

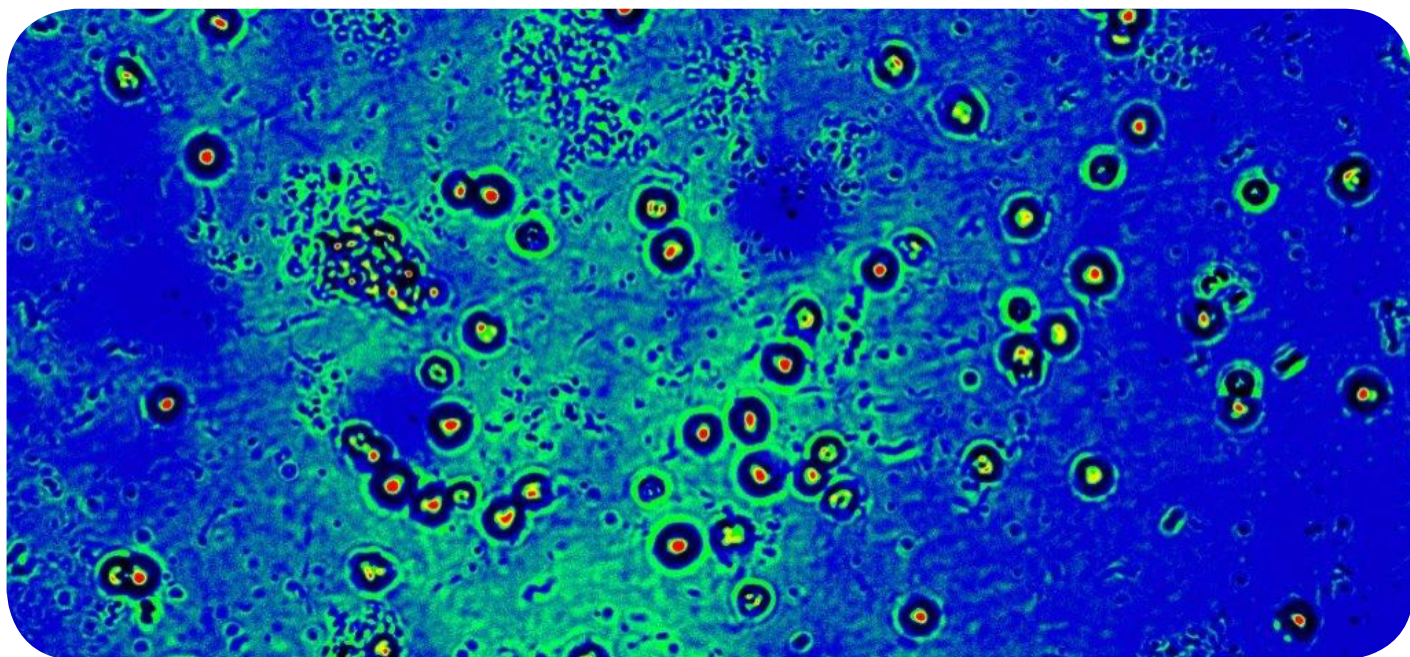
Meeting of Swiss Analytical Scientists

CHanalysis 2018

April 12–13, 2016

Dorint Hotel Beatenberg

Organized by the Division Analytical Sciences
of the Swiss Chemical Society



SCS
Swiss Chemical
Society

**Division of
Analytical Sciences**

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General Information

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Participation Fee (includes meals and accommodation)

Regular Fee: CHF 300.–

Students including PhD students: CHF 100.–

Scientific Program

Thursday, April 12

Session 1

13.00 Conference Opening

13.05 **Enrico Martionoia**, University of Zurich
Heavy metals and plants: how plants can be used in cleaning up soils and producing safe food

13.45 **Eric Bakker**, University of Geneva
Closed bipolar membrane electrodes to translate electrochemistry into colour

14.15 **Lu Wang, Stephanie Sadler, Eric Bakker**, University of Geneva
Tunable ion-selective optode microsensors based on hydrophobic solvatochromic dyes

14.30 **Felix Zelder**, University of Zurich,
Disassembly of metal-salen complexes for pyrophosphate detection

14.45 **Suphasinee Sateanchok, Nadezda Pankratova, Maria Cuartero, Eric Bakker**, University of Geneva
In-line thin layer sensors for phosphate determination in seawater

15.00 Coffee Break

Session 2

15.30 **Debora Käser, Joachim Koch, Detlef Günther**, ETH Zurich
Low coherence interferometry (LCI) for on-line monitoring of crater depths in ultrafast LA-ICPMS of conducting materials

15.45 **Lyndsey Hendriks, Debora Thöny, Alexander Gundlach-Graham, Detlef Günther**, ETH Zurich
Managing matrix effects for accurate nanoparticle sizing by single-particle ICP-TOFMS

- 16.00 **Lena Schinkel, Christian Bogdal, Ronan Cariou, Kristopher McNeill, Norbert Heeb**, Empa Dubendorf and ETH Zurich
In-source fragmentation of chlorinated paraffins impedes the analysis of chlorinated olefins by GC-ECNI-MS
- 16.15 **Luzia Gyr, Renato Zenobi**, ETH Zurich
Identification of reactive species in dielectric barrier discharge ionization mass spectrometry: A case study with perfluorinated compounds
- 16.30 **Alena Tierbach, Ksenia J Groh, Kristin Schirmer, Marc J-F Suter**, Eawag Dubendorf and ETH Zurich
*Glutathione S-transferase protein expression in different life stages of the vertebrate model zebrafish (*Danio rerio*)*
-

16.45 Poster Session

19.00 Dinner
followed by Muh-Bar for those interested

Friday, April 13

Session 3

- 09.00 **Bodo Hattendorf, Lorenzo Querci, Debora Käser, Joachim Koch, Detlef Günther**, ETH Zurich
Laser ablation under pressure for mass spectrometry-based element imaging without an ICP
- 09.30 **Renato Zenobi, Tobias Bruderer, Martin T Gaugg, Malcolm Kohler, Nora Nowak**, ETH Zurich
Exhalomics
-

10.00 Coffee Break

Session 4

- 10.30 **Vera I Slaveykova**, University of Geneva,
Environmental flow field-flow fractionation coupled to ICP-MS for exploring the bioavailability potential of metal-containing contaminants in the aquatic systems
- 10.45 **David Ruskic, Gérard Hopfgartner**, University of Geneva,
Liquid chromatography - mass spectrometry with modifier assisted differential mobility spectrometry for tuning multidimensional separation selectivity
- 11.00 **Marion Ort, Simon Bachler, Dominik Hümmer, Alexander Stettler, Stefanie D Krämer, Petra S Dittrich**, ETH Zurich and University Basel
Novel drug permeability screening platform combining microfluidics and LC-MS
- 11.15 **Carla Frege, Matthias Hill, Stefan Reimann, Martin K Vollmer**, Empa Dubendorf
APRECON-TOF-MS: A state-of-the art instrument for the analysis of halogenated greenhouse gases
- 11.30 **Christian Berchtold, Ralf Dumler, Boris Kolvenbach, Israel Joel Koenka, Veronika Butterweck, Peter C Hauser, Götz Schlotterbeck**, FHNW Muttenz and University of Basel
Microwave plasma desorption and ionization for direct analysis without sample preparation
- 11.45 **Rahel P Eberle, Stefan Schürch**, University of Bern
Interaction of antitumor metallocenes with nucleic acids
- 12.00 **Nora Nowak, Thomas Gaisl, Martin T Gaugg, Tobias Bruderer, Malcolm Kohler, Pablo Sinues, Renato Zenobi, Steven Brown**, ETH Zurich
How can real-time breath analysis provide new insights into metabolism during sleep?
- 12.15 **Caroline Davis, Kristopher McNeill, Elisabeth ML Janssen**, ETH Zurich and Eawag Dubendorf
Non-singlet oxygen kinetic solvent isotope effects in photochemistry
-

12.30 General Assembly of the Division Analytical Sciences (DAS) of
the Swiss Chemical Society

13.00 End of the Meeting

List of Posters

1. **Matthias Schild**, A new nitrogen microwave plasma source for mass spectrometry MICAP-TOFMS
2. **Marcel Burger**, Capabilities of inductively coupled plasma time-of-flight mass spectrometry in combination with collision/reaction cell technology
3. **Jovana Teofilovic**, Optimization method development for silica nanoparticles measurement using sp-ICPSFMS
4. **Alexander Gundlach-Graham**, Characterization of low-count-rate signals and noise in ICP-TOFMS
5. **Gunnar Schwarz**, Elemental imaging of bivalve mollusk shells with LA-ICP-TOFMS
6. **Fabrizio Mastrorocco**, Analysis of red figured samples from Apulia using LA-ICP-MS
7. **Stefan Kradolfer**, 'On-site' laser ablation – Insights into the trace elements of ancient gold artefacts
8. **Ralf Dumler**, RF Energy coaxial wave-guided atmospheric pressure ion sources for universal mass spectrometry
9. **Aline Mutabazi**, Evaluation of the potential of ion mobility combined with liquid chromatography and mass spectrometry (LC-IM/MS) for the analysis of pharmaceutical compounds
10. **Dajing Yuan**, Probing ion-ionophore interactions in thin layer polymeric membranes
11. **Sutida Jansod**, Colorimetric closed bipolar electrode for ion selective detection
12. **Stephanie Sadler**, Optical detection of common ions by solvatochromatic dye transducers doped into polystyrene microsensors
13. **Pitchnaree Kraikaew**, Electrochemical controlled fluorescence detection with localized ion transfer of lipophilic solvatochromic dyes
14. **Alina Osypova**, The pyranine-benzalkonium ion pair: a versatile sensor for biomedical purposes
15. **Hao Yin**, Plasmonic 'hot electrons' mediate nanoscale methylene blue molecular "blinking" without electric potential assistance
16. **Mengting Li**, Cocktail effect of TiO₂ nanoparticle mixtures with mercury to green alga *Chlamydomonas reinhardtii*

Abstracts of Oral Presentations

*Heavy metals and plants: how plants can be used in cleaning up soils and producing safe food***Enrico Martinoia**

Institute of Plant and Microbial Biology, University Zurich

All living organisms require heavy metals such as iron, copper or zinc, which are important co-factors for many enzymes. Therefore, plants have evolved uptake systems to take up the essential heavy metals and deliver them to the right targets. However, besides these essential heavy metals, non-essential, toxic metals and metalloids such as cadmium, lead or arsenic are also often present and widespread on agronomical soils. This contamination of agricultural soils can occur by the natural presence of toxic heavy metals or by anthropogenic deposition, mainly in mining areas. The uptake systems (transporters) of living organisms can in most cases not completely discriminate between essential and non-essential heavy metals. Due to this fact, toxic heavy metals and metalloids are taken up by plants and can enter the food chain, potentially causing serious health problems.

To reduce or even solve this problem two approaches have been undertaken. The first has the goal to use plants that can efficiently take up heavy metals from soils to clean up contaminate soils. This approach, called phytoremediation has the advantage that it is much less expensive than a physical decontamination of soils and would also allow to keep the soil structure, which is important for plant growth and productivity. Despite some progress, however, we are up to now far away to have an efficient phytoremediation system. The second approach has the goal to reduce or avoid the transfer of heavy metals to the edible parts of a plant and hence to avoid that toxic heavy metals enter in the food chain. Here the results obtained so far are much more promising.

In my talk I will introduce how plants take up heavy metals and how plants allocate heavy metals to the different organs. Based on this knowledge I will show how plants can detoxify toxic heavy metals and approaches that can be used to clean up soils or reduce the transfer of toxic heavy metals to the edible parts of a plant to reduce the health risks for humans.

Closed bipolar membrane electrodes to translate electrochemistry into color

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The realization of a fundamentally sound optical transduction of membrane electrodes has been a goal for many years. It all started by observing chromogenic ionophores that changed their optical properties upon binding with host molecules in a membrane film thinner than the ones used in potentiometric probes. In a sweeping paper by Morf where he aimed to impress the audience of the Matrafured conference, he put forward the principles by which so called bulk optodes must function, namely on the basis of ion-exchange and coextraction equilibria between the aqueous phase and sensing phase. Unfortunately, this meant that one could not realize an optical readout for single ions, which is really what one would like to achieve. Some progress in this direction has been recently achieved by the use of solvatochromic dyes that function not only as the exchanging reference ion but also as the transducing molecule as their optical properties change upon transfer into the aqueous phase. The lipophilization of these probes made it possible to confine this exchange just the sensor surface, realizing self-contained optical ion probes.

The innovation introduced here directly translates membrane electrode response to an optical readout by bipolar electrodes. This is a principle that overcomes the old limitations and results in optical sensors that are no more fundamentally compromised than potentiometric sensing probes. It is realized by an imposed potential across a free hanging (bipolar) electrode that makes contact on one end with the sample (the sensing probe) and on the other with a reference solution optimized for optical readout. As the sample concentration changes, the potential at the sample side changes predictably according to the Nernst equation, and this change must be compensated at the opposite end of the bipolar electrode and translated into an optically detectable change. A number of examples will be shown to illustrate the principle, one with ferroin on the detection side and either Ag/AgCl or a polymeric ion-selective membrane on the sample side, the other using solvatochromic dye transducers. The principle can be multiplexed for large arrays of electrodes to achieve chemical imaging applications where the sample does not need to be exposed to light.

Tunable ion-selective optode microsensors based on hydrophobic solvatochromic dyes

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Ion-selective optode sensors based on ion-exchange progress have been developed during the last few decades.¹ Reversible ion optodes are composed of a polymeric phase containing a lipophilic optode reporter which can be a pH indicator (also called chromoionophore) or, more recently, a positively charged solvatochromic dye (SD),² an ion exchanger and an optically silent ionophore selective for the analyte. For the traditional pH-dependent sensors with chromoionophore, the dynamic range depends on the pK_a of the chromoionophore and it can be also shifted by adjusting the sample pH. For the sensors based on lipophilic SD, the pH does not influence the response range. It is tunable to some extent by adjusting the ratio of the components. However, positive charge saturation on the sensor surface during the ion-exchange progress limits the range at higher sample concentrations. We present here a series of newly synthesized solvatochromic dyes that exhibit a range of hydrophobic properties, so that their response range can be tuned by the choice of the dye.

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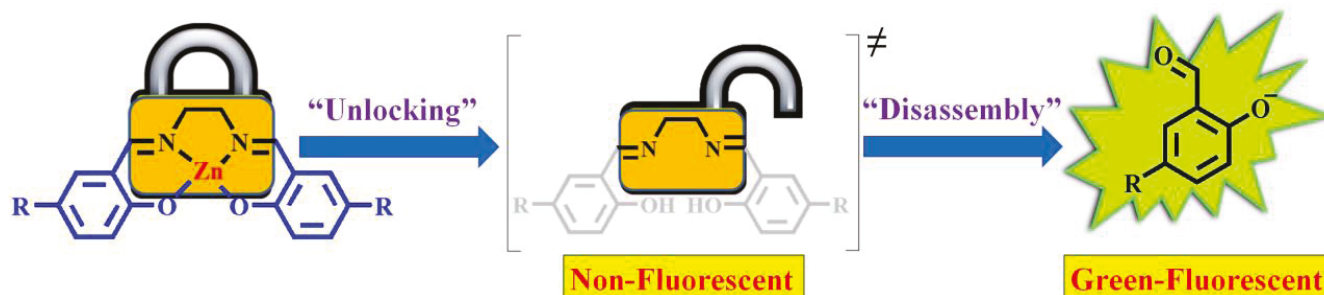
Disassembly of metal-salen complexes for pyrophosphate detection

Felix Zelder

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This contribution presents a stimulus-induced disassembly approach in water.¹ In particular, the selective fluorometric detection of pyrophosphate (PPi) in water and biological media is described.

In this method, PPi selectively sequesters a metal ion from a metal-chelate complex. The “unlocked” ligand subsequently hydrolyses into its molecular subunits.



Since the optical properties of the disassembled ligand and its ancestor are distinguishable, the PPi induced disassembly of the metal-complex is leading to a detectable signal.¹⁻³ Applications of this strategy for PPi detection in cells are presented.⁴

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*In-line thin layer sensors for phosphate determination in seawater*Suphasinee Sateanchok^{1,2}, Nadezda Pankratova¹, Maria Cuartero¹, Eric Bakker^{1*}¹Department of Inorganic and Analytical Chemistry, University of Geneva, Quai Ernest-Ansermet 30, CH-1211 Geneva, Switzerland²Department of Chemistry and Center of Excellence for Innovation in Analytical Science and Technology, Chiang Mai University, Chiang Mai, Thailand
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Phosphate is an essential nutrient for growth and energy transfer used by all living organisms. Also, it is an important key parameter of water quality and is often the limiting nutrient for primary production in marine ecosystems. Classical methods of phosphate determination commonly used for routine analysis include colorimetry, ion chromatography and flow injection analysis. However, these methods are still cumbersome for *in-situ* measurements, as their drawbacks include high cost, requirement of sample pre-treatment, reagent addition and storage. Here, an in-line microflow system for phosphate determination is established in view of realizing a monitoring system for the environmental sciences.

A microfluidic flow employing membrane based reagent delivery for phosphate determination will be presented. The key reagents (molybdate anions and hydrogen ions) are transported into a thin layer sample across anion-exchange and cation-exchange membranes, respectively. The formed phosphomolybdate complex is detectable by electrochemical as well as spectrophotometric means. Characterization of the applicable pH window and reagent concentration will be demonstrated. The system is applied to seawater samples.

References

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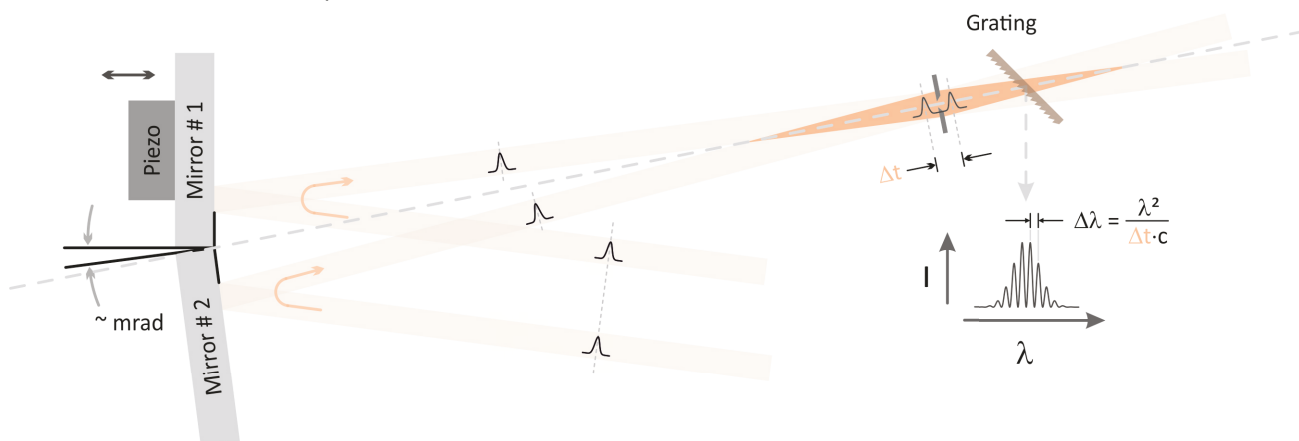
Low coherence interferometry (LCI) for on-line monitoring of crater depths in ultrafast LA-ICPMS of conducting materials

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Ultrafast laser ablation (LA) is being considered a versatile sampling tool for depth profile analyses (DPA) of conducting materials with resolutions in the sub-micrometer range. Over the years, LA-based DPA has been used in combination with different analytical techniques, such as laser-induced breakdown spectrometry (LIBS), LA mass spectrometry (MS) or inductively coupled plasma (ICP) MS [1-3]. The goal of any DPA is to measure the true concentration profile of elements as a function of sampling depth, which turns the morphology of craters as well as the material up-take rates to crucial parameters as both control the depth resolution (ultimately) achievable. Furthermore, on-line monitoring of crater depths and diameters would allow calculating ablated volumes and, thus, to even render absolute quantification possible as reported by Hattendorf et al. [4].

In this paper, we studied the feasibilities of Fourier domain low coherence interferometry (FD-LCI) to monitor the depths of craters in conducting materials using ultrashort bursts of white light [5]. A Fresnel double-mirror set-up served as proxy for crater rim and bottom to first split, delay and reflect, and then reassemble individual pulses for interference along an optical grating (see figure). Depending on whether interference patterns were processed by discrete Fourier transform (DFT) or by non-linear least squares regression (LSR) mirror displacements, i.e. depth resolutions, were found to range from several micrometers to less than 100 nm, respectively.



Fresnel double mirror set-up used for FD-LCI of bursts of white light pulses.

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Managing matrix effects for accurate nanoparticle sizing by single-particle ICP-TOFMS

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Single Particle Inductively Coupled Plasma Mass Spectrometry (sp-ICPMS) is a promising technique for nanoparticle (NP) analysis that enables concurrent measurement of individual NP mass and particle number concentrations (PNCs).¹ In sp-ICPMS, NPs introduced into the ICP are vaporized, atomized, and ionized, and each NP produces a bursts of ions that is measurable as a signal spike above the baseline.² Because the intensity of ICPMS signals depend on the mass of analyte that enters the plasma, appropriate mass-sensitivity calibration allows for the mass of each NP to be determined. In this study, we determine absolute mass sensitivity (counts/atom) of the ICPMS by introducing monodisperse droplets doped with the analyte of interest into the ICP; because the solution concentration and droplet size are known, the analyte mass entering the plasma can be readily calculated.^{3,4} It has been demonstrated that this approach yields accurate sizing in water matrices, but because the goal would be to apply sp-ICPMS to more complex matrices, such as food samples, environmental and biological samples, the effect of the sample matrix on the ICPMS sensitivities needs to be investigated. Indeed, the sample matrix could affect the ICPMS signals recorded for the NPs and an unmatched sensitivity for NPs and calibrant droplet will result in an error of the measured nanoparticle size, as the mass is related to the volume.

In order to investigate matrix effects on NP accurate sizing, we combined our ICP-TOFMS (icpTOF, TOFWERK AG, Switzerland), with a dual-sample introduction system first reported by Ramkorun-Schmidt et al.⁵ In this setup, microdroplets—which are used as calibrant to determine the instrument sensitivity—are introduced concurrently with the NP-containing samples and thereby experience the same plasma conditions. This type of online microdroplet “standard addition” approach can be used to compensate for plasma-related matrix effects. In results presented here, we investigated the sizing of gold NPs dispersed in matrices of ultra-pure water, fruit juices, and milk. For the fruit juices matrix, minimal signal enhancement was observed and Au NPs sizing was identical to that obtained in the water matrix. However, in the case of milk, signal intensities were decreased by ~50% for both the calibrant droplets and NP signals. Because the sensitivities of calibrant droplet and analyte NP were affected in the same way, Au NPs could be sized accurately despite signal attenuation due to the matrix. However, if the sensitivities had not been matched for the calibrant droplet and the NPs, a size underestimation of 27% would have been obtained.

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In-source fragmentation of chlorinated paraffins impedes the analysis of chlorinated olefins by GC-ECNI-MS

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Chlorinated paraffins (CPs) are high production volume chemicals (>1 Mio t a⁻¹) often applied as plasticizers, flame retardants or metal working fluids. CPs are persistent and of environmental concern. Their analysis is an analytical challenge due to complex mixtures of thousands of isomers, limited chromatographic resolution and complex isotopic patterns that often overlap. Recently, we showed that a thermal exposure of CPs during their applications induces the elimination of HCl resulting in the formation of chlorinated olefins (COs) [1,2]. COs have similar physicochemical properties and can be released to the environment together with CPs. The mass spectrometric analysis of CP/CO mixtures is even more problematic due to severe interferences.

Typically, CPs are analyzed by gas chromatography electron-capture negative ionization mass spectrometry (GC-ECNI-MS) in selected ion monitoring mode (SIM). Herein, we show that such methods falsely quantify COs as CPs in case of insufficient mass resolution ($R < 20'000$) and mass accuracy (>40 ppm) [3]. Further, this method can lead to an intense in-source formation of COs. ECNI is supposed to be a soft ionization method producing mainly $[M-Cl]^-$ fragment ions for CPs. However, we also observed $[M-HCl-Cl]^-$ fragment ions [4]. As shown in Figure 1a, when fragmented to $[M-HCl-Cl]^-$ ions, CPs have exactly the same mass as COs when fragmented to $[M-Cl]^-$ ions. Thus, COs that are present in the analyzed samples cannot be distinguished from COs formed in the ion source of the MS. Figure 1b shows that extracted $[M-Cl]^-$ ion chromatograms for C₁₃H₁₉Cl₇-COs and C₁₃H₂₀Cl₈-CPs interfere and are chromatographically irresolvable (red area) [3].

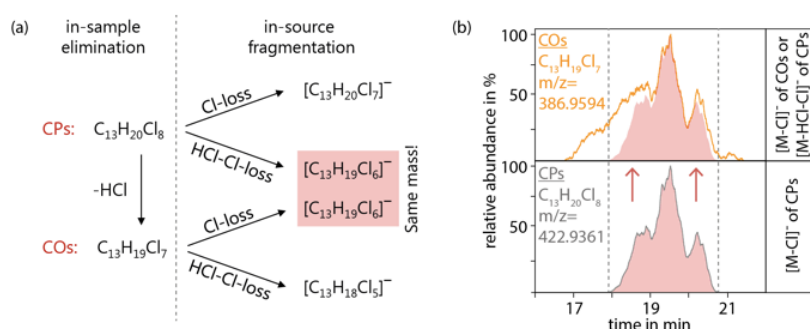


Figure 1. Interfering chlorinated olefin (CO) and chlorinated paraffin (CP) fragment ions. HCl elimination can occur in samples or in the ion source of the MS, leading to identical ions of CPs and COs.

Even if applying state-of-the-art high resolution MS technologies (e.g. Orbitrap-MS with $R > 100'000$), in-source fragmentation of chlorinated paraffins impedes the analysis of chlorinated olefins by GC-ECNI-MS. Besides, there is a risk that CPs thermally degrade to COs in hot GC injectors or columns, as well. As an alternative, we present a method based on liquid chromatography coupled to chlorine-enhanced atmospheric pressure chemical ionization

(APCI) MS. This method provides an even softer ionization of CPs, producing $[M+Cl]^-$ adduct ions. With this method, COs can be analyzed in presence of CPs without interfering fragment ions [1,4].

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Identification of reactive species in dielectric barrier discharge ionization mass spectrometry: A case study with perfluorinated compounds

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Ambient ionization techniques coupled with mass spectrometry attracted enormous attention in the last decade due to the fast chemical analysis with nearly no sample preparation. [1] However, the literature is currently dominated by applications of different ambient ionization sources, especially the development of new ionization sources with only minor improvements, while the basic understanding of the ionization mechanism of existing techniques is neglected. It is known that for both polar and non-polar analytes, protonated and radical cations are mostly generated through water clusters or via radical mediated pathways respectively. For halogenated or nitrated analytes, more diverse product ions are observed, such as the radical anion, the deprotonated molecule, anion attachment and/or oxidation of the analyte.

In this work, an active capillary plasma ionization source [2], based on dielectric barrier discharge, was used to study different perfluorinated compounds (PFCs). These compounds have unique properties resulting in many applications but are challenging to ionize efficiently with a soft ionization method.

The active capillary plasma ionization source consists of an inner electrode (ground) which is separated by a glass capillary from the outer electrode. A cold plasma is generated by applying a sine-modulated high voltage on the outer electrode. The plasma source was directly attached to the mass spectrometer (LTQ Orbitrap), providing a 100 % transport efficiency of the ions into the MS. Nitrogen, air or oxygen were used as carrier and discharge gas.

The ionization of perfluorinated compounds gave a characteristic spectrum of three ions: $[M]^-$, $[M-F]^-$ and $[M-F+O]^-$. The radical anion $[M]^-$ was mainly formed by electron capture (low plasma voltage). The loss of fluorine was mainly generated through electron capture dissociation (high plasma voltage and frequency). The substitution reaction product $[M-F+O]^-$ was mostly formed through reaction with O^- and at high plasma voltage. Through the identification of the reactive species, the selectivity and sensitivity for the three product ions of PFCs could be improved. [3] Thus, the active capillary plasma ionization source has the potential to analyze real samples containing PFCs, such as ski wax.

References

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Glutathione S-transferase protein expression in different life stages of the vertebrate model zebrafish (Danio rerio)

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Zebrafish has gained growing interest from the scientific community due to its multifaceted applications in biomedical sciences and toxicology. Yet, the development of defense systems, such as phase II biotransformation pathways, during zebrafish early life stages and in adulthood is largely unexplored.

Glutathione S-transferases (GSTs) is one enzyme family that plays a major role in phase II biotransformation processes. GST catalyzed conjugation reactions are considered a critical contributor to detoxification and clearance of various intracellular metabolites, but also natural toxins and xenobiotic compounds.

Given the important role of GSTs in xenobiotic metabolism, we analyzed cytosolic GST proteins in zebrafish early life stages and different organs of adult male and female fish, using a targeted proteomics approach. The MRM assays developed within the study enable the monitoring of specific GST isoenzymes and GST classes through a combination of proteotypic peptides and peptides shared within the same class.

We could show that some GST classes (alpha, mu, pi and rho) are present in zebrafish embryos as early as 4 hours post fertilization (hpf). The majority of GST enzymes, however, were expressed at 72 hpf followed by a continuous increase in expression thereafter. In adult zebrafish, GST expression is organ-dependent, with most of the GST classes showing the highest expression in the liver.

The early expression of GSTs during zebrafish embryogenesis and the wide range of cytosolic GST classes expressed in adult fish supports the use of zebrafish as a model organism in chemicals-related investigations.

*Laser ablation under pressure for mass spectrometry-based element imaging
without an ICP*

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Laser ablation / ionization mass spectrometry has recently seen a renaissance in several research labs. The major driving force for this may be the availability of femtosecond lasers, whose potential for quantitative analyses was shown superior to previously used nanosecond systems [1,2]. In particular, elemental imaging applications would benefit from the relatively simple instrumental setup and lower running cost of for example laser ablation-ICPMS [3]. Still ions generated in vacuum using a high-energy laser pulse exhibit a broad angular spread and wide energy distribution, making it a challenge to collect and transport them into a mass spectrometer with highest efficiency. Ion cooling in an inert buffer gas for example was shown to be a viable approach to reduce the energy spread but requires a suitable arrangement for efficient ion collection and transfer to the MS. The use of an Rf-only ring electrode assembly with decreasing inner diameter (aka ion funnel [4]), in combination with a convergent-divergent nozzle is currently studied as a method to thermalize laser-generated ions for mass spectrometric applications. This configuration provides a sufficient pressure drop between ion source and mass spectrometer, while allowing for multiple collisions and efficient ion cooling. At the same time, it significantly simplifies the configuration when compared with a conventional ion funnel with axial ion acceleration using a DC gradient [4,5]. Further development of this configuration [6] includes integration of a homogenized femtosecond laser beam to reduce matrix dependency of the ion yield and to enable a controlled removal of surface layers for depth profiling studies. Compared to the previously used nanosecond laser ablation, the new arrangement exhibits significantly smaller ablation rates. Transient signals were shorter than the ms regime, which would enable kHz sampling in depth and spatial profiling experiments. It further allows for ablation of transparent materials, which could not be analyzed in the previous setup. Still, transient signals exhibited a reduced dependency of signal duration on buffer gas pressure, indicating that a fraction of high energetic ions could not be thermalized completely in this case.

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Exhalomics

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Exhaled breath contains relevant information on a person's health status. Our vision is to use real-time and completely non-invasive chemical analysis of exhaled breath for applications such as medical diagnosis, monitoring progress and treatment of diseases, drug compliance, pharmacokinetics, and others. The methodology we use to analyze breath in real time is based on secondary electrospray ionization coupled to high-resolution mass spectrometry (SESI-HRMS). It affords ppb-ppt limits of detection, and analysis of even semi-volatile compounds with molecular weights up to 1000 Da. Using complementary UHPLC-HRMS and MS/MS measurements of exhaled breath condensate and reference standards, it is possible to identify compounds in these "breathprints".

A number of interesting questions can now be addressed via on-line mass spectrometric analysis of exhaled breath: is there a core pattern for individual phenotypes visible in mass spectrometric "breathprints"? Can diurnal changes be monitored via exhaled breath? Can diseases be diagnosed via exhaled breath, and if yes, which ones? Can proper drug use (or drug abuse) be detected via analysis of the chemical composition of exhaled breath? This presentation will focus on several examples in medical diagnosis, including the detection of novel biomarkers for diseases such as obstructive sleep apnea (OSA) [1] and chronic obstructive pulmonary disease (COPD) [2,3]. Monitoring of drug compliance and pharmacokinetics [4] via real-time SESI-MS will also be shown.



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Environmental flow field-flow fractionation coupled to ICP-MS for exploring the bioavailability potential of metal-containing contaminants in the aquatic systems

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Flow field-flow fractionation (FlFFF) is well suited state-of-the-art technique finding growing applications in the separation and characterization of natural and engineered nanoparticles. The hyphenation of the FlFFF with a very sensitive elemental detection, such as inductively coupled plasma-mass spectrometry (ICP-MS), opens novel opportunities to explore the interactions of metal-containing contaminants, e.g. traces metals and metal-containing nanoparticles, with different abiotic and biotic components in the aquatic systems. Some of the recent advances with respect to the understanding of the metal-containing contaminant behavior in the aquatic systems and their bioavailability potential obtained by using the asymmetrical FlFFF coupled to ICP-MS will be discussed. Bioavailability is a key concept allowing to relate different processes at the ambient medium with the biological effects (e.g., beneficial or toxic) on a specific (micro)organism. Capabilities of the FlFFF-diode array-fluorescence-ICP-MS to examine (i) the association, size or molar mass distribution of metal complexes with organic matter of pedogenic and biogenic origin; (ii) engineered nanoparticle interactions dissolved and colloidal organic matter, (iii) different contaminant forms e.g. dissolved and nanoparticulate will be illustrated. The implications of the obtained information for the bioavailability potential of metal-containing contaminants to microorganisms will be discussed. Specific examples of the interactions of trace metals and metal-containing nanoparticles with extracellular polymeric substances, humic substances, colloidal organic matter from the waste water treatment effluents, proteins, and their bioavailability to the microorganisms such as microalgae and protozoa will be provided to illustrate the versatility and potential of FlFFF-ICP-MS in the research area at the interface between the molecular organic and inorganic biogeochemistry.

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Liquid chromatography - mass spectrometry with modifier assisted differential mobility spectrometry for tuning multidimensional separation selectivity

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LC-MS analysis in complex biological samples often lacks of selectivity, especially for isobaric/isomeric analytes. Ion mobility has demonstrated its potential for resolving of isobars and isomers in combination of liquid chromatography-mass spectrometry. Separation of the analytes can even be enhanced with the use of organic modifiers (e.g. isopropanol) in differential mobility spectrometry (DMS) however very limited investigations on the effects of the solvents have been reported. [1,2]

In this work, we first explored the role of various modifiers (water, linear and branched alcohols, acetone, toluene and ethyl acetate) in relation to their physico-chemical properties on the separation of isomeric sulfonamides drugs (sulfameter, sulfamethoxypyridazine, sulfamonomethoxine, sulfamoxole, sulfisoxazole, sulfadimidine, sulfisomidine, sulfadimethoxine and sulfadoxine). A DMS cell (SelexIon, Sciex) was mounted in front of a triple quadrupole linear ion trap and quadrupole time-of flight instrument: Electrospray ionisation was used in positive and negative mode. Considering the clustering-declustering mechanism, ion-hydrogen bond interactions are the limiting factors of the cluster stability. It is predominant over dipole-dipole, dipole-induced dipole and ion- π interactions depending on the nature of the modifier. Consequently, cluster stability will depend on modifier functional groups as well as type and charge site of the analyte, which directly dictates the compensation voltage. Within the alcohol series, interacting with the same positively charged analyte, a linear correlation could be found between the reduced mass of the analyte-alcohol cluster and the separation performance of the analytes. Negatively charged analyte within the same alcohol series shows a different behaviour which can be explained by different type of ion-solvent interaction. In addition, toluene versus the alcohols showed a completely different selectivity.

Secondly, we investigated the potential of differential ion mobility (DMS) in multidimensional separation, as an alternative to LCxLC, in terms of modifier assisted selectivity tuning of the second separation dimension (LCxDMS versus LCxLC) for the analysis of isomeric sulfonamides drugs in plasma. While some isomeric compounds are coeluting in the first LC dimension (reversed phase chromatographic) they could be separated in the second DMS dimension with right selection of the modifier, for example ethyl-acetate. Furthermore, different selectivity in separation in the second DMS dimension could be observed with different modifiers opening new tuning possibilities in multidimensional LC-MS separation.

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Novel drug permeability screening platform combining microfluidics and LC-MS
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Membrane permeability of drug candidates is an important requirement, but also a challenge in drug discovery and development. Currently, the parallel artificial membrane permeability assay (PAMPA) and Caco-2 cellular monolayers are used for drug permeability screening [1]. To overcome the shortcomings of the state of the art, we use microfluidics, fluorescence microscopy, and liquid chromatography-mass spectrometry (LC-MS) to develop a novel platform consisting of droplet interface bilayers (DIBs), on a basis of a droplet formation and spotting as previously developed in our lab [2,3]. These DIBs are not only tunable; their characteristics as an artificial bilayer are also more physiologically relevant than those of PAMPA. Together with the advantages of microfluidics, our assay operates with small sample amounts and shortened incubation times, therefore improving throughput.

We generated aqueous droplets of 25 nL surrounded by a lipid monolayer with a microfluidic T-junction [3] and spotted them with micrometer-precision on a SU8-coated glass slide. Upon contact of two droplets, a bilayer formed. By varying the droplet content, we could observe permeation with fluorescence microscopy and LC-MS. The method was first optimized and evaluated with fluorescent dyes.

To date, we evaluated our method with the model-drug propranolol. We obtained a permeability coefficient $P_{app} = 3.41 \times 10^{-6} \text{ cm s}^{-1}$ after 5 h, while conventional PAMPA experiments reach a similar value ($PPAMPA = 2.82 \times 10^{-6} \text{ cm s}^{-1}$) in assay times of 16 h [4].

Overall, our platform allows on-demand droplet generation, spotting, on-site investigation, and subsequent LC-MS analysis, opening doors for membrane composition studies as well as pore formation experiments or even permeation over multiple compartments.

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APRECON-TOF-MS: A state-of-the art instrument for the analysis of halogenated greenhouse gases

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In the past 40 years, it became clear that halogenated compounds exert a powerful influence on the chemical composition of the troposphere and through that influence affect the fate of pollutants and climate. In particular regard to climate, halogenated compounds affect methane, ozone, and particles, all of which are powerful climate forcing agents through direct and indirect radiative effects[1]. The continuous measurement of halogenated greenhouse gases at remote stations (within the global AGAGE network) is currently performed by Gas Chromatography with Mass Spectrometry (Medusa GC-MS) systems, providing the continuous measurement of a list of 40 trace gas species ranging in concentration from a few tenths of a ppt (dry air mole fraction, part-per-trillion) to about 600 ppt [2].

Here we present a further development of instrumentation for halogenated greenhouse gases measurement, combining two new techniques: the Advanced Preconcentration system (APRECON) coupled with a time-of-flight mass spectrometer (TOF-MS). As a first step, a two-liter sample is preconcentrated by selective adsorption onto a polymer cooled to -180°C . Two copper cones are fixed on a copper plate on which preconcentration traps are mounted on detachable hats (NOAA/ESRL/GMD design). For the subsequent heating phase, the hats can be removed from the base plate for desorption of the analytes. This design allows fast switching of the traps between heating and cooling cycles. The sample is then injected into a gas chromatograph (Agilent 7890B) and finally to the TOF-MS. The pre-separation of the gas chromatograph, combined with the high resolution of the TOF-MS (with a resolving power around 4000 Th/Th and a mass accuracy better than 15 ppm), and the extraction of a full spectra between with 30 and 300 m/z, allows a more detailed analysis of the sample. The resulting system provides a more accurate detection of halogenated compounds compared to present techniques and the possibility to measure a wide range of substances even in concentration levels of ppq (part-per-quadrillion). First results from this state-of-the art instrument will be shown.

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Microwave plasma desorption and ionization for direct analysis without sample preparation

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No or only minor sample preparation is the main advantage of ambient ionization compared to other established ionization techniques. Therefore DART, DESI, laser desorption or other ambient techniques are very interesting for fast, high throughput or portable applications [1]. Microwave plasma ionization complements the evolving portfolio of ambient ionization technologies and allows new applications [2]. A solid-state RF amplifier coupled to plasma jet offers an extremely compact design and a precise energy regulation.

A first design of a new microwave plasma ion source driven by a solid-state microwave amplifier has been tested for quantitative analysis of drug standards, identification of active pharmaceutical ingredients in formulations, characterisation of bacteria and mammalian cells as well as for its potential for imaging experiments in combination with high resolution mass spectrometry.

A microwave atmospheric pressure plasma ion source (plasma jet based [3]), driven by a solid state 2.45 GHz microwave generator coupled to a stainless steel plasma torch using argon gas for ionization and nitrogen for cooling was used. The microwave power was controlled using an in house software based on the Arduino platform and Instrumentino framework [4]. An LTQ Orbitrap XL (Thermo) instrument with a DESI X-Y stage (Prosolia) were used for the measurements.

Quantitative measurement of drug standards

A total amount of 67ng acetaminophen was spotted in solution on a glass slide and dried, to achieve a signal to noise ratio of 3:1. Linearity was obtained up to 1.4 micrograms ($R^2 = 0.9981$). A CV of <30% was found (n = 6). The gas flow was 0,3 L/min Argon and 20 W were applied. Sensitivity and robustness needs to be improved by carefully adjusting angle, gas flow and applied power of the plasma.

Active pharmaceutical ingredient identification in formulated drugs

The $[M+H]^+$ and M^+ ions of active pharmaceutical ingredients were detected (Alkaselzer, Dafalgan, Oelefin) by adjusting the argon plasma jet directly towards the surface of the pill. A PCA (principal component analysis) based chemo metric model was developed, using triggered MRM and high-resolution mass spectrometry, for identification of the exposed formulation.

Bacteria and mammalian cells

Unique signal patterns were found for the tested biological samples. First tests with bacteria allowed a distinction between gram positive and negative strains. In addition, mammalian cells showed distinct signals. However, further experiments will be needed to assess the potential of this system to distinguish bacterial samples on the taxon or even species level and/or different kinds of cells.

Imaging experiments

A spatial resolution of 420 micrometers was achieved. Positioning, especially the angle of the

argon plasmajet, as well as the plasma gas temperature, gas flow rate and power-input were found to be critical for the resolution.

Conclusions

We could demonstrate very interesting new properties of atmospheric pressure plasma ionization by investigating a wide range of potential applications. However, the system still requires further optimization for robustness, reproducibility, sensitivity and spatial resolution.

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Interaction of antitumor metallocenes with nucleic acids

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Bent metallocene dichlorides (Cp_2MCl_2 , with Cp = cyclopentadienyl, M = Ti, V, Nb, Mo) and their derivatives are a class of metallodrugs with promising anticancer characteristics that are even active against cisplatin-resistant cell lines. Though the precise mechanism of action of metallocene-based agents still remains elusive, cell distribution studies revealed the accumulation of the corresponding metal ions in the nucleus, thus, pointing towards nuclear DNA as a primary biological target.

High-resolution ESI-MS/MS experiments were performed to study the interaction of metallocenes with nucleic acids. At first, metallocene adducts with dinucleoside monophosphates, the smallest nucleic acid model compounds that are able to provide information on the targeted functional groups were studied. Data revealed that the type of transition metal essentially determines the extent of adduct formation and the binding pattern. Titanocene primarily binds to the phosphate group and the oxygen-containing nucleobases, while molybdenocene mainly interacts with nucleobases. Such binding behavior is in good agreement with the hard and soft (Lewis) acids and bases concept. Subsequently, competition experiments on titanocene-hexanucleotide adducts were conducted to evaluate the effect of repetitive phosphate linkers and to elucidate the effect of the nucleobase composition and sequence on the binding characteristics. Though the interaction of titanocene with a phosphate group implies a nucleobase-independent binding motif, the adduct yield was considerably influenced by the nucleobase composition. MS/MS experiments further demonstrated a sequence-specific binding of the metallodrug to the oligonucleotide.

How can real-time breath analysis provide new insights into metabolism during sleep?

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The sleep-wake cycle influences circadian clocks and interacts with the human metabolism. Disruption or misalignment of circadian clocks as well as sleep deficiency are known to cause health problems like metabolic disorders. [1] Therefore, not only in fundamental research but also from a medical aspect, there is a great interest in obtaining a better understanding of the underlying molecular mechanisms. Effects of sleep restriction and sleep deprivation on our metabolism have been studied recently [2, 3], however metabolism during sleep is hard to assess. The main limitation is a lack of sampling methods for biofluids such as cerebrospinal fluid, urine or saliva during sleep. Blood sampling is possible, but it is invasive, and there are limitations of sample volume and sampling rate.

This limitation could be overcome by analyzing exhaled breath during sleep. Breath analysis provides real-time information and it is a non-invasive technique. Hundreds of metabolites have been reported from breath including fatty acids and amino acids. [4] These two classes of metabolites are known to be under circadian control. Also, fat metabolism was found to be altered under sleep restriction and deprivation. [3, 5]

Using a modified continuous positive airway pressure (CPAP) mask for uninterrupted breath sampling, we are measuring metabolites in exhaled breath with secondary electrospray ionization mass spectrometry (SESI-MS) during different stages of vigilance. SESI coupled to a high-resolution mass spectrometer allows molecular formula assignment, covers a broad m/z range and achieves high sensitivity. [6]

Our preliminary results indicate that even within a short nap, the breath metabolome undergoes significant changes. We found different groups of correlating features suggesting different metabolic pathways to be up- and down-regulated. Further overnight studies are planned, where changes in the metabolic breath pattern during different stages of sleep will be investigated.

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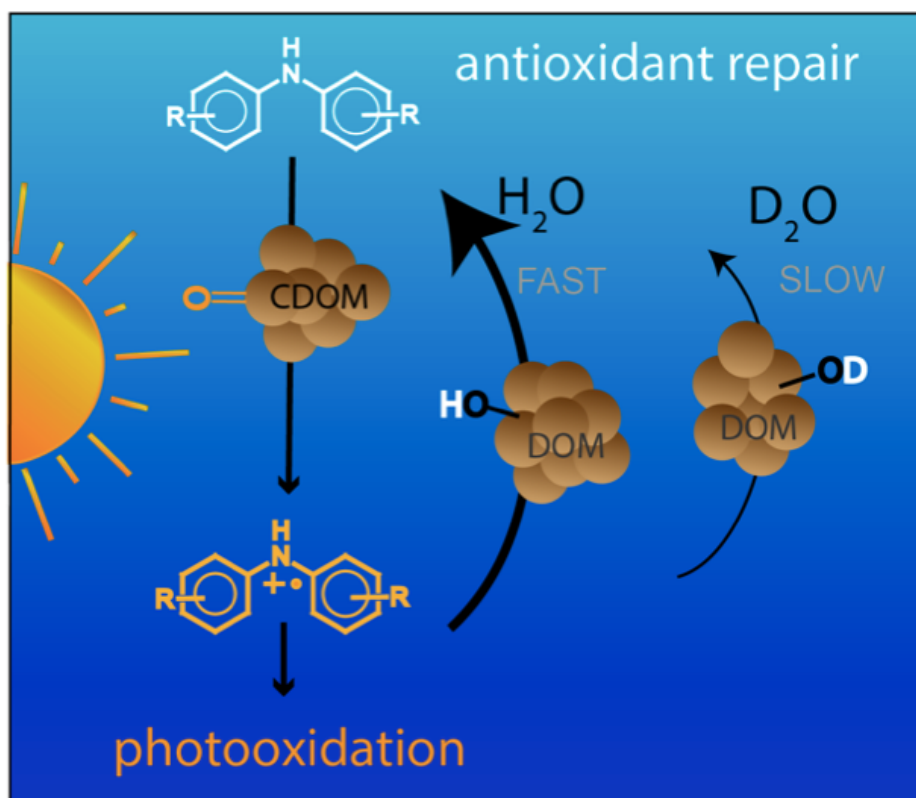
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*Non-singlet oxygen kinetic solvent isotope effects in photochemistry*Caroline Davis^{1,2}, Kristopher McNeill¹, Elisabeth ML Janssen²¹Institute of Biogeochemistry and Pollutant Dynamics, ETH Zurich, 8092 Zurich, Switzerland²Department of Environmental Chemistry, Swiss Federal Institute of Aquatic Science and Technology (Eawag), 8600 Dübendorf, Switzerland
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The kinetic solvent isotope effect (KSIE) is typically utilized in environmental photochemistry to elucidate whether a compound is susceptible to photooxidation by singlet oxygen ($^1\text{O}_2$), due to its known difference in lifetime in H_2O versus D_2O . Here, the overall indirect photodegradation rates of diarylamines in the presence of dissolved organic matter (DOM) were enhanced in D_2O to a greater extent than expected for a reaction purely with $^1\text{O}_2$. The relative contribution of the observed KSIE from reaction with $^1\text{O}_2$ was determined from high resolution data of $^1\text{O}_2$ lifetimes by time-resolved infrared luminescence spectroscopy. The additional enhancement in D_2O beyond reaction with $^1\text{O}_2$ contributed significantly to the observed KSIE for diarylamines (8-65%) and diclofenac (100%). The enhancement was ascribed to slower reduction of transient radical species of the diarylamines due to H/D exchange at DOM's phenolic antioxidant moieties. A slower bimolecular reaction rate constant with a model antioxidant was verified for mefenamic acid radicals using transient absorption spectroscopy. Changes in lifetimes and reactivities with triplet sensitizers were not responsible for the additional KSIE. Other pollutants with quenched radical intermediates may also be susceptible to such an additional KSIE, which has to be considered when using the KSIE as a diagnostic tool.



Schematic representation: Photodegradation and antioxidant repair of model diarylamines. Antioxidant repair proceeds slower when phenolic moieties undergo H/D exchange in D_2O .

Poster Abstracts

A new nitrogen microwave plasma source for mass spectrometry MICAP-TOFMS

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Inductively coupled plasma mass spectrometry (ICPMS) has been recognized as a state-of-the-art technique for trace-element quantification since its introduction in the early 1980s. In past years, substantial advances in sample introduction approaches and mass analyzer design have expanded the utility of ICP-MS. However, no fundamental changes to the ICP source have been adopted. The ICP is still argon-based, with the energy coupled into the plasma by a load coil at radio-frequencies (RF) of 27 or 40 MHz. Here, we report the coupling of a new nitrogen-based high-power Microwave-sustained Inductively Coupled Atmospheric-pressure Plasma (MICAP [1], RADOM, Milwaukee, WI) to a time of flight (TOF) mass analyzer [2] (TOFWERK AG, Thun). The MICAP is composed of a ceramic ring dielectric resonator across which a polarization current is generated by radiation with microwaves at 2.45 GHz. The plasma is sustained by an oscillating magnetic field originating from the polarization current not very different from the load coil of an RF Ar-ICP; in fact, plasma generation is so similar that a conventional ICP torch can be used for operation of the MICAP. However, unlike the Ar-ICP, the MICAP can be sustained in nitrogen or air, which offers substantial reduction in operating costs compared to the argon ICP.

In this study, a 1500 W MICAP ion source was used in combination with conventional liquid-sample introduction approaches (i.e. concentric pneumatic nebulizer with a cyclonic spray chamber or a desolvation system (Apex Q, ESI, Omaha), and performance of N₂-MICAP-TOFMS was compared with that of Ar-ICP-TOFMS. Initial inspection of the MICAP-TOF mass spectrum, shows a less spectrally dense and intense background. Usual argon-based interferences (e.g. Ar⁺, Ar₂, and ArO) are missing, and major background and plasma species include nitrogen species such as, NO⁺, N⁺, N₂⁺, N₃⁺, N₄⁺. Limits of detection (LODs) were found to be comparable (and, in select cases, improved) compared to those of the ICP-TOFMS, with LODs of heavy elements in the low ppt region. A dynamic range of at least five orders of magnitude was observed, which matches that of the ICP-TOFMS instrument configuration. A detailed comparison of ICP- and MICAP-TOFMS will be provided.

In general, we find that the MICAP offers comparable performance to an ICP source for liquid-sample introduction. Use of nitrogen as the operating gas results in fewer/different background species, lower operation cost, and a simpler design, while maintaining the familiar operating procedure of the Ar-ICP-MS.

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Capabilities of inductively coupled plasma time-of-flight mass spectrometry in combination with collision/reaction cell technology

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Fast and simultaneous full spectrum acquisition make inductively coupled plasma time-of-flight mass spectrometry (ICPTOFMS) ideally suited for the analysis of transient signals with durations as short as hundreds of μs . Simultaneous ion sampling enables matching of plasma excitation conditions and allows therefore for correction of correlated flicker noise. However, the limited mass resolving power offered by ICPTOFMS and the need for attenuation of the most abundant plasma species upstream of the TOF extraction region are major obstacles for accurate and precise elemental and isotope ratio analyses. Therefore, the most recent ICPTOFMS instrument is equipped with a collision/reaction cell to facilitate ion molecule reactions and thereby alleviate the need for attenuation of abundant plasma background ions.

This study evaluated analytical capabilities of this instrument with the use of (non-)reactive collision gases. Experiments were carried out using various sample introduction techniques including laser ablation (LA) with high and low aerosol dispersion, conventional solution nebulization (SN) and micro-droplet generation (MDG). We investigated H_2 , He and mixtures of the two for their influence on detection power, quantification capabilities, and transient signal structure. A particular focus was placed on studying effects of gas phase collisions on structure of shortest signals, originating from individual droplets. Importantly, the high spectral read out rate obtainable with recent ICPTOFMS instruments allows investigation of CCT effects on a much shorter time scale than it has been possible until now.

Experiments with these droplets showed that ion transit times between the ICP and the TOF extraction region are mass dependent. In absence of a collision gas, light ions arrive at the TOF extractor before heavy ones. The presence of a buffer gas in the collision cell slows down light ions more than heavy ones, so that arrival times at the TOF mass analyser can be made mass independent or even reversed. Changes in transit times, as well as signal broadening were observed on a time scale of tens to hundreds of μs . Signal structure in low-dispersion LA-ICPTOFMS remained practically unaffected from collisional effects, such that single pulse resolved imaging at 100 Hz laser repetition rate is still possible.

Optimization method development for silica nanoparticles measurement using sp-ICPSFMS**Jovana Teofilovic, Bodo Hattendorf, Detlef Günther**

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Due to their unique properties, nanoparticles (NPs) are used in different fields, such as biomedicine, consumer goods, energy production, etc. [1-3]

Silica NPs (SiO_2) are in particular widely used for various applications since they could be easily and inexpensively produced, nevertheless as they are not easily analyzed, nowadays little is known about them. Numerous techniques are available for the detection and the characterization of NPs, but still there is no existing method, which could be used for obtaining a reliable and reproducible characterization of NPs, on a routine basis. [4, 5] Single particle inductively coupled plasma mass spectrometry (sp-ICPMS) is a promising approach due to its high sensitivity however quantification of silica NPs using sp-ICPMS is challenging, due to the background arising from polyatomic interferences (N_2^+ and CO^+) and high background level arising from Si from the ICP instrument. We present a possible approach for characterization of silica NPs, exploiting capabilities of sector-field ICPMS offering highest detection efficiency (DE) and mass resolving power that allow for separating silica signal from the interferences.

In order to increase signal to background ratio for silicon, the optimization method is developed. To avoid Si memory effects from this step, it is investigated a possible proxy-element using a combination of wide range of parameters for auxiliary gas, sample gas and sampling depth. Upon testing dissolved ^{24}Mg , ^{27}Al and ^{49}Ti solutions, dissolved titania shown to be the most suitable element, behaving similar to ^{28}Si . Mass drift in medium resolution ($m/\Delta m \approx 4000$) was corrected via ^{23}Na signal before each acquisition, and ensured the accurate measurement position of the SFMS. Measurements were recorded in narrow scan range ($\Delta M \leq 5\%$), and at high time resolution (≤ 1 ms).

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Characterization of low-count-rate signals and noise in ICP-TOFMS

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Inductively Coupled Plasma Time-of-Flight Mass Spectrometry (ICP-TOFMS) is routinely used in our lab for the analysis of individual inorganic nanoparticles (NPs) in a measurement scheme termed single-particle ICPMS (sp-ICPMS) [1]. In sp-ICPMS, a dilute suspension of NPs is introduced into the ICP. When a NP passes into the ICP source, it is vaporized, atomized, and ionized, and produces a narrow bunch of ions that are measured as a burst of signal by the mass analyzer. The typical duration of signal from a NP event is 200-500 μ s. The frequency of NP-induced signals is proportional to particle-number concentration (PNC), and the integral of each transient peak correlates to the element mass in each particle [2]. For large nanoparticles, signal spikes can readily be distinguished from the steady signals of dissolved analyte; however, detection of small NPs with signal levels near that of the dissolved background poses a challenge. To accurately identify low-count NP signals from background signals, thorough characterization of this background must be performed, including identification of sources of instrument noise in order to accurately define limits of detection.

In this study, we report how the detection electronics of our TOF mass analyzer (icpTOF, TOFWERK AG) influence the shape of ion-signal distributions for low-count signals. To improve dynamic range for individual TOF measurements, ion signals on our TOFMS instrument are not counted with a time-to-digital converter, but rather measured with a high-speed 14-bit digitizer. With this detection setup, the major contributors to signal distribution at low count rates are Poisson noise and pulse-amplitude variation from the microchannel plate (MCP) detector. To investigate the influence of pulse-height distribution from MCPs, experimental evidence is matched with Monte Carlo simulations to empirically define the shape of low-count-rate signal distributions. We find that the shape of MCP response significantly affects (> 5% RSD increase) signal distributions up to average count rates of 10 counts/acquisition. From Monte Carlo simulations, we determine a modified definition of the limit of detection for our TOF mass analyzer (LOD) that replaces the widely accepted definition of LOD for count-limited analyses [3]. Additionally, this new “first-principle” understanding low-count signal distributions allows for deconvolution of NP and dissolved background signals, in a manner similar to that reported for ion-counting mass analyzers [4]. Here, we discuss how modelling signal background improves PNC determinations, even for challenging analyses of small NPs in the presence of large dissolved background.

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Elemental imaging of bivalve mollusk shells with LA-ICP-TOFMS

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Mollusk shells are mainly composed of CaCO₃ and are formed by a biologically-controlled mineralization that leads to a superimposition of calcified layers. The bicarbonate and calcium ions needed for the bio-mineralization are provided by food, the water adsorbed by filtration, or directly from the external medium by diffusion [1]. Large amounts of mollusk shells arise from the food industry, which have potential to serve as readily available sorbent material for heavy metal contaminations in natural waters, e.g. in proximity of mining sites.

We investigated the uptake of cadmium by bivalve mollusk shells from solutions. Shells from the Po Delta region (Italy) were treated with 0.1 or 1.0 mg kg⁻¹ cadmium solution for 24 h, cut and analyzed by both solution-based inductively-coupled plasma mass spectrometry (ICP-MS) and laser ablation (LA) ICP-MS. After acid digestion of pulverized shell samples, the solution-based analysis provides information about the overall uptake. In contrast, LA-ICPMS analysis was performed in a line-scan mode over shell cross sections and reveals the distribution of cadmium from the treatment. Preliminary results suggest that cadmium as well as other heavy metals already present is enriched in the outer (organic) layer of the shell and its color might indicate the capacity to incorporate cadmium.

In addition, we investigated elemental distributions of the treated samples by imaging of the mollusk shell hinge plate and middle sections with multi-elemental LA-ICP-TOFMS imaging [2-3] to reveal shell layers and examine differences in elemental concentrations at high resolution using 5 µm laser spot size. Elemental imaging confirms earlier observations regarding the accumulation and distribution of cadmium and other heavy metals in the outer layers.

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Analysis of red figured samples from Apulia using LA-ICP-MS

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Apulian red figure pottery – 5th - 4th centuries BCE – is a variant of the well-known Attic red figure production, based on painting on the vase a black glossy background, saving figures from the ceramic body, developed in Apulia (Southern Italy). This production quickly emerged like the most considerable manufacture class of figure pottery in Magna Graecia. It was defined by a significant value and exceptional drawing features, and largely marketed inside and outside the region. Nowadays, not much has changed, this ceramic production is still considered extraordinary relevant and most of the vases are located in archeological museums inside Italy and all around the world. Nevertheless, technological productive data are almost absent. Consequently, a systematic archaeometric study^{1,2,3} providing compositional and structural information of bulk and surfaces, could allow to recognize the manufacturing processes of ancient objects and to contribute in solving the wider question of the raw materials and objects provenance.

The elemental composition of red and black gloss coating of 22 fragments of Apulian red figure pottery, coming from different archeological sites in Apulia was determined by LA-ICP-MS (Perkin Elmer Elan 6100 DRC and GeoLaserC 193nm). Statistical multivariate analyses by PCA and HCA were performed on chemical compositional data.

The obtained results highlighted differences both in the black gloss and ceramic raw materials used in Apulia with respect to Attic ones, so providing an objective parameter of regional production discrimination. Further, Apulian differences in raw materials are also evident between the archaeological sites. This leads to well discriminate the production: Apulian respect to Attic and also intra-Apulian (different archaeological sites-different raw materials), supporting the hypothesis of a parceled production.



Fig. 1 Apulian red-figures vase of Lycurgus painter

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“On-site” laser ablation – Insights into the trace elements of ancient gold artefacts

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Laser Ablation Inductively Coupled Plasma Mass Spectrometry (LA-ICPMS) is nowadays the method of choice for the determination of the (ultra-)trace element composition of solids. The small sampling cross-section (10's of μm) of the LA in combination with the high sensitivity and multi-element capabilities of ICPMS allow for a quasi-non-destructive analysis with low limits of detection (ng/g) [1], compared to e.g. XRF (LOD as low as $\sim 5 \mu\text{g/g}$ with a spot size of $60 \mu\text{m}$) [2].

However, the instrumental and infrastructural requirements for the ICPMS part hinder the application of this method for the analysis of non-mobile or large samples impossible to transport or not removable due to regulatory restrictions.

The portable Laser Ablation system (pLA) developed in our laboratory [3] allows decoupling the LA sampling process from a subsequent elemental analysis. Basically it allows for quasi-non-destructive sampling of laser ablation in unrestricted, even field-deployable situations. The ablation process is performed in ambient conditions by a pulsed ns-laser (Nd:YAG, $\lambda = 532 \text{ nm}$) which is fibre-coupled to an ablation head and focused to a spot size of $\sim 100 \mu\text{m}$. The ablated material is extracted by a membrane pump and collected on polycarbonate filters for the subsequent analysis. These are carried out in the laboratory facilities and can either include the digestion or leaching [4] of the filters followed by conventional solution nebulization ICPMS or the re-ablation of the deposits by applying conventional LA-ICPMS.

The analytical approach has been evaluated in experiments with gold reference materials. We found that main element abundances were deviating by less than 10% from the reference concentrations. Relative deviations of trace element concentrations were usually smaller than 30%. Finally, we have used this approach to analyze a wide variety of archaeological gold artefacts from the “Treasure of Eberswalde” [5]. The collection of aerosols produced from application of 2×5000 laser pulses resulted in a deposition of $0.2 - 4 \mu\text{g}$ of gold per filter. These filters were digested and analyzed by conventional solution nebulization ICPMS in a laboratory environment.

These results show the potential for the general investigation by pLA into the (ultra-)trace element concentrations of metallic gold objects for archaeometric studies located all over the world.

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RF Energy coaxial wave-guided atmospheric pressure ion sources for universal mass spectrometry

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Solid-State RF Energy offers exciting opportunities to develop new ion sources for ambient ionization mass spectrometry [1]. In the last two decades, manufacturers of semiconductors specializing in high frequency transistors have made excellent progress developing affordable transistors in the frequency range of 2,45 GHz in gallium nitride (GaN) designs. Different from traditional magnetron designs, the GaN transistors offer unique and improved abilities. The most enhanced benefits are fast frequency-, phase- and power-agility complemented by hyper-precision. The solid-state RF Energy attributes an unprecedented process control range, even dynamic energy distribution, and fast adaption to changing load conditions in terms of load stability and sample introduction. NovionX GmbH introduces a unique power-controlled solid-state 2,45 GHz amplifier, designed to power a wide range of different ion sources for mass spectrometry. Ion sources can be easily connected to the solid-state RF generator unit by means of a coaxial waveguide. Applications range from small molecule plasma ambient ionization, plasma ablation imaging to direct plasma pyrolysis of small molecules, photoionization and element analysis of aerosols. All this can be achieved with a solid-state RF Energy amplifier connected to a single mass spectrometer, preferred a high-resolution time-of-flight instrument. Various interchangeable atmospheric pressure ion sources driven by a coaxial waveguide can be coupled to an atmospheric pressure interface of a mass spectrometer. The new system provides fast detection and analysis for a wide range of different analytes, as well as unparalleled flexibility. Solid-state RF Energy driven ion sources bridges the analysis of small molecules to classical elemental analysis running on a single mass spectrometer.

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Evaluation of the potential of ion mobility combined with liquid chromatography and mass spectrometry (LC-IM/MS) for the analysis of pharmaceutical compounds

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Over the last decade, analysis of pharmaceutical compounds has been mostly performed by liquid chromatography (LC) hyphenated to mass spectrometry (MS). In recent years, there was a growing interest in improving the performance of LC-MS, especially for the analysis of complex matrices. For this purpose, ion mobility spectrometry (IMS) adds an online orthogonal separation to LC which may solve some of the challenges observed when analyzing complex matrices in LC-MS (e.g. isobaric compounds). IMS is an analytical technique enabling the separation of ions in the gas phase based on their mobility, affected by their size, shape, and charge. Furthermore, for each ion, IMS allows the determination of an important and specific parameter: the collisional cross section (CCS). Then, the CCS can be considered as an important structural descriptor of the ions which gives a complementary information to identify pharmaceutical compounds by LC-MS [1].

The goal of the present study is to evaluate the performance of IM combined with LC-MS for the separation of closely related compounds of pharmaceutical interest. More than 100 compounds have been analyzed by LC-IM-MS including different families of pharmaceutical compounds from small molecules to peptides, presenting difficult separations and numerous isobaric substances (e.g. closely related compounds, positional isomers, cis-trans isomers, diastereoisomers...). The experimental IM resolutions between the different pairs of analogs, as well as CCS values have been measured and will be critically discussed. Finally, based on this work, it will be possible to understand if IMS has the potential to discriminate isobaric compounds, which is one of the main limitations of mass spectrometry.

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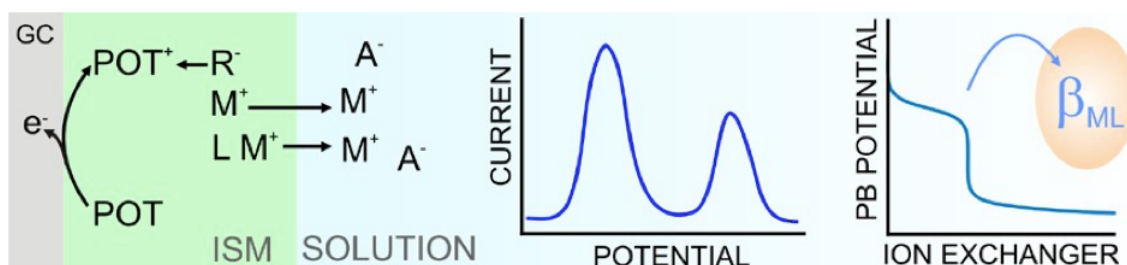
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Probing ion-ionophore interactions in thin layer polymeric membranes

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Ion-selective membranes of submicrometer thickness, backside contacted with an ion to electron transducing layer such as poly(3-octylthiophene) are attractive tools to electrochemically probe ion-ionophore interactions.[1] The main challenge with this approach is the poorly understood electrochemical behavior of the underlying transducing layer. This makes it difficult to isolate the ion transfer potential between membrane and aqueous phase. Earlier work either assumed a linear relationship between the charge and potential change for the underlying conducting polymer[1] or used a pseudo-Nernstian equation to describe the potential for polymer oxidation.[2] Unfortunately, both assumptions lack rigorous experimental confirmation and are additionally not extendable to other various transducing materials such as lipophilic redox probes.[3]



The problem is here overcome by recording the behavior of the membrane towards a bulky reference ion, tetrabutylammonium. This cation exhibits a voltammetric phase transfer that is well described theoretically and confirmed experimentally to be independent of ionophore. This information is used to arrive at a relationship between charge and potential for the transducing layer alone, which is then subtracted in subsequent experiments from the experimental cell potential. This allows one to describe, in a single linear scan, the change in phase boundary potential as a function of ion-exchanger concentration. Fitting of this function now gives direct information on complex stoichiometry, complex formation constants, and selectivity coefficient as a function of ion-exchanger. The principle is put forward with valinomycin as a model ionophore.[4] Other molecular receptors that exhibit reversible binding kinetics are also investigated.

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Colorimetric closed bipolar electrode for ion selective detection

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A proof of concept of closed bipolar electrodes (BPE) based on electrochemical chloride ion-selective electrode coupled to colorimetric ferriin redox probe is introduced here. The translation of electrochemical readout to an optical signal is imaged by a camera, which is then interpreted as a HUE value. The faradaic processes are generated by a potential difference at the extremities of the driving electrodes by applying a sufficient external voltage without direct contact with the bipolar electrode.

A change of the chloride concentration in the sample compartment (one end of the bipolar electrode) results in an opposite change in potential at the other end, to fulfil the magnitude of the applied external potential. This results in a change in the redox state of the redox indicator ferriin at the detection side of the BPE. Upon oxidation, the color changes from red (FeII) to blue (FeIII).

Quantitative analysis of chloride is demonstrated by plotting the HUE values in the detection cell as a function of logarithmic chloride concentration in the sample compartment. This concept expands the possibility to measure other analytes at different concentration levels in biological and environmental samples by modulating the external potential only from a single power supply.

Optical detection of common ions by solvatochromatic dye transducers doped into polystyrene microsensors

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Ion-selective optodes (ISOs) promise to translate concentration changes to optical readout and are facilitated by the availability of a multitude of ionophores. These sensors are applicable in a number of fields, such as clinical and environmental, but what is urgently needed is a universal approach that can selectively detect a wide variety of cations and anions without the use of a lipophilic pH indicator. The latter's severe drawback of cross responding to sample pH changes was recently overcome by charged solvatochromatic dyes (SDs) that can interact by ion-exchange with the ion of interest. This results in the extraction or expulsion of either compound into the organic sensing phase which can be spectrophotometrically followed due to the SDs' optical dependence on solvent environment. The use of polystyrene beads, known for their strong physical adsorption of lipophilic functional groups, doped with a SD, was successfully demonstrated to detect K^+ by Wang et al. [1]. ζ -potential measurements were performed for the first time to study the prevalent response mechanism of their SD polystyrene microsensor system. Based on this principle, the detection of a wider range of common anions and cations is here explored, testing a variety of ionophores and in-house synthesized SDs with the goal of unifying them under a single ISO principle.

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Electrochemical controlled fluorescence detection with localized ion transfer of lipophilic solvatochromic dyes

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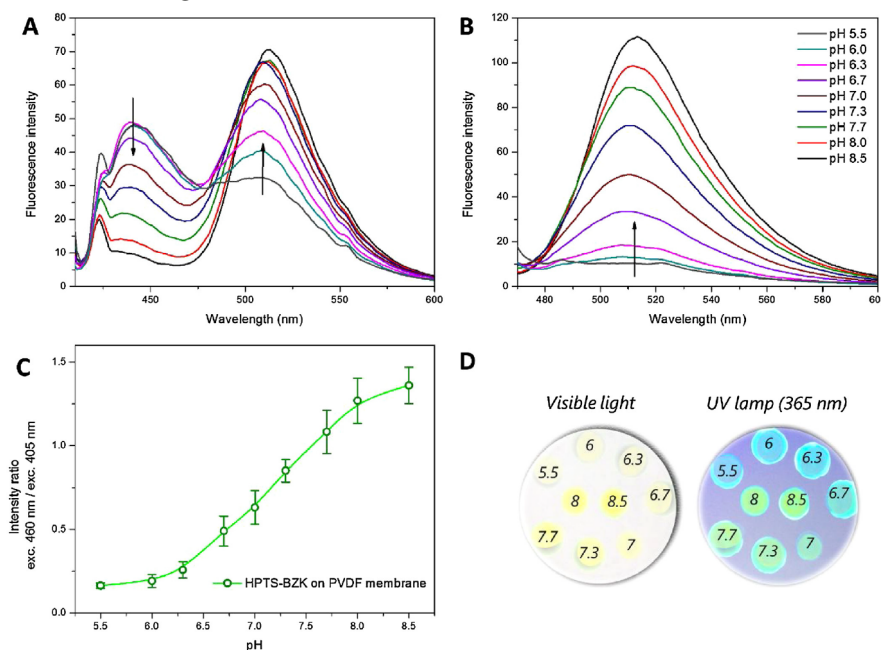
This work reports on a novel way to control fluorescence emission by electrochemical control. The change in fluorescence intensity of a solvatochromic dye (SD) upon electrochemical doping was investigated. Thin plasticized polyurethane membrane containing solvatochromic dye ((E)-1-methyl-4-(4-(methyl(2-(stearoyloxy)-ethyl)amino)styryl)pyridinium) and the lipophilic cation-exchanger (sodium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate) was spin coated over an electropolymerized poly-3-octyothiophene (POT) film as electron to ion transducer. The polymer film was then interrogated by cyclic voltammetry. At anodic potentials, POT is partially oxidized to POT⁺, which initiates the localized expulsion of the cationic chromogenic part of the solvatochromic dye from the membrane to the aqueous phase. This is manifested by a voltammetric ion transfer wave. Simultaneous fluorescence measurement show that the fluorescence of SD is quenched by this process. The principle may form the basis for constructing a massive ion detection array on the basis of closed bipolar electrodes for reading out the sensing chemistry by fluorescence imaging.

The pyranine-benzalkonium ion pair: a versatile sensor for biomedical purposes

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Fluorescent pH-sensitive dyes occupy a place of relevance in the domains of fluorescent analysis, biomedical labelling and sensing. Especially dyes allowing ratiometric pH detection within the physiological pH window, that is between 5 and 7, have always received special attention. Among this class of dyes, 8-hydroxypyrene-1,3,6-trisulfonic acid (HPTS or pyranine) has been one of the most studied thanks to its multifold positive properties, such as: non-toxicity and biocompatibility, chemical and photochemical stability, cheapness. Its high solubility in water, however, can be a remarkable drawback for *in situ* applications requiring long-term stability in aqueous environments. Usually, this problem has been overcome by coupling pyranine's sulphonate groups with hydrophobic cations, obtaining ion pairs which are virtually insoluble in water. Recently, the facile synthesis of a novel ion pair based on pyranine and benzalkonium (BZK) was reported.¹ Benzalkonium chloride is a quaternary ammonium salt, widely used as an antiseptic. Combined with pyranine, it produces an ion pair which is not only sufficiently hydrophobic, allowing incorporation in conventional membranes, while not impacting the pH-sensing behaviour of pyranine but also displays antimicrobial properties. The suitability of this system for the monitoring of wound pH has also been demonstrated.



(A,B) Emission spectra of the pyranine-BZK ion pair as a function of pH, obtained respectively with $\lambda_{exc} = 405$ nm and $\lambda_{exc} = 460$ nm. The resulting calibration line (C) is the ratio between the emission at 511 nm for two different excitation wavelengths. The color change of the immobilized ion pair as a function of pH is depicted in (D) under visible and UV light.

Acknowledgement: The work was performed in the frame of the FlusiTex and FlusiGate projects, funded by NanoTera.

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Plasmonic 'hot electrons' mediate nanoscale methylene blue molecular "blinking" without electric potential assistance

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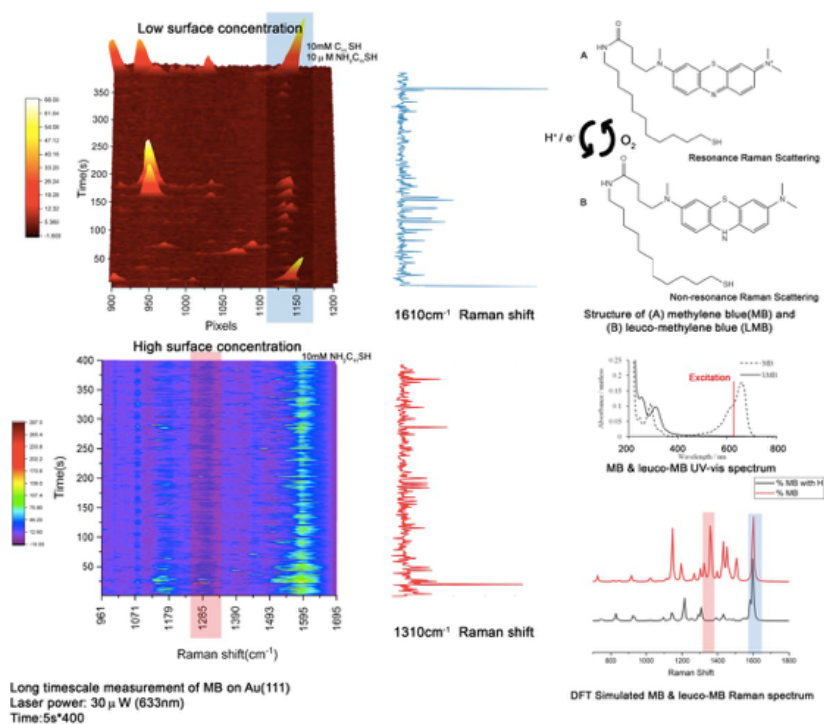
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The electrochemical characteristics of methylene blue (MB) have been widely studied and applied in many fields especially biochemistry and electrochemistry, because methylene blue, also known as a typical 'Lecuo' dye can switch between two chemical forms at different potentials; one is fluorescent and exhibits resonance Raman scattering (RRS), while the other one is colorless and has a much smaller Raman scattering cross-section.

In our recent tip-enhanced Raman spectroscopy (TERS) experiments, we observed significant Raman band intensity 'blinking', implying that this switching can be induced by plasmonic 'hot electrons' from the Ag tip without any external potential control. Atomically flat gold (111) surfaces have been derivatized with a mixture of 1-undecanethiol and 1-amino-1-undecanethiol to adjust the surface amino group concentration. NHS-ester modified methylene blue was chemically linked to the surface, and the surface concentration of methylene blue is related to the ratio of two types of thiols. Thus, by adjusting the surface dye concentration and the environmental O₂ concentration, we can tune the ratio of 'on/off' states (resonance-MB/non-resonance-LecuoMB), which indicates that some electrochemical reaction can also be achieved by 'hot electrons'.

The physical basis of the 'hot electrons' is an electron-phonon interaction known as surface plasmon (SP). The oscillating electrons produce an antenna effect, resulting in light collection and higher local electromagnetic field, which is the principle of most surface-enhanced processes (including TERS). Surface plasmon resonances in nanostructures can be damped radiatively by re-emission of a photon or non-radiatively through the creation of hot electron-hole pairs via Landau damping.



Cocktail effect of TiO₂ nanoparticle mixtures with mercury to green alga Chlamydomonas reinhardtii

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In aquatic environment nanoparticles are present as complex mixtures with other contaminants [1] which can result in synergism or antagonism of their combined action. Despite the fact that the toxicity and environmental risks of engineered nanoparticles have received extensive attention in recent years, their interactions with other contaminants and the consequent effects to aquatic microorganisms are to explore. In such a context, the present study aims to examine the interactions and effects of cocktails containing nTiO₂ and mercury, as a representative of priority hazardous substance, to *Chlamydomonas reinhardtii*, as a model phytoplankton specie. It was hypothesized that due to the its high reactivity nTiO₂ will adsorb Hg(II) and thus decrease its bioavailability and effects to alga, and that the effect will be more pronounced for cocktails containing nanoparticles of smaller primary size. The influence of nTiO₂ of different primary sizes, 5 nm (anatase, A5), 15 nm (anatase, A15) and 20 nm (anatase/rutile AR20) on Hg(II) effects to algae was studied. The effect of Hg, nTiO₂ and the mixture to the algal growth, generation of reactive oxygen species (ROS) and oxidative damage were determined by flow cytometry. In parallel, the stability of nTiO₂ in terms of hydrodynamic size and surface charge as well as Hg adsorptive capacity of nTiO₂ were measured. Results showed that the increasing concentrations of nTiO₂ with different primary size lead to a decrease of Hg-induced effects, due to the adsorption of Hg to nTiO₂. However, no dependence of nTiO₂ primary size was observed, due to significant agglomeration of the studied materials in the exposure medium. The results highlighted the need for improved understanding of the interactions of complex environmental settings containing mixtures of nanomaterials and other contaminants, central for sustainable development of nanotechnology.

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General Assembly of the DAS

Agenda:

1. Opening of the General Assembly by the president of the DAS
2. Nomination of the scrutineers
3. President's report
4. Treasurer's report
5. Election of board members – approval of the board
6. Individual proposals
7. Miscellaneous

