Abstract: A new concept for miniaturised analysis systems, based on a modular assembly of silicon system components on an anodically bonded base plate containing fluid channels, is presented. The proposed configuration allows the separate development of the different system elements as well as an easy modification of the system setup. Besides micropumps and flow-sensors, for detection, different ISFET-based chemical sensors for cations are presented. Using covalent attachment of all membrane components to the polymer matrix, a durable CHEMFET system is obtained. It is shown that such sensors can be very well incorporated in a continuous flow system, e.g. a Flow Injection Analysis (FIA) system. Finally, the realization of a liquid dosing module and a modular setup for a Micro Total Analysis System (μTAS) is illustrated. Possible applications of such μTAS are discussed, and future markets are indicated.

1. INTRODUCTION

During the past few decades a large variety of chemical microsensors has been developed. A large amount of sensor principles such as optical, electrochemical, mass-sensitive and calorimetric were developed [1]. However, few of these sensors have made the way to the market. In most cases very interesting laboratory prototypes were fabricated, but industries interested in the commercialization of the devices were lacking. This was on the one hand due to the technology-push rather than market-pull development, which meant that in many cases the market had to be created. Another important aspect, however, was the presence of sensor defaults. Chemical sensors inherently exhibit drift, temperature dependence and non-ideal selectivity, which leads to the need for a regular calibration. For industrial applications, a measurement system rather than a sensor is required.

The aforementioned shortcomings can be solved by integration of the sensor into a microsystem, in which apart from the sensing function also sample-preparation, sample handling and calibration can take place. Since all steps of the analysis are carried out in such system, it can be called a Miniaturized Total Analysis System (μTAS) [2]. With the recent upcoming of silicon micromachining such miniature elements for sample handling (micropumps, -valves, -channels) and preparation (mixers, injectors, filaments) have become available. The great challenge is to develop a general and modular way to integrate the elements into a system, so that the various components can be developed separately and the final configuration may simply be modified. Such a setup requires standardized interfaces: packaging, electrical and liquid or gas connections and feed-through's. The schematic layout of a microsystem representing a miniature Flow Injection Analysis (FIA) system is shown in fig. 1. The total system consists of several modules or subsystems, that should be preferably integrated in a monolithic way. The combination of the different subsystems is realized by hybrid integration. In terms of performance, such miniature analyzers can have impressive advantages over conventional analysis systems. The most direct advantage is the reduced use of chemical reagents. A recently published microanalyzer for phosphate measurement uses at least ten times less chemical reagents than a conventional analyzer, whereas its size (a few cubic cm’s) and price are far below that of a desk-top instrument of 50 kfl [3]. Another advantage is the improved analytical performance. reducing the dimensions of the system results either in the same performance with a shorter measurement time, or in the same measurement time but better resolution. An illustration of this is given by the recently published micro PCR-reactor [4], that enabled a extremely rapid analysis of various viruses through the use of a micro reactor chamber. Here the great advantage is found in the small thermal mass of the cell, resulting in fast thermal cycling.
Some examples of miniaturized chemical sensors will be discussed, as well as a subsystem for liquid dosing. Finally we will discuss different fields of applications of μTAS and the chances for future developments.

2. CHEMICAL MICROSENSORS

Since the first publication on ISFETs in 1970 [5], a lot of research has been carried out on ISFET-based ion sensors. The main effort has been devoted to the development of durable ion-sensitive membrane materials that can be applied to the ISFET with IC-compatible techniques. In addition, the approach was to use a thermodynamically well-defined system, which was realized through the use of an intermediate polyHEMA hydrogel layer [6]. With this approach, durable sensors for K⁺, Na⁺ [7], Ca²⁺ [8] and heavy metal ions like Ag⁺ and Pb²⁺ [9] were successfully realized. As strategy for this development the synthesis of a membrane system with as much as possible immobilized electroactive components (plasticizer, ionic sites, ionophore) was chosen. It appeared that polysiloxane based materials offer great flexibility in the realization of these membranes.

Although the above mentioned sensors have excellent properties with respect to sensitivity, selectivity and lifetime, their use in practical applications require incorporation in a so-called Micro Total Analysis System or μTAS [10]. In such a system, all aspect of the chemical determination, from sample-taking to measurement, are miniaturized and integrated. In this way the sensors can be regularly calibrated, and drift problems can be avoided. In a first stage, potassium sensitive CHEMFETs have been incorporated in a wall-jet flow cell, where they show a reproducible response (see fig.3).

Figure 2. Schematic setup of a CHEMFET mounted in a wall-jet flow cell [11].

The important advantage, however, lies in the fact that using a photosensitive polysiloxane membrane matrix, the realization of a multi-ion sensor on one chip has become possible. An interesting additional option is to use the photopatternable polysiloxane membrane to fabricate an on-chip sealing ring enabling the creation of a small cell volume [12].

3. MINIATURIZED LIQUID DOSING MODULE

One of the most essential parts of μTAS is the sample-taking part, for which a miniature pump is an indispensable element. The first piezo-electrically driven micropump was realized at our institute already in 1988 [11]. This pump, however, requires the hybrid integration of silicon parts with a small piezoelectric disc. A new thermopneumatic pumping principle, which was recently proposed, allows a wafer-wise fabrication technology [13]. An explanation of pumping principle is given in figure 4. In order to obtain well-controlled flow rates and to be able to actually dose precise liquid quantities, a flow sensor is integrated with the micropump. When applied in a...

Figure 3. Measurements with a K⁺ CHEMFET in a 0.1 M NaCl background solution [11].

Figure 4. Principle of thermopneumatic pumping [13].
feedback control system, the flow sensor can also be used to obtain a pressure independent flow rate. An important aspect is that the technologies for both elements are compatible, so that they can be integrated on the same chip. The fabrication procedure requires two anodic glass bonding steps, that can be carried out on the wafer level. Figure 5 shows a cross-section of the thermopneumatic micropump, whereas the basic concept of an integrated liquid dosing system (pump with monolithically integrated flow sensor) is shown in figure 6.

![Cross-section of a thermopneumatic micropump.](image)

Figure 5. Cross-section of a thermopneumatic micropump.

![Setup of liquid of a monolithic micro liquid dosing system.](image)

Figure 6. Setup of liquid of a monolithic micro liquid dosing system [12].

For the integration of this liquid dosing module and other modular system components into Micro Total Analysis Systems (μTAS), as shown in Fig. 7, vertical feed through technologies for liquids, gases and electronic connections are currently under development.

![Artist’s impression of μTAS realization.](image)

Figure 7. Artist’s impression of μTAS realization.

4. APPLICATIONS OF MICRO TOTAL ANALYSIS SYSTEMS (μTAS)

The applications of μTAS can roughly be divided in three areas: environmental, medical diagnostics and automotive applications (see figure 8). In all of these three areas, the market needs to be developed. On the one hand, this is an advantage since there are not many well-developed conventional systems to compete with. On the other hand, the disadvantage is that market chances and profits need to be conquered, at the price of a relatively high investment, which might make investors hesitant. To overcome the latter problem, a more strict legislation with respect to for instance environmental aspect would be a strong stimulus for further development.

![Application fields of Micro Total Analysis Systems (μTAS).](image)

Figure 8. Application fields of Micro Total Analysis Systems (μTAS).

**Environmental**

The environmental applications can be divided into off-line field monitors and on-line process monitoring systems. The latter is regaining more and more attention, as there is a tendency to go from end-of-pipe measurements to on-line monitoring and process control. For the field monitors probably the most important market is that of portable mini-labs, that are able to perform continuous measurements in an autonomous way together with indicative probes for water and soil pollution assessment. The latter probes are not meant to replace laboratory equipment by microsystems, but aim at using the laboratory capacity in a more efficient way. For on-line process monitoring and control miniature FIA-systems are the most obvious realization. For most of the chemical species a chemical procedure for FIA detection is established, often requiring substantial amounts of expensive reagents. This means that there is an economic benefit to be gained from the miniaturization, which is probably the best driving force for its development.

**Medical diagnostics**

In medical diagnostics one of the biggest advantages in using micro-analysis systems is the extremely small quantities that can be analyzed. With the use of planar capillary electrophoresis techniques, sample volumes of less than 1 nl can be accurately analyzed [14]. Also,
equipment with improved performance could be fabricated, as is very elegantly shown by the micro-PCR reactor cell fabricated with silicon microtechnology [15]. In mentioned system, a large number of viruses could be detected with a much faster analysis time than with conventional analyzers. Another important market is that of bed-side monitoring. Here, micro analysis systems allow simple by-pass arrangements for continuous blood monitoring, since the amount of consumed sample (blood) is extremely low.

Automotive

Finally, the automotive industry uses more and more sensors. Chemical analysis systems may be applied in cabin comfort control (humidity, detection of exhaust gases) and motor management. For both applications microsystems for gases rather than for liquids are required. A first concept for such gas measurement microsystems, based on the electrochemical detection of catalytically converted hydrocarbons, has recently been proposed [16]. Here, some important development work in the direction of gas valves and micropumps still needs to be carried out. Nevertheless, gas-phase chemical analysis appears to have a growing impact.

5. CONCLUSIONS

There is a large and still growing interest in microsystems for chemical analysis. The technological developments in silicon microtechnology provide a continuous stream of new microsystem components. For a modular and flexible integration of the different modules (vertical) feed through connection technologies as well as some sort of standardization need to be developed. The applications of micro analysis systems are found either in niche markets, where specific analysis for small samples is needed, or in large markets where conventional equipment already exists and can be replaced. Apart from this, new large markets are expected to be developed, especially in the field of environmental monitoring. The advantage of lower sample and reagents consumption, which is a strong economic driving factor, can however only be valorized if the same degree of reliability as in conventional systems can be obtained.

REFERENCES
