From Analytical to Chemical Information Technology

C-CIT AG undertakes development and commercialisation of projects and products in the field of advanced chemical sensors and analytical devices, and related services and measuring technology. The products aim at determining the concentration of biomarkers providing chemical information.

C-CIT (Centre for Chemical Information Technology) has evolved out of CCS, a seven-year old research organisation at the Swiss Federal Institute of Technology in Zürich (ETHZ).

In April 1994 Professor Dr. Ursula E. Spichiger-Keller founded CCS, the Center for Chemical Sensors, Biosensors and bioAnalytical Chemistry belonging to the Department of Applied Biological Sciences at ETHZ. CCS was designed as a vehicle to focus ETHZ's expertise in chemical sensor technology onto development of practical applications for the technology. In other words, a move towards creating a new interface for technology transfer between the science and the market-place in this field. CCS and its work has been recognised through a large number of publications and a number of industry, governmental and academic awards.

As a real interface between science and the market place, C-CIT will act as a development engine, focused on the development and commercialisation of selected, screened and feasibility-tested product concepts, in the field in which C-CIT has evolved from and is competent in. Beside the own developed products, which should be sold via companies active in the field, C-CIT will also undertake contract developments in order of third parties. C-CIT offers also the service of project management and consulting in the field of chemical sensors, bioassays and chemical information technology generally.

The C-CIT technology and products occupy a unique and interesting technological niche in the life science fields, in agriculture and food technology. The technology appears to be well placed to provide a range of innovative solutions to yield chemical information about bioprocesses in different fields. Potential end-user industries include life sciences, food, environmental, agri- and aquaculture.

zvg

Fig.1: The founders of C-CIT from left to right. Standing: U.E. Spichiger-Keller, Prof. Ph.D. (director CCS), A. Koch, Ph.D. (Koch Consulting), Mrs. C. Kern, F. Tschopp, Ph.D. (CEO Sensorix AG), front: S. Spichiger, Dipl.-Ing. (CCS, CEO C-CIT), G. Zhylyak Ph.D. (CCS and R&D C-CIT), M. Linnhoff Ph.D.(CCS).

Projects

One of the main projects running at C-CIT AG is the final development of the «Lab in the Bag®» concept. This is a small, portable case with a multianalytic system, connected to the Intra- or Internet. The flow-through system incorporates sensors that are able to measure more than one analyte from different analyte classes simultaneously (e.g. the activity of glucose and magnesium), without the use of reagents. The system is ideal for on-site measurements in real-time. It is modular and can be tailored for specific customer needs.

The advantages of such a system include:

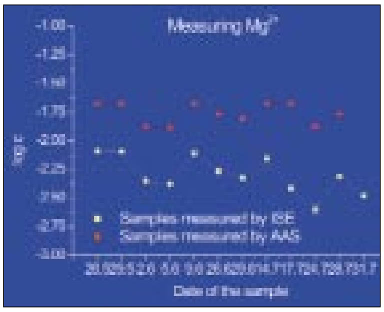
- Multiple readings at the same time. Multiple data points provide a chemical information pattern and a profile of the process.
- Reagent-less: ecologically friendly analysis. No bias in readings due to chemical reactions and mixing processes.
- Fast, continuous and real-time readings: no time-consuming packing and despatch of samples.
- On-the-spot analysis, allows timely response to specific conditions
- No sample transport = minimal risk of bias to results, ecologically friendly and reduced costs. Allows late recognition of changes in the sampling process.
- User-friendly instruments, high throughput, reduced cost per individual analysis, saves labour.
- Following substances can already be handled: glucose, lactate, electrolytes such as Mg^{2+}, Ca^{2+}, K^+, Na^+, NH_4^+, NO_3^- (nitrate), NO_2^- (nitrite). An example is shown in the case described below (quantification of the concentration of free, accessible ions in a nutrient solution for soilless cultures)
- Under development are: CN^- (cyanide), SO_3^- (sulfite), specific metal ions such as cadmium, lead, silver ions, alcohol, amines

Measuring of single ions in a nutrient solution

The task of this project was to prove the possibility to measure ions (specially Mg^{2+}, $K^+$and NO^{3-}) in a nutrient solution for soilless cultures continuously with ion selective electrodes. The question was if the membranes were sensitive and selective enough to measure the above mentioned ions in such a complex solution like the nutrient solution. By now the only analytical method, where similar results are accessible in a reasonable timeframe in order to study total concentrations of cations, is AAS (atomic absorption spectrometry). Anion concentrations such as nitrate may be addressed by ion chromatography or photometric wet-chemical assays (Merck, Boehringer, Lange AG). However, these methods are too complicated and too time consuming in order to receive the results in time, and to respond to concentration changes immediately. With a continuous monitoring system this problems can be solved.

It was shown that it is possible to measure all three ions in the nutrient solution. The three ion-selective a, one for each ion, were calibrated in a simulated nutrient solution. The electrodes showed an almost optimal slope. The detection limits of the three membranes were sufficiently low to measure the mentioned ions in the desired concentration range. In the next step, the analytical parameters were evaluated by spiking real specimens with the target ions. In the last step, the free ion concentrations were measured directly in real samples and the results were compared with analytical reference methods (AAS and HPLC). It was proved, that the different methods are equivalent in precision and reproducibility.

Selectivity problems were faced with the magnesium-selective electrode only, since serious interferences to background ions occurred in aqueous solutions. The electrode showed a high affinity to copper, zinc and manganese ions. Also, problems with the selectivity over free calcium ions were faced. However, experimental data showed that even if the nutrient solution contained all four ions, the selectivity coefficient of the magnesium-selective membrane was good enough to discriminate the mentioned ions sufficiently in order to quantify the concentration of free accessible magnesium ions with high reproducibility.



zvg

Fig. 2: Comparison between measurements of nutrient solutions by ISE and by AAS. The parallel shift is due to the different measuring techniques. By AAS the total concentration of Mg2+ ions is measured. By ISE the free ion concentration is measured and therefore lower than the total concentration.

zvg

Fig. 3: The present state of the Lab in the Bag®. The picture shows a box with the connectors for six potentiometric, one amperometric channels in the background. A small flow-through system with four potentiometric electrodes is shown in the front. For both measuring techniques a special reference electrode was designed. The box is connected to a lab-top for data processing.

The study proved, that continuous quantification of all three ions in the nutrient solution was feasible. In the meantime, the measuring system used for these experiments has been reduced from laboratory size to portable dimensions: the size of the «Lab in the Bag®».

Platform for measurements in active proteomics

This product concept is just emerging from research and the underlying idea is to test the activity of proteins / enzymes vs. various substrates. A specific application studied is to test sterile preparations (fluids, injections etc) for pyrogens, chemical compounds from the walls of micro-organisms that can create fever in a patient («LAL-endotoxin test»). This test is a must for companies producing such preparations with appropriate quality. The aim is to make the tests via a chip and put the chip into a cartridge.

In the «MIOSA»-project, a KTI-financed project, a platform for optical sensor arrays based on planar optical waveguides was developed. The goal of the project is to provide this platform technology for measuring the activity of enzymes and proteases especially. The technology is able to provide a solution to specific tasks in pharmaceutical and medical applications such as drug screening and point-of-care testing (POCT). The MIOSA-project especially was focused on the development of miniaturised-integrated-optical-sensor-arrays (MIOSA). As a prerequisite of this project, chromophore-labelled substrates were developed which will be immobilised on the surface of an optical chip.

C-CIT AG
c/o CCS /ETHZ
Technoparkstr. 1
CH-8005 Zürich
Tel: +41 (0)1 445 12 32
E-mail: info@c-cit.ch
www.c-cit.ch