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Evidence for laser-induced redox reactions in matrix-assisted laser desorption/ionization between cationizing agents and target plate material: a study with polystyrene and trifluoroacetate salts

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Matrix-assisted laser desorption/ionization mass spectrometry (MALDI-MS) is often applied to assess the dispersity and the end groups of synthetic polymers through the addition of cationizing agents. Here we address how these cation adducts are formed in a redox reaction context using polystyrene (PS) as a model polymer. The addition of several trifluoroacetate (TFA) salts as cationizing agents to a mixture of PS and matrix on a range of different target plate materials was systematically investigated, revealing the existence of laser-induced redox reactions between cationizing agents and target plate material during MALDI.

PS (M_w 1,920 Da) was mixed with a range of TFA salts (Li, Na, K, Cs, Ba, Cr, Pd, Cu, Ag, Zn, Al and In, as well as trifluoroacetic acid) and analyzed with MALDI using 2-[(2*E*)-3-(4-*tert*-butylphenyl)-2-methylprop-2-enylidene]malononitrile (DCTB) as matrix on different target plate materials (copper, Ti90/Al6/V4, Inconel® 625, stainless steel, as well as chrome-, silver- and gold-plated stainless steel) to evaluate the occurrence of redox reactions. Spectra, obtained on a Bruker Autoflex I MALDI-Time-of-Flight mass spectrometer, were processed with MATLAB to obtain PS- and DCTB-adduct ion signal intensities for direct comparison between chosen conditions.

It was found that on a stainless steel substrate the metal cations Al^+, Li^+, Na^+, Cu^+ and Ag^+ formed polystyrene adducts, whereas K^+, Cs^+, Ba^{2+}, Cr^{3+}, Pd^{2+}, In^{3+}, or their lower oxidation states, did not. For the copper and silver substrates, PS and DCTB adduct formation with cations liberated from these target plate materials was observed upon addition of a cationizing agent (unless TFA salt cluster ions were preferably formed), which indicates the occurrence of redox reactions between the added TFA salts and the target plate material. To understand at what point these ions were liberated from the substrate surface, control experiments employing salt solutions incubated with copper granules before mixing with matrix and polymer solutions were carried out. Judging from their standard electrode potentials, the redox reactions, which would not normally occur, leading to the observed Cu^+ complexation behavior when using a copper substrate in combination with a copper-free TFA salt, require an additional energy input, strongly suggesting that the observed redox reactions are laser-induced. Furthermore, copper granules were found to successfully sequester PS from a tetrahydrofuran (THF) solution, consistent with the view that adduct formation is preceded by complex formation with the copper target plate prior to the MALDI-MS measurement, facilitating the laser-induced redox reactions. The occurence of laser-induced redox reactions in MALDI-MS sheds new light on the underlying mechanism and provides a new analyte ionization strategy. It does, however, also raise questions to the reliability of MALDI-MS measurements carried out thus far in the presence of cationizing agents.

Quantifying positional uncertainties in NMR crystallography

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The structural characterization of complex materials is one of the key challenges in chemistry today.
Single crystal diffraction (SD-XRD) methods are capable of characterizing a big diversity of systems, from complicated inorganic structures over entire virus particles up to complex proteins. However in many cases, where the sample is either a powder or for example opaque, structural characterization with SD-XRD remains an enormous challenge. In this area, structure elucidation by a combined approach of solid-state NMR and computational methods holds great promise. In recent years the scope of this combined approach has been steadily improved and today there are many examples of structure validation by chemical shift measurements combined with density functional calculations (DFT). However in contrast to SD-XRD methods, for NMR crystallography there exists no method to quantify the positional uncertainties on individual atoms for the characterized structures.

We present a computational method to estimate the correlation between the root mean square deviation (RMSD) of the chemical shift and the positional RMSD of the investigated structure. This correlation allows us to quantify the positional uncertainties of individual atoms of the structures predicted by NMR crystallography, thereby making them directly comparable to structures characterized by SD-XRD methods. For several crystal structures comprised of organic molecules, we validate different methods of generating an ensemble of perturbed structures. For these perturbed structures we present a method to calculate and correlate the chemical shift RMSD and the positional RMSD of the whole ensembles. The presented method allows us to directly quantify the positional uncertainty of each individual atom in the investigated structure.

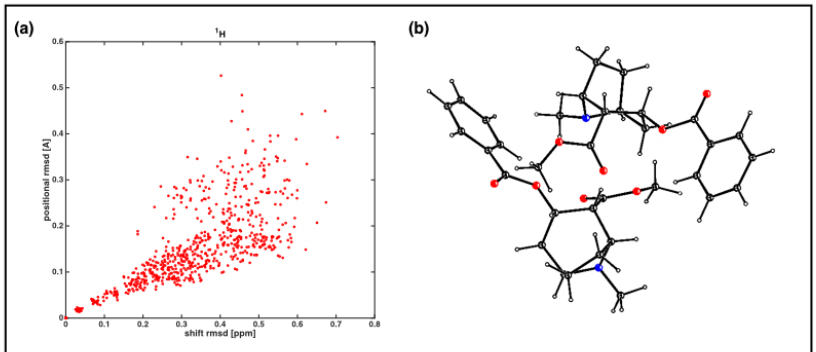

Figure (a): The figure shows the correlation between the positional RMSD [A] and the ^{1}H chemical shift RMSD [ppm] for an ensemble of perturbed Cocaine [$C_{17}H_{21}NO_4$] crystal structures. **(b)** Ortep plot of a Cocaine unit cell, illustrating the positional uncertainties [~0.12 A] correlated to a ^{1}H chemical shift uncertainty of ~0.3 ppm.

[1] Baias, M.; Widdifield, C.M.; Dumez, J.N.; Thompson, H.P.G.; Cooper, T.G.; Salager, E.; Bassil, S.; Stein, R.S.; Lesage, A.; Day, G.M.; Emsley,L., *Phys. Chem. Chem. Phys*., **2013**, 15, 8069.
[2] Salager, E.; Day, G.M.; Stein, R.S.; Pickard, C.J.; Elena, B.; Emsley, L.,*J. Am. Chem. Soc.* **2010**, 132, 2564.

SPRi-MALDI MS: How to follow non-covalent interactions in real time and identify the binding partners directly

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The coupling of SPRi and MALDI MS technologies meet the increasing demand for high-throughput analysis in pharma and life science research. In addition, it provides information on binding kinetics, binding affinity in real time and identifies the interaction partners with no need of purification, separation or labeling in real time. SPRi-MALDI MS enables the multiplexed investigation of specific interactions out of a crude mixture even in the low fmol range.

SPR imaging measurements were performed on the SPR Plex II (Horiba, France) working with polyoxyethylene functionalized gold slides including NHS-esters for immobilizing ligands. Mass spectrometric detection was done with a commercial MALDI TOF mass spectrometer (Ultraflex II TOF, Bruker Daltonics, Germany). The gold slide was mounted in an adapter. MS measurements were performed in the linear or reflected positive ion mode with standard settings and a “smartbeam” laser with proper energy. Each mass spectrum was the average of 2000 laser shots acquired at random sample position.

We will show an investigation of specific as well as off-target binding of various DARPins against ribosomal protein S6 kinase 2 (RPS6KA2), a potential drug target and suitable for the development of novel inhibitors for pancreatic cancer therapy. Designed ankyrin repeat proteins (DARPins) are a very promising class of non-immunoglobulin proteins that rival antibodies for target binding, but are genetically engineered. They are more robust than antibodies and can be tagged for an aligned chemical coupling to solid supports.

DARPins were immobilized, dissolved pure protein was injected, and the K_D was determined based on the measured SPR data (K_Ds of 0.4 to 2 nM resulted). When injecting a cell lysate, i. e. a complex mixture of proteins containing RPS6KA2, a MALDI MS measurement on the SPRi-chip directly after the SPRi experiment verifies the specific interaction between DARPins and RPS6KA2 even in the low fmol range. One problem of the matrix application with pipets is the low reproducibility due to spreading of the matrix solution spots and therefore the dilution of the sample. To boost the sensitivity, we developed a mask that combines the possibility of SPR imaging and upconcentrating the sample for MALDI detection.

Laser Ablation Time of Flight Mass Spectrometry using Ion Funnel for Trace Element Analysis in Solids

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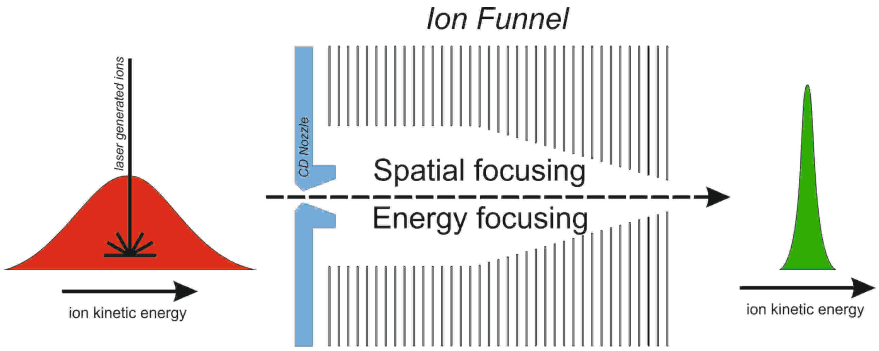
The aim of this research is to investigate and further develop a novel LAMS ion source providing both spatial and collisional focusing of laser produced ions with the use of a so called ion funnel. The ion funnel was first described by Shaffer et al [1] to improve ion transmission in electrospray ionization mass spectrometry and is based on the theoretical work of Gerlich [2]. Briefly, the ion funnel consists of stacked ring electrodes with decreasing diameter towards the mass spectrometer orifice. Radiofrequency (RF) power is applied to the ring electrodes at alternating phase (180° shift) between adjacent electrodes. Such an arrangement creates a repulsive quasi-stationary potential wall in the radial direction that confines ions along the funnel axis, and thus improves ion transmission. Classically a DC gradient is superimposed on the ion funnel to drive ions across the funnel; in the hereby presented setup the DC gradient is absent and the transmission relies solely on the gas dynamic effects produced by a convergent-divergent supersonic (CD) nozzle added in front of the sample. In addition to spatial focusing, the kinetic energy of the ions in the funnel is dissipated through collisions with a buffer gas (e.g. He) during their transit through the ion funnel.



In LAMS, the initial ion-energy distribution from the laser ablation process is very broad; energy focusing with an ion funnel should reduce this distribution to improve transport efficiency through the mass analyzer.
The first experiments with our LA-TOFMS instrument show a dramatic influence of collision-gas pressure, gas flow rate, and RF frequency and amplitude on signal intensity and transient evolution for ions across the elemental mass range. Specifically, we have observed a signal enhancement for species with lower mass to charge ratio (Cu^+) under higher pressure, higher RF frequency and lower RF amplitude. Species with higher mass to charge ratio (Pb^+) show an inverse trend regarding RF frequency and amplitude, but seems to be less affected by the pressure differences. Interestingly, the gas flow rate seems to cause changes the transient signal structure.

[1]Shaffer, S. A., Tang, K., Anderson, G. A., Prior, D. C., Udseth, H. R. and Smith, *Rapid Commun. in Mass Spectrometry* **1997**, 11, 1813-1817.
[2] Gerlich. Advances in Chemical Physics 1992.

In-vivo mass spectrometric analysis of yeast growth metabolism

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Introduction

Yeast (*Saccharomyces cerevisiae*) is widely used in the food industry. Maximizing the desired outcome and minimizing unwanted metabolic end-products is key to optimizing industrial production. Here we present a novel method capable of tracking in real time metabolic changes occurring during yeast growth.

Method

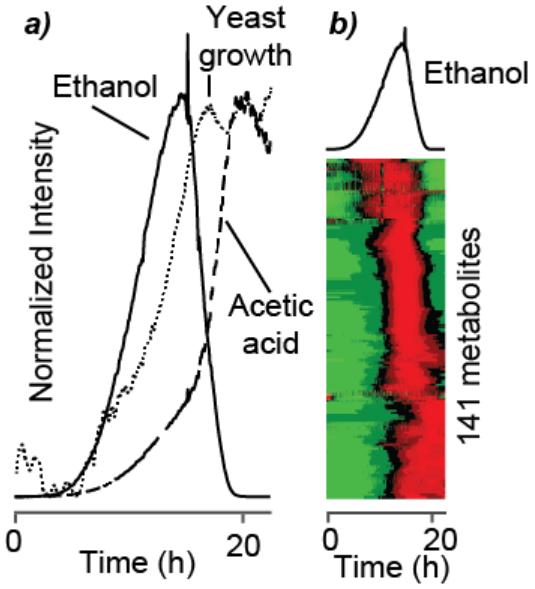
A commercially available Secondary Electrospray Ionization (SESI) source[1] was interfaced with an LTQ-Orbitrap mass spectrometer (MS). Volatile yeast metabolites in the mass range 50-400 Da were monitored with a time resolution of 1 min during starvation and growth after glucose injection.

Results

141 metabolites were detected simulataneously during yeast growth during 21 hours. For example, figure (a) shows the production of ethanol and acetic acid measured with SESI-MS, along with the yeast growth as measured with a time lapse camera. Lag-, exponential growth-, stationary- and dioxic shift-phases are clearly captured. Figure (b) shows a heat map of the 141 metabolites detected.

Conclusions

SESI-MS is an attractive chemical analysis method for the real-time monitoring of yeast bioreactors.



[1] C. Barrios-Collado, G. Vidal-de-Miguel, P. Martinez-Lozano Sinues, *Sensors Actuators B: Chem.* **2016**, *223*, 217.

A Laser ablation ICP-TOFMS setup with a 213 nm Laser for High-Resolution, High-Speed and Multielemental Imaging of Biological Tissues

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Laser ablation inductively coupled plasma mass spectrometry (LA-ICP-MS) can be utilized to map elemental distributions in solid materials. In this approach, ICP-MS signal is recorded as function of the position of the ablating laser beam on the surface of the sample. LA-ICPMS imaging is already applied in multiple disciplines such as geology, forensics, biology and medicine. There are, however, several challenges involved to develop this strategy into an even more applicable technique.

For example, in the emerging field of bio-imaging, spot sizes of a few micrometers and below are necessary to provide resolution on sub-cellular scale and therefore the optical setup must be able to focus the laser beam to such dimensions. In order to preserve the highest spatial resolution, ICP-MS signals from individual laser pulses must be clearly identifiably in a transient signal. This requires an ablation cell that provides gas dynamics for instantaneous aerosols transport with minimal dispersion in order to maintain reasonable total analysis times. Furthermore, the ICP-MS system has to be able to detect the short transient signals and record multi-elemental data.

The compact LA setup developed in this work addresses all the challenges mentioned above. It consists of a solid state Nd:YAG-based 213 nm laser, a low-dispersion ablation cell and an ICP-TOFMS (icpTOF, TOFWERK, Thun, Switzerland). While the optical system provides laser spot sizes as small as 1 µm, the low-dispersion tube cell maintains a compact aerosol plug with transient signals below 10 ms (full width at 1% peak maximum) for single ablation events. The LA setup was coupled to an ICP-TOFMS, which is able to acquire full-spectral data within a few milliseconds and is therefore suited for fast and high resolution multi-elemental imaging of geological and biological samples.

Gundlach-Graham et al., *Anal. Chem.*, **2015**, *87*, 8250.
Burger et al., *Anal Chem.*, **2015**, *87*, 8259.

Investigation of the $^{85}Rb^{+}$-$^{88}Sr^{+}$ Signal Separation by Online Electrothermal Vaporization in a fs-LA-ETV-SCICPMS Set-Up

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Laser ablation multiple collector inductively coupled plasma mass spectrometry (LA-MCICPMS) offers the possibility to determine Sr isotope ratios in solids online with minimal sample preparation. However, compared to solution-based analytical techniques, elements cannot be separated from the laser-generated aerosol before the ICP. Therefore, the isobaric interference of ^{87}Rb on ^{87}Sr, which limits the accuracy and precision ofthe $^{87}Sr/^{86}Sr$ ratio, cannot be suppressed. With the currently available mass resolving power, the two isotopes cannot be separated neither. Jackson et al. [1] concluded from their measurements, that 0.15 is the maximal value for the [Rb]/[Sr] concentration ratio, if one is aiming for an accuracy comparable to solution-based methods. When the aerosol is heated in an electrothermal vaporizer (ETV), changes in its chemical composition can be achieved. By using a commercial graphite-tube ETV system (HGA-600 MS), those changes were previously studied for temperatures up to 2’500° C [2]. A partial suppression of the Rb-signal was observed, leading to improved $^{87}Sr/^{86}Sr$ accuracy. Selective Rb-evaporation and condensation was suggested to lead to this effect, based on the different vaporization temperatures of Rb (‹ 1’000° C) and Sr (SrO ≈ 3’000° C). Beside this element-specific vaporization, a temperature regime was observed, where the signals of all elements were suppressed but increased again. It was shown in this work, that when a fs- instead of a ns-LA system is used, a less expressed or no non-specific suppression is observed, resulting in a larger temperature range that can be used to study the signal behavior. Therefore, a fs-laser (Excite Pharos operating at 257 nm) was used together with a sector field ICPMS (Element XR). Furthermore, the efficiency of Rb-separation of two ETV units (ETV-4000, Spectral Systems and HGA-600 MS, Perkin Elmer) was. The selective Rb-suppression was about one order of magnitude more pronounced when using the ETV-4000, while Sr-sensitivity was retained under optimized settings. The non-specific suppression regime was not observed, which supports the previous work done with the fs-laser. Further characterization of the set-up will be performed as a next step by investigating the influence of different parameters (carrier gas flow rate, laser scan rate and mass load of the furnace) on the Rb-elimination efficiency.

[1] M. G. Jackson et al. *Earth and Planetary Science Letters* **2006**, *245*, 260.
[2] R. Brogioli *ETH Diss.* **2012**,*Nr. 20795*.

A new twist to current understanding of pollen-induced asthma - non-allergenic, secondary metabolites in pollen induce non-inflammatory airways constriction?

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Plant pollen are known to be strong airborne elicitors of asthma in humans. *In vitro* data and clinical studies corroborate the involvement of small surface proteins present on the pollen grain. They modulate the immune system through IgE cross-linkage, thereby causing airway inflammation, and obstruction due to constriction of airways. At the physiological level, relaxation and constriction of airways is regulated by mechanisms involving proteins such as the lipid kinase PIP5Kγ and the cation channel TRPA1. While the role of pollen surface proteins is well established, a possible contribution of small molecules present in pollen to the clinical outcome of asthma has not been explored up to now.

Therefore, we analyzed and compared the phytochemical profiles of pollen originating from thirty plant species causing varying degrees of pollen allergenicity. Profiling was performed by HPLC coupled with PDA, ESIMS, and ELSD detectors, off-line microprobe NMR spectroscopy, and spectrophotometric analysis. The presence of conjugated polyamines, such as N^1,N^5,N^{10}-tricoumaroylspermidine, N^1-caffeoyl-N^5,N^{10}-dicoumaroylspermidine and N^1,N^5,N^{10},N^{15}-tetracoumaroylspermine was a characteristic feature of pollen from Asteraceae (*Ambrosia* and *Artemisia* ssp.). Compounds with Michael acceptor properties were also mainly present in Asteraceae pollen. Extracts were tested for activation of TRPA1 in murine dorsal root ganglia. Tetrahydrofuran extracts of selected pollen increased intracellular Ca^{2+} at concentrations comparable to the prototypical TRPA1 activator cinnamaldehyde. Characterization of active compounds will be presented.

[1]Erle DJ and Sheppard D. Cell biology of disease: the cell biology of asthma. J Cell Biol 2014; 205: 621–631.
[2]Avonto C, Taglialatela-Scafati O, Pollastro F, Minassi A,DiMarzo V, De Petrocellis L, Appendino G .An NMR spectroscopic method to identify and classify thiol-trapping agents: revival of michael acceptors for drug discovery? Angew Chem Int Ed2011; 50: 467 –471.br

Characterization of Membrane Proteins and their Complexes by High-Mass Matrix-Assisted Laser Desorption Ionization-Mass Spectrometry

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The structural investigation of membrane proteins is an important area of research due to their relevance in biochemical processes. These include the transport of ions and proteins, signaling, and cell-cell interactions. The characterization of the membrane proteins involved could lead to a better understanding of these processes, enabling novel approaches in medical research, e.g. the development of more specific drugs or the prevention of drug resistance in cancer therapy (1).

The investigation of membrane proteins via mass spectrometric techniques (e.g. ESI MS) (2) often requires extensive sample preparation prior to analysis, due to high concentrations of salts and detergents in “protein-friendly” buffers. To minimize such sample preparation we apply matrix-assisted laser desorption ionization (MALDI) MS combined with a high-mass detector for accurate mass determination and characterization of membrane proteins and their complexes (3).

In this study we investigated the complexes of a lipid-linked oligosaccharide flippase (PglK), known as an important biological actor for the translocation of lipid-linked oligosaccharides that serve as donors in N-linked protein glycosylation, with different nanobodies, designed to stabilize its native structure, in order to obtain pure crystals for x-ray crystallography. We applied chemical cross-linking to investigate the stoichiometry of the nanobody-PglK complexes. Furthermore, we incubated ATP and ADP with the ABC-transporter to observe structural changes of these proteins induced by nanobody-protein interactions.

[1] Leonard GD, Fojo T, Bates SE, *Oncologist,* **(2003)**, 8, 411-424.
[2] Whitelegge JP, Gundersen CB, Faull KF, *Protein Sci,* **(1998)**, 7, 1423-1430.
[3] Chen F*, et al., Analytical chemistry,* **(2013)**, 85, 3483-3488.

Response factor determination of oligomeric proteins in native ESI-MS Katharina Root, Yves Wittwer, Renato Zenobi Department of Chemistry and Applied Biosciences, ETH Zuurich, CH-8093 Zuurich, Switzerland

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Electrospray ionization mass spectrometry (ESI-MS) is increasingly used for determination of protein complexes and its constituents. However, it is not clear whether the classical definition of a response factor can be still applied for oligomeric biomolecular complexes. Here, we propose to use a model system based on chain like, covalently linked Maltose Binding Protein (MBP) units [1] to systematically study the behavior of oligomeric protein mixtures in terms of ion suppression effects and determine the response factors. The individual oligomers have the advantage to differ from each other by an increase in mass, while other properties should stay the same. Binary solutions including equimolar mixtures, titration series at constant total concentration as well as titrations with one component kept constant were studied by native ESI-MS. While the classical definition of a response factor was found to be still applicable for equimolar mixtures, this relationship is lost when titration series are performed. By using simulations, we were able to separate and quantify ion suppression effects. It was found that signals corresponding to lighter oligomers always suppressed signals from heavier ones.
The strength of ion suppression effects depending on oligomers present in the mixtures was evaluated. For highly concentrated solutions the ion suppression strength was explained by competition for available charges at the surface droplet. By using ion mobility (IMS) and calculations based on the theoretical Rayleigh limit, ion suppression strength behavior for low concentrated samples could be explained by using a discrimination based attempt. For mixtures with low concentrations the magnitude of ion suppression was explained by discrimination during the ionization process, which was confirmed by theoretical calculations and IMS. Titration experiments with anti-MBP binding to MBP ligand were performed using nanoESI-MS. The determined dissociation constant (K_D) using a 2:1 binding model was determined to be 100mM.

[1] S. Weidmann, K. Barylyuk, N. Nespovitaya, S. Mädler, R. Zenobi, Anal.Chem., 2013, 85, 3425-3432.

ICP-TOFMS analysis of transient signals generated by laser ablation

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Laser ablation inductively coupled plasma time-of-flight mass spectrometry (LA-ICP-TOFMS) is a versatile micro-analytical technique that has recently found great attention in many research fields such as geology, material sciences, biology and medicine.

In this presentation, we describe latest advances in the combination of discrete as well as continuous LA-based sample introduction systems with ICP-TOFMS instrumentation. Using low-dispersion LA cells, the ablated aerosol can be transported to the ICP within 5 ms, which leads to a higher instantaneous concentration of ablated aerosol in the ICP and improved signal-to-noise ratios. Current TOFMS instrumentation can provide real time and continuous full-spectrum recording at 1000 Hz, which provides sufficient sampling of each LA transient event. Moreover, because each batch of ions analyzed with TOFMS is extracted simultaneously from the ICP, spectral intensity skew error is eliminated and improved correction for ICP flicker noise is possible through ratioing.

In addition to its unique merits for use with low-dispersion LA, the latest generation ICP-TOFMS instruments provide characteristics also desirable for the analysis of continuous LA signals. A collision cell upstream of the TOF mass analyzer can be pressurized with a collision or reaction gas. Using He as collision gas, the ion beam is cooled so that mass resolving powers up to $RP_{(FWHM)}$=5000 can be achieved. Operating the cell with a reactive gas like H_2 allows for the suppression of Ar-based interferences (Ar^+, Ar_2^+ or ArO^+), which improves signal/background ratios for interfered isotopes such as ^{40}Ca, ^{56}Fe and ^{80}Se. Furthermore, preventing all Ar^+ and argon-based molecular ions from entering the TOF extraction region attenuates the total ion current to a level better manageable by a TOF mass spectrometer.

Applying a 44 µm diameter spot size and operating the laser at a repetition rate of 10 Hz allows accurate quantification for most elements in NIST reference glasses with limits of detection in the single ng/g range for most sensitive isotopes. Accurate full mass spectral quantification from a single laser pulse is possible with limits of detection ranging from single µg/g (5 µm diameter laser spot size) to single ng/g (90 µm diameter laser spot size) for most sensitive isotopes in NIST reference glasses. This corresponds to an absolute limit of detection in the tens of femtograms range.

Recording and storing complete elemental mass spectra across a time series provides the opportunity to perform mass spectral deconvolution of non-baseline resolved signals. This accounts for more flexibility regarding the isotope selection. Speed, sensitivity, spatial and mass spectral resolution offered by LA-ICP-TOFMS instrumentation are desirable for various applications including high-resolution qualitative and quantitative imaging of geological and biological specimens, depth profiling, and bulk quantification of solids with minimal sample consumption.

Small-drugs quantification from whole-blood within paper-based microstructures for Point-Of-Care Therapeutic Drug Monitoring

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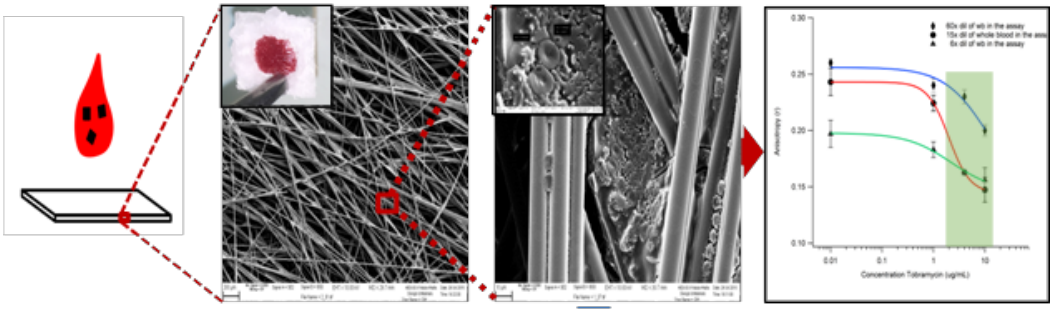
Therapeutic Drug Monitoring allows and controls personalized dosage during important therapeutic treatments and it is often mandatory for modern potent drugs against cancer, HIV or in organ transplantation cases. Currently, this process is demanding for the patient as several milliliters of blood are required, is slow and costly, as the sample needs to be transferred to a central laboratory and suffers of limited efficacy as the results are difficult to interpret for a non-specialist. In order to circumvent these problems, we aim to develop a minimally invasive Point-of-Care (POC) device that allows the quantification of small drug molecules in blood with fast turnaround, based on miniaturized fluorescence polarization immunoassays (FPIA).

Precisely, a fluorescence-polarization based immunoassay for Tobramycin, a 456 Da molecule, was miniaturized with significantly reduced human sample (just 1 µl), reagent consumption and number of steps, without compromising assay reliability. Furthermore, the miniaturized assay was transferred into paper-based microstructures, as we consider paper as an ideal platform for a POC device for clinical and analytical chemistry due to it is light weight, its biocompatibility, easy to use and dispose and its low cost[1]. However, Fluorescence polarization hasn't been yet associated with direct quantitative measurements into paper mainly due to the fluorescent background and the depolarizing scattering effect that might interfere with analytical performance.

For Tobramycin, we optimized the assay by developing a novel tracer whose fluorescence is not impacted by the biological samples and we managed to measure the anisotropy within human serum, directly into paper (Fig. 1). The novel approach showed good performance in terms of analytical parameters regarding the variation coefficients, recoveries and limit of detection and quantification demonstrating the feasibility of FPIA using only minute amounts of blood as it is available in point-of-care tests.



Connelly, Rolland, and Whitesides, "'Paper Machine' for Molecular Diagnostics.", Anal. Chem., **2015**, *87* (15), pp 7595–7601

LA-ICP-MS for quantification of minerals using matrix-matched glasses as external standards

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Since the early investigations of Laser-Ablation Inductively Coupled Mass Spectrometry (LA-ICP-MS) in 1985 [1], it has become an extremely important analytical technique for spatially resolved analysis of solids.

Although there have been promising results for non-matrix matched quantification using femtosecond lasers [2 - 4], it still remains a challenge. Non-matrix matched quantification possibilities are still limited by differences in ablated mass, particle size distribution, vaporization, ionization regions within the plasma of different particles etc. [5, 6]. Hence, a variety of certified reference materials (CRMs) not only broadens the possibility for matrix-matched quantification, but rather allows to validate calibration strategies of non-matrix matched quantifications.

Developments of pressed powder CRMs by for example Garbe-Schönberg et al. [7] opens the opportunity to validate matrix-matched, non-phase-matched quantifications, in order to account for different ablation behaviors or different behavior within the plasma.

Herein the feasibility to quantify samples in mineral phase with an external standard in glass phase was investigated, using LA-ICP-MS. The samples are pressed powder tablets from basalt rocks [7], produced without any additional binders, whereas the external calibrants are basalt glasses from USGS [8]. The effect of different laser-ablation parameters, such as wavelength, pulse duration and energy density were investigated. Results for nanosecond laser ablation at 193nm as well as for femtosecond laser ablation at 257nm, using calcium as internal standard and different spot sizes (60µm, 55 µm, 30µm), show significant overestimations for silicon, whereas aluminum and magnesium tend to be underestimated. Though, major elements, such as iron, manganese and titanium are accurately quantified. Quantifications using femtosecond laser ablation at lower energy density, higher photon energy (206nm) and smaller spot sizes (30µm), leads to higher accuracy for silicon, magnesium and aluminum. Possible explanations for these quantification errors using an external standard with a different chemical environment, but the same chemical composition will be part of this presentation.

[1] Alan L. Gray, Analyst (Cambridge, UK), 1985, 110, 551-556. [2] Jhanis Gonzalez, Chunyi Liu, Xianglei Mao, Richard E. Russo, J. Anal. At. Spectrom., 2004, 19, 1165-1168. [3] Helmar Wiltsche, Detlef Günther, Anal. Bioanal. Chem., 2011, 399, 2167-2174. [4] Veronika Mozná, Jorge Pisonero, Markéta Holá, Viktor Kanický, J. Anal. At. Spectrom., 2006, 21, 1194-1201. [5] Ivana Kroslakova, Detlef Günther, J. Anal. At. Spectrom., 2006, 22, 51-62. [6] Luca Flamigni, Joachim Koch, Detlef Günther, Spectrochim. Acta, Part B, 2012, 76, 70-76. [7] Dieter Garbe-Schönberg, Samuel Müller, J. Aanl. At. Spectrom., 2014, 29, 990-1000. [8] Shan Gao, Xiaomin Liu, Honglin Yuan, Bodo Hattendorf, Detlef Günther, Liang Chen, Shenhong Hu, J. Geostandards and Geoanalysis, 2002, 26, 181-196.

Observation of forbidden vibrational transitions in a plasmonic nanogap

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We demonstrate a breakdown of selection rules for vibrational spectroscopy in a plasmonic nanogap between a silver tip and a gold substrate.

Tip-enhanced Raman spectroscopic (TERS) measurements were performed for a model dipeptide (Phe-Phe) located in the tip-sample junction of a scanning tunneling microscope (STM). Tuning the junction geometry by modifying the STM feedback set point allowed observation of several IR-active modes, normally not observed in Raman spectroscopy. Conversely, certain Raman-active vibrations disappeared from the spectrum upon tightening the junction.

Appearance of new spectral features is mostly due to the high field gradient in the plasmonic nanogap, which affects the selection rules for vibrational transitions. The effect of tunneling current on the spectra was verified by direct comparison of spectra obtained in STM and AFM feedback using the same probe.

The observed phenomena are of general relevance for nanospectroscopy and may help to resolve the controversy about spectral discrepancies between confocal Raman and TERS.

Nanoscale molecular orientation mapping by Tip-Enhanced Raman Spectroscopy

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Molecular orientation plays an important role in molecular interactions, affecting intermolecular binding [1], catalytic properties [2], thermal stability [3], and solar cell performance [4]. For generation of monolayer sheets with a certain orientation, the Langmuir-Blodgett (LB) technique is often used. It relies on orientation of amphiphilic molecules floating on a liquid/airinterface. As the potential for applications utilizing oriented thin films grows, the need for accurate, reliable analysis of molecular orientation and surface coverage also tends to increase.

Tip-enhanced Raman spectroscopy (TERS) combines scanning probe microscopy (SPM) with Raman spectroscopy, and allows one to simultaneously record the topography and a chemical fingerprint of samples with nanoscale resolution [5]. Moreover, TERS has been shown to have a sensitivity down to the single molecule level [5].

Here, we investigate monolayer/sub-monolayer samples generated with different sample preparation methods, spin-coating and the LB technique, by using TERS with scanning tunneling microscope (STM) feedback at ambient conditions. We record high-resolution TERS maps of these samples and evaluate the distribution of molecular orientations by statistical analysis. Furthermore, utilizing density functional theory (DFT) calculations, we compare the confocal Raman spectra, TERS spectra and theoretical Raman spectra with different surface selection rule to get quantitative information on the orientation of our molecules [6].

[1]. P. Yang, *et al.*, PLoS ONE **8**, e82072 (2013).
[2]. K. Brandt, *et al.*, J. Am. Chem. Soc. **131**, 17286-17290 (2009).
[3]. S. S. Dalal, *et al.*, Proc. Natl. Acad. Sci. USA **112**, 4227-4232 (2015).
[4]. J. R. Tumbleston *et al.*, Nat. Photon. **8**, 385-391 (2014).
[5]. Schmid, T. *et al.*, Angew. Chem. Int. Edit.**52** (23), 5940-5954 (2013).
[6]. S. Jiang *et al.*, *Nat. Nano.* **10**, 865-869 (2015).

Constant Potential Coulometry for All-Solid-State Chloride-Selective Electrodes

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In recent years, the exploration and the development of chemical sensors have been the subjects of growing scientific attention. Today, a number of solid-contact ion-selective sensors exist for the recognition of ions in fundamental chemical science as well in modern applications, including environmental monitoring and clinical diagnostics.

Solid contact ion-selective electrodes (SC-ISEs) have been extensively characterized during the last two decades and their application allows one to develop a new generation of ion sensors. The SC-ISEs having a conducting polymer as ion-to-electron transducer display excellent and tunable analytical properties that make them advantageous to be used in sensor technology.[1,2]

We present here an extended experimental study of a novel signal transduction principle for SC-ISEs introduced by Bobacka et al.[2,3] The novel technique is based on constant potential coulometry and uses the redox capacitance of the internal solid-contact of the ion-selective membrane electrode to convert changes in ion activity into an electrical current (and charge) readout.[3,4] The potential of the SC-ISE vs the reference electrode is kept constant and the potential change at the interface between the ion-selective membrane and the sample solution is compensated by the oxidation/reduction of the conducting polymer PEDOT (poly(3,4-ethylenedioxythiophene)) that is covered by a cation-selective or anion-selective membrane. We provide here a systematic comparative study between constant potential coulometry and traditional potentiometry for detecting small changes in ion activity using chloride-selective SC-ISEs. The attention was focused on the optimization of analytical parameters by varying e.g. the thickness of the PEDOT layer and the chloride-sensitive membrane.

1. Bobacka, J., *Electroanalysis* **2006**, 18, 7-18.
2. Yuan, D.; Anthis, A. H. C.; Ghahraman Afshar, M.; Pankratova, N.; Cuartero, M.; Crespo, G. A.; Bakker, E., *Analytical Chemistry* **2015**, 87, 8640-8645.
3. Hupa, E.; Vanamo, U.; Bobacka, J., *Electroanalysis* **2015**, 27, 591-594.
4. Vanamo, U.; Hupa, E.; Yrjana, V.; Bobacka, J., *Analytical Chemistry* **2016**, 88, 4369-4373.

Ionization Mechanism of Perfluorinated Compounds Using an Active Capillary Plasma Ionization Source

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Active capillary plasma ionization is a soft ionization technique, which is based on a dielectric barrier discharge. This plasma source operates with air, N_2 or CO_2 as discharge gas and features a fully enclosed ionization volume, which facilitates mechanistic investigations. In this study, the ionization of perfluorinated compounds (PFC) was investigated, a class of compounds that can only be ionized with great difficulty by other ambient ionization techniques. More detailed knowledge about negative ion formation of perfluorinated compounds would allow us to better understand the ionization mechanisms taking place in our plasma source, compare it with other ambient ionization techniques, and find useful applications that can take advantage of the specific features of our source.

Several perfluorinated compounds (e.g. perfluorohexane, perfluoroheptane, perfluorooctane, perfluorotributylamine) were investigated in the gas phase. The samples were evaporated within a hollow heating cartridge held at 200 °C, and a preheated discharge-gas stream (air or N_2) was used to transport the vapors to the active capillary plasma ionization source, which was directly connected to the inlet of a mass spectrometer. The active capillary plasma ionization source contains a stainless steel capillary working inserted into a glass capillary as an electrode, and a copper ring surrounding the glass capillary functioning as the counter-electrode. The cold plasma was generated by applying a sine modulated (5750 Hz) high voltage (3.0 kV_{pp}) to the electrodes. For all measurements, a commercial ion trap instrument (LTQ Finnigan, Thermo Fischer) was used for the detection.

The perfluorinated alkanes were ionized to two main gas-phase products, namely by loss of a fluorine atom to form $[M\text{-}F]^-$ and by a substitution reaction of fluorine by oxygen to form $[M\text{-}F+O]^-$. The radical anion $[M]^{-\cdot}$ was only detected when applying a lower voltage. It was found that the applied voltage has a great impact on negative ion formation. The oxygen source for the substitution reaction ($[M\text{-}F+O]^-$) was successfully determined by operation under different conditions. H_2O and O_2 molecules present (in traces) in the discharge gas were identified to contribute as an oxygen source for the substitution reaction. NO_2 and NO_3 ions were generated in the plasma source, but it is not yet clear if they are able to react with the perfluorinated alkanes.

UV-fs-LA-ICP-TOF-MS for the quantitative analysis of $La_{1-x}Ca_xMnO_3$ PLD thin films in high spatial resolution

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The pulsed laser deposition (PLD) technique is a proven way of manufacturing films of a thickness below 200 nm. The subjects of interest in this study are thin films made from the raw material; perovskite-structured compound $La_{1-x}Ca_xMnO_3$ ($0 \leq x \leq 1$), the physical properties of which (e. g. electrical conductivity) are subjected to change depending on slight variations in the La/Ca stoichiometry[1]. Rutherford backscattering spectrometry (RBS) has been used to reliably quantify the immediate surface (first 5 nm) of these films so far [2]. However, considering the lateral resolution of RBS is in the mm-range, laser ablation inductively coupled plasma mass spectrometry (LA-ICP-MS) (lat. Resolution: µm-range) would qualify as a more efficient, swifter technique to obtain a 3-dimensional, quantitative profile of the stoichiometry within the film. The deployment of a novel UV-fs-LA system allowed a low uptake rate of 40 nm per pulse, whereas the quasi-simultaneous ion detection of TOF-MS prevented spectral intensity skew, enabling single pulse quantification.[3]

Initial UV-fs-LA-ICP-TOF-MS depth profiling, yielding novel elemental information on the thin films, as the layer depth could be analysed in its entirety, indicated relative homogeneity with depth (5% rsd) but less so laterally (up to 15% rsd). However, the average stoichiometry derived from the UV-fs-LA-ICP-TOF-MS depth profiling was similar (6% difference) to the values the RBS measurements yielded. Considering the discrepancy in actual sampling area between RBS and UV-fs-LA-ICP-TOF-MS (mm^2 vs μm^2), further analyses were conducted on the PLD films in an acquisition mode that emulated that of the RBS measurements, to produce valid comparisons between both techniques.

Results of the UV-fs-LA-ICP-TOF-MS analyses on the aforementioned films, i.e., quantification data and comparisons to RBS measurements will be presented and discussed.

[1] A. Ojeda, C.W. Schneider, M. Döbeli, T. Lippert, A. Wokaun, *Applied Surface Science*, **2015**,336, 150-156.
[2] M. Döbeli*, J. Phys. Condens. Mat*, **2008**,20, 1.
[3] A. W. Gundlach-Graham, et. al. *Anal. Chem.*, **2015**,87, 8250-8258.

Capillary Gap Sampler : a new microfluidic platform directly coupled to ESI-MS for fast analysis of low sample amounts

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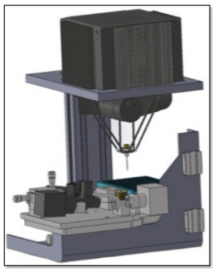
Miniaturized sampling devices hyphenated with ESI-MS are very attractive analytical tools for early drug discovery. ESI-MS is compatible with microfluidics, and allows comprehensive, label-free sample analysis yielding information that is orthogonal to that available from optical methods. This project aims at the development and implementation of a “capillary gap sampler”- a miniaturized sampling device as a platform for directly connecting microfluidics to µ-ESI-MS for fast and comprehensive sample analysis. The sampler is robust, light and compact, and allows precise liquid handling or extraction of very low sample amounts.



Important requirements for the sampler design come from an increasing interest in both site-specific sample pickup (e.g., for imaging applications) and for improved productivity in resource-saving screening procedures. The basic idea consists of creating an“ open” system for sample infusion, by forming a liquid bridge of several nanoliters within a micrometer-sized gap between two capillaries, which minimizes the system dead volume as well as sample adsorption/sticking on surfaces. One of the capillaries acts directly as the ESI-MS spray needle. This design allows for the system to be constantly ready for sample infusion. A solid pin is used for sample uptake and delivery, such that neither valves nor additional lines for sample introduction are needed. Other components includes onboard microrobotics, optics, and a sophisticated pressure and liquid flow regulation system that enables robust sample infusion without distressing the stability of the liquid bridge in the gap.

The system shows good performance characteristics such as symmetric peak shapes, low sample carryover (below 1%), and total injection cycle times of less than 15 s. This device thus has the potential for rapid analysis of biomedical and pharmaceutical samples with limited sample amounts in a high-throughput mode. Characterization of the liquid bridge as a new microfluidic element showed a miniaturization-friendly behavior based on self-stabilization, which opens the door for further reduction of injection volumes, gap dimensions, and capillary lengths, in order to further minimize the internal system volumes and the sample dilution factor. Performance tests of the sampler revealed promising figures of merit in terms of sensitivity, response linearity, and robustness for multiple sample analysis (1).

We present a coupling of solid phase microextraction with the capillary gap sampler to address challenges for small-volume sample cleanup prior to ESI-MS analysis (2). We have shown that the sampler is capable of extracting benzodiazepines from PBS. Experimental conditions are optimized and repeatability for 20 extractions of benzodiazepines from PBS with less than 17 % RSD, confirming the promising performance of the method. This would be interesting for less available or expensive biological samples within complicated matrices. Recently we also developed a specific extraction tool for a synthetic antineoplastic agent. This example opens the door for studying targeted drug delivery such as quantification of drug in targeted tissue.

1. Volker Neu, *Analytical Chemistry Journal*, **2013**, 85, 4628−4635
2. Fatemeh mirnaghi, *Analytical Chemistry Journal*, **2011**, 83, 6018–6025

Study of the Interaction Between p53 and DNA by Tip-Enhanced Raman Spectroscopy

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p53 is a tumor suppressor protein that plays an important role in cellular apoptosis, genomic stability, and inhibition of angiogenesis. The ability to bind DNA is crucial for the tumor suppressor activity of p53. [1] p53 forms tetramers that bind specifically to the DNA. [2] A chemical characterization of this binding behavior will contribute to better understand p53's mechanism of action.

Tip-enhanced Raman spectroscopy (TERS) is a near-field optical technique that combines the advantages of scanning probe microscopy (SPM) and Raman spectroscopy. A metal nanostructure can be deposited on the apex of tip, which amplifies the electromagnetic field of incident laser light and enhances the Raman signal of a sample located close to the tip. TERS possesses high spatial resolution and high sensitivity, down to the single molecule level. [3,4]

We investigated the interaction between p53 and DNA by atomic force microscopy (AFM)-TERS. After p53 and DNA were incubated in solution, Mg^{2+} was used to bridge the negatively charged mica surface and DNA backbone. [1,5] TER spectra of DNA, protein and DNA-protein complexes were collected. First results on spectral imaging of the DNA-protein complex with nanoscale spatial resolution will be presented.

[1] Y. Jiao, et al. *J. Mol. Biol.*, 2001, 314, 233-243.
[2] P. N. Friedman, et al. *Proc. Nat. Acad. Sci. USA*, 1993, 90, 3319-3323.
[3] T. Schmid, et al. *Angew. Chem. Int. Edit.*, 2013, 52, 5940-5954.
[4] M. D. Sonntag, et al. *J. Phys. Chem. Lett.,* 2014, 5, 3125.
[5] A. Japaridze, et al. *Macromolecules*, 2016, 49, 643-652.

Sample Acidification for Potentiometric Sensing of Anions in Environmental Samples

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The detection of inorganic and hydrophilic anions is essential in many areas of applied analytical chemistry, particularly for the analysis of environmental samples. For instance, the determination of phosphate and nitrite concentration is of great interest since aquatic ecosystems are highly affected by the levels of nutrients such as phosphorus and nitrogen. In the last decades potentiometric ion-selective sensors have become a very attractive tool for practical applications due to their reasonably fast response, small dimensions, portability, low energy consumption and simple operation.[1,2] However, due to strong hydroxide interference, most anion sensors reported so far are not suitable for application above pH 7 while the pH of environmental samples normally ranges from 6.5 to 8.5[3].
The hydroxide interference can be suppressed by means of sample acidification which is commonly achieved either with a cation exchanger column or a loop injector/mixing coil where the sample is mixed with acid in adequate proportion.[4,5] Here we report on two new principally different concepts for the sample acidification, coupled with potentiometric measurements.

The first concept suggests acidification of the bulk solution in a flow. The principle is based on the ion exchange process between cations present in the sample and protons released through the preconditioned cation-exchange membrane (FKL, fumasep) with constantly renewed hydrochloric acid reservoir behind the membrane. The acidification occurs in-line and allows for various resulting pH depending on the flow rate, cation concentration in the sample compartment and acid concentration in the acid compartment. Moreover, the concept can be relatively easily adapted for in-situ measurements and provides for long-term continuous determination. No additional valves are required unlike with ion exchange column where the latter needs to be periodically rinsed and reconditioned. A theoretical model was suggested for the description of acidification process within the proposed configuration.
The second concept requires no flow and is based on local electrode surface acidification by proton release in the thin layer adjacent to the electrode membrane. Three different approaches were developed for the implementation of the proposed concept. All three require no pre-treatment and suggest direct contact of the sensor with the natural sample. In a first approach, a concentrated acetic acid solution is placed in the inner filling solution of the PVC-based membrane electrode, forcing a significant acid gradient across the membrane. A second strategy achieves the same type of passive acidification by using an external proton source placed in front of a potentiometric solid contact anion selective electrode where the thin layer gap allows one to observe spontaneous acidification at the opposing detection electrode. The third approach shares the same configuration, but protons are here released by electrochemical control from the selective proton source into the thin layer sample.[6]

All concepts are explored with ionophore-based membrane electrodes selective for nitrite and phosphate as guiding examples. The suggested protocols improve the limit of detection by more than two orders of magnitude at environmental pH.

[1] Martijn M. G. Antonisse, David N. Reinhoudt, *Electroanalysis,* **1999**, 11, 1035-1048.
[2] Eric Bakker, Ernö Pretsch, *Angewandte Chemie, Int. Ed.* **2007**, 46, 5660-5668.
[3] Joy P. Michaud,A Citizens' Guide to Understanding and Monitoring Lakes and Streams. Washington State Department of Ecology: **1991**.
[4] Andrew G. Howard, C. Y. Yeh, *Analytical Chemistry,* **1998**, 70, 4868-4872.
[5] Glenn B. Martin, Mark E. Meyerhoff, *Analytica Chimica Acta,* **1986**, 186, 71-80.
[6] Nadezda Pankratova, Majid Ghahraman Afshar, Dajing Yuan, Gaston A. Crespo, Eric Bakker, *ACS Sensors,* **2016**, 1, 48-54.

Source apportionment of atmospheric mercury species measured at the high-alpine site Jungfraujoch

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Mercury is a heavy metal which can cause severe adverse health effects in humans and the environment [2]. It is released to the atmosphere, both from natural sources, including volcanic eruptions and anthropogenic activities, like fossil fuel combustion. The largest emissions of mercury are in the form of gaseous elemental mercury (GEM) which is distributed globally. Parts of it are oxidized in the atmosphere or bind to particles. However, in contrast to GEM, these compounds are deposited rapidly [1]. Anaerobic organisms in water can transform this deposited inorganic mercury to highly toxic methyl mercury which is known to accumulate in the food chain [1]. Thus, humans and animals are most exposed to it through their diet. The Minamata Convention aims to control anthropogenic mercury emissions globally, to protect humans and the environment.

Until now, the atmospheric anthropogenic mercury emissions have only been estimated with bottom up approaches based on activity data [1]. A focus lies on gaseous elemental mercury, which, due to its long residence time, is responsible for long range atmospheric transport. For a regional perspective it is important to investigate gaseous oxidized (GOM) and particle bound mercury (PBM) emissions as well, as these species are deposited quickly. To lay a basis for an improved estimation of atmospheric mercury emissions by human activities, we recently built a top down inventory for GEM emissions in Europe.

In the first part of this work a Tekran mercury analyzer was set up at the high alpine-site Jungfraujoch and GEM, GOM, and PBM concentrations were measured over a three months period.

In the second part GOM and PBM is analyzed during time periods with different influence of the planetary boundary layer (PBL) to our measurement location, in order to better understand the oxidation processes of mercury. Analogously to aircraft measurements [3] higher concentrations of GOM in situations with little PBL influence were measured, due to the fact that the oxidation potential in the free troposphere is higher. Furthermore, PBL air originates in Switzerland, whereas free tropospheric air can stem from all over Europe, thus allowing to compare Swiss and European emissions.

In a last part atmospheric emission sources and fluxes of GOM and PBM as well as their transport have been investigated. With the Lagrangian dispersion model FLEXPART backward trajectories of air parcels reaching Jungfraujoch were calculated. Thus, it was possible to establish a source receptor relationship. Subsequently, the emission fluxes were calculated with a Bayesian inversion method. By comparing and combining the modeled emissions with the AMAP mercury emission inventory an improved emission map of Europe has been obtained.

In Conclusion, the measurement done within the framework of this project allow to better understand reactions, emission sources and fluxes of atmospheric mercury. It is a first step toward the implementation of a novel top down inventory of human caused mercury emissions, which can be used to validate uncertain anthropogenic bottom-up approaches and provide additional support for decision-makers and politicians to better monitor, track and control mercury emissions.

[1] AMAP/UNEP, *Tech. rept. UNEP; AMAP*, **2013.**

[2] D. Mergler, H. Anderson, L. Chan, et al., *Ambio,* **2007**, 36(1),3-11.

[3] A. Weigelt, R. Ebinghaus, N. Pirrone, et al.,*Atmospheric Chemistry and Physics Discussions*, **2015**, 15(20), 28217-28247.

Gas-phase properties of natural and modified nucleic acid duplexes

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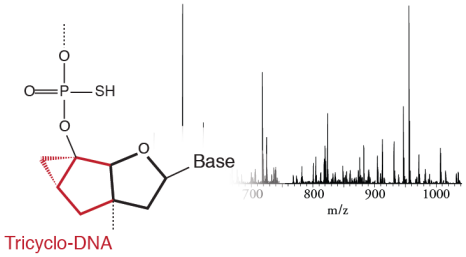
Antisense therapy aims at treating hereditary diseases by modifying the processing of mRNAs, for instance by inducing alternative splicing. For most effective treatment at minimal dose, the antisense oligonucleotides should selectively bind the targeted mRNA and evade fast enzymatic degradation. These properties are introduced by structural modifications in the synthetic oligonucleotide. One promising example of antisense chemistries is tricyclo-DNA (tcDNA), a DNA analogue comprising a three-membered ring system instead of the deoxyribose moiety.



The relative stability of natural and modified nucleic acid duplexes can be assessed by tandem mass spectrometric experiments. On one hand, these experiments probe the specificity of antisense oligonucleotides for their designated target and provide insight into the interaction between complementary strands. On the other hand, comparison of different types of nucleic acid duplexes illustrates the contribution of thermodynamic parameters to the gas-phase stability of duplexes. The entropy-favored strand separation is the dominant fragmentation channel in DNA duplexes. In modified heteroduplexes, by contrast, alternative reaction pathways compete with strand separation because the free activation enthalpies of the different channels converge.

The conformation and rigidity of higher-order nucleic acid structures were probed by ion-mobility spectrometry-mass spectrometry (IMS-MS). It was found that the modified sugar-moiety leads to a substantial increase of the collision cross-section in single strands and duplexes. Presumably, tcDNA adopts an extended conformation because the rigid sugar-moiety restricts the contraction of the molecule to a more compact, globular structure. Moreover, ion-mobility experiments evidence how the charge state influences the extension of the macromolecule as well as the rigidity of the structure.

Interaction of Metallocenes with Nucleic Acids

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Metallocene dichlorides (Cp_2MCl_2, Cp=cyclopentadienyl ligand, M=Ti, V, Nb, Mo) are metal-based compounds, which were found to be highly effective against several cancer cell lines [1]. Evidence for the accumulation of the transition metal in the cell nucleus suggests DNA as one of the major targets. However, the characteristics of the interaction between different types of metallocenes and nucleic acids remain largely unknown. The progress of this therapeutic approach comprises the development of cyclopentadienyl-modified metallocenes [2] and precise knowledge of their interaction with the target. Tandem mass spectrometry is the ideal method to investigate the formation of metallodrug adducts and to elucidate nucleobase selectivity and binding.

In this study, four different metallocenes were incubated with eight dinucleotide monophosphates (AT, TA, CG, GC, CT, TC, AG, GA) to elucidate the favored binding sites. ESI-MS experiments emphasized that adduct formation is primarily determined by the type of transition metal attached. While only titanocene and molybdenocene yield adducts including the two Cp ligands, vanadocene exhibits adducts that underwent extensive ligand exchange, and no niobocene adducts were detected at pH 7. ESI-MS/MS data of the adducts revealed that the nucleobase is involved in the binding of the metallocenes and that the type (pyrimidine or purine) and the position (3' or 5') of the nucleobase essentially determine the binding motif and the gas-phase fragmentation.

1. Köpf, H., Köpf-Maier, P.: Titanocene Dichloride - The First Metallocene with Cancerostatic Activity. *Angewandte Chemie* **18**, 477-478 (1979)
2. Kelter G., Sweeney N. J., Strohfeldt K., Fiebig H. H., Tacke, M.: In-vitro anti-tumor activity studies of bridged and unbridged benzyl-substituted titanocenes. *Anticancer Drugs* **16**, 1091-1098 (2005)b

Solid Contact Thin Layer Ionophore Based Membranes for Ion Activity Detection: Two sensing modes

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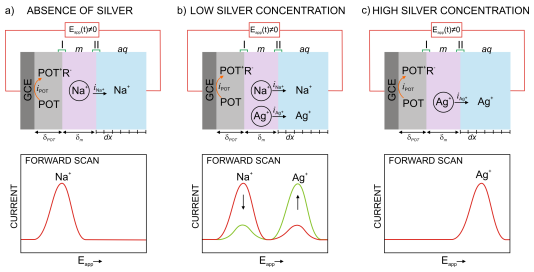
Solid contact thin layer ionophore-based membranes have recently gained much attention in the community of analytical chemistry for the sensing of small cations and anions both in environmental and physiological samples. Generally, this electrochemical sensor consists of two thin layers. The first layer is a conducting polymer such as poly-(3-octyl)thiophene (POT) that serves as reversible electron transfer layer in the electrochemical sensing process. The second layer is a thin layer liquid membrane which is spin coated on top of conducting polymer underlayer with a thickness of ~200 nm. This membrane usually contains selective receptors and cation/anion exchanger sites that facilitated the ion-transfer upon an applied potential triggered by the oxidation of the underlying conducting polymer. The application of the two thin layer configuration was primarily found in stripping voltammetric analysis of the nanomolar level of potassium, ammonium and perchlorate in drinking waters and ultrapure waters. This sensing mechanism is based on the linear relationship of voltammetric peak current or peak charge with increasing analyte concentration. In this mode, the membrane is not saturated and the current is mass transport controlled. Recently, our group found new applications of ionophore based membrane at relatively high analyte concentrations, at which the membrane is fully saturated and voltammetric peak potential exhibit a Nernstian displacement with increasing analyte concentration (so-called thin layer regime). Furthermore, a membrane incorporated with several ionophores is devised to acquire multi analyte information about the sample in a similar way as performing multiple potentiometric measurements with individual membranes. The transition between one mode to the other as well as the limiting conditions of these two approaches are here defined. A selective membrane containing silver ionophore is selected to study the transition from low analyte concentration to high analyte concentration due to an excellent discrimination of silver signal towards background sodium signal. The transition is successfully described by a model considering equilibrium at both aqueous/membrane and POT/GC interface and diffusion processes in the aqueous phase. A semi-empirical treatment was used and validated to distinguish the two sensing modes.



1.Benjamin Kabagambe et al., *Anal. Chem*. **2012**, 84, 7979–7986
2.Gaston A. Crespo et al.,*Anal. Chem.* **2015**, 87, 7729–7737

Mobile spectroscopic real-time monitoring of NO_2 for pollution maps of Zurich

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The concentration of air pollutants such as nitrogen dioxide (NO_2) in cities is highly variable because important determining factors (e.g. source activities and the density of the built environment) are changing on small spatial scales. Therefore, measurements at a small number of fixed sites can only provide incomplete information about the distribution of air pollutants in urban environments. Mobile measurement platforms are a powerful option for improving the knowledge of the small scale variability with high temporal resolution [1].

Recently, we developed a very compact (40x36x15cm) quantum cascade laser absorption spectrometer (QCLAS) for selective and rapid NO_2 detection and installed it on the roof of a tram travelling through Zurich on a regular schedule. The instrument is based on DFB-QCL operated in icw mode [2] and uses a paraboloid multipass cell with 12 m path length [3]. The NO_2 concentration is determined with a best precision of 30ppt using an integration time of 100 s. We present a detailed analysis of the variability of NO_2 in Zurich and demonstrate how the mobile high-frequency NO_2 data can complement the data from fixed traditional air quality monitoring sites for a thorough assessment of the urban NO_2 concentration field. Furthermore, we explore the potential of using the QCLAS concentration measurements in statistical Land Use Regression (LUR) modelling to create pollution maps of the city of Zurich at unprecedented resolution in time and space [1]. This is a promising tool to provide data for future health studies which will include highly resolved information of individual human activities, especially in the city environment. Furthermore, other air quality parameters, such as NO, can be implemented in the same optical setup using an additional or a multi-wavelength QCL [4].

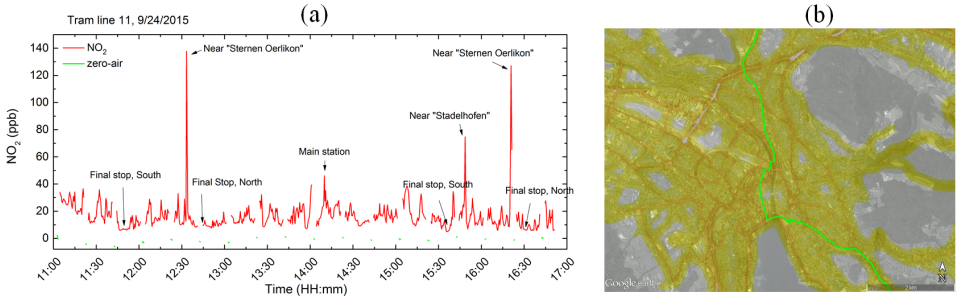

Figure 1: (a) The QCL spectrometer can resolve the large spatial and temporal variability of NO_2 in the city of Zurich. (b) Illustrative example of hourly resolved pollution map.

[1] M. Müller, D. Hasenfratz, O. Saukh, M. Fierz, Ch. Hüglin, *Atmospheric Environment,* **2016**, 126, 171-181.
[2] M. Fischer, B. Tuzson, A. Hugi, R. Brönnimann, M. Rochat, S. Blaser,A. Müller, and L. Emmenegger, *Optics Express*, **2014**, 22, 6.
[3] M. Mangold, B. Tuzson, M. Hundt, J. Jágerská, H. Looser, L. Emmenegger, *JOSA A,* **2016,** 33, 5.
[4] J. Jágerská, P. Jouy, B. Tuzson, H. Looser, M. Mangold, P. Soltic, A. Hugi, R. Brönnimann, J. Faist, and L.Emmenegger, *Optics Express,* **2015**, 23, 3.

Polyurethane Thin Layer Membranes for Multiion Detection in Blood and Serum

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[1]University of Geneva

The benefit of using thin layer ionophore-based membranes (~200 nm) backside contacted with a film of poly(3-octylthiophene) (POT) and interrogated by cyclic voltammetry for selectively triggering cation transfer processes has been recently demonstrated.[1] An anodic potential scan partially oxidizes the POT film (~50 nm), thereby initiating the release of hydrophilic cations present in the membrane to the sample solution at a characteristic potential. This ion transfer potential is related to the cation-ionophore binding constant and defines the cation release order, i.e. the less favorable cation is first expelled from the membrane.

An interesting selectivity pattern is observed with membranes containing multiple ionophores (selective for different cations). Voltammograms with multiple peaks are observed and each peak is associated with the transfer of the different cations.[2] The concept results really attractive to be applied for multiion detection in real samples such as blood. Importantly, in order to provide sensors capable of being implemented in routine analysis, it is necessary to improve the robustness found for thin layer membranes based on poly(vinyl chloride) (PVC) as the polymeric matrix. For instance, the peaks observed for different cations tend to disappear when the membrane is rinsed with water owing to the leaching of the membrane components.[1]

In order to find a suitable alternative to PVC thin layer membranes, several polymeric matrix and membrane compositions are explored. Interestingly, polyurethane-based membranes show similar analytical performances as PVC membranes with the additional overcoming of the rinsing effect. This material provides excellent mechanical, physical and chemical robustness, exhibiting no leaching of the lipophilic additives from the membrane.[3]

Simultaneous determination of lithium and potassium in blood and serum samples is successfully demonstrated as a proof-of-concept. Notably, the use of polyurethane membranes has many advantages regarding (bio)analytical applications. Biocompatibility, less nonspecific protein adsorption in biological samples and the use of a lower percentage of plasticizer in the membrane, which is often the cause of blood clotting and tissue inflammation when the sensor is used in biomedical applications are among these advantages.[4,5] In addition, polyurethane membranes present excellent adhesion conditions in order to fabricate miniaturized sensors with biodetection schemes providing a promising wave of sensors based on thin layer membranes for the detection of key ion analytes.

1. G. A. Crespo, M. Cuartero, E. Bakker, Anal. Chem. 2015, 87, 7729-7737.
2. M. Cuartero, G.A. Crespo, E. Bakker, Anal. Chem. 2016, 88, 1654-1660.
3. M. Cuartero, G.A. Crespo, E. Bakker, Anal. Chem. DOI:10.1021/acs.analchem.6b01085
4. E. Lindner et al., J. Biomed. Mat. Res. 1994, 28, 591-601.
5. C. Espadas-Torre, M. Meyerhoff, Anal. Chem. 1995, 67, 3108-3114.

Silver nanoparticle transformations in lake water explored by an asymmetrical flow field-flow fractionation and single particle ICP-MS characterization

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The continuously growing production and use of nano silver-based materials (nanoAg) in a wide range of applications and their unavoidable release into the environment, raise concerns about their fate and impact to the environment and human health. However, given the low concentrations of engineered nanomaterials in the natural water, the study of their fate and transformation requires the use of highly sensitive analytical techniques. In the present work a combination of an asymmetrical flow field-flow fractionation (AsFlFFF), surface plasmon resonance (SPR), and single particle inductively coupled plasma mass spectrometry (SP-ICP-MS) is used to examines the transformations of nanoAg with three different coatings – citrate (CIT), polyvinyl pyrrolidone (PVP) and lipoic acid (LIP) and size of 20 and 50nm in lake water. The influence of nanoAg size, surface coating, exposure time and the presence and nature of dissolved organic matter on the nanoAg transformations in terms of agglomeration, dissolution and surface modifications in lake water were investigated.

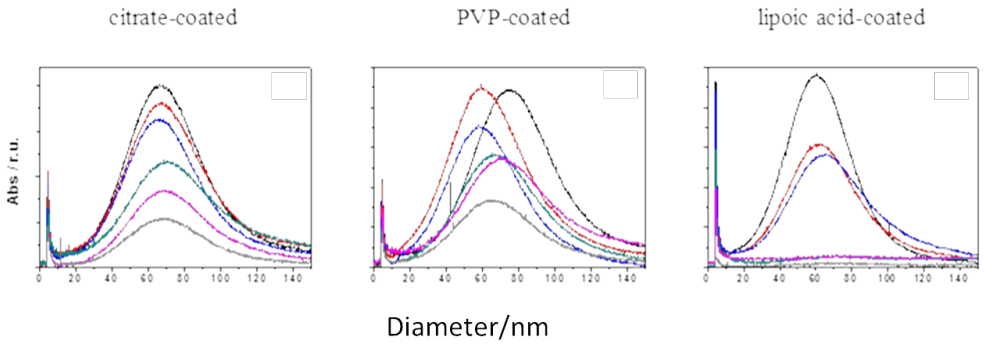

Figure 1. Size distributions of 50 nm citrate-coated nanoAg at different exposure times obtained by AsFlFFF-UV-Vis: 0h (black line), 1h (red line), 2h (blue line), 24h (green line), 48h (pink line) and 168h (gray line).

The results revealed that prevailing transformations e.g. agglomeration vs dissolution are complex interplay between the surface coating characteristics, exposure time and presence and nature of DOM rather the initial nanoAg size. The combination of the AsFlFFF-UV-Vis and SP-ICP-MS allows to better understand the persistence of different nanoAg in the aquatic systems.

Two-dimensional algal array combining AC-dielectrophoresis with ROS fluorescence detection as a contaminant biosensing chip

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An alternative current (AC) dielectrophoretic lab-on-chip setup was evaluated as a rapid tool of capture in two-dimensional (2D) arrays of microalga *Chlamydomonas reinhardtii.* Combined with fluorescence microscopy detection, the capability of using the 2D whole-cell arrays on chip to follow the reactive oxygen species production to several environmental contaminants, including mercury, methylmercury, copper, copper oxide nanoparticles (CuO-NPs), and diuron was explored. The results showed significant increase of the cellular reactive oxygen species when *C. reinhardtii* was exposed to increasing concentrations of methylmercury, CuO-NPs and 10^{-5} M Cu, as revealed by enhancement of the CellROX® stained cells proportion. Overall, this study demonstrates the potential of combining of AC-dielectrophoretically assembled two-dimensional algal array with single cell fluorescence analysis using a fluorescence stain, as a rapid biosensing tool for environmental contaminants and toxins at high exposure concentrations.

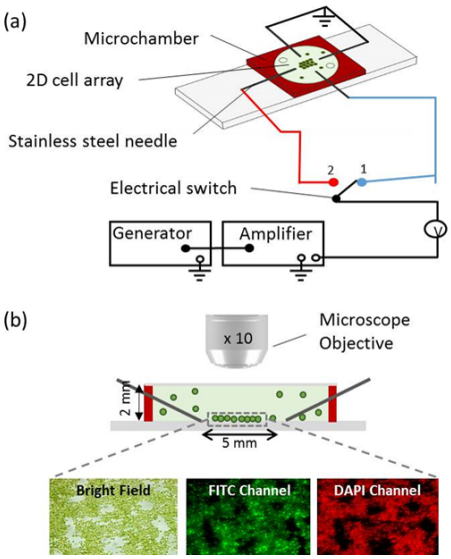

Figure 1. Schematic of the experimental set-up. The four stainless steel needle electrodes were orthogonally connected to the generator and amplifier. The electric field was applied to one pair of electrodes and switched to the other pair every 2 min allowing the formation of 2D cell array at the surface of the chamber. (b) Transverse section of the 2 mm high chamber, the 2D-array formed inside the 5 mm gap formed by the four point needle electrodes is observed under x10 magnification objective using bright field light, FITC channel and DAPI channel. The chamber and the cells sizes are not to scale.

Coralie Siebman, Orlin D. Velev and Vera I. Slaveykova, Biosensors 2015, 5 320.

Mathematical demodulation of interreflection based multi-modulation artefacts in Fourier transform infrared spectroscopy

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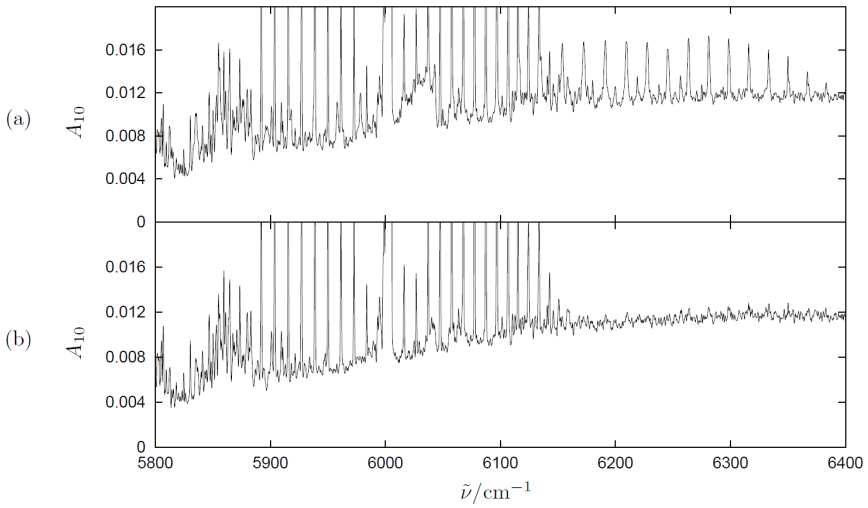
Fourier transform infrared spectroscopy (FTIR) is widely used to record rovibrational spectra of molecules in the gas-phase and to assign the corresponding transitions [1]. If reflected light in a FTIR spectrometer reaches the interferometer again and is being detected, double-modulation artefacts are observed in the spectra [2, 3].Those artefacts interfere with rovibrational transitions of overtones and combination bands at half the wavenumbers of the artefacts and therefore can perturb the transition intensities and line shapes in spectra. It is very desirable to eliminate those artefacts. We developed a demodulation scheme, which is applied directly to the interferogram. The contribution of the reflection interferogram is cancelled using the original interferogram at double the frequency in combination with a compensation coefficient γ. This coefficient is determined iteratively resulting in a complete compensation of the artefacts can be compensated completely.

In the figure below, the P_4 tetradecad band of CH_4 (5800 to 6150 cm^{-1}) and double modulation artefacts of the P_2 pentad region are shown. The original spectrum (a) was compensated (b) with a single iteration using γ= 0.004.



Using this demodulation scheme, intensity correction characteristics on the real signals have been identified. Implementing a few apparative modifications inside the spectrometer would in principle allow for a full automation [4, 5].

[1] M. Quack, F. Merkt, *Handbook of High-Resolution Spectroscopy*, vol. 1 2. Wiley, **2011**.
[2] J. R. Birch, F. J. J. Clarke. *Spectroscopy Europe*, **1995**, 4, 16.
[3] T. J. Johnson, R. L. Sams, T. A. Blake, S. W. Sharpe, P. M. Chu. *Applied Optics*, **2002**, 41, 2831.
[4] M. Schilling, MSc Thesis, ZHAW Wädenswil, **2016** (unpublished).
[5] M. Schilling, J. Stohner, In Jürgen Stohner and Chahan Yeretzian (Eds.), Proceedings of the 20th Symposium on Atomic, Cluster and Surface Physics 2016 in Davos, Innsbruck University Press, **2016**.

Implementing Plasma-based Extreme UV radiation for table-top nano-analytics

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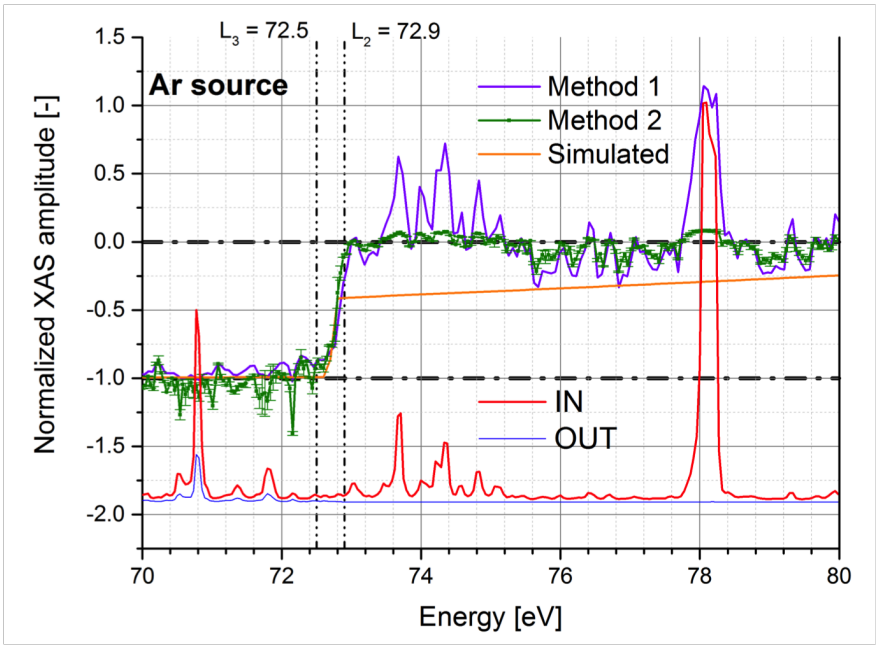
Laser action in the extreme ultraviolet and soft X-ray has been demonstrated on tabletop setups using laser-produced and discharge-produced hot/dense plasmas as single-pass high-gain media. In the time of large *accelerator-based* X-ray lasers, fundamental and applied research on compact *plasma-driven* X-ray laser carries the promise of bridging the gap between the user and the analytical tools. This demands contributions in (i) better quantitative understanding of the parameters' effect on plasma-lasing, and generalization of the empirical models, (ii) assembling compact "table-top" demonstrators with the required robustness to address research and industry challenges, (iii) performing proof-of-principle experiments on "real world" advanced materials.



Experiments were run using the newly installed *Beagle*[Plus] system at the Empa Laboratories. The "*back-end system*", i.e. compact and close to the application needs, uses also a self-developed pseudospark XUV source for imaging or spectroscopy. A parametric study is also presented.

Nano-analytics were indeed performed on certified reference materials (CRM) as well as catalysts. Imaging was performed using a self-developed Schwarzschild microscope, with a back-end resolution well-below the resolution of commodity confocal microscopes and without the sample prep for super-resolution techniques. Proof-of-principle spectroscopy experiments using a home-built FT-Time-of-Flight Spectrometer as well as X-ray absorption and fluorescence measurements in the so-called HEROS (High-Energy Resolution Off-resonance Spectroscopy) configuration are discussed (see figure, showing an absorption spectrum acquired on a table top without scanning).

SOLUTIONS for effective Non-target Screening in environmental samples

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Non-target screening using high resolution tandem mass spectrometry (HR-MS/MS) is essential to help prioritize and identify the tens of thousands of unknown chemicals detected in complex mixtures, but is also time-consuming and requires compilation of information from a plethora of sources. A high-throughput, consolidated non-target identification workflow for environmental HR-MS/MS screening was developed within the European project SOLUTIONS (www.solutions-project.eu). The *in silico* fragmenter MetFrag, first released in 2010, was expanded to include retention time (RT), reference and patent information, spectral similarity, suspect list screening, element and/or substructure selection and exclusion as well as user-defined scores [1], see also http://c-ruttkies.github.io/MetFrag/. References and patents provide vital clues for high-use substances. The suspect screening functionality allows candidate retrieval from large compound databases (such as PubChem and ChemSpider with several million entries) combined with tagging entries in various specialised suspect lists such as STOFF-IDENT (http://bb-x-stoffident.hswt.de/) and other lists on the NORMAN Network Suspect Exchange (http://www.norman-network.com/?q=node/236). User-defined scores allow the inclusion of exposure and toxicity predictions. Finally, the inclusion of mass spectral information from the MassBank of North America (http://mona.fiehnlab.ucdavis.edu/) via both a MetFusion spectral-structural similarity score [2] and per-substance best match gives users the chance to increase the confidence of the tentative identifications with spectral evidence, where available.

Firstly, MetFrag2.2 was evaluated on 473 merged spectra of environmental reference standards to determine the optimal weightings for the fragmentation, reference and retention time scores. The ranking results improved from 15 % structures ranked correctly in first place using MetFrag2010 to 89 % with MetFrag2.2 using the ChemSpider database. Comparable results were obtained for three independent Orbitrap datasets of 310, 289 and 225 substances [1], all from MassBank (contributed by Eawag and UFZ). Including an alternative fragmenter, CFM-ID [3], improved the results further. For high throughput use, MetFrag2.2 was applied within an R-based workflow using the packages enviPick, enviMass, enviPat, nontarget and RMassBank (http://www.eawag.ch/en/department/uchem/software/). Upstream, downstream and wastewater effluent samples from three small streams in the Rhine catchment were evaluated. Masses (159 positive, 137 negative mode) were prioritized for data-dependent MS/MS acquisition using peak picking, componentization and pattern analysis. Meaningful MS/MS was obtained for 182 (92 positive, 90 negative) of these masses, respectively. Of these, 28 and 16 (positive, negative) were prioritized as potentially high exposure and/or high risk substances from compiled (and partially confidential) registration data (S. Fischer, KEMI, Sweden, *pers. comm.*). Identification has yielded 5 confirmed, 5 probable and 27 tentative (structural) identifications (84 % of peaks with MS/MS), clearly showing the benefit of the increased metadata and mass spectral exchange. The entire SOLUTIONS non-target workflow greatly expedites high-throughput non-target screening and has huge potential to assist prioritization of substances for identification purposes.

[1] Ruttkies, Schymanski, Wolf, Hollender, Neumann, *J. Cheminformatics*, **2016**, *8*:3.
[2] Gerlich and Neumann, *J. Mass Specrom.*, **2013**, *48*, 291.
[3] Allen, Greiner, Wishart, *Metabolomics*, **2014**, DOI: 10.1007/s11306-014-0676-4

Solvent based Selective Titration Reagents for High Affinity Complexometric Titrations

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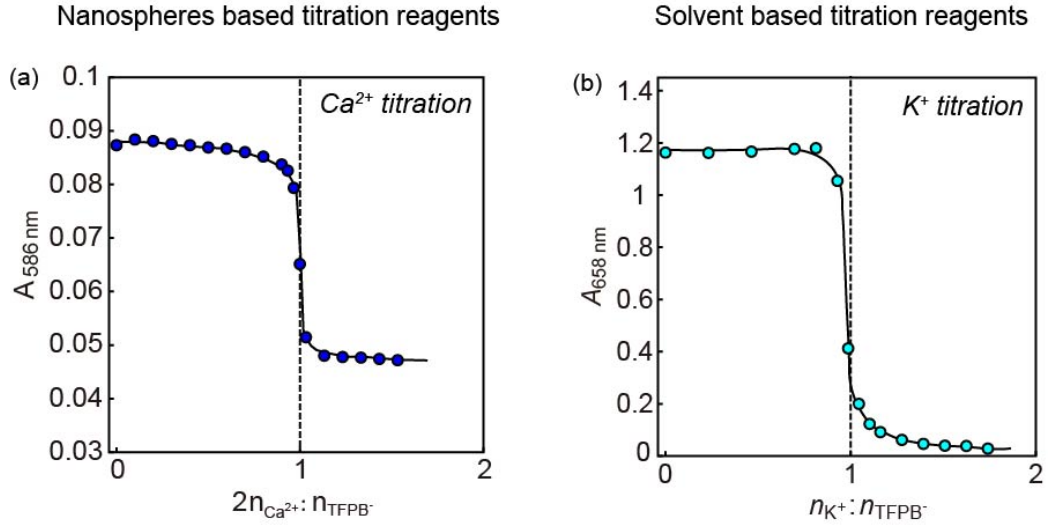
Complexometric titration is a mature analytical technique that is being used and taught all over the world in analytical science. Titrations are routinely used to determine ion concentration, speciation as well as complexation reactions in various fields such as environmental, clinical and bioanalytical chemistry. Traditionally, the titrations are performed with water soluble reagents such as EDTA. However, their pH dependent complexing ability and rather rigid selectivity remains problematic.

Recently, we reported ion selective nanospheres as a novel class of titration reagents capable of moving the titration process from homogeneous phase to heterogeneous phase. [1] [2] [3] Based on the ion exchange principle, the water soluble ions can be exchanged into the lipophilic core of the nanospheres which extends the use of lipophilic ionophores with high selectivity and sensitivity. Both the chelating and indicating nanospheres can be designed to be pH independent. However, only the ionophores with high affinity to the analyte could be successfully applied because of the relatively polar microenvironment of the nanospheres. Calcium and lead titrations were successfully demonstrated (Figure a).[4]

To expand the palette of useful ionophores by including those with relatively lower affinity for the analyte, solvent based titration reagents are presented here. An organic solvent doped with ionophore, ion exchanger and chromoionophore may also serve as titration reagent. With high amount of the ion exchanger and small amount of chromoionophore, the solvent based titration reagents possess the ability to act both as chelators and indicators. The use of organic solvent increased the affinity of the ionophores compared with the abovementioned nanospheres. The solvent based method also increased the doping capacity of the sensing components compared to the nanospheres (Figure b). Potassium, sodium and lithium titrations were successfully demonstrated by using solvent based reagents. Potassium concentrations in human serum were also accurately determined.



[1] Jingying Zhai, Xiaojiang Xie, Eric Bakker, *Chemical Communication*, **2014**, *50*, 12659-12661.
[2] Jingying Zhai, Xiaojiang Xie, Eric Bakker, *Analytical Chemistry*, **2015**, *87*, 8347-8352.
[3] Jingying Zhai, Xiaojiang Xie, Eric Bakker, *Analytical Chemistry*, **2015**, *87*, 2827-2831.
[4] Jingying Zhai, Xiaojiang Xie, Eric Bakker, *Analytical Chemistry*, **2015**, *87*, 12318-12323.

New SI-traceable reference gas mixtures for sulfur hexafluoride (SF_6) at the pmol/mol level

S. A. Wyss[1], S. Reimann[1], M. Vicar[3], M. K. Vollmer[1], C. Pascale[2], G. Nieuwenkamp[4], B. Niederhauser[2], L. Emmenegger[1]*

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We developed a SI-traceable method to produce reference gas mixtures for sulfur hexafluoride (SF_6) at pmol/mol. This research activity is conducted under the framework of the European EMRP HIGHGAS project, in support of the measurements of this important greenhouse gas in the Earth's atmosphere.

First, the single component mixture of SF_6 in synthetic air, which is a widely used gaseous dielectric in gas insulated switchgear power installations [1], was gravimetrically generated at a mole fraction of approximately 1 µmol/mol according to ISO 6142 and was pressurised into an aluminium cylinder at VSL.

In a second step this primary mixture was further dynamically diluted to the pmol/mol level. Two systems were independently developed and were checked for their performance in the course of this project. The first one was produced by the Federal Institute of Metrology (METAS) achieving the final molar fractions with a two-step dilution system, whereas the Czech Metrology Institute (CMI) used a three-step dilution system. In both systems the dilution is controlled by mass flow controllers. The final gas mixtures at near-ambient mole fraction, in the pmol/mol range, were measured with the use of a Medusa gas chromatography-mass spectrometry system (Medusa-GC/MS) against working standards calibrated on existing scales of the Scripps Institution of Oceanography (SIO) [2].

For both systems the assigned value of the primary reference mixture in the µmol/mol range was in excellent agreement with the measured values. This shows the ability of producing accurate SI-traceable standards at the pmol/mol level without laborious static dilution steps and could be a breakthrough in the efficient and precise production of standards, e.g. for newly emerging halogenated greenhouse gases in the atmosphere.

[1] Constantine T. Dervos, Panayota Vassiliou, *J. Air Waste Manag. Assoc.,* **2000**, *50*, 137.
[2] Benjamin R. Miller, Ray F. Weiss, Peter K. Salameh, Toste Tanhua, Brian R. Greally, Jens Mühle, Peter G. Simmonds, *Anal. Chem.,* **2008**, *80*, 1536.

Nucleotide and nucleotide sugar quantification in cell extracts by capillary electrophoresis

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In biotechnological processes the intracellular level of nucleotides and nucleotide sugars has direct impact on the post-translational modification (glycosylation) of therapeutic protein products and on the exopolysaccharide pattern of the cells. Thus, they are precursors and also key components in the production of glycoproteins and glycolipids [1].

The nucleotides and their sugar derivatives coexist in biological samples. Therefore, their simultaneous determination in biotechnological samples is reasonable and challenging. The most common approaches are the high pH anion exchange liquid chromatography [2], reverse-phase liquid chromatography [3] and capillary electrophoretic techniques [4]. The reported separation performance with even high performance LC methods is often not sufficient.

In our study nucleotides (AMP, CMP, GMP, ATP, ADP, GTP, CTP, GDP, UMP, UTP, UDP) and nucleotide sugars (GDP-Glc, UDP-GlcNAc, UDP-Glc, UDP-GalNAc, UDP-Gal) are analyzed with capillary electrophoresis similarly to [5]. The extracted nucleotides and sugar derivatives are separated in back ground buffer (pH 9.5) of 40mM borate containing 1% PEG (MW=35’000Da) under 30kV separation voltage. The capillary (ID=50µm, total length=75.7cm, length to the detection window=67.2cm) was treated with dynamic coating from CEofix Carbo Kit (Analis SA, Belgium). They are detected by direct detection at 260nm with an LOQ of about 10µM. The high efficiency of CE allows the separation / quantification of all compounds, the use of the dynamic coating from CEofix Carbo Kit allows reproducible migration times (RSD 0.5%, n=14). Therefore, their quantification in the cell extracts is possible.

[1]P. Van den Steen, P. M. Rudd, R. A. Dwek, and G. Opdenakker,*Crit. Rev. Biochem. Mol. Biol.*, **1998**, 33. 151–208.
[2]J. B. Ritter, Y. Genzel, and U. Reichl, *J. Chromatogr. B Anal. Technol. Biomed. Life Sci.*, **2006**, 843, 216–226.
[3] A. Ranogajec, S. Beluhan, and Z. Šmit, *J. Sep. Sci.*, **2010**, 33, 1024–1033.
[4] M. Uhrova, Z. Deyl, and M. Suchanek, *J. Chromatogr. B Biomed. Appl.*, **1996,** 681, 99–105.
[5] H. T. Feng, N. Wong, S. Wee, and M. M. Lee, *J. Chromatogr. B Anal. Technol. Biomed. Life Sci.*, **2008,** 870, 131–134.

Novel instrumentation for analysis of halogenated trace gases by GC-TOFMS (APRECON)

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A variety of halogenated trace gases in the atmosphere are of anthropogenic origin and derive from usage as refrigerant, foam blowing agents and solvents. The chlorine and bromine bearing compounds are typically ozone depleting substances and most of the halogenated trace gases are potent greenhouse gases. The measurement of these is demanding, as they occur in low concentrations. Especially difficult is monitoring the time trend of the concentration for some phased-out substances is particularly difficult as they are often very stable causing the concentration to change very slowly. This requires high measurement precision and accuracy.

Our new APRECON (Advancend PRECONcentration) instrumentation provides high precision, high sensitivity and high throughput using a sophisticated preconcentration unit in combination with gas chromatography time-of-flight mass spectrometry (GC TOF MS). Prior to measurement the sample is preconcentrated by adsorption onto a polymer under cryogenic conditions (-180 °C) using a Stirling cooler. The sample amount is quantified barometrically which is more precise than using mass flow controllers. For desorptive heating the traps are decoupled from the cold head. This minimizes the overall heat input and results in a rapid subsequent cooling in preparation for the next sample preconcentration. The desorbed fraction is injected into a gas chromatograph (Agilent 7890B) where it is separated into its compounds and finally analyzed in a MS. For comparison we tested two different MS for this set up: A quadrupole and a TOF. The later shows significant advantages such as virtually simultaneous measurement of all masses during the entire acquisition time and a mass resolution in the 4’000 range enabling fractional masses rather than the integer resolution of a quadrupole. First results of continuous measurements at the urban site of Duebendorf will be presented.

A novel analytical peak fitting tool for the integration of very noisy or overlapped peaks (for the inexperienced users)

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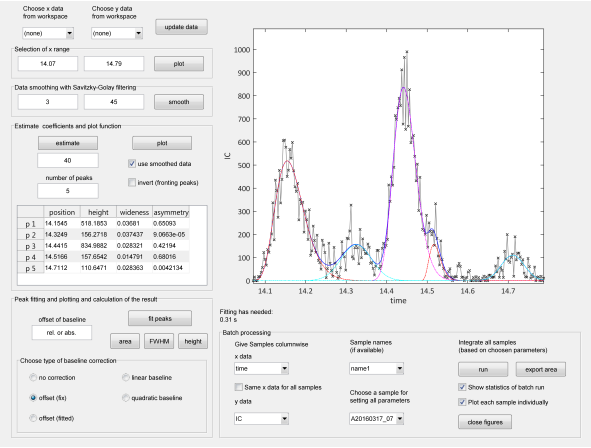
The analysis of volatile aroma compounds in products such as coffee is usually conducted by HS-GC-MS [1]. The complexity of the aroma leads to congested chromatograms with a large number of overlapping signals. As an additional challenge, many compounds appear only with very low intensities, near the limit of detection, and hidden by a strong noise. To extract information from such data, a reliable method for peak integration is needed.
Generally numeric peak integration is performed based on MS data. Each peak is defined by a start- and an end-point. Yet, for overlapped and/or noisy peaks, these are difficult to detect, leading to non-reproducible results. An alternative is analytical peak fitting, which circumvents the need of defining start- and end-point. Overlapped as well as very noisy peaks can easily be integrated individually. As an example for such an approach, the mathematical function published by Pap and Pápai [2], for describing chromatographic peaks, was considered as a starting point. Yet, this method has one big disadvantage. It requires a highly experienced user, with a hight level of expertise in mathematical least squares fitting and a profound knowing of probability density functions, in order to obtain accurate and reliable results.
The aim of the novel analytical peak fitting tool presented here was to develop a function, which enables for analytical peak fitting without prior knowledge, even in the presence of strong noise. This was integrated into an easy-to-use graphical user interface (figure). The function developed here is particularly suitable for the automatic, robust and fast analysis of chromatographic peaks, but was shown to give very good results for any peak shaped signal, such as spectroscopic peaks and electrochemical signals. The tool automatically estimates the number of peaks and their function coefficients, such that even inexperienced users can execute analytical peak fitting and therefore obtain reliable integration of overlapped and/or noisy peaks (plot window in figure). Batch processing of multiple samples is also possible as well. The time needed for each sample is usually below 0.5 s and the results are fully reliable, despite overlapping or noisy peaks. With this tool, analytical peak fitting becomes a good, reliable and fast alternative to conventional trapezoidal method for peak integration, also for users without prior knowledge.



Graphical user interface. Theaxes shows chromatographic data of coffee (Δt_R = 40 s). The signals are very noisy and overlapping. Five compounds were automatically detected and fitted in approx. 0.5 s.

[1] C. Yeretzian, in: A. Buettner (Ed.), *Springer Handbook of Odour*, **2016**, Springer.
[2] T.L. Pap and Zs. Pápai, *Journal of Chromatography A*, **2001**, 930, 53–60.

Can We Use Targeted Proteomics to Explore Dynamics in Glutathione S-Transferase Expression in Zebrafish Embryos?

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Zebrafish embryos are increasingly employed as alternative to the conventional acute fish toxicity test. One important requirement for the establishment of an alternative test model is that both models should be comparable in terms of uptake and biotransformation of xenobiotics. However, little is known about the expression of xenobiotic metabolizing enzymes in the developing zebrafish embryo.

In this study, we have developed a targeted proteomic approach to characterize the expression of Glutathione S-transferases. Selected members of the family were monitored in zebrafish embryos by mass spectrometry on the basis of proteotypic peptides and peptides characteristic for the enzyme groups of interest.

The basal expression of GSTs on the protein level was investigated at 4, 8, 24, 48, 72, 96, 120 hpf and compared to adult liver samples. Samples collected at 4 and 8 hpf were used to estimate the relevance of maternal mRNA transfer in zebrafish eggs - samples from the later time points give an insight into the dynamic of GST expression throughout the development. The expression pattern of selected GST enzymes is presented including members of the alpha and pi class – candidates that have been suggested to be involved in xenobiotic metabolism.

This study will help to fill existing knowledge gaps regarding the comparability of metabolic capacity of fish at different life stages.

Table-top XUV mass spectrometry for nano-scale chemical imaging

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Optical lasers for solid micro-sampling, coupled to mass spectrometry, e.g. laser-ablation-ionization mass spectrometry imaging (MSI), have combined spatial resolution down to a few microns with extremely high chemical sensitivity. Advanced capabilities for accessing nano-scale resolution are important to investigate chemical zoning at the -interfaces. Enhanced spatial resolution implies adopting shorter lasers wavelengths [1], since the smallest spot is ~l/2. Beyond the UV/Vis region of laboratory lasers, radiation in the XUV as found at Synchrotron and X-ray Free-Electron Lasers (XFEL), offers the sought-for capability. They permit to tune the wavelength, but it is clear that they suffer from beamtime limitation. Ideally, advanced analytical technologies should be also non-destructive. Aim of this work was to demonstrate XUV-assisted mass spectrometry for nano-scale imaging in a table-top setup in our home-lab.

A complete setup is shown in Fig. 1, as used for the XUV-assisted MSI measurements. A pseudospark XUV source was operated which gives, about 10^{13} photons/(2πsr pulse) (l between 7 nm and 16 nm) and repetition rate of up to 25 Hz. The source was operated with Ar at a pressure of 0.1 mbar and using an input voltage of 2.5 kV. The XUV radiation was delivered on Al samples using a Y/Mo-multilayer [2] that reflects about 30 % at 12 nm. A self-designed time-of-flight mass spectrometer was used as detector. The TOF spectrometer had a length of 500 mm and was based in 6 electrostatic lenses and one extraction/retarding electrode, all of them independently connected to 7 bipolar high voltage power supplies, adjusted in voltages from -50 V to 500 V. A Channeltron electron multiplier with gain of about 10^7 at 2.5 kV was used for the time-of-flight measurements. Fig. 2 shows preliminary analytical results irradiating a Al certified reference. XUV Al mass spectra show peaks for $Al^{2+}$and Al^{+}, as well as for ions originated from residual gas and metallic trace impurities. It should be noted that these measurements were realized without focusing the XUV beam and without destruction of the sample.

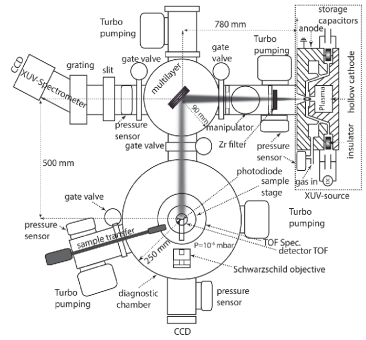

Fig. 1 Far field set up used to demonstrate XUV mass spectrometry. A Schwarzschild condenser and objective (NA=0.15 and expected resolution about 50 nm) are being integrated.

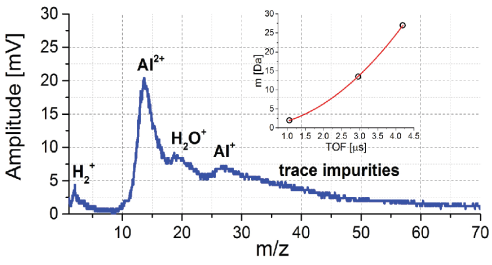

Fig. 2. XUV Al mass spectrum and calibration curve obtained for the TOF spectrometer.

In conclusion: (i) this lab-scale set up allows obtaining XUV MSI at nano-scale (ii) XUV photons are able to efficiently sample even without focusing.

[1] I. Kuznetsov, J. Filevich, F. Dong, M. Woolston, W. Chao, E. H. Anderson, E. R. Bernstein, D. C. Crick, J. J. Rocca, C. S. Menoni, "Three-dimensional nanoscale molecular imaging by extreme ultraviolet laser ablation mass spectrometry," *Nat. Commun.* **2015,** 6944.

[2] D. Bleiner, S. Yulin, J. Martynczuk, M. Ruiz, Y. Arbelo, J. E. Balmer, D. Günther, "Actinic damage of Y/Mo multilayer optics in a table-top plasma-driven x-ray laser," *Appl. Opt.* **2014,** 53, 22.

Distribution and speciation of Ag, Ce and Ti in natural freshwaters

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Engineered nanoparticles (NPs), including Ag, CeO_2 and TiO_2 NPs, are currently produced and incorporated in several consumer products. To evaluate risks related to their potential release into natural freshwaters from wastewater treatment plants (WWTPs), more information is urgently required on the natural background of the corresponding metals. Therefore, the aim of this project was to investigate the occurrence of Ag, Ce and Ti in natural freshwaters, focusing on their speciation and distribution among size fractions, and to evaluate possible anthropogenic inputs by comparing their occurrence up- and downstream of WWTPs.

Experimentally, we sampled several small streams in Switzerland before and after wastewater discharges. After successive filtrations (0.45 µm, 0.22 µm, 3kDa) and microwave assisted acid digestion, total, particulate and dissolved concentrations of Ag, Ce and Ti were determined by ICP-MS analysis. To further characterize dissolved and particulate fractions, we also used diffusive gradients in thin films (DGT) devices and we are currently testing and optimizing single-particle ICP-MS analysis. Additional experiments were carried out to investigate the bioaccumulation of Ag, Ce and Ti in biofilm communities of algae and bacteria collected at selected sites.

Ce and Ti were regularly detected in the particulate fraction and often in their dissolved form, even in the 3 kDa fraction, indicating the presence of very small Ce and Ti complexes, possibly stabilized by humic acids. Up- and downstream concentrations of Ti and Ce were similar at most sites. However, in few cases, Ti concentrations showed to be higher downstream compared to upstream, suggesting a possible discharge of anthropogenic Ti from the WWTPs. Ag was below the quantification limit in most of the considered water samples, but it was found to accumulate in the biofilms, confirming the potential of this approach to investigate the presence of target elements commonly expected at very low concentrations.

Deconvolution of chlorinated paraffins and their transformation products from DI-CE-APCI-qTOF mass spectra

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Chlorinated paraffins (CPs) are high production volume chemicals (1 Mio t/a in 2009) widely used as metal working fluids, plasticisers and flame retardants. They are of concern due to their persistence and bioaccumulation potential. Analysis of CPs in environmental samples is a challenge, but the analysis of their transformation products is a nightmare, considering the large number of congeners. Thus, information on environmental fate of selected congeners is limited. Recently, we developed a method overcoming the need for chromatographic separation using direct liquid injection (DI) and focussing on accurate mass determination [1]. Atmospheric pressure chemical ionisation (APCI) is applied under chlorine-enhanced (CE) conditions in negative ion mode followed by quadrupole time-of-flight (qTOF) mass spectrometry. This method allows rapid (Figure). In presence of chlorinated alkenes the respective isotopic distributions of the observed CP patterns are affected and vice versa. Here, we will present a deconvolution method that can be used to determine the relative contributions of CPs and respective alkenes within the measured pattern. The observed isotopic patterns are deconvoluted into a linear combination of both interfering patterns. After deconvolution, we are able to study alkane/alkene ratios and changes in chlorination degree after transformation and investigate corresponding transformation kinetics.

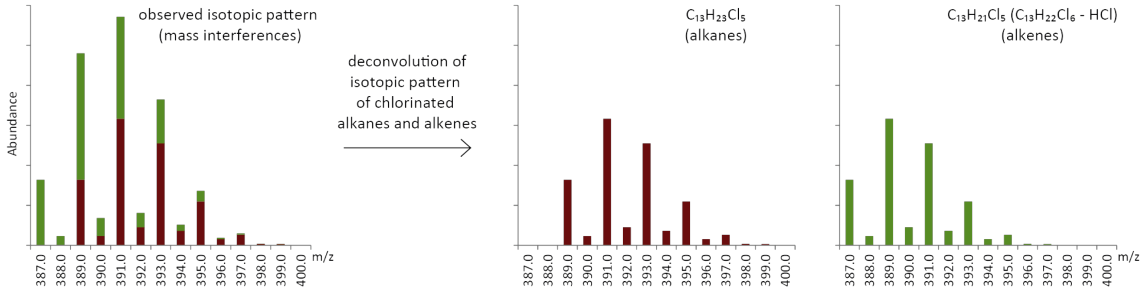

Figure: Principle of deconvolution of observed isotopic pattern into respective patterns of chlorinated alkanes (CP) and alkenes (transformation product).

[1] Bogdal, C., Alsberg, T., Diefenbacher, P.S., MacLeod, M., Berger, U.,*Analytical Chemistry.* **2015**, *87*, 2852-2860.

Biotransformation of chlorinated paraffins with LinA, a HCH-converting bacterial enzyme found in various Sphingomonadacea

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Chlorinated paraffins (CP)s are like hexachlorocyclohexanes (HCHs) high production volume chemicals. CPs are produced at about 1 million t/y and widely used as polymer additives e.g. as flame retardants, plasticizers or metal working fluids. HCHs on the other hand have been widely used as insecticides with production rates up to 270,000 t/y in 1980. HCH production and use is now prohibited and HCHs are classified as persistent organic pollutants (POP) in the Stockholm Convention. A risk profile recently published for short-chain chlorinated paraffins (SCCPs) by the POP review committee concludes that SCCPs too are persistent, bioaccumulating and have substantial long-range transport potential. In our contribution we study the biotransformation of selected CPs with LinA, a HCH-converting bacterial enzyme found in various *Sphingomonadacea* (**Figure**). LinA shows dehydrohalogenase activity when exposed to HCHs and hexabromocyclododecanes (HBCDs) [1]. Our newly developed analytical method [2] which is based on direct injection chlorine-enhanced atmospheric pressure chemical ionisation quadrupole time-of-flight mass spectrometry (DI-CE-APCI-qTOF-MS) is well suited to study such biotransformation reactions. The applied analytical method which will be presented separately [3] is capable to resolve the various mass interferences occurring in spectra of CPs and their transformation products.

Figure: 3D ribbon model of trimeric LinA. The enzyme supports dehydrohalogenase activity as recently shown for HCHs and HBCDs [1].

[1] Heeb N.V., Wyss, S.A., Geueke, B., Fleischmann, T., Kohler, H.-P. E., Schweizer, W. B., Moor, H., Lienemann, P., *Chemosphere.* **2015**, *122*, 70-80.
[2] Bogdal, C., Alsberg, T., Diefenbacher, P.S., MacLeod, M., Berger, U.,*Analytical Chemistry.* **2015**, *87*, 2852-2860.
[3] Schinkel et al. 2016 (contribution to SCS Fall Meeting, September 2016, Zürich)

Tracking biotransformation of hexachlorocyclohexane isomers by compound-specific isotope analysis

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Hexachlorocyclohexanes (HCHs) are frequently used in agriculture and medicine due to the pesticidal activity of the γ-isomer. The persistence of HCHs led to their frequent detection as diffuse pollution in the environment and as point sources at abandoned production and dumpsites. To date, production and use of HCHs is prohibited in many countries and the α-, β- and γ-isomers are listed as persistent organic pollutants in the Stockholm Convention. Remediation strategies rely on the biodegradation of HCH isomers under oxic conditions, which is initiated through a sequence of substitution and elimination reactions to chlorohydroquinones which are further metabolized via maleylacetate in the citric acid cycle.
In this work, we explore the use of compound-specific isotope analysis (CSIA) for assessing the extent and pathways of HCH biodegradation. As has been shown in studies with nitroaromatic compounds and fuel constituents such as methyl tert-butyl ether CSIA can give insight on the different predominant reaction mechanisms. To quantify the C- and H-kinetic isotope effects (KIEs) of HCH biodegradation by substitution and elimination reactions, we use experimental systems with purified LinA and LinB enzymes, originating from *Sphingobium japonicum* UT26 and *Sphingobium indicum* B90A, respectively. LinA and LinB are produced in our laboratory using arabinose and IPTG inducible expression systems in *E. coli* Bl21 and are then purified via fast-protein liquid chromatography (FPLC). Concentration and isotope signatures of HCHs and reaction products are measured in GC/MS and in GC/IRMS systems, respectively.
Experiments with LinA2 and γ-HCH show that at low and high turnover, C-isotope fractionation can be detected in the substrate and the products. Current work focuses on adapting and improving the experimental setup for model systems [1], in order to quantify H-KIEs using a chromium-oxidation reactor. Furthermore, different γ-pentachlorocyclohexene (γ-PCCH) isomers are synthesized to determine the C-KIEs of single reaction steps.

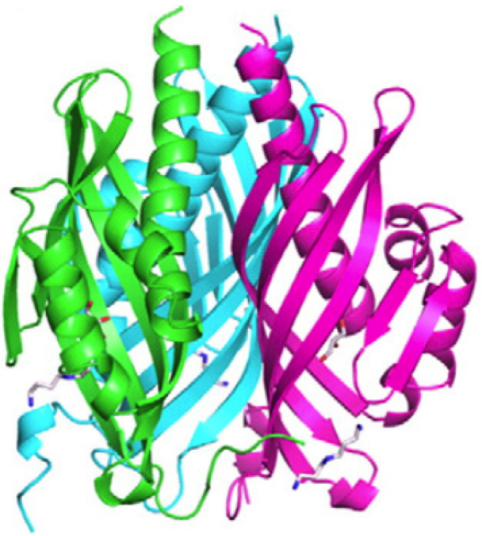

Figure 1: Strucure of LinA from *S. japonicum* UT26 [2]

[1] Renpenning, J., Kümmel, S., Hitzfeld, K., Schimmelmann, A., Gehre, M., *Analytical Chemistry*. **2015**, *87* (18), 9443.
[2] Okai, M., Kubota, K., Fukuda, M., Nagata, Y., Nagata, K., Tanokura, M., *Journal of Molecular Biology.* **2010**, *403*, 260.

The Swiss Army Knife of Analytics for Energy Storage

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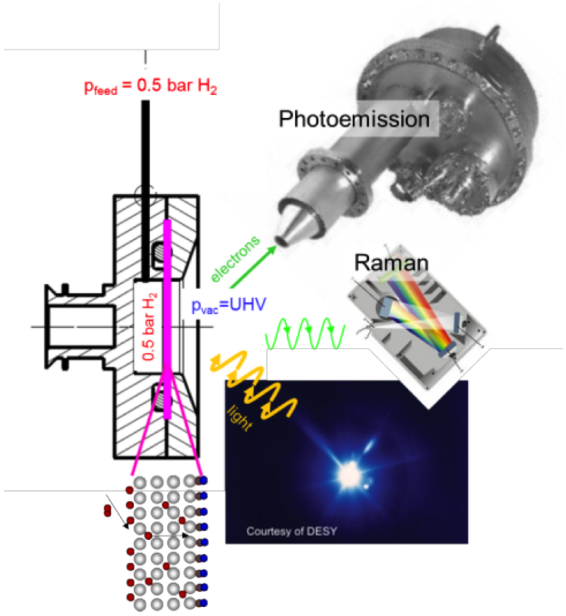
Traditional chemical analytics was driven by pushing the detection limit towards ultralow concentrations. Recently, this target has been upgraded in the sense of detecting lowest concentrations at ultrahigh spatial and temporal resolution. There are several reasons: the chemical gradient is very high at interfaces, where different media meet, and complicated phenomena (e.g. segregation phenomena) can occur. These may be used in technical applications, such as pn-junctions to separate charge carriers, and the triple phase boundary in fuel cells, where gas, conductive solid, and electrolyte have to be in contact to each other. However, from the viewpoint of the analytical chemist, these surfaces and interfaces are most difficult to characterize: either, the required interaction volume of probe and sample is much smaller than needed for a proper signal-to-noise ratio (an example is X-ray diffraction), or, vice versa, the strong interaction of probe with sample allows characterization of a few monolayers, i.e., a surface, but is then hindered by the surrounding material. A typical example is photoelectron spectroscopy. Resolving the kinetics of chemical processes taking place in an atomically confined space adds another challenge. The analytical tool of the future will thus be a kind of Swiss Army knife, which has various blades being selective for each specific target. I will highlight the idea on examples, that is surface enhanced Raman spectroscopy on silver nano-particles produced in biofilms and photoemission on promotion of hydrogen desorption from palladium surfaces by fluoropolymer coating. In both cases the analytical tools have to be adapted: the bulk method Raman has to be made interface selective by surface plasmon interactions, the surface sensitive XPS had to be adapted to be compatible to “bulk” conditions. Here, we propose a smart combination of time resolved photoemission and Raman spectroscopy to unravel kinetic and dynamic phenomena at interfaces relevant in catalysis and electro-catalysis for energy applications. For this we are developing a table-top pulsed laser-plasma source providing EUV-photons for (ns) time-resolved photoemission and ns pulsed visible photons for time-resolved Raman spectroscopy.



Soft X-ray HEROS on photoactive materials

C. Cirelli[1], F. Barbato[1], Y. Arbelo Pena[1], A. Borgschulte[1], L. Mewes[2], D. Kinschel[2], C. Arrell[2], J. Budarz[2], D. Leuenberger[3], B. D. Patterson[1,1], M. Chergui[2]*, D. Bleiner[1,4]*

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X-ray absorption spectroscopy (XAS) is a powerful tool to study the electronic structure of molecular species: *e.g.*, valence charge distribution and state energies, symmetries and interactions of molecular orbitals as well as oxidation and spin state of selected ions. Its main strength is its elemental selectivity. High-brightness, short-pulse X-ray sources have opened the possibility of time-resolved, pump-probe XAS measurements of photo-active molecular species. But such measurements generally require a series of measurements in which, besides the pump-probe delay, also the incoming X-ray photon energy must be varied. The new “high energy resolution off-resonant spectroscopy” (HEROS) technique [1,2], in which a sample is irradiated at a fixed photon energy slightly below an absorption edge and the resulting X-ray emission spectrum (XES) is analyzed in terms of the Kramers-Heisenberg expression for resonant X-ray scattering, in effect allows a single-shot XAS spectrum to be obtained without varying the incident X-ray energy [2].

In the present work we show the first application of the HEROS technique to soft X-rays, with the purpose of investigating time dependent chemical processes such as charge transfers, spin changes or photocatalytic reactions at the molecular level. Soft X-rays represent the ideal probe when the concentration of the interacting center is reduced, like in the case of thin films and interfaces or single molecules in solution, due to their high absorption cross section.

We have performed experiments at the GASPHASE beamline of the Elettra synchrotron facility in Trieste, using a high resolution XES spectrometer optimized for operation in the soft X-ray energy range [3].

After first test experiments on crystalline and amorphous solid samples aimed to identify the optimal incident X-ray energy for soft X-ray HEROS, we focused on the response of organic molecular systems diluted in solvents. Particularly, we measured static HEROS spectra of polypyrydil-based iron complexes [4, 5] and PV cyanine borate dyes [6].

Based on these preliminary results, pump-probe studies will be performed by exciting electronic states and charge transfer dynamics in the same systems with femtosecond laser pulses (pump) and probing the delay-dependent response of Co 3d and B 1s orbitals with core level HEROS spectroscopy.

[1] W. Błachucki et al., *Phys. Rev. Lett.* **112**, 173003 (2014).
[2] J. Szlachetko et al., *Chem. Commun.* **48**, 10898 (2014).
[3] L. Poletto et al., *Rev. Sci. Instrum.* **85**, 103112 (2014).
[4] A. Cannizzo et al., *Coord. Chem Rev.* **254**, 2677 (2010).
[5] G. Auböck and M. Chergui, *Nature Chem.* **7**, 629 (2015).
[6] J. De Jonghe-Risse et al., *J. Mater. Chem. A* **3**, 10935 (2015).

Table-top pseudo-spark XUV source for energy dispersive absorption spectroscopy

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X-ray absorption spectroscopy (XAS) is a powerful tool extensively used to study the chemical state and the local geometric and electronic structure of matter [1]. XAS offers the attractive capability to investigate the atomic environment of each separate element in a compound because it is non-destructive and elemental sensitive. Moreover, structures can be determined from samples that are both crystalline and amorphous [2]. The standard procedure is based on the measurement of the incoming and transmitted photon flux through the sample while scanning the energy across the absorption edge with a monochromatic beam. This is possible only at large scale facilities like synchrotrons able to offer tunable and monochromatic X-ray radiation.

There is thus a strong motivation to develop small laboratory scale systems to allow a larger number of researchers to explore new field of applications. To date available table top extreme ultraviolet (XUV or EUV) sources are not easily tunable, thus making energy scanning infeasible. A possible alternative is offered by the use of energy dispersive X-ray absorption [3]. The main advantage of such scheme is the simultaneous acquisition of all energies in a single-shot, which brings the additional advantage of being suited for time-resolved measurement. For instance in-situ energy reactions can be followed with a time resolution in the order of millisecond [6]. In the present work a table-top setup, composed by a source and a high resolution spectrometer, is tested as an energy dispersive absorption tool. The system operates in the EUV range, from 12 eV to 30 eV (12 - 5 nm). Several transition metals have *L* and *M*-edge in the EUV range. Studying the absorption spectra in this energy range is not easy due to the strong absorption of the element for EUV energies. But at the same time the use of EUV radiation makes the technique chemical sensitive, due to the inner shell electrons excited by such energies that are well defined and different in energy for each element [4,5].

[1] Durham, P. J., D. C. Koningsberger, and R. Prins, *WileySons, New York* **(1988)**: 53.
[2] Shahin, Ahmed M., et al., *Chemistry of materials* 17.2 **(2005)**: 315-321.
[3] Matsushita, Tadashi, and R. Paul Phizackerley, *Japanese Journal of Applied Physics* 20.11 **(1981)**: 2223.
[4] Wray, L. Andrew, et al. , *Frontiers in Physics* 3 **(2015)**: 0032.
[5] Guo, Jinghua, *Optics Photonics 2005*. International Society for Optics and Photonics, **2005**.
[6] Mathon, Olivier, Innokenty Kantor, and Sakura Pascarelli, *X-Ray Absorption and X-Ray Emission Spectroscopy: Theory and Applications* **(2016)**: 185.

Gaining a Comprehensive Picture of Transformation Products formed during Wastewater Treatment Processes

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It is known that thousands of compounds end up in wastewater treatment plants (WWTPs) and it is estimated that about half of these may be present in the effluent since they are either resistant to treatment or form transformation products (TPs) [1]. These unintended TPs therefore, through their discharge, may affect downstream aquatic communities or contaminate drinking water supplies. Lab studies and target screening can only provide a limited picture of the compounds present because many TPs are unknown. This project focused on nontarget screening methods using statistical tools to analyze data collected with liquid chromatography coupled to high-resolution tandem mass spectrometry (LC-HRMS/MS). The aim of this work was to characterize nontarget peaks at different points in a WWTP, prioritize peaks through a combination of statistics and chemical logic, and to identify new micropollutants.

Samples were collected at a full-scale WWTP after conventional activated sludge treatment, ozonation, and various post-treatments (e.g., sand filtration and granulated activated carbon). Data pre-processing included peak picking, profile building, and isotope/adduct clustering [2]. Nontarget peaks were classified into potential parent compounds and potential TPs with principal component analysis (PCA). Links between these groups were explored using known biotransformation (for activated sludge treatment) or chemical (for ozonation) reactions and a tentative transformation type was assigned. Compounds not falling into either of these categories were further investigated as possible persistent compounds.

The highest number of features was detected at the influent of the WWTP (14,268), and generally decreased along the treatment train. From the four ozone doses investigated (*i.e.*, 2, 3, 4, and 5 mg/L O_3), the highest number of features were found at 3 mg/L, but characteristics of nontarget peaks after ozonation were not substantially different in retention time, *m/z*, or intensity. Most commonly detected transformation from activated sludge was hydroxylation, while most common across the ozone doses was demethylation. There was little to no observable difference between the influent and effluent of the post-treatments and no peak classification could be done with PCA. From the biological treatment an unknown surfactant series was detected which was then eliminated during ozonation. Overall, results demonstrate that by applying a comprehensive workflow designed for nontarget analysis, relevant compounds can be found and unknown TPs can be identified.

[1] Eggen R. I. L., Hollender J., Joss A., Schärer M., Stamm C. 2014. Reducing the Discharge of Micropollutants in the Aquatic Environment: The Benefits of Upgrading Wastewater Treatment Plants. Environ Sci Technol. 48: 7683-7689.
[2] Loos M.. 2013. enviMass: Utilities to process mass spectrometry (LC-HRMS) data for environmental analysis. R package version 2.0.

A computational workflow for elucidating phytoplankton biotransformation using LC-HRMS

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Green algae and cyanobacteria, as part of the phytoplankton, are an important component of the biosphere in lakes and marine ecosystems. Despite their abundance and diversity, it is largely unknown if and how phytoplankton species contribute to the biotransformation of polar organic pollutants. However, recent reports have suggested an involvement of photosynthetically active organisms in the degradation of plant protection products [1]. Because of their diversity in metabolic functions as well as the scarce information available, unexpected transformation products could likely be found.

The advent of high-resolution mass spectrometry (HRMS) has spurred the development of a variety of computational tools for different tasks in the detection and structure elucidation of transformation products, using both suspect screening of hypothetical transformation products generated from transformation rules, and non-target screening for detection of possible transformation products via e.g. time trends.

With a set of 20 pesticides and pharmaceuticals, we investigated the biotransformation of model species Microcystis aeruginosa, and Synechococcus sp. (both cyanobacteria), and Chlamydomonas reinhardtii (unicellular green alga). We used a combination of computational approaches with LC-HRMS/MS data to detect transformation products and elucidate their structure: potential transformation products were detected through suspect screening and/or time trend analysis using R scripts and packages developed in-house [2], and spectra were acquired in positive and negative mode with 9 collision energies (15-180 NCE). For structure elucidation, we combined structure generation using MOLGEN [3] or SMIRKS reaction rules [4] with spectral simulation using CFM-ID [5] and MetFrag [6], as well as automatic spectrum annotation and shifting using RMassBank [7]. The used workflow was made accessible as an R package (https://github.com/meowcat/RMassScreening).

Using the workflow, we were able to detect and elucidate different classes of novel transformation products, among them multiple methylation products as well as amino acid conjugates.

[1] Thomas and Hand, *Environ. Toxicol. Chem.* **2011**, 30, 622-31.
[2] https://github.com/blosloos/enviPick; https://github.com/blosloos/enviMass; https://github.com/blosloos/nontarget; https://github.com/meowcat/RMassScreening
[3] Benecke et al. Fresenius, J. Anal. Chem. **1997**, 359 (1), 23-32
[4] http://www.daylight.com/dayhtml/doc/theory/theory.smirks.html
[5] Allen et al., *Metabolomics* **2015**, 11 (1), 98-110
[6] Ruttkies et al., *J. Cheminform.* **2016**, 8:3
[7] Stravs et al. *J. Mass Spectrom.* **2013**, 48, 89-99

Quantitative Atomistic Simulations of Solute Intercalation in Reversed Phase Liquid Chromatography

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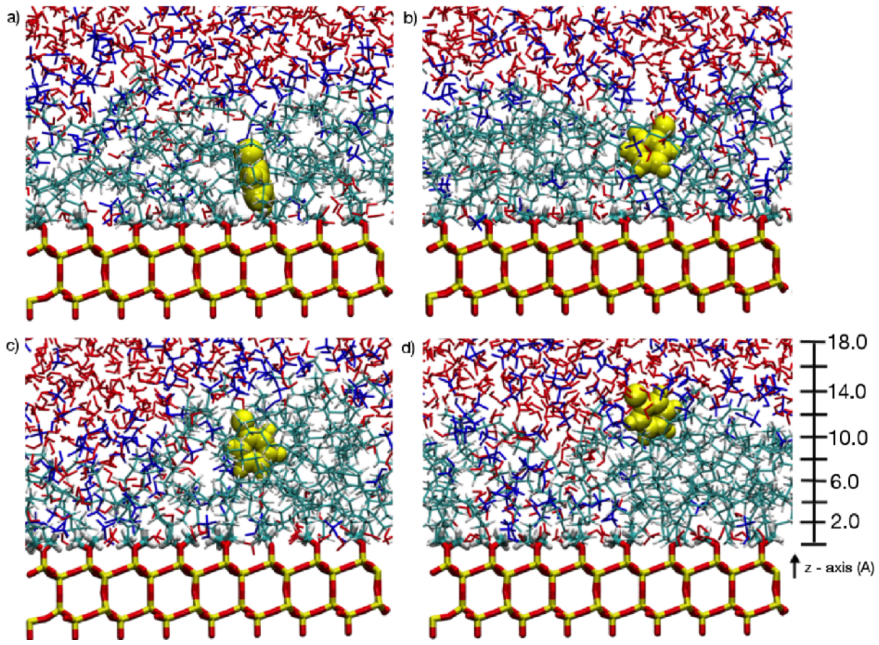
The separation mechanism in reversed-phase liquid chromatography (RPLC) is based on interactions between the solute and its environment which includes the solvent mixture and the functionalized alkyl chains chemically bonded to the support surface. [1] Despite the seemingly “simple” chemical composition of such systems, the atomistic understanding underlying the separation process remains elusive since the system is highly dynamical, heterogeneous and disordered.[2,3,4] During elution, the alkyl chains are highly flexible which modulates the intermolecular interactions at the stationary/mobile interface which significantly influences retention and chemical selectivity.[2-5] Recent work has shown that atomistic simulations with accurate force fields are ideally suited to describe the thermodynamics of complex systems.[6] Hence, in the present study the thermodynamics of intercalation of a range of benzene-derivatives is studied using state-of-the art atomistic simulations. The compounds include halogenated benzenes (PhX where X=F, Cl), phenol, nitrobenzene and toluene for which experimental data in C18 columns and different solvent mixtures is available.[1] Simulations (see Figure for desorption of PhCl from the surface) allow to explicitly determine the hydration free energy for desorption from the surface which is directly compared with the experimentally measured partition coefficients.[1] This provides the basis for an atomistically resolved picture of solute desorption from the surface in RPLC.



[1] Buszewski, B. *et al. J. Chromatography.* **1990**, *499*, 305-316.
[2] Fouqueau, A.; Bemish, R.; Meuwly, M. *J. Phys Chem. B* **2007**, *111,*10208-10216.
[3] Orzechowski, M.; Meuwly, M. *J. Phys Chem. B* **2010**, *114,*12203-12212.
[4] Gupta, P.; Meuwly, M. *J. Phys Chem. B* ,**2012**, *116,*10951-10959.
[5] Gupta, P.; Meuwly, M. *Chem. Phys. Chem.* **2016**, *in print*.
[6] ElHage, K., Bereau, T, Jakobsen, S., and Meuwly, M., *J. Chem. Theo. Comp.* **2016**, *in print*.

Advanced Trace Analysis Bridging Industrial Scientific Challenges

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The industry is confronted with a number of challenges, which often require the advanced capabilities of a research laboratory. In this poster two flag projects are discussed.

For the solar cell industry and RD, knowledge of the major to trace elements concentration is crucial for the performance. The quantitative analytical determination of different photo-cell types such as **CIGS** (**C**opper, **I**ndium, **G**allium, Di**S**elenide) and **CZTS** (**C**opper, **Z**inc, **T**in**S**ulfide), especially their impurities such as Na, K, Rb, Al, is a real challenge. The latter requires a complete understanding of the sample preparation, of the instrumental analysis, in order to obtain a robust information coverage.

In fact, for the dissolving processes of the solar cells two different procedures were used. For the CIGS cells a mixture of HNO_3 / H_2O_2 is used whereas for the CZTS[1] cells reversed aqua regia was preferred. For the main elements the quantification was carried out by ICP-OES (inductively coupled plasma emission spectrometry). Sulfur and trace elements (Na, K, Rb, Al) were measured by means QQQ-ICP-MS (triple quadrupole inductively coupled plasma mass spectrometry) using the reaction cell with different reaction gases such as He and O_2. The poster will highlight the advanced character of these analysis and how the combination of multiple techniques resulted decisive to drastically advance the analytical capabilities.

Data on primary and secondary raw materials are available in Europe, but scattered amongst a variety of institutions including government agencies, universities, NGOs and industry. By establishing an EU Information Network (EUIN), the project will coordinate efforts to collect secondary CRM data and collate maps of stocks and flows for materials and products of the “urban mine”. The scope is the particularly relevant sources for secondary CRMs: Electrical and electronic equipment, vehicles, batteries and mining tailings. The project will construct a comprehensive inventory identifying, quantifying and mapping CRM stocks and flows at national and regional levels across Europe. Via a user-friendly, open-access Urban Mine Knowledge Data Platform (EU-UMKDP), it will communicate the results online and combine them with primary raw materials data from the on-going Minerals4EU project. To maintain and expand the EU-UMKDP in the future, it will provide update protocols, standards and recommendations for additional statistics and improved reporting on CRM’s in waste flows required.

The development of consistent advanced analytical methods for the determination of traces and ultra traces of raw materials such as rare earth elements (REE) and more is necessary for the creation of the database.

Features of KF and NaF Postdeposition Treatments of Cu(In, Ga)Se2. Absorbers for High Efficiency Thin Film Solar Cells
Patrick Reinhard, Benjamin Bissig, Fabian Pianezzi, Enrico Avancini, Harald Hagendorfer, Debora Keller, Peter Fuchs, Max Döbeli, Carlos Vigo, Paolo Crivelli, Shiro Nishiwaki, Stephan Buecheler, Ayodhya N Tiwari, *Chemistry of Materials* 2015, *16*, 5755-5764.

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Chromatographic resolution of racemic compounds on optically active polymers as chiral stationary phases (KGF-SCS Senior Industrial Science Award Lecture 2016)

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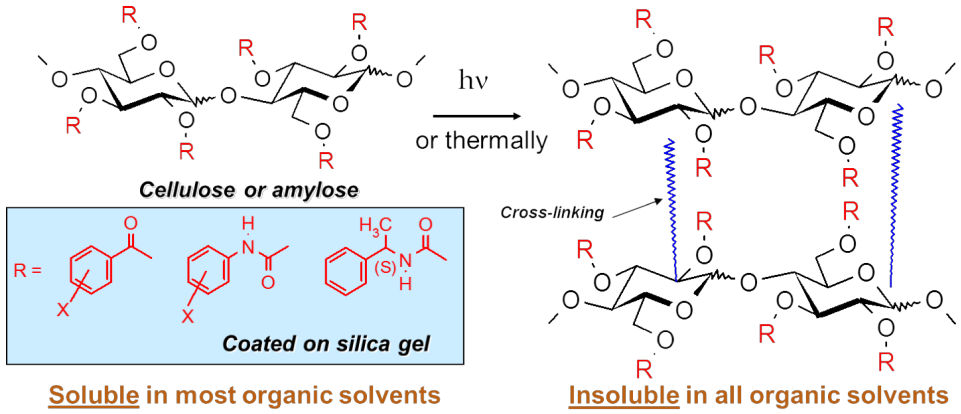
The awareness of the importance of chirality on the biological activity of chiral drugs, fungicides, insecticides, hormones, or fragrances is now well established. Over the last 30 years it has led to a rapidly increasing demand for tools addressing this fundamental question and for methodologies dealing with the chemistry challenges associated to this molecular feature.

Among all developed tools, enantioselective chromatography using chiral stationary phases has become a key technology for the analysis and preparative separation of the enantiomers of racemic compounds. It is now the standard technique for determining the optical purity of chiral substances, replacing almost completely the classical methods such as optical rotation.

In this context, polysaccharide derivatives have emerged as remarkably powerful chiral materials for the purpose of separating stereoisomers by chromatography, showing an exceptional chiral recognition capability not only for analytical determination of optical purity but also for the preparative utilization of this technology to produce optically pure compounds from mg to ton scale. The approach has now become the standard everyday process to access the single pure stereoisomers of potential new chiral drugs in drug discovery. Moreover, with the invention and introduction of immobilized polysaccharide-based chiral stationary phases, we have been able to considerably improve and extend the applicability of enantioselective chromatography to a broad variety of chiral molecules [1-3]. The process is based on a photochemical reaction which leads to a cross-linking of the polysaccharide chains.



The new generation (immobilized) of polysaccharide-based stationary phases has been gradually introduced on the market since 2004 and these phases are now used worldwide as the state-of-the art materials in almost all research laboratories dealing with chiral molecules both in academia and industry, as well as in many development and production units.

The advance of enantioselective chromatography has undeniably permitted to develop technological opportunities which were not conceivable some years ago in the field of large scale separation of stereoisomers of chiral drugs. Furthermore, this development has also favored the advent of the multi-column and continuous separation technology such as simulated moving bed (SMB) chromatography in the pharmaceutical environment, and the resurgence of the packed supercritical fluid chromatography (SFC) technique in general.

[1] E. Francotte, D. Huynh, *J. Pharm. Biomed. Anal*. **2002**, *27*, 421.
[2] E. Francotte, T. Zhang, Patent, PCT Int. Appl. (1997), WO 9704011 .
[3] E. Francotte, *Chimia.* **2009**, 63, 867.

Towards a better understanding of spectral similarity between structurally related compounds

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High-resolution tandem mass spectrometry (HR-MS/MS) is a vital tool in compound identification in environmental samples, *e.g.*, detecting unknown transformation products (TPs) that are produced when emerging contaminants are subjected to natural or anthropogenic processes. Fragmentation of a compound is induced during measurement and it has in general been assumed that structurally similar compounds will have similar spectra since they are likely to produce similar fragments. Furthermore, this tenet has been proposed as a way to improve unknown identification. This hypothesis was tested here using a set of 199 related pairs (parent compounds and their structurally related transformation products (TPs)) which were measured with HR-MS/MS using higher-energy collision-induced dissociation (HCD) fragmentation.

Using purchased reference standards, each compound was measured with liquid chromatography coupled to HR-MS/MS over a range of HCD energies. Spectra were cleaned and recalibrated with the R package “RMassBank”. TPs were paired with their respective parent compounds and included different modification reactions, such as N- or O-dealkylation, hydroxylation, or conjugation. The spectral similarity of a pair was calculated as the dot product of aligned intensity vectors. The influence of collision energy on the similarity of the spectra was investigated, as well as the use of merged spectra from different HCD energies. Additionally, it was hypothesized that shifting the MS/MS fragments of the TP by the mass difference of the transformation would lead to increased similarity between the spectra of each pair.

The highest spectral similarity scores were achieved at high collision energies, indicating that small fragments produced at these energies, or the combination of many small fragments, retained structure-specific information. Also critical was the removal of the precursor peak during comparison to reduce false positive matches. Merged spectra which included both the measured fragments and fragments which were adjusted for the mass of the transformation performed the best of all scenarios tested. Under these conditions, at an optimum similarity score of 0.12, 80% of related pairs had a spectral similarity above this value, while 90% of unrelated pairs were below this threshold. Still, structural similarity of pairs as estimated by the Tanimoto coefficient was not strongly correlated to the similarity of the spectra, indicating that even small changes in a molecule may influence fragmentation. The mechanisms governing this phenomenon need to be further investigated so that spectral similarity between known and unknown spectra can be successfully used for the purposes of prioritization of unknown for nontarget identification.

[1] Stravs, M. A., Schymanski, E. L., Singer, H. P., Hollender, J. (2013). Automatic recalibration and processing of tandem mass spectra using formula annotation. *Journal of Mass Spectrometry, 48*(1), 89-99. doi:10.1002/jms.3131

Understanding the cellular distribution and protein targets of a ruthenium (II) anti-cancer compound, RAPTA-T via mass spectrometry

R. F. Lee[1], C. Maclachlan[1], G. W. Knott[1], A. Meibom[1], R. Zubarev[2], A. Chernobrovkin[2], D. Rutishauser[2], K. P. Johnsson[1], P. J. Dyson[1]*

[1]EPF Lausanne, [2]Karolinska Institutet

Newer generation anti-cancer ruthenium (II) complexes such as RAPTA-T are promising clinical candidates which possess interesting anti-metastatic properties. However, the mechanism of action of RAPTA-T is poorly understood. Here we apply imaging mass spectrometry to elucidate the differences in distribution of RAPTA-T in highly metastatic breast cancer cells, MDA-MB-231 in contrast to MCF-7 cells which are lowly metastatic. We see clear nuclear accumulation of RAPTA-T in the metastatic cell line. We also find that unlike previously speculated, the activation of RAPTA-T involves not just aquation but possibly detachment of the arene. We then apply a novel proteomic profiling method to probe for interesting protein targets in these cells. We find two interesting targets phospholipase D3 and methionine adenosyltransferase 2A, the former being linked to metastasis and the latter being involved in cancer progression.

[1] R. F. S. Lee, S. Escrig, M. Croisier, S. Clerc-Rosset, G. W. Knott, A. Meibom, C. A. Davey, K. Johnsson and P. J. Dyson, *Chem. Commun.*, 2015, **51**, 16486–16489.
[2] A. Chernobrovkin, C. Marin-Vicente, N. Visa and R. A. Zubarev, *Scientific Reports*, 2015, **5**, 11176.

Combined GC- and UHPLC-HR-MS based metabolomics to analyze durable anti-fungal resistance processes in cereals

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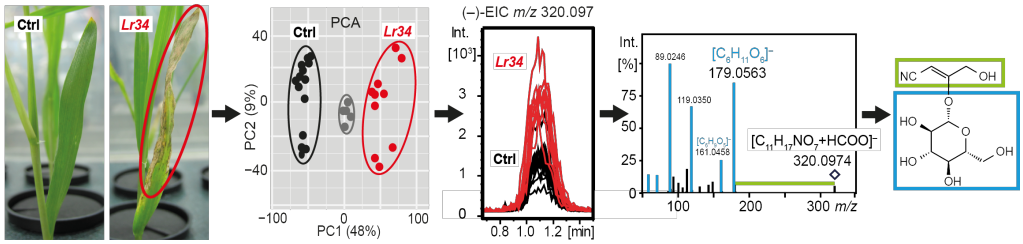
Introduction of durable resistance genes in crops is an important strategy to prevent yield loss caused by fungal pathogens and to maintain food security. The resistance gene *Lr34* of wheat (*Triticum aestivum*) durably confers resistance to four major fungal pathogens leaf rust, stripe rust, stem rust and powdery mildew. *Lr34* is functionally transferable to barley (*Hordeum vulgare*) [1] and rice (*Oryza sativa*). The molecular resistance mechanism of *Lr34*, encoding for an ATP-binding cassette transporter [2], is not known yet. The overall aim of this multi-disciplinary project was to increase the understanding of the molecular function and defense response of durable disease resistance in cereals.

To characterize *Lr34* functionality at metabolite level, a metabolomics approach based on combined UHPLC-HR-MS and GC-MS technology was applied. Comprehensive metabolic profiles of *Lr34* barley, rice and wheat grown under different conditions were investigated and a broad range of structurally diverse primary metabolites (e.g. amino- and organic acids, sugars), lipids and secondary metabolites (e.g. flavonoids) were identified. UHPLC-HR-MS/MS allowed the annotation of a variety of defensive secondary metabolites [1] contributing to the understanding of the durable, multi-pathogen resistance *Lr34* in different crop species.



[1] Harsh Chauhan, *et al.*, *Plant J.*, **2015**, *84*, 1, 202-215.
[2] Simon G. Krattinger, *et al.*, *Science,* **2009**, *323*, 1360-1363.

Compound-specific isotope analysis of environmental organic micropollutants: challenges and possibilities

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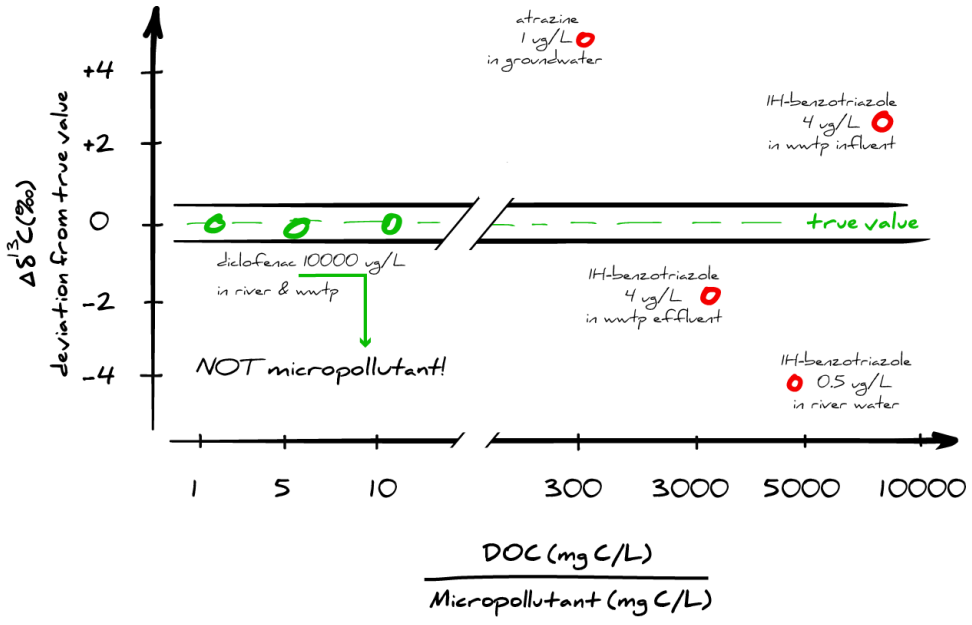
Occurrence of organic micropollutants in water raises major concern to both human health and the environment. Hence, it's necessary to assess the fate of these chemicals in the environment where compound-specific isotope analysis (CSIA) offers invaluable information that cannot be simply obtained by concentration dynamics. However, CSIA for environmental organic micropollutants currently encounters major challenges that impedes its use, especially for the polar micropollutants. These challenges can simply be summarized by two facts, among others: 1) organic micropollutants occur in natural systems at very low concentrations (i.e. ng/L - µg/L) which fall below the typical limits of gas chromatographs coupled to isotope-ratio mass spectrometer (i.e. mg/L) by factors easily exceeding 50000. 2) The latter fact dictates that very large volumes of water (e.g. ≥ 10 L) must be enriched by the corresponding factor. These two facts inevitably lead to partial co-extraction of interfering substances which consequently deteriorates the quality of the acquired isotopic data (see graph). Since there is no substitute for good chromatography in CSIA, there is a great interest in introducing selectivity in the sample preparation to get rid of the interfering substances.

In this scenario, we explore the use of molecularly-imprinted polymers (MIP), tailor-made synthetic materials specific for certain class of compounds, as a strategy for specific enrichment of typical anthropogenic micropollutants. Chloro-s-triazines and benzotriazoles were chosen as model compounds representative for pesticides in agricultural catchments and consumer chemicals in waste water, respectively. Characterization of the developed MIP-CSIA procedures demonstrates the viability of such an approach in eliminating the interfering matrices. Whereas, the studied model compounds are specifically retained on the corresponding MIP and recovered without interferences. Furthermore, comparison of $^{13}C/^{12}C$ and $^{15}N/^{14}N$ ratio measurements before and after the specific retention shows no consequences on the integrity of the isotopic ratios using the optimized methodologies. The developed strategy was tested in typical aquatic environments, such as leachates from soil lysimeters for triazines and domestic waste water from wastewater treatment plants for benzotriazoles.



Electrochemical Proton Transfer Based Polyaniline Films for Thin Layer Titrations

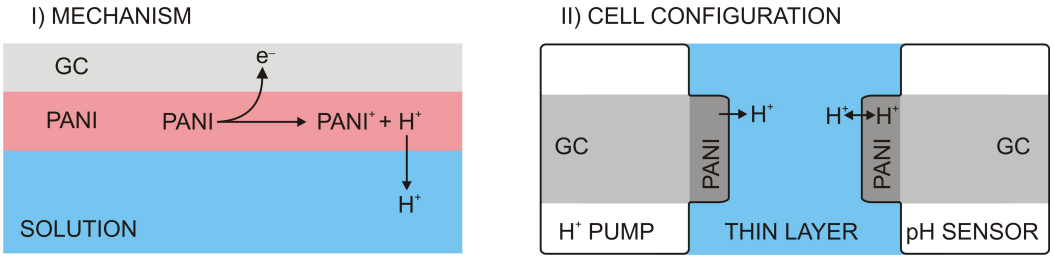
M. Ghahraman Afshar[1], G. A. Crespo[1], E. Bakker[1]*

[1]University of Geneva

Polyaniline (PANI) is univocally one of the most relevant electronic/conducting polymers, which has been applied for broad range of applications from batteries to sensors [1-3]. PANI is proposed here for the first time as a promising material for analytical applications where a targeted release of proton is required. Therefore, this research was mainly focused on the proton release properties of PANI layer. The PANI layer was synthesized by electropolymerization of aniline on the surface of glassy carbon (GC) by cyclic voltammetry [4, 5]. The coated PANI layer was then applied as a proton pump to release protons in thin layer coulometric mode (Scheme I).

The electrochemical arrangement consisted of one sensor and one pump placed opposite each in order to define a thin layer gap. The pump was used to release protons while the sensor was utilized as potentiometric readout to determine the local pH. A linear relationship between the duration of the applied pulse and the released charge (correlated with the potentiometric readout) allowed one to titrate the sample by adding a charge package, thereby mimicking a classical titration [6, 7]. Here, one PANI layer was used as a proton selective sensor and another PANI layer was applied as a proton pump (Scheme II).

We introduce here for the first time that a solid contact material such as PANI may provide an alternative technology with more pronounced mechanical and chemical robustness (compared to perm-selective membranes or other approaches based on water electrolysis) for both releasing and detecting protons in solution. Finally, the presented approach is applied for the titration of real samples including sea, river and lake waters for the determination of total alkalinity.



[1] Chetna Dhand, Maumita Das, Monika Datta, *Biosensors and Bioelectronics*, **2011**, *26,* 2811-2821.
[2] Alan G MacDiarmid, *Angewandte Chemie*, **2001**, *40,* 2581-2590.
[3] James Y Shimano, Alan G MacDiarmid, *Synthetic Metals*, **2001**, *123,* 251-262.
[4] M Radoicic, Z Saponjic, G Ciric-Marjanovic, *Applied Catalysis B: Environmental*, **2013**, *136,* 133-139.
[5] Shaolin Mu, *Synthetic Metals*, **2004**, *143,* 259-268.
[6] Majid Ghahraman Afshar, Gaston A Crespo, Eric Bakker, *Angewandte Chemie*, **2015**, *127,* 8228-8231.
[7] Majid Ghahraman Afshar, Gaston A Crespo, Eric Bakker, *Analytical Chemistry*, **2015**, *87,* 10125-10130.

Persistent organic pollutants in white-blooded Antarctic fish Champsocephalus gunnari and Chaenocephalus aceratus

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[1]Empa, Swiss Federal Laboratories for Materials Science and Technology, Laboratory for Advanced Analytical Technologies, CH-8600 Dübendorf, Switzerland, [2]University of Basel, Department of Environmental Sciences, Programme Man-Society-Environment MGU, CH-4051 Basel, Switzerland, [3]University of Bern, Vetsuisse Faculty, Centre of Fish and Wildlife Health, CH-3012 Bern, Switzerland, [4]Department of Biological Sciences, University of Alberta, Edmonton, AB Canada

Persistent organic pollutants (POPs) are ubiquitous environmental chemicals and can be found even at very remote areas such as the Antarctic Ocean. Via long-range atmospheric transport (LRAT), global distillation processes and cold condensation POPs reach the Antarctic ecosystem and bioaccumulate in aquatic biota. Polychlorinated biphenyls (PCBs), polybrominated diphenyl ethers (PBDEs), and former widely used pesticides such as g-hexachlorocyclohexane (g-HCH), hexachlorobenzene (HCB), and p,p'-DDT are lipophilic organic chemicals with high potential to bioaccumulate in Antarctic species. Antarctic fish, which hold high trophic positions, appear to possess low endogenous elimination rates for POPs and are expected to show increasing levels of these chemicals with rising anthropogenic pollution. Therefore two fish species of Antarctic icefish, originating from the Southern Ocean around Elephant Island, were caught and analyzed for their levels of PCBs, PBDEs, HCB, HCHs, and DDTs. The two species included the planktivorous *Champsocephalus gunnari* and the piscivorous *Chaenocephalus aceratus*. The species of white-blooded icefish were caught during a cruise with the research vessel 'Polarstern' during March 13 to April 9, 2012, around Elephant Island and the South Shetland Islands. POPs were analyzed in muscle and ovary tissue of mature, female fish. Lyophilized tissue of muscle or gonads was extracted using a speed-extractor (E-914, Büchi, Switzerland) with a mixture of n-hexane/dichloromethane (1:1). Extracted lipids were spiked with $^{13}C_{12}$ labeled internal standards and cleaned-up by treatment with concentrated sulfuric acid and liquid chromatography on multilayer silica gel. Quantitative determination of the target analytes was carried out by gas chromatography/high resolution mass spectrometry (GC/HRMS) at a mass resolution of 8'000.

Our results revealed higher contaminat levels in ovary than in muscle tissues of both species. Most analyte concentrations and the toxicity equivalents (TEQs), as well as the bioanalytical equivalents (BEQs) were lower as in temperate species. Comparison with data from the literature points to higher PCB and DDT concentrations than those measured in icefish in the 90's. For the other contaminants no temporal trend could be identified. Higher bioaccumulation was found for HCB and DDTs in C. aceratus compared to C. gunnari. However there was no general species-specific accumulation pattern of the different classes of POPs between the two icefish. Thus, the expected link between contaminant burdens of *C. aceratus and C. gunnari* and their ecological traits was only weakly supported for these species [1].

[1] Anneli Strobel, Peter Schmid, Helmut Segner, Patricia Burckhardt-Holm, Markus Zennegg, Chemosphere 2016, 1 - 8 (article in press)

Field-scale in-situ analysis of ambient N_2O isotopic composition to trace source processes in an intensively managed grassland

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[1]EMPA, Dübendorf, [2]KIT, IMK-IFU, [3]Sustainable Agroecosystems, [4]ETH Zurich, Sustainable Agroecosystems, [5]ETH Zurich

Nitrous oxide (N_2O), a strong greenhouse gas and an important ozone-depleting substance, is primarily emitted from pristine and fertilized soils. A multitude of biogenic and abiotic N_2O producing processes have been identified, but their relative contribution to total N_2O emission and relevance for different ecosystems is currently not known, as related processes are highly dispersed and variable. For the development of effective N_2O mitigation strategies, however, detailed knowledge of processes and their temporal and spatial variations is essential. Analysis of site-specific N_2O isotopic composition has proven potential to disentangle source processes based on their characteristic isotopic signatures (Wunderlin et al. 2013).

In recent years we developed an analytical technique for real-time high-precision analysis of N_2O site-specific isotopic composition, consisting of a quantum cascade laser absorption spectrometer (QCLAS) coupled to an automated preconcentration device, called TRace gas EXtractor (TREX) (Wächter et al. 2008, Eyer et al. 2016). In a pilot field study N_2O isotopic signatures could be interpreted in relation to management events and meteorological conditions (Wolf et al. 2015). Since then the field-applicability of the setup was significantly improved by advanced temperature control for both QCLAS and TREX, and installation of the instrumentation in a 19” rack. In addition, the novel device offers the possibility for simultanous analysis of $\delta^{17}O$-N_2O.

Here we present first results from a field study which will be carried out at an intensively managed grassland site in southern Bavaria, Germany (Fendt, 600 m.a.s.l.)between June and July 2016, as a sub-module of the ScaleX 2016 campaign organised by IMK-IFU. We will focus on the discussion of ambient N_2O isotopic composition measurements above the grassland site that are expected to shed light into different N_2O source processes based on their isotopic source signature. These results will be combined with atmospheric transport simulations and footprint analysis to interpret spatial variability. It is foreseen to evaluate N_2O isotopic information in conjunction with $\delta^{15}N$ values of nitrogen precursors (NH_4^+, NO_3^-), management events and additional supporting soil and metereological parameters. Results from the field study will be discussed in relation to complementary approaches: A biogeochemical soil model (L-DNDC) with an isotope sub-modul currently developed at IMK-IFU, and a ^{15}N tracer approach applied by Thünen Institute.

Wunderlin P., Lehmann M.F., Siegrist H., Tuzson B., Joss A., Emmenegger L., Mohn J. (2013): Environmental Science and Technology 47(3). 1339-1348.
Waechter H., Mohn J., Tuzson B., Emmenegger L., Sigrist M.W. (2008): Optics Express 16 (12). 9239-9244.
Eyer S., Tuzson B., Popa, M. E., van der Veen C., Röckmann T., Rothe M., Brand W. A., Fisher R., Lowry D., Nisbet E. G., Brennwald M. S., Harris E., Zellweger C., Emmenegger L., Fischer H., Mohn J. (2016): Atmospheric Measurement Technique 9, 263-280.
Wolf B., Merbold L., Decock C., Tuzson B., Harris E., Six J., Emmenegger L., Mohn J. (2015): Biogeosciences 12(8): 2517-2531.

At the interface between climate research and metrology: Gas adsorption and desorption on high pressure standard cylinders

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Long term atmospheric monitoring of trace gases require great attention to precision and accuracy. For a globally integrated and well established greenhouse gas observation network, World Meteorological Organization (WMO) has set recommended compatibility goals within the framework of its Global Atmosphere Watch (GAW) Programme. To achieve these challenging limits, the stability of the primary and secondary gas standards are of great importance.

For high pressure standard gas mixtures used in atmospheric trace gas analysis, there exists only a limited amount of data and few attempts to quantify the surface processes. Here, we focus on instabilities in gas composition due to surface processes, in particular, adsorption and desorption and it's temperature and pressure dependency. Specifically, we investigate adsorption/desorption phenomena on steel and aluminum cylinders for the species CO, CO_2 and CH_4 by using a cavity ring down spectroscopy analyzer. In the present study a set of experiments are designed to test the temperature dependency in the range of -10 °C to +50 °C and pressure dependency from over 100 bars to atmospheric pressure. Moreover, measured concentrations are fitted to a simple adsorption model in order to quantify the parameters of adsorption. For CH_4 no distinct difference between aluminum and steel cylinders are observed. CO_2 showed clear temperature dependency for steel and only minimal for aluminum cylinders, whereas CO needs further investigation.

Enyzme-Substrate Complexes Studied by Native Electrospray Mass Spectrometry: First Steps Towards Gas-Phase Enzymology

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The question of whether, and under what conditions, electrosprayed biological molecules and biomolecular complexes retain their "native" forms in the vacuum environment of a mass spectrometer remains an intense area of research [1-4]. To date, most experiments seeking to tackle this question have used a structural approach, relying on measures of ion size, reactivity, and dissociation properties. In this work, we attempt to address this question using a new, functional approach, with trypsin as a model enzyme. The aim was to isolate gaseous non-covalent trypsin-substrate complexes in the gas phase, and to see whether the acylenzyme (with the C-terminus of the substrate having dissociated after specific enzymatic cleavage) can be produced upon activation of these complexes. The successful formation of the gaseous acylenzyme would act as strong evidence for a correctly organized enzyme active site in the gas phase.

Electrospray ionization (ESI) mass spectra were acquired using gold-coated glass capillaries with a Waters Synapt G2 mass spectrometer. ESI solutions contained trypsin and/or model substrate (N-benzoyl-capped synthetic hexapeptides of type Bz-XXRGGG) at equimolar (10 micromolar) concentrations. Ammonium acetate (500 mM) was used for "native" ESI. Measurements at low pH were done in 1% aqueous acetic acid.

Native ESI mass spectra of trypsin-substrate mixtures indicate that, for many peptides, the hydrolysis reaction goes to completion in the nano-ESI emitters prior to MS analysis. However, trypsin-bound N-terminal fragments are clearly visible in the high mass regime, in accordance with trypsin's N-terminal recognition properties. Hydrolysis rates can be slowed by lowering pH, though this appears to hinder substrate binding affinity. Nonetheless, mass spectra of electrosprayed trypsin-substrate mixtures at low pH show peaks corresponding to the bound substrate, though these exist in low abundance. Upon isolation and collisional activation of these complexes, peaks corresponding to covalent detachment of the C-terminus of the substrate are apparent in tandem mass spectra. This is consistent with a gas-phase enzyme reaction having occurred in the gas phase. As a control experiment, trypsin complexes with peptides containing D amino acids (which react slowly in solution) were shown also to survive the electrospray process; however, in this case, no evidence for a gas-phase enzyme reaction is observed upon collisional activation. Building on these preliminary results, we are currently extending these studies to a larger library of peptides, to assess whether the specificity of the enzyme reaction depends on amino acid sequence in a manner similar to that in solution. Furthermore, to enable studies of the short-lived complexes of trypsin with good substrates under native solution conditions, we are currently working towards implementing a rapid-mixing device prior to MS analysis. In these experiments, the mass spectrometer acts as a useful readout to monitor potential proteolytic activity in the gas phase, as the trypsin-substrate complex and acylenzyme have distinct masses which are easily distinguishable in a mass spectrum. It is easily envisioned that this methodology could be implemented to study other enzyme reactions in the gas phase.

[1] K. Breuker, F.W. McLafferty, Proc. Natl. Acad. Sci. USA, **2008**, 105, 18145.
[2] E. Jurneczko, P.E. Barran, Analyst, **2011**, 136, 20.
[3] Z. Hall, C.V. Robinson, J. Am. Soc. Mass Spectrom., **2012**, 23, 1161.
[4] J. J. Brady, E. J. Judge and R.J. Levis, Proc. Natl. Acad. Sci. USA, **2012**, 109, E207.

Studies on discrete samples using a microdroplet generator combined with ICP-Time-of-Flight Mass Spectrometry

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Conventional liquid introduction for inductively coupled plasma optical emission (ICP-OES) and mass spectrometry (ICP-MS) is typically realized by means of pneumatic nebulizer combined with a spray chamber. However, drawbacks of this approach include sample consumption and incomplete sample transport, which can limit its application in various fields, namely forensic, toxicological, biological, and clinical studies, where only microliters of sample are available [1]. In this study, a microdroplet generator (MDG) was used as an alternative sample introduction system for ICP-MS. With this setup, monodisperse droplets (20-40 µm in diameter) are generated with a user defined frequency (1 Hz to 2000 Hz) and result in time-separated and discrete ICP-MS signals of about 300 µs in duration. Droplets are produced on-axis to the ICP and introduced into the plasma via a stream of helium and argon gas to focus their trajectories and partially dry them [2]. This system configuration routinely enables 100% transport efficiency. In combination with a recently developed ICP-Time-of-Flight Mass Spectrometer (ICP-TOFMS), we record complete elemental spectra from each generated droplet and can examine the composition of ICP-TOFMS signals from droplets at a time resolution of 30 µs. Thanks to the narrow size distribution of the droplets, the time required to undergo complete desolvation, atomization, excitation and ionization is highly reproducible from one droplet to another, making this discrete sample introduction system an ideal candidate tool for investigating fundamental ICP processes [3]. Here, we report studies on the effects of analyte mass and water load for multi-elemental detection from individual droplets. Importantly, because droplets serve as proxy for other mass-limited discrete samples, such as single cells or nanoparticles, these studies indicate the potential of multi-element ICP-TOFMS analysis for these species. Despite its numerous advantages, poor limits of detection (LODs) in terms of concentration (above 1 ng/g) for single-droplet analysis remain a limitation of MDG sample introduction. While absolute LODs are excellent (10s of attograms), the lowest concentration detection limit achievable was in the ng/g range for ^{238}U, which compares poorly to conventional solution-based introduction systems. To overcome this limitation, signal averaging may be employed. With this approach the concentration LOD for ^{238}U is improved to 2 pg/g with 500 droplets averaged. These results make MDG-ICP-TOFMS competitive with conventional solution-based sample introduction for ICP-MS. Finally, in this presentation, we will discuss how the characteristics of discrete microdroplets affect the performance of the ICP and how the fate of these individual entities directly correlates to nanoparticles behavior within the plasma.

[1] J. L. Todolí and J. M. Mermet, Sample introduction systems for the analysis of liquid microsamples by ICP-AES and ICP-MS, *Spectrochimica Acta Part B: Atomic Spectroscopy*, **61** (2006), 239-283.
[2] (a) Gschwind, S.; Hagendorfer, H.; Frick, D. A.; Gunther, D., Mass Quantification of Nanoparticles by Single Droplet Calibration Using Inductively Coupled Plasma Mass Spectrometry. *Anal Chem* **2013,** *85* (12), 5875-5883; (b) Borovinskaya, O.; Gschwind, S.; Hattendorf, B.; Tanner, M.; Gunther, D., Simultaneous Mass Quantification of Nanoparticles of Different Composition in a Mixture by Microdroplet Generator-ICPTOFMS. *Anal Chem* **2014,** *86* (16), 8142-8148.
[3] (a) Olesik, J. W., Investigating the fate of individual sample droplets in inductively coupled plasmas. *Appl Spectrosc* **1997,** *51* (5), A158-A175; (b) Borovinskaya, O.; Aghaei, M.; Flamigni, L.; Hattendorf, B.; Tanner, M.; Bogaerts, A.; Gunther, D., Diffusion- and velocity-driven spatial separation of analytes from single droplets entering an ICP off-axis. *J Anal Atom Spectrom* **2014,** *29* (2), 262-271.