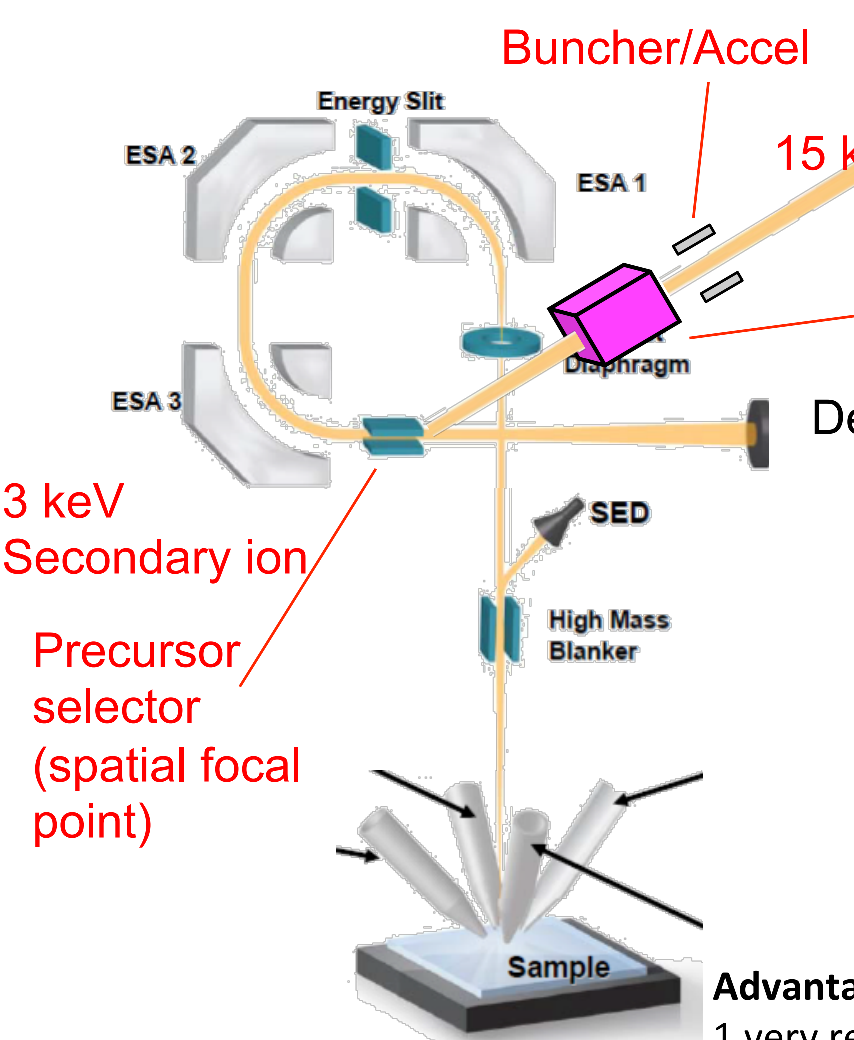
Fundamental, Instrumentation

報告者

兵庫県立大 盛谷浩右
山梨大 二宮啓

New *“nanoTOF II”* with MS/MS

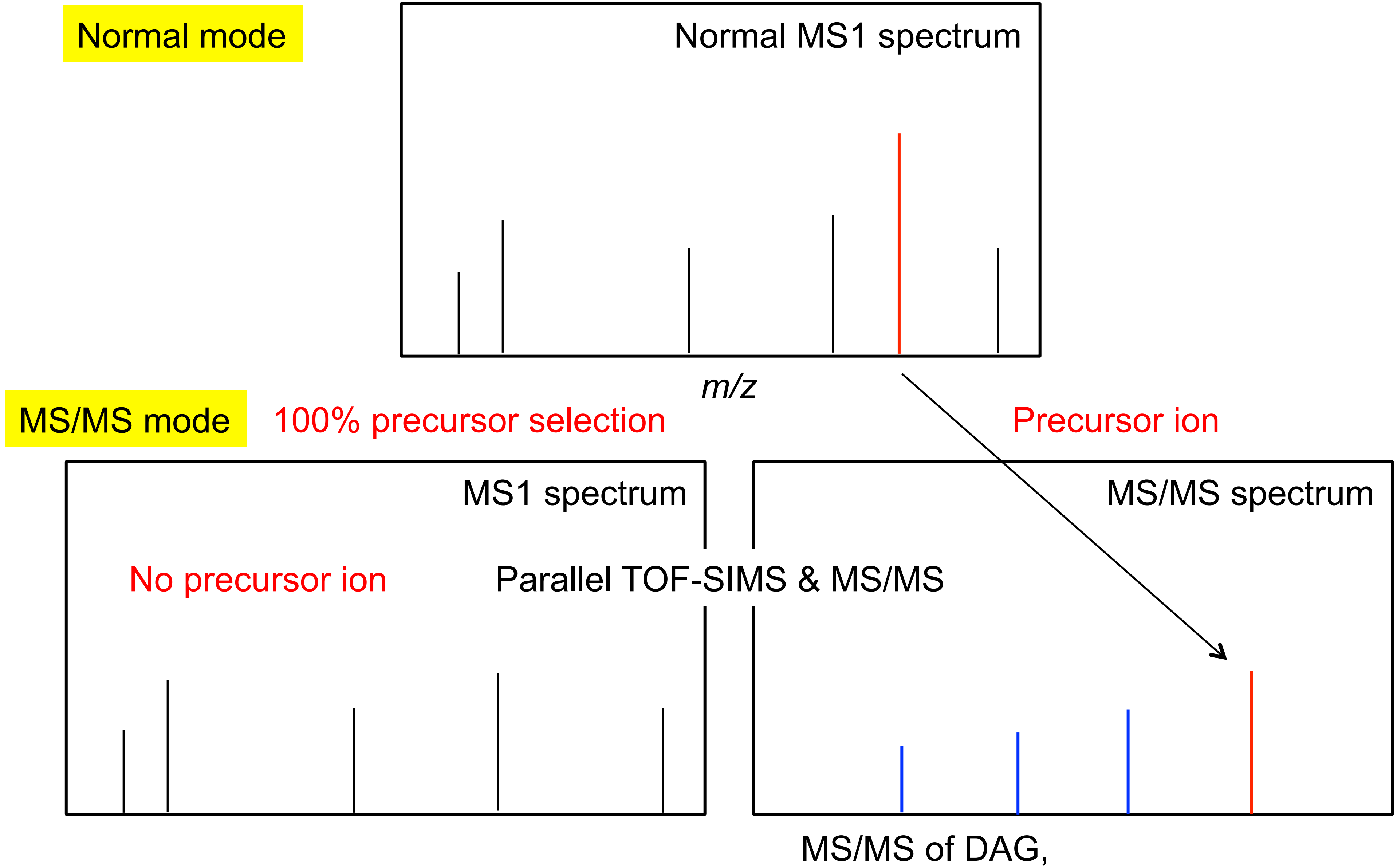


- 1 Da precursor window
- Parallel TOF-SIMS & MS/MS
- High conversion efficiency
  MS/MS spectra are generated with >25% average precursor fragmentation
- *m/Δm* of MS/MS spectrum: 3000
- Mass accuracy of MS/MS : 0.6~5 ppm

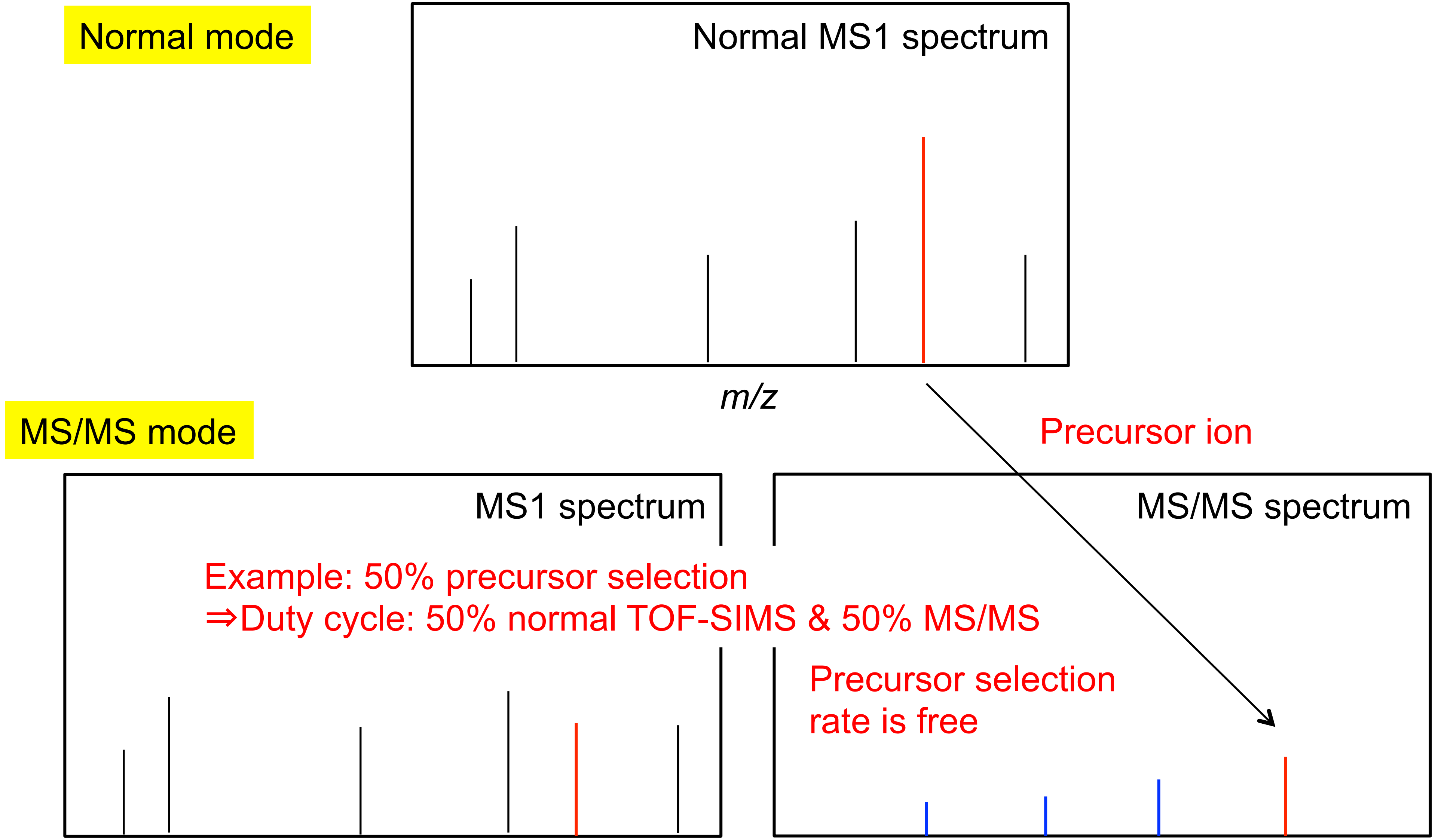
Advantages of High-Energy CID vs Low Energy CID

1 very reproducible → nearly independent of gas pressure and species
2. More fragmentation = more structural information
3. Less rearrangements = easier to interpret
4. Compatible with TOF-SIMS repetition rates

MS/MS spectra with “*nano-TOF II*” 1

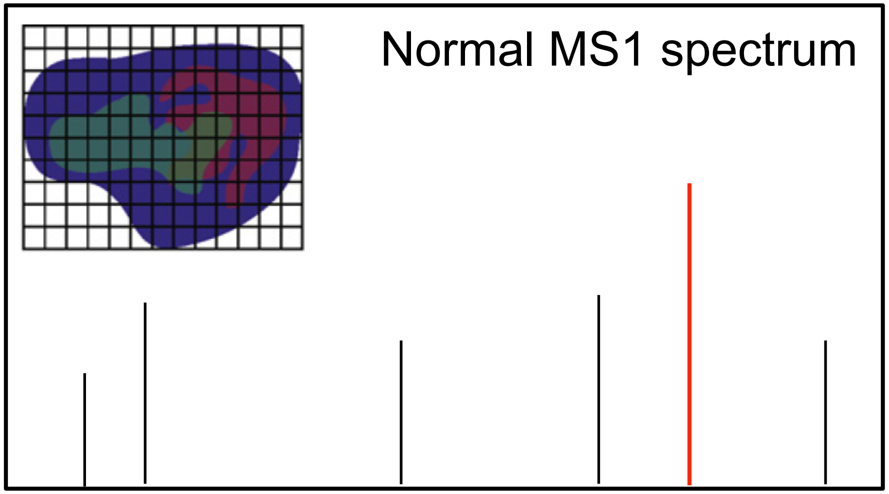


MS/MS spectra with "*nano-TOF II*" 2



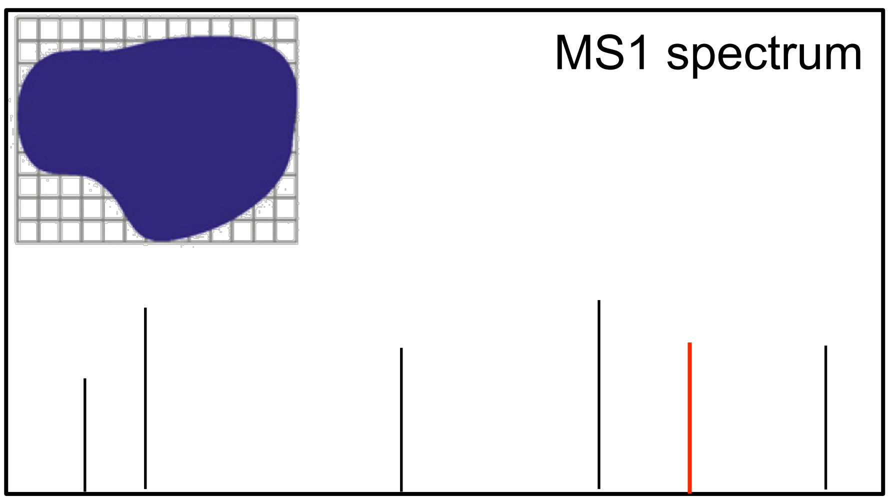
MS/MS spectra with "*nano-TOF II*" 3

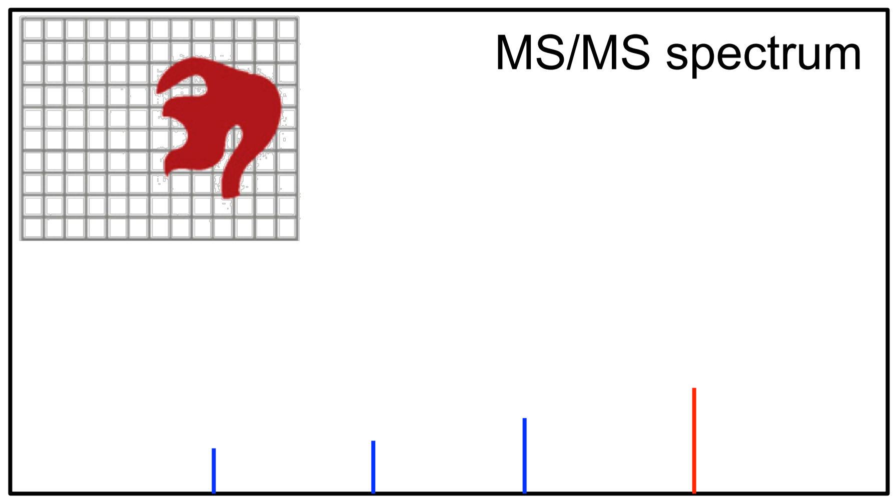
Normal mode



MS/MS mode

Parallel MS1 and MS/MS imaging





User presentation of MS/MS with *nano-TOF II*

"Biomolecular Investigation of Neurodegenerative Diseases and Brain Plasticity with TOF-SIMS Tandem Imaging MS"

N.O. Potocnik, *et al*., Maastricht University, Netherlands

BRAIN PATH
Molecular Imaging of Brain Pathophysiology

Research for Alzheimer's disease

MS/MS imaging of tissue sample
MS/MS of *m/z*888 (sulfatide) etc.

AMOLF(Institute for atomic and molecular physics) is led by Prof. Heeren. The Heeren group is one of the world leaders in high resolution molecular imaging of biological surfaces. It targets the development and application of state-of-art mass spectrometry based molecular imaging approaches. The application of molecular imaging using mass spectrometry in molecular histology is one of the breakthrough technologies in modern biomedical research.

Presentations of MS/MS @ SIMSXX conference

PHYSICAL ELECTRONICS
A DIVISION OF ULVAC-PHI

&

Prof. R.A. Heeren, AMOLF

5 oral presentations
@ SIMS conference

New TOF-SIMS Imaging MS/MS Presented @ SIMS XX

September 21, 2015

Last week at the 20th International Conference on Secondary Ion Mass Spectrometry (SIMS XX), PHI scientists authored or co-authored five papers with our collaborators from Maastricht University on the new parallel imaging MS/MS capability being developed for the PHI *nanoTOF* II. The following talks were presented;

A New Instrument for Parallel TOF-SIMS and MS/MS Data Acquisition, **Scott R. Bryan**, P.E. Larson, G.L. Fisher, J.S. Hammond, Physical Electronics, R.M.A. Heeren, Maastricht University

Imaging of Molecular Chemistry in Biological Specimens by Next-Generation TOF-SIMS, **Gregory L. Fisher**, Physical Electronics, N. Ogrinc Potocnik, A.L. Bruinen, B. Flinders, Maastricht University, T. Miyayama, S. Iida, ULVAC-PHI, J.S. Hammond, S.R. Bryan, Physical Electronics, R.M.A. Heeren, Maastricht University

TOF-SIMS Imaging MS/MS of Polymer Additives, **John S. Hammond**, P.E. Larson, G.L. Fisher, Physical Electronics, T. Miyayama, ULVAC-PHI, D.M. Carr, S.R. Bryan, Physical Electronics

Biomolecular Investigation of Neurodegenerative Diseases and Brain Plasticity with TOF-SIMS Tandem Imaging MS, **Nina Ogrinc Potocnik**, Maastricht University, G.L. Fisher, Physical Electronics, J. Praet, J. Hamaide, University of Antwerp, A.L. Bruinen, Maastricht University, A. Van Der Linden, University of Antwerp, R.M.A. Heeren, Maastricht University

High Resolution TOF-SIMS Tandem Imaging MS of Lipid Species in Infected Thin Tissue Sections, **Anne L. Bruinen**, Maastricht University, G.L. Fisher, Physical Electronics, A.M. Van Der Sar, VU University, N. Ogrinc Potocnik, R.M.A. Heeren, Maastricht University

This new capability generated a buzz at the meeting with many people making comments such as "we have needed this for years" and "I can finally identify my unknown peaks". The new patented PHI MS/MS approach offers a major step forward compared to conventional TOF-TOF tandem mass spectrometry. In our approach, the TOF-SIMS spectrum (MS^1) and the MS/MS spectrum (MS^2) are acquired in parallel. This high speed TOF-TOF method allows direct comparison of peaks, images or depth profiles from MS^1 and MS^2 from the same analytical volume of material.

Combination of SIMS and "Orbitrap"

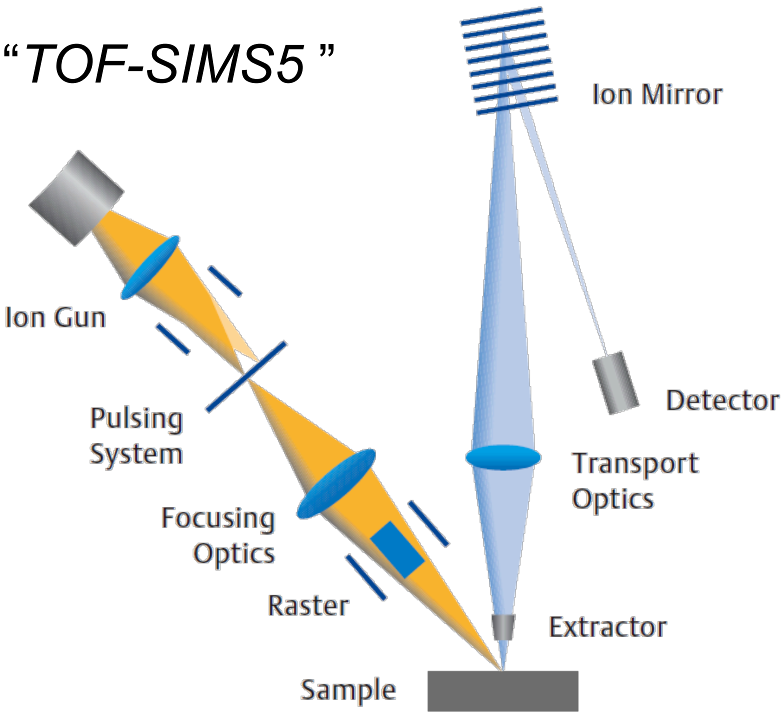
Dr. I. Gilmore of NPL, UK presented "A revolution in Chemical Imaging" including the first results from a "beyond state-of-the-art" SIMS instrument being developed with partners including ION-TOF & Thermo Fisher Scientific.

<u>Catchphrase</u>
"Surface analysis meets organic mass spectrometry"

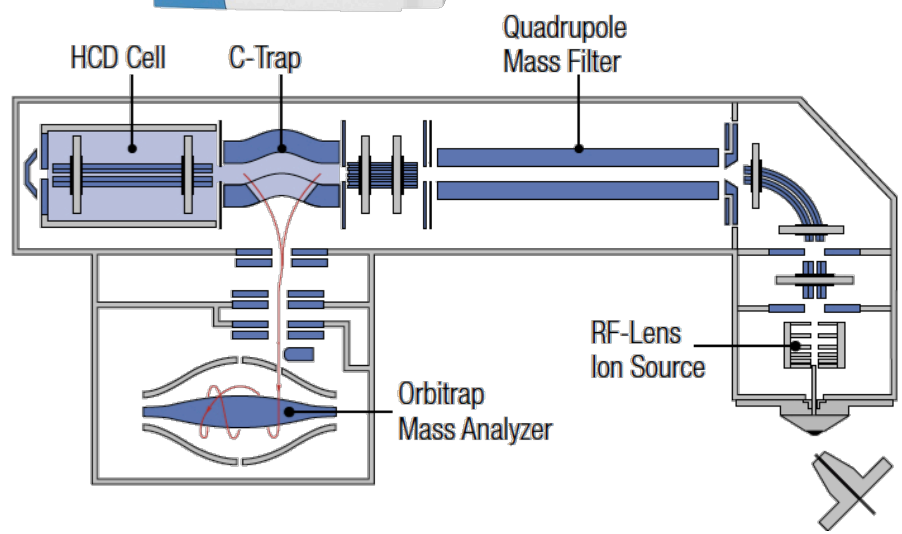
Highest mass resolution, real MS/MS and unambiguous peak identification for SIMS

"TOF-SIMS5" and "Q-Exactive"

"TOF-SIMS5"

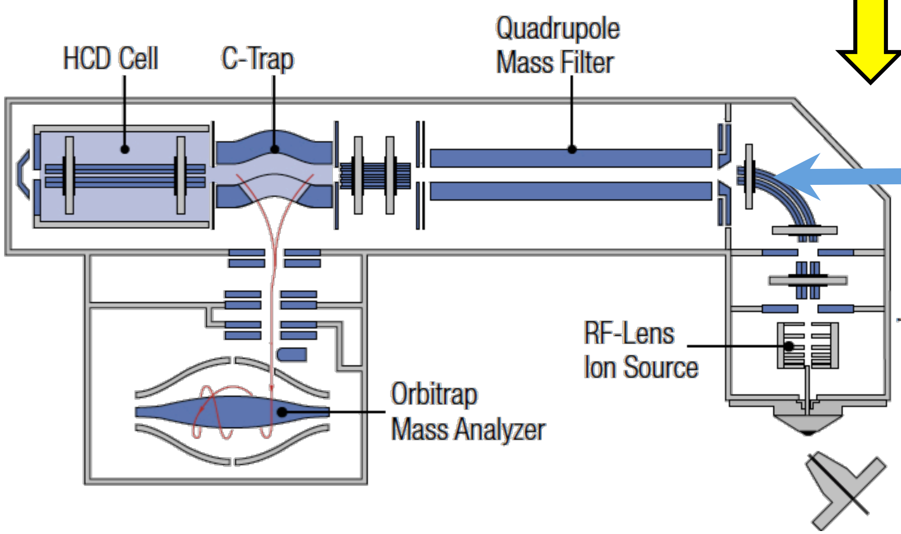


"Q-Exactive"

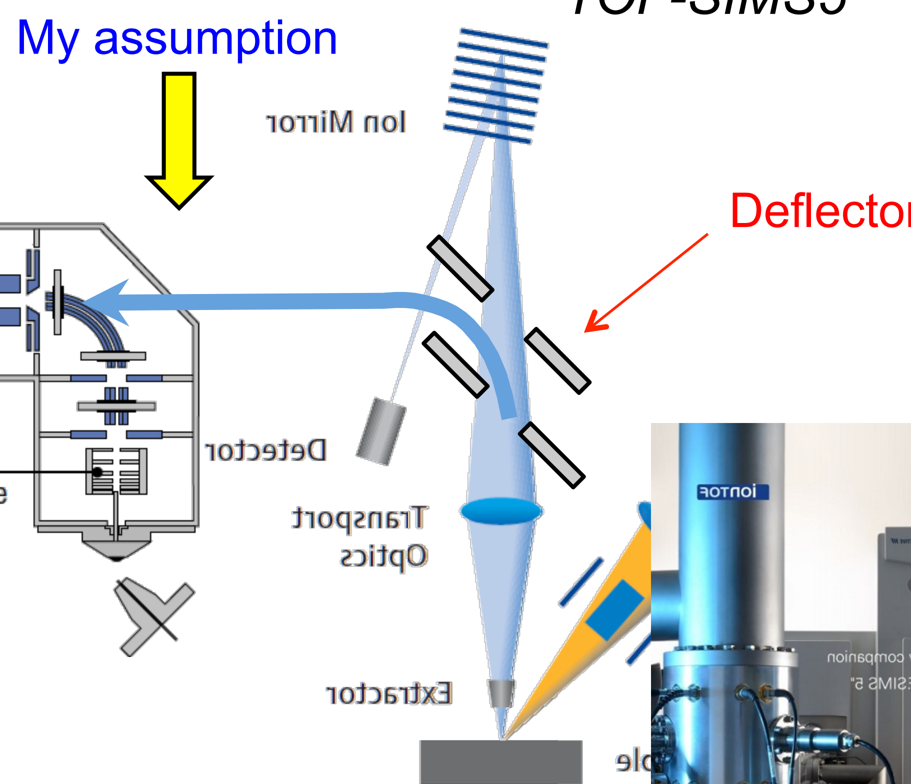


Joint of *“TOF-SIMS5”* and *”Q-Exactive”*

“Q-Exactive”



“TOF-SIMS5 ”



- *m/Δm* : 240000@*m/z*200
- Max. frequency: 18 Hz
- Imaging with Q-Exactive: 256×256 pixels
  Ar-GCIB<2 μm, LMIG<100 nm
- MS/MS available

Bioimaging by Massive Cluster Impact (MCI), Peter Williams group

Massive cluster

・electrosprayed glycerol in vacuum （$(Glycerol_{40000})^{130}$ ~4MDa
1.7 MeV@13 kV; 0.4 eV/nucleaon; *v* ~ 9 km/s

・Sputtering mechanism; shock heating followed by explosion.
(ΔT up to ~1000 K) (Peter Williams 1992)

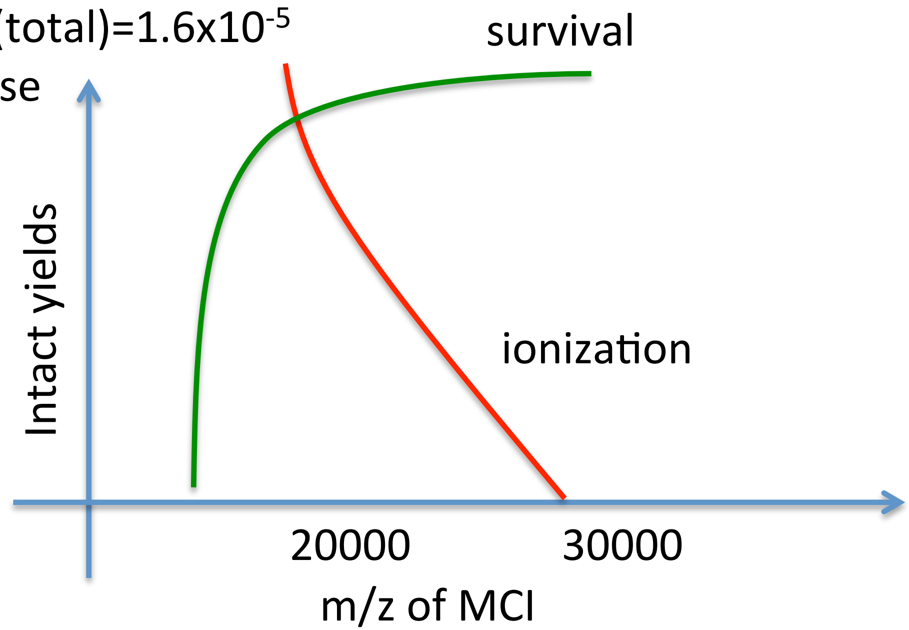
Experimental

・MCI-TRIFT system

Useful ion yields (UY)

・UY = (No. of detected intact and ionized molecules)/(No. of sputtered molecules)

・UY of MCI 1〜3 X 10^{-5} → 260 counts @ 3x3 μm^2 (for intact lipid); not sufficient
for example, insulin(+1)=0.9 insulin(+2)=0.7 insulin(total)=1.6×10^{-5}
※ UY for Ar_n, Ar_n+H_2O: ~ 10^{-6} for Lipid and Treharose



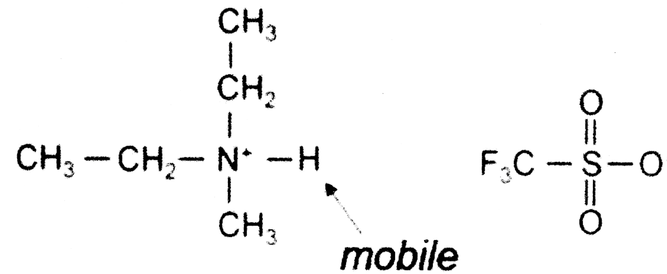
Future Solution

→ MCI-Cameca Xf

1. Microscope imaging: few µm resolution
2. DC secondary ion beam
3. M/dM ~ 1000

Development of a vacuum-electrospray beam source using a proton-conducting ionic liquid[dema][TfO], Y. Fujiwara's group

- Vacuum electrospray
- Protic ionic liquid
- Sample:
  ①Arginine → enhance
  ②PEG3000 → not enhance
- Proton affinities for ①, ② and [dema] can explain the difference.



$[dema]^+$ $[TfO]^-$

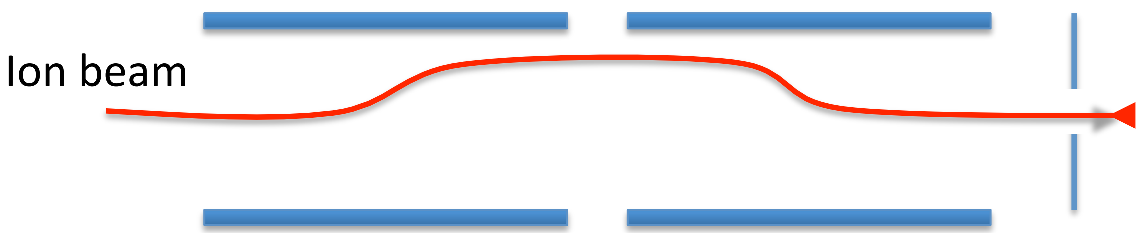
Secondary ions produced by electrosprayed droplet impacts with m/z selection from 10^3 to 10^6, S. Ninomiya's group

- Vacuum electrospray
- Va = 8～9 keV

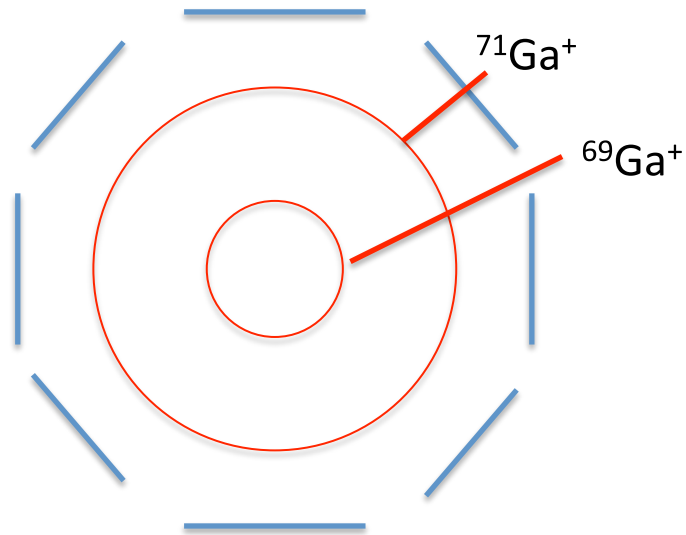
- Indium, SUS → Smaller droplets（10^2～10^4 Da）
- arginine intact → Larger droplets (~40～50 kDa, but decreased above ~50 kDa.)

Development of a Mass Spectrometer using Two Rotating Electric Fields, M. Nojima Group

Vertical section



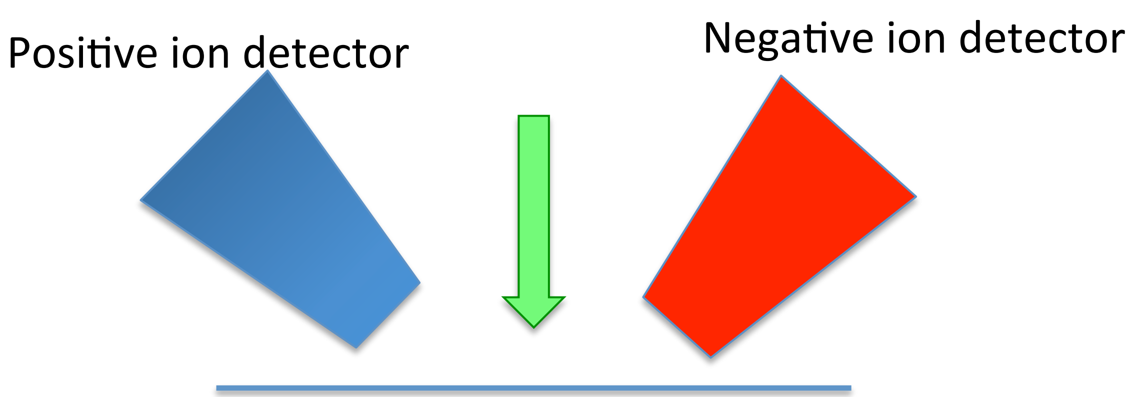
Cross section



- Compact, wide mass range mass spectrometer

Simultaneous Detection of Positive and Negative Secondary Ions On Focused Ion Beam Tool, HIDEN Analytical

- Quadrupole SIMS detectors
- Ga FIB



Parallel Ion Electron Spectrometry (PIES); TEM-SIMS, Luxembourg group

Complemetarity SIMS-TEM

TEM

○

・Spatial resolution
・Crystallographic information
・EELS and EDX at high spatial resolution
・Quantitative

x

・Concentrations > 0.1%
・Low-Z elements (H, Li)
・No isotopic information

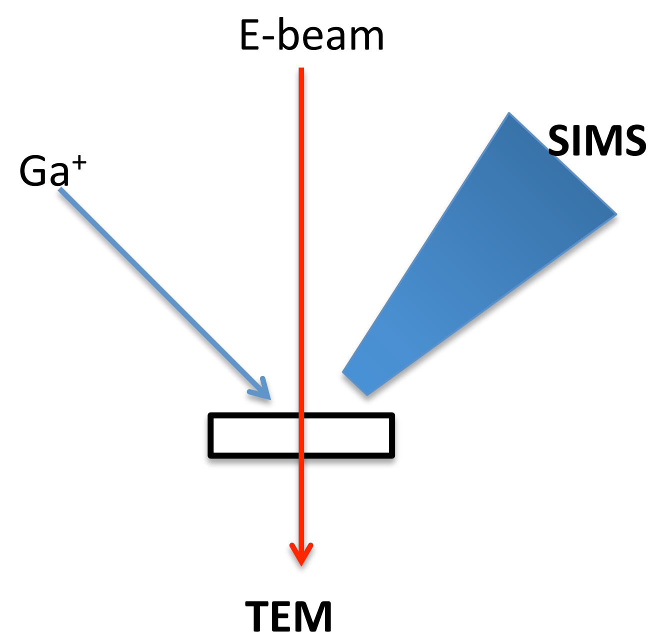
SIMS

○

Low detection limits (ppm)
All Masses/Isotopes

x

Lateral resolution
Quantification



Application

Sample: Li_2TiO_3

Ar cluster SIMS and XPS, UPS, Kratos Analytical

Sample

Thiol-based SAMs on Gold

・Depth profiling → TOF-SIMS, XPS, UPS
・Work-function changes → UPS
・Quantification C1, O1s, S2p → XPS

Application

Sample: organic solar cell material

Others

Beyond Defect Formation: Characterization of Structural and Electronic Modifications in Graphene due to Plasma Treatment by ToF- SIMS, XPS and Raman, JOSEPH GARDELLA, JR., J.S. WALLACE, A. QUINN, University at Buffalo, The State University of New York, J. HU, E. KONG, Shanghai Jiao Tong University, H. JOH, Korean Institute of Technology

Combining XPS Atomic Concentration Data with a ToF- SIMS Chemical Image Map using Image and Data Fusion, **TAMMY MILILLO**, University at Buffalo, The State University of New York, M.E. MILLER, Michigan Tech Research Institute, R.V. FISCHIONE, CUBRIC Inc., J.A. GARDELLA, University at Buffalo, The State University of New York

XPS/UPS Depth Profiling with Gas Cluster Ion Beam for Characterization of Interfaces in Thin Multilayer Organic Structures, MATEUSZ M. MARZEC, AGH University of Science and Technology, Poland, J. RYSZ, Jagiellonian University, Poland, J. HABERKO, A. BERNASIK, AGH University of Science and Technology, Poland, A. BUDKOWSKI, Jagiellonian University, Poland

…などなど

Glyoxal Aqueous Surface Chemistry by SALVI and Liquid ToF-SIMS, Xiao-Ying Yu@Pacific Northewest National Laboratory

・Keep 10^{-7} mbar vacuum
・2～3 μm Microchannel

Application

・In situ chemical probing of the electrode–electrolyte interface by ToF-SIMS
（Lab Chip, 2014, 14, 855）

・In situ molecular imaging of a hydrated biofilm
（Analyst, 2014, 139, 1609）

・Two-dimensional and three-dimensional dynamic imaging of live biofilms ToF-SIMS
（BIOMICROFLUIDICS 9, 031101 (2015)）

・Photochemical reaction of glyoxal (CHOCHO) oxidation
（This conference）

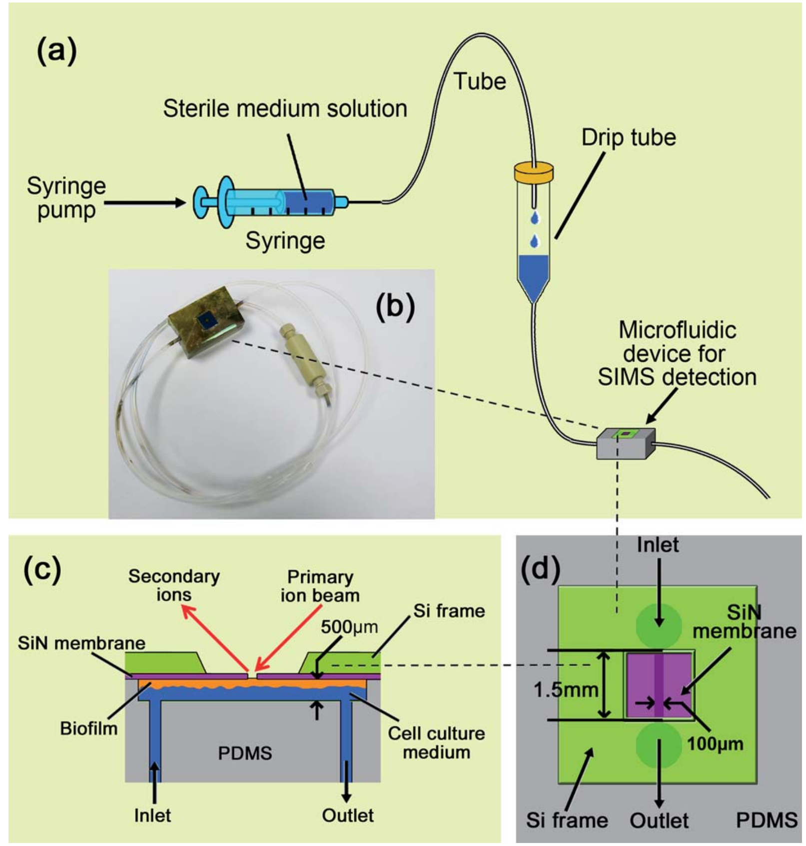
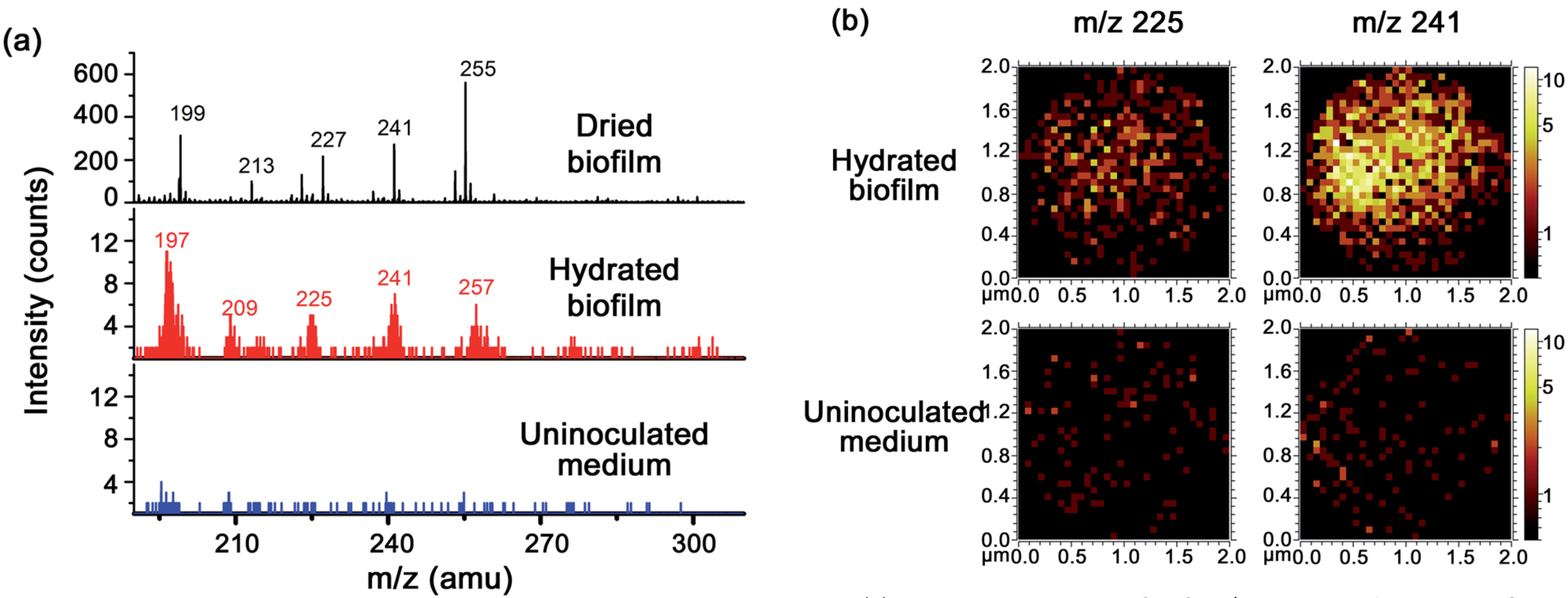


Fig. 1 Schematic of the single-channel growth microfluidic reactor and ToF-SIMS detection including (a) the setup of the biofilm growth experiment, (b) a photo of the device used for biofilm growth; (c) schematic showing the cross-sectional view of the grown biofilm during ToF-SIMS probing; and (d) a top view of the device during biofilm growth.

（Analyst, 2014, 139, 1609）

Glyoxal Aqueous Surface Chemistry by SALVI and Liquid ToF-SIMS, Xiao-Ying Yu@Pacific Northewest National Laboratory



(Analyst, 2014, 139, 1609)

Fig. 2 (a) Representative ToF-SIMS *m*/*z* spectra of the dried *Shewanella* sp. biofilm deposited on a clean Si wafer, the hydrated biofilm, and the uninoculated medium solution and (b) 2D images of *m*/*z* 225 (C_{14} FA) and *m*/*z* 241 (C_{15} FA) fragments obtained from the hydrated biofilm and uninoculated medium samples. The false-colour scale shown on the right of (b) indicates the relative SIMS signal intensity from high (white/yellow) to low (black/red).

Glyoxal Aqueous Surface Chemistry by SALVI and Liquid ToF-SIMS, Xiao-Ying Yu@Pacific Northewest National Laboratory

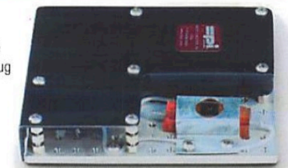
SPI Supplies Wet Cell II

The Wet Cell II is the next generation device for the examination of liquids in an EM environment. The self-contained high vacuum compatible device enables the analyst to characterize a fluid in its natural state. And as it is a self-contained device, there is no need for modification of the existing microscope. Once the liquid is loaded into the device platform, it is inserted into the microscope and is ready for analysis.

The device can be used for in-situ chemical probing or molecular imaging of a sample in liquid. Potential application areas include liquid surface chemistry, microbiology, drug delivery & reaction.

Wet Cell II Specifications:

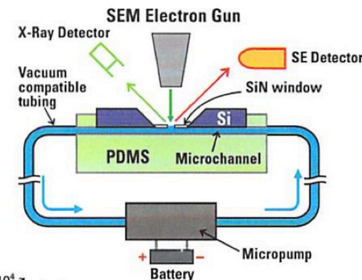
- Self-contained high vacuum compatible device
- Battery driven pump for up to 4 hours operation
- Microfluidic block for sample characterization
- Electron transparent SiN membrane

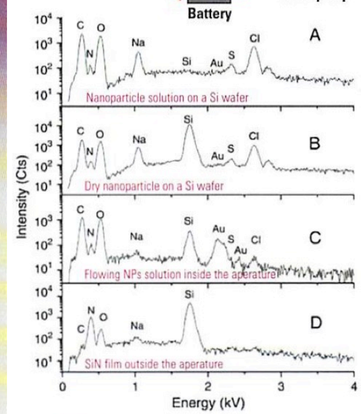


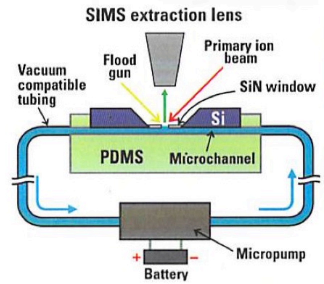
- ~200 µl reservoir
- Flow rate < 2 µl/min
- Low cost replaceable components allow contaminant-free work.
- Platform size: 3″ × 4″ (75 × 100 mm), Height: 20 to 25 mm

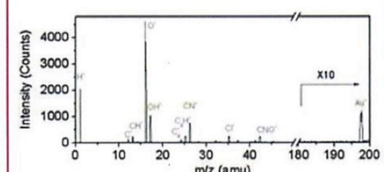
The 75 x 100 mm platform contains all the components needed to run your sample and is adaptable to most electron microscopes.

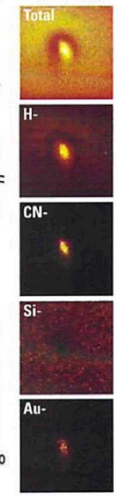
A degassed fluid is loaded by the micropump on the device or a syringe pump into the reservoir. The main chamber is composed of PDMS with a SiN window. This block is easily replaced, avoiding the need to try to clean it between runs. Vacuum compatible tubing connects the sample block to the pump, which operates at a flow rate < 2 µl/min.











References:

1. Yang, L., Zhu, Z., Yu, X. Y., Rodek, E., Saraf, L., Thevuthasan, T., & Cowin, J. P. (2014). In situ SEM and ToF-SIMS analysis of IgG conjugated gold nanoparticles at aqueous surfaces. Surface and Interface Analysis, 46(4), 224-228.

Analysis of mixed organic/inorganic hybrid multilayers

Oral presentations related to this topic

- "Sputtering with Large O_n^+ Cluster Projectiles on Inorganic Surfaces "
  by W. Vandervorst (IMEC, Belgium) → 10 keV $(O)_{1500}$, ripple formation, not good
- "Low Temperature Plasma for Crater Edge Depth Profiling of Inorganic Multilayers"
  by S. Muramoto (NIST, USA)
  → LTP etching + Bi_3 analysis, No damage detection for inorganic and organic samples
- "Recent Developments in TOF-SIMS Depth Profiling of Inorganic and Organic Thin Films"
  by E. Niehuis (ION-TOF, Germany)→Next slide
- "Low Energy Cesium Depth Profiling of Hybrid Materials"
  by L. Houssiau (Univ. of Namur, Belgium)
  →GCIB: damage removal mode, Cs: damage controlled mode
  500 eV Cs^+⇒Tyr/Au(Cr)/Si, Au(Cr)/Tyr/Si, Tyr/Au(Cr)/Tyr/Si
  Tyr/Au(Cr)/Si：very sharp interface, no diffusion of metal into Tyr
  Au(Cr)/Tyr/Si：metal diffusion into Tyr (Cr is stronger) , sharp Tyr rise
  ※Sputter Yields by 500 eV Cs^+：0.05 (Au), 0.016(Cr), 0.28(Tyr) [nm^3/ion]
  Simulation of recoil (injection into organic layers) of metals by SRIM

Depth profile with gas cluster ion beam (GCIB)

"Recent Developments in TOF-SIMS Depth Profiling of Inorganic and Organic Thin Films"
by E. Niehuis (ION-TOF, Germany)

★Depth profiling of MRFA peptide with "*TOF-SIMS5*"／"*Q-Exactive*"
Probe: Ar-GCIB (5 keV, Ar_{2500})
Mass resolution @ depth profiling: 119000~343000
Mass accuracy: 1~2 ppm

★Inorganic/organic multilayer analysis with various GCIBs
Problem of Ar-GCIB: Low etching rate for inorganic samples
Improve by chemical effects？
O_2-GCIB：Not good, but excellent oxidation

SF_6-GCIB→Polymer(styrene methacrylate)/SiO_2/Polymer/SiO_2/…/Si
20 keV $(SF_6)_{570}$, Y_{pol}/Y_{SiO2}=5.4, RMS@bottom=8nm, RMS(Pol/SiO_2)=4.5
7.5 keV $(SF_6)_{370}$, Y_{pol}/Y_{SiO2}=10.7, RMS@bottom=10nm, RMS(Pol/SiO_2)=8.1
Depth profile of polymer/SiO_2 multilayers may be possible,
but how about metal/organic multilayers?

Comparison of SI yields for Ar- & H_2O-GCIBs

"Enhanced Ionization Using Water-containing Cluster Ion Beams"
"Matrix Effects in Biological SIMS using Cluster Ion Beams of Different Chemical Composition"
by N. Lockyer & J.C. Vickerman (Univ. of Manchester, UK)

1. The chemistry of the primary ion cluster becomes significant at low energy per atom (molecule) ($E/n < 10$ eV) in terms of the ionisation of analyte molecules.

2. The water cluster beam increase ionisation efficiency by x3~90 (depending on the kind of molecules and the E/n). The SI yield is highest at E/n ~3 eV

3. At $E/n > 10$ eV, the water cluster beam behave similarly to Ar cluster beam.

Matrix enhanced SIMS

"Peptide yields for various primary ions in SIMS and ME-SIMS"
M. Körsgen, *et al*., University of Münster, Germany

Bi cluster (LMIG)
SIMS: strong increase of molecular ion signal with increasing cluster size
ME-SIMS (DHB, HCCA): show nearly comparable yields of molecular ions

Ar-GCIB
SIMS: strong decrease of molecular ion signal with increasing cluster size
ME-SIMS (DHB, HCCA): increase of molecular ion signal with increasing cluster size

Investigation of Surface-adsorbate Interaction of Surface- adsorbed (bio-) Molecules Using Desorption/Ionization Induced by Neutral Clusters $(SO_2)_n$, M. Dürr

- Proton attachment to the intact occur during $(SO_2)_n$ beam irradiation.
- They tested $(SO_2)_n$ beam irradiation to peptides in D_2O atmosphere.
  SO_2 is necessary for H/D exchange reaction.
  H/D exchange reaction : $SO_2 + D_2O \rightarrow D_2SO_3 \rightarrow D^+ + DSO_3^-$

(Poster) Measuring the Internal Energy of Secondary Ion Sputtered with Argon Cluster Beams with N-substituted Benzylpyridinium Thermometer Molecules,
MELISSA PASSARELLI, NPL, UK, I.S. GILMORE, National Physical Laboratory, UK, United Kingdom of Great Britain and Northern Ireland

・The energy transfer from the primary ion beam to the secondary ions during the bombardment process generates ‘hot' secondary ion fragments in the gas phase, which result in complex mass spectra and reduced molecular ion yields.

・Because The efficiency of this energy transfer is unknown, they tried to measure the internal energies of secondary ion produced from argon cluster beam using a series of thermometer molecules which have well-defined internal energy thresholds.

・Internal energy determined the extent of fragmentation.

・They plotted 'Survival yield' for the chlorine-substituted benzylpyridium ions vs E/n values of Ar GCIB projectile.

'Survival yield' = I(M)/[I(M+) + I(F+)]

・The E/n value at the inflection point represents the maximum dissociation energy, which is consistent with the known bond energy.

・The internal energy of secondary ions was found to be linear with the primary ion beams E/n value.

SIMS XX 報告会＠東京理科大学 2015年 11月4日

Biological application
Biological
Biological imaging

成蹊大学　理工学部　物質生命理工学科
物質計測・イメージング研究室
横山　有太、青柳　里果

SIMS XX (20th International Conference on Secondary Ion Mass Spectrometry)

期間; 2015年9月13日～18日
場所; The Westin Seattle, シアトル

http://www.westinseattle.com/gallery

Topics

- 3D 3D Imaging of Complex Materials
- AE Archeology/Environment/Forensics
- BI Biological Imaging
- CI Cluster Ions
- CT Complementary Techniques and Multi-Technique Approaches
- DG Depth Profiling/General
- DI Depth Profiling/Inorganics
- DO Depth Profiling/Organics
- DP Data Processing and Interpretation
- FE Forensics & Environment
- FN Fundamentals
- FS FIB-SIMS
- GC Geology, Geo- and Cosmochemistry
- IA Industrial Applications
- ID Image and Data Fusion
- IN Instrument Development
- IP Ionization Processes
- IS In-Situ Liquid SIMS
- LS Life Science and Biotechnology
- MA Medical Applications
- MI Microelectronics
- MS MeV-SIMS
- NN Nanomaterials and Nanotechnology
- PM Polymers and Molecular Films
- PS Plenary Session
- RE Renewable Energy and Energy Storage
- SI Surface & Interface Analysis
- SM SIMS Analysis of Materials
- SP Sample Prep & Analysis of Biological Samples
- SR Ultra High Spatial Resolution SIMS
- ST SIMS Tutorial
- TC Tribology and Corrosion

発表件数（バイオ関連のトピックス）

	Oral	Poster	Total
BI; Biological Imaging	19	12	31
LS; Life Science and Biotechnology	8	6	14
SP; Sample Prep & Analysis of Biological Samples	6	9	15
合計(総件数)	33 (168)	27 (112)	60 (280)

* “バイオ”関連のトピックスの発表は全体の約20 %
* 他のトピックスでもバイオ関係の発表あり
* データ解析やクラスターイオン、3Dイメージング等との関連が深い

SIMS XX について

【バイオ関連の印象】

- Arクラスターなどのクラスターイオン源を用いた研究
- データ解析への多変量解析（特に主成分分析）の適用
- 生体試料中の特定成分の高感度イメージング

【全体の印象】

- 深さ方向分析、マトリックス効果の補正
- 2次イオン収率の向上（装置、サンプル調整）
- 生体イメージング（ラットの脳など）

Invited Talks

【BI; Biological Imaging】

DaeWon Moon (DGIST, Korea, Republic of Korea)

"Alternative Pathways for Generating Breakthroughs in Biological SIMS Imaging"

・バイオイメージングへのToF-SIMSの適用、クラスターイオンの発展がブレークスルー
・2次イオン強度（たんぱく質やペプチド）が小さい ⇒ 金属（希土類金属）を付加する

【LS; Life Science and Biotechnology】

Gregory L. Fisher (Physical Electronics)

"Imaging of Molecular Chemistry in Biological Specimens by Next-Generation TOF-SIMS"

・PHI *nanoTOF*IIとタンデムIMSを組み合わせた測定

【SP; Sample Prep & Analysis of Biological Samples】

Lara Gamble, Blake Bluestein, Daniel Graham (University of Washington)

"Tissue Analysis with SIMS: Turning Challenges into Opportunities"

・ホルマリン固定パラフィン包埋(FFPE)法で作製した試料のToF-SIMS測定

・データ解析に主成分分析を使用

研究紹介　BI; Biological Imaging

【BI1-TuA-1】

John Vickerman et al.

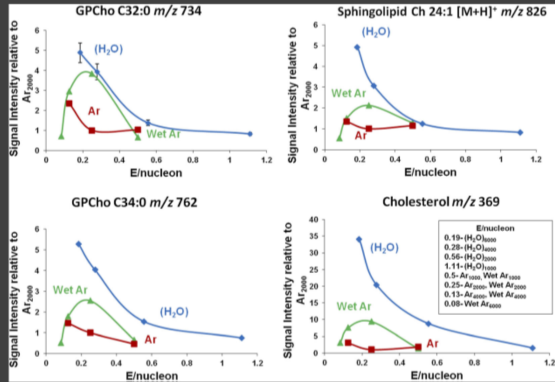
“Comparing Polyatomic Ion Beams for Mass Spectrometric Imaging of Mouse Brain Tissue by ToF-SIMS”

・20 kV C_{60}^{+}, Ar_{2000}^{+}, $(H_2O)_{6000}^{+}$, water-doped Ar_{2000}^{+}によるDPPCやラットの脳のイメージング

・$(H_2O)_{6000}^{+}$, water-doped Ar_{2000}^{+}では2次イオン収率が高い（特に$[M+H]^{+}$）

⇒ 生体組織のイメージングに有効

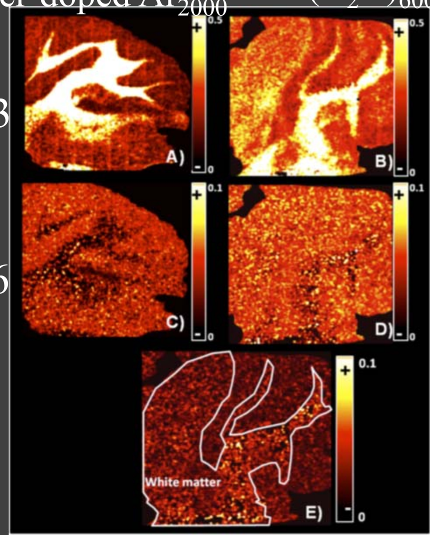
[1] S. Sheraz (née Rabbani) *et al.*, Anal. Chem. 2013 , 85 , 5654 – 5658.
[2] S. Sheraz (née Rabbani *et al.*, Surf. Interface Anal., 2014, 46, 51 – 53 .
[3] I. Berrueta Razo, *et al.*, Surf. Interface Anal., 46, 2014, 136 – 139 .



water-doped Ar_{2000}^{+}　$(H_2O)_{6000}^{+}$

m/z 369.3

m/z 788.6



I. Berrueta Razo *et al.*, Rapid Commun. Mass Specrtom. 2015, 29, 1851–1862.

研究紹介　BI; Biological Imaging

【BI2-FrM-1】
Tae Geol Lee et al.
"TOF-SIMS Imaging Analysis of Rats with Focal Cerebral Ischemia by Using Ar Cluster Ion Beams"

・主にラットの脳を用いたイメージング（脳梗塞？）
・BiおよびArクラスターを用いたToF-SIMS測定
　⇒ *m/z* 1000 以上でもきれいなイメージング
・MALDI-ToFを補完するデータやあらたな2次イオンを発見
・PCAやNMF (non-negative Matrix Factorization; 非負値行列因子分解)によるデータ解析

Anal. Chem. **83**, 9298 (2011)
J. Lip. Res. **53**, 1823 (2012)

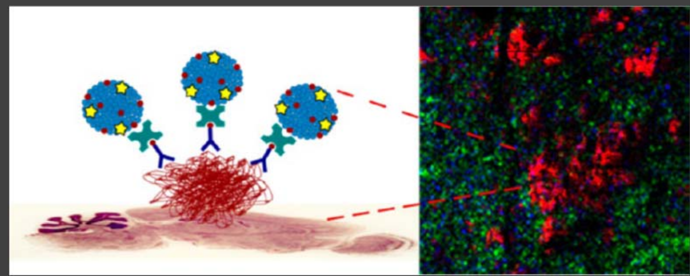
研究紹介　BI; Biological Imaging

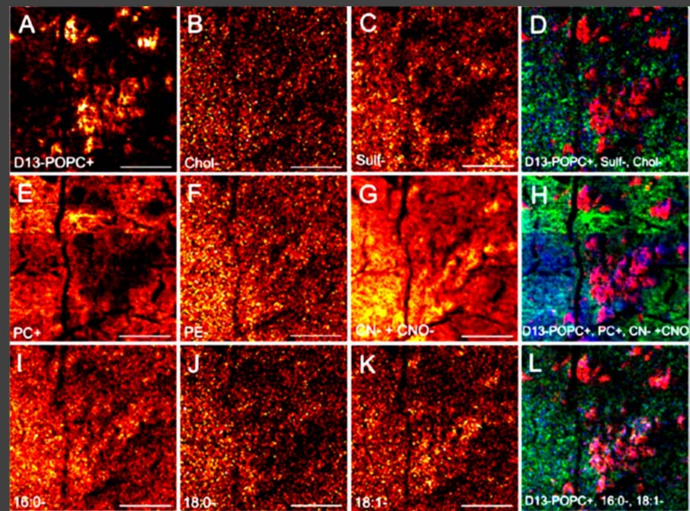
【BI2-FrM-2】

Louise Carlred et al.

“Imaging of Lipids and Proteins in Alzheimer’s Disease Transgenic Mouse Brains Using Immunoliposomes and ToF-SIMS”

- Liposomeを用いたToF-SIMSイメージング
- 抗体を接合したliposome (immunoliposome)を目的のタンパク質に結合
- Liposomeの分布から目的タンパク質の分布が分かる
- 検出したいタンパク質に合う抗体を接合することで、さまざまなタンパク質の検出が可能
- 異なるタンパク質の同時測定も可能





J. Am. Chem. Soc. **136**, 9973 (2014).

研究紹介　BI; Biological Imaging

【BI2-FrM-10】
Zhanping Li et al.
"TOF-SIMS Analysis of Pharmacological Active Components in Cordyceps Sinensis"


https://ja.wikipedia.org/wiki/%E5%86%AC%E8%99%AB%E5%A4%8F%E8%8D%89

・Cordyceps（冬虫夏草）に含まれる有効成分のToF-SIMS測定
・30 kV Bi_3^{++}, (TRIFT V nanoToF)
・いくつかの2次イオン強度に注目
例えば*m/z* 251 (cordycepin; $C_{10}H_{13}N_5O_3$)や*m/z* 181 (mannitol $(M-H)^-$; $C_6H_{14}O_6$)
・ToF-SIMSはこれらの有効成分由来の2次イオンの検出に有効
・種類の異なる冬虫夏草で有効成分の量（2次イオン強度）を比較
（高価なものの方が有効成分多い？）

[1] Committee of National Pharmacopoeia, Pharmacopoeia of People's Republic of China, China Medicine Science and Technology Press, Beijing, 2012: p.106.
[2] J. Pharmaceutical and Biomedical Analysis, 2006, 41: 1571–1584
[3] J. Pharmaceutical and Biomedical Analysis, 2006, 40: 623–630

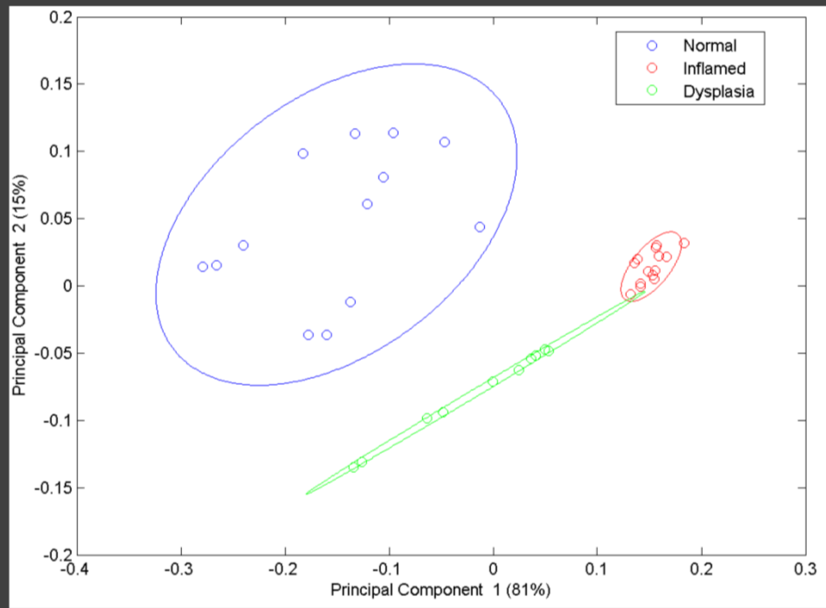
研究紹介　LS; Life Science and Biotechnology

【LS1-WeM-9】

Marco Urbini et al.

"Identification of Biomarkers for Human Inflamed and Dysplastic Colon Tissues by Time-Of-Flight Secondary Ion Mass Spectrometry and Multivariate Analysis"

- 大腸がん組織のToF-SIMS測定 (Bi_3^{++})
- 主成分分析によるデータ解析
  m/z 58（グルタミン酸）⇒ 炎症組織
  m/z 91（チロシン）⇒ 形成異常組織
- ToF-SIMSと多変量解析を合わせた手法は大腸がんなどの診断に有効



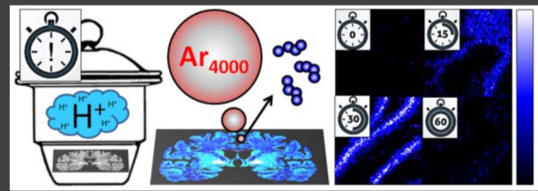
研究紹介　SP; Sample Prep & Analysis of Biological Samples

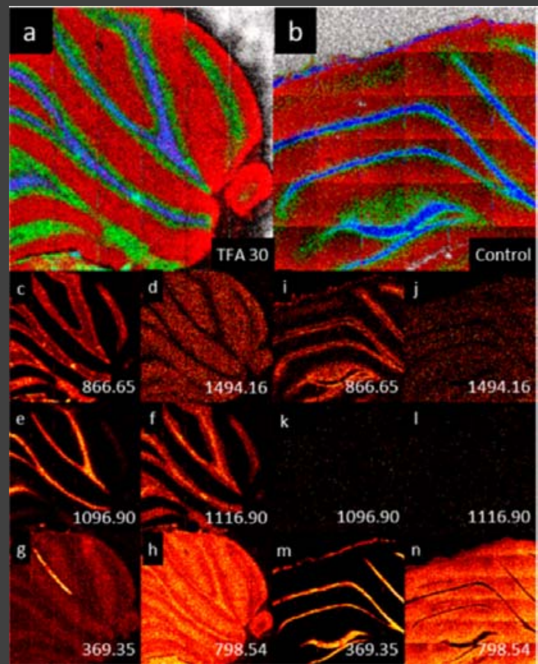
【SP1-TuM-4】

Tina Bernadette Angerer et al.

"Improving Sensitivity and Broadening Chemical Coverage in Brain Imaging using ToF-SIMS and GCIBs"

- 40 keV GCIB (Ar_{4000}^{+})によるイメージング
  (J105-*3D Chemical Imager*)
  高いイオン化効率、ビームスポット径　<3 μm
- Trifluoracetic acid (TFA)などのガスを曝露することで高質量ピーク強度が増大したり、これまでは検出できなかった新たなピークが現れる。
- TFA曝露によりコレステロールが多く、結晶化した部分が取り除かれる。
  ⇒ 神経学分野のToF-SIMSイメージングにおいて有効な前処理方法





[1] D. Touboul *et al.*, *J. Lipid Res.* 2005, 46, 1388-1395.
[2] T. B. Angerer *et al.*, *Int. J. Mass Spectrom.* 2015, 377, 591-598.
[3] T. B. Angerer *et al.*, *Anal. Chem.* 2015, 87, 4305-4313.

研究紹介 SP; Sample Prep & Analysis of Biological Samples

【SP1-TuP-7】

Bonnie J. Tyler et al.

"ToF-SIMS imaging of Capsaicinoids in Scotch Bonnet Peppers"

- トウガラシ(スコッチボネット)に含まれるカプサイシノイド類(カプサイシンなど)の分布をToF-SIMSにより計測(Bi_3^+)
- 液体プロパンで凍結した試料を-110℃で測定
- 6種類のカプサイシノイド及びその前駆体イオンを観測
  ⇒ 果皮や胎座に多く分布
- ToF-SIMSイメージングは、ラベルなしで目的物質をイメージングできるため、植物中の代謝物のイメージングに有効

Scotch Bonnet

Species	*Capsicum chinense*
Cultivar	'Scotch Bonnet'
Heat	Exceptionally hot
Scoville scale	100,000–350,000 SHU

https://en.wikipedia.org/wiki/Scotch_bonnet_(pepper)

Tutorial

(1) **Arnaud Delcorte** (Université catholique de Louvain, Institut de la Matière Condensée et des Nanosciences (IMCN)

"Fundamental Aspects of SIMS"

・スパッタ収率、クラスターイオン、マトリックス効果など（主にクラスターに関する解説）

(2) **Rasmus Havelund** (National Physical Laboratory, UK)

"Organic Depth Profiling"

Tutorial

(3) **Daniel Graham** (University of Washington)

“Successfully Navigating the Sea of ToF-SIMS Data with Multivariate Analysis”

- 多変量解析（特にPCA）の適用例

(4) **Marinus Hopstaken**

(IBM T.J. Watson Research Center)

“SIMS Depth Profiling in Thin film Materials for Advanced Microelectronics and Photovoltaic Devices”

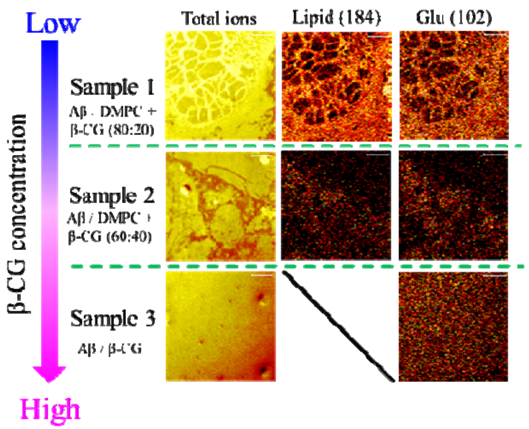
発表紹介 （成蹊大学 物質計測・イメージング研究室）

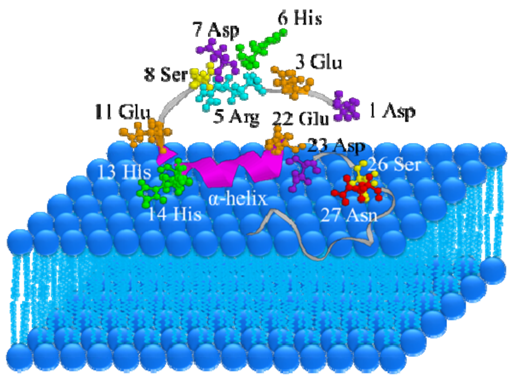
【LS1-WeM-4】

Yuta Yokoyama, Toshinori Shimanouchi, Hideo Iwai, Satoka Aoyagi

"ToF-SIMS Analysis of Amyloid Beta Aggregation forms on Different Lipid Membranes"

- 脂質とグルコシド混合膜上でのAβの吸着状態の評価 (PCA, MCR)
- Aβは局在化したDMPC上で特定の配向をもって吸着





PDB ID: 2LFM

n-Asp-Ala-Glu-Phe-Arg-His-Asp-Ser-Gly-Tyr-Glu-Val-His-His-Gln-Lys-Leu-Val-Phe-Phe-Ala-Glu-Asp-Val-Gly-Ser-Asn-Lys-Gly-Ala-Ile-Ile-Gly-Leu-Met-Val-Gly-Gly-Val-Val-c

α-らせん構造部分がDMPC上に吸着している？

発表紹介　（成蹊大学　物質計測・イメージング研究室）

【LS1-WeM-6】

Satoka Aoyagi, Yuta Yokoyama, Makiko Fujii, Jiro Matsuo, John S. Fletcher, Nicholas Lockyer, John Vickerman

"The Influence of Primary Ion Beam Energy on Peptide Fragmentation by Means of ToF-SIMS Using Huge Cluster Ion Sources"

- ペプチドのフラグメント化傾向の1次イオンエネルギー及びイオン種依存性の評価

【DO1-ThA-5】

Kazuma Takahashi, Yuta Yokoyama, Satoka

"The Comparison of Matrix Effects Depending on the Combination of Polymers in a Sample for Depth Profiles Using Ar Cluster Ion Beams"

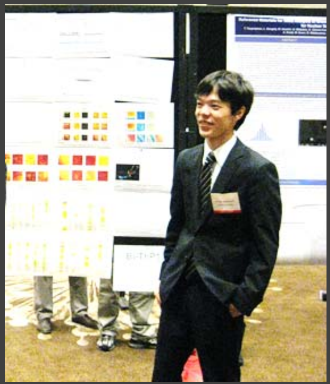
- 高分子試料の深さ方向分析における マトリックス効果の評価

発表紹介　（成蹊大学　物質計測・イメージング研究室）

【LS1-ThP-1】

Yusei Takahashi, Toshinori Shimanouchi, Yuta Yokoyama, Hideo Iwai, Satoka Aoyagi

“Evaluation of Structural Change of Amyloid Beta caused by Interaction between Amyloid Beta and Lipids”



- 3種類の脂質(DOPC, DMPC, DPPC)上でのAβの吸着状態の評価

【LS1-ThP-2】

Shusuke Nakano, Naoyuki Himi, John S. Fletcher, Sadia Sheraz née Rabbani, Nicholas Lockyer, Alex Henderson, John Vickerman, Yuta Yokoyama, Satoka Aoyagi

“The Evaluation of Biomolecular Distributions in Rat Brain Tissues by means of TOF-SIMS Using a Continuous Beam of Ar Clusters”

- ラットの脳梗塞部分に存在する生体分子のイメージング評価

SIMS XX報告

2015.11.4

(株)東レリサーチセンター
赤堀誠至

講演内容のアウトライン

3D Imaging of Complex Materials
Archeology/Environment/Forensics
Biological Imaging
Cluster Ions
Complementary Techniques and Multi-Technique Approaches
Depth Profiling/General
Depth Profiling/Inorganics
Depth Profiling/Organics
Data Processing and Interpretation
Forensics & Environment
Fundamentals
FIB-SIMS
Geology, Geo- and Cosmochemistry
Industrial Applications
Image and Data Fusion
Instrument Development
Ionization Processes
In-Situ Liquid SIMS
Life Science and Biotechnology
Medical Applications
Microelectronics
MeV-SIMS
Nanomaterials and Nanotechnology
Polymers and Molecular Films
Renewable Energy and Energy Storage
Surface & Interface Analysis
SIMS Analysis of Materials
Sample Prep & Analysis of Biological Samples
Ultra High Spatial Resolution SIMS
Tribology and Corrosion

Depth Profiling/Inorganics
FIB-SIMS
Microelectronics

TORAY

講演内容のアウトライン

発表件数推移
D-SIMS
1992 60%
2013 20%
2015 <10%?（22件?／口頭193件＋ポスター113件）

Cluster (Ion bombardment)
1992 0%
2013 70%
2015 many

TOF-SIMS, Imaging, 3-D, バイオ、環境、医薬などがほとんど
APTの発表ほほとんど見られない。

Inorganics, Microelectronics, FIB-SIMS, Depth/Inorganics

キーワードに関連するセッション：

Microelectronic関連：半日（6件）、ポスター（1件）

FIB-SIMS+MeV-SIMS関連：半日（9件）　、ポスター（3件）

Depth Profiling / Inorganic：半日（8件）、ポスター（7件）

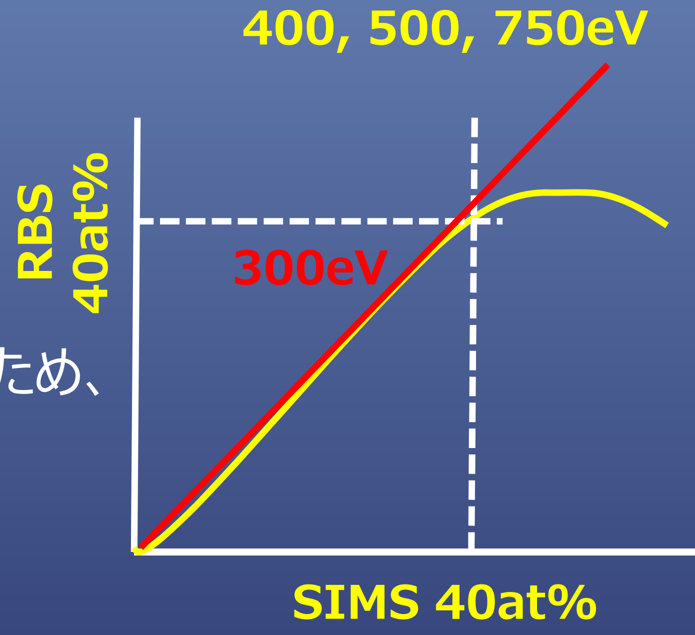
D-SIMSは、セミコンダクター、マテリアルサイエンス分野ではまだまだ需要は有るものの、装置開発、新規測定技術という意味では限界に近い？
産学で少しギャップが感じられる。

TORAY

Microelectronics

SiGe, III-V(GaN, InGaAs, InP･･･)

SiGe, III-Vにおけるドーパントの定量精度に関する報告
（イオン種、一次イオンエネルギー、入射角度など）



IBM(MI1-MoM6)
【CMOS channel用途SiGeのGe濃度、B濃度の定量分析】
サブ20nmノードのFinFETでは、Ge濃度が50at%以上に達するため、
高濃度領域でのB濃度を正確に定量する必要がある。

Ge=20-90at%のSiGe膜でCs+, O2+を用いてそれぞれ検討

40at%まではRBSの結果と一致
一次イオンエネルギー(400, 500, 750eV以上)→40at%以上の濃度でドロップ
一次イオンエネルギー(300eV)→一致

50at%以上のGe、Bを定量する際は、300eV以下の一次イオンエネルギーが有効
→酸素のretentionが起きているのでは？SiGeOの生成によるイオン化率の変化？

TORAY

Microelectronics

IBM（DI1+TuA1）7nm FinFET SiGe試作チップを作製

SIMSに求められているもの･･･高信頼性（精度、繰り返し再現性）
ただし、検出できる原子の絶対数が限りなく少なくなっているため、
SIMSの良さ（検出下限、深さ分解能、定量精度、繰り返し再現性）が
失われつつある（発揮しにくい）。→TEM, APTに期待

アトムプローブの問題点･･･
・（針状）の試料加工が難しい→TEM試料より加工難？
・分析深さの制限→試料形状から、数十nm～100nm程度？
・定量精度

SIMSでできること･･･
FIB-(TOF)-SIMSを用いた深さ方向のイメージング
（FIB+）Nano-SIMSを用いた深さ方向プロファイル

Microelectronics

NPL (National Physical Laboratory, UK)

ION-TOF, Thermo
→3D nanoSIMS project (Hybrid SIMS Instrument)

このような取り組みをD-SIMSでもしていかなければ、今後の発展は望めない
（感度、分解能向上への取り組み→新たな情報、知見）

TORAY

Depth Profiling / General

● CAMECA(DG1-ThM4)
IMS-7f Autoの紹介
6ホルダー導入予備室
繰り返し再現性

軽元素のバックグラウンド
低減

- **Light elements analyses** performed on Si float-zone samples:
  - Cs^+ 15keV high impact energy for high sputter rate (22nm/sec)
  - Optimized vacuum in the analysis chamber (<5 E-10 mbar)
  - Measured species: H^-, C^-, O^-, SiN^-
- **After an overnight pump-down in the storage chamber** for sample outgassing, results showed that optimized detection limits for H, C, N and O were obtained without further pump-down time in the analytical chamber. **Analyses can be started immediately after loading the sample from storage to analytical chamber.**
- **Bulk detection limits (DL)** obtained in Si are :

Element	H	C	N	O
Detection Limit (at/cm^3)	3.0 E16	1.1 E16	1.9 E15	2.0 E16

H, C, O limited by vacuum,
N limited by ionization.
LN2 cryo-trap on.

- **Throughput:**
  - After overnight outgassing, up to 24 samples can be analyzed the same day (6 holders x 4 samples)
  - **Total duration of ~7 hours for 48 depth profiles** (2 runs per sample, 24 samples, 8 min per analysis, and 3 min per holder exchange).
- **Conclusion: excellent Throughput together with excellent DLs** (not accessible by other techniques)

ちなみに
弊社の7fでは、

Element	H	C	N	O
Detection limit (atoms/cm^3)	1E17	**1-5E15**	**1-5E14**	1-5E16

TORAY

Depth Profiling/Inorganics

● NIST (DI1-TuA8)
Creating Depth Profile Standards for Inorganic Materials Using Inkjet Deposition, Joe Bennett (NIST)

標準試料の新しい作り方（新材料）
新材料では、イオン注入するためのターゲット材料を探すのが難しいため、
イオン注入ではなく、インクジェット方式を採用。

Si, SiO2, GaAs, Cu材料でイオン注入、インクジェット方式でRSFを算出
Siはどちらもほぼ同じRSF
SiO2は20回滴下時にばらつきが最も少ない
GaAsは10回滴下時にばらつき少ないが、イオン注入のRSFと10倍近く変化
Cuはイオン注入のRSFと約30倍変化

表面状態、表面反応なのかはまだわかっていない。

TORAY

FIB-SIMS（FIB-TOF-SIMS）

TEM、SEM(EPMA)では検出できない（二次元、三次元）元素分布情報
表面ラフネス、ノックオンの影響が少ない（深さ分解能の低下を回避できる）
通常のD-SIMSでは分析が困難な極深のデプスプロファイル

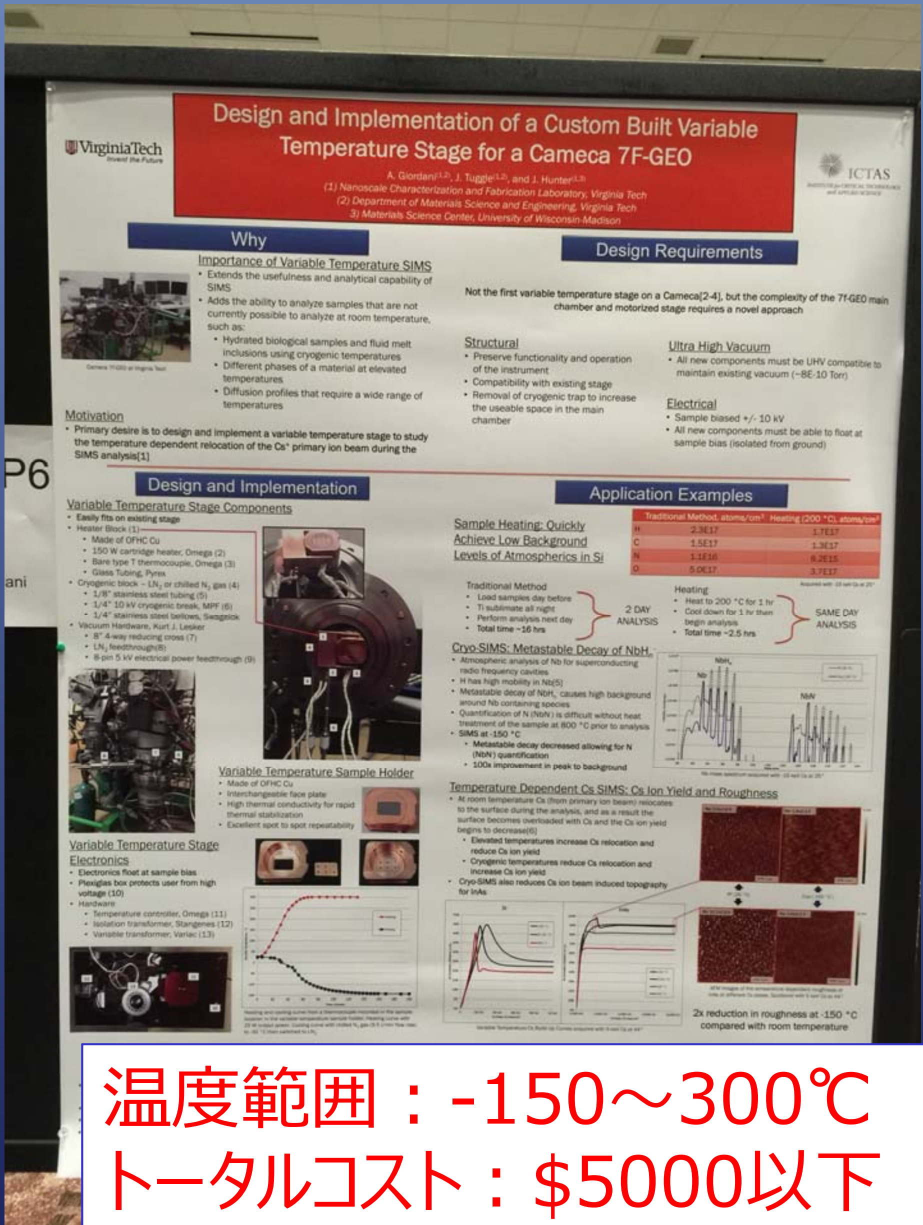
リチウムイオン電池、固体酸化物型燃料電池（SOFC）、シリコン貫通ビア（TSV）等の縦（深さ）方向に比較的深い（～数十μm）元素情報が必要な材料が対象
（3件がION-TOF TOF.SIMS 5へFIBを取り付けた装置で分析→in-situで分析可能）

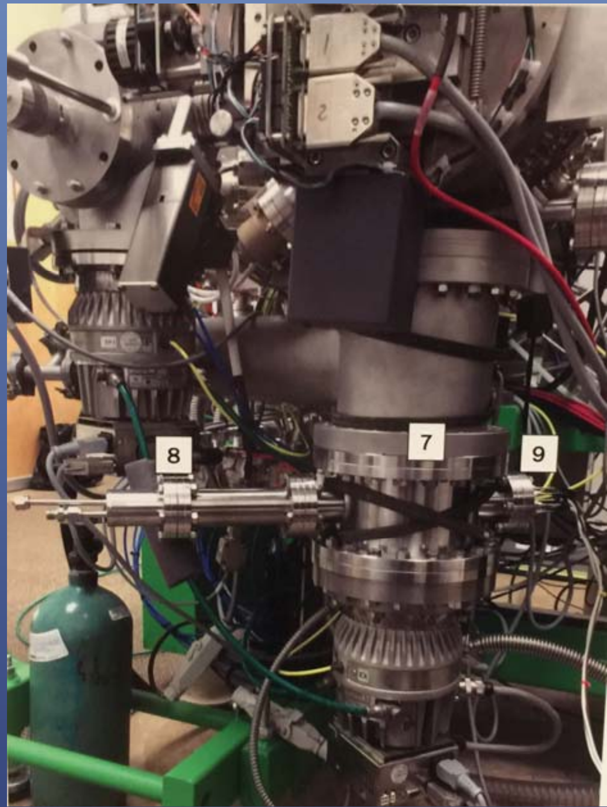
【FS1+MS1+MoA4】
●リチウムイオン電池の充放電時における、脱Li・充LiしたときのSi構造の変化
【FS1+MS1+MoA5】
●SOFCインターコネクタ（Crofer 22 APUステンレス鋼）の表面酸化状態や酸素拡散評価
【FS1+MS1+MoA1】
●**Plasma-FIB**を併用したTSV (Through Silicon Via)の解析

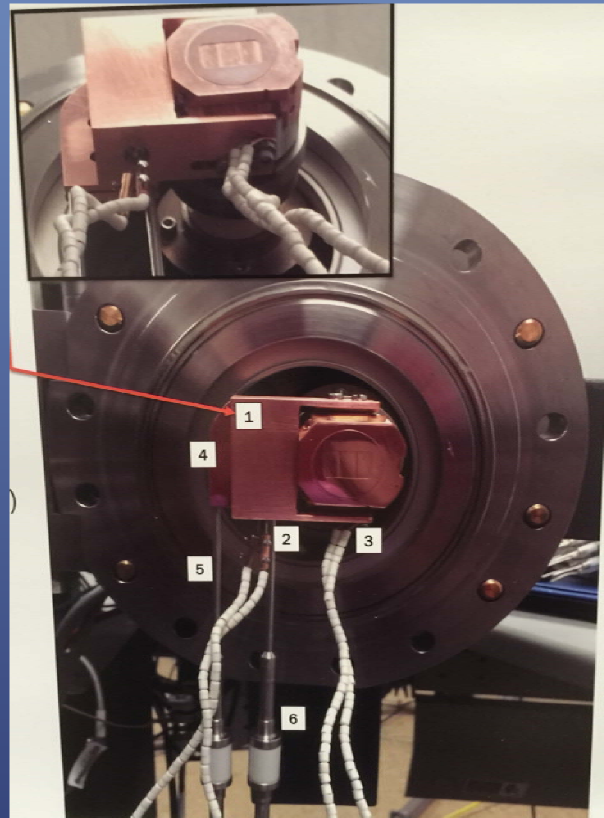
アスペクト比8:1（Full depth of TSV image (4days 40GB)）

パワーデバイス（IGBT、SiC、GaN etc.）へ応用可能？

Instruments/Poster session







温度範囲：-150～300℃
トータルコスト：$5000以下

TORAY

Application Examples

Sample Heating: Quickly Achieve Low Background Levels of Atmospherics in Si

	Traditional Method, atoms/cm^3	Heating (200 °C), atoms/cm^3
H	2.3E17	1.7E17
C	1.5E17	1.3E17
N	1.1E16	8.2E15
O	5.0E17	3.7E17

Acquired with -15 keV Cs at 25°

Traditional Method
- Load samples day before
- Ti sublimate all night
- Perform analysis next day
- Total time ~16 hrs

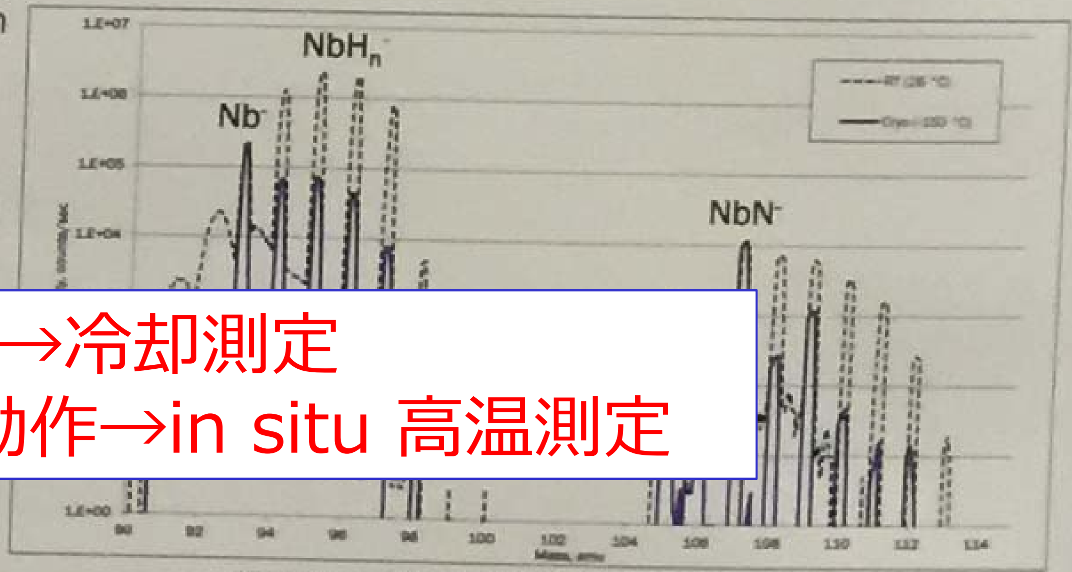
2 DAY ANALYSIS

Heating
- Heat to 200 °C for 1 hr
- Cool down for 1 hr then begin analysis
- Total time ~2.5 hrs

SAME DAY ANALYSIS

Cryo-SIMS: Metastable Decay of NbH_n^-

- Atmospheric analysis of Nb for superconducting radio frequency cavities
- H has high mobility in Nb[5]
- Metastable decay of NbH_n^- causes high background around Nb containing species
- Qu… tre…
- SIM…
  - … (NbN^-) quantification
  - 100x improvement in peak to background

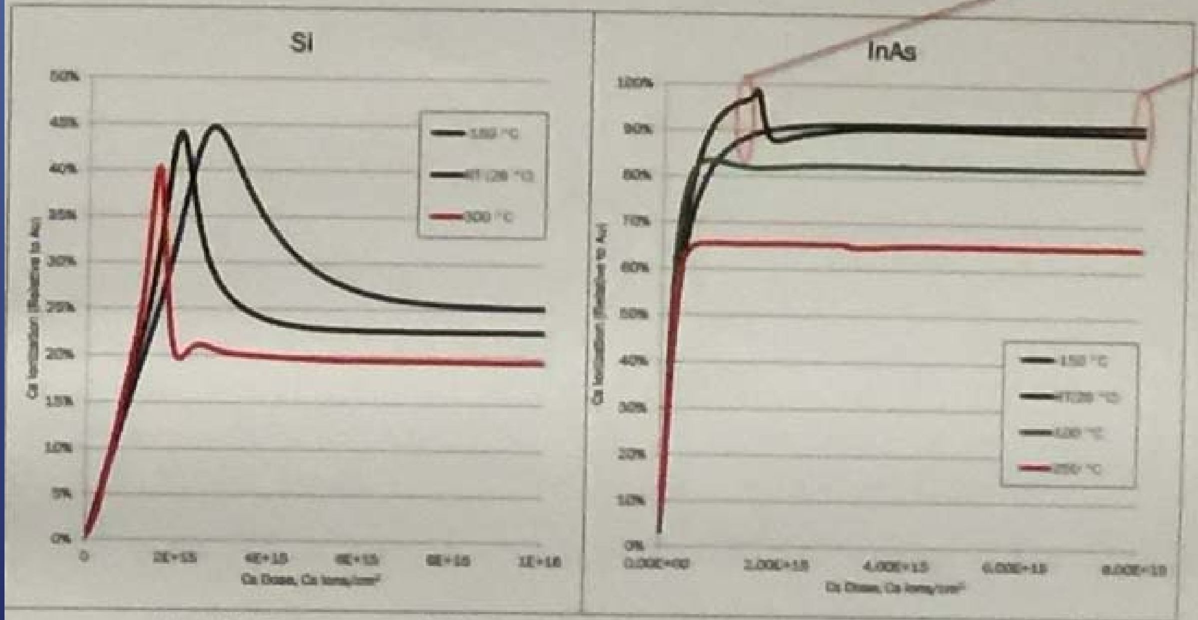


Nb mass spectrum acquired with -15 keV Cs at 25°

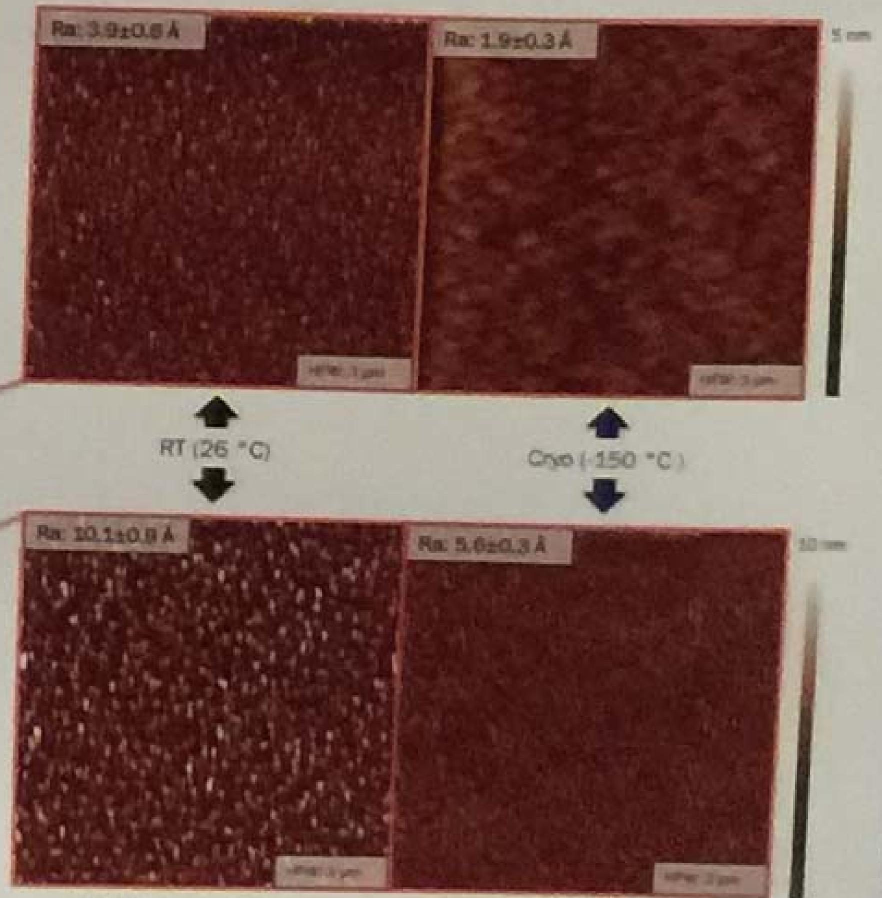
金属中の水素→移動しやすい→冷却測定
高耐圧素子（SiC）→高温動作→in situ 高温測定

Temperature Dependent Cs SIMS: Cs Ion Yield and Roughness

- At room temperature Cs (from primary ion beam) relocates to the surface during the analysis, and as a result the surface becomes overloaded with Cs and the Cs ion yield begins to decrease[6]
  - Elevated temperatures increase Cs relocation and reduce Cs ion yield
  - Cryogenic temperatures reduce Cs relocation and increase Cs ion yield
- Cryo-SIMS also reduces Cs ion beam induced topography for InAs



Variable Temperature Cs Build Up Curves acquired with 5 keV Cs at 44°



AFM images of the temperature dependent roughness of InAs at different Cs doses. Sputtered with 5 keV Cs at 44°

2x reduction in roughness at -150 °C compared with room temperature

全体を通じて

D-SIMS・・・
発表件数を見ても明らかで、下火傾向
SIMS（イオンスパッタリング）における現象に関する発表は少数
アプリケーションに関する発表がほとんど

TOF-SIMS、FIBを組み合わせたD-SIMS・・・
今後の展開に大いに期待できる
深さ分解能、空間分解能、イメージングといった点では魅力的だが、
検出感度（下限）をどうやってD-SIMSに近づけていくか？
データ容量の増大、転送、演算、処理等のPCの能力も今後は課題

TORAY

Innovation by Chemistry

2015.11.4
SIMS研究会（SIMSXX報告会）

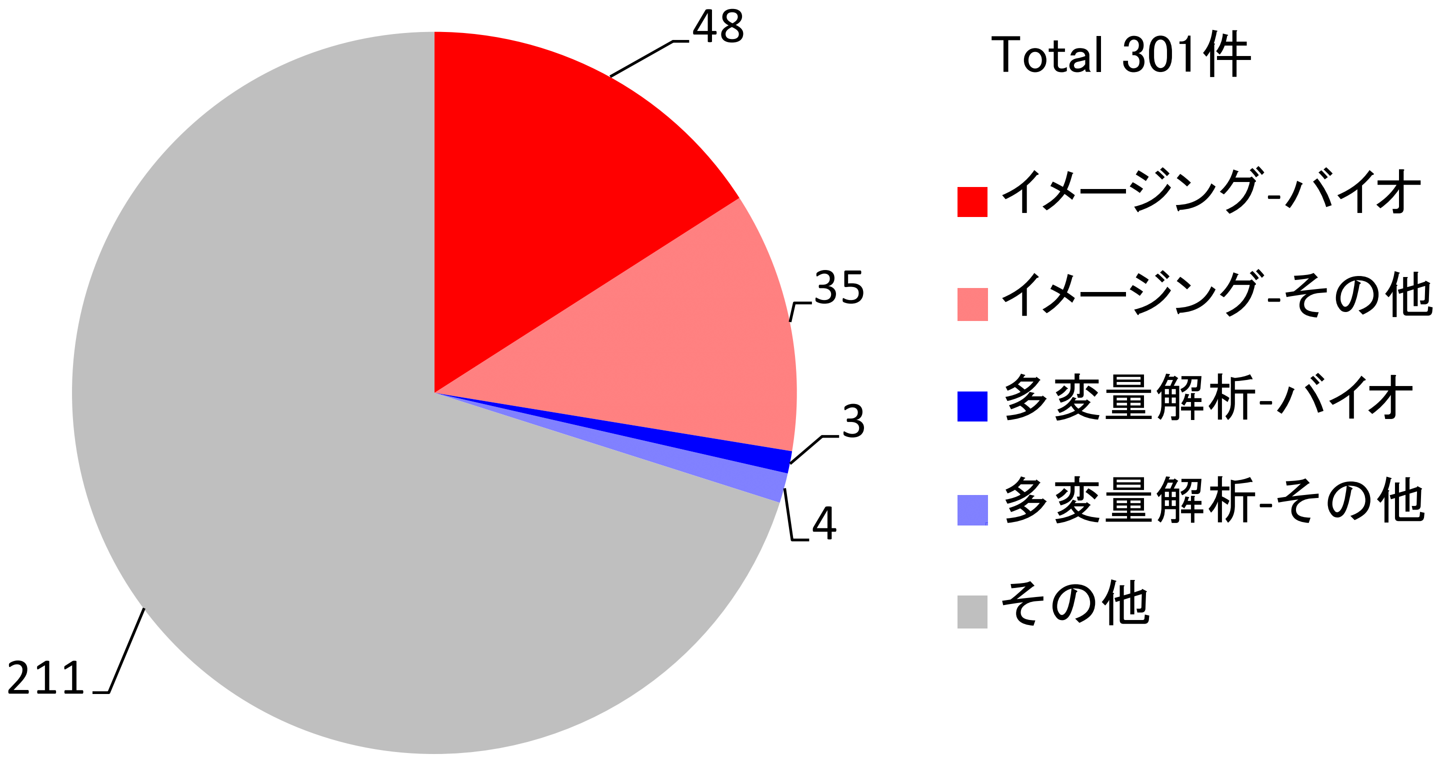
④Imaging, Data processing 3D, Data processing

→ イメージング
多変量解析

旭硝子(株) 小林大介

SIMSXXにおけるイメージング・多変量解析の件数

タイトルからキーワード検索
イメージング： Imaging, FIB/TOF-SIMS, 2D, 3D, nanoSIMS
多変量解析： Chemometrics, PCA



所感： SIMSのイメージング能力に大きな期待が寄せられている（特にバイオ関係）。

トピックス

1. イメージング

   ① Data Fusion

   ② 同位体マーキング法

   ③ TOF-MS/MS

   ④ その他

2. 多変量解析

トピックス

1. イメージング

① Data Fusion

② 同位体マーキング法

③ TOF-MS/MS

④ その他

2. 多変量解析

①Data Fusion

3D1+ID1-MoA7
Mass Spectrometry Image Fusion: What Works and What Doesn't
Bonnie J. Tyler, National Physical Laboratory, UK.

3D1+ID1-MoA9
The Benefits and Pitfalls of Image Fusion
Alex Henderson, University of Manchester, UK.

3D1+ID1-MoA10
Combining XPS Atomic Concentration Data with a ToF-SIMS Chemical Image Map using Image and Data Fusion
Tammy Milillo, University at Buffalo, USA.

3D1+ID1-MoA11
Exploring New Source of High Resolution Data for Image Fusion
Jay G. Tarolli, Penn State University, USA.

①Data Fusion

Data Fusion:
画像融合により化学情報を有する高空間分解能のマッピング像を得ること

化学情報
（例：TOF−SIMS）

＋

形状情報
（例：SEM）

＝

問題点:
・データサイズが大きくなること
・画像をマッチングさせる必要があること

など・・・

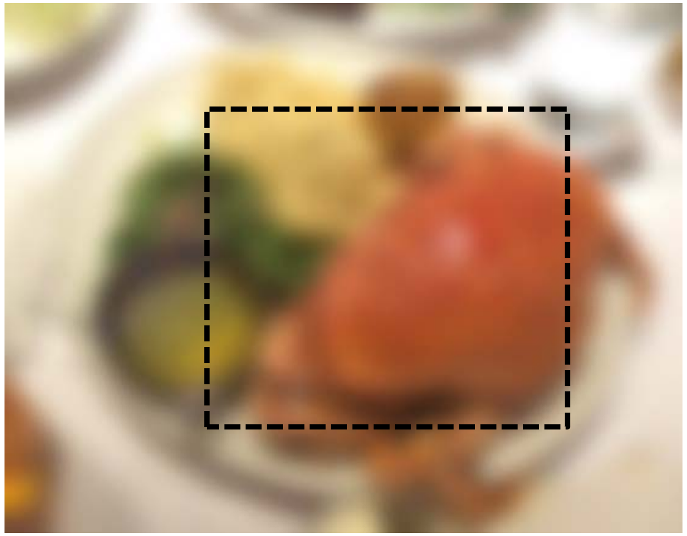
①Data Fusion

3D1+ID1-MoA11

Exploring New Source of High Resolution Data for Image Fusion

Jay G. Tarolli, Penn State University, USA.

化学情報



＋

形状情報

＝

化学情報と形状情報のエリアを人為的にマッチング

※本内容についてはBiointerphasesへ投稿予定とのこと。

SIA, **46** (2014) 217-220.

J. Am. Soc. Mass Spectrom. **25** (2014) 2154-2162.

②同位体マーキング法

<u>SR1-ThM4</u>

High-Resolution Imaging of the Distributions of Cholesterol and Sphingolipids in Cellular Membranes

Mary Kraft, University of Illinois, USA.

＜背景＞

スフィンゴ脂質の面内分布は、生物活性のシグナル分子の代謝に関係する。これまで、分布分析が困難とされてきた。同位体マーキング法で解決を図る。

＜実験＞

18O-コレステロールと15N-スフィンゴ脂質を細胞中に培養で組み込む。

⇒強度エンハンス効果を狙ってイリジウム薄膜2nmをコート。

⇒CAMECA NanoSIMS 50にて観察。

＜結論＞

スフィンゴ脂質は細胞膜中でドメインを有するが、コレステロールは分布を持たない。

＜参考文献＞

J Biol Chem **2013**, 288, 16855-16861

PNAS **2013**, 110, E613-E622

③TOF-MS/MS

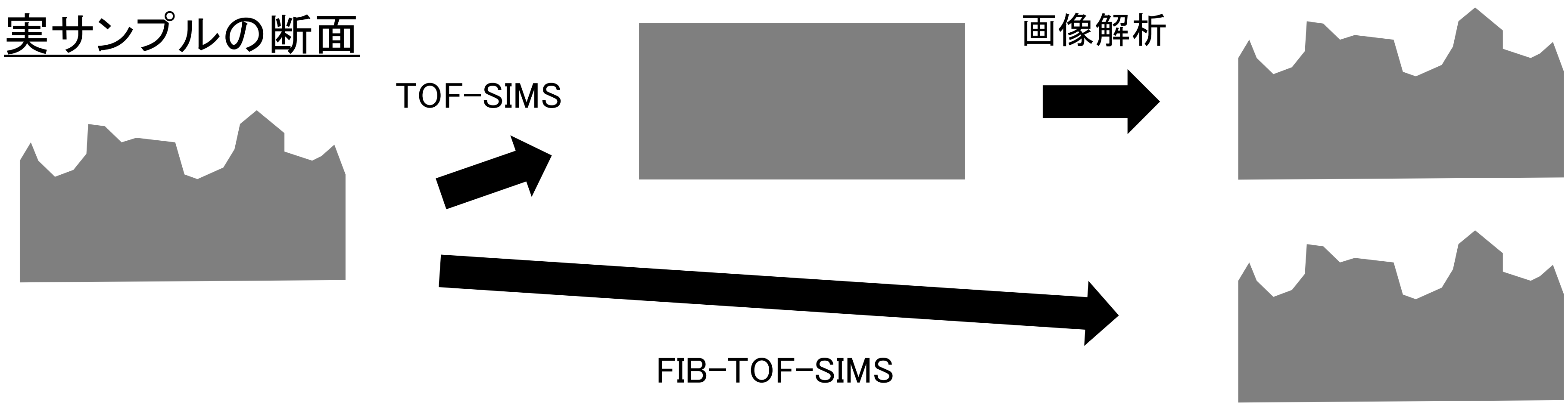
<u>PM1-WeM6</u>
TOF-SIMS Imaging MS/MS of Polymer Additives
John Hammond, Physical Electronics, USA.

＜概要＞
加熱により生成するPET表面の析出物を分析している。質量干渉フリーなMS1とMS2のパラレルイメージング機能を搭載しており、MS2ではバックグラウンドの低いイメージ像の取得が可能である。

④その他

<u>CT1-MoM1</u>
SIMS Based Correlative Microscopy for High Resolution Multi-technique Analysis
David Dowsett, Luxembourg Institute of Science and Technology, Luxembourg.

TOF-SIMSと画像解析の合わせ技



FIB-TOF-SIMSによる直接観察

例えば・・・
<u>FS1+MS1-MoA3</u>
Comparison of Conventional Dual Beam SIMS Depth Profiling with FIB/SIMS Cross Section Analysis
Felix Kollmer, ION-TOF GmbH, Germany.

トピックス

1. イメージング

① Data Fusion

② 同位体マーキング法

③ TOF-MS/MS

④ その他

2. 多変量解析

⇒解析例を4つ紹介

解析例1

<u>AE-TuP2</u>

Evaluation of TOF-SIMS with PCA to Identify Pigments in Artist's Paints in Post War Art

Naoko Sano, National EPSRC XPS Users' Service, UK.

＜背景＞

合成塗料には多くの顔料(pigment)が含有。

顔料を特定するには分子構造情報の入手が鍵。

しかしながら、顔料の化学式はとても類似している。。。

＜実験＞

作品のピンクフレーク（1点）と既知のフレーク（5点）を用いてTOF-SIMS分析およびPCA解析をトライ。

＜結論＞

・TOF-SIMSスペクトルのPCA解析結果から既知のフレーク（5点）を分別。

・PC1, PC2は分子情報に由来すると推察。

・作品のフレークは、PV19-4R and/or PR122に近いと推定。

解析例2, 3

BI-ThP1

Evaluation of Structual Change of Amyloid Beta caused by Interaction between Amyloid Beta and Lipids

Yusei Takahashi, Seikei University, Japan.

異なる脂質膜上でのペプチドの吸着状態の違いの評価に、PCAを利用。PCA得点イメージから、吸着状態を考察し、さらに比較対象の主成分の負荷量から、注目する吸着状態に起因する二次イオンピーク(フラグメントイオン)を見つけた。

BI-ThP2

The Evaluation of Biomolecular Distributions in Rat Brain Tissues by means of TOF-SIMS Using a Continuous Beam of Ar Clusters

Shusuke Nakano, Seikei University, Japan

動物組織イメージの解析にPCAを利用。ピークの自動検索ができないので、測定の全チャネル (0.05 u刻みで19405個)を対象にして主成分分析した。PCA得点イメージから、対象部位を表す主成分を見つけて、その負荷量から、特徴的なピークを見つけた。そのおかげで、やみくもに数千のピークを調べずに必要なイメージを得ることができた。

解析例4

DO1-ThA5

The comparison of matrix effects depending on the combination of polymers in a sample for depth profiles using Ar cluster ion beams

Kazuma Takahashi, Seikei University, Japan

各高分子の特徴的な二次イオンがあらかじめ分からない場合、PCAやMCRによって特徴的なピークを見つけることができた。影響が複雑な高分子の組み合わせ（もう一方の高分子の影響を受けていない二次イオンがほとんどないような場合）ではMCRの方が有効な場合が多かった。

謝辞

ご協力ありがとうございました。

アルバック・ファイ(株)　宮山卓也　様
成蹊大学　青柳里果　先生

SIMSXX報告会　20151104@東京理科大

Organics

Cluster ions, Polymers and Molecular Films, Depth/Organics

京都大学大学院工学研究科
附属量子理工学教育研究センター
日本学術振興会特別研究員
藤井 麻樹子

セッション分けと発表件数

		Plenary	Oral	Poster	計
3D+ID	3D Imaging of Complex Materials + Image and Data Infusion	0	8	4	12
AE	Archeology/Environment/Forensics	0	0	6	6
BI	Biological Imaging	0	19	12	31
CI	Cluster Ions	0	10	7	17
CT	Complementary Techniques and Multi-Technique Approaches	0	16	12	28
DG	Depth Profiling/General	0	9	0	9
DI	Depth Profiling/Inorganics	0	9	8	17
DO	Depth Profiling/Organics	0	10	4	14
DP	Data Processing and Interpretation	0	9	5	14
FE	Forensics & Environment	0	8	0	8
FN	Funfamentals	0	6	7	13
FS+MS	FIB-SIMS + MeV-SIMS	0	9	7	16
GC	Geology, Geo- and Cosmochemistry	0	0	3	3
IA	Industrial Applications	0	0	3	3
IN	Instrument Development	0	7	3	10
IP	Ionization Processes	0	0	3	3
IS	In-Situ Liquid SIMS	0	8	3	11
LS	Life Science and Biotechnology	0	8	6	14
MA	Medical Applications	0	0	1	1
MI	Microelectronics	0	7	1	8
NN	Nanomaterials and Nanotechnology	0	9	3	12
PM	Polymers and Molecular Films	0	9	3	12
PS	Plenary Session	2	0	0	2
RE	Renewable Energy and Energy Strage	0	0	1	1
SI	Surface & Interface Analysis	0	6	0	6
SM	SIMS analysis of Materials	0	10	0	10
SP	Sample Prep & Analysis of Biological Samples	0	6	9	15
SR	Ultra High Spatial Resolution SIMS	0	4	1	5
TC	Tribology and Corrosion	0	0	1	1
計		2	187	113	302

SIMSXIXとの比較

Topics

Topic	Oral	Poster	Invited	Total
Fundamentals on Sputtering and Ionization Mechanisms	12	11	3	26
Cluster Sputtering	7	9	1	17
Biomedical Application (Cell)	4	34		54
Biomedical Application (General)	8		1	
Biomedical Application (Tissue)	5		2	
Depth Profiling (Inorganics)	7	17	1	25
Depth Profiling (Organics)	14	9	1	24
Data Processing (Imaging)	4	4	1	14
Data Processing (General)	4		1	
Ultra High Spatial Resolution SIMS	6	3	3	12
Semiconductor / Display	3	8	1	12
USJ Depth	1	1	2	4
Polymers and Molecular Surfaces	7	9	2	18
Instrumentation	7	8	3	18
Art / Archeology / Forensics	2	2	2	6
Geochemistry and Cosmochemisty	9	4	2	15
Energy / Nano-material	5	7		12
Complementary MALDI Imaging	3	5	1	9
Atom Probe	4		1	5
Combination of SIMS with other characterization techniques	14	14	1	29
Vickerman	2		1	3
Total	128	145	30	303

Oral
158 (SIMSXIX)
↓
189 (SIMSXX)

Poster
145 (SIMSXIX)
↓
113 (SIMSXX)

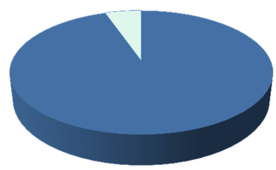
Total
303 (SIMSXIX)
↓
302 (SIMSXX)

日本からの発表数

		Plenary	Oral	Poster	計
3D+ID	3D Imaging of Complex Materials + Image and Data Infusion	0	0	1	1
AE	Archeology/Environment/Forensics	0	0	0	0
BI	Biological Imaging	0	0	3	3
CI	Cluster Ions	0	2	1	3
CT	Complementary Techniques and Multi-Technique Approaches	0	0	0	0
DG	Depth Profiling/General	0	0	0	0
DI	Depth Profiling/Inorganics	0	0	2	2
DO	Depth Profiling/Organics	0	2	1	3
DP	Data Processing and Interpretation	0	0	0	0
FE	Forensics & Environment	0	0	0	0
FN	Funfamentals	0	0	2	2
FS+MS	FIB-SIMS + MeV-SIMS	0	1	0	1
GC	Geology, Geo- and Cosmochemistry	0	0	0	0
IA	Industrial Applications	0	0	0	0
IN	Instrument Development	0	3	0	3
IP	Ionization Processes	0	0	0	0
IS	In-Situ Liquid SIMS	0	0	0	0
LS	Life Science and Biotechnology	0	2	0	2
MA	Medical Applications	0	0	0	0
MI	Microelectronics	0	0	0	0
NN	Nanomaterials and Nanotechnology	0	0	0	0
PM	Polymers and Molecular Films	0	0	1	1
PS	Plenary Session	1	0	0	1
RE	Renewable Energy and Energy Strage	0	0	0	0
SI	Surface & Interface Analysis	0	0	0	0
SM	SIMS analysis of Materials	0	0	0	0
SP	Sample Prep & Analysis of Biological Samples	0	0	1	1
SR	Ultra High Spatial Resolution SIMS	0	0	0	0
TC	Tribology and Corrosion	0	0	0	0
計		1	10	12	23

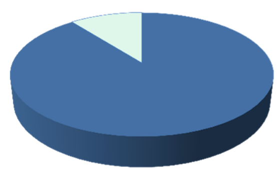
全Oral発表に占める
日本からの発表

5.3%



全Poster発表に占め
る日本からの発表

11%



SIMSXIXとの比較

Abstracts

Country	Oral	Poster	Total
Korea	16	39	55
Japan	21	23	44
China	6	3	9
Taiwan	3	5	8
Hong Kong	1	1	2
Singapore	1		1
United States	34	20	54
Australia	1		1
Austria	1		1
Belgium	10	6	16
Czech		1	1
France	14	8	22
Germany	18	10	28
Italy	4	3	7
Luxembourg	5	4	9
Netherlands	1	1	2
Poland	5		5
Russia		1	1
Slovenia		2	2
Sweden	11	9	20
Switzerland	3	1	4
United Kingdom	14	6	20
Uzbekistan		2	2
Total	169	145	314

日本からの発表
44 (SIMSXIX)
↓
23 (SIMSXX)

SIMS XXI

Important dates (tentative)

- Abstract submission deadline April 30, 2017
- Abstract acceptance notification June, 2017
- Early registration deadline July, 2017
- Hotel reservation deadline July, 2017
- Paper submission deadline October 30, 2017

http://sims.confer.uj.edu.pl/index.php

Cluster Ion

Oral 10件，Poster 7件

Cluster Ion

- Derk Rading (ION-TOF GmbH, Germany)
- Wilfred Vandervorst (IMEC, Belgium)

酸素クラスタービームを用いた無機膜の深さ方向分析・表面分析

- Makiko Fujii (Kyoto Univ., Japan)

アルゴンクラスタービームによる生体分析・有機分子クラスターエミッション

- Hubert Gnaser (Univ. of Kaiserslautern, Germany)
- Anders Barlow (NEXUS, UK)

アルゴンクラスタービームによるスパッタ率の半経験的予測モデル

- Jitao Zhang (Arizona State Univ., USA)

MCIにおけるマトリクス効果

- Nicholas Lockyer (Univ. of Manchester, UK)
- Kosuke Moritani (Univ. of Hyogo, Japan)

水・メタノール・メタン、複合クラスターによるイオン収率

- Michael Dürr, (Justus Liebig Univ. Giessen, Germany)

中性クラスターによる表面吸着分子の分析

- Paula Clark (Tascon USA, USA)

市販のコンタクトレンズの表面分析と深さ分析

Depth Profiling (Organic)

Oral 10件，Poster 4件

Depth Profiling (Organic)

Morgan Alexander (The Univ. of Nottingham, UK) Frozen Hydrated Hydrogelsの分析

Tanguy Terlier (CEA-Leti, France) CsとC_{60}とAr-GCIBの比較

Kan Shen (The Pennsylvania State Univ., USA) C_{60}とAr-GCIBの比較

Rasmus Havelund (National Physical Laboratory, UK) Ar-GCIBエッチングにおける入射角・試料温度・組成の影響

Kazuma Takahashi (Seikei Univ., Japan) 試料組成によるマトリクス効果の比較

Lars Breuer (The Pennsylvania State Univ., USA) レーザーポストイオン化によるマトリクス効果の低減

Michael Clark, Jr. (The Dow Chemical Company, South Korea) フォトレジスト中の添加剤の分析

Supriya Surana (IMEC & KU Leuven, Belgium) Organic BHJ の分析

Jakub Rysz (Jagiellonian Univ. Poland) Organic BHJ の分析

Kazutaka Ishikawa (Kao Corporation, Japan) 毛髪表面の分析

Polymers and Molecular Films

Oral 9件，Poster 3件

Polymers and Molecular Films

- Vanina Cristaudo (Univ. catholique de Louvain, Belgium) プラズマ処理したPolyethylene
- Jean-Paul Barnes (CEA-Leti, France) iCVD法を用いたMethacrylate
- Heng-Yong Nie (The Univ. of Western Ontario, Canada) $C_{2n}H^-$イオンを用いた架橋構造の解析
- Fan Yang (Texas A&M Univ. USA) Au_{400}^+ビームを用いたナノドメインの分析
- John Hammond (Physical Electronics, USA) MS/MSを用いたポリマー添加剤の分析
- Lu-Tao Weng (The Hong Kong Univ. of Sci. & Tech., Hong Kong)
- Andreas Pelster, Univ. of Münster, Germany) SIMSとLaser-SNMSを用いた2D, 3D分析
- Wenjing Xie (The Hong Kong Univ. of Sci. & Tech., Hong Kong) グラフェンとグラファイト
- Laetitia Bernard (Swiss Federal Laboratories of Material Sci. & Tech., Switzerland) 自己組織化単分子膜

Cluster Ion

- Derk Rading (ION-TOF GmbH, Germany)
- Wilfred Vandervorst (IMEC, Belgium)
- Makiko Fujii (Kyoto Univ., Japan)
- Hubert Gnaser (Univ. of Kaiserslautern, Germany)
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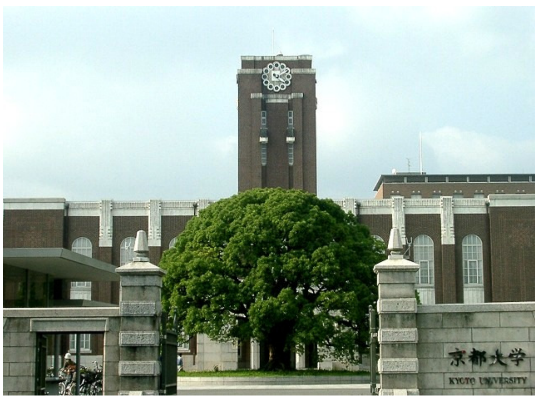
- Kosuke Moritani (Univ. of Hyogo, Japan)
- Michael Dürr, (Justus Liebig Univ. Giessen, Germany)
- Paula Clark (Tascon USA, USA)

Molecular cluster emission in sputtering of amino acids by argon gas-cluster ions

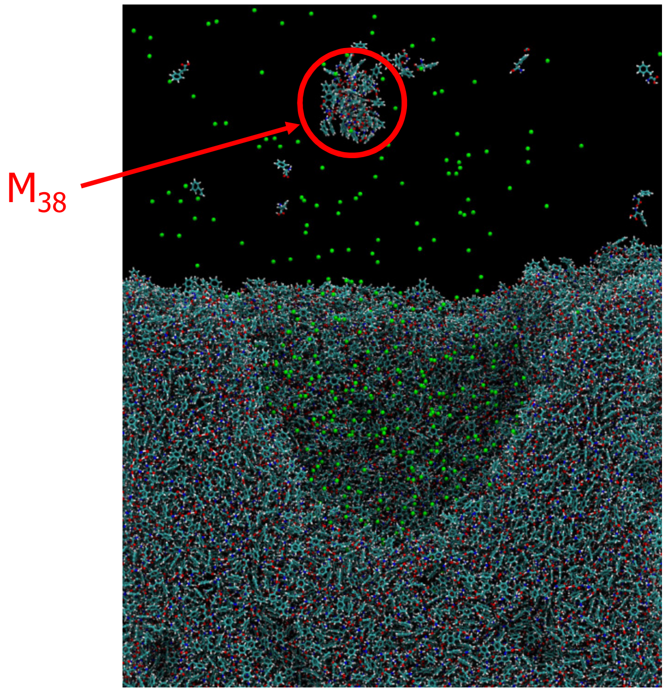
Hubert Gnaser, Masakazu Kusakari, Makiko Fujii, Toshio Seki, Takaaki Aoki, Jiro Matsuo

Quantum Science and Engineering Center, Kyoto University, Kyoto, Japan
Department of Physics, University of Kaiserslautern, Germany



Cluster emission from phenylalanine

Emission of phenylalanine cluster



MD simulation:

10 keV Ar_{1000} (green)

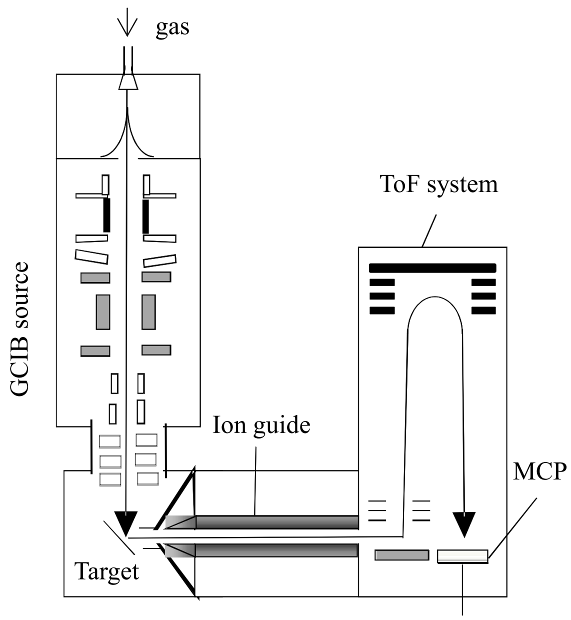
→ phenylalanine

(21.5 ps after impact)

Mücksch et al, J Phys Chem C 118, 7962 (2014)

Orthogonal TOF-SIMS with gas-cluster ion source

Kyoto University



Instrument:

- Gas-cluster ion source
  - Ar_n^+ cluster size: n = ~ 1500
  - Ar_n^+ cluster energy: 10 keV
  - Fluence: 1×10^{13} cm^{-2}
- Quadrupole ion guide (Cooling of ions)
- Positive SIMS with orthogonal TOF

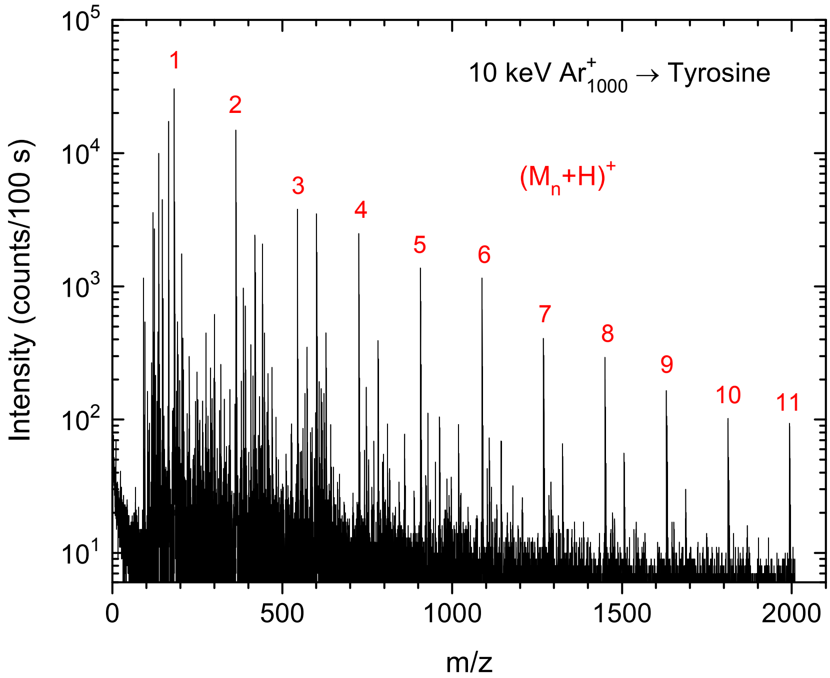
Samples: Deposits on Si wafers

- 10 pure amino acids
  Ala, Arg, Asn, Gln, Glu, Ile, Leu, Phe, Thr, Tyr
- 3 mixed amino acids (1:1)
  Phe-Arg, Phe-Tyr, Arg-Tyr

Matsuo et al, Appl Phys Exp 7, 056602 (2014)

Cluster emission from pure amino acids

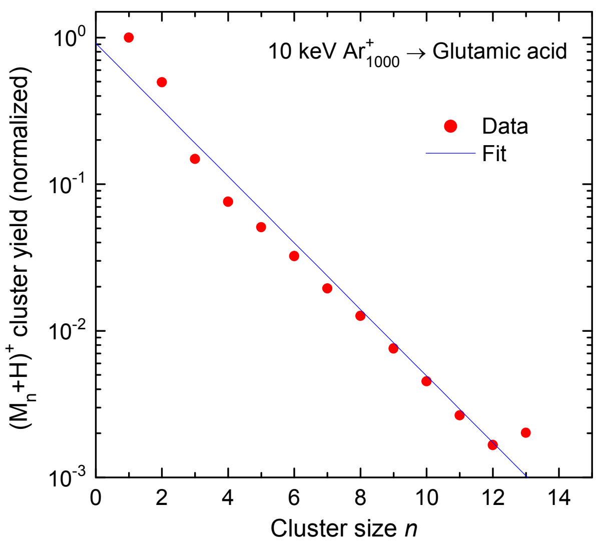
Mass spectrum of tyrosine cluster

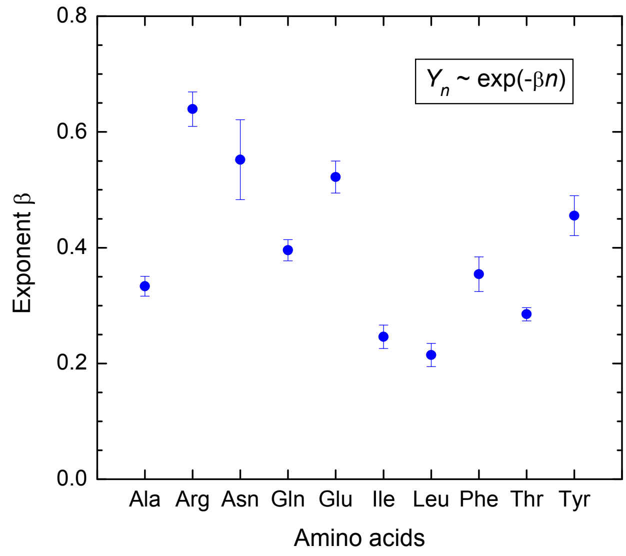


Kusakari et al, Int J Mass Spectr 383-384, 31 (2015)

Cluster emission from pure amino acids

Cluster yield vs cluster size *n*



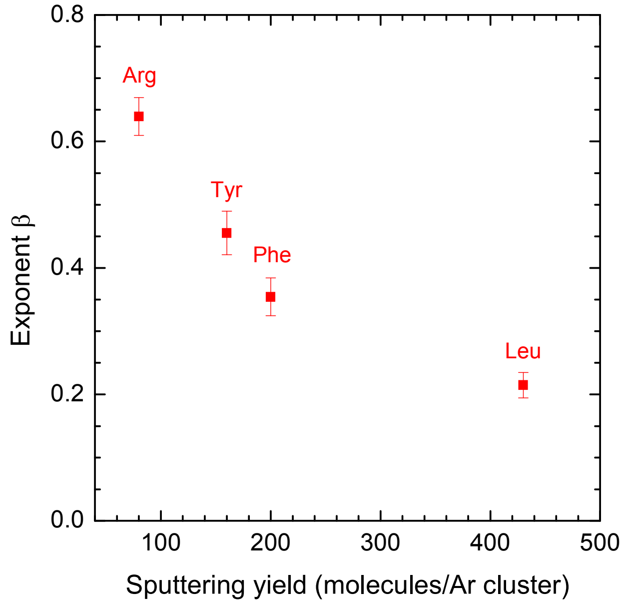


$$Y_n \propto \exp(-\beta n)$$

Kusakari et al, Int J Mass Spectr 383-384, 31 (2015)

Cluster emission from pure amino acids

Exponent vs sputtering yield

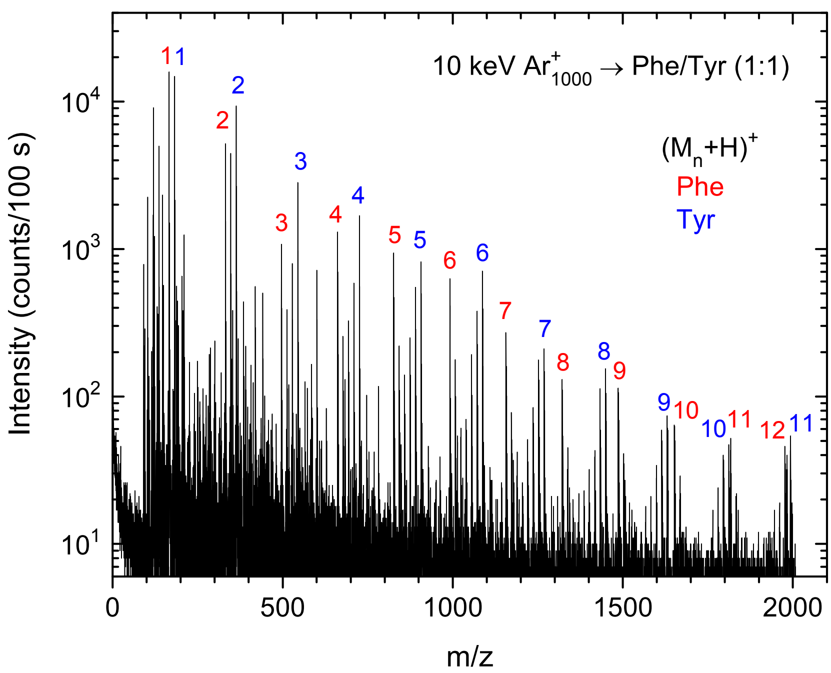


$Y_n \propto \exp(-\beta n)$

Kusakari et al, Int J Mass Spectr 383-384, 31 (2015)

Cluster emission from mixed amino acids

Mass spectrum of mixture Phe-Tyr

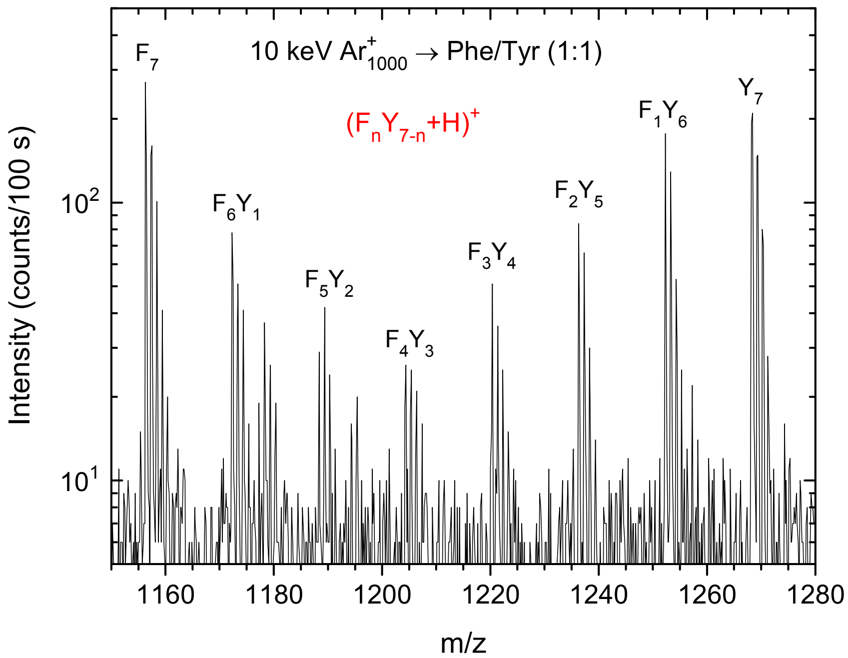


Homo- and heteromolecular cluster ions

Kusakari et al, Int J Mass Spectr 383-384, 31 (2015)

Cluster emission from mixed amino acids

Mass spectrum of mixture Phe-Tyr



Homo- and heteromolecular cluster ions

Mixture is inhomogeneous

Kusakari et al, Int J Mass Spectr 383-384, 31 (2015)

Summary

- Emission of molecular ion $(M+H)^+$ from all (20) amino acids:
  Little fragmentation, if E/n not too high
- Abundant cluster emission $(M_n+H)^+$ from (10) amino acids
- Cluster abundances depend on sputtering yields
- Spectra of mixed samples:
  Inhomogeneous compositions from mixed cluster
- Similar spectra from isoleucine & leucine:
  Doubly-charged cluster ions

個人的な印象

■ イオンビームだけでなく新しい質量分析器の採用

オービトラップ・直交加速型**TOF**・**MS/MS**など

■ 有機物試料におけるマトリクス効果に着目

２相系の基礎検討が主体

■ 相補的分析手法についての調査検討

MALDI-MS, APT, XPS, LA-ICP-MS, UHPLC-ESI-MS …

表面科学会@つくば

2015年12月3日（木）

「表面分析・評価技術」（13:00～16:00）

福満仁志（住化分析センター）：GCIB およびXAS を用いたIr(ppy)$_3$:TPBi 混合薄膜の深さ方向評価,

藤井麻樹子（京都大）：クラスターSIMS 法を用いた生体試料分析の現状と課題,

松尾二郎（京都大院工学）：クラスターSIMS 法による生体分子の高空間分解能イメージング,

青柳里果（成蹊大理工）：ToF-SIMS の低エネルギー一次イオンビームによる ペプチドフラグメントイオン生成評価,

高橋一真（成蹊大理工）：高分子混合試料のAr クラスタースパッタリング正・負二次イオン スペクトルにおけるマトリックス効果の評価,

村谷直紀（日本電子）：Ar イオンビームの有機・無機材料に対するエッチングレートの加速電圧とクラスターサイズ依存性,

永田翔吾（兵庫県立大院）：水およびメタノールクラスターイオンビームを用いた有機材料のSIMS 測定,

飯田真一（アルバック・ファイ）：MS/MS を搭載したTOF-SIMS によるポリマーのスペクトル解析,

石川丈晴（トヤマ）：高面分解能TOF-SIMS を用いたミクロンからサブミクロンサイズの単一微粒子表面および内部の成分分布取得,

中嶋薫（京大院工）：高速C$_{60}$ イオンを用いた透過型二次イオン質量分析,

齋藤玲子（東芝生産技術センター）：SIMS とレーザSNMS による不純物分析におけるマトリックス効果の検証,

ご清聴ありがとうございました

2015/11/4

SIMS20報告会(Organic)

Cluster Ions (CI)
Depth Profiling/Organics (DO)
Polymers and Molecular Films (PM)

<担当>
藤井 麻樹子(京都大学大学院 工学研究科)
岡本 昌幸 (花王株式会社)

セッションの概要

Depth Profiling/Organic, General（Organic関連）

	Applications	Priciple/Fundamentals
Oral	7	6+ Invited 1
Poster	2	2

Applications ：Hydrogel, ﾌｫﾄﾚｼﾞｽﾄ, 太陽光電池, 毛髪
Principle/Fundamentals ：ｲｵﾝ源の比較, GCIB条件検討, ﾏﾄﾘｯｸｽ効果

Polymers and Molecular Films

	Applications	Principle/Instrumentation
Oral	4 (1件講演中止)	4
Poster	3	

Applications ：ﾌﾟﾗｽﾞﾏ処理PE, Polymerﾌﾞﾗｼ, ｸﾞﾗﾌｪﾝ, SAM膜
Principle/Instrumentation ：ｽﾍﾟｸﾄﾙ解析(架橋, 表面Tg), MS/MSｲﾒｰｼﾞﾝｸﾞ
Laser-SNMS

セッションの概要

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Polymers and Molecular Films

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Laser-SNMS

Depth Profiling/Organic, General(Organic関連)

Depth profiling / Organic　　Oral　10件　　Poster　4件

(DO1-ThA1)
ToF-SIMS of Frozen Hydrated Hydrogels
MORGAN ALEXANDER, The University of Nottingham, UK

(DO1-ThA2)
Comparison of Cs+, C60+ and Arn+ for ToF-SIMS Sputtering of PS-b-PMMA
TANGUY TERLIER, University of Catania, Italy

(DO1-ThA3)
Direct Comparison of Argon Gas Cluster Ion Beams and C60 in Molecular Depth Profiling of Organic Thin Films
KAN SHEN, The Pennsylvania State University

(DO1-ThA4)
Argon Cluster Sputtering – Effects of Angle of Incidence, Sample Temperature and Composition
RASMUS HAVELUND, National Physical Laboratory, UK

アルゴンガスクラスターによる有機物のスパッタリング現象の基礎的研究。
Irganox1010/Irganox1098, Irganox1010/Fmoc-pentafluoro-L-phenylalanineの系
→ 照射角度については45°が最もスパッタレート高。
　角度依存性はアルゴン1原子あたりのエネルギーが低い(2eV＞2.5＞5＞10)ほど顕著。
→ 試料温度を上げるとスパッタレートは徐々に高くなるが、Tgを超えると顕著に増加。
　膜厚解析等を安定して行うためには、Tg以下の温度で計測する方が良い。

Depth Profiling/Organic, General(Organic関連)

Depth profiling / Organic　　　Oral　10件　　　Poster　4件

(DO1-ThA5)
The Comparison of Matrix Effects Depending on the Combination of Polymers in a Sample for Depth Profiles Using Ar Cluster Ion Beams

KAZUMA TAKAHASHI, Seikei University, Japan

Irganox1010/Irganox1098, Irganox1010/Fmoc-pentafluoro-L-phenylalanineの系

- DepthprofilingのﾃﾞｰﾀをPCA, MCRで解析 → 各剤に特徴的なﾋﾟｰｸの識別に有効
- Irganox1010/FmocPFLPA ：Irganox1010由来の正ｲｵﾝ発生を促進、Irgnox1010由来の負ｲｵﾝ抑制
- Irganox1010/Irganox1098 ：Irganox1010由来の正ｲｵﾝ発生を抑制、負イオンでは大きな影響なし

(DO1-ThA7)
Molecular Depth Profiling with Strong Field Post-Ionization

LARS BREUER, The Pennsylvania State University

(DO1-ThA8)
Additive Chemistry and Distributions in Photoresist Thin Films

MICHAEL CLARK, JR., The Dow Chemical Company

Depth Profiling/Organic, General(Organic関連)

Depth profiling / Organic　　Oral 10件　　Poster 4件

(DO1-ThA9)
Depth Profiling and Composition Analysis of Polymer:Fullerene Blend Layers for Organic Photovoltaics

S. SURANA, imec & KU Leuven, Belgium

(DO1-ThA10)
Interdiffusion of Fullerene Derivative into Conjugated Polymer Matrix upon Solvent Vapor Annealing

JAKUB RYSZ, Jagiellonian University, Poland

(DO1-ThA11)
Structural Analysis of the Outermost Hair Surface using TOF-SIMS with GCIB Sputtering,

KAZUTAKA ISHIKAWA, Kao Corporation, Japan

毛髪表面に存在する層状組織(キューティクル)を、Ar_{2500}によるスパッタで深さ方向分析。キューティクル表面は段差が存在するため、平坦部のデータを解析した方が深さ方向分解能高。
最表面の脂質層、およびその下層のnmオーダーの特異的なアミノ酸組成を持つ層が存在。
→ 毛髪科学で提唱されている最表面構造を実験的に直接示した。

Depth Profiling/Organic, General(Organic関連)

Depth profiling / General(Organic関連)　Oral　10件　　Poster　4件

有機物:GCIB1次ｲｵﾝ源, Orbitrap検出器, MS/MS capability
無機物:Large O_2 gas cluster, $(SF_6)_{370}$

(DG1-ThM7) Invited
Invited Recent Developments in ToF-SIMS Depth Profiling of Inorganic and Organic Thin Films
EWALD NIEHUIS, ION-TOF GmbH, Germany

(DG1-ThM9)
Low Energy Cesium Depth Profiling of Hybrid Materials
LAURENT HOUSSIAU, University of Namur, Belgium

(DG1-ThM10)
Surface Analysis and Depth Profiling of Polymer Multilayers by ToF-SIMS and XPS: A Possible Model for Complex Matrices Analysis
GIACOMO CECCONE, EC-JRC-IHCP, Ispra , Italy

(DG1-ThM11)
Reconstructing Accurate ToF-SIMS Depth Profiles for Organic Materials with Differential Sputter Rates
DAVID CASTNER, University of Washington

アルゴンガスクラスターによるスパッタリング挙動を、PS/PMMA二成分膜を用いて検討。
Ar_{1000}クラスターによるスパッタリングでは、PSよりもPMMAの方が約2倍速くスパッタされる。
ポリマーをブレンドした場合のスパッタレートの変化は、組成比に対応してほぼリニアに変化する。
→ より正確な深さ方向分析を行うには、組成変化によるｽﾊﾟｯﾀﾚｰﾄの変化を把握しておくことが重要。

その他(Organic Depthprofiling)

深さ方向分析のﾏﾄﾘｯｸｽ効果(Data processing and Interpretation)

(DP1-ThM3)
The Matrix Effect in SIMS Organic Depth Profiling: A VAMAS Inter-laboratory Comparison
Alexander G. Shard, National Physical Laboratory, UK

Irganox1010/Irganox1098, Irganox1010/Fmoc-pentafluoro-L-phenylalanineの系
Irganox1098, Fmoc-PFLPAのﾏﾄﾘｯｸｽ効果(二次ｲｵﾝ種, 一次ｲｵﾝ源の影響)
- Lowﾏｽの二次ｲｵﾝ(59Da.以下)ではﾏﾄﾘｯｸｽ効果低い
- 分子ｲｵﾝが最も大きい, ﾀﾞｲﾏｰは影響を受けにくい
- 一次ｲｵﾝ種が多原子になるほどﾏﾄﾘｯｸｽ効果が大きくなる傾向有り

FIB-SIMSによる有機物の深さ方向分析(FIB-SIMS)

(3D1+ID1-MoA3)
3D Organic Structure Characterization by FIB-TOF Tomography
DAVID M. CARR, Physical Electronics

FIB sectioning ＋ Polishing(C_{60} or Ar_{2500})
→ 有機物と金属の混合試料の分析

セッションの概要

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Polymers and Molecular Films

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Applications ：ﾌﾟﾗｽﾞﾏ処理PE, Polymerﾌﾞﾗｼ, ｸﾞﾗﾌｪﾝ, SAM膜
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Laser-SNMS

Polymers and Molecular Films

Polymers and Molecular Films　　Oral　10件　　Poster　4件

(PM1-WeM1)

ToF-SIMS Investigation of Polyethylene Modified by an Atmospheric Ar-D2O Post-discharge

VANINA CRISTAUDO,Université catholique de Louvain (UCL), Belgium

(PM1-WeM3)

Negative Hydrocarbon Species $C_{2n}H^-$: How Useful Can They Be?

HENG-YONG NIE, The University of Western Ontario, Canada

$C_{2n}H^-$ピークでポリマーの構造を解析。PE, PP, PS, PMMAなどのポリマーでC_6H^-/C_4H^-強度比を調べた結果、C-C間の結合数が多いもの(分岐や二重結合等)ほどが値が大。分岐度を変えたPMMAの測定結果でも、分岐の増大と共にC_6H^-/C_4H^-強度比が大に。

→ 直鎖の構造よりも分岐の方が、スパッタリングの過程で結合解裂/Crosslinkingを発生し易いからと説明。

(PM1-WeM4)

Compositional and Structural Characterization of Nanodomains

FAN YANG, Texas A&M University

(PM1-WeM6)

TOF-SIMS Imaging MS/MS of Polymer Additives

JOHN HAMMOND, Physical Electronics

Polymers and Molecular Films

Polymers and Molecular Films　　Oral　10件　　Poster　4件

（PM1-WeM7）
TOF-SIMS Analysis of Polymer Conformations at Surfaces and Interfaces
LU-TAO WENG, The Hong Kong University of Science & Technology

PSのTOF-SIMSスペクトルを温度可変で計測し、その変化を主成分分析(PCA)で解析することで表面コンフォメーションの変化を調べた。ローディングプロットにより、0～85℃と90～100℃のデータが異なる群として明瞭に区別された。
→ PSの表面ガラス転移温度(表面Tg)による変化を捉えていると解釈される。

（PM1-WeM8）
ToF-SIMS and Laser-SNMS 2D and 3D Investigations of Different Polymer Systems
ANDREAS PELSTER, University of Münster, Germany

（PM1-WeM9）
ToF-SIMS Analysis of Clean Graphene and Graphite
WENJING XIE, Hong Kong University of Science and Technology

（PM1-WeM10）
ToF-SIMS Characterization of Self-Assembled Oriented Carborane Dipoles on Silver Surface
LAETITIA BERNARD, Swiss Federal Laboratories for Material Science and Technology, Switzerland

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Laser-SNMS

SIMS XX

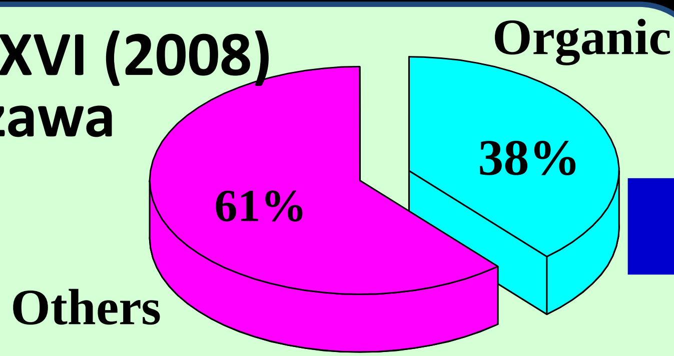
John Fletcher

Tokyo 2015

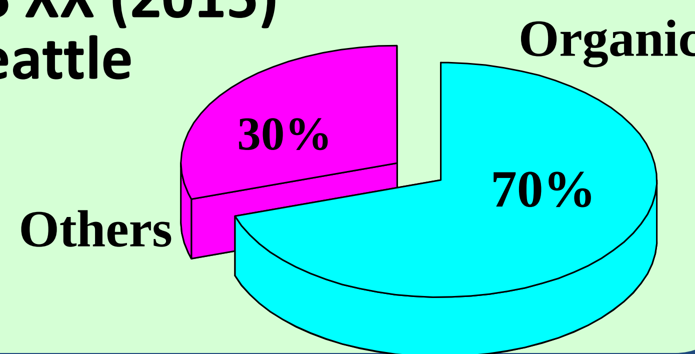
Statistic in SIMS Conference (2015)

Plenary Session		
Microelectronics	Complementary Techniques	Fundamentals
3D Imaging	Cluster Ions	FIB-SIMS & MeV SIMS
Plenary Session		
Instrument Development	Sample Prep Analysis of Bio. Samples	Surface & Interface Analysis
Depth Profiling Inorganics	Biological Imaging	Multi-Technique
Nanomaterials and Nanotechnology	Depth Profiling/Organics	In-Situ Liquid SIMS
SIMS Analysis of Materials	Biological Imaging	

SIMS XVI (2008)
Kanazawa



SIMS XX (2015)
Seattle



Organic and Biological materials are main topics!

Ian Gilmore (NPL) opened the conference with a presentation that included the first data from the Iontof/Thermo ToF/Orbitrap hybrid instrument.

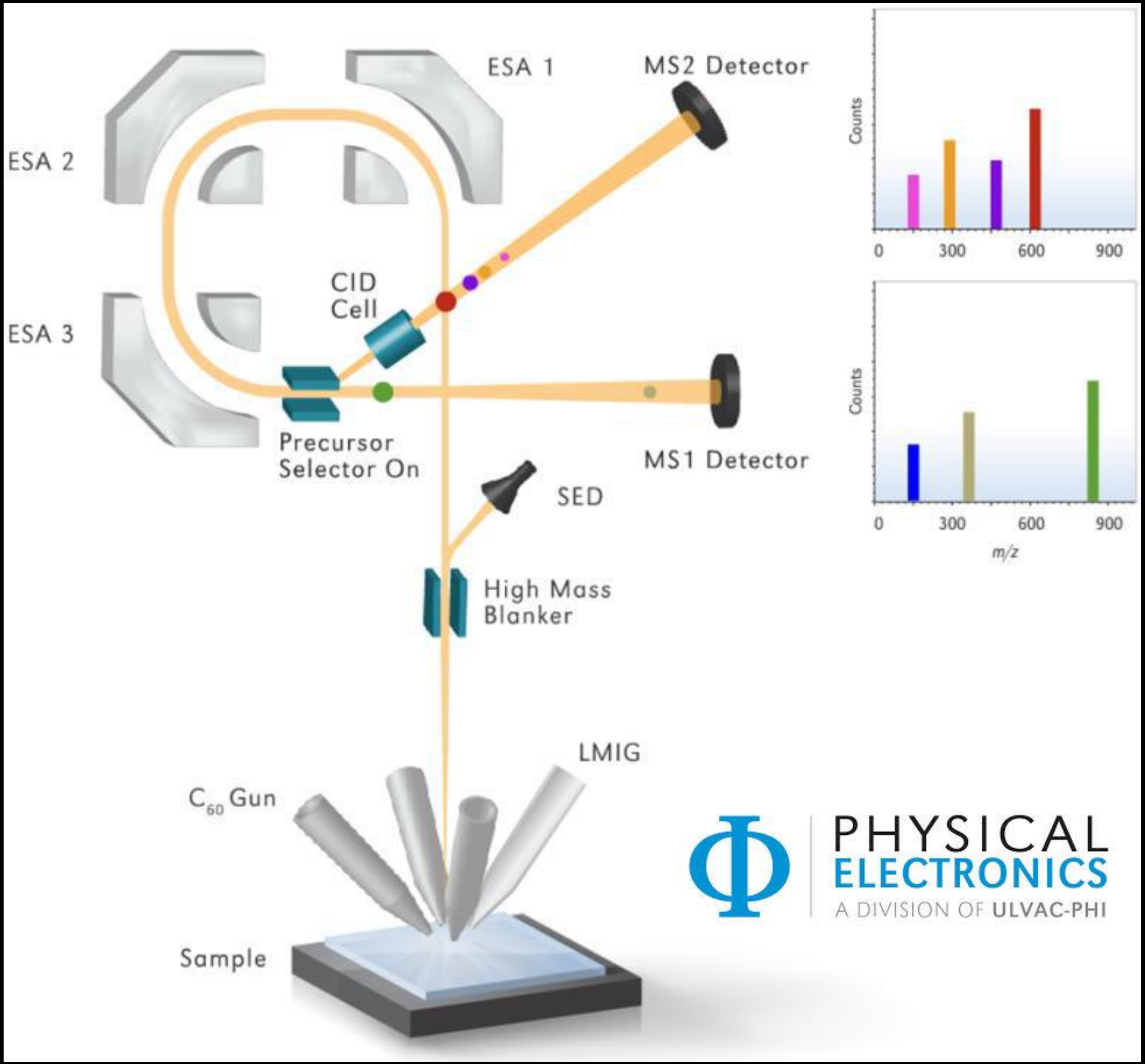
Presentation included tissue imaging with a new GCIB.

230,000 mass resolution at m/z 200

20,000 mass resolution at 18 Hz.

http://planetorbitrap.com/

ULVAC-PHI introduce MSMS on the TRIFT



ToF-ToF configuration

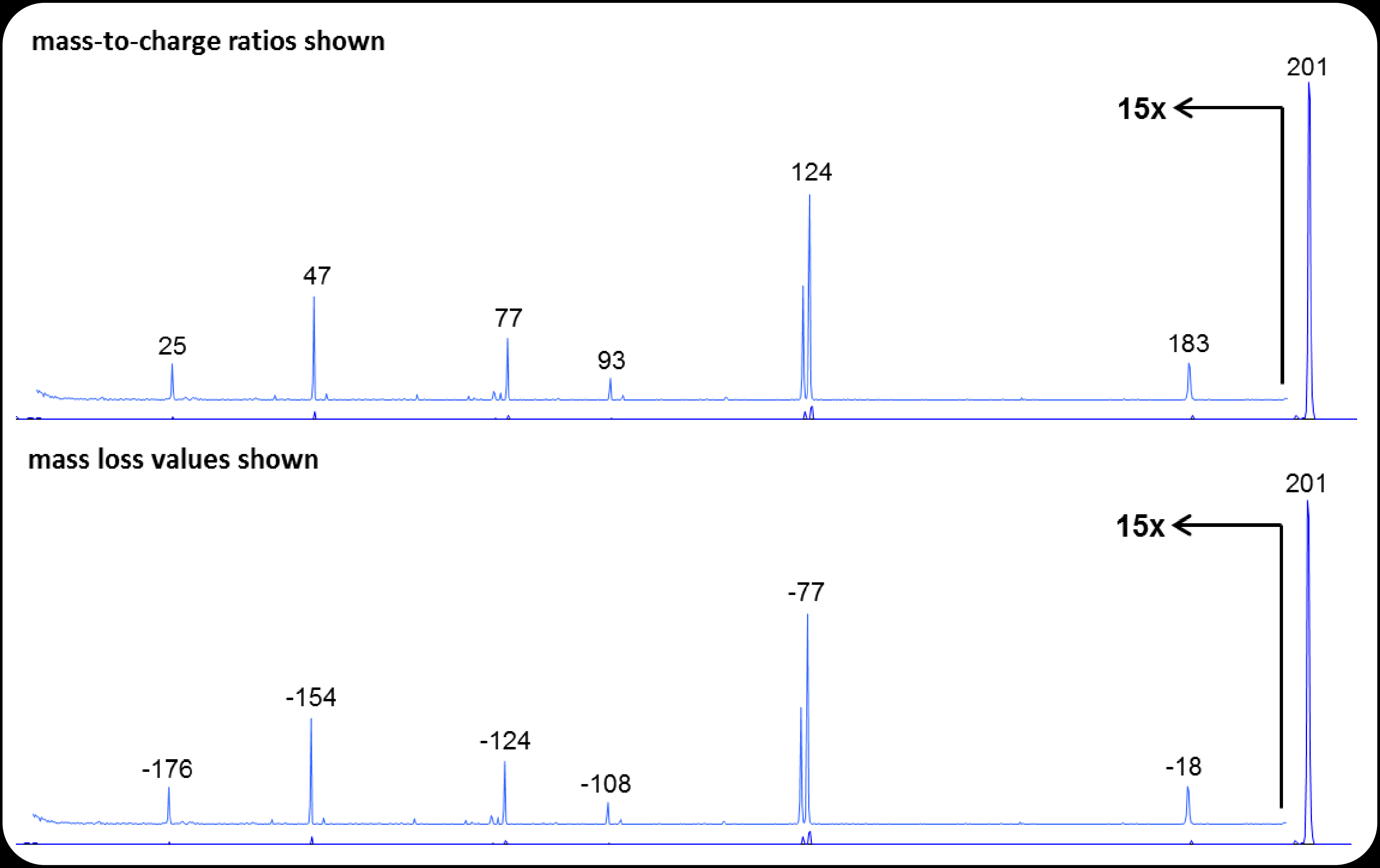
"high" energy CID

Linear MS for product ion identification.

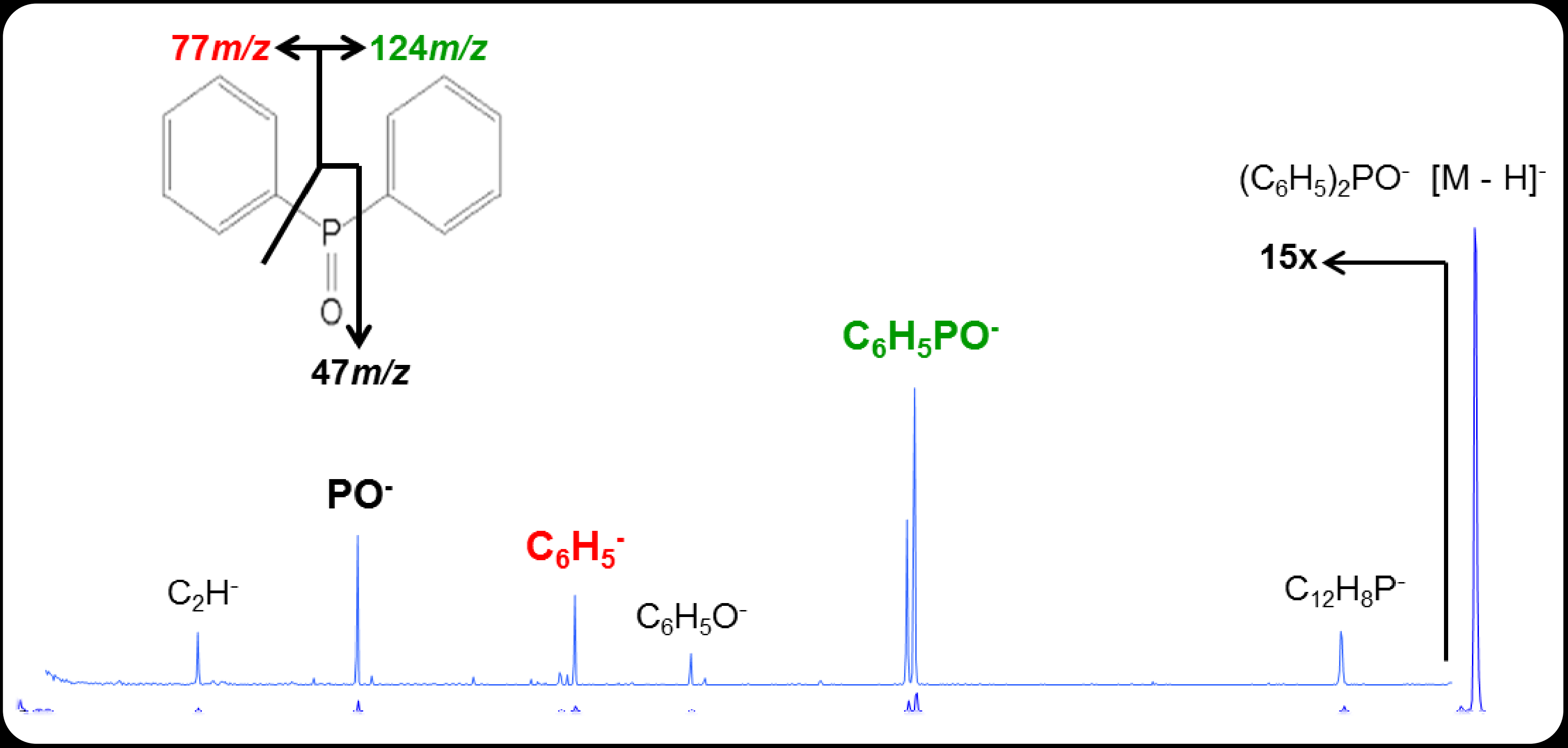
Normal MS spectrum is collected simultaneously with MSMS spectrum.

www.phi.com

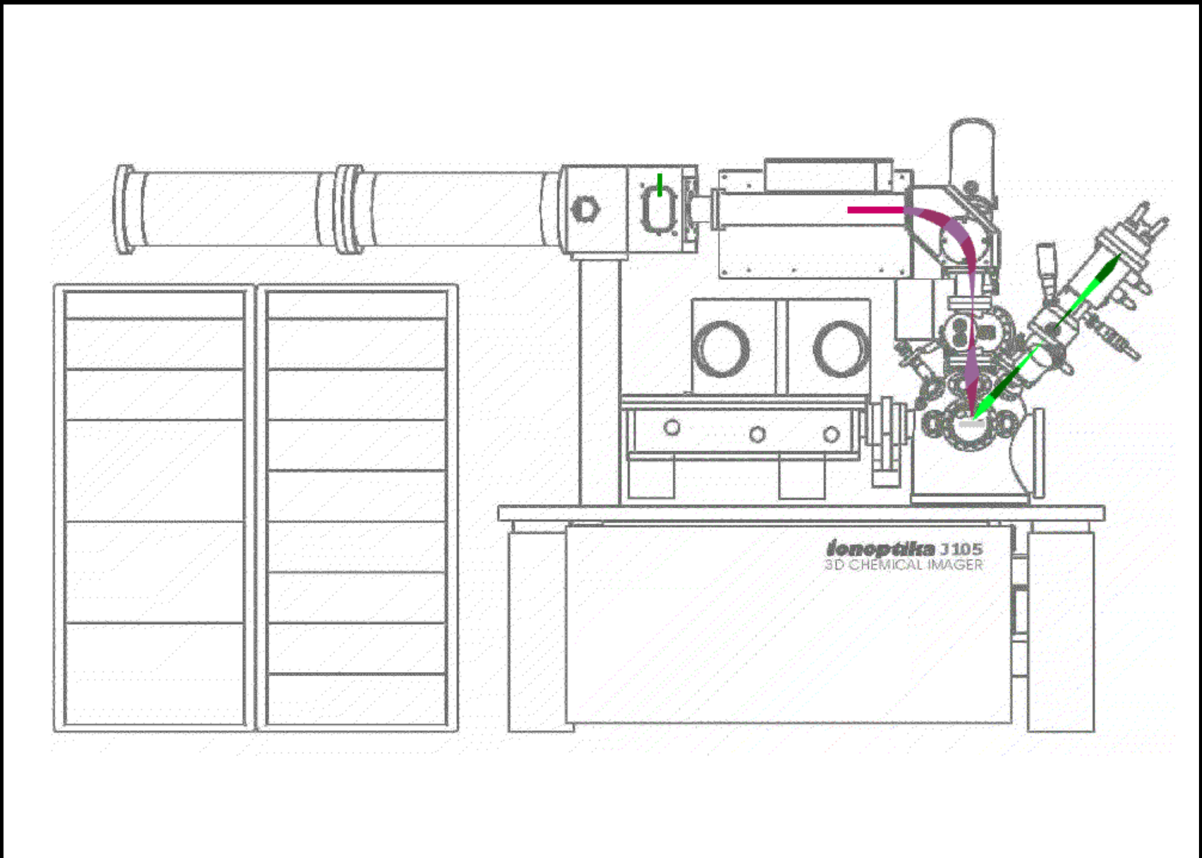
Additive Identification using TOF-SIMS Parallel MSMS Analysis



Fragments suggest the m/z 201 peak to originate from DPPO, a photo-initiator that was likely to be an additive in the material analysed



J105 SIMS Instrument has led the way!



No effect of sample topography on calibration.

Better than 5 ppm mass accuracy

MSMS

www.Ionoptika.com

J. S. Fletcher, et al. *Analytical Chemistry,* 2008

Lipid Imaging of Invertebrate Model Systems by Secondary Ion Mass Spectrometry

NHU PHAN, University of Gothenburg, Sweden, A.G. EWING, J.S. FLETCHER, Chalmers University of Technology, Sweden

Effects of Methylphenidate (Ritalin) on Fly Brain Chemistry

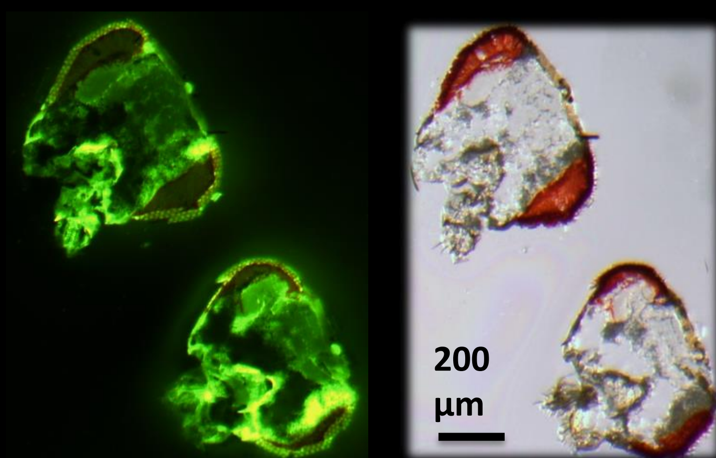
Live flies on collar

Fly collar in gelatin

Fly collar attached to gelatin block

Fly heads on frozen gelatin blocks

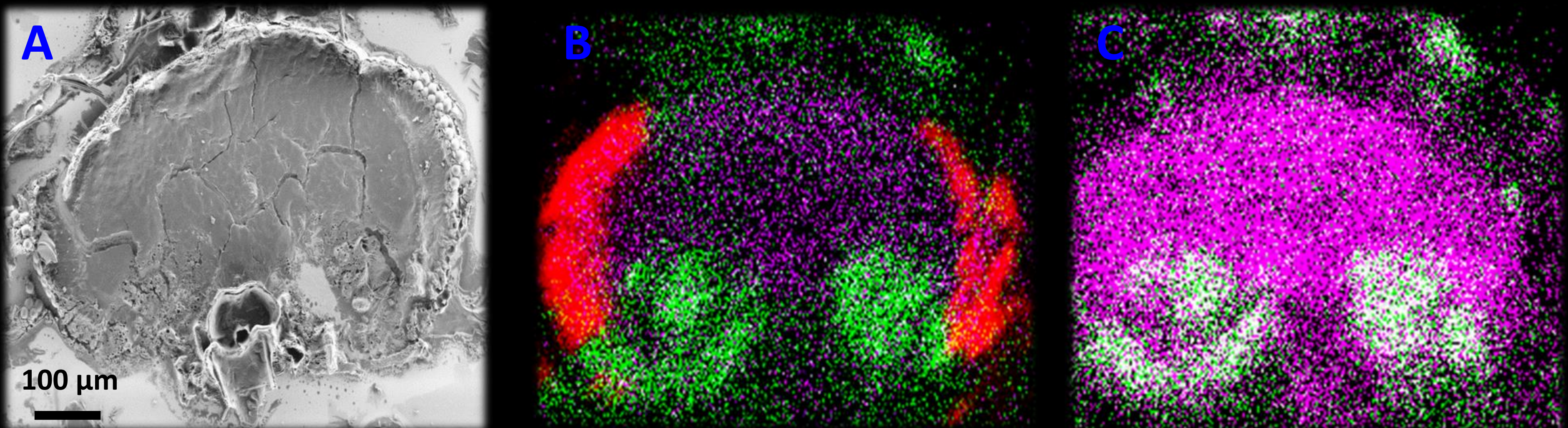
Sectioned using a cryo-microtome



Fly brain section 15 µm thickness

ToF-SIMS Imaging of the Fly Brain

ToF-SIMS ion images of a fly brain with the GCIB show different distributions of bio-molecules which implies their biological functions in the brain. **(A)** SEM image **(B)** Positive mode **(C)** Negative mode



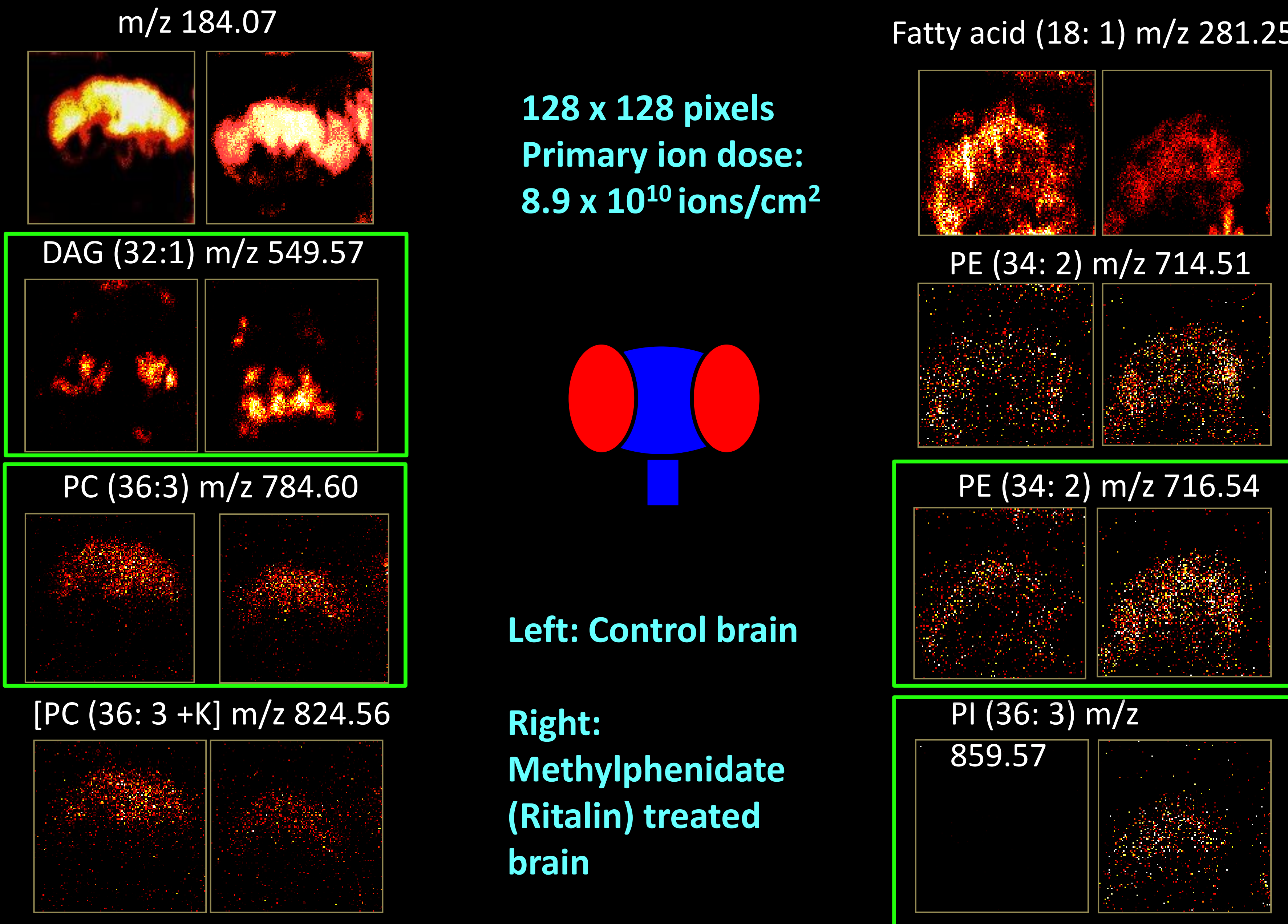
SEM image

Drosopterins m/z 369.16
DAGs m/z 521.47, m/z 549.58
Lipids PC (32:1) m/z 732.67
PC (34:1) m/z 760.68

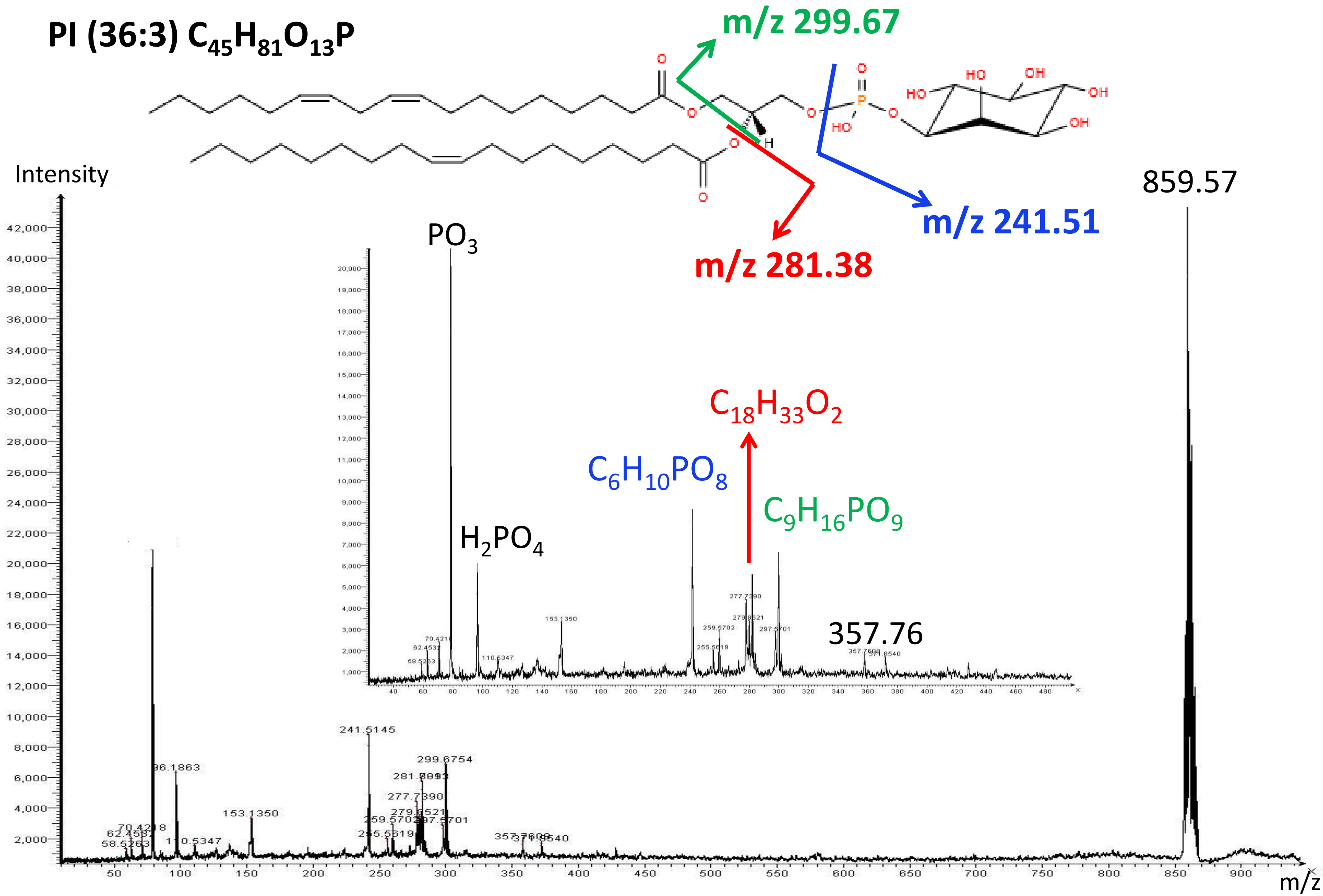
Fatty acid (C14:0) m/z 227.18
Fatty acid (C18:1) m/z 281.21

N. Phan *et al. Anal. Chem.* 2015

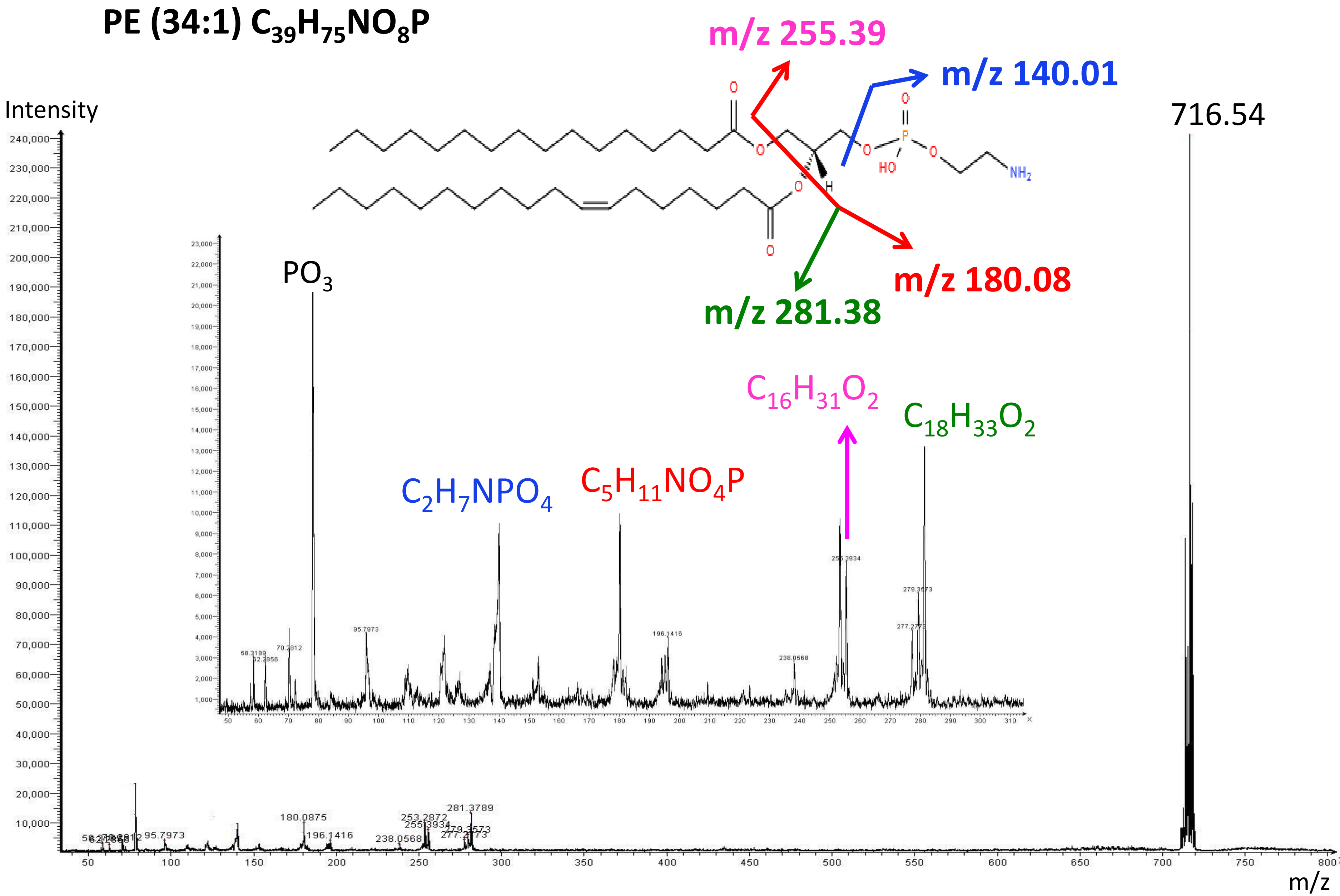
Lipid Changes after Methylphenidate Exposure



Structural Study of m/z 859.57 by MSMS



Structural study of m/z 716.54 by MSMS



Gas Cluster Ion Beams are Still a Hot Topic

Application of beams for analysis is increasing.

More people are experimenting with different beam types:

Projectile Assisted Surface Chemistry: A Possible Route to Enhance Molecular Secondary Ion Yields?, H. TIAN, The Pennsylvania State University, **ANDREAS WUCHER**, University Duisburg-Essen, Germany, N.X. WINOGRAD, The Pennsylvania State University

Argon Cluster Total Sputter Yield: Quartz Crystal Microbalance Measurements and Semi-Empirical Predictive Model, P.J. CUMPSON, **ANDERS BARLOW**, J.F. PORTOLES, N. SANO, National EPSRC XPS Users' Service (NEXUS), UK

Depth Profiling of Inorganic Thin Films Using Large Oxygen Gas Clusters, DERK RADING, R. MOELLERS, E. NIEHUIS, ION-TOF GmbH, Germany

Current Prospects of Organic Analysis with Ar-GCIB SIMS, from Synthetic Polymers and Organic Devices toward Biological Materials, MAKIKO FUJII, T. SEKI, T. AOKI, J. MATSUO, Kyoto University, Japan

Quantitative Studies of Matrix Effects in Massive Cluster Impact (MCI) Sputtering of Intact Lipid and Peptide Ions, JITAO ZHANG, P. WILLIAMS, A. LEE, Arizona State University

Enhanced Ionisation Using Water-containing Cluster Ion Beams - A Fundamental Study, S. SHERAZ, I. BERRUETA RAZO, T. KOHN, **NICHOLAS LOCKYER**, J.C. VICKERMAN, University of Manchester, UK

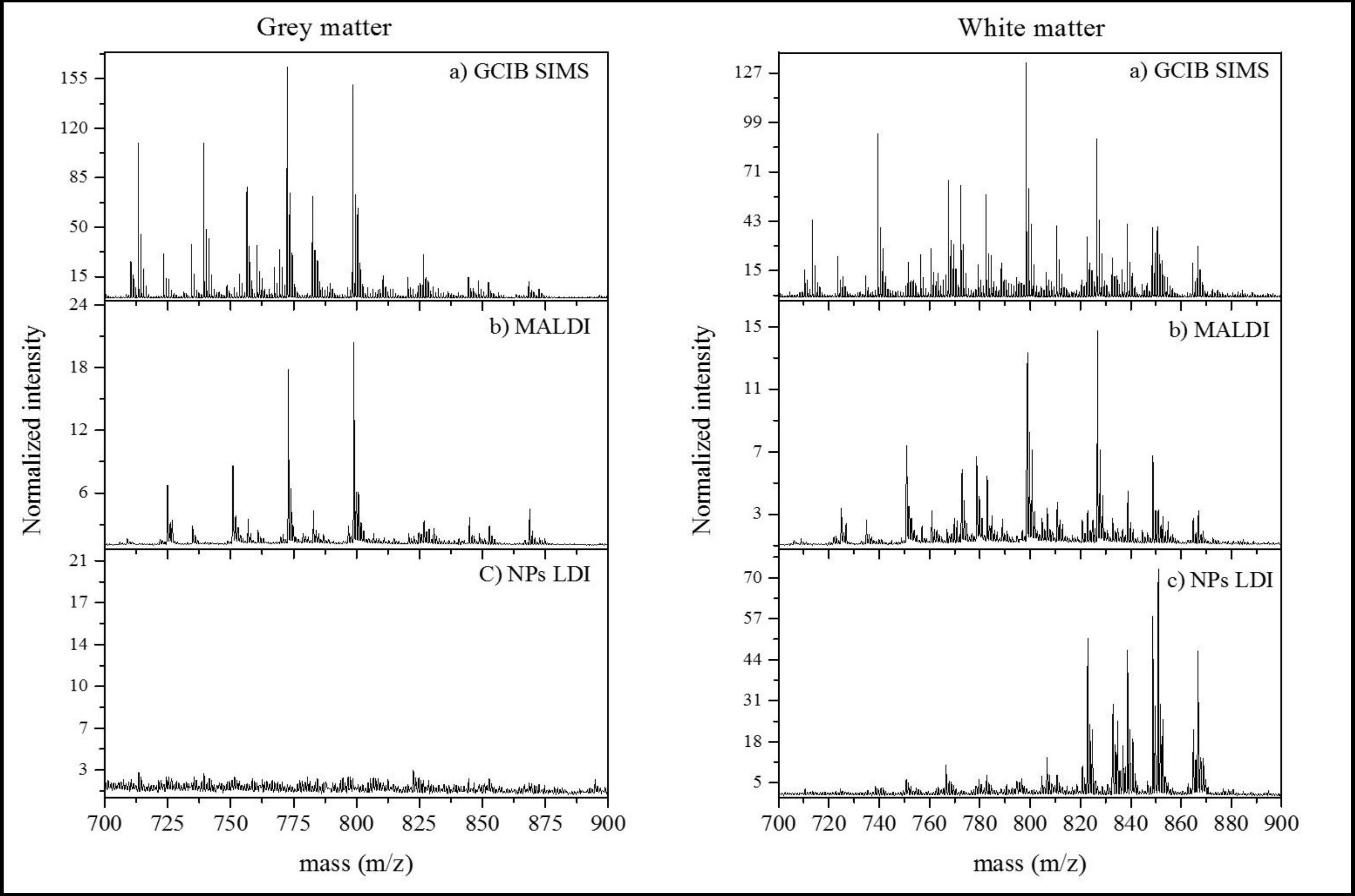
Investigation of Surface-adsorbate Interaction of Surface-adsorbed (bio-) Molecules Using Desorption/Ionization Induced by Neutral Clusters, A. PORTZ, Institute of Applied Physics, Justus Liebig University Giessen, S. ABB, S. RAUSCHENBACH, K. KERN, MPI for Solid State Research, Stuttgart, C.R. GEBHARDT, Bruker Daltonik GmbH, Bremen, **MICHAEL DÜRR**, Institute of Applied Physics, Justus Liebig University Giessen, Germany

Benninghoven Lecture: An Evolution in SIMS Instruments: How Far are we from the Goal?, JIRO MATSUO, Kyoto University, Japan

Comparative Study of Secondary Ion Emission from Organic Thin Film Bombarded with Water, Methanol and Methane Cluster Ions, KOUSUKE MORITANI, S. NAGATA, Y. HIGASHIHARA, N. INUI, K. MOCHIJI, University of Hyogo, Japan

MD Simulations of Polymer Sputtering by Large Gas Clusters: Effects of Cluster Nature (Ar, CH4), incidence angle and sample molecular weight, ARNAUD DELCORTE, Université catholique de Louvain, Belgium, M. DEBONGNIE, Université catholique de Louvain, Institut de la Matière Condensée et des Nanosciences (IMCN), Bio & Soft Matter (BSMA), 1 Croix du Sud box L7.04.01, B-1348 Louvain-la-Neuve, Belgium.

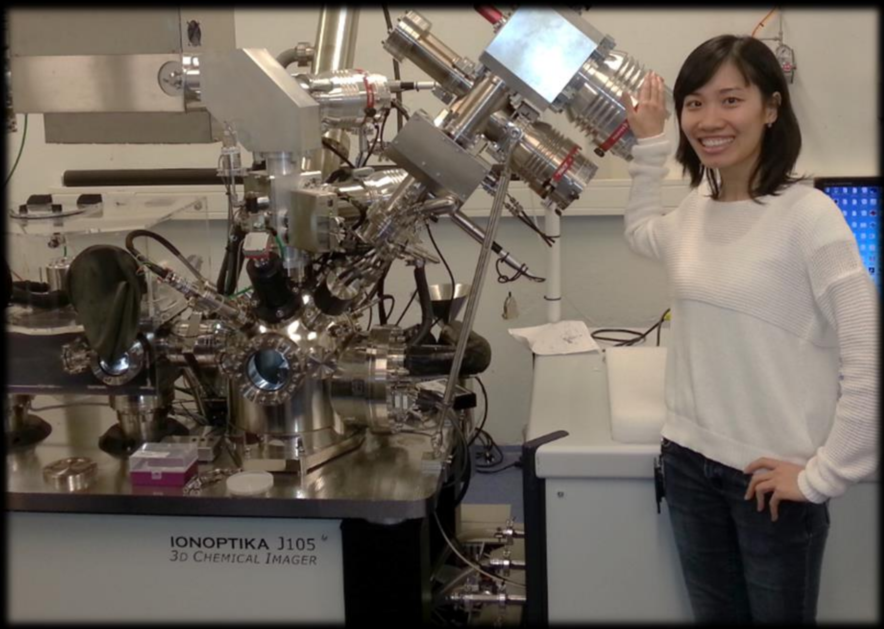
GCIB SIMS Starts to Compete with MALDI

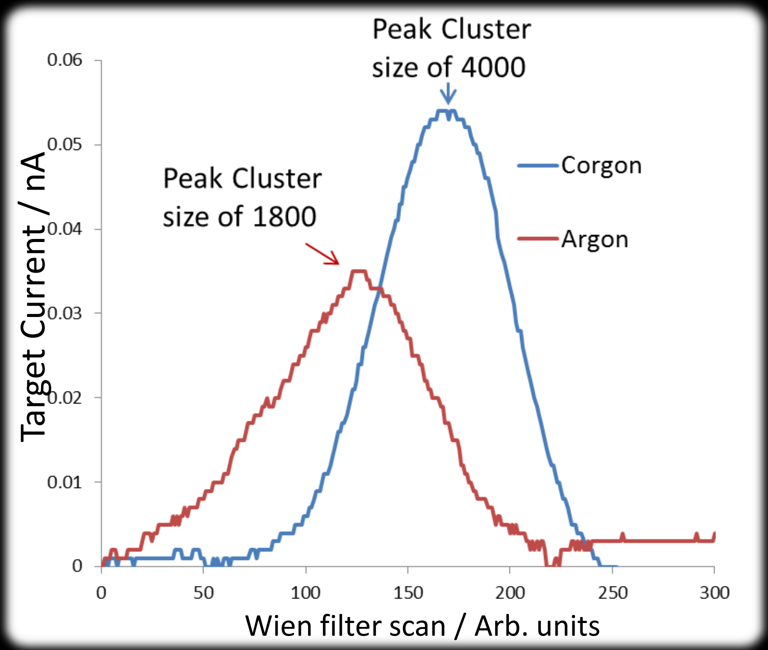


Amir Mohammadi. Andrew Ewing Group

40 kV GCIB

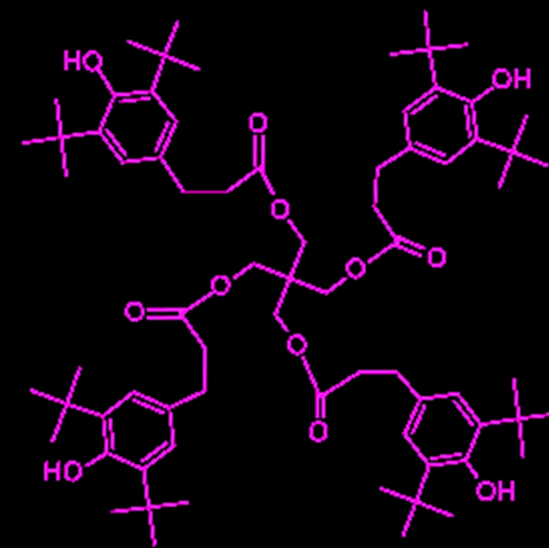
Higher energy GCIB system tested to improve spatial resolution and ion yield

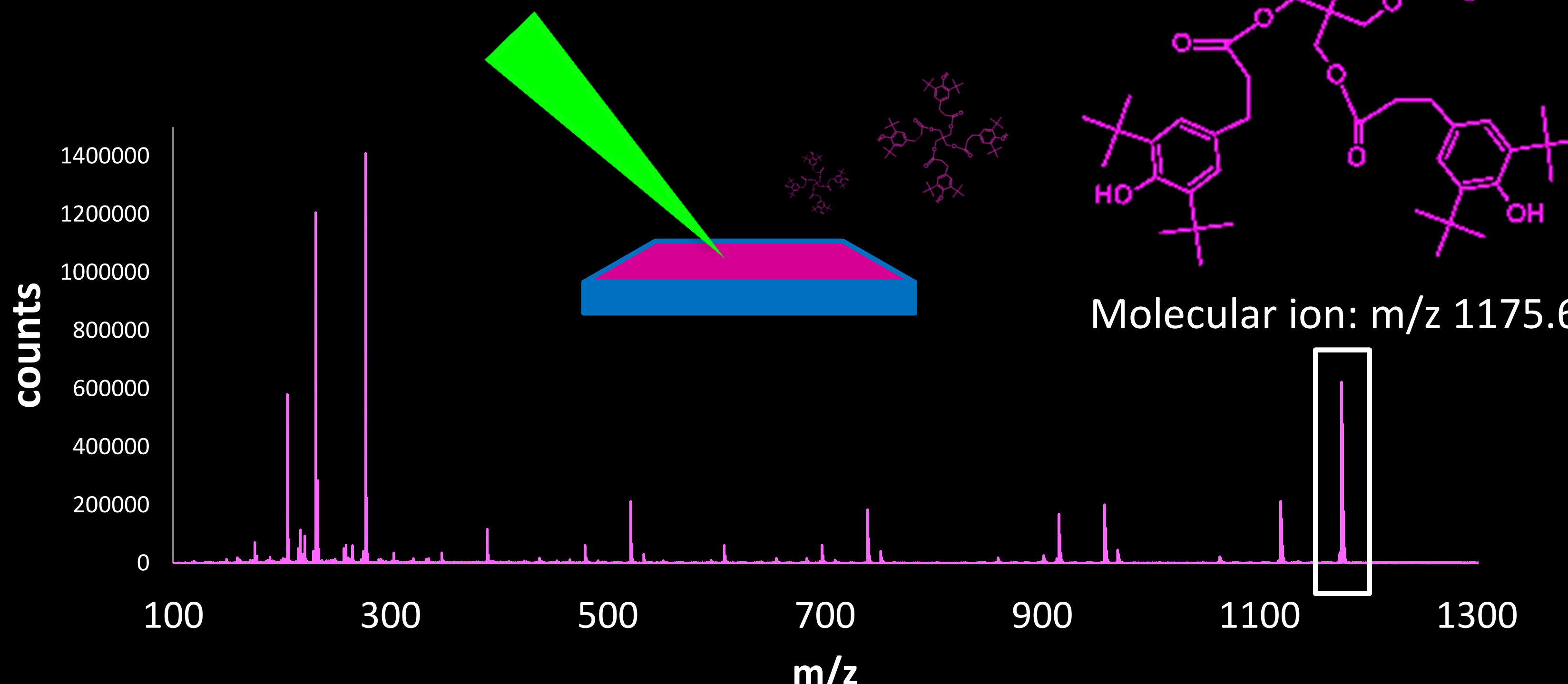




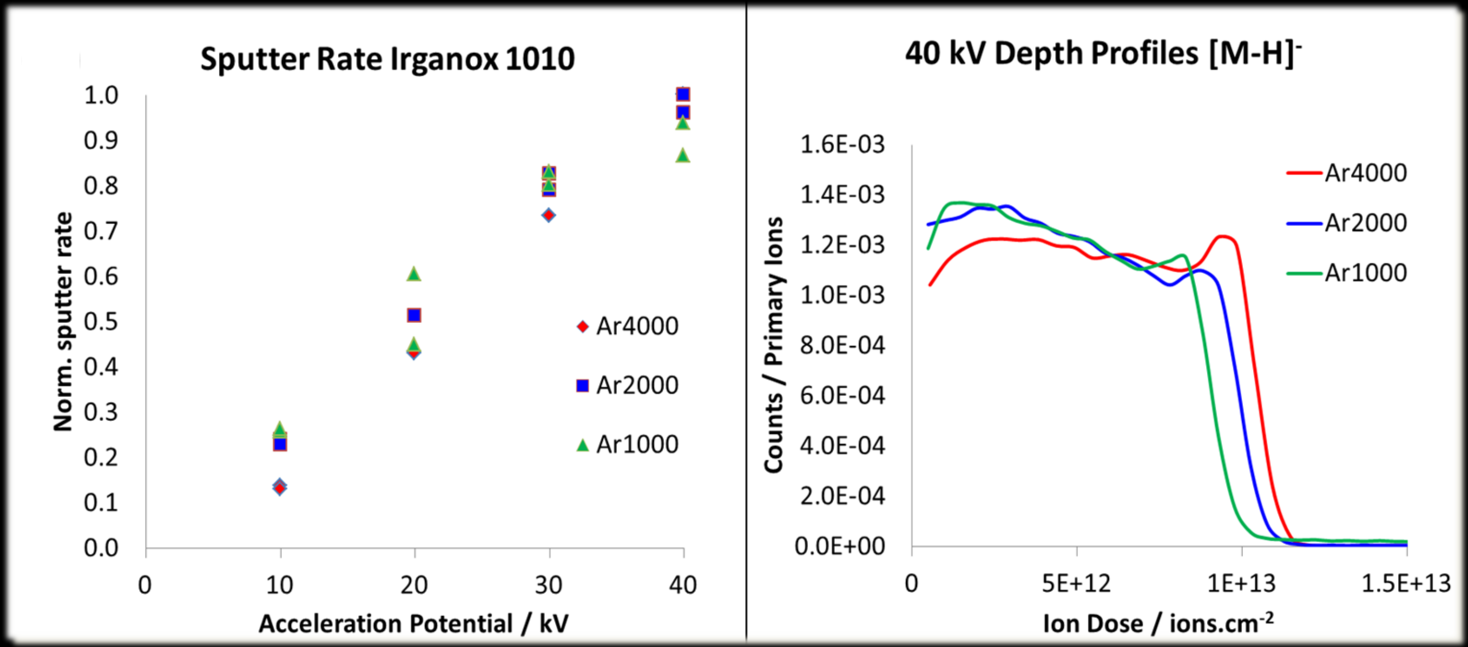
Beam Characterisation with Irganox 1010

- Standard sample used for beam characterisation → Comparison with previously studied primary ion beams possible
- In this study: 50 nm thick Irganox 1010 film from NPL (UK)





Sputter Rate and Steady State through Irganox 1010



An approximately linear increase in sputter rate is observed as the acceleration potential is increased from 10 to 40 kV.

At 40 kV there is little if any difference in sputter rate between the different size clusters used in this study.

The Matrix Effect in SIMS Organic Depth Profiling: A VAMAS Inter-laboratory Comparison

ALEXANDER G. SHARD, S.J. SPENCER, R. HAVELUND, I.S. GILMORE, National Physical Laboratory, UK

The Comparison of Matrix Effects Depending on the Combination of Polymers in a Sample for Depth Profiles Using Ar Cluster Ion Beams

KAZUMA TAKAHASHI, Y. YOKOYAMA, S. AOYAGI, Seikei University, Japan

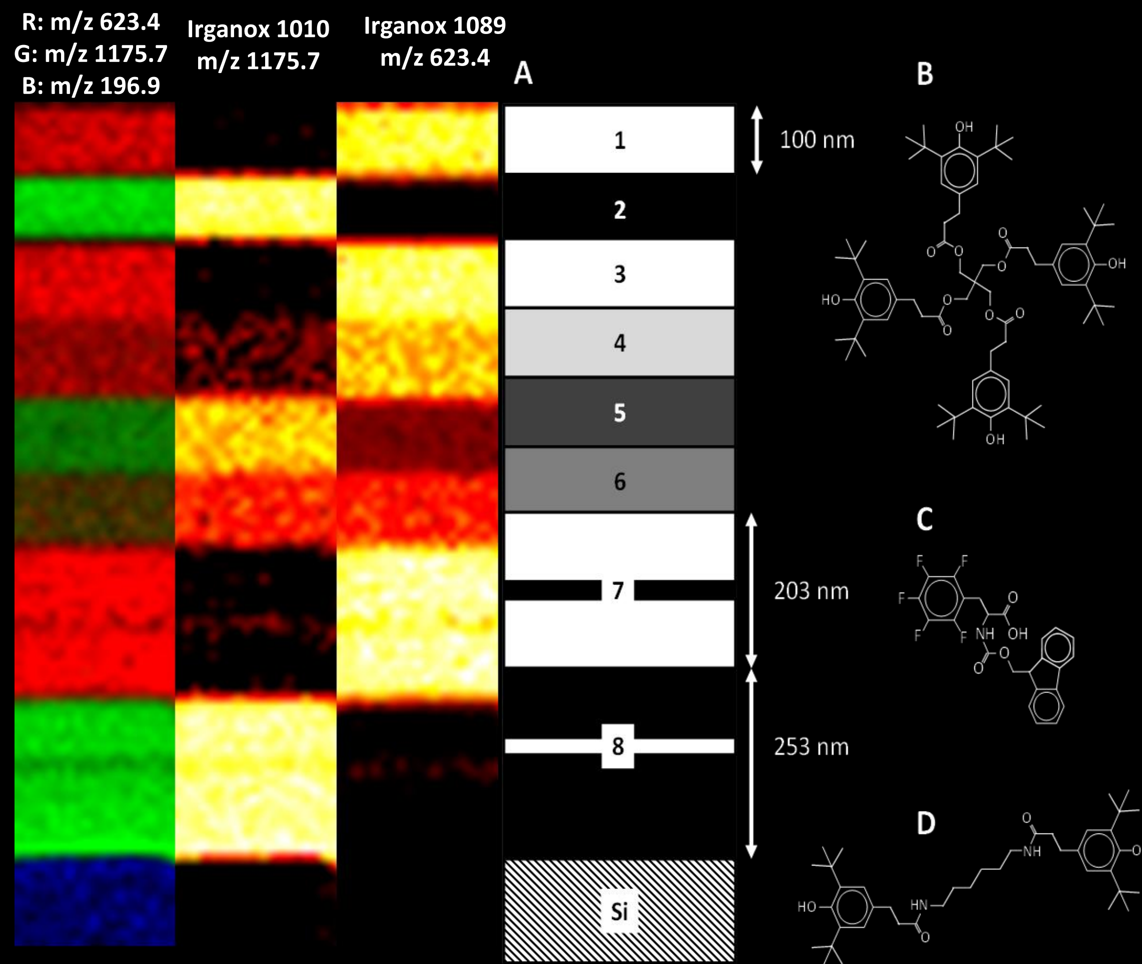
3D Imaging ToF-SIMS for Biology – Are We Living the Dream?

JOHN S. FLETCHER, University of Gothenburg, Sweden

Irganox – Matrix effects in depth profiles

Measuring Compositions in Organic Depth Profiling: Results from a VAMAS Interlaboratory Study

Alexander G. Shard, Rasmus Havelund, Steve J. Spencer, Ian S. Gilmore, Morgan R. Alexander, Tina B. Angerer, Satoka Aoyagi, Jean-Paul Barnes, Anass Benayad, Andrzej Bernasik, Giacomo Ceccone, Jonathan D. P. Counsell, Christopher Deeks, John S. Fletcher, Daniel J. Graham, Christian Heuser, Tae Geol Lee, Camille Marie, Mateusz M. Marzeco, Gautam Mishra, Derk Rading, Olivier Renault, David J. Scurr, Hyun Kyong Shon, Valentina Spampinato, Hua Tian, Fuyi Wang, Nicholas Winograd, Kui Wu, Andreas Wucher, Yufan Zhou, and Zihua Zhu

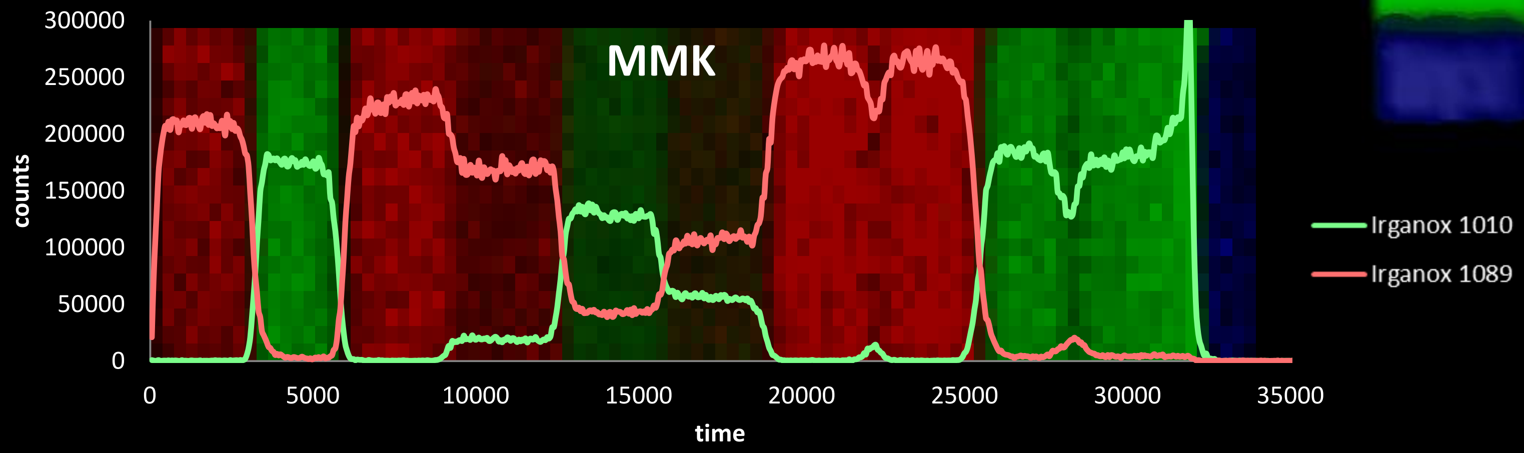


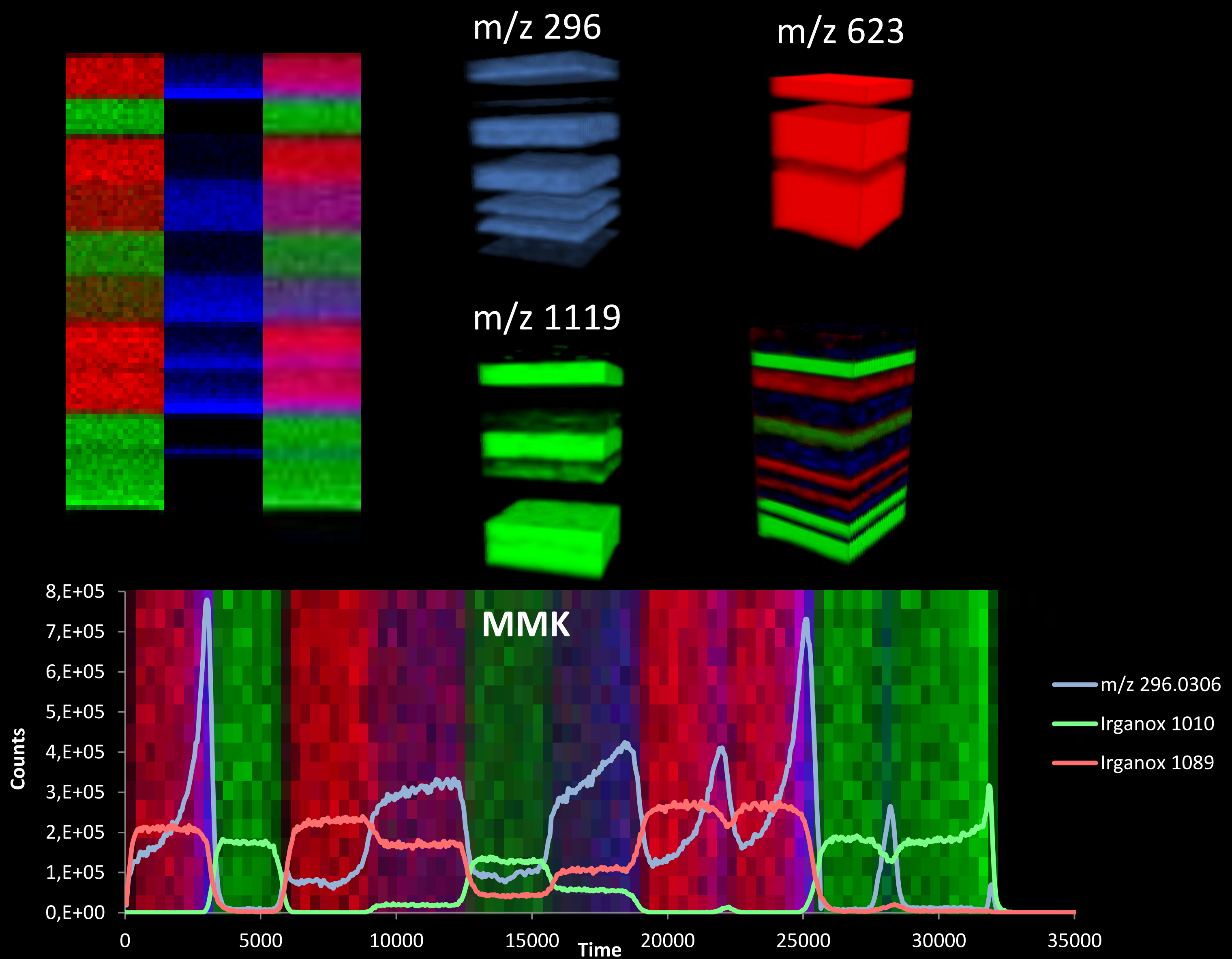
J. Phys. Chem. B, **2015**, *119* (33), pp 10784–10797

40 kV GCIB Result

If the “right” peaks are selected nice looking, quantitative(ish) depth profiles and 3D images can be generated.

Choosing the “wrong” peaks shows a strong matrix effect with interfaces and relative compositions distorted.





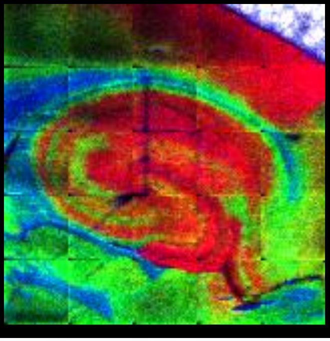
Shard et al. J. Phys. Chem. B, **2015**, *119* (33), pp 10784–10797

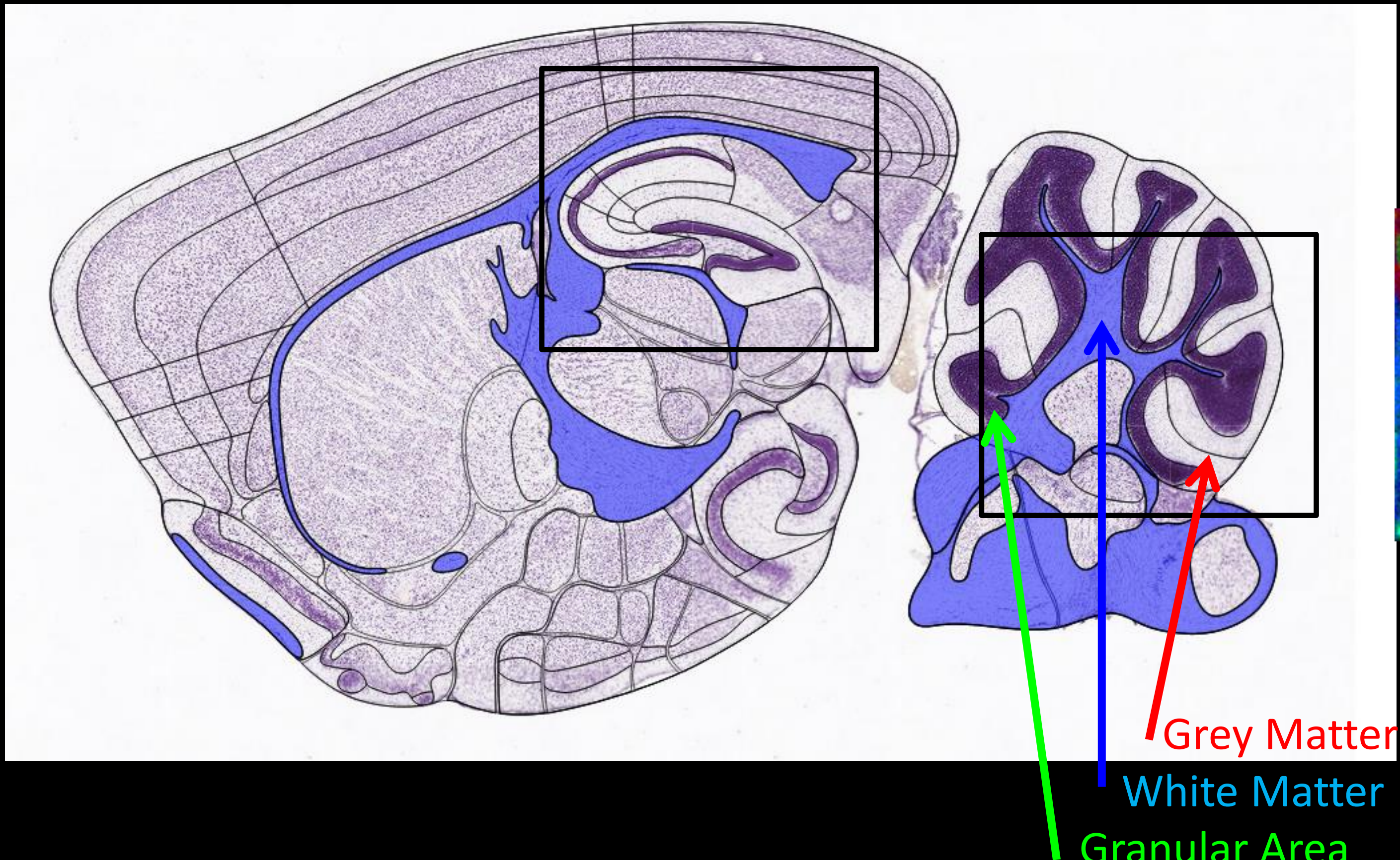
Improving Sensitivity and Broadening Chemical Coverage in Brain Imaging using ToF-SIMS and GCIBs

TINA BERNADETTE ANGERER, University of Gothenburg, Sweden, J.S. FLETCHER, Chalmers University of Technology, Sweden

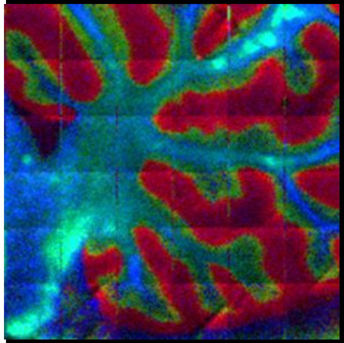
Brain Regions Mouse – Sagittal Section

FH and NH_3 Study:
Hippocampal Formation

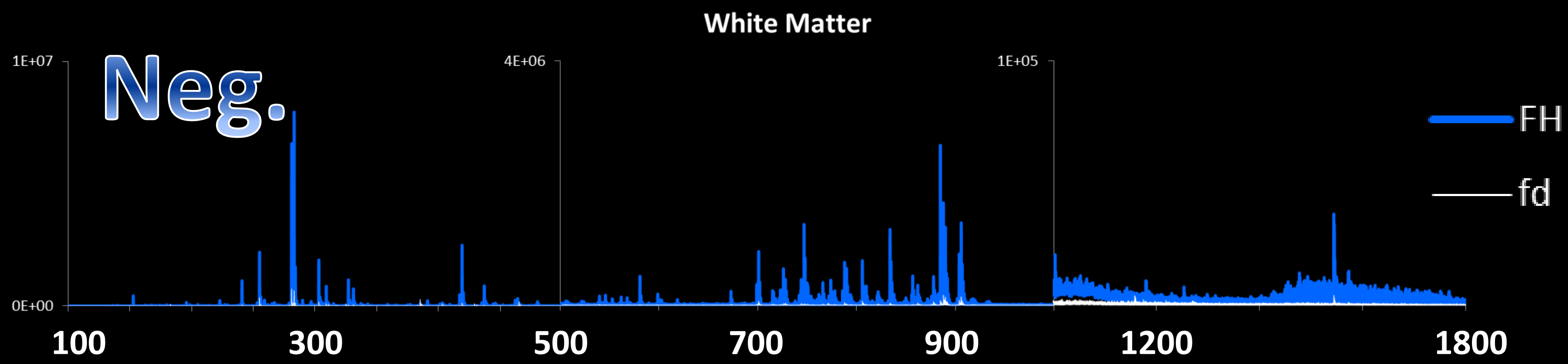


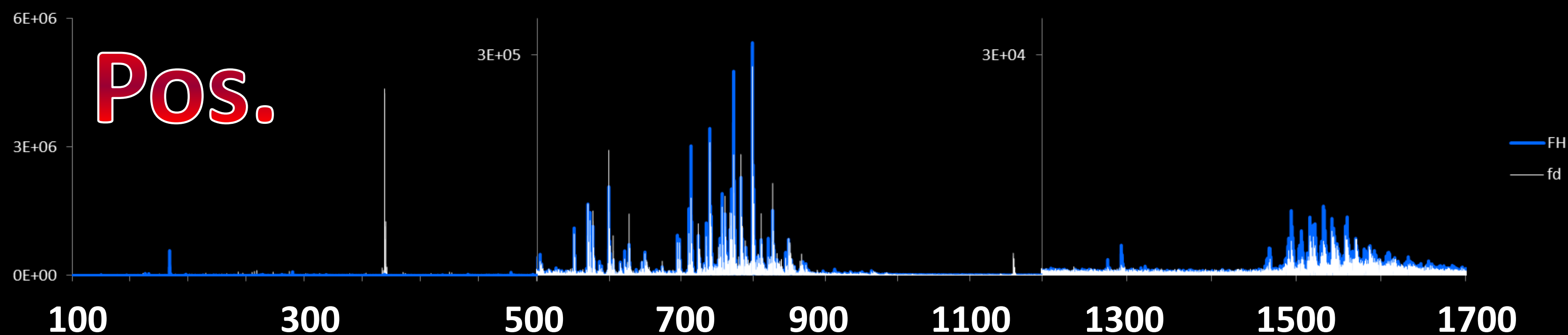


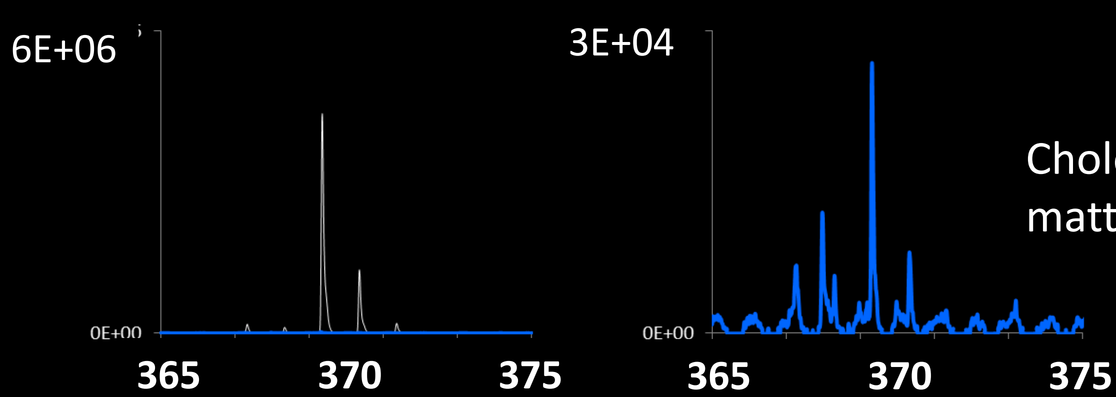
TFA Study:
Cerebellum



Frozen Hydrated vs. Freeze Dried – Signal Changes

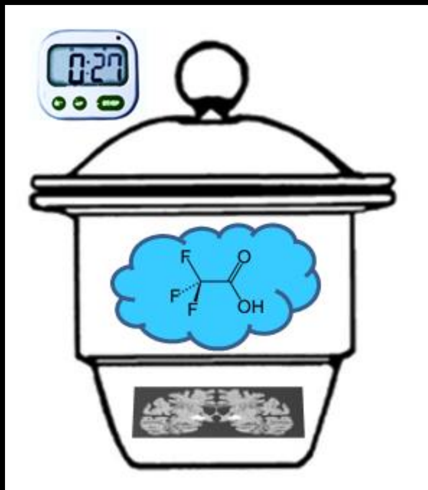


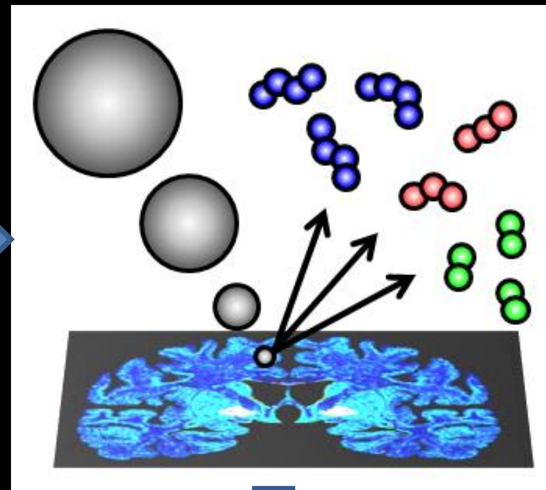




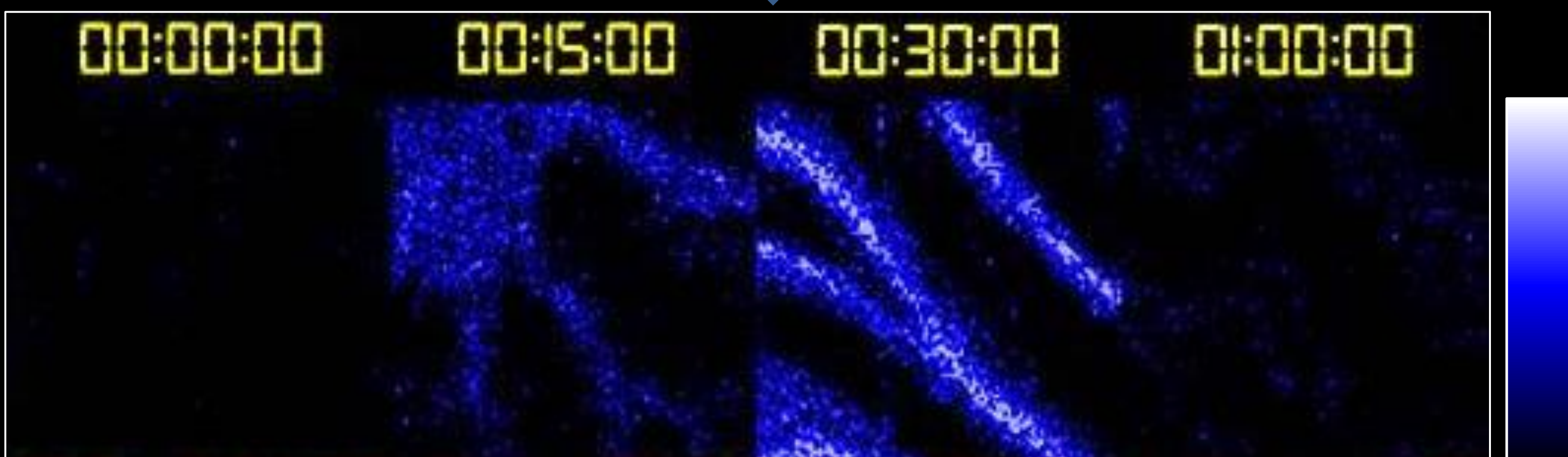
Cholesterol dominates white matter spectra when tissue is dry

Optimisation of Pre-Analysis Sample Treatment with Ammonia (NH_3) and Trifluoroacetic acid (TFA)



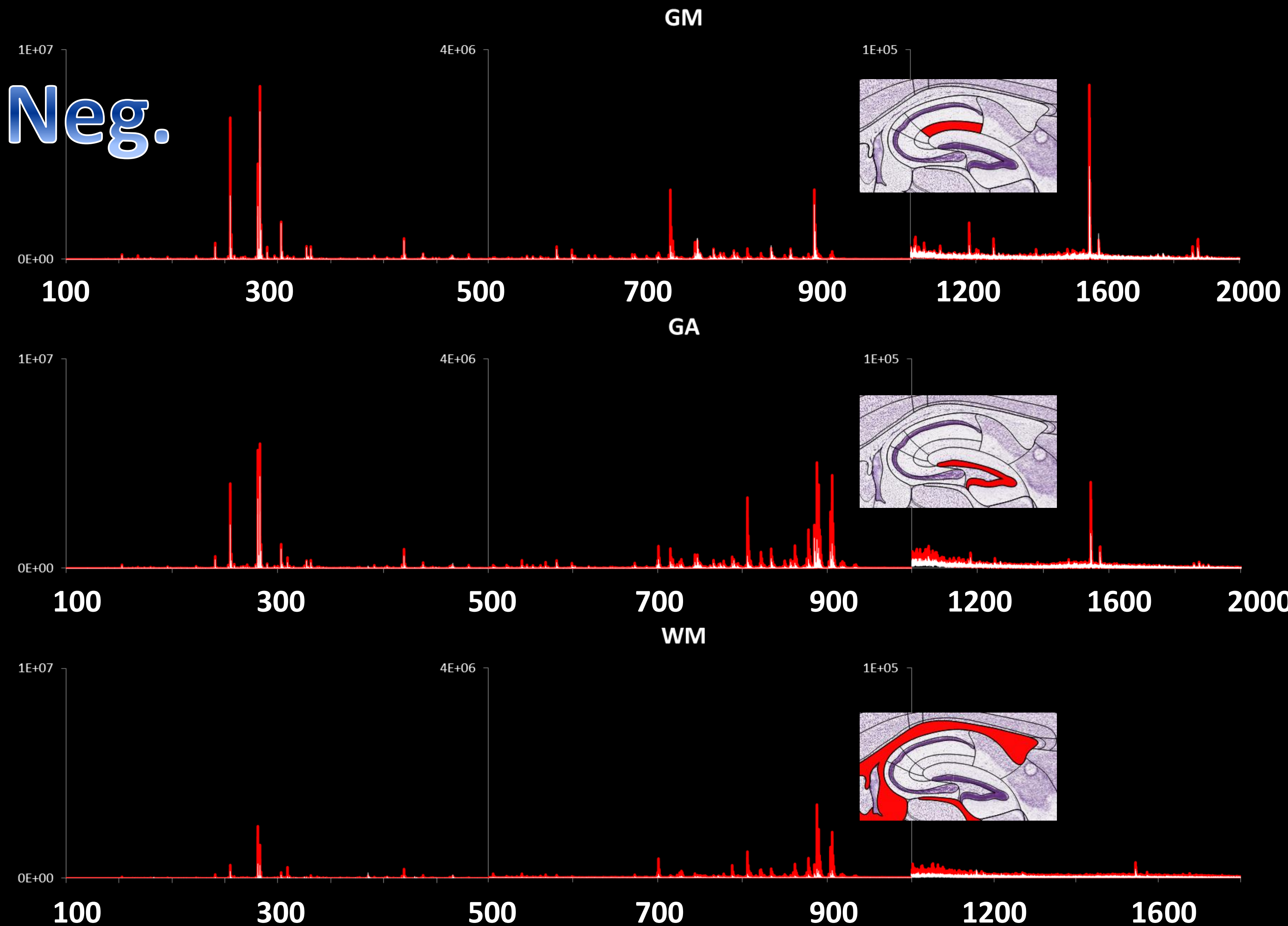


- **60 min NH_3 vapour exposure → signal enhancement neg. mode**
- **30 min TFA vapour exposure → signal enhancement pos. mode**



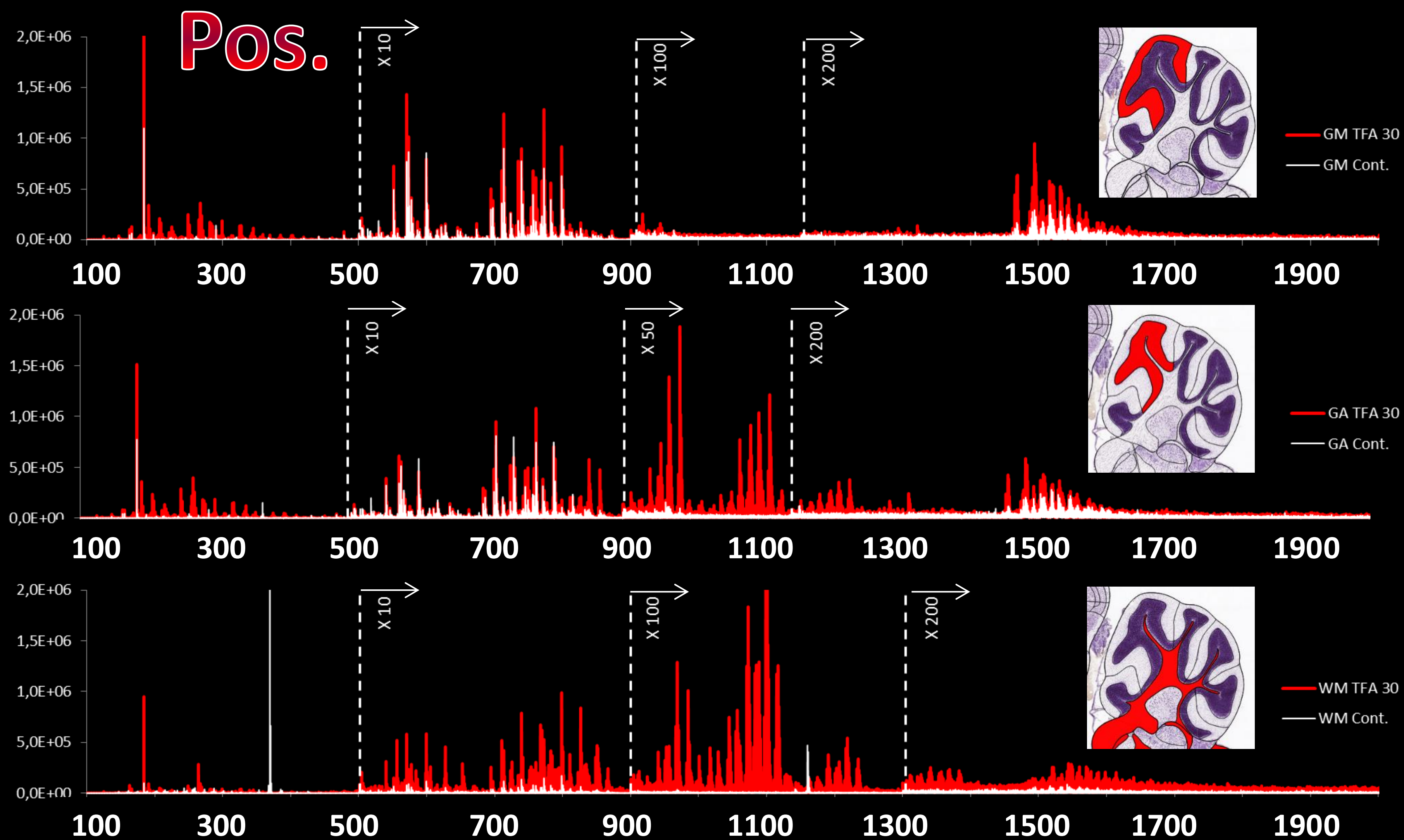
T. B. Angerer, et al. *Analytical Chemistry*, (2015).

Results for Ammonia (NH_3) Treatment



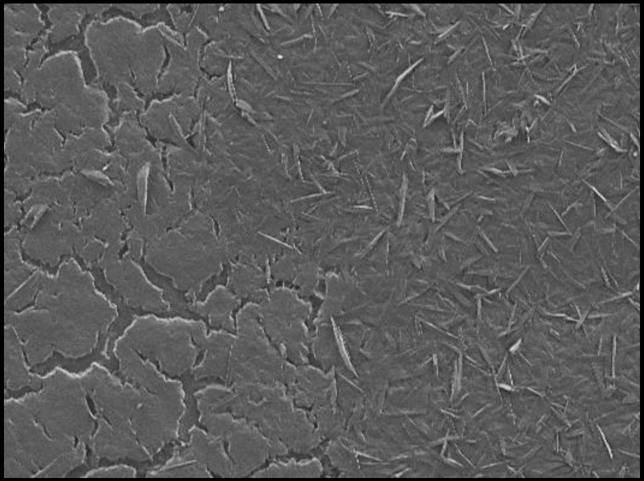
Seetharaman Vaidyanathan, et al. *Surface and Interface Analysis*, (2013).

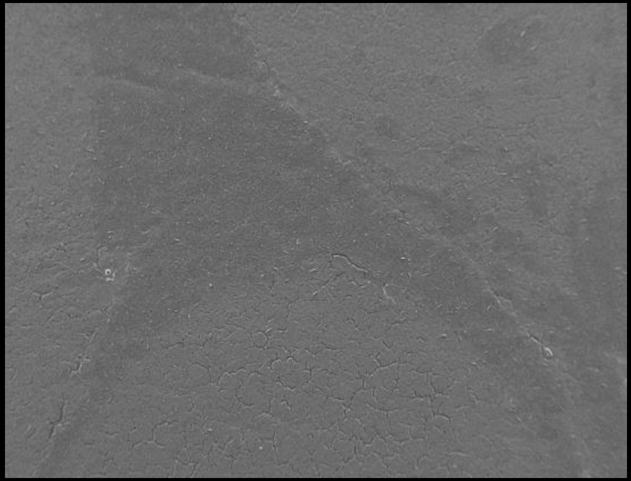
TFA - Spectral Changes in Different Brain Regions



T. B. Angerer, et al. *Analytical Chemistry*, (2015).

SEM of brain tissue with and without TFA

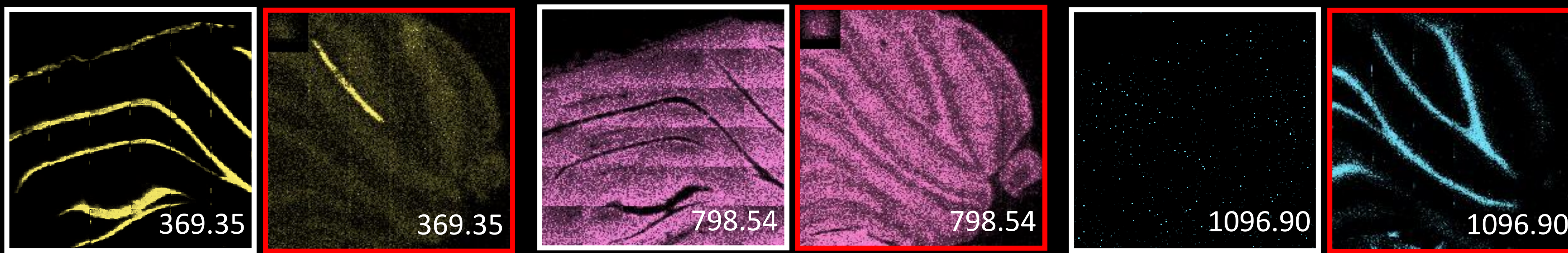




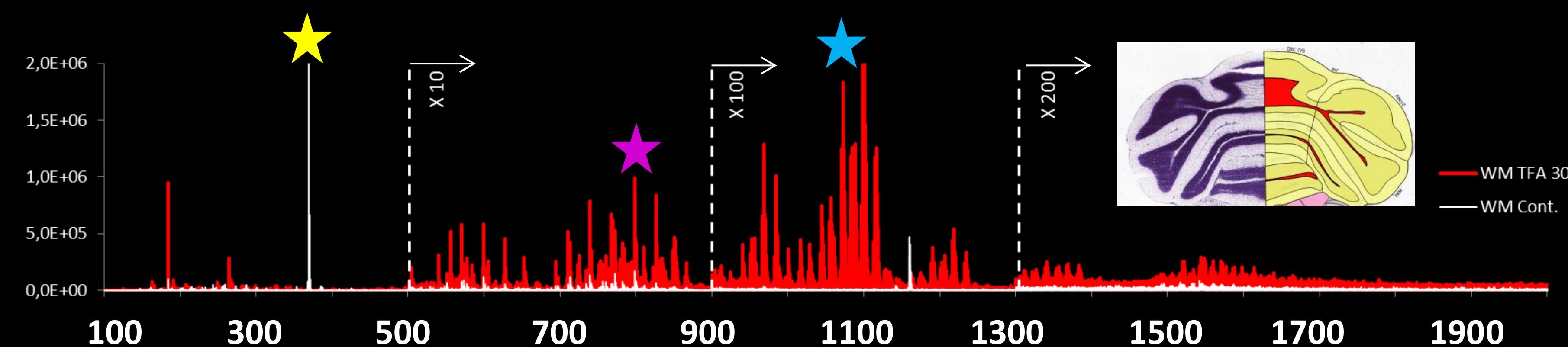
Crystalline features visible on white matter in dry untreated tissue.

Crystals not visible after TFA exposure.

30 min TFA Treatment
-Effects on White Matter

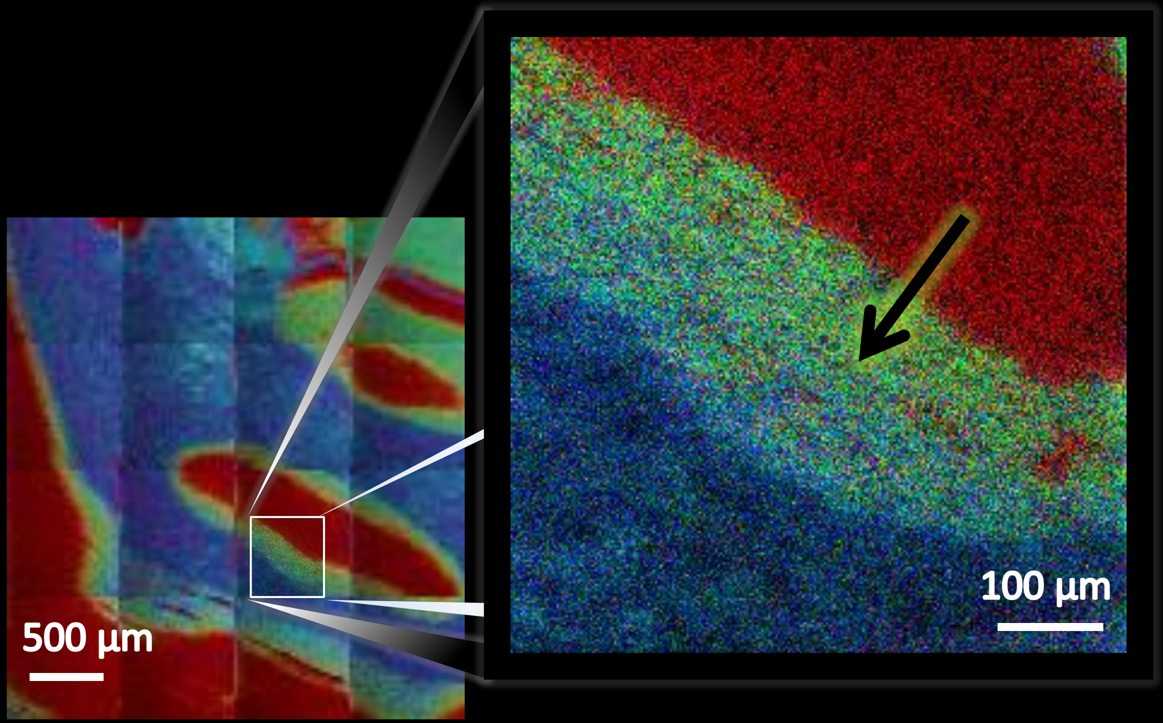


- SIMS + SEM studies confirm cholesterol removal due to TFA exposure
- Abundance of lipids in white matter higher than previously observed
- Cholesterol removal + new ionisation source uncovers unseen molecules



T. B. Angerer, et al. *Analytical Chemistry*, (2015).

High Spatial Resolution Imaging now done on Intact Lipids with Ar_{4000}



m/z	Exact	Δppm	Label	Species	Formula
890.6385	890.6391	-0.64	C24 Sulfatide	$[M-H]^-$	$C_{48}H_{92}SNO_{11}$
906.6328	906.6340	-1.31	C24-OH Sulfatide	$[M-H]^-$	$C_{48}H_{92}SNO_{12}$
885.5509	885.5493	1.83	PI(38:4)	$[M-H]^-$	$C_{47}H_{82}O_{13}P$

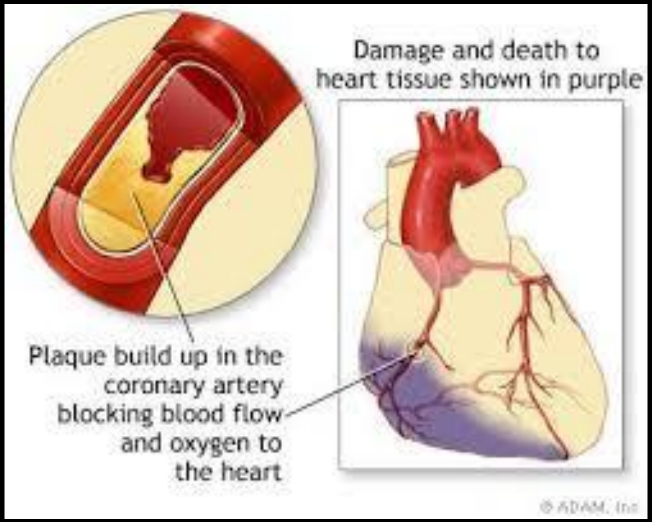
T. B. Angerer, et al. Analytical Chemistry, (2015).

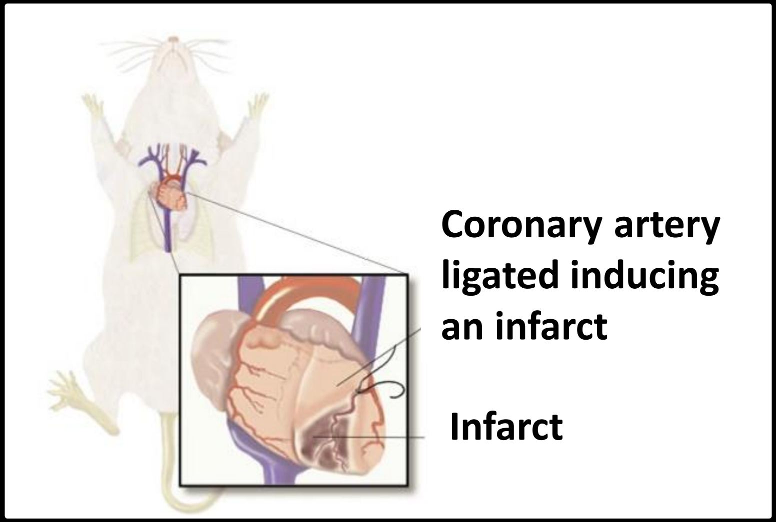
ToF-SIMS using a GCIB for Studies on Lipid Distribution following Myocardial Infarction

SANNA SÄMFORS, Chalmers University of Technology, Sweden, M. HEYDEN, J. BORÉN, University of Gothenburg, Sweden, A.G. EWING, J.S. FLETCHER, Chalmers University of Technology, Sweden

Myocardial Infaction

- Myocardial infarction = heart attack
- Blocking of a vessel going to the heart
- Know risk factors of getting heart attack
- Mechanism of recovery?

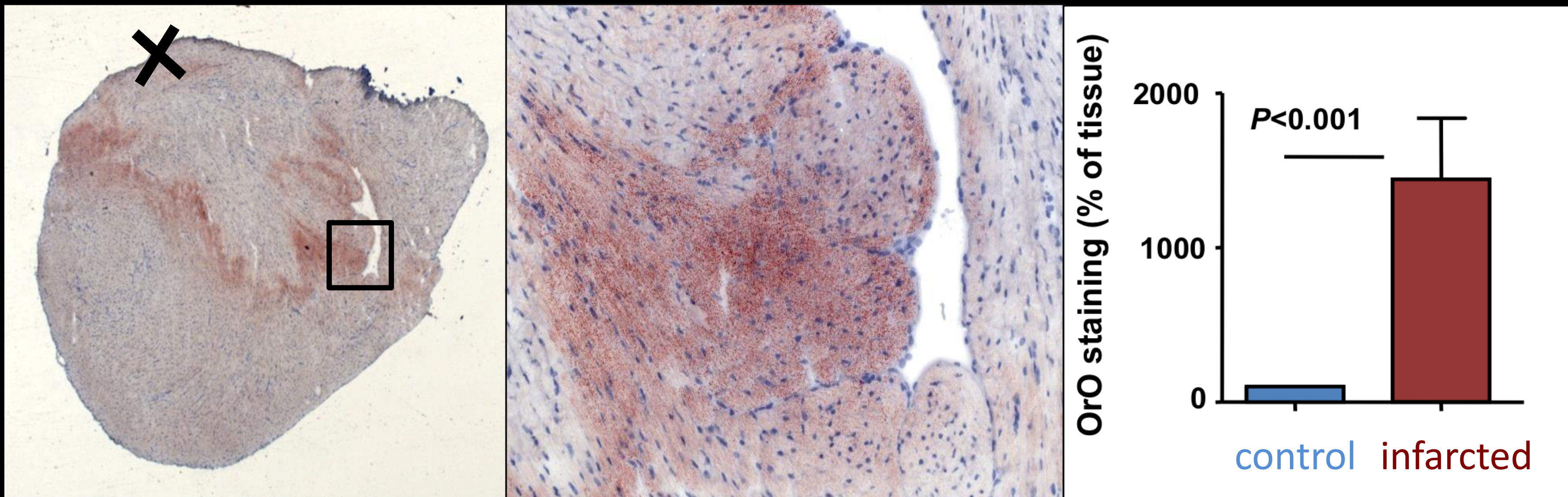




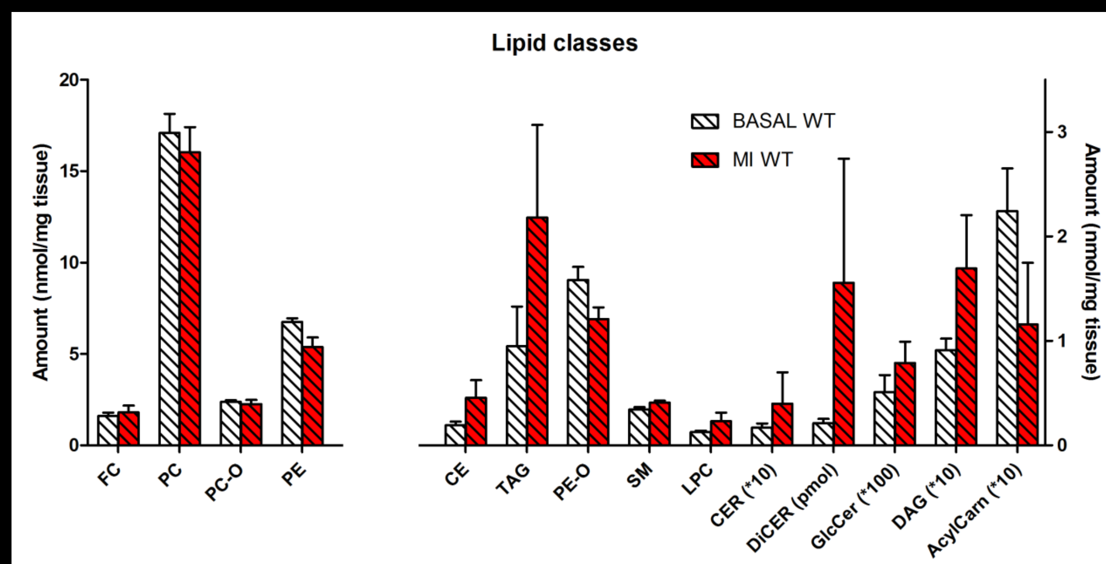
Infarcted heart tissue was imaged after 6 hours of recovery time.

Sham samples (operation but no infarction) were analysed for comparison.

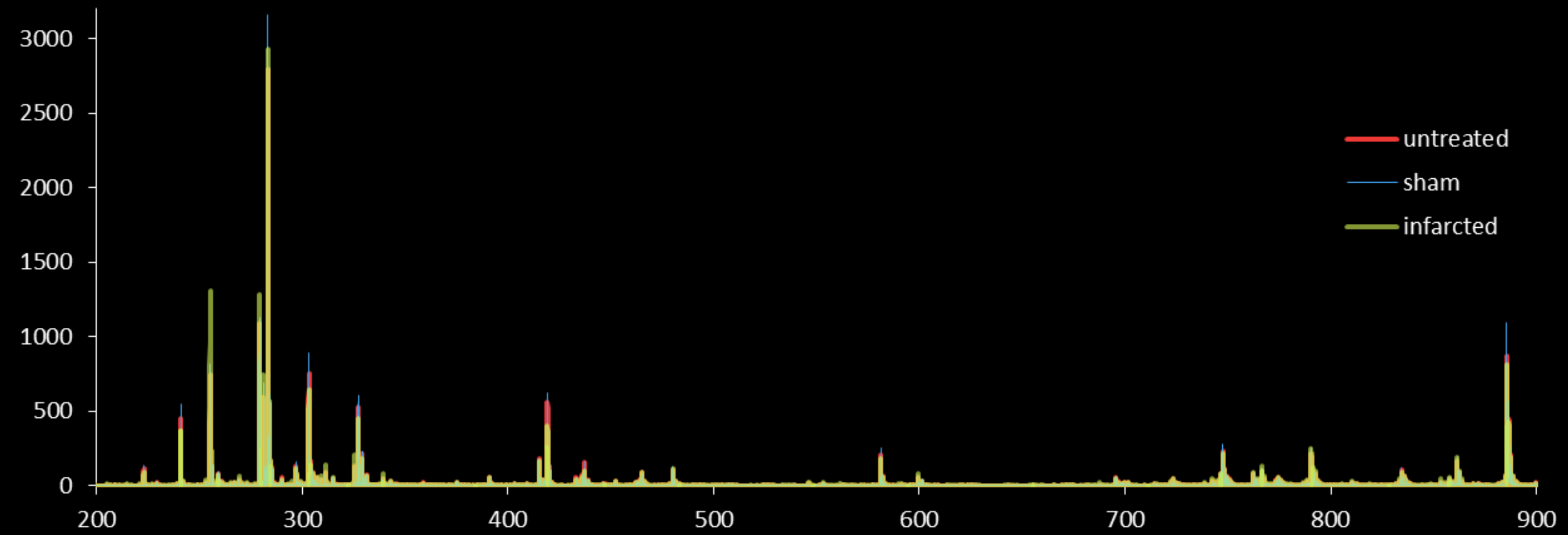
Hypoxia-Induced Cardiac Lipid Accumulation

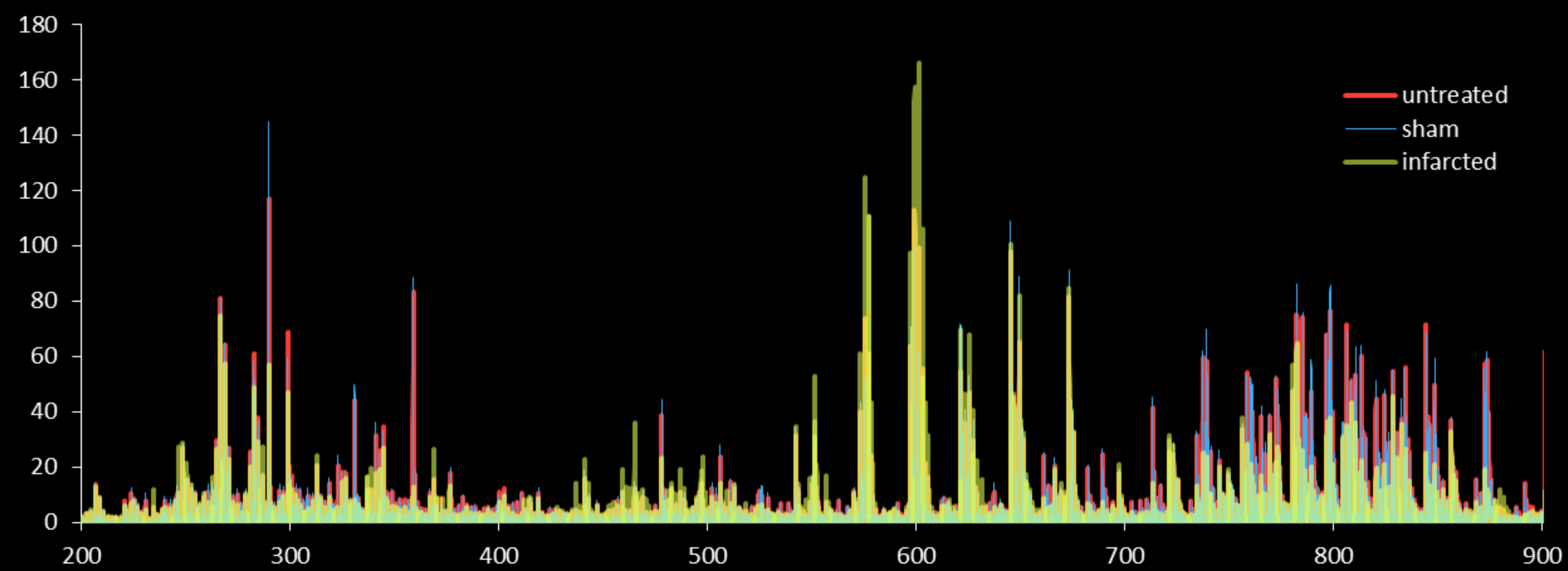


- Accumulation of lipids after infarction ➔ heart failure
- Which lipids are accumulating and how are they distributed?

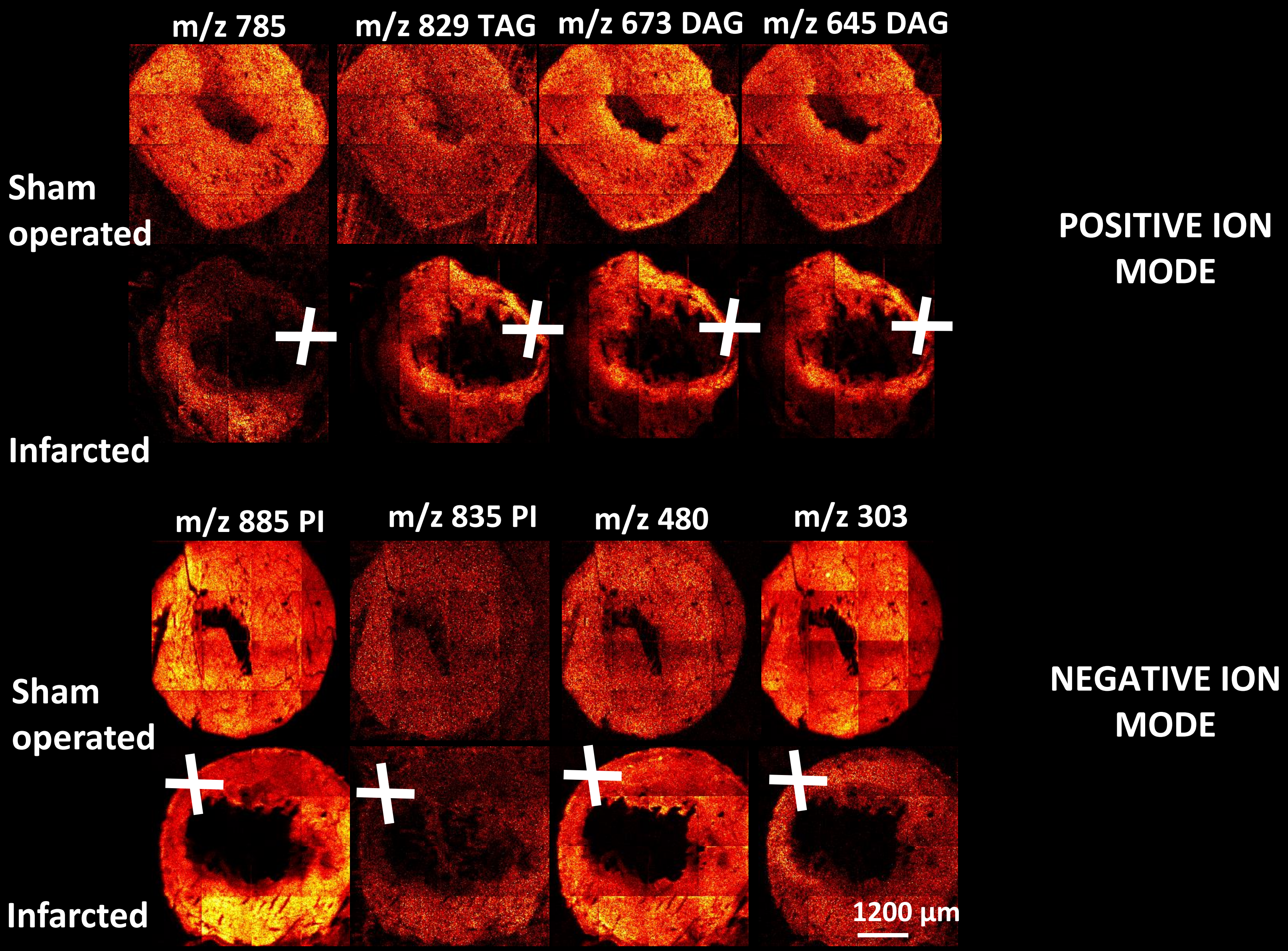


Representative Spectra

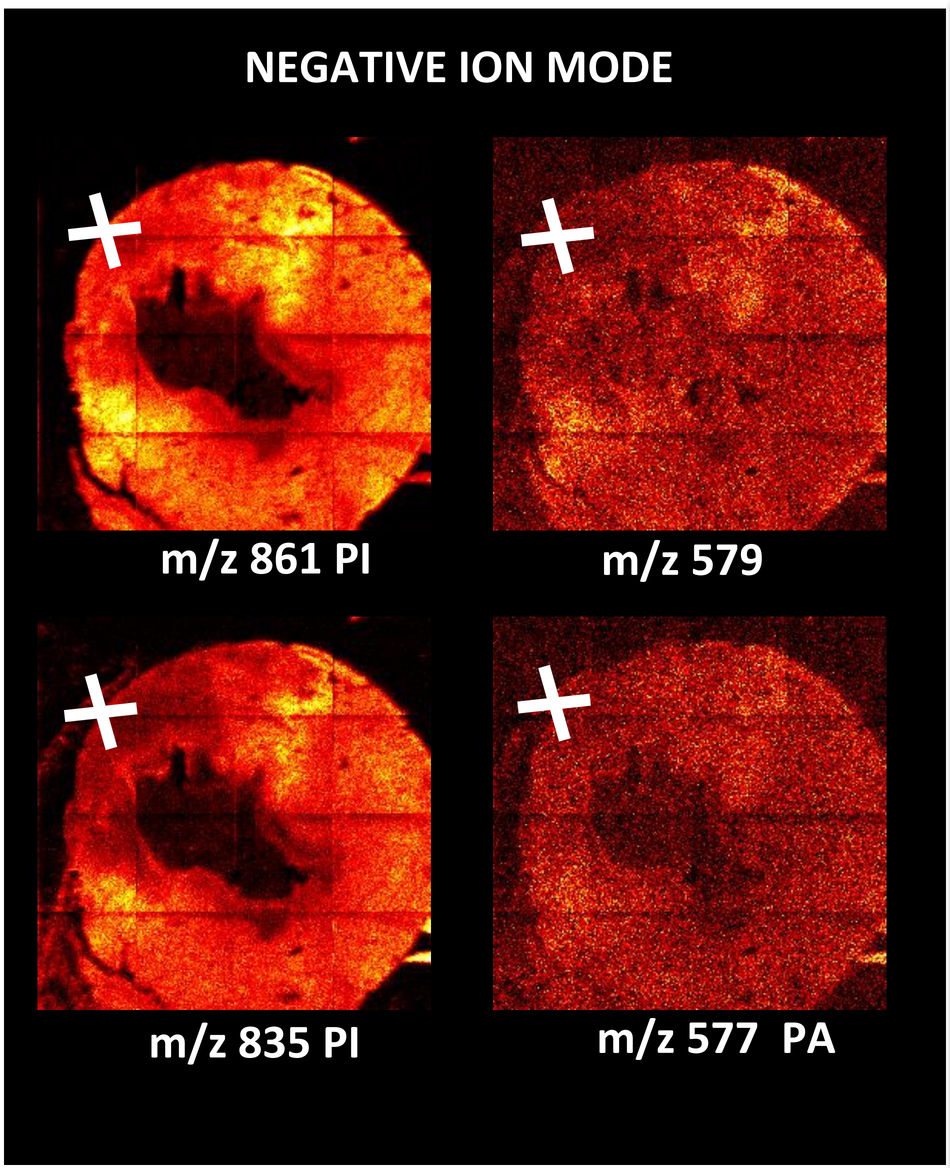


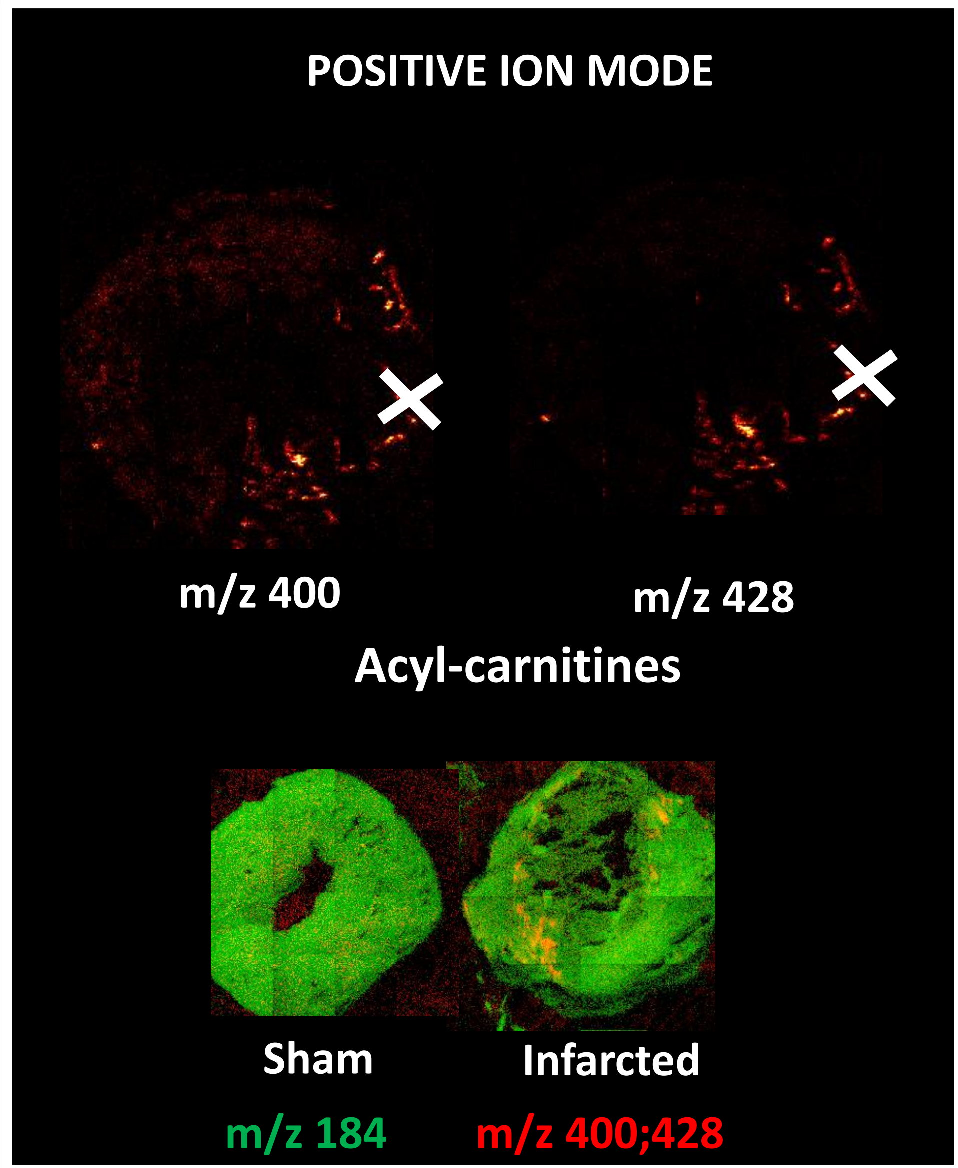


Different Lipid Distribution in Infarcted Heart

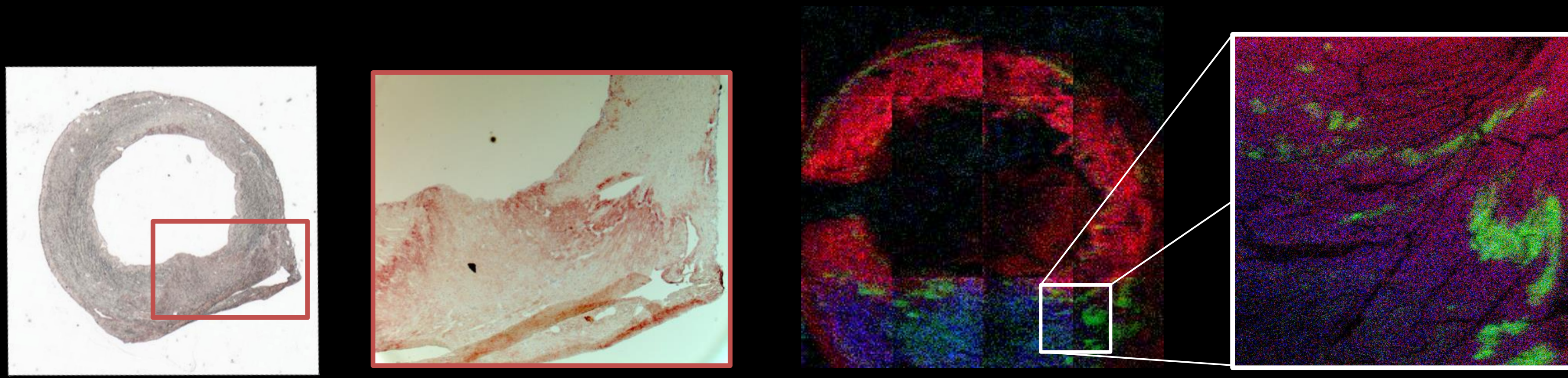


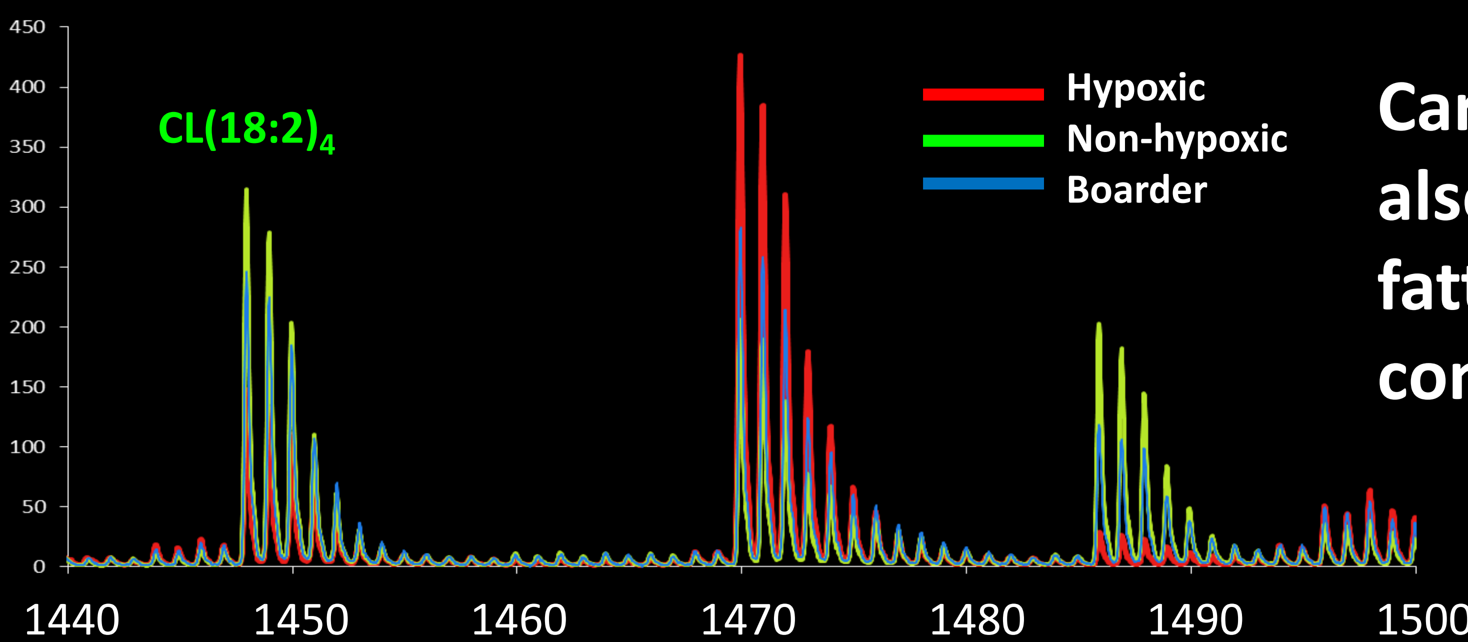
Lipid Distribution in the Border Region





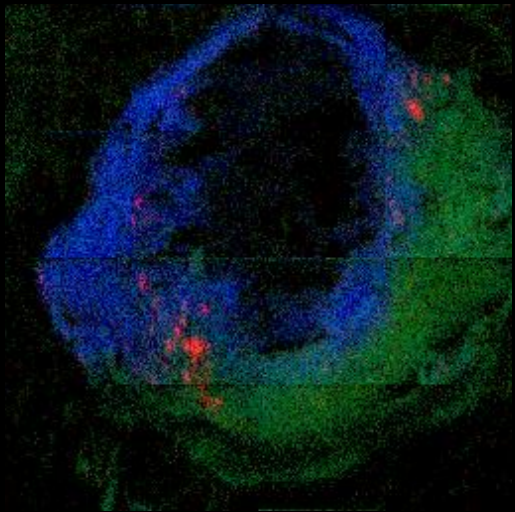
Acyl-carnitines Correlate with Stained Tissue



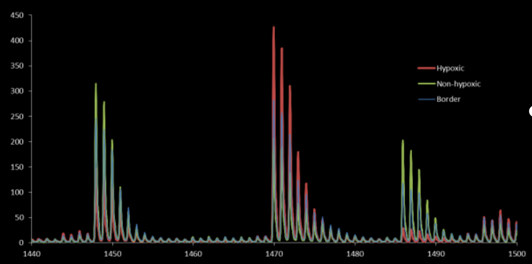


Cardiolipins also change fatty acid composition.

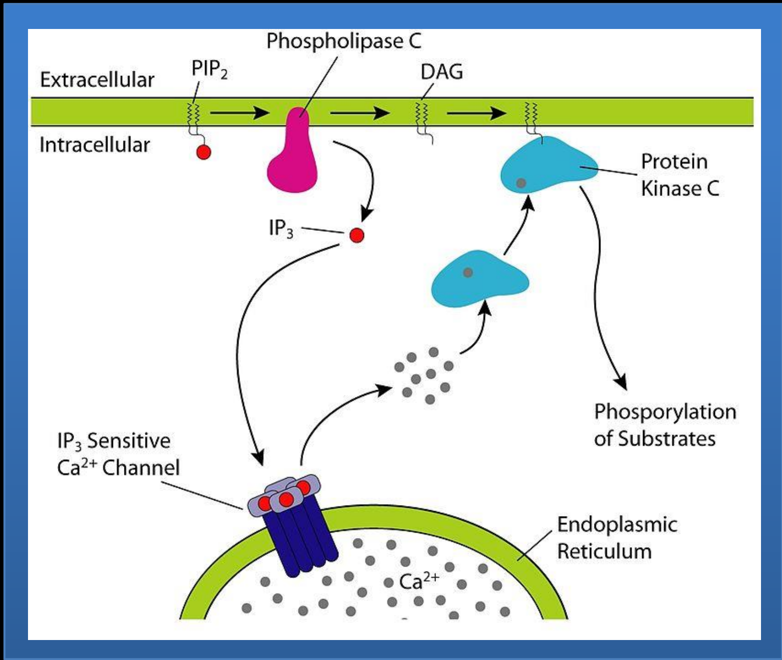
Biological Implications

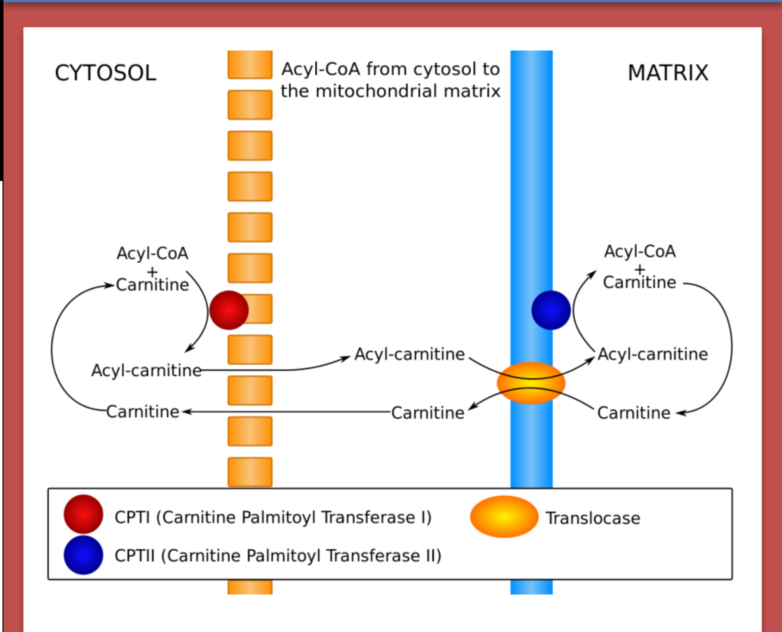


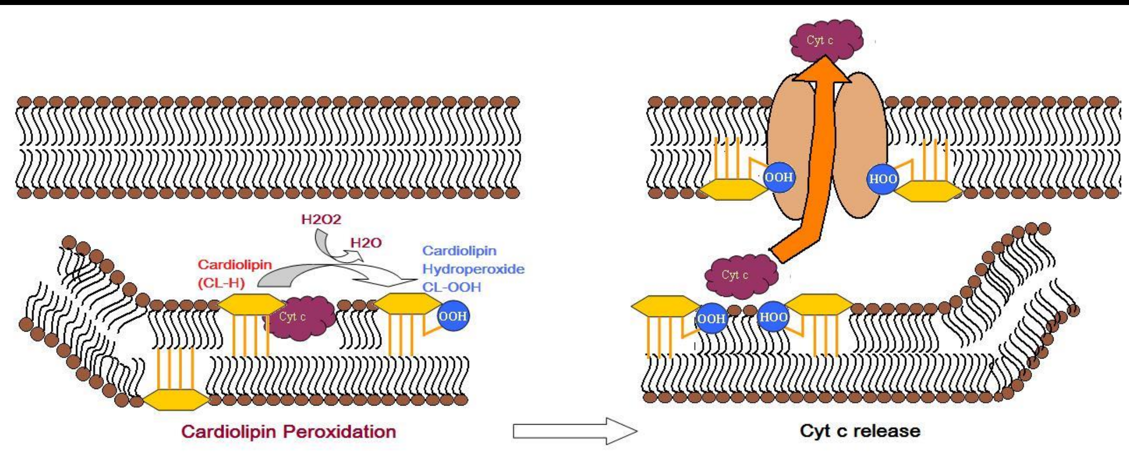
- Hypoxic region: High on DAG + depletion of PI
- Border region: Localisation of acyl-carnitines



- Cardiolipins change FA composition







Conclusions

An increase in demand for improved analysis capabilities for biological samples has led to a series of new instrumental developments.

GCIBs are still an exciting area for development.

We always want more signal!

The use of GCIBs for SIMS facilitates the application of SIMS for biomedical analysis.

The developments do not only benefit bio-research but improved molecular sensitivity, mass accuracy and MSMS benefit a wide range of research areas.