Universität Rostock
HELMHOLTZ MUNICH
JOINT MASS SPECTROMETRY CENTRE

# “How to mine a complex spectrum”

or

# Dealing with Complex Mass Spectrometric Data in the Framework of the EU_FT-ICR_MS Project

**Christopher P. Rüger**
University of Rostock

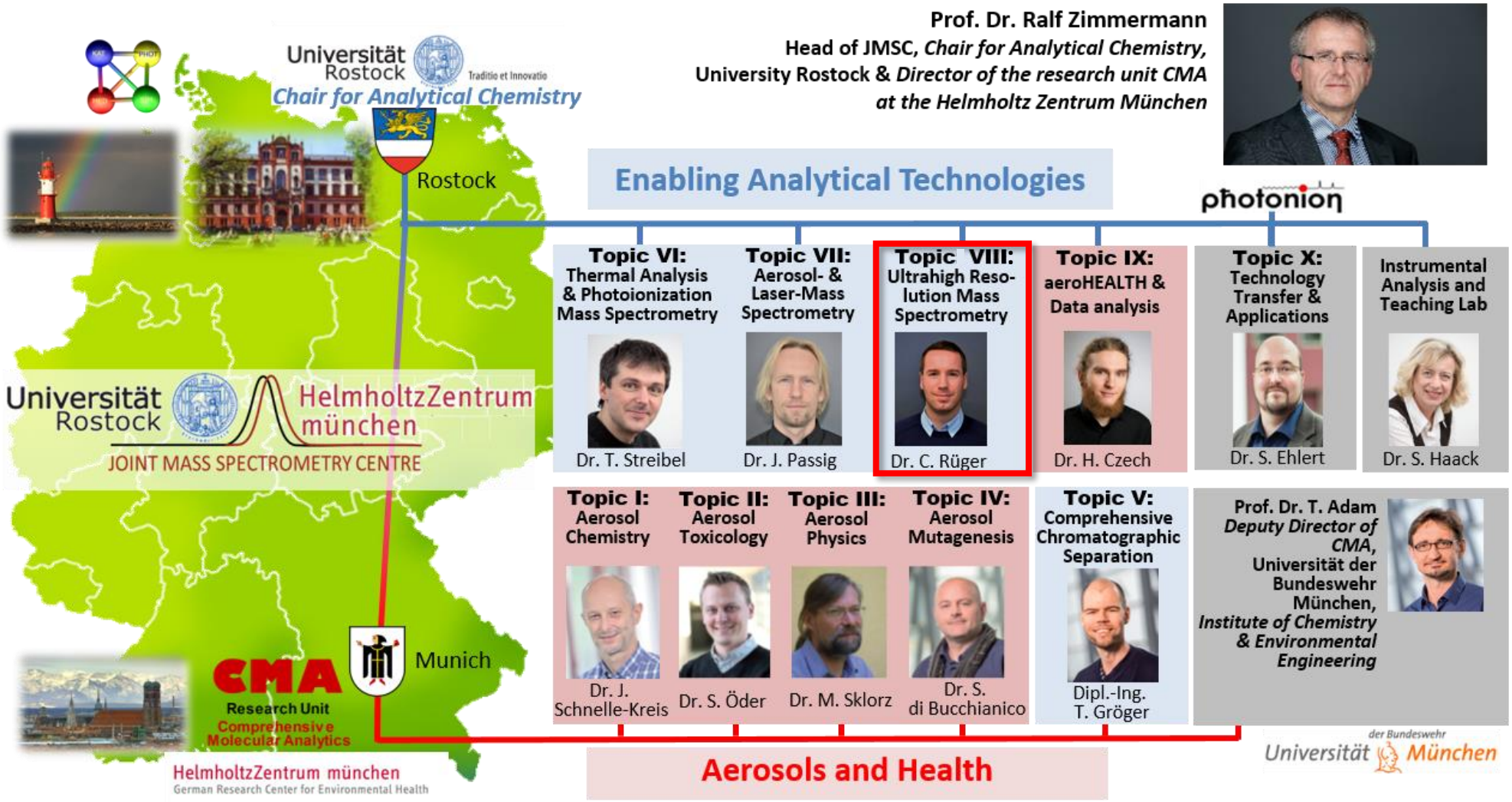
EU FT-ICR MS

**End User School, 12.-16. December 2022, Lille**

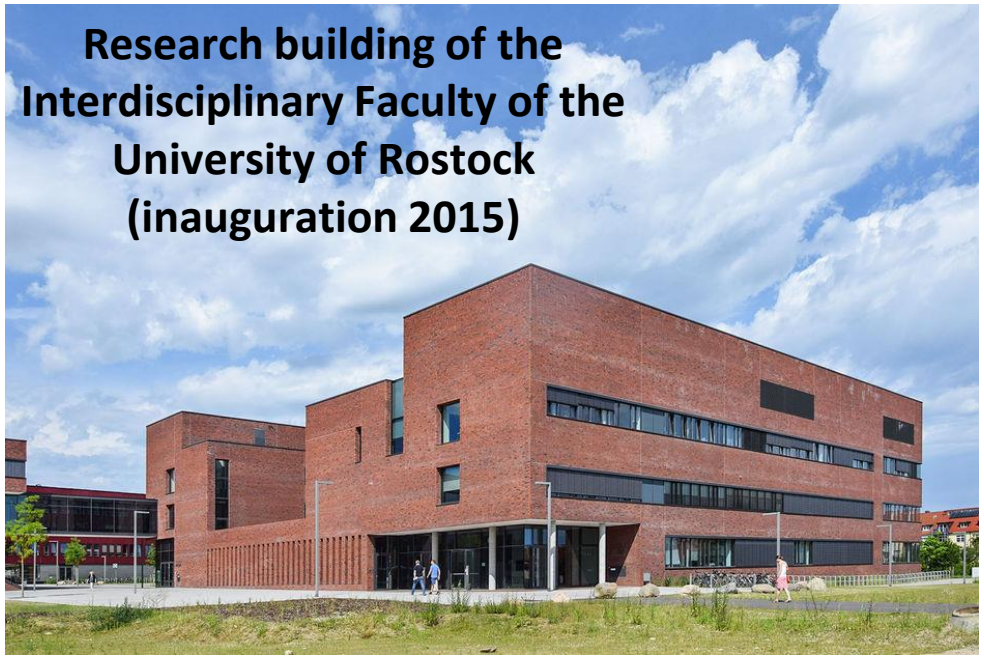
# Lecture Outline

- **Chemical Complexity and Analytical Capabilities** “What does complexity really means?”
- **Challenges in High-Resolution Mass Spectrometry** “Can we cope with the complexity by FT-ICR MS?”
- **From Transient to Mass Spectrum**
- **Utilizing the Mass Spectrum Data and Feature Detection** “Where are the good data?”
- **From Mass to Chemistry** “How to convert numbers to science?”
- **Handling Attribution Data** “Thousands of Elemental Compositions and now?
- **Research Examples from our Group** – From Energy Transition to Environmental Sciences
- **Summary and Outlook** “Are we there yet?”

# Joint Mass Spectrometry Centre



# Analytical Chemistry at University of Rostock



**Research building of the Interdisciplinary Faculty of the University of Rostock (inauguration 2015)**

**New extension building of the Institute of Chemistry of the University of Rostock (inauguration 2022)**


**Some insights into the mass spectrometry laboratories**

# Topic: High-Resolution Mass Spectrometry

## Group leader: Christopher Rüger







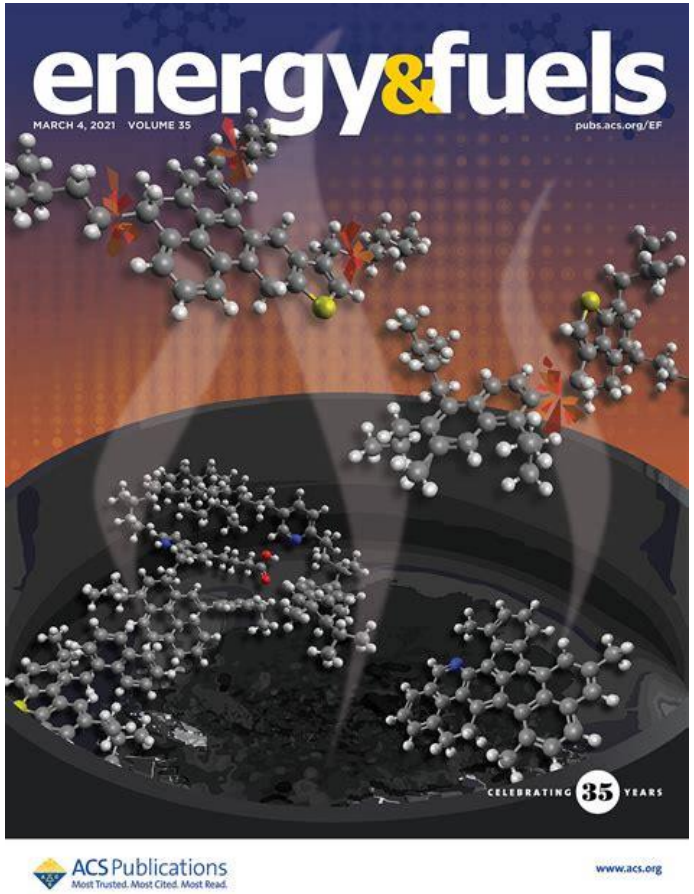
Ole Tiemann
Lars Kurths
Abdulghani Ebtini
Eric Schneider
Silvia Vesga-Martinez
Jan Heide
Lukas Fried
Julian Schade
Paul Kösling
Anika Neumann



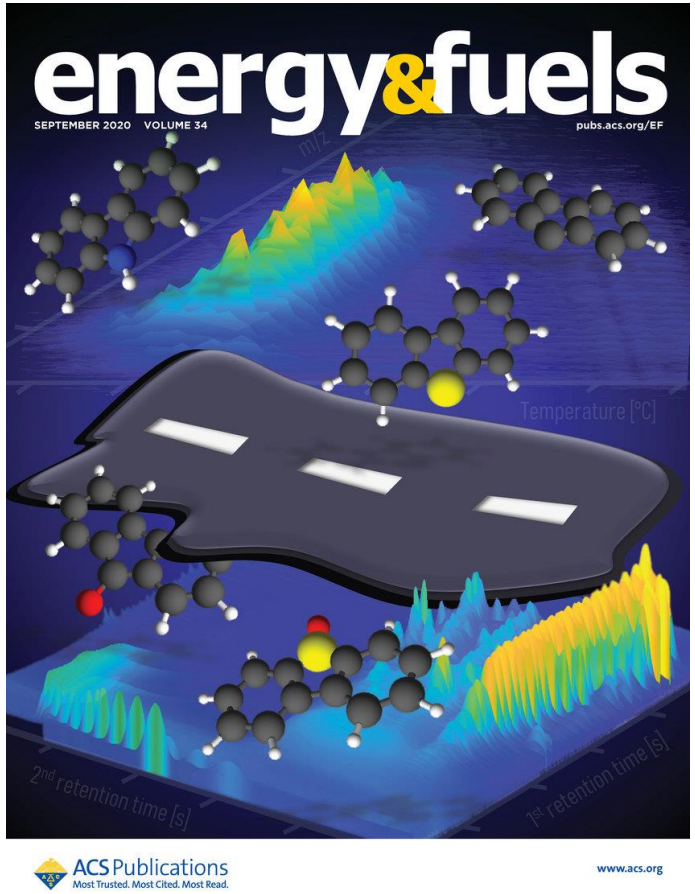

**Main research aim:**
Developing high-resolution mass spectrometry based technologies based on soft (photo) ionization and evolved gas analysis for complex mixtures (fuels, materials, and environment).

# Impact of EU_FT-ICR_MS on Univ. of Rostock

January 2021 – Thesis Defense Anika Neumann (COVID-19 affected)




Neumann et al., Energy and Fuels 2021, 35, 5, 3808–3824



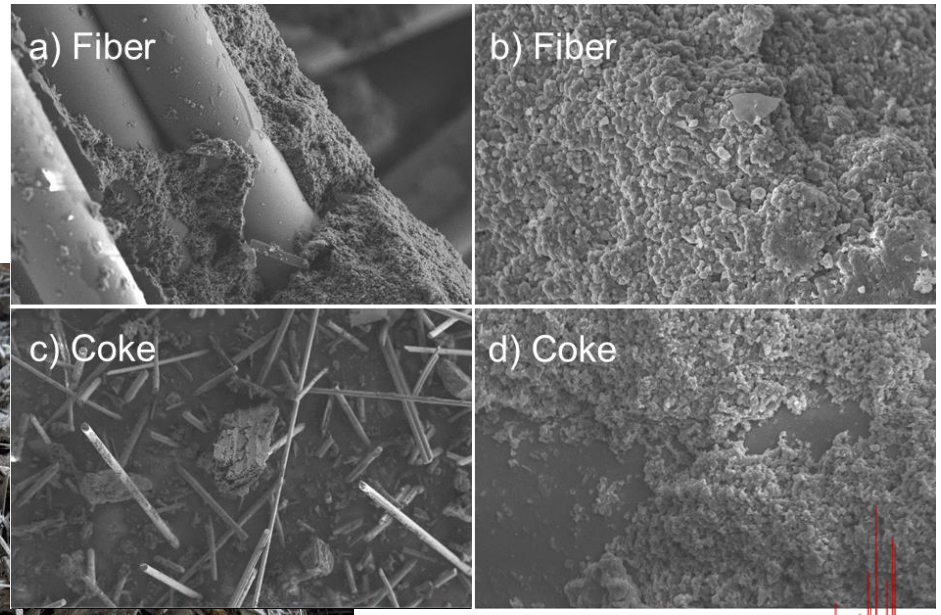

Neumann et al., Energy and Fuels 2020, 34, 9, 10641–10654

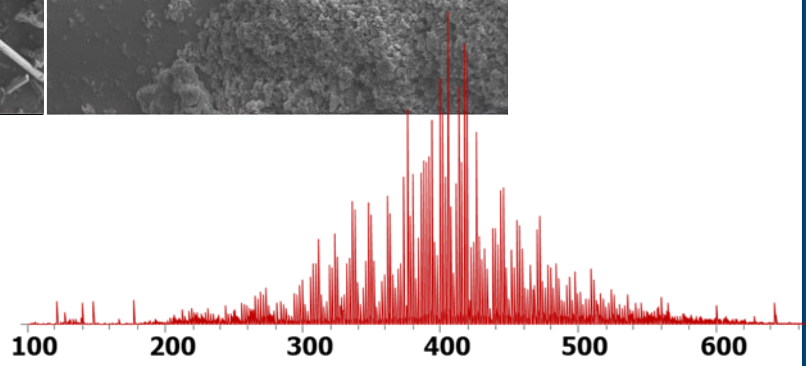
# Impact of EU_FT-ICR_MS on Univ. of Rostock

**Fostering Energy Transition and Recycling as Research Topics**

PhD Thesis of Lukas Friederici on composite recycling guided by thermal analysis mass spectrometry

Sampling next to pilot plant for pyrolytic composite recycling



# Impact of EU_FT-ICR_MS on Univ. of Rostock

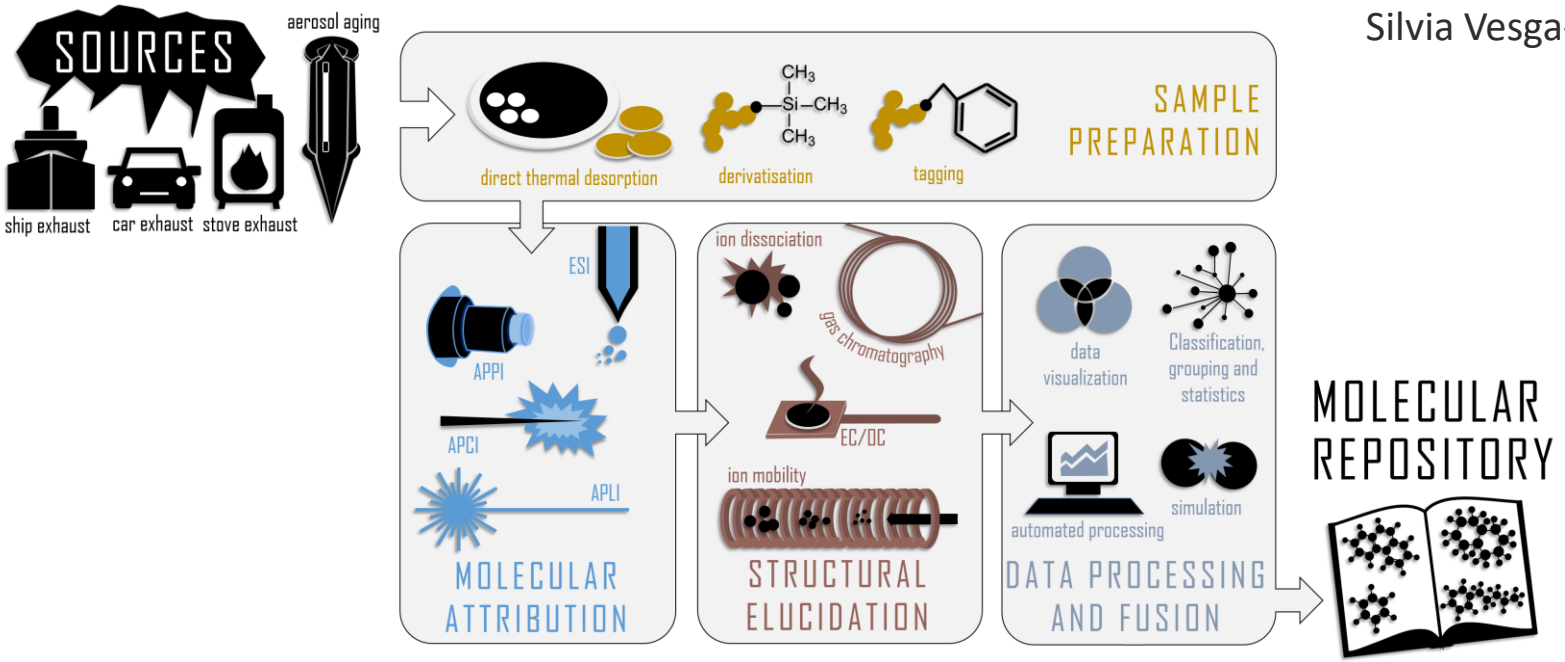
New Projects Resulted from the Network with New Faces:

DFG Deutsche Forschungsgemeinschaft

ANR AGENCE NATIONALE DE LA RECHERCHE

**DFG-ANR 3-year research project TIMSAC**

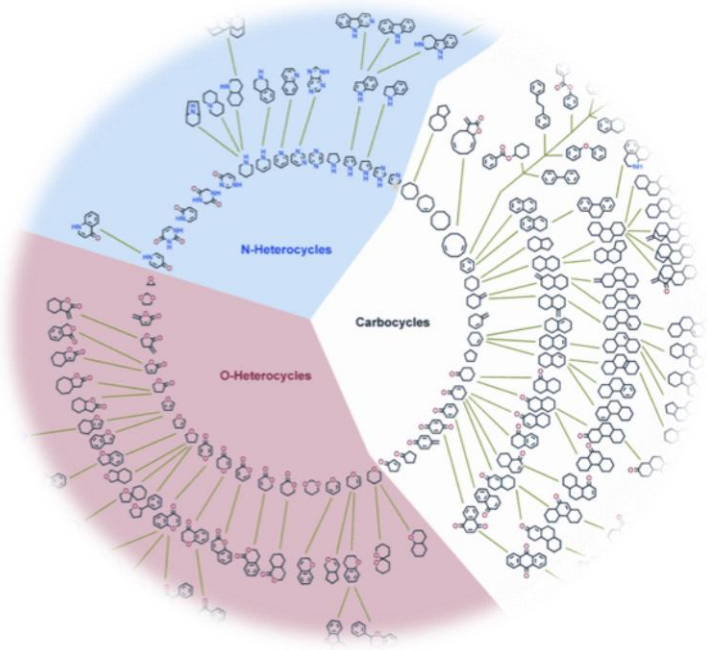
**Thermal analysis and ion mobility coupled to high-resolution mass spectrometry for organic aerosol characterization**

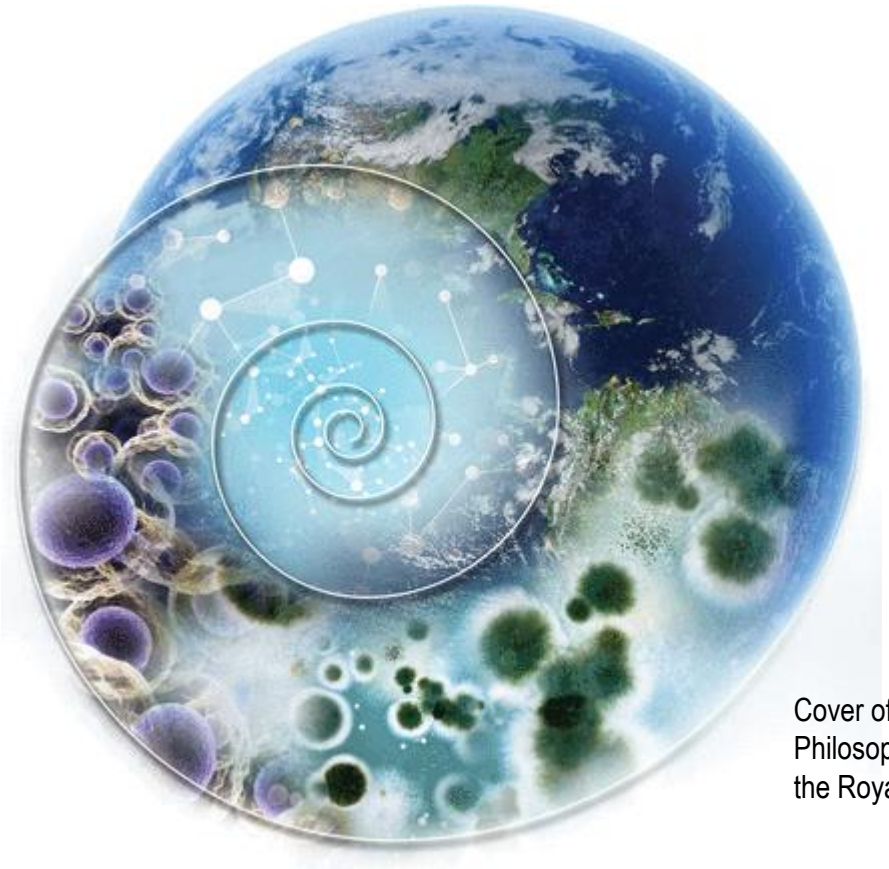



Maxime Sueur &
Silvia Vesga-Martinez

# Complex Mixtures - Motivation

## Complexity of organic mixtures – The chemical space



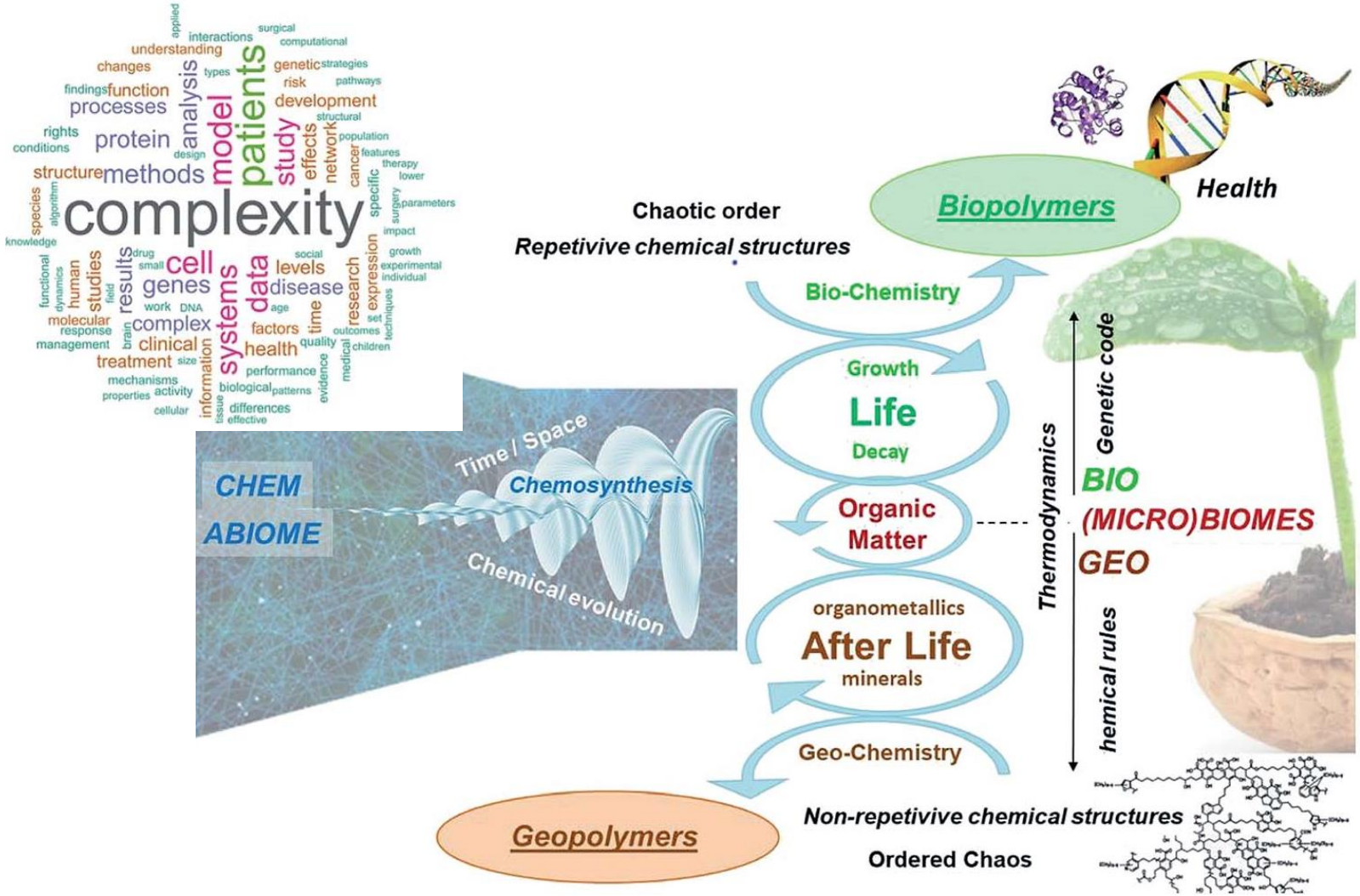



Cover of Vol. 375, 2109,
Philosophical Transactions of
the Royal Society A, Dec. 2017

Estimated number of organic molecules with MW < 500: $10^{62}$

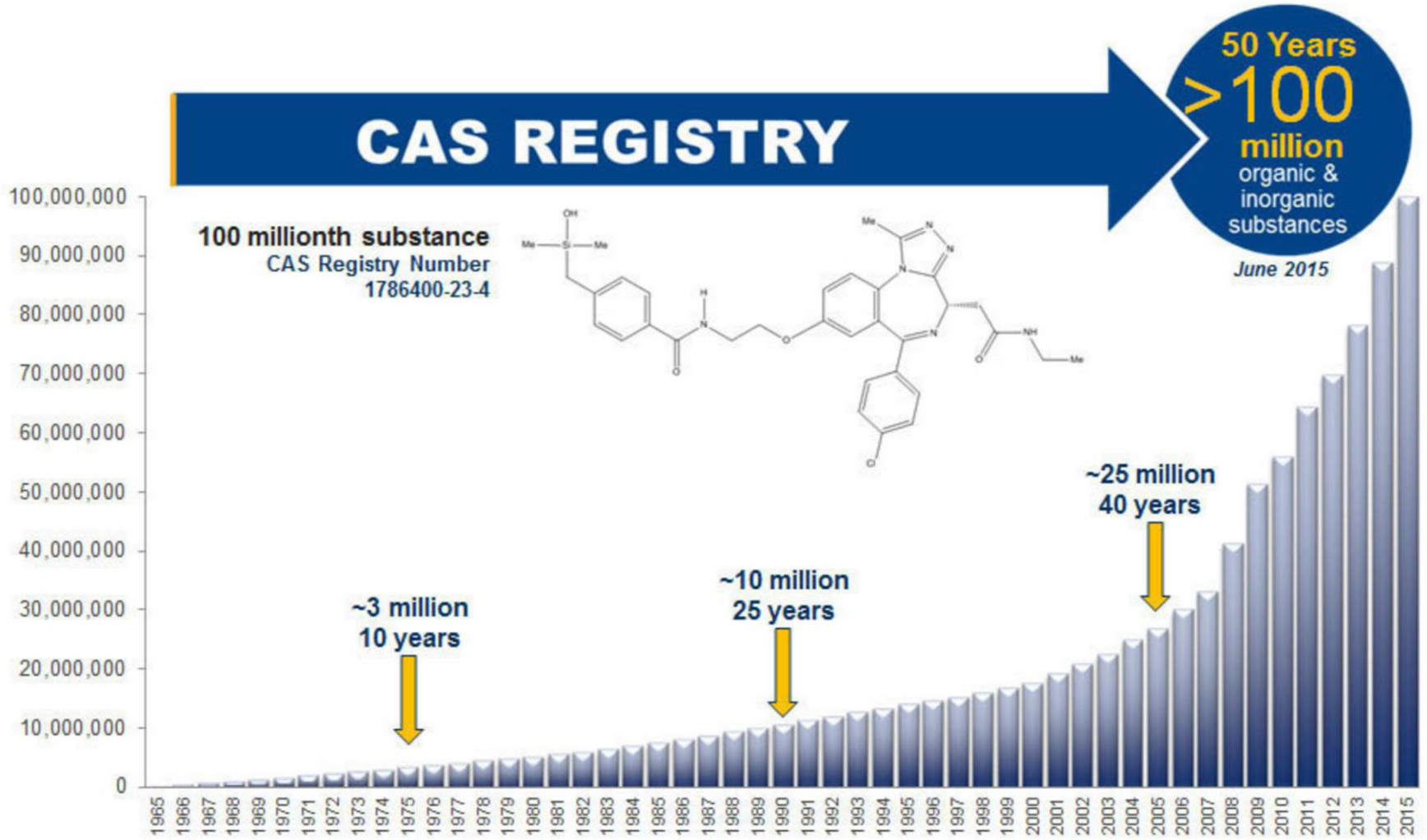
Bohacek, R. S., McMartin, C., and Guida, W. C. (1996), Med. Res. Rev. 16, 3−50

# Complex Mixtures – Everywhere in Science



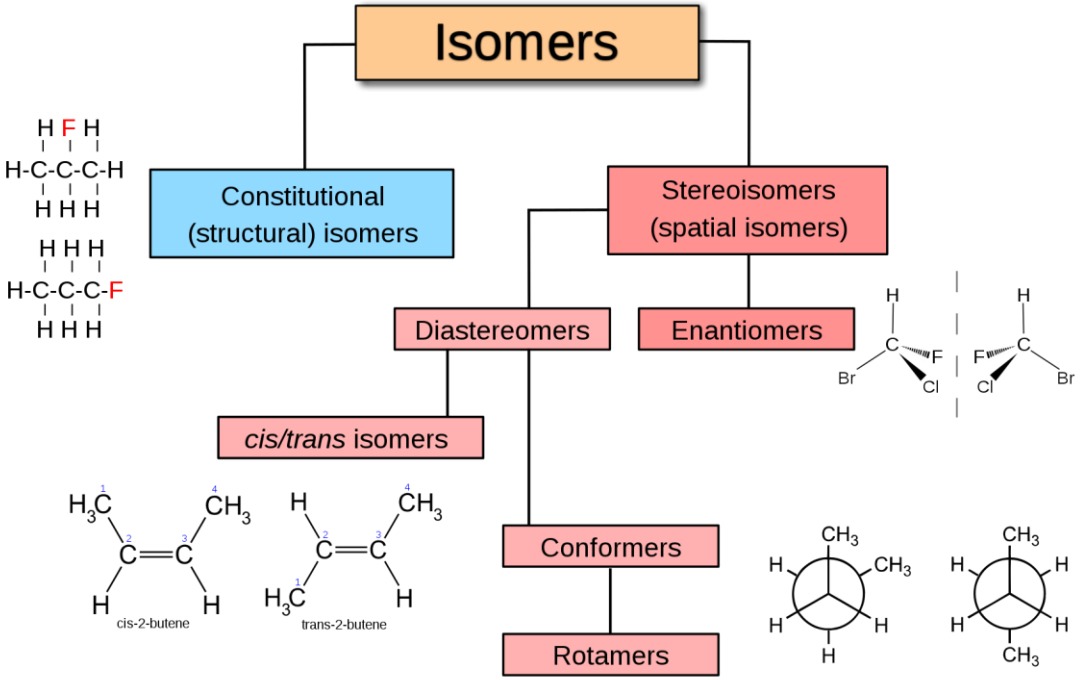

Schmitt-Kopplin et al., *Faraday Discussions*, **2019**, *218, 9-28*

# Complex Mixtures – Data Bases



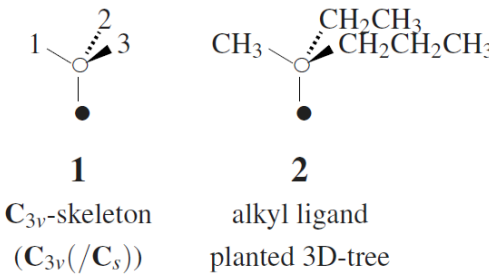

**Other useful general databases:** NIST Webbook (US), ChemSpider (RCS), Pubchem (NIH), HMDB, …

# Complex Mixtures – Isomers




**Isomers in complex mixtures to be tackled by:**

- fragmentation, MS/MS
- pre-ionization separation, *e.g.*, LC, GC
- post-ionization separation, *e.g.*, IMS



**1** $C_{3v}$-skeleton ($C_{3v}(/C_s)$)

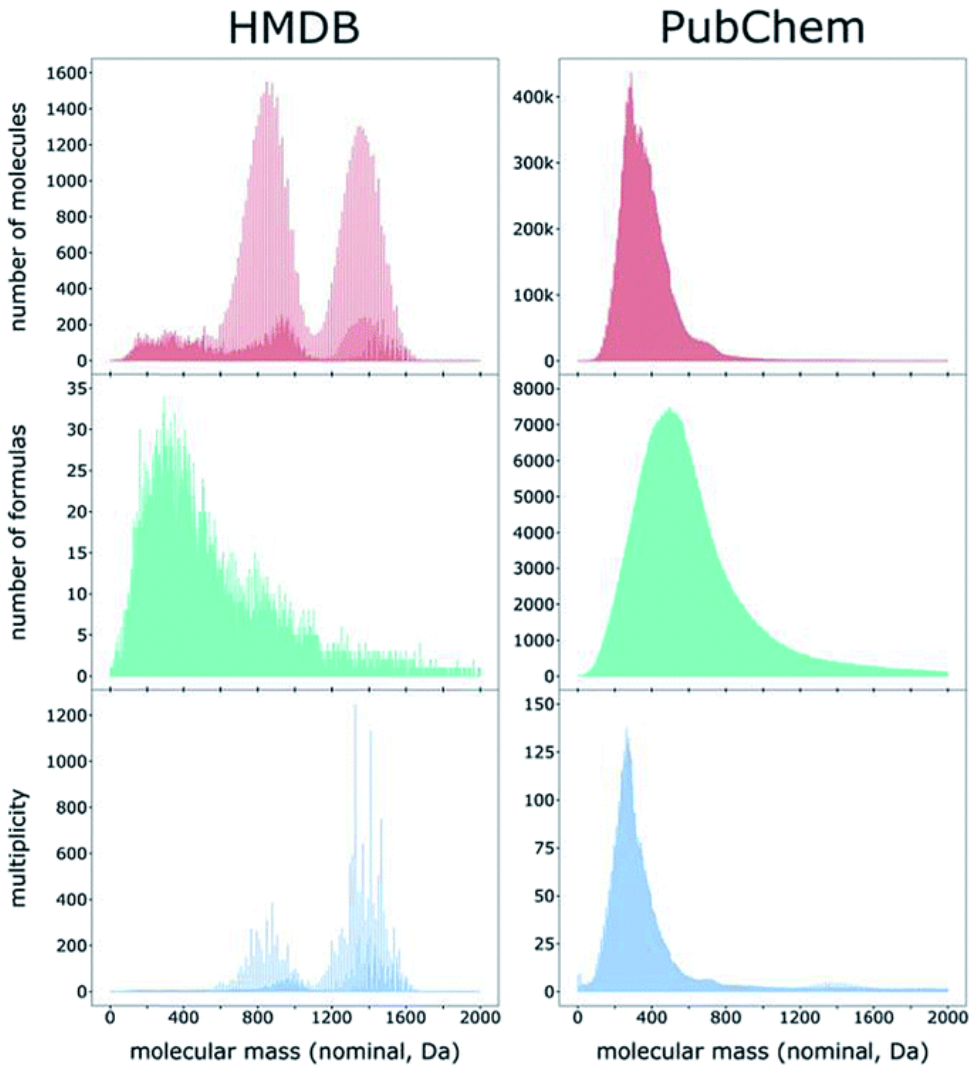
**2** alkyl ligand planted 3D-tree

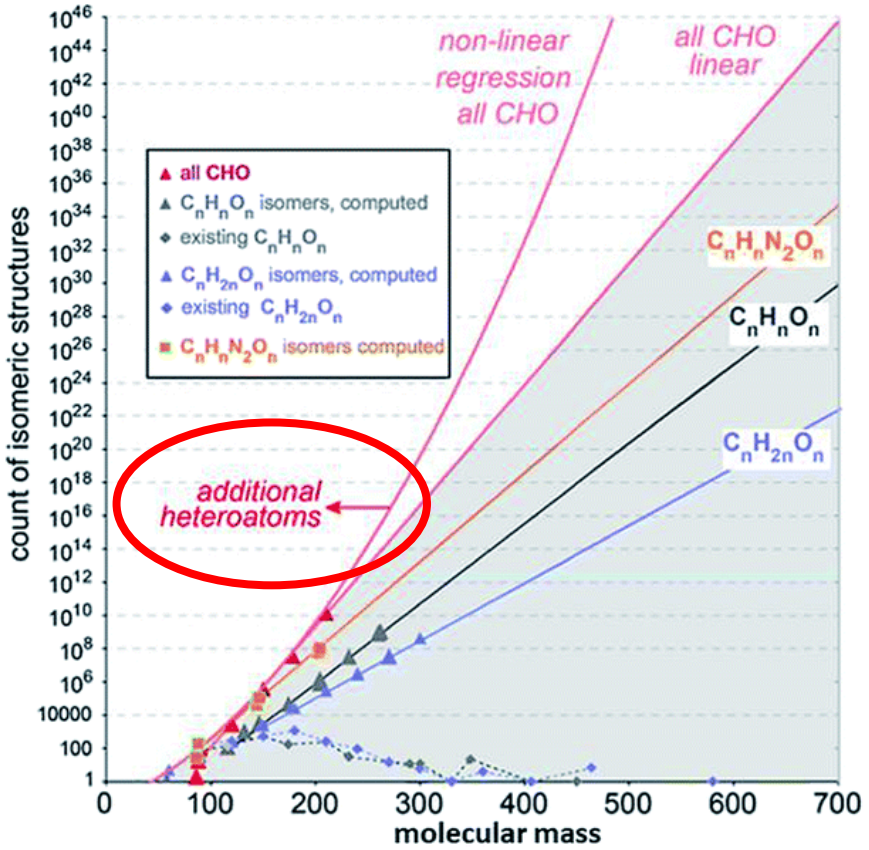
Fujita, *MATCH Commun. Math. Comput. Chem.* **57** (2007) 299-340

Table 1: Numbers of Centroidal Alkanes as Stereoisomers

| $k$ | $\widehat{B}_k$ (Total) | $\widehat{A}_k$ (Achiral) | $\widehat{C}_k$ (Chiral) |
|---|---|---|---|
| 1 | 1 | 1 | 0 |
| 2 | 0 | 0 | 0 |
| 3 | 1 | 1 | 0 |
| 4 | 1 | 1 | 0 |
| 5 | 3 | 3 | 0 |
| 6 | 2 | 2 | 0 |
| 7 | 9 | 7 | 2 |
| 8 | 8 | 7 | 1 |
| 9 | 38 | 21 | 17 |
| 10 | 46 | 22 | 24 |
| 11 | 203 | 61 | 142 |
| 12 | 283 | 72 | 211 |
| 13 | 1299 | 186 | 1113 |
| 14 | 2004 | 220 | 1784 |
| 15 | 9347 | 567 | 8780 |
| 16 | 15758 | 717 | 15041 |
| 17 | 72505 | 1755 | 70750 |
| 18 | 129281 | 2209 | 127072 |
| 19 | 589612 | 5454 | 584158 |
| 20 | 1098656 | 7149 | 1091507 |
| 21 | 4954686 | 17070 | 4937616 |
| 22 | 9576645 | 22476 | 9554169 |
| 23 | 42671509 | 53628 | 42617881 |
| 24 | 84998202 | 72656 | 84925546 |
| 25 | 374749447 | 169175 | 374580272 |
| 26 | 765965475 | 229676 | 765735799 |
| 27 | 3344714436 | 535267 | 3344179169 |
| 28 | 6992429665 | 743026 | 6991686639 |
| 29 | 30264120901 | 1698322 | 30262422579 |
| 30 | 64538102227 | 2361476 | 64535740751 |
| 31 | 277096805630 | 5400908 | 277091404722 |
| 32 | 601441729659 | 7642893 | 601434086766 |
| 33 | 2563418291362 | 17211368 | 2563401079994 |
| 34 | 5652900424627 | 24394779 | 5652876029848 |
| 35 | 23931052067297 | 54947147 | 23930997120150 |
| 36 | 53534903586744 | 79009726 | 53534824577018 |
| 37 | 225226025743122 | 175702378 | 225225850040744 |
| 38 | 510446528635659 | 252964410 | 510446275671249 |
| 39 | 2135109239262173 | 562645937 | 2135108676616236 |
| 40 | 4896889667780240 | 819922295 | 4896888847857945 |
| 41 | 20372876580255143 | 1804088396 | 20372874776166747 |
| 42 | 47238614063478058 | 2631820744 | 47238611431657314 |
| 43 | 195544793394384827 | 5791497722 | 195544876022887105 |
| 44 | 457999560484205773 | 8536377160 | 457999551947828613 |
| 45 | 1886989279103128211 | 18611821161 | 1886989260491307050 |
| 46 | 4461040396950967790 | 27458156708 | 4461040369492811082 |
| 47 | 18298681742426380229 | 59870273288 | 18298681682556106941 |
| 48 | 43636081544149901047 | 89120741244 | 43636081455029159803 |
| 49 | 178246302614039769705 | 192762694240 | 178246302421277075465 |
| 50 | 428497965173462968567 | 287167536146 | 428497964886295432421 |
| 51 | 1743475977870305954708 | 621145058010 | 1743475977249160896698 |
| 52 | 4222957579213874326998 | 932636649624 | 4222957578281237677374 |
| 53 | 17118606500538110493165 | 2003060193783 | 17118606498535050299382 |
| 54 | 41757573020631974557921 | 3009644412440 | 41757573017622330145481 |
| 55 | 168676827177458246245600 | 6464001746606 | 168676827170994244498994 |
| 56 | 414192406700454644211608 | 9780036558542 | 414192406690674607653066 |
| 57 | 1667507044106396700614662 | 20873421744449 | 1667507044085523278870213 |
| 58 | 4120269449060079231919190 | 31600908341722 | 4120269449028478323577468 |
| 59 | 16535111535321800418856805 | 67445191538640 | 16535111535254355227318165 |
| 60 | 41098222466126905529132145 | 102743321459580 | 41098222466024162207672565 |
| 61 | 164431691004690928193898010 | 218049903481679 | 164431691004472878290416331 |
| 62 | 410979018222119235952994626 | 332350277618212 | 410979018221786885675376414 |
| 63 | 1639544206288762558253253718 | 705330165952872 | 1639544206288057228087300846 |
| 64 | 4119529788256533749220428115 | 1081087049647181 | 4119529788255452666170780934 |
| 65 | 16388819934893627771459167067 | 2282686396696017 | 16388819934891345085062471050 |
| 66 | 41385225782249836799266208327 | 3500478814410329 | 41385225782246336320451797998 |
| 67 | 164207682036849477130738064324 | 739101628996713O | 164207682036842086114448097194 |
| 68 | 416635607643584641443966956505 | 1139163403768010 | 416635607643573249809932188495 |
| 69 | 1648923729893987703415359750119 | 2394165796780820O | 1648923729893963761757391941910 |
| 70 | 4202708638020682863979777378556 | 3691716157758059O | 4202708638020645946818199797966 |
| 71 | 16592589875613236090913193392688 | 7758638146603494 7 | 16592589875613158504531727357741 |
| 72 | 42473372537692324926023951462175 | 1201893096912942 16 | 42473372537692204736714260167959 |
| 73 | 167295424464204241785279087528744 | 2515289353493067 93 | 167295424464203990256343738221951 |
| 74 | 430006772381311411463428100669081 | 3898007823996770 01 | 430006772381311021662645700992080 |
| 75 | 168991183506456475023017071834985 5 | 8157411403380682 27 | 168991183506456393448903038028162 8 |
| 76 | 436078672683084004824169032135154 0 | 1269537929599135 156 | 436078672683083877870376433000038 4 |
| 77 | 171006097510741442171745608077683 66 | 2646489896299591 485 | 171006097510741415706846645081768 81 |
| 78 | 442943541852221868207691241535217 49 | 4120240983149128 308 | 442943541852221827005281410043934 41 |
| 79 | 173335468778163787515568474781956550 | 8588824555686539622 | 173335468778163758926743919095416928 |
| 80 | 450600427378156845559982800702584531 | 1342390357338998107 | 450600427378156832136079227317086424 |
| 81 | 175976731349647795595013618543623711 3 | 2788274845723029086 2 | 175976731349647792806738772820594625 1 |

# Complexity – Molecules and Multiplicity



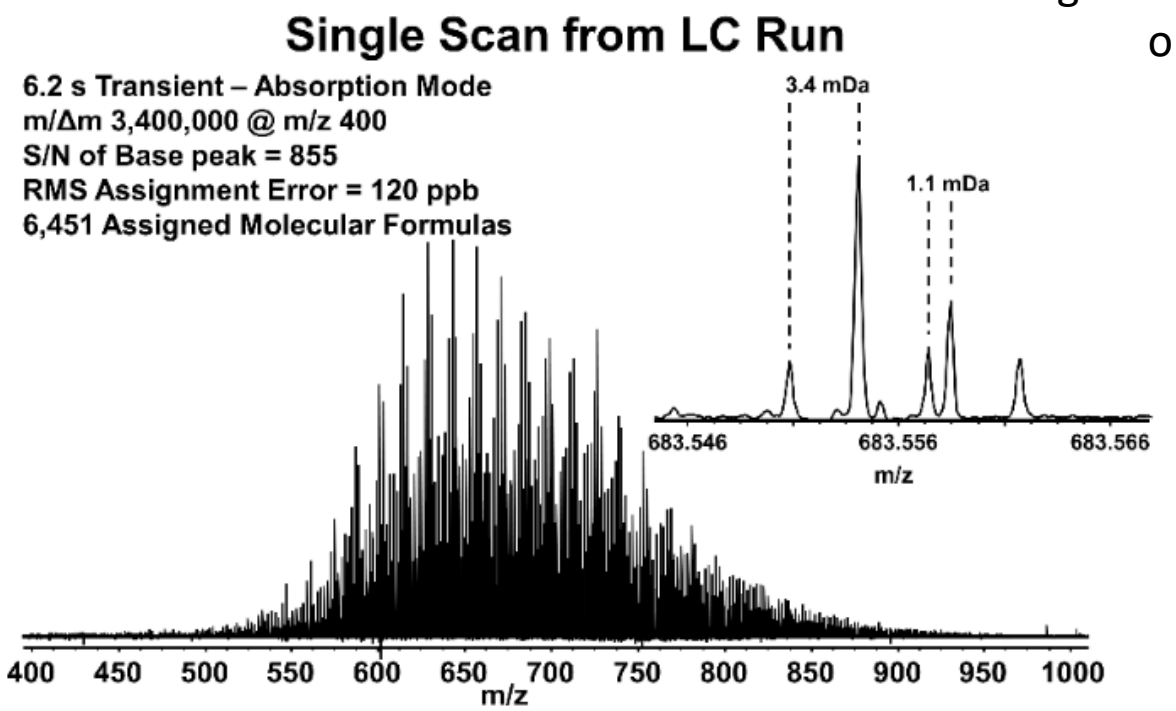




Schmitt-Kopplin et al., *Faraday Discussions*, **2019**, *218, 9-28*

# The Concept of Challenging Complex Mixtures

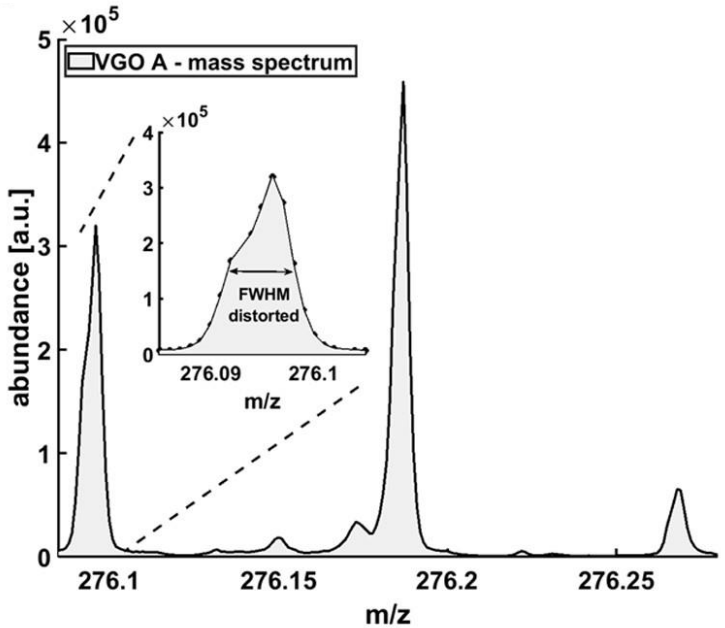
**What is complexity really? How do we define a complex mixture?**

a single doublet of not resolved (mass spectrometrically or analytically in general) compounds




unpublished data – 21T FT-ICR MS platform NHMFL

**or**




Rüger, et al., *Analytical Chemistry* 93 (14), S. 5872–5881.

Challenging complex mixture as somewhat philosophical question (courtesy to Prof. Jan Andersson, Univ. Munster)

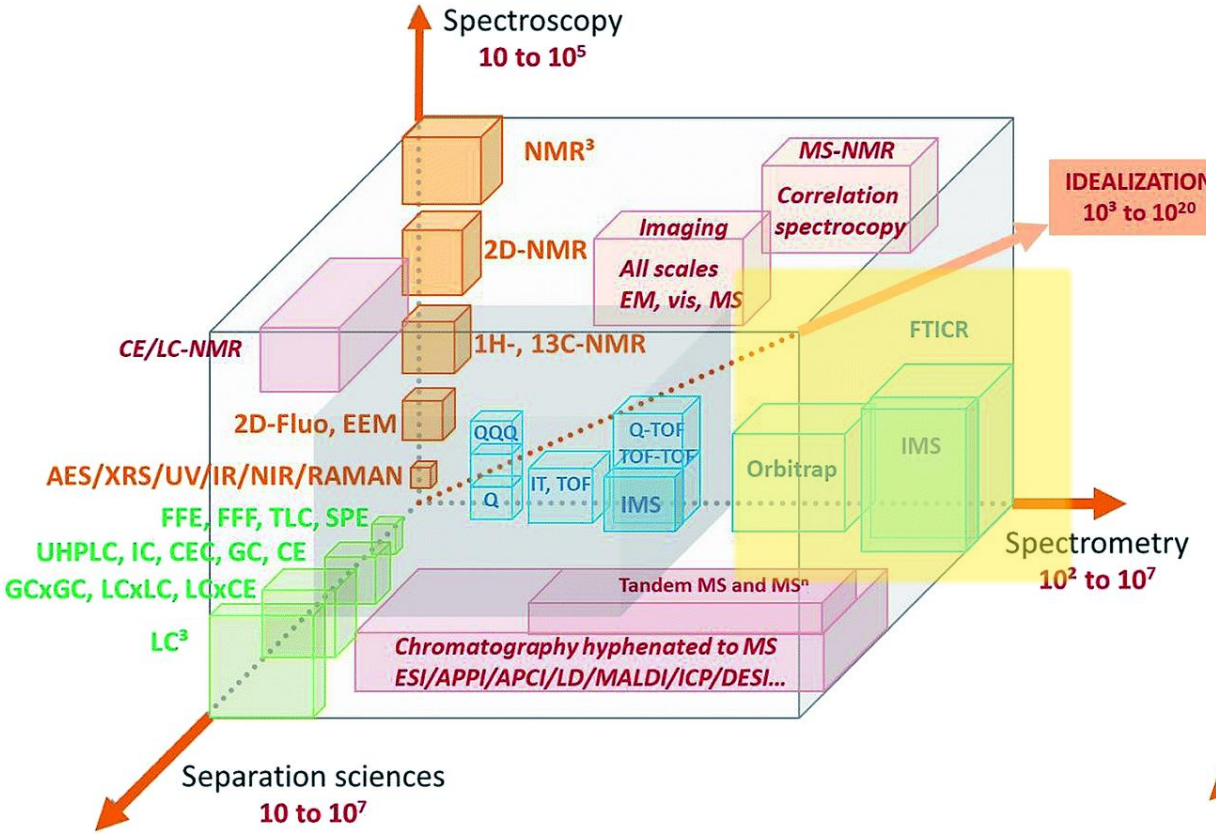
# Deciphering Complex Mixtures

*"I have a friend who's an artist and has sometimes taken a view which I don't agree with very well. He'll hold up a flower and say "look how beautiful it is," and I'll agree. Then he says "I as an artist can see how beautiful this is but you as a scientist take this all apart and it becomes a dull thing," and I think that he's kind of nutty. First of all, the beauty that he sees is available to other people and to me too, I believe… I can appreciate the beauty of a flower. At the same time, I see much more about the flower than he sees. I could imagine the cells in there, the complicated actions inside, which also have a beauty. I mean it's not just beauty at this dimension, at one centimeter; there's also beauty at smaller dimensions, the inner structure, also the processes. The fact that the colors in the flower evolved in order to attract insects to pollinate it is interesting; it means that insects can see the color. It adds a question: does this aesthetic sense also exist in the lower forms? Why is it aesthetic? All kinds of interesting questions which the science knowledge only adds to the excitement, the mystery and the awe of a flower. It only adds. I don't understand how it subtracts."*

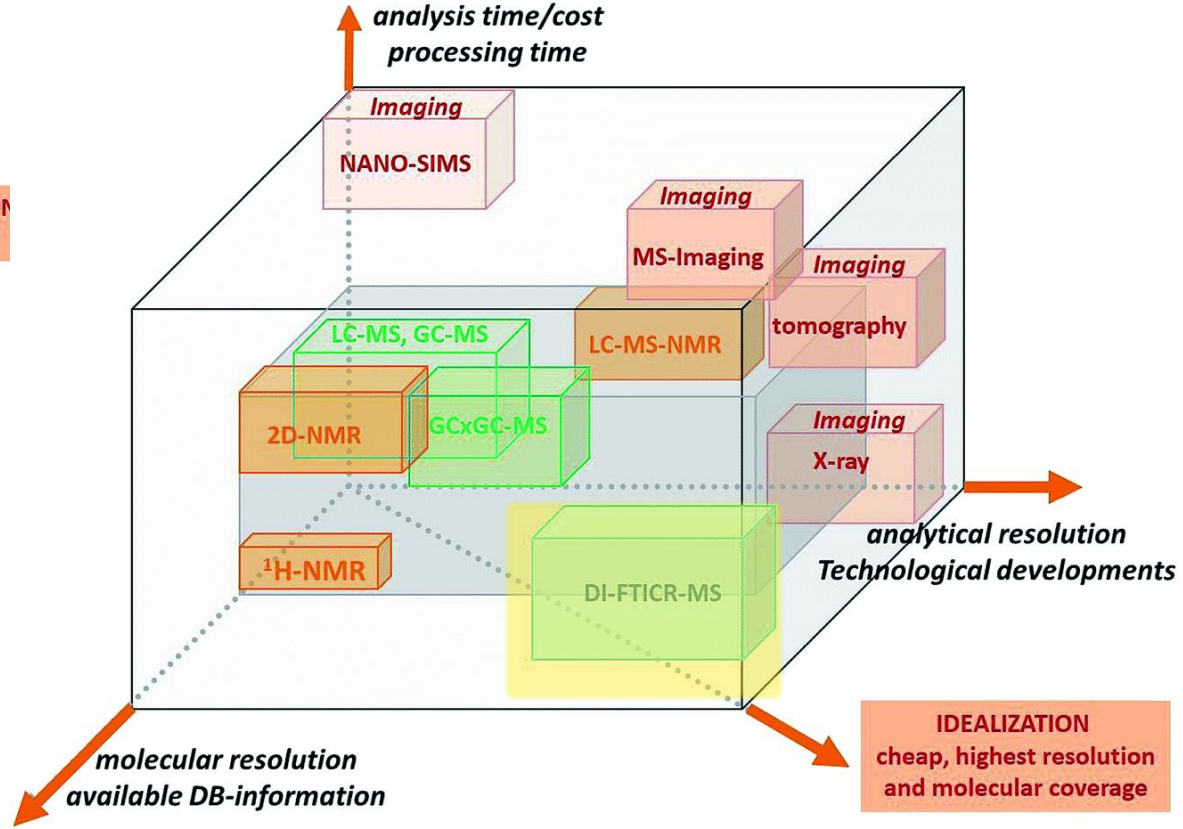
*Richard Feynman, Nobel-laureate in physics (from BBC Interview for Horizon 'The Pleasure of Finding Things Out' (https://www.bbc.co.uk/sn/tvradio/programmes/horizon/broadband/archive/feynman/) animated by Fraser Davidson/https://vimeo.com/55874553).*

# Analytical Platforms

**Separation capabilities according to the three main domains:**



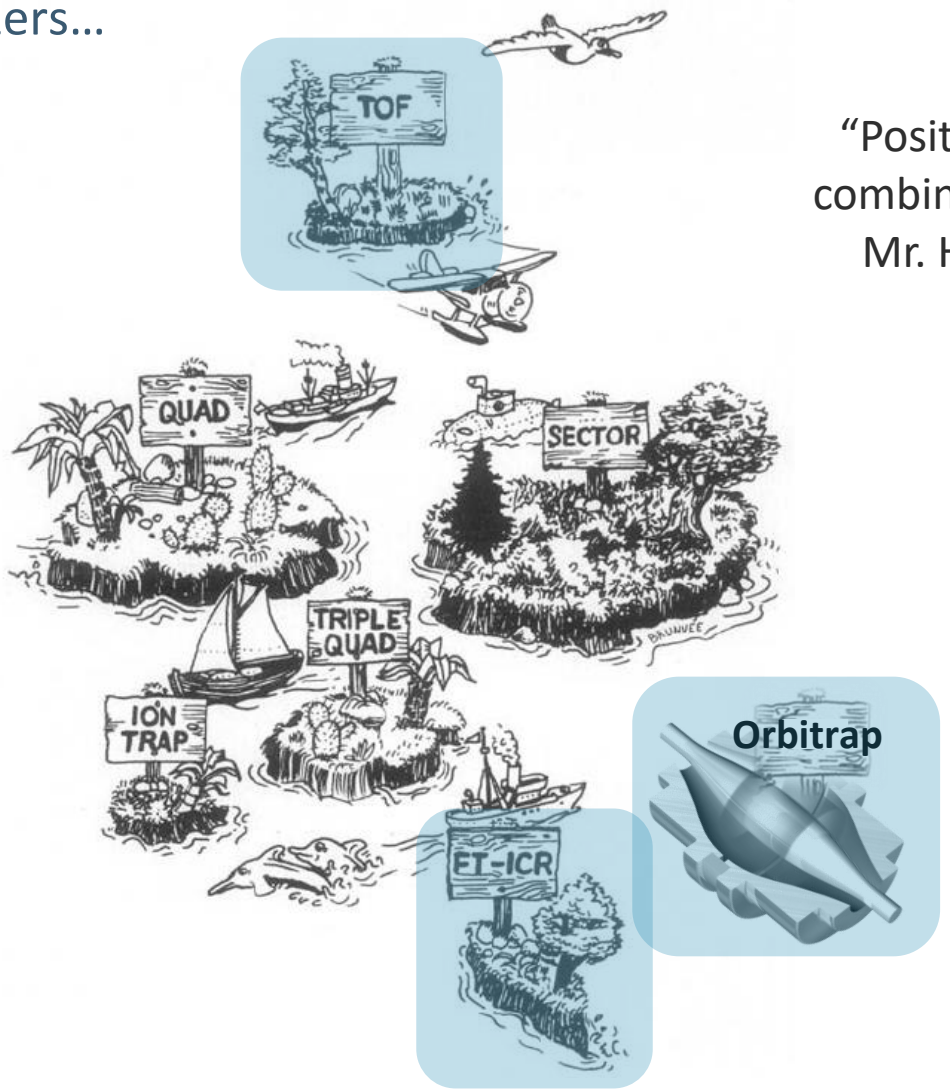

**Pragmatic combination of coverage, price/time, etc.:**




Schmitt-Kopplin et al., *Faraday Discussions*, **2019**, *218, 9-28*

# Which Mass Spectrometric Platform?

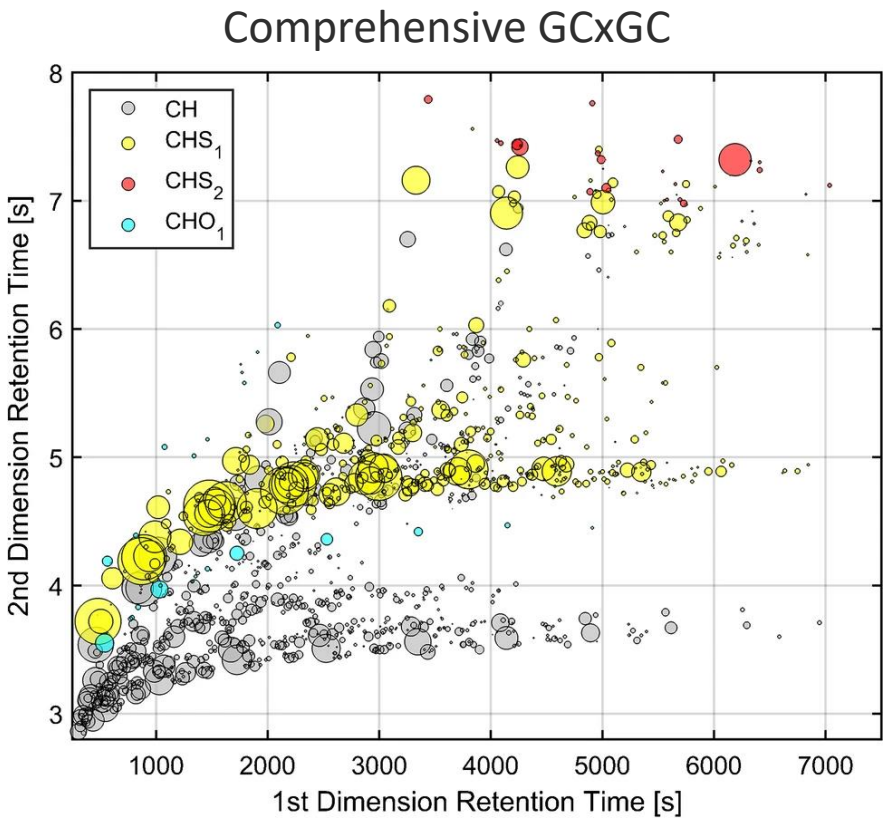
## The realm of mass analyzers…




"Positive and negative features are always combined in one instrument as Dr. Jekyll and Mr. Hyde are combined in one person."

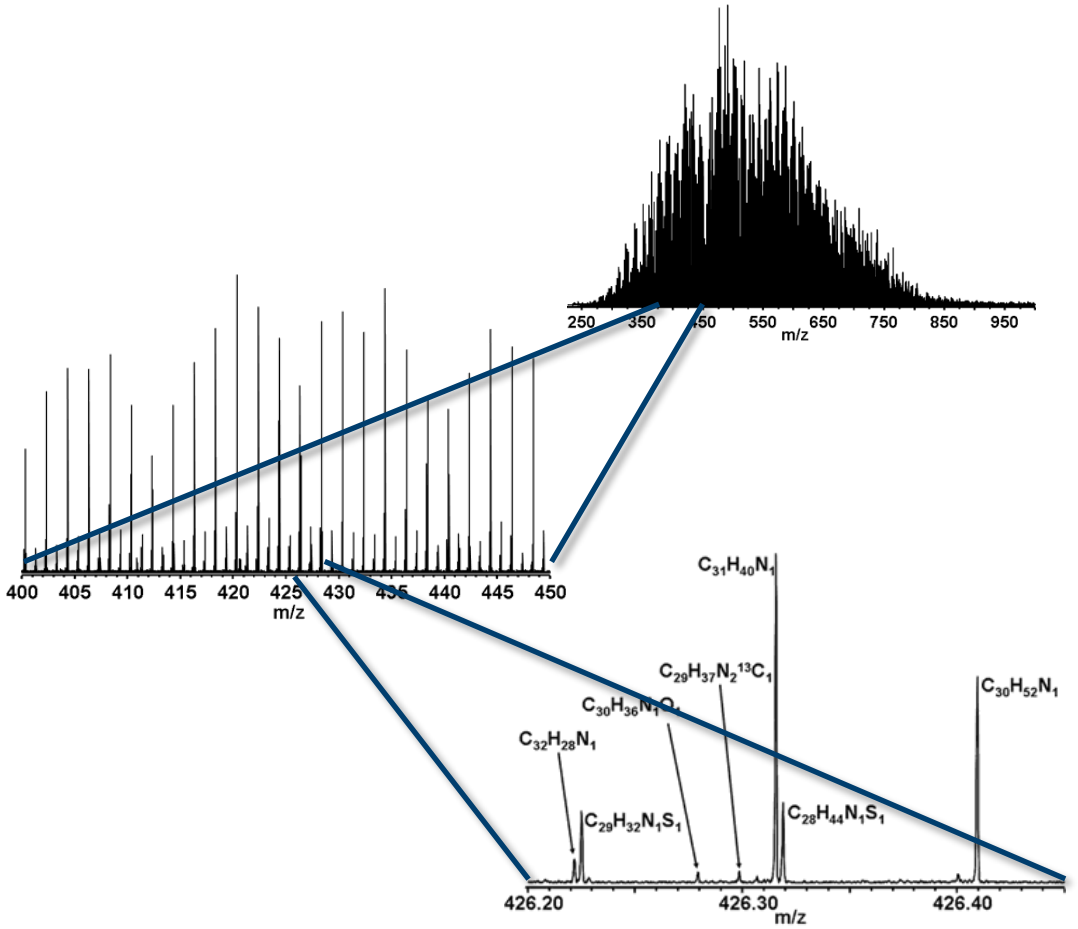
adapted based on:
Curt Brunnée, The Ideal Mass Analyzer Fact or Fiction, *Int. J. Mass Spectrom and Ion Processes*, 76 (**1987**), 125-237

# Orthogonality and Peak Coverage




Schwalb et al. *Analytical and Bioanalytical Chemistry*. DOI: 10.1007/s00216-022-04393-w.

**Peak capacity:** Maximum theoretical number of components that can be separated. → Reality check: peak coverage




Even highly complex mixtures are not covering the entire *m/z*-domain giving a limited peak coverage and utilization of the FTMS peak capacity (naturally by the mass defect)

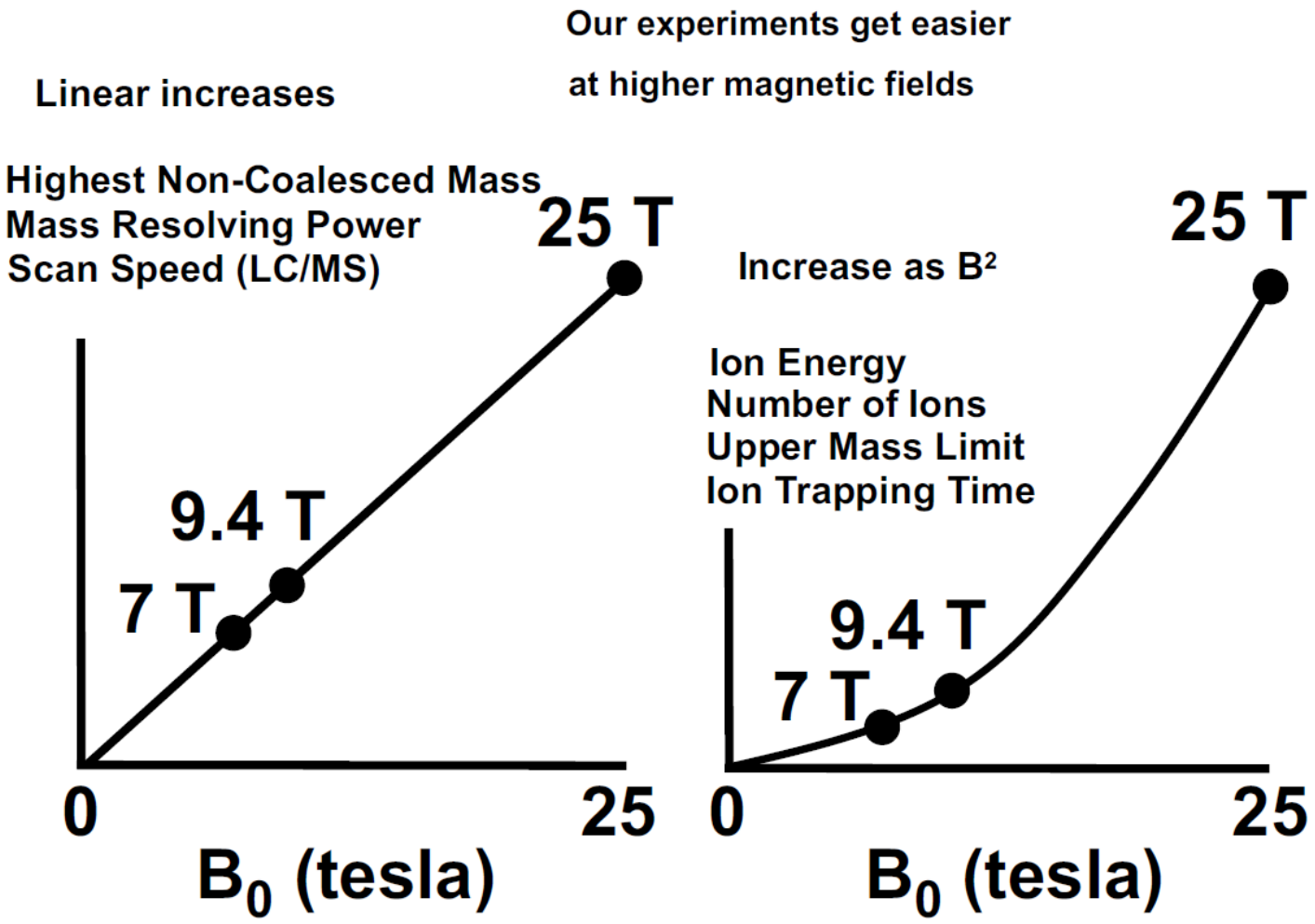
# Challenges in High-Resolution Mass Spectrometry

## "Can we cope with the complexity by FT-ICR MS?" – Wishful thinking

- analytical challenges: classical direct infusion versus hyphenated solution (some covered here)
- expanding the accessible chemical space via ionization techniques (see talk from Janne Jänis and Carlos Afonso)
- fragmentation techniques and novel unique 2D solutions (see talk from Pete O'Connor and Maria van Agthoven)
- open-code/access software solutions for data processing, visualization and comparison (see talk from Maxim Sueur)

→ **Limitation for this lecture:** Classical 'omics sciences (biomedical/biochemistry/biopolymers via proteomics, metabolomics, lipidomics, etc.) excluded and not covered in this talk!

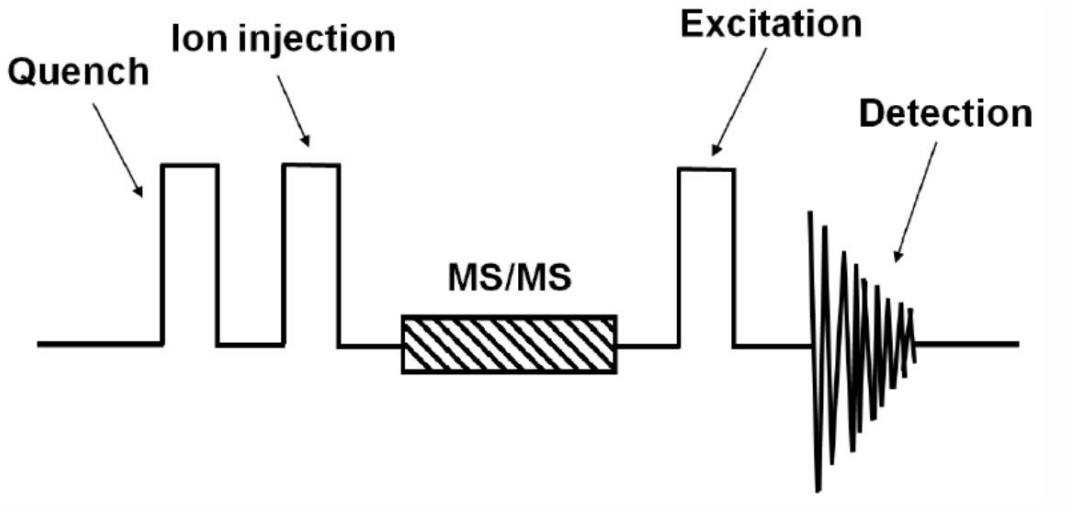
# From Transient to Mass Spectrum

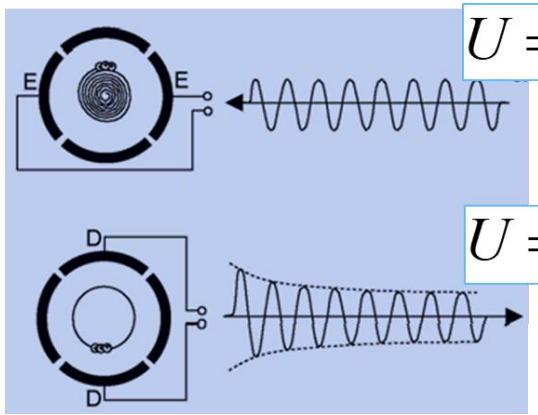



Marshall et al., *Mass Spectrometry Reviews* (**1998**) 17, 1-35

21T FT-ICR MS platform at the NHMFL
(2nd comparable system at PNNL)

# From Transient to Mass Spectrum




$$U = U_1 \sin(\omega \cdot t)$$

$$U = U_0 \cdot e^{-k \cdot t} \cdot \sin(\omega \cdot t)$$

Cyclotron frequency (~1 Mhz)

$$\omega_c = \frac{q}{m} \cdot B$$

simplest case, only the value of the magnetic field is considered

Trapping frequency (~1 khz)

$$\omega_T = \frac{2}{a} \cdot \sqrt{\alpha \cdot U_T \cdot \frac{q}{m}}$$

A more accurate equation takes into account the reduction of $\omega_c$ relative to the application of the trapping electric field

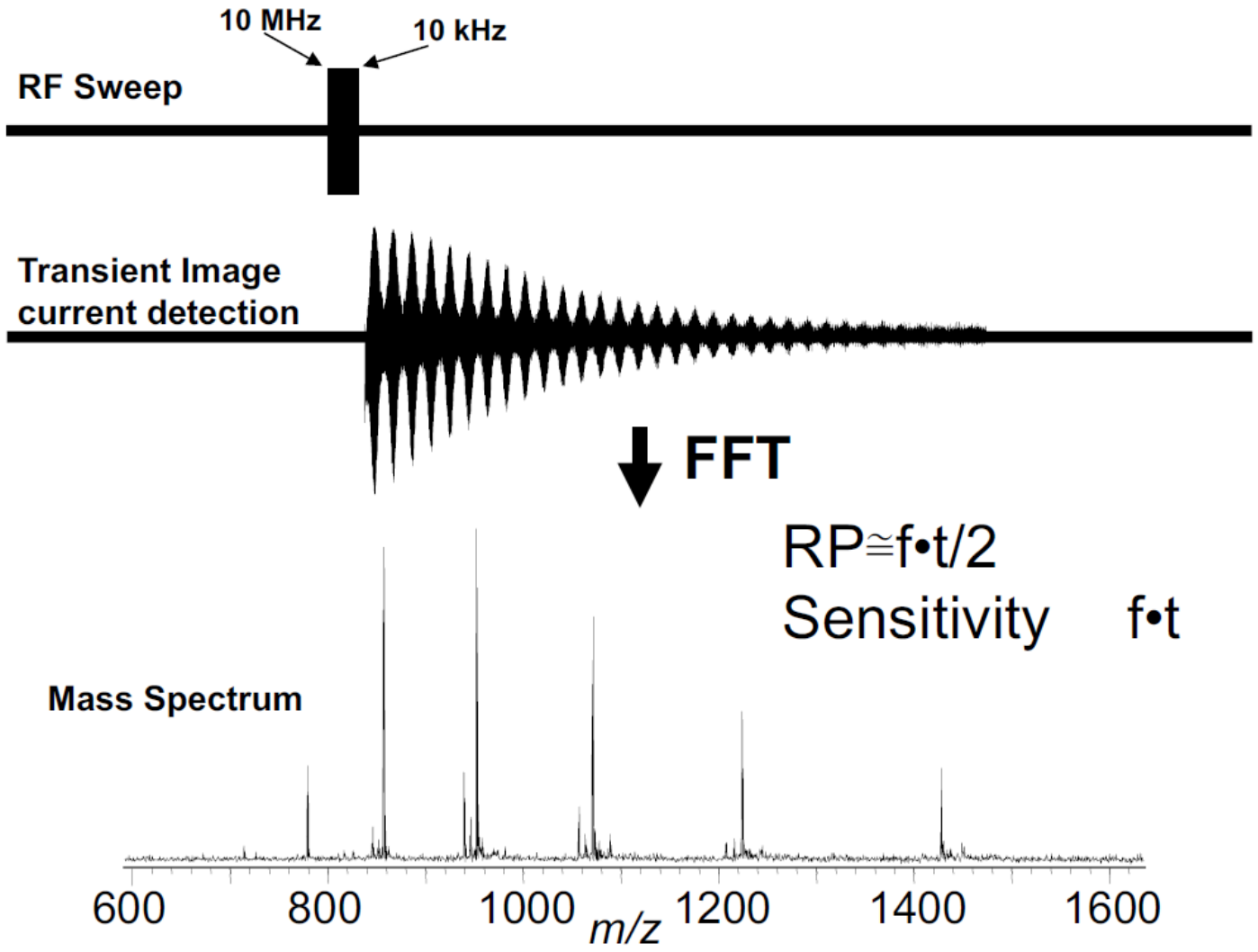
Effective Frequency

$$\omega_{eff} \cong \omega_c - \omega_m \qquad \omega_m \cong \frac{\omega_T^2}{2 \cdot \omega_c} = \frac{2 \cdot \alpha \cdot U_T}{a^2 \cdot B}$$

so called “magnetron frequency” (~ 10 Hz)

Qi, Y.; O'Connor, P. B., Data processing in Fourier transform ion cyclotron resonance mass Spectrometry; *Mass Spectrometry Reviews* ***2014,*** *33, 333-352.*

# From Transient to Mass Spectrum




**What to do with the time domain signal:**

- Zero-filling
- Windowing (Apodization)
- Fourier-transformation
- Phasing
- Calibration

**Software Solutions:**

- vendor-based (Bruker/Thermo)
- custom free solutions, *e.g.*, EU_FT-ICR_MS development, phasing (Pete O'Connor) or Predator
- external companies, *e.g.*, Spectroswiss

Slide courtesy mostly to Pete O'Connor

# From Transient to Mass Spectrum

## Peak Picking – From profile data to line centroided data

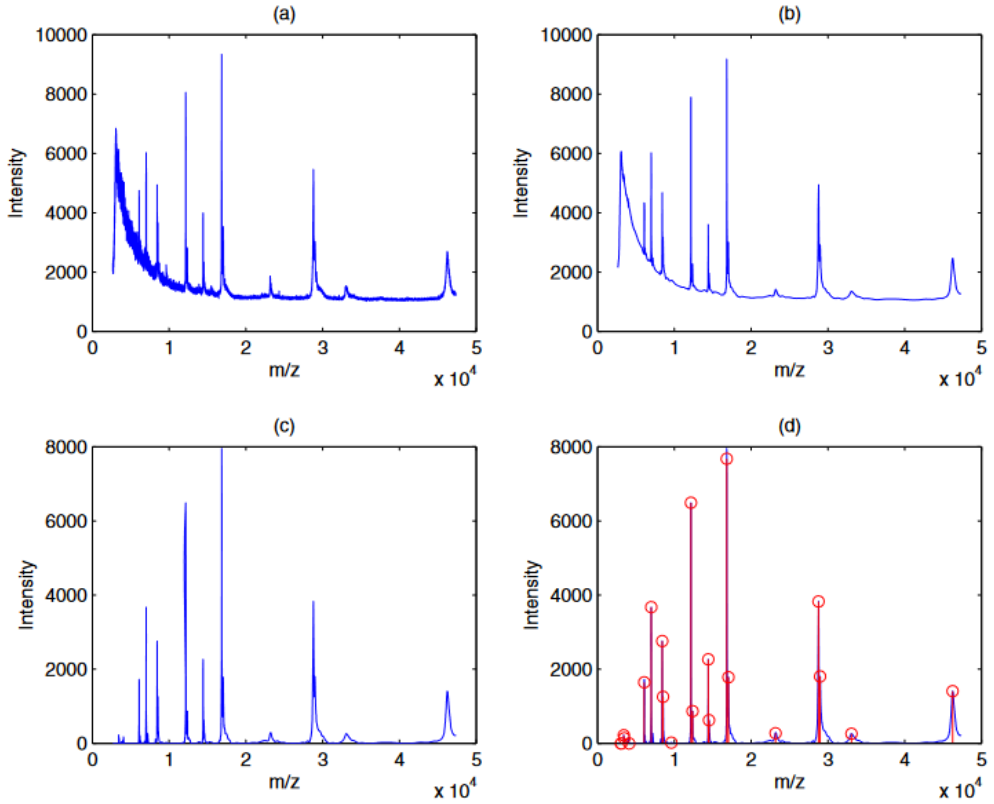



**Figure 2**
**An example of the peak detection process.** (a) A raw spectrum, (b) the spectrum after smoothing, (c) the spectrum after smoothing and baseline correction and (d) final peak detection results with peaks marked as circles.

Yang et al., *BMC Bioinformatics* **2009**, 10:4


J. Am. Soc. Mass Spectrom. (2017) 28:253-262
DOI: 10.1007/s13361-016-1549-z

RESEARCH ARTICLE

**Autopiquer - a Robust and Reliable Peak Detection Algorithm for Mass Spectrometry**

David P. A. Kilgour,[1] Sam Hughes,[2] Samantha L. Kilgour,[3] C. Logan Mackay,[2] Magnus Palmblad,[4] Bao Quoc Tran,[5] Young Ah Goo,[5] Robert K. Ernst,[3] David J. Clarke,[2] David R. Goodlett[5]

[1]Department of Chemistry and Forensics, Nottingham Trent University, Nottingham, NG11 8NS, UK
[2]EastCHEM School of Chemistry, University of Edinburgh, Edinburgh, EH9 3FJ, UK
[3]Department of Microbial Pathogenesis, School of Dentistry, University of Maryland, Baltimore, MD 21201, USA
[4]Center for Proteomics and Metabolomics, Leiden University Medical Center, 2300 RC, Leiden, The Netherlands
[5]Department of Pharmaceutical Sciences, School of Pharmacy, University of Maryland, Baltimore, MD 21201, USA

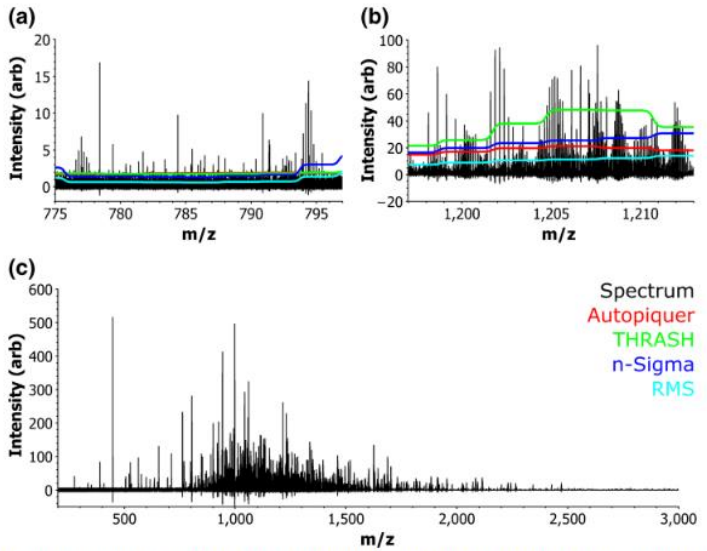



Figure 4. Showing peak detection thresholds being set for an absorption mode FT-ICR MS spectrum of the electron capture dissociation product ions of denatured horse heart myoglobin. The complete spectrum is shown in panel (c), bottom row. Panels (a) and (b), top row, show the peak detection thresholds generated by different algorithms in two regions of interest – one with low peak density and the other with high peak density. For all methods, the window width is 3 Da. The spectrum is shown in black and the thresholds calculated by the Autopiquer, THRASH, *n*-Sigma, and RMS methods are shown in red, green, blue, and cyan, respectively

# From Transient to Mass Spectrum

## Peak Picking – “Where to cut the noise?”

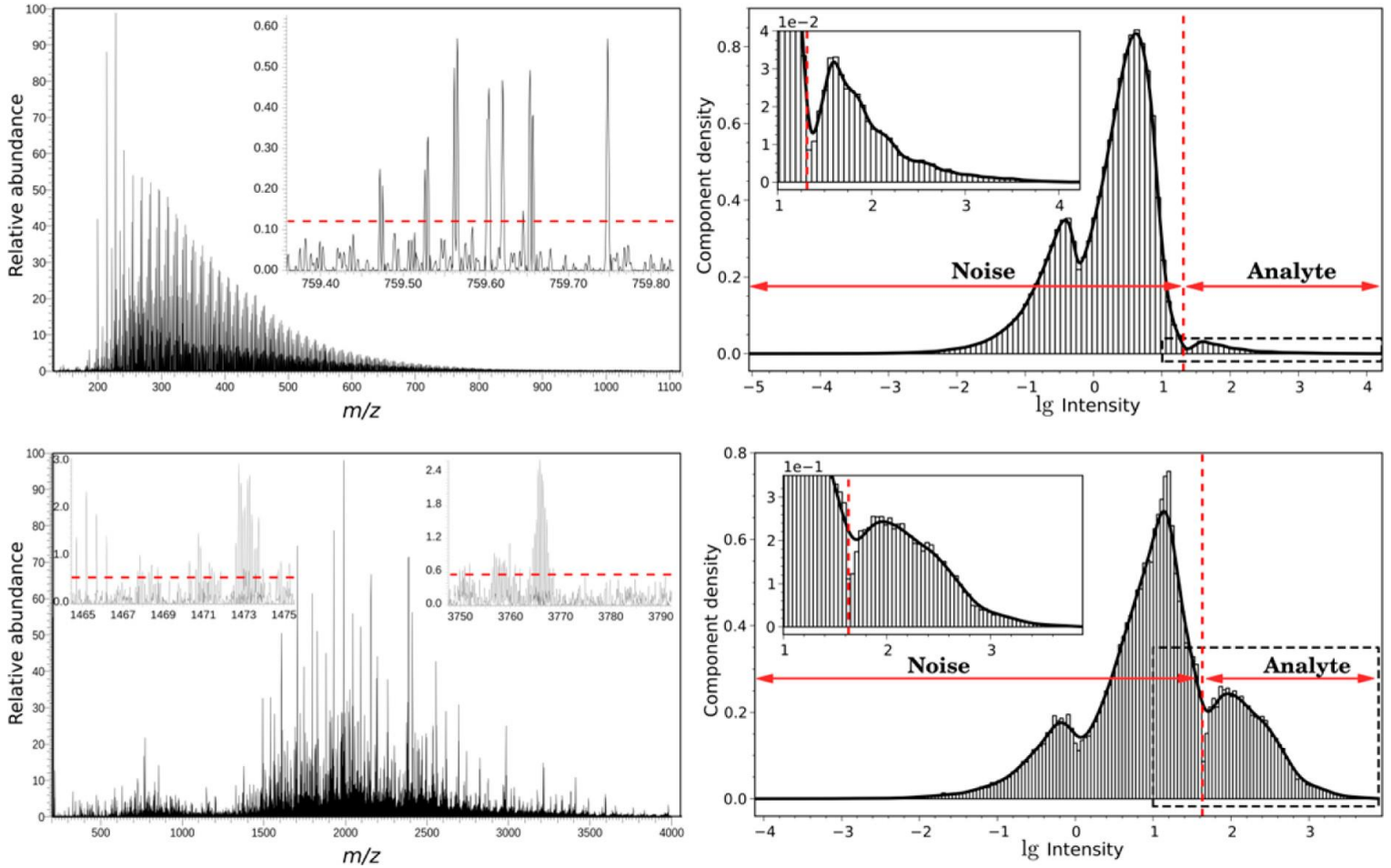
analytical chemistry Article pubs.acs.org/ac

**Distinguishing Analyte from Noise Components in Mass Spectra of Complex Samples: Where to Cut the Noise?**

Konstantin O. Zhurov, Anton N. Kozhinov, Luca Fornelli, and Yury O. Tsybin*

Biomolecular Mass Spectrometry Laboratory, Ecole Polytechnique Fédérale de Lausanne, 1015 Lausanne, Switzerland

Analysis of full-profile mass spectra of South American crude oil fraction (top) and Humira IgG (bottom). Left panels: absorption-mode-type mass spectra acquired on Orbitrap Elite FTMS. Right panels: distributions of logarithmic intensity. Red lines indicate the noise threshold values.

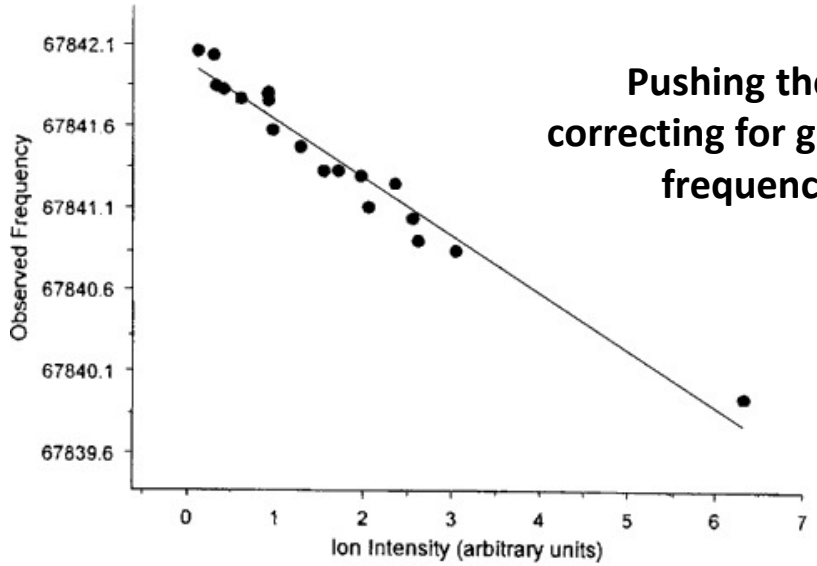


# From Transient to Mass Spectrum

## Mass Spectral Calibration – the ion trap behaviour and physics of FTMS

**TABLE 1.** Proposed calibration procedures

| | |
|---|---|
| $f = \frac{a}{m}$ | basic law of ions in a B field |
| $f^2 = \frac{a}{m^2} + \frac{b}{m}$ | (Beauchamp-Armstrong et al., 1969) |
| $f^2 = \frac{a}{m^2} + \frac{b}{m} + c$ | (Ledford et al., 1980) |
| $f_{sideband} = \frac{a}{m}$ | (Allemann et al., 1981) |
| $f = \frac{a}{m} + c$ | (Francl et al., 1983) |
| $\left(\frac{M}{Z}\right) = \frac{a}{f_{obsd}} + \frac{b}{f_{obsd}^2}$ | (Ledford et al., 1984b) |
| $f_{estimated} = f_{measured} + c(I_{calibrant} - I_{analyte})$<br>$\frac{m}{z} = \frac{A}{f_{estimated}} + \frac{B}{f_{estimated}^2} + \frac{C}{f_{estimated}^3}$ | (Easterling et al., 1999) |
| $M = (\frac{kB}{f_n + \Delta f})n - n(M_e)$ | (Bruce et al., 2000) |
| $\left(\frac{M}{Z}\right)_i = \frac{a}{f_{obsd}} + \frac{b}{f_{obsd}^2} + \frac{CI_i}{f_{obsd}^2}$ | (Masselon et al., 2002) |
| $\frac{m}{z} = \frac{A}{v} + \frac{B}{v^2} + \frac{C}{v^3} + \frac{BC}{Av^4}$ | (Wang et al., 1988) |




**Pushing the limits by correcting for global and local frequency shifts!**

Frequency shift as a function of ion population for the monoisotopic peak of bradykinin, showing the change in observed frequency as a function of total ion intensity as ions from a single laser shot are remeasured.

Zhang, L. K.; Rempel, D.; Pramanik, B. N.; Gross, M. L.; Accurate mass measurements by Fourier transform mass spectrometry *Mass Spectrom. Rev.* **2005**, *24*, 286-309.
T. J. Francl, M. G. Sherman, R. L. Hunter, M. H. Locke, W. D. Bowers, R. T. McIver, *Int. J. Mass Spec.* 1983, *54*. 189-199.
M. L. Easterling, T. H. Mize, I. J. Amster, *Anal. Chem.* 1999, *71*. 624-632.
C. Masselon, A. V. Tolmachev, G. A. Anderson, R. Harkewicz, R. D. Smith, *J. Am. Soc. Mass Spectrom.* 2002, *13*. 99-106.

# From Transient to Mass Spectrum

## Mass Spectral Calibration – "Walking" Calibration Equation

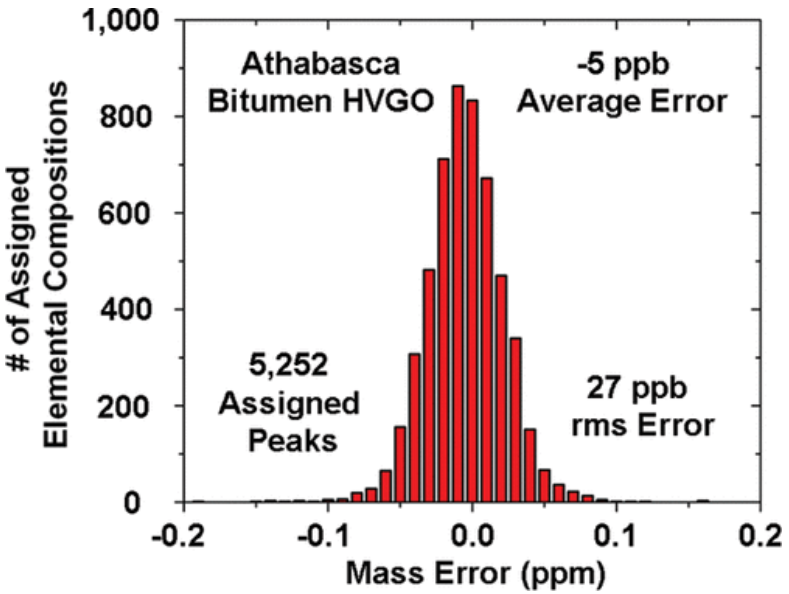
analytical chemistry ARTICLE
pubs.acs.org/ac

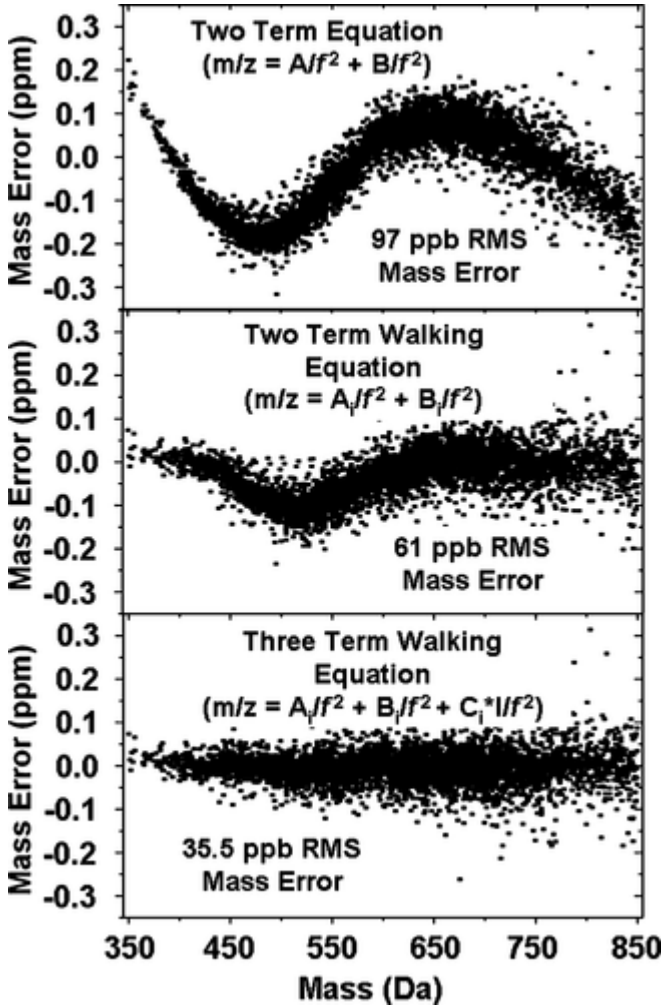
Parts-Per-Billion Fourier Transform Ion Cyclotron Resonance Mass Measurement Accuracy with a "Walking" Calibration Equation

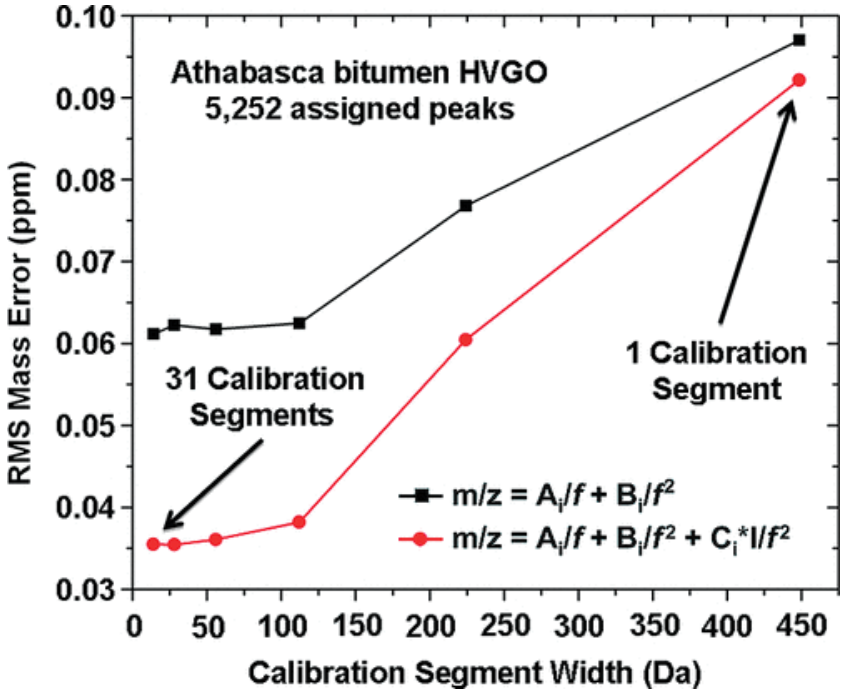
Joshua J. Savory,[†] Nathan K. Kaiser,[†] Amy M. McKenna,[†] Feng Xian,[‡] Greg T. Blakney,[†] Ryan P. Rodgers,[†,‡] Christopher L. Hendrickson,[*,†,‡] and Alan G. Marshall[*,†,‡]

[†]National High Magnetic Field Laboratory, Florida State University, 1800 East Paul Dirac Drive, Tallahassee, Florida 32310-4005, United States

[‡]Department of Chemistry, Florida State University, 95 Chieftain Way, Tallahassee, Florida 32306, United States




"Addition of an abundance-dependent term to the walking calibration equation and 13C isotopomers to the calibration series was also advantageous."

# From Transient to Mass Spectrum

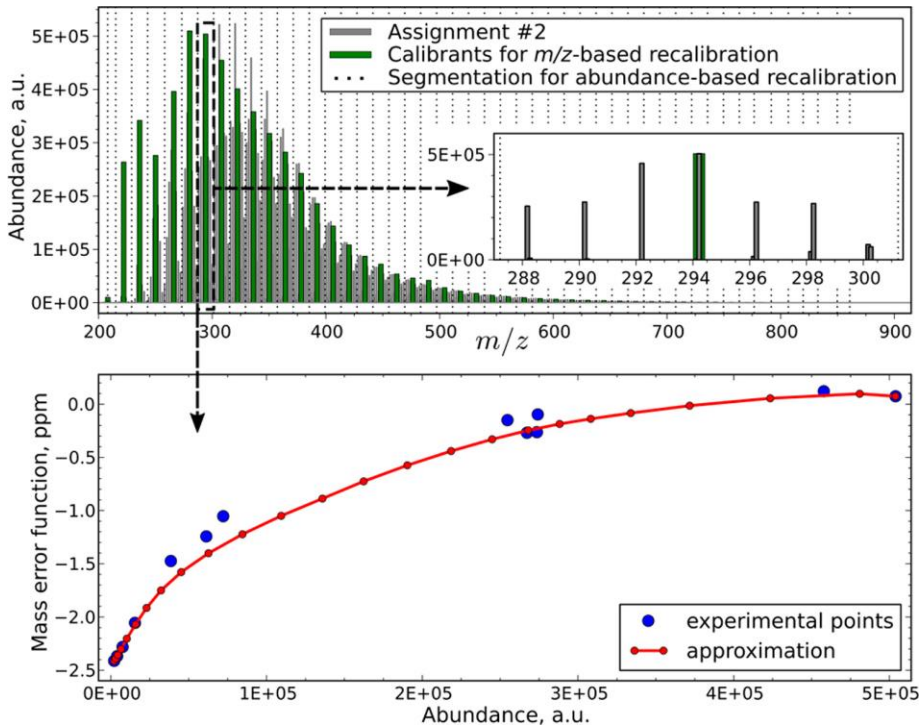
## Mass Spectral Calibration – Iterative Recalibration

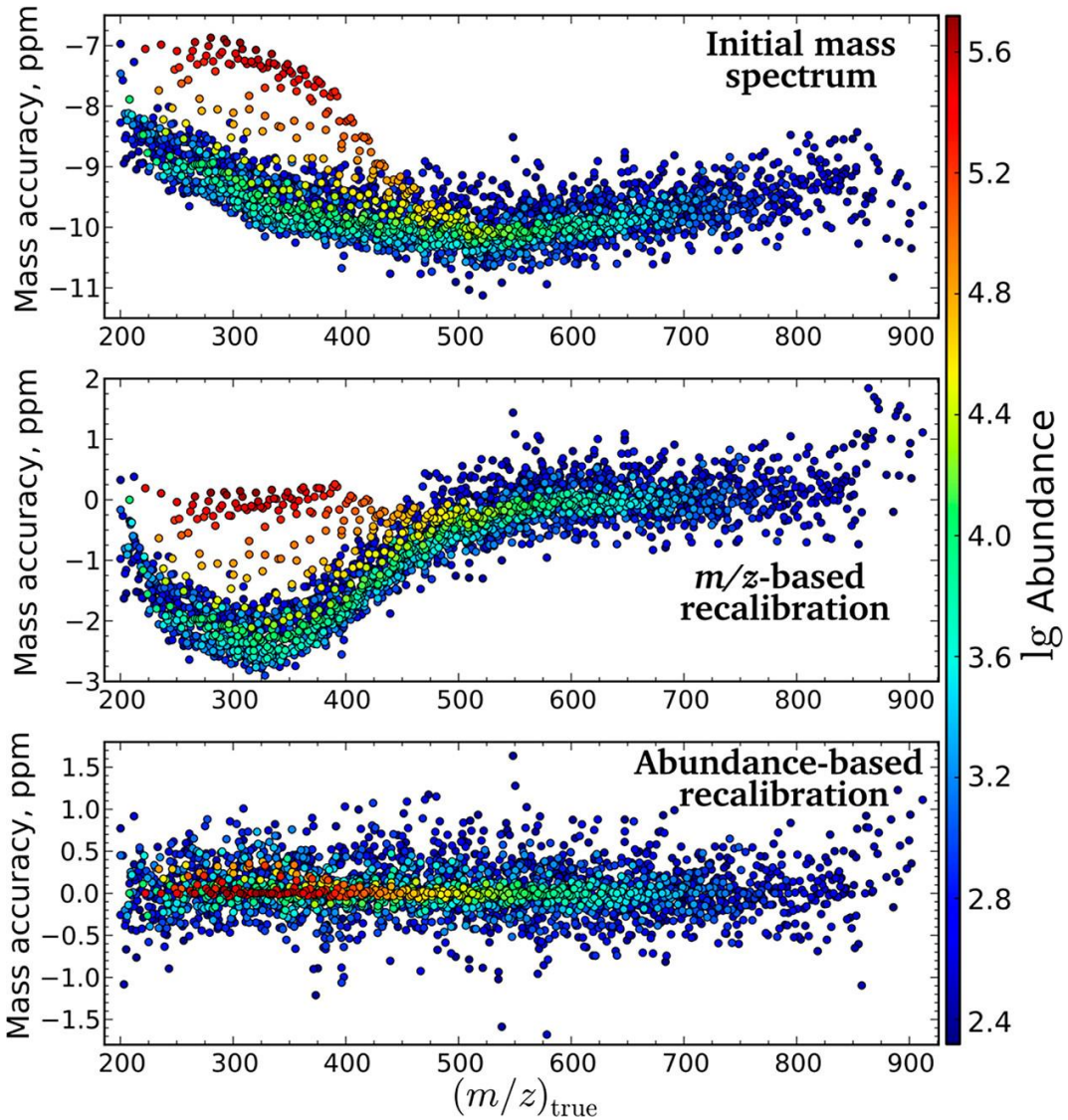
analytical chemistry Article pubs.acs.org/ac

**Iterative Method for Mass Spectra Recalibration via Empirical Estimation of the Mass Calibration Function for Fourier Transform Mass Spectrometry-Based Petroleomics**

Anton N. Kozhinov, Konstantin O. Zhurov, and Yury O. Tsybin*

Biomolecular Mass Spectrometry Laboratory, Ecole Polytechnique Fédérale de Lausanne, 1015 Lausanne, Switzerland



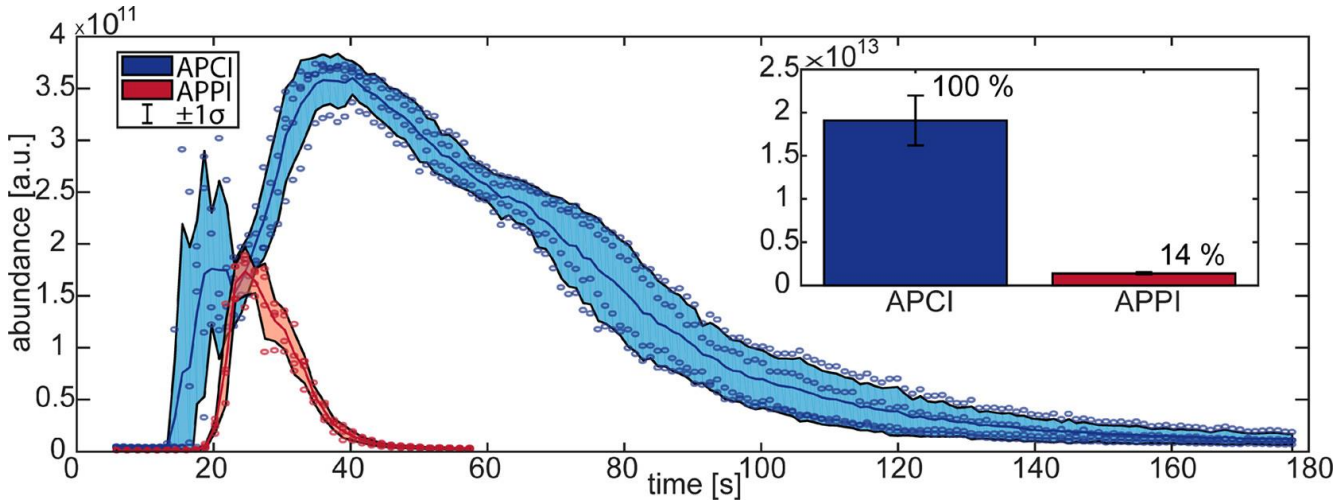
# Mass Spectrometric Recalibration

## Hyphenated Solutions – Time-Dependent Data

pubs.acs.org/jasms Research Article

**Direct Inlet Probe Atmospheric Pressure Photo and Chemical Ionization Coupled to Ultrahigh Resolution Mass Spectrometry for the Description of Lignocellulosic Biomass**

Clément Castilla, Christopher P. Rüger, Stéphane Marcotte, Hélène Lavanant,* and Carlos Afonso




Time-resolved total ion count (TIC) for the DIP experiment conducted with APCI (blue) and APPI (red) on ground beech pellets. The shaded area corresponds to ±1σ, and the scattered circles are derived from individual mass spectra. The averaged summed TIC with the respective standard deviation is given in the inset.

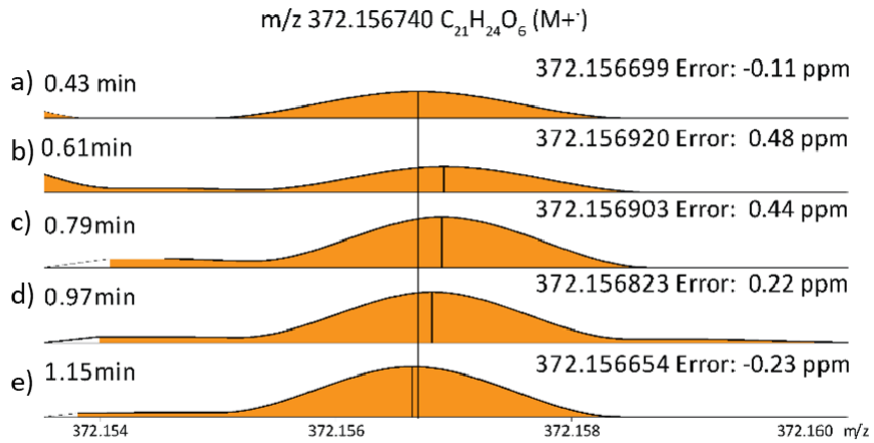



**Figure S4.** Mass shifts observed during pyrolysis process of beech pellet for *m/z 372.15640* ion. With mass shift observed at a) 0.43 min, b) 0.61 min, c) 0.79 min, d) 0.97 min, e) 1.15 min

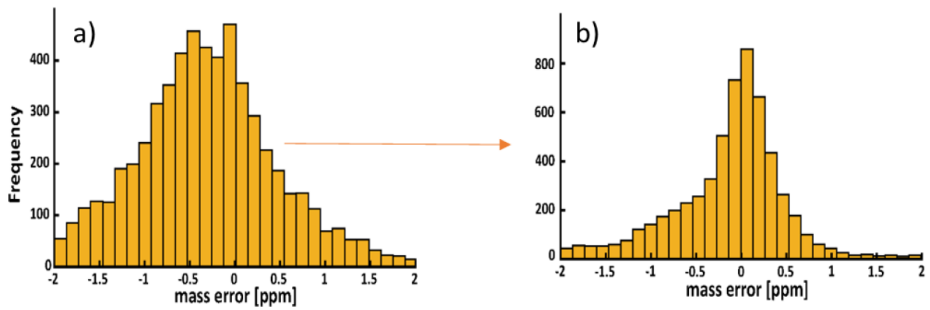



**Figure S5.** Improvement of attribution error using scan–to-scan recalibration, with a), the mass error before calibration and b), the mass error after scan to scan calibration

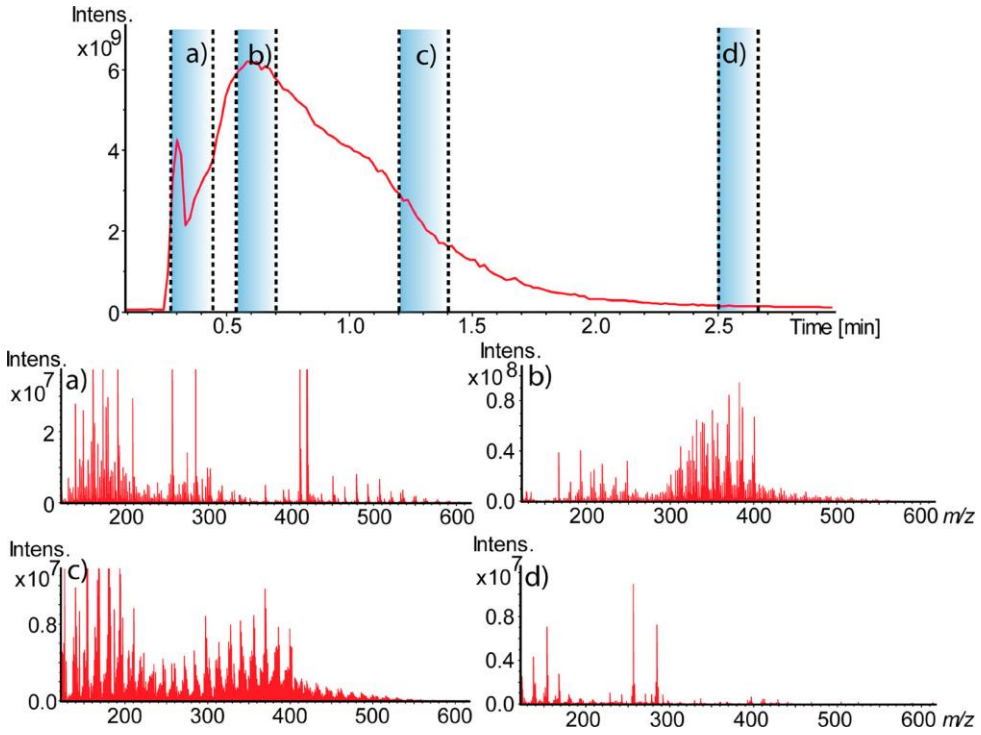
# Mass Spectrometric Recalibration

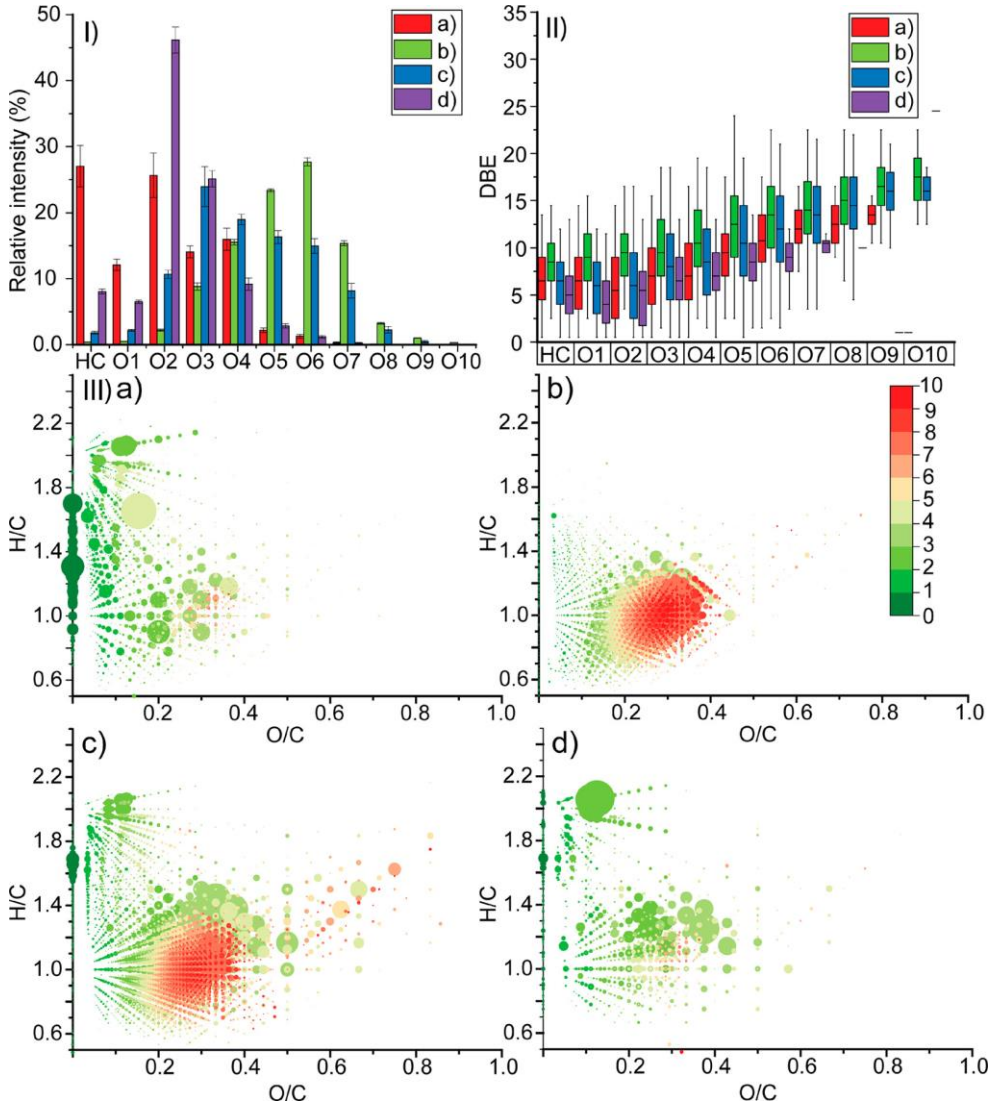
## Hyphenated Solutions – Time-Dependent Data

pubs.acs.org/jasms Research Article

**Direct Inlet Probe Atmospheric Pressure Photo and Chemical Ionization Coupled to Ultrahigh Resolution Mass Spectrometry for the Description of Lignocellulosic Biomass**

Clément Castilla, Christopher P. Rüger, Stéphane Marcotte, Hélène Lavanant,* and Carlos Afonso



# From Transient to Mass Spectrum

## Software Solutions – Example: Kairos MS

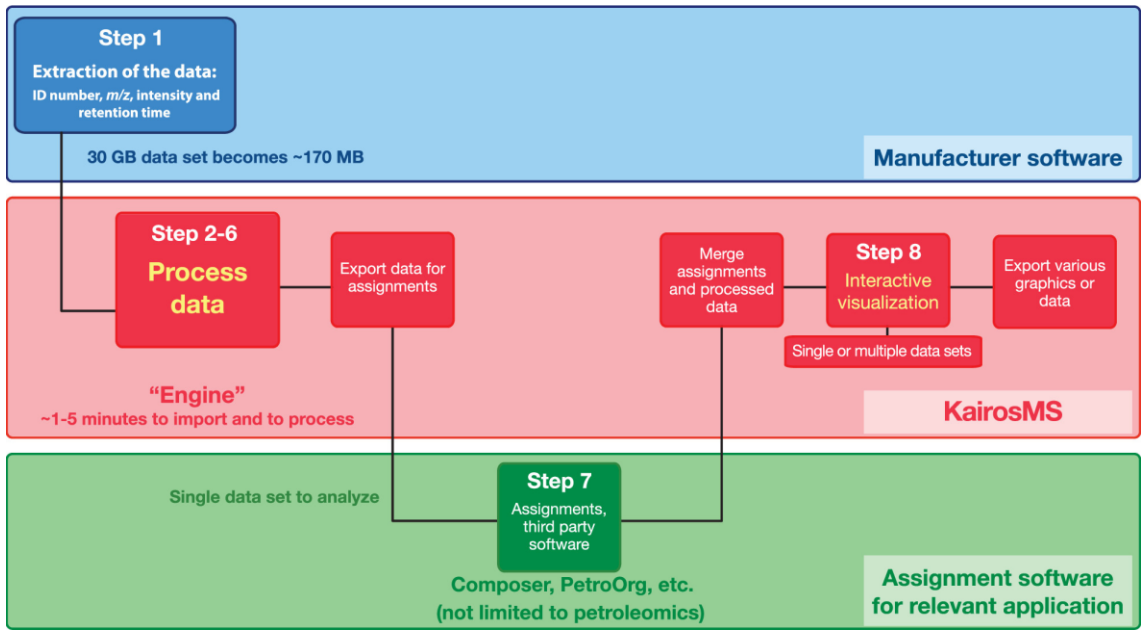
analytical chemistry

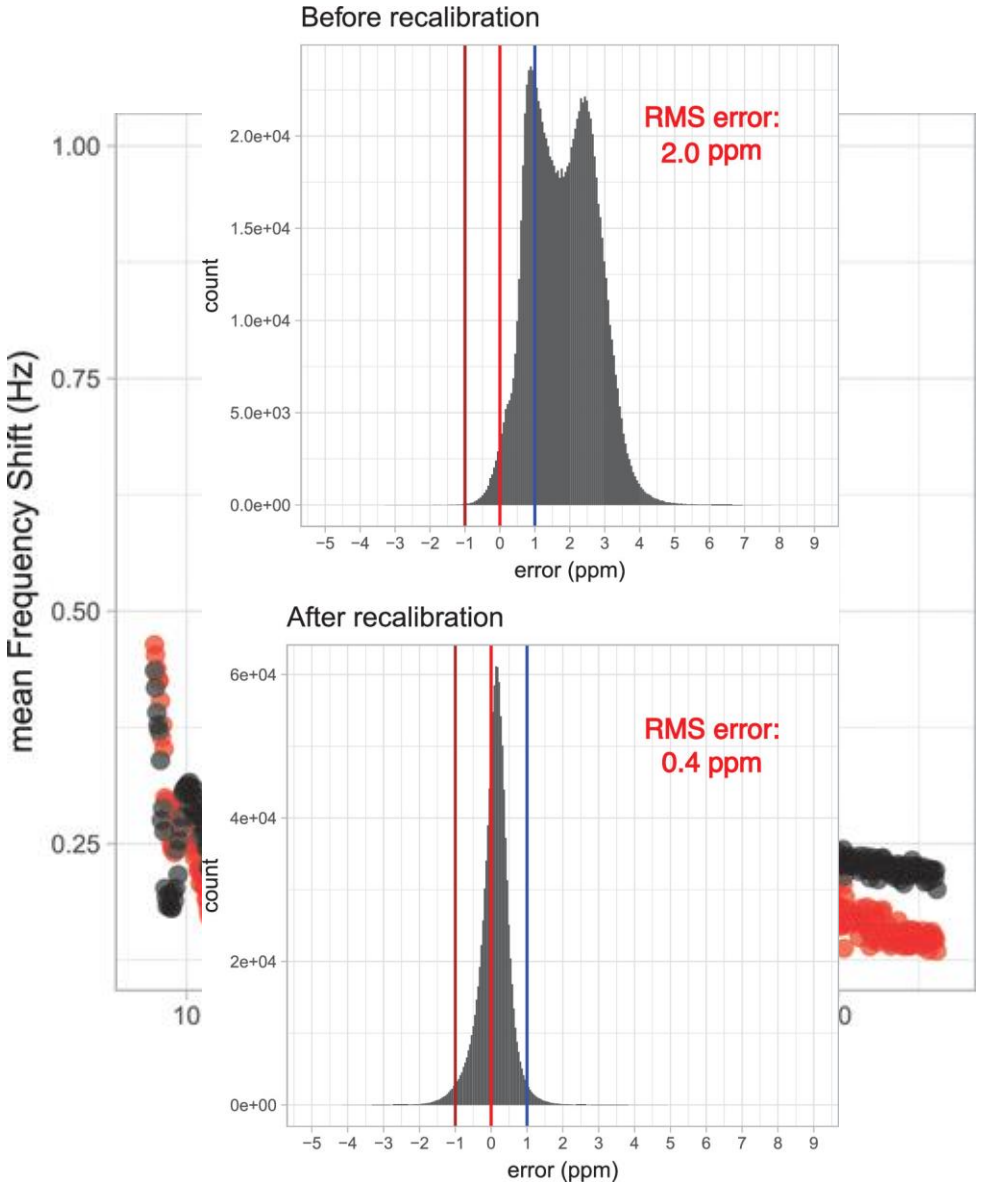
pubs.acs.org/ac Article

**KairosMS: A New Solution for the Processing of Hyphenated Ultrahigh Resolution Mass Spectrometry Data**

Remy Gavard, Hugh E. Jones, Diana Catalina Palacio Lozano, Mary J. Thomas, David Rossell, Simon E. F. Spencer, and Mark P. Barrow*

Cite This: *Anal. Chem.* 2020, 92, 3775–3786 Read Online



# Feature Detection

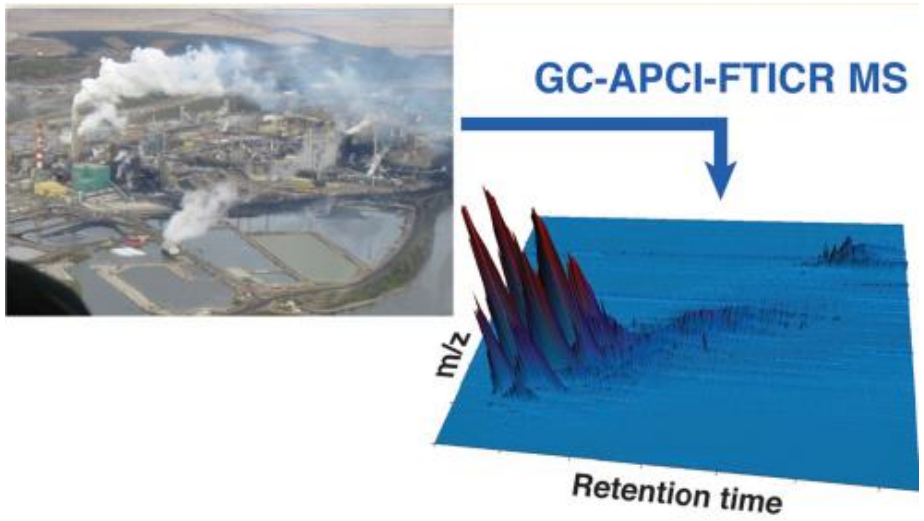
## “Where are the good data?” – Hyphenated Solutions – Example Gas Chromatographic Hyphenation

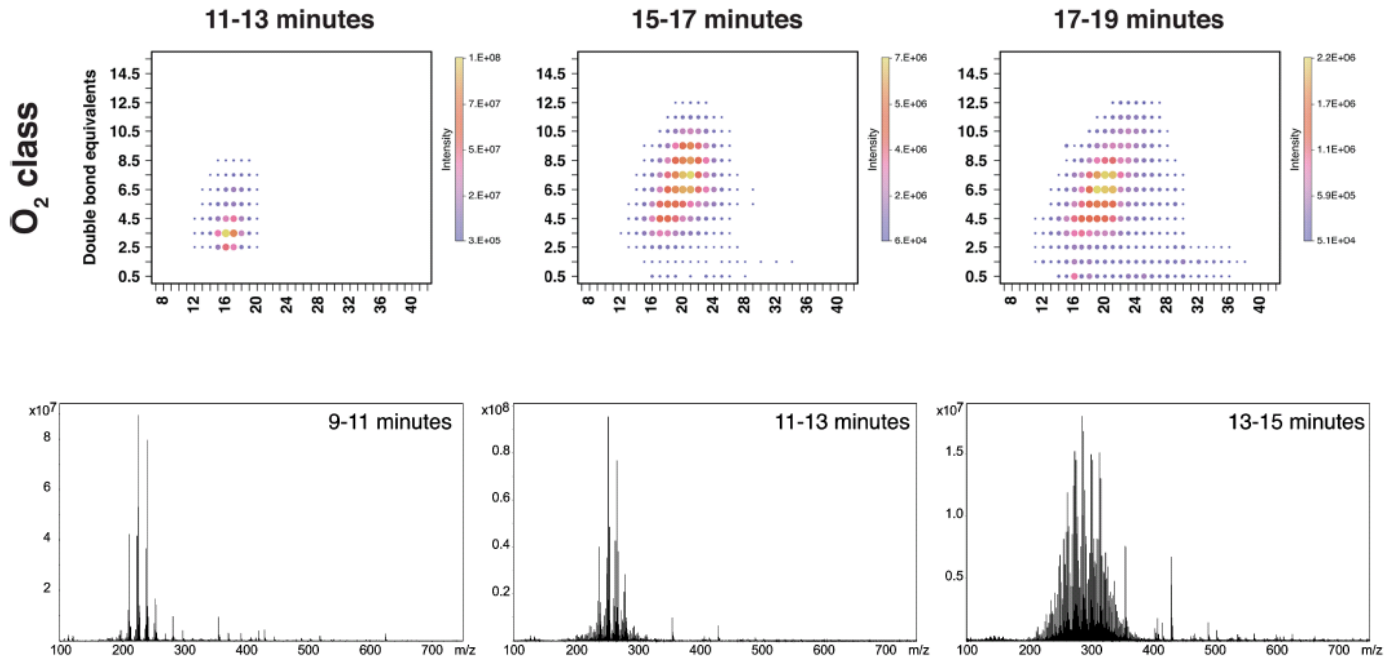
### An Added Dimension: GC Atmospheric Pressure Chemical Ionization FTICR MS and the Athabasca Oil Sands

Mark P. Barrow,*,† Kerry M. Peru,‡ and John V. Headley‡

†Department of Chemistry, University of Warwick, Coventry, CV4 7AL United Kingdom

‡Water Science and Technology Division, Environment Canada, 11 Innovation Boulevard, Saskatoon, Saskatchewan S7N 3H5 Canada



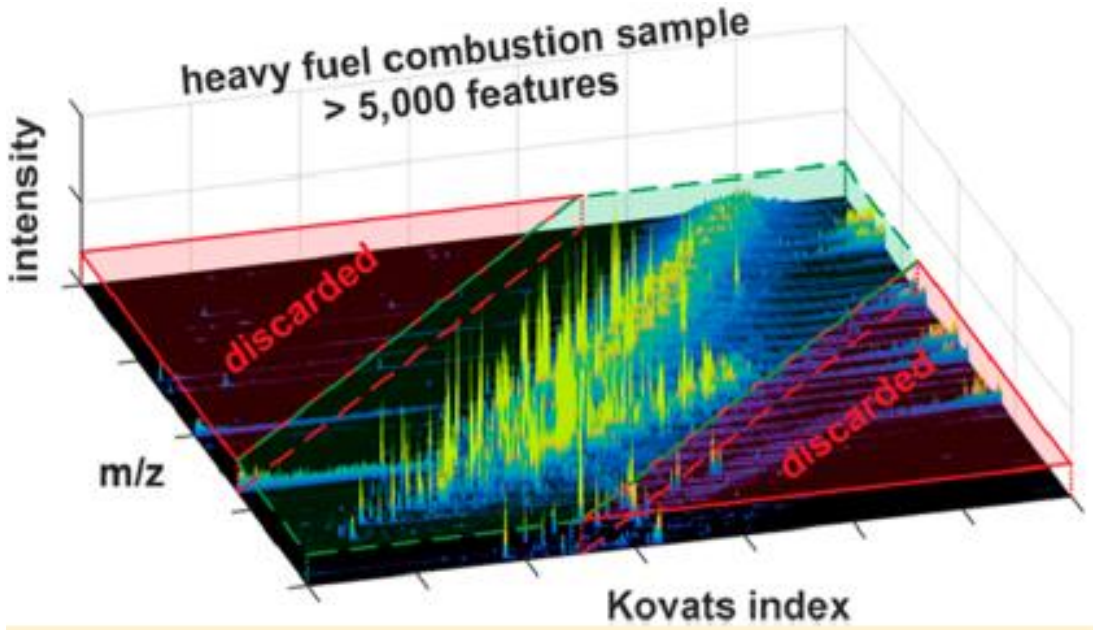
# Feature Detection

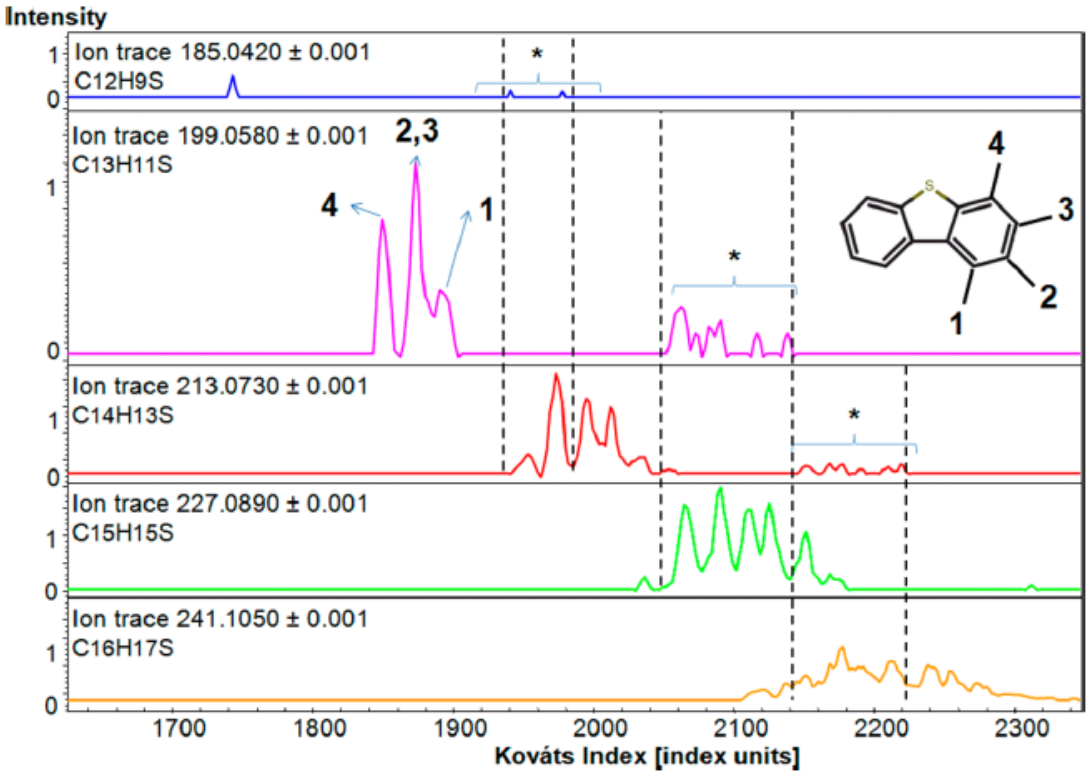
## “Where are the good data?” – Hyphenated Solutions – Example Gas Chromatographic Hyphenation

**Gas Chromatography Coupled to Atmospheric Pressure Chemical Ionization FT-ICR Mass Spectrometry for Improvement of Data Reliability**

Theo Schwemer,[†,‡] Christopher P. Rüger,[†] Martin Sklorz,[*,†,§] and Ralf Zimmermann[†,‡,§]

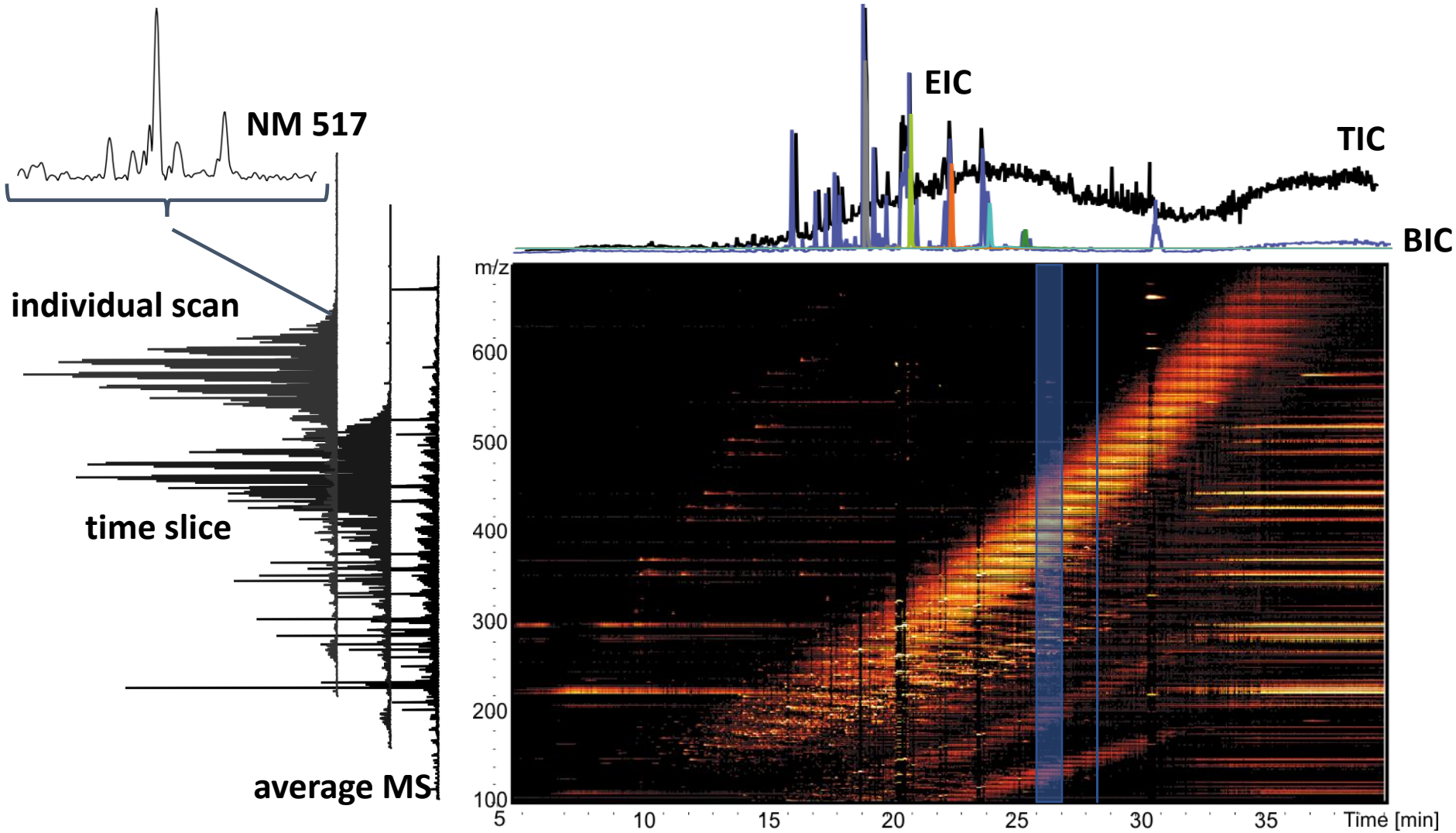
[†]Joint Mass Spectrometry Centre/Chair of Analytical Chemistry, University of Rostock, 18051 Rostock, Germany
[‡]HICE – Helmholtz Virtual Institute of Complex Molecular Systems in Environmental Health – Aerosols and Health, 85764 Neuherberg, Germany, www.hice-vi.eu
[§]Joint Mass Spectrometry Centre/Cooperation Group Comprehensive Molecular Analytics, Helmholtz Zentrum München, 85764 Neuherberg, Germany



# Feature Detection

## "Where are the good data?" – Hyphenated Solutions – Example Gas Chromatographic Hyphenation



# Feature Detection

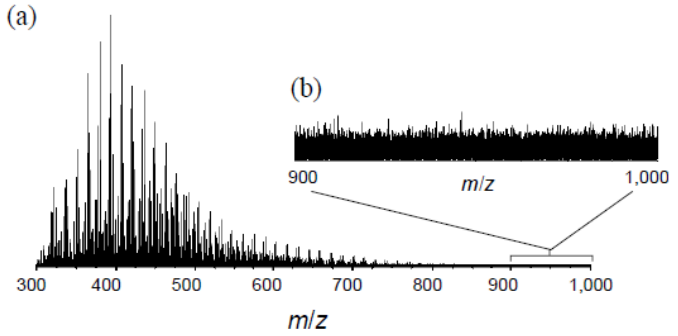
## “Where are the good data?” – Hyphenated Solutions – Example Gas Chromatographic Hyphenation

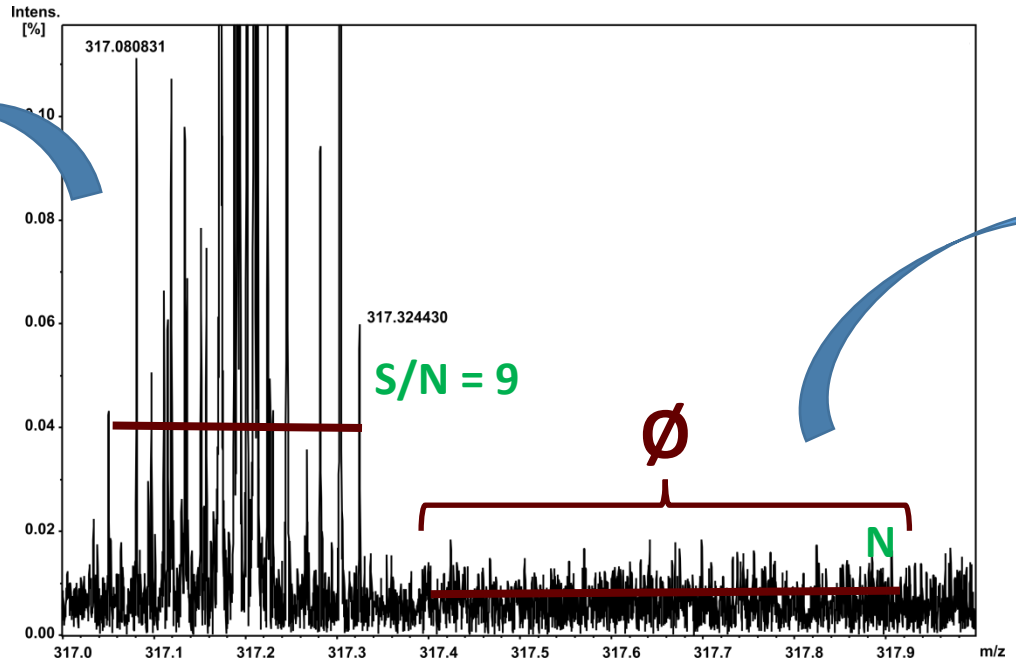
*Optimized Automatic Noise Level Calculations for FT-ICR MS Data* *Bull. Korean Chem. Soc.* **2009**, Vol. 30, No. 11 2665

**Optimized Automatic Noise Level Calculations for Broadband FT-ICR Mass Spectra of Petroleum Give More Reliable and Faster Peak Picking Results**

**Manhoi Hur, Han Bin Oh,† and Sunghwan Kim‡,***

*BNF Technology Inc., Daejeon 305-500, Korea*
*†Department of Chemistry, Sogang University, Seoul 121-742, Korea (200811036)*
*‡Kyungpook National University, Department of Chemistry, Daegu 702-701, Korea. *E-mail: sunghwank@knu.ac.kr*
*Received July 4, 2009, Accepted September 17, 2009*



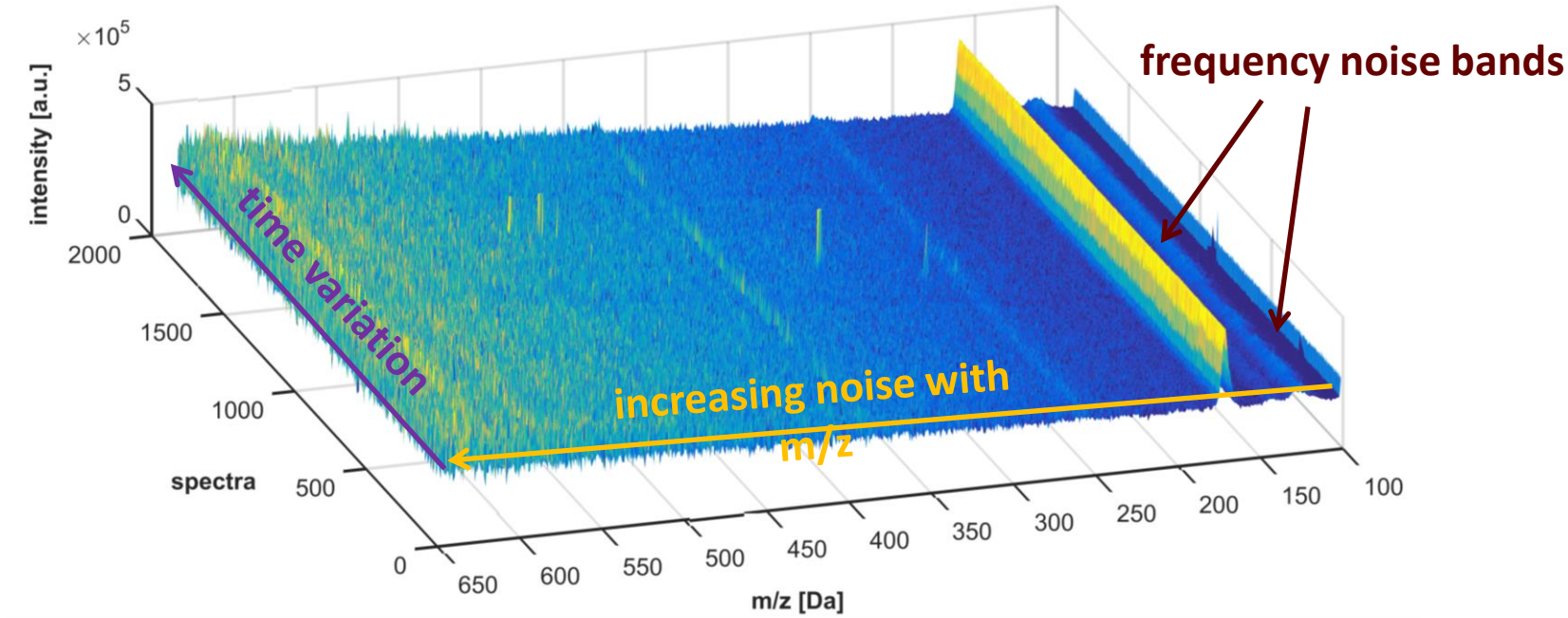

chemically accessed “island” for Petroleum

chemically not accessed space – noise

# Feature Detection

## "Where are the good data?" – Hyphenated Solutions – Example Gas Chromatographic Hyphenation

**Noise estimation for GC-APCI run:**
(550 nominal m/z-values * 2000 spectra = 1.1e6 noise values)




Noise estimation based on the signal height at the *m/z* interval chemically not accessible for each nominal mass

# Feature Detection

## “Where are the good data?” – Hyphenated Solutions – Example Gas Chromatographic Hyphenation

Analytica Chimica Acta 1173 (2021) 338674

Contents lists available at ScienceDirect

Analytica Chimica Acta

journal homepage: www.elsevier.com/locate/aca

### Dynamic binning peak detection and assessment of various lipidomics liquid chromatography-mass spectrometry pre-processing platforms

Xiaodong Feng [a], Wenxuan Zhang [b, c], Folkert Kuipers [a, b], Ido Kema [a], Andrei Barcaru [a, 1], Péter Horvatovich [c, *, 1]

[a] Department of Laboratory Medicine, University Medical Center Groningen, Hanzeplein 1, 9713, GZ Groningen, the Netherlands
[b] Department of Pediatrics, University Medical Center Groningen, Hanzeplein 1, 9713, GZ Groningen, the Netherlands
[c] Department of Analytical Biochemistry, University of Groningen, Antonius Deusinglaan 1, 9713, AV Groningen, the Netherlands

This uncertainty is dependent on the *m/z*, so a fixed mass tolerance value for peak detection may result in peak merging and/or failure to detect peaks at a specific *m/z* range. An alternative is to use a dynamic mass tolerance according to the uncertainty of acquired ions. Thus, the peak detection mass tolerance (*PDMT*) should be set as a function of the MF (usually defined in ppm) and MD. The PDMT in Da ($PDMT_{Da}$) can be calculated by

$$PDMT_{Da} = MD_{Da} + MF \cdot \frac{m}{z} \cdot 10^{-6} \quad (1)$$

FTICR:

$$PDMT_{Da} = \left(\frac{A_{fti}}{2.35482}\right) \cdot \left(\frac{m}{z}\right)^2 + MF \cdot \frac{m}{z} \cdot 10^{-6} \quad (1a)$$

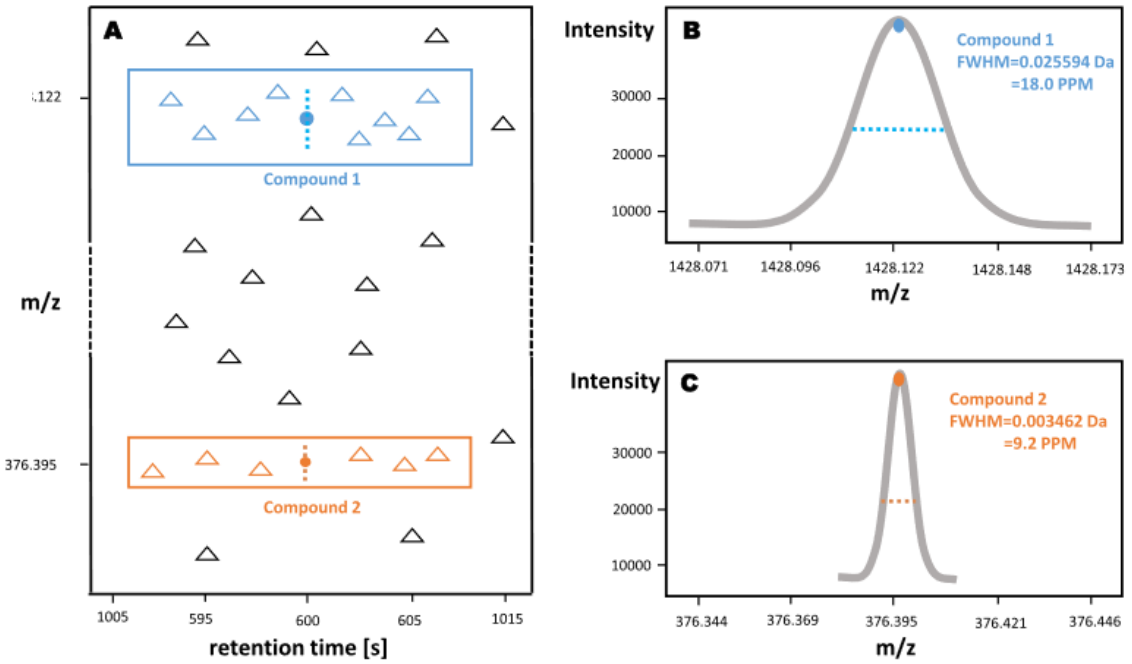
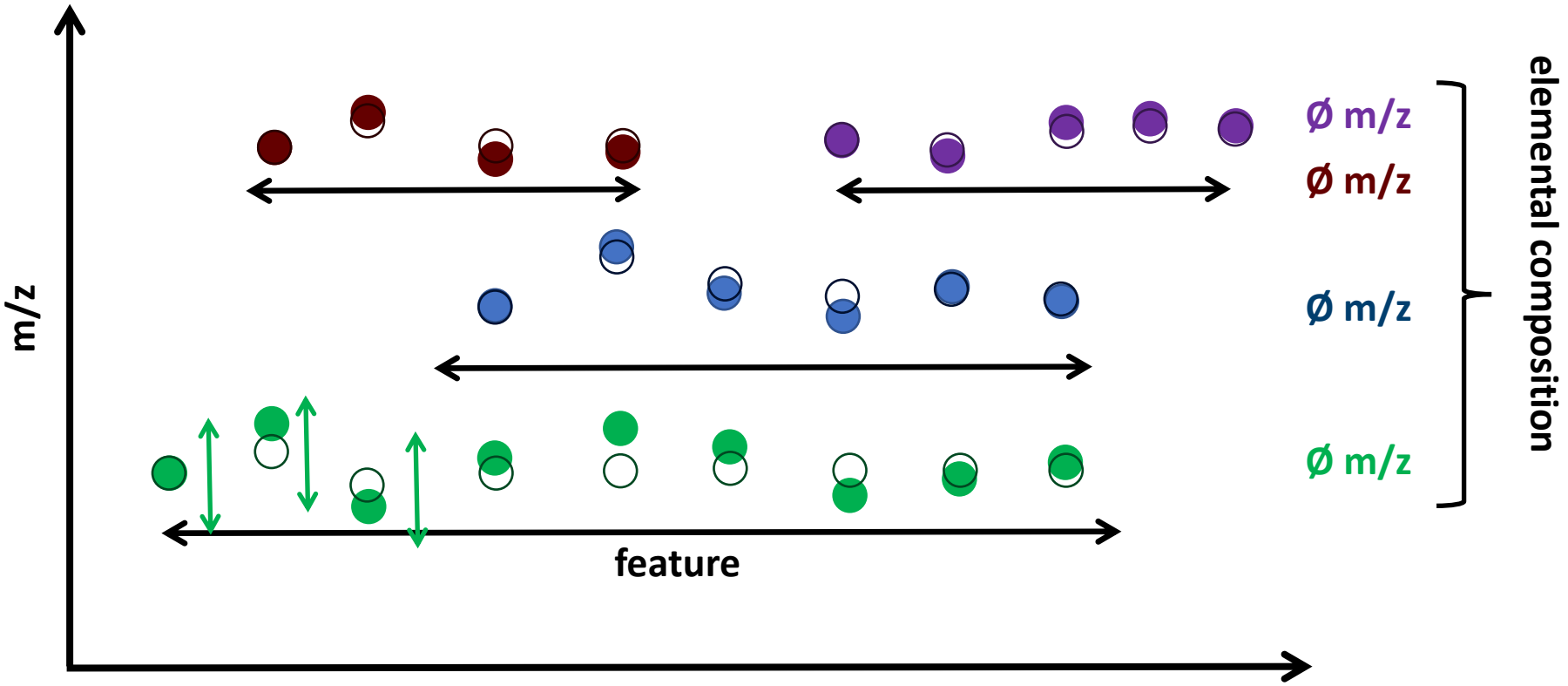



**Fig. 1.** Scheme showing the main aspects of the dynamic binning method demonstrating the change of peak width defined as *FWHM* (Full Width at Half Maximum) in function of *m/z*. (A) Scatter plot of detected peaks, with retention time in the x-axis and *m/z* in the y-axis. (B) Compound 1 is located at a high *m/z* 1428.1220 Da, which has a large *FWHM*, around 0.025594 Da (18.0 ppm). (C) Compound 2 is situated at a low *m/z* of 376.3950 Da, which has a small *FWHM*, around 0.003462 Da (9.2 ppm).

# Feature Detection

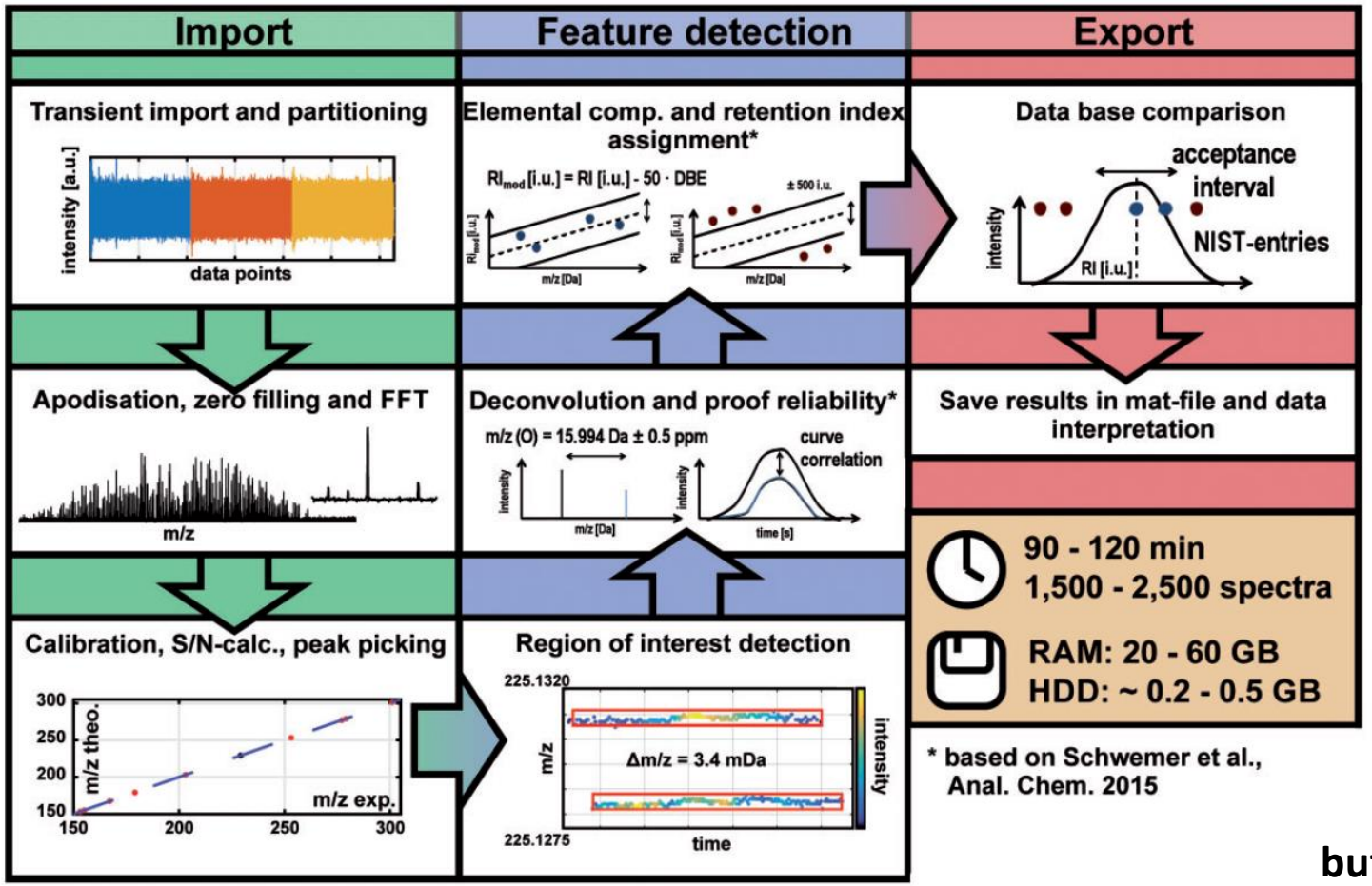
## "Where are the good data?" – Hyphenated Solutions – Example Gas Chromatographic Hyphenation

- feature detection based on time trace and moving mass window
- automatic discarding of non-chromatographic, to low intense and to short features and deconvolution



# Feature Detection

## "Where are the good data?" – Hyphenated Solutions – Example Gas Chromatographic Hyphenation

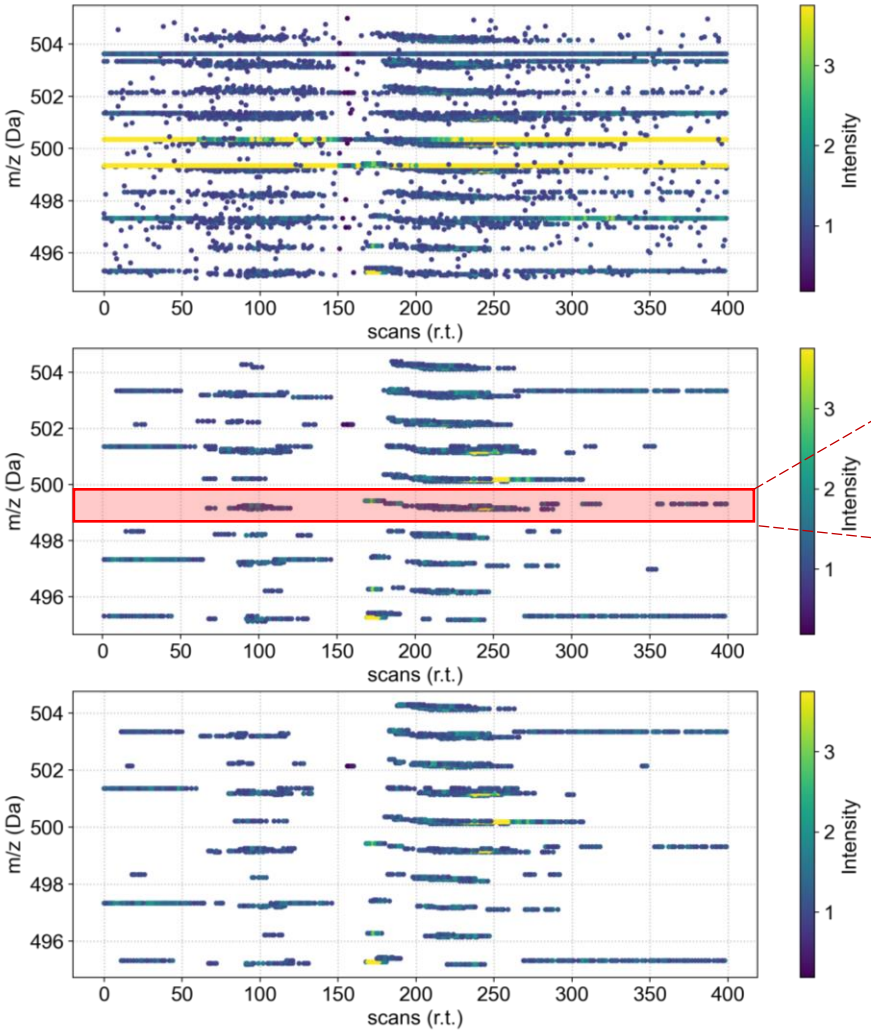



**but** poor scaling for larger data sets

Rüger, *European Journal of Mass Spectrometry* 23, S. 28–39. DOI: 10.1177/1469066717694286.

# Feature Detection

## “Where are the good data?”

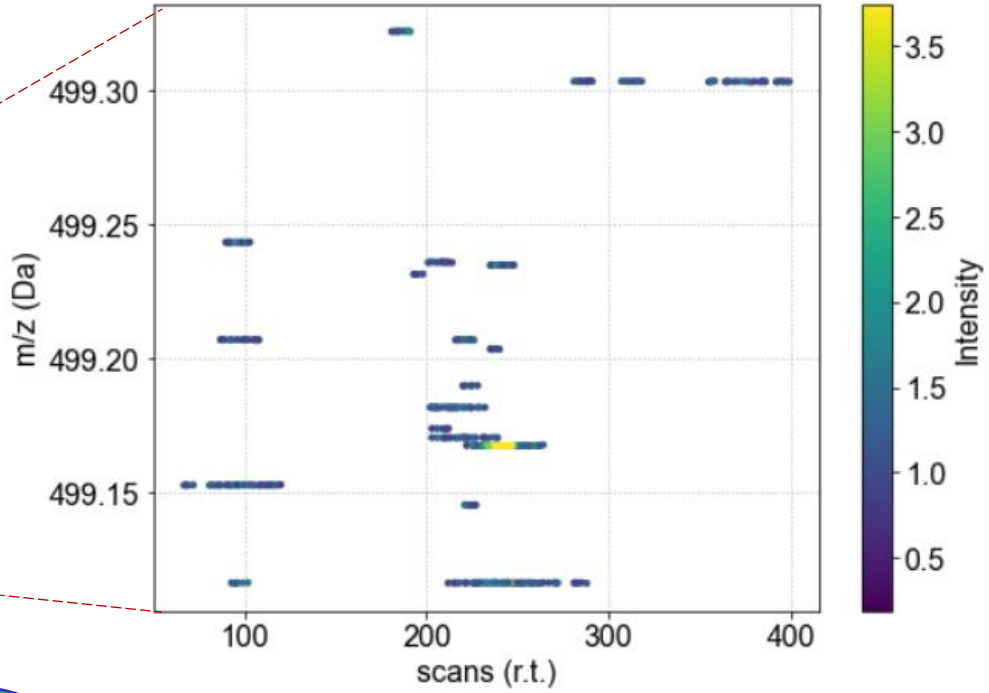



**RAW DATA**

**K-means**
Time: 10.9 s
ROIs detected: 26896

**Iterative method:**
Time: 3min 7.2s
ROIs detected: 23350

Zoom: 499 – 499.4 Da



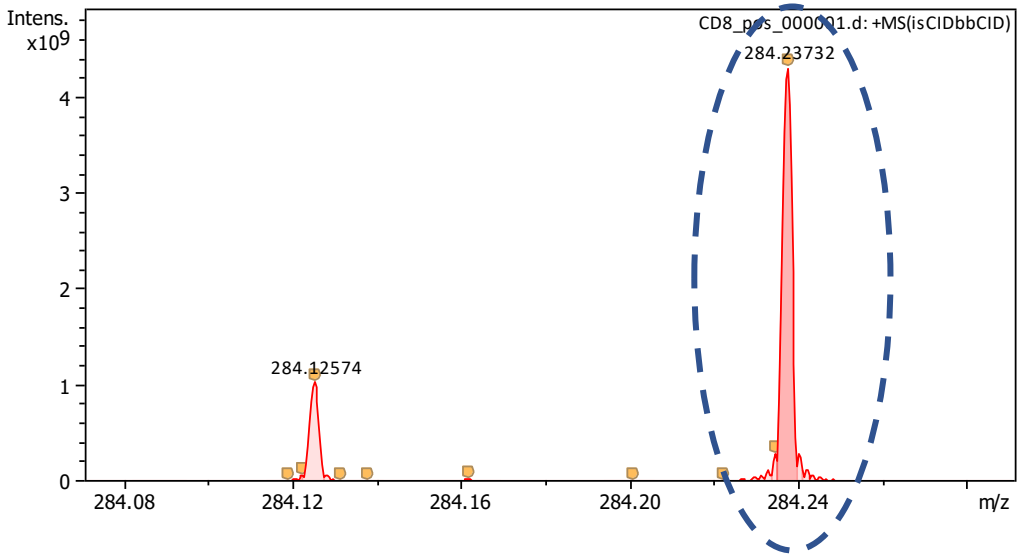

Local grouping approach by nominal mass

**Enhanced Iterative method:**
Time: 27.5 s
ROIs detected: 23642

PyC2MC
Python Framework for Complex Matrices Molecular Characterization

# From Mass to Chemistry

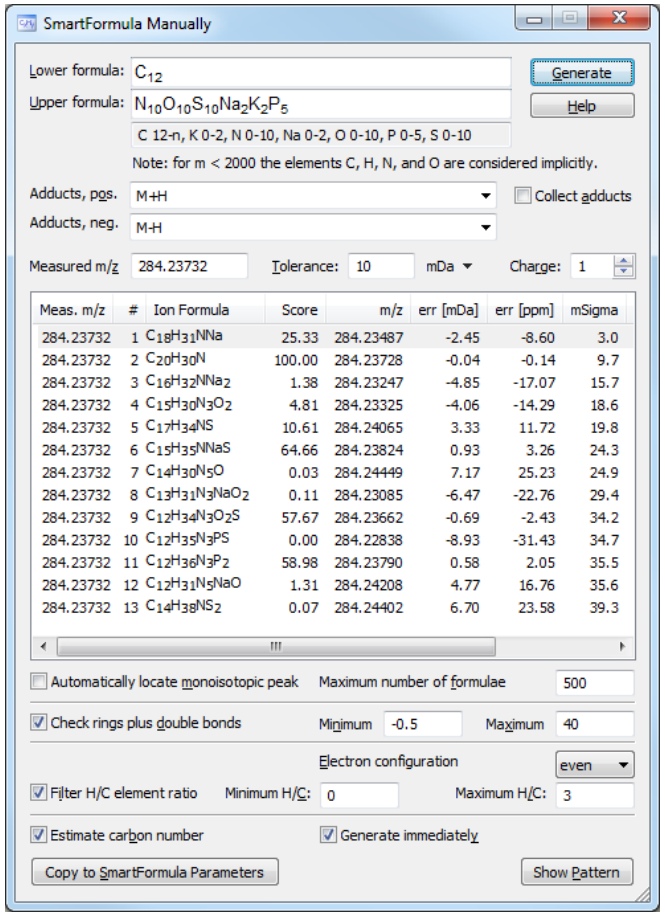
## Now we have a list of mass spectrometric features – What to do?



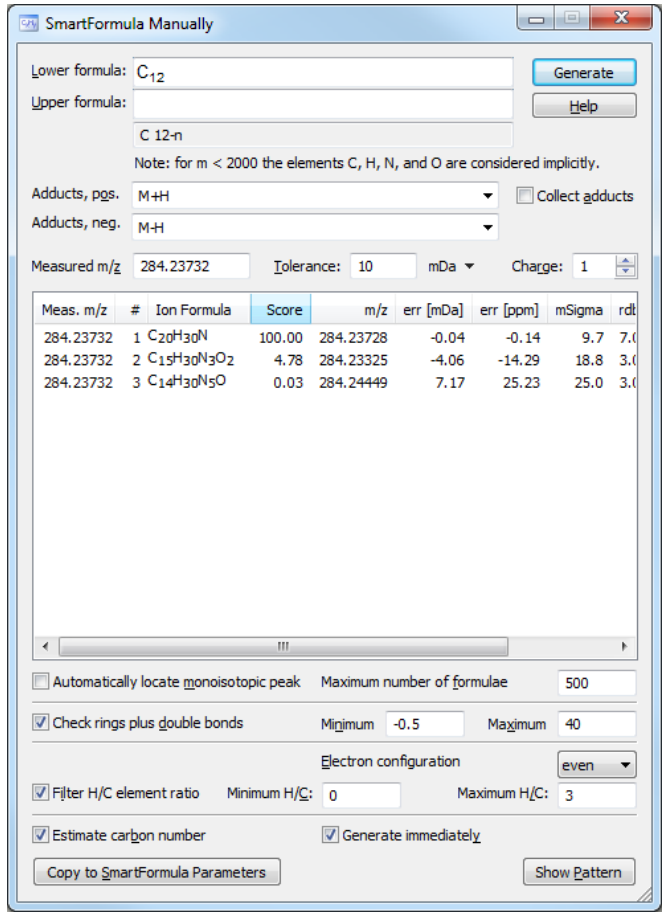

- even with ppm mass accuracy several mathematical possibilities – pure ab-initio calculation difficult / not possible

→ selection rules needed!

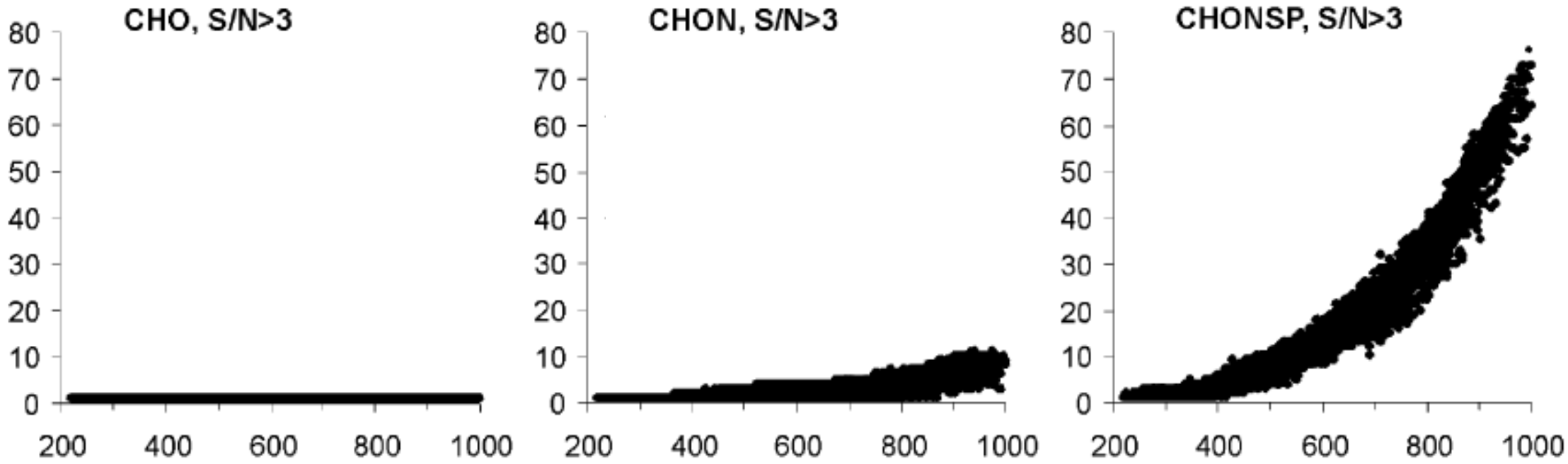
some heteroelements




CHNO only



# From Mass to Chemistry




$\Delta m/m < 1ppm$

Suwannee River Fulvic Acid Standard, ESI negativ ≈ 8,500 Peaks

Koch et al., *Anal.Chem.*, 1758-1763 (**2007**)

**Attribution of elemental compositions:**

"Seven golden rules"

**1 . Restriction to element numbers**

**Table 1: Restrictions for number of elements during formula generation for small molecules based on examination of the DNP and Wiley mass spectral databases. For each element, the higher count was taken for denominating the element restriction rule #1**

| Mass Range [Da] | Library | C max | H max | N max | O max | P max | S max | F max | Cl max | Br max | Si max |
|---|---|---|---|---|---|---|---|---|---|---|---|
| < 500 | DNP | 29 | 72 | 10 | 18 | 4 | 7 | 15 | 8 | 5 | |
| | Wiley | 39 | 72 | 20 | 20 | 9 | 10 | 16 | 10 | 4 | 8 |
| < 1000 | DNP | 66 | 126 | 25 | 27 | 6 | 8 | 16 | 11 | 8 | |
| | Wiley | 78 | 126 | 20 | 27 | 9 | 14 | 34 | 12 | 8 | 14 |
| < 2000 | DNP | 115 | 236 | 32 | 63 | 6 | 8 | 16 | 11 | 8 | |
| | Wiley | 156 | 180 | 20 | 40 | 9 | 14 | 48 | 12 | 10 | 15 |
| < 3000 | DNP | 162 | 208 | 48 | 78 | 6 | 9 | 16 | 11 | 8 | |

# From Mass to Chemistry

**Attribution of elemental compositions:**

"Seven golden rules"

**2. LEWIS and SENIOR check**

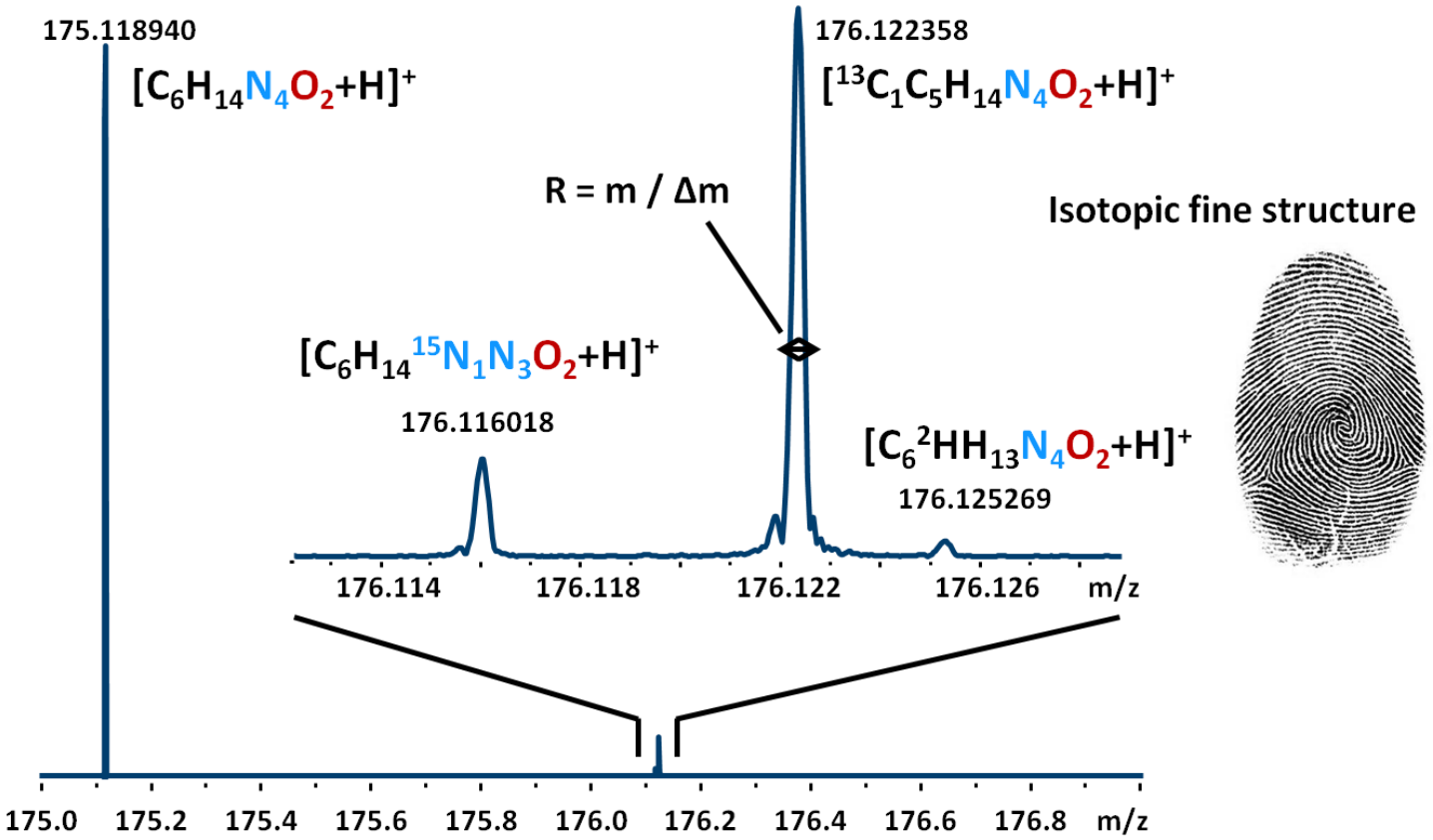
> i) The sum of valences or the total number of atoms having odd valences is even;
>
> ii) The sum of valences is greater than or equal to twice the maximum valence;
>
> iii) The sum of valences is greater than or equal to twice the number of atoms minus 1.

# From Mass to Chemistry

**Attribution of elemental compositions:**

"Seven golden rules"

**3. Isotopic pattern filter**



# From Mass to Chemistry

**Attribution of elemental compositions:**

"Seven golden rules"

1) apply heuristic restrictions for number of elements during formula generation

2) perform LEWIS and SENIOR check

3) perform isotopic pattern filter

4) perform H/C ratio check (hydrogen/carbon ratio)

5) perform NOPS ratio check (N, O, P, S/C ratios)

6) perform heuristic HNOPS probability check (H, N, O, P, S/C high probability ratios)

7) perform -TMS check (for GC-MS if a silylation step is involved)

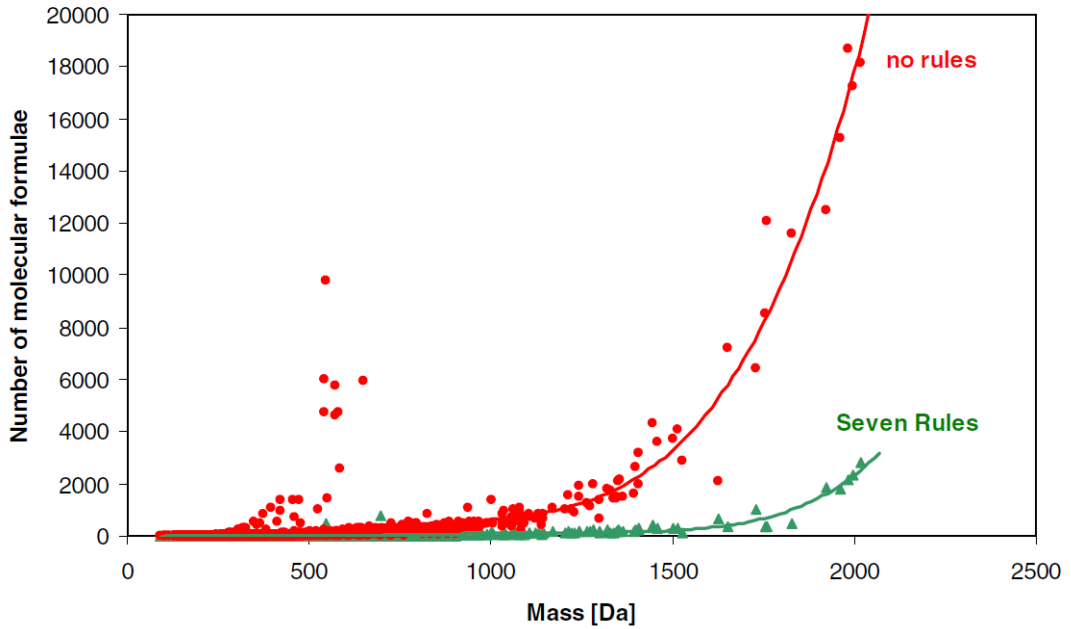



**Figure 5**
**Mass dependence of calculated, chemically possible formulas derived from 1,200 randomly selected DNP molecules, imposed with simulated 3 ppm mass accuracy ± 5% isotope ratio measurement errors**. Red graph: number of calculated formulas with common molecular generators. Green graph: number of formulas constrained by the seven rules. Outliers around 600 Dalton were found to be halogen containing compounds.

# From Mass to Chemistry

**Available Software Solutions**

- vendor Solutions, *e.g.*, Bruker Data Analysis, ThermoFisher Xcalibur, Agilent Mass Hunter, etc.

→ but most often strong limitations in-handling complex data, isotpologues, validation concepts,…

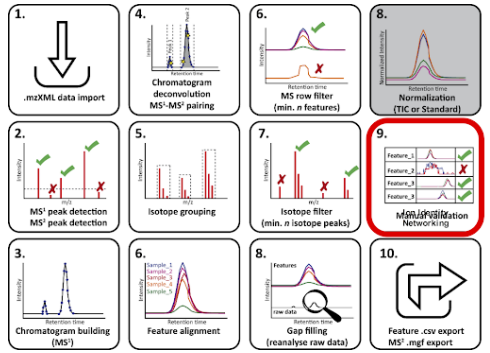
<u>Custom Software Solution:</u>

- Commercial: PetroOrg

Sierra Analytics Composer

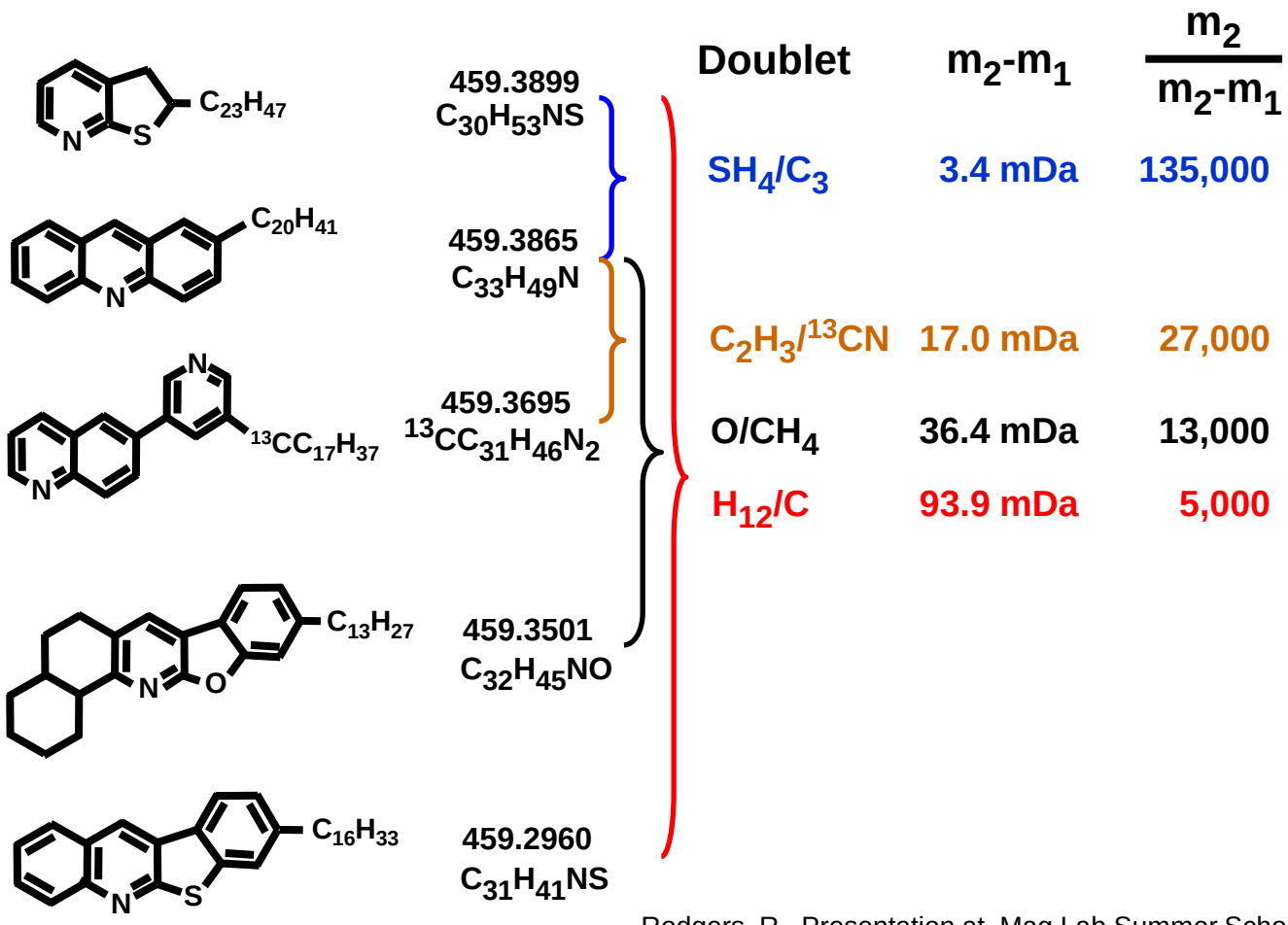
Peak-by-Peak

- Free Software: CERES (Univ. Rostock), OpenMS, mMass, MZmine / MZmine2
- Specialized Solutions:
  - OCEAN (Univ. Oldenburg for DOM)
  - …



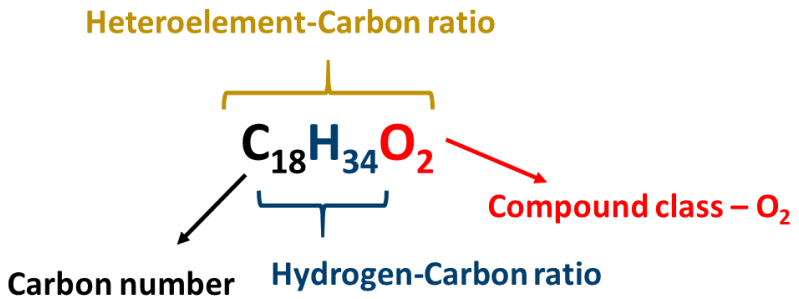
# From Mass to Chemistry

**Characteristic mass splits and critical aspects in elemental composition attribution:**




| Doublet | $m_2$-$m_1$ | $\frac{m_2}{m_2\text{-}m_1}$ |
|---|---|---|
| $SH_4/C_3$ | 3.4 mDa | 135,000 |
| $C_2H_3/^{13}CN$ | 17.0 mDa | 27,000 |
| $O/CH_4$ | 36.4 mDa | 13,000 |
| $H_{12}/C$ | 93.9 mDa | 5,000 |

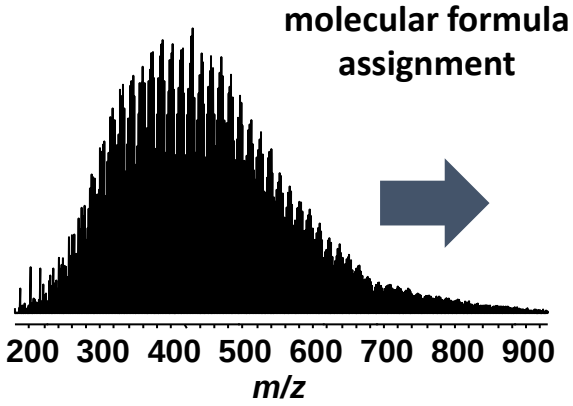
→ **Let us imagine we attributed the correct elemental compositions. How to handle several thousands of formula efficiently?**




Rodgers, R., Presentation at Mag Lab Summer School 2009

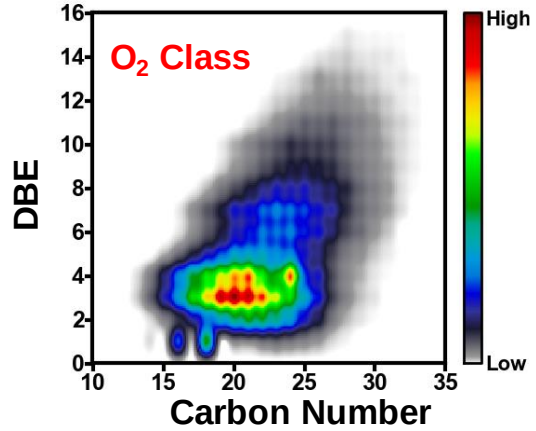
# Handling Attribution Data

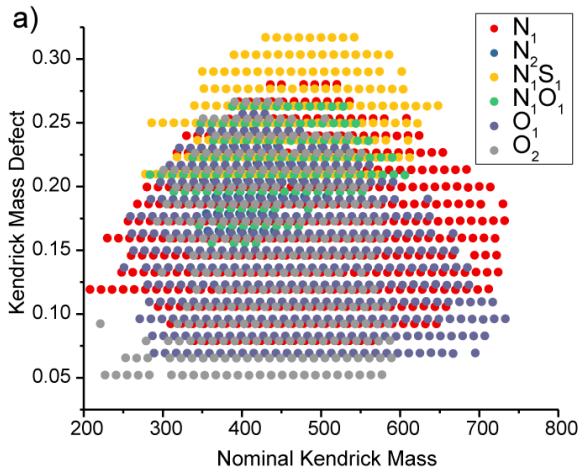
## Complex Mixture



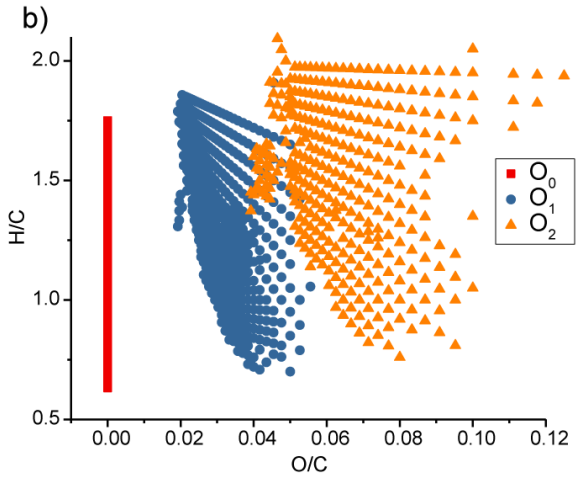

| Molecular Formula | Measured Mass | Calculated Mass | ppm error |
|---|---|---|---|
| $C_{29}H_{42}N_1$ | 404.3323 | 404.33227 | 0.16 |
| $C_{30}H_{44}N_1$ | 418.348 | 418.34792 | 0.18 |
| $C_{31}H_{46}N_1$ | 432.3638 | 432.36357 | 0.48 |
| $C_{32}H_{50}N_1$ | 446.3793 | 446.37922 | 0.15 |
| $C_{27}H_{47}O_2$ | 403.3582 | 403.35815 | 0.09 |
| $C_{28}H_{49}O_2$ | 417.3738 | 417.37380 | -0.13 |
| $C_{29}H_{51}O_2$ | 431.3895 | 431.38945 | 0.18 |
| $C_{30}H_{53}O_2$ | 445.4052 | 445.40510 | 0.12 |
| $C_{31}H_{55}O_2$ | 459.4210 | 459.42075 | 0.49 |
| $C_{32}H_{57}O_2$ | 473.4364 | 473.43640 | -0.07 |

data grouping and visualization

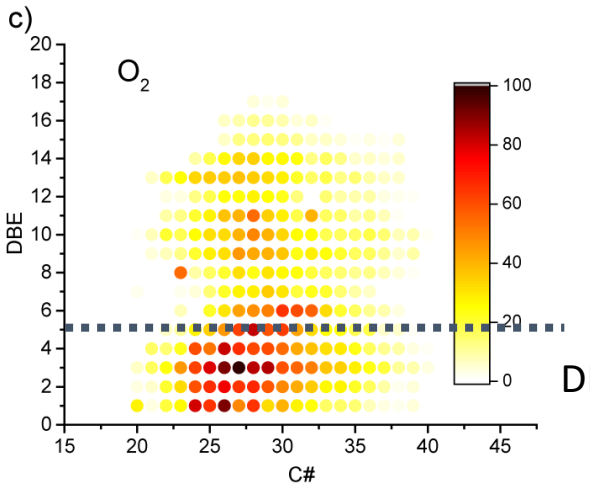


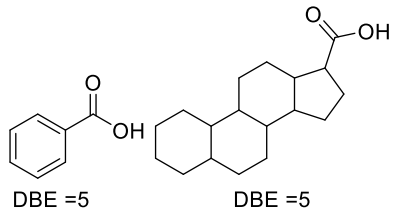

Kendrick Diagram




van Krevelen Diagram




DBE vs C#




$$DBE = 1 + \#C - \#H/2 + \#N/2$$

S. Gutierrez Sama et al., *Energy and Fuels* **(2018)**

# Handling Attribution Data

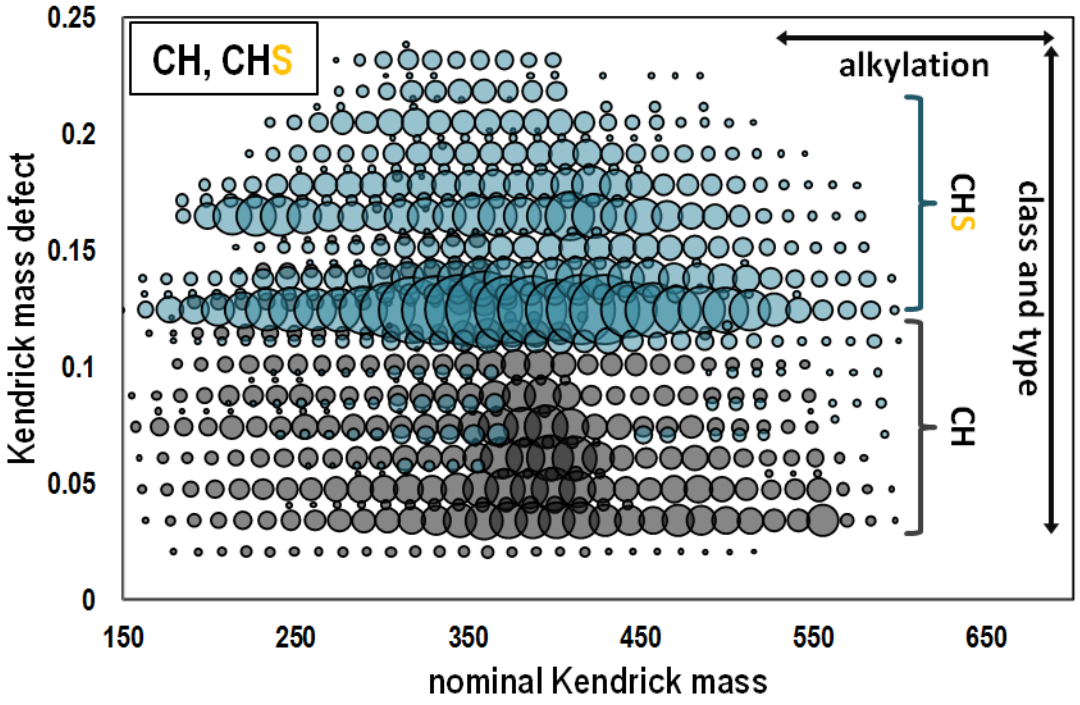
## Visualization and grouping of elemental compositions – Kendrick Mass Defect Diagram

$$KM = mass_{detect}\left(\frac{14.00000}{14.01565}\right)$$

$$KMD = mass_{integer} - KM$$

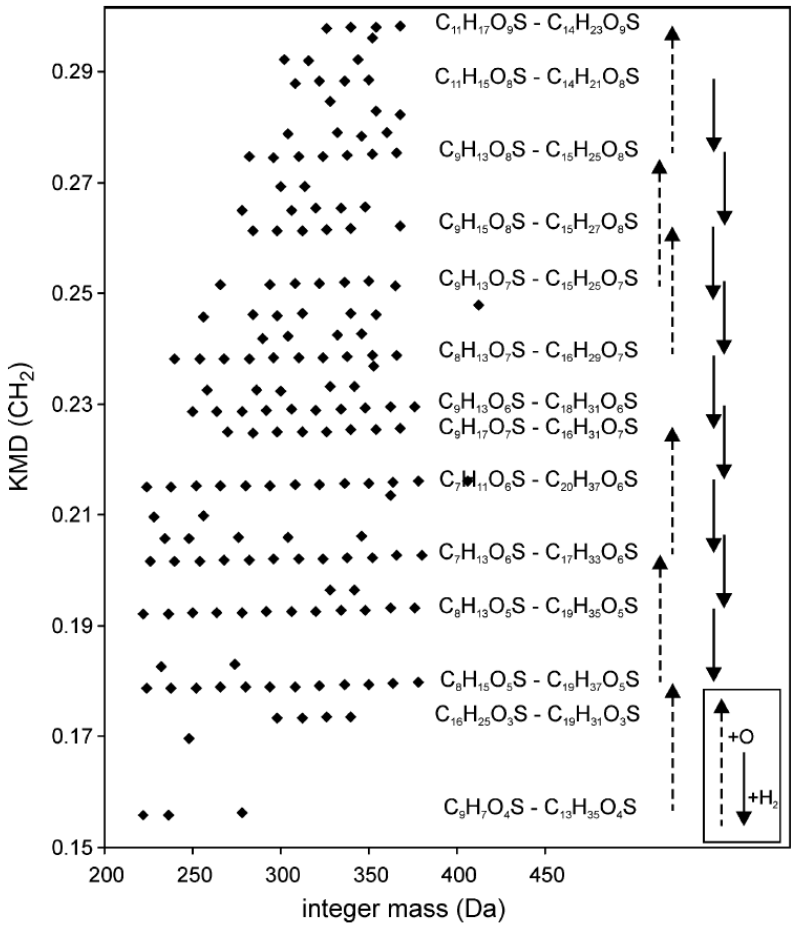
$$KMD\ (C_6H_6) = 78.04695 \times (14.0000/14.01565) - 78 = 0.9598$$

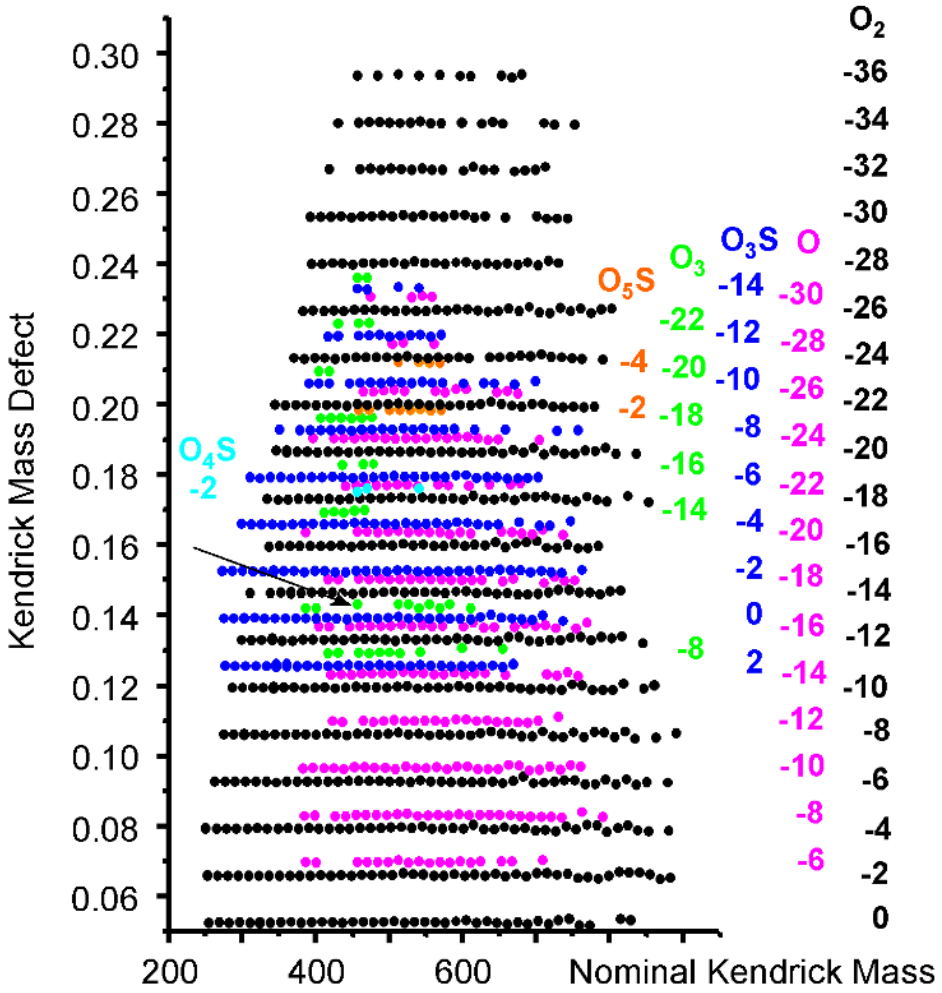
$$KMD\ (C_7H_8) = 92.06300 \times (14.0000/14.01565) - 92 = 0.9598$$



# Handling Attribution Data

## Visualization and grouping of elemental compositions – Kendrick Mass Defect Diagram



# Handling Attribution Data

Contents lists available at ScienceDirect

Fuel

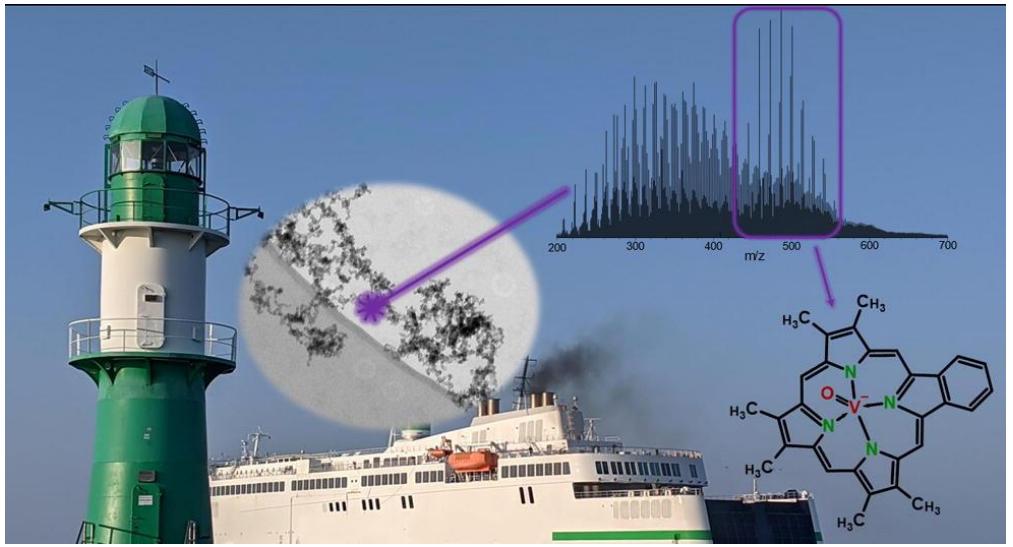
journal homepage: www.elsevier.com/locate/fuel

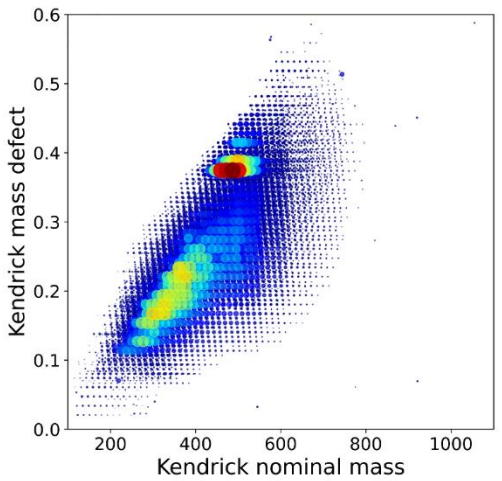
Full Length Article

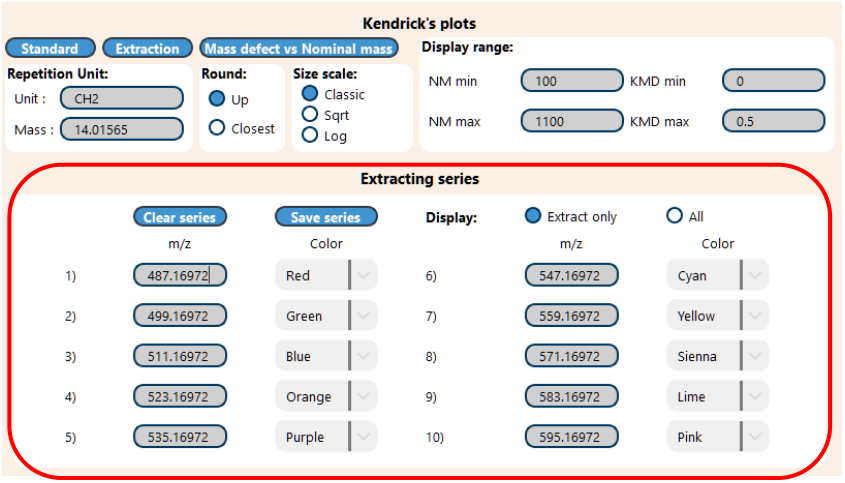
Selective characterization of petroporphyrins in shipping fuels and their corresponding emissions using electron-transfer matrix-assisted laser desorption/ionization Fourier transform ion cyclotron resonance mass spectrometry

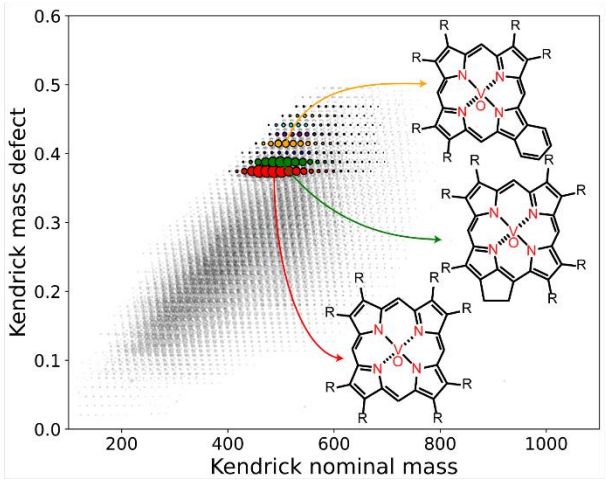
Maxime Sueur [a,b], Christopher P. Rüger [b,c,d,*], Julien F. Maillard [a,b], Hélène Lavanant [a], Ralf Zimmermann [c,d], Carlos Afonso [a,b]

[a] Normandie Université, COBRA, UMR 6014 et FR 3038, Université de Rouen, INSA de Rouen-Normandie, CNRS, IRCOF, Mont Saint Aignan Cedex, France
[b] International Joint Laboratory – iC2MC: Complex Matrices Molecular Characterization, TRTG, BP 27, 76700 Harfleur, France
[c] Joint Mass Spectrometry Centre/Chair of Analytical Chemistry, University of Rostock, 18059 Rostock, Germany
[d] Department Life, Light & Matter (LLM), University of Rostock, 18051 Rostock, Germany



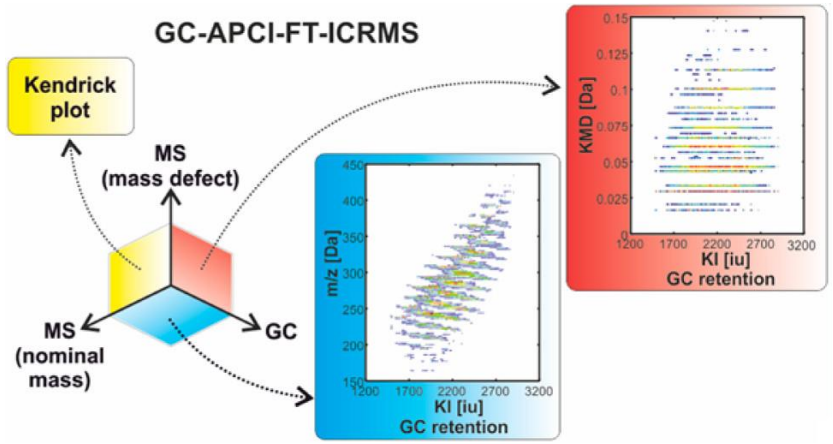
# Handling Attribution Data

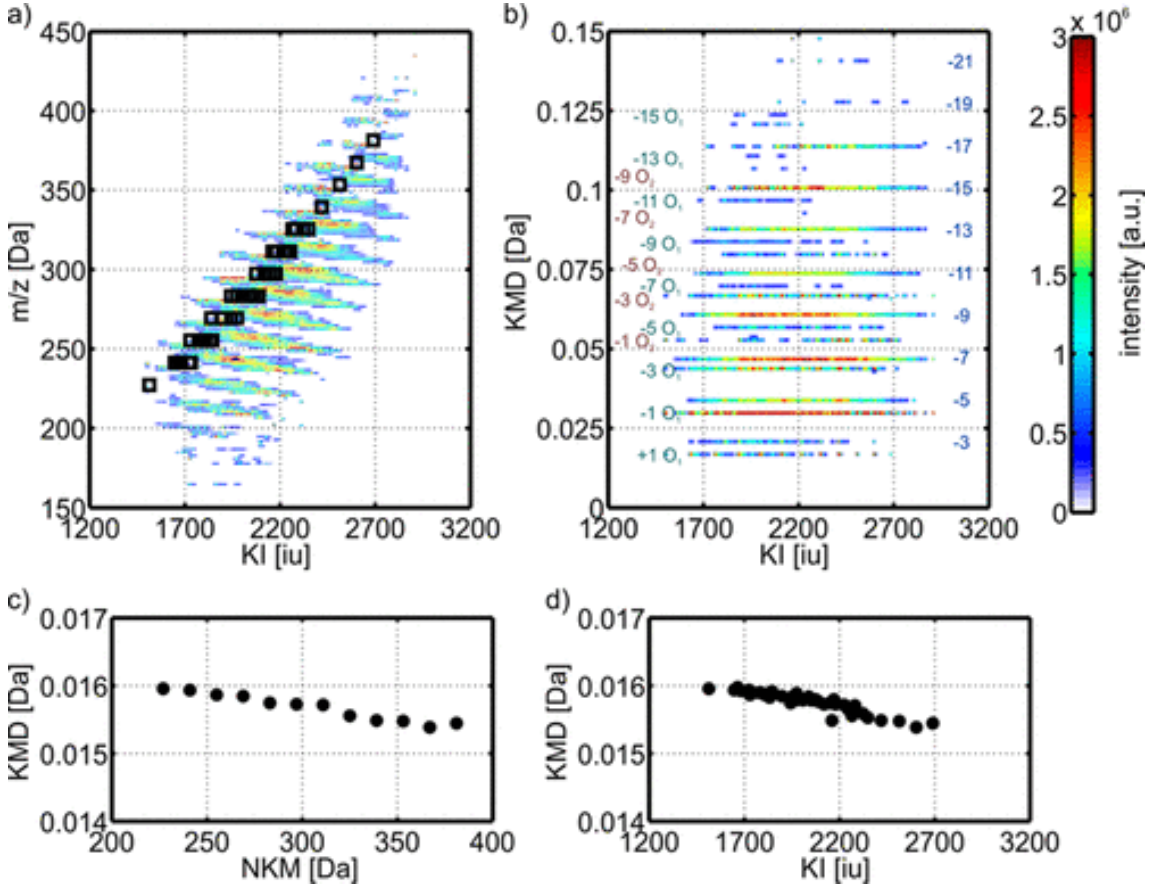
energy&fuels
Article
pubs.acs.org/EF

**Investigating the Trace Polar Species Present in Diesel Using High-Resolution Mass Spectrometry and Selective Ionization Techniques**

Elize Smit,[*,†] Christopher P. Rüger,[‡] Martin Sklorz,[‡,§] Stefan De Goede,[▽] Ralf Zimmermann,[‡,§] and Egmont R. Rohwer[†]

[†]Department of Chemistry, University of Pretoria, Lynnwood Road, Pretoria, South Africa
[‡]Joint Mass Spectrometry Centre/Chair of Analytical Chemistry, University of Rostock, Rostock, Germany
[§]Joint Mass Spectrometry Centre/Cooperation Group Comprehensive Molecular Analytics, Helmholtz Zentrum München, Neuherberg, Germany
[▽]Sasol Southern Africa Energy, Energy Technology, Klasie Havenga Street, Sasolburg, South Africa

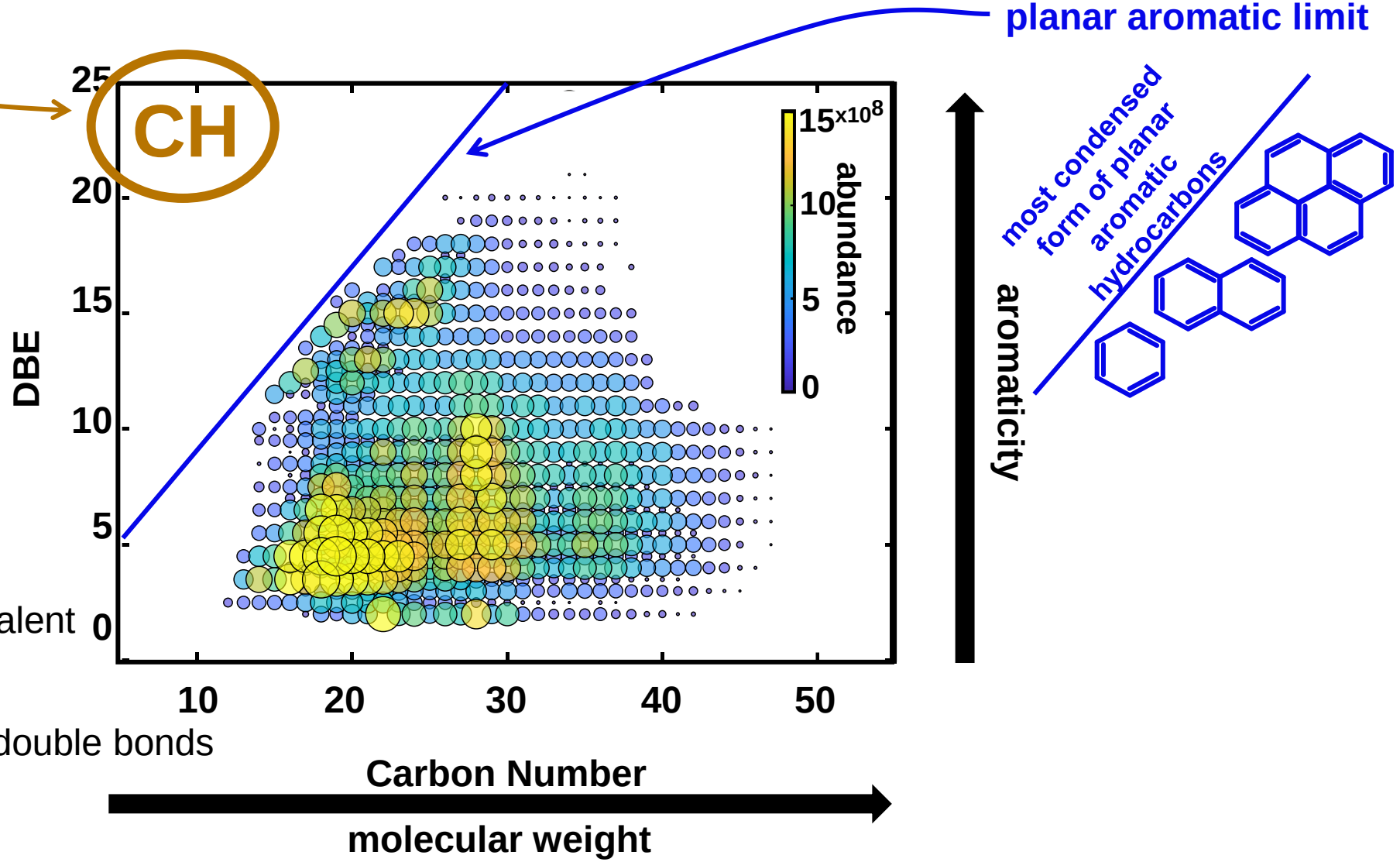



Different graphical representations of the chromatographic separation and mass spectral data obtained by GC-APCI-FT-ICRMS for sample CD5: (a) m/z vs KI values, with peaks of the $+1O_1$ subclass highlighted in black. (b) Plot of Kendrick mass defect vs KI values showing a more orthogonal distribution of peaks throughout the two-dimensional space. (c,d) Comparison of the $+1O_1$ subclass with (panel d) and without (panel c) chromatographic separation being taken into account.

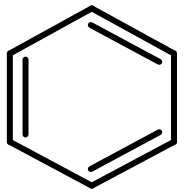
# Handling Attribution Data – DBE/#C

All compounds containing only CH are summarized in the CH-class, species containing C, H, and one O-atom are summarized in the O1-class




$$DBE = \#C - \frac{\#H}{2} + \frac{\#N}{2}$$

Ring and double bond equivalent



one ring + three double bonds
DBE = 4

# Handling Attribution Data

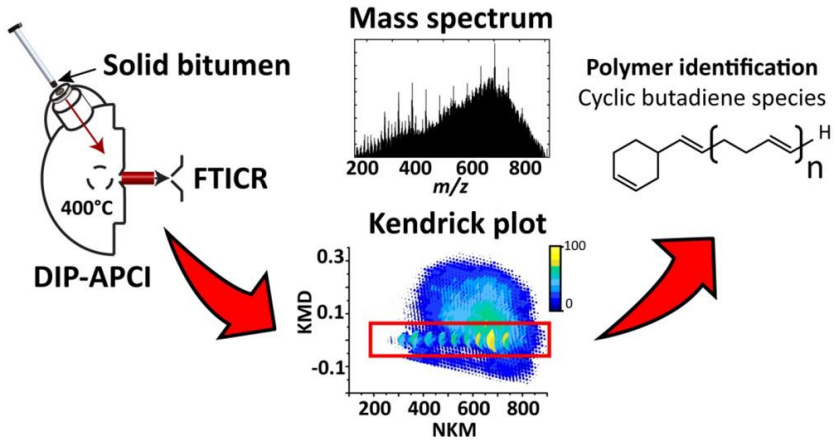
energy&fuels

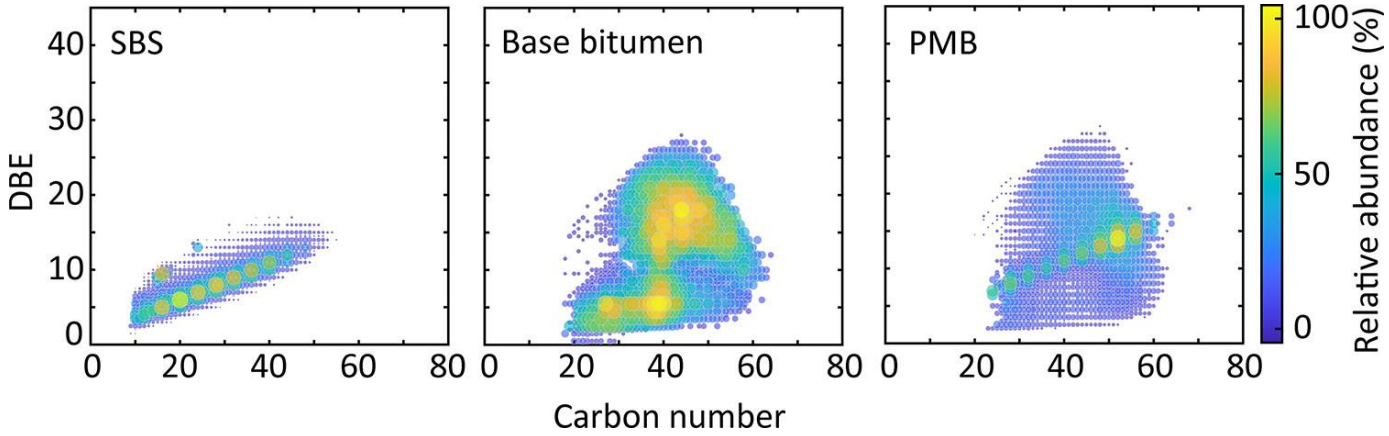
pubs.acs.org/EF Article

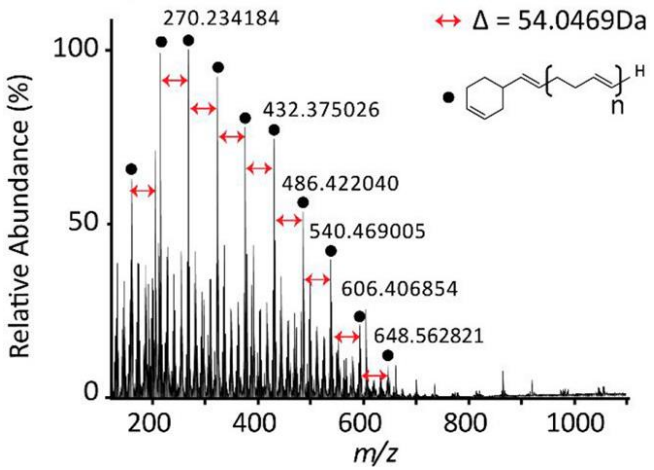
**Direct Insertion Analysis of Polymer-Modified Bitumen by Atmospheric Pressure Chemical Ionization Ultrahigh-Resolution Mass Spectrometry**

Oscar Lacroix-Andrivet, Clément Castilla, Christopher Rüger, Marie Hubert-Roux, Anna Luiza Mendes Siqueira, Pierre Giusti, and Carlos Afonso*

Cite This: *Energy Fuels* 2021, 35, 2165–2173 Read Online



# Handling Attribution Data

## Visualization and grouping of elemental compositions – Van Krevelen Diagram

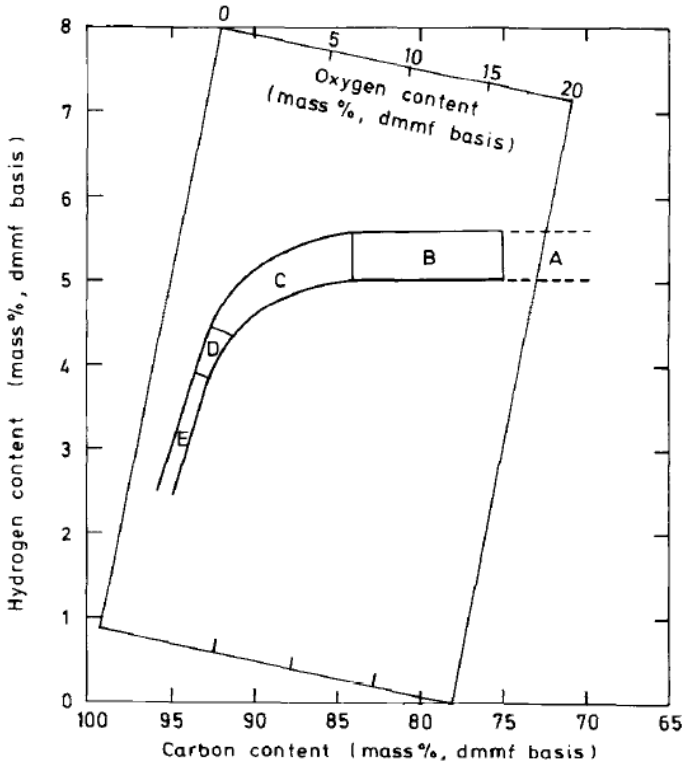



*Figure 1* Seyler's coal chart (adapted from Figure 5.23, Reference 1): A, brown coal and lignite; B, lignitous coal; C, bituminous coal; D, carbonaceous coal; E, anthracite. The broken lines for the brown coal band presumably indicate lack of experience in the classification of such coals in the U.K.

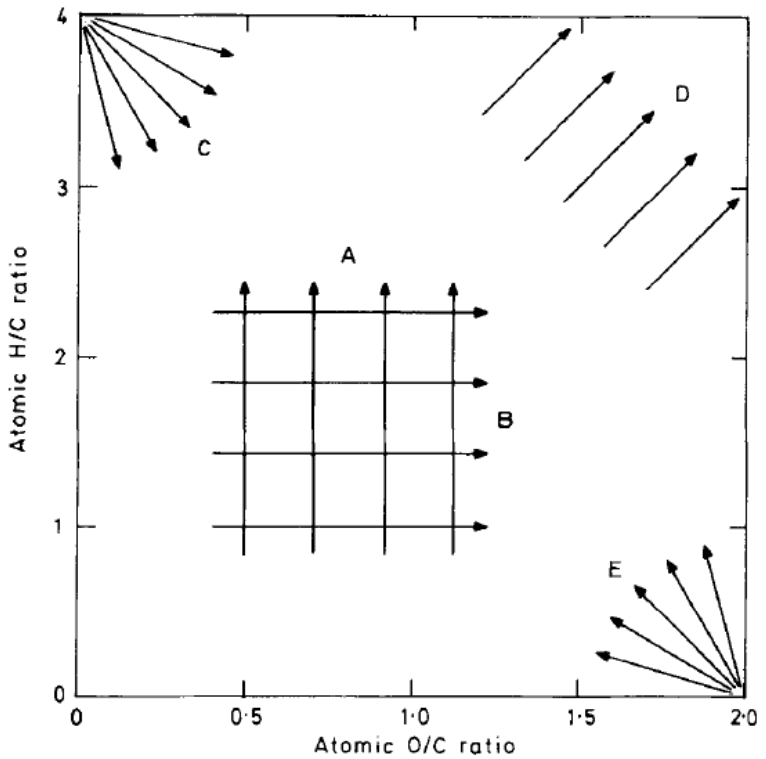
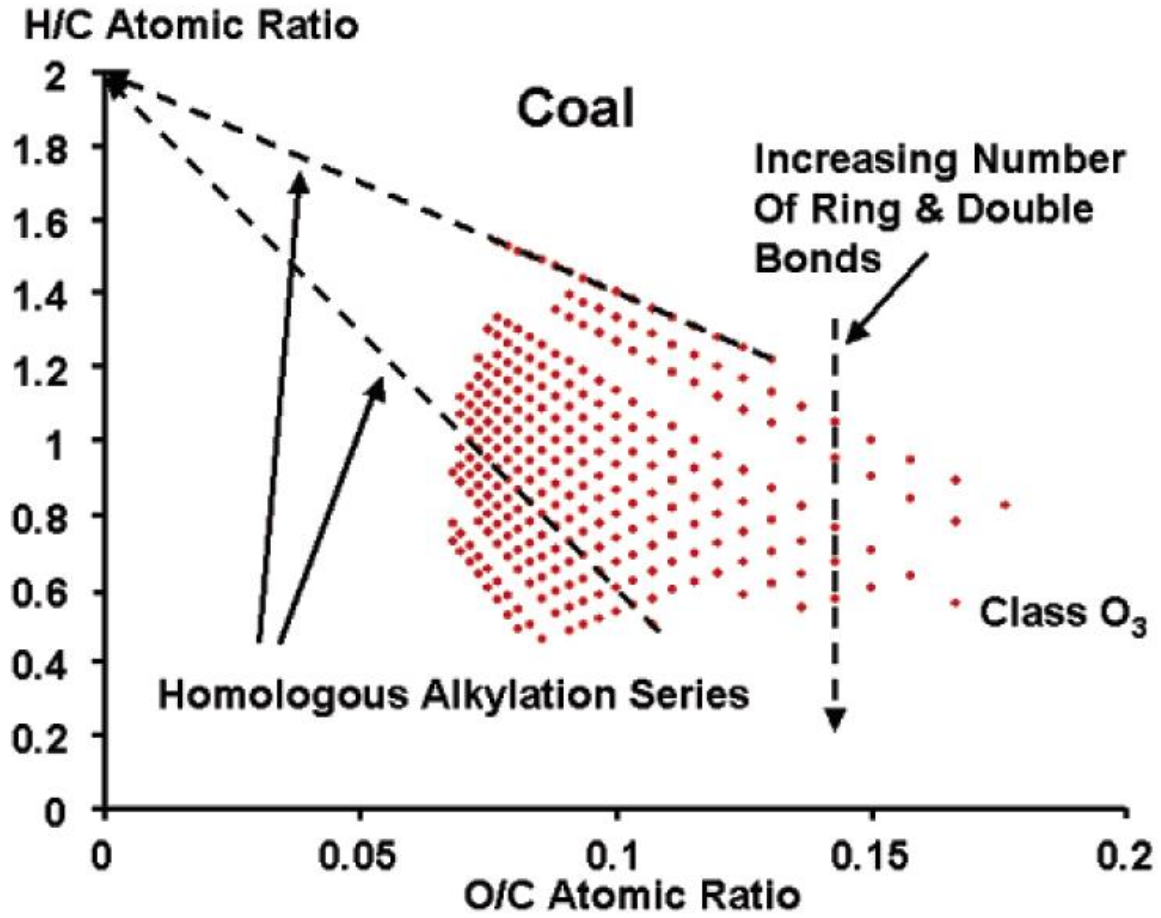
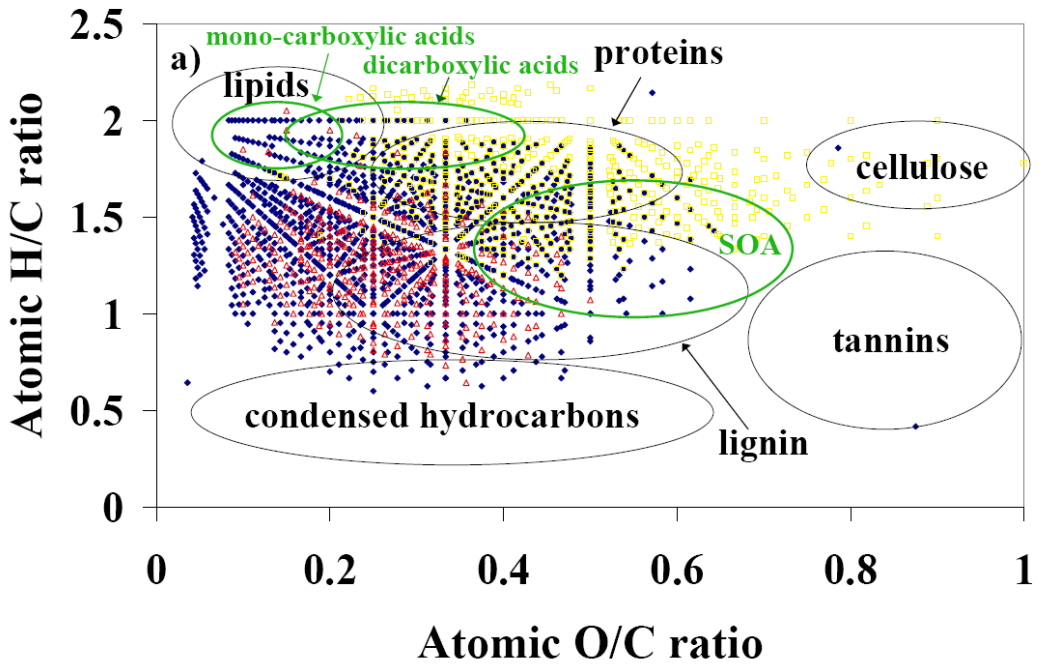



*Figure 2* Van Krevelen chart: A, hydrogenation trajectories; B, oxidation trajectories; C, demethanation trajectories; D, dehydration trajectories; E, decarboxylation trajectories

# Handling Attribution Data

## Visualization and grouping of elemental compositions – Van Krevelen Diagram




Wozniak et al., ACP (2008)

# Handling Attribution Data

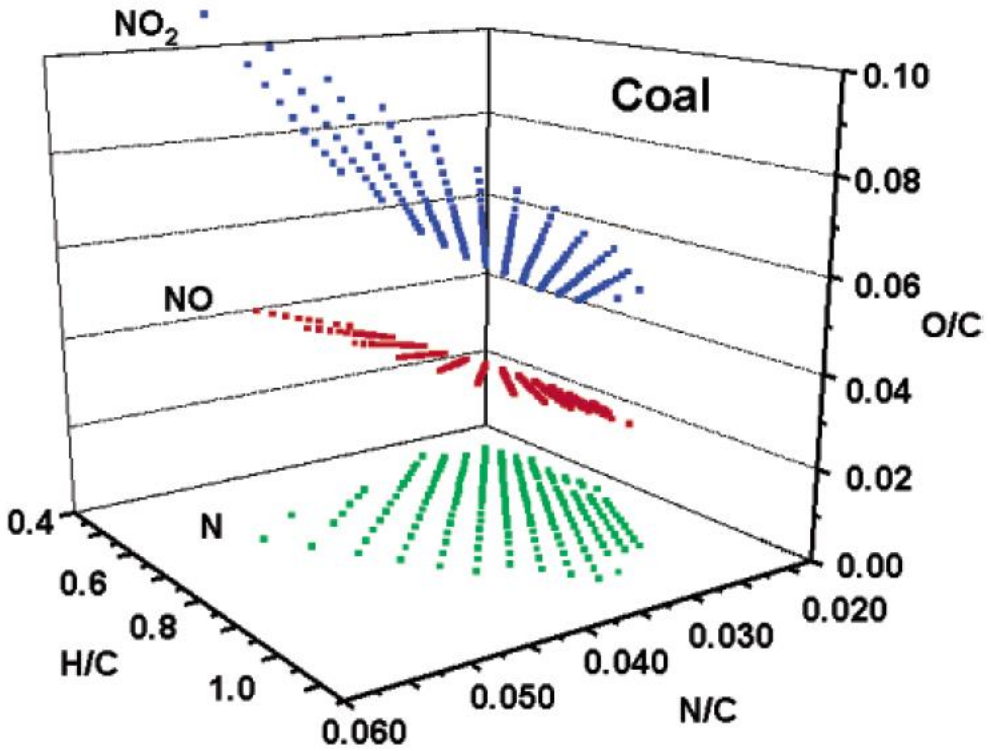



**Figure 6.** Three-dimensional van Krevelen diagram for members of the classes, N, NO, and $NO_2$, from pyridine-extracted Pocahontas No. 3 coal. Each class differs by at least one heteroatom (by definition) and is thus shifted to a different plane. Different classes are thus completely separated in the three-dimensional display.

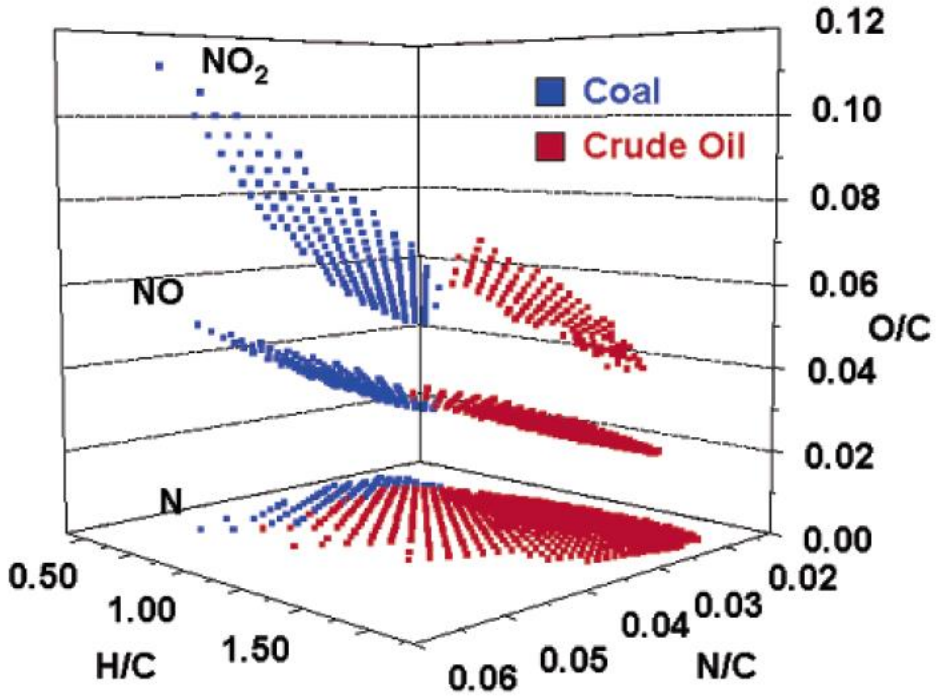



**Figure 7.** Three-dimensional van Krevelen diagram for the *same* classes (N, NO, $NO_2$) for two *different* fossil fuels: coal (blue) and crude oil (red). Because the coal components are more aromatic than are the constituents of crude oil, the two fuels are readily distinguished graphically in the diagram.

Pocahontas #3 Coal

# Handling Attribution Data

Green Chemistry

ROYAL SOCIETY OF CHEMISTRY

PAPER

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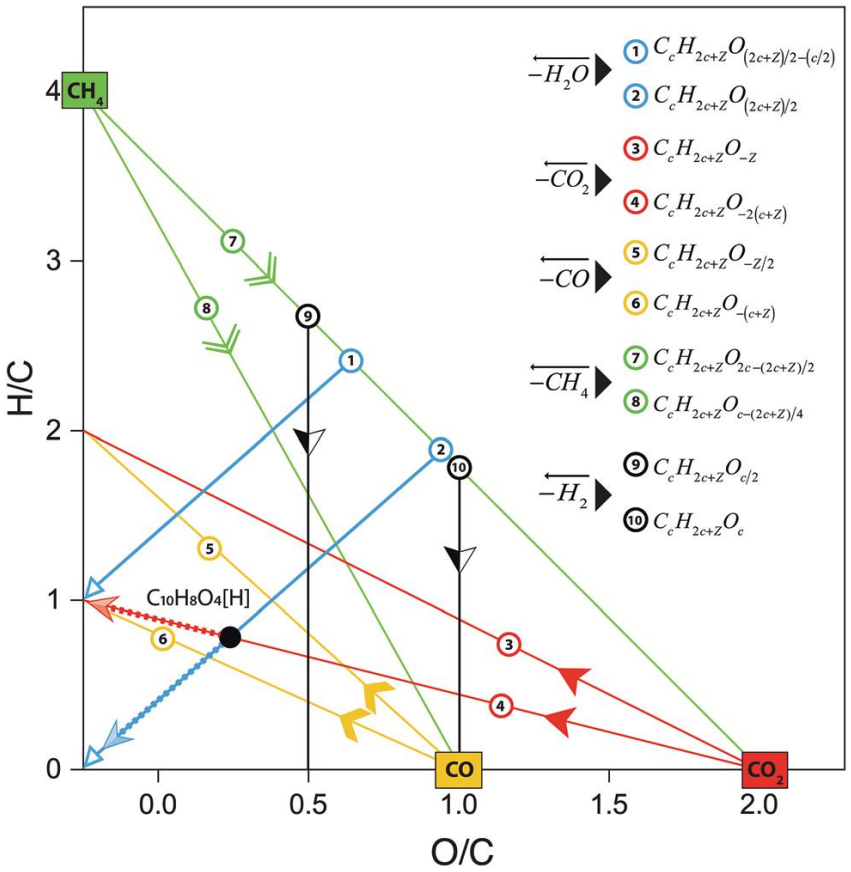
Cite this: *Green Chem.*, 2021, **23**, 8949

## Unlocking the potential of biofuels *via* reaction pathways in van Krevelen diagrams†

Diana Catalina Palacio Lozano, [a] Hugh E. Jones, [a,b] Tomas Ramirez Reina, [c] Roberto Volpe [d] and Mark P. Barrow *[a]

**Table 2** General equations of the magnitude of the displacement along the axis H/C and O/C corresponding to losses of molecules of $H_2O$, $H_2$, $CH_4$, CO, and $CO_2$ of a molecule with a general chemical formula $C_cH_{2n+Z}O_o$

| Principal reactions | Reaction vector (c,h,o) | Δ(O/C) | Δ(H/C) |
|---|---|---|---|
| Dehydration ($-H_2O$) | (0,−2,−1) | $-\frac{1}{c}$ | $-\frac{2}{c}$ |
| Dehydrogenation ($-H_2$) | (0,−2,0) | 0 | $-\frac{2}{c}$ |
| Decarbonylation (−CO) | (−1,0,−1) | $\frac{1}{c-1}\left(\frac{o}{c}-1\right)$ | $\frac{1}{c-1}\left(2+\frac{Z}{c}\right)$ |
| Decarboxylation ($-CO_2$) | (−1,0,−2) | $\frac{1}{c-1}\left(\frac{o}{c}-2\right)$ | $\frac{1}{c-1}\left(2+\frac{Z}{c}\right)$ |
| Demethanation ($-CH_4$) | (−1,−4,0) | $\frac{1}{c-1}\left(\frac{o}{c}\right)$ | $\frac{1}{c-1}\left[\left(2+\frac{Z}{c}\right)-4\right]$ |




Example of reaction processing lines in van Krevelen diagrams corresponding to losses of molecules of water, carbon dioxide, carbon monoxide, methane, and hydrogen. The characteristic molecular formulae of molecules in each line are shown on the right corner and the CO, CO2, and CH4 poles are shown along the axis, 2c + Z correspond to the total hydrogen atoms within the molecule.

# Handling Attribution Data

Green Chemistry

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## Unlocking the potential of biofuels *via* reaction pathways in van Krevelen diagrams†

Diana Catalina Palacio Lozano, [a] Hugh E. Jones, [a,b] Tomas Ramirez Reina, [c] Roberto Volpe [d] and Mark P. Barrow [*a]

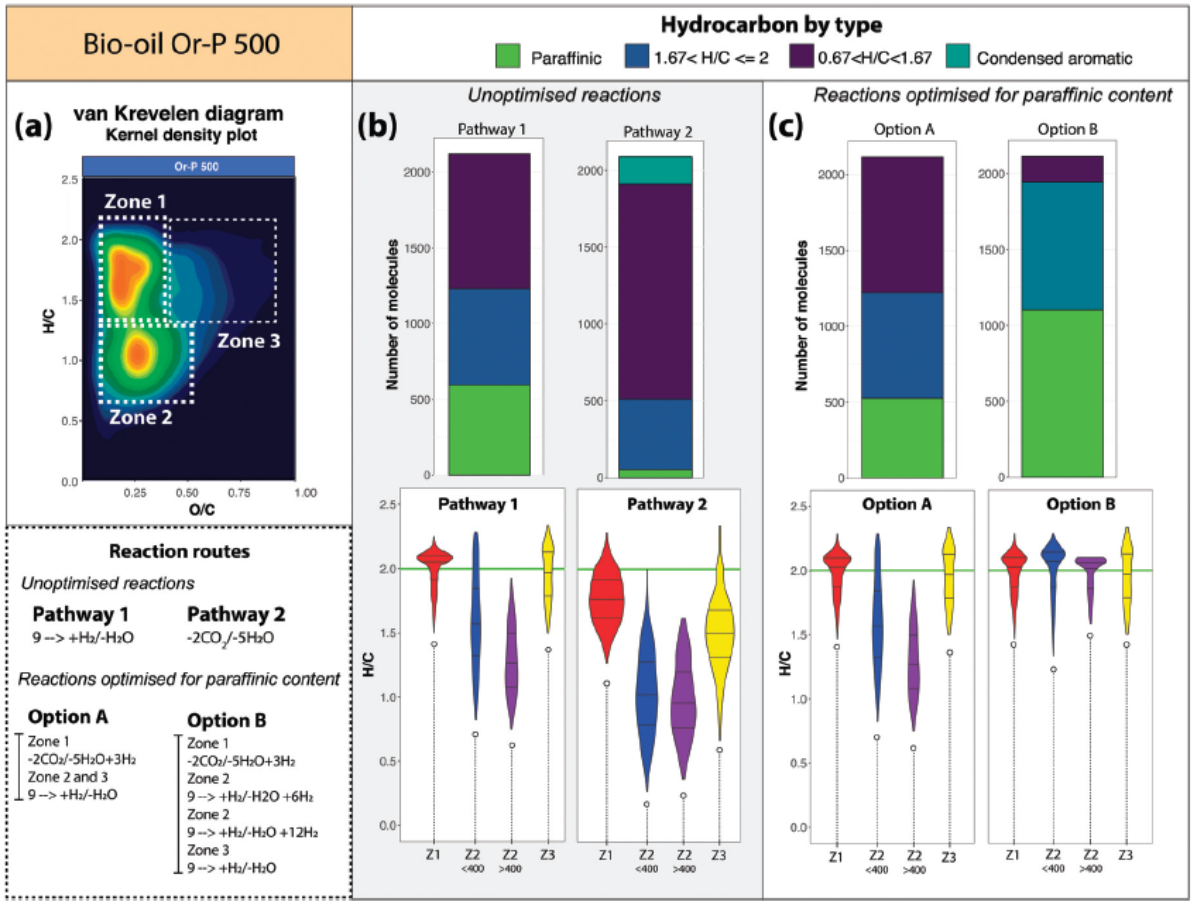



Fig. 7 Comparison of the starting material and the hydrocarbon distribution by type obtained after the simulation of different reaction pathways. (a) van Krevelen diagrams of the oxygenated species of the bio-oil obtained from orange pulp plotted as Kernel density plot. (b) and (c) – Distributions of the hydrocarbons obtained by the simulation of unoptimised reactions and reactions optimised for paraffinic content, respectively. Violin plots are used to illustrate the distribution of the hydrocarbons in the H/C-value by zone. The reactions were applied to four different fractions of the bio-oil Or-P 500. Zone 1 (Z1) $1.5 \leq H/C < 2$, $0 < O/C \leq 0.3$ (652 molecules), zone 2 (Z2) $0.5 < H/C < 1.5$, $0 < O/C < 0.67$ (1283 molecules), and zone 3 (Z3) $1.5 < H/C < 2$, $O/C > 0.3$ (402), the fraction of molecules in zone 2 was also divided by mass: <400 Da and >400 Da (697 and 586 molecules respectively). All the reactions were performed to reduce 9 oxygen atoms from the molecular formulae. About 2100 hydrocarbon molecules were obtained after the deoxidation reactions were applied.

# Research Examples by EU_FT-ICR_MS

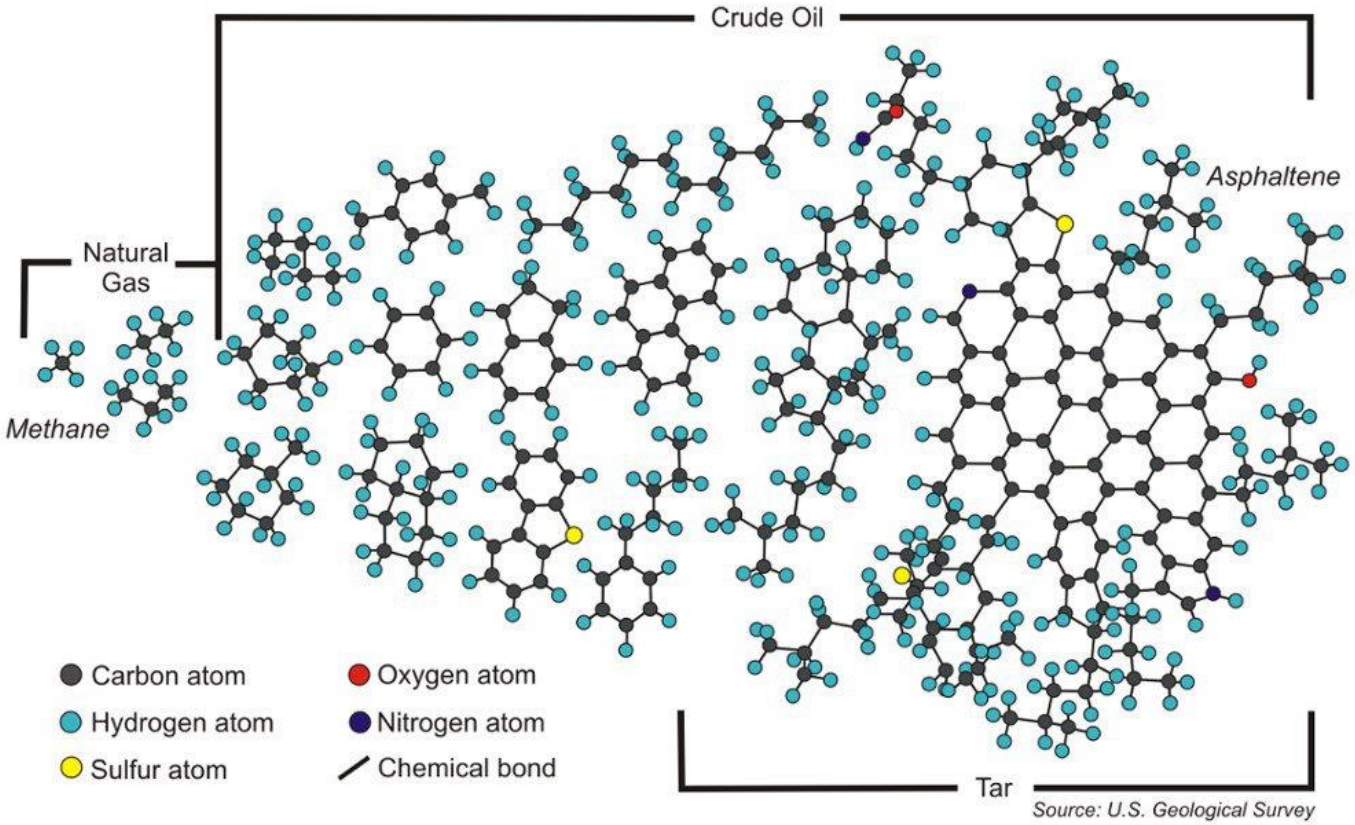
**Hyphenated Solutions – here Thermal Analysis Coupled to High-Resolution Mass Spectrometry**

→ time-dependent processing of the temperature-resolved complex mass spectra needed applying the shown concept and steps for data mining

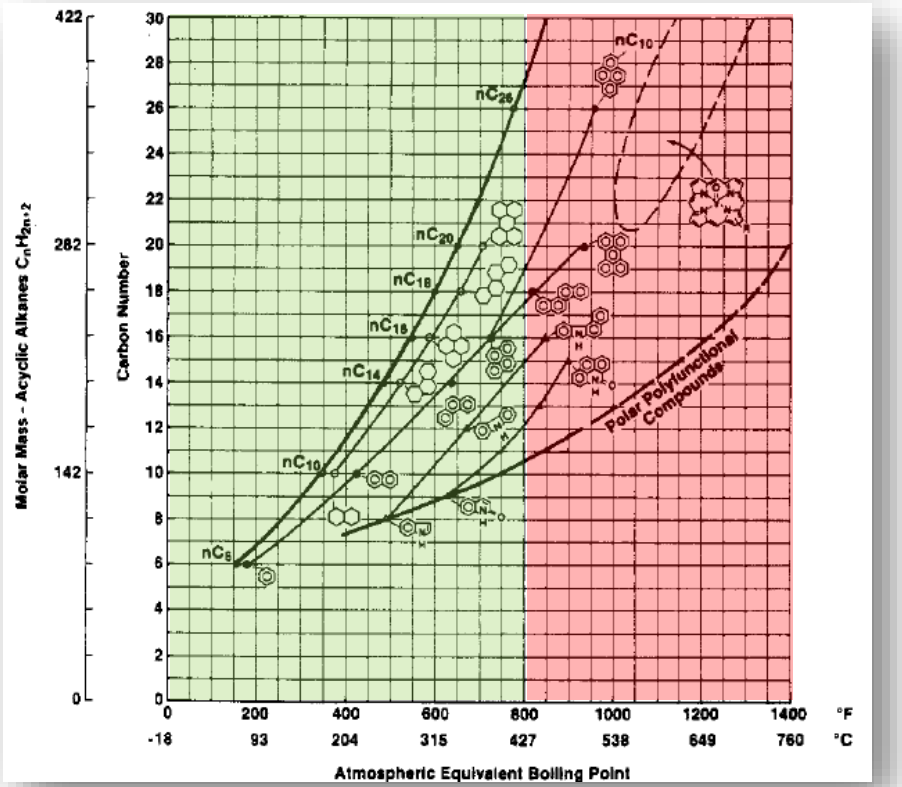
- **Aging of Bitumen** – Combing FT-ICR MS and GCxGC Data
- **Plastic Pyrolysis Chars** – Combination of Several Thermal Analysis Techniques
- **Carbon Fibers from Bitumen Feedstocks** – Cooperation with the 21T platform at NHMFL
- **Orbitrap Thermal Analysis and Online Emission Tracking** – non-ICR but deploying the same concepts

# Methodology -Thermal Analysis

# Complex Mixtures: Heavy Fractions and Residues



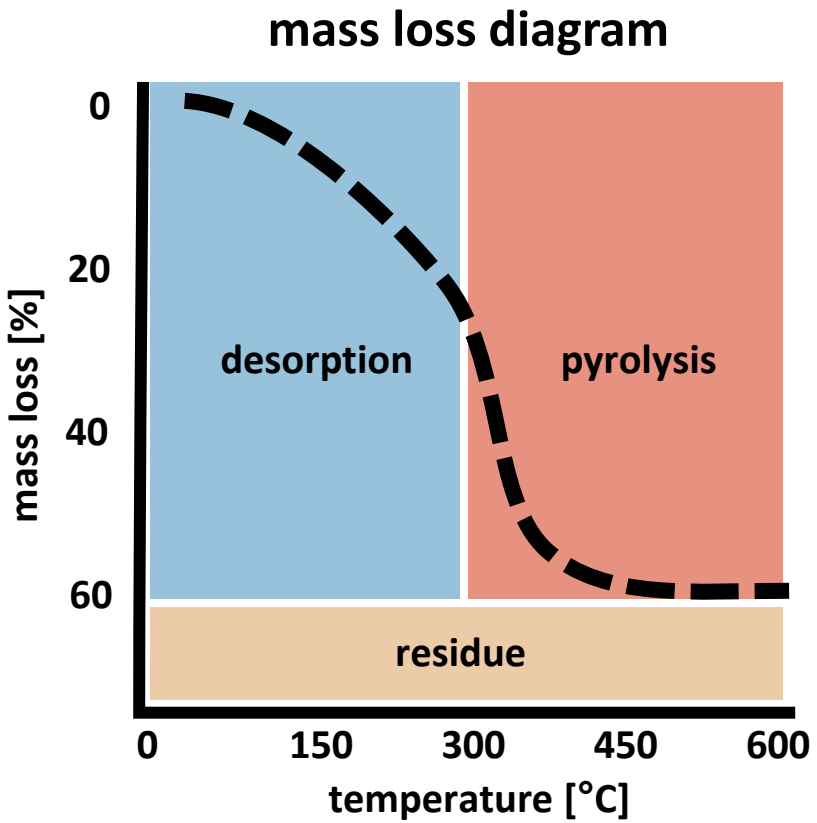

**GC/GCxGC-MS accessible**

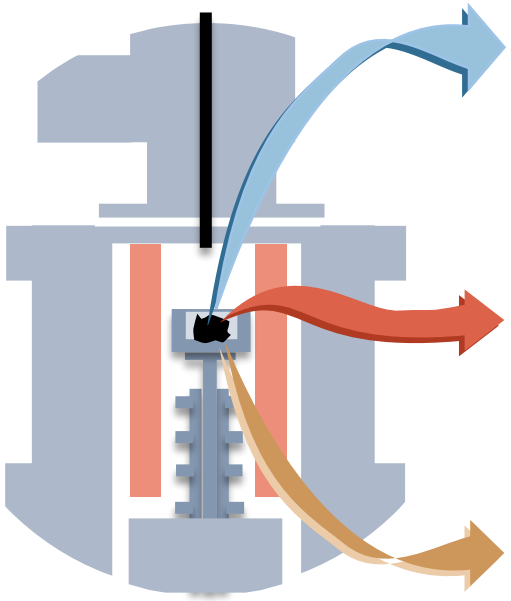


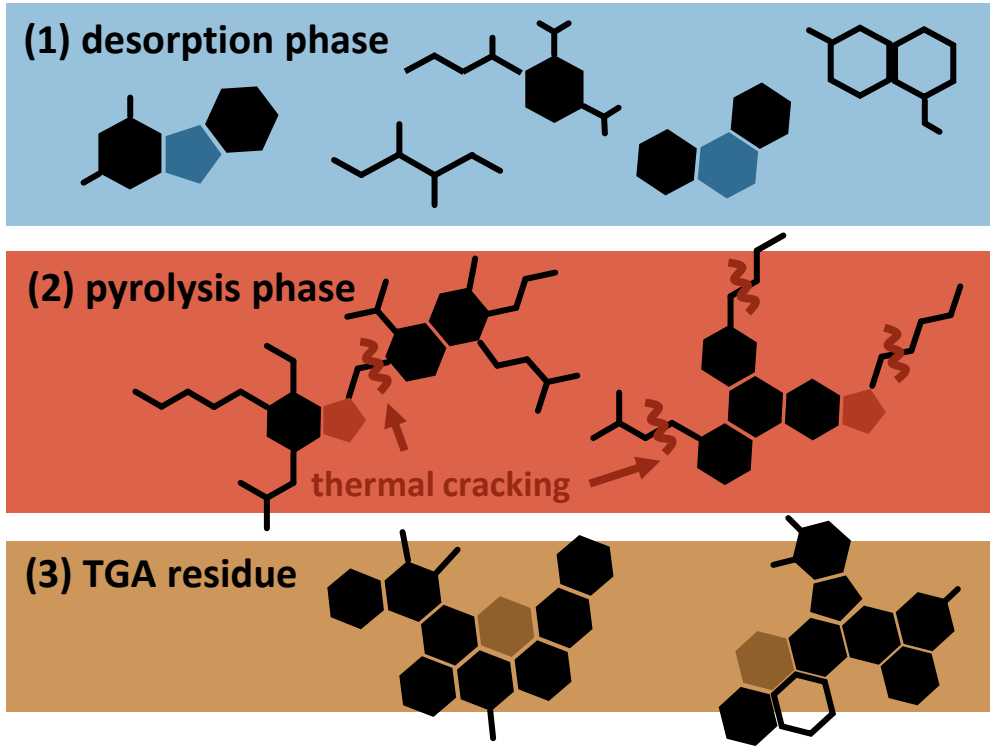

- Petroleum (fossil/**biomass/pyrolysis**) are ultra complex mixtures → *Petroleomics*

**Challenging heavy fractions**

# Insights via Thermogravimetric Processes



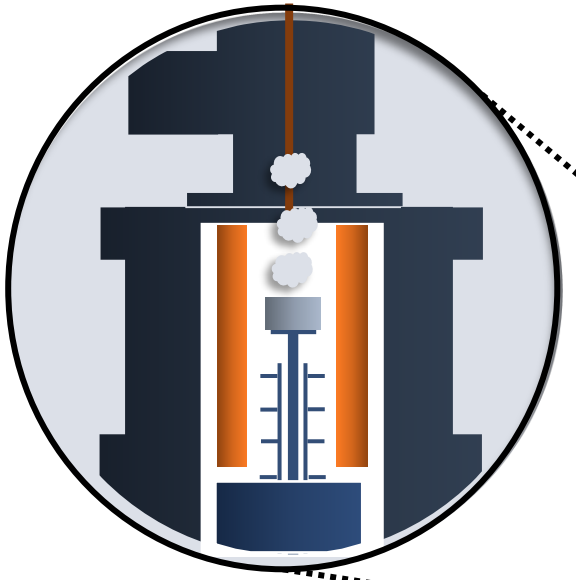



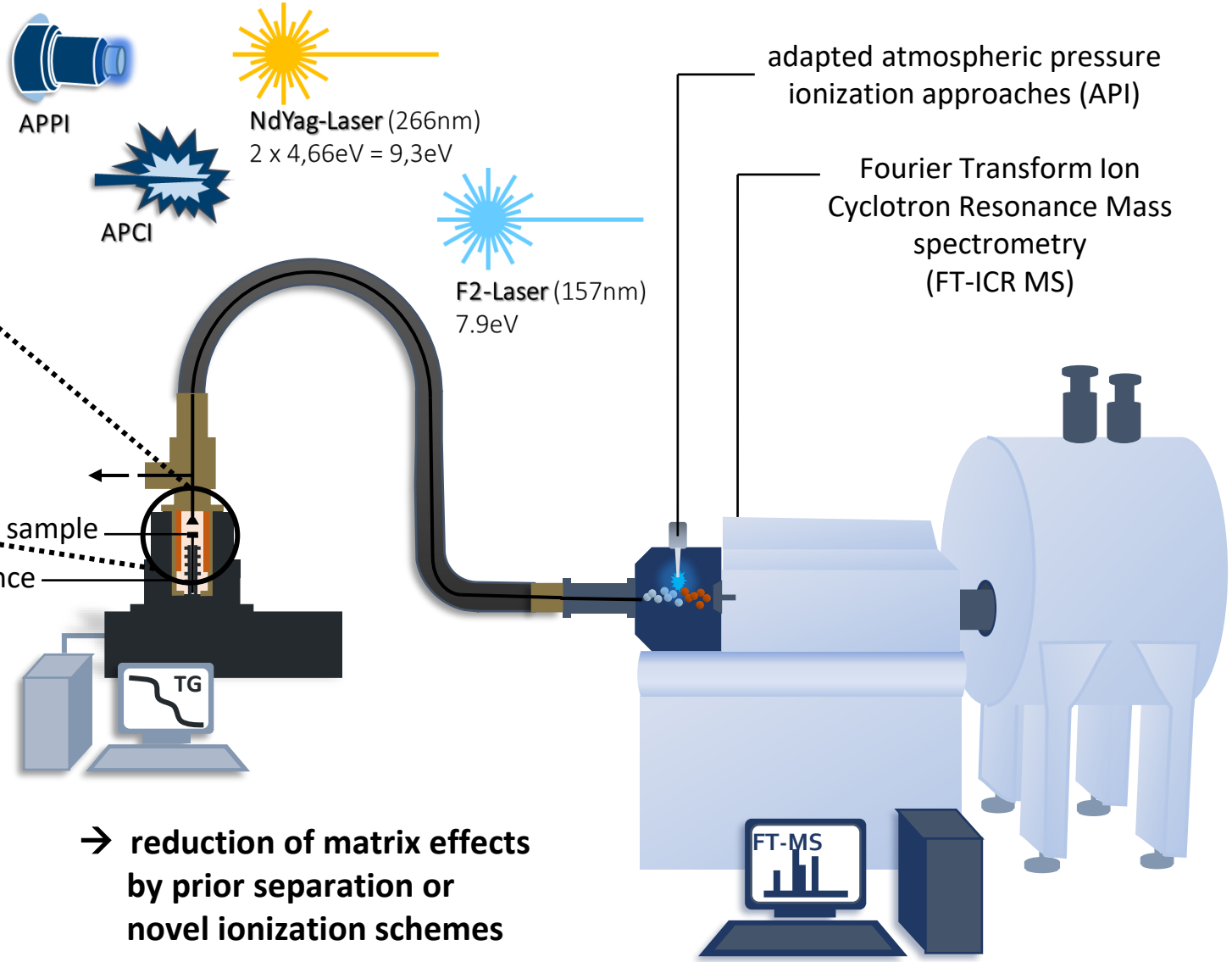



**Three processes occur during the thermogravimetric heating process:**

(1) Desorption: mostly evaporation of intact compounds
(2) Pyrolysis: thermal decomposition of high molecular weight species (starting at 300-350 °C)
(3) Residue: coke formation of high aromatic compounds and highly stable aggregates

# Mass Spectrometric Platform – FT-ICR MS





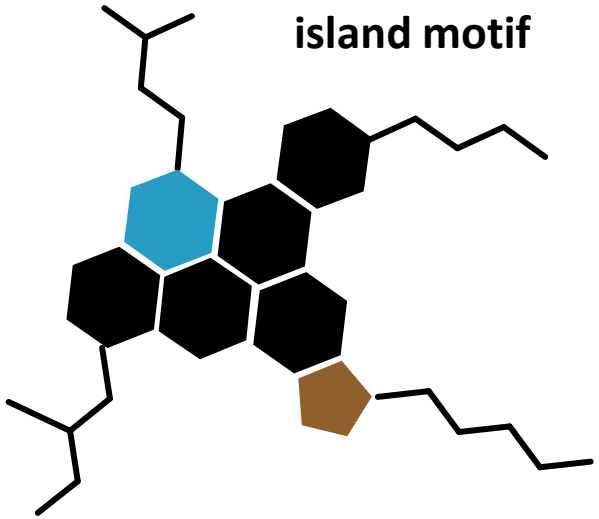

- thermal separation by a defined heating ramp leading to less matrix effects
- tracing mass loss during the heating process

→ **reduction of matrix effects by prior separation or novel ionization schemes**

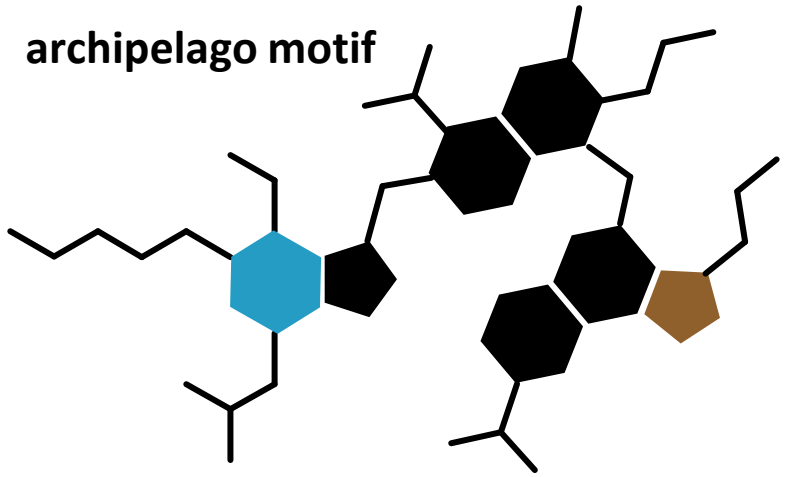
Rüger et al., *Anal. Chem.* 2015, 87, 13, 6493–6499
Rüger et al., *Anal. Chem*. 2021, 93, 8, 3691–3697

# Asphaltenes – Molecular Architecture Debate

## Architecture of asphaltenes strongly discussed in literature




Wyoming Deposit asphaltenes

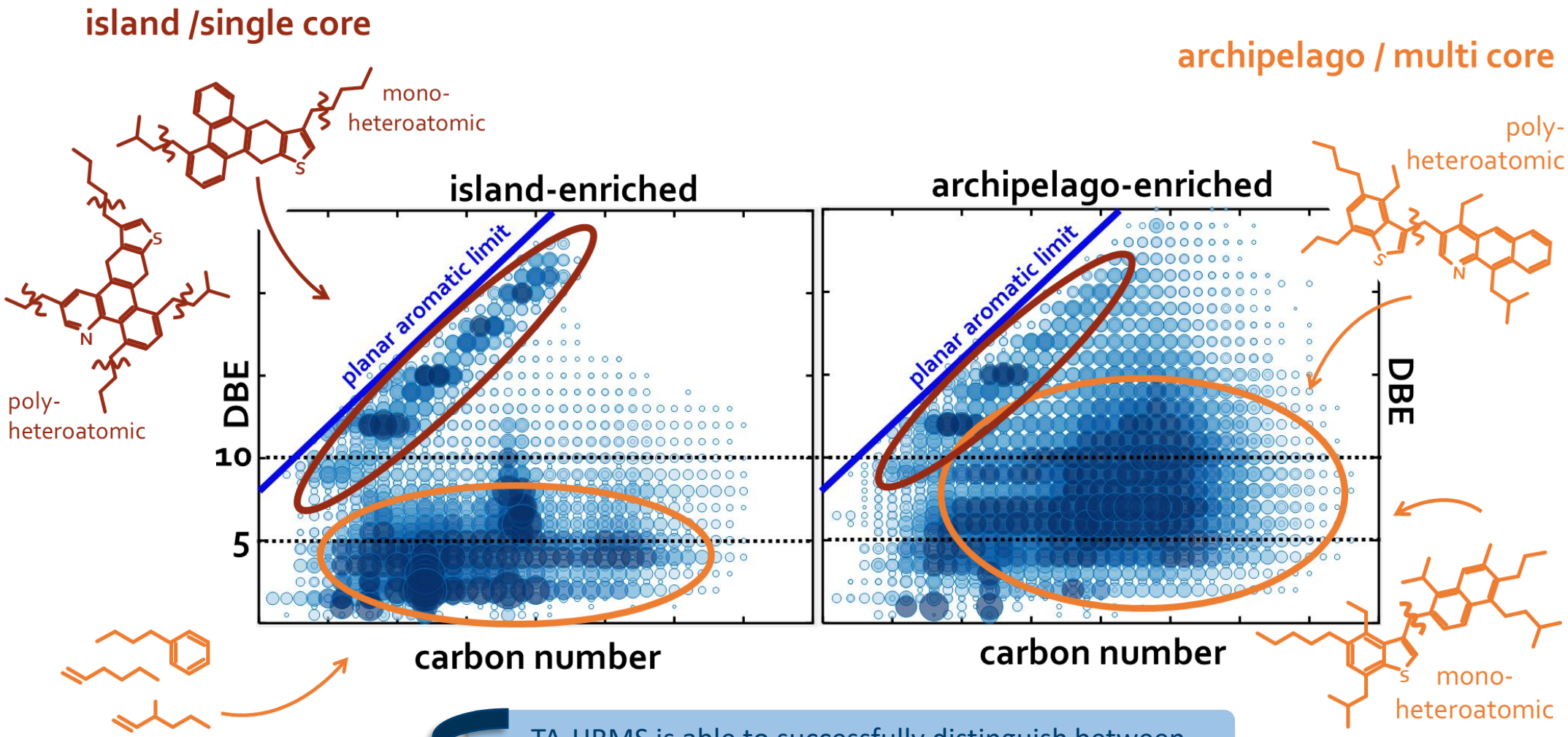



Athabasca Bitumen asphaltenes

Only limited analytical techniques available, which show evidence for both types of asphaltenes.
→ A structural motif is most often highlighted by a specific analytical technique.

**Is TG-FT-ICR MS able to distinguish between both structural motifs?**

# Asphaltene Pyrolysis Products

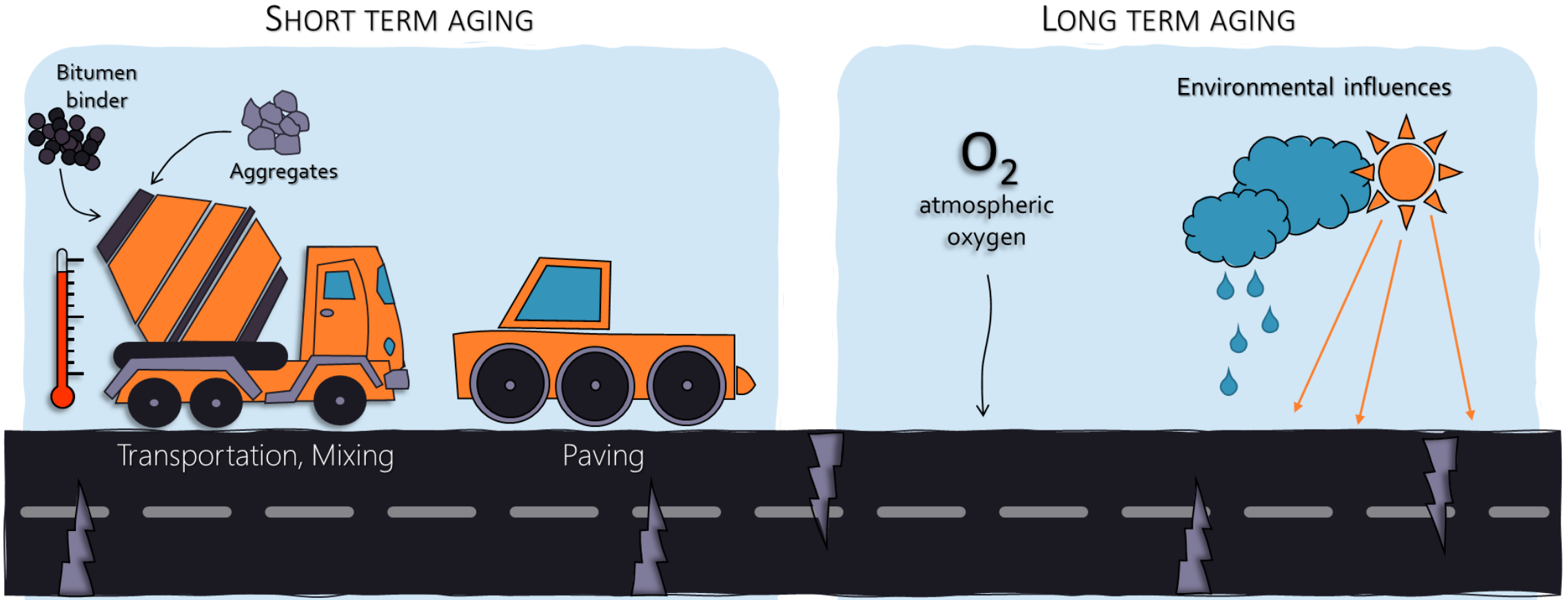



TA-HRMS is able to successfully distinguish between the structural motifs in those ultra-complex mixtures

Neumann et al., *Energy and Fuels* **2021**, 35, 5, 3808–3824

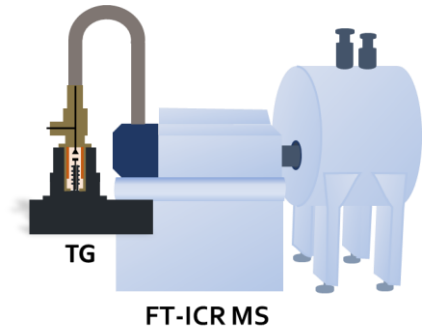
# Case Study I – Bitumen Aging

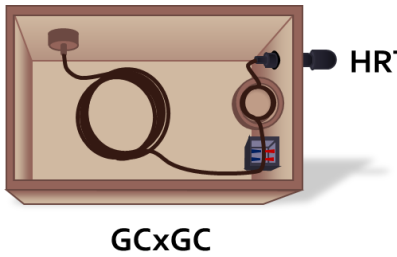
# Bitumen Ageing – Combining FTMS and GCxGC

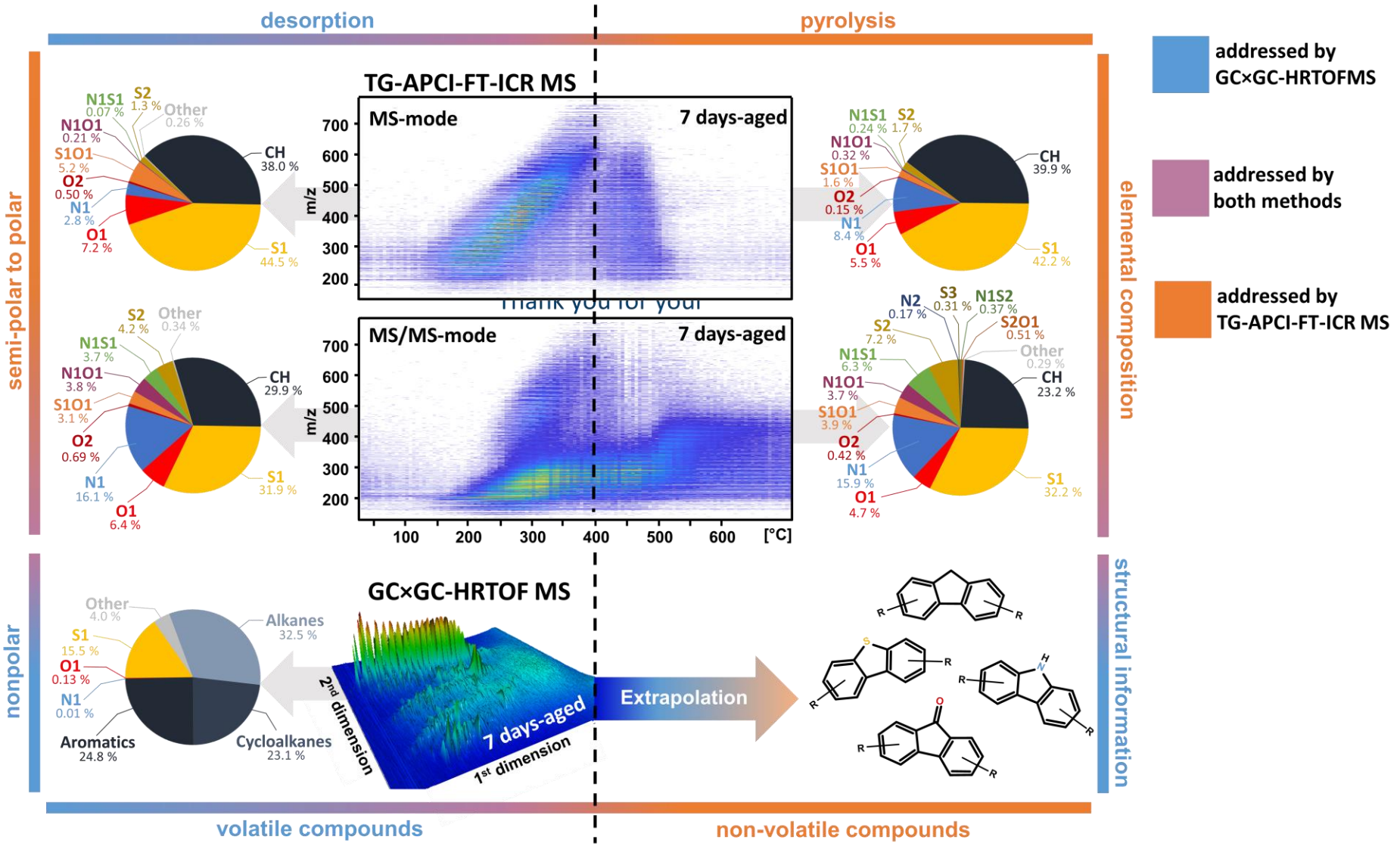



Neumann et al., *Energy and Fuels* **2020**, 34, 9, 10641–10654

# Bitumen Ageing – Combining FTMS and GCxGC



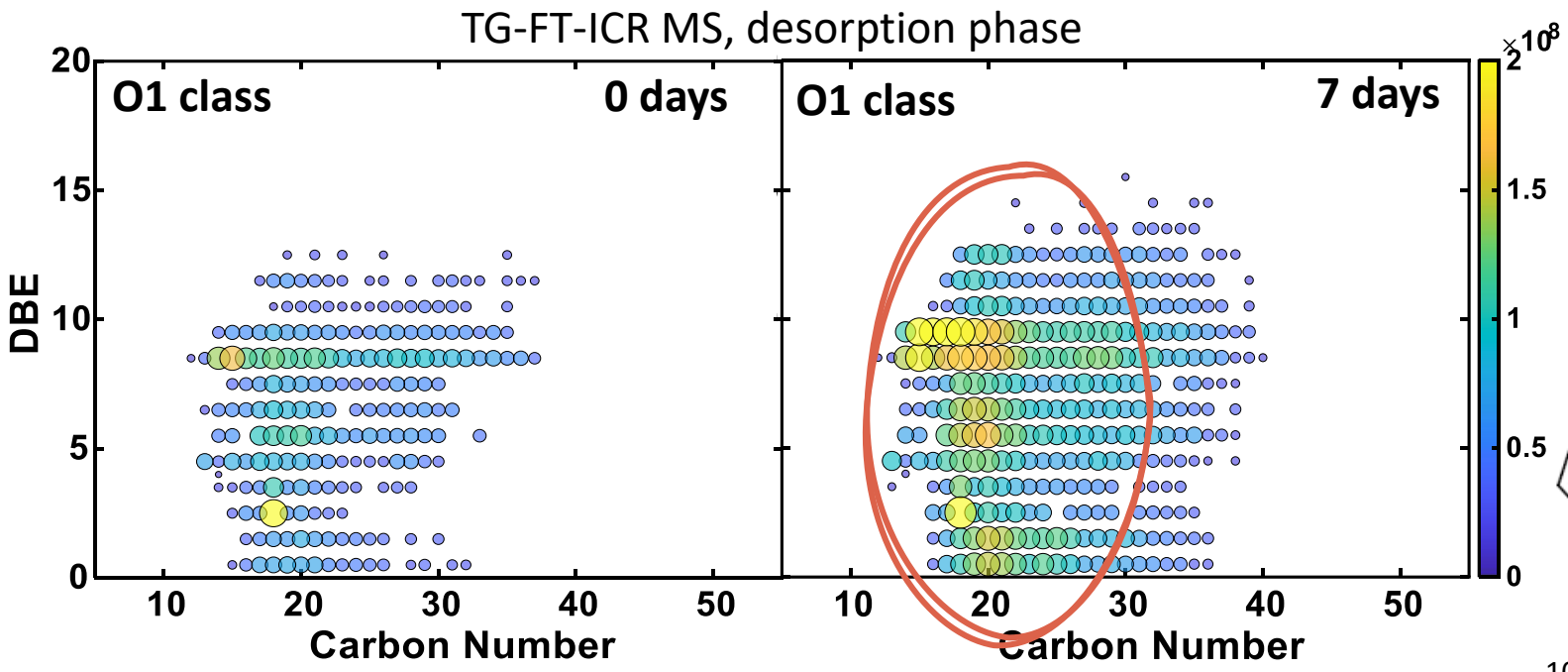

addressed by GC×GC-HRTOFMS

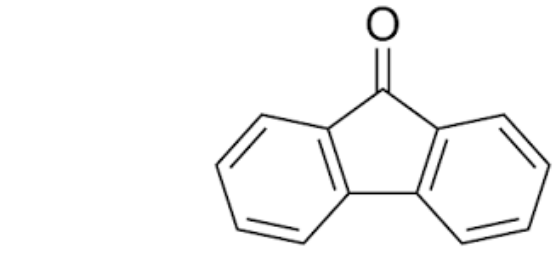
addressed by both methods

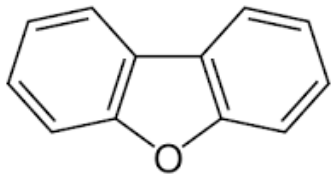
addressed by TG-APCI-FT-ICR MS

Neumann et al., *Energy and Fuels* **2020**, 34, 9, 10641–10654

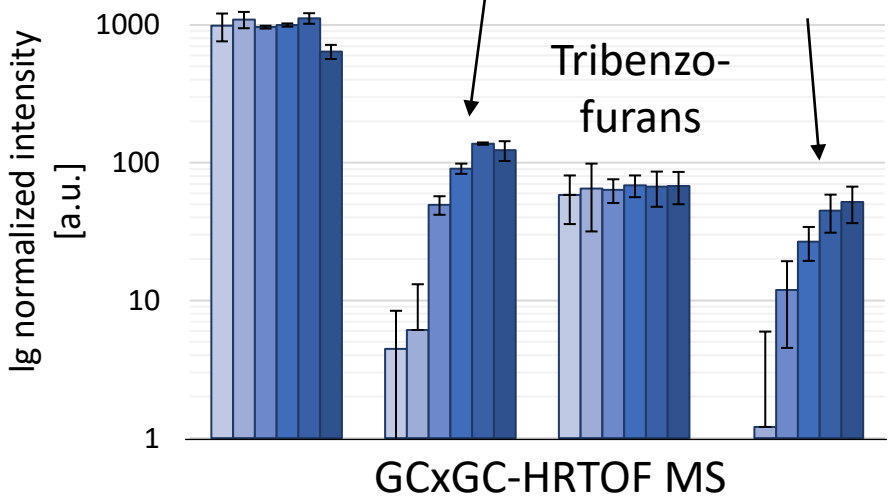
# Bitumen Ageing – Combining FTMS and GCxGC




Benzo-fluorenones

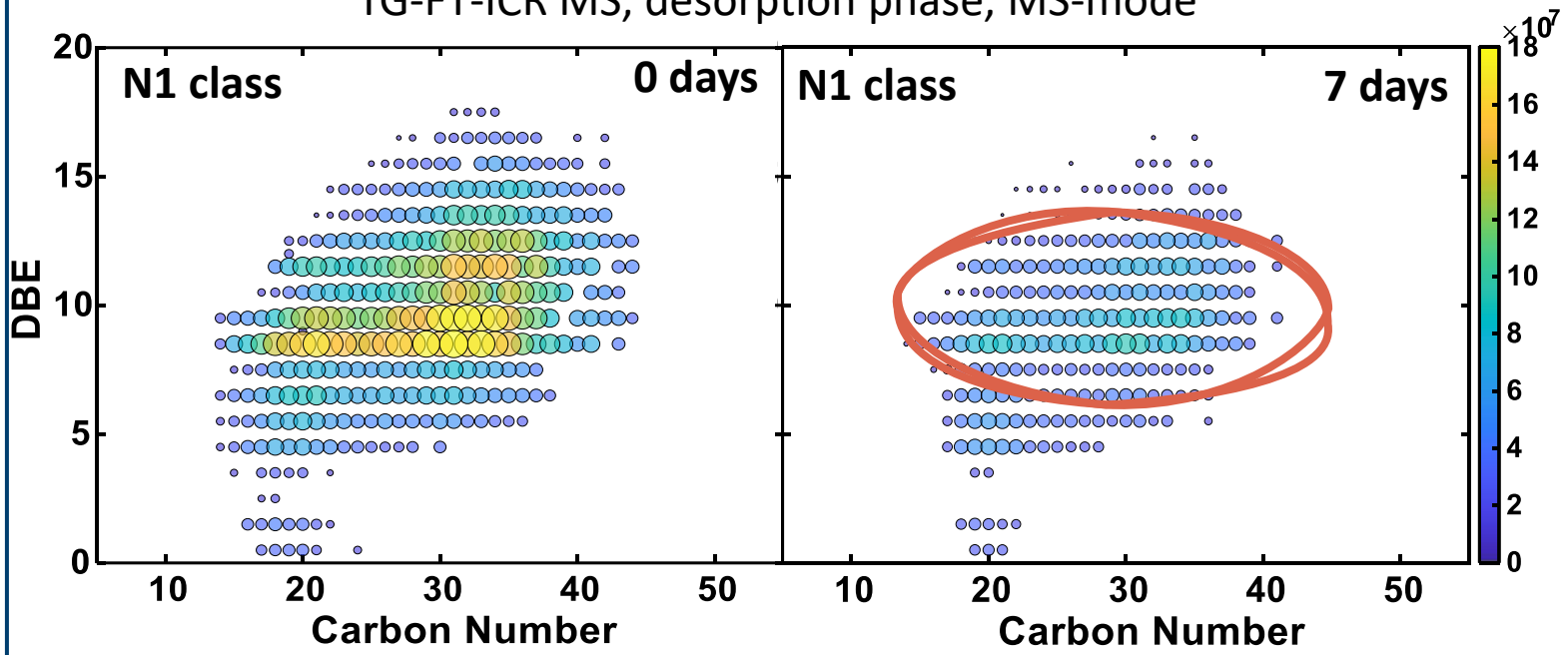


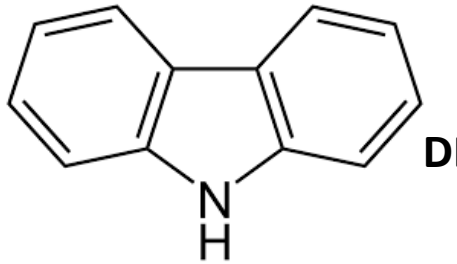

- significant **increase** for **oxidized compounds**
- especially species with **DBE 9 and 10 are pronounced** in FT-ICR MS data
- GCxGC HRTOF MS shows **significant increase** for **fluorenones**, but no changes for furans

Neumann et al., *Energy and Fuels* **2020**, 34, 9, 10641–10654

# Bitumen Ageing – Combining FTMS and GCxGC

TG-FT-ICR MS, desorption phase, MS-mode

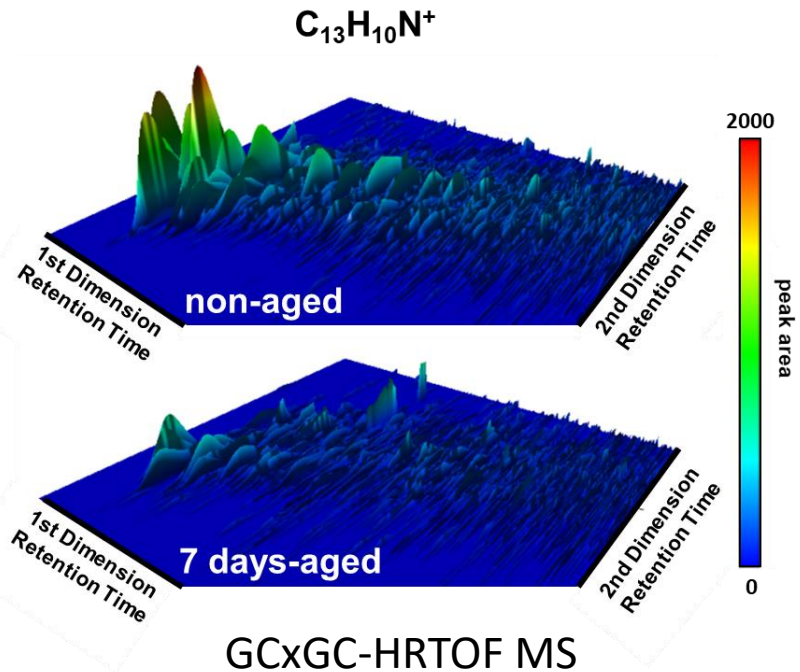



DBE 9

Carbazoles

- strong **decrease** for **all N-containing species** revealed by both techniques, especially species with DBE greater than 9 (carbazoles)
- **oxidized N-compounds** are **near detection** limit, but evidence for further oxidation



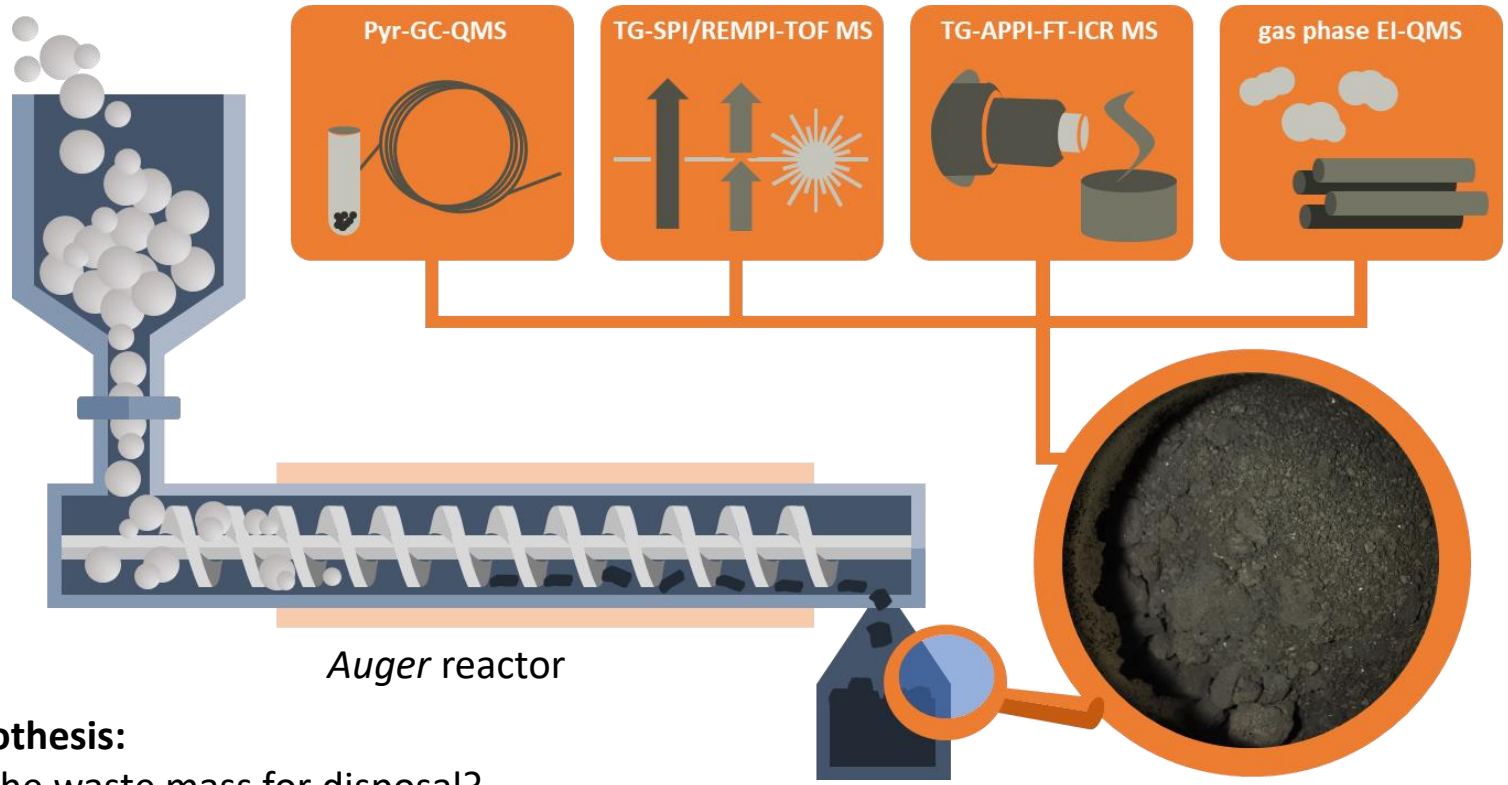

GCxGC-HRTOF MS

Neumann et al., *Energy and Fuels* **2020**, 34, 9, 10641–10654

# Case Study II – Plastic Pyrolysis Chars

# Plastic Pyrolysis Coke

## Chemical description of plastic pyrolysis coke residues for improved recycling




*Auger* reactor

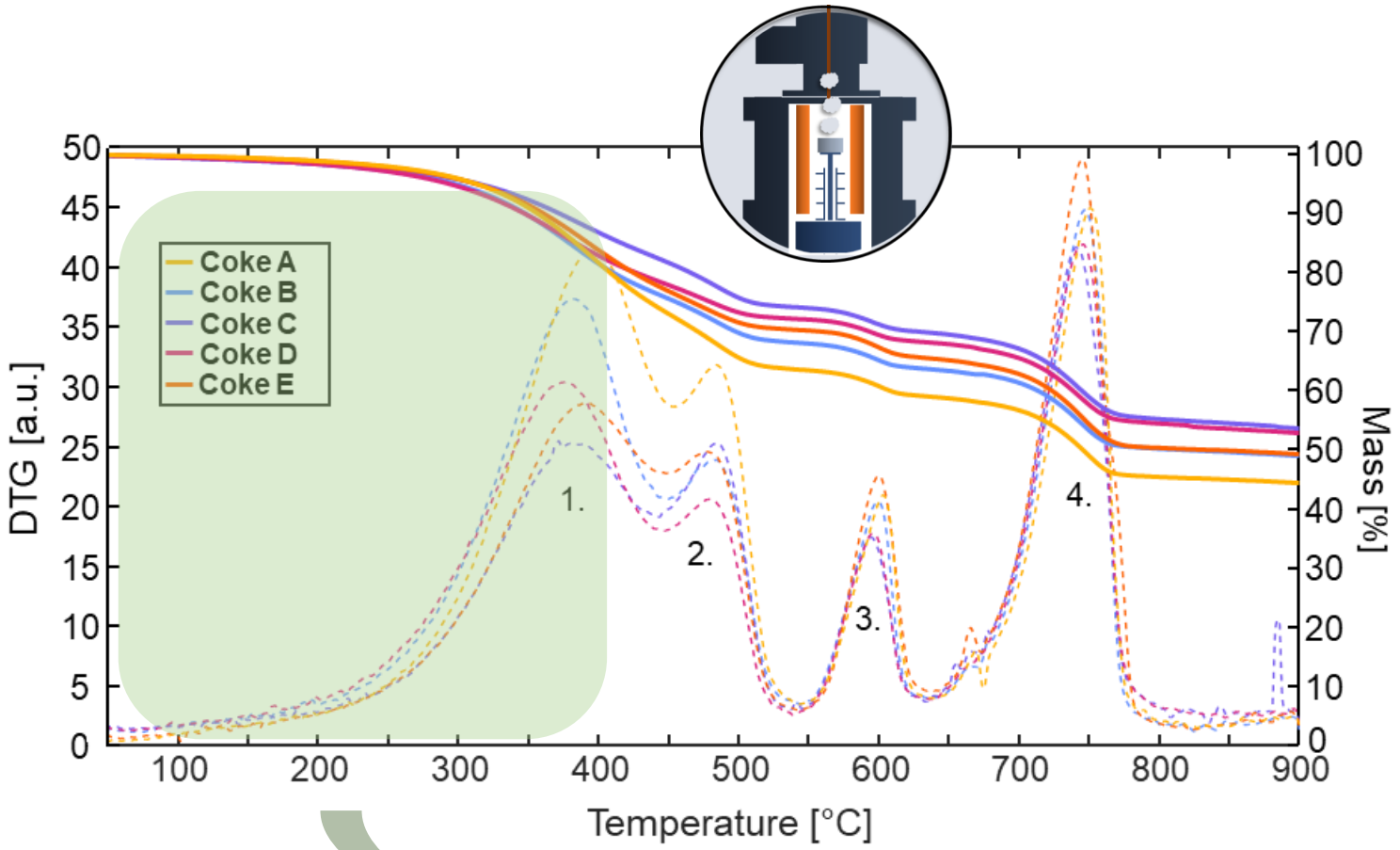
**Main research hypothesis:**

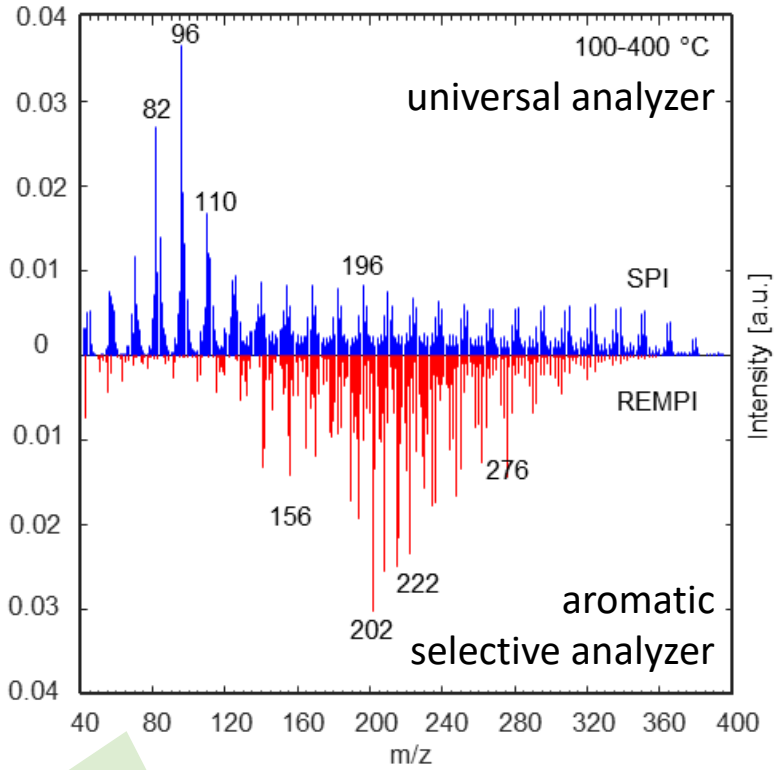
- Can we reduce the waste mass for disposal?
- Can we examine the quality and purity/toxicity of the coke?
- Are valuable chemicals be accessible based on a second pyrolysis step?
- Is there a potential for usage of the residue in material science?

TotalEnergies

# Plastic Pyrolysis Coke

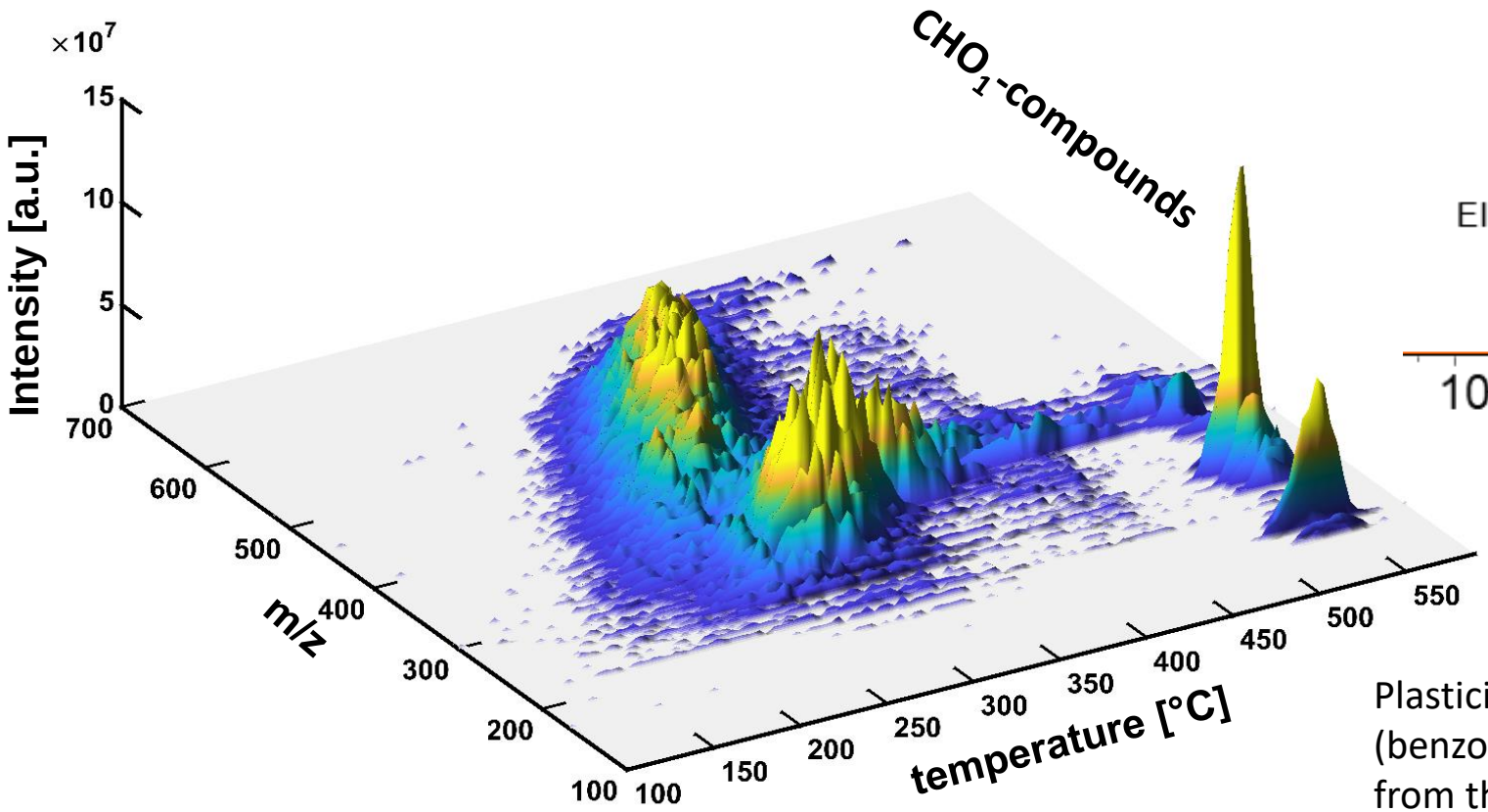
## Unique thermogravimetric behavior with several distinct mass loss events



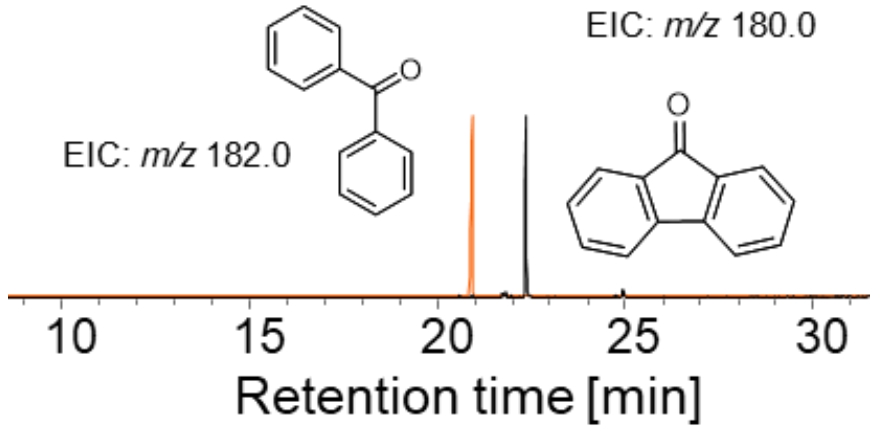



# Plastic Pyrolysis Coke

## Polymer additives and plasticizers cause unique pyrolysis chemistry



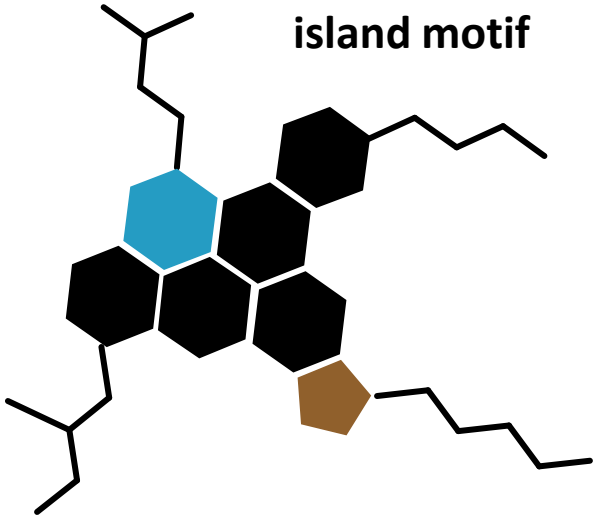

Survey view of the thermal analysis high-resolution mass spectrometric data

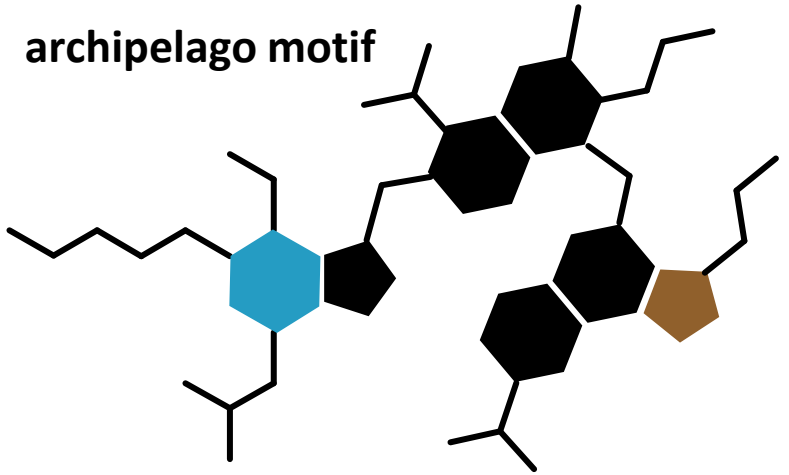



Plasticizer derivatives, such as UV-stabilizers (benzophenones) released at elevated temperatures from the char network (strongly bound and/or integrated in the macromolecular structure.

# Plastic Pyrolysis Coke

## Architecture of graphitized materials strongly discussed in literature…



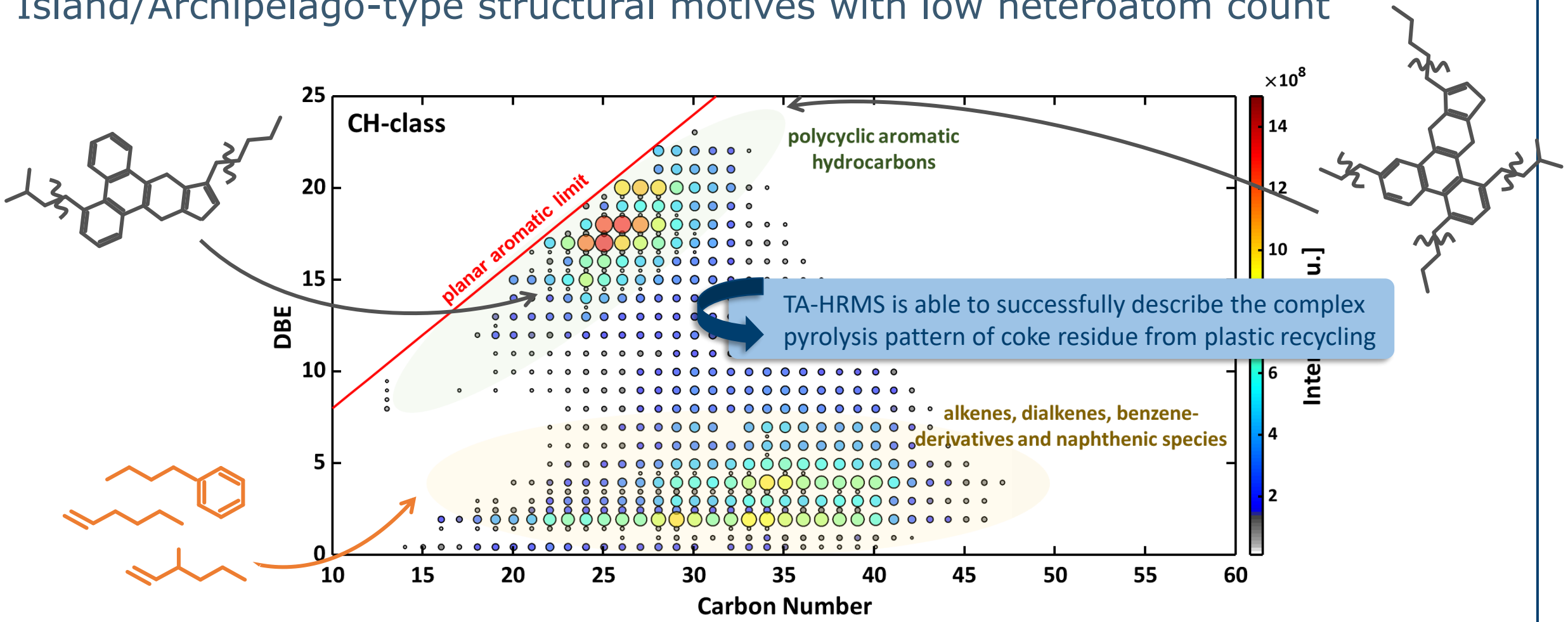




**Is TG-FT-ICR MS able to distinguish between both structural motifs?**

Neumann *et. al.*, *Energy Fuels* 2021, 35, 3808-3824; DOI: 10.1021/acs.energyfuels.0c03751

# Plastic Pyrolysis Coke

## Island/Archipelago-type structural motives with low heteroatom count

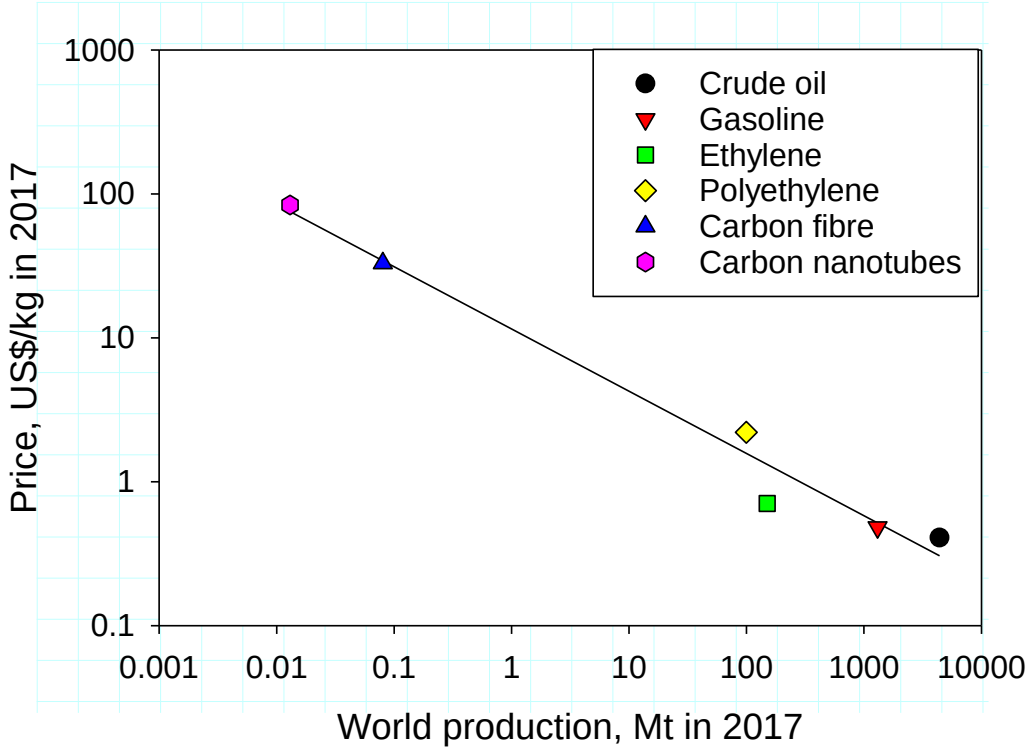


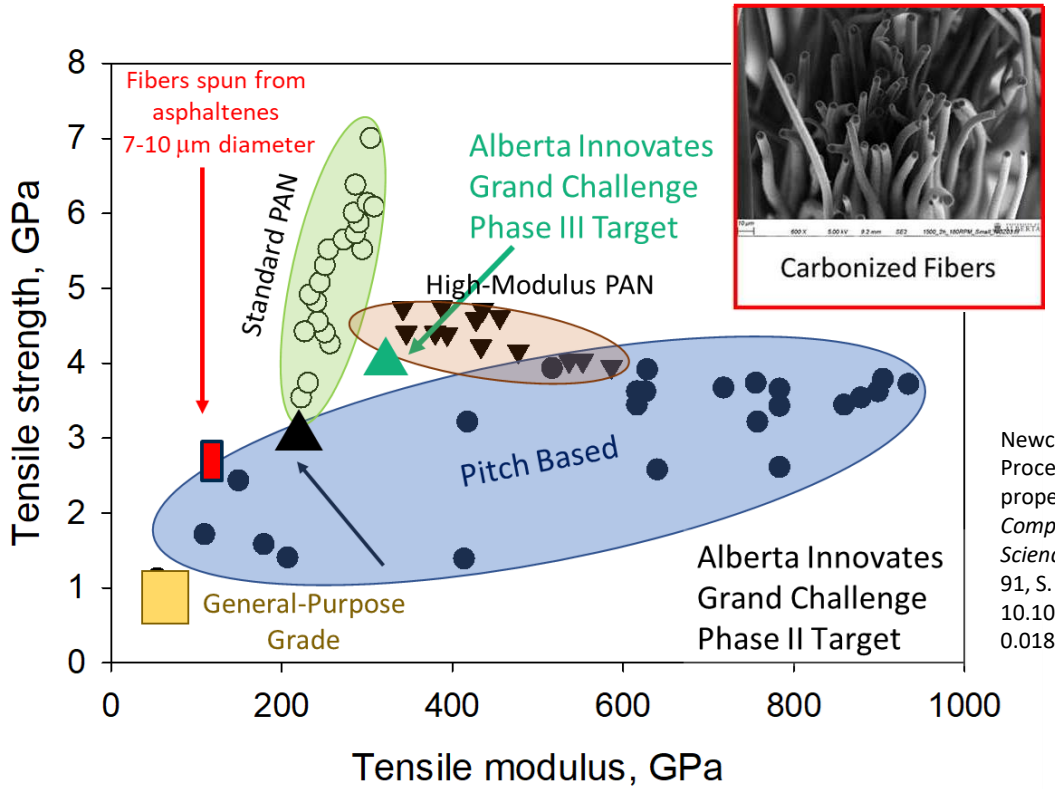

Comprehensive Chemical Description of Pyrolysis Chars from Low-Density Polyethylene by Thermal Analysis Hyphenated to Different Mass Spectrometric Approaches, Friederici et al., *Energy and Fuels*, 2021, DOI 10.1021/acs.energyfuels.1c01994

# Case Study III – Bitumen Carbon Fibers

# Carbon Fibers from Bitumen Feedstocks

- production of asphalt binder, activated carbon and **carbon fibers** from asphaltene-rich bitumen (15-30 wt%)
- carbon fibers are widely used in applications ranging from aerospace to **blades for wind turbines**
- **light weight**, **corrosion resistance**, and **conductivity**
- increasing demand for carbon fibers (58k tons in 2015 to more than 100k tons in 2020)
- PAN serves as the principal precursor (96%) => greenhouse gas emissions for PAN and fiber production

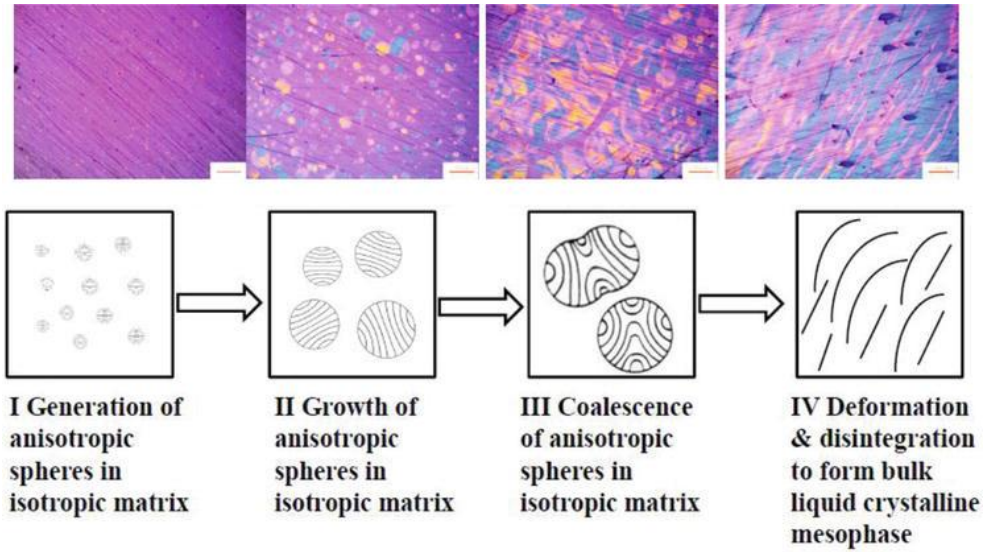



Newcomb, Bradley A. (2016): Processing, structure, and properties of carbon fibers. In: *Composites Part A: Applied Science and Manufacturing* 91, S. 262–282. DOI: 10.1016/j.compositesa.2016.10.018.

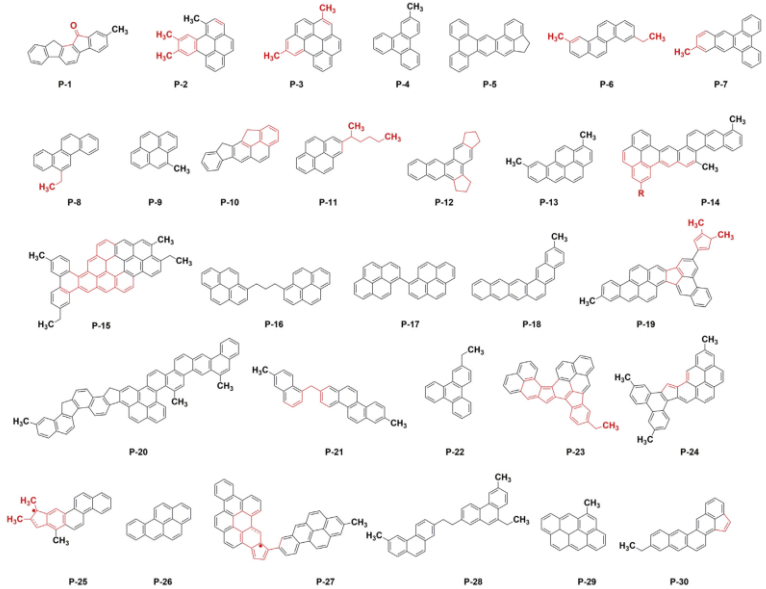
# Carbon Fibers from Bitumen Feedstocks

- large aromatics separate to form a liquid crystal phase
- stacking of aromatics detected by diffraction of light
- liquid crystal phase is called mesophase




Sasani Ghamsari, Morteza; Carlescu, Irina (Hg.) (2020): Liquid Crystals and Display Technology: IntechOpen.

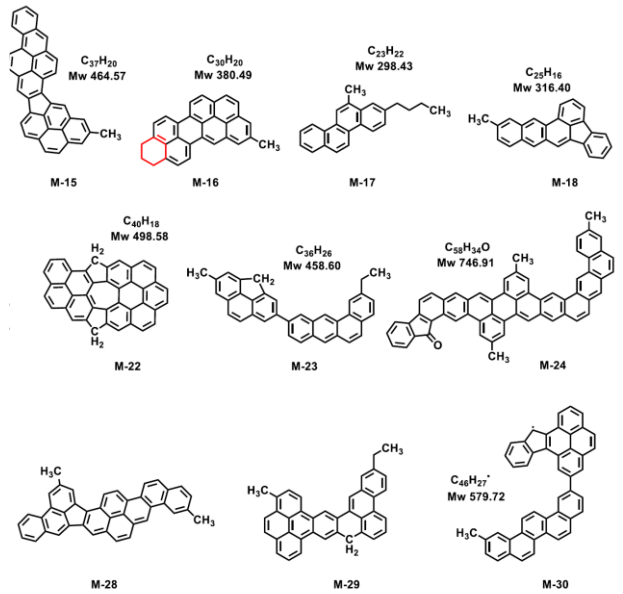
**Isotropic Pitch**




**React at 400 °C for 3h**

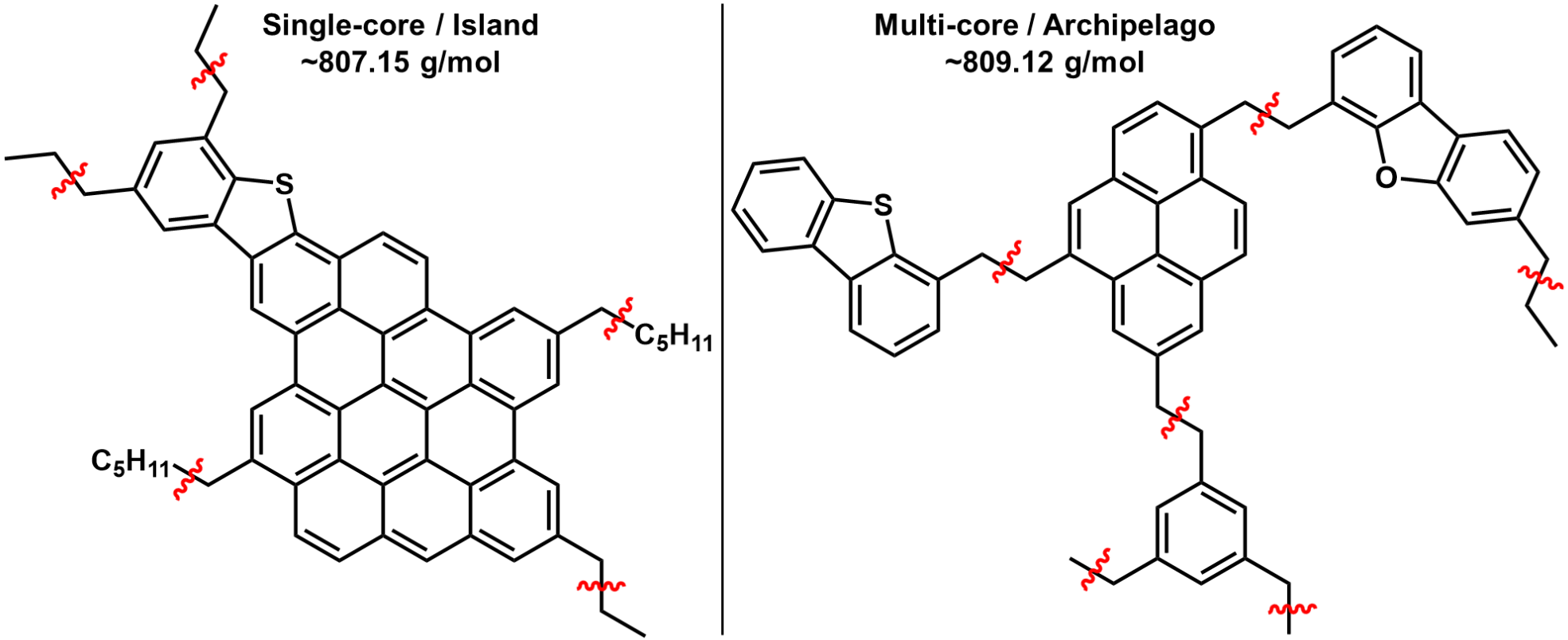
**Addition reactions give dimers, trimers etc.**
**Methyl groups contribute to addition reactions**

**Mesophase Pitch**



# Carbon Fibers from Bitumen Feedstocks

## Which one makes “good” carbon fibers?



# Carbon Fibres from Bitumen Feedstocks

**Chemistry and Properties of Carbon Fiber Feedstocks from Bitumen Asphaltenes.**

*Martha L. Chacón-Patiño[1,2*#], Anika Neumann[3,4#], Christopher P. Rüger[2,3,4*], Paolo G. Bomben[5], Lukas Friederici[3,4], Ralf Zimmermann[3,4], Erik Frank[6], Philipp Kreis[6], Michael R. Buchmeiser[6,8], Murray R. Gray[6,7]*

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[2]International Joint Laboratory−iC2MC: Complex Matrices Molecular Characterization, TRTG, 76700 Harfleur, France.
[3]Joint Mass Spectrometry Centre (JMSC)/Chair of Analytical Chemistry, University of Rostock, 18059 Rostock, Germany
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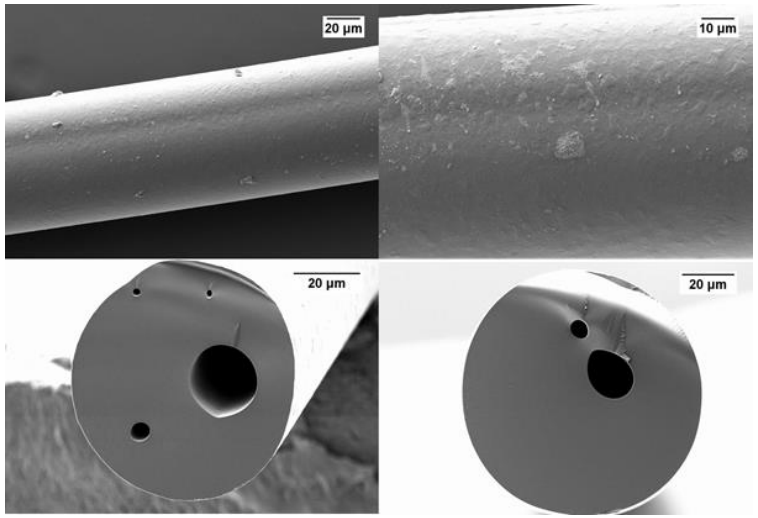
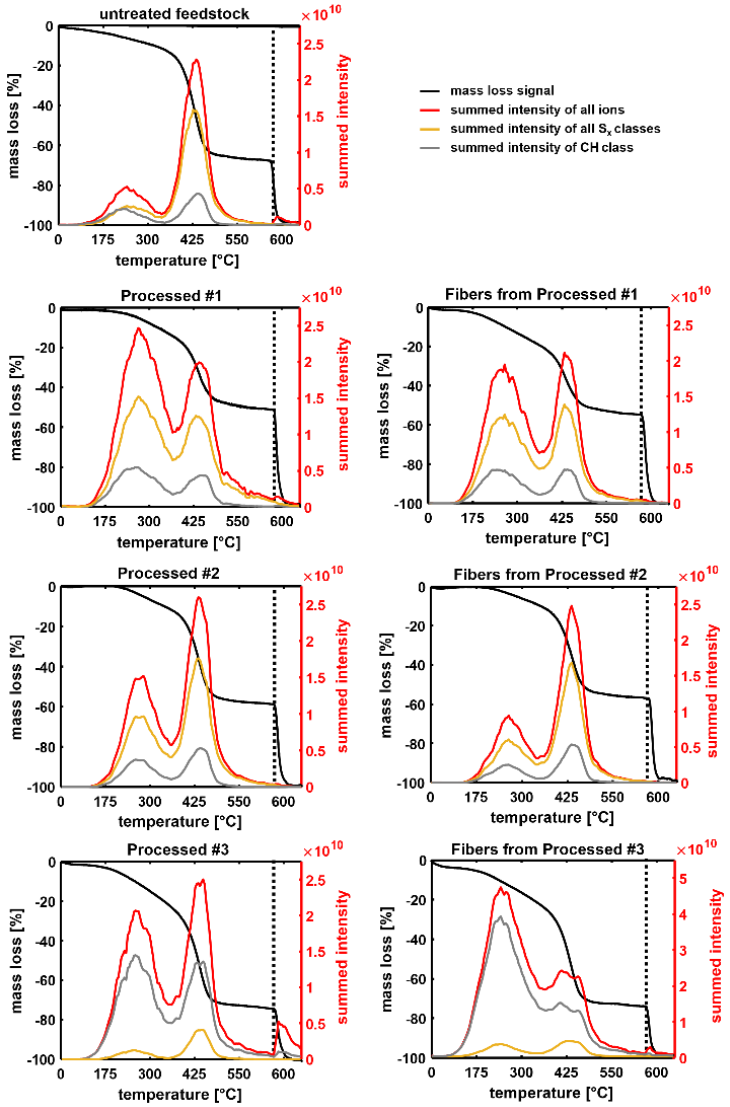
[5]Alberta Innovates Suite 2540, 801-6th Ave SW, Calgary AB, T2P 3W2, Canada
[6]German Institutes of Textile- and Fiber Research (DITF) Denkendorf, Körschtalstr. 26, D-73770 Denkendorf, Germany.
[7]Department of Chemical and Materials Engineering, University of Alberta. Edmonton, AB T6G 1H9, Canada
[8] Institute of Polymer Chemistry, University of Stuttgart, Pfaffenwaldring 55, 70569 Stuttgart, Germany

submission to ACS Energy and Fuels

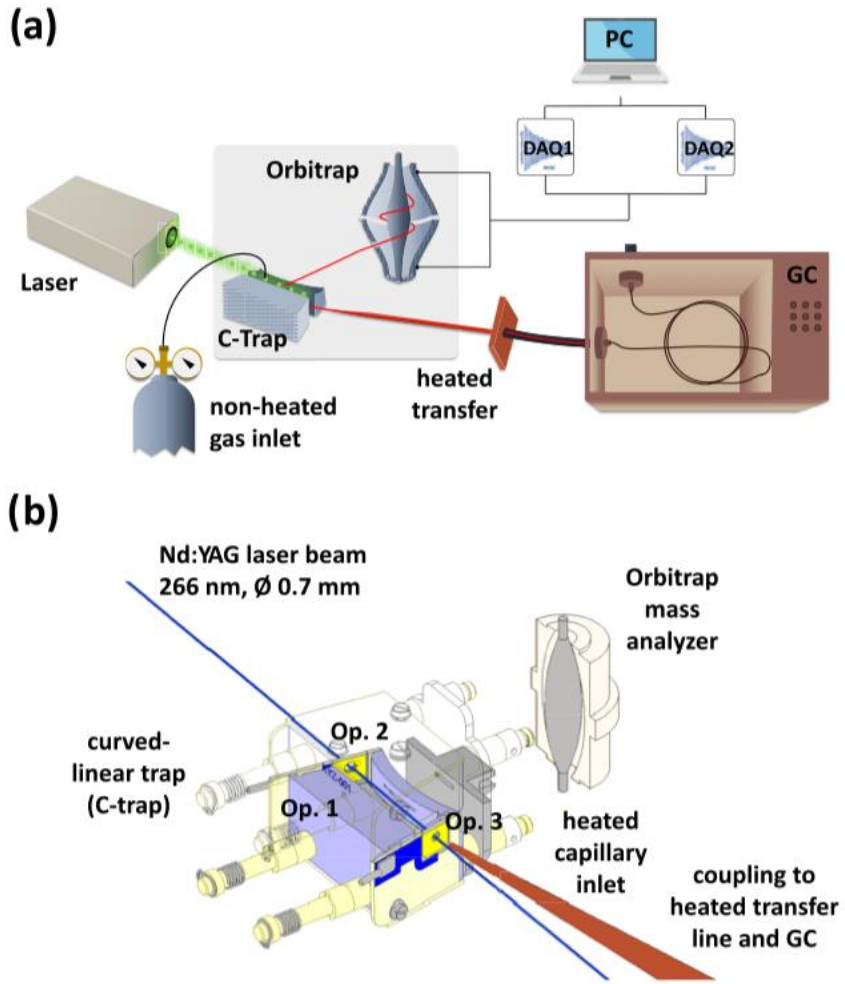



Mass loss data (black) from TG measurements and summed intensity of all ions (red), summed intensity of all Sx-classes (yellow), and summed intensity of the HC-class (grey) from HRMS measurements for the asphaltene feedstock, the three processed samples, and the fibers. The dotted line indicates the change of the atmosphere from nitrogen to oxygen at 600 ° C at the end of the TG measurement.

# Case Study IV – Application on Orbitrap

# Photoionization Orbitrap Time-Dependent Data




analytical chemistry

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## Vacuum Laser Photoionization inside the C-trap of an Orbitrap Mass Spectrometer: Resonance-Enhanced Multiphoton Ionization High-Resolution Mass Spectrometry

Paul Kösling, Christopher P. Rüger,* Julian Schade, Kyle L. Fort, Sven Ehlert, Robert Irsig, Anton N. Kozhinov, Konstantin O. Nagornov, Alexander Makarov, Martin Rigler, Yury O. Tsybin, Andreas Walte, and Ralf Zimmermann

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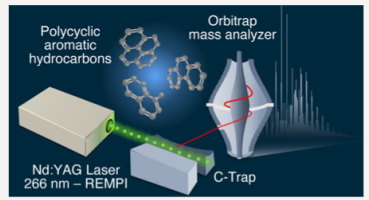
**ABSTRACT:** State-of-the-art mass spectrometry with ultraviolet (UV) photoionization is mostly limited to time-of-flight (ToF) mass spectrometers with 1000−10 000 $m/\Delta m$ mass resolution. However, higher resolution and higher spectral dynamic range mass spectrometry may be indispensable in complex mixture characterization. Here, we present the concept, implementation, and initial evaluation of a compact ultrahigh-resolution mass spectrometer with gas-phase laser ionization. The concept is based on direct laser photoionization in the ion accumulation and ejection trap (C-trap) of an Orbitrap mass spectrometer. Resonance-enhanced multiphoton ionization (REMPI) using 266 nm UV pulses from a frequency-quadrupled Nd:YAG laser was applied for selective and efficient ionization of monocyclic and polycyclic aromatic hydrocarbons. The system is equipped with a gas inlet for volatile compounds and a heated gas chromatography coupling. The former can be employed for rapid system $m/z$-calibration and performance evaluation, whereas the latter enables analysis of semivolatile and higher-molecular-weight compounds. The capability to evaluate complex mixtures is demonstrated for selected petrochemical materials. In these experiments, several hundred to over a thousand compounds could be attributed with a root-mean-square mass error generally below 1 ppm and a mass resolution of over 140 000 at 200 $m/z$. Isobaric interferences could be resolved, and narrow mass splits, such as 3.4 mDa ($SH_4/C_3$), are determined. Single laser shots provided limits of detection in the 20-ppb range for p-xylene and 1,2,4-trimethylbenzene, similar to compact vacuum REMPI-ToF systems.



# Photoionization Orbitrap Time-Dependent Data

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**Addressing Thermal Behavior and Molecular Architecture of Asphaltenes by a Thermal-Optical Carbon Analyzer Coupled to High-Resolution Mass Spectrometry**

Christopher P. Rüger,* Anika Neumann, Paul Kösling, Silvia Juliana Vesga Martínez, Martha Liliana Chacón-Patiño, Ryan P. Rodgers, and Ralf Zimmermann

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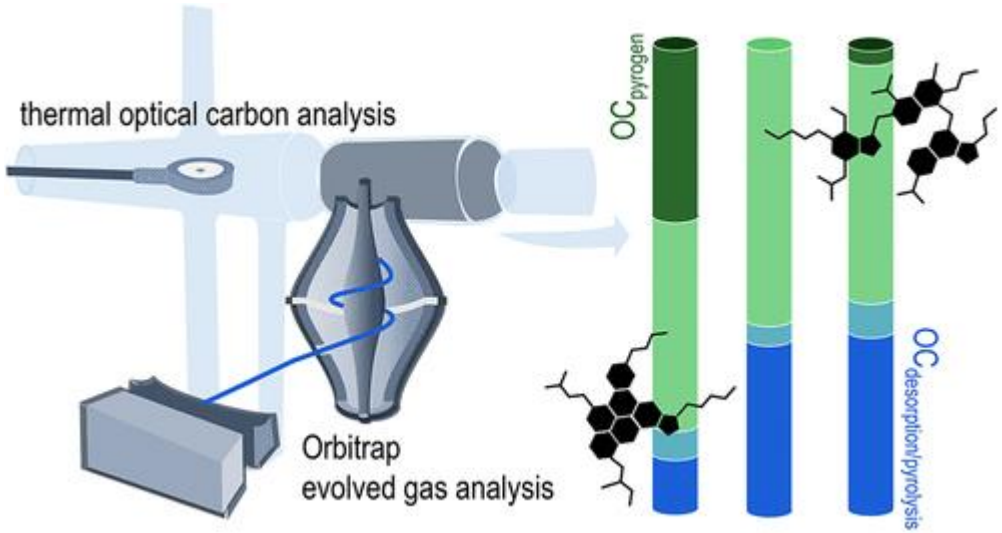


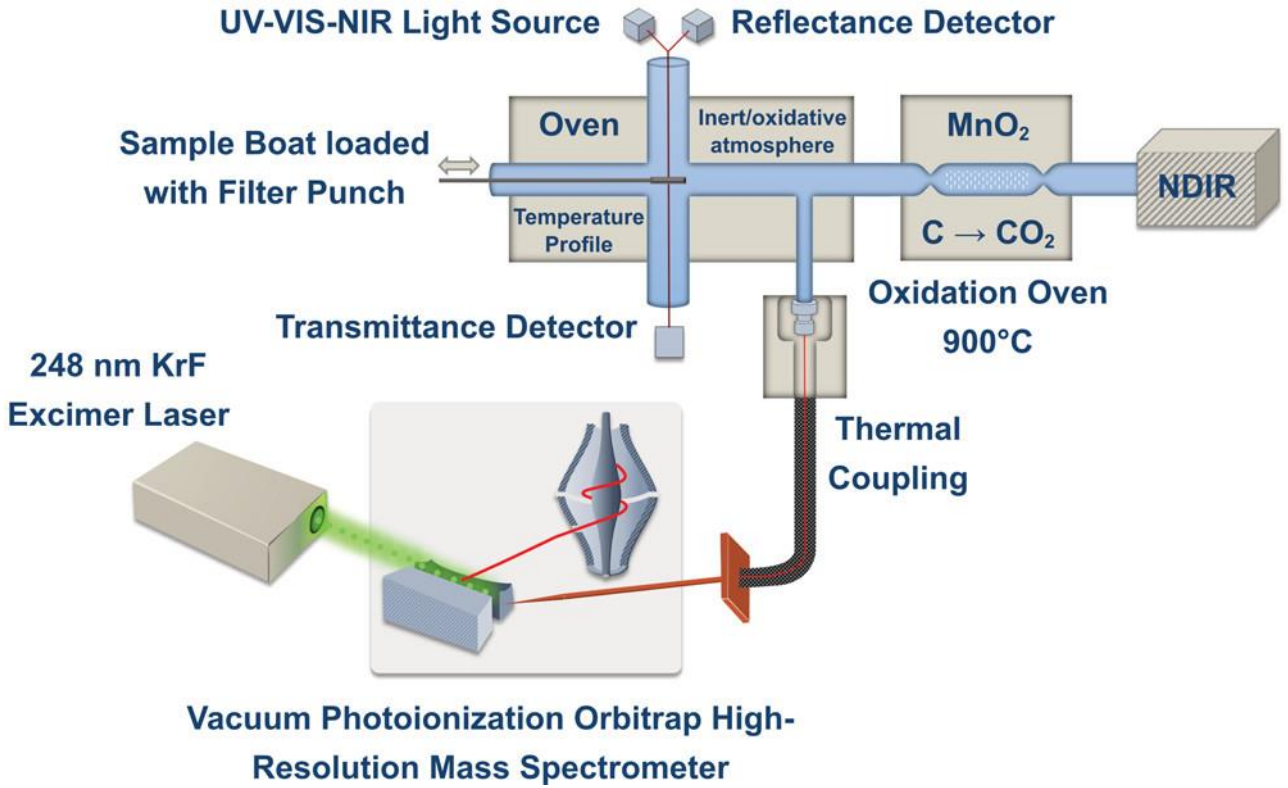

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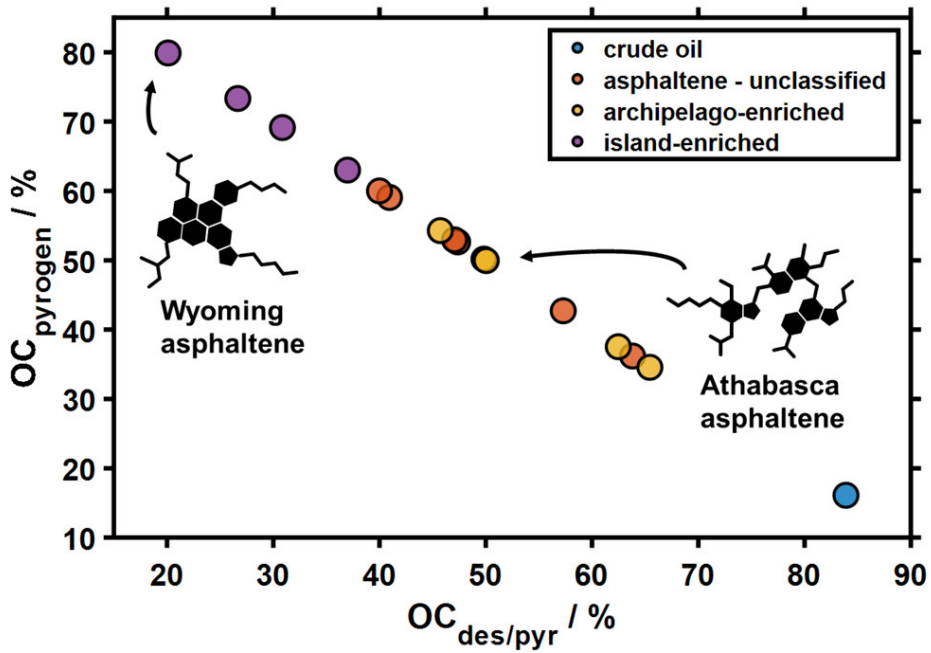
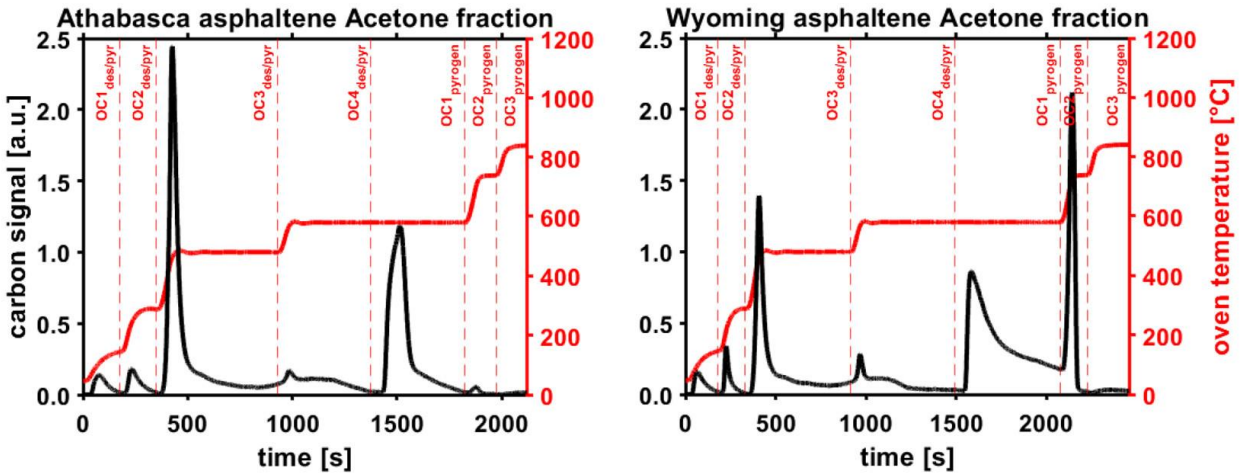
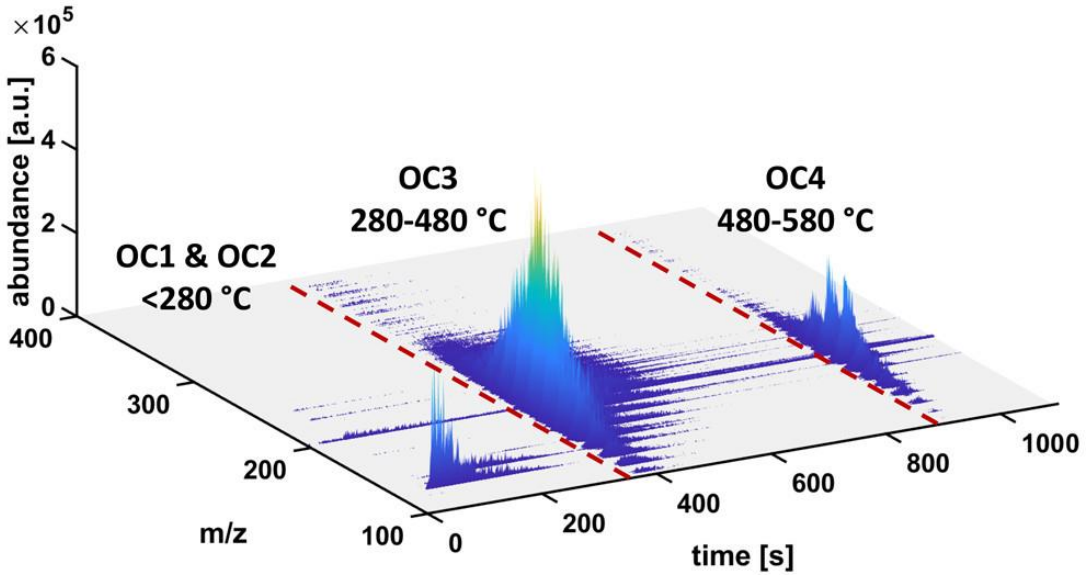


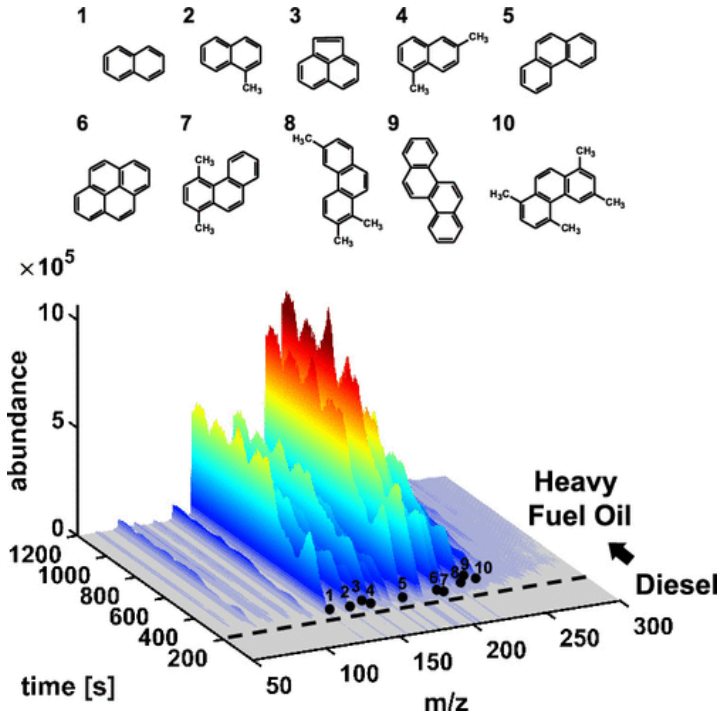
# Photoionization Orbitrap Time-Dependent Data

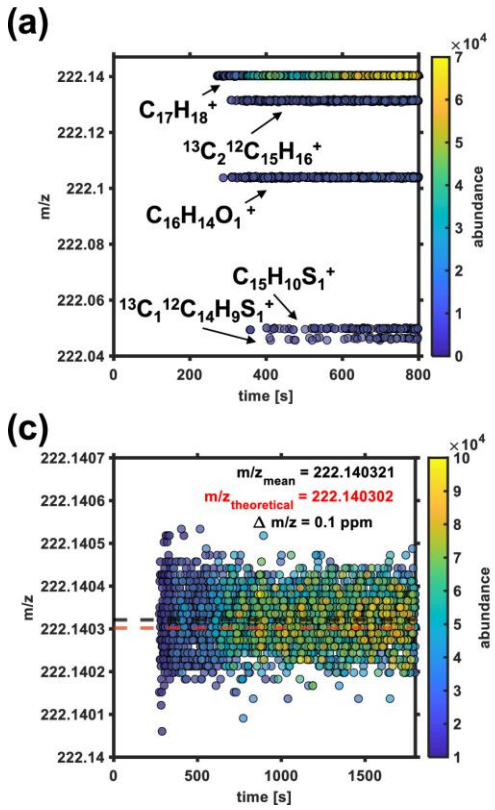
## Online Tracing of Ship Emission via High-Resolution Mass Spectrometry

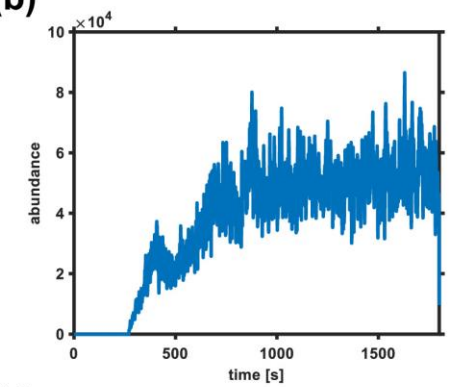
analytical chemistry
pubs.acs.org/ac Article

**Real-Time Investigation of Primary Ship Engine Emissions by Vacuum Resonance-Enhanced Multiphoton Ionization High-Resolution Orbitrap Mass Spectrometry**

Paul Kösling, Christopher P. Rüger,* Julian Schade, Sven Ehlert, Uwe Etzien, Anton N. Kozhinov, Yury O. Tsybin, Martin Rigler, Thomas Adam, Andreas Walte, Bert Buchholz, and Ralf Zimmermann

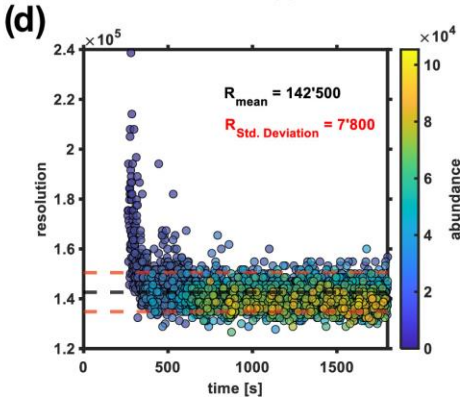


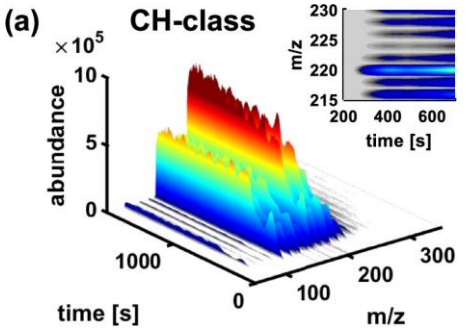



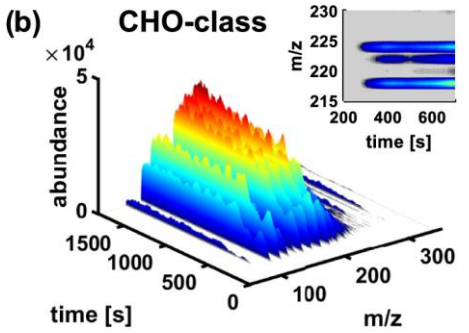



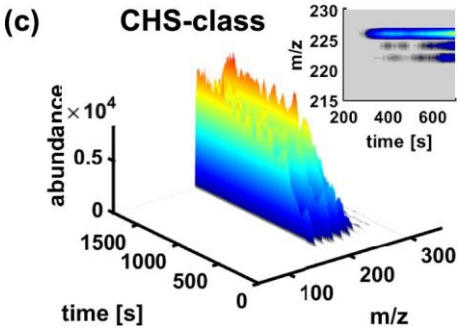






# Finishing – Review Recommendation

*Annual Review of Analytical Chemistry*

## Petroleomics: Tools, Challenges, and Developments

Diana Catalina Palacio Lozano,[1] Mary J. Thomas,[1,2] Hugh E. Jones,[1,2] and Mark P. Barrow[1]

[1]Department of Chemistry, University of Warwick, Coventry CV4 7AL, United Kingdom; email: M.P.Barrow@warwick.ac.uk

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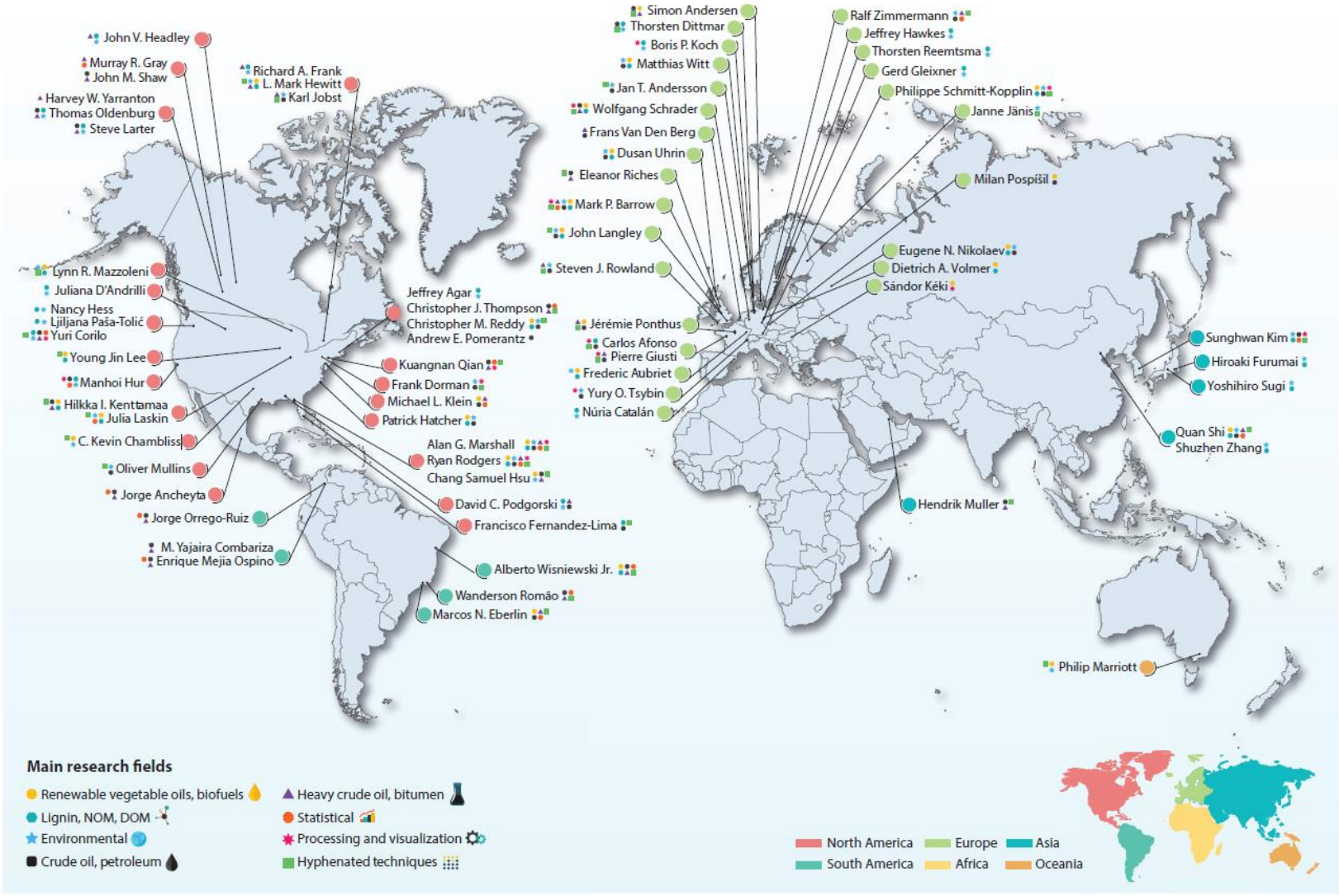


# Finishing – Chemometrics - Petroinformatics



## 4. Petroinformatics

Manhoi Hur, Sunghwan Kim, Chang Samuel Hsu

Studies on petroleomics have been focused on advanced molecular-level characterization of compounds that could not be analyzed by conventional techniques. The next stage of the development would be more discussions on the information obtained and relationships with the properties and functions. The relationship between molecular composition and bulk properties or functions can be explicitly expressed by *petroinformatics*, which utilizes statistics, mathematics, and computational visualization technology to interpret or correlate analytical results with bulk properties and experimental data. This provides explicit or implicit information for underlying science and engineering.
In this chapter, several examples of petroinformatics are presented. Statistical methods, such as principle component analysis (PCA) for dimensionality reduction in multivariate analysis, and hierarchical clustering analysis (HCA), have been applied to interpret complex petroleum mass spectra obtained by ultrahigh-resolution Fourier transform ion cyclotron resonance mass spectrometry (FT-ICR MS). The mass spectral peaks were statistically analyzed by Spearman's rank correlation, and by correlation diagrams showing relationships between composition and bulk properties. Additionally, the chapter demonstrates quantitative analyses for petroleum samples by PCA for multivariate analysis and *t*-tests for univariate analysis. Volcano plots are utilized to visualize the quantitative change or difference between samples in detail.

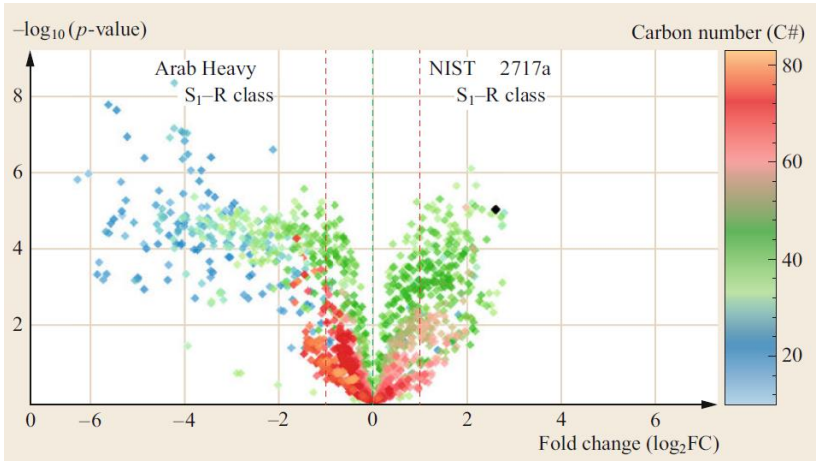


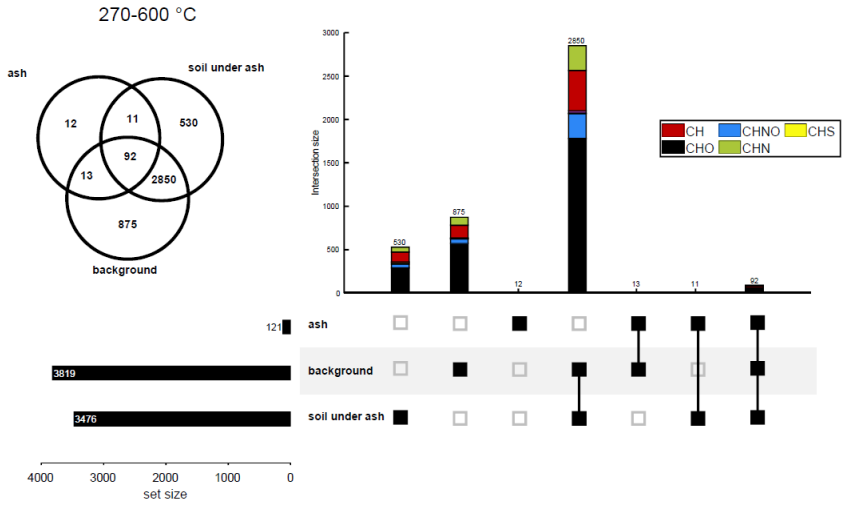
The software platform, which integrates data from many samples obtained from different analytical instruments, is a very important tool to achieve more comprehensive understanding of complex analytes such as crude oils. The learnings from other research fields, such as metabolomics, genomics, and proteomics, are important and valuable for the next steps of petroinformatics development, i. e., standardization of data and retrieval of its metadata information.

In modern society, information is generated by studies, experiments, surveys, experience and other communications. Information technology, or informatics, vastly improves access to such information by people who support education, research, practice, development, and decision making. Thanks to advances in computer technology, a huge amount of information from various sources can be digitized, integrated, stored, and processed by computers with high speed and efficiency. *Petroinformatics*, which utilizes statistics, mathematics, and computational visualization technology to interpret or correlate analytical results with bulk properties and experimental data, is particularly needed for very complex petroleum mixtures, ranging from light gas to solid residue that can contain millions of molecules. Sophisticated analytical techniques generate data that often


C.S. Hsu, P.R. Robinson (Eds.), *Springer Handbook of Petroleum Technology*, DOI 10.1007/978-3-319-49347-3_4

- **supervised and unsupervised multivariate data analysis** for accessing similarities and differences in large attribution data sets
- always take hypothesis tests into account (if data set allows it), such as **ANOVA**/MANOVA for creating powerful and easy significance and fold-change visualizations (Volcano Plot)
- primarily via principle component analysis (**PCA**), clustering approaches (e.g. hierarchical clustering – **HCA**), matrix factorization (NNMF/PMF)
- **Venn plots** as starting point for elucidation shared and unique chemical space (upset plots for nice visualization)



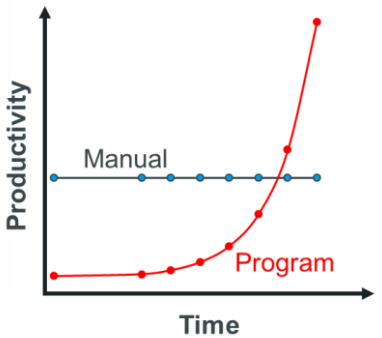
# Summary and Outlook

**“Are we there yet?”**

- all steps of data processing are important in FT-ICR MS and require attention for pushing to the best results
- but peak-picking and transient processing (FT/non-FT, absorption/magnitude mode, etc.) are very well advanced

- current challenges are primarily for elemental composition attribution with **optimized validation strategies**
- efficient open-code and free workflows **tackling big data from hyphenated solutions** remain rare
- for most complex mixture fields (energy transition, environmental, etc.) we are just at the starting point for **comprehensive data treatment with supervised/non-supervised statistics** (ANOVA, HCA/PCA; NMR

- plenty of roam for future (your?) research → learn a programming language
  – it will always help you either in academia or industry



# Acknowledgment

TotalEnergies
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Spectroswiss
photonion
DFG Deutsche Forschungsgemeinschaft
iC2MC INTERNATIONAL – COMPLEX MATRICES MOLECULAR CHARACTERIZATION
ThermoFisher SCIENTIFIC
Aerosol

*Complete team of:*

**Joint Mass Spectrometry Centre Rostock and Munich - JMSC**

**International Joint Laboratory Complex Matrices Molecular Characterization- iC2MC**

EU FT-ICR MS

**Thank you for the kind attention!**

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