# *CH*analysis 2024

## April 10-12, 2024,
## Dorint Resort Blüemlisalp Beatenberg

SCS
Swiss Chemical
Society

The Division Analytical Sciences (DAS) of the Swiss Chemical Society (SCS) is organizing *CH*analysis, a meeting of Swiss analytical scientists on a yearly basis.

The goal of this two-day conference series is to stimulate a stronger interaction among persons working in different areas of analytical sciences. Scientists from applied and fundamental research, from industry, education, and regulation are welcome.

Confirmed Speakers:
Hanspeter Andres (METAS)
Christoph Meyer (Lonza)
Götz Schlotterbeck (Uni BS)
Jens Jacobsen (Waters)
Rok Roškar (Swiss Data Science Center)
Jacob Shelley (Rensselaer Polytechnic Institute)

Topics:
Analytical Instrumentation
Micro/Nano Sampling
Environmental Methods
On-line Processes for QA/QC
Data and Digitalization
Omics
Isotopic Fingerprint
METAS Award

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# Program

## Wed, April 10, 2024

| | |
|---|---|
| 18.00 | Registration |
| 18.45 | Welcome & Opening by the DAS President<br>*Davide Bleiner*, President DAS |
| 19.00 | *Jacob Shelley,* Rensselaer Polytechnic Institute<br>«Use of Acoustic Fields to Gate, Focus, and Separate Ions at Atmospheric Pressure» |
| 19.45 | Aperitif riche |

## Thu, April 11, 2024

| | |
|---|---|
| 09.00 | *Christoph Meyer*, Lonza<br>«The Commercialization of Cell and Gene Therapies – a Perspective from the Analytical Quality Control function» |
| 09.25 | *Christoph Jansen*, Metrohm<br>«Evolving Vibrational Spectroscopy<br>From scientific curiosity to outstanding routine analysis applications» |
| 09.50 | Contributed Lectures<br>*Chan Cao,* University of Geneva<br>«Single-molecule discrimination of different types of glycosaminoglycans by nanopore sensing»<br>*Mihai-Ovidiu Degeratu*, Eawag<br>«Proteomics profiling questions morphological classification of zebrafish cell line» |
| 10.40 | Coffee Break |
| 11.00 | *Hanspeter Andres*, METAS<br>«Chemical and biological references at the Federal Institute of Metrology METAS» |
| 11.25 | METAS Award lecture 2024<br>*Andrea Rösch,* Agroscope<br>«A multi-residue method for trace analysis of pesticides in soil with special emphasis on rigorous quality control» |
| 11.50 | Contributed Lectures<br>*Naresh Kumar*, ETZ Zurich<br>«Mechanistic Insights in Oxygen Activation on Bulk Au(111) Surface Using Tip-Enhanced»<br>*Sharath Rameshbabu*, Empa<br>«Strategies for the characterization of epitaxial thin films as Röntgen Materials» |
| 12.40 | Lunch Break |
| 14.00 | *Jens Jacobsen*, Waters<br>«Markers and Methods for the Identification of Recycled Polymeric Materials» |
| 14.25 | Contributed Lectures<br>*Gabriel Junquetti*, University of Geneva<br>«Integrated electrochemical systems for enzyme-linked immunoassays»<br>*Nikolai Tiuftiakov*, University of Geneva<br>«Exploring the Limits of Ionic Liquid Reference Electrodes»<br>*Robin Nussbaum*, University of Geneva<br>«Improving the Sensitivity of pH Glass Electrodes with an Alternative Readout» |
| 15.40 | Coffee Break & Networking |
| 16.00 | *Fabian Tolle*, Agilent<br>«Forever Chemicals – Workflows to detect PFAS in Water, Soil and Food» |
| 16.25 | Poster pitches |
| 17.45 | Poster Session |
| 19.30 | Dinner & Get-together |

## Fri, April 12, 2024

09.00 *Götz Schlotterbeck*, Institute of Legal Medicine Basel
«Analytical Chemistry in Forensic Chemistry and Toxicology at the Institute of Legal Medicine Basel (IRM Basel)»

09.25 Contributed Lectures
*Andres Kordikowski*, Novartis
«To Humidity and Beyond»

*Fabian Weyand,* Empa
«Electrochemical Sensing coupled to Liquid-Liquid Phase Extraction using Hydrophobic Deep Eutectic Solvents»

*Jawad Alzeer*, University of Zurich
«Exploring the Complexity of Entropy: Harmonizing Disorder and Energy Dynamics»

10.40 Coffee Break

11.00 *Rok Roskar*, Swiss Data Science Center
«Collaborative Data Science at the Swiss Data Science Center»

11.50 Contributed Lectures
*Oscar Mendo Diaz*, Empa
«Levels of Short-Chain Chlorinated Paraffins in Consumer Products of the Swiss Market: From a Semi-Quantitative Approach to Specific C- and Cl-Homologue Quantification»

*Diana Roos*, METAS
«METAS: the new WMO-GAW Central Calibration Laboratory for halogenated VOCs»

12.40 Lunch Break

14.00 Panel Discussion “Analytical Reliability”

14.30 Awards and Closing Remarks

15.00 End of Meeting

# TALKS

# Use of Acoustic Fields to Gate, Focus, and Separate Ions at Atmospheric Pressure

Jacob T. Shelley[1], Yi You[2], Julia L. Danischewski[1], Jens Riedel[2]

[1] Department of Chemistry and Chemical Biology, Rensselaer Polytechnic Institute,
110 8th St., Troy, NY 12180 USA
[2] Department of Instrumental Analytics, Federal Institute for Materials Research and Testing (BAM),
Richard-Willstätter-Straße 11, Berlin 12489 Germany
shellj@rpi.edu

Approaches to control the motion and direction of ionized atoms and molecules are an essential aspect of ion-based analytical methods, such as mass spectrometry (MS) and ion-mobility spectrometry (IMS). Because these species are inherently charged, most ion-manipulation approaches rely upon electrostatic and/or Lorentz forces in electric fields and magnetic fields, respectively. The ability to produce intact gaseous ions for MS and IMS is often performed at atmospheric-pressure (AP) due ease of sample introduction, high ionization efficiencies, and minimal fragmentation. However, diffusion and electrostatic repulsion between ions hinders the transport of gaseous ions into the lower-pressure environment of the analyzers. Conventional ion optics, that use electric or magnetic fields, can guide ions at AP, but require high field strengths to overcome the dominating aerodynamic effects.

Here, we describe a remarkable phenomenon whereby low-power acoustic fields are used to move, shape, gate, and separate beams of gaseous ions at atmospheric pressure. We refer to this approach as Acoustic Ion Manipulation Spectrometry (AIMS). Gaseous ions formed by AP electrical plasmas and other ionization approaches are directed towards and separated by the presence of the acoustic field. To better understand the phenomenon, an ion-detector array provided a measure of bulk ion movement, while mass spectrometry (MS) offered chemical-specific information. As one example of an AIMS setup, a standing acoustic wave was formed with two ultrasonic speakers and placed between an ionization source and ion detector. Ion beams are deflected away from unstable pressure regions (i.e. antinodes) into the pressure-stable nodal areas. Shadowgraphy revealed that the ions are separated from a neutral gas stream. Specific examples of ion focusing, gating, and separation (based on ion size) will be shown. In addition, experimental findings will be used to postulate a theory to develop a better understand of the behavior of gas-phase ions in acoustic fields. This discovery could have profound impacts in analytical ion-based spectrometries, like MS and IMS, as well as in materials processing and characterization.

# The Commercialization of Cell and Gene Therapies – a Perspective from the Analytical Quality Control function

Christoph Meyer

Global Head Quality Control Lonza Cell and Gene Technologies, Basel, Switzerland
christoph.meyer@lonza.com

Cell and Gene Therapies (CGTs) can be highly curative. The response rate for advanced therapy medicinal products like CGTs is unprecedented. The Lonza New Product Introduction and Lifecycle process for CGTs enables a streamlined product development and allows to achieve a robust commercially viable manufacturing and quality control process. The key modalities in cell and gene therapies each present unique challenges and opportunities also leading to a need for different analytical method requirements. Challenges in CGTs include accelerated clinical development which requires faster timelines for Chemistry, Manufacturing and Controls (CMC) thus faster timelines for analytical development as well. Manufacturing comparability evidence must be supported by fit for purpose analytical methods and linked to clinical evidence. This specifically applies for potency assay methods mimicking and confirming clinical outcomes . Short shelf life of the products or immediate medical need impose specific challenges to analytical methods to be fast and efficient, respectively interim read-out of results may be needed for fast track product release. In this presentation, a general approach to development, commercialization, industrialization, and delivery in line with cGMP is outlined from an analytical quality control perspective.

# Evolving Vibrational Spectroscopy

## From scientific curiosity to outstanding routine analysis applications

Christoph Jansen

Metrohm Schweiz AG, CH Zofingen

Christoph.jansen@metrohm.ch

Fundamental science sometimes can take long until it is useful for practical applications. So did Raman Spectroscopy. For a long time, it lacked powerful excitation and sensitive detectors.

Since the technology evolved, the number of exciting applications was booming. Modern Raman spectroscopy has significant advantages, especially in sample preparation.

While MIR (mid IR) samples often must be prepared with some effort, modern Raman spectrometers can just easily point at the sample and measure. No cut out, just leave the sample as it is.

Non-destructive measurements obviously are important in gemmology [1] and mineralogy, even in space [2]. In the field of Archaeology [3,4,5,6], pigments in precious ancient paintings, scrolls or books can be identified. This application is also used to identify fraud and falsification.

Studies of a medical school reported that Raman can be applied to distinguish cancer tissue from healthy one [7].

Due to the mobility and ruggedness of the hardware, Raman spectroscopy can be used for police, firefighters, and military applications: identification of explosives and illicit drugs or warfare substances.

With SERS (Signal Enhanced Raman Spectroscopy), Raman can even be used for trace analysis. The SERS effect enhances the sensitivity of the Raman signal by a factor of up to $10^7$. This enables, e.g. measuring pesticide residuals [8, 9] on fruit or vegetables surface for food safety. It can as well be used to identify traces of drugs e.g. in urine [10].

However, one of the most common Raman-applications is the identity check or verification of incoming goods in the pharma industries. Users appreciate the ease of use and the ruggedness of the Raman hardware.

A complementary technology is NIRS (Near InfraRed Spectroscopy) which offers some additional advantages: It can quantify water, which is impossible for Raman. NIRS enables the simultaneous quantification of several ingredients, including some physical parameters such as viscosity, density and crystallinity. Here also the technology is evolving towards compacter instruments, faster measurements and easy model generation, which all end in increasing efficiency and reducing operational cost.

[1] http://bwtek.com/videos/gem-identification-with-expert-gemologist-using-portable-raman-spectroscopy/
[2] E.L. Lalla et al, Advances in Space Research 57 (2016) 2385–2395

[3] Dominguez-Vidal, Ana & Torre-Lopez, Maria & Rubio-Domene, Ramon & Cañada, Maria. (2012). In situ noninvasive Raman microspectroscopic investigation of polychrome plasterworks in the Alhambra. The Analyst. 137. 10.1039/c2an36027f.
[4] N. Prieto-Taboada, M. Veneranda, H. Morillas, I. Marcaida, S. Fdez-Ortiz de Vallejuelo, M. Maguregui, K. Castro, D. Rau, D. Yang, E. De Carolis, M. Osanna and J. M. Madariaga. IRUG 2016
[5] http://bwtek.com/videos/portable-raman-spectroscopy-in-pompeii-italy/
[6] http://bwtek.com/videos/mineral-identification-with-portable-raman-at-the-sterling-hill-mining-museum/
[7] Willie c. Zúñiga, Veronica Jones, Sarah M. Anderson, Alex Echevarria, Nathaniel L. Miller, Connor Stashko, Daniel Schmolze, Philip D. Cha, Ragini Kothari, Yuman Fong, Michael C. Storrie-Lombardi, Raman Spectroscopy for Rapid Evaluation of Surgical Margins during Breast Cancer Lumpectomy www.nature.com/scientificreports, https://doi.org/10.1038/s41598-019-51112-0, (2019)
[8] Nekvapil, Fran, et al. "Citrus fruits freshness assessment using Raman spectroscopy." *Food chemistry* 242 (2018): 560-567.
*[9] Anal. Chem.* 2018, 90, 13647−13654
[10] Weng, Shizhuang, et al. "Dynamic surface-enhanced Raman spectroscopy and Chemometric methods for fast detection and intelligent identification of methamphetamine and 3, 4-Methylenedioxy methamphetamine in human urine." *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy* 189 (2018): 1-7.

# Single-molecule discrimination of different types of glycosaminoglycans by nanopore sensing

Chan Cao[1], Yuelin Luo[1,2], Junyi Liu[3], Verena Rukes[1,2], Ekaterina Pyatova[2], Juan Francisco Bada Juarez[1,2], Romain R. Vivès[4]

1 Department of Inorganic and Analytical Chemistry, University of Geneva, 1211 Geneva, Switzerland
2 School of Life Sciences, Ecole Polytechnique Fédérale de Lausanne, Lausanne 1015, Switzerland
3 Weiyang college, Tsinghua University, Beijing 100084, China
4 Univ. Grenoble Alpes, CNRS, CEA, IBS, Grenoble, France
chan.cao@unige.ch

Glycosaminoglycans (GAGs) are polysaccharides, which play critical roles in various physiological and pathological processes. The characterization of GAGs remains challenging due to a lack of tools to probe their highly diverse, heterogeneous and complex structures [1]. Nanopore technology has emerged as a powerful single-molecule approach with extensive applications in personalized medicine and disease research [2]. Here, we developed nanopore technique for discrimination of several types of GAGs. By investigated a range of different electrolytes, our results showed that different types of GAGs can be clearly identified. A deep learning model was developed to automatically classify different GAGs with a high accuracy, which is confirmed by different mixture samples. These results provide a valuable step towards analysis and sequencing of long GAGs with nanopores.

[1] Perez, S. *et al.* Glycosaminoglycans: What Remains To Be Deciphered? *JACS Au* **3**, 628–656 (2023).
[2] Cao, C. *et al.* Deep Learning-Assisted Single-Molecule Detection of Protein Post-translational Modifications with a Biological Nanopore. *ACS Nano*, **18**, 2, 1504–1515. (2024)

# Proteomics profiling questions morphological classification of zebrafish cell line

Mihai-Ovidiu Degeratu, René Schönenberger, Nikolai Huwa, Ksenia Groh

Eawag, ETH domain, Ueberlandstrasse 133, 8600 Dübendorf, Switzerland
Mihaiovidiu.degeratu@eawag.ch

Chemical testing for aquatic risk assessment currently requires high numbers of fish and ample resources, which raises ethical and economical concerns. Cell lines derived from fish tissues/organs represent promising alternative (animal-free) test models for predicting chemical toxicity to fish, but their regulatory uptake has been slow. One hurdle has been the insufficient knowledge about the properties of these cell lines, which could be enhanced by looking at molecular profiles (e.g. proteome). This could help improve our understanding of the cell lines` general characteristics (e.g. cell morphology) as well as their (potential) functional capacity.

Here I present the case of the zebrafish (*Danio rerio*) embryonic cell line, PAC2, which was originally classified as a fibroblast cell line, based on visual inspection. However, this view has been challenged, as PAC2 cells also resemble epithelial-like morphology, especially when they are in a confluent monolayer. To investigate this, I performed mass spectrometry-based bottom-up global proteomics analysis of the PAC2 cell line. Cells were sampled at three cell culture growth phases: early (lag), exponential and stationary. Proteins were digested with trypsin and analysed by nano liquid chromatography (nanoLC) and tandem mass spectrometry (MS/MS) on the Orbitrap Fusion™ Lumos™ Tribrid™ mass spectrometer (Thermo Scientific), operated in a data-independent acquisition (DIA) mode. Direct DIA analysis was performed with Spectronaut® 18 (Biognosys AG). Further data analysis was done in RStudio.

Our method allowed measuring ca. 7000 proteins in the PAC2 cells. The protein abundance profiles were clearly distinct between the three growth phases. Notably, multiple epithelial cell markers were identified in addition to proteins characteristic of fibroblasts. This calls into question the morphological classification of PAC2 as a purely “fibroblast” cell line. Ongoing work focuses on comparative analyses of proteins and pathways expressed in the three growth phases, seeking to elucidate further the general characteristics and to deduce the (potential) functional capacities of the PAC2 cell line.

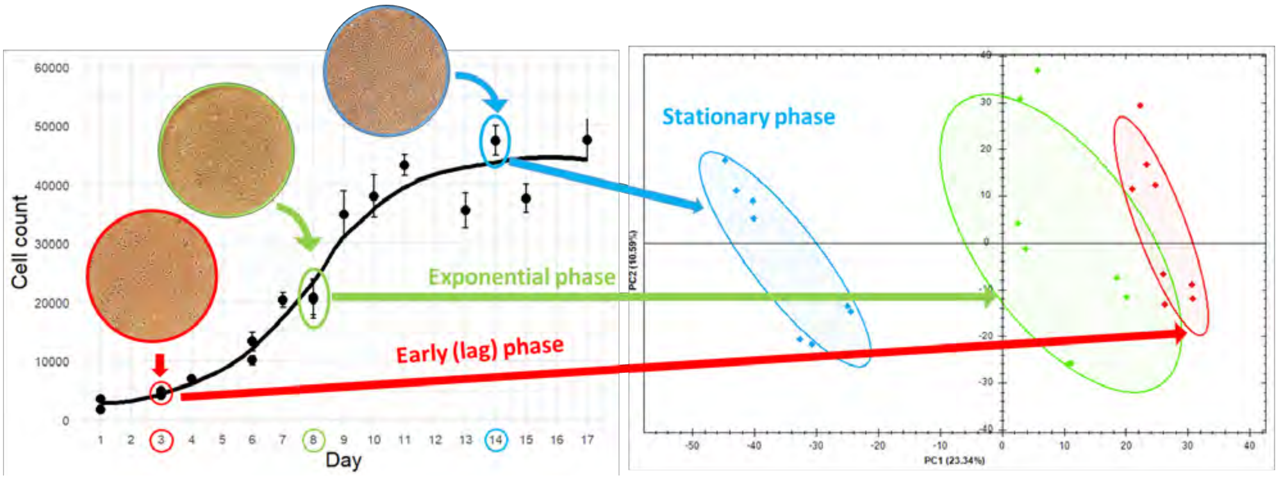

Figure. **Proteomics profiling of PAC2, a fish cell line derived from zebrafish embryos**. Fish cells collected at the early (lag; day 3 post seeding), exponential (day 6 post seeding) and stationary (day 15 post seeding) phases of the cell culture growth display distinct protein abundance profiles, as revealed by the PCA analysis.

# Chemical and biological references at the Federal Institute of Metrology METAS

Hanspeter Andres

Deputy Director, Federal Institute of Metrology METAS
hanspeter.andres@metas.ch

The Federal Institute of Metrology (METAS) serves as the federal centre of competence for all issues related to measurement, to measuring equipment and measuring procedures. It is the Swiss national metrology institute. As such, its mandate is to ensure the availability in Switzerland of measurement and testing facilities with the degree of accuracy needed to meet the requirements of the economy, research and administration. METAS stands at the cutting edge of measurement accuracy in Switzerland.

In chemistry and biology, the classical concepts of metrology (traceability and measurement uncertainty) are only partially established. Traceability of measurement values to the international system of units SI can make significant contributions to technical and scientific progress in various areas. At METAS we focus on the areas of environmental, health and life sciences that are relevant to the Swiss economy, administration and science. Results of four recent collaborative R&D projects advancing measurement science in chemistry and biology will be presented.

[1] M. Guillevic et al.; Dynamic–gravimetric preparation of metrologically traceable primary calibration standards for halogenated greenhouse gases, *Atmospheric Measurement Techniques*, 11, 3351–3372 (2018); DOI: 10.5194/amt-11-3351-2018

[2] K. Vasilatou et al,; Extending traceability in airborne particle size distribution measurements beyond 10 µm: Counting efficiency and unit-to-unit variability of four aerodynamic particle size spectrometers, *Aerosol Science and Technology*, 57:1, 24-34 (2023); DOI: 10.1080/02786826.2022.2139659.

[3] S. Lobsiger et al.; Development of a novel certified reference material for the determination of polycyclic aromatic hydrocarbons (PAHs) in whey protein powder*, Anal Bioanal Chem* 415, 5819–5832 (2023). DOI: 10.1007/s00216-023-04863-9.

[4] S. Flütsch et al.; Vibrio-Sequins - dPCR-traceable DNA standards for quantitative genomics of Vibrio spp. *BMC Genomics* 24, 375 (2023). DOI: 10.1186/s12864-023-09429-8

# A multi-residue method for trace analysis of pesticides in soil with special emphasis on rigorous quality control

Andrea Rösch[1,2], Felix E. Wettstein[1], Vanessa Reininger[2], Thomas D. Bucheli[1]

[1]Environmental Analytics, Agroscope, 8046 Zurich, Switzerland
[2]Soil Quality and Soil Use, Agroscope, 8046 Zurich, Switzerland

andrea.roesch@agroscope.admin.ch

Pesticides are applied on agricultural fields to fight or prevent crop pests, diseases, and weeds in order to maintain crop yield. Whereas knowledge on chemical pollution in surface water bodies located in agriculturally influenced areas is constantly improving, information on soil contamination with agrochemicals is relatively scarce. Therefore, within the *Swiss Action Plan for Risk Minimization and Sustainable Use of Plant Protection Products* (*AP PPP*) one measure focuses on developing a long-term monitoring of pesticide residues in agricultural soils. As part of this measure, a multi-residue trace analytical method was developed to accurately quantify ~150 pesticides in (agricultural) soils with varying soil properties. An optimized quick, easy, cheap, effective, rugged, and safe (QuEChERS) approach was selected to extract pesticides from soil. Chemical analysis was carried out by liquid chromatography coupled to tandem mass spectrometry using electrospray ionization. Accurate quantification was guaranteed by the use of ~100 isotopically labelled internal standards to compensate soil specific matrix effects. In contrast to the common approach of method validation using soil samples spiked with pesticides shortly before the extraction, our method was additionally validated via an in-house prepared partly aged soil that contained all target analytes and via agricultural field soils with native pesticide residues. In this way, a highly sensitive (median method limit of quantification 0.2 ng/g), precise (median intra-day and inter-day precision both 4% based on field soils), and true ((i) quantified pesticide concentrations of the partly-aged soil remained stable during 6 months and were close to the initially spiked nominal concentration; (ii) median freshly spiked relative recovery: 103%; and (iii) participation in a ring trial: median *z*-scores close to one (good to satisfactory result)) analytical method is presented, which is already in use for routine monitoring as part of the *AP PPP* to evaluate soil quality.

[1] A. Rösch, F. E. Wettstein, D. Wächter, V. Reininger, R. G. Meuli, T. D. Bucheli, *Analytical and Bioanalytical Chemistry*, **2023**, *415*, 6009-6025.

# Mechanistic Insights in Oxygen Activation on Bulk Au(111) Surface Using Tip-Enhanced Raman Spectroscopy

Naresh Kumar

ETH Zurich, Vladimir-Prelog-Weg 3, 8093 Zurich, Switzerland
kumar@org.chem.ethz.ch

Over the past two decades, Tip-Enhanced Raman Spectroscopy (TERS) has emerged as a powerful tool for surface chemical analysis at the nanoscale [1]. By combining the high spatial resolution of scanning probe microscopy with the chemical sensitivity and specificity of surface-enhanced Raman spectroscopy, TERS allows visualization of surface chemical processes beyond the diffraction limit of visible light [2].

In this talk, I will first provide a brief overview of the fundamental principle of TERS, with a particular focus on the strengths and limitations of AFM- and STM-based TERS techniques for nanoanalysis of heterogenous catalytic systems. In the second part of my talk, I will demonstrate the practical application of TERS in the field of heterogeneous catalysis by sharing findings from a recent study conducted in our laboratory [3]. Specifically, we investigated oxidation of 4-aminothiophenol (4-ATP) to 4-nitrothiophenol (4-NTP) on Au(111) surface using hyperspectral TERS imaging as schematically illustrated in Figure 1. Nanoscale TERS images revealed a markedly higher oxidation efficiency in disordered 4-ATP adlayers compared to the ordered adlayers signifying that the oxidation of 4-ATP molecules proceeds via interaction with the on-surface oxidative species. These results were further validated via direct oxidation of the 4-ATP adlayers with $H_2O_2$ solution. Finally, TERS measurements of oxidized 4-ATP adlayers in the presence of $H_2O^{18}$ provided the first empirical evidence for the generation of oxidative species on bulk Au(111) surface via water-mediated activation of molecular oxygen [3]. This study expands our mechanistic understanding of oxidation chemistry on Au by elucidating the oxygen activation pathway.

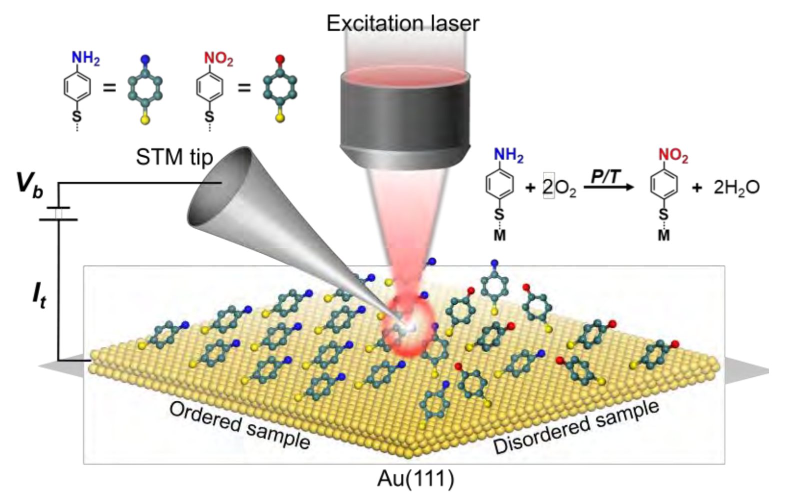

**Figure 1.** Schematic diagram of the scanning tunnelling microscopy (STM) based TERS setup used in this study to investigate the on-surface oxidation of ordered and disordered 4-ATP adlayers on Au(111) surface.

Overall, this talk will highlight the potential of TERS in the nanoscale investigation of surface catalytic processes. Through high sensitivity and nanoscale hyperspectral imaging, TERS can offer valuable insights to advance our mechanistic understanding of surface chemistry.

[1] Z.-F. Cai, N. Kumar, R. Zenobi, *CCS Chem.*, **2023**, *5*, 55-71
[2] N. Kumar, S. Mignuzzi, W. Su, D. Roy, *EPJ Tech. Instrum.*, **2015**, *2*, 9
[3] Z.-F. Cai, Z.-X. Tang, Y. Zhang, N. Kumar, *Angew. Chem. Int. Ed.*, **2024**, e202318682

# Strategies for the characterization of epitaxial thin films as Röntgen Materials

Sharath Rameshbabu[1,2], Christof Vockenhuber[3], Arnold Müller[3], Davide Bleiner[1,2]

[1]Swiss Federal Laboratories for Materials Science and Technology (Empa), Überlandstrasse 129, 8600 Dübendorf, Switzerland

[3]Laboratory of Ion Beam Physics, ETH Zürich, 8093 Zürich, Switzerland.

[2]University of Zurich, Winterthurerstrasse 190, 8057 Zurich, Switzerland.
Sharath.rameshbabu@empa.ch

About 50 years ago, Fisher [1] proposed the utilization of single crystals as distributed feedback resonators for compact X-ray lasers. However, the realization of a compact X-ray laser has been hindered by challenges associated with the usage of single crystals. In our previous work [2], we classified a new class of Röntgen materials and detailed their gain parameters for X-ray laser on a chip. We found that the quality of single crystals, particularly in terms of their stoichiometry and geometry, plays a crucial role in achieving the desired results. Moreover, we determined that only 100 $nm^3$ crystals are required for our purposes, leading us to propose the use of pulsed laser deposition (PLD) for their fabrication.

PLD is renowned for its epitaxial growth with stoichiometry transfer. We demonstrated the growth of a complex oxide, $La_{0.5}Sr_{0.5}CoO_3$, epitaxial thin film using a homemade compact PLD system. Extensive analysis of the crystal quality was performed through X-ray studies. Atomic force microscopy (AFM) was utilized to analyze the topography of the grown thin film, with the roughness estimated to be approximately 3.5 nm.

Resonance nuclear elastic scattering (RENS), a specialized technique akin to Rutherford backscattering spectroscopy (RBS), was employed to probe lighter elements within a heavier matrix. In our case, the thin film was grown on a strontium titanate substrate. RENS was employed to accurately estimate the oxygen content in the grown thin film. Furthermore, the thickness and stoichiometry of the grown film were analyzed using RENS. The thickness of the film was calculated to be 100 nm, assuming a theoretical density of 6.5 $g/cm^3$.

[1] Fisher, Robert A, Applied Physics Letters 24, **1974**, 12, 598-599.
[2] Rameshbabu, Sharath, and Bleiner, Davide, SPIE, **2023**, 12582, 95-103.

# Markers and Methods for the Identification of Recycled Polymeric Materials

Jens A. Jacobsen[1], Rachel Sanig[1], James A. Browne[1], Jennifer Gough[1], Donald A. Trinite[1], Ben MacCreath[1], Falk-Thilo Ferse[1], Agnieszka Kalinowska[2], Christoph Rethmann[2] ,Pascal Tuszewski[2], and Cristian I. Cojocariu[1]
1. Waters Corporation, 2.thyssenkrupp Presta AG
jens_jacobsen@waters.com

The Analysis of polymeric materials is amongst the most diverse pallet of methodoglogies and tools due to the polymeric and non soluble substance matter. Material Characeristation vary from Physical and Thermodynamic testing to surface analysis. Recently, a comprehensive literature review looking at the application of recycled plastics in safety-related components was reported [1]. When recycling such parts, it is critical to assess both mechanical properties and chemical properties of the finished product to ensure that performance is not affected. However, due to the uncertainties of the material properties in mechanical recycling, there are limited studies on the use of regranulates in safety-relevant components. As a result, the literature recommends that no more than 25% recyclate should be used, especially for technical parts. A proportion of less than 5%, on the other hand, is considered tolerable and can be done without further testing of the properties. This case study describes a combined analytical approach to test the structure and properties of polyamide gears processed by extrusion/injection molding of virgin or recycled (regrind) pellets. The workflow described is aimed at analyzing the potential differences of the virgin and recycled pellets and gears.

1. Rethmann, C., 2022. Evaluation of polymer recycling for safety-relevant components in the automotive industry, Masterthesis, University of Applied Sciences/Hochschule Osnabrück.

# Integrated electrochemical systems for enzyme-linked immunoassays

Gabriel Junquetti, Thomas Cherubini, and Eric Bakker

University of Geneva, Department of Inorganic and Analytical Chemistry, Quai E.-Ansermet 30, CH-1211,
Geneva, Switzerland
gabriel.junquettimattos@unige.ch

Enzyme-linked immunoassays such as ELISA require labor intensive manipulation (washing steps) to remove unbound enzyme-labeled detection antibodies that would otherwise interfere with the output signal. Restricting the substrate delivery to the immunocomplexes site would greatly simplify those assays. Here we propose an integrated sensing system in a flow-cell for enzyme-linked immunoassays, where a dispersible magnetic probe containing a sandwich-type enzyme-immunocomplex is spatially resolved from the excess detection conjugate in the bulk solution by applying a magnetic field. Once the beads are on the surface of an ion selective membrane (ISM), an electrochemical excitation pulse delivers the enzyme substrate from the back side inner solution to the immunocomplex side (see Figure 1 below) [1]. In the presence of the enzyme-linked immunocomplex on the surface of the ISM, the enzyme substrate ions instrumentally delivered are now partially consumed by the enzyme label. The potential changes with time since the membrane is selective to the substrate activity and proportional to the concentration of enzyme-immunocomplex. This allows for the quantification of the target analyte [2]. This integrated electrochemical immunosensor comprises the immunobinding, enzyme reaction, and electrochemical detection all occurring in the same system, controlled by electrochemistry and magnetic forces.

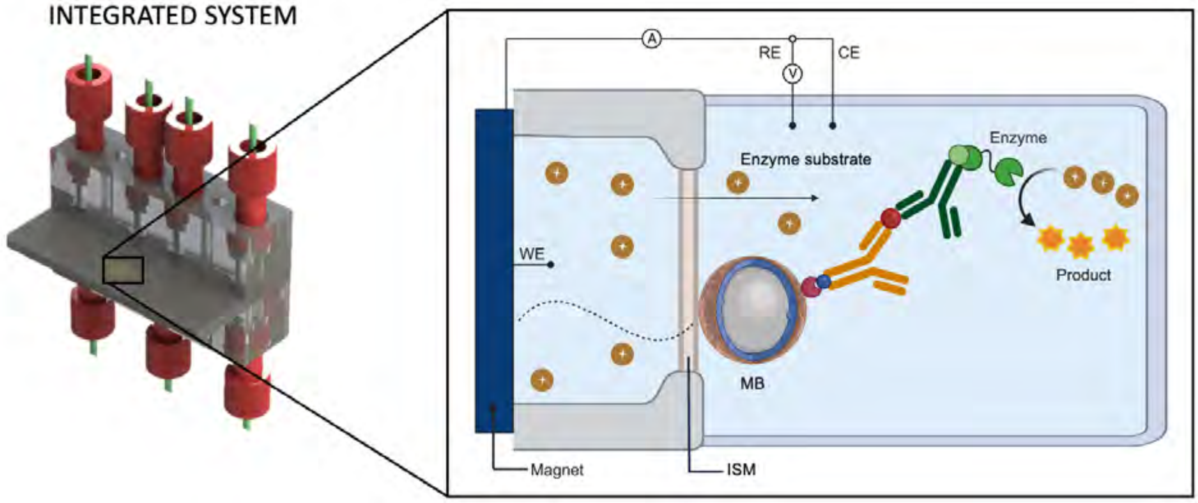

**Figure 1.** Schematic view of the integrated system and sensing principle. ISM represents the ion-selective membrane. A three-electrode cell contains the working electrode (WE), reference electrode (RE), and the counter electrode (CE).

[1] G. J. Mattos, E. Bakker, *Biosensors & Bioelectronics*, **2023**, *14*, 100351.
[2] J. Ding, X. Wang, W. Qin, *ACS Appl. Mater. Interfaces*, **2013**, *5*, 9488-9493.

# Improving the Sensitivity of pH Glass Electrodes with an Alternative Readout

Robin Nussbaum, Stéphane Jeanneret, Eric Bakker

Department of Inorganic and Analytical Chemistry, University of Geneva, Quai Ernest-Ansermet 30, 1211 Geneva, Switzerland
Robin.Nussbaum@unige.ch

Glass electrodes are the gold standard for day-to-day pH determination. They are typically operated at zero current and the phase boundary potential at the electrode-sample interface relates to the sample pH. The sensitivity of such electrodes is dictated by the Nernst equation and is equal to -59.2 mV/pH at 25°C. This limited value makes very small pH variations challenging to measure. Yet, their accurate monitoring is crucial to keep track of environmental processes such as ocean acidification (-0.002 pH $y^{-1}$) or metal speciation [1].

Constant potential coulometry was introduced to improve the sensitivity of ion-selective electrodes (ISEs) compared to the Nernstian response [2]. In this protocol, a constant potential is imposed between the reference electrode (RE) and the ISE. Thus, any potential change at the ISE-sample interface induces an opposite potential change on an electronic capacitor placed in series, resulting in a transient current. The charge is obtained from the latter and used as amplified analytical signal. Unfortunately, the transient current must flow through the electrochemical cell, which may induce measurement errors and makes it impossible to use high impedance ISEs such as glass electrodes.

We report here on an electronic circuit that overcomes these limitations through the combination of (i) zero-current measurement at the ISE and (ii) a high-impedance input voltage follower [3]. As the transient current does not flow though the ISE, its potential is left intact and a counter electrode is no longer required. The setup is first evaluated for chloride sensing as model system and compared with classical potentiometry. The procedure is then successfully applied with a glass electrode (i) to narrow pH ranges comparable to the values found in environmental samples with 0.01 pH steps (64 µpH precision) and (ii) to a wider pH range (4 to 10) with 1 pH steps to assess the versatility of the proposed method.

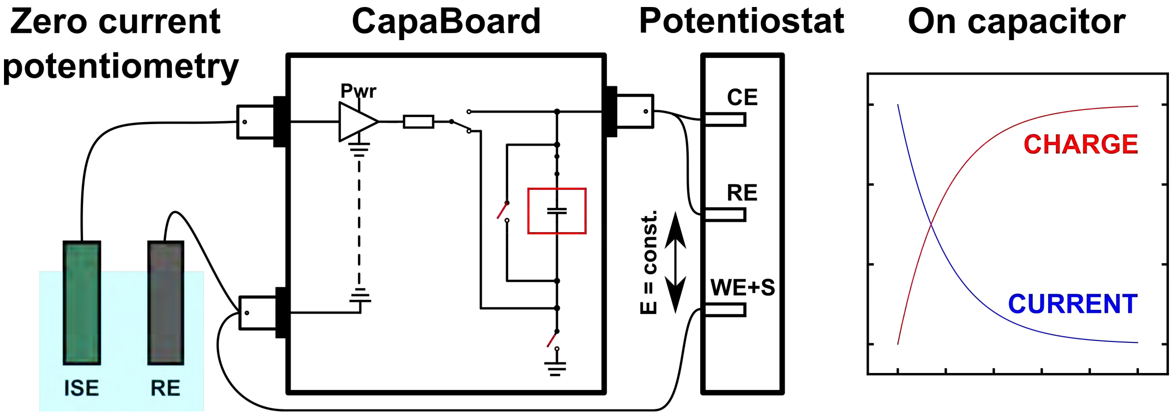

Figure 1. Scheme of the novel experimental setup for enhanced pH sensitivity.

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# Exploring the Limits of Ionic Liquid Reference Electrodes

Nikolai Yu. Tiuftiakov, Elena Zdrachek and Eric Bakker

Department of Inorganic and Analytical Chemistry, University of Geneva,
Quai Ernest-Ansermet 30, CH-1211, Geneva, Switzerland
Nikolai.Tiuftiakov@unige.ch

Reference electrodes (REs) without liquid junction have attracted significant attention over the last 20 years. These REs typically utilize ionic liquids (ILs) as free-flowing, water-immiscible salt bridges or as lipophilic electrolytes within plasticized polymeric reference membranes. Upon contact with a sample, the IL partitions into the aqueous phase (Fig. 1a), establishing an equilibrium distribution across the interface and a corresponding phase boundary potential, that is generally independent of the sample composition (Fig. 1b). IL-based REs offer an alternative to conventional REs employing aqueous salt bridge electrolytes and present opportunities for achieving integrated potentiometric sensing systems [1]. However, despite their advantages, IL-based REs have yet to achieve widespread commercial adoption, partly due to a lack of comprehensive understanding regarding their limitations. One major concern revolves around the reference membrane lifetime, as there is little quantitative data available on IL partitioning and leaching. The RE potential stability in complex samples is also of great importance. Lipophilic ions and surfactants are known to affect the response of IL-based REs, making it crucial to understand and investigate the underlying mechanisms in more detail.

In this study we explore the working limits of REs based on polymeric reference membranes incorporating ILs. A theoretical framework is developed and experimentally verified to describe the failure of REs in the presence of lipophilic solution ions [2]. The critical concentration at which the RE potential begins to deviate noticeably from its equilibrium value is estimated as the intersection of the separate Nernstian responses to the IL and the solution ion (Fig. 1c). Furthermore, reference membrane lifetimes are assessed based on the IL partition constants acquired for the sensing matrix used in this study. Lastly, we discuss the effectiveness of potential stabilization with highly lipophilic electrolytes to establish the optimal range of IL lipophilicity for RE design.

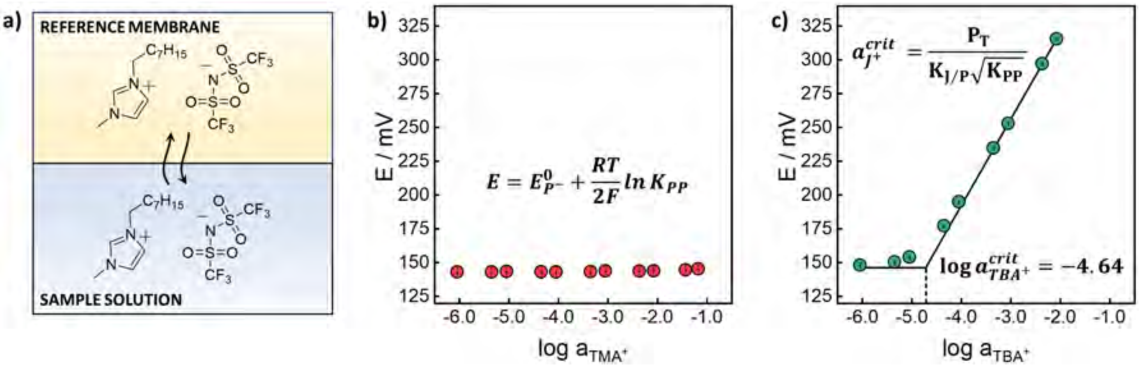

Figure 1. a) Partitioning of the ionic liquid $[C_8mim^+][C_1C_1N^-]$ between the electrode membrane and the sample and the response of the corresponding REs in the presence of different concentrations of b) tetramethylammonium ($TMA^+$) and c) tetrabutylammonium ($TBA^+$).

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# Forever Chemicals – Workflows to detect PFAS in Water, Soil and Food

Fabian Tolle, PhD

Agilent Technologies Switzerland AG, Lautengartenstrasse 6, CH-4052 Basel; Fabian.Tolle@agilent.com

Per- and polyfluoroalkyl substances (PFAS) are a set of manufactured substances that have been used since the 1940s in various industrial and consumer products like nonstick cookware, stain repellent clothing, food contact materials, detergents and other cleaning products, and firefighting foams. They have been widely detected in drinking water, wastewater, ground and surface water, soil, food, body fluids and other complex matrices. This contamination of the environment with PFAS is a serious concern worldwide, due to their ubiquitous presence, persistence, and toxicity. Their chain of strong fluorine-carbon bonds makes these chemicals persistent and bio-accumulative – linking them to health hazards in humans and wildlife.

Therefore, PFAS testing methods, like EPA methods for chemical analysis of water and wastes, are needed for quantification and screening of PFAS in the environment, for example, for water and soil quality. Key challenges in the analysis of per and poly-fluoroalkyl substances (PFAS) are the potential of adsorption of target compounds or the introduction of interferences during sample handling. To address the clients' needs to fulfil PFAS regulations and overcome analytical challenges, Agilent provides start-to-finish solutions that covers a growing list of PFAS. These solutions include sample containment, sample preparation, extraction, and liquid chromatography/mass spectrometry (LC/MS) analysis.

During this presentation, we will provide you an overview about Agilent's workflows for PFAS analysis in water, food, and soil, implementing different LC/MS instrument according to required sensitivity and targeted or non-targeted strategies to detect the "Forever Chemicals" in various matrices.

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# Analytical Chemistry in Forensic Chemistry and Toxicology at the Institute of Legal Medicine Basel (IRM Basel)

Götz Schlotterbeck

Head Department Forensic Chemistry and Toxicology, Institute of Forensic Medicine, University of Basel
goetz.schlotterbeck@bs.ch

The Institute of Forensic Medicine (IRM), with its three specialised departments of Forensic Chemistry and Toxicology, Forensic Genetics and Forensic Medicine and Traffic Medicine, offers its clients from the fields of law enforcement a comprehensive range of forensic-medical and scientific-criminalistic services. Forensic toxicological analyses for drugs, alcohol and medication are carried out on deceased persons, persons involved in bodily injury offences, road users and persons for whom a fitness to drive assessment has been ordered. Forensic chemical analyses of narcotics provide information on the purity and active ingredient content of illegal seized drugs.

At IRM Basel in the department of Forensic Chemistry and Toxicology we focus on research on synthetic cannabinoids, target and non-targeted analytical method development and perform studies to support legislative bodies. With our drug checking service we provide analytical support to increase safety for consumers of recreational drugs. Results of selected research projects, examples of forensic chemistry and forensic toxicology case work and drug checking services will be presented.

# To Humidity and Beyond

Andreas Kordikowski

Novartis Pharma AG, Fabrikstrasse 2, 4056 Basel, Switzerland
andreas.kordikowski@novartis.com

Dynamic vapor sorption (DVS) has long been used as a tool to determine the hygroscopicity of food stuffs and functional materials. It is increasingly used in the pharmaceutical industry in the investigation for drug substances and drug products. Pro's and con's of DVS analyses and hardware configurations will be presented. Applications from early and late phase development regarding form selection and confirmation as well as RA-CMC and HA support will be discussed.

# Electrochemical Sensing coupled to Liquid-Liquid Phase Extraction using Hydrophobic Deep Eutectic Solvents

Fabian Weyand[a,b], Vasily Grebennikov[a], Adrian Wichser[a], Jing Wang[a,b]

[a]Advanced Analytical Technologies, EMPA
[b]Institute of Environmental Engineering, D-BAUG, ETH Zürich

In-field measurements of hydrophobic biomarkers have gained increasing attention in clinical research. For instance, the detection of hydrophobic quinones, usually employed as biological key molecules in the redox machinery for photosynthesis and respiration, set up also the chemical entity of antibiotics, cofactors and vitamins.[1] However, their sensitive and selective analysis is challenging due to their low solubility in aqueous solutions.[2] Amperometric electrochemical sensing exhibits an auspicious approach owing to portable equipment, low limit of detections (LoDs, micromolar) and the direct conversion of the target signal into an electrical signal, allowing miniaturization and thus small sample volume (microliters).[3] However, real-world samples typically contain a wide range of redox-active molecules and, unless equipped with bioreceptors, the selectivity and specificity of the resulting abiotic sensor is often inadequate. Moreover, the very low upper concentration limit of hydrophobic biomarkers, which may be below the sensor's own LoD, prevents the detection in aqueous solutions.

Here, we propose an approach based on the electrochemical sensing of prototypical quinone/hydroquinone (Q/$H_2Q$) redox couples interconnected to liquid-liquid phase extraction (LLPE) using Hydrophobic Deep Eutectic Solvents (HDES). HDES are promising environmental benign quasi-water immiscible solvents formed by mixing a hydrogen bond acceptor (e.g., decanoid acid (DA)) and a hydrogen bond donor (e.g., *tetra*-butylammonium chloride (TBACl)) in an appropriate molar ratio. Since one of the precursors is ionic, the LLPE can subsequently be coupled with electrochemistry. By using drop-size volume of the HDES as extractant, which is brought into contact with a larger amount of sample, fast extraction equilibria and high preconcentration factors are reached. Thus, beforehand inaccessible concentrations are enriched via preconcentration and become electrochemically accessible. In addition, hydrophobic analytes are preferably extracted so that enrichment comes along with both, an increase in specificity and lower LoDs.

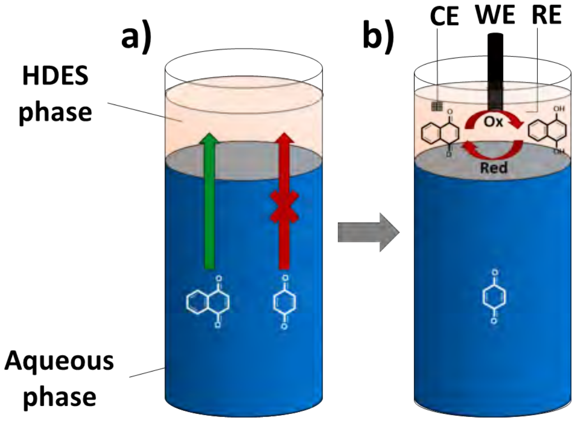

**Fig. 1:** a) Schematic representation of the selective partition of hydrophobic naphtoquinone priorhydrophilic benzoquinone via LLPE using HDES and b) subsequent electrochemical sensing.

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# Exploring the Complexity of Entropy: Harmonizing Disorder and Energy Dynamics

Jawad Alzeer

Swiss Scientific Society for Developing Countries, Zürichstrasse 70, Dübendorf, Switzerland
jawad.alzeer@uzh.ch

Entropy, a cornerstone of chemistry, often presents a challenge due to its perceived duality between disorder and energy. This complexity stems from the multifaceted nature of entropy, necessitating a shift from a simplistic, disorder-centred perspective towards an integrated approach that considers both disorder and energy dynamics. Chemical transformations involve more than disorder; they encompass exchanges of energy and molecular rearrangements, with entropy and enthalpy changes playing pivotal roles in determining reaction outcomes. By recognizing entropy not only as a measure of disorder but also as a form of energy, chemists can develop a more comprehensive understanding of its role in chemical reactions. Gibbs free energy, which considers both enthalpy and entropy influences, emerges as a vital tool for predicting reaction spontaneity under varying conditions. Moreover, this refined understanding of entropy, acknowledging potential energy as anti-entropy, holds transformative potential across scientific fields, fostering a unified comprehension of entropy's role in physical and biological phenomena. Through embracing disorder and energy dynamics, scientists can pave the way for transformative advancements in chemistry and beyond, unlocking new insights into fundamental processes and phenomena.

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# Collaborative Data Science at the Swiss Data Science Center

Rok Roškar, Guillaume Obozinski

Swiss Data Science Center, ETH Zürich
rok.roskar@sdsc.ethz.ch

Collaborating efficiently on data science projects is a difficult task that requires a good knowledge of many different technologies and practices. At the Swiss Data Science Center (SDSC), we are building Renku, a platform for sustainable data science, whose aim is to make collaboration easier and future-proof. Renku strives to serve as the connector between the different needs of data-centric projects by brokering access to code, sources of data, and computational environments. The relationships between these entities are preserved in a knowledge graph which can be used for building an understanding about the propagation of data and results within an individual project, among a research group, or across institutions and communities. In this contribution, we will present Renku, its current features and roadmap. In addition, we will share a few examples of projects carried out in collaboration with research groups in the ETH domain, where SDSC machine learning expertise has been applied to help answer scientific questions.

# Levels of Short-Chain Chlorinated Paraffins in Consumer Products of the Swiss Market: From a Semi-Quantitative Approach to Specific C- and Cl-Homologue Quantification

O. Mendo Diaz *, [1, 2], A. Tell [1, 3], U. Stalder [2], L. Bigler [2], S. Kern [3], D. Bleiner [1, 2], N. V. Heeb [1]

[1] Swiss Federal Laboratories for Materials Science and Technology Empa, Überlandstrasse 129, 8600 Dübendorf, Switzerland

[2] Department of Chemistry, University of Zürich, Winterthurerstrasse 190, 8057 Zürich, Switzerland

[3] Zürich University of Applied Sciences ZHAW, Einsiedlerstrasse 31, 8820 Wädenswil, Switzerland

Chlorinated paraffins (CPs) are polychlorinated *n*-alkanes with the general molecular formula $C_nH_{2n+2-x}Cl_x$. CPs are commonly used as plasticizers, flame retardants or coolant fluids and are currently produced at a rate of 1.5 Mt/y.[1] Depending on their carbon-chain length, CPs are classified as very short-chain (vSC-, $C_{<10}$) short-chain (SC-, $C_{10}$–$C_{13}$), medium-chain (MC-, $C_{14}$–$C_{17}$), long-chain (LC-, $C_{18}$–$C_{21}$) and very long-chain (vLC-, $C_{>21}$) CPs. Since 2017, SCCPs are labeled as persistent organic pollutants by the Stockholm Convention and MCCPs are under evaluation since 2022. According to a regulation introduced in 2017, SCCP levels in consumer products in Switzerland should not exceed 0.15 % in mass. Due to evolving legislations, the levels of SC- and MCCPs are of concern in various markets. [2]

Technical CP mixtures can contain a broad range of carbon- (C-, $n_C$=9–30) and chlorine- (Cl-, $n_{Cl}$=2–20) homologues with millions of constitutional isomers and stereoisomers. CPs are commonly analyzed by liquid chromatography coupled with mass spectrometry (LC-MS). Due to the lack of representative standard materials, the levels of CPs are often determined only semi-quantitatively, assuming similar MS-response factors for different homologues. This means that the amount of CPs in a standard material are compared with the amount of CPs in a sample, regardless whether their C- and Cl-homologue composition match. This approach fails when homologue distributions of standards and samples are different due to different MS-response. We developed a method where the MS-responses of each C- and Cl-homologue are quantified individually in a standard material and can now be compared with the ones found in the samples.

Herein, 30 plastic items collected from the Swiss market in 2021 were analyzed by an LC system coupled with an atmospheric pressure chemical ionization source and an Orbitrap mass analyzer (LC-APCI-Orbitrap-MS). Adduct ions of $[M+Cl]^-$ were monitored and the corresponding high-resolution MS data were evaluated by the newly developed data evaluation tool CP Hunter. Carbon- and chlorine-homologue distributions were obtained as qualitative analysis. Quantification of the SCCP content was achieved by the C- and Cl-homologue approach. [3]

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# METAS: the new WMO-GAW Central Calibration Laboratory for halogenated VOCs

Diana Roos, Tobias Bühlmann

Federal Institute of Metrology METAS, Lindenweg 50, 3003 Berne-Wabern, Switzerland
diana.roos@metas.ch

Many halogenated volatile organic compounds (VOCs) are found in the atmosphere in the pmol/mol range. These halogenated VOCs have negative impacts on the environment as they are strong greenhouse gases and/or contribute to the depletion of the stratospheric ozone layer or their degradation products may have a negative impact on the environment. This underpins the importance to accurately measure the amount fractions of these substances in the atmosphere on the long-term.

The Global Atmosphere Watch (GAW) Programme of the World Meteorological Organization (WMO) is a long-term international global programme that coordinates observations and analysis of atmospheric composition changes. The GAW Programme is a collaboration of more than 100 countries and it relies fundamentally on the contributions of its members to help to build a single, coordinated global understanding of atmospheric composition and its change. For most substances there is a Central Calibration Laboratory (CCL) that is responsible for maintaining and distributing the WMO references for instrument calibration for a specified gas in air. However, until summer 2023 there was no CCL for halogenated VOCs. METAS applied successfully for the CCL function for a total of ten halogenated VOCs because METAS' gas analysis laboratory has a decade of experience in the production of reference gas mixtures for halogenated VOCs. Here, we will present our new function as CCL including our services, the work done in the past and the planned work for the next years.

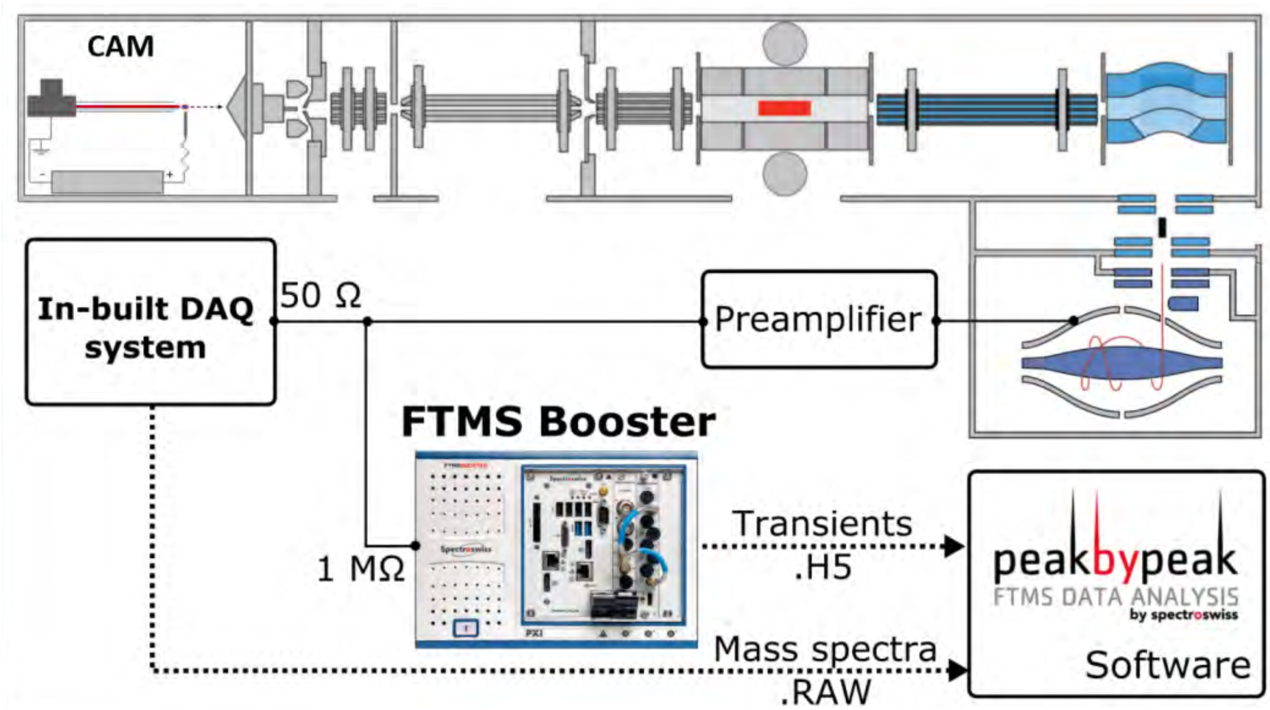
# POSTERS

# The Swiss Army Knife of Operando Chemical Mass Spectrometry: EWMS Spectroscopy

Vasily Grebennikov[1,2], Adrian Wichser[1], Davide Bleiner[1,2]

[1]Swiss Federal Laboratories for Materials Science and Technology (Empa), Überlandstrasse 129, 8600 Dübendorf, Switzerland

[2]University of Zurich, Winterthurerstrasse 190, 8057 Zurich, Switzerland.
Author email: adrian.wichser@empa.ch



Mass Spectrometry is split into traditional categories such as elemental (or inorganic) and molecular (mainly organic), despite more and more application are cross-field. This is due to the different kind of ionization sources, harder for elemental, e.g. ICP, or softer for molecular, e.g. APCI, ESI. However it is desirable to develop new analytical platform that offer the required flexibility between elemental and molecular analysis. Furthermore, traditional mass spectrometry can only indirectly infer the molecular structure. This happens as a jigsaw puzzle on the fragments. In the case of complex mixture of many isomers and compounds, e.g. wastewater samples with halogenated pollutants, such data analysis is virtually impossible. Thereafter, there should be "orthogonal dimensions" of analysis that besides the mass-to-charge would give the collisional cross-section. The latter happen in ion mobility.

In particular, FAIMS is an effective method for adding a new dimension to separation, namely the compensation voltage of a sample. This new dimensionality allows for the separation of constitutional isomers, enabling the study of complex mixtures as previously mentioned. Furthermore, due to the non-destructive nature of FAIMS, it provides valuable insights into molecular studies, as opposed to fragmentation studies, which are often complicated and challenging to follow.

In turn, the analytical characteristics of mass-to-charge data should also correspond to the sample complexity. These include resolution, mass accuracy, sensitivity, and dynamic range. To maximize the analytical performance of our Orbitrap-based MS set-up, we interfaced it with a high-performance data acquisition and processing system, FTMS Booster.

Aim of this project was to develop a unique "Swiss Army Knife" that would combine all the needs above. As chemistry continues to evolve, so will the complexity of chemical samples, rendering normal mass spectrometers obsolete as they may not provide enough information about an analyte. Therefore, the development of new dimensionalities provided by mass spectrometers is crucial to keep up with the demands of modern chemical analysis.

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# Toward a mechanistic understanding of trace-element influence on corrosion at the magnesium-biology interface

Maxence Hannard[1,2], Martina Cihova[1], Adrian Wischer[2], Patrik Schmutz[1], Davide Bleiner[2]

1) Laboratory for Joining Technologies and Corrosion, Empa - Swiss Federal
Laboratories for Materials Science and Technology, Dübendorf 8600, Switzerland
2) Laboratory for Advanced Analytical Technologies, Empa - Swiss Federal
Laboratories for Materials Science and Technology, Dübendorf 8600, Switzerland
maxence.hannard@empa.ch

Biodegradable magnesium (Mg) implants are a promising alternative to permanent metallic implants in biomedical applications. Yet, their effectiveness is hampered by unpredictable corrosion in the physiological environment, resulting in premature implant failure and potential toxicity [1]. A key parameter influencing this phenomenon is the behavior of trace elements (Fe, Zn, Cu) present in the peri-implant microenvironment and as impurities in Mg. These elements are known to impact Mg dissolution by creating active cathodic sites, though their behavior in physiological conditions is still unknown.

Conventional chemical analysis methods, such as SEM/EDS or XPS, lack the necessary elemental sensitivity and spatial resolution to understand the chemical nature of the interfacial layer forming on corroding implants. In this study, laser ablation coupled with inductively coupled plasma mass spectrometry (LA-ICP-MS) was employed for trace-element analysis of corrosion products [2].

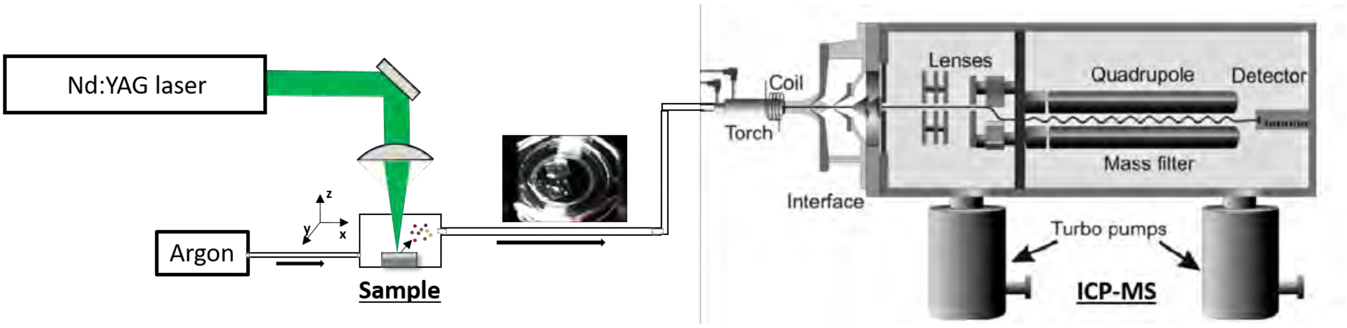

*Figure 1: Laser Ablation – Inductively Coupled Plasma – Mass Spectrometry device used to characterize Mg corrosion layer [3].*

Through the optimization of lateral probing and trace-element analysis on Mg model systems of varying trace element purity exposed to Simulated Body Fluids (SBF), the study achieved sufficient sensitivity (3.6 ppm) to distinguish purity levels based on the Fe content in the Mg Matrix. This data correlates with the dissolved Fe content quantified by ICP-MS liquid-phase analysis (SBF composition) following contact of SBF with Mg. The interplay of Fe with complex electrolytes is further studied by electrochemical quartz crystal microbalance (eQCM) at potentials establishing on Mg surfaces, which revealed insights into Fe-redeposition kinetics and trace-element quantification, particularly in the electrochemical potential range where strong hydrogen reduction dominates the current signal. This comprehensive approach sheds light on the intricacies of Mg implant corrosion, offering valuable insights for the development of more robust and reliable biodegradable implants in biomedical applications.

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# Biomonitoring of phthalates in the Swiss population

Joëlle Houriet [1], Alexandra Jaus [1], Gisela Umbricht [1], Beat J. Brüschweiler [2]

[1] Federal Institute of Metrology, Bern-Wabern, Switzerland
[2] Federal Food Safety and Veterinary Office, Bern, Switzerland
joelle.houriet@metas.ch

Phthalates are found in many everyday objects, mainly as plasticizers, but some have been classified as endocrine disruptors, and their use has been restricted or banned in recent years [1]. The Federal Food Safety and Veterinary Office has organized two large-scale human biomonitoring campaigns in Switzerland as part of health studies, and various substances, including phthalates, are measured in the biofluids of adults and children.

Population exposure is measured by analyzing phthalate metabolites in human urine, thus avoiding the need to deal with ubiquitous environmental contamination. Thirty metabolites, representing 16 phthalates, are selected and analyzed with liquid chromatography–mass spectrometry. The mass spectrometer is operated in negative ionization mode, using a scheduled multiple reaction method by selecting two transitions per standard (one quantifying and one qualifying transition) to ensure selectivity. Corresponding isotopically-labelled standards are added in equal amounts to all samples to ensure robustness and follow up with two transitions.

The analytical challenge of this study is to handle more than 2500 samples. Method development efforts focus on optimizing sample preparation and analysis time based on a published method [2]. First, a transfer from a column of high-pressure to ultra-high-pressure is evaluated to shorten the analysis time. Secondly, simplified sample preparation is evaluated by comparing online and offline solid-phase extraction. These two steps are currently being evaluated, and initial results are presented.

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# Optimization of Manufacturing Method for Solid-Contact Ion-Selective Electrodes: Towards Sensor Reproducibility and Operational Stability

Sara Krivačić[a], Eric Bakker[b]

[a] Department of General and Inorganic Chemistry, University of Zagreb, Faculty of Chemical Engineering and Technology, Trg Marka Marulića 19, HR-10000 Zagreb, Croatia.

[b] Department of Inorganic and Analytical Chemistry, University of Geneva, Quai Ernest-Ansermet 30, 1221 Genève, Switzerland.

skrivacic@fkit.unizg.hr

High demand for easily accessible chemical information provoked the shifting of traditionally laboratory-based analyses to distributed, simplified designs aimed for application in various environments, and not strictly by trained individuals. Owing to mechanistic simplicity and improvements in analytical selectivity, electrochemical sensing platforms are chosen for integration into devices for rapid screening of complex matrixes, such as biological and environmental samples [1]. As mass-production methods are evolving, ensuring sensor reproducibility becomes very important for quality assurance [2]. With the simplest operational principle of potentiometric sensing, reproducibility is defined by the uniformity of the standard potential, $E^0$, as well as response stability. These prerequisites can be achieved by properly selecting ion-selective membrane materials and careful optimization of production parameters.

A fluid dispenser was used to deposit ion-selective membranes on screen-printed carbon electrodes. The reproducibility of the electrodes was optimized by adjusting the membrane composition and deposition parameters such as the spotting pressure and substrate temperature. The electrodes were evaluated using a new colorimetric absorbance method [3]. The analytical performance of the devices were assessed by calibrating potassium-selective membranes. Additionally, the stability of the sensor's operation was examined by identifying the impact of sample introduction on the underlying ion-to-electron transducer layer.

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# Zero-Current Chronopotentiometry with Wired Biosensors

Andrea Nonis, Polyxeni Damala, Eric Bakker

Department of Inorganic and Analytical Chemistry, (University of Geneva, Quai Ernest-Ansermet 30,
1211 Geneva, Switzerland)
Andrea.Nonis@unige.ch

Glucose biosensors are extremely important for point of care measurements and one of the major applications of electroanalytical chemistry. Theses sensors often use amperometric detection methods in which a redox mediator is used to shuttle electron between the electrode and the enzyme reaction site. Heller et al. developed the “wired” biosensor where the redox mediators are bound to the polymer containing the enzyme, thereby providing a connection to the electrode surface. [1] To achieve selectivity and avoid interference, a permselective layer is normally deposited which will also limit the diffusion of the analyte to the enzyme. The sensor is then no longer governed by the enzyme turnover rate but by the analyte diffusion, resulting in some protection from variations in enzyme kinetics and enzyme degradation. [2] Unfortunately, these sensors are subject to signal drift, which was attributed by Damala et al. to the charging of the redox polymer through the oxidation/reduction of redox center not connected to the enzyme. [3] Passive detection methods at open circuit may overcome some of these limitations. Nagy et al. introduced a chronopotentiometric method mased on the measurement of the open circuit potential (OCP) decay resulting from the reduction of an oxidized a redox mediator absorbed the electrode by NADH in solution. They correlated the initial slope of the potential decay to the NADH concentration. [4]

In this work we propose a new chronopotentiometric time dependent readout for a “wired” glucose biosensor based on glucose oxidase. A two-step process involving the oxidation of the redox polymer (ferrocene-modified branched poly(ethylenimine)) followed by the monitoring of the OCP over time allows one to measure a transition time characteristic to the glucose concentration in solution. The transition time ($t_r$) correspond to the potential jump due to the reduction of the previously oxidized ferrocene moieties by the electron generated by the enzyme converting glucose in gluconolactone. Thanks to an outer diffusion limiting membrane $t_r$ is related to the concentration of glucose Nafion and a blend of hydrophilic polyurethane and polyvinyl alcohol/vinyl butyral copolymer are used as outer permselective membrane to repel interference in phosphate buffered saline solution.

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# Protamine/Heparin Detection with Nanosensors: From Research to Point of Care Device

Marialaura Russo, Robin Nussbaum, Eric Bakker

Department of Inorganic and Analytical Chemistry, University of Geneva, Quai Ernest-Ansermet 30, 1211
Geneva, Switzerland
marialauara.russo@etu.unige.ch

Heparin is a natural polyanion widely used as an anticoagulant during surgical procedures. As it is metabolized after injection in the bloodstream, minimizing the measurement time is critical to prevent clotting at too low concentration or uncontrolled bleeding at too high concentration. These needs are not compatible with the heparin quantification gold standard, the anti-Xa assay, because it requires sample preparation as fluorescence cannot be performed in whole blood, owing to its high background signal. Heparin effects may be reversed by addition of protamine, an arginine rich protein, via polyionic interaction.

Meyerhoff and coworkers achieved pioneering work on protamine and heparin detection since 1994 with ion-selective electrodes [1] and optical sensors [2]. More recently, our group developed protamine nanosensors with a solvatochromic dye as signal transducer [3]. The protamine ionophore dinonylnaphthalenesulfonic ($DNNS^-$) was found to strongly polarize the dye environment within the nanoparticles. With protamine binding, the dye interacts with a much more apolar environment, resulting in an absorbance shift. The particles response was found to be independent of pH, which is a significant advantage compared to typical optical nanosensors. Heparin was successfully quantified in patients' plasma and the mechanism of the nanosensors was investigated. However, this approach still required consequent sample preparation as it was not suitable for whole blood measurement. Thus, the nanosensors were embedded in an agarose gel, known to filter out the red blood cells, and poured in polystyrene cuvettes for absorbance measurement [4]. Protamine diffusion though the gel induced a color change, which was recorded with a camera. Heparin quantification in whole blood was achieved with this very simple setup. Yet, this was still far from a point of care device.

We report here on the development of a novel heparin assay that that combines paper-based devices and agarose gels to detect heparin in whole blood samples via protamine titration. The device is composed of multiple layer stacked onto each other. A few µl of sample is dropped on the top layer that traps the red blood cells to prevent color interference. The sample components then diffuse through a filter paper preloaded with protamine and enters a thin layer of agarose gel containing the nanosensors where unbound protamine induces a color change. A camera is placed below to quantify the sensor response and correlate it to heparin concentration. This avoids sample pretreament and provides a rapid assay for heparin. As the nanosensors function in exhaustive mode (taking up all protamine until saturation), adjusting their composition may tune the response to different heparin ranges depending on the desired application.

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# An experiment for undergraduate students: Element analysis of dietary supplements using a nitrogen microwave inductively coupled atmospheric-pressure plasma optical emission spectrometer (MICAP-OES)

Gunnar Schwarz, Chiara Fabbretti, Bodo Hattendorf

Laboratory of Inorganic Chemistry, Department of Chemistry and Applied Biosciences, ETH Zürich,
Vladimir-Prelog-Weg 1, CH-8093 Zurich, Switzerland, schwarz@inorg.chem.ethz.ch

Quantitative analyses are a major part of analytical chemistry in academia, public service, and industry. Incorrect analyses can end in false conclusions in research, losses of production or for example incorrect drug compositions and therefore may have severe health consequences, respectively. Thus, laboratory experiments for quantitative analyses should be a part of academic education in chemistry and related sciences and train student in matters of related theory and practice.

A large portion of the considerable running costs of ICP-OES are caused by the required supply of argon as plasma gas, whereas the use of a nitrogen-based microwave inductively coupled atmospheric-pressure plasma optical emission spectrometer (MICAP-OES)[1,2] is more affordable and well-suited for lab courses in undergraduate education.

Some educational activities were presented in which nitrogen plasmas sources have already been presented for element analyses: Ricca et al. used a microwave plasma to identify cereal brands based on their element composition[3] and Muna reported on soil analyses using microwave plasma atomic emission spectroscopy.[4]

We present a new laboratory experiment in which students use a $N_2$MICAP-OES to determine several elements in dietary supplements and other consumer products. In contrast to most other lab experiments carried out in typical analytical lab courses, this experiment was designed so that students could and should follow their own approach to the task. Experimental details were not provided to the students in advance. Appropriate procedures included dissolving the sample and acid digestions that students could perform within the given time frame of 4 hours. We also show various ways in which the experiment can be adapted to provide different emphases on samples, sample preparation, calibration, the use of internal standards, and spectral interference. An evaluation revealed that this experiment was well received by students, but they asked for a more detailed handout.

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# Microfabricated Self-Referencing Pulstrodes

Ayian Speck[1], Elena Zdrachek[1], Tara Forrest[1], Davide Migliorelli[2], Silvia Generelli[2], Guillaume Bouilly[2],
Loïc Burr[2], Eric Bakker[1]

[1]Department of Inorganic and Analytical Chemistry, University of Geneva, Quai Ernest-Ansermet 30, 1221 Genève, Switzerland
[2] Swiss Center for Electronics and Microtechnology, Rue Jaquet-Droz 1, 2002 Neuchâtel, Switzerland
Ayian.Speck@unige.ch

With an ever-increasing world population and life expectancy, public health often ranks as the second sector in terms of budgetary spending worldwide. Finding ways to reduce the costs, whether it is in the preventive care or therapeutic domain, is a crucial component of developing a sustainable health system. As a result, Point-of-Care Testings (POCTs) and wearable sensors have attracted a tremendous interest in the past decades. As opposed to traditional analysis, which are costly and time-consuming, POCTs and wearable sensors present, among others, the following advantages: they are cost-effective and allow rapid or continuous measurements, which lead to better reaction time and thus fewer costly complications [1]. Electrochemical sensors in that regards represent a good example of POCTs.

The reference electrode is an essential component of an electrochemical system, resulting in a high research activity in that domain [2]. The gold standard remains the Ag/AgCl double junction reference electrode. However, owing to its electrolyte-filled inner compartment its design is cumbersome and impractical for wearable sensors applications, which require miniaturization. From that point of view, all-solid state reference electrodes provide a promising alternative.

Gao *et al.* proposed a solid-state reference electrode which relies on an Ag/AgI element and acts as a pulstrode to self-generate a reference potential [3]. The pulstrode protocol consists of four distinct steps: 1) potentiometric measurement of the initial state of the system (OCP), 2) a cathodic current pulse, leading to the reduction of $Ag^+$ into Ag and the local release of a controlled amount of iodide, 3) measurement of the EMF (reference pulse) 4) application of the original OCP to regenerate the system into its initial state. The protocol has proven its reliability in terms of precision and stability over cycles on a macro-electrode.

In the present context of finding a reference electrode suitable for miniaturized systems, this work investigates the use of the pulstrode protocol on inkjet-printed electrodes in collaboration with the Swiss Center for Electronics and Microtechnology (CSEM). The performance of the inkjet-printed electrodes as reference element are compared to a classical reference element (double-junction silver chloride reference electrode) for the quantification of major ions in biological matrixes.

Additionally, an attempt to improve the robustness of the described system against sample convection and sample density fluctuations was made by covering the electrode surface with an agarose gel layer.

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# Induction Mass Spectrometry Using a Hollow-Core Toroidal Coil

Janosch von Ballmoos[1], Davide Bleiner[1,2]

[1]Swiss Federal Laboratories for Materials Science and Technology (Empa), Überlandstrasse 129, 8600 Dübendorf, Switzerland
[2]University of Zurich, Winterthurerstrasse 190, 8057 Zurich, Switzerland
Author email: janosch.vonballmoos@empa.ch

Current state-of-the-art detectors used in mass spectrometry are based on electron multipliers. These detectors show a number of drawbacks, such as fast-signal distortion, dead time and the requirement of a trigger, and they require complex and expensive instruments. The ion signal is dispersed upfront by means of a mass analyzer (e.g. TOF) or filter (e.g. QMS). All these technologies are dead-end, in the sense they cannot be carried out online for process monitoring.

The use of a hollow-core toroidal coil (HTC) [1] as an induction sensor was previously shown [2] to be a powerful tool that can overcome all these limitations. The induced voltage in the HTC allows measuring changes in the magnetic flux, e.g. a plasma released through laser ablation. The Fourier spectrum of this response signal can then be used to serve as a fingerprint of each material. This sensor offers ultrafast ion spectroscopy of fast transients at high sensitivity and simplicity, requiring very small amounts of material.

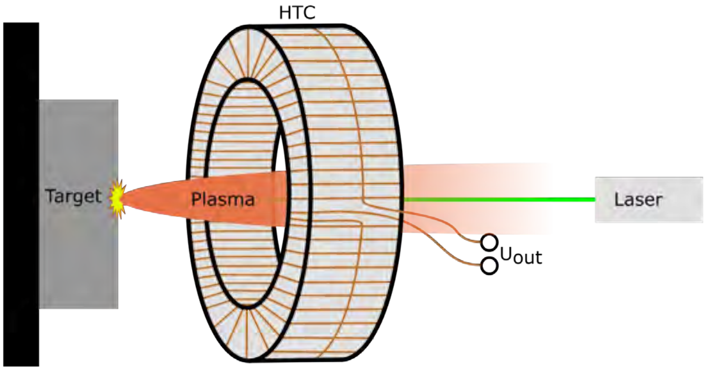

*Figure 1: Experimental setup*

In our work, we further investigated the characteristics of the HTC sensor by calibrating using ten metallic elements ranging from Aluminum as the lightest to Gold as the heaviest element. We show that the HTC sensor proves effective in enabling the differentiation of pure metals based on their unique response signal, revealing distinct patterns indicative of the respective elements. Through a newly written program, we were able to use cluster analysis or machine learning to assign measurements to the respective material automatically, achieving prediction accuracies between 73% and 100% depending on the metal. In addition, we also investigated the response signal for non-metallic compounds by measuring Lithium Fluoride as well as Calcium Fluoride.

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# Analytical Strategy to characterize Lake Geneva Colloidal Matter and associated Trace Metals

Isabelle Worms,[1] Nicolas Layglon,[2] Kevin Trindade,[1] Vera Slaveykova,[1] Laura Maloriol[2] and Mary-Lou Tercier-Waeber[2]

Department F.-A. Forel for Environmental and Aquatic Sciences[1] and Department of Inorganic and Analytical Chemistry [2], University of Geneva, 30 Quai Ernest Ansermet, Geneva

Isabelle.worms@unige.ch

This ongoing project is motivated by two important phenomena observed in summer 2022: significant blooms of cyanobacteria on Lake Geneva and Rhône River, downstream, and very high intensity with low frequency precipitations. These two phenomena, related to a severe heat wave, were expected to alter the natural cycle of organic matter (OM), and thus must affect the remanence of trace metals (TMs) whatever their forms (OM-complex; natural nanoparticles (NNPs)) in the surface of lakes.[1] It is thus important to set-up methodologies enabling the quantitative measurements of TMs preferential association to either OM or NNPs, both acting as TMs nano-carriers from sources to water reservoirs. In this study we present the first step towards the development of a methodology able to determine size-distribution of TMs, in low OM and NNPs containing waters: Lake Geneva, sampled at 2 different depths, 2 different seasons (summer, winter), impacted or not by precipitation events. A centrifugal-ultrafiltration method was first applied to concentrate the colloidal matter. Its impact on the losses of OM components, TMs, and effect on NNCs size distribution was addressed. Asymmetrical-flow fractionation link to multi-detectors including ICP-MS (AF4-MD-ICP-MS) analysis enable the in-depth size-elemental fingerprint of natural nanocomponents and associated TMs.[2] The methodology presented here allowed to gain in sensitivity for TMs size-speciation measurements compared to our previous study performed on Lake Geneva.[3] Our results also show that despite discrete changes in OM composition (based on fluorophores types and abundances), the elemental size-profiles of NNCs clearly varied according to depths and seasons but was not impacted by storm scenario, at the location chosen for the sampling. To date, the effects of external conditions, such as changes in OM composition, on toxic TMs behaviour under relevant environmental scenario (other than in polluted systems) is unclear and hinders our understanding of the key risks and issues associated to TMs detection according to their physico-chemical forms. The development and optimization of procedures which allow to maintain size-based speciation of TMs at ultra-low concentrations, open new opportunities to make a link between environmental toxic metals exposure doses, their bioavailability to aquatic organisms and their potential ecotoxicological impacts.

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# Self-Powered Smart Potentiometric Sensor with Relational Operation Function to Capture Concentration Excursions

Yaotian Wu and Eric Bakker

Department of Inorganic and Analytical Chemistry, University of Geneva, Quai Ernest-Ansermet 30, CH-1211 Geneva, Switzerland.

Yaotian.wu@etu.unige.ch

Potentiometric sensors give a spontaneous voltage response to ion concentration changes in the sample, which makes the technique promising for the realization of self-powered sensors. Previous work from our group has demonstrated that the ion-selective electrode (ISE) voltage signal may be harvested and stored by a capacitor connected in series with the electrodes. This voltage signal can be read out with a simple multimeter[1].

Based on this, our group proposed the first type of self-powered potentiometric sensor with memory.[2] A diode was placed in series with a capacitor in the circuit and with this design, only positive voltage changes may be recorded in the capacitor for the later readout at the end of the measurement. A $Zn/Zn^{2+}$ electrode was used as the reference electrode (RE) to overcome the forward voltage by hundreds of millivolts. Compared to a conventional Ag/AgCl electrode, the EMF of the ion-selective electrode against the Zn RE was lifted by about 1V, sufficient to charge the capacitor with a diode placed in series. Unfortunately, however, this sensor can only record the voltage deviation in a positive direction. The voltage change in the other direction cannot be remembered because of the single direction conductivity of the diode.

In this work, we describe a self-powered sensor capable of recording both positive and negative voltage fluctuations during a period of few hours for later readout. The principle is shown in Figure 1 below and uses two different operators to capture fluctuations in the positive and negative direction. Capacitor $C_1$ and diode $D_1$ are connected to the ISE and the Zn RE for recording the positive voltage change, as established.[2] To record the negative voltage change, the capacitor was first charged by the ISE and the Zn RE and subsequently the switch $S_{L1}$ was placed to position $P_2$ to place the diode into the circuit. The switch SL2 was then moved from position $P_3$ to $P_4$ to generate a voltage drop of about 1V across the capacitor $C_2$ and to overcome the forward voltage across the diode D2. Any further voltage decrease from the ISE is then recorded on the capacitor C2.

This work demonstrates a novel self-powered sensing principle that can record voltage perturbations away from a normal range over a period of hours. This sensor may be deployed as an affordable alternative option to monitor chemical changes in agriculture, aquaculture and biomedical applications.

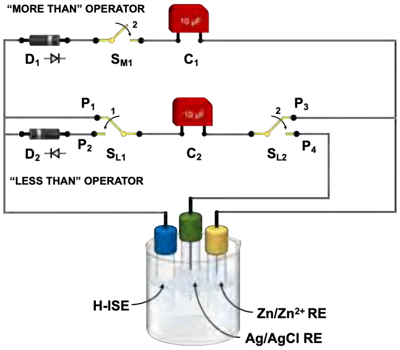

*Figure 1. Scheme of the sensor circuit. To overcome the forward voltage of the diode blocking the charge transfer, a dual reference electrode system was used here. By switching from the $Zn^{2+}$ RE to the Ag/AgCl RE, one may generate a voltage change of about 1V, which is sufficient to discharge the capacitor in series with the diode and transfer the chemical information into the capacitor.*

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# Probing Deuteration-Induced Phase Separation in Supported Lipid Monolayers using Tip-Enhanced Raman Spectroscopy

Chengcheng Xu, Naresh Kumar, Renato Zenobi

Department of Chemistry and Applied Biosciences, ETH Zurich
Vladimir-Prelog-Weg 3, 8093 Zurich (Switzerland)
chengxu@ethz.ch

Deuterium labelling is a common strategy to track the distribution of molecules in biological samples.[1][2] However, the alteration of biophysical properties caused by deuteration is not well understood yet. Conventional analytical tool lacks the sensitivity and spatial resolution to investigate this at the nanoscale. Herein, we demonstrate that hyperspectral tip-enhanced Raman spectroscopy (TERS) imaging is an effective tool to visualize deuteration-induced phase separation in a mixed dipalmitoylphosphatidylcholine monolayer (DPPC:$d_{62}$-DPPC at 1:1) supported on Au(111) surface. The DPPC:$d_{62}$-DPPC monolayer was transferred onto the Au(111) surface via the Langmuir Blodgett technique. Successful monolayer transfer was confirmed via topography measurements using atomic force microscopy. Since $d_{62}$-DPPC has a strong C-D stretching signal ($I_{C\text{-}D}$) in the silent region of the Raman spectrum from 2000 cm$^{-1}$ to 2200 cm$^{-1}$, and DPPC has a strong C-H stretching signal ($I_{C\text{-}H}$) from 2800 cm$^{-1}$ to 3000 cm$^{-1}$, the $I_{C\text{-}D}$ / $I_{C\text{-}H}$ ratio was used to visualize the phase separation. In TERS images, there were distinct DPPC-rich and $d_{62}$-DPPC-rich domains, which can be attributed to the differences in the molecular size and polar/non-polar interaction between the deuterated and non-deuterated chains of the $d_{62}$-DPPC and DPPC molecules. Finally, the size and polarity of $d_{62}$-DPPC and DPPC were quantitatively examined using LC-MS and correlated with their phase separation behaviour. The novel insights gained in this work expand our biophysical understanding of supported lipid membranes.

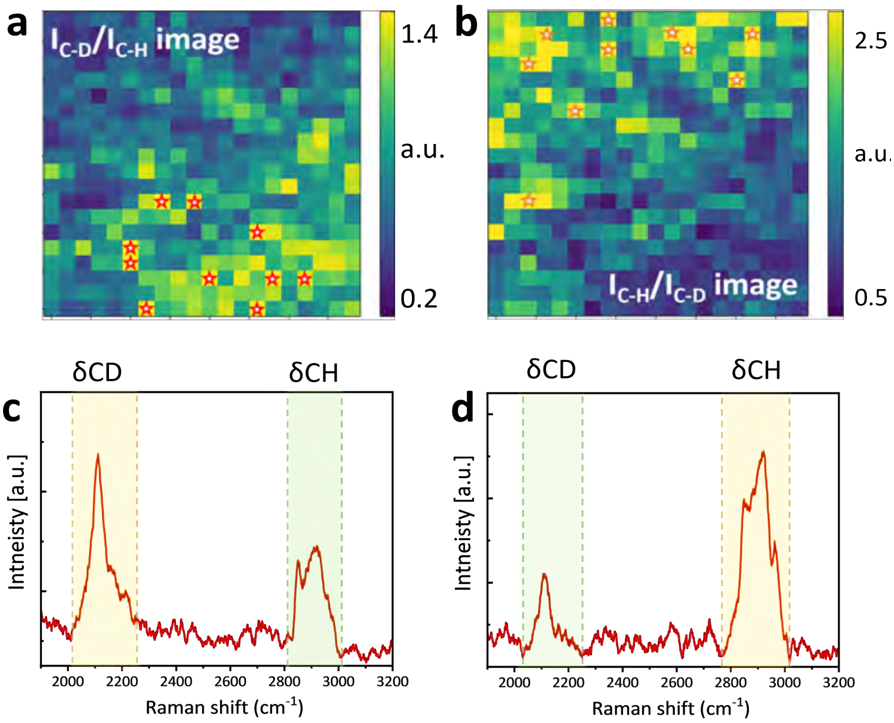

**Figure 1.** TERS images of the (a) $I_{C\text{-}D}/I_{C\text{-}H}$ and (b) $I_{C\text{-}H}/I_{C\text{-}D}$ ratio showing phase separation of the DPPC:$d_{62}$-DPPC domains. Averaged TERS spectra at the locations marked in Panels (c) a and (d) b.

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# Direct Covalent Attachment of Ion-Selective PVC Membrane Onto the Substrate for Improved Characteristics

Yupu Zhang, Tara Forrest, Eric Bakker*

Department of Inorganic and Analytical Chemistry, University of Geneva, Quai Ernest-Ansermet 30, CH-1211 Geneva, Switzerland

Yupu.zhang@unige.ch

Solid-contact ion-selective electrodes (SC-ISEs) have demonstrated considerable potential in various fields such as environmental monitoring, bioanalytical measurements, and wearable sensors over the past decades. In recent works, conducting polymers including POT, PEDOT, and PPy have been widely used as ion-to-electron transducers for SC-ISEs, which significantly improve their ion response stability by preventing water layer formation. However, the reproducibility of standard potential (E0) is still one of the most significant and common problems to be solved [1]. Otherwise, it is necessary to calibrate each electrode before use, which is not desired.

To improve the E0 reproducibility for SC-ISEs utilizing conducting polymer as transducers, various strategies have been employed, such as the prepolarization of the conducting polymer layer or outer coating methods. [2, 3] For instance, the Lindfors group achieved significant enhancement in E0 reproducibility by prepolarizing the conducting polymer before the deposition of the polymer membrane cocktail [2]. Joon et al. improved the stability of the E0 by simply adding an outer layer of silicone rubber, which also exhibited potential in reducing biofouling [3].

We present here a novel strategy by creating a direct covalent linkage between the ion-to-electron transducer layer and the ion-selective membrane layer using click reaction. Specifically, CuAAC-based click chemistry was employed to covalently attach a thin layer of PVC onto the transducer layer that is either directly functionalized with ion sensing components or followed by the deposition of a second PVC layer with ionophores, ion exchangers, and plasticizer either through spin coating and drop-casting.

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