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SELECTION IN SYSTEM AND SENSOR

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Introduction

Since the dawn of chemical sensors, there were high hopes of rapid and widespread utilization of these devices. This predicted success, however, has not yet been achieved, due to several causes: (bio)chemical fouling of the sensor, unstability in the sensor signal resulting in drift, and lack of available selector materials, specific for all species to be detected.

In this paper, a more realistic approach is pursued, i.e., the incorporation of the sensing element in a Total Analysis System (TAS). This system comprises a double-lumen microdialysis probe, providing a coarse first-stage selection of molecules, to be allowed into the system, decreasing the possibility of sensor fouling. Additionally, the system is provided with integrated electrochemically driven pumps to precisely dose nanoliter amounts of calibration liquid, for periodic calibration of the possibly drifting sensing element.

A possible and simple sensing element in these kind of TAS's is a conductivity probe. Electrolyte Conductivity (EC) is not selective for specific ions. It is shown in this paper, however, that separate ion concentrations can be calculated, when the EC is measured at several temperatures, using the characteristic temperature responses of the ionic conductivities of these ions.

Selection with a Total Analysis System (TAS)

General

An ideal chemical sensor would transfer concentration information of a specific chemical compound with 100 per cent selectivity, i.e., without any cross-sensitivity to the electrical (or optical) domain. Additionally, such a sensor must be able to operate directly in the sample solution. Despite all efforts, such sensors do not exist. Nevertheless, with full scale laboratory equipment, analysts are often able, off-line, to specifically characterize a certain sample after laborious sample pre-treatment. The development of a TAS is an attempt to integrate component-wise the several relevant sub-systems involved in laboratory equipment on a small scale. The functions these components should fulfill are typically sampling, transport, mixing, reaction, separation and detection. If this TAS is very close to the place of the actual measurement, then the system is commonly referred to as micro- or µ-TAS[1]. It is beyond the scope of this paper to describe all the possible advantages of µ-TAS, already partly realized and described in, e.g., [2].

In this section, we restrict ourselves to two problems, related to the direct use of chemical sensors, i.e., (bio)chemical fouling and unstability of the sensor signal, which can to a certain extent be solved by using a TAS, as shown in the next sub-sections.

Microdialysis probe

A realistic approach to the problem of fouling of the sensor surface, especially by large, solid particles and proteins is by separating these interfering compounds from the chemical sensor. Precisely this is accomplished by the microdialysis technique[3]. A perfusion liquid is pumped through a hollow fiber, in contact with the sample solution to be investigated. A part of this fiber consists of a semi-permeable membrane, such as cellulose acetate. During the passage of the perfusion liquid through the fiber, only substances of small molecular weight can diffuse through the membrane, preventing the fouling substances from entering the system. Subsequent analysis of the dialysate and detection of the species of interest is carried out off-site, but on-line in the TAS on a semi-continuous base.

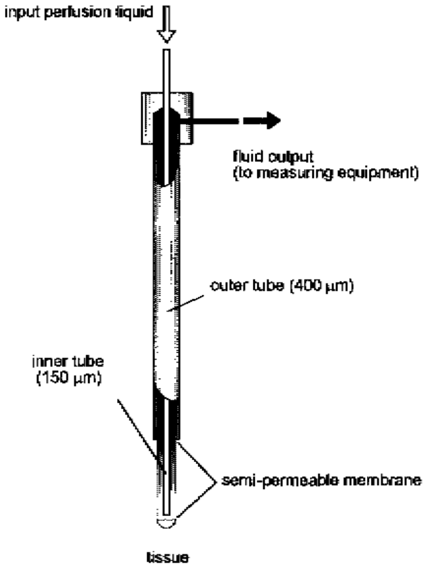


Fig. 1. Microdialysis probe

Microdialysis as a sampling tool for a µ-TAS is even more favourable, when a double-lumen microdialysis probe is used[4]. Now, the perfusate is driven through a small inner tube, located within an outer tube. The fluid leaves the inner tube at the probe-tip and subsequently flows past the semi-permeable membrane back via the outer tube as schematically shown in fig. 1. There are many parameters determining how well the concentration of the analyte in the dialysate agrees with that in the sample solution. This property is expressed by the relative recovery ratio R:

$$R = \frac{[analyte]_{dialysate}}{[analyte]_{sample}} * 100\% \tag{1}$$

Within the framework of this paper it is important to know, that R is inversely proportional to the volumetric flow rate of the perfusate. In order to obtain a R-value near 100 per cent, which is favourable, because calibration of the probe is then not necessary, the flow rate should be low. However, to maintain a reasonable response time of the TAS, any dead volume between the sampling probe and the detection in the TAS should be minimized. Better still, the probe and the sensors should be integrated as much as possible, resulting in a true µ-TAS. Therefore, a silicon micromachined connector was designed and realized, as schematically shown in fig. 2. The funnel-like structure between the large opening surrounding the outer tube of the lumen and the V-shaped channel for the inner tube act as a guide for the insertion of the inner tube. A dead volume remained of only 180 nl, being only a fraction of that of a conventional probe, which is ca. 1.5 µl. Thus, the lag time of the TAS, equipped with this micromachined probe, is considerably reduced. An array of five finished probes, ready for cutting apart is shown in fig. 3.

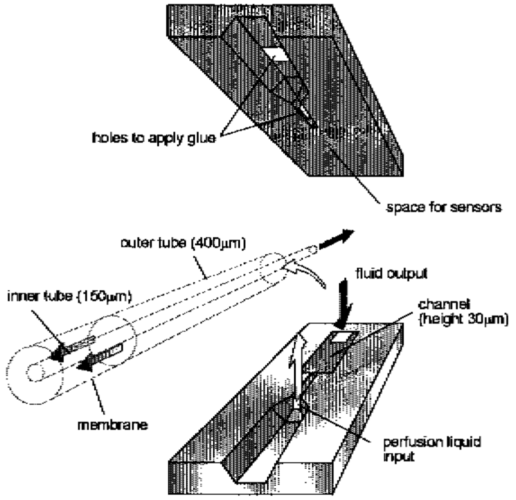


Fig. 2. Exploded view of the microdialysis probe with connector

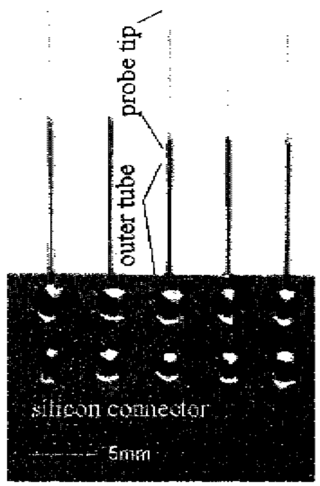


Fig. 3. Realized Si-micromachined probe with microdialysis probes, The two rows of dots are glue for fixing the inner and outer tube, respectively.

Calibration system

Although the sensor in the TAS as proposed in this paper can operate in a relatively clean solution, due to the microdialysis probe as sample inlet, regular calibration of the sensor is still required. The system performing this calibration should of course preferably be a part of the TAS itself. For this purpose a dosing system is required, capable of dispensing calibration liquid in the carrier channel, leading to the sensor. The response to this plug of calibration liquid can be applied to determine the off-set and sensitivity of the sensor (i.e., if two reservoirs of calibration liquid are implemented). The system proposed in this paper is based on the displacement of a fluid from a reservoir by the electrochemical production of gas bubbles[5].

In the realized structure, the calibration liquid to be dispensed is stored in a meander-shaped channel, starting in a reservoir filled with an electrolyte in which two electrodes are placed, as schematically shown in fig. 4. By sending an electric current through the electrodes, gas bubbles are produced by the well-known anodic and cathodic electrolysis of water. These bubbles expand in the reservoir and drive out the calibration liquid, stored in the meander. After saturating the electrolyte with hydrogen and oxygen, the volume, V, of the gas bubbles and thus of the calibration plug can be precisely controlled according to

$$V = \frac{3i\Delta t}{4F} V_m \qquad (2)$$

with i and Δt the amplitude and duration of the applied current pulse, respectively, F Faraday's constant, and V_m the molar gas volume at given temperature and (atmospheric) pressure.

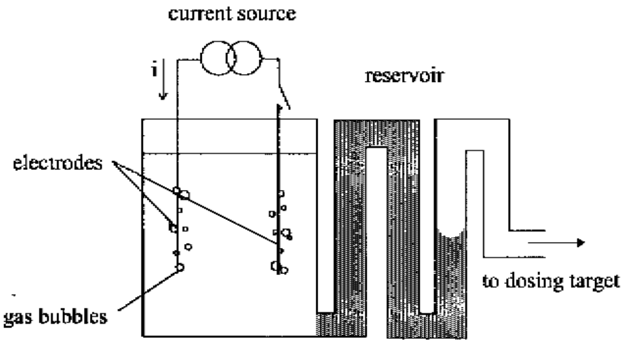
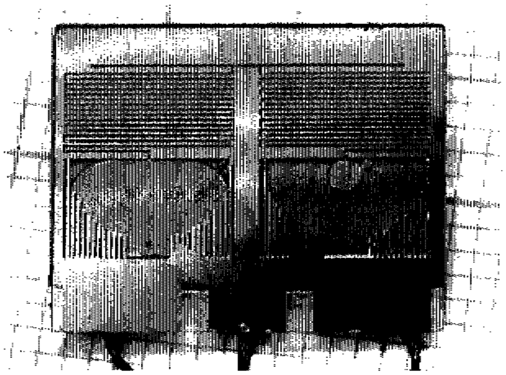


Fig. 4. Principle of the proposed electrochemically actuated pump and dosing system.

The proposed system has been realized in Si micromachining technology and a photograph of the device, including two integrated electrochemical pumps and meander-shaped reservoirs for calibration liquid is shown in fig. 5[6]. Precise dosing is shown to be possible in fig. 6, where the measured volumetric flow for $\Delta t=5$ s at the mentioned current values is shown, including the theoretical curve from eqn. 2.



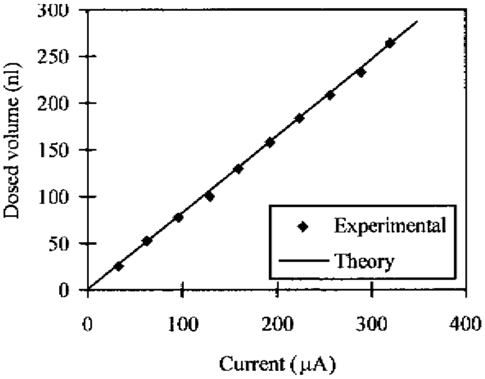


Fig. 5. Photograph of the realized device, showing two complete calibration units.

Fig. 6. Measured dosed volumes after 5 s current actuation with given current amplitudes.

Selection with an Electrolyte Conductivity (EC) sensor

One of the important sub-systems in any TAS is the detection. In many cases, optical techniques, such as luminiscence, fluorescence or spectroscopy are applied, using full-size optical equipment. Only in a few cases, the optics, necessary for the detection, are integrated as well, which is a prerequisite for a real TAS[7,8]. Considering size, electrochemical sensors seem to be better suited as detector in a TAS. Two regularly encountered types of sensors are amperometric and conductometric sensors[9,10]. Due to their simple construction and the fact that selectivity is often already obtained during separation, these sensors can give satisfying results. Better results, however, can possibly be obtained, when some selectivity is built-in in the detector. Although this seems to be impossible with an EC sensor, due to the inherently non-selective nature of EC, we will in the remaining part of this paper, present a method to add selectivity to EC sensing.

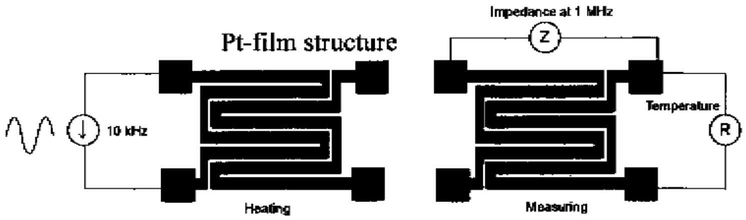


Fig. 7. Integrated sensor-actuator device for local heating and temperature/conductivity measurement.

Operational principle

A single EC measurement does not give any specific information on the ion concentrations that are present in the solution, when more than 2 types of ions are involved. However, a range of measurements at various temperatures of the electrolyte does, since the temperature dependence of the mobility of an ion is unique for that ion[11].

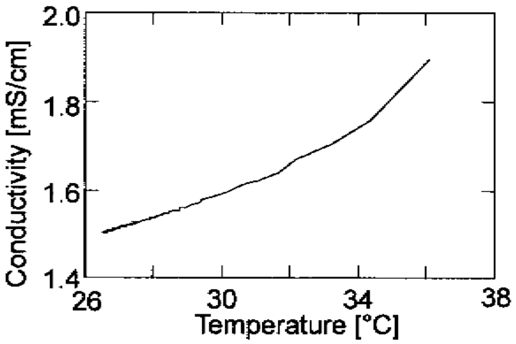
The total electrolyte conductivity Λ in terms of the separate ion contributions is given by

$$\Lambda = \sum_{ions} \lambda_i c_i |z_i| \tag{3}$$

with c_i the concentration, z_i the charge and λ_i the limiting molar conductivity of ion *i*. This last factor is dependent on temperature T and can be approximated by a polynomial fit[12]:

$$\lambda_i(T) = \lambda_i^0 \sum_{n=0}^{N} \alpha_{i,n}(T - T_0)^n \tag{4}$$

with λ_i^0 the limiting molar conductivity for ion *i* at $T=T_0$. Since the coefficients $\alpha_{i,n}$ are unique for ion *i*, the total conductivity Λ is a unique linear combination of the limiting molar conductivities $\lambda_i(T)$ with the specific ion concentrations as coefficients.



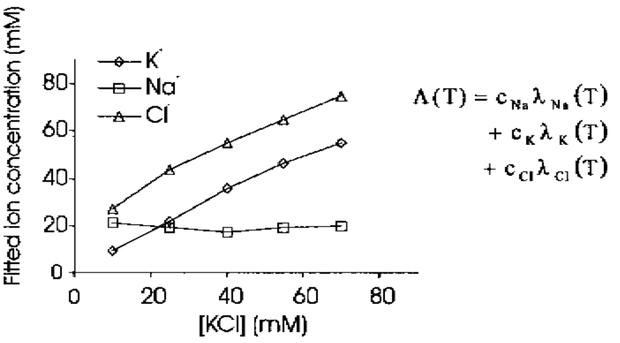


Fig. 8. Measured conductivity versus temperature plot.

Fig. 9. Fitted ion concentrations in five solutions with 25 mM NaCl and several KCl concentrations.

Implementation and results

The operational principle requires heating of the electrolyte. It is the benefit of a µ-TAS that local heating in a small measuring volume can be applied to rapidly heat the electrolyte locally. For this purpose, a dedicated EC-and-temperature sensor / thermal actuator was designed and developed. The device is shown in fig. 7 and consists of a 1x1 mm^2 platinum structure on a glass substrate. By applying an AC-current to one of the Pt-meanders, as shown at the left-hand part of fig. 7, the electrolyte can be heated locally. An increase of about 10ºC in temperature is obtained after a few milliseconds. Directly after switching off the heating current, both the EC and the local temperature are measured, as shown at the right-hand part of fig. 7: the structure now functions both as an interdigitated EC probe and resistive Pt-film temperature sensor. From the measured results, a conductivity versus temperature plot can be constructed, as shown in fig. 8. After some calculations, using eqns. 3 and 4, a unique fit can be obtained from which the specific ion concentrations can be calculated. A result, showing the successful application of the method is shown in fig. 9, in which the separate concentrations of 3 different ions in an electrolyte are determined.

Concluding remarks

Research groups can continue to pursue the development of the ideal chemical sensor, or they can use the existing devices and micromachining techniques favourably in Total Analysis Systems. The flaws of existing detectors can thereby be circumvented. Amongst several other advantages, it is shown in this paper, that µ-TAS's can offer a type of sample inlet, the microdialysis technique, which prevents severe fouling of the detector. Furthermore, it is shown that the function of calibration can be integrated in a µ-TAS by using electrochemically driven pumps.

Selection in EC sensing can be obtained by local heating, temperature- and EC-measuring. All these functions are shown to be performed with a device, comparably simple as an EC probe itself: properly shaped metal films. Only because of the small dimensions of a µ-TAS and the use of smart signal processing, the specific ion concentration determination by EC sensing is made possible.

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