,21,24 The resistivity/conductance measurement is done either via a Wheatstone bridge arrangement or by recording the current at an applied voltage in a DC (direct current) mode or in a low-amplitude, low-frequency AC (alternating current) mode to avoid electrode polarization. The contact resistance should be much lower than the sample resistance and be minimized, so that the bulk contribution dominates the measured overall conductance.

There is two major classes of chemoresistors: (1) high-temperature chemoresistors (200–600 °C) with semiconductor metal oxide coatings and (2) low-temperature chemoresistors (room temperature) with polymeric and organic sensitive coatings. We will focus on the technologically more challenging high-temperature sensors and only briefly mention the second type with the applications.

The sensitive materials used with high-temperature chemoresistors include wide-bandgap semiconducting metal oxides such as tin oxide, gallium oxide, indium oxide, or zinc oxide, all of which can only be operated as sensing materials at high temperature (> 200 °C). In general, gaseous electron donors (hydrogen) or acceptors (nitrogen oxide) adsorb on the metal oxides and form surface states, which, at high temperature, can exchange electrons with the semiconductor. An acceptor molecule will extract electrons from the semiconductor metal oxide and thus decrease its conductivity. The opposite holds true for an electron–donating surface state. The reaction between gases and oxide surface depends on the sensor temperature, the gas involved, and the sensor material.20,140–144

Semiconductor metal oxide sensors usually are not very selective, but respond to almost any analyte (carbon monoxide, nitrogen oxide, hydrogen, hydrocarbons). One method to modify the selectivity pattern includes surface doping of the metal oxide with catalytic metals such as platinum, palladium, gold, and iridium.20,21,140–144

The device requirements for a high-temperature chemoresistor include a thermally well-isolated stage such as a membrane, which allows for keeping the sensing materials at a high temperature without heating the bulk chip (protection of electronic components), an integrated heater, and a temperature sensor (Fig. 11).145,146

Fig. 11 shows a front-side-etched microhotplate on a CMOS substrate.145,146 The microhotplate components include a polysilicon resistive heater, an aluminum metal plate for heat distribution and temperature measurement and four noble metal-coated aluminum or tungsten contacts for electrical connection to the sensing film.145,146 Tin dioxide is then deposited on top of the metal electrodes.

Since microhotplates have a very low thermal mass, they allow for applying temperature-programmed operation modes, which enhance the gas detection capability.147,148

The fabrication of hotplates on CMOS-substrates is described in refs. 145, 146, 149 and 150. Complete processing sequences are detailed in refs. 150 and 151. First results with hotplates and circuitry on a single CMOS-chip have been presented recently.152,153 Multi-chip solutions have been proposed in refs. 154 and 155. Reliability tests with CMOS hotplates have been conducted.156 The CMOS-hotplates realized on SOI (silicon on insulator) and SIMOX (separation by implantation of oxygen) substrates are presented in refs. 157 and 158.

Typical microhotplate applications include the detection of inorganic gases such as hydrogen,145,146,150 oxygen,145,146 nitrogen oxide,147,159 carbon monoxide,145–148,155,159 and a variety of organic volatiles145,146,150,159–161 using predominantly tin oxide as sensitive layer.

Several classes of predominantly organic materials are used for application with chemoresistors at room temperature (electrode spacing typically 5 to 100 µm, applied voltage 1–5 V). Conducting polymers such as polypyrroles, polyaniline and polythiophene are used to monitor a variety of polar organic volatiles like ethanol, methanol, and components of aro- mas.162–165 Conducting carbon black can be dispersed in non-conducting polymers so that if the polymer absorbs vapor molecules and swells, the particles are, on average, further apart and the conductivity of the film is reduced (conductivity by particle-to-particle charge percolation).166 Applications also include organic solvents such as hydrocarbons, chlorinated compounds, and alcohols.166–170

CMOS-based monolithic sensor systems coated with carbon black/polymer blends are detailed in refs. 160,170 (two-chip solutions with a CMOS circuitry chip and a separate sensor chip based on conducting polymers can be found in refs. 164 and 165. A CMOS-compatible monolithic conductivity sensor for liquid phase (Pt electrodes) was presented in ref. 171.

4.4.3.2 Chemocapacitors. Chemocapacitors (dielectrometers) rely on changes in the dielectric properties of a sensing material upon analyte exposure. Interdigitated electrode structures are predominantly used.172,173 The capacitances usually are measured at an AC frequency of a few kHz up to 500 kHz.

The interdigitated capacitors described here exhibit an electrode width and spacing of 1.6 µm. The total footprint of a capacitor is 800 × 800 µm². Since the nominal capacitance of such a microstructure is on the order of 1 pF and the expected capacitance changes (sensor signals) in the range of some attoFarads, an integrated solution with on-chip circuitry is
required. There is no possibility to transfer such minute analog signals via bond wires and cables to desktop instruments. The integrated solution includes two capacitors, a polymer-coated sensing capacitor and a silicon nitride-passivated reference capacitor in a switched-capacitor scheme (Fig. 12). The sensor response is read out as a differential signal between the polymer-coated sensing and a passivated reference capacitor. A digital output signal is then generated by comparing the minute loading currents of both capacitors using a fully differential second-order Sigma–Delta-modulator circuitry. A counter to decimate the output bit stream is co-integrated on-chip. A schematic of a capacitive chemical sensor microsystem is shown in Fig. 12.

Two effects change the capacitance of a polymeric sensitive layer upon absorption of an analyte: (i) swelling and (ii) change of the dielectric constant due to incorporation of the analyte molecules into the polymer matrix. The capacitance change for a polymer layer with a thickness of approximately half the periodicity of the electrodes is determined by the ratio of the dielectric constants of analyte and polymer. If the dielectric constant of the polymer is lower than that of the analyte, the capacitance will be increased. Conversely, if the polymer dielectric constant is larger, the capacitance will be decreased (see Fig. 15 later). These effects have been further discussed and supported by simulations in ref. 176.

For conducting measurements at defined temperatures, sensor and reference capacitors can be placed on thermally isolated membrane structures. The fabrication of capacitors integrated with CMOS circuitry components is described in refs. 46, 173–178.

Typical applications include humidity sensing with polyimide films since water has a high dielectric constant of 78.5 (liquid state) at 298 K leading to large capacitance changes. CMOS-based integrated capacitive humidity sensors are commercially available, e.g., Sensirion AG, Switzerland. More recent applications also include the detection of organic volatiles in the gas phase using polymeric layers.

4.5 Monolithic integration of different transducers

Another significant advantage of CMOS-based chemical sensors is the possibility to integrate several different transducers along with all the driving circuitry on a single chip. Additional components that can be integrated include signal conditioning circuitry (amplifiers, references), multiplexers to reduce the number of output pins, analog/digital and digital/analog converters, chip memory (calibration values) or other smart features, an intra-chip communication or bus system and a serial interface to communicate with off-chip microcontrollers or instruments. In the following we will present two prototype monolithic CMOS multisensor systems, (1) a multiparameter biochemical sensor and (2) a smart gas sensor microsystem.

4.5.1 CMOS multiparameter biochemical microsensor

The microsensor system is aimed at continuous monitoring of ions, dissolved gases and biomolecules in liquid phase such as blood (Fig. 13), and is based on an earlier design by Gumbrech et al. The eight integrated chemical sensors comprise six ion-sensitive field-effect transistors (ISFETs; 1–6 in Fig. 13), one oxygen sensor (7 in Fig. 13) and one conductometric sensor (8a,b in Fig. 13), all of which can be operated in parallel. An Ag/AgCl reference electrode was also integrated on the CMOS chip to get rid of external references. A flow channel (polyimide) restricts the liquid phase access to the sensor area.

The six ISFETs allow for direct contact of the electrolyte with the gate oxide. The gate oxide itself is pH-sensitive (see ISFET section), or the ISFET can be used as a ‘Severinghaus’-type pH-FET to measure dissolved carbon dioxide (detection of carbon dioxide via dissolution in water, formation of ‘carbonic acid’ and monitoring of the pH change). The gate oxide can also be covered with different ion-selective membranes to achieve sensitivity to a range of target ions such as potassium. All six ISFETs or only a subset can be used. The idea is to make a standard chip to reduce manufacturing costs and then modify the chip with selective coatings according to user needs.

The integrated amperometric sensor can be used as a Clark-type oxygen sensor, which is based on a two-step-reduction of gaseous oxygen in aqueous solution via hydrogen peroxide to hydroxyl ions.

The conductometric sensor consists of two parallel sensors (8a), which share one common electrode (8b). A sinusoidal AC potential is applied to the electrodes, and the current, which depends on the solution composition (concentration of charged particles or ions) is recorded. The eight sensors can continuously monitor ions, dissolved gases and biomolecules via enzymatic reactions that produce charged particles.

The full system is produced in a 1.2 μm single-metal, single-poly CMOS process and the chip size is 4.11 × 6.25 mm. The chip is operated at 5 V and hosts all driving circuitry for the sensors such as ISFET buffer amplifiers, a potentiostatic setup for the amperometric sensor and the circuitry necessary to perform a four-point conductometric measurement on chip. In addition the chip exhibits a temperature control unit to keep the system temperature at an adjusted value (physiological conditions). This temperature control unit includes a temperature

![Fig. 12](image) Schematic of a capacitive chemical sensor microsystem including a polymer-coated sensing capacitor and a Si-nitride-protected reference capacitor. The on-chip circuitry includes a ΣA-converter.

![Fig. 13](image) Micrograph of the CMOS multi-parameter biochemical sensor chip, which includes 6 ISFETs (1–6), one conductometric sensor (8a,b) and an (amperometric) oxygen sensor (7). The on-chip circuitry includes an EPROM, a multiplexer and counter, a driver unit, a conductometric and potentiostatic circuit and a heater. Reprinted with permission from ref. 181.

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sensor (parasitic vertical p–n–p bipolar transistor) and a NMOS transistor heater. A single-bit EPROM (electrically programmable read-only memory) was implemented on chip to make sure the chip is only used once and then is disposed, which is a crucial feature in medical applications. Additional on-chip electronics include units to control the chip (multiplexer, demultiplexer, 4-bit Gray counter and decoder) and units to provide the biasing and the communication to off-chip instrumentation. Due to the high level of on-chip integration only 5 external connections are needed: two for power supply, two for bi-directional communication and one for a clock signal.

First tests including amperometric oxygen measurements, the assessment of potassium concentrations with ISFETs, and conductimetric measurements with a buffer solution have been performed.\textsuperscript{181}

4.5.2 CMOS single-chip gas sensor microsystem\textsuperscript{182}. The CMOS single-chip chemical microsensor system combines three different transducers, a mass-sensitive cantilever, a capacitive sensor, and a calorimetric sensor, all of which rely on polymeric coatings as sensitive layers to detect airborne volatile organic compounds (VOCs). The three transducers respond to fundamentally different analyte molecule properties. One of them responds to the mass of sorbed molecules, another responds to the heat of absorption, and the third responds to the dielectric properties of the absorbates. The monolithic system such simultaneously provides three different ("orthogonal") sensor responses, which are used to classify or quantify analytes in the gas phase.

The capacitive sensor as previously described in section 4.4.3.2 is integrated with a fully differential second-order Sigma-Delta-modulator circuitry and a counter to decimate the output bit stream.\textsuperscript{185}

The micromachined cantilever, the operation principle of which has also been already described in section 4.1.2, is 150 \( \mu \text{m} \) long and consists of silicon as well as vapor-deposited and thermal oxide. The cantilever acts as the frequency-determining element in a feedback oscillation circuit, which is entirely integrated on the chip with a counter. For more details on the electronics, see refs. 43 and 185.

The third transducer is a thermodiagnostic calorimeter based on the Seebeck effect with 256 polysilicon/aluminum thermocouples connected in series (500 \( \mu \text{m} \) by 500 \( \mu \text{m} \) dielectric membranes). Details have been described in section 4.2.2. The thermovoltage is translated into a digital signal on chip using a Sigma–Delta analog/digital converter and a decimation filter. The overall system chip additionally includes a temperature sensor, (6) mass-sensitive resonant cantilever, and (7) digital circuitry, which has been described in the context of the different transducers. The analog/digital conversion is done on chip, which allows for achieving a favorable signal-to-noise ratio, since noisy connections are avoided and a robust digital signal is generated on chip and then transmitted to an off-chip data port over an I2C serial interface.\textsuperscript{186} The I2C bus interface offers the additional advantage of having only very few signal lines (essentially two) for bi-directional communication and also allows for operating multiple chips on the same bus system. An on-chip digital controller manages the sensor timing and the chip power budget. The sensors are located in the center of a metal frame, which is used to apply a flip-chip packaging technique.\textsuperscript{187}

Fig. 15 displays simultaneously recorded sensor signals of all three transducers upon exposure to 1200 and 3000 ppm (parts per million) of ethanol, and 1000 and 3000 ppm of toluene at 30\textdegree C.\textsuperscript{181,185} The sensors were alternately exposed to analyte gas and pure carrier gas. The polymeric coating consisted of poly(etherurethane), PEUT\textsuperscript{46} at a thickness of approximately 4 \( \mu \text{m} \).

Fig. 15a shows the measured frequency signals (Sigma–Delta converter output) of the capacitor. Ethanol exhibiting a dielectric constant of 24.5, which is larger than that of PEUT (2.9), causes a capacitance increase and hence positive frequency shifts, toluene with a dielectric constant of 2.4 causes a capacitance decrease and negative frequency shifts. Fig. 15b displays the cantilever response. The resonance frequency decreases with increasing oscillating mass as a consequence of volatile absorption. Ethanol shows rather low signals as compared to toluene due to its lower molecular mass and due to its lower enrichment (partitioning) in the polymeric phase.

The calorimetric results in Fig. 15c represent a superposition of already discussed partitioning and heat budget change due to analyte ab/desorption. The absorbing analyte liberates heat (heat of condensation) causing a positive transient signal (positive peak), whereas the desorbing analyte abstracts vaporization heat from the environment generating a negative transient signal (negative peak upon purging, see Fig. 15c). The close-up in the upper left corner shows the time-resolved response upon 3000 ppm of toluene within the first 6 s.

The signals of all three transducers linearly correlate with analyte concentration at low concentrations (less than 3\% of saturation vapour pressure at the operating temperature). To further improve analyte identification/quantification, an array of microsystem chips coated with different polymers can be used. The monolithic CMOS gas microsystem is targeted at identifying organic solvents in transport containers or providing workplace safety in, e.g., chemical industry. It will form part of a handheld or credit card size detection unit.

5 Outlook

The field of CMOS-integrated chemical sensors is currently expanding as can be seen from the growing number of publications in the last years. As can be concluded from the article, the research and development thrusts go in the direction of integrating more and more electronic functions on the sensor chip such as adaptive circuits for signal evaluation and discrimination,\textsuperscript{188,189} or telemetry units for wireless communication. Telemetry functions will encompass, e.g., communication from implanted chips (glucose sensors) through the...
frequencies in environmental and building control scenarios by using radio and distributed chemical sensor responses to a central terminal CMOS-assisted electronic detection rather than optical detection. This will gain momentum and will most probably also include monitoring stimulators, 20 or neural prostheses, which is at an early stage but will function correctly, which then makes up for the costly development. Of thousands of pieces are sold, or if the devices provide unique costs) and only pays off, if either millions or at least hundreds of users are using these devices. CMOS sensor development is expensive (mask and processing were reported on by Kovacs and coworkers. 195,196 The interfacing of neurons or nerve ends with CMOS circuits provided by the huge development efforts of the IC-industry, only a small fraction of which has been used for semiconductor devices so far. It has to be kept in mind, however, that CMOS-MEMS technology and processes offer a great deal of readily available electronic circuits provided by the huge development efforts of the IC-industry, only a small fraction of which has been used for chemical sensors so far. It has to be kept in mind, however, that CMOS sensor development is expensive (mask and processing costs) and only pays off, if either millions or at least hundreds of thousands of pieces are sold, or if the devices provide unique functionality, which then makes up for the costly development. The ‘killer-applications’ involving large numbers of chemical sensors have not emerged yet. They may be in the field of automotive applications, domestic gas alarms, HVAC (humidity, ventilation, air conditioning) units, or in the field of disposable medical devices (e.g., DNA or blood tests).

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7 References
