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Societal Challenges, Analytical Solutions

Keynote speakers

K-01 Analytical chemistry for a sustainable world

Peter Kuipers Munneke

“Analytical chemistry is indispensible in understanding past climate, in monitoring current environmental pollution, and in shaping the future of energy, materials, and food.”

Peter Kuipers Munneke Peter Kuipers Munneke (1980) is polar researcher at the Institute for Marine and Atmospheric research Utrecht at Utrecht University. He investigates how the large ice sheets in Greenland and Antarctica respond to global warming. He has (co-)authored more than 50 peer-reviewed papers. He is also tv weatherman at NOS, the largest public broadcast organization of The Netherlands. In recent years, he reported about climate change from the polar regions, presented a podcast on the weather, and toured Dutch theatres together with pianist Ralph van Raat with their music and science programme “Counting Eskimo Words for Snow”.

K02 Analytical tools in support of a toxic-free environment

Juliane Hollender

“Analytical chemists can support regulators and industry to address global challenges and improve environmental quality and human health”

Juliane Hollender is head of the department Environmental Chemistry at Eawag as well as adjunct professor at ETH Zurich. After a diploma in chemistry and a PhD in environmental engineering, she worked for 10 years at the RWTH Aachen in Germany before she moved to Switzerland in 2005. Her research concentrates on target, suspect and non-target screening of micropollutants combining high resolution mass spectrometry with chemometrics and the fate of organic micropollutants in the natural and engineered aquatic environment. She has coauthored more than 200 peer-reviewed publications (h-index 66, google scholar) and belonged in 2019 and 2020 to the highly cited scientist in the field of environment and ecology (web of science). She is member of the research council of the Swiss National Science Foundation and part of the steering committee of the network of reference laboratories, research centres and related organisations for monitoring of emerging environmental substances (NORMAN).

K03 Analytical chemistry for a sustainable world

Emmanuel Delamarche

“It is easy to make complicated devices and concepts, but much harder to find simple and elegant solutions - and this is so true with microfluidics and diagnostic devices!”

Dr. Delamarche is leading activities on Precision Diagnostics at IBM Research - Zurich with the goal of using expertise in micro/nanotechnology and biochemistry for solving important problems in biology and medicine. His main projects deal with the development of portable and precise diagnostic devices and the development of a non-contact scanning microfluidic probe for analyzing biological interfaces. He is also a Lecturer at ETH Zurich and a contributor to scientific panels for governmental agencies and research institutions. He published over 120 papers and is co-inventor on more than 70 patent families. He has received numerous awards from IBM, was named “Master Inventor” by IBM, and received the Werner prize of the Swiss Chemical Society in 2006 and Langmuir Lecture Award in 2020. Dr. Delamarche studied chemistry and received a degree in supramolecular chemistry in 1992 from the University Paul Sabatier of Toulouse in France and his Ph.D. in biochemistry in 1995 from the University of Zurich.

K-04 Vaccine Development and the COVID-19 pandemic

Jerome Custers

“Advances in analytical chemistry will be one of the key enablers in vaccine development supporting progress in vaccine characterization, release and quality control”

Jerome Custers, Ph.D., is Senior Scientific Director Vaccine Research, Viral Vaccines at Janssen, Pharmaceutical Companies of Johnson and Johnson. He joined Janssen in 2011 through the acquisition of Crucell Holland BV, a Dutch Biotech company he joined back in 2002 as a research scientist to work on the development of vaccines against a variety of infectious diseases based on adenoviral vectors. Genetic engineering of viruses has been at the core of the vaccine research performed with the last years expanding into structural vaccinology for antigen design and RNA vaccines for antigen delivery. Jerome co-authored more than 50 peer-reviewed scientific articles and more than 25 patent applications. Jerome was trained as a molecular biologist and prior to joining Crucell he worked for 8 years in the biotechnology industry (Syngenta). He obtained his PhD from the University of Wageningen, The Netherlands in 2007. Jerome’s current responsibilities include vaccine platform development, design of novel vaccine candidates and prototype vaccine development. His team has been instrumental in developing the Adenoviral vector platform technology that has resulted in the successful development of two authorized vaccines (Ebola and COVID-19) and several investigational vaccines in development. His team developed >10 prototype covid-19 vaccines and selected the Janssen Ad26.COV2.S vaccine as lead candidate, now licensed under Emergency Use in several countries across the globe.

K-05 Infrared Ion Spectroscopy: new opportunities for small-molecule identification in MS analysis

Jos Oomens

“Integrating mass spectrometry with IR spectroscopy brings us the best of both worlds: sensitivity, selectivity & structure!”

Jos Oomens obtained his PhD degree from Radboud University (Nijmegen, NL) in 1996 on a topic in molecular laser spectroscopy. Since 1999, he has been developing methods that integrate mass spectrometry and infrared spectroscopy applying the radiation from the free-electron laser FELIX. IR spectra can now be routinely recorded for mass-selected molecular ions and this is exploited in fundamental molecular sciences as well as in analytical applications. The ability to record an IR spectrum for a single mass peak within complex mixtures provides unique opportunities to assign accurate molecular structures in mass spectrometry workflows, which is applied for instance in metabolomics, environmental sciences and forensics. In 2009, Oomens became Professor by special appointment at the University of Amsterdam (UvA) and in 2011, he received an NWO VICI grant to investigate fundamentals of the dissociation chemistry occurring in MS/MS reactions using ion spectroscopy. In 2013, he was appointed as full professor at Radboud University. He (co-)authored more than 350 peer-reviewed papers (H-index 50), the large majority of which on IR ion spectroscopy and its various applications.

K-06 Spectral imaging for direct analysis of foods: overcoming challenges through chemometrics?

Aoife Gowen

Aoife Gowen is a Professor in the School of Biosystems and Food Engineering at University College Dublin in Ireland. Her research area is multidisciplinary, involving applications of Spectral Imaging and chemometrics to biological systems, including foods, microbes and biomaterials.
After completing her undergraduate degree in Theoretical Physics in 2000, she moved to the highly applied research area of Food Science. Her PhD thesis, completed in 2006, concerned mathematical modeling of food quality parameters and optimization of food process operations. During her time as a post-doctoral researcher and Marie Curie fellow in Dublin and Japan she investigated the intersection of near infrared spectroscopy, imaging and chemometrics for characterization of biological systems.
In 2014 she set up the Spectral Imaging research group in UCD and has expanded her team through EU and nationally funded grants, including European Research Council starting and proof of concept grants. She is editor in chief of the Journal of Spectral Imaging and has developed new research-informed modules in spectral imaging and sensors for undergraduate and graduate students.

K-07 Emerging global food security and food Safety challenges and related analytical solutions

Rudolf Krska[1,2] and Martin Wagner [3]

[1] *University of Natural Resources and Life Sciences, Vienna, Department of Agrobiotechnology IFA-Tulln, Institute of Bioanalytics and Agro-Metabolomics , Konrad-Lorenz-Str. 20, 3430 Tulln, Austria (rudolf.krska@boku.ac.at)*
[2] *Institute for Global Food Security, School of Biological Sciences, Queens University Belfast, University Road, Belfast, BT7 1NN, Northern Ireland, United Kingdom*
[3] *Unit of Food Microbiology, Institute of Food Safety, Food Technology and Veterinary Public Health, University of Veterinary Medicine Vienna, 1210 Vienna, Austria*
[4] *Austrian Competence Center for Feed and Food Quality, Safety and Innovation (FFOQSI GmbH), 3430 Tulln, Austria*

Abstract

Zoonoses and extreme weather events in Europe, compounded by the COVID-19 pandemic, have shone a spotlight on the underlying vulnerability of our global food systems[1], they are a wakeup call that must be heeded. Weaknesses triggered by isolated events such as a zoonotic agent or a carcinogenic mycotoxin will be heavily compounded in the years to come by climate change, a shift in our food system towards a more plant-based diet, and the need for a recircular economy. Food safety management systems which have been established to tackle foodborne hazards, including bacteria, parasites, toxins (chemical hazards) and allergens in European farming and food businesses need to be adapted to make them more robust towards changes affecting our global food systems, resulting in proactive risk management that can make the EU food system future-proof.

The contamination of food by microbial agents is a worldwide public health concern and results in a dramatic loss of food due to raw food spoilage, most likely in developing countries, food wasting or even foodborne poisoning. Climate-based impacts, such as heavy rainfalls, lead to a higher contamination rate of plant food sources and extensively housed farm animals. Re- and cross-contamination scenarios including the growing research on persistence of microbiota highly adapted to conditions of modern food production triggered by microbiome studies show an emerging risk for microbial transmission at the processing level. Chemical contaminants in food are still an important food-borne public health concern in Europe [2] . Particularly, unintentionally present chemical contaminants in food, such as environmental and food process contaminants (e.g. furans) and natural toxins (esp. mycotoxins and plant toxins), can pose public health concerns if their concentrations are not kept at appropriately low levels as dictated by legislation.

This paper will centre on the advancement of innovations to combat selected (emerging) microbial and chemical contaminants based on cutting edge science. In cooperation with stakeholders the authors have also identified areas of microbial and chemical food safety that have not been adequately or sufficiently been addressed by previous research.

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K-08 What data analysis and chemometrics methods can offer to solve environmental problems?

Romà Tauler

IDAEA-CSIC, Barcelona

Roma.Tauler@idaea.csic.es

Chemometrics has consolidated and expanded its contribution to different scientific and technological fields, because of its success in the resolution of problems in various fields, like for example, in environmental and omics sciences, and in general because of its role in the analysis of large volumes of data (BigData). Application of data analysis and chemometric methods helps us to improve the understanding of global challenges and of human impacts on the environment and provide efficient tools for environmental risk assessment and management. Pollution and toxic chemical compounds are a threat for the environment and human health which need urgent measures and actions. Environmental monitoring studies produce huge amounts of multivariate analytical data stored in large data sets. The bottle neck in the study of these environmental data tables is their analysis and interpretation. There is a need for chemometrics analysis of these big data tables. There is also at present an urgent need for an improvement, dissemination and automation of all the steps of data analysis of high throughput analytical 'big' omics type of data (genomic, transcriptomics, proteomics, metabonomics, lipidomics,…) using chemometric methods to assess the effects and risks of environmental pollutants and stressors. Examples of application of recently developed chemometric methods to solve environmental problems related with water and air quality and to assess the effects and risk of environmental pollutants and hazards will be presented and discussed.

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Oral presentations

O-00 Advancing mass spectrometry to study nucleic acid structures and interactions

Valérie Gabelica

[1] *Univ. Bordeaux, Inserm & CNRS, ARNA Laboratory, Institut Européen de Chimie et Biologie, 2 rue Robert Escarpit, 33600 Pessac, France.* v.gabelica@iecb.u-bordeaux.fr

Abstract

Our aim is to decipher the relationships between structures and energetics—Angstroms and Calories—in non-covalent complexes. Non-covalent interactions govern the structure and function of myriads of systems, from supramolecular assemblies to biological complexes. Function is linked to structure, but also to energetics: How prevalent is a structural form? How does it switch to other states? How fast? To bridge the gap between structure and energetics, our team develops new mass spectrometry approaches to separate, quantify, and structurally characterize the different ensembles of structures (the different states) simultaneously present in solution.

This presentation will survey recent developments of mass spectrometry and associated techniques (ion mobility spectrometry and ion spectroscopy) for nucleic acids biophysics. Specifically, with mass spectrometry, we characterize the stoichiometries of all complexes simultaneously present. Experiments can be carried out at equilibrium,[1] as a function of time,[2] or as a function of temperature.[3] Another dimension of information is provided by ion mobility spectrometry, which measures the electric drag of ions at each *m/z* in an inert gas such as helium. The collision cross sections inform us on the shape of each population, and we use molecular modelling to deduce the shapes of each structure.[4-8] Finally, ion spectroscopy measures spectroscopic properties (either vibrational[9,10] or electronic[10,11]) of each ion packet, to get additional insight into the secondary structures.

We will present here in more detail the feasibility of circular dichroism ion spectroscopy to characterize nucleic acid complexes, for which the secondary structure is defined by the base stacking arrangements.[12] The groundbreaking aspect was to make circular dichroism ion spectroscopy feasible for large biomolecule ions. But our work also opens new doors to measure chirality directly within the mass spectrometer. Indeed, mass spectrometry is essentially blind to chirality. Our research opens the door to a wide range of applications, taking advantage of the mass separation and circularly polarized light to characterize other chiral molecules.

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O-01 Fate of Gd-based contrast agents in the body and the environment

Marcel Macke[1], Patrick Bücker[1], Sabrina Funke[1], C. Derrick Quarles, Jr.[2], Michael Sperling[1,3] and Uwe Karst[1]

[1]University of Münster, Institute of Inorganic and Analytical Chemistry, Corrensstr. 30, 48149 Münster, Germany
[2]Elemental Scientific, Inc., 7277 World Communications Drive, Omaha, NE 68122, USA
[3]European Virtual Institute for Speciation Analysis, Corrensstr. 30, 48149 Münster, Germany

Since more than 25 years, gadolinium-based contrast agents (GBCAs) are successfully used in magnetic resonance imaging, one of the most important modern tools for medical diagnostics. As the contrast agents are excreted via the kidneys, these highly polar compounds enter the wastewater streams and mostly pass through the wastewater treatment plants to enter the aquatic environment.

To investigate the distribution and fate of GBCAs in water samples, powerful methods of speciation analysis are required. A fully automated single platform approach for total metal analysis and syringe-driven anion exchange chromatography in combination with ICP-MS was developed to identify and quantify several contrast agents in environmental and in drinking water samples with limits of detection in the mid-picomolar range.

As many studies have recently shown a deposition of Gd from GBCAs in the human body, including bones, skin and several areas of the brain, laser ablation (LA)-ICP-MS methods were developed for the analysis of gadolinium and endogenous elements in human and animal tissue samples.

O-02 Modern voltammetric methods 100 years after the discovery of polarography Where we are and where we are heading

Jiri Barek

Charles University, Faculty of Science, UNESCO Laboratory of Environmental Electrochemistry, Hlavova 2030/8, CZ-128 43 Prague 2, Czech Republic;
e-mail : barek@natur.cuni.cz

Abstract

The discovery of polarography 100 years ago [1] opened new possibilities in analytical chemistry which are strongly reflected in recent research of our UNESCO laboratory of environmental electrochemistry. The presentation will focus on novel electrode materials (e.g. boron doped diamond [2], glassy carbon [3], silver solid amalgam [4], carbon film composites [5], carbo nanotube paste [6], reduced graphene oxide [7] and some other non-traditional materials and arrangements and their application for monitoring of biologically important organic compounds important from the point of view of the protection of human health and environment. Critical comparison of different novel electrode materials and their advantages and disadvantages in comparison with liquid mercury (as so far unsurpassed and nearly ideal electrode material) will be presented.

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O-03 Multimodal characterization of microplastics in drinking water

Clementina Vitali[1], Ruud J.B. Peters[1], Hans-Gerd Janssen[2,3], and Michel W.F. Nielen[1,3]

1 Wageningen Food Safety Research, Wageningen University & Research, Akkermaalsbos 2, 6708 WB Wageningen, NL.

2 Unilever Foods Innovation Centre – Hive, Bronland 14, 6708 WH Wageningen, NL.

3 Wageningen University, Laboratory of Organic Chemistry, Stippeneng 4, 6708WE, Wageningen, NL

Abstract

The mismanagement of plastic waste and its accumulation in the environment has resulted in the presence of microplastic (MPs) and nanoplastics (NPs) in the food chain and the exposure of consumers. A new drinking water directive was published in 2019 by the European Commission (EC) stating that water companies will need to measure concentrations of microplastics within two years for positive release and inspection. The Marie Sklodowska-Curie MONPLAS project – involving academic institutions and equipment manufacturers and end-users – aims to develop methodologies and technologies for the robust, easy and low cost determination of MPs and NPs.

Several parameters have to be assessed in order to fully characterize MP contamination: number of particles, particle size, particle size distribution, particle shape, chemical composition, and particle mass. Currently, no single analytical of physical method is able to provide all this information. Optical techniques, used to measure and count the particles, can be combined with vibrational spectroscopic techniques for their chemical characterization. However, those techniques are subject to interference related to aging, weathering, surface contamination, and chemical damage of the micro and nano particles' surface.

In this presentation we propose the combined detection and quantification of MPs by Nile red staining and fluorescence microscopy plus chemical characterization of individual particles by ambient ionization mass spectrometry (MS) using an Atmospheric Solids Analysis Probe (ASAP). Compared to infrared techniques, this multimodal characterization method excels in the discrimination of MP polymers belonging to the same chemical class and in the identification of polymer mixtures. The method overcomes the interference from MP surface contamination and, as a bonus, enables the MS characterization of the adsorbed contaminants.

Acknowledgement

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Contact information

Clementina Vitali, MSc | clementina.vitali@wur.nl | +31 634329983
Ruud J.B. Peters, PhD | ruudj.peters@wur.nl
Hans-Gerd Janssen, prof.dr.ir. | hans-gerd.janssen@wur.nl
Michel W.F. Nielen, Prof.dr. | michel.nielen@wur.nl

O-04 Automated analysis of biopharmaceuticals using multidimensional liquid chromatography - mass spectrometry

Christoph Gstöttner[1], Elena Domínguez-Vega[1]

[1]*Center for Proteomics and Metabolomics, Leiden University Medical Center, Leiden, the Netherlands*

Abstract

Novel biopharmaceuticals are very diverse ranging from proteins to viruses. Monoclonal antibodies (mAbs) have been employed already for many years and still continue being the most selling biopharmaceuticals in the market. On the other hand, gene therapy products based on adeno-associated viruses (AAVs) are recently receiving a lot of attention due to their capabilities to treat genetic diseases. Both, mAbs and AAVs, consist in complex molecules, exhibiting a wide range of structural and functional heterogeneities that need to be extensively assessed. This assessment is very time consuming and often rely on multiplatform approaches contributing to the high cost of these type of molecules. Automation is key for speeding the process and save hands-on time contributing to a decrease on production cost.

We have been exploiting the capabilities of multidimensional liquid chromatography hyphenated with mass spectrometry for the automation of sample preparation and analysis of biopharmaceuticals. We have employed a commercial 2D-LC system from Agilent Technologies complemented with additional modules and an additional macro. MS detection was performed using an Impact QToF from Bruker.

Characterization of mAbs is commonly performed by bottom-up approaches, involving sample preparation and peptide analysis by liquid chromatography-mass spectrometry (LC-MS). Sample preparation for conventional bottom-up approaches is very time consuming and can increase the risk of inducing artificial modifications as many off-line steps (denaturation, reduction, alkylation and digestion) have to be performed. Other drawbacks, includes long incubation times (several hours) and low efficiency of tryptic digestion. To overcome these issues, we developed a multidimensional LC (mD-LC) set-up for fast routine analysis of formulated conventional mAbs and newer antibody formats. The applicability of the method was demonstrated by the analysis of different (stressed and non-stressed) mAbs. This new automated approach enables mAb characterization in less than 2h with sequences coverages between 96-98%. The proposed mD-LC approach permitted the direct injection of formulated mAb samples without the need of any sample preparation or pre-separation of antibody variants. Furthermore, we extended this concept to characterize new therapeutic products, such as gene therapy products. AAV quality assessment require between others assessment of empty/full AAV ratios and characterization of viral proteins after manual disassembly. We developed an automated approach, which is able to separate full and empty viruses, allows online capsid disassembly and permits separation of viral proteins (VP1, VP2, VP3) and their mass spectrometric and fluorescence detection in one single platform.

Optional:

O-05 Analysis of short-chain fatty acids in exhaled breath for non-invasive monitoring of gut microbiome health

Joris Meurs[1], Ben Henderson[1], Evangelia Sakkoula[1], Carlijn R. Lamers[2,3], Guilherme Lopes Batista[1], Dušan Materić[1,4], Carlo G. Bertinetto[1], Coen C.W.G. Bongers[5], Neeltje A.E. Allard[5], Thijs M.H. Eijsvogels[5], Rupert Holzinger[4], Frans J.M. Harren[1], Jeroen J. Jansen[1], Maria T.E. Hopman[5] and Simona M. Cristescu[1]

[1] Radboud University Nijmegen, the Netherlands; [2] Wageningen University & Research, the Netherlands; [3] Hospital Gelderse Vallei, Ede, the Netherlands; [4] Utrecht University, the Netherlands; [5] Radboud University Medical Center, Nijmegen, the Netherlands

Abstract

Short-chain fatty acids (SCFAs) are metabolites formed in the gut as a result of bacterial fermentation of dietary fibers and resistant starches. These metabolites play an important role in regulating human health, particularly helping to reduce the risk of inflammatory diseases, digestive disorders and type 2 diabetes. SCFAs are also important mediators for microbiota-gut-brain crosstalk. Among all the SCFAs present in the human colon, acetic, propionic and butyric acid account for 95%. Acetic acid is an energy source for muscles and regulates the pH in the gut. Both propionic and butyric acid have anti-inflammatory properties.

During a study investigating the potential use of exhaled breath in relation to dietary quality (https://nutrishield-project.eu/), we were able to identify these SCFAs in exhaled breath using proton transfer reaction – time-of-flight – mass spectrometry. With the use of random forest regression, SCFAs, among other volatile organic compounds (VOCs) in exhaled breath, were identified as predictive VOCs for assessing dietary quality. Furthermore, we optimized the PTR-ToF-MS instrumental parameters, defined which product ions were formed and validated the methodology using chemical standards and exhaled breath samples. Excellent linearity ($R^2 > 0.99$) over a wide part-per-billion volume (ppbV) range and breath-to-breath repeatability (<15% relative variation) were achieved. With a validated method, new opportunities for real-time monitoring of SCFAs in exhaled breath during e.g. drug or dietary intervention studies become possible.

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O-06 Sulfated Glycans in the Gas Phase: An Infrared Spectroscopy Study

M. Lettow[1,2], M. Grabarics[1,2], K. Greis[1,2], G. Meijer[1], G. von Helden[1], K. Pagel[1,2]

[1]*Fritz Haber Institute of the Max Planck Society, Berlin, Germany,*
[2]*Institute of Chemistry and Biochemistry, Freie Universität Berlin, Berlin, Germany*
**Contact information presenting author: maikelettow@fhi-berlin.mpg.de, 0049 30 8413 5741*
grabarics@fhi-berlin.mpg.de, greiskim@fhi-berlin.mpg.de, meijer@fhi-berlin.mpg.de, helden@fhi-berlin.mpg.de, kevin.pagel@fu-berlin.de

Abstract

Glycosaminoglycans are a class of complex, often highly sulfated saccharides possessing a linear, repetitive core of disaccharide units. They are especially prominent on cell surfaces and in the extracellular matrix. Involved in various physiological and pathological pathways, they can interact with soluble and membrane proteins, as well as components of the extracellular matrix. The analysis and sequencing of glycosaminoglycans is generally challenging due to the coexistence of isomers from possible sulfation at various sites and epimerization of hexuronic acid residues. The spontaneous neutral loss of sulfates further complicates their identification in mass spectrometry (MS) experiments.

The potential of (MS)-based infrared (IR) spectroscopy for the structural analysis of peptides, proteins and smaller glycans has been successfully demonstrated throughout the last years. Recently, we explored its potential to record highly resolved IR spectra of sulfated glycans. We found that the spectral region, in which vibrational modes of sulfate functional groups are typically found, contains a number of well-resolved spectral features. Cryogenic temperatures and the choice of the charge state have been found to significantly improve the spectral resolution. Cryogenic IR spectra of glycosaminoglycans up to pentasaccharides were recorded.[1] Chondroitin disaccharides with extensive variation in sulfation[2] and heparan sulfate diastereomers[3] were unambiguously distinguishable based on their IR signature. Combined with quantum chemical calculations, the IR spectra revealed an interesting insight into the conformational landscape of the sulfated glycans in MS experiments. In the future, cryogenic IR spectroscopy could complement existing MS-based workflows in the structural analysis and sequencing of glycosaminoglycans.

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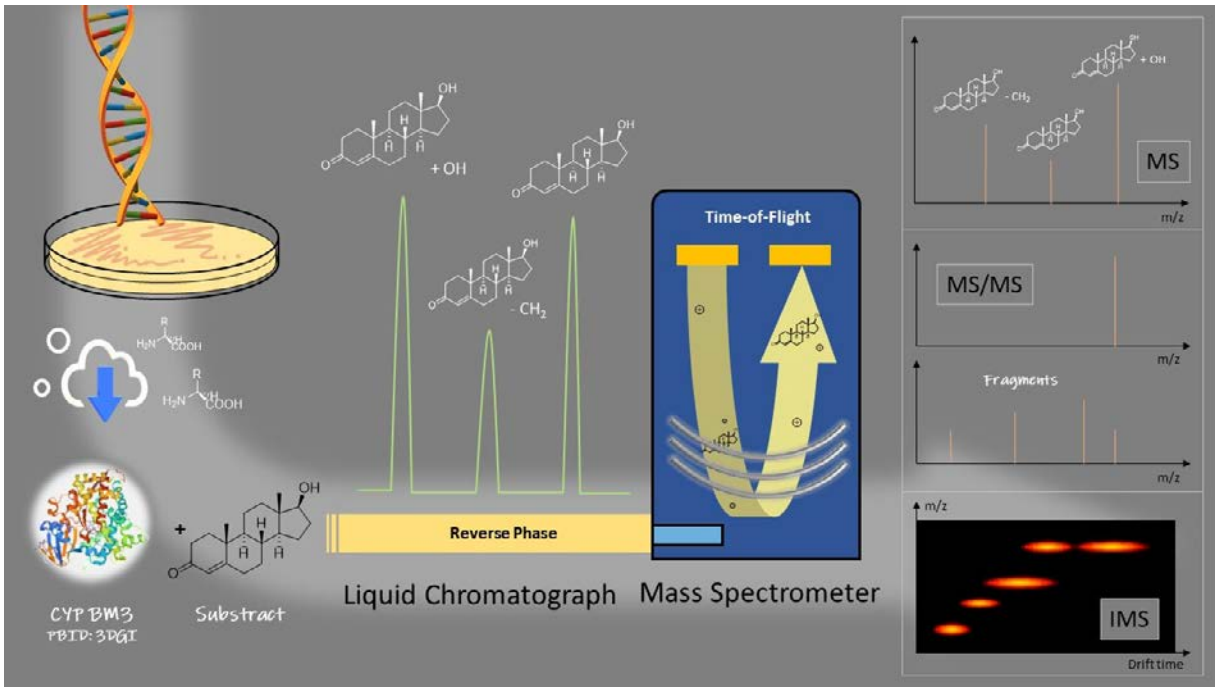
O-07 LC-MS/MS-IMS METHOD FOR UNKNOWN METABOLITES IDENTIFICATION

Yuandi Zhao[1], Kim Freulings[1, 2] and Maarten Honing[1]

[1] Maastricht Multimodal Molecular Imaging Institute (M4i), University of Maastricht, the Netherlands

[2] Zuyd University of Applied Sciences, the Netherlands



Cytochrome P450 monooxygenases (CYPs) play an essential role in metabolizing a wide range of xenobiotics. Among CYPs family, CYP BM3 from Bacillus megaterium is a very interesting candidate, which is a highly stable enzyme and possesses the highest activity.
A liquid chromatograph-tandem mass spectrometry-ion mobility spectrometry (LC-MS/MS-IMS) method has been developed to screen the mutants biocatalytic activity, besides the structural identification of the metabolites formed. Here, MS/MS is expected to generate structural information of the unknowns based on the fragments formed after collisional activation. However, in the case, the mass-to-charge ratios (m/z) of the metabolites and their fragments remain identical, since they cannot be distinguished. An IMS method can be added to the separation. The unknown metabolites can be differentiated based on their shapes, which will lead to possible several peaks observed in the mobilogram. Therefore, LC-MS/MS-IMS can be used as a novel method not only for the screening of bioactivity metabolism, but also can be used for the structure identification of unknown metabolites.
In this communication we will discuss the application of different analytical strategies using LC hyphenated MS/MS – IMS for the tentative structural identification of unknown small molecules.

O-08 Method development for the monitoring of various components in cell culture medium by capillary and microchip electrophoresis

Debbie van der Burg[1,2], Leila Josefsson[3], Saara Mikkonen[3], Véronique Chotteau[3], Åsa Emmer[3], Hermann Wätzig[2], Cari E Sänger – van de Griend[1,4]

[1] Kantisto BV, Baarn, the Netherlands, [2] TU Braunschweig, Braunschweig, Germany, [3] KTH Royal Institute of Technology, Stockholm, Sweden, [4] Uppsala University, Uppsala, Sweden

Abstract

Efficient and safe bio-production is critical for biopharmaceuticals; hence it is essential to improve upstream process monitoring. We work on developing an analytical control and sensing platform for continuous monitoring and automated feedback control of the upstream process. The platform consists of on-line and at-line sensors and detection methods to analyse multiple factors in the cell culture and the produced drug protein. Methodologies available in literature are generally not suitable, as the platform is a miniaturised closed system, supposed to run unattended for the duration of the upstream process with automated sample preparation, analysis and data processing. This means that requirements for robustness, precision, accuracy, sensitivity, flexibility etc. are high. The current presentation will show preliminary results of vitamin and mAb quantification using conventional CE and the quantification of mono- and disaccharides in cell culture medium on microchip CE.

Experiments were performed on capillary and microchip electrophoresis systems. BGEs were developed to enhance selectivity of the analytes against the complex cell culture medium, to avoid absorption of cell culture media components, to increase tolerability for antifoaming agents, cell debris, and other components in the cell culture medium, and to enhance the overall robustness of the system, keeping in mind the transferability to microchip CE.

The saccharide quantification method was developed on conventional CE and then transferred to CE-chip. The LIF-derivatisation protocol for saccharide quantification was developed to fit into an automated monitoring platform, so drying steps were avoided and toxic chemicals were replaced. The derivatisation process was optimised using design of experiments (DoE). As proof-of-principle for the use of this method in an integrated monitoring system, a standard saccharide mixture, cell culture medium, and spent cell culture medium were analysed with microchip CE. Separation was comparable to separation on capillary and all five saccharides were separated within 5 minutes. The medium and the spent medium sample show a glucose peak and no interfering peaks from the cell culture medium.

The developed saccharide method showed good transferability from conventional CE to microchip CE. With additional testing on microchip CE and online APTS-derivatisation, the method can be integrated in an automated monitoring platform with integrated calibration and data analysis. This good transferability also shows potential for the transfer of the vitamin and mAb quantification methods from conventional CE to microchip CE.

Acknowledgement

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Contact details: Debbie van der Burg, vdburg@kth.se, +46734821255

O-09 Glycoproteomic Analysis of Plasma PSA by RP-LC-MS using Isobaric Labels

Wei Wang[1], Jan Nouta, Peter van Veelen[1], Manfred Wuhrer[1], Guinevere S.M. Lageveen-Kammeijer[1]

[1] Center for Proteomics and Metabolomics, Leiden University Medical Center, Netherlands

Abstract

Prostate cancer (PCa) is one of the most frequent cancers in men.[1] As an early screening method the concentration of the glycoprotein prostate-specific antigen (PSA) is measured in serum. Even though this clinical test is applied worldwide, it exhibits a rather low sensitivity, specificity and moreover a poor predictive value.[2] Literature suggests that knowledge on specific alterations in the glycosylation profile of PSA may provide a way for more specific yet non-invasive PCa diagnosis.[3] To gain a better understanding of the alterations of molecular features of PSA glycosylation (*e.g.* antenna modification and core fucosylation) as well as its many different proteoforms, this study is focused on the in-depth analysis of the PSA *N*-glycome derived from the circulation in a highly sensitive manner (PSA concentration > 3 ng/mL).

PSA was captured from 4 mL of plasma using an antiPSA antibody followed by tryptic digestion. To distinguish differently linked sialylated isomers, sialic acids were derivatizated in a linkage specific manner. As, the peptide backbone of tryptic glycopeptide of PSA is only two amino acids long (sequence NK), the glycopeptides are not retained on a C18 column.. Therefore, tandem mass tag (TMT) labeling was introduced to increase the hydrophobicity of the glycopeptides. In addition, TMT labeling opens up the opportunity to introduce multiplexed quantification. Reverse phase liquid chromatography hyphenated with mass spectrometry (RPLC-MS) was used for the analysis.

PSA was succesfuly isolated from plasma by immunoaffinty capture based upon a previous study[4] (capturing efficiency > 57%). Subsequently, the sample was digested and the sialic acids derivatized, which resulted in a derivatization efficiency of 94%[5]. The TMT labeling effiency of the peptide backbone was estimate at 84%. Moreover, LC parameters were optimized to allow optimal separation of PSA glycopeptides, including isomeric separation. Preliminary results revealed that a concentration of 3 ng/mL PSA, from 4 mL plasma, resulted in the identification of 10 PSA glycoforms on the peptide NK, including the distinction of various isomers with different sialic acid linkages and diverse glycosylation features (mono-/di-sialylation, (non-)fucosylation, with/without LacdiNAc). Further improvements are envisioned to enabe high-throughput analysis by multiplexing several samples in a single analysis. Finally, we intend to investigate the diagnostic and prognostic potential of PSA glycosylation derived from plasma for the early diagnosis of PCa as well as for the differentiation between aggressive and indolent PCa.

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O-10 Advancement NMR technologies for deep insights into plant-based food

Klaartje Houben[1], Elwin van der Cruijsen[1], Tim Rietkerk[1], Rob van der Hoeven[1], Wim Bijleveld[1], Adriana Carvalho de Souza[1] and Maurien Olsthoorn[1]

[1] *Center for Analytical Innovation, Biodata & Translation, DSM Science & Innovation, Delft, the Netherlands*

Abstract

DSM is a company active in Health, Nutrition and Bioscience. Supporting the protein transition towards more sustainable food production, requires deep insights into the food matrix to create plant-based foods while maintaining good taste, texture and health. In this presentation, we will show how we develop our advanced analytical toolbox to characterize ingredients and their interactions in food (related) matrices to steer the food properties.

Texturized Vegetable Proteins (TVPs) are used in meat alternative products and prior to application they are hydrated. We developed a Time Domain NMR method including robust python data-fitting to follow and optimize hydration times of these TVPs and correlated those to their composition (*i.e*. type of protein source) and processing conditions. To assure the quality of our plant and/or fermentative proteins during product development and shelf-life, characterization the quality and stability of the protein 3D structure is very relevant. Making use of methyl groups (CH_3) as sensitive reporters for overall protein structural quality, we implemented natural abundance methyl ^{1}H-^{13}C HSQC NMR fingerprinting [1] of some of our protein products. Comparison to standards allowed us to determine the weight % of well-folded protein.

Furthermore, enzymes can be used during food processing to obtain the right food properties. Time resolved NMR is an insightful tool for studying enzyme kinetics on application relevant substrates. We will show how we developed specific enzyme reaction monitoring in an automated way using the InsightXpress (Bruker). Finally, with Saturation Difference NMR, we study interactions between astringent compounds, such as polyphenols present in plant protein products, and saliva proteins with the goal of finding strategies to mitigate these interactions.

In conclusion, the protein transition brings complex analytical challenges to create deep insights to improve plant-based food.

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O-11 Automated identification of potential pesticides residues in fruit samples using HRMS data"

Ismael Zamora[1], Elisabeth Ortega[1]; Pol Giménez-Xavier[1]; Xavier Pascual[1]; Roberto Romero-gonzález[2]; Rosalía López-Ruiz[2]; Antonia Garrido Frenich[2]
[1]Lead Molecular Design, S.L., Sant Cugat del Valles, Spain; [2]Research Group 'Analytical Chemistry of Contaminants', Department of Chemistry and Physics, Research Centre for Agricultural and Food Biotechnology (BITAL), Agrifood Campus of International Excellence, University of Almeria, Almeria, Spain

Introduction

In food safety and related fields, High Resolution Mass Spectrometry techniques applied for multiresidue analysis had become an alternative to the historical routine procedures involving triple quadrupole instruments. This evolution was mainly driven by the possibility to interrogate hundreds or thousands of compounds without a prior individual study of all of them. However, due to the big amount of information that can be generated during the data acquisition, the later data processing and data analysis steps can be quite time demanding. In this presentation we will show how this late step could be automized using Chemical Monitoring workflow included in MassChemSite 3.1.

Methods

For chromatographic analysis, Thermo Fisher Scientific Vanquish Flex Quaternary LC (Thermo Scientific Transcend™, Thermo Fisher Scientific, San Jose, CA, USA) was used. The chromatographic system is coupled to a hybrid mass spectrometer Q-Exactive Orbitrap Thermo Fisher Scientific (ExactiveTM, Thermo Fisher Scientific, Bremen, Germany) using an electrospray interface (ESI) (HESI-II, Thermo Fisher Scientific, San Jose, CA, USA) in positive-negative mode. ESI parameters were as follows: spray voltage, 4 kV; sheath gas (N2, 95%), 35 (adimensional); auxiliary gas (N2, 95%), 10 (adimensional); S-lens RF level, 50 (adimensional); heater temperature, 305 °C; and capillary temperature, 300 °C.
Data processing has been done using MassChemSite 3.1 (Molecular Discovery, Ltd. Borehamwood, UK). Data analysis was performed in ONIRO server (Molecular Discovery, Ltd. Borehamwood, UK).

Preliminary Data

Strawberry, white grape and orange samples providing from Almeria (Spain) greenhouses were acquired in the University of Almería and processed using the Chemical Monitoring data workflow included in MassChemSite 3.1. Data was interrogated against an in-house pesticide database generated by literature search including up to 1500 different pesticides. From the total, up to 10 different pesticides were detected in all the samples in less than five minutes of data processing.
The identification step was performed using the MS and MSMS information: MS was used to detect the pesticide in the sample, while fragmentation information was used to finally elucidate the structure of the detected pesticide, by means of a computational fragmentation of the detected pesticide and a later assignation to the MSMS data provided by the instrument. The fitting among computed and experimental fragments is reported as "score" which can be used to discriminate among other structural isobaric compounds associated to the same chromatographic peak.
Data analysis and reporting were done in ONIRO server after an automatic uploading of the raw data. Later filtering steps were applied and tracked by the application for further inspection. Additionally, a final report was generated automatically once the experiment was reviewed. Data generated during the acquisition remained on the server for later use or further re-analysis.

Novel Aspect

MassChemSite 3.1 and ONIRO are valuable tools perform an automatic pesticide indentification in food samples.

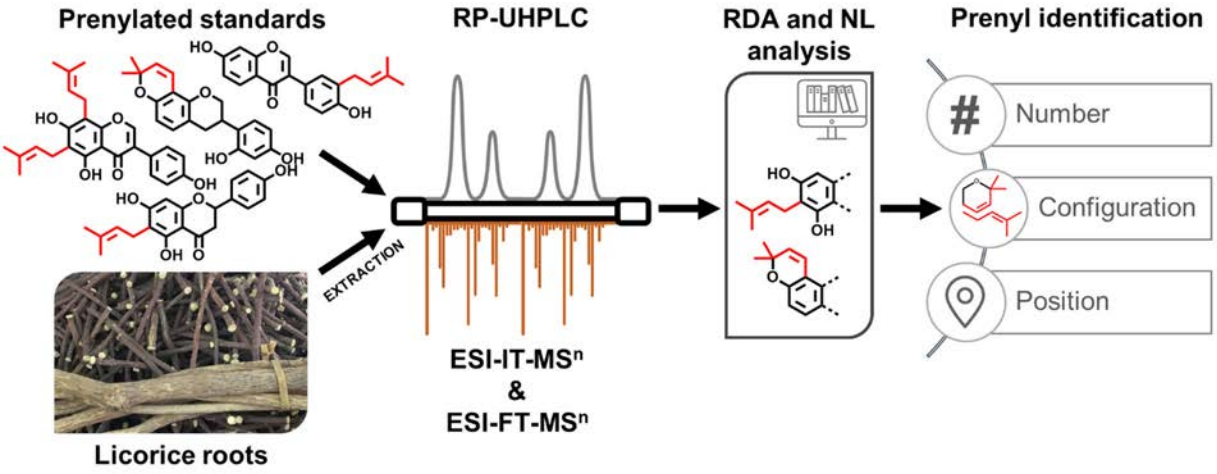
O-12 Mass spectrometry as tool for identification and characterization of prenyl number, configuration, and position in different subclasses of (iso)flavonoids

Sarah van Dinteren MSc[1,2], Dr. Carla Araya-Cloutier[1], Dr. Wouter J.C. de Bruijn[1], Prof. Jean-Paul Vincken[1]

[1]*University of Wageningen, The Netherlands; sarah.vandinteren@wur.nl, carla.arayacloutier@wur.nl, wouter.debruijn@wur.nl, jean-paul.vincken@wur.nl;* [2]*(+31) 651790927*

Abstract

In the search for new antimicrobials, plant secondary metabolites provide unlimited opportunities due to their vast chemical diversity. Under (a)biotic stress, plants from the Fabaceae family, including *Glycyrrhiza* spp., produce prenylated (iso)flavonoids with potent antimicrobial activity. However, identification of these prenylated (iso)flavonoids in complex plant extracts is a laborious manual process that is prone to errors. Therefore, in this study, we developed a mass spectrometric decision guideline that easily identifies prenylation in complex plant extracts. We investigated fragmentation of prenylated (iso)flavonoid standards by using electrospray ionization ion trap mass spectrometry (ESI-IT-MS^n) with fragmentation by collision induced dissociation (CID) and Orbitrap-MS (ESI-FT-MS^n) with fragmentation by higher energy C-trap dissociation (HCD). By combining IT-MS^n and FT-MS^n, we determined fragmentation pathways of different subclasses of prenylated (iso)flavonoids and elucidated characteristic fragmentations and neutral losses of different prenyl configurations. The decision guideline enables to annotate (i) prenyl number, (ii) prenyl configuration, and (iii) prenyl position of unknown prenylated (iso)flavonoids analyzed by ESI-IT-MS. High resolution MS with HCD fragmentation was used to confirm molecular formulas of fragments and led to the new insights, which uncovered inconsistencies in previously proposed annotation guidelines. With this guideline, we annotated 196 prenylated (iso)flavonoids in a *G. glabra* root extract; 75 skeletons were single prenylated, 104 were double prenylated, and for merely 17 skeletons prenyl number could not unambiguously be annotated. In conclusion, our prenylation guideline facilitates rapid identification of prenyl number, prenyl configuration, and prenyl position in (iso)flavonoids in complex plant extracts. With this guideline, a more comprehensive characterization of complex antimicrobial extracts is within reach, which ultimately leads to better understanding structure antimicrobial activity relationships.



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O-13 Structural elucidation of agrochemical derivatives using infrared ion spectroscopy

Matthias.J.A. Vink[1], Giel Berden[1], Timothy J. C. O'Riordan[2], Peter W.A. Howe[2], Jos Oomens[1], Simon J. Perry[2], Jonathan Martens[1]

[1]Radboud University, Institute for Molecules and Materials, FELIX Laboratory, Toernooiveld 7, 6525ED Nijmegen, the Netherlands

[2]Syngenta, Jealott's Hill International Research Centre, Bracknell, Berkshire, RG42 6EY, the United Kingdom

Abstract

The development of novel agrochemical compounds is required for a growing population. However, the characterization of their environmental degradation products is a major analytical challenge as many chemical derivatives often arise following their application. The complete profile of these derivatives must be established to assess their impact on environmental and human safety. A common issue is that various structural isomers can be present, and their precise molecular assignment based on LC-MS(/MS) characterization can be very challenging. In this study, we focus on the differentiation between various isomeric byproducts of agrochemicals in complex biological agricultural matrixes using infrared ion spectroscopy (IRIS).

We have focused on the differentiation of oxidized structural isomers of two common agrochemicals, which present challenges using common LC-MS(/MS) approaches. We used density-functional theory (DFT) to obtain computationally predicted IR spectra and compared those to measured IRIS spectra for reference standards. Based on these analyses, we differentiated several structural- and diastereo-isomers based on fingerprint IR features. Subsequently, we aimed to replicate those findings in spiked matrix samples, for which we investigated two approaches for measuring IRIS spectra.

We examined the possibility of using direct analysis and compared those with samples using HPLC fractionation. In the direct analyses approach, we isolated the ion of interest in an ion trap mass spectrometer from the spiked matrix directly infused into the MS by ESI. This approach yielded IRIS spectra for agrochemicals present at relatively high concentrations of more than 3 µg/ml; however, this is relatively high for agrochemicals in a real-world setting. In the second approach, we employed LC-MS to fractionate the relevant agrochemical from the spiked matrix sample, which could subsequently be infused into the MS for IRIS characterization. Both approaches yielded equivalent IR spectra; however, the fractionation approach yielded spectra from significantly lower concentrations, allowing IRIS spectra to be measured from samples with a 95 ng/ml concentration of the relevant agrochemical using 10 µl of sample for HPLC fractionation. An IRIS-based characterization workflow for elucidating the structure of unknown byproducts, guided by computationally predicted spectra at the DFT level, allows for improved identification of agrochemical byproducts.

MSc. Matthias.J.A. Vink	matthias.vink@ru.nl Toernooiveld 7 6525 ED NIJMEGEN	+31 24 36 52416
Dr. Giel Berden	giel.berden@ru.nl	
Dr. Timothy J. C. O'Riordan	tim.o_riordan@syngenta.com	
Dr. Peter W.A. Howe	peter.howe@syngenta.com	
Prof. Dr. Jos Oomens	Jos.Oomens@ru.nl	
Dr. Simon J. Perry	simon.perry@syngenta.com	
Dr. Jonathan Martens	jonathan.martens@science.ru.nl	

O-14 Predicting the uniqueness of single non-negative profiles estimated by multivariate curve resolution methods

Mahsa Akbari Lakeh[1], Hamid Abdollahi[1], Róbert Rajkó[2]

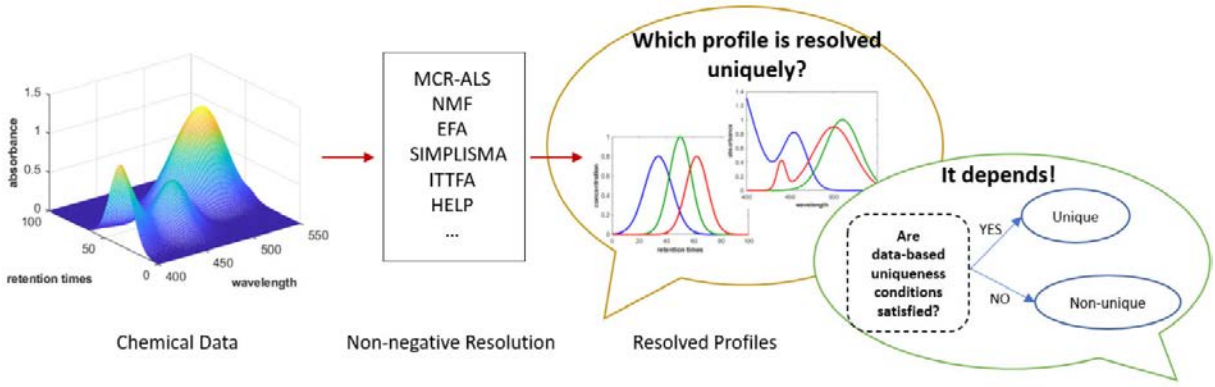
[1] *Department of Chemistry, Institute for Advanced Studies in Basic Sciences, P.O. Box 45195-1159, Zanjan, Iran;*

[2] *Institute of Mathematics and Informatics, University of Pécs, Ifjúság u. 6, H-7624 Pécs, Hungary*

Abstract

In many kinds of chemical data, one or more species are unknown and the only efficient way to identify and/or quantify them is by mathematical resolution of the mixture spectra. The major problem with such mathematical decompositions is the possibility of obtaining a range of feasible solutions instead of a unique solution due to insufficient prior information about the system under study [1]. However, even with the minimal non-negativity assumptions, there may be some levels of uniqueness, i.e., full/partial/fractional, in the results of the bilinear decomposition of chemical data which is very important to detect. In the lecture, a procedure is explained which can predict the uniqueness of the resolved non-negative profiles obtained by MCR-ALS (or analogous methods like NMF, EFA, SIMPLISMA, ITTFA, HELP, etc.). Because the proposed method works on the already resolved profiles, the remaining noise effect only depends on the quality of the used non-negative curve resolution method. For each experimental data, a noise level should be defined, depending on the chemical system and the type of signal, to estimate the presence window of each component. Defining this level may not be an easy task but it is necessary for getting reliable MCR solutions.
The proposed uniqueness prediction is based on the data-based uniqueness (DBU) theorem [2] and the general rule of uniqueness (GRU) [3] - all in all, on duality concept. It is easy to implement, has no additional computational cost, and is general for different systems with any number of components.

Illustration



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O-15 Continuous monitoring of small molecules for industrial process control

Chris Vu[1, 2], Yu-Ting Lin[3], Junhong Yan[3], Julia Marshall[4], Annemarie Hummel[4], Simone F. A. Wouters[4], Jos M.H. Raats[4], Arthur M. de Jong[2, 5] and Menno W. J. Prins[1, 2, 3, 5]

[1] Department of Biomedical Engineering, Eindhoven University of Technology, The Netherlands; [2] Institute for Complex Molecular Systems (ICMS), Eindhoven University of Technology, The Netherlands; [3] Helia Biomonitoring, The Netherlands; [4] AbSano, Oss, The Netherlands; [5] Department of Applied Physics, Eindhoven University of Technology, The Netherlands.

Abstract

Monitoring of biochemical substances is applied in downstream food processing for process control and quality assurance purposes. Here, we describe a sensing technology that will allow for real-time continuous monitoring of small molecules, so that processes can be adjusted and optimized in real-time. This can help to minimize under- and over-processing, improve efficiency, reduce waste, and reduce the use of resources.

The continuous sensing technology is called BPM, Biosensing by Particle Mobility[1-3]. Biofunctionalized micrometer-sized particles are attached by a flexible tether to a biofunctionalized substrate. The sensor response is based on the mobility of the particles, which is changed by reversible affinity-based interactions (see Fig. 1a). Hundreds of particles are measured and their mobilities dynamically reflect the concentration of analyte molecules in solution.

Here we demonstrate the feasibility of small-molecule monitoring in protein solutions using the BPM sensor. We have synthesized analogue molecules and selected recombinant antibodies from large phage display libraries for a competitive assay design (see Fig. 1a). The sensor is shown to be sensitive in the micromolar concentration range, in aqueous buffers and in complex matrices (see Fig. 1b). We will present the measurement principle, the development of analogue and antibodies, show monitoring results, and discuss how BPM can generally be applied for real-time monitoring of small molecules in industrial food processes.

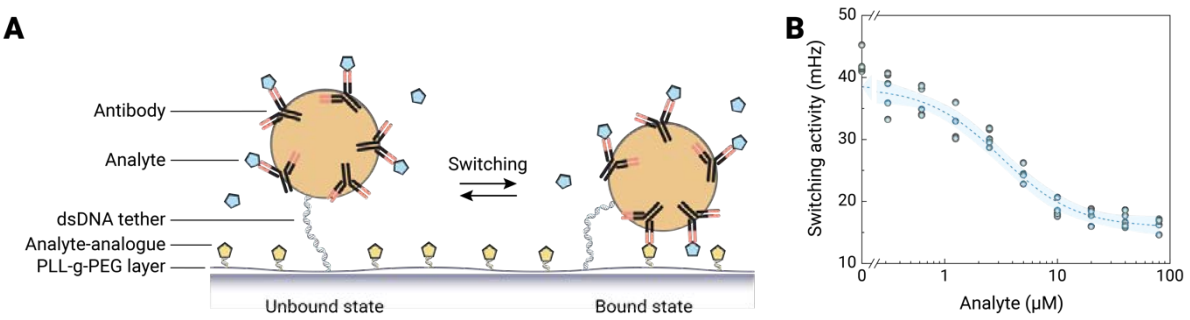

Figure 1. Quantification of small molecules using Biosensing by Particle Mobility (BPM). (A) Schematic overview of the BPM sensor design, with a competitive assay format. The sensor surface is provided with analyte-analogue molecules. The particles are tethered to the surface via double-stranded DNA and a low-fouling PLL-g-PEG polymer layer. The particles are functionalized with antibodies that reversibly bind to the analogue and to the analyte molecules. The switching events between bound and unbound states are detected by tracking the movement of the particles using brightfield microscopy. (B) Dose-response curve measured in the competitive BPM assay.

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O-16

Infrared Absorption Nanospectroscopy towards the Single Molecule Scale

Francesco Simone Ruggeri

Laboratory of Organic Chemistry, Stippeneng 4, 6703 WE, Wageningen University & Research, the Netherlands

Physical Chemistry and Soft Matter, Stippeneng 4, 6703 WE, Wageningen University & Research, the Netherlands

Biological processes rely on a wide class of biomolecular and macromolecular machines that have nanoscale physical dimensions and whose function emerges from a correlation between their chemical and structural properties. A fundamental objective of modern analytical methods in physics, chemistry and biology is the comprehension of how physical-chemical properties and heterogeneity of single biomolecules underlie their role in cellular function and disease. While innovative nanoscale imaging methods have been developed to characterise biomolecules, imaging microscopies are to the most part chemically blind; thus hampering the characterisation of inhomogeneous and complex systems.

Here, we show the application of infrared absorption nanospectroscopy (AFM-IR) as a real breakthrough for the analysis of heterogeneous biomolecules and their interactions from the single molecule scale to several multiple biological length scales in air and liquid environment. As a major advance in the field, we demonstrate the achievement of single protein molecule detection of infrared absorption spectra and maps by introducing off-resonance, low power and short pulse ORS-nanoIR.[1] The technique enables the accurate determination of the secondary structure elements of single proteins in the amide band I region, such as α-helices and β-sheets. Then, we show the application of this single molecule sensitivity to unravel the molecular interaction fingerprint between a small molecule and its target [2], the surface properties of artificial model membranes [3] and the structure of functional protein self-assemblies to be exploited as a novel class of biomaterials in bioscience [4-7].

Overall, our aim is to expand the capabilities of analytical nanoscience to shed light on the structure-activity relationship of biomolecules for nano- and bio-science applications.

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O-17 Multilayer Plastic Sorting Based on Multi-Block Non-Negative Matrix Factorization

Mahdiyeh Ghaffari, Geert Postma, and Jeroen Jansen

Radboud University, Institute for Molecules and Materials, Analytical Chemistry, P.O. Box 9010, 6500, GL, Nijmegen, the Netherlands

Abstract

Multilayer plastics are widely employed to improve functional properties of packaging i.e. thickness of packaging, mechanical strength, and heat tolerance. On one hand, 26% of the flexible packaging market is multilayer plastic packaging. On the other hand, one of the main challenges in plastic sorting is the detection, identification, and separation of multilayer packaging. Although some companies succeeded in the post-industrial multilayer packaging sorting, the available technologies are limited to some particular polymer types [1].

In recent years, automated sorting of plastic packaging significantly increased thanks to technology improvement, especially ones based on Near Infrared-Hyperspectral Imaging (NIR-HSI) [1]. HSIs are non-destructive and fast with minimum sample preparation steps which help for the identification of single/multilayer plastic stream integrated with pattern recognition and/or curve resolution techniques.

In this contribution, a Multi-Block Non-negative Matrix Factorization model (MB-NMF) [2] is conducted for the identification of single/multilayer plastics. In the proposed strategy, the recorded HSI of single/multilayer plastics is jointly analyzed using Multi-Block-NMF under predefined constraints to tackle the possible collinearity of concentration contribution maps of polymers in the multilayer block. For this, augmented HIS images are analyzed by MB-NMF and the results are present in figure 1. The first two sub-matrices in figure 1 are hyperspectral images of two different polymers (Polypropylene and Polyethylene). However, the last image contains multilayer packaging and is made of both Polypropylene and Polyethylene. Joint analysis of HSIs with zero-region constraints together with selecting appropriate spectral-domain resulted in the accurate unraveling of hyperspectral images and correct identification.

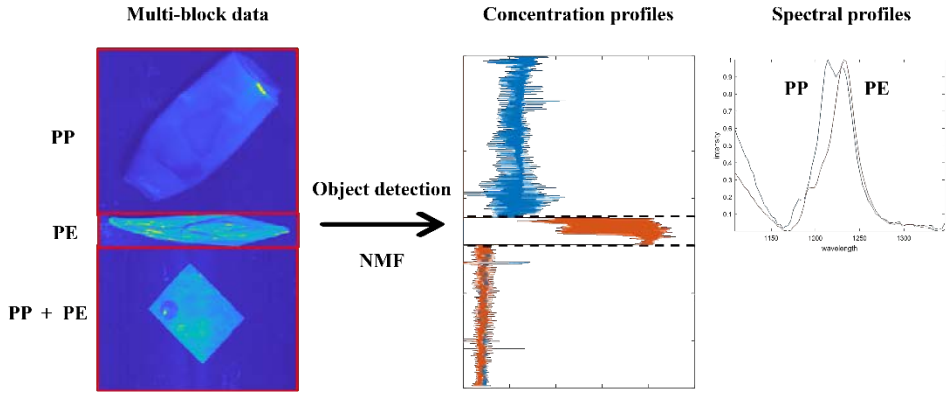

Figure 1. A summary of the proposed strategy to join analysis of multilayer plastics. The left panel shows recorded HSIs (PP; PE; PP/PE). The middle panel shows the unfolded concentration contribution map of PP and PE. The right panel indicates the spectral profile of identified polymers.

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O-18 Covalent surface modification for flow control & sensing in paper microfluidics

Canan Aksoy[1,2], Han Zuilhof[1,3,4] and Gert Salentijn[1,2]

[1] *Wageningen University, Laboratory of Organic Chemistry, Helix Building 124, Stippeneng 4. 6708 WE Wageningen, The Netherlands.*
[2] *Wageningen Food Safety Research, Wageningen University & Research, P.O Box 230, 6700 AE Wageningen, The Netherlands.*
[3] *Key Laboratory of Phytochemical R&D of Hunan Province and Key Laboratory of Chemical Biology & Traditional Chinese Medicine Research of Ministry of Education, Hunan Normal University, Changsha 410081, China*
[4] *Department of Chemical and Materials Engineering, Faculty of Engineering, King Abdulaziz University, Jeddah 21589, Saudi Arabia*

Microfluidic paper-based devices (μPADs) are promising candidates for on-site sensing platforms that bring the lab to the sample, since they allow passive, capillary-action-driven flow, and precise flow control by manipulating the (properties of) paper. Here, we propose the use of simple covalent modification of cellulose paper, to tune its surface properties, and thereby open a new range of functionality and applicability.

Paper-based analytical devices, such as μPADs and lateral flow immunoassays are convenient and popular approaches for quick on-site screening for a wide range of analytes in different matrices. However, their use is somewhat limited by the fact that it is difficult to integrate advanced functionality and flow control. Recent progress in this area has led to development of on/off valving and timing of the flow by changing chemical and physical properties of paper [1, 2]. However, precise control over flow in paper microfluidics remains challenging.

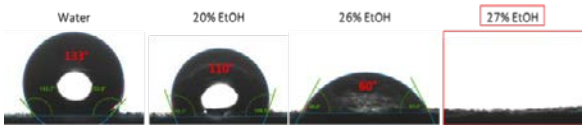

Figure 1 CA of various EtOH solutions and CWC of C4-Paper

Here, we have modified the surface of cellulose paper hydrophobically with fatty acyl chlorides of different chain lengths to tune its microfluidic properties. These properties were defined as permeability (does it wick the solution or not), maximum flow distance (how far does the solution flow before it stops), and flow rate (how fast does the solution wick through paper). Modified papers were characterized by IR spectroscopy, contact angle (CA) measurements, and by using aqueous ethanol (EtOH) solutions of varying surface tensions to monitor wicking behavior. Differently modified papers were then applied in several proof-of-concept devices, to demonstrate their future implementation for sensing and actuating towards improved on-site analysis.

The modified papers repelled water due to their hydrophobic surfaces. In binary mixtures of water and EtOH, an increase in EtOH content, resulted in lower contact angle, i.e. higher wettability due to the decreasing surface tension (Fig 1). Permeability measurements also showed that every modified paper had a critical wicking concentration (CWC), which is the minimum EtOH content required for the binary solution to wick into a specific modified paper, e.g. the CWC for the paper modified with butyryl chloride (C4) is 27% EtOH (Fig 1). These properties could be correlated to the non-polarity of the used reagent, as well as to the amount of reagent use. Lower polarity of reagents resulted in higher CWCs and larger contact angles. The maximum distance traveled on a modified paper by water/EtOH solution, could be linked to its composition. Longer distances were measured with both higher EtOH content for the same paper and with less hydrophobic paper for the same solution. It is hypothesized that maximum distance is obtained by the evaporation of the more volatile EtOH, thereby increasing the surface tension of the solution, thereby reducing the wettability of the modified paper.

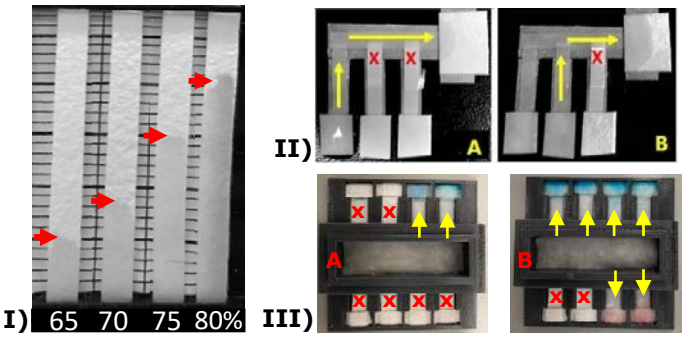

Figure 2 I) Maximum flow distance of EtOH solutions on C12-Paper, II) Valving application for sequential flow without backflow for (A) 15% and (B) 30% EtOH solutions, III) Permeability-based colorimetric surface tension sensing with (A) 15% and (B) 45% EtOH solutions

Hydrophobic papers with varying and controllable properties have a wide range of potential applications. Here, we demonstrate how they can be used for the indirect measurement of the surface tension of a solution based on maximum flow distance. This can e.g. be used in the determination of the ethanol content of alcoholic beverages (Fig 2-I), for solvent-dependent valving (Fig 2-II), or for permeability-based surface tension sensing (Fig 2-III).

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Societal Challenges, Analytical Solutions

Poster presentations

P-01 Identification and characterization of in vivo, in vitro and reactive metabolites of zorifertinib using Liquid Chromatography Ion Trap Mass Spectrometry

N. Alshakliah

Abstract

Zorifertinib is a novel, potent, oral, small molecule used to treat non-small cell lung cancer (NSCLC). zorifertinib is Epidermal Growth Factor Receptor (EGFR) inhibitor and has good blood–brain barrier permeability for (NSCLC) patients with EGFR mutations. zorifertinib is currently at a phase II/III clinical trials. The current research reports the characterization and identification of *in vitro*, *in vivo* and reactive intermediates of zorifertinib. Prediction of susceptible sites of metabolism and reactivity pathways (cyanide and GSH) of zorifertinib were performed by Xenosite web predictor tool. *In-vitro* metabolites of zorifertinib were performed by incubation with rat liver microsomes (RLMs) and isolated perfused rat liver hepatocytes. Extraction of zorifertinib and its in vitro metabolites from the incubation mixtures were done by protein precipitation. *In vivo* metabolism was done by giving single oral dose of zorifertinib (10 mg/Kg) to Sprague Dawely rats in metabolic cages by using oral gavage. Urine was gathered and filtered at specific time intervals (0, 6, 12, 18, 24, 48, 72, 96 and 120 hr) from zorifertinib dosing. A similar volume of ACN was added to each collected urine sample. Both layers (organic and aqueous) were injected into liquid chromatography ion trap mass spectrometry (LC-IT-MS) to detect in vivo zorifertinib metabolites. N-methyl piperizine ring and quinazoline group of zorifertinib undergoe metabolism forming iminium and electro deficient conjugated system respectively, which are very reactive toward nucleophilic macromolecules. Incubation of zorifertinib with RLMs in the presence of 1.0 mM KCN and 1.0 Mm glutathione were made to check reactive metabolites as it is often responsible for toxicities associated with this drug. For in vitro metabolites there were nine *in vitro* phase I metabolites, four in vitro phase II metabolites, eleven reactive metabolites (three cyano adducts, five GSH conjugates metabolites and three methoxy metabolites of zorifertinib were detected by LC-IT-MS. For in vivo metabolites there were eight *in vivo* phase I, ten *in vivo* phase II metabolites of zorifertinib were detected by LC-IT-MS. *In vitro* and *in vivo* phase I metabolic pathways were N- demthylation, O-demethylation, hydroxylation, reduction, defluorination and dechlorination. *In vivo* phase II metabolic reaction was direct conjugation of zorifertinib with glucuronic acid and sulphate.

Keywords: N-methyl piperizine; zorifertinib; *In vivo* metabolites; *In vitro* metabolites; Cyano conjugates, GSH conjugate.

P-02 Tube plasma: a soft ionization for the GC-MS analysis of complex food samples

Juan F. Ayala-Cabrera[1,2], Lidia Montero[1,2], Florian Uteschil[1,2], Sven W. Meckelmann[1,2], Oliver J. Schmitz[1,2]

[1]*Applied Analytical Chemistry, University of Duisburg-Essen, Universitaetstrasse 5, 45141 Essen, Germany*
[2]*Teaching and Research Center for Separation, University of Duisburg-Essen, Universitaetstrasse 5, 45141 Essen, Germany*

juan.ayala-cabrera@uni-due.de, +49 (0) 2011834599

The use of atmospheric pressure ionization (API) sources for gas chromatography-mass spectrometry (GC-MS) applications has exponentially grown during the last decade. In contrast to vacuum ionization techniques such as electron ionization (EI), API sources provide a soft ionization which largely preserve the molecular or quasi-molecular ion, overcoming the compromise between sensitivity and selectivity required with EI as well as promoting new ionization mechanisms which may open new fields of applications for GC-MS determinations [1]. Some sources such as atmospheric pressure chemical ionization (APCI), photoionization (APPI) and laser ionization (APLI) are showing a great performance in different fields such as food, environmental or clinical analysis [2]. However, there is still a long way of improvement and, thereby, new API sources and set-ups have been recently investigated to provide new ionization mechanisms as well as to overcome some difficulties such as response stability or memory effects. Recently, we developed a tube plasma ionization (TPI) source for GC-MS. TPI consists of a half dielectric barrier discharge based on an inverse low temperature plasma configuration where the high voltage is applied to a stainless-steel pin electrode and the virtual grounded electrode is the housing itself (Illustration 1). Preliminary tests showed that TPI provide a soft ionization yielding the formation of the protonated molecules for most of the compounds. Due to the low in-source fragmentation and the simplicity of the mass spectra, TPI could have a great performance for non-targeted analyses of complex samples.

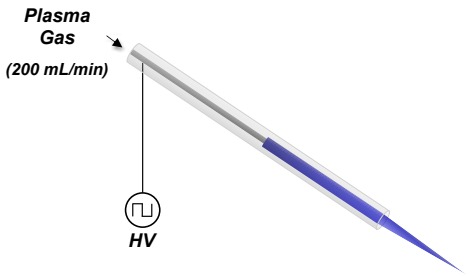

Illustration 1. Schematic of the TPI configuration

The main goal of this works lies on the evaluation of TPI as a potential source for the non-targeted analysis of herbal liqueurs. Herbal liqueurs are complex matrices including a wide range of non-polar compounds which are related to their organoleptic properties. Most of them are low molecular weight compounds that usually show a high fragmentation by EI, which could difficult their identification. Thus, GC-TPI-HRMS (QTOF) was proposed for the characterization of 7 commercial herbal liqueurs. The soft ionization led to the formation of the protonated molecule for most of these fragile compounds. Additionally, the mass accuracy and the possibility to carry out tandem mass spectrometry experiments from the $[M+H]^+$ ion in the GC-TPI-QTOF allowed ensuring the identification of non-polar compounds present in the herbal liqueurs. The results obtained have been compared to those achieved by GC-EI-HRMS (QTOF). While for the EI mass spectra interpretation, libraries which could lead to false positive/negative results depending on the threshold stablished for the match score are required, TPI strongly simplifies and guarantees the correct identification in the non-targeted analysis of complex food samples. Finally, multivariable statistical analyses have been done to differentiate between all the herbal liqueurs establishing a model that could help on the identification of fraudulent activities.

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Co-authors details: lidia.montero@uni-due.de, florian.uteschil@uni-due.de, sven.meckelmann@uni-due.de, oliver.schmitz@uni-due.de

P-03 Possibilities of using boron-doped diamond electrode materials for non-enzymatic cortisol detection

Simona Baluchová[1], Zhichao Liu[1], and Josephus G. Buijnsters[1]

[1] *Delft University of Technology, The Netherlands*

Abstract

Cortisol (also called hydrocortisone; its structure is depicted in Fig. 1A) is a glucocorticoid hormone that is predominantly produced by the adrenal glands as a reaction to physiological stimulus and stress. Cortisol has a crucial role in a wide range of essential physiological functions associated with the regulation of blood pressure, metabolic pathways of carbohydrates (including glucose), proteins and lipids, immunosuppressive and anti-inflammatory actions [1]. Abnormal fluctuations of cortisol levels in physiological fluids may indicate numerous diseases, and therefore monitoring and detection of cortisol in the human body is of a high importance.

Electrochemical methods can be favorably used in clinical analysis due to their simplicity, reliability, short analysis time and low cost, compared to the other routine analytical techniques, while they still fulfil high requirements on sensitivity and selectivity. Nevertheless, up to date, only a few electrochemical sensors have been developed for cortisol detection [1]. Surprisingly, none of the sensors has been based on utilization of boron-doped diamond (BDD) materials possessing exceptional characteristics for applications in clinical chemistry, such as chemically inert surfaces contributing to resistance towards (bio)fouling and biocompatibility, low capacitance and background currents, and wide potential window [2], even in cathodic region where cortisol reduction occurs.

Therefore, this work reports, for the first time, on examination of various BDD-based electrodes for non-enzymatic cortisol detection. The tested BDD materials, including but not limiting to (i) BDD thin film deposited on a p-Si wafer and (ii) polished growth side of the free-standing BDD electrode (see scanning electron micrographs in Fig. 1B), differ in surface roughness and termination (H- *vs*. O-), boron-doping level, and sp^2 carbon content (*i.e.*, conductivity). These are all factors having a significant impact on electrochemical properties of BDD electrodes and their suitability and applicability for electroanalysis of cortisol, carried out by differential pulse and square-wave voltammetry.

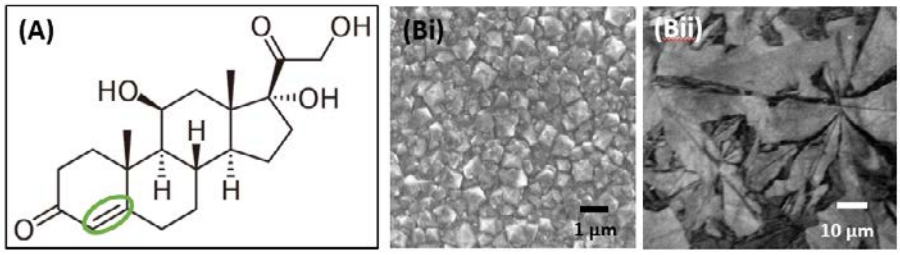

Fig. 1 (A) Chemical structure of cortisol with highlighted reducible double-bond. (B) SEM images of (Bi) BDD film deposited on a p-Si wafer and (Bii) polished growth side of the free-standing BDD electrode.

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Acknowledgements

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P-04 Role of sp^2 carbon in non-enzymatic electrochemical sensing of glucose using boron-doped diamond electrodes

Zhichao Liu[1], Simona Baluchová[1], André F. Sartori[1], and Josephus G. Buijnsters[1]

[1] *Delft University of Technology, The Netherlands*

Abstract

Boron-doped diamond (BDD) is of increasing interest for applications in electrochemical sensing. It is well known that the sp^2 carbon content in BDD influences its electrochemical properties as electrode material. In this work, evidence is provided that the surface sp^2 carbon content plays a crucial role in the electrochemical sensitivity of BDD towards glucose. Single-crystal BDD, freestanding polycrystalline BDD and glassy carbon (sp^2 carbon reference material) were examined by voltammetry. Neither single-crystal BDD, which is free of sp^2 carbon, nor pure sp^2 glassy carbon could detect glucose in the range of +0.2 − +1.0 V *vs* Ag/AgCl. On the other hand, glucose oxidation was observed on polycrystalline BDD, and with increasing intensity with increase of sp^2 carbon content (see Fig. 1). Thus, an optimum amount of (B-doped) sp^2 carbon in the BDD electrode is needed for best sensing performance. Understanding this, and being able to control the composition of BDD, are not only important to glucose detection but to any electrochemical sensing application involving BDD.

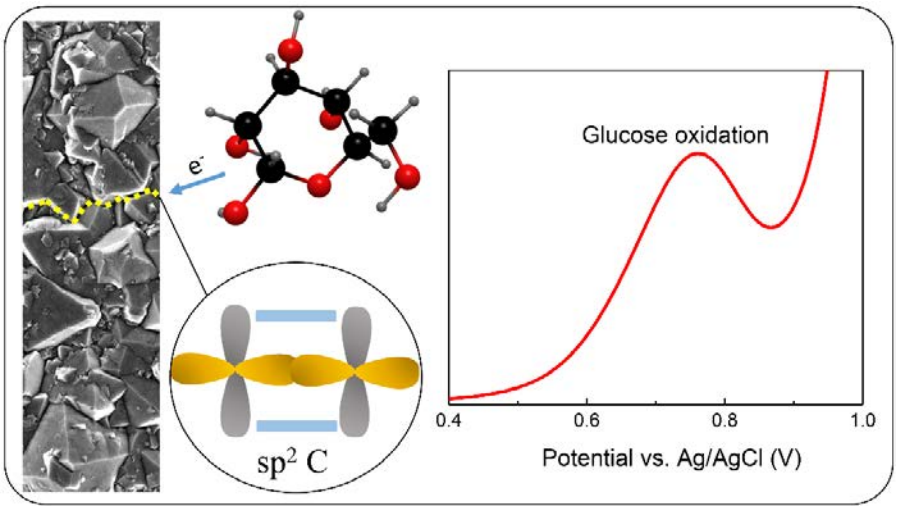

Fig. 1 Sp^2 carbon related glucose sensing on BDD electrode.

Reference

Zhichao Liu, André F. Sartori, Josephus G. Buijnsters, Role of sp^2 carbon in non-enzymatic electrochemical sensing of glucose using boron-doped diamond electrodes, *Electrochemistry Communications,* Volume 130, 2021, 107096, ISSN 1388-2481, https://doi.org/10.1016/j.elecom.2021.107096.

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P-05

On-site food contaminant detection by infrared spectroscopy in paper-based analytical devices

Anouk J. Bosman [1,2], Georgina M.S. Ross [1,2], Michel W.F. Nielen [1,2], Hans-Gerd Janssen[1,4], Francesco S. Ruggeri [1,3], Gert IJ. Salentijn [1,2]

[1] *Wageningen University, Laboratory of Organic Chemistry, Helix Building 124, Stippeneng 4. 6708 WE Wageningen, The Netherlands.*

[2] *Wageningen Food Safety Research, Wageningen University & Research, P.O Box 230, 6700 AE Wageningen, The Netherlands.*

[3] *Wageningen University, Laboratory of Physical Chemistry and Soft Matter, Helix Building 124, Stippeneng 4. 6708 WE Wageningen, The Netherlands.*

[4] *Unilever Foods Innovation Centre - Hive, Bronland 14, 6708 WH Wageningen*

The increasing demand for food and feed products is stretching the capacity of the food value chain to the extent that in the forthcoming years it will reach a limit. Moreover, the food industry needs to comply to ever more stringent standards for food and feed safety, and other sharpened guidelines. Achieving food safety along the entire food value chain requires fast, easy and accessible monitoring of food contaminants. However, to date samples are often taken at the production location and then sent to an accredited laboratory for analysis. Analysis is performed with high-end instrumentation, after extensive sample preparation, which can take days. Therefore, there is a pressing challenge to translate laboratory-based procedures into a rapid and truly on-site device suited for non-experts. This challenge includes (i) sample acquisition & extraction, (ii) selective capture & enrichment, (iii) detection and (iv) interpretation.

Here, a solution is proposed to tackle this challenge in the context of the analysis of a potent mycotoxin, deoxynivalenol (DON) from wheat samples, and first results will be discussed. Sample acquisition and extraction were integrated into a modular device by which the user can perform laboratory procedures such as weighing, grinding and extraction on-site. Several interconnectable modules were envisioned that can process hard or soft food commodities (Fig. 1, (i)). To achieve this objective, rapid prototyping using 3D-printing was applied to design the modules. These designs are tested for compatibility with standard laboratory procedures, by analyzing the particle size distributions of processed wheat and determining extraction efficiency by LC-MS/MS. Next, the selective capture and enrichment of deoxynivalenol was achieved using paper-based microfluidics and was demonstrated using IR sample assessment. Here, an immunoaffinity zone on a paper substrate is used to selectively enrich deoxynivalenol (Fig.1 (ii)). In order to obtain chemical information from the enrichment zone, mid-infrared spectroscopy was used. Such detection of the analyte on a paper substrate requires careful design of methodology. Criteria were established for the detection of deoxynivalenol on a selective paper substrate, as a framework for a standardized mid-infrared spectroscopy detection, exploiting ATR-FTIR (Fig.1 (iii)). This is the first demonstration of the discrimination of DON on a paper substrate. We aim to achieve a proof-of-concept for the on-paper detection of DON, extracted from a real-life wheat sample, around the maximum residue level (MRL) using multivariate data analysis (Fig. 1 (iv)). The established framework can be adjusted for the detection of other types of mycotoxins as well. In the future, this framework can be implemented with miniaturized MIR techniques that are developed within the EU PhotonFood project, as a novel approach for food contaminant detection.

The proposed concept, of hyphenating sample acquisition and extraction, with paper-based enrichment and miniaturized mid-infrared spectroscopy is a promising solution for the integration of the entire 'sample-to-result' procedure into one device to tackle the challenge of fast, easy and accessible food safety monitoring.

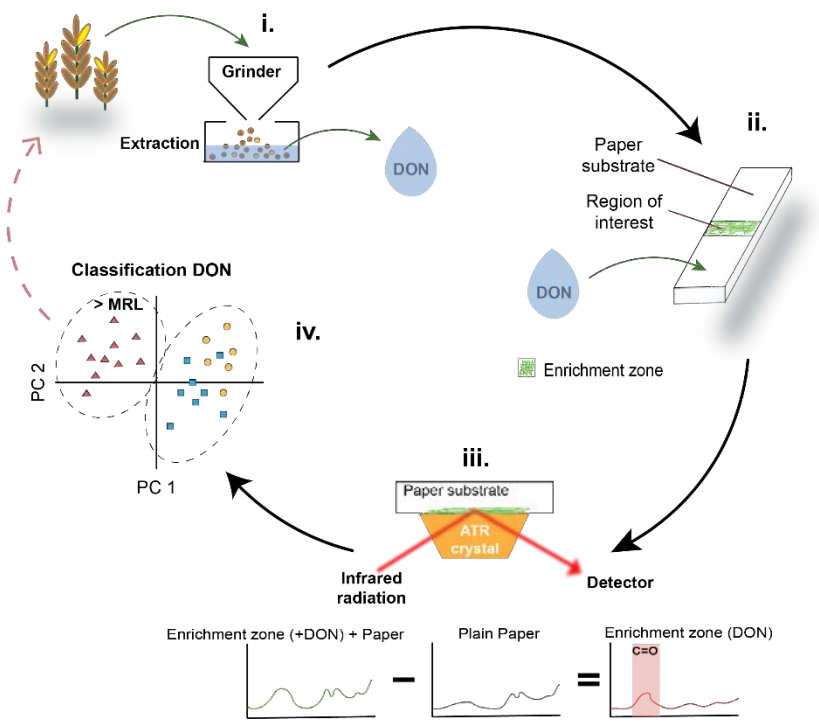

Figure 1: Establishing criteria for an on-site food contaminant detection device exploiting paper-based microfluidics and mid-infrared spectroscopy

This research is part of the PHOTONFOOD project, which received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No. 101016444 and is part of the PHOTONICS PUBLIC PRIVATE PARTNERSHIP

P-06 Evaluating chloride-water discharge relationship during high-flow events: comparison and validation of hydrograph separation methods with model simulation

Maria Cairoli[1], Gerard J. Stroomberg[2], Geert J. Postma[1], Jeroen J. Jansen[1]

[1] *Radboud University, Institute for Molecules and Materials, Heyendaalseweg 135, 6526 AJ Nijmegen, The Netherlands*

[2] *RIWA Rijn, Groenendael 6, 3439 LV, Nieuwegein, The Netherlands*
e-mail: maria.cairoli@ru.nl

Abstract

Understanding the relationship between water discharge and contaminant concentration in conditions of high-flow is pivotal for a comprehensive description of the sources of contamination, the storage, reaction and transport processes involving solutes in the river [1]. This relationship is often non-linear, and represented via *hysteretic* loops, which reproduce a time-lagged response between the observed variables [2]. In absence of a-priori information, an accurate procedure for baseflow estimation and direct runoff events isolation is essential to optimally model hysteresis [3]. We propose a combined data- and process-driven approach to evaluate and accurately describe chloride-water discharge hysteresis at Lobith (NL). We compare the performance of automatic hydrograph separation techniques on diagnostic indices for hysteresis description and quantification. We validate the choice of the optimal methodology with hysteresis simulation from metereological and water quality variables. We correlate the *hysteretic* events with antecedent metereological and watershed conditions. We report on a dilution behavior for chloride throughout 30 years of monitoring, with an emission source prevalently close to the monitoring point and high influence of sesonality on event-scale hysteresis. The proposed procedure, further extended to multiple compounds and several monitoring points, may be vital to exhaustively explain all the dynamics involving the river-based contaminants, ultimately pointing to potential sources of contamination. Moreover, the improved modeling may facilitate the understanding of flow-based analytical technologies.

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P-07 Alternative approaches to untargeted LC/GC-MS data analysis

Andrea Jr Carnoli[1], Gerke Spaling[2] , Petra Oude Lohuis[2], Gerjen Tinnevelt[1], Francisco Souza[1], Christina Precht[3], Arend Heerschap[4], Geert Postma[1],Jeroen Jansen[1]

[1] Department of Analytical Chemistry/Chemometrics. Radboud University, Institute for Molecules and Materials (IMM), The Netherlands;

[2] Teijin Aramid, Tivolilaan 50, 6824 BV Arnhem, The Netherlands;

[3] Clinical Radiology, Vetsuisse Faculty University of Bern, Bern;

[4]Department of Radiology, Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands

Abstract

Untargeted LC/GC-MS data are difficult to analyze compared to targeted MS analysis due to data analytical challenges, such as high data dimensionality, data collinearity and data artefacts (also caused by high data variety). Therefore, chemometrics is required to retrieve information regarding similarity among samples and feature importance. For untargeted MS analysis, the response within the measurement may be non-linear with respect to the concentration of the molecules/ions/fragments. Therefore, we explore the application of CMIM feature selection and a combined qualitative and quantitative information analysis to effectively extract and interpret untargeted LC/GC-MS data.

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Acknowledgement

This research was founded by Teijin Aramid

P-08 Conversion factors for the comparison of antioxidant capacity through DPPH assay detected by UV-VIS and EPR spectroscopy.

Marco Consumi[1], Flavia Bisozzi[1], Maria Camilla Baratto[1] and Gabriella Tamasi[1]

[1]*Department of Biotechnology, Chemistry and Pharmacy, University of Siena, Via Aldo Moro, 2, 53100 Siena, Italy*

Abstract

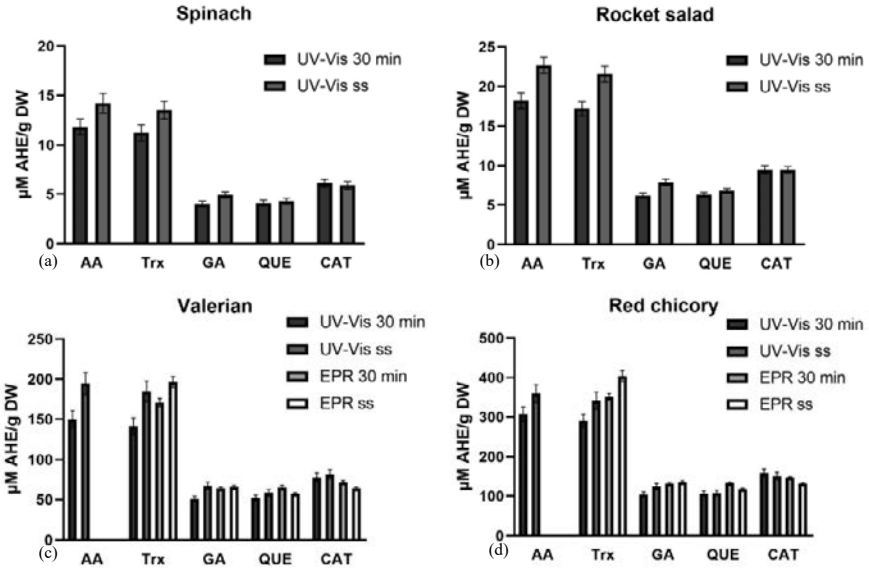
The purpose of this research is the determination of conversion factors which can be used to compare results from different equivalent antioxidant capacity measurements using different compounds as standard, in particular ascorbic acid, Trolox, gallic acid, quercetin and catechin.

The conversion factors between results obtained through two different spectroscopic techniques, UV-VIS spectroscopy and electron paramagnetic resonance EPR, were tested on four varieties of salad (Spinacia oleracea, Eruca sativa, Valerianella locusta and Cichorium intybus) used as benchmark.

The stable radical 1,1-diphenyl-2-picrylhydrazyl ($DPPH^{\cdot}$) colorimetric assays were carried out either with UV-Vis spectroscopy or EPR, to determine the EC_{50} values through linear regression and a non-linear regression fitting models.

The reliability of the conversion factor was demonstrated by Student's t-test performed on the antioxidant capacities of the samples obtained by different standards as well as by UV-Vis spectroscopy and EPR, which showed no statistical difference ($p > 0.05$).

The attainment of steady state in the quenching reaction between $DPPH^{\cdot}$ and antioxidant is an important parameter in determining the EC_{50} values of standards and samples and consequently in quantifying the antioxidant capacity of the samples. This result was confirmed by using conversion factors between the measurements performed with UV-Vis spectroscopy and EPR, where the converted antioxidant capacities were not statistically different using the EC_{50} values at steady state (Student's t-test, $p > 0.05$).



AH-equivalent antioxidant capacity of (a) spinach, (b) rocket salad, (c) valerian and (d) red chicory obtained with the EC_{50} values after 30 min and at the steady state (concentration express as µmol AHE/g DW) for UV-Vis and EPR measurements. The values are expressed as mean ± SD.

P-09 Towards future high-throughput analytical workflows in industrial biotechnology

Andre Vente[1], Wouter Coppes[1], Emilie Usureau[1], Rob van der Hoeven[1], Erwin Kaal[1], Maurien Olsthoorn, Nicolas Abello[1], Leon Coulier[1*]

* presenter

[1] *Center for Analytical Innovation, Biodata & Translation, DSM Science & Innovation, Delft, the Netherlands*

Abstract

DSM is a company active in Health, Nutrition and Bioscience. In our bioprocess and bioproducts development, mass spectrometry (MS) is a core technology in our labs for both metabolite and protein analysis to generate insight for microbial strain development and screening.

In Biotech R&D, analytical throughput and turnaround time of these advanced technologies can be a limiting factor for broad adoption. Therefore, we investigated different technologies for high-throughput MS analysis of metabolites and proteins and we developed and streamlined the whole workflow from sample preparation to data reporting for high-throughput proteomics.

We will show different examples of fast LC-MS analysis, application of dual LC/multiplexing LC-MS and flow injection analysis (FIA)-MS for metabolite screening. In addition, we also investigated external technologies like fast solid-phase extraction (SPE)-MS and acoustic droplet injection (ADE)-MS as high-throughput alternatives. Each of the technologies that will be presented have their specific advantages and the specific bioproduct development requirements will determine which approach for metabolite analysis is the most appropriate. The balance between speed, quantification, robustness and deployment costs will determine which of these technologies are the right analytical strategy for each new MS-based metabolite screening set-up.

We will also show possible enhancements for label-free quantitative proteomics for improving throughput and quality from fermentation sample to data reporting. Elements we will touch upon are protein/peptide normalization, sample preparation automation, application of quality controls, faster and more reproducible LC-MS analysis, and automation of data handling, visualization and reporting. LC-MS improvements consisted notably in the adoption of a dual-LC system coupled to Data-Independent Acquisition (DIA) on an Orbitrap Exploris™ 480 mass spectrometer (Thermo Scientific™). using the Spectronaut™ (Biognosys) data analysis software together with the Proteome Discoverer (Thermo Scientific™) software. Overall, we demonstrate a significantly improved Proteomics platform for characterization of yeast strains concomitant with improved data quality and turnaround time.

This presentation shows that with novel developments in mass spectrometry, from sample preparation, rapid measurements to data reporting, we are able to develop high-throughput analytical workflows that are fit for future biotech innovations.

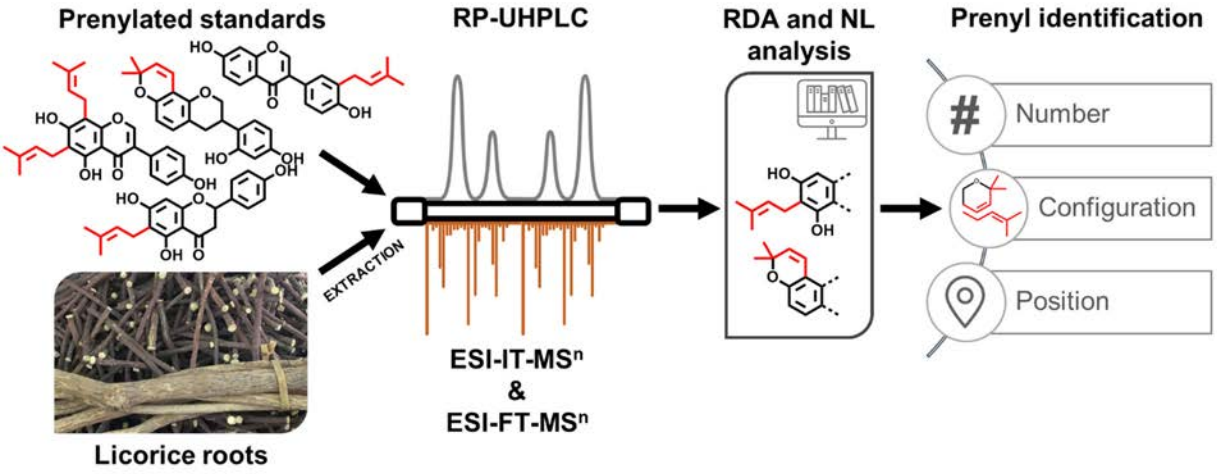
P-10 Mass spectrometry as tool for identification and characterization of prenyl number, configuration, and position in different subclasses of (iso)flavonoids

Sarah van Dinteren MSc[1,2], Dr. Carla Araya-Cloutier[1], Dr. Wouter J.C. de Bruijn[1], Prof. Jean-Paul Vincken[1]

[1]*University of Wageningen, The Netherlands; sarah.vandinteren@wur.nl, carla.arayacloutier@wur.nl, wouter.debruijn@wur.nl, jean-paul.vincken@wur.nl;* [2]*(+31) 651790927*

Abstract

In the search for new antimicrobials, plant secondary metabolites provide unlimited opportunities due to their vast chemical diversity. Under (a)biotic stress, plants from the Fabaceae family, including *Glycyrrhiza* spp., produce prenylated (iso)flavonoids with potent antimicrobial activity. However, identification of these prenylated (iso)flavonoids in complex plant extracts is a laborious manual process that is prone to errors. Therefore, in this study, we developed a mass spectrometric decision guideline that easily identifies prenylation in complex plant extracts. We investigated fragmentation of prenylated (iso)flavonoid standards by using electrospray ionization ion trap mass spectrometry (ESI-IT-MS^n) with fragmentation by collision induced dissociation (CID) and Orbitrap-MS (ESI-FT-MS^n) with fragmentation by higher energy C-trap dissociation (HCD). By combining IT-MS^n and FT-MS^n, we determined fragmentation pathways of different subclasses of prenylated (iso)flavonoids and elucidated characteristic fragmentations and neutral losses of different prenyl configurations. The decision guideline enables to annotate (i) prenyl number, (ii) prenyl configuration, and (iii) prenyl position of unknown prenylated (iso)flavonoids analyzed by ESI-IT-MS. High resolution MS with HCD fragmentation was used to confirm molecular formulas of fragments and led to the new insights, which uncovered inconsistencies in previously proposed annotation guidelines. With this guideline, we annotated 196 prenylated (iso)flavonoids in a *G. glabra* root extract; 75 skeletons were single prenylated, 104 were double prenylated, and for merely 17 skeletons prenyl number could not unambiguously be annotated. In conclusion, our prenylation guideline facilitates rapid identification of prenyl number, prenyl configuration, and prenyl position in (iso)flavonoids in complex plant extracts. With this guideline, a more comprehensive characterization of complex antimicrobial extracts is within reach, which ultimately leads to better understanding structure antimicrobial activity relationships.



Acknowledgements

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P-11 Integrated bio-recognition mass spectrometry approaches for improved food-safety testing

Ariadni Geballa-Koukoula[1], Arjen Gerssen[1], Marco Blokland[1] and Michel W.F. Nielen[2]

[1] Wageningen Food Safety Research, Wageningen University and Research, P.O. Box 230, 6700 AE Wageningen, The Netherlands;
ariadni.geballakoukoula@wur.nl +31628494266, arjen.gerssen@wur.nl, marco.blokland@wur.nl
[2] Wageningen University, Laboratory of Organic Chemistry, Stippeneng 4, 6708 WE Wageningen, The Netherlands, michel.nielen@wur.nl

Abstract

The standard strategy for monitoring food contaminants in the EU consists of a two-tiered approach. First, screening is performed with various tools, including bioassays, such as immunoassays. If the screening result is suspect, the second step is confirmation with liquid or gas chromatography coupled with mass spectrometry (MS), which aims at the unequivocal identification and, when possible, quantitation of the contaminants that led to the suspect screening. Despite screening being fast, it only provides a yes/no answer for the presence of contaminants, while in the case of immunoassays, cross-reaction with the biorecognition element might lead to a false-positive result. Contrary, confirmation is time-consuming but is based on strict criteria to identify the screened contaminant with high certainty. Incorporating bio-recognition elements with direct MS analysis, eliminating the time-consuming chromatographic separation, leads to improved analysis performance, rapid specific and selective contaminant identification, and high-throughput, which are valuable in future regulatory settings for contaminant monitoring. In this line, different approaches of direct MS analysis of immuno-captured contaminants were developed, optimized, and validated [1-3]. In all approaches, specificity is achieved using highly selective monoclonal antibodies, and direct MS identification is achieved with direct infusion electrospray ionization (ESI), direct analysis in real time (DART), or blade spray ionization. The target analytes were the mycotoxin deoxynivalenol (DON) and the marine toxin domoic acid. Those analytes are strictly regulated in the EU, with a specified maximum permitted level, but their structural analogs that cross-react with the biorecognition element, i.e., masked forms of DON and kainic acid, respectively, are not regulated. This cross-reactivity makes a screening assay insufficient to differentiate between the regulated and the non-regulated forms; thus, confirmation is essential. When using an integrated bio-recognition MS approach, screening and confirmation are combined. These approaches are of high scientific interest and undoubtful societal significance because they will cause a paradigm shift in how food safety testing could be conducted in the near future.

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P-12 Making viticultural decisions based on spectroscopic and chemometric analysis of grape clusters in a vineyard

Daniel Schorn-García[1], Barbara Giussani[2], Olga Busto[1], Laura Aceña[1], Ricard Boqué[3], Montserrat Mestres[1]
[1&3]Universitat Rovira i Virgili, Department of Analytical Chemistry and Organic Chemistry, [1]Instrumental Sensometry (iSens) & [3]Chemometrics, Qualimetrics and Nanosensors Group, Campus Sescelades, 43007 Tarragona, Spain
[2]Dipartimento di Scienza e Alta Tecnologia, Università degli Studi dell'Insubria, Via Valleggio, 9, 22100 Como (Italy)

Abstract

One of the most critical decisions for the winemaker is the date of harvest as it is different in each vintage and conditions the quality of the final wine. Once picked, grapes do not improve in flavour, colour, or sugar content, so it is mandatory to properly monitor the ripening of grapes to harvest them exactly when the desired quality parameters are reached[1].

The content of sugars and pH are the common oenological indicators of grape ripeness, which can be quite easily determined with a portable refractometer and a pH meter. Total acidity is another common indicator, and in this case an acid-base titration of the grape juice is required. Other subjective attributes such as colour, texture from touch and after a bite, and flavour (recognizable varietal aroma) are periodically checked by growers and vintners.

To determine these parameters, a representative sample of the field to be harvested is necessary, and guaranteeing this representativeness is not an obvious task. This is because the ripening of the grapes shows great heterogeneity depending on the position of the vine in the field, the position of the cluster on the vine and even the position of the grape within the cluster[1].

This study aims to lay the foundations on three ambitious objectives:

i) to propose a method to monitor the maturity of grapes directly on the field based on middle infrared (MIR) portable spectroscopy and chemometric data analysis;
ii) to study the different sources of variability in grape samples in a vineyard using ANOVA Simultaneous Component Analysis (ASCA)[2] to determine the better sampling strategy;
iii) to build multivariate statistical process control (MSPC)[3] charts to help the winemakers/winegrowers to make decisions concerning the time of harvest.

To achieve these objectives, an extensive sampling campaign was carried out in the summer of 2021 in the experimental vineyard Mas dels Frares of the Faculty of Enology in Tarragona (Catalunya). Grapes of the variety Muscat of Alexandria were harvested during five ripening periods, with time 4 being the optimal time to harvest according to oenologists. Samples were collected considering different vineyard positions and different plant and cluster levels.

The grape juice (must) was analysed without any pretreatment by a portable 4100 ExoScan FTIR spectrometer (Agilent, California, USA). Chemometric calculations were performed using Matlab R2015 (The MathWorks, Natick, USA) and PLS Toolbox v8.7 (Eigenvector Research Inc., Eaglerock, USA).

The proposed methodology allowed to determine the main grape chemical parameters, to study the variability of samples throughout the investigated vineyard, and to prove that MSPC charts can help growers and vintners in viticultural decisions.

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P-13 On the monitoring of kefir fermentation using a low-cost miniaturized NIR spectrometer: developing analytical strategies and facing challenges

Giulia Gorla[1], Carlo Bertinetto[2], Jeroen J. Jansen[2], Alberto Ferrer[3], Barbara Giussani[1]

[1]*Department of Science and High Technology, University of Insubria, Como, Italy*
[2]*Institute for Molecules and Materials (Analytical Chemistry), Radboud University, Nijmegen, The Netherlands*
[3]*Multivariate Statistical Engineering Group, Department of Applied Statistics and Operational Research, and Quality, Valencia Polytechnic University, Valencia, Spain*

Abstract

In recent years, low cost miniaturized NIR spectrometers have been used to address quantification, discrimination and classification problems in many fields of application [1]. Indeed, different analytical strategies were employed to investigate the potentialities of this instrumentation for field and industrial applications. A key aspect to take into account when investigating new applications is surely the analytical set-up and the strategy of spectra acquisition. As for liquid and fluid samples, some retailers present their instruments with dedicated accessories, while in other cases it is the researcher who has to find and test analytical strategies suitable for their samples [2,3].
In this context, the dairy industry is showing particular interest in using portable near-infrared spectroscopy as a quality assessment method or process analytical tool [4]. Kefir is a dairy drink with raising interest due to its health beneficial effects [5]. The fermentation process involved chemicals and physical transformations that bring to the final product starting from milk by inoculating the so-called “kefir grains”.
In this study, the potentialities and limits of a handheld spectrometer (1350-2550 nm) in gaining information about kefir fermentation were investigated. Semi-skimmed milk was chosen as fermentation media. After adding the kefir grains, spectra were acquired at interval times during the evolution of the process that was carried out under temperature control. Sample pH was also measured since this property is a usual indicator of the process progress.
As the used NIR portable instrument has no cell for liquids analysis, several acquisition strategies were studied and optimized in the way of at-line and in-line analysis. The spectral variability related to the experimental set-up and the heterogeneity of the samples were explored.
To catch all the information included in the spectra and to pave the way for real-time monitoring, different approaches relied on multivariate analysis were employed.

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P-14

Leaky Waveguide Sensors

Ruchi Gupta, School of Chemistry, University of Birmingham, UK
r.gupta.3@bham.ac.uk

Being able to sense and quantify is ubiquitous to for instance, water monitoring and clinical diagnostics. There is a drive towards point-of-use analysis, which requires sensors and analytical microsystems. Current point-of-use analysis based on lateral flow devices provide qualitative and at best semi-quantitative information. Label-free optical sensors based on refractive index measurements can overcome this limitation. In this presentation, I will discuss some of our research on leaky waveguide (LW) sensors. I will discuss capabilities of LW sensors and challenges that need to be addressed.

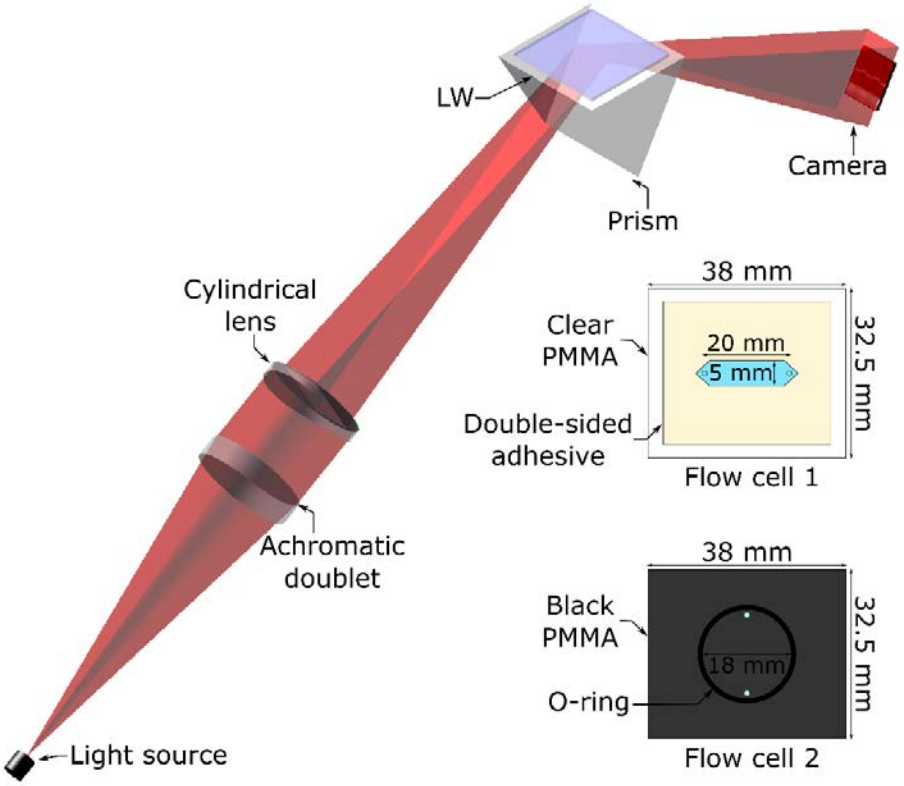
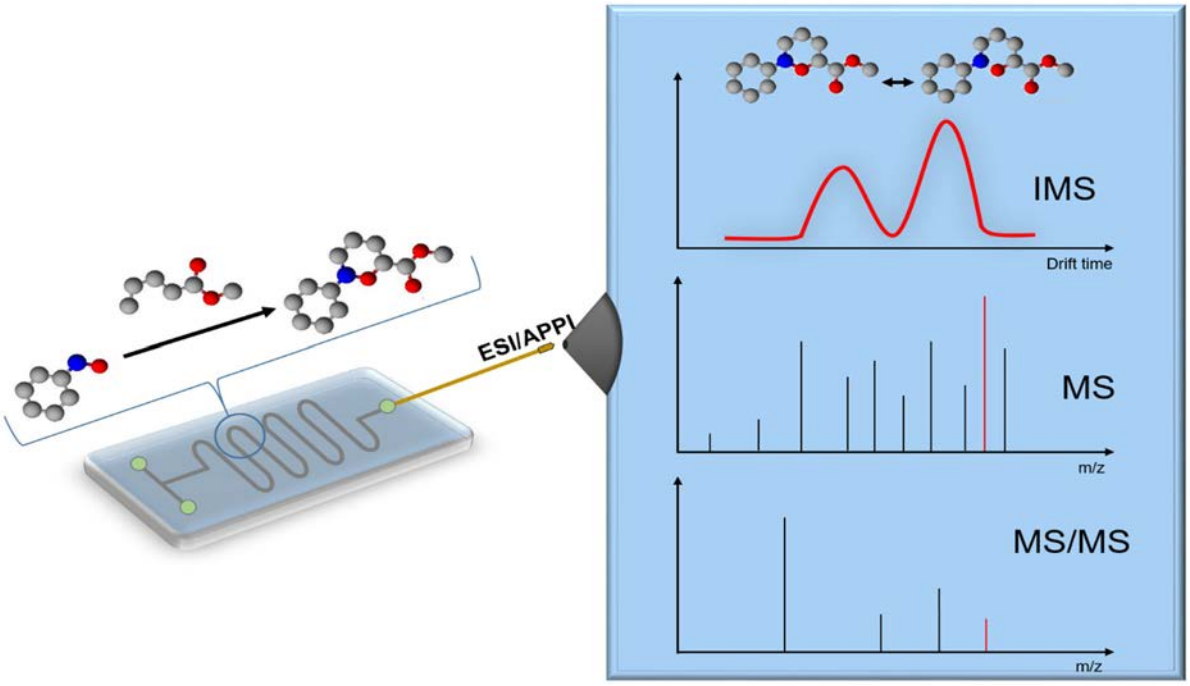


Figure 1: Schematic of our Leaky Waveguide (LW) Instrumentation

P-15 ION MOBILITY SPECTROMETRY-TANDEM MASS SPECTROMETRY STRATEGIES FOR THE ON-LINE MONITORING OF A CONTINUOUS MICROFLOW REACTION

Darya Hadavi[1], Peiliang Han[1], Maarten Honing[1]

[1] Maastricht Multimodal Molecular Imaging Institute (M4i), University of Maastricht, The Netherlands



Continuous flow chemistry is an efficient and green approach for chemical synthesis. Moreover, it could be directly connected to the analytical techniques for on-line monitoring. Here, we aim to use ion mobility, mass and tandem mass spectrometry (IMS-MS and MS/MS) for the on-line analysis of a pharmaceutically relevant chemical flow reaction. We carried out a model hetero-Diels Alder (DA) reaction in a microflow reactor directly connected to the IMS-MS and MS/MS using electrospray ionization method. We were able to monitor the reaction mechanism of the DA reaction and structurally characterize the reaction product and side-products. The chosen approach enabled identification of two isomers of the main reaction product. A new strategy to annotate the ion mobility spectrum in the absence of standard molecules was introduced and tested for its validity. This was achieved by determining the survival yield of each isomer upon ion mobility separation and density functional theory calculations. This approach was verified by comparing the theoretically driven collision cross section values to the experimental data. Here, we introduced the potential of combined MS-IMS and MS/MS on-line analysis platform to investigate, monitor and characterize structural isomers.

P-16 Fast, online three-phase electroextraction for the analysis of trace-level basic and acidic pharmaceuticals in biofluids

Yupeng He[1], Nicolas Drouin[1], Paul Miggiels[1], Peter W. Lindenburg[1,2], Bert Wouters[1], Thomas Hankemeier[1]

[1] Analytical Biosciences and Metabolomics, Systems Biomedicine and Pharmacology, Leiden Academic Centre for Drug Research, Leiden University, The Netherlands
[2] Research Group Metabolomics, Leiden Center for Applied Bioscience, University of Applied Sciences Leiden, The Netherlands

Abstract
Sample preparation is a challenge for high-throughput analysis, especially for volume-limited samples with low-abundant analytes. Ideally, sample preparation enriches the analytes of interest while removing the interferents to reduce the matrix effect and improves both sensitivity and quantification. In this study, a three-phase electroextraction (EE) method hyphenated to mass spectrometry (MS) was developed. Four model basic drugs (propranolol, amitriptyline, bupivacaine, and oxeladin) and four model acidic drugs (naproxen, fenoprofen, flurbiprofen, and ibuprofen) were utilized for the optimization and evaluation of the method. The critical parameters for the EE were optimized, *i.e.*, the type of organic solvent, pH of the sample and acceptor phase, and the extraction voltage and time. For basic compounds, the highest enrichment factors (EF) of 105–569 and extraction recoveries (ER) of 10.2%–55.7% were achieved within only 30 s, with limits of detection (LODs) ranging between 0.36 to 3.21 ng mL^{-1}, good linear response function ($R^2 > 0.99$), low relative standard deviation (0.6%–17.8%) and acceptable accuracy (73–112%). For acidic compounds, EF up to 190 and ER up to 38% were achieved in less than 2 min. Finally, the optimized three-phase EE methods was successfully applied to human plasma and urine samples. The developed three-phase EE method is easy to operate and provides fast and online extraction of trace-level basic and acidic analytes from volume-limited biological samples. Therefore, this method can provide a potential solution for sample-preparation bottlenecks in high-throughput bioanalysis workflows. To further improve the throughput and ease-of-use, we are integrating three-phase EE into an automated robot-based workflow.

P-17 Selectivity and Sensitivity without Chromatography: Real-time Mobile Mass Spectrometry for Trace Gas Analysis in Environment, Food and Consumer Goods

Arnd Ingendoh[1], Christopher Pfaff[1], Vaughan Langford[2], Mark Perkins[3]

[1]Syft Technologies, Darmstadt, Germany and [2]Christchurch, New Zealand, [3]Antune Ltd., Cambridge, UK

Abstract

Conventional methods for the analysis of trace volatile organic compounds (VOC) like GC/MS, GC-O (gas chromatography-olfactometry) or LC/MS usually involve significant sample preparation followed by time-consuming chromatographic analysis. Direct mass spectrometry (DMS) provides opportunities for simplifying or even complete elimination of sample preparation and for very short analysis times suitable for real-time monitoring or ultrahigh sample throughput. SIFT-MS (Selected Ion Flow Tube - Mass Spectrometry, [1]) is a DMS technique that utilizes a variety of precisely controlled soft chemical ionization reactions to detect and quantify trace VOC amounts at high selectivity without the need of chromatography.

SIFT uses eight reagent ions – H_3O^+, NO^+, O_2^+, O^-, O_2^-, OH^-, NO_2^- and NO_3^- – which are generated by plasma microwave discharge from simply moist air. These reactants exhibit a significant variety of ion-molecule reactions, i.e. often react differently with each compound, and thus enhance selectivity and allow to detect a wide range of VOC. The reagent ion selection is done in a first quadrupole mass filter with switching times in the ms range. This enables real time monitoring of dynamic processes even when multiple reagents are used for the analysis of various different compounds. The selected reagent ion interacts with the sample in a gas flow tube under well-defined conditions. Product ions and unreacted reagent ions are detected in a second quadrupole mass spectrometer. Utilizing a compound library with known rate coefficients (k), the software instantaneously calculates each analyte's absolute concentration from the specific reagent and product ion count rates. Typical run times for individual samples are in the range of less than one minute.

The technology is used in a wide range of applications where either real-time process monitoring or accelerated sample throughput is required. These cover environmental areas like wastewater [2] or exhaust control from factories or vehicles, consumer goods like flavor analysis or the evaporation of volatiles from packaging [3] in food and pharma, quality control of new fuels like hydrogen or e-car batteries, cleanroom monitoring in semiconductor production and others [4]. Presented here are typical examples that illustrate the features and benefits of DMS in comparison to conventional techniques. SIFT-MS is not that much seen in direct competition to those methods but as a most useful complementary addition to enhance productivity and data confidence.

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P-18 Production of Graphite-Based Conductive Filaments for the Fabrication of Ready-to-Use 3D Printed Electrochemical Sensors

Jéssica S. Stefano[1], Luiz Ricardo G. Silva[1], Raquel G. Rocha[2], Eduardo M. Richter[2], Rodrigo A. A. Muñoz[2], Bruno C. Janegitz[1]*

[1] *Laboratory of Sensors, Nanomedicine, and Nanostructured Materials, Federal University of São Carlos, Araras, São Paulo, 13600-970, Brazil.*
[2] *Institute of Chemistry, Federal University of Uberlândia, Uberlândia, Minas Gerais, 38400-902, Brazil.*

The 3D printing technology has gained ground due to its wide range of applicability. The development of new conductive filaments contributes significantly to the production of improved electrochemical devices. However, the production of conductive filaments is a challenge due to the difficulties of incorporating high percentages of conductive material. In this context, we report a simple method to producing an efficient conductive filament, containing graphite within the polymer matrix of PLA, and applied in conjunction with 3D printing technology to generate (bio)sensors without the need for surface activation. The proposed method for producing the conductive filament consists of the solubilization of PLA and incorporation of graphite powder. For this, a mixture of solvents (acetone and chloroform (3:1 v/v)) was employed in a reflux system under vigorous stirring for 3h at 70 ºC. A homogeneous mixture was obtained and immediate recrystallization was performed, transferring all the content into a recipient containing ethanol, a Gpt-PLA composite was obtained and dried overnight after a filtration process. The acquisition of the filaments was carried out with the insertion of the composite in an extruder and, finally, a 3D printer provided the three electrodes system and a non-conductive base was also printed using PLA for the coupling of the electrodes, forming the analysis system.

The produced filament was used for the manufacture of electrochemical 3D printed sensors. The filament and sensor were characterized by physicochemical techniques, such as SEM, TGA, Raman, FTIR as well as electrochemical techniques (EIS and CV). The $[Fe(CN)_6]^{3-/4-}$ electrochemical probe (1.0 mmol L^{-1}) in 0.1 mol L^{-1} KCl was explored to evaluate the electrochemical response of the obtained Gpt-PLA electrodes facing the use of commercial filaments containing graphene and carbon black (G-PLA and CB-PLA, respectively). It was observed that Gpt-PLA does not require surface treatment and presented superior electrochemical response (higher Ip and lower ΔEp), even in comparison to electrochemically treated G-PLA and CB-PLA electrodes, with a current ratio closer to unity, indicating better reversibility of the process.

Higher electroactive area was observed for the electrodes obtained from the manufactured filament, as well as faster HET and lower Rct values when compared with commercial filaments, with the advantage of being a ready-to-use filament (no pre-treatment step is necessary), additionally to be a lab-made material is of simple fabrication and relatively low-cost. Therefore, the lab-made produced filament is promising and can become an alternative route for the production of different 3D electrochemical (bio)sensors and other types of conductive devices by 3D printing, which has been applied in the analysis of analytes for clinical, food and environmental diagnosis.

P-19 Capillary and microchip electrophoresis for amino acid monitoring during biopharmaceutical cultivation

Saara Mikkonen[1], Leila Josefsson[1,2], Meeri Mäkinen[1], Veronique Chotteau[1,3], Åsa Emmer[1]
[1]KTH Royal Institute of Technology, Stockholm, Sweden, [2]Kantisto BV, Baarn, TheNetherlands, [3]AdBIOPRO, Stockholm, Sweden

Abstract
The biopharmaceuticals market is extremely fast-growing, and monoclonal antibody drugs produced by Chinese hamster ovary (CHO) cells are increasingly used to treat several diseases. There is a need for improved means of bioprocess monitoring in terms of speed, throughput, and amount of gained information. The culture medium is a complex mixture of nutrients and additives to create optimal conditions for the cells, and components produced or released by the cells, e.g. metabolites, product of interest, host cell proteins, and nucleic acid. Monitoring the concentrations of free amino acids (AAs) is important to obtain information about the culture's state, prevent depletion or unfavourable excess. Capillary electrophoresis (CE) and microchip-CE (MCE) can achieve fast, high-resolution separations consuming only nanolitres of sample, they are promising tools for bioprocess monitoring of AAs (figure 1). Samples of culture medium before addition of CHO cells (FMX-8) and spent CHO cell culture media at different days, were analysed using the two techniques. The results were compared to a currently used high performance liquid chromatography (HPLC). In samples from different days of a CHO cell cultivation process, all 19 proteinogenic AAs containing primary amine groups could be detected using CE, and 17 out of 19 AAs using MCE. The relative concentration changes in different samples of the spent cell culture agreed well with those measured by HPLC, R-values of 0.96 (CE vs. HPLC), 0.93 (CE vs. MCE) and 0.90 (HPLC vs. MCE) were obtained (after exclusion of outliers). Compared to the more commonly employed HPLC analysis, the CE and MCE methods resulted in faster analysis, while significantly lowering both the sample and reagent consumption, and the cost per analysis.

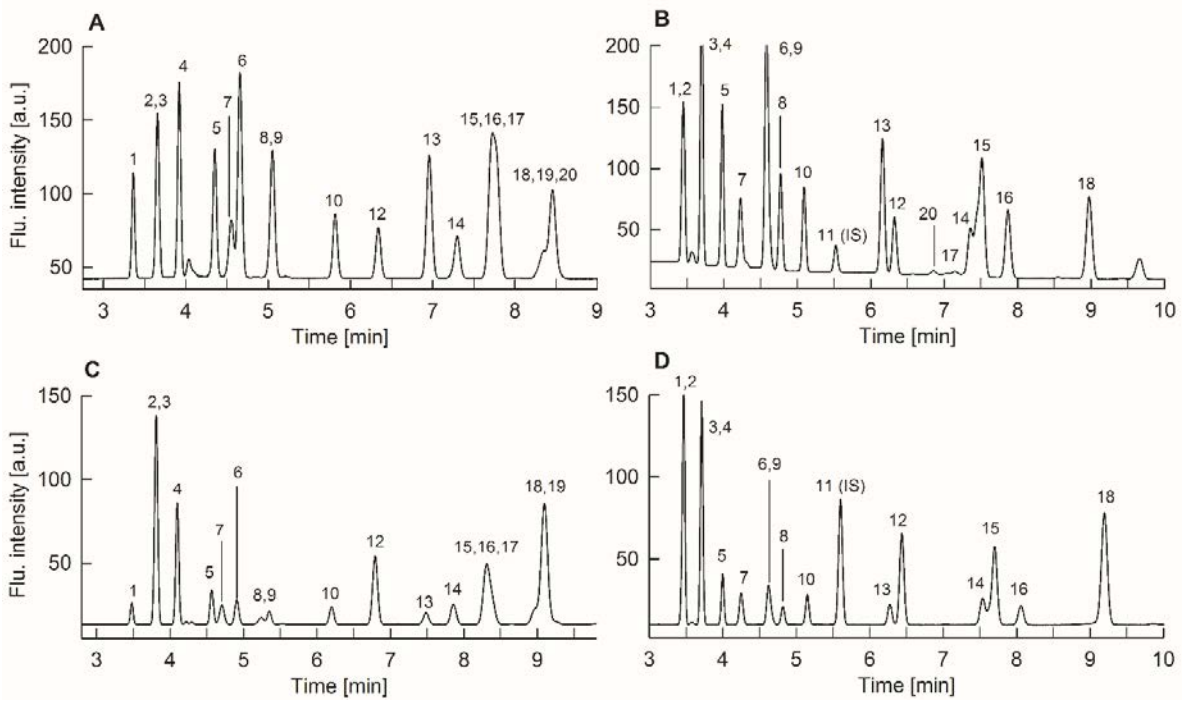

Figure 1- MCE-fluorescence of NDA derivatised AAs in a 7.9 cm chip. A) Method A, sample: AA stds, B) Method B), sample: AA stds, C) Method A, sample: FMX-8 cell culture medium. D) Method B, sample: FMX-8 cell culture medium. 1: Ser, 2: Asn, 3: Thr, 4: Gln, 5: His, 6: Gly, 7: Glu, 8: Ala, 9: Asp, 10: Tyr, 11: AABA (IS), 12: Val, 13: Met, 14: Ile, 15: Leu, 16: Phe, 17: Trp, 18: Arg, 19: Lys, 20: Cys.

P-20

Voltammetric determination of 4-(4-aminophenyl)morpholin-3-one

M. Kartashov[1,2], J. Barek[1,2], E.I. Korotkova[2]

[1] Charles University, Faculty of Science, UNESCO Laboratory of Environmental Electrochemistry, Hlavova 2030/8, CZ-128 43 Prague 2, Czech Republic
[2] National Research Tomsk Polytechnic University, Tomsk, Russia
E-mail: maks99661@gmail.com

Rivaroxaban is an oral anticoagulant from the group of direct factor Xa inhibitors. It is used to treat deep vein thrombosis and pulmonary embolism, as well as to prevent thrombi formation during atrial fibrillation and after hip or knee surgery [1]. Rivaroxaban could be considered for thromboprophylaxis in high VTE risk COVID-19 outpatients [2].

At the moment, there are only two voltammetric techniques intended for the determination of rivaroxaban [3,4], which shows the need to develop new voltammetric techniques and to study the electrochemical behavior of rivaroxaban in more details.

4-(4-Aminophenyl)morpholin-3-one (AM) is used as the model compound of rivaroxaban in the pilot study.

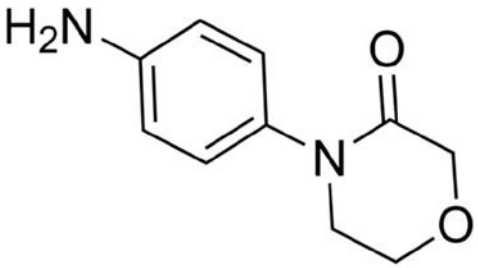

Figure 1 – Chemical structure of 4-(4-Aminophenyl)morpholin-3-one

The results of the voltammetric study of AM using HMDE as the working electrode, Ag|AgCl (3M KCl) as the reference electrode and platinum wire as the auxiliary electrode will be presented including optimization of instrumental parameters of cyclic voltammetry and differential pulse voltammetry employed for this investigation

Acknowledgement
This research was funded by the RFBR (project 19-53-26001), by the Czech Science Foundation (project GACR 20-01417J), and the Russian State assignment “Science” FSWW-2020-0022. We appreciate efficient material, technical and intellectual support of Metrohm.CZ (https://www.metrohm.com/cs-cz/).

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P-21 Unambiguous identification of ricin in complex samples using a combination of mass spectrometry methods, immuno- and activity assays

Jelle de Koning, Daan Noort, Marcel J. van der Schans, Alex Fidder, Debora van der Riet-van Oeveren, Ad de Jong, Roland van den Berg, Saskia de Kant

TNO Defense, Safety and Security, Department of CBRN Protection, Rijswijk, The Netherlands

Abstract

Ricin is a highly toxic protein which can cause cell death by inhibiting protein synthesis. Ricin is a so-called Schedule 1 compound under the Chemical Weapons Convention (CWC) and can be isolated from seeds of the castor bean plant. The widespread availability of castor beans renders ricin an agent of concern.

To verify the presence or to prove alleged use of ricin, methods for rapid, sensitive and (most importantly) unambiguous identification of ricin have been developed. These methods have been put to use in the context of a biotoxin exercise, organized by the Organization for Prohibition of Chemical Weapons (OPCW). Several test samples (provided by OPCW) were analyzed for the presence of ricin. After tryptic digestion, untargeted LC-HRMS measurements were done on the samples, leading to identification of peptides from both the A- and B-chain of the protein. The activity of ricin was assessed by a targeted LC-MS assay displaying the depurination effect of ricin on an oligonucleotide, resulting in free adenine. The protein identity was further confirmed by ELISA, which also allowed for semi-quantitation of the protein.

P-22 Structural annotation of novel biomarkers for inborn errors of metabolism with infrared ion spectroscopy

Pieter C. Kooijman[1], Tessa Peters[2], Karlien L.M. Coene[2], Udo Engelke[2], Jona Merx[3], Thomas J. Boltje[3], Jos Oomens[1,4], Jonathan Martens[1]

[1]Radboud University, Institute for Molecules and Materials, FELIX Laboratory, Nijmegen, the Netherlands; [2]Radboud University Medical Center, Translational Metabolic Laboratory, Nijmegen, the Netherlands; [3]Radboud University, Institute for Molecules and Materials, Synthetic Organic Chemistry, Nijmegen, the Netherlands; [4]van't Hoff Institute for Molecular Sciences, University of Amsterdam, Amsterdam, the Netherlands

Abstract

Modern metabolic approaches, such as untargeted liquid chromatography mass spectrometry (LC-MS) screening, make it possible to confidently link low abundant molecular features found in patients to metabolic disease states. Assigning the molecular structure of these features can often lead to the discovery or refinement of metabolic pathways and provide novel insights to the underlying biochemistry and pathophysiology.
Standard MS/MS or NMR approaches are often not able to distinguish the subtle structural differences (e.g. isomerism) between low-abundant isobaric features in a metabolic pathway. Infrared ion spectroscopy (IRIS) fills this gap, as it can be performed directly on patient samples by coupling to an LC-MS method. The vibrational bands of an infrared spectrum often contain the information needed to confidently assign the structure of biomarkers.

Features were detected using untargeted LC-MS in patient materials such as cerebrospinal fluid, blood plasma and urine. These compounds, often the nM range, were fractioned by heart-cut reversed phase (RP) or hydrophilic interaction liquid chromatography (HILIC) and analysed by infrared ion spectroscopy (IRIS) in an ion trap mass spectrometer coupled to the free-electron laser at the FELIX laboratory. Quantum-chemical calculations were used to determine the optimal wavelength range for IRIS on each target feature and to direct further investigation. Final confirmation was obtained by comparison to IRIS analysis of synthesized standards.

Using the method described above multiple previously unknown features have been assigned in patients with inborn errors of metabolism, such as AICA-ribosiduria, SSADH deficiency and GLUT1 deficiency syndrome. These identifications have led to new hypotheses on the pathways of the disease states and further discovery is ongoing.

We have successfully combined online heart-cutting HILIC and RPLC methods with our IRIS methodology to generate IR spectra from nM range components of patient samples in that enable and confident assignments of molecular structures.

P-23

Alternative strategies based on easy and cost effectiveness colorimetric assays for drug monitoring in Parkinson's patients

Mariagrazia Lettieri[1], Simona Scarano[1], Pasquale Palladino[1], Maria Minunni[1]

Department of Chemistry "Ugo Schiff", University of Florence,50019, Sesto Fiorentino, FI, Italy

Abstract

Over the past decade, the efforts of the scientists have increasingly been moving towards the development of pocket, easy-to-use, low-cost and fast-response diagnostics devices to ensure a continuous monitoring of the patient's health. In this context, we focused on the development of detection strategies for the drug monitoring in Parkinson's patients.

Parkinson's disease is neurodegenerative disorder caused by the degeneration of dopaminergic neurons upon pH-dependent oxidative conversion of neurotransmitters like dopamine into cytotoxic molecules. This lead to neuronal death and, consequently, characteristic symptoms of Parkinson's disease which are muscle rigidity, hypo- and bradykinesia and resting tremor. Unfortunately, there is no cure for Parkinson, but several medications may improve the quality of life of patients.

Dopamine cannot be straightly administered since it is a polar molecule unable to cross the blood brain barrier but levodopa, a precursor of dopamine, appears effective. In addition, Parkinson's drugs usually contain also decarboxylase and/or catechol-Omethyltransferase inhibitor like carbidopa which avoid levodopa metabolization prior to reach the brain. Hence, levodopa and carbidopa are the mainstays in the Parkinson's pharmacological therapy.

In this work, we proposed colorimetric detection strategies able to sensitively and selectively detect levodopa and carbidopa in commercial available Parkinson's drugs. Levodopa was detected exploiting the synthesis of purple melanochrome[1], here generated and stabilized for the first time. Levodopa was firstly quantified in two commercial drug formulations showing a common linear trend between 10 mg L^{-1} and 40 mg L^{-1} with levodopa alone or in combination with carbidopa in standard solutions, with very good reproducibility (CV_{av}% 3.3% for both brand and generic drug) and very good sensitivity, with limit of quantification about 0.6 mg L^{-1} in any case. Then, levodopa was detected in urine samples with a limit of quantification equal to 2.76 ± 1.03 x 10-4 mg L^{-1}, far below to levodopa reference values usually find in urine Parkinson's patients [2]. Then, we proceed to detect carbidopa through the synthesis of yellow and fluorescent dimetliylamitiobenzalazine obtaining low limit of quantification value (3.36 ± 0.11 mg L^{-1}) and high reproducibility (CV_{av}% 2).

The colorimetric methods, here developed, could revolutionize the monitoring of Parkinson's drugs in patients. In addition, the proposed tests are very simple and effective appearing as a rapid and low-cost alternative to other methodologies [3], that usually involves large and expensive instrumentations, for drug estimation and quality control of pharmaceutical formulations.

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P-24 Oriented Antibody coupling to a Low Fouling Polymer for Continuous Biomarker Monitoring by Particle Mobility

Maud Linssen[1], Sebastian van den Wildenberg[1], Yu-Ting Lin[2], Arthur de Jong[2,3], Menno Prins[1,2,3,4]

[1] Department of Biomedical Engineering, Eindhoven University of Technology, Eindhoven, The Netherlands; [2] Department of Applied Physics, Eindhoven University of Technology, Eindhoven, The Netherlands; [3] Institute for Complex Molecular Systems (ICMS), Eindhoven University of Technology, Eindhoven, The Netherlands; [4] Helia Biomonitoring, Eindhoven, The Netherlands

Abstract

Biosensing by Particle Mobility (BPM) is a novel sensing technology for continuous biomarker monitoring with single-molecule resolution [1-3]. To suppress the non-specific binding of biomolecules, Lin *et al* [3] introduced a low-fouling PLL-g-PEG bottlebrush polymer for surface functionalization. Here, we demonstrate the directional coupling of antibodies on a PLL-g-PEG surface to enable immunoassay biosensing with high sensitivity. Directional coupling of the antibodies was achieved by glycan remodeling, as illustrated in Figure 1. The glycans were first trimmed by endoglycosidase. Next, a modeled sugar containing an azide group, UDP-GalNac6N_3, was coupled to the glycosylation site by glycosyltransferase. In the final modification step, a single-stranded DNA-DBCO conjugate was connected to the azide via second-generation click-chemistry. The modified antibody was consecutively coupled to single-stranded DNA on the PLL-g-PEG surface by DNA hybridization. Directional binding of the antibodies was confirmed with DNA-PAINT using imagers that specifically bind to either the Fc or Fab part of the antibody. The surface functionalization was applied in BPM for the detection of Procalcitonin (PCT), an inflammation biomarker that is used in the intensive care. In this talk, we will describe the BPM sensing principle and the antibody coupling method. We will also present PCT biosensing using oriented as well as non-oriented antibodies.

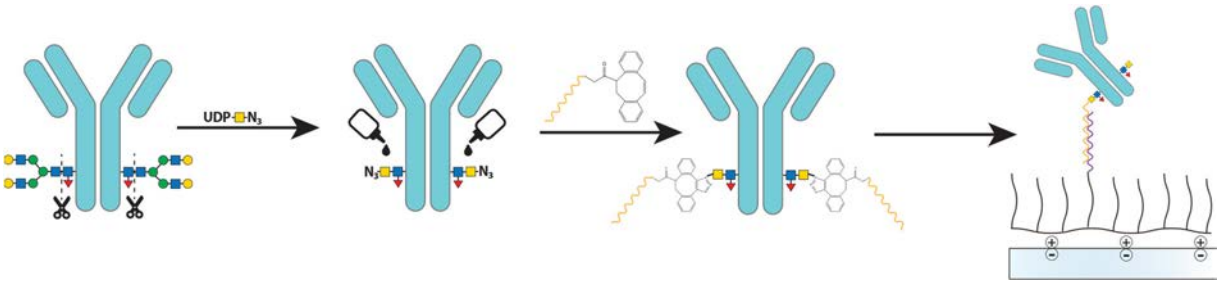

Figure 1: Oriented antibody coupling to PLL-g-PEG using glycan remodeling. The coupling method is studied in Biosensing by Particle Mobility (BPM) and applied for the monitoring of Procalcitonin (PCT).

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Acknowledgement: We thank Sander van Berkel (Synaffix) for providing us with the materials and knowledge for performing the glycan remodeling. We thank Marrit Tholen for performing measurements that proved that the antibodies were bound directionally.

P-25

Voltammetric determination of S-nitrosothiols in biological samples

L.Loskutova[1,2], J. Barek[1,2], E.I. Korotkova[2]

[1] Charles University, Faculty of Science, UNESCO Laboratory of Environmental Electrochemistry, Hlavova 2030/8, CZ-128 43 Prague 2, Czech Republic
[2] National Research Tomsk Polytechnic University, Tomsk, Russia
E-mail: loskuto4ek@mail.ru

Interest in S-nitrosothiols (RSNOs) has increased since their identification as key biologically important participants in nitric oxide-induced reactions [1]. Despite the large number of described methods for monitoring of S-nitrosothiols [2], there is still a need to develop new, more sensitive methods to understand the role of these compounds in various processes in the human body.

The immense potential of modern electroanalytical methods in the monitoring of S-nitrosothiols is generally recognized and appreciated because of their low investment and running costs, reasonable and in many cases "fit for the purpose" sensitivity and selectivity, easy automatization, easy miniaturization resulting in portability of corresponding instrumentation, user friendliness and environmental friendliness ("green electroanalytical chemistry") [3].

Nevertheless, the big problem connected with the use of modern electrochemical techniques in analysis of biological objects remains to be the passivation of working electrodes by products/intermediates of electrochemical reactions or by components of matrix sample which can adsorb on the electrode surface thus fouling the electrode and complicating the determination or even making it impossible.

We shall present voltammetric investigation of Diazald as the model compound containing the SNO-group.

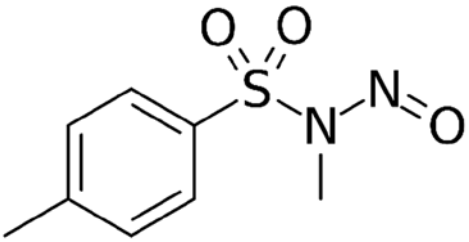

Figure 1 - Chemical structure of Diazald

The results of the voltammetric study of Diazald using HMDE as the working electrode, Ag|AgCl (3M KCl) as the reference electrode and platinum wire as the auxiliary electrode will be presented including optimization of instrumental parameters of cyclic voltammetry and differential pulse voltammetry employed for this investigation.

Acknowledgement
This research was funded by the RFBR (project 19-53-26001), by the Czech Science Foundation (project GACR 20-01417J), and the Russian State assignment "Science" FSWW-2020-0022. We appreciate efficient material, technical and intellectual support of Metrohm.CZ (https://www.metrohm.com/cs-cz/).

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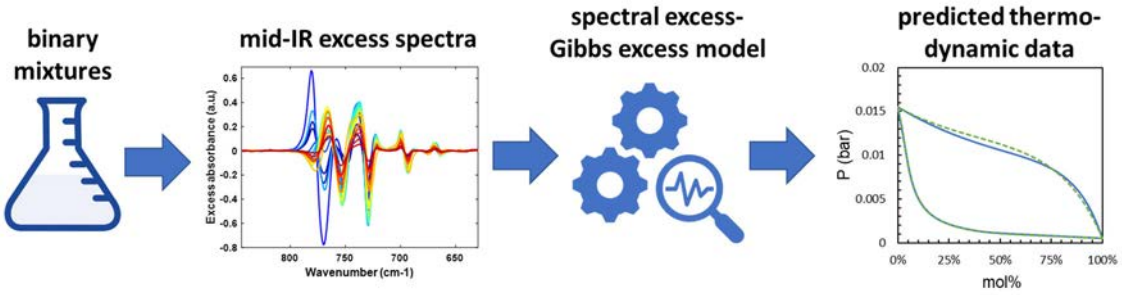
P-26 Predicting thermodynamic data from excess vibrational spectroscopy

Henk-Jan van Manen[1], Antoon ten Kate[1], Jan Gerretzen[1], Georgios M. Kontogeorgis[2], and Gerrald Bargeman[3,4]

[1] Nouryon Specialty Chemicals B.V., The Netherlands; [2] Technical University of Denmark, Denmark; [3] Nobian Industrial Chemicals B.V., The Netherlands; [4]University of Twente, The Netherlands



Abstract

There's a strong drive in the processing industries (e.g. chemical, pharmaceutical, materials) to move towards more sustainable processes and renewable products. Currently available process simulation tools are indispensable for process and product R&D and rely mostly on conventional thermodynamic models, which are often (semi)empirical and require a substantial amount of input data [1]. The generation of such data is time-consuming and application of models to complex mixtures of industrial interest is cumbersome. Consequently, there's a need for more accurate and predictive thermodynamic models and fast-track the generation of the required input data [1].

It is known that vibrational spectroscopies such as near- and mid-infrared absorption and Raman scattering provide useful information about intermolecular interactions and non-ideal behavior in liquid mixtures. Using this phenomenon, we have developed a methodology to predict thermodynamic data such as vapor-liquid equilibria from spectroscopic information [1]. The proof-of-principle work that will be presented in this contribution was performed on 45 binary mixtures, which were both formulated and analyzed spectroscopically using automated high-throughput experimentation. The backbone of our methodology is the successful prediction of Gibbs excess energy from excess mid-infrared spectra using multivariate partial least squares (PLS) regression. Within binary component families (e.g. alcohols-ketones), we have shown that PLS models based on a limited number of binary mixtures (e.g. for a few alcohol-ketone binary mixtures) can also predict Gibbs excess energy for other component mixtures within that family (e.g. for other alcohol-ketone mixtures) that were not included in the PLS calibration step. Furthermore, we have proven that, based on these predicted Gibbs excess energies, quite accurate vapor-liquid equilibrium envelopes can be obtained for component mixtures within that family that were not included in the PLS modelling [1].

The benefits of our methodology are the cost-effective, accurate and rapid measurement of non-ideality information and improved thermodynamic predictive models, even for complex mixtures. It therefore has the potential to contribute to the efficient development of improved sustainable processes.

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P-27

Continuous monitoring of Lactoferrin for real-time process control

Claire Michielsen[1], Arthur de Jong[2,3], Menno Prins[1,2,3,4]

[1] Department of Biomedical Engineering, Eindhoven University of Technology, The Netherlands; [2] Department of Applied Physics, Eindhoven University of Technology, The Netherlands; [3] Institute for Complex Molecular Systems(ICMS), Eindhoven University of Technology, The Netherlands; [4] Helia Biomonitoring, The Netherlands.

Abstract

Lactoferrin is a multifunctional iron-binding glycoprotein that supports the immune system and is present in secretory fluids. Due to its beneficial properties (a.o. antiviral, antibacterial, anti-inflammatory, anti-tumor, antioxidant)[1], Lactoferrin is extracted from bovine milk and used as a nutritional supplement. The manufacturing process has to deal with inherent fluctuations of the Lactoferrin concentration in bovine milk. Currently, the Lactoferrin concentration is measured in centralized laboratories, which is time-consuming and does not allow for immediate adjustments in the manufacturing process. Here, we describe a biosensor technology that creates a continuous stream of data, so that insights are gained and processes can be adapted in real time. The sensor is based on Biosensing by Particle Mobility (BPM), a reversible sensing principle with single-molecule resolution, as sketched in Fig. 1[2,3,4]. Antibodies are selected as molecular binders for Lactoferrin and changes of particle motion reflect the concentration in solution. In this talk, I will discuss the Lactoferrin protein, describe the BPM biosensing principle, explain the design of the biomolecular components and the sensing results, and will present how the sensor can be applied for continuous monitoring of Lactoferrin in bovine milk to improve the extraction process.

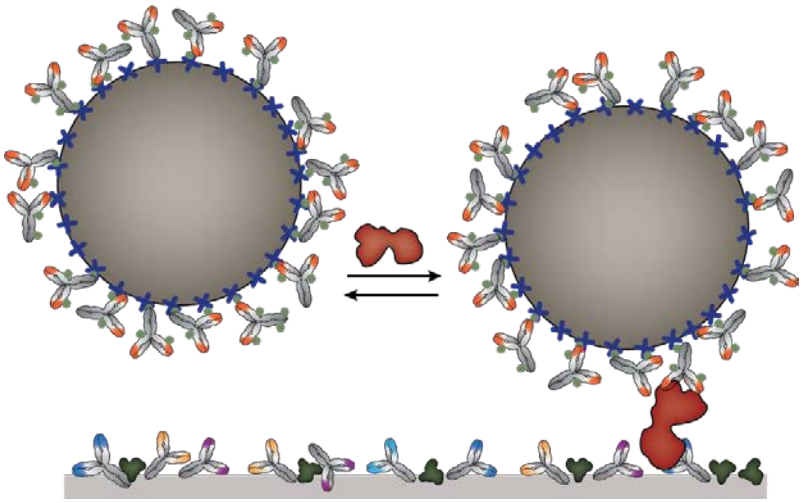

Figure 1. Schematic representation of the BPM biosensing principle for real time Lactoferrin monitoring. The substrate and the particle are functionalized with antibodies. In the presence of Lactoferrin, the particles switch between bound and unbound states.

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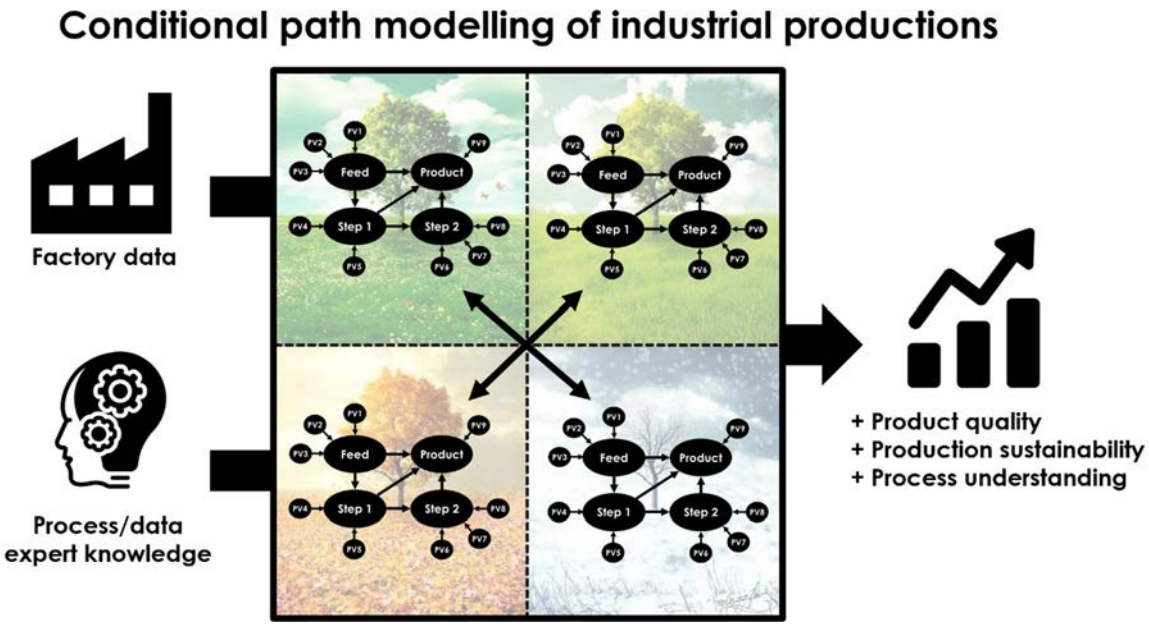
P-28 Improved understanding of production relationships with conditional Process-PLS

Tim Offermans[1], Geert van Kollenburg[1], Ewa Szymańska[2] and Jeroen Jansen[1]

[1] Radboud University, Nijmegen (the Netherlands); [2] FrieslandCampina, Amersfoort (the Netherlands)

Abstract

Understanding how different units of an industrial production plant are operationally related is key to improving production quality and sustainability. Path modelling is a valuable statistical tool to obtain such information from historical production data. Investigating how relationships within a process are affected by multiple production conditions and their interactions can however an even deeper understanding of the plant's daily operation. We therefore present conditional path modelling as an approach to obtain such improved understanding. For a milk powder production plant we studied how the relationships between different production units and steps depend on factors like production line, different seasons and product quality range. We show how the interaction of such factors can be quantified and interpreted in context of daily plant operation. Process PLS, which is a path modelling method recently developed to be optimally suited for analyzing industrial data, is used for this study. Our analysis revealed an augmented insight into the process that can be readily placed in the context of the plant's structure and behavior. Such insights can be vital to identify and improve upon shortcomings in current plant-wide monitoring and control routines.



P-29 Metabolite identification using infrared ion spectroscopy – Novel biomarkers for pyridoxine-dependent epilepsy

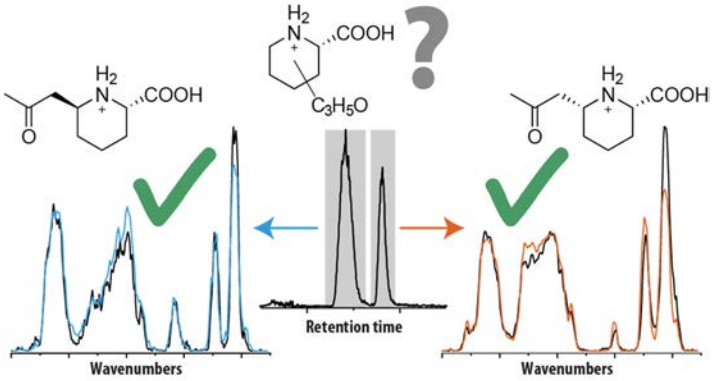
Rianne E. van Outersterp[1], Udo F.H. Engelke[2], Jona Merx[3], Giel Berden[1], Mathias Paul[4], Thomas Thomulka[4], Albrecht Berkessel[4], Marleen C.D.G. Huigen[2], Leo A.J. Kluijtmans[2], Jasmin Mecinović[5], Floris P.J.T. Rutjes[3], Clara D.M. van Karnebeek[6], Ron A. Wevers[2], Thomas J. Boltje[3], Karlien L.M. Coene[2], Jonathan Martens[1], and Jos Oomens[1]

[1]Institute for Molecules and Materials, FELIX Laboratory, Radboud University, 6525 ED Nijmegen, The Netherlands; [2] Department of Laboratory Medicine, Translational Metabolic Laboratory, Radboud University Medical Center, 6525 GA Nijmegen, The Netherlands; [3]Institute for Molecules and Materials, Synthetic Organic Chemistry, Radboud University, 6525 AJ Nijmegen, The Netherland; [4]Department of Chemistry, University of Cologne, 50939 Cologne, Germany; [5]University of Southern Denmark, Department of Physics, Chemistry and Pharmacy, 5230 Odense, Denmark; [6]Department of Pediatrics-Metabolic Diseases, Radboud Center for Mitochondrial Medicine, Radboud University Medical Center, 6525 GA Nijmegen, The Netherlands; [7]van't Hoff Institute for Molecular Sciences, University of Amsterdam, 1098XH Amsterdam, The Netherlands

Abstract

Untargeted liquid chromatography-mass spectrometry (LC-MS) is commonly used to find new biomarkers for metabolic disorders. However, assigning a full molecular structure to the detected *m/z*-values remains a significant challenge. To address this, we have developed a novel workflow for biomarker discovery combining untargeted LC-MS metabolite screening with targeted molecular identification using infrared ion spectroscopy (IRIS). IRIS can often distinguish between closely related isomers and has as significant advantage that *in silico*-predicted IR spectra of candidate chemical structures can be used to suggest the molecular structure of unknown features, thus mitigating the need for the synthesis of a broad range of physical reference standards.

Pyridoxine-dependent epilepsy (PDE) is a metabolic disorder caused by the deficiency of one of the enzymes responsible for lysine catabolism, leading to severe epilepsy in newborns. The defect leads to the accumulation of α-aminoadipic semialdehyde (α-AASA), piperideine-6-carboxylate (P6C), and pipecolic acid in body fluids. The main cause of symptoms is thought to be depletion of vitamin B6 through its reaction with P6C. However, supplementation of vitamin B6 incompletely resolves disease symptoms, suggesting that the biochemistry is incompletely understood. Additionally, while early diagnosis is crucial for successful treatment outcomes, PDE is yet not part of the national newborn screening program as all currently known biomarkers are too chemically unstable for analysis from dried bloodspots. Here, we demonstrate the identification of four new metabolites accumulating in PDE. These biomarkers are chemically stable and suitable for use in newborn screening programs. Additionally, we show that the identification of these novel metabolites directly provides novel insights into the pathophysiology of PDE.



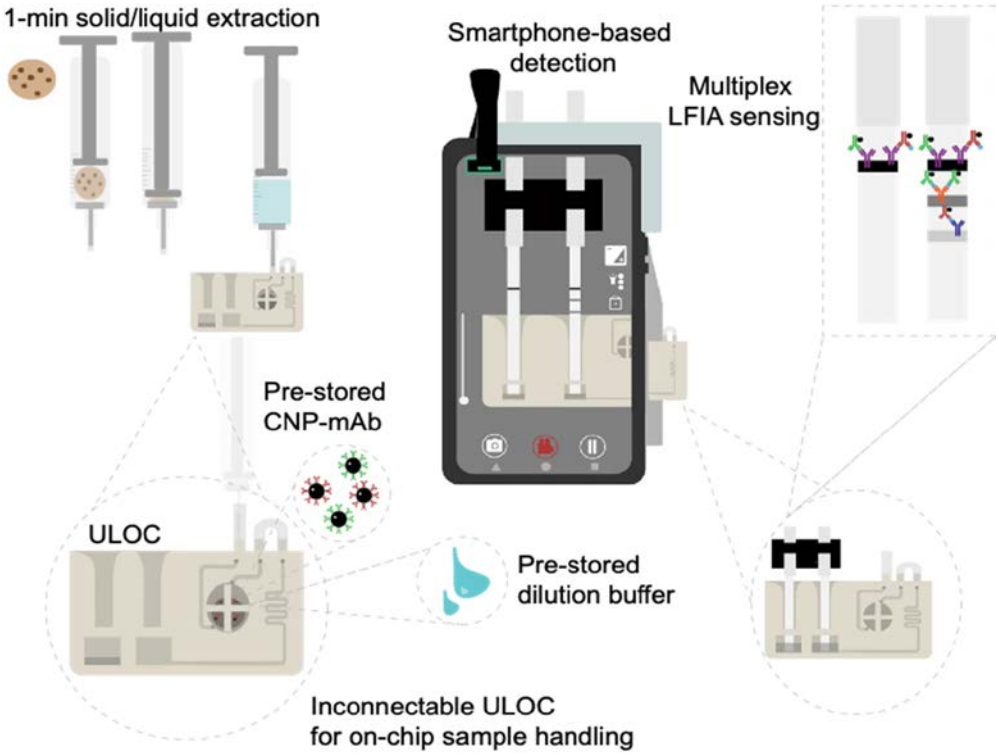
P-30

Smart allergen detection: a consumer-operable platform for total on-site analysis of food allergens

Ross, G.M.S[1,2]. Filippini, D[3]. Nielen, M.W.F[1,2]. Salentijn, G.IJ[1,2].

1. Wageningen Food Safety Research (WFSR), Wageningen University & Research, P.O. Box 230, Wageningen 6700 AE, The Netherlands
2. Laboratory of Organic Chemistry, Wageningen University, Stippeneng 4, Wageningen 6708 WE, The Netherlands
3. Optical Devices Laboratory, Division of Sensor and Actuator Systems, IFM - Linköping University, S58183, Linköping, Sweden

Undeclared allergens in foods pose a severe risk for allergic consumers. Considering that allergen monitoring, and management are key priorities for the food industry, there is an evident need for simplified, rapid, ubiquitous, screening methods that allow for the near real-time detection of allergens by food producers on-site, and by consumers on-the-go. While consumer-focused food analysis is upcoming, the need for multiple sample preparation and handling steps is limiting. On-site and consumer-friendly analysis paradoxically still requires laboratory-based and skill-intensive sample preparation methods. To target this, a compact, inexpensive, and novel prototype immunosensor combining sample preparation and on-chip reagent storage for multiplex allergen lateral flow immunosensing has been developed. The comprehensive approach paves the way for personalized consumer diagnostics. The prototype allows for handheld solid-liquid extraction, pipette-free on-chip dilution, and controllable adjustment of sample concentrations into the appropriate assay dynamic working range (0.1 - 100 ppm). The disposable and interconnectable sample-preparation-syringe allows for the solid-liquid extraction of allergenic proteins from solid bakery products in 1 min. The sample-preparation-syringe interconnects with a 3D-printed unibody lab-on-a-chip (ULOC) microdevice, which is used to deliver precise volumes of sample extract to a reagent reservoir. The reagent reservoir is implemented for on-chip storage of carbon nanoparticle labeled antibodies and running buffer for sample dilution. The handheld prototype allows for total homogenization of solid samples, solid-liquid protein extraction, 3D-printed sieve based filtration, ULOC-enabled dilution, mixing, transport, and smartphone-based detection of hazelnut and peanut allergens in solid bakery products with limited operational complexity. The multiplex lateral flow immunoassay (LFIA) detects allergens as low as 0.1 ppm in real bakery products, and the system is already consumer-operable (having been tested by a 15 year old participant), demonstrating its potential for future citizen science approaches. The designed system is suitable for a wide range of analytical applications outside of food safety, provided an LFIA is available. Moreover, by using a smartphone-based video method for monitoring the LFIA signal development in real-time, it is possible to distinguish between different concentration dependent effects in LFIAs that can lead to false results. Digitally analysing this data allows clear differentiation of highly positive samples and false negative samples and can indicate whether the LFIA is in the dynamic working range to at critically high concentrations.



This project has received funding from the European Union's Horizon 2020 research and innovation program under the Marie Sklodowska-Curie grant agreement no. 720325.

P-31

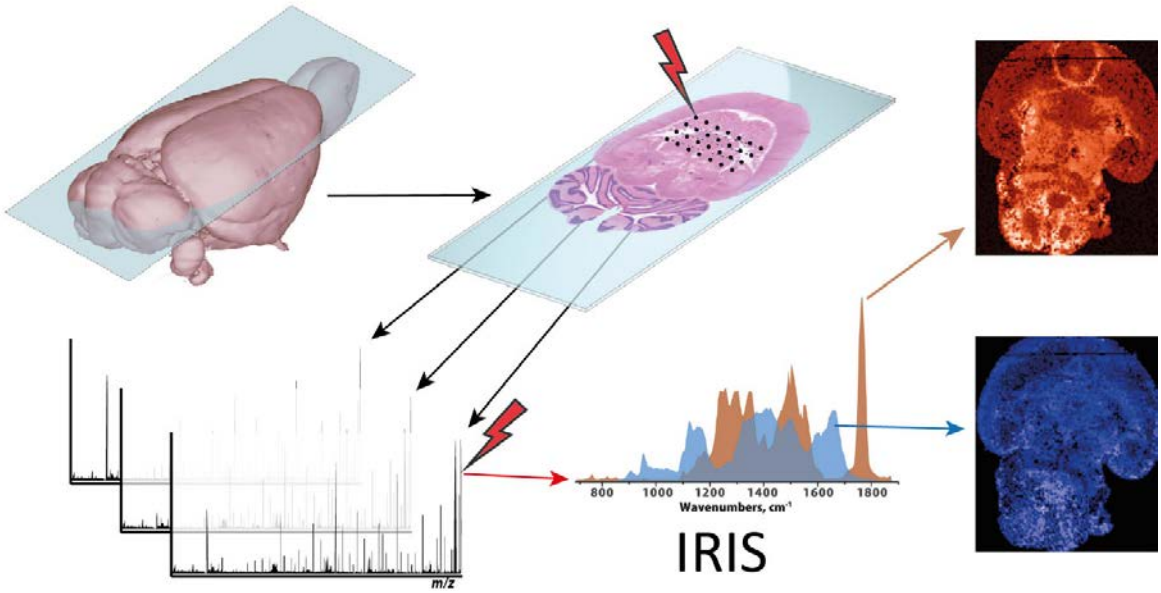
STRUCTURAL ELUCIDATION IN MALDI MASS SPECTROMETRY IMAGING WITH INFRARED ION SPECTROSCOPY

Jelle Schuurman[1], Pieter Kooijman[1], Kas Houthuijs, Jos Oomens[1] , Jonathan Martens[1]

[1] *FELIX Laboratory, Radboud University, Nijmegen, the Netherlands*

Abstract

Mass spectrometry imaging (MSI) is a powerful technique used to study the spatial distribution of molecules in a sample. An interesting and recent application of MSI is in the study of spatially resolved metabolomics which aims to generate an improved understanding of metabolic diseases. Even though MSI is mass-selective and can be highly sensitive, distinguishing isomers and identifying previously unknown *m/z*-features remains a major limitation. InfraRed Ion Spectroscopy (IRIS) is an increasingly popular mass spectrometry-based method that provides an orthogonal spectroscopic basis for structural characterization of ions detected in the mass spectrometer. Here we present recent results highlighting the progress towards combining MSI and IRIS for spectroscopic characterization of spatially resolved ions. It is impossible to record an entire IR spectrum at each pixel in the MSI experiment as IRIS requires one mass spectrum for every frequency point in the IR spectrum. Instead, we implement either an imaging- or a spectroscopy-favoured experiment. The first experiment uses isomer-selective photo-dissociation to distinguish the presence of a particular isomer using known vibrational resonances unique to that species. The very short time scale of the laser pulse (microseconds) allows the MSI experiment to continue normally as it would under common tandem MS conditions. The second experiment aims to measure a full IR spectrum by exploring a region of the sample where the *m/z* of interest is present rather than considering only that *m/z* from a single pixel. The frequency of the IR laser can be tuned between pixels to generate an IR spectrum of the *m/z* of interest over tens or hundreds of pixels. To demonstrate the technique, we apply combined MSI+IRIS to study the metabolic disease pyridoxine dependent epilepsy (PDE), aiming to generate spatial resolved detection of metabolites associated with this disease in a mouse model. Our preliminary MSI data contains several known as well as a handful of unknown metabolites (*m/z*-features) that correlate with our knockout group. Using this example, we will highlight how IRIS can be combined with MSI and used to confirm the molecular structures of ions detected in MSI.



P-32 Determination of uremic retention solutes in human biological samples: sample treatment features

Andreia N. Meireles [1], Sara R. Fernandes [1, 2], Luisa Barreiros [1, 2], Benedita Sampaio-Maia [3, 4] and Marcela A. Segundo[1]

[1] LAQV/REQUIMTE, University of Porto, Portugal; [2] Escola Superior de Saúde, Instituto Politécnico do Porto, Portugal; [3] FMDUP, University of Porto, Portugal; [4] INEB/I3S, Portugal

Abstract

Healthy kidneys are responsible for the excretion of a large number of compounds from the organism. However, when renal function is compromised, several compounds tend to be progressively retained in the organism, due to a decrease in their renal clearance. The retained compounds are named uremic retention solutes (1). Indole-3-acetic acid, indoxyl sulfate, p-cresol and p-cresol sulfate are examples of uremic retention solutes, which are associated with the development of several pathologies, namely renal, cardiovascular and bone toxicities, due to their possible accumulation in the body.

The present work aims to compare recent methods proposed for the determination of uremic retention solutes using chromatographic techniques. Emphasis is given to sample treatment strategies targeting serum, plasma, urine, and saliva, which includes protein precipitation, pH adjustment, separation of phases by centrifugation, solid-phase extraction, and salting-out assisted liquid-liquid extraction. Particular aspects according to the type of sample are critically discussed, namely the existence of target compounds bound to proteins and the strategies applied to distinguish bound and free analytes. Automated solid-phase extraction using the bead injection concept is also introduced for determination of indoxyl sulfate and p-cresol sulfate in plasma samples. Adicionally, the greenness of the different sample treatment strategies is evaluated using the AGREEprep metric (2), where ten criteria are considered, including the minimization of sample, chemicals, materials and waste; the maximization of sample throughput; and the minimization of energy consumption, among others.

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Acknowledgements

This work received financial support from FCT/MCTES through grant UIDB/50006/2020, from IUPAC through project 2021-015-2-500, and from the Competitiveness and Internationalisation Operational Programme (POCI), under the PORTUGAL 2020 Partnership Agreement (European Regional Development Fund (ERDF) and FCT funds) through project POCI-01-0145-FEDER-029777. S. R. Fernandes thanks FCT and POCH (Programa Operacional Capital Humano) for her PhD grant (SFRH/BD/130948/2017). L. Barreiros acknowledges funding from FCT through program DL 57/2016 – Norma transitória.

P-33

Contextual-based soft sensors: Integrating expert knowledge and extracting insights from predictive modeling

Francisco Souza[1], Tim Offermans[1], Geert Postma[1], Jeroen Jansen[1]

[1] *Radboud University, Institute for Molecules and Materials, Analytical Chemistry & Chemometrics, Heyendaalseweg 135 6525 AJ Nijmegen, The Netherlands*

Abstract

There is an increasing demand for industrialization towards a more sustainable and greener industrial future. Artificial intelligence (AI) is at the front of the 4th industrial revolution by redefining decision-making at the operational and technical levels, allowing faster, data-driven, and automatic decision-making along the value chain. Also, with further growth in industrial data infrastructure, many companies are implementing data-driven predictive models to improve energy efficiencies and industrial sustainability. These policies can reduce production costs and environmental impact while increasing process efficiency. In that sense, there is an increased demand for explainable AI models, to provide valuable insights on the process to be modeled, instead of the pure black-box modeling in which the focus is only on predictive performance. In this work, we discuss using the contextual mixture of experts, a new family of models capable of integrating the process-specific characteristics into the learning. The Contextual Mixture of Experts explicitly uses process knowledge along the model learning stage to mold the historical data to represent operators' context related to the process. A schematic of this approach is illustrated in Fig. 1a. The results will be presented with two real case studies for quality prediction in a sulfur recovery unit and a polymerization process. The contextual mixture of experts was employed to represent different contexts in both experiments. The results indicate that integrating process knowledge has increased predictive performance while improving interpretability by providing insights into the variables affecting the process's different regimes.

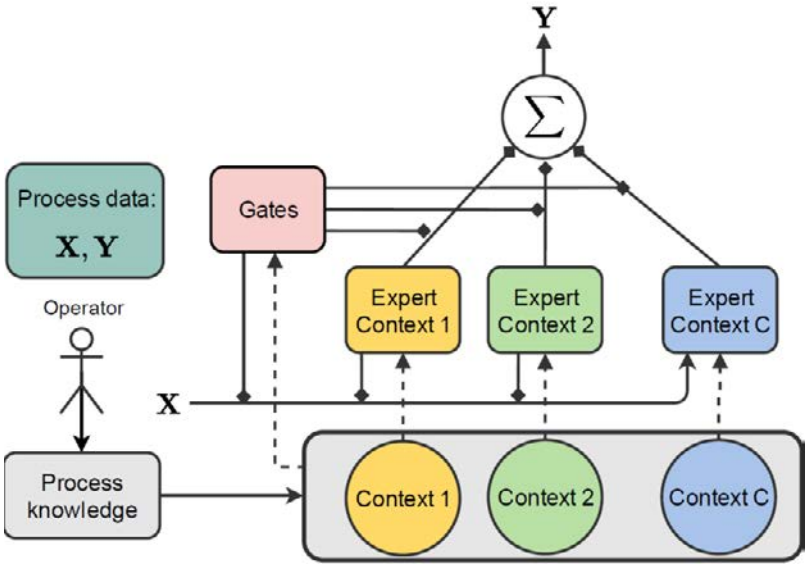

Figure 1. Representation of the contextual mixture of experts for learning different phases for a batch process

P-34 Revealing the structure of chemokine-glycosaminoglycan complexes by native mass spectrometry

Gergo Peter Szekeres[1,2], Douglas P. Dyer[3], Weston Struwe[4], Kevin Pagel[1,2], Rebecca Miller[5]

[1]Freie Universität Berlin, Germany; [2]Fritz Haber Institute of the Max Planck Society, Berlin, Germany; [3]Wellcome Trust Centre for Cell Matrix Research, University of Manchester, United Kingdom; [4]University of Oxford, United Kingdom; [5]Copenhagen Center for Glycomics, University of Copenhagen, Denmark

Abstract

Chemokines play a central role in our immune system by combating infection and trauma [1]. One of the most well-known chemokines called platelet factor 4 (PF4 or CXCL4) aids the clotting process upon injury to prevent excessive bleeding, among other regulatory tasks. In atypical cases, these molecules can be linked to adverse physiological phenomena, such as autoimmune processes or cancer. The concentration of CXCL4 can also increase in viral infections, leading to negative consequences [2]: most recently, in SARS-COV-2 patients with severe symptoms, the infection resulted in chemokine activation and abnormal blood clot formation similar to heparin-induced thrombocytopenia and thrombosis (HITT). Such a response is based on chemokine-glycosaminoglycan interactions. In these interactions, some chemokines remain monomeric (e.g., CCL7) or form dimers and tetramers (e.g., CCL2), while others like CXCL4 and CCL5 form massive complexes, which in rare events can induce HITT [3]. Although research in this direction is abundant, our knowledge on the properties of the complex-forming glycosaminoglycan chains or the complex size range necessary to induce HITT is currently limited.

In this work, we use native mass spectrometry and mass photometry to study the interaction of different chemokines with glycosaminoglycans of different lengths and charges, and to learn about the mechanism of chemokine-glycosaminoglycan oligomerization. Our analysis confirms monomeric CCL7, dimeric CCL2, and tetrameric CCL2 and CXCL4 complexes upon glycosaminoglycan binding. The collision-induced dissociation of CXCL4-glycosaminoglycan complexes allowed for insight into the interactions that result in complexes in the range of hundreds of kilodaltons observed by mass photometry.

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Acknowledgement

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P-35

Chemsy: Simultaneous feature selection, pre-processing search, model selection, and hyper-parameter optimization in Python

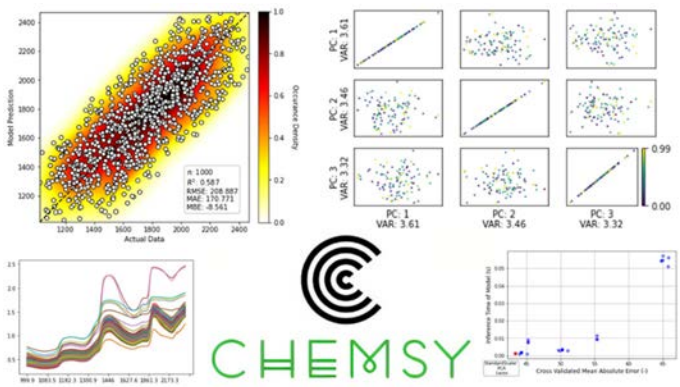
Sin Yong Teng[1], Martijn Dingemans[1], Maria Cairoli[1], Jeroen J. Jansen[1]
(presenting author underlined)

[1] *Radboud University, 6525 AJ Nijmegen, the Netherlands*

Abstract

Chemsy is a chemometrics and machine-learning framework written in Python with a *sklearn* syntax to allow for flexible usage. The Chemsy framework was designed to provide automated data modelling features with the consideration of full flexibility of the user. Here, we demonstrate the simultaneous capabilities of Chemsy in feature selection, pre-processing search, model selection, and hyperparameter optimization in spectroscopic modelling via examples of regression and classification using standard benchmark dataset. With the Chemsy framework, specific optimization algorithms can also be customized to be used for automatic pipeline search. For example, we demonstrate the use of Chemsy with various different optimization solvers such as brute force search, random search, design of experiment strategy (Gerretzen et al., 2015), genetic algorithm, particle swarm optimization, etc. The use of Chemsy allows for a simplistic, yet fully customizable chemometrics platform for upcoming applications.

Illustration



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Acknowledgement

This project is co-funded by TKI-E&I with the supplementary grant 'TKI- Toeslag' for Topconsortia for Knowledge and Innovation (TKI's) of the Ministry of Economic Affairs and Climate Policy. The authors thank all partners within the project 'Measure for Management (M4M)', managed by the Institute for Sustainable Process Technology (ISPT) in Amersfoort, The Netherlands.

P-36 Water quality based on the analysis of high-resolution phytoplankton data

Gerjen H. Tinnevelt,[1,2] Olga Lushchikova[1,2], Mathijs Lochs[1,2], Dillen Augustijn[1,2], Rinze W. Geertsma[3], Machteld Rijkeboer[3], Harrie Kools[4], George Dubelaar[4], Arnold Veen[3], Lutgarde M.C. Buydens[1], Jeroen J. Jansen[1]

[1]Radboud University, Institute for Molecules and Materials, (Analytical Chemistry), Nijmegen, The Netherlands; [2]TI-COAST, Amsterdam, The Netherlands; [3]Laboratory for Hydrobiological Analysis, Rijkswaterstaat (RWS), Lelystad, The Netherlands; [4]CytoBuoy bv, Woerden, The Netherlands.

Abstract

River water is an important source for Dutch drinking water. For this reason, continuous monitoring of river water quality is needed. However, comprehensive chemical analyses with high resolution mass spectrometry (GC-MS/LC-MS) are quite tedious and time consuming, making them poorly fit for routine water quality monitoring and therefore many pollution events are missed. Phytoplankton are highly sensitive and responsive to toxicity, which makes them highly usable for effect-based water quality monitoring. Flow cytometry can measure the optical properties of phytoplankton every hour, generating a large amount of information-rich data in one year. This however requires chemometrics, as the resulting fingerprints need to be processed into information about abnormal phytoplankton behavior. We developed the Discriminant Analysis of Multi-Aspect CYtometry (DAMACY) to model the "normal condition" of the phytoplankton community imposed by diurnal, meteorological and other exogenous influences, see Figure 1. DAMACY first describes the cellular variability and distribution of phytoplankton in each measurement using PCA, and then aims to find subtle differences in these phytoplankton distributions that predict normal environmental conditions using (O)-PLS-DA. Deviations from these normal environmental conditions indicated abnormal phytoplankton behavior that happened alongside pollution events measured with the GC/MS and LC/MS systems. Thus, our results demonstrate that flow cytometry in combination with chemometrics may be used for an automated hourly assessment of river water quality and as a near real-time early warning for detecting harmful (un)known contaminants. Additionally we use automatic updating of the model to account for year-to-year variance. We are currently working on implementing this warning system such that drinking water companies can temporary stop pumping water whenever abnormal phytoplankton behavior is detected. In the case of prolonged abnormal phytoplankton behavior, comprehensive chemical analysis can still be used to identify the (un)known chemical compound, its origin and toxicity.

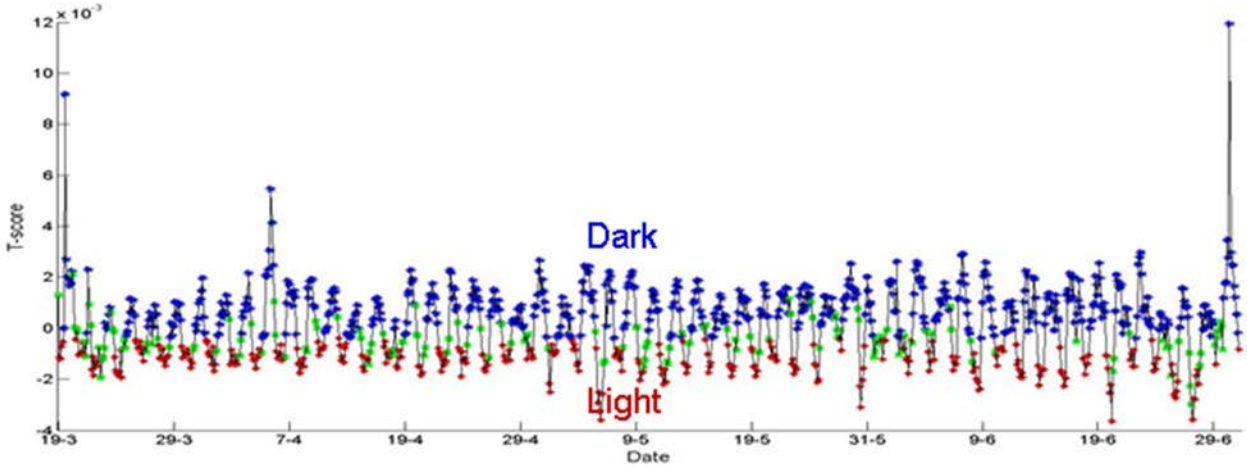

Figure 1: DAMACY on flow cytometry data of phytoplankton can successfully predict diurnal rhythms.

P-37 Simultaneous Electron and Chemical Ionization used for GC- and Real Time – MS applications for improved Targeted and Non-Targeted Analysis

Marleen Vetter[1], Steffen Bräkling[1, 2] and Sonja Klee[1]
(presenting author underlined)

[1] *Tofwerk AG, Thun, Switzerland;* [2] *University of Wuppertal, Wuppertal, Germany*

Abstract

A time of flight (TOF) mass spectrometer operating an electron ionization (EI) and a chemical ionization (CI) source simultaneously is presented. The instrument offers multiple setup options that provide the opportunity to use gas chromatographic as well as real time samplings.
Via parallel coupling of both ionization sources directly to one single gas chromatograph (GC) target and suspect screening analysis is improved as well as effective non-target analysis via GC-MS is rendered possible. Simultaneous structural as well as accurate mass molecular ion information is generated via one GC-MS analysis step.
Real time-CI-TOFMS is well known to allow direct measurements of complex mixtures during rapid sample changes, coping with large dynamic ranges of analyte concentration. The high resolution, accurate mass TOF full-mass spectrum creates a full picture of the sample all the time. Simultaneous GC-TOF analysis of the same sample allows for effective separation and identification of isomers via divergent EI mass spectra using one singe analyzer. High resolution mass analysis increases the information on analytes that would be concealed in nominal mass spectrometry.

Various types of experiments will be presented to depict the performance of the instruments for different applications. The advantages for targeted and non-targeted approaches will be elaborated using multiple common GC-MS standards including pesticides, allergens, phthalates etc. The information increase on a sample using simultaneous analysis via GC and real time mass spectrometry is presented for a biomass burning process depicting the burning emissions in high time resolution. In addition, the parallel GC-TOF measurements show isomer separation and improved compound identification.

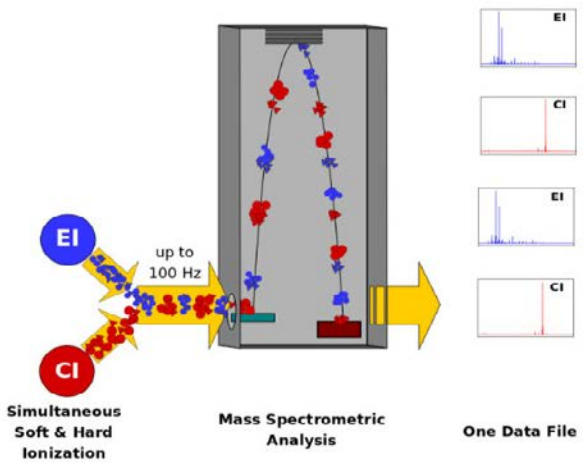

Figure 1: Principle of operation for quasi-simultaneous generation of EI and CI mass spectra on one single TOF mass analyzer

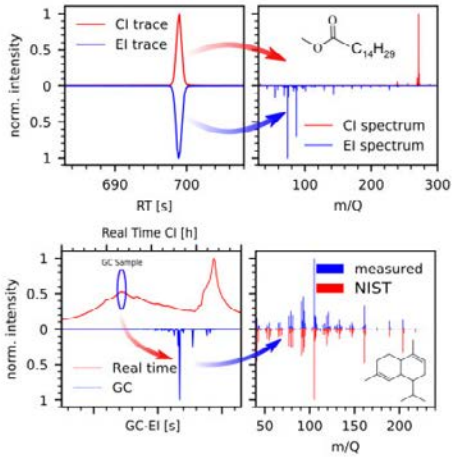

Figure 2: Top - Data generated via GC-EI&CI-TOF MS within one seperation run. Bottom - Data of real time-CI and GC-EI-TOF analysis of a bio mass burning process

P-38 Multimodal characterization of microplastics in drinking water

Clementina Vitali[1], Ruud J.B. Peters[1], Hans-Gerd Janssen[2,3], and Michel W.F. Nielen[1,3]

1 Wageningen Food Safety Research, Wageningen University & Research, Akkermaalsbos 2, 6708 WB Wageningen, NL.

2 Unilever Foods Innovation Centre – Hive, Bronland 14, 6708 WH Wageningen, NL.

3 Wageningen University, Laboratory of Organic Chemistry, Stippeneng 4, 6708WE, Wageningen, NL

Abstract

The mismanagement of plastic waste and its accumulation in the environment has resulted in the presence of microplastic (MPs) and nanoplastics (NPs) in the food chain and the exposure of consumers. A new drinking water directive was published in 2019 by the European Commission (EC) stating that water companies will need to measure concentrations of microplastics within two years for positive release and inspection. The Marie Sklodowska-Curie MONPLAS project – involving academic institutions and equipment manufacturers and end-users – aims to develop methodologies and technologies for the robust, easy and low cost determination of MPs and NPs.

Several parameters have to be assessed in order to fully characterize MP contamination: number of particles, particle size, particle size distribution, particle shape, chemical composition, and particle mass. Currently, no single analytical of physical method is able to provide all this information. Optical techniques, used to measure and count the particles, can be combined with vibrational spectroscopic techniques for their chemical characterization. However, those techniques are subject to interference related to aging, weathering, surface contamination, and chemical damage of the micro and nano particles' surface.

In this presentation we propose the combined detection and quantification of MPs by Nile red staining and fluorescence microscopy plus chemical characterization of individual particles by ambient ionization mass spectrometry (MS) using an Atmospheric Solids Analysis Probe (ASAP). Compared to infrared techniques, this multimodal characterization method excels in the discrimination of MP polymers belonging to the same chemical class and in the identification of polymer mixtures. The method overcomes the interference from MP surface contamination and, as a bonus, enables the MS characterization of the adsorbed contaminants.

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Contact information

Clementina Vitali, MSc | clementina.vitali@wur.nl | +31 634329983
Ruud J.B. Peters, PhD | ruudj.peters@wur.nl
Hans-Gerd Janssen, prof.dr.ir. | hans-gerd.janssen@wur.nl
Michel W.F. Nielen, Prof.dr. | michel.nielen@wur.nl

P-39 Continuous monitoring of small molecules for industrial process control

Chris Vu[1, 2], Yu-Ting Lin[3], Junhong Yan[3], Julia Marshall[4], Annemarie Hummel[4], Simone F. A. Wouters[4], Jos M.H. Raats[4], Arthur M. de Jong[2, 5] and Menno W. J. Prins[1, 2, 3, 5]

[1] Department of Biomedical Engineering, Eindhoven University of Technology, The Netherlands; [2] Institute for Complex Molecular Systems (ICMS), Eindhoven University of Technology, The Netherlands; [3] Helia Biomonitoring, The Netherlands; [4] AbSano, Oss, The Netherlands; [5] Department of Applied Physics, Eindhoven University of Technology, The Netherlands.

Abstract

Monitoring of biochemical substances is applied in downstream food processing for process control and quality assurance purposes. Here, we describe a sensing technology that will allow for real-time continuous monitoring of small molecules, so that processes can be adjusted and optimized in real-time. This can help to minimize under- and over-processing, improve efficiency, reduce waste, and reduce the use of resources.

The continuous sensing technology is called BPM, Biosensing by Particle Mobility[1-3]. Biofunctionalized micrometer-sized particles are attached by a flexible tether to a biofunctionalized substrate. The sensor response is based on the mobility of the particles, which is changed by reversible affinity-based interactions (see Fig. 1a). Hundreds of particles are measured and their mobilities dynamically reflect the concentration of analyte molecules in solution.

Here we demonstrate the feasibility of small-molecule monitoring in protein solutions using the BPM sensor. We have synthesized analogue molecules and selected recombinant antibodies from large phage display libraries for a competitive assay design (see Fig. 1a). The sensor is shown to be sensitive in the micromolar concentration range, in aqueous buffers and in complex matrices (see Fig. 1b). We will present the measurement principle, the development of analogue and antibodies, show monitoring results, and discuss how BPM can generally be applied for real-time monitoring of small molecules in industrial food processes.

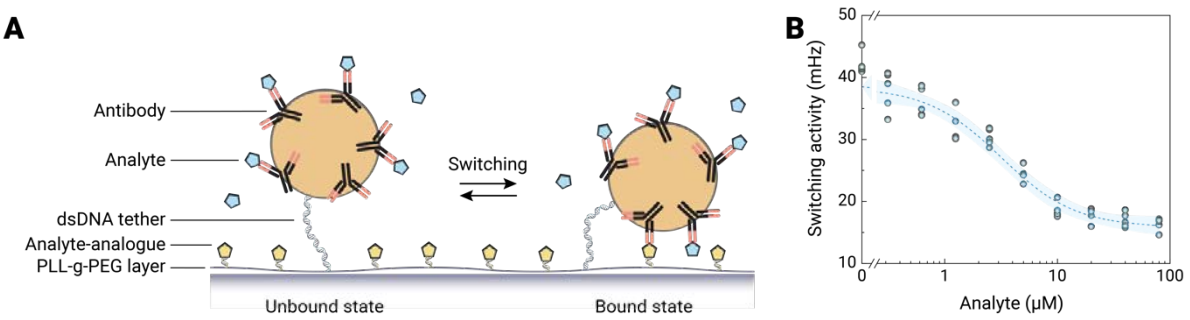

Figure 1. Quantification of small molecules using Biosensing by Particle Mobility (BPM). (A) Schematic overview of the BPM sensor design, with a competitive assay format. The sensor surface is provided with analyte-analogue molecules. The particles are tethered to the surface via double-stranded DNA and a low-fouling PLL-g-PEG polymer layer. The particles are functionalized with antibodies that reversibly bind to the analogue and to the analyte molecules. The switching events between bound and unbound states are detected by tracking the movement of the particles using brightfield microscopy. (B) Dose-response curve measured in the competitive BPM assay.

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P-40

PANACEA – Pan-European solid-state NMR Infrastructure for Chemistry-Enabling Access

Evan Wenbo Zhao, Radboud University Nijmegen

European Union's Horizon 2020 research and innovation programme

The development of modern chemistry relies on our capacity to investigate with atomic-level resolution increasingly complex solid substrates in frontier research areas crossing disciplines from catalysis and energy materials through polymers to pharmaceutical formulations and medical implants. Thanks to a number of recent breakthroughs in instrumentation and methodology, solid-state NMR spectroscopy is uniquely positioned today to characterize the structure and dynamics at the atomic-level, and reveal morphology in solids. However, state-of-the-art methods rely on the use of sophisticated and costly solid-state NMR equipment that is only available in a handful of national facilities. The rarity of the instrumentation and associated operational know-how has restricted the uptake of these enabling methods by the broader base.

PANACEA addresses this issue by bringing together, and integrating on the European scale, seven national infrastructures across Europe and incorporating one infrastructure in the United States, and opening them to all European chemists, from both academia and industry.

P-41 Determination of pesticide residues in cucumber using GC-MS/MS with APGC after extraction and clean up using QuEChERS

Janitha de Alwis, Simon Hird, Stuart Adams, Rhys Jones
Waters Corporation

ABSTRACT:
Reliable analytical methods are needed for detection, quantification, and identification of hundreds of pesticide residues in many different commodities. This application note describes the development and validation of a comprehensive method based on GC–MS/MS for the determination of over 200 pesticides. Extracts of cucumber were prepared using the CEN version of QuEChERS, including a dispersive solid-phase extraction (dSPE) step followed by determination with GC-MS/MS. The use of GC-MS/MS utilizing atmospheric pressure ionization (APGC) has been shown to offer significant improvements in performance over electron ionization (EI) for pesticide residue analysis, in terms of selectivity, specificity, and speed of analysis. The extremely high sensitivity of the APGC Xevo TQ-XS system was demonstrated with reliable detection for all the analytes at concentrations as low as 0.001 mg/kg, even when injection volume was limited to 1µL. The method was successfully validated in cucumber using the SANTE guidelines document. The results from analysis of the spikes @ 0.001 mg/kg showed that 94 % and 99 % of the analytes were within the required tolerances for recovery and repeatability, respectively. The method is considered sensitive, specific, accurate, and suitable for the determination of residues of a wide range of GC-amenable pesticides in agricultural commodities for checking compliance with MRLs and has the potential for determination at much lower concentrations.

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P-42 Routine Determination of Per- and Polyfluoronated Alkyl Substances (PFAS) in Drinking Water by Direct Injection Using UPLC-MS/MS to Meet the EU Drinking Water Directive 2020/2184 Requirements

Hannah Willmer, Kari L. Organtini, Stuart Adams

Waters corporation

Abstract

The purpose of this work is to demonstrate a direct injection UPLC-MS/MS method for the determination of PFAS compounds in drinking water in response to the parametric level requirements in the 2020 recast EU Drinking Water Directive.[1] The method performance study was completed on an ACQUITY UPLC I-Class PLUS System with a Xevo TQ-XS and UniSpray ion source combination using an ACQUITY Premier BEH Shield RP_{18} Column. Samples were prepared by dilution with an acidified organic solution containing internal standard directly into an autosampler vial.

A method validation study was carried out on 3 common drinking water matrices; tap water from known soft and hardwater areas and bottled mineral water. The method performance was assessed using 3 spike levels at 2, 10, and 100 ng/L (1.2, 6, and 60 ng/L in vial concentration) for all analytes, with 7 replicates at each level. Average method performance for trueness was 89 to 112% across all matrices. RSDs were all at or below 14%.

All calibration graphs had residuals within 20% and R^2 values of 0.99 or higher with linear regression fit. Retention time stability across all the method validation study batches for all analytes was below RSD 3.2%.

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P-43 Introduction to PARADISE (Propelling Analysts by Removing Analytical-, Data, Instrument-, and Sample-related Encumbrances)

Joshka Verduin[1,2], Rick S. van den Hurk[2,3], Nino B.L. Milani[2,3], Govert W. Somsen[1,2], Bob W.J. Pirok[2,3], Arian C. van Asten[2,3,4]

[1] *Vrije Universiteit, De Boelelaan 1105, 1081 HV Amsterdam, The Netherlands*

[2] *Centre for Analytical Sciences Amsterdam, Amsterdam, The Netherlands*

[3] *Universiteit van Amsterdam, Science Park 904, 1098 XH, Amsterdam, The Netherlands*

[4] *Co van Ledden Hulsebosch Center (CLHC), Amsterdam Center for Forensic Science and Medicine, Amsterdam 1090 GD, The Netherlands*

Abstract

Today, more than ever, science has provided us with more and more high-tech solutions to improve our lives and our world. While these new developments make our day-to-day life much easier, they also make our work on the lab much more difficult. For instance, imagine a special particle that is carrying an important drug through our body and is designed to release that drug only at the place where it is needed. Before giving it to a patient, we need to test if this particle is of good quality. We may for instance want to know how its size, and whether the particle has the correct drug content. We could determine the size distribution of the particles and the average drug content. However, the relationship between the particle size and the drug content remains unknown. Sometimes a sample is just too complex to describe in one analysis. If a sample contains hundreds or even thousands of different compounds, we often use multiple systems to enable the characterization of these compounds. If we want to measure them all in only one system, we need more so-called “separation space”. A bigger separation space means that more compounds can be identified simultaneously. While there are techniques to analyze these samples with many different compounds in them, interpreting the data remains challenging, because they yield gigabytes full of numbers that need to be translated into useful information. Therefore, the goal of the PARADISE project is to get more and faster useful information from samples by not only determining multiple properties of a sample at once, but also linking these properties and making the data interpretation much easier.

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P-44 Understanding the atypical chromatographic behavior of semi-crystalline polyamides

Kruijswijk, J.D.[1,2*], Philipsen, H.J.A.[3], Schoenmakers, P.J.[2,4], and Somsen, G.W.[1,2]

[1] *Division of BioAnalytical Chemistry, Amsterdam Institute of Molecular and Life Sciences, Vrije Universiteit Amsterdam, De Boelelaan 1085, 1081 HV Amsterdam, The Netherlands*

[2] *Center for Analytical Sciences Amsterdam (CASA)*

[3] *DSM Materials Science Center, Chemelot Campus, Urmonderbaan 22, 6167 RD Geleen, The Netherlands*

[4] *Analytical Chemistry Group, van 't Hoff Institute for Molecular Sciences, Faculty of Science, University of Amsterdam, Science Park 904, 1098 XH Amsterdam, The Netherlands*

*Corresponding author: J.D.Kruijswijk@vu.nl

Abstract

The application of gradient elution liquid chromatography (GELC) to semi-crystalline polyamide (PA) is hampered by irregular and often irreproducible retention and performance issues. The chromatographic behavior of these PAs is marked by a broad band that obeys conventional chemistry-based retention followed by one or more atypical sharp peak(s). The obtained peak pattern depends heavily on the selected experimental conditions. The retention times of the later eluting peaks are not according what can be expected from the PAs' chemistry, and crystallization phenomena are thought to be the origin of the irregular behavior. In order to understand the observed performance, various conditions were studied that affect the separation and the relative magnitudes of the elution patterns. The gradient was performed at different starting conditions of water + 0.1% formic acid to 100% hexafluoro-2-propanol (HFIP) as eluent. The column temperature was varied from 5 to 80 degrees Celsius. For injection, the sample concentration was changed with both equivalent and increased mass loads. To create conditions at which the PAs could crystallize more easily, formic acid was added as an injection solvent. Parameters that induced or alleviated potential crystallization were evaluated. By selecting proper conditions, the crystallization phenomena and related adverse effects would be fully mitigated, resulting in a separation of the polymer that would solely be based on the chemistry. The most promising result came when employing a gradient from 50% water (+0.1% formic acid) to 100% HIFP and a column temperature of five degrees Celsius.

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