10
Integrated Electronic Noses and Microsystems for Chemical Analysis

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Abstract
There is considerable interest in the miniaturization and mass production of electronic noses through the exploitation of recent advances in the emergent field of microsystems technology. In this chapter we explore the future outlook for integrated electronic noses by first reviewing the different types of microfluidic components that have been reported in the literature, such as microchannels, microvalves, and micropumps. Next, we describe recent efforts to develop microelectronic noses based upon the integration of sensor arrays and smart interfaces. Finally we report upon work in the related field of micro total analysis systems, in which, for example, a micro gas chromatograph or a micro mass spectrometer are being fabricated; these physically-based microinstruments may be regarded as a type of micronose and thus in competition with integrated electronic micronoses.

10.1
Introduction

The integration of gas microsensors and signal processing circuitry is a subject of ever-increasing importance in the chemical sensor community. It offers lower unit cost through batch production of wafers, smaller device size, better reproducibility, superior signal conditioning by less noise generated in the transmission of the sensor signals to the processing electronics, and an improved limit of detection for the whole sensing system. The full integration of gas microsensors and signal processing circuitry has been brought a step nearer with reports of an increase in sensor reproducibility by the integration of arrays of sensors onto the same substrate [1–4], improvements in sensor sensitivity through advances in individual microsensor technologies [5, 6] and finally the development of novel gas-sensitive materials, for example see Gardner and Bartlett [7], and Attard et al. [8]. Many commercial (non-chemical) sensors have been realized in recent years through the integration of both the electronic signal processing circuitry and the sensing part on the same silicon die. Some examples include pressure sensors, ultrasound sensors and gas flow sensors, proximity and temperature sensors.
For a review of silicon sensors, readers are referred to Gardner et al. [13]. The field of gas sensors is covered in Chapter 9 of this book where a detailed description of the design of the single-chip multisensor system comprising four different sensors, as well as driving and signal-conditioning circuitry, can be found.

Recent years have also seen substantial efforts in the development of smart and intelligent sensor technology. The main advantages of intelligent sensors are their improved performance and reliability – achieved through the addition of self-testing and self-diagnostic functions [14]. Emphasis has also been given to the development of application-specific integrated circuits (ASICs) for intelligent sensors. Taner and Brignell [15] have studied the advantages of ASIC technology, which enables intelligent devices to deal both with systematic variation in sensor parameters and provides good solutions for sensor communications.

Parallel with the integration of microsensors and signal processing electronics, and the realization of smart sensor interfaces, sampling and fluid-handling techniques have been rapidly developing. Micro flow sensors, micropumps and microvalves started emerging in the late 1980s marking the beginning of the field of microfluidics. So far, life sciences and chemistry have been the main application areas of microfluidics in the liquid phase. Considering that sample handling is a critical area, which has an enormous influence on the performance of e-noses (see Chapter 3), microfluidics should have a significant impact on the future development of superior, integrated electronic nose (e-nose) systems. Microfluidic technology combined with smart silicon sensor arrays could lead to the development of cheap, and possibly disposable devices, particularly important in medical applications such as chemical and biological assays.

In this chapter, a review of different solid-state sensor systems and smart sensor interfaces for e-noses will be given together with an overview of existing microfabricated components for fluid handling, such as microvalves, micropumps, and micro-
channels. A block diagram of the basic components that make up an integrated e-nose system is shown in Fig. 10.1 and will be described below. The integration of different components into microsystems and microinstruments will also be discussed, and the future outlook concerning sensor arrays, biological assay devices, and neuromorphic systems will be briefly outlined. Microsystems for chemical analysis based on gas chromatography, mass spectrometry, and optical spectrometry techniques will also be reviewed. Finally, a future outlook is given of e-noses and microsystems for chemical analysis.

10.2 Microcomponents for Fluid Handling

In the early 1990s, microfluidics was established as a general term for the research discipline dealing with fluid transport phenomena on the micrometer scale and fluidic components, devices, and systems built with microfabrication technologies. The major applications of microfluidics are in the fields of medical diagnostics, genetic sequencing, drug discovery, and proteomics. This section focuses on microcomponents for fluid handling, such as microchannels, microchambers, microvalves and micropumps that could be applicable to the development of integrated e-noses and microsystems for chemical rather than biological analysis.

Advancements in photolithography turned the possibility of miniaturizing analytical systems into reality. Initially, only simple channels and reservoirs could be made by photolithography on glass or silicon wafers, and electro-osmosis was the only way to move liquids. Over the last 10 years, the fabrication of new microfluidic components, such as valves, pressure systems, metering systems, reaction chambers, and detection systems, has led towards the development of more complex manufacturing technologies, e.g. deep reactive ion etching (DRIE), and multiplayer processes such as the five-layer polysilicon Sandia process) and hence the possibility for lab-on-a-chip prototypes [16]. Apart from their use in research, microfluidic devices also have significant commercial potential. In 1999, the Systems Planning Corporation, Arlington, VA, released a market study on microelectromechanical systems (MEMS) that projected a microfluidics market of 3 to 4.5 billion euros by 2003. 30% of this total is split equally between sensors and lab-on-a-chip applications. Another microsystems market study completed in 1996 by a task force of the European Commission’s Network of Excellence in Multi-functional Microsystems (NEXUS) forecasted a market of €2.8 billion for microstructure-based disposable assay devices alone by 2002.

10.2.1 Microchannels and Mixing Chambers

Microchannels are essential components of microfluidic systems. They provide the connections between pumps, valves and sensors [17], and they are used as separation columns for different types of gas or liquid chromatographs [18, 19]. They also act as
Fig. 10.2 Scanning electron microscope (SEM) images of several types of microchannels, fabricated with: (a) bulk micromachining and wafer bonding, (b) surface micromachining, and (c) buried channel technology. From Boer et al. [21]
heat exchangers in the cooling of electronic chips [20]. Common methods used for the fabrication of microchannels include bulk etching with wafer-to-wafer bonding, bulk etching with sealing using low-pressure chemical vapour deposition (LPCVD) materials, conventional surface micromachining of channels, imprinting plastic substrates, X-ray LIGA (German acronym: Lithographie, Galvanoformung, Abformung) technology and DRIE, and channel forming from UV photodefiable SU-8 photoresist using LIGA (sometimes called UV LIGA). Figure 10.2 shows scanning electron micrograph (SEM) images of several types of microchannels fabricated with bulk micromachining and wafer bonding (Fig. 10.2a), surface micromachining (Fig. 10.2b), and buried channel technology (BCT) (Fig. 10.2c). One problem with wafer-to-wafer techniques, such as anodic bonding or direct fusion bonding, is the possible creation of wafer-to-wafer misalignments and the formation of microvoids at the bonding interface, which may affect the functional performance of the device. Another difficulty is that electronic circuitry (e.g., CMOS) cannot be incorporated on the same substrate because of the high process temperatures and voltages needed to perform anodic bonds. The use of surface micromachining obviates the need for accurate wafer alignment. In this approach, structural parts are embedded in layers of a suitable sacrificial material on the surface of a substrate. Dissolving the sacrificial material forms a complete microchannel. By this method microchannels can be fabricated in various different passive materials, e.g., silicon nitride, polysilicon, metal, polymer, and silicon dioxide. One major disadvantage of this technique has been that the vertical dimension of such channels is restricted by the maximum sacrificial layer thickness that can be deposited and etched within an acceptable time period. Researchers at the University of Twente have proposed BCT as an alternative to conventional bulk and surface micromachining [21]. BCT allows the fabrication of complete microchannels in a single wafer with only one lithographic mask, and processing on one side of the wafer. The microstructures are constructed by trench etching, coating of the sidewalls of the trench, removal of the coating at the bottom of the trench, and finally etching into the bulk of the silicon substrate. This method for the fabrication of these devices was derived from the SCREAM (single-crystal reactive etching and metallization) process [22]. The structure can be sealed by the deposition of a suitable layer that closes the trench. Using the above procedure it is possible to construct cavities, reaction chambers or crossing channels. A spiral-shaped channel with a length of 10 m and a diameter of 30 μm was also developed by the same research group for possible application as a separation element in gas chromatography.

The method of imprinting plastic substrates involves the low-temperature patterning of plastic substrates using either small diameter wire or a micromachined silicon template. Silicon templates have also been used as a negative master tool for fabrication of polymer microchannels and mixers by hot embossing and microinjection molding [23]. Templates have also been made in metals and, more recently, diamond. Figure 10.3 shows a micrograph of a mixer, which has been replicated on a hot embossed polymethylmethacrylate wafer. The advantage of this method is that the resultant channels are robust, easy to fabricate at low cost, and compatible with biological fluids (unlike silicon); it also allows the integration of other microfluidic elements and the sensors but not electronic circuitry. Another technology that
Fig. 10.3 Micrograph of an embossed mixer (smallest channel dimensions: 50 μm × 50 μm). From Greschke et al. [22]

Fig. 10.4 Process steps for fabricating the MWμCs (a) etch channel, (b) form porous silicon (PS), (c) under-etch PS. From Tjerkstra et al. [24]
could be used is LIGA technology. The principal advantage of the LIGA process is that microdevices can be fabricated with a height-to-width aspect ratio of up to 200, typically several millimeters in height and 10 μm in width, but the microchannels fabricated using this technology are usually made from plastics, metals, and ceramics rather than silicon. The process is also very expensive because it requires a synchrotron source. Finally, channels can be made using thick UV LIGA. Using this method only the sidewalls of the channel can be formed, so to seal them some method of bonding is required. The advantage is that the thickness of the wall can be easily controlled and a high aspect ratio achieved.

Releasing electrochemically formed porous silicon from the bulk silicon substrate by under-etching at increased current density is another technique that can be used for the microfabrication of microchannels, in particular multi-walled microchannels (MWµCs) [24]. Figure 10.4 shows the main processing steps for the formation of a MWµC by etching channels in a p-type silicon wafer using LPCVD silicon-rich silicon nitride as the mask material. Figure 10.5 shows an SEM image of a MWµC containing two porous layers. To create more robust devices, i.e. to increase the strength of the structure, microchannels can be fabricated with a porous silicon membrane suspended halfway across an etched cavity surrounded by silicon nitride walls.

Most of the above methods allow for some integration with sensors, but external integration with the electronic circuitry is typically used, e.g. hybrid packaging or multi-chip modules. In order to allow direct integration of sensors, actuators, and other electronics with the microchannels, Rasmussen et al. have proposed two methods for the fabrication of microchannels using the standard CMOS process and simple and inexpensive post-processing steps [25]. In the first method, shallow microchannels of the order of 0.4 μm are realized by removing surface layers incorporated in a standard CMOS integrated circuit process. Larger channels with depth of 30 to 300 μm can be fabricated through the second method that employs bulk micromachining techniques. Both methods offer the possibility to create a complete smart microfluidic sys-
tem that possesses integrated microfluidic elements, sensors and electronics as shown in Fig. 10.6.

10.2.2 Microvalves

Microvalves are one of the most important building blocks of microfluidic systems used for fluid flow control. They can be classified in two categories: active valves (with an actuator) and passive check valves (without an actuator).

10.2.2.1 Active Microvalves

An active microvalve consists of a device body that contains the fluid under pressure, a valve seat to modify the fluid flow, and an actuator to control the position of the valve seat. The first reported microvalve was designed as an injection valve for use in integrated gas chromatography [26]. It had a silicon valve seat and a nickel diaphragm actuated by an external solenoid. Following this first design, a large number of microvalves have been designed and reported, and they can be classified on the basis of the actuation method employed. These methods include pneumatic, thermopneumatic, thermomechanic, piezoelectric, electrostatic, electromagnetic, electrochemical, and capillary force microvalves. Figure 10.7 shows some of these actuating devices.

Pneumatic valves have a membrane structure as the valve seat. Although pneumatic actuation is based upon a very simple principle it requires an external pressure source, which makes the pneumatic valves unsuitable for most compact applications. A low spring constant is also an important parameter and in order to achieve it thin membranes or corrugated membranes have to be designed. Soft elastic materials, such as
Silicon rubber or Parylene, can be used to realize the low spring constant [27], whereas hard materials such as silicon and glass are problematic.

Thermopneumatic valves utilize a sealed pressure cavity filled with a liquid. Actuation is based on the change in volume of the sealed liquid. The phase change from liquid to gas or from solid to liquid can also be used if a larger volume expansion is required. The disadvantage of these types of valves is the incompatibility of the technology, since the liquid has to be primed, filled, and sealed individually. Thin films of solid paraffin material could be used as an alternative [28] since they could be integrated in the batch fabrication.

Thermomechanic microvalves utilize the principle of the conversion of thermal energy directly into mechanical stress. There are three types of thermomechanic actuators: solid-expansion [29], shape-memory alloy [30], and bimetallic actuators. A bimetallic valve as shown in Fig. 10.7a, was introduced by Jerman [31] and was one of the first commercialized microfluidic components. The valve was designed for a gas flow controller, and its actuator consists of a central boss, a circular diaphragm made of bimetallic materials, and a circular heater. The temperature, controlled by the heater, of the bimetallic structure on the diaphragm was used to vary the force applied to the boss by the diaphragm so that the gas flow can be adjusted. The valve was designed to control the gas volumetric flow-rate from 0 to 90 mL min⁻¹.

Piezoelectric microvalves utilize the piezoelectric effect as an actuation principle. The thin-film piezoelectric actuators do not deliver sufficient force/displacement for valve...
application, so all reported piezoelectric microvalves use external stack-type piezoelectric actuators, bimorph piezocantilevers, or bimorph piezodisks. Bimorph actuators are used if larger deflections are required. They either consist of two bonded piezoelectric layers, with anti-parallel polarization [32], or of a piezoelectric layer bonded to a non-piezoelectric layer [33].

**Electrostatically actuated microvalves** have typically been designed with a valve seat in the form of a cantilever. Figure 10.7b shows a cantilever structure fabricated by surface micromachining. The valve seat could also have a form of flexible metal bridge. Such a design of microvalve was fabricated by Shikida and Sato [34] in order to allow an adequate gas flow-rate under low pressure. The valve is suitable for rarefied gas control systems but it requires a large actuating voltage of 100 V. In order for a large deflection to be achieved with a relatively small drive voltage, a combination of the electrostatic force, buckling effect, and pneumatic force were used. This arrangement was utilize for a bistable valve in an implantable drug delivery system [35]. Vandelli et al. have designed a microvalve array for fluid flow control with the valve membrane and one electrode made out of a polysilicon layer, whereas the other electrode was bulk silicon fabricated using surface micromachining. The valves were arranged in an array so that the flow rate could be controlled digitally [36].

**Electromagnetic microvalve** with a valve cap made out of a soft magnetic Ni-Fe alloy supported by a spring is shown in Fig. 10.7c [37]. It moves vertically in the magnetic field gradient applied by the external electromagnet. This valve was designed as a flow regulator for a high vacuum application. A microvalve activated by a combination of electromagnetic and electrostatic forces has also been fabricated [38]. The structure consists of a gas flow inlet having a counter electrode, a deflectable membrane coated with a metal conductor and two permanent magnets. Current pulses of 200 mA and a voltage of 30 V were typically applied for electromagnetic and electrostatic actuation. The response time was below 0.4 ms.

There are also some reported examples of so-called electrochemical and capillary-force valves. Electrochemical valves are actuated gas bubbles generated by the electrolysis reaction, where the pressure inside the bubble is proportional to the surface tension and the radius of curvature. Capillary-force valves use capillary-force actuation where the surface tension and the capillary force can be controlled actively or passively by different means: electrocapillary, thermocapillary, and passive capillary. The use of some of these effects are described in two published papers [39, 40].

10.2.2.2 Passive Microvalves (Check Valves)
This type of microvalve is typically designed for use in micropumps where a very small leakage under reverse applied pressure and a large reverse-to-forward flow resistance ratio is required. The dimensions of check valves are small in comparison with the valves with integrated or external actuators. A review paper by Shoji and Esashi describes a wide variety of check valve structures [41]. A typical cantilever-type structure is shown in Fig. 10.8. Oosterbroek et al. have reported on the design, simulation, and realization of in-plane operating passive microvalves [42]. Figure 10.9 shows functional, art, and SEM impressions of a 2 × 5 high-density in-plane check valve array.
10.2.3 Micropumps

Micropumps can be classified into two categories: mechanical pumps with moving parts and non-mechanical without moving parts. Mechanical pumps can be further divided into three major groups: reciprocating, peristaltic, and valve-less rectification pumps. Non-mechanical pumps are mainly used to move liquids and constituents in liquids, which need to avoid any moving mechanical parts. Electrohydrodynamic, electro-osmotic, or ultrasonic effects are normally employed in the operation of non-mechanical micropumps.

10.2.3.1 Mechanical Micropumps

A reciprocating-type micropump consists of a pump pressure chamber with a flexible membrane driven by an actuator unit and passive microvalves (check valves). Two main conditions have to be satisfied in order for reciprocating micropumps to function correctly. First, the minimum compression ratio of micropumps (the ratio between the stroke volume and the dead volume that causes serious constraints in most micropump designs) has to be determined and secondly the pump pressure has to be high. For the gas micropumps that are of interest in integrated e-nose ap-
applications, the criterion for the minimum compression ratio \( \varepsilon \) is given by Richter et al. [43]:

\[
\varepsilon > \left( \frac{P_0}{P_0 - |\Delta P_{crit}|} \right)^{1/\gamma} - 1
\]

where \( P_0 \) is atmospheric pressure, \( \Delta P_{crit} \) is the critical pressure required for the opening of the check valve, and \( \gamma \) is the adiabatic coefficient (for air \( \gamma \) takes a value of 1.4).

(The above equation could be simplified at small critical pressures and low pump frequencies where there is isothermal behaviour.)

The maximum output pressure of the micropump depends directly on the available force of the actuator used. The different types of actuators that have been employed to date are piezoelectric, pneumatic, electrostatic, and thermopneumatic. The first piezoelectric micropump (Fig. 10.10), developed and reported in 1988 by van Lintel et al. [44], was made in silicon and used a piezoelectric disk. Since then, various different types of micropumps have been designed in order to satisfy the two requirements mentioned above. Over the years the dead volume of the pump chamber has become smaller, and the check valves and the pump membranes have been made out of softer materials with low spring constants. An example of a self-priming micropump [45] with a small dead volume able to pump gas is shown in Fig. 10.11. Here the dead volume was minimised by minimising the dead volume of the valve unit down to 500 nL, hence increasing the compression ratio to 0.111. In another development [46] van Lintel’s original design was improved to achieve a compression ratio of 1.16. Another way to achieve improvements in the micropump design is through the design of flexible check-valves. The valves, in the forms of cantilever, have been used with integrated electrostatic [47] or bimorph piezoelectric disks [48] as actuators. Materials that are more flexible than silicon, such as polyimide, polyester, and parylene, have also been used in the design of flexible check-valves. A thermo-pneumatically driven micropump was fabricated using the LIGA process [49]. In this the pump case is made by injection moulding of polysulphone (PSU) and the pump chamber is covered by a polyimide membrane. A similar design was fabricated by plastic injection moulding and uses a polyester valve [50] whereas the design reported in [51] has a pump membrane made out of silicone rubber, and the disk valve from parylene.

![Piezoelectric disk reciprocating micropump. From van Lintel et al. [44]](image-url)
deposited through CVD process. Maximum flow rates reported for reciprocating type micropumps range from 4 to 13 000 µL min⁻¹.

Functionality of peristaltic micropumps is based on the peristaltic motion of the pump chambers, and theoretically, peristaltic pumps should have three or more pump chambers with reciprocating membranes. These types of pumps do not require passive valves for the flow rectification, nor do they require a high chamber pressure, so the two main conditions that have to be satisfied are a large stroke volume and a large compression ratio. Three types of actuation principles have been employed in reported peristaltic micropumps: piezoelectric, electrostatic and thermopneumatic along with several types of fabrication processes, such as bulk micromachining, surface micromachining, plastic moulding, and a combination of bulk micromachining and anodic bonding. Maximum reported flow rates range from 3 to 30 000 µL min⁻¹ (for air). Examples include a surface micromachined pump with electrostatic actuators [52], a thermopneumatically driven micropump having three active pressure chambers with flexible membranes [53], a micropump with curved pump chambers and a flexible plastic membrane with electrostatic actuation [54]. A new pumping principle called dual-diaphragm pump, which consists of two actuating membranes in the pump chamber, is reported by Cabuz et al. [55]. This type of pump is able to pump up to the maximum reported flow-rate 30 mL min⁻¹ of air.

Valveless rectification micropumps are similar to check-valve pumps except that, instead of check-valves, diffusers/nozzles are used for the flow rectification. In order to optimize the valveless pump designs, the stroke volume has to be maximized while the dead volume has to be minimized. The first piezoelectric micropump using nozzle/diffuser elements instead of check-valves [56] was presented in 1993. The original valve was fabricated in brass using precision machining. The same research group in 1997 presented the first valveless diffuser pump [57] fabricated using DRIE fabrication process shown in Fig. 10.12. The maximum pump pressure was 74 kPa and the maximum pump volumetric flow-rate was 2.3 mL min⁻¹ for water. Two different thermoplastic replication methods for the fabrication of valveless pumps: hot embossing and injection moulding have also been tested [58]. Deep precision-milled brass mould inserts and deep microelectroformed nickel mould inserts defined from DRIE silicon wafers were used for these designs. Figure 10.13 shows the design of the precision-
milled brass mould insert pump. Tested pumps had a maximum volumetric flow-rate of 1.2 mL min$^{-1}$. Nguyen and Huang [59] have demonstrated the design of miniature valveless pumps based on a printed circuit board technique. The pump could be operated as a single diffuser/nozzle pump (or a peristaltic pump) and has a maximum flow-rate of 3 mL min$^{-1}$.

Fig. 10.12 Fabrication process of the DRIE diffuser pump. From Olsson et al. [57]

![DIagram](image1)

Fig. 10.13 (a) Top layout view of single-chamber diffuser pump, and cross-sectional views of (b) a single-chamber pump unit, and (c) two pump units stacked in parallel arrangement for high pump flow. From Olsson et al. [58]
10.2.3.2 Nonmechanical Micropumps

Nonmechanical pumps are based on non-mechanical pumping principles and can be driven by capillary-force, thermal, chemical, electrical or magnetic means. Micropumps using electrohydrodynamic and electrokinetic effects have been reported.

Electrohydrodynamic (EHD) actuation is based on electrostatic forces acting on dielectric fluids, such as organic solutions. Two main types of electrohydrodynamic micropumps have been reported: the EHD induction [60] and the EHD injection pumps [61].

Electrokinetic micropumps use the electrical field for pumping conductive fluid. They can be divided into two categories: pumps based on the electrophoresis effect and pumps based on the electro-osmosis effect. Electrophoresis can be described as the motion of charged particles under an electric field in a fluid relative to the uncharged fluid molecules. The velocity of the charged species is proportional to the applied electrical field. Electrophoresis pumps have their application in processes such as the separation of large molecules such as DNA or proteins [62]. The separation, performed in microchannels, is called capillary electrophoresis. Electro-osmosis is the effect of pumping fluid in a channel under an applied electric field. Changing the applied electric field or the pH of the solution that affects the potential arising from the charge on the channel wall can control the electro-osmotic flow velocity. In microanalysis systems, the electro-osmosis effect is used for delivering buffer solutions [63] and, when combined with the electrophoretic effect, for separating out different molecules. The drawbacks of electro-osmosis are that it cannot be used when several interconnected channels are required for sample processing, and it is not compatible with high-ionic-strength buffers.

Information on various other types of micropumps, such as surface-tension driven pumps, magnetohydrodynamic pumps, and ferrofluidic magnetic pumps can also be found in the literature.

10.3 Integrated E-Nose Systems

10.3.1 Monotype Sensor Arrays

The performance of integrated e-nose systems largely depends upon the performance of the sensor array used. The integration of the sensor array on to the same substrate offers a reduction in sensor variation and also improves device reliability. Other advantages include reduced fabrication cost, smaller dimensions and lower power consumption. The majority of sensor arrays reported to date are monotype and can be divided into several categories based upon either the sensor material or type employed, such as conducting polymer, tin oxide, quartz resonator, surface acoustic wave (SAW) and FET sensor arrays. Readers are referred to Chapter 4 for a full description of the different types of chemical sensors.
Conducting polymers are very attractive for gas-sensing applications because of their ease of deposition, the large variety of available polymer combinations, and their ability to operate at room temperature [64, 65]. Neaves and Hatfield [66, 67] reported on one of the first ASIC chips for conducting polymer sensor arrays. In this, the integrated sensor array consists of 64 parallel gold electrodes (forming 32 resistive sensors) and a ground plane fabricated on a ceramic substrate. Each conducting polymer sensor consists of a two-layer composite: the poly(pyrrole) as the base polymer and a second polymer grown electrochemically onto this base. Figure 10.14 shows a micrograph of a resistance-measuring ASIC used in the final design of the integrated nose system for interrogation of 32 conducting polymer resistors. Another sensor array consisting of five conducting polymers in a microbridge configuration has been developed at Warwick University [68]. The microbridge arrangement was used in order to reduce the temperature dependence of the discrete polymer elements. The array, which has been fabricated in a standard 0.8 \mu m CMOS technology, is shown in Fig. 10.15. P-type silicon (or metal electrodes) is used to form resistors for either electrochemical deposition of polymers or spray coating of carbon-black polymer composite materials, such as those reported by Lewis [69] (Caltech). These polymer materials can also be deposited on co-fired ceramic substrates, glass slides, and silicon. These materials have also been used for other micromachined gas sensor arrays. Zee and Judy [70] reported two types of devices, bulk micromachined and patterned thick-film sensors. The micromachined, so-called ‘wells’, have been designed to contain the liquid volume during deposition. This type of design permits good reproducibility in the deposition and creates larger exposure areas for sensing while minimizing the chip area. It also allows for the integration of on-chip electronics for signal conditioning and processing. Figure 10.16 shows photographs of micromachined gas sensor arrays with polymer carbon black composite materials.
A novel ChemFET sensor array reported by Covington et al. [71] also uses carbon-black composite polymer materials. A linear dependence to toluene concentration and sensitivity of up to 2.8 μV ppm$^{-1}$ was observed. The device comprises an array of four $n$-type enhanced MOSFET sensors, fabricated by the Institute of Microtechnology (IMT, University of Neuchatel, Switzerland). Briand et al. [72] first reported on these devices as catalytic field-effect gas sensors in 2000. In this case, three of the MOSFETs had their gate covered with thin catalytic metals and were used as gas sensors, while the fourth one had a standard gate covered with nitride and acted as a reference. Sensitivities to the gases hydrogen and ammonia were tested.

Most of the reported integrated gas array sensors are based on tin oxide technology. Gardner et al. [73] reported on an array of six MOS odour sensors on single silicon substrate with six separate integrated heaters in 1995. A sensor array reported by Das et al. [74] consists of four integrated thick-film tin-oxide gas sensors. The array was fabricated on a single substrate and the sensor responses to different concentrations of various alcohols and alcoholic beverages were reported. Another micromachined tin oxide gas sensor array composed of three different devices on the same rectangular membrane and working at different temperatures was used for the detection of NO$_2$, CO, and toluene [75]. A sensor array consisting of 40 monolithic sensor elements with different sensitivities achieved by gradient techniques was used for halitosis analysis [76]. Forty-one parallel platinum strips partitioned the surface of the device into 40 gas-sensitive segments (SnO$_2$ and WO$_3$ were used). Four heating elements were based on the reverse side and the sensitivity of the array to malodour components was tested.

Flexural plate wave (FPW) sensors and SAW devices have both been used as the elements for analytical sensor systems. In both sensors acoustic waves are generated within a piezoelectric substrate that has usually been coated with a chemically sensitive film. A pair of interdigital transducers is normally used to generate and receive acoustic waves. The difference between these two types of devices is that the active region of the FPW sensor is the membrane of thickness much smaller than the acoustic wave-
length. SAW sensor arrays have often been used and reported in gas analysis instruments [77, 78] but rarely as integrated arrays. Baca et al. [79], from the Sandia National Laboratories (USA), have reported on the development of a GaAs monolithic surface acoustic wave integrated circuit (Fig. 10.17) aimed at chemical sensing applications. A prototype instrument describing an integrated array of six polymer-coated FPWs used together with an absorbent pre-concentrator is reported by Cai et al. [80]. Each FPW membrane is a layered composite, 5-µm thick, consisting of a silicon nitride layer, a polished layer of p-doped polysilicon, and a ZnO piezoelectric layer attached peripherally to the silicon substrate. The whole system is shown in Fig. 10.18. Responses to thermally desorbed samples of individual organic solvent vapours and binary and ternary vapour mixtures are reported. Another example of an integrated FPW sensor array has been recently reported by Cunningham et al. [81] of the Draper Laboratory. They have designed a chemical-vapour detection and biosensor array based on microfabricated silicon resonators (FPW sensors) coated with thin-film polymer sorption layers. The devices were fabricated on silicon-on-insulator (SOI) wafers and the work was an initial step towards the development of a large multi-element FPW array with several hundred devices operating within a single silicon chip.

Bulk acoustic wave sensors, in particular the thickness mode quartz-crystal microbalances (QCM), have also been used in e-nose applications but not as integrated microsensor arrays. A monolithic sensor array based on six elements integrated on the same quartz crystal designed for monitoring agricultural emissions was reported.
by Boeker et al. [82]. The dimensions of the quartz substrate are 12 mm × 20 mm edge length and 168 μm thickness with resonant frequency of 10 MHz.

Optical sensor arrays using image processing are another attractive technique for application in e-nose systems (see Chapter 8). A fibre-optic bead-based sensor array has been designed at Tufts University and employed to discriminate between different odours [83]. The system incorporates high-density arrays of micrometer-scale optical fibres, with polymer beads doped with fluorescent dyes placed at the end of each fibre. The binding of vapor molecules to the polymers changes the light emitted from the dyes, forming a colour signature. A similar technique has been used for the characterization of multicomponent monosaccharide solutions. In this, a chip-based sensor array composed of individually addressable polystyrene-poly(ethylene glycol) and agarose microspheres has been used. The microspheres are arranged in anisotropically etched cavities that are designed to serve as miniaturized reaction vessels and analysis chambers (Fig. 10.19). Identification of analytes takes place through colorimetric and fluorescence changes to receptor and indicator molecules, which are covalently attached to termination sites on the polymeric microspheres [84].
ical chemical microsensors reported by Datskos et al. [85] should also be mentioned. In this work it was demonstrated that photo-induced bending of microcantilevers depends on the number of absorbed molecules on their surface. The authors claim that by choosing different wavelengths tuneable chemical selectivity could be achieved. Apart from identification, a real time visualisation of gas/odour flow has also been studied (see Chapter 16 on odour tracing). A portable homogeneous gas sensor array was used to visualize the flow of a target gas, and the direction of the gas source was estimated using a real-time image-processing algorithm [86].

Finally, silicon-based microelectrode arrays for chemical analysis have been reported. An array consisting of various electrode shapes and sizes designed and used for a systematic study on some aspects of electrochemical sensing (i.e. influence of electrode geometry) was reported by Schoning et al. [87]. Sensor arrays with different electrode geometries have been studied at Warwick University for organic crystals, metal oxide, and polymer resistive devices [88–90] and offer certain functional improvements, such as faster responses or higher common-mode rejection ratios.

### 10.3.2 Multi-type Sensor Arrays

A study on the advantage of hybrid modular systems over monosystems, aimed at the possibility of achieving optimum discrimination power of an e-nose system, has been conducted by Ulmer et al. [91] at Tuebingen University. The system used for this comparative study consisted of 16 QCMs and MOSs. The results suggest that whenever high reliability and a high degree of reproducibility and separation power are required in the analysis of a complex gas matrix hybrid modular systems should be used. Another hybrid instrument, designed by Dyer and Gardner [92] at Warwick University, employs both resistive and piezoelectric sensors in arrays with improved
dynamic characteristics, and agrees with the above findings. High-precision programmable interface circuitry was developed for this system and a resolution of 0.05% was achieved. Recently, two examples of multi-type sensor arrays have been reported. The first one consisting of four different sensors designed at ETH Zurich has been described in Chapter 9. The second system is a result of collaboration between Cambridge and Warwick Universities. In this, an integrated smart sensor has been developed consisting of two types of devices, chemo-resistive gas sensors and microcalorimetric devices with active microFET heaters and temperature sensors on an SOI membrane [93]. The smart SOI sensors can operate at temperatures up to 350°C and offer excellent, uniform thermal distribution over the sensing area.

A method for selecting an optimum sensor array has been suggested by Chaudry et al. [94]. A step-wise elimination procedure, which ranks the inclusion of sensors in an array according to their contribution to the overall sensitivity and selectivity values, was adopted in this study. Various other techniques could be used to optimize sensor array response through either smart sensor interfacing [95] or smart signal processing (i.e. adaptive thresholding for improving selectivity or signal processing for improving gas sensor response time using analogue VLSI) [96, 97]. A combination of microfluidic technology, sensor arrays, smart sensor interfacing and signals processing should result in the development of superior e-nose systems and they may, perhaps, be comparable to the conventional chemical analysis microsystems currently being developed. These micro, total analysis systems (μTAS) are described in the next section.

10.4 Microsystems for Chemical Analysis

10.4.1 Gas Chromatographs

Chromatography is a popular analytical tool commonly employed by chemists to analyze liquid and gas mixtures. Figure 10.20 illustrates the basic components of a typical gas chromatograph (GC) [98], namely, a carrier gas bottle, an injection port, a long separation column through which the gas components pass down, a detector, and a data processing system. The components in the gas mixture are separated out because the column is either coated or packed with a stationary-phase film that absorbs the different components to differing degrees. Consequently, the components travel down the tube at different rates depending on their specific sorptive properties, and

![Fig. 10.20 Basic set-up of a gas chromatography system used to analyze gas mixtures](image-url)
hence are partitioned out. Ideally, the components will be totally separated out in time when they emerge from the column and hence can be measured by a single detector. The ideal graph is illustrated in Fig. 10.21 with five major components clearly visible. This technique is widely used and a description can be found of it in most analytical chemistry books. However, GC systems tend to be bulky, fragile and expensive items of equipment with limited sensitivity.

Gas chromatography has been used in olfaction to help analyze complex odours with only limited success. They can be used to separate out fairly large concentrations of certain organic components for which specific coatings (stationary phases) exist. GCs are also used as the front-end of an olfactometer with a person sniffing the output, instead of the sensor, and recording the specific notes as they emerge. This so-called GC olfactometer can help organoleptic panels identify the presence of certain notes in complex odors. In fact, there is some evidence that the human olfactory system generates its own spatio-temporal sorption patterns in the olfactory mucosa and so is itself a type of GC [99].

The first attempts to make a micromachined version of a GC were initially reported as long ago as 1975 by Terry at Stanford University (USA). The separation column was made from the isotropic wet etching of a silicon wafer. Figure 10.22 shows a cross-section of the device reported later in 1979 [100] with a pyrex glass lid. The system included a sample injector (silicon valve) and integrated thermal conductivity sensor but not the air supply. From 1975 to 1998 this research group further developed the micro GC and a recent review of the field has been published by Kolesar et al. [101]. Figure 10.23 shows a photograph of a micromachined GC column that is 10 μm deep, 300 μm wide, and 0.9 m to 1.5 m in length. In this case copper phthalocyanine has
been sputtered down to act as the stationary phase sensitive to reactive gases. The micro column was shown to separate mixtures of ammonia and nitrogen dioxide in air.

In 1997 a Japanese group led by Hannoe et al. [102] (Japanese Integrated Information and Energy Systems Laboratories) reported on the use of an ultrasonic etching technique to produce the micro channel, again with a pyrex lid, but this time a PCTFE-sputtered thin-film coating. The GC micro column has the dimensions of 10 $\mu$m deep, 100 $\mu$m across and 2 m long. Then Wiranto et al. [103], an Australian group, isotropically etched a GC column again with a pyrex lid; this time the column was 20 $\mu$m deep, 200 $\mu$m wide and only 125 cm long.

The problem associated with the etching of deep channels was solved in the late 1990s with the advent of the DRIE process, and so it is now possible to make micro GC columns more accurately and with superior properties. Perhaps the most sophisticated system is that being developed by Matzke et al. [104] of the Sandia Laboratories using a plasma-etched (DRIE Bosch process) pyrex lid. The GC column is part of what is referred to as the ChemLab and Fig. 10.24a shows the schematic arrangement of this chip. The columns are now 200 to 400 $\mu$m deep with width of 10, 40 and 80 $\mu$m and lengths of only 10, 30 and 100 cm. The group plans to microfabricate a pre-concentrator and pump thus making the entire instrument on a chip as shown in Fig. 10.24a. It is also possible to try and simplify the integration process through the combination of electrophoresis to pump the mobile phase, and chromatography to separate with stationary phases, a method called micro capillary electrochromatography [105]. However this technique is mainly suitable for a liquid mobile phase, and requires a high voltage supply which are incompatible with standard integrated circuit processes.
Fig. 10.24 (a) Schematic layout of the ChemLab (Sandia Laboratories, USA). The chip is envisaged to be the size of a dime coin, (b) commercial portable ‘micro’ GC called the Chrompack and used widely for environmental gas analysis.
GC is a useful analytical tool for chemists and there are a number of companies that make portable micro GC with some micro machined parts in them – but still about the size of a computer tower case. For example, the company AST make a battery-operated unit that contains two micro GC columns with a silicon micromachined thermal conductivity sensor. Similar units are made by MTI (see Fig. 10.24b) and by Chrompack International; these so-called Chrompack units are widely used to analyze the air for organic pollutants [106]; modifications to this basic unit by Tuan et al. [107] have also been reported that seek to enhance its basic performance. However, all of these micro GCs have some major drawbacks as regards analyzing complex odours. Firstly, the time it takes for the odorant components to travel down the columns and partition can be tens or even hundreds of seconds and, secondly, the separation for some important classes of odours is relatively poor. However, there are two other analytical tools used by chemists alongside the GC, namely, the mass spectrometer and the optical spectrometer that may be regarded as complementary techniques. We shall now discuss them in turn.

10.4.2 Mass Spectrometers

The composition of a liquid (or vapour) can be analyzed using a mass spectrometer (MS). Figure 10.25 shows the general layout of an MS in which the sample is injected in to the mobile phase (normally helium gas) and the molecules ionized [108]. The ions are first accelerated in a vacuum by applying a voltage and finally separated by a magnetic field according to the ratio of their mass to charge. The number of ions is counted for each particular mass (the ions are usually singly charged species) using an ion gauge and this is commonly referred to as the abundance. The magnetic sector can be replaced by either a quadrupole electrostatic lens or a time-of-flight element to produce a more compact unit. Indeed a quadrupole mass spectrometer is now marketed by Agilent Technologies Inc. (USA) as the Chemical Sensor (Agilent 4440) and

![Fig. 10.25 Layout of a magnetic sector mass spectrometer. From Gardner and Bartlett [108]](image-url)
comprises a headspace autosampler connected up to a quadrupole mass spectrometer unit and a PC for data analysis (see Fig. 10.26). This unit has been used to analyze various odorant problems and Fig. 10.27 shows the mass spectra for a complex odour generated from the headspace of a bacterial sample and covers a mass range from 45 to 550 Daltons [109]. As can be seen, the mass spectra for natural odours is complex and a pattern recognition system is needed to analyze the differences. In this example, a linear technique such as discriminant function analysis was able to resolve the differences between the growth phases.

The MS, like the GC, is a fairly large, heavy, and expensive instrument. Recent efforts have been made to miniaturize parts of the MS, such as the quadrupole lens and the sampling orifice, using various micromachining techniques. For example, Fig. 10.28a shows a miniature quadrupole lens system produced by Syms et al. [110] in 1996 together with a more recent version reported by Friedhoff [111] in
Fig. 10.28  Micro mass spectrometer: (a) schematic parts of a quadrupole electrostatic lens, (b) photograph of a micro quadrupole lens (from Syms et al. [110]), and (c) mass spectrum from a micro mass spectrometer.
1999 (Fig. 10.28b). These relatively crude microsystems are capable of separating out a small number of different light masses as shown in Fig. 10.28c.

Further advances are being made in the development of micro-injection ports for micro-MS instruments but the challenges associated with making a miniature ion-source detector and a vacuum system are significant. Nevertheless an integrated microfluidic-tandem MS has been reported by Figeys et al. [112] for the analysis of protein and peptide masses (in solution). This instrument examines the higher masses of 500 to 1,000 Daltons and is aimed at analyzing biological systems at the protein level rather than odours – by definition, odours have lower weights otherwise they are not volatile.

Finally, it should also be noted that there are clearly many examples in which molecules of the same mass have quite different odors. For example, the position of a ketone group in undecanone causes the smell to change from fruity to rue-like. Similar changes occur when comparing cis and trans isomers of unsaturated compounds. The other examples of this phenomenon may be found in Chapter 1. Consequently, there is no simple mass-activity relationship for odours. The situation is further complicated by the fact that the ionization of a single fragile odorant molecule can lead to its fragmentation and so the mass spectrum is more complicated. Consequently, the mass spectra should really be considered as a chemical signature rather than an accurate measure of the mass content in the original complex odour, and of course, there may not be a unique mapping between smell and mass signature. The combination of a GC followed by an MS instrument is a powerful and sensitive analytical tool but is clearly an extremely large and expensive unit. Making a micro GC-MS would be the ultimate challenge!

10.4.3
Optical Spectrometers

Molecules have characteristic modes of mechanical vibration and rotation, and these can be detected by looking at the amount of light at different frequencies that is absorbed by the molecules. The technique is called optical spectroscopy and the molecules are usually analyzed using light in the UV to IR range. Although the technique is generally much less sensitive to odorant molecules than GC or MS, micro spectrometer integrated circuits are being developed rapidly for the telecommunications industry. For example, Fig. 10.29 shows the principle in which light from a fibre-optic is split by a deflection grating in to its various frequencies, and these are detected using a 256-element CCD array [113]. The combination of these technologies with a microfluidic system could lead to a low-cost solution for the screening of simple odours. However, that will require improvements in both the sensitivity of the optical sensor array and the width of the frequency spectrum.
Fig. 10.29 Optical micro spectrometer integrated circuit chip: (a) schematic and (b) actual device. From Gardner et al. [113]
10.5 Future Outlook

A nose in its totality comprises a sampling system (i.e. sniffing mechanism), and a fluid flow system as well as a distributed sensor array and complex signal processing architecture. In this chapter we have described some of the current efforts towards making a micro nose that integrates the sampling and fluidic system with the actual sensing system. It is clear that the integration of a sampling system will improve the reliability and performance of an electronic nose, as it is also evident that the creation of multi-type sensor arrays enhances its dynamic range. The latter may also be further extended through the use of biological materials within the sensing elements; however the lack of stability of most biological materials exposed to the environment suggests that such bio-electronic noses could only really be used for a very short period of time. This lack of stability creates the need for a micro cassette that holds a sequence of biosensors that can be employed at the appropriate time, somewhat analogous to a photographic film cassette. Based on an analogy with the human olfactory system, the cassette would need to be wound on every 20 or so days.

The production of a reliable sampling microsystem will also enable the use of the dynamical part of the sensor signal, which has been shown to be very useful [114]. However, miniaturization of the system is essential so that the time-constants associated with the physical transport of the odour around the channels and chambers are much smaller than the response times of the sensors themselves. This permits the different rate kinetics of the chemical sensors for the different analytes to be observed, and thus used to help the discrimination process. The micro channels, micro chambers and micro pumps will permit the delivery of odours extremely quickly and reproducibly to the sensor array (or mass filter), and so this should permit the creation of a new generation of dynamical micronoses.

Nevertheless, the technological advances that permit the creation of such a physical embodiment of e-noses will not, in our opinion, be sufficient to solve the more complex odour problems. It is difficult to visualize a mass/optical spectrum from a mass/optical spectrometer (miniaturized or not) resolving subtle differences in the headspace of such as cheeses and beverages. Instead, the spatio-temporal information generated by GC-based and/or sensor-based micronoses will require quite different types of signal processing algorithms from the customary the principal components analysis, discriminant function analysis and neural networking methods described in earlier chapters. The types of nonlinear dynamical filters that will be required may well be neuromorphic algorithms similar to those used in our human olfactory systems. Consequently, the future emphasis will turn from the construction of the miniature hardware towards the identification of suitable dynamical models, which could either be data-driven or parametric. Of course this generic approach is challenging and will lead to integrated noses whose cost may be unacceptable in some application fields. For instance, the most likely competitor to e-noses in the medical domain may be disposable biochips that seek specific proteins or protein sequences. It is unlikely that a generic micronose can compete with such a low-cost screening method. However, there are other biomedical applications in which it is possible to use an e-nose to
screen for whole viable micro-organisms (see Chapter 18) because a protein biochip lacks such a capability.

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