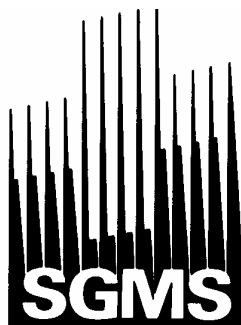


Swiss group for mass spectrometry
Schweizerische Gruppe für Massenspektrometrie



Groupe suisse de spectrométrie de masse
Gruppo svizzero di spettrometria di massa

Newsletter

Rigi Meeting 2004

and

General Assembly 2004

Dorint Hotel Blüemlisalp, Beatenberg

November 25 and 26, 2004

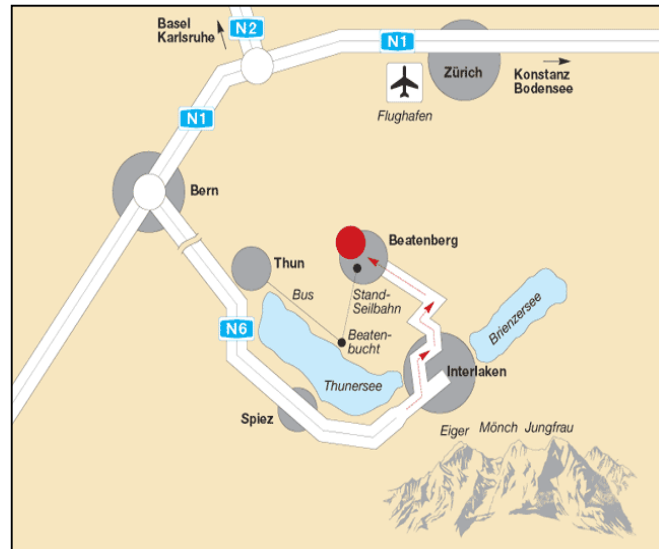
In this Newsletter:

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Travel information

Please note that the Beatenbucht-Beatenberg mountain railway will be out of order in November.

By car: Take highway no. 6 from Berne to Thun, then no. 8 direction Interlaken. Right before reaching Interlaken follow directions to Gunten/Unterseen/**Beatenberg**.



In Beatenberg: Don't be afraid of having missed the Dorint Hotel Blüemlisalp. Beatenberg is a stretched-out village - probably the longest in Europe. Our destination is located at the very far end. Parking at the Hotel is free of charge. Please check-in first at the lobby.

By train (travel date November 25, 2005):

Genève: IC713 at 07:30, Lausanne 08:06 and Fribourg 08:51 then Bern.

Basel: IC965 at 08:04 arriving in Bern at 09:11. Please stay in the train. It will continue to Interlaken West.

Schaffhausen: D2559 at 07:07 then Zürich.

Zürich: IC810 at 08:04 then Bern.

Bern: IC965 at 09:26 arriving in Interlaken West at 10:15.

Interlaken: Bus 109 in front of the main station at 10:23.

The bus will arrive at 10:53 in front of the Hotel Dorint Blüemlisalp.

Proposed new members for the committee

The committee was looking for two new members for 2004, to replace Hanspeter Moser and Raphaele Tabacchi who decided to resign at the General Assembly 2004. We have found the following willing candidates:

Dr. Laurent Bigler
University of Zürich
Institute for Organic Chemistry

and

Dr. Stephan Brombacher
Novartis Pharma
Basel

More detailed information will be given at the General Assembly.

Their election will be proposed by the committee members, but other suggestions are of course welcome as well. Election of the new members of the committee will take place during the General Assembly 2004.



November 25, 2004

11:15 – 11:30 Welcome Notes***Starting Session:***

Chair: Hanspeter Moser

11:30 - 12:15 The Microscope - History of a versatile tool

Paulus Kurt

12:30 - 14h00 Lunch**Session 1**

Chair: Hansjörg Walther

14:00–14h45 Supramolecular mass spectrometry : a new technology for the study of non covalent interactions in biology

Alain Van Dorsselaer

14:45 - 15:05 Segmented post column analyte addition; a tool for real time response control of ESI LC-MS signals affected by signal suppression

Anton Kaufmann

15:05 – 15:25 Organosulfates – A Major Component of Humic–Like Substances in Atmospheric Aerosol?

Fernando Romero

15:25 – 15:45 Two-Step Laser Mass Spectrometry: Analysis of Size-Segregated Aerosol-Bound Polycyclic Aromatic Hydrocarbons with High Time Resolution

Christian Emmenegger

15:45 - 16:15 Coffee Break**Session 2**

Chair: Andreas Staempfli

16:15 – 16:35 Fourier Transform Mass Spectrometry: an invaluable tool for the analysis of small molecules

Christian Guenat

16:35 – 16:55 Parallel Processing in a Hybrid Instrument - A new dimension in LC-MS and LC-MSMS

Winfried Redeker

16:55 – 17:15 Identification and structure determination of protein nitrations by high resolution FT-ICR mass spectrometry

Michael Przybylski

17:20 General Assembly 2004**19:00 Apéro****20:00 Blüemlisalp Dinner Buffet**

November 26, 2004

Session 3		Chair: Laurent Bigler
08:30 - 09:15	Mass spectrometric imagery and flash photography: Rapid analysis of the molecular organization of biomolecules at surfaces	Ron M.A. Heeren
09:15 - 09:35	Novel Approaches for High Throughput Metabolites Identification and Structural Characterization using Chip Based Infusion and MALDI Mass Spectrometry	Roland Staack
09:35 - 09:55	The State-of-the-Art in Capillary Electrophoresis/Mass Spectrometry Coupling	Martin Schär
09:55 - 10:15	Isotope Ratio Mass Spectrometry of underivatised amino acids and peptides using LC IsoLink interface	Jean-Philippe Godin
10:15 - 10:45	Coffee Break	
Session 4		Chair: Jean-Luc Wolfender
10:45 - 11:30	Chromatographic and Mass Spectrometric Characterization of Polymers	Peter Schoenmakers
11:30 - 11:50	Characterization of very long chain fatty acid composition of human blood using a novel HPLC-MS approach based on non miscible solvents	Kornél Nagy
11:50 - 12:10	Are there alternatives to quantitation with quadrupole instruments?	Friedrich Mandel
12:10 - 12:30	Exact Mass Determinations and Elemental Compositions -- Where are we at present?	Uwe Rapp
12:30 - 12:40	Closing Remarks	
13:00 - ???	Lunch at Dorint Beatenberg (voluntary, therefore not included in package)	



The Microscope - History of a versatile tool

***Kurt Paulus
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4002 Basel, Switzerland***

In the mid of the 17th century, different scientists in Europe, started to dissect insects and to prepare slices of plants. One discovered bacteria, cells, sperms (so called animalculae) and much more. The instrument microscope was the most important tool of these scientists. But, how important is the microscope today in the field of science?

In my talk, I will show details of the development of the light microscope and different microscopic methods in medicine, biology and chemistry since 350 years.

Especially I will present some archeological problems, solved in my laboratory within Novartis.

***Supramolecular mass spectrometry:
a new technology for the study of non covalent
interactions in biology***

***Noelle Potier, Guillaume Chevreux, Emmanuelle Leize,
Alain Van Dorsselaer
Laboratoire de Spectrométrie de Masse Bio-Organique
Louis Pasteur University, UMR 7509 CNRS, Strasbourg
France***

Mass spectrometry was always dealing with molecules. In addition, to this molecular mass spectrometry, about 10 years ago, a new type of mass spectrometry emerged: supramolecular mass spectrometry, which allowed to measure the mass of non covalent complexes. Complexes of several molecules attached by specific interactions can be volatilized without destruction of the specific non covalent interactions.

It took 30 years research effort to the mass spectrometrists community to develop the methodology for the characterization of tryptic peptides at attomole level and the automatic interpretation of fragmentation spectra are. Today, this is routinely used as the key step for the identification of proteins in proteomic studies. Huge amounts of data are now collected in proteomic studies allowing to establish the proteomes of cells, tissues, ...

We believe that supramolecular mass spectrometry will play a role in what is the next step after proteomics; the complexomics, but several years of efforts, if not several decades, will be necessary to fully develop this technology.

In Supra Molecular Mass Spectrometry, the instrument is modified and tuned so that specific interactions are maintained during the ionisation/volatilization process.



In these conditions, answers may be given to the following questions:

1. Is there a specific interaction between a protein and a possible ligand?
2. What is the stoichiometry of a multi-protein complex ?
3. Can we detect a cooperativity in the addition of a cofactor?
4. Is there a cooperative effect in the addition of a cofactor ?

Data will be presented where enzyme/ligand interactions are detected and characterized. Mass measurement of multi-protein complexes of more than 2 million Daltons were obtained and will be discussed.

***Segmented post column analyte addition:
a tool for real time response control of ESI LC-MS signals
affected by signal suppression***

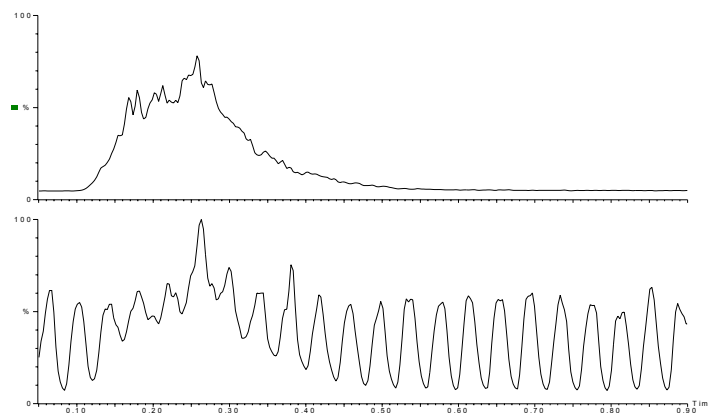
***Anton Kaufmann
Kantonales Labor, Postfach, 8030 Zürich***

The introduction of LC-MS-MS improved the selectivity and sensitivity for trace analysis to previous unknown levels. This caused some analysts to abandon sample preparation at all and to simply dissolve and inject unprocessed samples into the instrument. Such approaches are less frequently propagated today. Compounds present in the sample were found out to suppress or enhance the target substance signal intensity, hence affecting quantification. Prolonged chromatography and the use of stable-isotope labeled internal standards is currently the best strategy to avoid such interferences. Matrix effects have been visualized by the post column addition of analyte solution. Valleys and hills on the elevated baseline indicate the presence of signal suppression or enhancement. Quantification of the analyte in a sample is not anymore possible by this technique, because of the superimposed noisy post column analyte signal.

The proposed segmented post column analyte addition is a novel approach to visualize signal suppression and to correct peak areas of target substances being affected. Instead of supplying a constant post-column stream of analyte solution, a regularly switching valve is employed to add well defined segments of analyte- containing solvent and analyte-free solvent to the eluent leaving the analytical column.

The feasibility of this technique has been shown. Large volumes (30 μ l) of sulfathiazole in water were injected into a mobile phase consisting of acetic acid in acetonitrile. No column was employed, hence the core of the sample

plug could not mix anymore with the eluent. As ionization conditions were more favorable in the eluent than in the solvent plug, a peak distortion was observed. See top signal in figure. The superimposed segmented post-column analyte addition spikes were equally affected. This is clearly visible as indicated in figure (bottom).



Appropriate mathematical approaches like fast Fourier transformation should enable the deconvolution of the signals. The amplitudes of the spikes can be used to correct the analyte peak area and to possibly quantify the signal without injecting external standards.

Organosulfates – A Major Component of Humic-Like Substances in Atmospheric Aerosol?

***Fernando Romero and Michael Oehme
Organic Analytical Chemistry, University of Basel,
Neuhausstrasse 31, 4057 Basel, Switzerland***

Atmospheric aerosols can act as cloud condensation nuclei and control transmission of light through the atmosphere by scattering and absorption. Furthermore, health may be affected by inhaling them [1]. Little is known about polar and water soluble organic compounds (WSOC) in atmospheric aerosols, which account for 20 to 70% of the total organic carbon [2]. Inorganic sulfate constitutes approximately 40% of all water soluble compounds and polycarboxylic acids or humic-like substances (HULIS) represent around one quarter of the WSOC. However, hitherto mass spectrometric information about HULIS is scarce.

Aerosol particles of 10 μm diameter (PM_{10}) were collected with quartz fiber filters for 24 h in the region of Basel and extracted with water. Separation of HULIS was performed with size exclusion chromatography (SEC). ESI- MS^n in the negative mode was chosen for characterisation of HULIS. Full scan mass spectra of the extracts showed a mass distribution pattern, which was also observed for fulvic and humic acids. This suggested a polymeric structure of HULIS. Furthermore, fragment spectra showed repetitive mass losses of 18 u (H_2O), 28 u (C_2H_4 , CO) and 44 u (CO_2), which indicated a highly oxidated state of HULIS and confirms their polycarboxylic nature. Moreover, MS^2 -spectra of selected molecular ions showed the fragment m/z 97 which was identified as sulfate. The appearance of m/z 97 in MS^3 -fragment spectra confirmed the existence of covalently bounded sulfate to the HULIS. This points to a possible sulfation of HULIS in the atmosphere contributing to their high polarity and water solubility.

- [1] Brimblecombe, P.; Air composition & chemistry, Cambridge Environmental chemistry series 6, Cambridge University Press, 1996.
- [2] Saxena, P.; Hildemann, L. M.; *J. Atmos. Chem.*, 1996, 24, 57-109.



Two-Step Laser Mass Spectrometry: Analysis of Size-Segregated Aerosol-Bound Polycyclic Aromatic Hydrocarbons with High Time Resolution

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Department of Chemistry and Applied Biosciences
Swiss Federal Institute of Technology (ETH)
Hönggerberg, Wolfgang-Pauli-Str. 10, CH-8093 Zürich, Switzerland

Polycyclic aromatic hydrocarbons (PAHs) are of major concern in all environmental compartments due to their mutagenic and carcinogenic properties. Two-Step Laser Mass Spectrometry (L2MS) is a sensitive and selective method to measure PAHs in complex matrices.

A new combination of methods has been developed to monitor PAHs in ambient aerosols with a high time and size resolution. The sampling with a three-stage rotating drum impactor (10-1, 1-0.3, 0.3-0.1 μm) has been combined with the analysis by two-step laser mass spectrometry (L2MS), resulting in a time resolution of 20 minutes (Emmenegger, C.; Kalberer, M.; Samburova, V.; Zenobi, R.; *The Analyst* 2004, 129, 416-420). A new design for a highly compact, vacuum compatible translation stage to move the sample strips (160 x 12 mm) generated by the Rotating Drum Impactor relative to the desorption laser focus was developed.

The usefulness and value of this combined method has been validated and is demonstrated in a field campaign during summer and winter 2002/2003 in downtown Zurich. The dominant peaks in the spectra are skeletal PAHs such as m/z 178, 202, 228, 252, 276. However, the spectra show that there are many more polycyclic aromatic compounds present in the aerosol, than the 16 PAHs declared as high priority pollutants by the US Environmental Protection Agency. The diurnal cycle with day/night ratios of 0.1 was only altered during intensive atmospheric mixing periods (changing the day/night ratios up to 8) where cleaner air from upper atmosphere layers was mixed into the boundary layer. In summer, particle bound PAH were about a factor of 2-10 lower than during winter.

Fourier Transform Mass Spectrometry: an invaluable tool for the analysis of small molecules

***Christian Guenat
Novartis Pharma AG
WSJ-503-11.06
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Fourier Transform Mass Spectrometry (FTMS) is certainly most often used for biomolecule analysis, but it is also an invaluable tool for the characterization of small molecules with molecular weight up to 1'500 Da. Thank to its very high mass resolution and high mass accuracy, FTMS is especially useful for the determination of elemental compositions and, thus contribute to the structure elucidation process of unknown molecules, such as natural products.

After an introduction and a review of some of the basics of FTMS some examples obtained on our 9.4T FTMS instrument operated for two years in our laboratory will be presented, such as natural products, isotopically labelled compounds or molecules from the chemistry laboratories.

A comparison with the double focusing sector instrument used previously for accurate mass determination shows that the FTMS is faster, more accurate, more sensitive and offers more possibilities for the analysis of small molecules.



***Parallel Processing in a Hybrid Instrument:
A new dimension in LC-MS and LC-MSMS***

Winfried Wagner-Redeker¹, Helmut Münster²

¹Spectronex AG, Hochstrasse 48, CH-4002 Basel

²Thermo Electron (Bremen) GmbH, Barkhausenstr.2, D-28197 Bremen

A key objective of proteomics projects is to develop biochemical and instrumental approaches to increase coverage and confidence of protein identification. Recent advantages in mass spectrometry have placed this technology solidly at the center of proteomics research. To cope with the complexity of samples, the demands on the power of the analytical setup are steadily increasing. The ideal workstation will yield both, excellent LC-separation, and even more importantly, fast and sensitive mass detection. Accurate mass analysis of the precursor ion in combination with MS/MS yields high reliability in peptide and hence in protein identification. Ideally, high mass accuracy and MS/MS information are achieved within a very short time in order to acquire as many scans as possible during the elution of a chromatographic peak. High speed of mass analyzers combined with dynamic exclusion enables to receive sequence information of low-level components in highly complex samples.

The Finnigan LTQ FT consists of two mass analyzers which can work both, independently from as well as in combination with each other: a linear ion trap and a FTICR MS. The linear ion trap is characterized by high scan rates and excellent sensitivity, also in MS/MS mode of operation. The FT ICR analyzer routinely achieves high mass resolution at a scan rate of 1 scan/s, while providing excellent mass accuracies utilizing external calibration.

Great care has been taken to fully exploit the benefits of both mass analyzers working in tandem.

While the FTICR is collecting high resolution/high mass accuracy data of all peptides eluting at a given retention time, the linear ion traps collects MS/MS spectra of these candidate peptides in data dependent mode.

The data dependent information for the MS/MS experiments is derived from a short preview FFT (Fast Fourier Transform), while the full transient acquisition for ultimate resolution is ongoing. This capability allows the acquisition of four to five spectra per second, one HRMS and three to four MSMS spectra.

The presentation describes the experimental technique and discusses a number of recent analyses from our laboratory.



Identification and structure determination of protein nitrations by high resolution FT-ICR mass spectrometry

Michael Przybylski, Nikolay Youhnovski, Alina Petre, Juho Lukkari, Patrick Schmidt, and Volker Ullrich

University of Konstanz, Laboratories of Analytical Chemistry and Biological Chemistry, 78457 Konstanz, Germany

Nitration of proteins has recently been shown – and suggested – to exert important physiological functions and play a significant pathophysiological role in diseases such as Alzheimer's disease, Parkinson, atherosclerosis, and in bronchio-alveolar diseases. The identification of nitrated tyrosine residues has been found difficult and is hampered by (i) low levels of modifications in proteins and (ii) structural changes introduced by the nitro group. The reduced chemical stability of nitro-tyrosine residues in proteins renders both Edman sequencing and proteome analysis with standard mass spectrometry (peptide mass fingerprinting) difficult. High resolution mass spectrometric methods using Fouriertransform – ion cyclotron resonance (FTICR-MS), in combination with micro-LC-MS / MS have been developed as powerful tools for the unequivocal and sensitive identification of nitrations. Specific nitrations were recently identified upon peroxynitrite treatment at the active site – Tyr-430 residue of bovine prostacyclin synthase [1], and at Tyr-488 of eosinophil- peroxidase using specific proteolytic digestion and ESI-FTICR-MS at isotopic resolution. Detailed studies were performed with Tyr-nitrated model peptides prepared by solid phase peptide synthesis, and peroxynitrite and nitromethane nitration. Using MALDI-MS with the standard UV-nitrogen laser, 3-nitro-tyrosyl-peptides were found to undergo rapid photochemical fragmentation of the nitrophenyl-group, which renders this MS method critical or unfeasible for nitro-Tyr identification. In contrast, intact molecular ions of nitrated peptides are obtained using infrared(IR)-MALDI-FTICR-MS (with a 2.94 μm NdYAG-laser) recently introduced in our laboratory [2]. First IR-MALDI studies of protein nitrations will be presented.

[1] Schmidt, P, Youhnovski, N, Daiber, A, Balan, B.-A., Przybylski, M, Ullrich, V, *J. Biol. Chem.*, (2003) **278**, 12813-12819.

[2] Youhnovski, N., Petre, A., Przybylski, M. *Eur. J. Mass Spectrom.* (2004), in press.

***Mass spectrometric imagery and flash photography:
Rapid analysis of the molecular organization of
biomolecules at surfaces***

***Ron M.A. Heeren
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Kruislaan 407, 1098 SJ Amsterdam
The Netherlands***

MALDI-MS imaging is one of the emerging technologies in the study of biomolecules at surfaces. It provides a wealth of information on the spatial organization of biomolecules at surfaces. It has the potential of becoming an important diagnostic tool in biomedical sciences for the differential analysis of diseased versus healthy tissue. The characterization of the spatial organisation of macromolecules that are present in complex systems such as cells or ensembles of cells (tissue) with mass spectrometry can be realized through two approaches: spatial resolved ion generation (microprobe) or spatial resolved ion detection (microscope) of the macromolecule(s) of interest.

The highest resolution microprobe images of surfaces are generally obtained by scanning tightly focused ion beams over surfaces (i.e. SIMS). This technique is generally used for the study of semi-conductor surfaces as it provides detailed information on the distribution of a variety of elements and fragment fingerprints of organic surface molecules. The addition of an acidic matrix to biological surfaces (similar to the MALDI sample preparation process) aids in the generation of intact biological molecules, a technique referred to as ME-SIMS. We will show how this microprobe approach can be used to generate images of biomolecular distributions in nervous tissue with subcellular spatial resolution.

The fastest mass spectrometric imaging technique is without doubt the mass microscope approach. The instrumental features and benefits for the rapid study of spatial organization of macromolecules on biological surfaces with sub-micron spatial resolution will be described and discussed. It will be shown to improve the combination of spatial resolution and speed of analysis. This novel stigmatic mass spectrometric ion imaging instrument records the spatial distribution of MALDI generated peptide ions over an area of 150 by 150 micrometer with a spatial resolution exceeding 1 micrometer in a single laser shot. In this new approach the MALDI-MS spatial resolution is no longer determined by the spot size or the wavelength of the desorption beam but by the quality of the ion optics and the spatial resolution of the 2 D detector. Moreover, the molecular flash-photography approach also allows the usage of different desorption and ionization techniques that would not deliver useful images with the microprobe approach.

Novel Approaches for High-Throughput Metabolites Identification and Structural Characterization using Chip-Based Infusion and MALDI Mass Spectrometry

Roland F. Staack, Emmanuel Varesio and Gérard Hopfgartner, University of Geneva, Laboratory of Pharmaceutical Analytical Chemistry Life Sciences Mass Spectrometry, CH-1211 Geneva 4, Switzerland.

Drug metabolism is playing more and more an important role in drug discovery and early development. Besides metabolite stability, identification and structural characterisation of metabolites is crucial for lead optimization. For this purpose, efficient strategies based on non-radiolabeled parent drugs are needed. At that stage and due to the need of high sensitivity, LC-MS/MS is currently the method of choice for early drug metabolism studies. However, LC-MS/MS has an intrinsic problem for qualitative analysis because most LC peaks elute too fast to perform all necessary MS experiments in one run. Therefore, structural characterization of metabolites often requires re-analysis on various types of mass spectrometers. Moreover, good chromatographic separation is crucial for detection of isobaric metabolites, resulting in long LC analysis times.

Two different strategies in order to increase throughput and sensitivity were explored. The first one combines micro-LC/MS fraction collection via a post-column split into a 96-well plate, with simultaneous online MS monitoring, followed by automated nanoelectrospray chip-based infusion for rapid re-analysis of the fractions of interest. The second one is based on parallel column-switching nano-LC fraction collection onto a MALDI plate followed by o-MALDI analysis. Both strategies allow to freeze the LC separation either in 96-well format or onto a MALDI target. MALDI mass spectrometry showed to be an interesting and sensitive alternative to electrospray for the analysis of low molecular compounds.

Selected examples demonstrating the efficiency of these approaches will be presented on various pharmaceutical compounds.

The State-of-the-Art in Capillary Electrophoresis/Mass Spectrometry Coupling

Martin Schär

LABOR SPIEZ, Organische Analytik, Austrasse, CH-3700 Spiez

The combination of capillary electrophoresis (CE) with electrospray mass spectrometry (ESI-MS) for bioanalytical, biotechnological and pharmaceutical tasks offers intrinsic advantages:

CE offers high theoretical plate numbers, a host of different separation mechanisms for selectivity, ruggedness, automation and last but not least, it is a low cost technique. Mass spectrometry (MS) on the other hand provides high sensitivity with a very high selectivity. The separation power of an on-line CE/MS system is thereby twofold: CE separates the analytes by their charge-to-size ratio while MS subsequently differentiates the analytes by their mass-to-charge ratio.

Several types of on-line interfaces have been described and at least three are in use today: the liquid junction, the coaxial sheath flow and the sheathless interface. Although several manufacturers have commercialized CE/MS systems nowadays, it is still considered as a niche technique. What are the obstacles and the challenges today and what can be expected in the near future?

This presentation will give an overview about the properties and details of the different CE/MS interfaces and a novel coaxial sheath flow interface with a floating sheath liquid feed will be presented. Based on selected examples, specific advantages and limitations of the technique will be pointed out.

Isotope Ratio Monitoring Mass Spectrometry of Underivatised Amino Acids and Peptides using the LC IsoLink Interface

J-P Godin¹, L-B Fay¹ and G Hopfgartner²

¹ Nestec Ltd, Nestlé Research Center, Vers-Chez-les-Blanc, PO BOX 44, CH-1000 Lausanne 26, Switzerland ;

² University of Geneva, Laboratory of Pharmaceutical Analytical Chemistry, Life Sciences Mass Spectrometry, 20 Bd d'Yvoy, CH-1211 Geneva 4

For a long time, the determination of the $^{13}\text{C}/^{12}\text{C}$ isotope ratios of natural organic compounds has been restricted to the analysis of bulk samples. For 20 years, the high-precision isotope ratio analysis has been mostly conducted through gas chromatography coupled to an isotope ratio mass spectrometer (IRMS) via a combustion furnace (GC/C/IRMS) or pyrolysis furnace (GC/P/IRMS), depending on the isotopes studied (combustion furnace for ^{13}C and ^{15}N , pyrolysis furnace for ^{18}O and ^2H). Currently, GC-IRMS is the "technique of choice" for isotopic analysis of organic compounds in complex mixtures. However, these techniques suffer from the common limitations of gas chromatographs, in particular the restriction to volatile samples. The requirement for sample preparation (derivatisation), can be time-consuming, cumbersome and is not always reliable (isotopic fractionation can alter the isotopic ratio).

Several efforts to couple liquid chromatography to a high-precision IRMS have been conducted up to now: Caimi et al.[1] first introduced a moving transport interface. Abramson et al. [2] reported an interface using a thermospray/particle beam interface, referred to as LC/CRI-IRMS ("CRI" for "chemical reaction interface"). None of these solutions have been commercialised or routinely used. However, very recently, Thermo Electron GmbH (Bremen, Germany) developed a new interface, "LC IsoLink", to

perform the LC-IRMS coupling [3]. This interface is designed to convert organic compounds present in inorganic buffers into CO₂ gas by a wet chemical oxidation process. The CO₂ gas generated is then transferred into a helium flow that is dried into a Nafion tube and finally introduced into the IRMS ion source.

In this presentation, the principle of the interface will be briefly described. Our preliminary data obtained for different underivatized amino acids and peptides in terms of sensitivity, precision and linearity will be highlighted. The accuracy of measurement of the natural enrichment of those compounds will be compared to the results obtained versus an alternative technique: the elemental analyser-IRMS (EA-IRMS). Additionally, different sample preparations of insulin will be discussed with respect to sensitivity using direct injection mode (FIA-IRMS).

- [1] R. J. Caimi and J. T. Brenna, *Anal. Chem.* 65 (1993) 3497.
- [2] F. P. Abramson, G. E. Black, and P. Lecchi, *Journal of Chromatography A* 913 (2001) 269.
- [3] M. Krummen, A.W. Hilker, D. Juchelka, A. Duhr, H.J. Schluter, R. Pesh, *Rapid. Comm. Mass Spectrom.* Accepted.

Chromatographic and Mass Spectrometric Characterization of Polymers

***Peter Schoenmakers and Petra Aarnoutse
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***Dutch Polymer Institute, P.O. Box 902
5600 AX Eindhoven
The Netherlands***

Polymer samples constitute complex mixtures of large molecules. The different molecules vary in size (molecular-weight distribution), chemical composition (chemical-composition distribution), functional groups and end-groups (functionality-type distribution), architecture (e.g. degree-of-branching distribution, block-length distribution), regularity (tacticity distribution). Also, many of the properties of polymers and materials are affected by these variations in molecular structure. Unavoidably, the characterization of molecular distributions requires separation techniques.

For polymers, liquid-phase separations appear the obvious choice. Soluble polymers can be separated according to size using size-exclusion chromatography, field-flow fractionation or hydrodynamic chromatography. Interactive liquid chromatography allows separation of macromolecules according to chemical composition or functionality. Capillary electrophoresis and related techniques provide options for high-resolution separations.

When several distributions must be characterized simultaneously, multi-dimensional separation techniques are required. Comprehensive two-dimensional liquid chromatography is a very useful tool for separation polymers. However, it also poses challenges by requiring both high-resolution miniaturized separations (first dimension) and fast, yet efficient separations

in the second dimension. If only because of these requirements contemporary developments in the field of LC, such as the use of monolithic columns or very high pressures are highly relevant in the area.

Perhaps more surprising, but equally relevant have been the developments in mass spectrometry for the characterization of polymers. The emergence of soft ionization techniques (matrix-assisted laser-desorption ionization, MALDI, and electrospray ionization, ESI) in combination with Time-of-Flight MS has created fantastic possibilities. Yet, for characterizing polymer distributions MS techniques still have their limitations. Both MALDI and ESI are limited to specific classes of polymers and, most of all, require samples with relatively narrow distributions.

The narrow fractions obtained from one- and two-dimensional separations are very suitable for analysis by MS. Inversely, the mass and structural information obtained by MS is invaluable for calibrating and interpreting separation data. Thus, liquid-phase separations and MS are harmoniously complementary for the characterization of polymers.

(pjschoen@science.uva.nl)

Characterization of very long chain fatty acid composition of human blood using a novel HPLC-MS approach based on non miscible solvents

Kornél Nagy

***Chemical Research Center of the Hungarian Academy of Sciences
Institute of Structural Chemistry, Mass Spectrometry Department
1025 Budapest; Pustaszeri út 59-67. Hungary***

The main point of the talk is to present a novel HPLC-MS approach for the characterization of apolar compounds in biological matrices. In the presented study common octadecyl-silica columns and partly miscible solvents are used for stepwise gradient elution starting with a methanol/water and ending with a methanol/n-hexane binary mixture. The applied solvents and the ultra fast gradient allow very fast analysis of apolar compounds, comparable or better to those obtained on monolithic columns, while the solvent consumption is only small fraction of that required by monolithic columns. The combination of fast analysis time and low solvent consumption is of particular importance in high throughput studies. The separation mechanism is believed to occur in the pores at the beginning of the column and not along the column, thus it is significantly different from the traditional approaches. The developed method is also very sensitive, quantitation limit in the low pg range was achieved for fatty acids. Example is presented for fatty acid characterization in human blood which is an important clinical application of mass spectrometry. Determination of very long chain fatty acids has diagnostic potential for the screening of Zellweger syndrome, Infantile Refsum disease and so on... Advantages of the presented technique are discussed and quantitation is illustrated in the case of blood analysis. Triacylglycerol and sterol analysis in biological matrices using the same method is also presented in combination with multivariate data exploratory techniques (principal component analysis and linear discriminant analysis). Pointers for successful data evaluation of HPLC-MS chromatograms in large scale experiments will be also suggested and illustrated.



***Are there alternatives to
quantitation with quadrupole instruments?***

***Friedrich Mandel
Agilent Technologies, Waldbronn***

The majority of LC/MS(/MS) quantitation methods is based on the use of quadrupole mass spectrometers, either single-quadrupole or triple-quadrupole instruments. Alternative mass analyzers such as ion traps or time-of-flight systems are frequently blamed in publications on not being capable of delivering quantitative results of good reproducibility and linearity. This judgment usually is based on design-related properties of first generation instruments. In this lecture we will present and discuss application examples which have been generated by mass spectrometers utilizing state-of-the-art instrument design. Besides others, these examples will describe the quantitation of derivatized isocyanates in ambient air and the determination of nitrofurans derivatives and chloramphenicol in food of animal origin.

Exact Mass Determinations and Elemental Compositions -- Where are we at present?

***Uwe Rapp, Holger Nagel and Mathias Pelzing
Bruker Daltonik GmbH, Bremen and Leipzig, Germany***

ESI and MALDI as ionization techniques have revolutionized mass spectrometry for more than 10 years. Traditionally, the determination of elemental compositions via mass spectrometry largely has been performed using electron impact/chemical ionization (EI/CI) techniques and sector field instrumentation. For more polar substances LiquidSIMS (FAB) has been introduced successfully, later.

Presently, the analytical goal of many research groups is moving towards life-sciences and large molecule work. One main advantage of ESI and MALDI is that these two techniques ionize "nearly everything". As a result, a lot of Chemistry Departments prefer these techniques, especially when considering that in comparison to sector field instruments the new systems are significantly smaller in size and more intuitive to use.

TOF is an established technology and very well known for good mass resolution and excellent exact mass determinations even with external calibration. The requirements in terms of mass accuracy required for the determination of the elemental composition can be divided into two different areas:

1. Confirmation of expected masses and
2. De-novo work, meaning no assumption a priori, the latter being not that often reality.

For the confirmation of even larger molecules an accuracy of 1-5 ppm is sufficient, whereas for the de-novo approach accuracies have to be in the ppb range for being unambiguous for higher molecular weights.



Several examples from different substance classes will illustrate the performance characteristics. The instrument used consists of an ESI orthogonal TOF arrangement, which yields even for larger molecules e.g. beyond m/z 4,000 exact masses in the 1 ppm range. Furthermore, we will discuss some new developments with respect to the evaluation software which considers not only the chemical rules (e.g. N-rule), but also the correctly measured isotopic pattern which is a second dimension of information in a mass spectrum. The different parameters are combined to yield a scoring factor for the quality of the elemental composition proposition.

Swiss group for mass spectrometry
Schweizerische Gruppe für Massenspektrometrie



Groupe suisse de spectrométrie de masse
Gruppo svizzero di spettrometria di massa

General Assembly of the SGMS 2004

Thursday, November 25, 2004

~1720 h

Dorint Hotel Blüemlisalp, Beatenberg

Agenda (preliminary)

1. Nomination of the scrutinizers.
2. Approval of the minutes of the 2003 general assembly.
3. President's report and its approval.
4. Treasurer's report.
5. Auditor's report and approval of treasurer's and auditor's report.
6. Decision on the 2005 membership fee.
7. Admission of new members.
8. Election of the President.
9. Election of new members and members of the SGMS committee.
10. Statutes
11. News from the NSCG - HJ. Walther.
12. News from ESMS - R.Tabacchi.
13. News about the SGMS homepage.
14. Individual proposals.
15. Miscellaneous.

Individual proposals must be **sent by (e)-mail before November 9, 2004**
to: andreas.staempfli@roche.com

The President
Andreas A. Staempfli

Changes of statutes: GA 2004 (proposal)

The present state of the membership: by today we do have a total of 183 active individual members and only 2 active collective members. During the last years 7 companies - either manufacturers or suppliers in the field of mass spectrometry – were established as sponsors of the SGMS.

The committee proposes to change the statutes in a way to dismiss the term of active collective member and to add the new membership active sponsoring member of the SGMS.

An active sponsor of the SGMS gets a total of three memberships at no extra costs, one of them being the spokesperson in contact with the committee of the SGMS. In addition, a direct link of the SGMS homepage guides directly to the homepage of the sponsor. The sponsor has the right to place also advertisements of courses strongly related to the field of mass spectrometry on our special section of the SGMS homepage and the logo is printed on the back cover of our newsletter.

The active sponsoring membership package is available starting from 1000 Fr. The sponsors define the amount of their donation. A change of the amount is possible, but must be communicated to the contact person of the SGMS committee prior to the beginning of the fiscal year.

The active collective membership was available for only 100 sfr. and included just a listing on the back cover of the newsletter. The active collective membership was initiated at a time without all the possibilities of the network and a homepage of the SGMS did not exist either.

The committee of the SGMS proposes therefore the following changes of the statutes (changes in ***bold/italic***):

2. Membership

2.1 Conditions for membership

2.1.1 The group consists of

- active individual members
- ***active sponsoring members***
- honorary members

All members have the right to vote. Only ***active sponsoring members*** have the right to be represented by another person. The representatives of the ***active sponsoring members*** must fulfil the condition mentioned under 2.1.1.1.

2.1.1.1 Persons working in the field of mass spectrometry are eligible to apply for enrolment as active individual members.

2.1.1.2 Industrial companies, as well as private and university research institutes, are eligible to apply for enrolment as ***active sponsoring members***.

2.1.1.3 The committee can propose to the general assembly to accept persons, having a valuable influence on the group or providing excellent contributions in the field of mass spectrometry, as honorary members.

2.1.2 The procedure for application of membership is as follows:

a) ***active individual members***: The committee checks all applications submitted and makes a proposal to the general assembly.

b) ***active sponsoring member***: ***The committee decides upon acceptance by simple voting upon request of a company fulfilling the conditions stated in 2.1.1.2.***

The new members must pay the membership fee upon acceptance. The honorary members do not need to pay a membership fee.

3. Finances

3.1 Assets of the group

The assets of the group consist of the membership fees, sponsor fees and donations.

3.2 Membership fee

The active members must pay an annual membership fee. The committee proposes the amount to the general assembly, which may discuss it and change it. The membership fee must be approved annually by the general assembly.

The active sponsoring members must contribute an annual sponsoring fee communicated to the committee.

Complete section of the current statutes to be replaced:

2. Membership

2.1 Conditions for membership

2.1.1 The group consists of

- active individual members
- active collective members
- honorary members

All members have the right to vote. Only active collective members have the right to be represented by another person. The representatives of the active collective members must fulfil the condition mentioned under 2.1.1.1.

2.1.1.1 Persons working in the field of mass spectrometry are eligible to apply for enrolment as active individual members.

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