Annual Report

CEAC

Center of Excellence
in Analytical Chemistry

2006

Impressum

Eidgenössische Technische Hochschule Zürich
Switzerland

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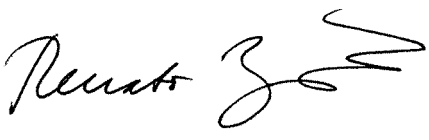
Preface

Preface
by Renato Zenobi

The past year marked a certain consolidation and stabilization within the activities of the CEAC. Contacts between the participating institutions of the ETH domain and ETHZ institutes and laboratories are well established. For example, it becomes more and more straightforward to find external placements for undergraduate research projects or M.Sc. theses of students with special interests, to tap into ETH-external expertise for advanced lecture courses in analytical chemistry, to apply for and run collaborative research projects, or have joint Ph.D. students, e.g., with the practical work being carried out at EMPA, Eawag, or PSI, and an ETH faculty member as formal research advisor. The key to this is certainly the active representation of CEAC interests at the research institutions of the ETH domain, and a true "bottom up" spirit for making collaborations on many levels possible. A special thanks for this goes to the members of the CEAC board of directors!

In 2006, the CEAC seminars have found what I would consider a permanent home in one of the beautifully renovated lecture halls in the Old Chemistry Building of the ETH. It is considerably easier to reach than the Hönggerberg campus, and accordingly, seminar attendance is up. We enjoyed many excellent lectures during the past year; a highlight both in terms of attendance and "sensory experience" was certainly the lecture by Roman Kaiser from Givaudan, who presented a story about the hunt for new fragrances and smells in the canopy of tropical rain forests to a completely packed lecture hall. The 2006 CEAC Summer Workshops on "Nanoanalysis" was also a success. It was organized jointly with the OptETH network and the Micro / Nano Science Platform at ETH. This had the advantage that automatically a broader audience was targeted. Already, the organization of the 2007 workshop is well underway. It will be run jointly by the CEAC and the Division of Analytical Chemistry, Swiss Chemical Society, and be held in honor of Prof. Ernö Pretsch, a long-time board member of the CEAC. In 2006, we were able to grant two Simon fellowships, one at the Ph.D. student and one at the postdoctoral level. The reports of the two fellows are contained in a special section in this annual report. One of the fellowships was financed by the NIDECO network of ETHZ, which is gratefully acknowledged here.

On behalf of the board of the CEAC, I would like to thank all contributors to this annual report, and the ETH Zürich, EAWAG, EMPA, and PSI for the financial support for continuing our activities.

Zürich, February 2006 

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Joint CEAC Activities

Summer Workshop on Nanoanalysis July 10 & 11, 2006 at the Swiss Federal Institute of Technology (ETH) in Zürich

Organisation: D. Günther, V. Sandoghdar, R. Spolenak, R. Zenobi & F.T. Ford (ETH Zürich), H.-J. Hug (Empa Dübendorf), Th. Jung (PSI Villigen)

Monday, July 10, 2006

09.00 **S. Kawata,** Department of Applied Physics, Osaka University, Japan
Nanoanalysis and nano diagnosis for users of nano-tech

10.00 **A. Engel,** M.E. Müller Institute, Biozentrum, University of Basel, Switzerland
Travelling through proteomes using 3D-EM

10.30 **A. Fraile-Rodriguez,** Swiss Light Source, PSI Villigen, Switzerland
X-ray Imaging and Spectroscopy of Individual Nanoparticles using Photoemission Electron Microscopy

11.30 **E. Arzt,** Max-Planck-Institute for Metals Research, University of Stuttgart, Germany
Micro/nanomechanics of adhesion in biological and artificial systems

14.00 **E. Gnecco,** Institute for Physics, University of Basel, Switzerland
Organic molecules on insulating surfaces investigated by NC-AFM

14.20 **F. Krumeich,** Laboratory for Inorganic Chemistry, ETH Zürich, Switzerland
Electron Microscopy Analysis of nm-sized Particles and Segregations

14.40 **C. Mocuta,** ESRF – Grenoble, France
X-Ray Microdiffraction on Individual Semiconductor Rolled-Up Nanotubes

15.00 **R. J. Hamers,** University of Wisconsin, Madison, USA
Physical and Chemical characterization of nanostructured carbon-based materials

Tuesday, July 11, 2006

09.00 **S. Morita,** Graduate School of Engineering, Osaka University, Japan
Site-Specific Force Spectroscopy, Atom Manipulation and Artificial Nanostructuring

10.00 **O. Hollricher,** WITec GmbH, Ulm, Germany
Nanoscale analysis: properties of individual wires, layers, atomic and molecular structures

10.30 **D. Klenerman,** Department of Chemistry, Cambridge University, England
The scanned nanopipette: a new tool for functional imaging of living cells

11.30 **A. Benninghoven,** IHK Nord Westfalen, Münster, Germany
High Resolution Surface Mass Spectrometry by TOF-SIMS

14.30 **A. Hartschuh,** Physical & Theoretical Chemistry,
University of Tübingen, Germany
Tip-enhanced Raman and photoluminescence spectroscopy of nanoscale systems

15.00 **P. Gehr,** Institute of Anatomy, University of Bern, Switzerland
The fate of inhaled particles after touch down on the internal lung surface

15.30 **J. Stöhr,** Stanford Synchrotron Radiation Laboratory, Stanford, USA
X-Ray Studies of the Nanoworld – Motivation, Concepts and Applications

CEAC Seminars – Summer & Winter Semesters 2006

27.04.2006	**Dr. Douglas R. Worsnop, Center for Aerosol & Cloud Chemistry, Aerodyne Res. Inc., Billerica/MA, USA** *Are Particles in the Lab the same as in the Atmosphere? Results from Aerosol Mass Spectrometry*
18.05.2006	**Dr. Walter Huber, F. Hoffmann-La Roche Ltd, Department of Pharma Research, Basel, Switzerland** *Biological interaction analysis based on surface plasmon resonance techniques in drug discovery and drug development*
16.06.2006	**Dr. Alexander Makarov, Thermo Electron (Bremen) GmbH, Bremen, Germany** *Tandem Mass Spectrometry using LTQ Orbitrap Hybrid Mass Spectrometer*
29.06.2006	**Prof. Beat Ernst, Institute of Molecular Pharmacy, University of Basel, Switzerland** *From Carbohydrate Leads to Drugs: Why is it so Difficult?*
26.10.2006	**Dr. Thomas A. Jung, Laboratory for Micro- & Nanotechnology, Paul Scherrer Institute, Villigen, Switzerland** *Molecular and Supra-Molecular Self Assembly at Surfaces: A Walk between Surface Chemistry and Physics*
23.11.2006	**CEAC Wilhelm Simon Fellowship Winners** **Dr. Huanwen Chen, Laboratory for Organic Chemistry, ETH Zürich, Switzerland** *Extractive Electrospray Ionization Time-of-Flight Mass Spectrometry for Direct Fingerprinting of Ambient Samples* **Mrs. Ratna Karuna, Institute for Clinical Chemistry, University Hospital Zürich, Switzerland** *Development of analytical methods for lipids as biomarkers for cardiovascular disease*
14.12.2006	**Prof. John P. Giesy, Dept. of Veterinary Biomedical Sciences at the University of Saskatchewan, Saskatoon, Canada** *Perfluorinated Chemicals in the Environmental the history of an Environmental Issue*
18.01.2007	**Prof. Huan-Cheng Chang, Institute of Atomic and Molecular Sciences, Academia Sinica, Taipei, Taiwan** *Measuring masses of single viruses and biological cells with quadropole ion trap*
01.02.2007	**Prof. René Schwarzenbach & Dr. Thomas Hofstetter, Institute for Environmental Chemistry, ETH Zürich, Switzerland** *Using compound-specific stable isotope analysis to assess organic pollutant transformation in the environment*

WWW

The CEAC WWW address is: www.ceac.ethz.ch

Currently the following information and links can be found on the CEAC web page:

- **Who is Who:** Who belongs to the Center of Excellence in Analytical Chemistry. A list of the CEAC board of directors, with links to their WWW home pages.
- **Seminars:** a list of the special analytical seminars organized by the CEAC.
- **Workshops:** Information on the CEAC summer workshop, including registration information
- **Links:** long list of interesting analytical and chemistry links
- **CEAC Research Projects**
- **Annual Report:** The Annual Report 2006 will be made available online.

3

Feature Project

Reporter Gene Assays – A Tool for Effect-Orientated Analysis of Endocrine Disruptors

Daniela Wenger[1,2], Andreas Gerecke[1], Norbert Heeb[3], Hanspeter Nägeli[4], Renato Zenobi[2]

[1]Laboratory for Analytical Chemistry and [3]Laboratory for Solid State Chemistry and Catalysis, Empa, Swiss Federal Laboratories for Materials Testing and Research, Dübendorf, Switzerland; [2]Department of Chemistry and Applied Biosciences, ETH Zürich, Zürich, Switzerland; [4]Institute of Pharmacology and Toxicology, University of Zürich, Zürich, Switzerland

Introduction

Endocrine disrupting chemicals (EDCs) are compounds that interfere with the hormone system and thus may cause adverse health effects in humans and animals. The presence of EDCs in the biosphere has become a worldwide environmental concern. In 1999, a report released by the Swiss Federal Office for the Environment concluded that EDCs have already left their mark on the Swiss landscape. The report implicated EDCs as a general cause of population changes in wildlife such as the extinction of European otter in Switzerland [1]. The potential contribution of endocrine disruptors to the increased incidences of a number of diseases and developmental disorders in humans and animal is alarming, but the establishment of dose-response relationships requires further scientific investigation [2]. As a consequence, the Swiss Federal Council approved in 2001 the implementation of a National Research Programme (NRP) entitled "Endocrine Disruptors – Relevance to Humans, Animals and Ecosystems". Herein, the NRP project ENDAIR will be presented. The project aims to provide insights into the exposure of humans and animals to endocrine disruptors in the air. Inhalation of EDCs may represent an important exposure pathway and should be considered in human risk assessment. For exposure investigation, we focused on samples such as diesel engine exhaust, a source for EDCs in the air, and inhalable ambient air particulate matter, a representative for general exposure levels.

Traditionally, a toxicological risk characterization of mixtures is based on an evaluation of a selection of constituents. To investigate the endocrine disrupting potency of environmental samples, this approach is not feasible as not all potential EDCs in a sample are known and as it is virtually impossible to analyze all of the individual constituents. Moreover, compounds may still contribute to the overall endocrine disrupting potency of a mixture, although their individual levels are too low to be detected or to cause any effects [3]. Therefore, it is a better approach to assess the integrated endocrine disrupting potency and the overall effect of a sample by measuring biomarkers that specifically respond to major categories of constituents. Biomarkers are xenobiotically induced alterations in cellular or biochemical components or processes, structures, functions or behavior that are measurable in a biological system [4]. *In vitro* bioassays such as reporter gene assays are an example of biological test systems that are applied to measure xenobiotically induced alterations. In the project ENDAIR, we use *in vitro* reporter gene assays to qualify and quantify receptor-mediated alterations in mammalian cells.

Reporter Gene Assays

The general principle of reporter gene assays is based on a genetically modified cell line or bacteria strain in which a so-called reporter gene has been implemented. Expression of this gene construct is only triggered when a specific interaction takes place between xenobiotics and a cellular component present in the cytoplasm or in the nucleus (e.g., a hormone receptor). After transcription of the reporter gene the reporter messenger RNA is subsequently translated into a reporter enzyme of which the activity can easily be quantified.

The reporter gene assays that are used in the project ENDAIR are described as Chemically Activated LUciferase eXpression (CALUX) bioassays. The ER-CALUX® assay (BioDetection Systems, Amsterdam, The Netherlands) is applied to detect and quantify estrogenic activity mediated by the estrogen receptor (ER) and the DR-CALUX® assay (BDS) to measure activity mediated by the aryl hydrocarbon receptor (AhR). Both assays are based on mammalian cell lines that have incorporated the luciferase gene of firefly (*Photinus pyralis*) as reporter gene. Receptor-mediated gene expression with subsequent production of the reporter enzyme luciferase is used as biomarker (**Figure 1**). Luciferase activity is quantified in a luminometer via the enzymatic catalyzed transformation of luciferin to oxyluciferin. The light production of this chemiluminescent transformation is a direct measure for the exposure level of the cells to receptor agonists.

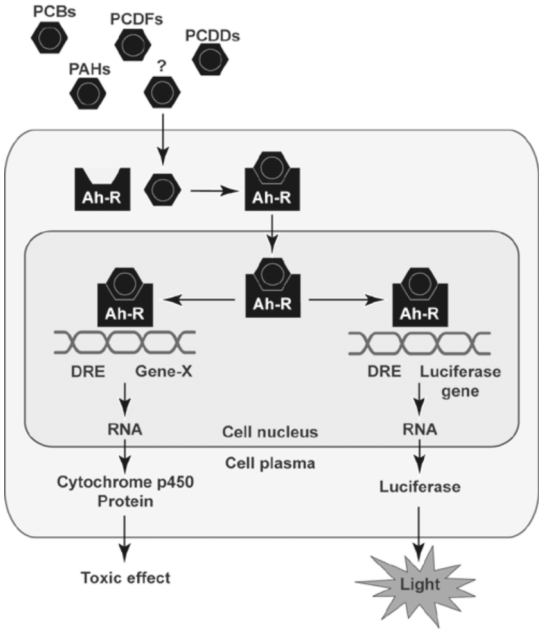

Figure 1. Mode of action of the DR-CALUX® assay, a reporter gene assay (AhR: aryl hydrocarbon receptor; DRE: dioxin responsive elements; modified from [5]).

The ER-CALUX® (Estrogen Responsive-Chemically Activated LUciferase eXpression) assay was developed by Legler et al. [6] and is based on a human breast adenocarcinoma cell line (T47D). It responds specifically to compounds that can mimic the activity of the female sex hormone estradiol. This category of EDCs, called xeno-estrogens, can cause effects on reproductive success. Similar to estradiol, xeno-estrogens bind to the estrogen receptor (ER) and induce an activation of the receptor. After dimerization, activated ER-ligand complexes specifically bind to estrogen receptor elements (EREs) in the DNA. This induces transcription of genes under control of the ERE, amongst them the incorporated luciferase gene. Using the major endogenous estrogen 17β-estradiol (E2) as a reference compound, ER-CALUX® responses to environmental samples were expressed as E2 CALUX equivalent (E2-CEQ) concentrations. The assay's limit of detection (LOD) is at 0.5 pM E2 (14 fg/100 µl exposure medium in a microtiter plate well) and the limit of quantification (LOQ) is at 1.5 pM E2 (42 fg/100 µl exposure medium).

The DR-CALUX® (Dioxin Responsive-Chemically Activated LUciferase eXpression) assay was developed by Aarts et al. [7] and is based on a rat hepatoma cell line (H4IIE). It responds

specifically to compounds that bind to the aryl hydrocarbon receptor (AhR), such as polyhalogenated aromatic hydrocarbons (PHAHs) and polycyclic aromatic hydrocarbons (PAHs). Although the AhR is traditionally not seen as a hormone receptor, AhR agonists may directly or indirectly modulate multiple endocrine signaling pathways. For example, it has been reported that AhR agonists exhibit antiestrogenic and antiandrogenic effects [8, 9]. Upon binding, the AhR is activated and the AhR-ligand complex is translocated to the nucleus. There it specifically binds to dioxin-responsive elements (DREs) and induces or inhibits the transcription of genes under control of DREs. 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (2,3,7,8-TCDD) is the most potent AhR agonist known and was used as reference compound. DR-CALUX® responses to environmental samples were expressed as 2,3,7,8-TCDD CALUX equivalent (TCDD-CEQ) concentrations. The assay has a LOD of 0.3 pM 2,3,7,8-TCDD (19 fg/200 µl exposure medium) and a LOQ of 1 pM 2,3,7,8-TCDD (63 fg/200 µl exposure medium).

Prior to assay analysis, extracts of environmental samples are transferred to dimethyl sulfoxide (DMSO). This solvent is not toxic for cells when used in low concentrations and serves as a carrier for receptor agonists to enter the CALUX cells. To perform assay analysis, CALUX cells are cultivated in 96-well microtiter plates and are exposed to sample extracts in DMSO with a final solvent concentration of 0.1 and 0.8%, respectively. An exposure time of 24 h is applied to quantify luciferase activity induced by receptor agonists in each well. Also shorter or longer exposure times can be applied if metabolic degradation of receptor agonists is investigated.

Endocrine Disruptors in Diesel Exhaust

Diesel engines emit a complex mixture of carbonaceous soot particles and thousands of gaseous and particle-sorbed combustion products or unburned fuel ingredients [10]. Some of these diesel exhaust (DE) constituents are potential endocrine disruptors [11] that may show different modes of action such as triggering receptor-mediated pathways. In our study we focused on the detection and quantification of ER- and AhR-mediated activity. We used the ER- and DR-CALUX® assays to conduct effect-orientated analysis on exhaust samples generated by a heavy duty diesel engine. The samples comprised particulate matter, as well as non- and semi-volatile compounds. To assess effects of diesel particulate filters (DPFs) on receptor agonists, we collected samples without and with exhaust treatment by fuel additive-regenerated filters.

DPFs are devices for exhaust treatment that were developed to counteract adverse health effects caused by diesel particulate matter. Heavy duty diesel engines and diesel-powered vehicles are known to contribute appreciable numbers of fine (<2.5 µm aerodynamic diameter) and ultrafine (<0.1 µm) particles to the atmosphere [12]. Diesel exhaust particles are associated with airway inflammation, asthma, allergies, and cardiovascular diseases [13, 14]. DPFs reduce particulate emissions by >95% with respect to particle number for a size range of 20-300 nm [15]. However, certain DPF systems favor unwanted chemical processes that produce toxic compounds, as shown by studies conducted at Empa [16, 17]. In principle, secondary emissions may form in any catalytically active system including for example fuel additive-regenerated DPFs, which depend on metal-containing additives that catalyze particle combustion. Consequently, DPFs are expected to alter the composition of DE by efficient retention of particulate matter and particle-sorbed compounds and by possible formation of secondary exhaust constituents. Therefore, we hypothesized that exhaust treatment by catalytic DPFs would (i) result in DE with decreased receptor-mediated activity if most agonists are sorbed to particles, (ii) that it would result in DE with no distinct change in activity if most agonists are not sorbed to particles, and (iii) that it would result in DE with

increased receptor-mediated activity if additional agonists are formed in the DPF. We tested an iron- and a copper/iron-catalyzed DPF. Herein, we discuss data of the iron-based DPF system.

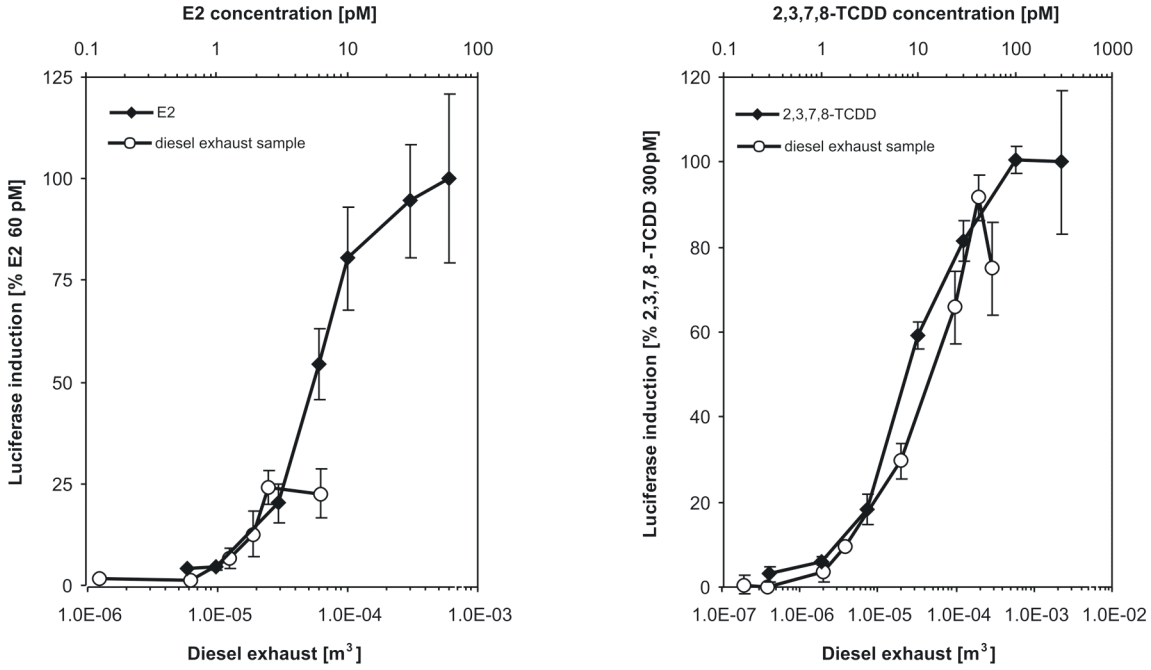

Figure 2. Dose-response curves of a diesel exhaust sample (circles) determined in the ER-CALUX® assay with 17β-estradiol (E2, rhombs) as reference compound and in the DR-CALUX® assay with 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (2,3,7,8-TCDD, rhombs) as reference compound.

Figure 2 shows the dose-response curves of the DE reference sample (*R*) measured in the ER- and DR-CALUX® assay, respectively, after an exposure time of 24h. In both assays, the DE extract induced a dose-dependent response similar to the curve of the reference compound, either E2 or 2,3,7,8-TCDD, allowing quantification of receptor agonists. In the DR-CALUX® assay, the DE extract exhibited a maximum induction of about 90% relative to 2,3,7,8-TCDD (**Figure 2**, right diagram). In the ER-CALUX® assay, a full dose-response curve for the DE sample could not be achieved due to high viscosity and precipitation during sample concentration (**Figure 2**, left diagram). Nevertheless, quantitative analysis was possible as ER-mediated activity could be measured between the limit of quantification (LOQ) and the 25% effect concentration (EC_{25}) of the E2 standard curve. For both assays, we chose sample dilutions that induced luciferase activity near to the LOQ, where quantifications are very reproducible [18]. The selected sample dilutions for ER-CALUX® assay analysis did not exhibit luciferase induction above the EC_{20} of the fitted E2 standard curve.

Applying the ER-CALUX® assay with an exposure time of 24 h, we found an ER agonist concentration of 1.7 ± 0.3 ng E2-CEQs per m^3 DE (E2-CEQs/m^3) in the reference sample generated without exhaust treatment (*R*). Doping of fuel with the iron additive resulted in a minor but significant decrease in ER agonist concentration (t-test; $p = 0.006$). We measured 1.3 ± 0.2 ng E2-CEQ/m^3 in the iron additive-based DE extract (*Fe*). In the DPF-treated sample (*FeP*), ER agonist emissions were clearly reduced to a concentration of 0.7 ± 0.1 ng E2-CEQ/m^3 (t-test; $p = 0.000$). Thus, the iron additive-regenerated DPF system decreased the

concentration of ER agonists by 55% (**Figure 3**, left diagram). This is an important result in respect to secondary effects of catalytic DPFs. We showed that exhaust treatment by the tested DPF reduced the ER-mediated endocrine disrupting potency of DE. The 55%-decline, calculated in relation to the reference concentration, reflects both the filter effect and the moderate influence of the iron additive on estrogenic DE constituents. These types of catalytic DPFs operate properly only in combination with adequate fuel additives. Hence, the situation described by the iron additive-based DE extract (*Fe*) does not exist in practice. It has to be mentioned that the use of blended fuels others than specified by Swiss legislation is prohibited. The application of metal-based fuel additives, which unavoidably leads to the formation of secondary nano particles, is allowed only in combination with efficient trap technology [15].

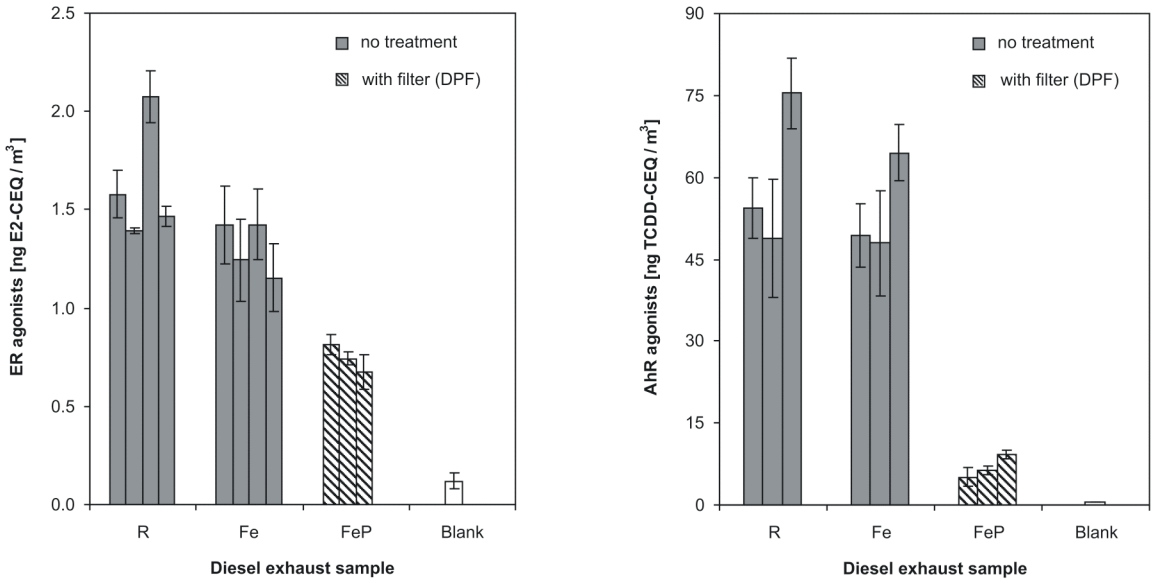

Figure 3. Receptor agonist concentrations in diesel exhaust detected after 24 h experiments with the ER-CALUX® assay (left diagram) and the DR-CALUX® assay (right diagram). Concentrations were expressed as 17β-estradiol CALUX equivalents per m^3 diesel exhaust (E2-CEQ/m^3) and as 2,3,7,8-tetrachlorodibenzo-p-dioxin CEQs per m^3 (TCDD-CEQ/m^3), respectively. Each sample was measured in triplicate on 3-4 independent microtiter plates. Experimental conditions: *R*: reference diesel fuel; *Fe*: fuel doped with iron additive (4.5 µg/g Fe); *FeP*: exhaust treatment by diesel particulate filter (DPF).

Using the DR-CALUX® assay, luciferase activity of the reference DE sample (*R*) amounted to 60 ± 14 ng TCDD-CEQ/m^3 (24 h exposure experiments). **Figure 3** (right diagram) illustrates that doping with the iron fuel additive (*Fe*) had no significant effect on the agonist concentration. In the iron additive-based DE extract, we measured 54 ± 10 ng TCDD-CEQ/m^3. Also in the case of AhR agonists, the effect of the DPF on agonist emissions was beneficial with regard to health aspects. The DPF system distinctly decreased agonist concentrations to 6.9 ± 2.1 ng TCDD-CEQ/m^3 (*FeP*). A reduction of AhR agonist emissions by 88% was observed, when comparing sample *FeP* to sample *R*. Thus, the iron-catalyzed DPF system did not favor *de novo* formation of AhR agonists. This was in contrast to the copper/iron-catalyzed DPF system (data not shown), where we observed secondary formation

of polychlorinated dibenzodioxins/furans (PCDD/Fs) [16, 17], which are among the most potent AhR agonists.

Conclusions

Reporter gene assays have proven to be valuable tools for exposure assessment of inhalable compounds with an ER- or AhR-mediated mode of action. We showed that diesel engines are a source of potential EDCs in the air. Diesel exhaust contains ER agonists and AhR agonists. Emissions of these agonists are clearly decreased by the employment of diesel particulate filters.

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4

Simon Fellowship Awards

Simon Fellowship Recipients: Project Descriptions

The Wilhelm Simon Scholarship Program in Analytical and Environmental Chemistry is intended to provide research opportunities for young scientists from developing countries and from Eastern Europe / Newly Emerging States at laboratories participating in the Center of Excellence in Analytical Chemistry of ETH Zürich. It was formally started in the summer of 1995, after an agreement between the ICSC-World Laboratory in Lausanne and CEAC-ETHZ had been signed by Prof. A. Zichichi (President, World Laboratory), Prof. R. Hütter (Vice President of Research, ETH Zürich), and Prof. R. Zenobi (presenting CEAC). This support terminated in 2004. We have since contimed and extended this program with own resources and in collaboration with NIDECO, the network for international development and cooperation at ETHZ. The latter funding is for post-docs (6 months) and Ph.D. students (12 months) from developing countries.

14 applications were received by the End of August 2005, and the fellowships for 2006 were awarded in November 2005. The fellows chosen for 2006 were:

- Ratna KARUNA (Leiden University, Amsterdam, The Netherlands)
- Huanwen CHEN (Purdue University, West Lafayette, Indiana, USA)

Development of Analytical Methods for Lipids as Biomarkers for Cardiovascular Disease

Ratna Karuna, Arnold von Eckardstein[1], Renato Zenobi[2], Katharina Rentsch[1]

[1]Institut für Klinische Chemie, Universitätsspital Zürich
[2]Laboratorium für Organische Chemie, ETH-Hönggerberg

Overview of Novel Biomarkers for Cardiovascular Disease

Cardiovascular disease (CVD), for which atherosclerosis is the major contributor, is the leading cause of mortality and disability in developed countries. Reports have also appeared on an alarming increase of CVD in developing countries, suggesting that the prevention and treatment of CVD is one of the most important public health issues worldwide [1].

Substantial data indicate that CVD is a life course disease that begins with the evolution of risk factors that in turn contribute to the development of subclinical atherosclerosis [2]. As a number of CVD events occur in asymptomatic patients with intermediate risk for CVD, prevention includes not only secondary prevention in patients who survive an event but also primary prevention and hence the early identification and treatment of patients at significant risk. Global risk assessment is necessary for accurate risk prediction and for the development of appropriate treatment strategies [1].

The presence of several moderately expressed risk factors in a given individual - such as hypercholesterolaemia, hypertriglyceridaemia, low HDL cholesterol, hypertension, smoking, diabetes, age, male gender, a positive family history of premature atherosclerotic disease - can produce a significant increase in CVD risk. Therefore, at present the most advanced strategy for CVD global risk assessment is to combine the information of several risk factors in algorithms or scores. This procedure allows calculation of an individual's absolute risk within the next 10 years [3].

An estimated global risk of >20% per 10 years in an asymptomatic patient is considered to be high. The affected patient is given advice to be treated as aggressively as a symptomatic patient. This implies lowering of LDL cholesterol and systolic blood pressure. An estimated risk ranging between 10 and 20% in 10 years is considered as moderate, and treatment is also targeted to lower LDL cholesterol and systolic blood pressure. An estimated risk <10% is considered as low. In this case, drug treatment recommendations are not offered to the majority of individuals [3].

The finding of an estimated global risk of <10% has a negative predictive value of 97%. However, the positive predictive value of high risk estimates (>20%) amounts to maximally only 32%, implying the false positive rate as high as 68%. The intermediate risk of 10–20% has positive and negative predictive values of 14 and 86%, respectively [3]. A better risk stratification is clearly needed to optimize the cost-benefit relationship of preventive measures. Biomarkers are one such tool to aid clinical assessment and improve risk prediction.

Amongst the many candidate biomarkers are those relevant to the pathophysiology of atherosclerosis. Atherosclerosis can be categorized as disorder in lipid (lipoprotein) metabolism, in which several different lipids other than cholesterol are also involved in the major events and different stages of the disease progression. In this project two forms of oxidized sterols (oxysterols), 27-hydroxy-cholesterol and 5,6-secosterol, as well as sphingolipids are hypothesized as potential novel biomarkers, as based on the literature [4-7].

Experimental Approaches

The first critical point in evaluating candidate biomarkers is the need of sensitive and robust quantitative analytical methods. Liquid chromatography – mass spectrometry (LC-MS) serves as a useful tool for high-throughput analysis in broad clinical applications. APPI (Atmospheric Pressure Photo Ionization) has been reported to improve the method sensitivity of some lipids, e.g. phytosterols which have similar structures as oxysterols [8]. As biomarker evaluation studies would be conducted not only in the lipoprotein subfractions of human plasma but also in plasma samples of genetically modified mice, highly sensitive methods are needed to allow low sample volume ($\leq$ 100 μL plasma). It could be then possible also to analyze biomarkers from the blood obtained locally at the side of ruptured plaque, e.g. using a balloon-based embolization protection device and aspiration catheter (PercuSurge) [9].

In order to define the "abnormal" biomarker levels reflecting certain events in atherosclerotic pathophysiology, reference values in healthy individuals (clinically inapparant controls) have to be established. Subsequent studies could then analyze the plasma levels in patients with clinically relevant atherosclerosis, e.g. by relating plasma levels with the extent of atherosclerotic plaque loads as assessed by quantitative coronary angiography and intravascular ultrasound.

In this project, after development and/or optimization and validation of analytical methods, the reference values will be established for sphingolipids. Studies in atherosclerotic patients, e.g. in acute coronary syndrome, will subsequently be conducted both for oxysterols and sphingolipids.

Result and Discussion

The first part of the project was the improvement of the method sensitivity for the analysis of 27-hydroxy-cholesterol. An analytical method for the quantification of 27-hydroxy-cholesterol in plasma using LC-APCI-MS has been developed and used to establish a normal reference range in healthy volunteers [10]. However, the sample volume (0.5 ml plasma) has been too large for studies in mice and/or special subfractions of plasma. Therefore, the method needs to be improved by way of increasing sensitivity.

Sensitive analysis requires the separation of oxysterols from cholesterol, which is present at a 10^3-10^6 higher levels, as well as from other lipids and contaminants in the plasma matrix. The use of silica column for SPE (solid phase extraction) was compared with the hydrophobic C18 material. Since cholesterol is more hydrophobic than its oxidized products, using a hydrophilic silica column resulted in cleaner plasma sample as compared to the C18 material used in the previously published LC-MS method [10]. On the other hand, the duration and work for sample pre-treatment using C18 material was less, which would be advantageous in routine analysis of hundreds of samples. Also chloroform extraction prior to silica-based SPE was needed after the hydrolysis of the fatty acid esters of endogenous 27-hydroxy-cholesterol. At this moment, both pre-treatments are being used in comparison during the optimization of LC and ionization condition for bio-analysis in plasma.

Ionization techniques interfacing HPLC and mass spectrometry include ESI, APCI and APPI. Regarding sensitivity enhancement, ESI offers the possibility for downscaling to nano-(LC)-ESI. However, the ionization efficiency of 27-hydroxy-cholesterol during ESI is very low and needs prior derivatization, as often applied to steroids. Most published sensitive methods on ESI analysis of steroids, e.g. progesterone and estradiol, include the derivatization of the keto- or phenolic hydroxy- moieties of the steroid rings. The 27-hydroxy-cholesterol has a different moiety of its steroid ring, limiting the choices of reagents for successful derivatization.

Moreover, an LC-MS-based method for oxidized cholesterols with prior derivatization offers little advantage compared to the established GC-MS method (which also needs prior silylation).

As mentioned previously, APPI has been reported to improve the sensitivity in the analysis of some lipids. Photoionization in atmospheric pressure, particularly if dopant-assisted or solvent-mediated, tends to produce $[M+H]^+$ ions [11]. However, although producing the same type of 27-hydroxy-cholesterol ions, $[M+H-H_2O]^+ = 385.2$, the dual ionization with APCI-APPI did not increase the signal (Fig 1). For this analyte, the highest signal was obtained using APPI alone with the assistance of 50 µL/min toluene as dopant. As mentioned in the literature, the solvent (LC mobile phase) could also mediate or interfere with the ionization. As shown in Fig 2, MeOH gave a dramatic increase in the signal.

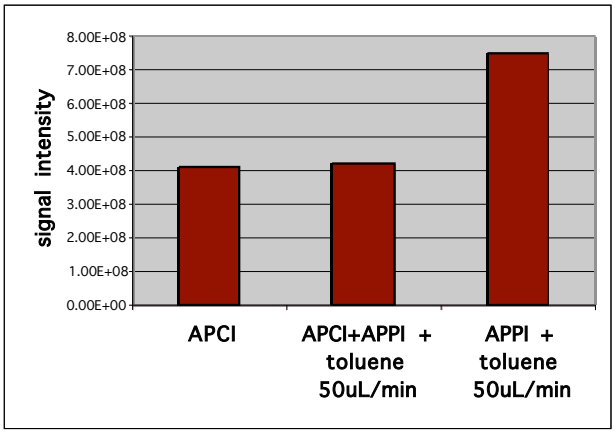

Fig 1

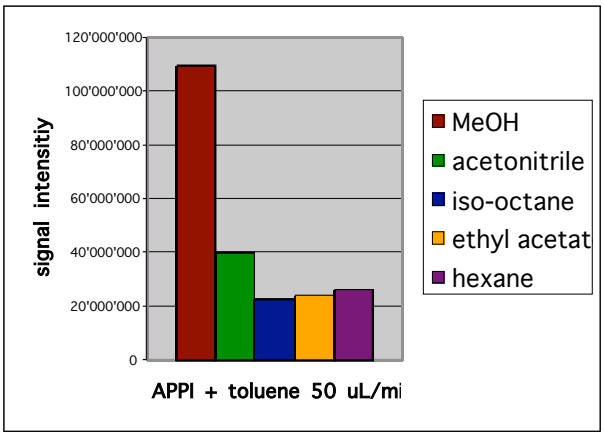

Fig 2

Using dopant-assisted APPI, improvement in the detection limit of 27-hydroxy-cholesterol could be achieved. However, large sample volumes (500 µL plasma) resulted in non-linearity, as the calibration curve of 27-hydroxy-cholesterol reached a plateau with higher concentrations. Probably the high level of endogenous 27-hydroxy-cholesterol or other endogenous contaminants interfered or saturated the ionization process. Better linearity was achieved using 100 µL plasma. Upon dilution of the 100 µL plasma sample, endogenous 27-hydroxy-cholesterol was still detected even in 25x dilution of a normal plasma sample prior to sample pre-treatment, indicating that the quantification of 27-hydroxy-cholesterol in as little as 50µL plasma is feasible. The next steps of the experiments will be further optimization for the use of smaller sample volumes (50µL plasma) and the determination of the Limit of Quantification as well as subsequent clinical validation of the method.

Acknowledgement:
Financial support from CEAC - NIDECO for the first year of the project is greatly appreciated. We would like also to thank Prof. Arnold von Eckardstein as the head of the Institute of Clinical Chemistry for his continuing interest and support, as well as to all members of Lab D OPS 14 to 18 for the help and the good working atmosphere.

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Extractive Electrospray Ionization Time-of-Flight Mass Spectrometry for Direct Fingerprinting of Ambient Samples

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Department of Chemistry and Applied Biosciences, ETH Zurich, Switzerland

1. Overview

Extractive electrospray ionization (EESI) mass spectrometry was initially demonstrated for direct real time online mass spectrometric analysis of ambient samples with dirty matrices using a Finnigan LTQ mass spectrometer coupled with a home-built EESI source.[1] Various samples including raw urine, serum, milk and solid powders can be analyzed directly by EESI-MS with neither sample pretreatment nor dilution. However, a commercial LTQ instrument requires a specially designed EESI source, which imposes difficulty on ordinary users. Alternatively, time-of-flight mass spectrometers offer good mass accuracy, high mass resolution and a fast scan rate. Some commercially available instruments such as the QTOF-MS provide a unique interface, thus EESI-MS can be implemented conveniently without any modification of the source.
In this work, QTOF-MS has been employed for the first time to demonstrate the capability of EESI-QTOF-MS for direct online analyses of various samples. Besides the intrinsic advantages of mass spectrometry such as high sensitivity and specificity, EESI-QTOF-MS allows fast quantitative detection of trace analytes without sample pretreatment and facilitates ion/molecule reactions at atmospheric pressure. Results on exhaled gas analysis and experimental data for online monitoring of various fruits for quality control and maturity screening have been obtained. The data reveal valuable information about body metabolism,[2,3] providing an alternative way to probe the health status of a human subject. Most recently, a neutral reagent desorption technique was developed to interrogate surfaces of various biological samples for EESI-MS analysis, showing the potential for more sophisticated applications in multiple disciplines, including food regulation analysis[4], homeland security, in vivo metabolomics, and clinical diagnosis.

2. Experimental Approach

2.1 Breath Analysis

Experiments were carried out using a commercial QTOF-MS instrument (QTOF Ultima, Waters Micromass, Manchester, UK) without further modification. Breath was directly blown into the ESI source (maintained at 80 °C) through the desolvation gas transfer line that has an outlet oriented orthogonally to the ESI spray. Neutral analytes are subjected to numerous collisions with protons when spraying an acetic acid/water solution (1:5), such that EESI is easily established (Figure 1). A practical example for EESI breath analysis is given in Figure 2, showing that exhaled breath can be fingerprinted *in vivo*. An $AgNO_3$ water solution (10 ppm) was used instead of a HAc solution for selective detection of S-containing molecules in breath. CID was performed with 10-25 units of collision energy.

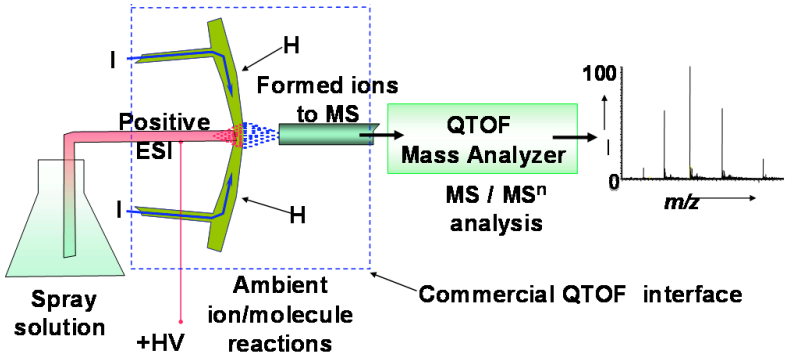

Fig. 1 Schematic illustration of the concept and setup of EESI-QTOF-MS. I: desolvation gas inlet, used for sampling of breath; H: heating region in the desolvation gas outlet; Breath compounds will be ionized in the region between the ESI spray and the breath stream. Note the intrinsic flexibility of EESI allows ambient ion/molecule reactions, including but not limited to protonation and cationization.

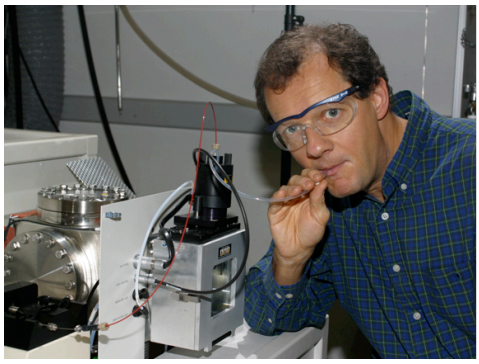

Fig. 2 A practical example of in vivo breath analysis using EESI-MS.

2.2 Fruit Analysis

Fruits such as bananas, grapes and strawberries, bought from local stores, were selected from three different maturity stages. A sample set was about 200 grams of each type of fruit. Fruits are measured multiple times to test the reproducibility of the measurement. All bananas were produced in the same location, as were all the grapes and strawberries. All the fruits were used directly without washing or other pretreatment.

To avoid potential chemical contamination, fruits were placed in a clean and dry glass container, which was specially designed so that the compounds released from the fruits inside the container could be directed into the gas inlet of the EESI source (Figure 3). Air of about 45% relative humidity was infused as carrier gas into the container at 200 mL/min, and the sample mixture was introduced into the EESI source through the desolvation gas transfer line, which is part of the original ESI interface and oriented orthogonal to the ESI spray. During this study, ESI was achieved with a 3.5 kV bias voltage and data were collected using positive ion mode.

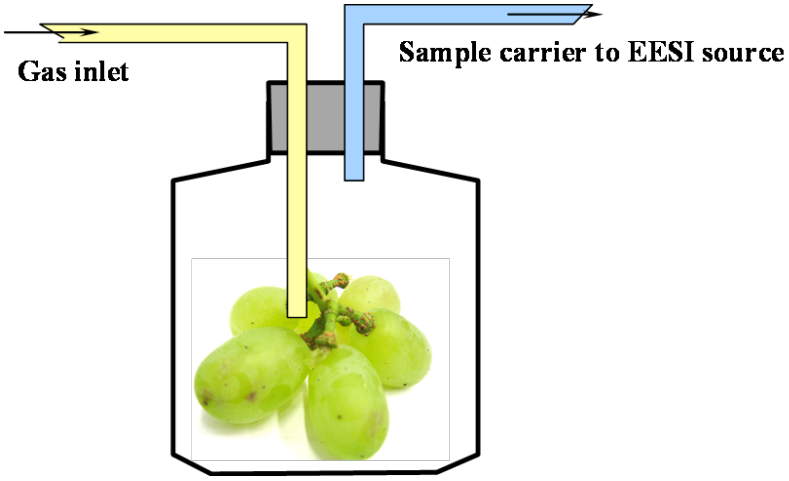

Fig. 3 Fruit sampling technique coupled to EESI-MS.

2.3 Differentiation of Biosamples by Metabolomic Fingerprinting

A simple approach that allows interrogation of virtually any kind of sample by a gentle stream of air or gas, followed by efficient ionization of the neutral molecules released in an extractive electrospray ionization (EESI) step (Figure 4). The sample molecules are transported to the ion source using the normal "desolvation gas" line, a standard feature of every commercial ESI instrument. Figure 4 shows the schematic diagram of atmospheric pressure neutral molecular desorption extractive electrospray ionization QTOF mass spectrometry: the compounds from the surface of biological samples such as frozen meat are desorbed without sample pre-treatment by a room temperature nitrogen gas flow, which creates an neutral aerosol mixture containing molecular metabolites. The aerosol is transported to the EESI source through the desolvation gas inlet (I). The aerosol passes through the heated region (H) which is maintained at 80 °C. The distance between the desorption gas flow tip and the sample surface was 5-10 mm, the desorption (a) and collecting (b) angles are both 60°. The aerosol transfer line is a flexible Teflon tube (i.d. 5 mm and 120 cm in length), thus the possibility for remote analysis is demonstrated.

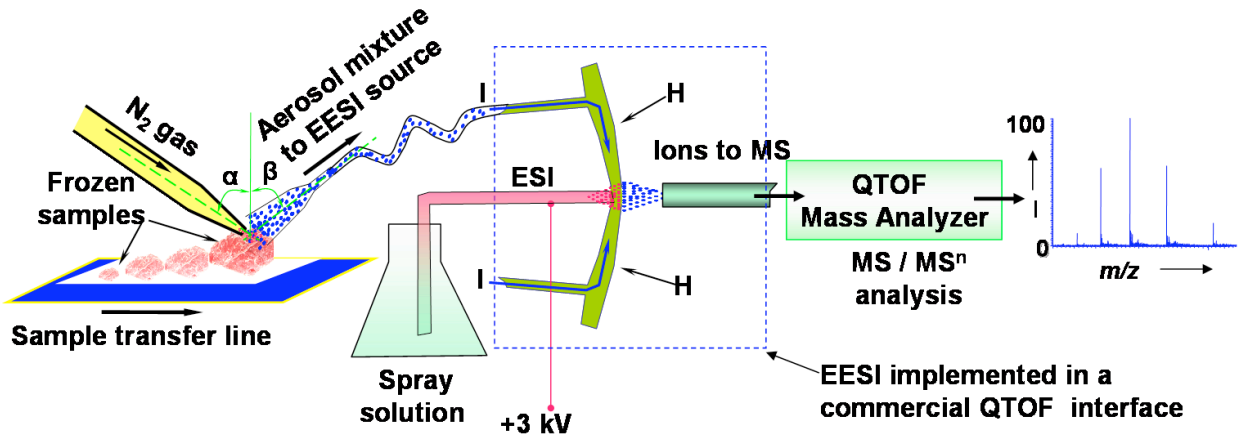

Fig. 4 Schematic diagram of atmospheric pressure neutral molecular desorption extractive electrospray ionization QTOF mass spectrometry.

3. Results

3.1 In vivo breath analysis

A simple and rapid method for analysing both volatile and non-volatile compounds in breath as it is exhaled is based on EESI was demonstrated.[3] It has the capability to analyse the gaseous components in breath as well as the volatile and non-volatile compounds held in exhaled microdroplets. For example, urea was detected in the breath of a healthy male after an overnight fast, and also 2 hours after eating a high-protein diet (cheese). Glucose was also detected from breath after taking plenty of sugar. Metabolic dynamics was followed easily after drinking different amounts of beer. Biomarkers in the breath of a smoker were also detected successfully. Nonpolar sulphur-containing compounds were detected in the breath after subjects had eaten garlic by adding silver nitrate to the spray solution (Figure 5). The silver ions formed adducts with the metabolites, allowing them to be detected in the mass spectrometer. The ease of the technique and the ability to acquire mass spectral information for both volatile and non-volatile metabolites directly from the breath should provide a valuable new way for in vivo research into the human metabolism. The method really worked right away, proved to be robust, and can be implemented on virtually any ESI interface.

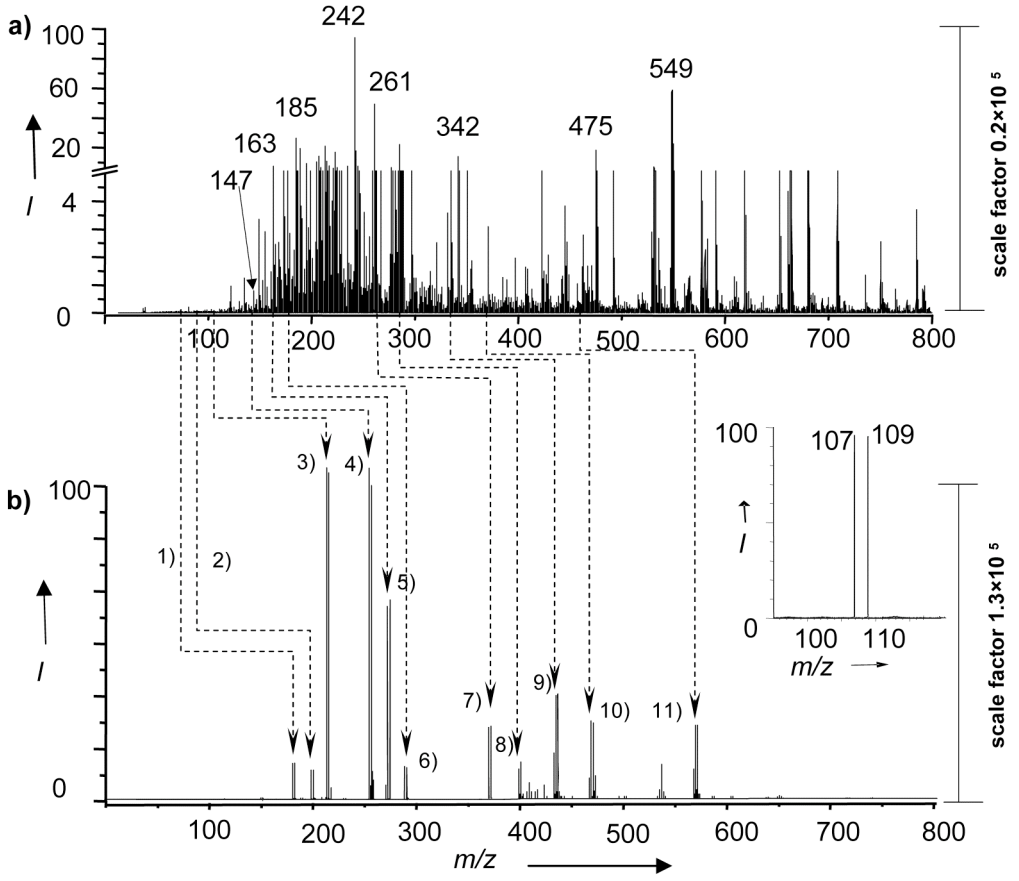

Fig. 5. Highly selective detection of S-containing species present in breath after eating garlic: a) breath fingerprint showing no non-polar compounds without Ag+/molecule reaction; insert shows the isotope peaks of silver produced by electrospraying the AgNO3 water solution; b) clear spectrum generated by adducts formed between silver isotopes and S-containing molecules. 1) m/z 181,183; 2) m/z 195,197; 3) m/z 212,214; 4) m/z 253,255; 5) m/z 269,271; 6) m/z 288,290; 7) m/z 371,373; 8) m/z 399,401; 9) m/z 435,437; 10) m/z 466,468; 11) m/z 570,572.

3.2 Fruit analysis

In this study, EESI-QTOF-MS was developed to fully meet the requirements for fruit maturity monitoring.[4] Successful differentiations of various fruits including bananas, grapes and strawberries were shown to provide different spectral fingerprints of the untreated fruit samples in the EESI-QTOF-MS; further discrimination was visualized by using cluster pattern recognition based on PCA of the raw data obtained in EESI-QTOF-MS. Due to the good long-term stability of EESI, very reproducible spectra were obtained and good reproducibility of the measurements was also confirmed by PCA results (Figure 6). Since no sample collection and separation are necessary, EESI-QTOF-MS affords high analysis speed; in a favorable case, a spectral fingerprint can be obtained in a few seconds. Therefore, EESI-QTOF-MS can be used as a tool for maturity differentiation with high sensitivity, high analysis speed, and good reproducibility and without any chemical contamination of the samples.

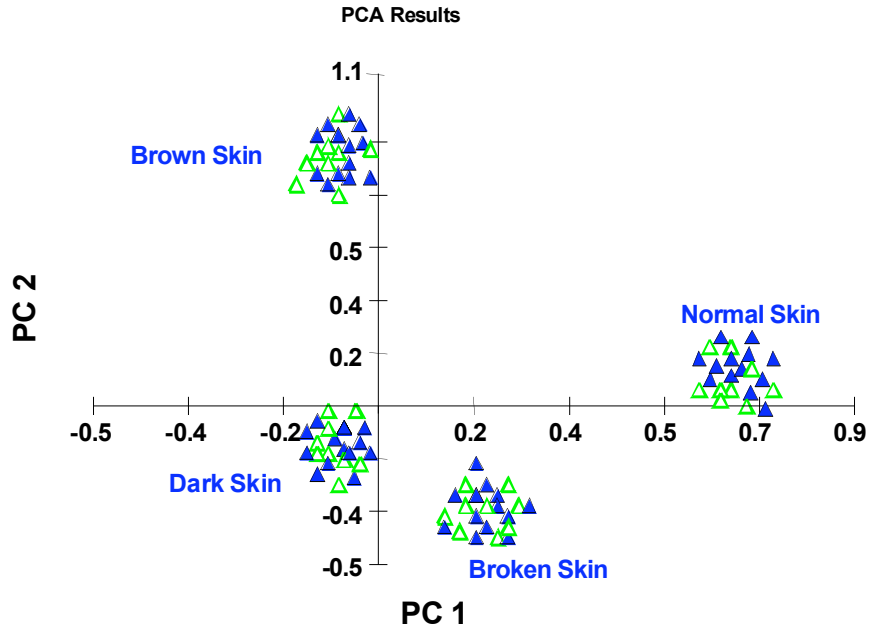

Fig. 6 PCA score plots of bananas at different maturity stages: unfilled triangles refer to data sets obtained 4 hours before the filled ones.

3.3 Differentiation of Biosamples by Metabolomic Fingerprinting

Frozen meat, spinach, and human skin can be sampled directly, in an on-line fashion by gentle desorption of neutrals coupled with EESI-MS for rapid monitoring without any chemical contamination or sample pre-treatment.[5] The mass spectral fingerprints reveal metabolites originating either from growing micro-organisms (Figure 7) or from the sample itself and thus a molecular signature for a wide variety of biological samples. This novel metabolomics-based strategy provides a "green" procedure for fast food quality differentiation. It was validated by studying 15 meat samples from different origins, and was successfully applied to fast screening of spinach samples contaminated by E. coli, and to in vivo analysis of human skin. The physiological and/or pathological status of animals or plants can potentially be diagnosed in vivo based on a molecular signature using the new technique reported here. We

expect this strategy to be used in many disciplines, including but not limited to food quality monitoring, homeland security, in vivo metabolomics, and clinical diagnosis.

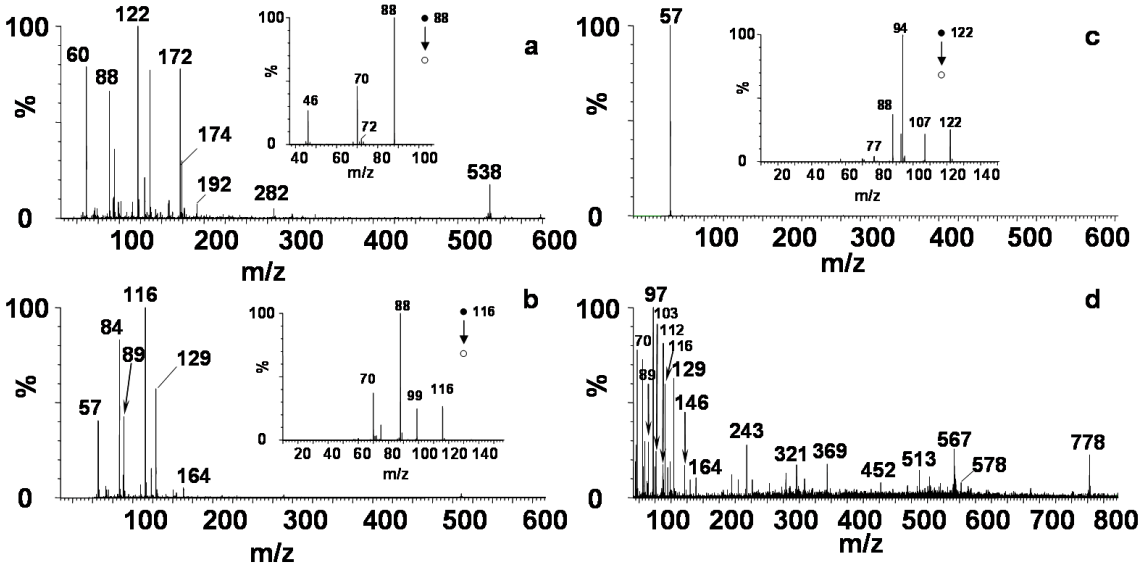

Fig. 7 Desorption extractive electrospray ionization mass spectra of fish meat at different stages: a) frozen fish exposed to room temperature (22 °C) for 0 day; b) frozen fish after exposure to room temperature for 1 day; c) frozen fish after exposure to room temperature for 2 days; d) zoomed view of the spectrum in c), numerous peaks were detected in mass range from m/z 70-800. Tyramine (MW 137), tryptamine (MW 160) and spermine (MW 202) were not detectable in samples after exposure for a time less than 2 days; but they were detected as protonated molecules with relatively low intensities in sample after exposure for 2 days.

4. Conclusions

EESI-QTOF-MS was established for the first time on commercial instrumentation without hardware modification, and was applied successfully for rapid *in vivo* fingerprinting of breath without sample pre-treatment. Metabolic dynamics is promptly reflected by breath fingerprints, providing a rapid and convenient method for *in vivo* metabolism research[3]. After further development, EESI-QTOF-MS fully meets the requirements for fruit maturity monitoring[4], thus it can be used as a tool for maturity differentiation with high sensitivity, high analysis speed, and good reproducibility and without any chemical contamination of the samples. While a neutral desorption technique is successfully developed to sample various biological samples for EESI-MS detection, frozen meat, spinach, and human skin can be monitored directly, in an on-line fashion by gentle desorption of neutrals coupled with EESI-MS for rapid monitoring without any chemical contamination or sample pre-treatment. The mass spectral fingerprints reveal metabolites originating either from growing micro-organisms or from the sample itself and thus a molecular signature for a wide variety of biological samples[5], showing promising potential for numerous applications in multiple disciplines.

Extractive electrospray ionization time-of-flight mass spectrometry has been developed for direct fingerprinting of a wide variety of ambient samples. Using practical examples, including in vivo breath analysis, fruit analysis and other biological samples, has validated the newly established method.

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5

Active Research at CEAC Member Laboratories

Title: **Ablation and ionization related studies on quantification of phase change materials (PCM) using LA-ICP-MS**

Researchers: Christian Frei, Detlef Günther

Institute/Group: Laboratory of Inorganic Chemistry,
Group of Trace Element and Micro Analysis, ETH Zurich

Project Description:
Phase change materials (PCM) are based on the reversible transition between a crystalline and an amorphous state. Phase change materials are widely used in commercial rewriteable optical data storage devices such as CD-RW and DVD-RW [1]. The fast and accurate determination of stoichiometry, homogeneity and purity is an important task in industrial quality control. In LA-ICP-MS minimum sample preparation is required and high spatial resolution is accessible, which favors this technique for such routine analysis.

Due to the lack of matrix-matched reference materials and the matrix dependent ablation behavior of these materials, detailed studies on their ablation and ionization behavior are required. Since it had been shown that particle size distribution of the laser induced aerosol has a significant influence on the ICP-MS response [2], particle size distributions for materials with different stoichiometry were investigated in detail.
To quantify various AgInSbTe materials an in-house reference sample was analysed by using solution nebulisation ICP-MS. A 100% normalization approach was used to correct for differences in the amount of ablated material and the ionization process within the plasma [3]. For data reduction standard procedures descript in [4] was used.
The ablation behavior of these phase change materials was studied in detail under different fluence conditions using raster and drilling mode. The results in raster mode are more precise due to the fact that sample fractionation during the ablation is reduced. Relative standard deviations (RSD) as low as 1% can be achieved using raster mode. Furthermore the raster mode ablation leads to improved accuracy in comparison to single hole drilling. For the four component materials a total deviation between initial weight and quantified value of less than 1.5 wt% was obtained.

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Collaboration:
Umicore Materials AG, Balzers, Liechtenstein

Title: **Single Aerosol Studies by LIBS**

Researchers: Christopher Latkoczy, Raphael Ruch, Raphael Felber, Pere Cabre-Verdiell, Ulrich Krieger and Detlef Günther

Institute/Group: Laboratory of Inorganic Chemistry, D-CHAB, ETH Zurich

Project Description:

Knowledge of the chemical composition of aerosol particles in the atmosphere is important due to the impact of heterogeneous chemistry on gas phase species in various regions of the atmosphere, understanding the atmospheric budget of aerosols and their associated light scattering and the impact of chemical composition on the cloud nucleating ability of particles. Various analytical techniques are used to determine the composition of atmospheric aerosols. They may be distinguished in on-line and off-line techniques and whether they are able to perform analysis of single aerosol particles or on a larger sample of collected aerosol. Most existing techniques for off-line analysis of single aerosol particles require that particles be collected on a substrate and stored under vacuum before analysis, limiting the analysis of volatile species. General problems associated with off-line techniques are potential transfer and sampling errors. Additionally they are not able to provide data with a high temporal resolution, which also requests further developments of on-line techniques.

An alternative to mass spectroscopy for real time in-situ analysis of single aerosols may become laser-induced breakdown spectroscopy (LIBS). The application of LIBS to the composition measurement of natural aerosol particles however require information about single particles, measured with a single laser shot, which significantly reduces the measurement precision. For example Hahn et al. [1] quantified the uncertainty of single particle measurements by sampling monodisperse aerosols, illustrating both the potential of single-particle LIBS measurements and the limitations due to precision in standard implementations of LIBS. Shot-to-shot uncertainties in LIBS composition measurements are attributed to fluctuations in laser pulse characteristics and variations in laser-plasma interaction inducing fluctuations in bulk-plasma parameters such as temperature and electron density. In this project, we developed a single particle levitation apparatus, which allows to perform subsequent single shot LIBS measurements on individual single particles. First results were obtained on mixed $NaNO_3/Ca(NO_3)_2$ aerosol particles with a diameter of 5 μm. Absolute limits of detection of 0.5 pg were reached. For quantification purposes, calibration-free Saha-Boltzmann-Plots from for 10 consecutive measurements were established with an agreement of around 30% for concentration determinations in the lower picogram range [2]. Further improvements might be possible using different approaches, like dual-pulse LIBS strategies and a modified electrodynamic balance setup to overcome current limitations.

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Collaborations:

U. Krieger, T. Peter: Inst for Atmospheric and Climate Science, D-UWIS (ETH Zurich)

Title: **Elemental Response in LA-ICPMS**

Researchers: Bodo Hattendorf, Zhongke Wang and Detlef Günther

Institute/Group: Laboratory of Inorganic Chemistry, D-CHAB, ETH Zurich

Project Description:

Accuracy in elemental analysis by laser ablation inductively coupled plasma mass spectrometry (LA-ICPMS) is affected by several processes originating in the ion source of the ICPMS. In order to better understand these processes and to improve the quality of analytical data, the influence of the operating conditions of the ion source on the elemental response for a variety of elements was investigated.

Major results from these studies [1,2] are:

- Vaporization is the rate determining step in ion generation in the ICP, especially when a large fraction of bigger particles is present in the aerosol.
- Ionization efficiency is significantly affected by the position of the sampling orifice relative to the plasma.
- Helium addition to the ICP changes the rates of diffusion and vaporization significantly leading to more homogeneous distributions of ions across the ICP
- Analyte loss in the ICP by radial diffusion is greater for Helium as carrier gas than for Argon.
- Higher analyte sensitivity with the use of Helium as carrier gas in LA-ICPMS is caused by better vaporization of the aerosol rather than changes in the ablation characteristics.

Thus, in order to improve sensitivity and accuracy of LA-ICPMS measurements the ICP-ion source leaves significant room for improvement. Modified sources are required that ensure a greater radial acceptance of ion sampling from the ICP, which also affects the vacuum interface design and the ion transfer towards the MS. Current research is aiming at such improved interfaces and ion sources.

References:

[1] Wang. Z., Hattendorf B., Günther D.; *Analyte Response in Laser Ablation Inductively Coupled Plasma Mass Spectrometry*, J. Am. Soc. Mass Spectrom., 2006, 17, 641-651

[2] Wang, Z., Hattendorf, B., Günther, D., *Vaporization and ionization of laser ablation generated aerosols in an inductively coupled plasma mass spectrometer—implications from ion distribution maps*, J. Anal. At. Spectrom., 2006, 21, 1143 - 1151

Title: **Developments of an online quantification method to characterise CeO_2 nanoparticle uptake into lung cells**

Researchers: Karin Birbaum, Detlef Günther

Institute/Group: Laboratory of Inorganic Chemistry, D-CHAB, ETH Zurich

Project Description:

The production and the use of Nanoparticles (NP) is an increasing research field due to the manifold applications of such materials. However, together with the production of these materials a number of health risks have been reported. Most of these reports are based on high concentration responses, which do not reflect "real world" scenarios. Therefore, NP-uptake experiments with physiologically relevant concentrations of NP were carried out with human lung cells. Due to the large amount of industrial production of CeO_2 particles (e.g. milling agent), these types of NP were used to study their uptake into human lung cells. It has been shown that simultaneously agglomeration, sedimentation and diffusion of NP are important for cell uptake [1].

The quantifications of the transferred NP into cells were realized by using solution nebulisation inductively coupled plasma mass spectrometry (ICP-MS).

The cells were exposed to various suspensions of NP. Therefore slurries with different particle size distributions and various concentrations were prepared.

Afterwards, cells were extracted, digested and analysed. It was found that the sample preparation procedure (digestion) is the most time-consuming step. Therefore, direct introduction of cell cultures into the ICP-MS is a major aim to provide a fast technique for their analysis. To provide a suitable quantification procedure, different suspensions (slurries) of different size fractions of NP were prepared and introduced into the ICP-MS. The concentration of the NP was determined using external solution calibration. The 'completeness' of particle vaporization within the ICP is a prerequisite to apply such a quantification procedure. Slurries with up to 300 ppb Ce concentration have a Ce recovery of 75-100 %.

References:

[1] Limbach L., Li Y., Grass R., Brunner T., Hintermann M., Müller M., Gunther D., Stark W.J., *Environ. Sci. Technol.*, **2005**, *39*, 9370

Collaborations:

L. Limbach, W. Stark (ICB, ETH)

Title: **Improving and characterization of a pulsed glow discharge time of flight mass spectrometer of GC coupling and solid aerosol sampling**

Researchers: Daniel Fliegel[1], Marc Gonin[2], Katrin Fuhrer[2] and Detlef Günther[1]

Institute/Group: [1]Laboratory of Inorganic Chemistry, D-CHAB, ETH Zurich
[2]Tofwerk, Thun, Switzerland

Project Description:

Pulsed glow discharges are ion sources that provide time dependent formation of elemental, fragmented and molecular ions within one plasma pulse [1].
Coupled to gas chromatography and in combination with mass spectrometry, quantification of organic analytes is possible and the figures of merit of today's GD-TOFMS instruments are improved compared to early instruments in terms of mass resolution, sensitivity and data acquisition speed [2,3].
Coupling the pulsed glow discharge to separation techniques like gas chromatography or other methods nevertheless remains a challenge due to the lack of adequate interfaces which is limiting the achievable sensitivity.
Moreover the huge amount of data acquired during measurements in less than a second still is exceeding the performance of current personal computer hardware.
The properties of the pulsed glow discharge plasma are highly sensitive to quenching agents as H_2, water or organic solvents.
Especially the population of the metastable argon species, which is responsible for the "soft" Penning-ionization, is dependent on the plasma operating parameters.
A aim was to describe the influence of the timing of the glow discharge in respect to the ion distribution within a GD pulse.
Finally the pulsed glow discharge was coupled to solid and aerosol sampling like laser ablation of organic samples or aerosol sampling. The possibilities of fingerprinting of organic polymers like Teflon and PVC by LA-GD-TOFMS could be proofed. Furthermore the possibility for stoichiometric analysis of chlorinated polymers could be demonstrated successfully. The possibility for aerosol sampling and identification has been shown on sampling of smoke from cigarettes. Further work will focus on the aerosol sampling of environmental samples and a further improvement of the system for low amounts of transient environmental relevant samples, like Zn, Pb, Se and Hg complexes, separated and introduced by GC.

References:

[1] Majidi V, Moser M, Lewis C, Hang W, King FL; J. Anal. At. Spectrom. (2000), 15, 19-25
[2] Fliegel D, Waddell R, Majidi V, Günther D, Lewis CL; Anal. Chem. (2005), 77, 1847-1852
[3] Fliegel D, Fuhrer K, Gonin M, Günther D; Anal. Bioanal. Chem. (2006), 386, 169-179

Collaborations:

Tofwerk, Thun, Switzerland

Title: **Ultra-violet femtosecond laser ablation inductively coupled plasma mass spectrometry**

Researchers: Joachim Koch, Markus Wälle, Jorge Pisonero, Detlef Günther

Institute/Group: Laboratory of Inorganic Chemistry, D-CHAB, ETH Zurich

Project description

The utilization of ultra-violet femtosecond (UV-fs) laser radiation is being considered as a promising approach to improve the general prospects of laser ablation inductively-coupled plasma mass spectrometry (LA-ICP-MS) concerning the isotope-selective trace element analysis of various materials. Nevertheless, the application of UV nanosecond (ns) LA emitting at 266 nm, 213 nm, and 193 nm still represents the most common way of solid sampling [1]. However, the analysis of, particularly, metals and semi-conducting material by non-matrix matched calibration has been demonstrated to be problematic since local zone heating often results in cumulative material re-distribution. As a consequence, the over-all composition of aerosols released can considerably deviate from the actual bulk value. In order to suppress zone heating, the laser pulse duration is supposed to fall below the thermal relaxation time. According to Ref. [2], thermal relaxation of metals takes place on a time-scale of a few hundred fs, slightly depending on the physical properties of the material considered. Therefore, reducing the laser pulse duration down to this range has been suggested to improve the ablation characteristics and to get closer to the concept of matrix-independent, stoichiometric sampling. In the scope of this project, the general prospects of UV-fs-LA concerning the analysis of dielectrics and metals by ICP-MS are being examined.

Recent findings reveal ICP-MS intensity ratios of strongly and less fractionating elemental systems such as Zn / Cu, Pb / U, and U / Th to be hardly affected by the wavelength or laser repetition rate chosen [3]. The complete suppression of particle size-related fractionation quantified on the basis of the U / Th-ratio turned out to comply with the absence of micrometer particles which were measured by optical particle counting (OPC). The relative fraction of particles > 0.5 µm was found to be less than 5 %. It could, furthermore, be shown that the quantification of certain elements remains difficult due to the occurrence of severe matrix and mass-dependent plasma load effects during analysis which, particularly, concerns the degree of ionization for, e.g., Zn, Cd, and Pb. In this context, the application of minor or excessive ICP mass loading on the basis of aerosol dilution and/or simultaneous aspiration of liquids as possible strategies to overcome these limitations have been discussed [4].

To provide information about the degree of aerosol dispersion during fs-LA, lately, expansion patterns of particles generated by near infrared (NIR) fs-LA of metals at atmospheric pressures were explored by laser-induced scattering [5]. Initial aerosol velocities derived from corresponding expansion plots varied from 10 m/s up to 30 m/s for fs-LA using argon and helium, respectively. It could, moreover, be shown that fs-LA carried out under helium atmosphere favours a chaotic, less reproducible aerosol expansion although particles were found to be strongly confined within cohesive fragments. Analytical implications addressing the choice of the LA protocol and physical dimensions of future ablation cell designs were given.

[1] B. J. Fryer, S. E. Jackson, H. P. Longerich, Can. Mineral., 1995, 33, 303
[2] B. Rethfeld, K. Sokolowski-Tinten, D. von der Linde, S. I. Anisimov, Appl. Phys. A, 2004, 79, 767
[3] J. Koch, M. Wälle, J. Pisonero, D. Günther, J. Anal. At. Spectrom., 2006, 21, 932
[4] J. Koch, D. Günther, Anal. Bioanal. Chem., 2007, 387, 149
[5] J. Koch, S. Schlamp, T. Rösgen, D. Fliegel, D. Günther, 2007, Spectrochim. Acta B, 62, 20

Title: **Laser Ablation-ICP-MS: Quantification of femtosecond laser ablation generated aerosols using solutions for calibration**

Researchers: Markus Wälle, Joachim Koch, Jorge Pisonero, Detlef Günther

Institute/Group: Laboratory of Inorganic Chemistry, D-CHAB, ETH Zurich

Project Description:

The quantification of laser generated aerosols using solution nebulization for calibration has been successfully applied in a variety of applications. The quantification is based on the assumption that a solution behaves similarly to a laser-generated aerosol within the ICP. Quantitative analyses of solids reported using solution based calibration show excellent results for selected elements, but also significant deviations in dependence on the matrix ablated and the elements determined [1-3].

Femtosecond laser ablation is suitable as a sampling tool to generate particles small enough for complete vaporization and ionization within the ICP. Furthermore it has been reported [4] that the ablated material represents the stoichiometric composition of the original sample when entering the ICP.

Recently it has been shown that matrix effects in LA-ICP-MS for dry plasma conditions are induced by different mass loads of the plasma (e.g. up to 25 % relative signal reduction for Cd under high mass load conditions) [5]. Therefore, the existence of mass load dependent matrix effects should question the capabilities of solution based calibration strategies for LA-ICP-MS. However it might be possible that already a very small amount of water could significantly influence the plasma conditions and might contribute to a reduction in matrix effects. First indications for such an effect have already been given in the literature [3].

This project focuses on the quantification of femtosecond laser (265 nm) generated aerosols using solution based calibration. For most of the elements the deviation of measured concentration versus certified values of reference glass and brass samples lies within a few percent. However, in glass some elements like Zinc, Selenium or Arsenic are more problematic and show deviations of 10% to 50%, whereas for brass samples Zinc shows a deviation up to a few percent only.

References:

[1] M. Thompson, S. Chenery and L. Brett, *Calibration Studies in Laser Micropobe – Inductively Coupled Plasma Atomic Emission Spectrometry*, J. Anal. At. Spectrom. **4**, 11 - 16 (1989)

[2] D. Günther, H. Cousin, B. Magyar and I. Leopold, *Calibration Studies on Dried Aerosols for Laser Ablation-Inductively Coupled Plasma Mass Spectrometry*, J. Anal. At. Spectrom. **12**, 165 - 170 (1997)

[3] C. O'Connor, B. L. Sharp and P. Evans, *On-line additions of aqueous standards for calibration of laser ablation inductively coupled plasma mass spectrometry: theory and comparison of wet and dry plasma conditions*, J. Anal. At. Spectrom. **21**, 556 - 565 (2006)

[4] J. Koch, D. Günther, *Femtosecond laser ablation inductively coupled plasma mass spectrometry: achievements and remaining problems*, Anal. Bioanal. Chem. **387**, 149 - 153 (2007)

[5] I. Kroslakova, D. Günther, *Elemental fractionation in laser ablation-inductively coupled plasma-mass spectrometry: evidence for mass load induced matrix effects in the ICP during ablation of a silicate glass*, J. Anal. At. Spectrom. **22**, 51 - 62 (2007)

Title: **Potentiometric Biosensors**

Researchers: Tamás Vigassy, Adam Malon, Ernö Pretsch

Institute/Group: Laboratorium für Organische Chemie, ETH Zürich

Project Description:
Subfemtomole amounts of Ca^{2+}, Pb^{2+}, and Ag^{+} have been determined at 100 picomolar concentrations by direct potentiometric measurements in small samples of 3 μL. Thanks to these improvements, potentiometry now belongs to the most sensitive techniques of ion analysis. By using the recently established labeling of biomolecules with nanoparticle-based metal (Ag) or semiconductor (CdSe) tags and dissolving these metals in small sample volumes, highly sensitive potentiometric immunoassays have been introduced.

References:
[1] Potentiometry at trace levels in confined samples: Ion-selective electrodes with sub-femtomole detection limits
A. Malon, T. Vigassy, E. Bakker, E. Pretsch
J. Am. Chem. Soc. **2006**, *128*, 8154–8155.
[2] Potentiometric biosensing of proteins with ultrasensitive ion-selective microelectrodes and nanoparticle labels
K.Y. Chumbimuni-Torres, Z. Dai, N. Rubinova, Y. Xiang, E. Pretsch, J. Wang, E. Bakker
J. Am. Chem. Soc. **2006**, 128, 13676–13677.
[3] Potentiometric immunoassay with quantum dot labels
R. Thürer, T. Vigassy, M. Hirayama, J. Wang, E. Bakker, E. Pretsch
Anal. Chem., submitted.

Collaborations:
Prof. E. Bakker, Purdue University, West Lafayette, IN, USA
Prof. M. Hirayama, Zürcher Hochschule Winterthur, CH-8400 Winterthur,
Prof. J Wang, Arizona State University, Tempe, AZ, USA

Title: **Backside Calibration Potentiometry**

Researchers: Károly Tompa, Adam Malon, Tamás Vigassy, Ernö Pretsch

Institute/Group: Laboratorium für Organische Chemie, ETH Zürich

Project Description:
Recently, we have shown that ion fluxes through supported liquid membranes are so fast that steady-state concentration profiles across ion-selective membranes are established rapidly and reproducibly [1]. At concentrations below ca. 10^{-4} M, the potentiometric response depends on the compositions of the solutions on both sides of the sensing membrane. Chemical asymmetries across the membranes are assessed by determining the direction of potential drift upon changing the stirring rate on either side of the membrane. Disappearance of this drift indicates the disappearance of concentration gradients across the membrane and is used to determine the sample composition if the solution composition at the backside of the membrane is known. The practical applicability of the method has been demonstrated with different environmental water samples, for which the results obtained with the novel method have been compared with those got by traditional calibration using standard additions.

References:
[1] Ion-selective supported liquid membranes placed under steady-state diffusion control
K. Tompa, K. Birbaum, A. Malon, T. Vigassy, E. Bakker, E. Pretsch
Anal. Chem. **2005**, *77*, 7801–7809.
[2] Ion activity measurements with selective supported liquid membranes by calibrating from the back side of the membrane
A. Malon, E. Bakker, E. Pretsch
Anal. Chem. **2007**, 79, 632–638.

Collaborations:
Prof. E. Bakker, Purdue University, West Lafayette, IN, USA

Title: **A Novel Spectral Similarity Measure**

Researchers: Lóránt Bódis, Ernö Pretsch

Institute/Group: Laboratorium für Organische Chemie, ETH Zürich

Project Description:
A novel similarity measure of related patterns has been introduced. In contrast to traditional quantities, like the correlation coefficient, it is less sensitive to small deviations in the position of the signals. Its utility has been demonstrated with infrared as well as one and two-dimensional NMR spectra. For testing the compatibility of a spectrum with the proposed structure, first the spectrum is predicted from the structure and then the novel similarity test is used to compare the predicted and measured spectra.

Collaborations:
Dr. A. Ross, F. Hoffmann-La Roche Ltd. CH-4070 Basel
Dr. P. Portmann, Porta Nova Software GmbH, CH-8037 Zürich

References:
[1] L. Bodis, A. Ross, E. Pretsch
A novel spectral similarity measure
Chemom. Intell. Lab. Syst. **2007**, 85, 1–8.

Title: **Nanoscale Chemical Analysis and Spectroscopy**

Researchers: Patrick Setz, Gerardo Gamez, Thomas Schmid, Thomas Schmitz, Jason Yeo, Weihua Zhang, Renato Zenobi

Institute/Group: Laboratorium für Organische Chemie, ETH Hönggerberg

Project Description:

For developments in nanoscience and nanotechnology, powerful nanodiagnostic tools capable of recording chemical/molecular information with exquisite spatial resolution will become increasingly important. Scanning near-field optical microscopy (SNOM) is particularly well suited as a tool for nanoscale molecular analysis [1]. SNOM is the "optical member" of the family of scanning probe microscopies and based on a subwavelength light source that is scanned above the object of interest at a distance of a few nm. In the optical near field, the illuminated area is not limited by diffraction, but merely by the size of the illumination source (50 - 100 nm). Questions that are being addressed in this project include the determination of the composition of thin solid films, the characterization of novel materials and elements of molecular electronics, the investigation of biological objects in their natural environment, the chemical analysis of polymer blends, and the study of chemical reactions on the surface of heterogenous catalysts.

The studies are based on two main methodologies: (i) Aperture SNOM with tips designed for high optical transmission and for sustaining pulsed laser radiation, for laser ablation mass spectrometry [2, 3], and (ii) apertureless SNOM, employing an external CW laser field and a metallic tip to greatly enhance the local field for “tip-enhanced” Raman spectroscopy (TERS) [4 - 6]. The latter method has a resolution that exceeds that of aperture SNOM. Much progress has been achieved in the area of TERS during the past year. In particular, ways for the production of robust and highly enhancing TERS tips were found [5]. Using “gap mode” TERS, we even achieved single molecule sensitivity [6]. The combination of chemical identification (via the Raman spectral signature), spatial resolution of ≈ 20 nm, and a detection limit at the single molecule level has never before been possible.

References:

[1] T. Schmid, T. A. Schmitz, P. D. Setz, B.-S. Yeo, W. Zhang, and R Zenobi, *Methods for Molecular Nanoanalysis*, Chimia (special issue on Nanoanalysis) 60, 783 - 788 (2006).

[2] C. Vannier, B.-S. Yeo, J. Melanson, and R. Zenobi, *Versatile Instrument for Micro- and Nano Raman Spectroscopy*, Rev. Sci. Instrum. 77, 023104 (2006).

[3] P. D. Setz, T. A. Schmitz, and R. Zenobi, *Design and Performance of an Atmospheric Pressure Sampling Interface for Ion Trap / Time-of-Flight Mass Spectrometry*, Rev. Sci. Instrum. 77, 024101 (2006).

[4] M. De Serio, H. Mohaparta, R. Zenobi, and V. Deckert, *Towards High Resolution Near-Field Raman Measurements of Liquid-Liquid Interfaces*, Chem. Phys. Lett. 417, 452 - 456 (2006).

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[6] W. Zhang, B.-S. Yeo, T. Schmid, and R. Zenobi, *Single Molecule Tip-enhanced Raman Spectroscopy with Ag tips*, J. Phys. Chem. C 111, 1733 - 1738 (2007).

Collaborations:

V. Deckert (ISAS, Dortmund/D), NT-MDT (Zelenograd/Russia), Goodyear (Luxembourg).

Title: **Environmental Trace Analysis and Aerosol Chemistry**

Researchers: Christian Emmenegger, Markus Kalberer, Alain Reinhardt, Vera Samburova, Renato Zenobi

Institute/Group: Laboratorium für Organische Chemie, ETH Hönggerberg

Project Description:
Organic aerosols are of importance in such different fields as global climate change, regional air quality and human health. Of particular interest to us is the analysis of organics in the atmosphere and especially of organic aerosol particles. The scientific goals of this project are to study the formation, composition, and chemical fate of secondary organic aerosol in detail, to better define the high-molecular weight fraction (so called humic acid like substances, HULIS) in ambient urban aerosols, and to push the limits for trace detection of organics in environmental samples [1]. The tools we are using are mass spectrometric, chromatographic [2] and optical spectroscopy methods that are applied to controlled laboratory experiments in a flow tube reactor as well as in a smog chamber, built in collaboration with the PSI [1]. These are complemented with field experiments from urban and rural areas.
An important recent advance is based on the application of ultra-high FTICR-MS. Studying the ozonolysis of a-pinene in the smog chamber, about 450 compounds were detected in the mass range between m/z 200 and 700. The mass spectrum is clearly divided into a low molecular weight (monomer) range and a high molecular weight (oligomer) range, where dimers and trimers are distinguishable. Using Kendrick mass analysis, the elemental composition of about 60% of all peaks could be determined throughout the entire mass range, and O:C ratios could be calculated. The results suggest that condensation reactions such as loss of water are important in the oligomer formation process. A second recent study focused on quantification of carboxylic, arylic, phenolic and aliphatic functional groups of HULIS, performed by a specially adapted and optimized H-NMR method. The concentrations of carboxylic, arylic, phenolic and aliphatic functional groups were between $9x10^{-11}$ – $6x10^{-8}$ mol/m^3 for all samples, corresponding up to 14% of the total HULIS mass. A good correlation between the H-NMR results and potentiometric titration of carboxylic groups was observed. A third focus is the investigation of particle-lung cell interactions and the identification of particle properties causing negative health effects, a project started in collaboration with the University of Bern.

References:
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[2] C. Emmenegger, et al., *Evaporative Light Scattering: a Novel Detection Method for the Quantitative Analysis of Humic-like Substances in Aerosols*, Envir. Sci. Technol. (accepted, Jan. 2007)
[3] A. Reinhardt et al., *Ultra-high Mass Resolution and Accurate Mass Measurements as a New Tool to Characterize Oligomers in Secondary Organic Aerosol*, Anal. Chem. (revised, Feb. 2007).
[3] V. Samburova et al., *Functional Group Analysis of High Molecular Weight Comounds in the Water-soluble Fraction of Organic Aerosols*, J. Atmos. Chem. (revised, Feb. 2007).

Collaborations: U. Baltensperger (PSI), H. Gaeggeler (Univ. Bern / PSI), C. Hüglin (EMPA), P. Gehr, M. Geiser (Univ. Bern), Functional Genomics Center Zurich.

Title: **Electrospray Ionization Mass Spectrometry for Studying Noncovalent Interactions**

Researchers: Cédric Bovet, Matthias Jecklin, Sonal Mathur, Alexis Nazabal, Tatiana Pimenova, David Touboul, Arno Wortmann, Renato Zenobi

Institute/Group: Laboratorium für Organische Chemie, ETH Hönggerberg

Project Description:

Electrospray ionization (ESI), and variations thereof such as electrosonic spray ionization (ESSI) or chip-based nanoelectrospray ionization allow, under carefully chosen conditions, the preservation of noncovalently bound complexes and supramolecular assemblies in the gas phase. We are working on a better understanding of the fundamentals for the detection of noncovalent complexes with ESI-MS based methods. This knowledge is also used to further develop mass spectrometry based methods to for quantitative study of noncovalent binding interactions [1].

Using ESI, nanospray, and ESSI, we pursue the following projects: (i) Study of complex, real-world noncovalent interactions such as the inhibition or activation of the endocrine receptor by small molecules that occur in the environment, so-called endocrine disruptors. (ii) Determination of binding constants by mass spectrometry. This sub-project is currently heavily focused on fast classification of human kinase inhibitors by automated nanoESI-MS. Protein kinases have become one of the most important drug targets. A lot of effort is being put in developing fast screening methods for active and specific inhibitors; we are convinced that MS-based methods can make an important contribution to the solution of this challenge. Different methods are used for this, such as ESI titration, competition methods, or H/D exchange followed by MALDI readout (a novel methods called SUPREX). (iii) We also validate these measurements by comparing against standard methods for K_d determination, such as circular dichroism and surface plasmon resonance studies. (iv) We conduct detailed investigations of the influence of the ESI spray on chemical equilibria in solution and its dependence on the time scale of droplet evolution relative to the time scale of the equilibrium kinetics [2]. A thorough understanding of these effects is key for further development of ESI-MS based methods to determine accurate binding constants.

References:

[1] J. M. Daniel, S. D. Friess, S. Rajagopalan, S. Wendt, and R. Zenobi, *Quantitative Determination of Noncovalent Binding Interactions using Soft Ionization Mass Spectrometry*, Int. J. Mass Spectrom. 216, 1 - 27 (2002).

[2] A. Wortmann, M. C. Heine, O. Wilhelm, A. Kistler-Momotova, S. E. Pratsinis, and R. Zenobi, *Shrinking Dtoplets in Electrospray Ionization and their Influence on Chemical Equilibria*, J. Am. Soc. Mass Spectrom. 18, 385 - 393(2007).

Collaborations: S. E. Pratsinis (ETHZ), D. Moras (IGBMC / CNRS, Strasbourg, France), Functional Genomics Center Zurich, Novartis Institutes for BioMedical Research (Cambridge).

Title: **MALDI Mass Spectrometry - Applications and Fundamentals**

Researchers: Stefanie Mädler, Alexis Nazabal, Tatiana Pimenova, Ryan Wenzel, Renato Zenobi

Institute/Group: Laboratorium für Organische Chemie, ETH Hönggerberg

Project Description:
MALDI Mass Spectrometry has emerged as an effective analytical tool for soft ionization of complex (bio-) molecules up to several 100 000 Da. In MALDI, the sample is embedded in an excess of a solid matrix, which, upon laser irradiation, assists in the volatilization and ionization of the analyte. We are contributing to both the fundamental understanding of the MALDI process as well as to application of MALDI to study high-mass biomolecules and their complexes.
As one of the very few groups in the world, we operate a novel MALDI mass spectrometer equipped with a superconducting tunnel junctions detector; similarly, a special high mass detector for MALDI based on discrete dynode technology is also available in our lab. These new detector technologies circumvent the familiar drop-off of the detection efficiency with increasing mass and allow detection up to 1 MDa and beyond. We are using high-mass MALDI for the following projects: (i) Detection of high-mass protein complexes by direct mass analysis of unfragmented, undigested, intact protein complexes by MALDI [1]. The method consists of a chemical stabilization of the non-covalent interaction partners prior to high-mass MALDI-MS analysis. In this context, the cross-linking chemistry (reactivity, amino acid specificity, kinetics, …) is also investigated in detail. (ii) epitope mapping, using the intensity fading approach [2]. Here, the high-mass MALDI is employed to ensure efficient cross-linking of the epitope to an antibody. This is then followed up with high-resolution FT-ICR measurements of the digested, cross-linked complex.
Our longstanding efforts in studying the fundamental principles of the MALDI process [3, 4] are currently focused on researching the effect of photoelectrons produced in the MALDI process, on the effect these have on ion yield, and on investigating the origin of the "first shot" phenomenon in MALDI, using a combination of MALDI-MS and fluorescence resonance energy transfer methodologies.

References:
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[4] A. Wortmann, T. Pimenova, an R. Zenobi, *Investigation of the First Shot Pheonmenon in MALDI,* The Analyst 132, 199 - 207 (2007).

Collaborations:
Franz Hillenkamp (University of Münster/D), S. Hornemann (ETHZ), A. Trkola (University Hospital, Zurich), Institute for Systems Biology (ETHZ), Functional Genomics Center Zurich, CovalX GmbH (Zürich).

Title: **Fourier-Transform Ion Cyclotron Resonance (FT-ICR)**

Researchers: Huanwen Chen, Konstantin Chingin, Maxim Dashtiev, Renato Zenobi

Institute/Group: Laboratorium für Organische Chemie, ETH Hönggerberg

Project Description:

Fourier-transform ion cyclotron resonance (FT-ICR) is a very powerful mass spectrometric method, celebrated for its extremely high mass accuracy and resolting power. For many applications, high-resolution measurements are very important to correctly assign peaks in the spectrum, for example to unambiguously determine a molecule's elemental composition. Since the FT-ICR instrument is an ion trap, it is very well suited for studying ion-molecule reactions, for example charge transfer processes that take place after desorption in MALDI, such as gas phase protonation (cationization) reactions in the plume. We have also employed this instrumentation for the study of electron emission from MALDI targets.

In a project more related to our investigations of noncovalent complexes, we are currently studying the conformation of biomolecules in the gas phase, by combining FT-ICR with fluorescence spectroscopy of trapped ions. For example, there are many current debates about whether biomolecules ionized by MALDI or ESI retain their native conformation. We plan to utilize the fluorescence emission of green fluorescent protein (GFP) and fluorescence resonant energy transfer in doubly labeled proteins and in molecular beacons based on self-complementary DNA strands. The fluorescence properties of such biomolecular ions brought into the gas phase by MALDI or ESI should give important new insights about conformation of gas-phase-ions. Using single photon counting, we have already demonstrated the capability to observe fluorescence resonance energy transfer in doubly labeled trapped gas-phase ions [1, 2].

References:

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Collaborations:

B. Schuler (University of Zurich), M. Gorshkov (Moscow State Univ.)

Title: **Single Cell Metabolomics**

Researchers: Andrea Amantonico, Nils Goedecke, Matthias Heinemann, Andreas Hierlemann, Kai-Uwe Kirstein, Oliver Kotte, Joo-Yeon Oh, Sven Panke, Markus Rottmar, Benjamin Volkmer, Renato Zenobi

Institute/Group: Bioprocess Laboratory, Institut für Verfahrenstechnik, ETH Zentrum
Laboratorium für Organische Chemie, ETH Hönggerberg
Physical Electronics Laboratory, ETH Hönggerberg
Institute for Systems Biology, ETH Hönggerberg

Project Description:
Despite a large body of knowledge about cellular components little is known about how all these work together as a system. The holistic, system-wide approach to modern biology is dramatically altering our view on the molecular key questions of cellular function and interplay. The ultimate goal of systems biology is to obtain a quantitative and mechanistic under-standing of the complex and highly interrelated processes occurring in cells. This in-depth understanding will be achieved by an integration of experimental data into predictive models. Almost all current quantitative informations aggregate data from an entire cell population, while even cells in monoclonal cultures display strong differences on all levels. Thus a single cell approach to '-omics' research is essential to create accurate models that include consideration of intracellular stochasticity. This project, funded through an ETHZ "INIT" proposal, has started in mid-2005.
For the purpose of detecting metabolites in single cells, we are developing highly sensitive methods that can detect on the order of 10^5 molecules in the volume of a single cell, which is in the femtoliter range. Furthermore, the technology should be amenable to high-throughput operation. We should reach this goal soon, through the coupling of a microfluidic cell processing and sample preparation step to an extremely sensitive version of MALDI mass spectrometry. We have recently shown that metabolites - even in cellular extracts - can be detected by MALDI with sufficient sensitivity, using nanoliter spotting of the samples onto a specially prepared matrix layer, in negative ion mode.
The project aims at establishing the proof of principle of the instrumental technology and at providing a first assessment of its performance and usability for biological systems science.

Collaborations:
Functional Genomics Center Zurich.

Title: **Detection and discrimination capabilities of a multitransducer single-chip gas sensor system**

Researchers: Petra Kurzawski, Christoph Hagleitner, Andreas Hierlemann

Institute/Group: Laboratorium für Physikalische Elektronik, Dept. Physik, ETH Hönggerberg

Project Description:

The performance of a single-chip three-transducer CMOS gas sensor microsystem has been thoroughly evaluated. The monolithic gas sensor system includes three polymer-coated transducers, a mass-sensitive cantilever, a thermoelectric calorimetric sensor and an interdigitated capacitive sensor that are integrated along with all electronic circuits needed to operate these sensors. The system additionally includes a temperature sensor and a serial interface unit so that it can be directly connected to, e.g., a microcontroller. Several multi-transducer chips have been coated with various partially selective polymers and then have been exposed to different volatile organic compounds. The sensitivities of the three different polymer-coated transducers to defined sets of gaseous analytes have been determined. The obtained sensitivity values have then been normalized with regard to the partition coefficients of the respective analyte/polymer combination to reveal the transducer-specific effects. The results of this investigation show that the three different transducers respond to fundamentally different molecular properties, such as the analyte molecular mass (mass-sensitive), its dielectric coefficient (capacitive), and its sorption heat (calorimetric) so that correlations between the determined sensitivity values and the different molecular properties of the absorbed analytes could be established.

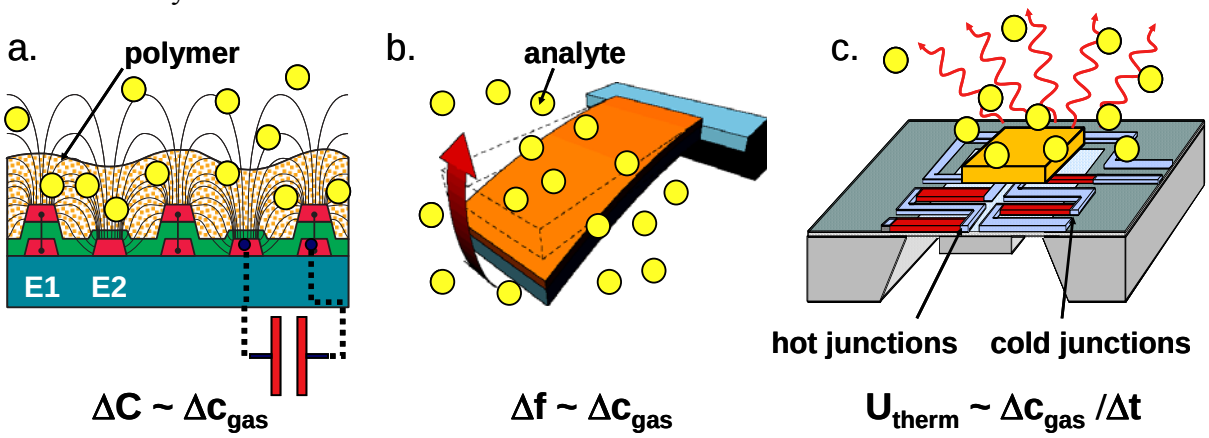

Fig1. Three different transducer principles: (a) microcapacitor sensitive to changes in dielectric properties, (b) resonant cantilever sensitive to mass changes, and (c) microcalorimeter measuring the absorption or desorption heat upon interaction of organic volatiles with the polymer.

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Title: **ADE: An integrated workflow for comprehensive bioinformatic characterization and statistical evaluation of protein species identified by mass spectrometry based proteomics**

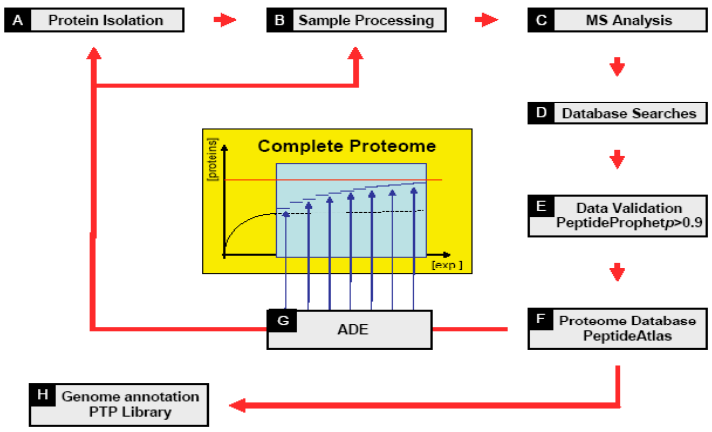
Researchers: Christian Ahrens, Hansruedi Baetschmann, Erich Brunner and Ralph Schlapbach

Institute/Group: Functional Genomics Center Zurich, UZH/ETH Zurich

Project Description:

The comprehensive analysis of proteins, which carry out most cellular functions, is an important pre-requisite to understand cellular processes in a systems biology context. However, a complete annotation of all the elements of a proteome has not yet been achieved for any organism. For the very complex eukaryotic proteomes, high-throughput shotgun proteomics approaches promise to achieve a greater coverage than traditional 2-D gel-based approaches. A partially automated platform for shotgun proteomics data handling, searching, and storage has been established at the FGCZ.

In order to identify deficiencies in the experimental setup that prevent whole proteome coverage, we use datasetd from large-scale shotgun approach that cover a large portion of the respective proteomes. Statistically significant differences can be observed for a number of parameters, and are used to adjust the experimental protocols, subsequently leading to the identification of a higher proportion of the proteome. Integration of data from other systematic large scale studies (e.g. gene expression datasets), further improves the ability to predict which proteins will be very difficult to identify by the experimental approaches. The project aims to develop a generally applicable rotational workflow that cycles from experiments through thorough bioinformatic and statistical analysis, delivering parameters that allow to fine-tune, amend or even change the experimental approaches eventually leading to a comprehensive proteome annotation.



Selected Collaborations:

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R.Aebersold (D-BIOL, ETH Zurich)
J. Jiricny (IMCR, University of Zurich)
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U. Grossniklaus (Inst. of Plant Biology, University of Zurich)

Title: **Determination of complex PTM-profiles using high-accuracy mass spectrometery**

Researchers: Bertran Gerrits, Dorothea Rutishauser, Bernd Roschitzki, Peter Gehrig, Simon Barkow, Christian Panse, and Ralph Schlapbach

Institute/Group: Functional Genomics Center Zurich, UZH/ETH Zurich

Project Description:

The dynamics and vast diversity of post-translational modifications (PTMs) pose an enormous challenge for the identification and positional mapping of the protein modifications. Combining latest proteomics technologies, in particular high accuracy and high resolution mass spectrometers, with sophisticated bioinformatics approaches, the project aims to characterize the complex PTM patterns of biological specimens.

The project focuses on indispensable proteomics data for the identification of novel circulating protein factors and PTMs that are important for the onset, dynamics and progression of complex diseases like diabetes and obesity. The polygenic basis for obesity and type-2 diabetes in inbred mouse strains (such as New Zealand Obese (NZO) mice) likely reflects the genetic architecture relevant for the human disease. Thus, inbred mouse models for the polygenic metabolic syndrome provide a powerful experimental platform for studying the pathophysiology of environmentally (i.e. diet) induced obesity and diabetes in humans. Data generation focuses in the project focuses on high-accuracy FT mass spectrometric analysis of mouse tissues. Supporting data available from transcriptomics approaches is integrated with the proteomics data to provide a solid fundament for the development of computational analysis methods for these data types and the creation of an adequate modeling technology.

Selected References:

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Database independent detection of isotopically labeled MS/MS spectrum peptide pairs.
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The mass distance fingerprint: a statistical framework for de novo detection of predominant modifications using high-accuracy mass spectrometry
J. Chromatogr. B. in press.

Selected Collaborations:

A. Malik, MicroDiscovery GmbH, Berlin, Germany
H. Al-Hasani, Deutsches Institut für Ernährungsforschung, Nuthetal, Germany
R. Cramer, The University of Reading, Reading, Great Britain
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Title: **Project to set-up a metrological infrastructure for electrochemical analysis applied to chemistry, biotechnology and laboratory medicine at the Swiss Federal Office for Metrology and Accreditation (METAS)**

Researchers: Aymeric Pellisier, Stefan Spichiger, Hans Gerber, Ursula E. Spichiger-Keller

Institute/Group: Centre for Chemical Sensors and Chemical Information Technology (CCS), D-CHAB, ETHZ, Zurich

Project Description:

It's a fundamental truth that classical analytical procedures do not respond to the same quantities as chemical sensors, biosensors and bioassays. Especially when these methods are applied and exposed to a complex specimens directly, the results deviate from wet chemical methods such as spectroscopy, AAS, chromatography etc. Remarkably, quantities such as molality and active molality and their units recommended by IUPAC are rarely used in practical analytical chemistry even if method comparisons reveal the differences in the results.

Enterprises frequently suffer from the drawback of being unable to refer the results of chemical sensors and bioassays, even of pH-electrodes, developed in-house to an independent primary analytical procedure based on sensor technology. This situation is especially crucial for start-up enterprises.

The collaboration between the Swiss Federal Office of Metrology and Accreditation. CCS is focused on the development and installation of primary standard methods, primarily of electrochemical methods, on which the data collected by commercialized electrodes and electrochemical instruments can be traced back.

The fundamentals of electrochemical analysis were published in teaching books long ago, and they are generally well accepted in the scientific community. Therefore, the goal of the project is to compare the results yielded from electrochemical experiments under very well controlled conditions with results which are yielded mathematically based on generally accepted physico-chemical models and algorithms. Results yielded by using electrochemical basic equipment must coincide with the results yielded by calculations within defined limits of uncertainty.

Fundamental quantities such as molality and active molality are defined by IUPAC, and are referred to the amount of solvent in a sample. These quantities need to get generally accepted in analytical chemistry. METAS has the legal power to contribute to the efforts of European and International Bodies to achieve the international comparability of analytical results and to get through data reporting in the appropriate units.

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(DK), Kuwa K, Tsukuba (JP), Külpmann W, Hannover (DE), Larsson L, Linkoping (SE), Lewenstam A, Åbo-Turku (FI), Maas AHJ, Utrecht (NL), Mager G, Bad Homburg (DE), Spichiger-Keller U, Zürich (CH). GUIDELINES FOR SAMPLING, MEASURING AND REPORTING IONIZED MAGNESIUM IN UNDILUTED SERUM, PLASMA OR WHOLE BLOOD.

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Collaborations:

Swiss Federal Office of Metrology, Bern-Wabern, Switzerland
C-CIT AG, Wadenswil

Title:	**The Development of a Fluorescence Optode Selective for Orthophosphate ($H_2PO_4^-$ and HPO_4^{2-}) and, Alternatively, for Nitrate and Nitrite**
Researchers:	Rita Cannas, Laurent Quebatte, Jolanta Kurz-Glebska, Stefan Spichiger, Ursula E. Spichiger-Keller
Institute/Group:	Centre for Chemical Sensors and Chemical Information Technology (CCS), D-CHAB, ETHZ, Zurich

Project Description:

Almost all methods assaying inorganic phosphate go back to the method by Fiske-Subbarow introduced in 1925 (Fiske and Subbarow 1925): The method relies on the formation of a polyoxometalate complex (Katsoulis 1998) between inorganic phosphate and molybdenum(VI)oxide salts. If inorganic phosphate has to be discriminated from organically bound P, the specimen is pretreated with trichloroacetic acid (Zilversmith and Davis 1950).

Phosphorus is an essential nutrient for all plants and is supplied as a fertilizer in agriculture. If phosphorus is transported from the terrestrial to the aquatic ecosystem, the consequence is the eutrophication of lakes and coastal water. Therefore the concentration of this element in water running off from sewage works is strictly controlled. In Switzerland such water samples must contain <0.8 mgP/L (26 umol/L phosphate) .[1].

Ideally a method to determine inorganic phosphate in water samples should be highly sensitive, mobile, reliable and, for continuous monitoring, a probe should react reversibly. Ideally, chemical sensors combine these properties and show, therefore, a high economic potential. However, the preconditions to develop a sensor system are to have access to an ionophore which complexes phosphate effectively and reversibly and is stable in contact with water over weeks.

The project involved a search for the most promising ionophores [2-5], to modify the ionophores synthetically in order to get the required features, to incorporate the ionophores into polymer films along with other compounds such as plasticizers and additives, and to prepare ion-selective electrodes (ISEs) and optodes. The relevant analytical parameters of the sensors were investigated in a stepwise screening process.

After a period where optodes were primarily investigated, the industrial partner decided to focus on improving ion-selective electrodes in a first step. The development is ongoing.

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Title: **A nanoparticulate matrix for the development of gas-selective Sensors**

Researchers: Jorge F. Fernández-Sánchez, Rita Cannas, Tomas Nezel, Thomas Roth, Stefan Spichiger, Ursula E. Spichiger-Keller

Institute/Group: Centre for Chemical Sensors and Chemical Information Technology (CCS), D-CHAB, ETHZ, Zurich

Project Description:
Nanoparticulate inorganic materials constitute a promising substrate to develop gas-selective chemical sensors with high resistance to heat and gamma irradiation. CCS recently got access to nanostructured ink-jet papers produced at Ilford, Marly, Switzerland. Various paper qualities made from different metal oxides and additives are accessible where the porosity, the pore volume and the pore size are well defined [US 6,156,419 patent]. Referred to the chemistry of the metal oxide, the surface charge of the pores can be negative or positive. The influence of electrostatic interactions on the specific chemical reaction of the organometallic compound adsorbed within the pores and the target gas was studied. The ink-jet papers were shown to be indeed resistant to gamma-irradiation and to autoclavation (humidity and heat) opposite to plasticized polymer membranes. Organometallic complexes (OMCs) such as phtalocyaninato Fe(II), Ru(II)- and Ir(III) complexes as well as pH- and pCO_2-sensitive indicators with appropriate pK, in addition to additives were dissolved in a volatile solvent and applied to the nanostructured film by spin-coating. The analytical performance of these films to the varying partial pressure of specific gases was investigated. Organometallic compounds were synthesized and synthetically modified in collaboration with the group of Prof. M. Graetzel, EPFL, in order to study the interactions between the surface of the mesopores and the specific OMC. In conclusion, the stability of the chemical compounds insulated within the mesopores and the homogeneity of the films is improved compared to solvent polymeric membranes. In addition, the chemically modified nanostructured film responds within seconds to the target gas. The chemical reactions going on within the nanoporous structure were investigated using the internal special optical equipment for the investigation of gas-selective sensors and sensor arrays. The chemical mechanisms were investigated by solution NMR and the SBSR-technique which is used with FTIR-ATR-spectroscopy at CCS. The characteristics of the films were correlated to the specific parameters of nanoporosity (see results).

Abstract:
Transparent nanoparticulate ink-jet paper is an excellent matrix to create optical gas-selective sensors. Specific organometallic compounds are added by spin-coating and react with a change in the electromagnetic spectrum to the partial pressure.

Materials and methods:
Nanostructured materials such as aluminum oxide (AlOOH), silicon oxide (SiO_2) and zirconium oxide (ZrO_2) embedded into PVA were investigated as potential matrices to incorporate organometallic compounds (OMCs) for the development of optical oxygen-sensitive sensors based on luminescence quenching. The OMCs used in this work were: ETHT-3003 (tris(4,7-bis(4-octylphenyl)-1,10-phenanthroline) ruthenium(II)), N-926 (bis(2-phenylpyridinyl)-N4,N4,N4',N4'-tetramethyl-(4,4'-diamine-2,2'-bipyridine) iridium(III) chlorate), N-833 (tetrabutylammonium bis(isothiocyanate) bis(2-phenylpyridinyl)-iridium(III)) and N-837 (tetrabutylammonium bis(cyanate) bis(2-phenylpyridinyl)-

iridium(III)) [5]; iron phthalocyaninato complexes solubilized in a number of amine solvents such as p-decylaniline, benzylamine and dioctylamine [6]. The organometallic compounds (OMCs) as well as pH- and pCO_2-sensitive indicators with appropriate pKa were incorporated into the nanostructured films and the analytical performance of these materials were investigated. Compounds were synthesized and synthetically modified in collaboration with the group of Prof. M. Graetzel, EPFL, in order to study interactions between the mesopores and the OMCs.

Equipment:
Luminescence measurements used for O_2: Perkin-Elmer LS-50B luminescence spectrometer fitted with a xenon flash lamp and a Hamamatsu R-928 red-sensitive photomultiplier which has ±1 nm accuracy at the specified wavelength and a reproducibility of ±0.5 nm with the usual 30°/60° excitation/emission geometry. A self-built flow-through cell was used in all the experiments [2].
For NO_2, CO and CO_2-sensitive sensors: The chemical reactions going on within the nanoporous structure were investigated by changes in the electromagnetic spectrum (internal special equipment for the investigation of optical gas-selective sensors and sensor arrays by optical transmission spectroscopy). The reaction mechanism of CO_2-sensitive sensors was investigated by FT-IR-spectroscopy using a special ATR sample cell and the SBSR-equipment offered by OPTISPEC, Neerach (Prof. U. Fringeli).
The chemical mechanisms involved in the molecular interactions between NO_2, an amine solubilizing the OMC and the iron phthalocyaninato-complex were investigated by solution NMR and by an X-ray structural study in collaboration with P.S. Pregosin, ETHZ.
Sterilization protocols: (1) An autoclave from Napco (Model 8000) at a temperature of 121°C and a pressure of 1 bar for 20 minutes were used. (2) chemical cleaning (cleaning in place; CIP and (3) gamma irradiation. The CIP protocol consisted in treating the membranes by NaOH (1 M) or H_3PO_4 (2.5%) at 50°C during 30 min, then purged with de-ionized water and, finally, drying under ambient conditions. The gamma-irradiation protocol consisted in the exposition of the membrane to 14.5 KGy during 30 min.

Summary of a selection of relevant results:
Oxygen-selective films based on luminescence quenching: The incorporation of the OMCs into the nanopores increases their luminescence quantum yield up to 85% (excitation at 400 nm, emission at 530 nm) for the Ir(III) complexes (bis(2-phenylpyridinyl)-N4,N4,N4',N4'-tetramethyl-(4,4'-diamine-2,2'-bipyridine) iridium(III) chlorate) and the sensitivity to molecular oxygen by a factor of >40 (Stern-Volmer constant) for the Ru(II)-complex ETHT 3003 (tris(4,7-bis(4-octylphenyl)-1,10-phenanthroline) ruthenium(II)) (excitation at 460 nm, emission at 620 nm).
Surprisingly, the total pore volume and the pore size played a crucial role for the sensitivity of the luminescence quenching reaction whereas the reaction was insensitive to the chemistry of the nanostructured metal oxides. The critical limit was a pore diameter.

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[5] R. Steiger, R. Beer, J.F. Fernández Sánchez and U.E. Spichiger-Keller. "Large area, nanoparticulate metal oxide coatings for consumer nanotechnologies". Solid State Phenomena 121-123 (2007) 1193.

Title: **The development of a magnesium-selective sensor**

Researchers: Jolanta Kurz-Glebska, Stefan Spichiger, Ursula E. Spichiger-Keller

Institute/Group: Centre for Chemical Sensors and Chemical Information Technology (CCS), D-CHAB, ETHZ, Zurich

Project Description:
Magnesium-selective electrodes based on ionophores developed at ETHZ achieve the highest-selectivity to monovalent ions. Additionally, the basic theories to achieve the best performance of the electrodes were developed in our group. This know-how was transferred to the industrial partner.

References:
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Collaboration:
Radiometer Medical ApS, Åkandevej 21, 2700 Brønshøj, Denmark

Title:	**ChemIT / Active Proteomics: Chemically modified integrated optical waveguide for yielding chemical information (Chem-IT)**
Researchers:	Jolanta Kurz-Glebska[1], Rita Cannas[1], Gleb Zhylyak [1], Michael Linnhoff[l], Ursula E. Spichiger-Keller [1], Uwe Pieles[2]
Institute/Group:	[1] Centre for Chemical Sensors and Chemical Information Technology (CCS), D-CHAB, ETHZ, Zurich [2] Fachhochschule Nordwestschweiz, Gründenstr. 40, Muttenz, BL

Project Description:
The goal of the **m**iniaturized **i**ntegrated **o**ptical **s**ensor **a**pplication (**MIOSA**) project is to develop an optical assay for measuring the activity of proteolytic enzymes.
Currently, the MIOSA project is aimed at two fields of applications: endotoxin detection assay (*Limulus* clotting enzyme) and monitoring of enzymatic tumour markers (Matrix metalloproteinases).
An appropriately designed interface, between a planar waveguide and a specific labelled peptide substrate, should allow the cleaving enzyme to attack the labelled peptide giving the possibility to trace the activity of this enzyme in solutions and in physiological fluids. Positive results on the development of the effective functional surface would contribute to a common platform technology applicable to a range of other proteases and transferable to other relevant enzymes.
A light beam propagating within the planar waveguide creates an evanescent field of penetration depth < 100 nm above the surface. Changes in the light absorption within this adjacent layer correlate with the concentration changes of the specific chromophore. The proteolytic activity of the enzyme is reflected by the increase in the light intensity upon cleavage of a peptide bond, at a specific recognition sequence, what results in chromophore dissociation out of the evanescent field.

Cleaning studies:
Mechanically washed or piranha cleaned chips were silanized and functionalized with a dye-labelled substrate. Except for the cleaning step all chips were prepared within the same batch.
The applied cleaning procedure strongly influences the system response. Instability of the sensing layer indicates that the SGR-LM 46 is primarily coupled to the sensor surface by adsorption; dye diffusion out of the evanescent field area is due to energy of the laser light, which seems to be stronger than the effective bond strength of coating. Higher thermal stability of chromogenic substrate molecules immobilized to the piranha cleaned surface are more likely due to stronger electrostatic interaction forces than due to covalent binding.
Piranha treated chips, contrary to these mechanically washed, showed no optical effects at all (Fig. 2, cf. Fig. 3).

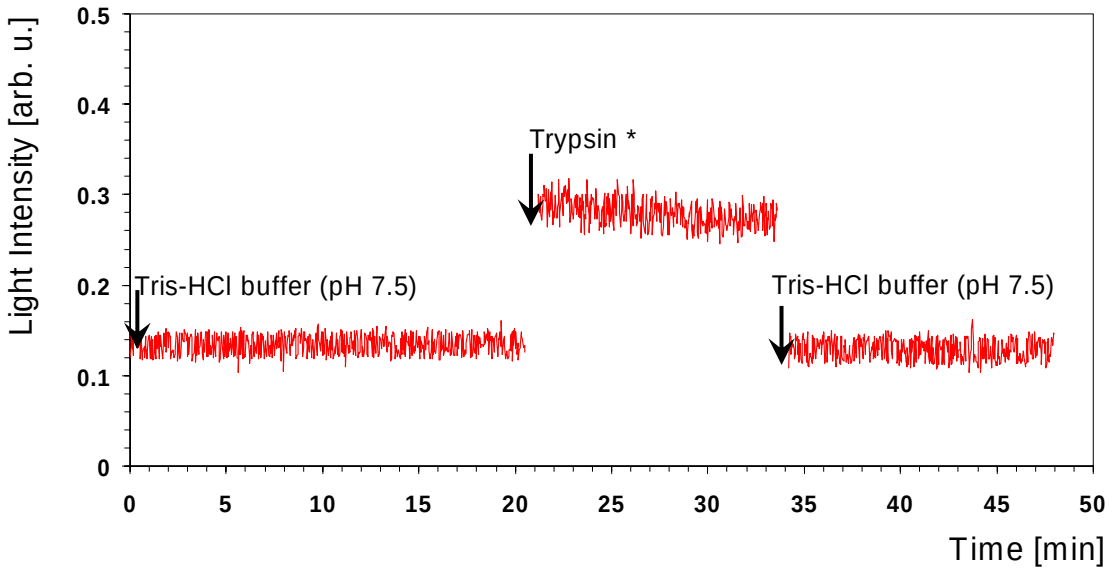


Fig.2 Changes in the light intensity, at 640 nm, after the exposure of a chip to the laser beam in the presence of Tris-HCl buffer or trypsin protease (* this change is due to the solution's refractive index change)

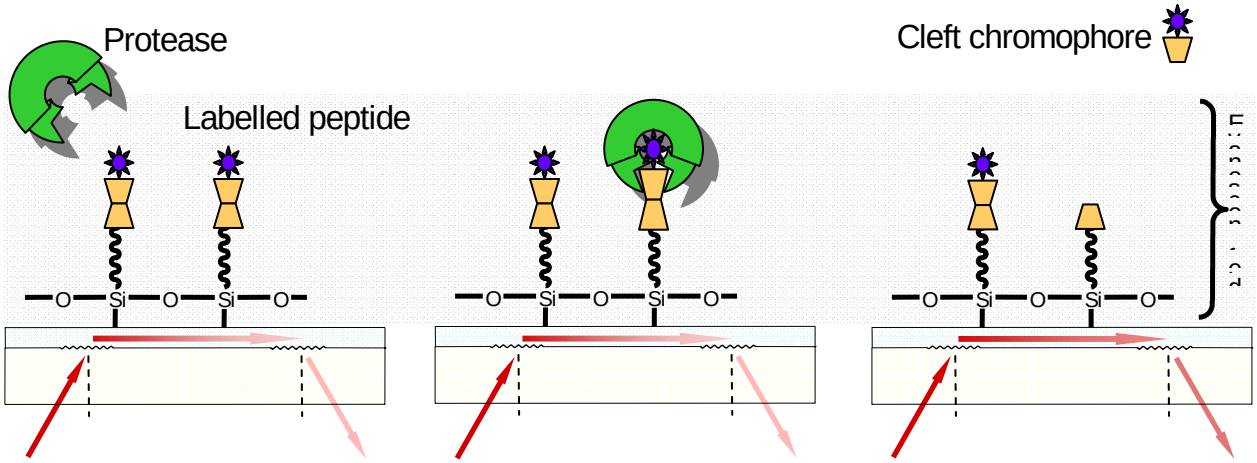
Surprisingly, there was no correlation between the optical characteristics of the chip and the amount of the silane on the surface (the relevant ratio is Si/Ta).
XPS results for pre-treated, GOPS silanized and SGR-LM 46 functionalized chips
A comparative study of mechanical cleaning method vs. piranha surface treatment reveals the importance of cleaning conditions for a successful chip functionalization. Acid cleaning methods (piranha, chromerge) are supposed to give results comparable to those of gas plasma treatment, the most common technology applied currently for optimal surface cleaning and activation. This is of current interest to determine the influence of this technique on the performance of the sensing layer.

Silanization \ Cleaning (Elemental composition (in norm. %))		C 1s	O 1s	N 1s	Si 2p	Ta 4f
GOPS, RT, 24h	mechanical cleaning	29	49	3	3	18
	piranha	33	45	2	4	16
GOPS, 95°C, 5h	mechanical cleaning	31	44	3	6	16
	piranha	25	50	2	5	18

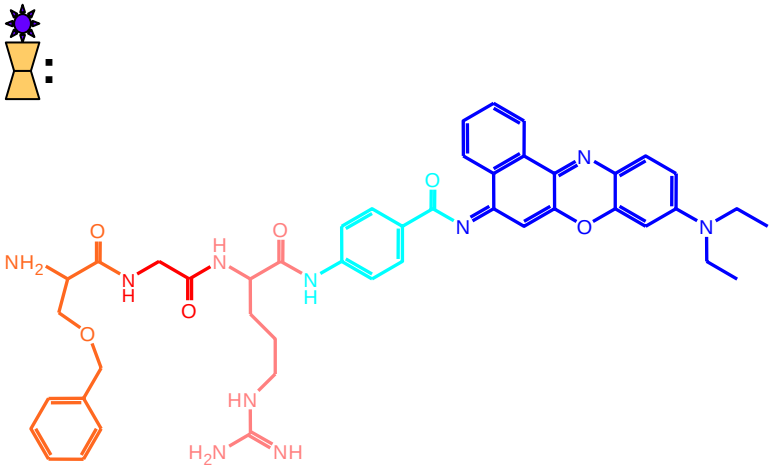
The goal of the **m**iniaturized **i**ntegrated **o**ptical **s**ensor **a**pplication (**MIOSA**) project is to develop an optical assay for measuring the activity of proteolytic enzymes.
Currently, the MIOSA project is aimed at two fields of applications: endotoxin detection assay (*Limulus* clotting enzyme) and monitoring of enzymatic tumour markers (Matrix metalloproteinases).
An appropriately designed interface, between a planar waveguide and a specific labelled peptide substrate, should allow the cleaving enzyme to attack the labelled peptide giving

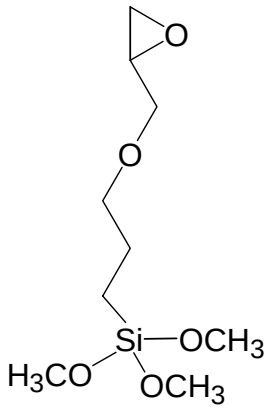
the possibility to trace the activity of this enzyme in solutions and in physiological fluids. Positive results on the development of the effective functional surface would contribute to a common platform technology applicable to a range of other proteases and transferable to other relevant enzymes.

Surface functionalization:



Chromophore labeled tripeptide:





GOPS: (3-glycidyloxy propyl)trimethoxysilane

The formation of sensing layers follows three to four steps procedure:
(1) **Cleaning** and **activation** (mechanical or chemical cleaning)
(2) **Immobilization** of organosilanes (APTES, GOPS) providing epoxy or amine groups
(3,4) **Covalent attachment** of a **linker**/spacer and the **specific chromophore**; SGR-LM 46

References:

G. Zhylyak *et al.*, Optics and Lasers in Engineering **2005**, 43, 603.

Collaborations

Prof. Marcus Textor, Dr. Samuele Tosatti, Mr. Vincent Zoulalian, Surface Science and Technology, ETH Zurich, Switzerland
Prof. Uwe Pieles, Applied University, Muttenz, Switzerland
Prof. T. Merseburger, Applied University Wadenswil, Switzerland
Prof. R. Steiger, CSEM, Neuchâtel, and Ilford Schweiz, Marly, Switzerland
C-CIT AG, Wadenswil, Switzerland

Title: **A Micro-capillary System Coupled to an ICP-MS as a Novel Technique for Investigation of Micro-Corrosion Processes**

Researchers: Nadzeya Homazava, Andrea Ulrich

Institute/Group: Laboratory for Analytical Chemistry, Empa

Project Description:

Detailed information on corrosion processes provides the key to effective prediction and minimization of corrosion damages. The initiation stage of material decomposition plays a special role, since the corrosion starts mainly on weakest locations such as surface defects, grain boundaries, segregations or inclusions. However, surface analysis or electrochemical methods commonly used in corrosion research can not present local element-specific and online in-situ information at the same time.

As a solution a combination of a device for localized investigations of corrosion based on a micro-capillary system coupled to an ICP-MS has been proposed. The online coupling of the micro-capillary system with controllable solution flow to an ICP-MS should allow continuous or time-dependent introduction of investigated in-situ samples and enable both element specific as well as spatially and time-resolved investigations of corrosion processes and mechanisms. The hyphenated technique can become an excellent tool to obtain essential data for reliable modelling of local surface degradation processes and mechanisms.

The minimization of the micro-capillary spot diameter is essential in the investigation of the initiation stage of complex corrosion processes. However, the development of a suitable flow cell is challenging and requires a careful optimization. Detection sensitivity is limited by several factors such as blank levels of used materials and chemicals, dissolution rates of the materials of interest, matrix content of the investigated corrosive media, possible dilution factors and maximum salt charge for the ICP-MS.

Strategies for suitable inter-element correction equations as well as detector calibration (e.g. custom resolution, dual detector calibration) are required. Investigations on method development and first results were already achieved on different aluminium alloys and enlighten how far the wetted surface area can be reduced and which spatial resolution capabilities the technique offers.

References:

[1] M. Gysler, *Charakterisierung der Korrosionsbeständigkeit von Aluminiumlegierungen*, Diplomarbeit EMPA/ZHW (2005).

[2] N. Homazava, A. Ulrich, U. Kraehenbuehl, *Element-Specific Investigation of Micro-corrosion Processes in Al Alloys by ICP-MS*, Poster at the 2006 PhD Symposium, October 19 2006, Empa St. Gallen.

Collaborations:

Prof. Krähenbühl, Prof. Siegenthaler (University of Bern); P. Schmutz, T. Suter, F. Eckermann (Empa); Alcan AG

Title: **An Analytical Task: The Analysis of the Ancient Material Copper and its Alloys**

Researchers: Adrian Wichser, Marianne Senn and Andrea Ulrich

Institute/Group: Laboratory for Analytical Chemistry, Empa

Project Description:

The chemical characterization of ancient copper alloy objects is an often requested task in the Laboratory of Analytical Chemistry. Information on chemical compositions of the copper alloys helps archaeologists to identify origin, production processes as well as transport and trade routes of ancient objects. Private collectors are mainly interested in authentication and the interest of museums is more focused on restoration/conservation.

Since preservation of ancient objects is a main goal, small sample quantities and invisible sampling is required. Moreover, it has to be ensured that the metal is analyzed and not the surrounding corrosion layer, which usually shows different composition. A well established standard method is the determination of the metal composition after acid digestion using atomic absorption spectrometry (AAS), plasma optical emission spectrometry (ICP-OES) or plasma mass spectrometry (ICP-MS). However, analysis with prior digestion require a minimum sample amount of about 50 mg for double determinations, which results in a drill hole of about 1-3 mm diameter in the object.

Thus, a direct analyzing method using LASER ablation plasma mass spectrometry (LA-ICP-MS) has been developed. Since a mountable cell was used, the method can also be applied for analysis of bigger objects. The analysis results in craters of usually 50-100 µm. Due to inhomogeneities of ancient copper alloy objects, for example lead bronzes often show lead inclusions or segregations of a diameter up to 100 µm, a larger number of sampling spots is needed to achieve reliable bulk analysis of the alloy. Also the crater sizes must be optimized with respect to the heterogeneity of the material. Calibration with matrix matched standards is mandatory. But the highly spatial resolution of LA-ICP-MS also allows detailed investigations of the corrosion layers. Metallurgic analysis using microscopic methods and also synchrotron analysis offer additional information on the form and composition of the corrosion.

The new analytical possibilities of LA-ICP-MS with mountable cell for the determination of copper alloys allowed the start of a new research project on Neolithic and Early Bronze Age copper alloy objects from Western Switzerland, with the goal to investigate origin, production and trade routes. The project is a cooperation with Université de Genève. A second research project studies Chinese leaded bronze objects with the goal to proof authenticity and to identify artificial corrosion processes.

References:

[1] A. Wichser, A. Ulrich, *LA-ICP-MS for Authentication of Antique Bronze Objects – Potential and Limitations*, Poster on the 8th European Workshop on LASER Ablation in Elemental Analysis, July 19-21, 2006, Zürich.

Collaborations:

Florence Cattin, Université de Genève, Laboratoire d'archéologie préhistorique et d'histoire des peuplements, Département d'anthropologie et d'écologie.

Title: **Occurrence of UV Filters in Fish from Swiss Rivers**

Researchers: Hans-Rudolf Buser[1], Marianne E. Balmer[1], Peter Schmid[2], Martin Kohler[2], Andreas C. Gerecke[2]

Institute/Group: [1]Agroscope Changins-Wädenswil ACW
[2]Laboratory of Analytical Chemistry, Empa

Project Description:

UV filters are chemicals that are used to protect the human skin and polymer based materials against damaging effects of sunlight. 4-methylbenzylidene camphor (4-MBC) and octocrylene (OC) are UV filter compounds which exhibit some of the typical characteristics of persistent organic pollutants (POPs). They have been shown to accumulate in the food chain due to their lipophilicity and stability against biotic degradation. In addition, 4-MBC was reported to show estrogenic activity in cell cultures and animals. In order to gain more insight into the environmental occurrence and behavior of UV filters, we analyzed fish which acts as a "sampling device" by accumulating persistent lipophilic compounds.

Fish (brown trout, *Salmo trutta fario*) were caught at short distances downstream from the discharge points of waste water treatment plants (WWTP) in 7 Swiss midland rivers and analyzed for 4-MBC and OC using gas chromatography / mass spectrometry. In order to link the concentrations to the WWTP input for each river, methyl triclosan (MT), a chemical marker for the domestic wastewater load to surface waters, was included in the analytical protocol [1, 2].

The UV filters 4-MBC, OC, and the chemical marker MT were detected in all 19 fish samples from 7 rivers. Average concentrations were 50 – 1800, 40 – 2400, and 130 – 2100 ng/g lipid weight for 4-MBC, OC, and MT, respectively. Generally, the levels of OC were higher than those of 4-MBC. As a general trend, UV filter concentrations increase with MT levels, indicating that WWTP are major sources of UV filters. This finding was different than for various Swiss lakes where in earlier studies direct inputs from swimming and bathing were identified as an important entry pathway of UV filters during summer.

Comparison of the results with concentrations of UV filters in fish from Swiss lakes [3] indicates further different behavior of 4-MBC and OC in the environment: Whereas concentrations of 4-MBC were somewhat lower in lake fish than in river fish, OC was not even detectable in lake fish. Lower levels can be explained by a higher dilution of the contaminants in lakes; however, the absence of OC may be due to compound specific environmental behavior.

References:

[1] H.-R. Buser, M. E. Balmer, P. Schmid, M. Kohler, Environmental Science & Technology **40**, 1427 (2006).
[2] Environmental Science & Technology Online News of January 18, 2006: http://pubs.acs.org/subscribe/journals/esthag-w/2006/jan/science/te_sunscreens.html
[3] M. E. Balmer, H.-R. Buser, M. D. Müller, T. Poiger, Environmental Science & Technology **39**, 953 (2005).

Collaborations:

Federal Office for the Environment (FOEN)

Title: **Plant Physiological Analysis at Norway Spruce Drill Cores using LA-HR-ICP-MS**

Researchers: Andrea Ulrich, Timothee Barrelet

Institute/Group: Laboratory of Analytical Chemistry, Empa

Project Description:

Investigations on the distribution of macronutrients such as sulphur, phosphorous, potassium or calcium in trees are of high interest in plant physiological research. Especially information about seasonal element variations within single tree rings could improve metabolism studies but were so far not accessible. Thus, a micro-analytical method involving LASER ablation coupled to a double-focusing magnetic sector field inductively coupled plasma mass spectrometer has been developed for this task. Method development is especially challenging because of the difficult sample consistency, the relatively low P and S concentrations in wood, a relatively high sulphur background levels in ICP-MS and the unavailability of appropriate calibration standards. Thus, careful optimization and suitable quantification strategies for direct micro-analysis were required.

Critical aspects in method development and possible strategies to reduce background levels were discussed as well as different calibration strategies. The method was applied to investigations in Norway spruce drill cores from different sampling sites. Results of analyses in distinct zones within single tree rings for selected elements could be archived and were interpreted.

References:

[1] T. Barrelet, A. Ulrich, H. Rennenberg, U. Krähenbühl, *Seasonal profiles of sulphur, phosphorus and potassium in Norway spruce wood*, Plant Biology 462-469 (2006)

[2] T. Barrlet, *Norway Spruce as an Environmental Archive for Sulphur Dioxide*, Inauguraldissertation der Philosophisch-naturwissenschaftlichen Fakultät der Universität Bern, January 2006

Collaborations:

Prof. Krähenbühl (University of Bern); F. H. Schweingruber, D. Nievergelt and J. Esper (WSL); J. Kaplan (Botanical Institute, University of Bern); H. Rennenberg (University of Freiburg im Breisgau, Germany); R. Struis (PSI); C. Ludwig (EPFL)

Title: **Tracer Doped Lubrication Oils: A New Method to Investigate the Influence on Particle Formation**

Researchers: Andrea Ulrich, Adrian Wichser

Institute/Group: Laboratory of Analytical Chemistry, Empa

Project Description:
Due to increasing concern about health effects of fine and ultra-fine particles (nanoparticles) from combustion engines, diesel particle filters (DPF) became a key technology for minimising soot emission of heavy duty engines and passenger cars in the last years. In this respect, a very important parameter is the irreversible plugging of the DPF with non-combustible ashes. Lubrication oil has a significant influence. Thus, the effects of different lubrication oils on particle formation and emission are of major interest. The quality of lubrication oil, especially the ash and the sulphur content has a certain influence on loading and required regeneration intervals of a diesel particle filter system.
It is evident to investigate how different lubrication oils influence the particle formation and the contribution of oil to total particle emissions. Therefore, a tracer study on a modern diesel engine has been performed with different lubrication oils. The comparison of non-doped oils with oils doped with defined tracers should enlighten the contribution of the oil to the particle formation.

References:
A. Ulrich, Wichser, J. Czerwinski, *Tracer doped lubrication oils: A new method to investigate the influence on particle formation*, Proceedings 10th International ETH-Conference on Combustion Generated Particles, August 21-23, 2006, Zürich.

Collaborations:
Prof. J. Czerwinski (University of Applied Sciences, Biel)

Title: **Chlorinated Paraffins (CPs) in Swiss Environmental Samples**

Researchers: Saverio Iozza[1)3)], Claudia Müller[2)], Peter Schmid[1)], Michael Oehme[3)]

Institute/Group: [1)]Laboratory for Analytical Chemistry, Empa
[2)]ETHZ (master thesis, carried out at Empa)
[3)]Department of Chemistry, University of Basel

Project Description:

Our research presents a general analytical approach suitable for the determination of chlorinated paraffins (CPs) in various matrices (fish, sea birds, sediment, human milk, soil, compost and spruce needles). Electron ionisation tandem mass spectrometry (EI-MS/MS) was used for a fast determination of the total CP amount (sum of short, medium and long chain CPs) and electron capture negative ion mass spectrometry (ECNI-MS) was employed for the evaluation of congener group patterns (specification of chain length and chlorination degree). An overview of the analytical method for all these matrices is described elsewhere [1].

Actually, only few data about CP environment levels in Switzerland are available. For the first time, CPs were determined in soils and composts. Furthermore, one sediment core from Lake Thun was analysed to get a time chart of the CP deposition of the last 120 years.

CPs were determined in nine selected soil samples (0-10 cm layer) collected by the Swiss national soil monitoring network (NABO). CPs were found in all nine sample sites. Total CP concentrations were between 34 and 151 ng/g dw (dry weight) (median: 45 ng/g dw). The ratio between short chain and medium chain CPs varied between 8 and 51% (median: 37%). The calculated chlorine content was similar for all samples. The mean calculated chlorine content of the short chain and medium chain CPs was 61% (60.1-62.5%) and 55% (53.9-55.6%), respectively.

Compost can contain significant amounts of pollutants that enter via aerial deposition on green waste or via direct contamination to input material. Three compost samples were analysed to determine CPs. The total CP level was between 182-614 ng/g dw. Short and medium chain CP concentrations were 58-138 ng/g dw and 29-248 ng/g dw, respectively. The average calculated chlorine content of the short chain CPs was 62% (61.0-63.3%) and of the medium chain CPs 59% (57.9-59.5%).

A dated sediment core from Lake Thun was analysed to investigate the historical record of the CP deposition of the last 120 years. In this core CPs started around 1965 (19 ng/g dw) followed by a slow increase. In the 1980s, CP concentrations showed a fast raise. The maximum level which is between 46 and 58 ng/g dw is reached around 1985 and is held till the surface sediment slice (2005). No decrease can be observed in this time span.

References:

S. Iozza, J. Hüttig, M. Reth, Z. Zencak, M. Oehme, Organohalogen Compounds **68**, 2404-2407 (2006).

Collaborations:

Renato Zenobi (Joint Master Thesis, Laboratory of Organic Chemistry/ETHZ and Laboratory of Analytical Chemistry/Empa, carried out by Claudia Müller at Empa), André Desaules (Agroscope Reckenholz-Tänikon ART), Rahel Brändli (ART), Thomas Kupper (Eawag), Christian Bogdal (Empa).

Title: **Brominated Flame Retardants and other Endocrine Disrupting Chemicals in the Ecosystem of Lake Thun - Environmental Fate and Correlation to Biological Effects (FLEET)**

Researchers: Christian Bogdal[1], Martin Kohler[1], Peter Schmid[1], Heinz Vonmont[1], Martin Scheringer[2], Konrad Hungerbühler[2]

Institute/Group: [1]Laboratory for Analytical Chemistry, Empa
[2]Institute for Chemical and Bioengineering, ETH

Project Description:
The main goal of this project consists in assessing the environmental behaviour of some prominent persistent organic pollutants (POP) as well as in studying possible correlations between the presence of endocrine disrupting chemicals (EDC) in Lake Thun and whitefish malformations, occurring since the year 2000. A comprehensive appraisal of the fate of POP, once they are released into the environment, is targeted first by sampling and analysing their concentrations in different matrices of a local ecosystem. In a second step, the partitioning of environmental contaminants between water, air, sediments and biota will be modelled by a multicompartmental mass balance model.
The chemicals under close scrutiny in this research are primarily brominated flame retardants, including decabromodiphenylether (deca-BDE) and hexabromocyclododecanes (HBCD), currently used to reduce the flammability of numerous combustible materials and consumer goods. Next to flame retardants, formerly used industrial chemicals with endocrine disrupting effects, like polychlorinated biphenyls (PCB) and polychlorinated naphthalenes (PCN) are considered, too.
The issue of fate and temporal trend of POP in the environmental has first been addressed by the analysis of a dated sediment core recovered from the deepest point (217 m) in the middle of Lake Thun. Dating of sediments combined with their chemical profile determinations clearly confirmed the effectiveness of a phase-out of hazardous substances on the environmental burden, even if previously used chemicals like PCB and PCN can persist in the environment over several decades. Indeed, the profile of PCB concentrations is characterised by a maximum around 1958 (21 ng/g dry weight). Since the 1960s, concentrations have gradually decreased (3.8 ng/g dry weight in surface sediments). Similarly, PCN concentrations peaked around 1930 (2.1 ng/g dry weight) and are currently 0.3 ng/g dry weight.
Besides the decreasing levels of legacy pollutants in Lake Thun sediments, investigation of emerging pollutants like the brominated flame retardants raise serious concerns. Concentrations of deca-BDE and HBCD, two currently used high volume production chemicals, have steadily been increasing since the 1980s. Compared to the historical record of legacy pollutants (PCB and PCN), concentrations of these flame retardants remain low (<1 ng/g dry weight) in recent sediment layers. However, the sharp increase of residues of these substances in the environment certainly needs closer attention.

Collaborations:
Rik Eggen, Erwin Grieder, Anja Liedtke, Michael Sturm, (Eawag); Daniel Bernet, David Bittner, Helmut Segner, Thomas Wahli, (University of Bern); Ueli Ochsenbein, Daniel Scheidegger, Markus Zeh (Canton of Bern).

Title: **Elemental Analysis of Ancient Bronze and Silver Objects by LA-ICP-MS: An Optimized Methodology Using a new Mountable Cell Design**

Researchers: Adrian Wichser, Andrea Ulrich

Institute/Group: Laboratory for Analytical Chemistry, Empa

Project Description:
Element patterns are important criteria for dating, origin determination and authenticity verification in archeometallurgy and evident to define appropriate restoration methods. The chemical characterisation requires an exact quantification in concentration ranges of lower ppm levels (impurities) to % levels of the main alloy element components. Non- or low-destructive methods are preferable especially with regard to preserve antique objects.
LASER ablation inductively coupled plasma mass spectrometry (LA-ICP-MS) is a sensitive micro-analytical method with high detection power. A mountable LASER cell design provides the advantages of low destruction because no sampling is necessary as required for LA-ICP-MS with conventional cells or for usually applied techniques such as NAA or digestion methods prior to AAS, ICP-OES or ICP-MS analysis.
Empa developed a first mountable cell for the analysis of artificial antique silver objects some years ago. However, problems in positioning, especially at uneven surface areas, a reduced transport efficiency and long washout time lead to development of a novel cell design. Thanks to the new cell design, the positioning is easier and more precise also on uneven surfaces. Moreover, the washout is much faster due to a new nozzle gas inlet. The cell was applied to analysis of several antique silver and bronze objects. Methods and calibration strategies for the analysis of bronze and silver objects have been developed and validated by comparison to established methods such as NAA and acid digestions prior ICP-OES or ICP-MS analysis. Potential and limitations of the LA-ICP-MS for the analysis of antique metal objects will be discussed in a planned paper.

References:
A. Wichser, A. Ulrich, *LA-ICP-MS for Authentication of Antique Bronze Objects Potentials and Limitations*, Poster at the 8th European Workshop on LASER Ablation in Elemental Analysis, July 19-21, 2006, Zürich.

Collaborations:
University of Oxford; archaeologists, museums and art collectors

Title: **Investigation of Isotope Fractionation and Composition Variation Effect in Deformed Double Chamber Hunting Munitions by ICP-MS**

Researchers: Andrea Ulrich, Adrian Wichser

Institute/Group: Laboratory for Analytical Chemistry, Empa

Project Description:

Twin-core projectiles belong to recent generation of high performance cartridge hunting munitions and consist of two lead cores with different hardness, coated by tombak or steel jackets. Some back tail cores are additionally jacketed for separation from the softer tip core. The core weight ratio is mostly 50:50. A tail groove at the rear end of the projectile reliably bonds the tail core with the external jacket. The shooting velocity varies for twin-core types between 800 and 900 m/s at shooting start with an average decrease by 10-15 m/s. Due to friction and collision energy, the lead is exposed to high temperature which can reach even melting temperature. Thus, transformations or enrichment or depletion effects are likely, which could change composition in fragments and residuals. The presented study investigates, if an effect on trace element patterns or lead isotope ratios occurs by comparison of new and fired projectiles of the same munitions type and manufacturing lot. Effects of melting processes due to high friction and collision energy could be clearly detected for the tip core lead. Certain elements clearly shown a trend to depletion, e.g. Sb and As, whereas other element concentrations remained stable (e.g. Ag, Bi). No melting effects were observed for the tail core lead. Thus, no fractionation or change in composition was detectable. Neither for tail nor for tip core lead isotopic fractionations of lead isotope ratios was observed.

References:

[1] A. Ulrich, Ch. Moor, H. Vonmont, H.-R. Jordi, M. Lory, *ICP-MS trace-element analysis as a forensic tool*, Analytical and Bioanalytical Chemistry, **378** (4), 1059 – 1068 (2004).

[2] A. Ulrich, A. Wichser, M. Vogler, *Investigation of isotope fractionation and composition variation effect in deformed double chamber hunting munition by ICP-MS*, Contribution to 2007 European Winter Plasma Conference, 18.-23.2.2007,Taormina, Italy.

Collaborations:

Wissenschaftlicher Dienst der Stadtpolizei Zürich

Title: **Concentrations of particulate matter (PM10, PM2.5, PM1) in Switzerland; Annual and seasonal trends and spatial variability**

Researchers: Robert Gehrig, Christoph Hüglin, Brigitte Buchmann

Institute/Group: Empa; Swiss Federal Laboratories for Materials Testing and Research
CH-8600 Dübendorf

Project Description:
Measurements of PM10, which is considered to represent the thoracic fraction of the ambient particles, have been performed within the Swiss National Monitoring Network (NABEL) already since 1997. Due to the increasing public interest for the finer alveolar fraction (PM2.5), the measurement programme of the network has been extended to PM2.5 measurements at seven sites in 1998 [1]. From 2003 also PM1 measurements were added to the measurement programme. This fraction provides, better than PM2.5, information on the particle sources, as PM1 represents in reasonable approximation combustion particles and secondary aerosol, while PM10-1 can be attributed to mechanically produced and geogenic particles. Long-term data sets of parallel measurements of the different PM fractions are still scarce if not lacking for Europe. Therefore, the Swiss data set forms a unique data basis for investigating the temporal and spatial behaviour of PM1 and PM2.5 compared to PM10. It includes meanwhile eight years of parallel PM2.5 and PM10 data and three years of parallel PM1 and PM10 data at various sites representing different important situations with respect to human PM exposure.
From the analysis of long-term parallel measurements of PM1, PM2.5 and PM10 concentrations in Switzerland the following conclusions can be drawn:
• At all sites the concentrations of the different size fractions were highly correlated on the level of daily values. Unless strong and variable local sources of coarse particles are present, parallel measurements of PM1, PM2.5 and PM10 provide only limited additional information. In order to make efficient use of the financial and personal resources, such parallel measurements can be restricted to a few carefully selected sites in a monitoring network.
• Also the comparison of daily PM values from different sites often show quite high correlation. The analysis of the Swiss data indicates that this has primarily meteorological reasons. Even distant sites show good correlations if they are situated in an area with similar meteorological conditions. However, the correlations drop drastically if this is not the case i.e. if the sites are divided by high topographical obstacles (Alps) or by an inversion layer.

References:
[1] R. Gehrig. and B. Buchmann, Characterising seasonal variations and spatial distribution of ambient PM10 and PM2.5 concentrations based on long-term Swiss monitoring data, Atmos. Environ. 37(19): 2571-2580 (2003).

Collaborations:
Federal Office for the Environment (FOEN) Bern

Title: **Trace gas and δ13C - CO2 analysis by FTIR spectroscopy**

Researchers: Joachim Mohn and Lukas Emmenegger

Institute/Group: Empa, Laboratory for Air Pollution and Environmental Technology

Project Description:
Fourier Transform Infrared (FTIR) spectroscopy is a powerful technique, widely used for gas analysis in environmental and industrial studies 1-3. We have developed a method, based on a portable, commercially available, 0.5 cm-1 resolution FTIR spectrometer, which allows simultaneous on-line analysis of most important atmospheric trace gases (CO2, CH4, N2O, CO) as well as the 13C/12C isotopic ratio of ambient CO2 (δ13C-CO2). The setup was optimized to yield very high temperature and pressure stability, and an excellent spectral signal to noise ratio. A precision of 0.06-0.10 % for CO2, CH4, N2O and 0.19 % for CO was obtained, which is competitive with accepted single-component trace gas measurement techniques.
The 13C/12C ratio of atmospheric CO2 (δ13C-CO2) is a powerful tool to quantify CO2 flux strength of different ecosystem compartments. To date, the majority of CO2 isotope studies have required air sample collection at remote locations, followed by laboratory analysis with isotope ratio mass spectrometry (IRMS), which limits the number and frequency of measurements. In our project we demonstrate the utility of Fourier transform infrared spectroscopy (FTIR) for online analysis of δ13C-CO2 in ambient air. Quantification relies on a novel calibration strategy based on a robust partial least squares (PLS) algorithm in combination with a set of multi-component standard spectra. Typically the instrument achieves a precision of 0.15 per mil an accuracy of 0.4 per mil for δ13C-CO2 4. The ability of the analyzer for on-line δ13C-CO2 was also tested outdoors at the Chamau micrometeorologic grassland station and compared to standard laboratory-based MS measurements made on field-collected flask samples. The average difference for δ13C-CO2 between FTIR and IRMS after removal of two outliers was 0.5 per mil (n = 83). Very good agreement was also found for the carbon isotope content of respired CO2 (δ13CR) determined by either FTIR spectroscopy or IRMS.

References:
[1] Mohn, J.; Forrs, A. M.; Brühlmann, S.; Zeyer, K.; Lüscher, R.; Emmenegger, L., Time-resolved ammonia measurement in vehicle exhaust. Int. J. of Environment and Pollution 2004, 22, (3), 342-356.
[2] Mohn, J.; Beck, U.; Zeyer, K.; Emmenegger, L., Calibration of reactive process gases for the characterization of semiconductor processes by FTIR. Journal of Molecular Structure 2005, (744-747), 247-253.
[3] Mohn, J.; Galli, R.; Emmenegger, L., Real-time measurement of reactive process gases in microelectronics by means of FTIR spectroscopy. Chemie Ingenieur Technik 2006, 78, (10), 1524-1530.
[4] Mohn, J.; Werner, R. A.; Buchmann, B.; Emmenegger, L., High-precision δ13CO2 analysis by FTIR spectroscopy using a novel calibration strategy. Journal of Molecular Structure 2007, in press.

Collaborations:
N. Buchmann, W. Eugster, R.A. Werner, M.J. Zeeman (ETH Zürich, Inst. of Plant Science)

Title: **Diesel exhaust or wood smoke? Source speciation of aerosol particles in ambient samples with X-ray microscopy**

Researchers: Martine Vernooij[1], Martin Mohr[1], Ralf Kägi[2], Robert Gehrig[1]

Institute/Group: [1]Empa, Swiss Federal Laboratories for Materials Testing and Research CH-8600 Dübendorf,
[2]EAWAG, Swiss Federal Institute for Environmental Science and Technology, CH-8600 Dübendorf.

Project Description:

In urban areas, carbonaceous particulate matter typically accounts for 25-50% of the ambient PM 2.5 (particles with a diameter < 2.5 μm). The major constituents of these carbonaceous aerosols are soot particles from diesel and wood combustion. With scanning transmission X-ray microscopy (STXM), it is now for the first time possible to gain more detailed information on the variation in structures of single soot particles depending on the combustion source.

The morphology of diesel and wood smoke soot particles is very similar. Both consist of chains of primary particles with a graphitic structure (Fig. 1a). First STXM results, however, indicate a clear difference between the chemical structures of the particles from the two different sources. Diesel soot particles contain a dominant spectral signature at 285 eV from unsaturated (multiple) carbon bonds in the solid cores of the primary particles and a very sharp exciton resonance at 290 eV (Fig. 1b). The spectra from graphite also show these features, confirming the partial graphitic nature of diesel soot. The spectra of wood soot have a less graphitic nature (Fig. 1b), but show a firm peak at 287.2 eV from C-OH bonds. These source specific signatures may allow discrimination between wood and diesel soot particles in ambient air samples. We collected such samples (with particle sizes<1mm) directly next to an arterial road in Zurich. First results show that the specific C(1s) NEXAFS peaks of the two combustion sources can be assigned to individual particles (Fig. 1c). The spectrum of particle 1 shows the characteristics of a diesel combustion source, the spectrum of particle 2 of wood combustion. Spectra, however, do not exactly match. Additional peaks are found, for example, between 295 and 300 eV in particle 1, which might be the result of particle aging. Future measurements are planned to investigate this aging effect and to quantify the relative abundance of diesel and wood combustion particles in ambient samples from different rural and urban locations (i.e. wood or diesel combustion dominated).

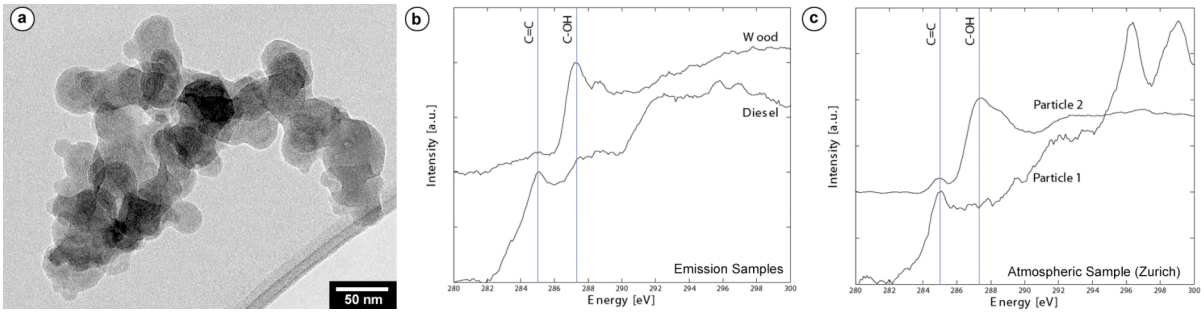


Figure 1: a) TEM bright field image of soot particle from wood combustion, b) C(1s) NEXAFS spectra of single soot particles from wood and diesel combustion, c) C(1s) NEXAFS spectra from two particles in an atmospheric sample that was collected along an arterial road in Zurich.

Collaborations:
Thomas Huthwelker, George Tzvetkov, Jörg Raabe, Paul Scherrer Institute, CH-5232 Villigen
Norbert Klippel, Verenum, Langmauerstrasse 109, CH-80006 Zurich

Title: **Evidence for increasing NO2 emissions from road traffic as deduced from long-term measurements**

Researchers: Christoph Hueglin, Brigitte Buchmann

Institute/Group: Empa; Swiss Federal Laboratories for Materials Testing and Research
CH-8600 Dübendorf

Project Description:
Road traffic is a major source of nitrogen dioxide (NO2) and nitrogen oxide (NO), the latter compound rapidly oxidizes in the atmosphere to NO2. NO2 is an important air pollutant, concerns over health effects of NO2 led to the enforcement of air quality standards in Switzerland and in many other countries.
Long-term trends of road traffic emissions of NO2 and NO have been investigated by analysis of air quality data from a measurement site near Haerkingen, Switzerland [1]. The Haerkingen site belongs to the Swiss national air pollution monitoring network NABEL. It is a roadside site located about 20m north of a four-lane motorway with 55'000–80'000 vehicles per day.
Depending on wind direction, the site is influenced either by regional background air (background sector) or by emissions from the adjacent motorway (traffic sector). Trends of road traffic emissions can be assessed from the difference of average air pollutant levels at winds from traffic and background sectors.
NO and NOx (NOx = NO + NO2) emissions from road traffic steadily decreased from 1992 to 2004 mainly due to the introduction of catalytic converters in the early 1990s and the subsequent specification of emission standards for road traffic vehicles. During the last years NO shows a steeper decline than NOx, which is due to increasing NO2 road traffic emissions as also indicated by an increasing NO2/NOx ratio.
A significant fraction of NO2 measured at the Haerkingen site results from secondary formation via reaction of NO with O3. However, the observed increase in NO2 cannot be caused by increasing secondary NO2 formation, because the difference of O3 at traffic and background sector conditions remained constant during the last years. We conclude that the observed trend of primary NO2 emissions from road traffic is due to the increasing penetration of diesel vehicles in Switzerland. The NO2/NOx emissions ratio of diesel vehicles is much higher compared to gasoline vehicles. New engine and exhaust gas after-treatment systems such as particle filters for diesel engines might have also contributed to the observed trend.

References:
[1] Ch. Hueglin, B. Buchmann, and R.O. Weber, Long-term observation of real-world road traffic emission factors on a motorway in Switzerland, Atmos. Environ. 40: 3696-3709 (2006).

Collaborations:
Federal Office for the Environment (FOEN) Bern.

Title: **Oxygenated Volatile Organic Compounds (OVOCs) in Switzerland: From the polluted boundary layer to the free troposphere**

Researchers: Geir Legreid, Stefan Reimann, Martin Steinbacher, Johannes Stähelin, Jacob Balzani Lööv

Institute/Group: Empa; Swiss Federal Laboratories for Materials Testing and Research CH-8600 Dübendorf

Project Description:

Oxygenated organic compounds (OVOCs) play an important role in tropospheric chemistry. Such compounds are, for example, important intermediates in the oxidation of many primary pollutants and precursors for peroxyacylnitrates (PANs). PANs are carriers of reactive nitrogen potentially releasing free radicals at remote sites. In other words, the OVOCs influence the oxidizing capacity and the ozone-forming potential of the atmosphere.
They may also contribute significantly to the formation of secondary organic aerosols (SOAs). Knowledge of their distribution and sources is still restricted to mostly short-time measurements of few compounds.
In this study 21 OVOCs and selected non-methane hydrocarbons (NMHCs) were measured with a recently developed double adsorbent sampler coupled to a gas chromatograph-mass spectrometer (GC-MS). Measured compounds were aldehydes and ketones, key intermediates of tropospheric chemistry as well as primary anthropogenic and biogenic compounds; alcohols, emitted by both anthropogenic and biogenic sources; and ethers and esters, which are mostly emitted by anthropogenic sources. Furthermore, selected anthropogenic and biogenic NMHCs were measured. Measurement locations were a highway tunnel (near Zürich), an urban background station in Zürich, a remote Alpine site and a village in the Swiss Alps (Roveredo), in which the air was highly influenced by wood burning emissions in winter.
The OVOC measurements in the highway tunnel were used to estimate the contribution of the Swiss vehicle fleet to OVOC emissions [1]. Ethanol was the most abundant compound found in this study with an emission factor (EF) of 10 mg/km. This compound was not only related to exhaust emissions, but also to the use of window wiper fluids. In total, the OVOCs represented 54 % of the measured volatile organic compounds (VOCs) from mobile sources.
The measurements indicated that OVOCs were mainly emitted by the heavy-duty vehicles (HDV), whereas the light-duty vehicles (LDV) dominated the emissions of the NMHCs. The comparison with earlier campaigns at the same site confirmed the large decrease of organic exhaust emissions under highway conditions, due to steady improvements of vehicle technology.
The measurement campaigns in Zürich were performed in order to gather information about the sources of the OVOCs in Switzerland. These were the first data collected for many of the OVOCs in the Swiss boundary layer, and are therefore unique in this respect. Also in Zürich, ethanol was the dominating compound measured throughout all seasons. Its anthropogenic origin was indicated by higher mixing ratios in winter than in summer, which was also the case for known anthropogenic pollutants like benzene and acrolein. On the other hand, compounds with additional biogenic sources like methanol, acetone and isoprene had higher levels during summer. Local sources were estimated to contribute to 40 % and 49 % to the OVOC mixing ratios in summer and winter, respectively. Combustion was responsible forabout 75 % of these local sources independent of the season. About 50% of both the OVOC and NMHC levels in Zürich were explained by the regional background, which

included regional biogenic and anthropogenic sources in addition to secondary production. From the calculation of the incremental ozone production, it was estimated that the OVOCs explained 40 % of the total VOC ozone production. Local OVOC sources were responsible for 16 %.
The campaigns at the high-alpine station Jungfraujoch aimed at a climatological description of OVOCs within the free troposphere above Europe and at a European source allocation. At this site acetone, methanol and acetaldehyde were the most abundant OVOCs, being responsible for 82 % of the measured VOCs in summer and 51 % in fall. The measured mixing ratios of these compounds were generally in accordance with other studies from remote locations. Source regions for the pollutants at Jungfraujoch were estimated from measurement days with influence from the polluted boundary layer (PBL) by applying a statistical trajectory model. The mainly anthropogenic compounds ethanol, ethyl acetate, butane and benzene had two main source regions; southern Germany and northern Italy, both heavily populated and industrialized areas. For the two industrial solvents methyl acetate and butanone the main source region was solely northern Italy. Methanol and acetone, compounds which also have large biogenic sources, had their main contribution from northern Italy as well. This is probably due to the higher biogenic activity south of the Alps compared to the north.

References:

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Collaborations:

A. Prevot (PSI), J. Stähelin (ETH Zürich)

Title: **The Influence of Climate Conditions on Weighing Results**

Researchers: Samuel Wunderli, Veronika R. Meyer

Institute/Group: Swiss Federal Laboratories for Materials Testing and Research EMPA St. Gallen

Project Description:
Climate conditions have an influence on weighing values which can easily be observed. Weighing operations can be accomplished at a relative uncertainty in the 10-5 range with regard to the technical performance of the balance but the buoyancy effect is in the 10-3 range for objects with density around 1000 kg m-3. The uncertainty of buoyancy can easily dominate the uncertainty of a mass determination. Therefore it is wrong to display the uncertainty of a weighing operation by the technical data of the balance alone. Buoyancy and its cause, the air density, depend on the climate parameters atmospheric pressure, air temperature, and air humidity; as a consequence, the uncertainty of the buoyancy depends on the uncertainty of the climate data.
The influence of atmospheric pressure, air temperature, and relative air humidity on weighing results was determined in a long-term experiment. Two magnesium and three aluminium cylinders were weighed in a room without air conditioning over a period of more than three months. The climate parameters were automatically registered every 10 minutes. The climate data allow to calculate the masses from the weighing values which are subject to air buoyancy. It is then possible to check the validity of the empirical Schwartz equation for the calculation of the air density. The match between theory and experimental results is excellent for the influence of pressure and temperature and is weaker for the influence of humidity. The influence of this latter parameter on weight values is rather low and may be corrupted by water adsorption effects on the surfaces. It was found that the climate parameters can be looked at as triangular distributions rather than the previously proposed rectangular ones for the calculation of the weighing uncertainty budget.
For mass determinations with an accuracy of approx. 10-3 (depending on the density of the weighing object) it is necessary to correct the weight value by the buoyancy factor. An air-conditioned weighing laboratory is to be preferred although it only eliminates the influences of temperature and humidity but not the one of atmospheric pressure; this latter effect is the most prominent one.
The step from weighing values to masses reduces the long-term relative standard deviation from typically 2-5 ppm to less than 1 ppm.

Reference:
M. Pozivil, W. Winiger, S. Wunderli, and V.R. Meyer, The Influence of Climate Conditions on Weighing Results, Microchim. Acta 154, 55-63 (2006).

Collaborations:
Martin Pozivil, Walter Winiger, Kantonsschule Heerbrugg

Title: **Arsenite and Arsenate Binding to Dissolved Humic Acids: Influence of pH, Type of Humic Acid and Aluminum**

Researchers: Johanna Buschmann, Alexandra Kappeler, Ursula Lindauer, David Kistler, Michael Berg, Laura Sigg

Institute/Group: Department of Water Resources and Drinking Water, Eawag

Project Description:

The fate of arsenic in the aquatic environment is influenced by dissolved natural organic matter (DOM). Using an equilibrium dialysis method, conditional distribution coefficients (Dom) for As(III) and As(V) binding onto two commercial humic acids were determined at environmentally relevant As/dissolved organic carbon (DOC) ratios and as a function of pH. At all pH values, As(V) was more strongly bound than As(III). Maximum binding was observed around pH 7, which is consistent with H+ competition for binding sites at low pH values and OH- competition for the arsenic center at high pH. For both oxidation states, Dom values increased with decreasing As/DOC ratios. Dom values were fitted as a function of the As/DOC ratio for As(III) and As(V). Compared to the aquatic humic acid, the terrestrial humic acid had a higher affinity for arsenic binding with 1.5-3 times higher Dom values under the same conditions. Al3+ in excess to arsenic successfully competed for strong binding sites at low As/DOC ratios. Under environmentally relevant conditions, about 10% of total As(V) may be bound to DOM, whereas >10% of As(III) is bound to DOM at very low As/DOC ratios only. Binding of arsenic to DOM should be considered in natural systems.

References:

J. Buschmann, A. Kappeler, U. Lindauer, D. Kistler, M. Berg, and L. Sigg,. *Environ. Sci. Technol.*, **40**, 6015–6020 (2006).

Title: **A Micro-Flowsensor Reveals the Structure of the Bottom Boundary Layer of Lakes**

Researchers: Andreas Brand, Beat Müller, Alfred Wüest, Christian Dinkel, Bernhard Wehrli

Institute/Group: Swiss Federal Institute of Aquatic Science and Technology, Eawag, CH-6047 Kastanienbaum, Switzerland

Project Description:

The currents in the lowest few mm of the bottom boundary layer of lakes are highly important for the dissipation of kinetic energy and for chemical processes like oxygen transfer into the sediment. So far, no high-resolution flow velocity profiles close to the sediment water interface have been reported for such systems because a suitable flow meter was lacking. We developed a novel method for the *in situ* measurement of extremely low flow velocities. The sensor used (Figure 1 left) is based on a hydrogen transducer that is surrounded by a gas reservoir. It measures the change in the partial pressure of a tracer gas due to advective transport on the outside of the reservoir tip. The sensor was tested in the laboratory for its suitability for in situ measurements on lake floors. These tests were focusing on the sensitivity of the sensor to pressure, temperature and direction dependence of its signal. The flow sensor proved to be insensitive to temperature changes between 5 and 15 °C. The sensor is robust against relative pressure changes, and angular differences in the sensitivity can be calibrated. First field campaigns provided promising results and gave detailed insight into the structure of vertical flow in the last millimeters above the sediment-water interface at shear velocities as low as 0.13 ± 0.02 cm s^{-1} [1].

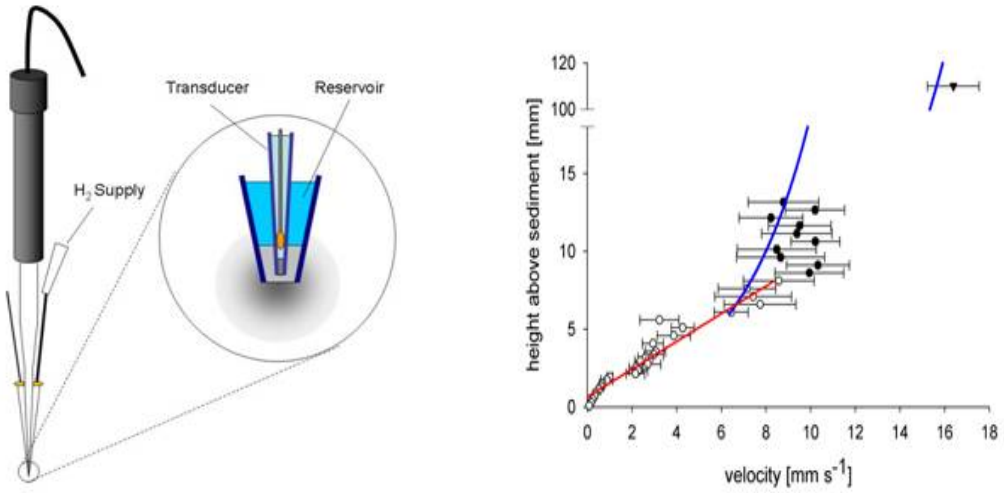

Figure 1. Left: Design of the flow sensor. A hydrogen transducer is surrounded by a perma-nently flushed reservoir. Right: Flow profile recorded in Lake Alpnach. The linear viscous boundary layer (red line) merges into the logarithmic profile (blue line).

References:

[1] A. Brand, B. Müller, A. Wüest, C. Dinkel, N.P. Revsbech, L.P. Nielsen, O. Pedersen, L.R. Damgaard, L.H. Larsen, and B. Wehrli, *Microsensor for in-situ flow measurements in benthic boundary layers at sub-millimeter resolution with extremely slow flow,* L&O: Methods (in print).

Collaborations:

L. R. Damgaard, H. Larsen (Unisense A/S), N. P. Revsbech (University of Aarhus)

Title: **Carbon and hydrogen isotopes on methane of the Lake Kivu water column**

Researchers: Carsten J. Schubert, Francisco Vazquez

Institute/Group: Department of Biogeochemistry, Surf, Eawag

Project Description:

The analysis of trace gases in aquatic systems is an area of increasing importance. Especially the green house gases CO2, CH4, and N2O are of particular interest. Lake Kivu is an East African rift lake between Rwanda and the Democratic Republic of Congo (Figure 1) with maximum depth of 485 m and a volume of 550 km3. Seasonal mixing reaches only a depth of 50–80 m. Below, about 300 km3 STP (gas volume at 0° C and 1 atm) carbon dioxide (CO2) and 60 km3 STP methane (CH4) are dissolved in the permanently stratified deep waters [1].

We were especially interested in the origin of the methane and used carbon and hydrogen isotopic measurements to get some insights into its source. There are basically three scenarios plausible: (1) thermogenic origin, i.e. methane was produced during the break down of organic matter under higher temperatures, (2) methane was produced by bacteria via CO2 reduction (dominant in the marine environment), and/or (3) methane was produced via acetate fermentation (dominant in freshwater environments). Methane in marine sediments can be defined isotopically by δ13C values from- 110 to -60 ‰, and δD values from -250 to -170 ‰. In contrast, methane from freshwater sediments ranges from δ13C = -65 to -50 ‰ and δD = -400 to -250 ‰ [2]. Thermal methane shows δ13C values of below - 50 ‰. We used two different devices to measure the isotopic composition. For carbon isotopes we used a Trace gas pre concentrating device connected to an Isoprime mass spectrometer (GV Instruments), where methane is oxidized to CO2 at 850 °C and then trapped in liquid nitrogen before the measurement in the mass spectrometer. For hydrogen isotopes we used a gas chromatograph in which methane was separated from other gases and then cracked in a ceramic tube at 1450 °C before being measured as H2.

The methane showed δ13C values around - 62 ‰ below 260 m. Due to methane oxidation by microorganisms the δ13C values increased to -42 ‰ towards the surface. Deuterium isotope values were around - 250 ‰ and increased like the carbon values due to oxidation to -142 ‰ at 60 m.

Unfortunately these values lie exactly in the mixing zone of methane that would have been produced by either of the processes, namely carbonate production or acetate fermentation.

Since much of the CO2 in the Lake comes from volcanic activity, 14C dating of the prevailing gases might give a hint to the processes that formed the methane in Lake Kivu.

References:

[1] M. Schmid, M. Halbwachs, B. Wehrli, and A. Wüest, *Weak mixing in Lake Kivu: New insights indicate increasing risk of uncontrolled gas eruption,* Geochem. Geophys. Geosyst., **6,** Q07009, doi:10.1029/2004GC000892 (2005).

[2] M.J. Whiticar, E. Faber, and M. Schoell, *Biogenic methane formation in marine and freshwater environments: CO2 reduction vs. acetate fermentation-Isotope evidence*, Geochimica et Cosmochimica Acta 50, 693 - 709 (1986).

Title: **Endocrine Disrupting Compounds in the Aquatic Environment**

Researchers: Marc J-F Suter, Rik IL Eggen, Beate I Escher, Anja Liedtke, Victor Nesatyy, René Schönenberger, Etiënne LM Vermeirssen, A Christiane Vögeli

Institute/Group: Department of Environmental Toxicology, Eawag

Project Description:

After more than a decade of research, the actual exposure to endocrine disrupting compounds in the aquatic environment is well documented. Very often, direct chemical target analysis is combined with modeling based on information available for a given catchment. However, less information is available on the effect side, and it is rarely possible to link chemical data to biological effects. Possible reasons are that i) exposure dynamics are rarely taken into account, ii) one popular in vitro test, the yeast estrogen screen, is based on nuclear receptor mediated pathways, missing other modes of action, iii) it is not entirely clear how to deal with mixtures, particularly for chemicals with dissimilar modes of action, and iv) the effects of combinations of chemical and physical stress, like for instance UV and temperature, are not well understood.

For these reasons our research focuses on analyzing exposure dynamics [1], determining internal concentrations of anthropogenic chemicals in aquatic organisms and linking them with biological endpoints. Bile and gonadal fat samples have been analyzed in bream from various sites in The Netherlands and in white fish from Lake Thun, using bioassay-directed fractionation [2]. Furthermore, passive samplers have been investigated for their usefulness to mimic bioaccumulation, thus potentially reducing the need for animal exposure experiments [3].

The effects of multiple stressors are investigated on model organisms (green algae, zebra fish), specifically looking at the organismic stress response on the protein level, using two-dimensional LC coupled to mass spectrometry.

References:

[1] E.L.M. Vermeirssen, M.J.-F. Suter, P. Burkhardt-Holm, *Estrogenicity patterns in the Swiss midland river Lützelmurg in relation to treated domestic sewage effluent discharges and hydrology*, Environ. Toxicol. Chem. **25**, 2413-2422 (2006).

[2] A.C. Vögeli, PhD Thesis, ETHZ, in preparation.

[3] E.L.M. Vermeirssen, O. Korner, R. Schönenberger, M.J.-F. Suter, P. Burkhardt-Holm,*Characterization of environmental estrogens in river water using a three pronged approach: active and passive water sampling and the analysis of accumulated estrogens in the bile of caged fish*, Environ. Sci. Technol. **39**, 8191-8198 (2005)

Collaborations:

Swiss National Research Programme 50

R Zenobi (ETHZ), H Segner (Uni Bern), P Burkhardt-Holm (Uni Basel)

EU-Project EDEN, member of the CREDO cluster

Title: **Using Nitrogen Isotope Fractionation to Asses Abiotic Reduction of Nitroaromatic Compounds**

Researchers: Akané Hartenbach, Thomas B. Hofstetter, Michael Berg, Jakov Bolotin, René P. Schwarzenbach

Institute/Group: Water Resources and Drinking Water, Eawag

Project Description:

Compound-specific isotope analysis (CSIA) is an increasingly important tool for the qualitative and quantitative assessment of transformations of organic compounds in contaminated environments. To date, the use of CSIA has been mainly restricted to the elements *C* and *H*, although *N* constitutes a very important reactive center for many priority contaminants. To evaluate the potential use of *N* isotope effects in the fate assessment of organic contaminants, we investigated the *N* isotope enrichment during the abiotic reduction of 4 substituted nitroaromatic compounds (NACs), using two abiotic model reductants, namely Fe(II) sorbed to goethite (α-FeOOH) and juglone (8-hydroxy-1,4-naphthoquinone) in the presence of H2S. Substantial and virtually identical isotope enrichment factors, ε*N*, of about -30‰, indicative of the breaking of one N-O bond, were found for all NACs, regardless of the reductant involved and the substitution of the NAC. These results indicate that the ε*N*-values determined in our study could be representative for the reduction of aromatic NO2-groups and thus be used to assess the abiotic transformation of NACs qualitatively and quantitatively in complex anoxic environments.

References:

A. Hartenbach, T.B. Hofstetter, M. Berg, J. Bolotin, and R.P. Schwarzenbach, *Environ. Sci. Technol.*, **40**, 7710–7716 (2006).

Collaborations:

Eawag and ETH Zurich, Department of Environmental Sciences

Title: **Arsenic speciation by gradient anion exchange chromatography and high resolution ICP MS detection**

Researchers: Adrian A. Ammann

Institute/Group: Department of Environmental Toxicology, Eawag

Project Description:

Accumulating evidence on multiple toxicity aspects [1] of several arsenic species [2] curbed down regulatory limits (WHO, US-EPA) to 10 μg/L As. Considering chronic toxicological effects in combination with As-mobilisation from geological deposits into ground water [3], as is likely to pose one of the greatest threat to human health worldwide and it might be only the visible tip of the iceberg [4].

These intensified As-problems initiated many investigations to reassess the mobilisation, transformation and toxicity of even low concentrated As-species. Common As-species cover the whole range of molecule polarities, e.g. anions, cations and, depending on the pH, neutral molecules. This diversity and the growing number of As-compounds is a permanent challenge to ion chromatography (IC), as the over helming part of As-speciation is done by this method. A new strategy in As speciation by anion exchange chromatography was investigated. Using the high sensitivity of a HR ICP MS coupled to an anion exchange column allowed higher sample dilution factors. While analyte concentrations down to 100 ng/L were quantified, less sample matrix is loaded to the column which rendered the separation more robust and reliable. The narrow bore format of the exchanger provided flow rates (<300 μL/min) compatible to higher efficiency nebulizers which allowed a split less direct inlet to the MS. The gradient separation with a pH flexible and perfectly ICP-compatible eluent resulted in high efficiency As-speciation. The high throughput of the method proved to be very useful in an extended arsenite oxidation kinetic study [5].

References:

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[3] P.L. Smedley and D.G. Kinniburgh, *Applied Geochemistry* **17**, 517 (2002).
[4] D. Chakraborti, M.M. Rahman, K. Paul, U.K. Chowdhury, M.K. Sengupta, D. Lodh, C.R. Chanda, K.C. Saha, and S.C. Mukherjee, *Talanta*, **58**, 3 (2002).
[5] M.C. Dodd, N.D. Vu, A.A. Ammann, V.C. Le, R. Kissner, H.V. Pham, T.H. Cao, M. Berg, and U. von Gunten. *Environ. Sci. & Technol.* **40**, 3285 (2006).

Title: **Arsenic Removal from Groundwater by Household Sand Filters: Comparative Field Study, Model Calculations, and Health Benefits**

Researchers: Michael Berg, Samuel Luzi, Walter Giger

Institute/Group: Department of Water Resources and Drinking Water, Eawag

Project Description:
Arsenic removal efficiencies of 43 household sand filters (SFs) were studied in rural areas of the Red River Delta in Vietnam. Simultaneously, raw groundwater from the same households and additional 31 tubewells were sampled to investigate arsenic co-precipitation (CP) with hydrous ferric iron from solution, i.e. without contact to sand surfaces. From the groundwaters containing 10–382 μg/L As, <0.1–48 mg/L Fe, <0.01–3.7 mg/L P, and 0.05–3.3 mg/L Mn, similar average removal rates of 80% and 76% were found for the SF and CP experiments, respectively. The filtering process requires only a few minutes. Removal efficiencies of Fe, phosphate and Mn were >99%, 90% and 71%, respectively. The concentration of dissolved iron in groundwater was the decisive factor for the removal of arsenic. Residual arsenic levels below 50 μg/L were achieved by 90% of the studied SFs, and 40% were even below 10 μg/L. Fe/As ratios of ≥50 or ≥250 were required to ensure arsenic removal to levels below 50 or 10 μg/L, respectively. Phosphate concentrations >2.5 mg P/L slightly hampered the filter SF and CP efficiencies. Interestingly, the overall arsenic elimination was higher than predicted from model calculations based on sorption constants determined from CP experiments with artificialgroundwater. This observation is assumed to result from As(III) oxidation involving Mn, microorganisms and possibly dissolved organic matter present in the natural groundwaters. Clear evidence of health benefits (i.e. lowered arsenic burden) for people consuming sand-filtered water is demonstrated based on the results of hair analyses. The investigated SFs proved to operate fast and robust for a broad range of groundwater composition. SFs are thus also a viable option for mitigation in other arsenic affected regions. An estimation conducted for Bangladesh indicates that a median residual level of 25 μg/L arsenic could be reached in 84% of the polluted groundwater. The easily observable removal of iron from the pumped water makes the effect of a SF immediately recognizable even to people who are not aware of the arsenic problem.

References:
M. Berg, S. Luzi, P.K.T. Trang, P.H. Viet, W. Giger, and D. Stüben, *Environ. Sci. Technol.*, **40**, 5567–5573 (2006).

Collaborations:
Doris Stüben (University of Karlsruhe, Institute for Mineralogy and Geochemistry)
Pham Thi Kim Trang, Pham Hung Viet (Hanoi University of Science)

Title: **Kinetics and Mechanistic Aspects of As(III) Oxidation by Aqueous Chlorine, Chloramines, and Ozone: Relevance to Drinking Water Treatment**

Researcher: Michael C. Dodd, Adrian A. Ammann, Michael Berg, Urs von Gunten

Institute/Group: Department of Water Resources and Drinking Water, Eawag

Project Description:

Kinetics and mechanisms of As(III) oxidation by free available chlorine (FAC - the sum of HOCl and OCl-), ozone (O3), and monochloramine (NH2Cl) were investigated in buffered reagent solutions. Each reaction was found to be first order in oxidant and in As(III), with 1:1 stoichiometry. FAC-As(III) and O3-As(III) reactions were extremely fast, with pH-dependent, apparent second-order rate constants, , of 2.6 (±0.1) × 10"*appk* 5 M-1s-1 and 1.5 (±0.1) × 106 M- 1 s-1 at pH 7, whereas the NH2Cl-As(III) reaction was relatively slow (= 4.3 (±1.7) ×10"*appk* -1 M-1s-1 at pH 7). Experiments conducted in real water samples spiked with 50 (6.7 × 10-7 M) showed that a 0.1 mg/L Cl2 (1.4 × 10-6 M) FAC dose was sufficient to achieve depletion of As(III) to <1 μg/L As(III) within 10 s of oxidant addition to waters containing negligible NH3 concentrations and DOC concentrations <2 mg-C/L. Even in a water containing 1 mg-N/L (7.1 × 10-5 M) of NH3, >75% As(III) oxidation could be achieved within 10 s of dosing 1-2 mg/L Cl2 (1.4-2.8 × 10-5 M) of FAC. As(III) residuals remaining in NH3- containing waters 10 s after dosing FAC were slowly oxidized ($t1/2 \geq 4$ h) in the presence of NH2Cl formed by the FAC-NH3 reaction. Ozonation was sufficient to yield >99% depletion of 50 μg/L As(III) within 10 s of dosing 0.25 mg/L O3 (5.2 × 10-6 M) to real waters containing <2 mg-C/L of DOC, while 0.8 mg/L O3 (1.7 × 10-5 M) was sufficient for a water containing 5.4 mg-C/L of DOC. NH3 had negligible effect on the efficiency of As(III) oxidation by O3, due to the slow kinetics of the O3-NH3 reaction at circumneutral pH. Time-resolved measurements of As(III) loss during chlorination and ozonation of real waters were accurately modeled using the rate constants determined in this investigation.

References:

M.C. Dodd, N.D. Vu, A.A. Ammann, V.C. Le, R. Kissner, H.V. Pham, T.H. Cao, M. Berg, and U. von Gunten, *Environ. Sci. Technol.*, **40**, 3285–3292 (2006).

Collaborations:

Rainhard Kissner (Laboratory of Inorganic Chemistry, ETH Zurich)
Le Van Chieu, Pham Hung Viet, Cao The Ha, (Hanoi University of Science)

Title: **Compound-Specific Nitrogen and Carbon Isotope Analysis of Nitroaromatic Compounds in Aqueous Environmental Samples Using SPME Coupled to GC-IRMS**

Researchers: Michael Berg, Jakov Bolotin, Thomas B. Hofstetter

Institute/Group: Department of Water Resources and Drinking Water, Eawag

Project Description:
Solid phase microextraction (SPME) coupled to gas chromatography/isotope ratio mass spectrometry was used to determine the δ15N- and δ13C-signatures of selected nitroaromatic contaminants such as the explosive 2,4,6-trinitrotoluene (TNT) for derivation of isotopic enrichment factors of contaminant transformation. Parameters for efficient extraction of nitroaromatic compounds (NACs) and substituted anilines from water samples were evaluated by SPME-GC/MS. δ13C-signatures determined by SPME-GC/IRMS and elemental analyzer IRMS (EA-IRMS) were in good agreement, generally within ±0.7‰, except for 2,4-dinitrotoluene (2,4-DNT) and TNT, which showed slight deviations (<1.3‰). Limits of detection (LOD) for δ13C-analysis by SPME-GC/IRMS were between 73 and 780 μg L-1 and correlated with the extraction efficiencies of the compounds determined by SPME-GC/MS. Nitrogen isotope measurements by SPME-GC/IRMS were of similar precision (standard deviations <0.8‰) for all NACs except for TNT. δ15N-signatures matched the reference values obtained by EA-IRMS within ±1.3‰ (+2.5‰ for TNT) but no systematic trend was found for the deviations. LODs of δ15N-measurements ranged from 1.6 to 9.6 mg L-1 for nitrotoluenes, chlorinated NACs and DNTs (22 mg L-1 for TNT). The SPME-GC/IRMS method is well suited for the determination of isotopic enrichment factors of various NAC transformation processes and provides so far unexplored possibilities to elucidate behavior and degradation mechanisms of nitroaromatic contaminants in soils and groundwaters.

References:
M. Berg, J. Bolotin, and T.B. Hofstetter, *Anal. Chem.*, **in press** (2007).

Collaborations:
Eawag and ETH Zurich, Department of Environmental Sciences

Title: **Pharmaceuticals and pesticides in groundwater of Switzerland**

Researchers: Christa S. McArdell, Irene Hanke, Heinz Singer

Institute/Group: Eawag: Swiss Federal Institute of Aquatic Science and Technology

Project Description:

Groundwater is the most important drinking water resource in Switzerland. It is therefore important to keep groundwater reserves free of artificial long-lived pollutants as far as possible. Due to progresses in trace analysis of organic contaminants more and more chemicals can also be detected in groundwater. Therefore, the criteria for quality of groundwater must be redefined continuously. In particular, pollution by chemicals developed and used in order to have a specific effect on organisms, such as pharmaceuticals or pesticides, should be avoided. Several substances are routinely analyzed in groundwater. However, sophisticated analytical methods are needed to determine micropollutants like pharmaceuticals or pesticides in the low nanogram per Liter range, which are not yet available in all analytical labs. To determine the groundwater pollution by these compounds, a broad range of pharmaceuticals as well as a selection of pesticides and some of their metabolites were analyzed at selected NAQUA sampling stations of the Federal Office for the Environment (BAFU) [1]. In a study in collaboration with the cantonal environmental protection agency (AWEL), the behavior of pharmaceuticals during infiltration of river water to groundwater was investigated [2]. LC/MS/MS was used for the analysis, and an online SPE-LC/MS/MS was used for pesticides and sulfonamide antibiotics [3]. One or more of 84 analyzed pharmaceuticals were detected in 27% of all investigated groundwater stations. The X-ray contrast media iopamidole and amidotrizoic acid were found in the highest concentrations up to 88 ng/L. Sulfamethoxazole was the most important antibiotic occurring at nearly every fifth investigated groundwater station with the highest concentration around 30 ng/L. Only in 2 out of 61 groundwater sites no pesticide was found above the detection limit. In 18% of the sites concentrations of pesticides exceeded the requirement level of the water protection regulation (GSchV) of 100 ng/L. Atrazine and its metabolite desethylatrazine were the most abundant representatives in concentrations up to 300 ng/L. While the pesticide metolachlor occurred only in concentrations up to 32 ng/L, its metabolites metolachlor-ESA and -OXA were detected in concentrations of up to 480 ng/L and 210 ng/L, respectively.

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[1] I. Hanke, H. Singer, C.S. McArdell, D. Traber, R. Muralt, M.S. Brennwald, T. Herold, R. Oechslin, R. Kipfer, Arzneimittel und Pestizide im Schweizer Grundwasser. GWA 3, 1-10 (2007).

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[3] K. Stoob, H.P. Singer, C.W. Goetz, M. Ruff, S.R. Mueller, Fully automated online solid phase extraction coupled directly to liquid chromatography–tandem mass spectrometry. J. Chromatogr. A 1097, 138-147 (2005).

Collaborations:

D. Traber, R. Muralt, T. Herold, Gruppe NAQUA, Bundesamt für Umwelt (BAFU)
W. Blüm, Amt für Abfall, Wasser, Energie und Luft (AWEL)

Title: **Analysis of N-nitrosamines in wastewater by LC-MS/MS using the linear iontrap-orbitrap hybrid mass spectrometer**

Researchers: Martin Krauss, Juliane Hollender

Institute/Group: Swiss Federal Institute of Aquatic Science and Technology (Eawag), Department of Environmental Chemistry

Project Description:
The presence of N-nitrosamines, particularly N-nitrosodimethylamine (NDMA) in wastewater, groundwater and drinking water is of great concern as these compounds act as strong human carcinogens. Our objective was to develop a method capable of identifying and quantifying nine N-nitrosamines in wastewater and groundwater samples at the low ng/L range utilizing solid-phase extraction preceded by LC-MS/MS. Solid phase extraction from 500 mL samples was achieved with stacked cartridges of a crosslinked copolymer sorbent (Waters Oasis HLB, top) and a carbonaceous sorbent (JT Baker Bakerbond Carbon, bottom). The SPE method was highly effective and breakthrough was less than 20 % for the most polar NDMA and < 5 % for all other nitrosamines when 500 mL samples were extracted. Low-resolution tandem mass spectrometry on two different triple-quadrupole instruments was not sufficiently selective to unambiguously identify all nitrosamines in wastewater samples. Therefore we used the LTQ Orbitrap (Thermo Electron) high-resolution mass spectrometer, combining a linear quadrupole ion trap MS with an Orbitrap MS capable of high mass resolution analysis (R=7500-100000). We were able to detect nitrosamines selectively using either the precursor ions in full scan mode or one to three product ions of each nitrosamine in MS2 experiments at R=15000. The corresponding method detection limits for wastewater samples were about 0.3-3 ng/L when deuterated internal standards were used for quantification. The recoveries of the individual nitrosamines spiked to sewage treatment plat effluent samples ranged from 54 to 119%. Our study shows that LC-MS/HRMS is a powerful technique to identify and quantify nitrosamines in water samples and is also promising for other polar contaminants of low molecular weight.

Collaborations:
This project was funded within the EU project RECLAIM Water within FP6 (Project no. 018309)

Title: **Detection and identification of polar contaminants and their transformation products in environmental water samples using liquid chromatography-linear iontrap-orbitrap hybrid mass spectrometry**

Researchers: Heinz Singer, Susanne Kern, Kathrin Fenner, Juliane Hollender

Institute/Group: Swiss Federal Institute of Aquatic Science and Technology (Eawag), Department of Environmental Chemistry

Project Description:
The challenges in analysing polar organic chemicals and their transformation products in environmental samples by LC-MS are twofold. First, the generally low but nevertheless potentially toxicologically relevant concentrations, which usually lie in the ng/L range, require enrichment, separation of the matrix and sensitive detection. The second challenge is the identification of unknown peaks in LC-MS, where the interpretation of fragmentation pattern without large spectra libraries as those available for GC-MS is more difficult. In recent years the combination of LC-TOF (providing accurate mass measurements to generate elemental compositions of ions) with LC ion trap (providing structural information from fragmentation studies) has a few times been applied in non-target-screening of environmental samples (Thurman et al., 2005; Hernandez et al., 2004; 2005). The limitation of TOF instruments in comparison to quadrupoles is their lower sensitivity, which hampers the detection and identification of analytes at low concentrations (Hernandez et al., 2005).

The scope of our ongoing study is to determine the potential of the new hybrid system linear ion trap and orbitrap analyzer to detect and identify polar organic contaminants like pesticides and their metabolites in environmental water samples without using reference standards. Surface and groundwater samples were enriched and analyzed by LTQ Orbitrap using automatic data dependent scanning, enabling the simultaneous acquisition of high resolution MS spectra and several MS/MS scans of the most abundant mass peaks. Screening for stable transformation products was focused by intensive literature surveys as well as the use of chemical fate models and biodegradation pathway prediction tools to produce a list of transformation products that are likely to occur. We managed to identify several pesticides and their transformation products in the lower ng/L concentration range by this method, but it is still an important issue to achieve sufficient detection sensitivity. Upon further refinement, the approach presented opens up an avenue to more realistically assess water quality with regard to emerging contaminants and their transformation products.

Literature:
Hernández, F., Ibánez, M., Sancho, J.V., Pozo, O.J., 2004. Anal. Chem. 76, 4349-4357.
Hernández, F., Pozo, Ó.J., Sancho, J.V., López, F.J., Marín, J.M., Ibánez M., 2005. TrAC 24, 596-612.
Thurman, E.M., Ferrer, I., Zweigenbaum, J.A., García-Reyes, J.F., Woodman, M., Fernández-Alba, A.R., 2005. J. Chromatogr. A, 1082, 71-80.

Collaborations:
This project was partly funded by the Swiss Federal Office for the Environment FOEN

Title: **Soft X-ray spectromicroscopy of phase-change microcapsules**

Researchers: G. Tzvetkov, J. Raabe, C. Quitmann

Institute/Group: Swiss Light Source (SLS), Paul Scherrer Institute (PSI), Villigen

Project Description:

In this work, Micronal® (BASF) phase-change microcapsules were examined with a newly installed PolLux scanning transmission X-ray microscope (STXM) at SLS. STXM combines excellent compositional sensitivity via near-edge X-ray absorption fine structure spectroscopy (NEXAFS) with high spatial resolution (~ 40 nm). Phase-change materials (PCMs) are using latent heat to store energy, i.e. they are able to absorb and release heat when the temperature increases and decreases while the material changes from a solid to a liquid and *vice versa*. Micronal® PCM is composed of microscopically small acrylic polymer shell capsules (diameter of ~5 μm) containing a paraffin wax droplets in their cores.

Radiation damage induced by the STXM microscope has been observed in the investigation of Micronal® PCM microcapsules (Fig. 1). Radiation-induced effects after a prolonged X-ray illumination (absorption of $8x10^4$ photons per pixel in the 282-315 eV photon range) lead to the severe changes in the microcapsules' morphology. Spectromicroscopy analysis of the most damaged particles reveal that a cracking of the microcapsules' polymer shell and partial separation of the core-shell components in nanometer scale occurs upon irradiation. Paraffin wax and acrylic polymer ingredients of the Micronal® microcapsules have been characterized by carbon K-edge NEXAFS.

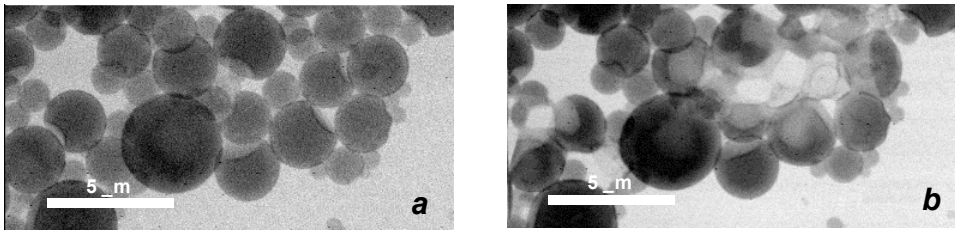

Fig. 1. STXM images of pristine (a) and beam-damaged (b) microcapsules.

References:

[1] G. Tzvetkov, B. Graf, R. Wiegner, J. Raabe, C. Quitmann, R. Fink, Soft X-ray spectromicroscopy of phase-change microcapsules, *submitted to Micron.*

Collaborations:

B. Graf, R. Wiegner, R. Fink (University of Erlangen-Nürnberg, Germany)

Title: **Determination of fission gas pressures in pores in high burnup nuclear fuel using Laser Ablation ICP-MS**

Researchers: Matthias I. Horvath, Andrei Izmer*, Niko Kivel, Renato Restani, Marcel Guillong**, Ines Günther-Leopold, Christian Hellwig, and Detlef Günther***

Institute/Group: Laboratory for Materials Behavior, Nuclear Energy and Safety, Paul Scherrer Institut, Villigen, Switzerland
*Current address: Environmental and Resource Studies, Trent University, Peterborough, Canada
**Institute for Isotope Geology/Mineralogic Elements, ETH Zürich, Switzerland
***Laboratory for Inorganic Chemistry, Trace Elements and Microanalysis Group, ETH Zürich, Switzerland

Project Description:

Roughly 20% of all fission products are gaseous, the most important are Kr- and mainly Xe-isotopes. By reaching high burnups, the High Burnup Structure (HBS) is formed in the rim of the fuel, where a depletion of the noble Fission Gases (FG) in the matrix and an enrichment of FG in the pores can be observed. In model calculations it has been estimated that the pressure in these pores reaches up to 30 MPa [1]. The knowledge of the FG distribution in the fuel is important to understand the high burnup fuel behaviour under accident conditions. This includes the local appearance of the FG and the microstructure.

With analytical methods routinely used for the characterization of solid samples like EPMA or SIMS the quantification of FG in pores is difficult. The combination of a laser ablation system (LA) with an inductively coupled plasma mass spectrometer (ICP-MS) is a powerful tool for this challenging task. It offers the advantages of high spatial resolution with laser spot sizes down to 10 μm and very low detection limits. The development of a suitable calibration technique for gases allows the quantification of Xe amounts in pores of the HBS. Via coupling with scanning electron microscope analysis (SEM) for the determination of the pore size distribution, the pressures in the pores can be estimated. Measurements were performed on PWR fuel with a rod average burnup of 105 GWd/tHM.

The laser ablation system in the Hotlab of PSI is custom built to fit the needs of a shielded ablation environment [2]. For the calibration the direct injection of a known concentration of Xe gas with a syringe into the carrier gas system of the LA-ICP-MS was applied.

Besides the LA-ICP-MS system, measurements were also performed with a shielded SEM/EPMA and a shielded optical microscope. Firstly EPMA/SEM measurements were carried out on the surface to determine pore sizes and porosity and to get some first impressions on the elemental distribution [3]. Two LA methods called: „single shot“ and „single hole“ were applied. The “single shot” method analyses each single LA shot which opens 1 to several surface near pores depending on the spot size of the laser. With the “single hole” method a fixed number of laser shots is applied to remove a defined fuel volume. This volume can be determined by optical microscopy. With the known porosity, determined by SEM, the removed porosity volume can be calculated. Fig. 1 shows the analyzed fuel sample across the whole diameter.

Based on the determined pore sizes, a range of pore pressures of 1-30 MPa was estimated by assuming opening of 2-4 pores of 2-7 μm diameter [4] with one “single shot” of 25 μm. With the “single hole” method, the detected pressure range was 10-50 MPa. Fig. 2 shows the pressure distribution across the whole fuel diameter, divided in regions depending on the

microstructure, i.e. porosity [5]. Experimentally determined pressures are in the range of the modelled and calculated values. Thus, the potential of the LA-ICP-MS method to determine FG pressures of pores in nuclear fuel has been successfully demonstrated.

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[2]M. Guillong et al./JAAS (2007) DOI : 10.1039/ b616364e
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[4]A. Romano et al./JNM (2007) DOI : 10.1016/ j.jnucmat.2006.09.016
[5]J. Spino et al./JNM 354 (2006) 66-84

Collaborations:

Swissnuclear, Institute of Polymer Physics ETHZ

Figures:

Fig. 1: Overview of the analyzed fuel sample divided in regions: on the rim the ultra high burnup structure (UHBS), followed by the high burnup structure (HBS), then a transition zone of a mixture of HBS and unrestructured fuel and finally in the center the unrestructured fuel region.

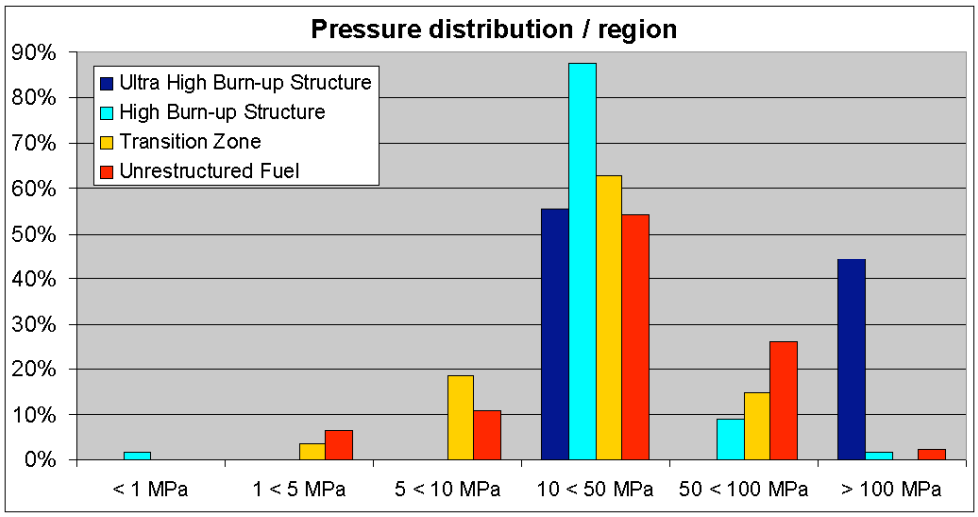

Fig. 2: Distribution of determined gas pressures in the porosity of the fuel. The majority of the pressures is in the range of 10-50 MPa. The porosity itself is also depending on the radial position in the fuel [5].

Title: **Toxicological screening after the REMEDI™ – Establishment of a GC-MS screening procedure**

Researchers: Sandra Zgraggen, Rosa Bonafini, Ursula Gutteck, Katharina Rentsch

Institute/Group: Institut für Klinische Chemie, Universitätsspital Zürich

Project Description:

The REMEDI™ from Bio-Rad is an automated HPLC system, which uses a scanning UV detector to identify a broad spectrum of drugs for toxicological screening in urine and serum. It will no longer be supported after 2007. Therefore, we had to introduce a new procedure for the general unknown screening for intoxicated patients. We introduced the GC-MS screening procedure published by Maurer et al. (1) and compared its performance with the REMEDI™ for the four different drug classes: antidepressants, antipsychotics, non-opioid analgetics and anticonvulsants.

Half of the urine sample has been hydrolysed by acid hydrolyses and then been combined with the other half. Trimipramine-d3 has been added as internal standard and liquid-liquid extraction was performed with dichloromethane/ isopropanol/ethylacetate. The organic phase was evaporated and the residue derivatized with acetanhydride/pyridine using microwave energy. After evaporation, the residue was dissolved in 50 µl toluene/ethylacetate and injected into a TraceTM GC 2000 coupled to a MD 800 mass spectrometer (ThermoQuest, San José, USA).

With the exception of sertraline, all antidepressants used in Switzerland could be detected with both methods below the calculated steady-state concentration in urine (c_{ssU}). The GC-MS procedure had a higher sensitivity for all compounds analysed. Many antipsychotic drugs are only minimally excreted in urine as unchanged drug. Therefore, the detection limit of the parent drug was often much higher than the c_{ssU}. The metabolites however could be detected sufficiently. With the exception of amisulpride, sulpiride and tiapride, all antipsychotics had a higher sensitivity with the GC-MS procedure.

The two drug classes non-opioide analgetics and anticonvulsants can only incompletely be detected by the REMEDI™. With the GC-MS procedure described above all acid drugs of the before mentioned drug classes cannot be detected, therefore a second extraction step using an acidic pH has been introduced into the screening procedure.

In conclusion, the modified GC-MS screening procedure allows a very complete detection of the antidepressants, antipsychotics, non-opioide analgetics and anticonvulsants. The disadvantage of this new procedure is a turnaround time of about 2 hours.

References:

[1] Sandra Zgraggen, *Toxikologisches Screening im Urin mit GC-MS*, Diplomarbeit ETHZ, September 2006

[2] Rosa Bonafini, *Toxikologisches Screening im Urin nach Antiepileptika und Analgetika mittels GC-MS,* Diplomarbeit ETHZ, Januar 2007

Title: **Lipidomics in Clinical Diagnostics**

Researchers: Ines Burkard, Ratna Karuna, Arnold von Eckardstein, Katharina Rentsch

Institute/Group: Institut für Klinische Chemie, Universitätsspital Zürich

Project Description:
Lipids comprise a family of biomolecules that play prominent roles in many critical metabolic and biochemical processes such as energy production and storage, the formation and functioning of cellular membranes, signal transduction, and steroidgenesis. The critical point in studying the in-vivo metabolism and the clinical impact of the different lipids is the need of one or several analytical methods which enable the sensitive, specific determination of the different lipid classes in their unaltered state. The title which has recently been given to the theme of studying lipids in their natural environment is lipidomics. As yet only cholesterol and its distribution in different lipoproteins as well as triglycerides have been used as diagnostic and prognostic markers. We are interested in the diagnostic and prognostic value of various lipids including oxysterols, bile acids, phospholipids and sphingolipids in human disease. Liquid chromatography mass spectrometry (LC-MS/(MS)) methods will be developed and used as analytical tools for the determination of the various lipid classes in serum and lipoprotein subfractions. Healthy individuals will be analyzed to establish reference values of the different markers and to unravel associations and correlations with demographic and anthropometric measures as well as clinical biochemical markers. Well defined patient cohorts will be evaluated to unravel the association of candidate lipids with diseases, for example cardiovascular or metabolic diseases.

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Collaborations:
HDLomics, Functional genomics of inborn errors and therapeutic interventions in high density lipoprotein (HDL) metabolism (EU, 6th framework programme)

6

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Group of E. Pretsch, Laboratorium für Organische Chemie, ETH Hönggerberg

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Research activities: Biogeochemical processes in surface waters (rivers, lakes, wetlands).

Swiss Federal Laboratories for Materials Testing and Research (Empa):

- Dr. Peter Hofer, Mobility and Environment, Ueberlandstrasse 129, CH-8600 Dübendorf, Tel.: 044 / 823 4110, Fax: 044 / 821 6244, e-mail: Peter.Hofer@empa.ch

Research activities: Mobility and environment.

- Prof. Hans-Josef Hug, Nanoscale Materials Science, Ueberlandstrasse 129, CH-8600 Dübendorf, Tel.: 044 / 823 4125, e-mail: Hans-Josef.Hug@empa.ch

Research activities: Forces, surfaces & magnetism.

- Dr. Martin Kohler, Organic Chemistry, Ueberlandstrasse 129, CH-8600 Dübendorf, Tel.: 044 / 823 4334, Fax: 044 / 823 4041, e-mail: Martin.Kohler@empa.ch

Research activities: Analytical chemistry of pollutants.

- Dr. Heinz Vonmont, Solid State Chemistry and Analyses, Ueberlandstrasse 129, CH-8600 Dübendorf, Tel.: 044 / 823 4131, Fax: 044 / 821 6244, e-mail: Heinz.Vonmont@empa.ch

Research activities: Inorganic analytical chemistry / Characterization of solids.

- Dr. Martin Mohr, Combustion Engines Internal, Ueberlandstrasse 129, CH-8600 Dübendorf, Tel.: 044 / 823 4190, e-mail: Martin.Mohr@empa.ch

Research activities: Internal combustion engines.

- Dr. Brigitte Buchmann, Air Pollution/Environmental Technology, Ueberlandstrasse 129, CH-8600 Dübendorf, Tel.: 044 / 823 4134, Fax: 044 / 823 6244, e-mail: brigitte.buchmann@empa.ch

Research activities: Air pollution & climate change, long-term analysis of reactive & greenhouse gases

- Dr. Andrea Ulrich, Analytical Chemistry, Ueberlandstrasse 129, CH-8600 Dübendorf, Tel.: 044 / 823 4661, e-mail: Andrea.Ulrich@empa.ch

Research activities: Analytical chemistry

- Dr. Veronika Meyer, Biocompatible Materials, Lerchenfeldstrasse 5, CH-9014 St. Gallen, Tel.: 071 / 274 7787, e-mail: Veronika.Meyer@empa.ch

Research activities: Analytical chemistry, HPLC, measurement uncertainty

Paul Scherrer Institut (PSI):

- PD Dr. Urs Baltensperger, Paul Scherrer Institut, CH-5232 Villigen, Tel.: 056 / 310 2184, Fax: 056 / 310 4435, e-mail: urs.baltensperger@psi.ch

Research activities: Aerosols, inorganic chemical analysis, radiochemical methods.

- Dr. André Scheidegger, Paul Scherer Institut, CH-5232 Villigen, Tel.: 056 / 310 2184, Fax: 056 / 310 3171, e-mail: andre.scheidegger@psi.ch

Research activities: Molecular-level investigations of physiochemical processes in geochemical systems using synchrotron-based X-ray absorption spectroscopy (XAS) and X-ray fluorescence (XRF), Micro-scale chemical speciation fo contaminants in heterogeneous natural and men-made materials.

- Dr. Thomas A. Jung, Paul Scherrer Institut, CH-5232 Villigen, Tel.: 056 / 310 4518, Fax: 056 / 310 2646, e-mail: thomas.jung@psi.ch

Research activities: Micro- and nanotechnology.

- Dr. Ines Günther-Leopold, Paul Scherrer Institut, CH-5232 Villigen, Tel.: 056 / 310 2286, Fax: 056 / 310 2203, e-mail: ines.guenther@psi.ch

Research activities: Nuclear fuels.

- Prof. Friso Van der Veen, Paul Scherrer Institut, CH-5232 Villigen, Tel.: 056 / 310 5118, Fax: 056 / 310 3151, e-mail: friso.vanderveen@psi.ch

Research activities: Synchrotron radiation and nanotechnology.

- PD Dr. Thomas Lippert, Paul Scherrer Institut, CH-5232 Villigen, Tel.: 056 / 310 4076, Fax: 056 / 310 2688, e-mail: thomas.lippert@psi.ch

Research activities: Electrochemistry.

- Prof. August Schubiger, Paul Scherrer Institut, CH-5232 Villigen,
Tel.: 056 / 310 2813, Fax: 056 / 310 2849, e-mail: august.schubiger@psi.ch oder august.schubiger@pharma.ethz.ch

Research activities: Radiopharmaceutical chemistry, biochemistry, molecular biology, pharmacy and pharmacology.

Institute for Clinical Chemistry, University Hospital Zürich:

● Dr. Katharina Rentsch, Clinical Chemistry, University Hospital Zürich, Rämistrasse 100, CH-8091 Zürich, Tel.: 044 / 255 4590, Fax: 044 / 255 2290,
e-mail: rentsch@ikc.unizh.ch

Research activities: Development of mass spectrometric methods for the determination of small molecules and clinical validation of new markers for the monitoring of drug treatment or diagnosis of disease.

Currently the following members serve on the CEAC-ETHZ Board of Directors

C. Quittmann, M. Suter, P. Hofer, R. Zenobi, J. Hollender, E. Pretsch, M. Kohler, U. Baltensperger