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Electron Ionization Source Parameters in GC-MS

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Content

Common source parameters for electron impact ionization

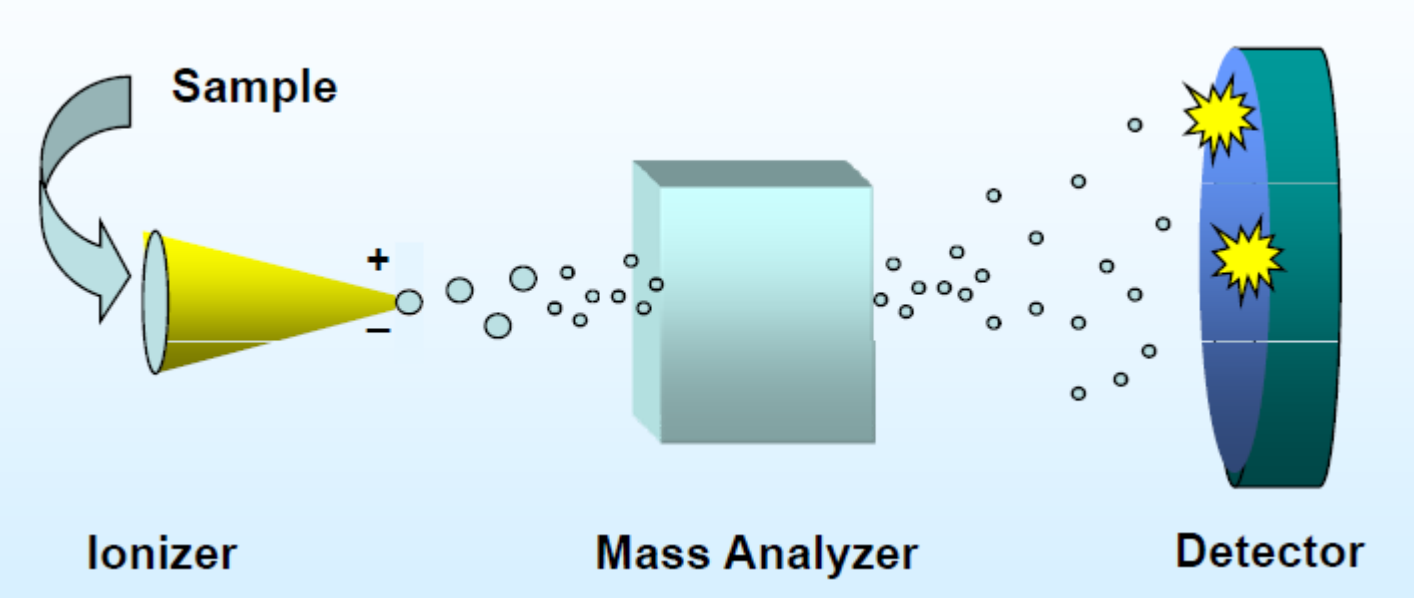
Setting up a SIM method

Setting up a MS/MS method

Sensitivity and selectivity: Choosing the right technology

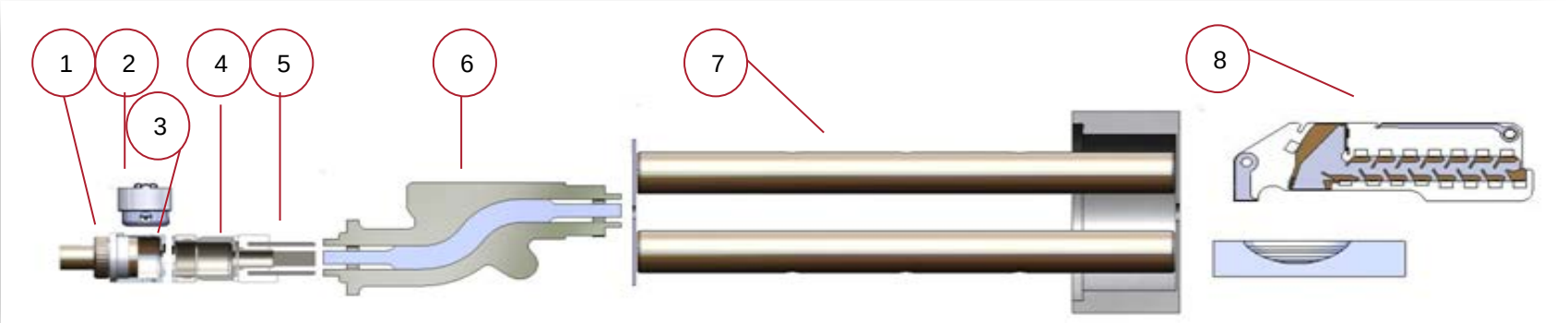
Troubleshooting tips and tricks

What is MS?



The basis of MS (Mass spectrometry) is the **production of ions that are subsequently separated or filtered according to their mass-to-charge (m/z) ratio, and detected. The resulting mass spectrum is a plot of the (Relative) abundance of the produced ions as a function of the m/z ratio."**

Components of a Single Quadrupole MS



- Ion source components
  - 1: Repellor
  - 2: Filament
  - 3: Ion volume
  - 4: Lenses
  - 5: Heated prefilter
- 6: Ion guide
- 7: Quadrupole
- 8: Multiplier

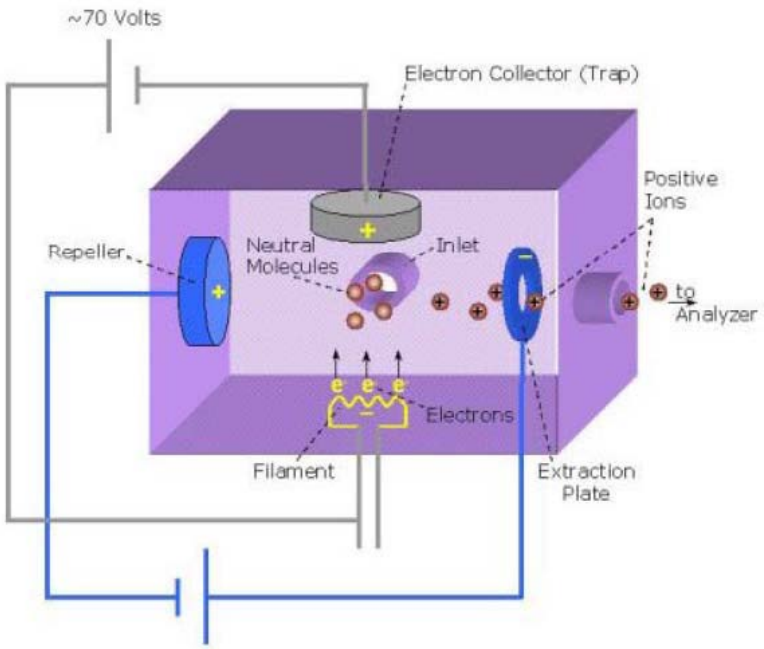
Step 1: Ion creation and guidance

Step 2: Ion separation

Step 3: Ion detection

Electron Impact Source Parameters

Source temperature, emission current, electron voltage



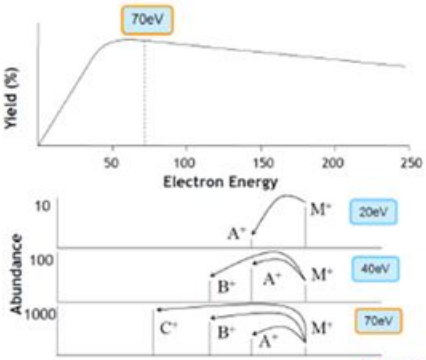
- Sample is introduced into the ionization chamber in a gaseous form through a heated transfer line
- Gas phase sample is bombarded with an energy-rich electron beam coming from rhenium or tungsten filament (Energy = 70 eV)
- Molecule is “shattered” into fragments (70 eV >> 5 eV bonds)
- Fragments (positive ions) are pushed under an electrical field to the mass analyzer
- Extended fragmentation -> *high structural information*

Parameters

- **Source temperature**
- Typical temperature range is **250-300° C**, compounds should be in a gaseous phase
- Recommendation 1: Use the temperature of the applicaton also for tuning
- Recommendation 2: Follow the guidelines from the manufacturer, source designs vary

- **Electron energy**
- Typically 70 eV
- Energy more than sufficient to break hydrocarbons
- Commercially available libraries are generated with 70 eV

- **Emission current**
- Typical emission current in uA, 50 to 100
- High emission current will yield in more ions but can lead to ion-molecule reactions
- Low emission currents can be used in case there is enough sensitivity
- Recommendation: Follw guidelines from manufacturer, source designs vary



Compound dependent

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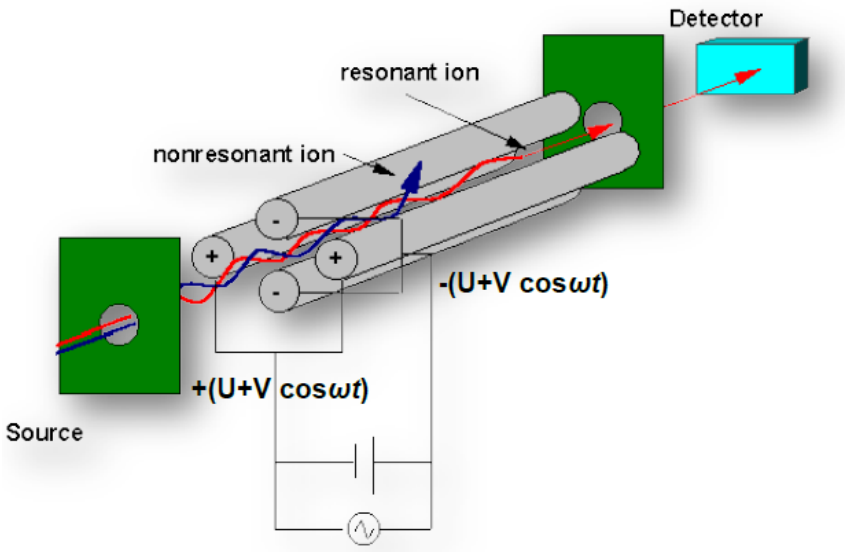
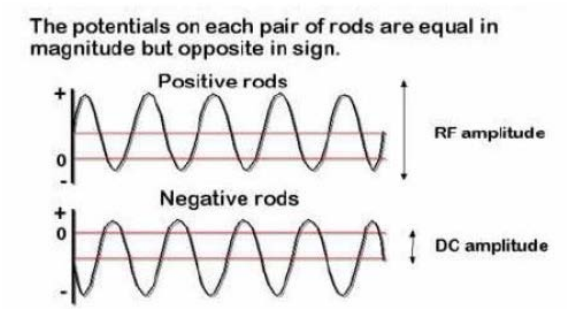
Separating the Ions in a Quadrupole

Parameters are defined by “tuning”



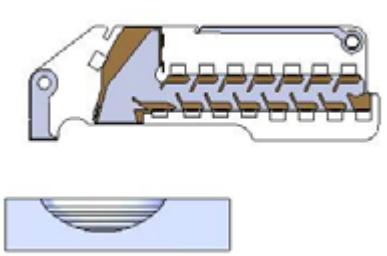


- The combination of DC and RF potentials applied to the quadrupoles are varied with time to separate the ions.
- Only specific ions are transmitted (Resonant ions) while the others collide with the rods having an unstable trajectory.
- Only ions that differ of one mass unit (1 amu) can be resolved by modulating the AC/DC potential (Low resolution)
- Increasing the resolution decreases the number of ions that reach the detector

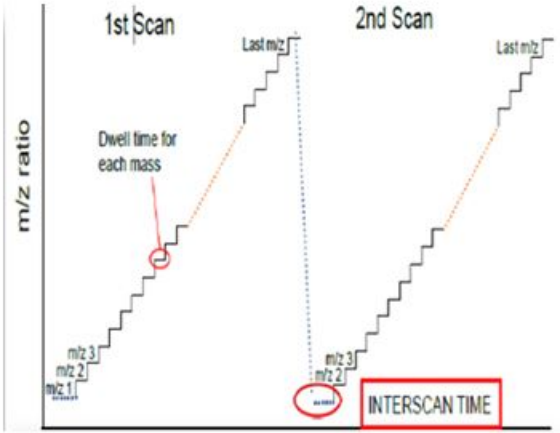
Electron Multiplier and Gain

- Typically optimized by “tuning”

- **Gain:**
- The gain is the number of electrons generated for every ion that strikes the detector.
- This is typically set between **1 x10^5 and 3x10^5 electrons per ion**.
- Gains larger than this will generate more electrons per ion, but both the analyte ion and the noise ion signals will be larger.
- As the electron multiplier ages, the voltage required for a given gain will increase.



FullScan Method

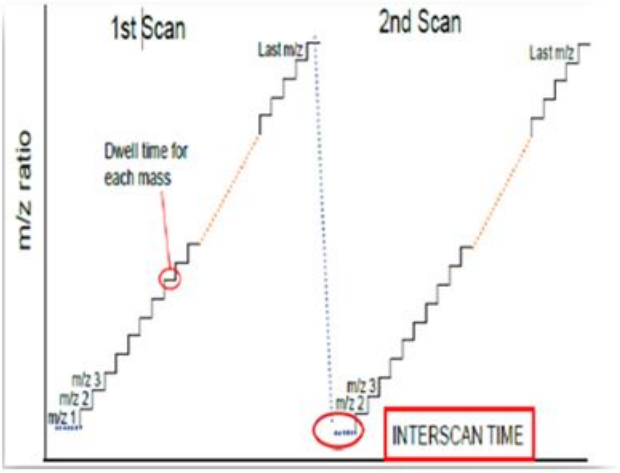


- Classic systems: You will need to add appr. 0.1s for interscan delay
- Thermo Scientific™ ISQ™ series single quadrupole GC-MS: Much lower interscan delay and scan speed in method equals actual scan speed

Parameters in the method

- **1: Mass range**
- **Typical range starts from 50 to 500 Da**, but of course analyte dependent. For instant some drugs have a strong 44 ion, where as polybrominated have ions above 900 Da.
- **2: Scan speed**
- **Typical 10 scans across a peak are needed for good integration.**
- Calculation example: Peak 3 sec, 10 scans across the peak, scan time 0.3 sec yields 10 scans

FullScan Method

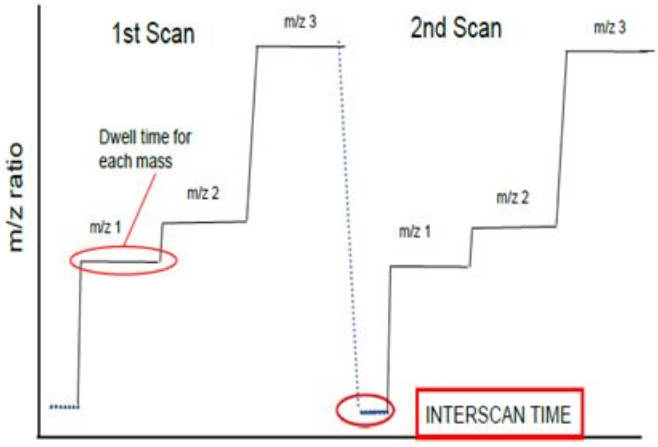


- Classic systems: Dwell time is affecting the **response**
- ISQ single quadrupole GC-MS series: Dwell time is **affecting S/N**
- **Why? See timed SIM/SRM**

Pro's and con's

- **1: Screening**
  - FullScan spectra can be library search
  - Full information available
- **2. Dwell time**
  - Measuring time of an ion = dwell time
  - In full scan mode this is low per definition
  - Dwell times and S/N are interdependent

SIM Method



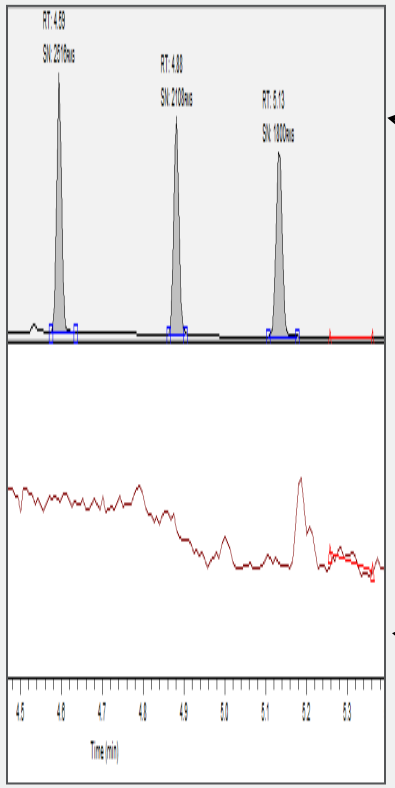
- Classic systems: Dwell time is affecting the response
- Thermo Scientific ISQ ™ series: Dwell time is affecting S/N
- **Why? See timed SIM/SRM**

Parameters

- **1: SIM ions**
  - Typically 3 ions per analyte are needed.
  - Choice: **Most selective** i.e.mostly ions with heavier m/z are preferred, or ions with high S/N ratio.
- **2: Dwell time**
  - Trade off between number of datapoints and measuring time

Single Quad Measurements: FullScan and SIM

Chromatogram FullScan

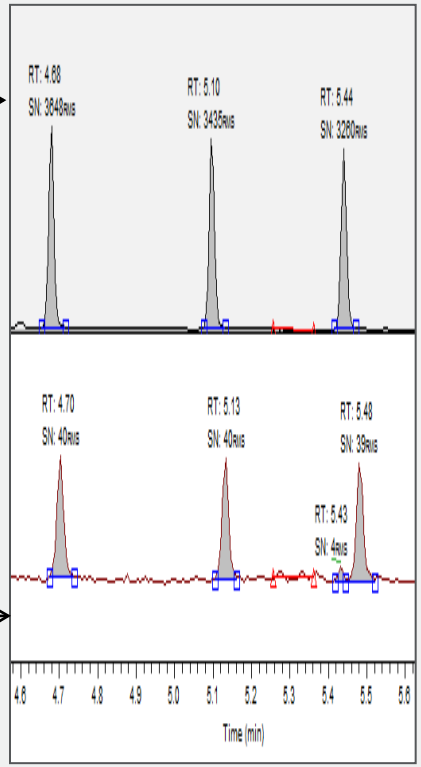


Experiments

Standard solution of trichlorobenzenes in FS (Left) and SIM (Right)

Sample extract showing trichlorobenzenes In FS (Left) and SIM (Right)

Chromatogram SIM



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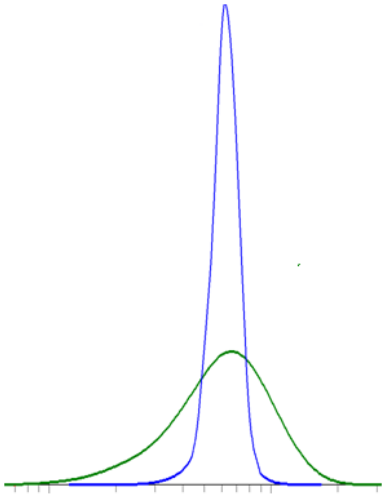
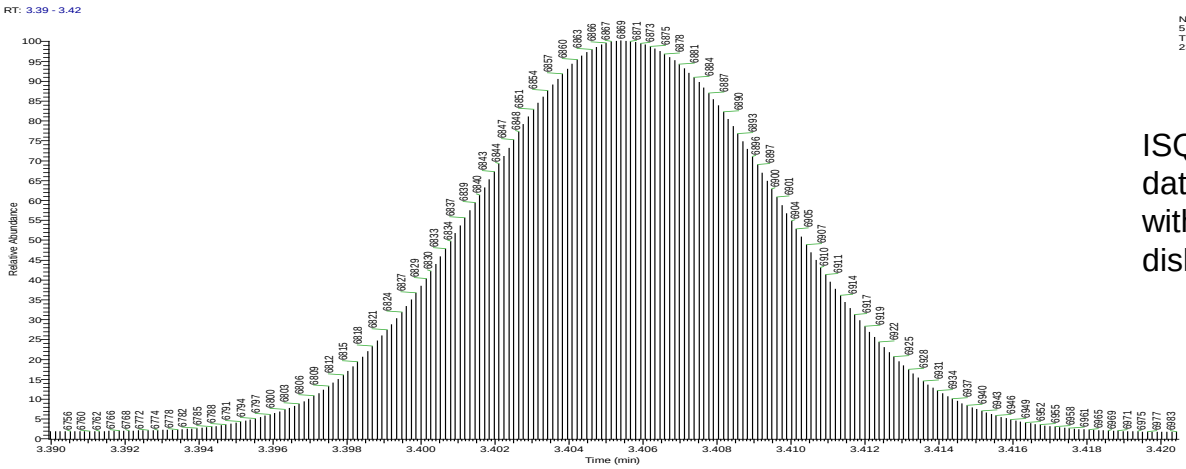
Why is Scan Speed Important – Part 1



- You can…..
  - …speed up your chromatography
  - …use narrower columns
- Narrower peaks = Better S/N= Better sensitivity
- Faster run times **and** faster *run to run* times = More productivity



ISQ QD GC.MS FullScan data over 50 u mass range with 127 scans/s written to disk

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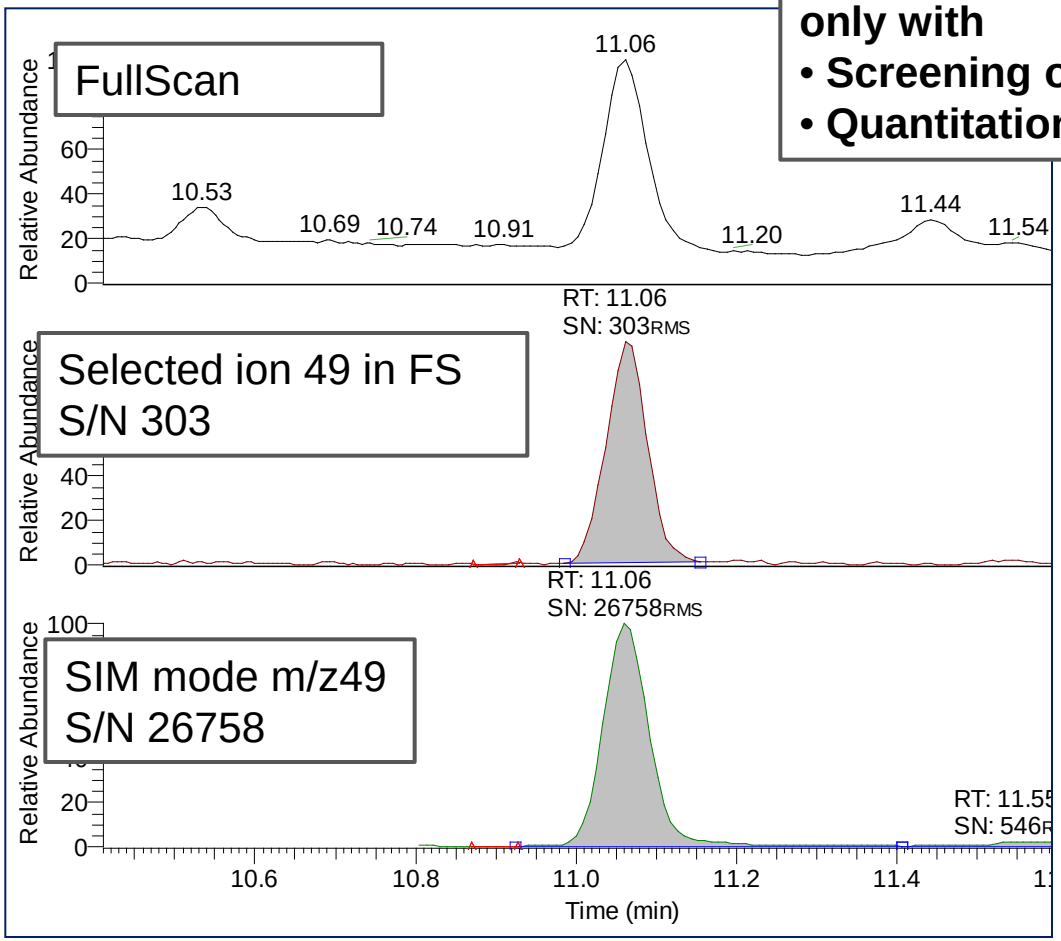
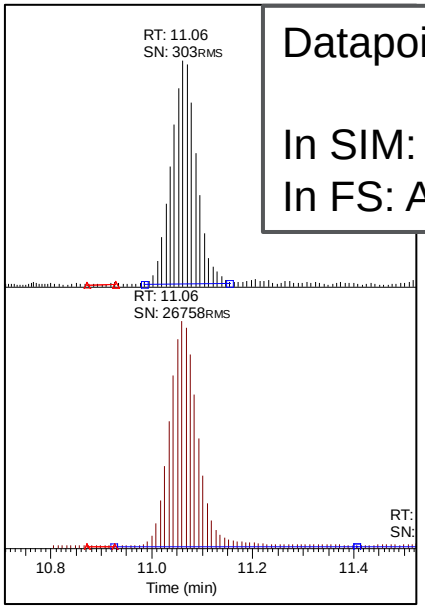
Why is Scan Speed Important – Part 2

Simultaneous FullScan and SIM: One injection only with
- **Screening of unknowns**
- **Quantitation of known compounds at low level**





Datapoints

In SIM: Approx 20
In FS: Approx 20

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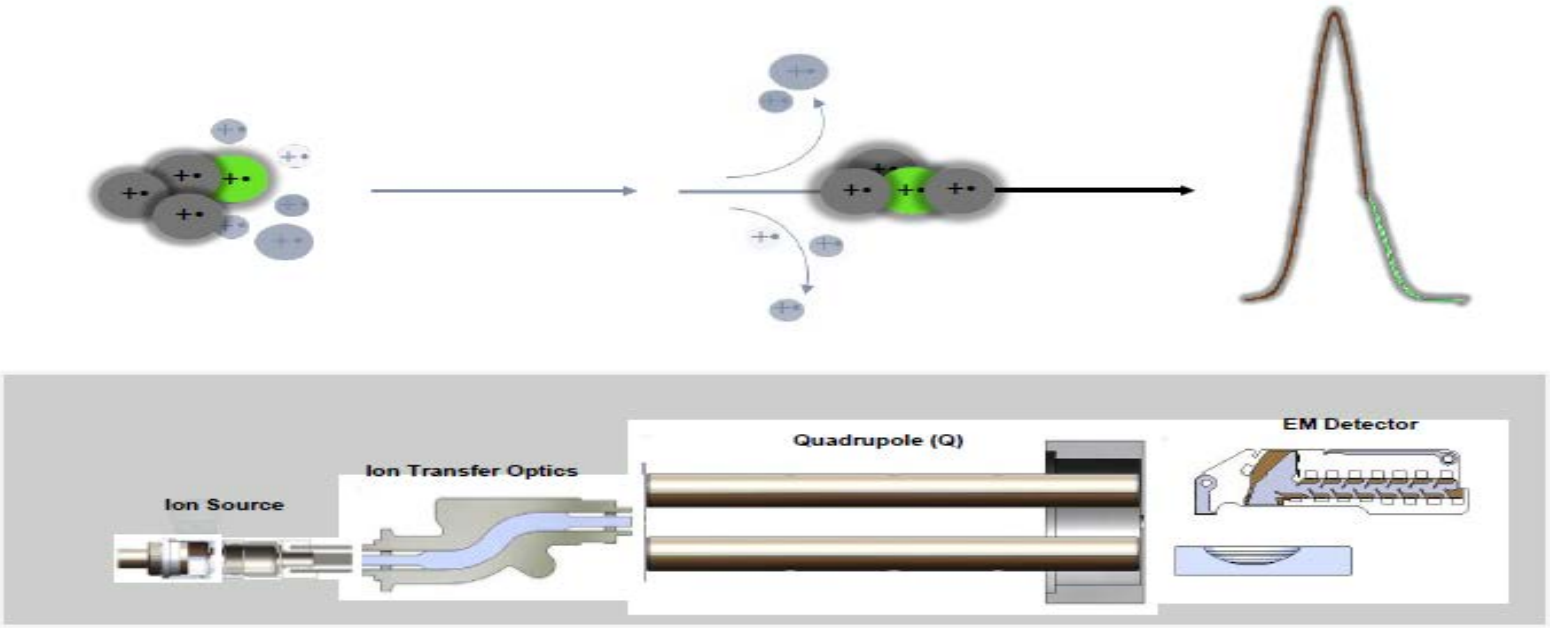
Going from Single to Triple Quadrupole

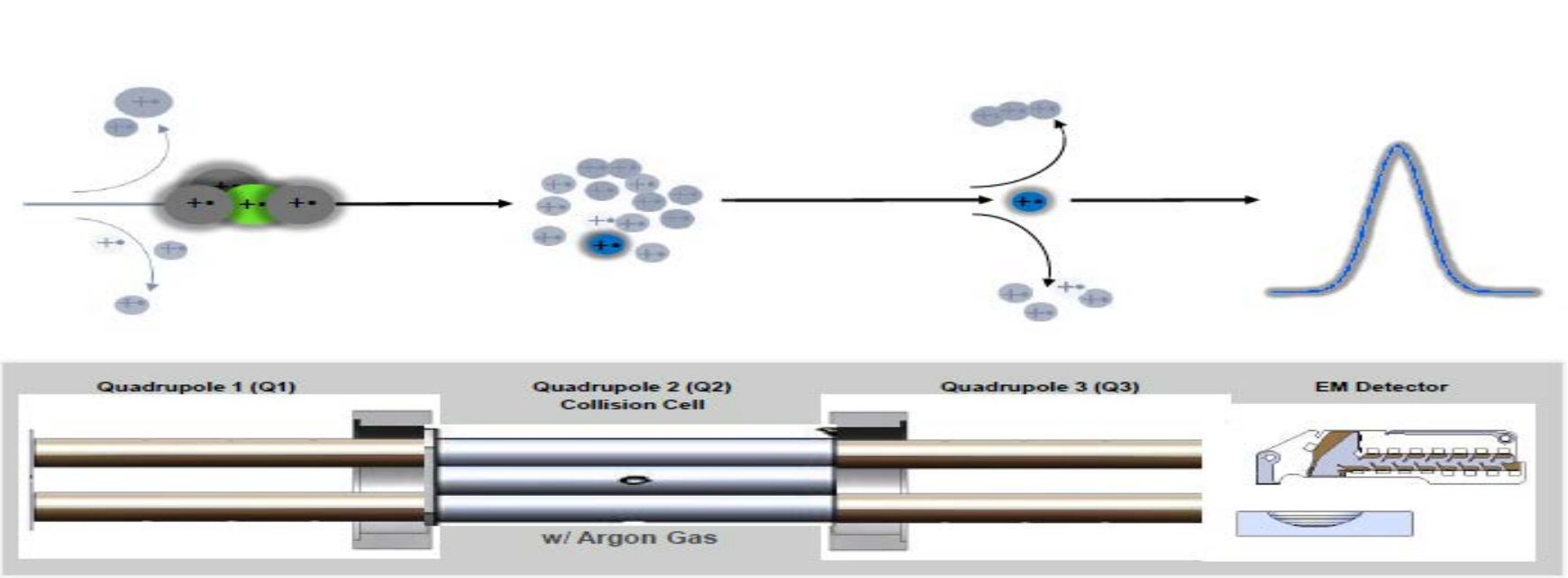
Some reasons to consider using QQQ

SIM Measurement in Heavy Matrix



- Matrix and analyte ions are isobaric, so the response contains analyte ions and matrix ions possibly leading to
  - No ion ration confirmation (3 ions are not in the correct ratio), false negative
  - Or increased detection limits

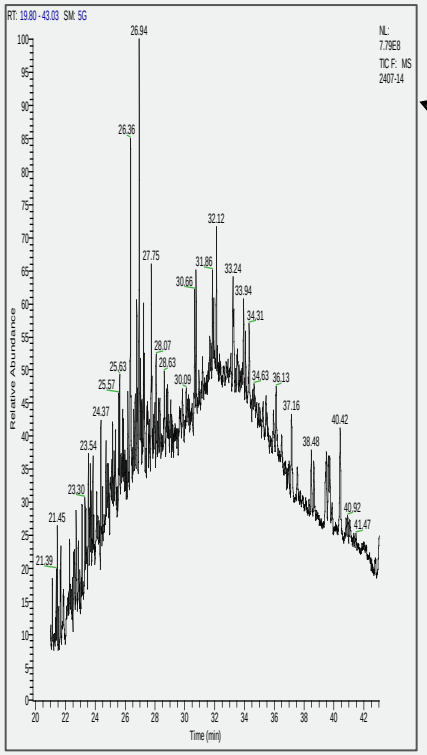
SRM or Triple Quad measurement in Heavy Matrix



- The second fragmentation in the collison cell yields in a selective and more unique ion, and eliminates the isobaric matrix ion.
  - Ion ration confirmation OK
  - Better noise reduction, increased S/N
  - Lower detection limints

Triple Quad Measurements: FullScan and SRM

Chromatogram FullScan



Experiments

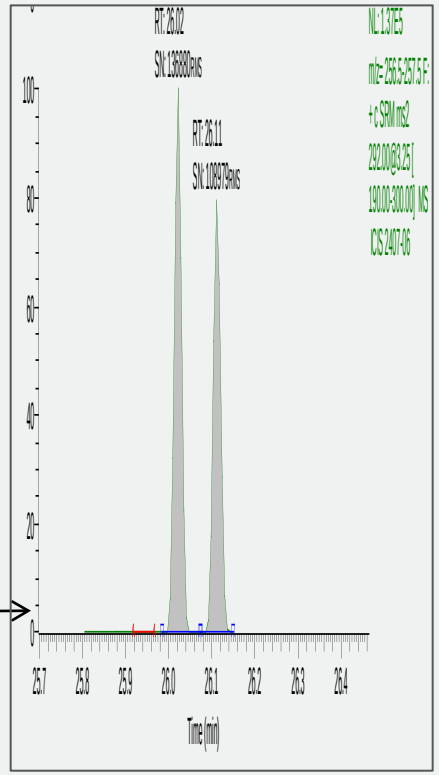
PCB in sediment

1000-s of peaks > 10% organic matter

PCB in sediments

Clear defined peaks in MS/MS mode

Chromatogram SRM



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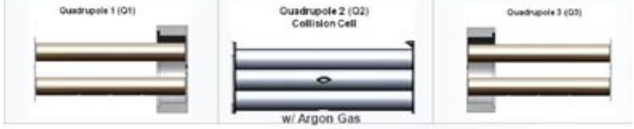
SRM Method

182	>	153
Precursor Ion	CID	Product Ion



- Classic systems: Manual optimization
- NEW: Automated method development

Parameters:
We need 2 ions in total

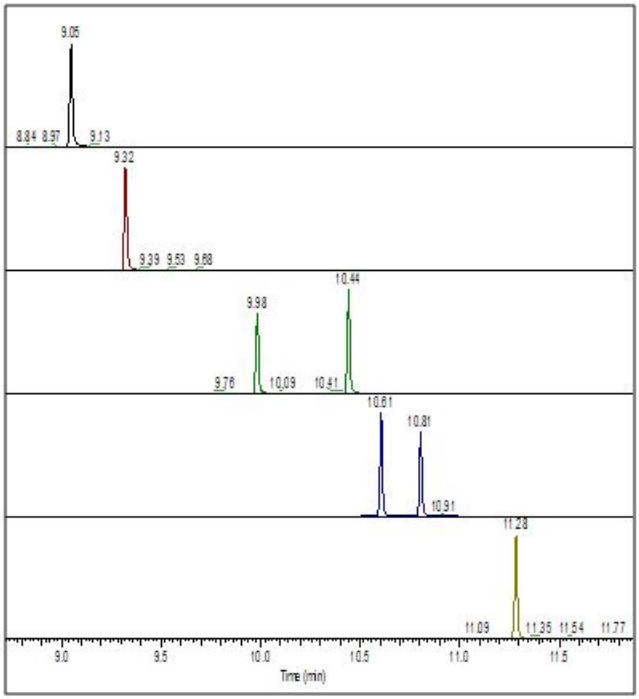
- **1: Precursor ion**
  - Typically 1 or 2
  - Choice: **Most selective**
- **2: Dwell time**
  - Trade off between number of datapoints and measuring time
- **3: Product ion**
  - To be determined with increased voltage in Q2 = Collision energy

Timed SIM and Timed SRM

Classical ways of SIM and SRM methods

Timed SIM/SRM

Classic Methods - Segmented SIM or SRM



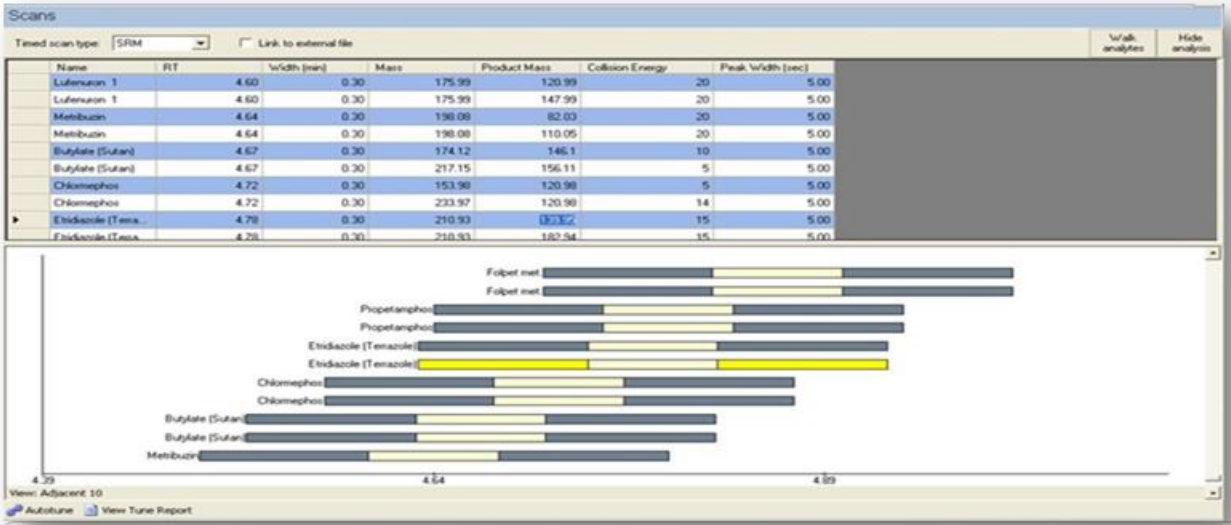
- Example of segmented scanning
- Fairly easy in the case of low number of analytes
- But when number of analytes increases, there are downsides

  1: More analytes per segment = Lower dwell times and lower S/N

  2: Increasingly more difficult to define start and stop times of a segment

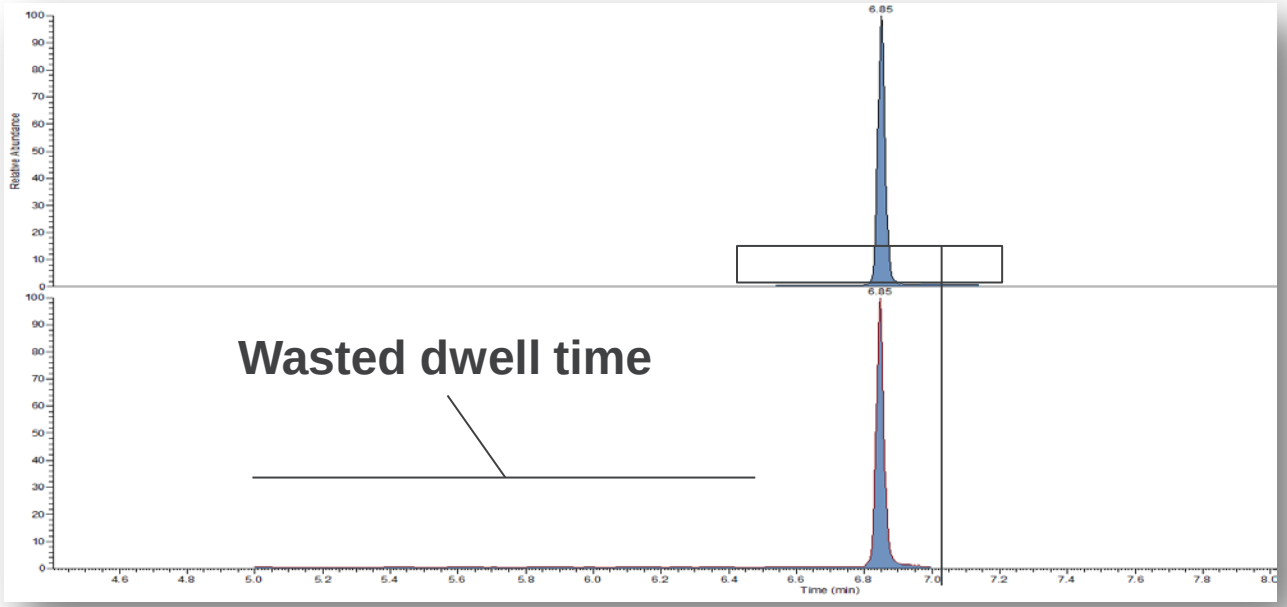
ISQ and TSQ 8000 GC-MS Series: Timed SIM and SRM

Thermo Scientific™ ISQ™ single quadrupole and TSQ™ triple quadrupole GC-MS systems



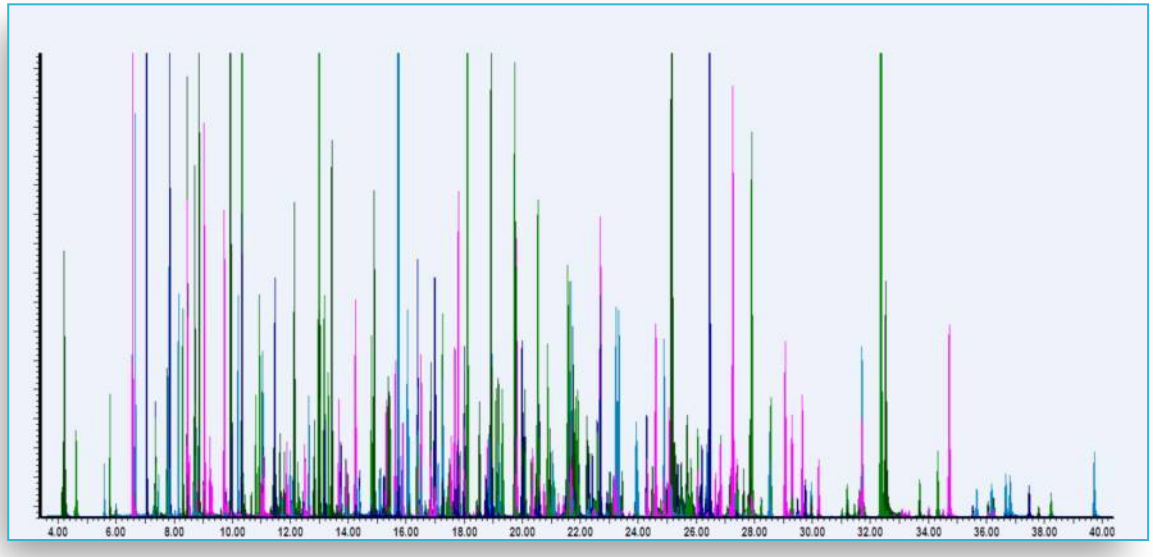
- Measuring window around RT of analyte
- Overlapping in time
- Only possible because SIM or SRM dwell times have effect on S/N, not on area counts

ISQ and TSQ 8000 GC-MS Series: Timed SIM and SRM Benefits



- Timed scanning: Overall higher dwell times, for more sensitivity
- Timed scanning: Peaks are not cut off near segment break

A Practical Example of Multiresidue Analysis



- Segmented SRM
  - Closest compound to segment break:

    5 seconds
  - Average number of simultaneous transitions:

    55

- Timed SRM
  - Closest compound to segment break:

    15 seconds
  - Average number of simultaneous transitions:

    15 (4X higher dwell times)

Automated Method Development

Auto SIM and Auto SRM

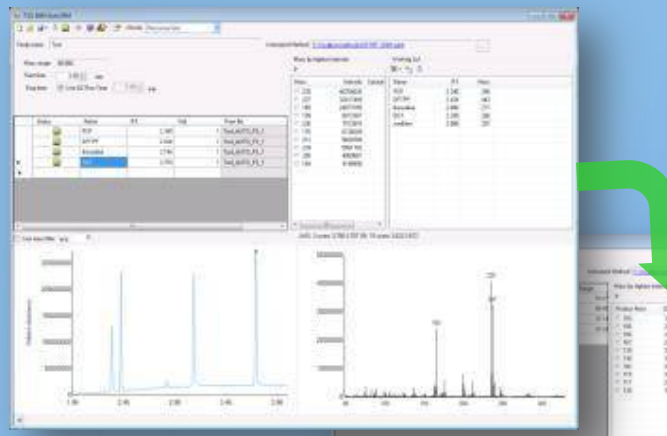
"Give a man a fish, feed him for a day.
Teach a man to fish, feed him for a lifetime"

Lao Tzu circa 5th Century BC

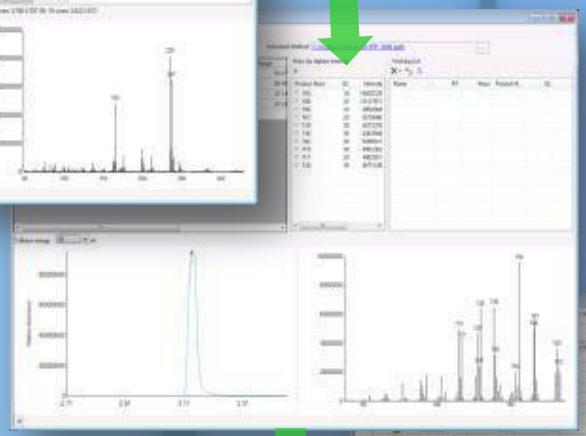
AutoSRM Overview

SRM creation workflow

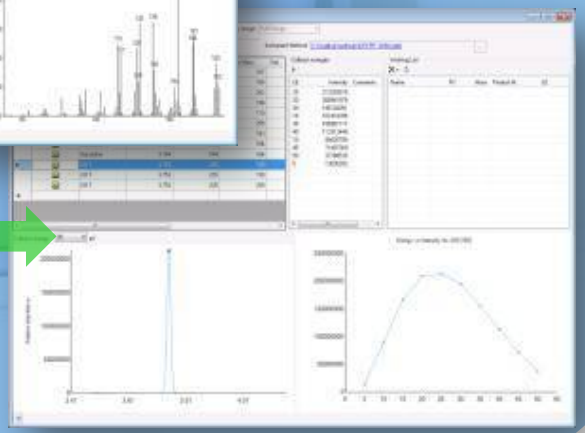
1) Precursor ion selection



2) Product ion selection

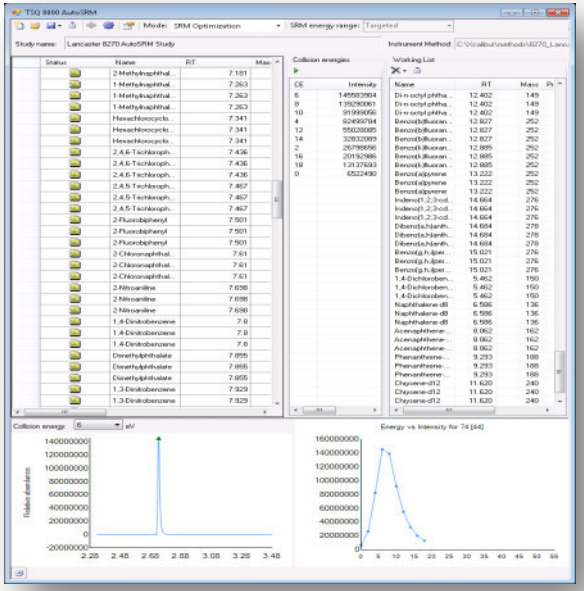


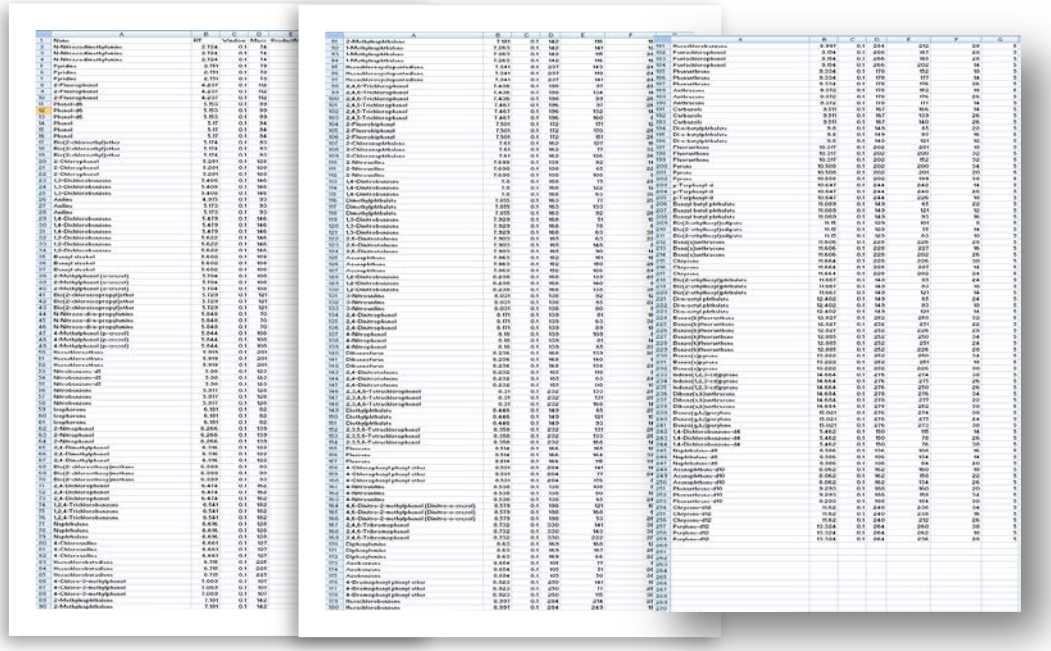
3) Collision energy optimization



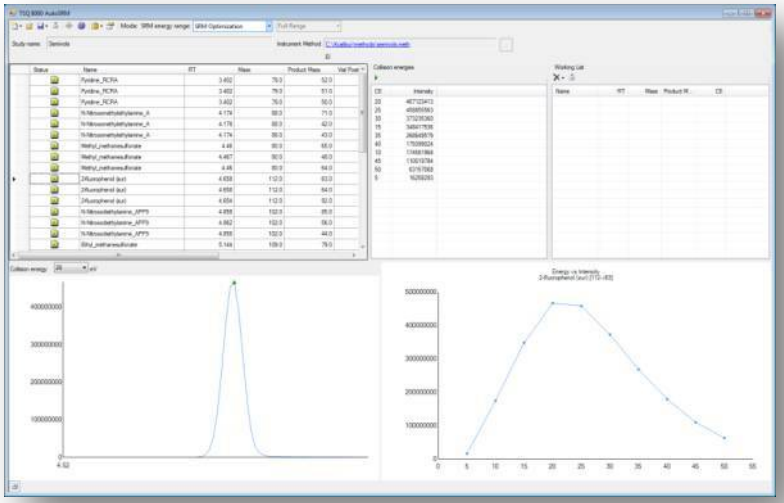
AutoSRM Use Case

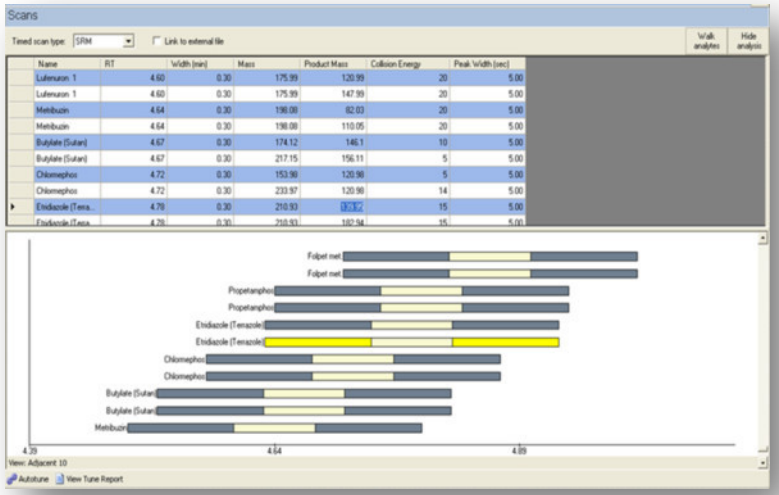
- Created and optimized > 250 transitions for > 80 compounds
- Minimal user interaction over 24 hours





Export form AutoSRM to Instrument Method





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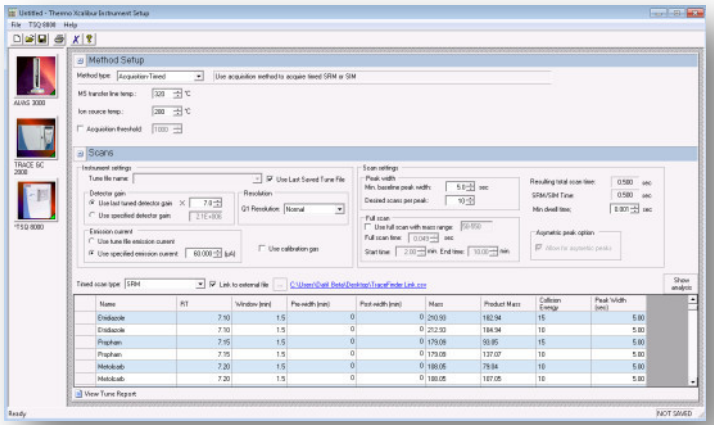
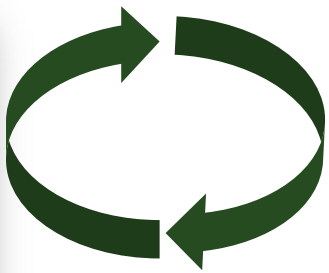
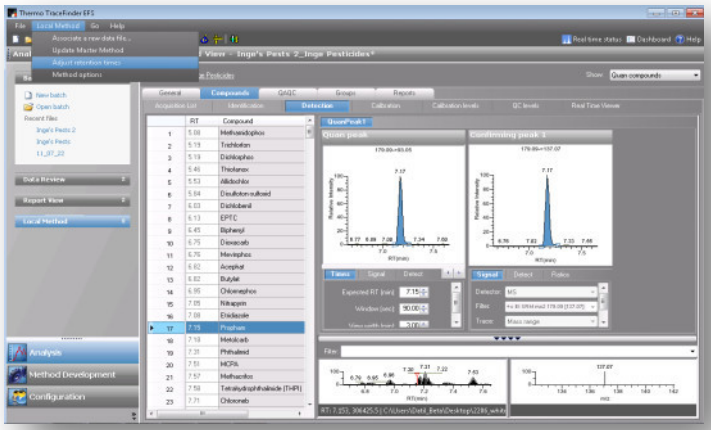
Method Sync

- **Links Thermo Scientific™ TraceFinder™ and Thermo Scientific™ Chromeleon™ software method with instrument method**

- **Enables:**
  - Compound based acquisition setup
  - Automated update of acquisition windows and RT







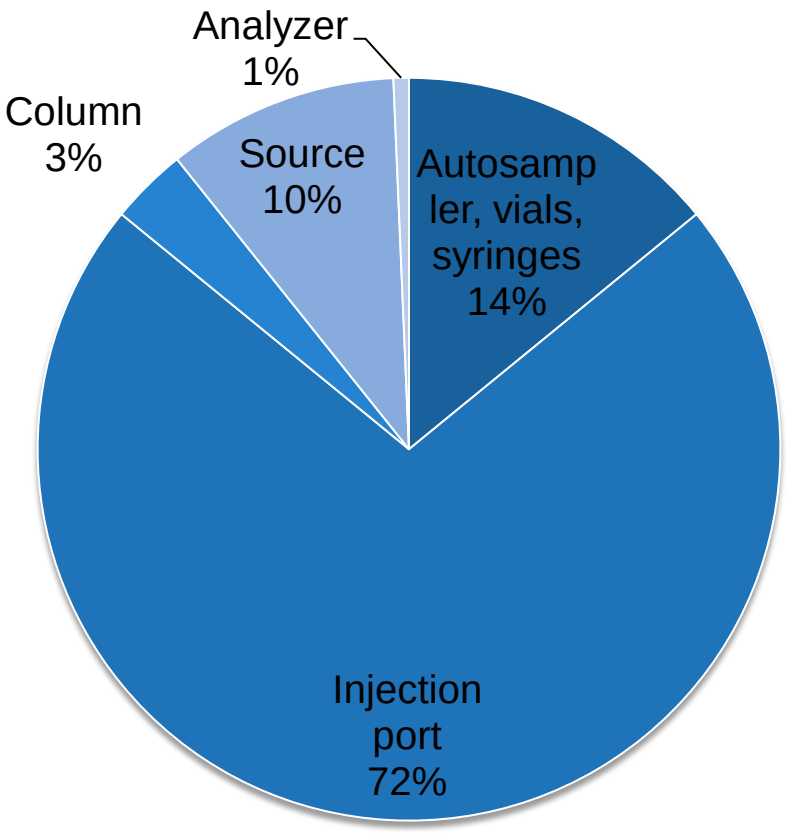
Your Main Benefits in One Slide

- Source replacement without venting the MS, including switch from EI to CI
- Wireless source
- Up and running again in 15 min

- Timed SIM and SRM
- Automated method development
- Active links:
  - From database to instrument method and vice versa
  - From database to quantitation method and vice versa
  - From instrument method to quantitation method and vice versa
- No more typing errors

Troubleshooting

Overall most common problems in a GC-MS system, one year of support gathered



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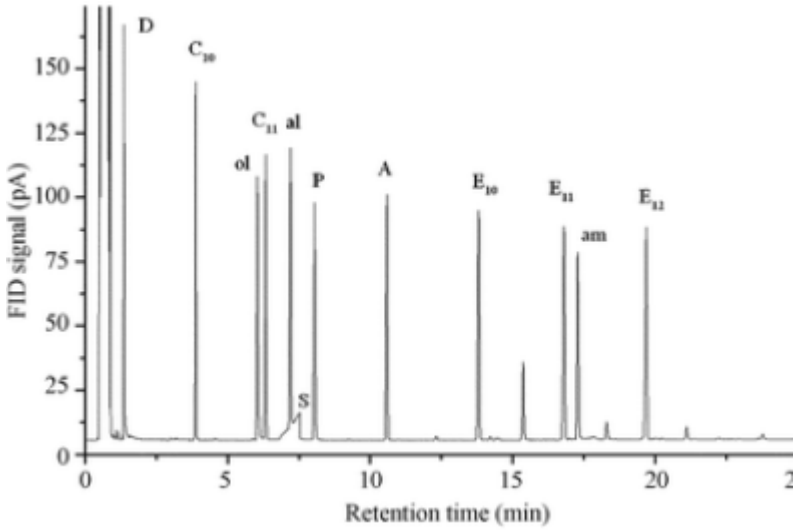
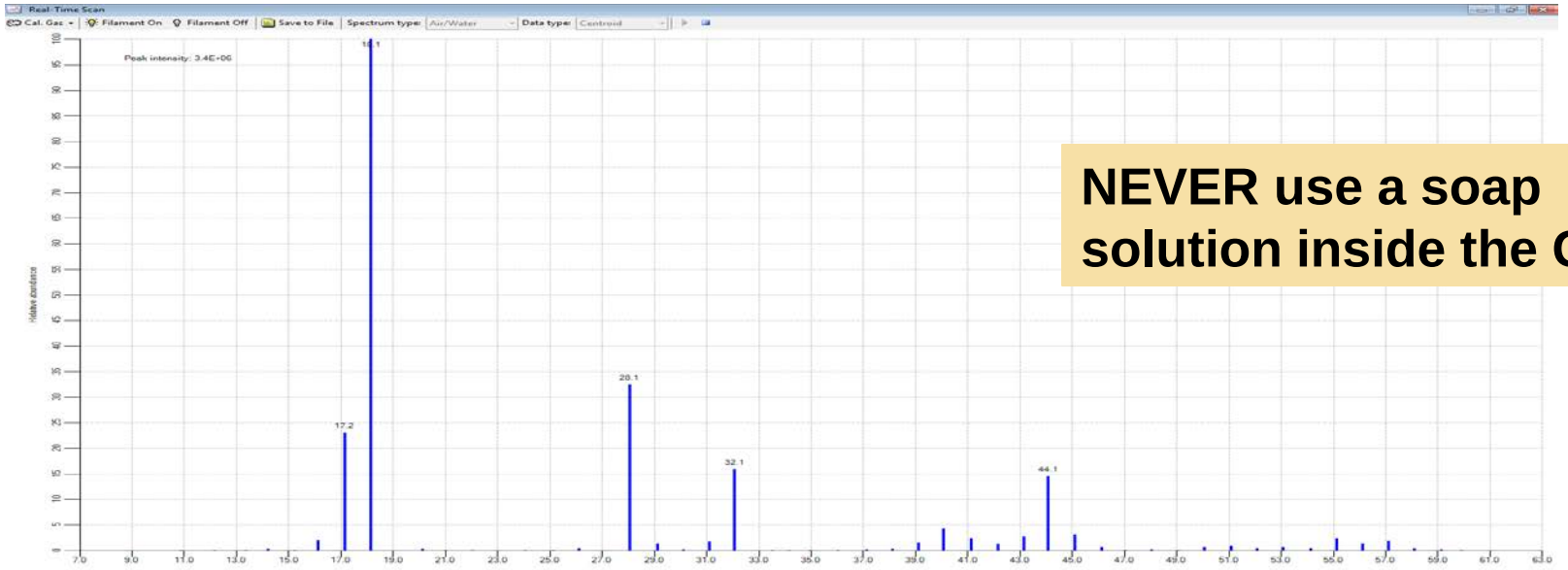
Two Troubleshooting Tools

- Air duster spray with freon gas
- Check for m/z 69 and 83
- Cost 5-10 euro

- Column test mix (E.g. Grob mix)
- Cost 40 euro approx



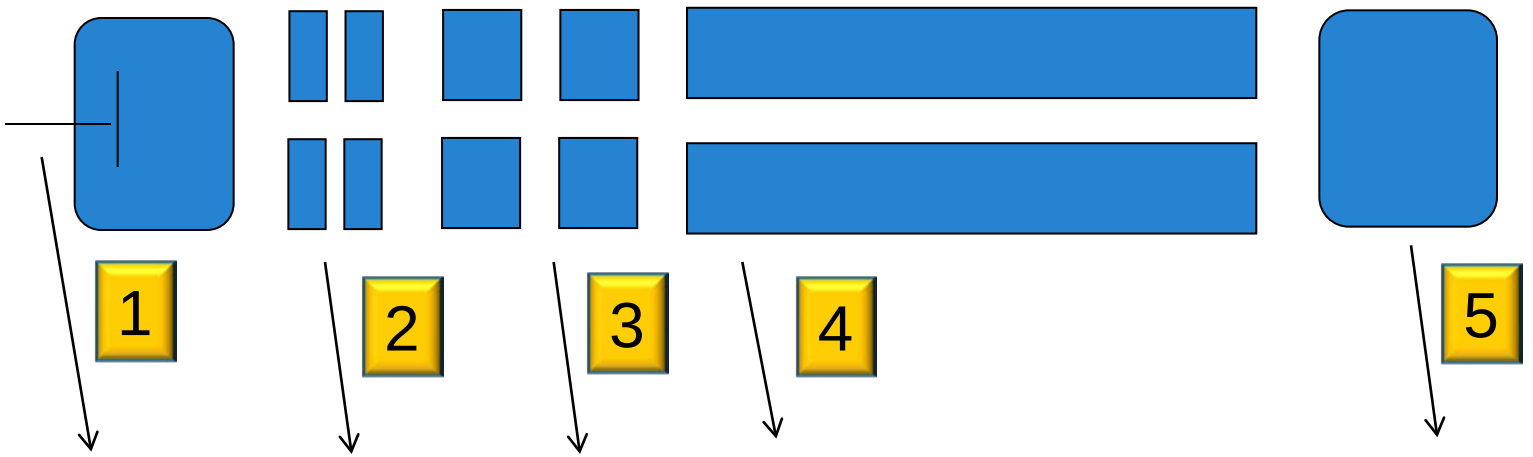
Air/Water Background



NEVER use a soap solution inside the GC

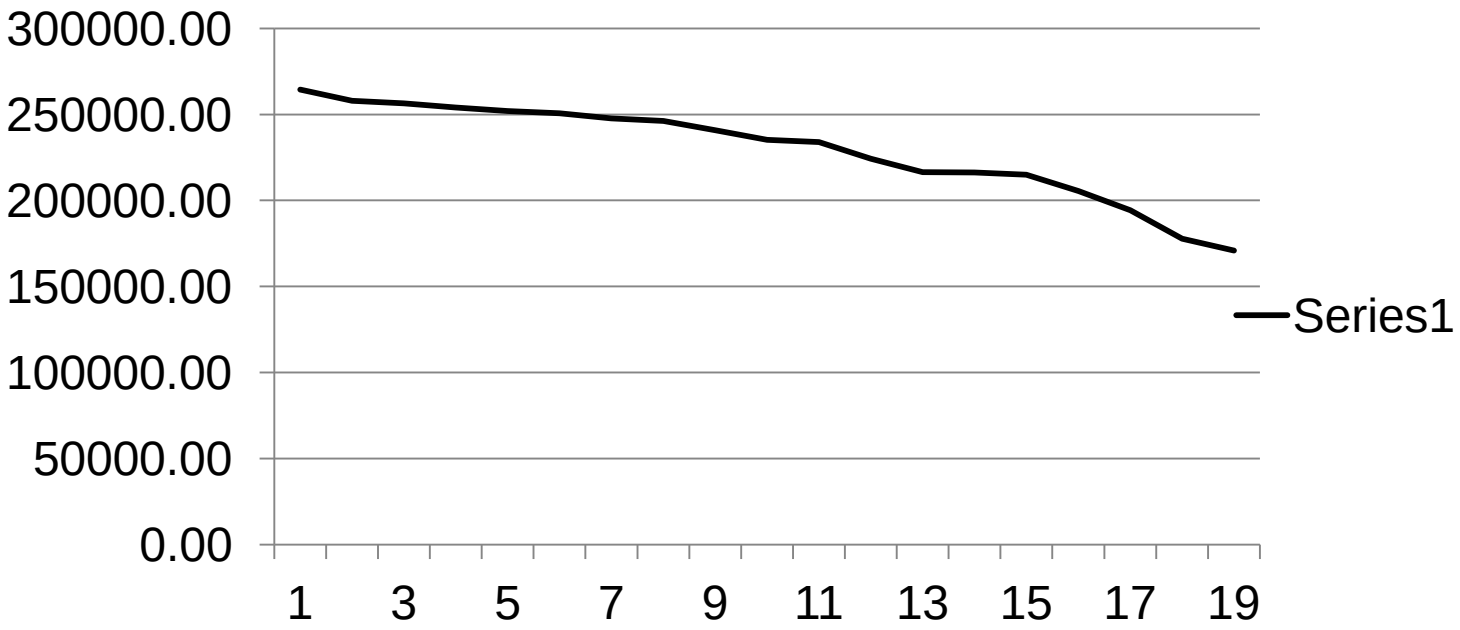
- A cheap investment in air duster spray will help you enormously
- Scan for m/z69 and 85
- Spray on the suspect points: If there is a leak this will show up
- Leaks will cause (Next to bad analysis):
  - Reduced lifetime of the filament
  - Reduced lifetime of the multiplier

Tuning of the Mass Spec



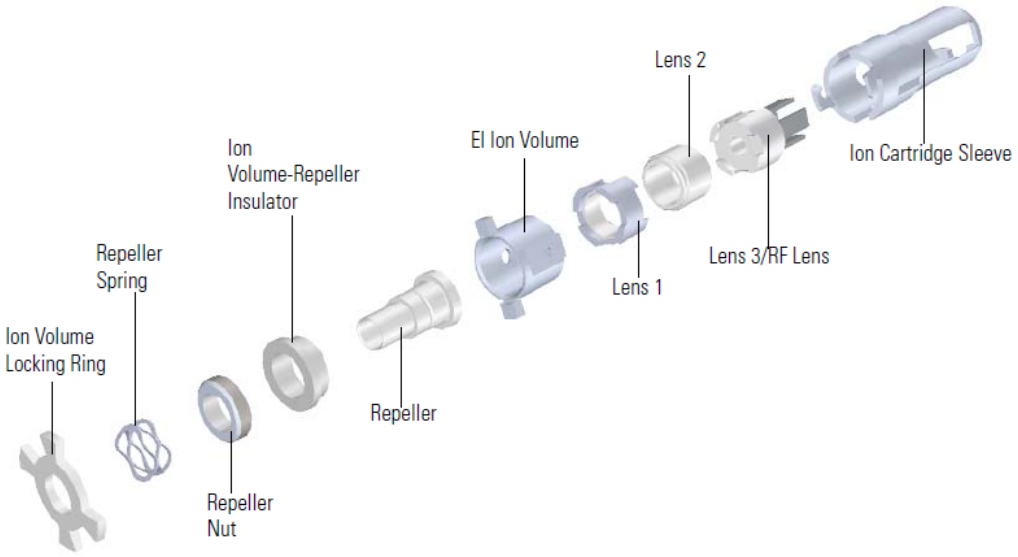
1. Repellor: Set to positive value, increases with increasing dirt on source
2. Lenses: Focussing and accelerating
3. Prefilter (Not with all brands) first ion selection and accelerating
4. Quad ion offset
5. Detector voltage

Dirty MS Source: What are the Consequences



- Repeat injection of neat solution
- Downward trend, and usually over 20% area reduced
- First signs: Low intensity and noisy peak of m/z 502
- TIP: Always check the intensity of the cal gas.
  It should be diminished in the same ratio

How to Clean an MS Source?



Parts that always need cleaning are: Repellor, lens 2 and ion volume

Typically only parts with ion burn are cleaned

Step 1: Clean with a cotton tip dipped in a slurry of glycerol and aluminiumoxide

Step 2: Rinse thoroughly under tap water

Step 3: Put the parts in detergent and sonicate for 15 min, rinse again

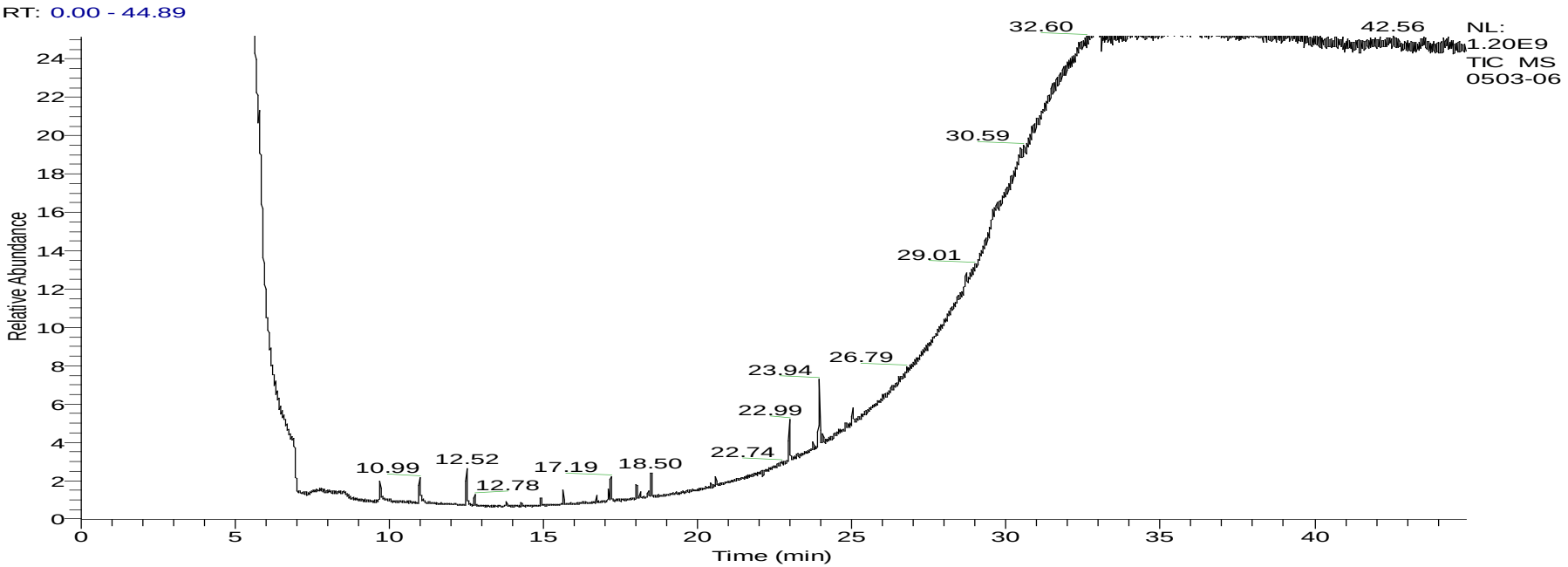
Step 4: Sonicate in MeOH for 15 min, let dry

Step 5: Assemble wearing dust free gloves

Inspect the cleaned dry parts for “grey”hue. This means aluminiumoxide is still there.

Read the guidelines in the manual first!

Column Bleed – Most Common Cause



- Chromatogram in FullScan mode ia showing excessive column bleed.
- Normal column bleed has intensities below 1e7.

- Column bleed will end up in the MS Source and dirty it up quickly.
- It is not visible in SIM or in MS/MS, so often this is a “hidden” problem.

Grob Test Mix - From 1978 Still Used Today

Journal of Chromatography, 156 (1978) 1-20

COMPREHENSIVE, STANDARDISED QUALITY TEST FOR GLASS CAPILLARY COLUMNS

J. Sep. Sci. 2007, *30*, 2480 – 2492

Jim Luong[1]
Ronda Gras[1]
Walter Jennings[2]

[1]Dow Chemical Canada, Fort Saskatchewan, Alberta, Canada
[2]Professor Emeritus, University of California, Davis, CA, USA

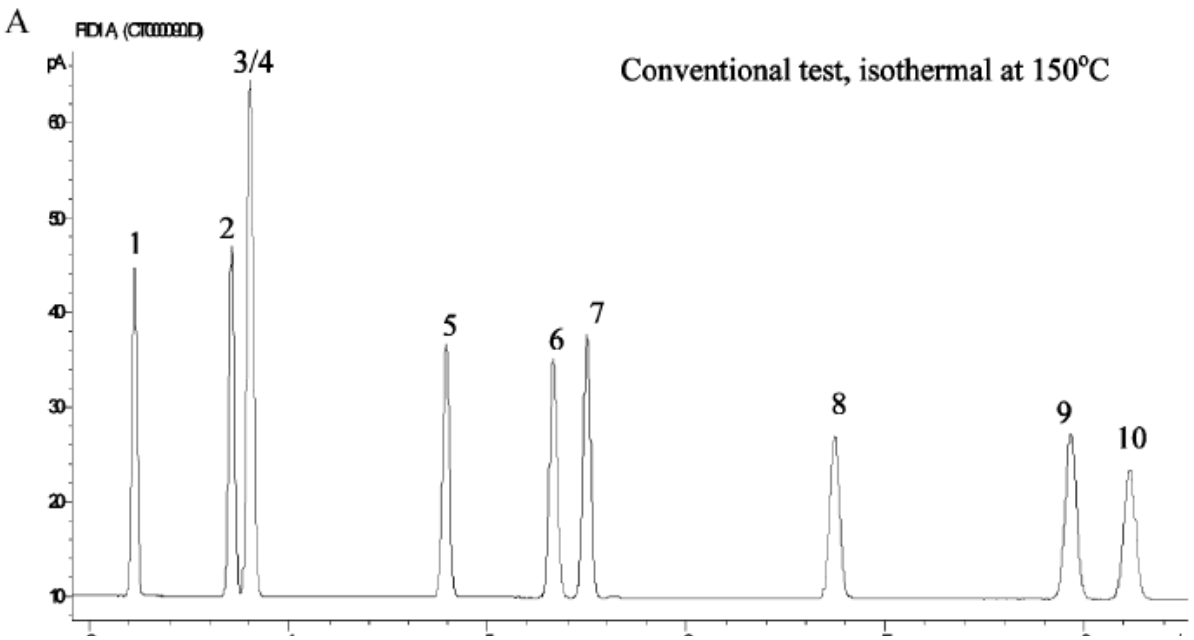
Original Paper

An advanced solventless column test for capillary GC columns

Manufacturing skills for capillary GC columns have improved to a point where the commonly used tests no longer distinguish between "adequate" and "excellent" col-

Use for monitoring column quality but offers more uses……

Grob test Mix for Repeatability and System Check



1. Octanol
2. *n*-Undecane
3. Octanoic acid methyl ester
4. 2,6-Dimethyl phenol
5. 2,6-Dimethylaniline
6. *n*-Dodecane
7. Naphthalene
8. 1-Decanol
9. *n*-Tridecane
10. Decanoic acid

Check the complete system using this mix:

- Typical RSD for MS detection should be below 5%
- Typical RSD for analogue detection should be below 2%
- Typical RSD for retention times should be below 0.1%

Resources

- Liner selection guide
- Chrom expert site

- Downloadable applications

Any Questions?

Do you have additional questions or do you want to talk to an expert from Thermo Fisher Scientific?

Please send an E-Mail to **analyze.eu@thermofisher.com** and we will get back to you.