

SCIENTIFIC

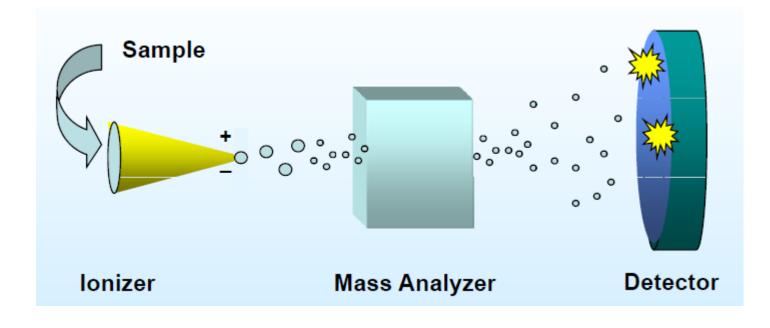
Electron Ionization Source Parameters in GC-MS

Inge De Dobbeleer Regional Marketing Manager GC and GC-MS, EMEA Thermo Fisher Scientific, Breda/The Netherlands

The world leader in serving science

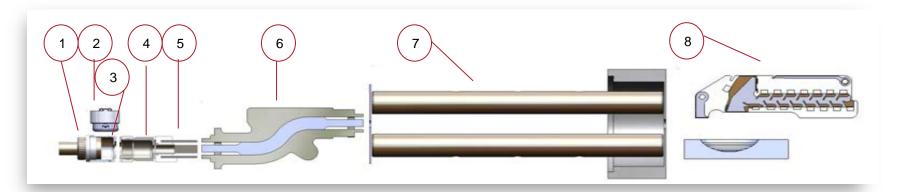
Content

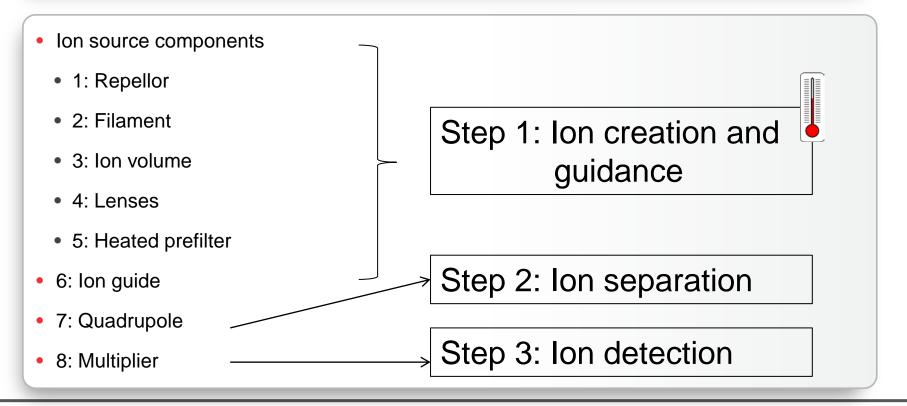
Common source parameters for electron impact ionization Setting up a SIM method Setting up a MS/MS method Sensitivity and selectivity: Choosing the right technology Troubleshooting tips and tricks



The basis of MS (Mass spectrometry) is the production of ions that are subsequently separated or filtered according to their mass-tocharge (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

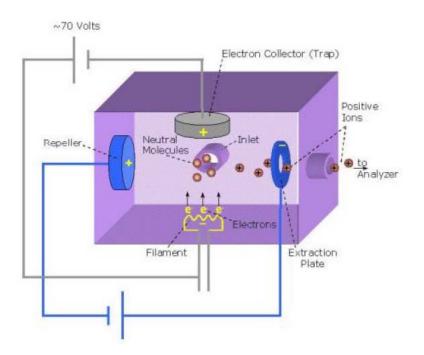






Electron Impact Source Parameters

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

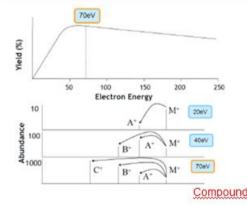


Parameters

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



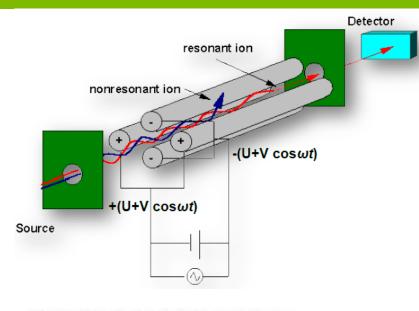
Compound dependent



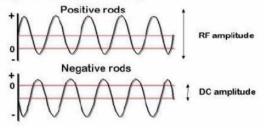
- **Emission current**
- Typical emission current in uA, 50 to 100
- High emission current will yield in more ions but can lead to ion-molecule reactions
- Low emission currents can be used in case there is enough sensitivity
- Recommendation: Follw guidelines from manufacturer, source designs vary

Separating the lons in a Quadrupole

Parameters are defined by "tuning"



The potentials on each pair of rods are equal in magnitude but opposite in sign.



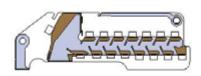
- •The combination of DC and RF potentials applied to the quadrupoles are varied with time to separate the ions.
- •Only specific ions are transmitted (Resonant ions) while the others collide with the rods having an unstable trajectory.
- •Only ions that differ of one mass unit (1 amu) can be resolved 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:

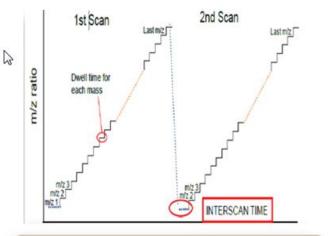
- The gain is the number of electrons generated for every ion that strikes the detector.
- This is typically set between 1 x10⁵ and 3x10⁵ electrons per ion.
- Gains larger than this will generate more electrons per ion, but both the analyte ion and the noise ion signals will be larger.
- As the electron multiplier ages, the voltage required for a given gain will increase.



\checkmark



FullScan Method



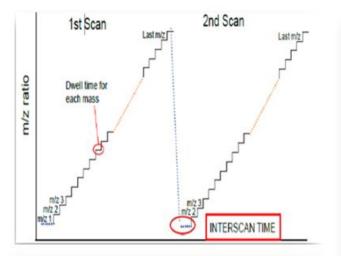
- Classic systems: You will need to add appr. 0.1s for interscan delay
- Thermo Scientific [™] ISQ[™] series single quadrupole GC-MS: Much lower interscan delay and scan speed in method equals actual scan speed

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

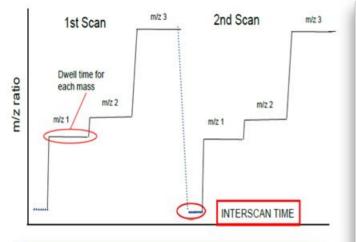
- 1: Screening
 - FullScan spectra can be library search
 - · Full information available

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

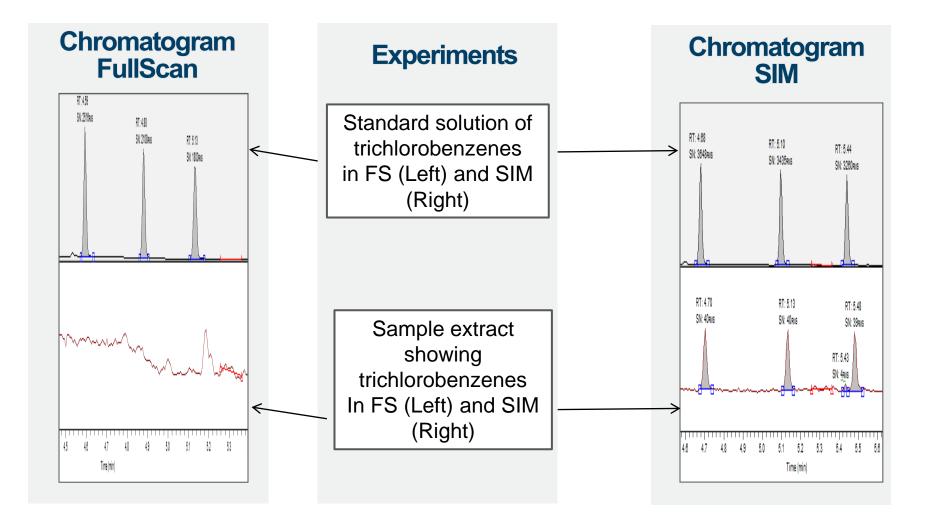
- 1: SIM ions
 - Typically 3 ions per analyte are needed.
 - Choice: Most selective i.e.mostly ions with heavier m/z are preferred, or ions with high S/N ratio.

2: Dwell time

 Trade off between number of datapoints and measuring time

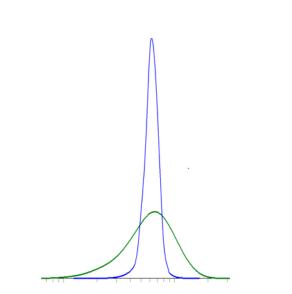


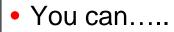
Single Quad Measurements: FullScan and SIM



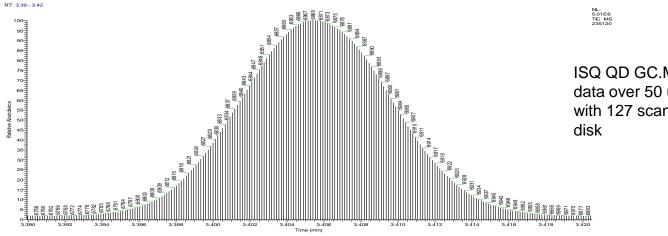


Why is Scan Speed Important – Part 1



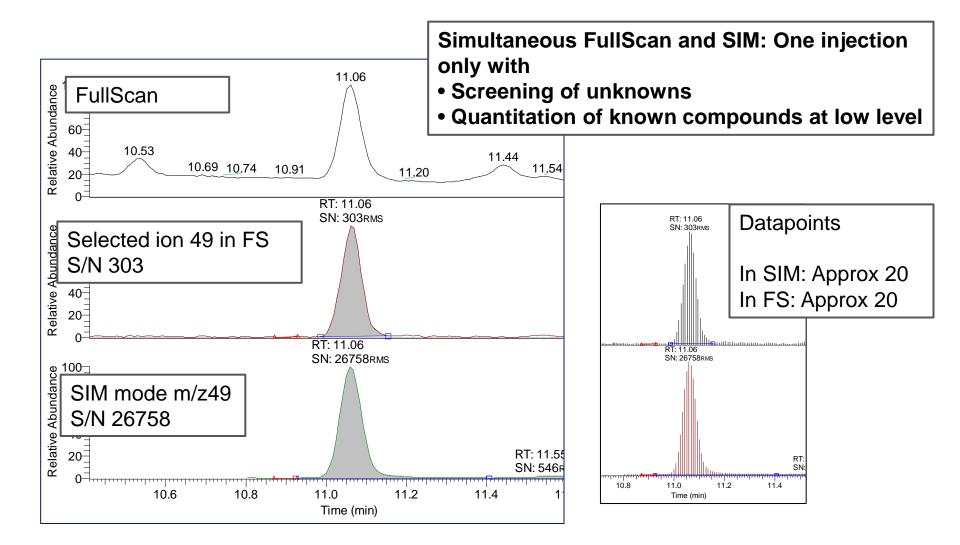


- ...speed up your chromatography
- ... use narrower columns
- Narrower peaks = Better S/N= Better sensitivity
- Faster run times **and** faster run to run times = More productivity



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

Why is Scan Speed Important – Part 2



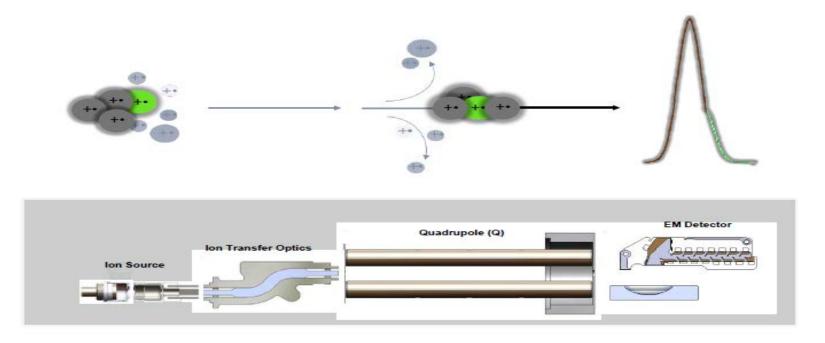


Going from Single to Triple Quadrupole

Some reasons to consider using QQQ



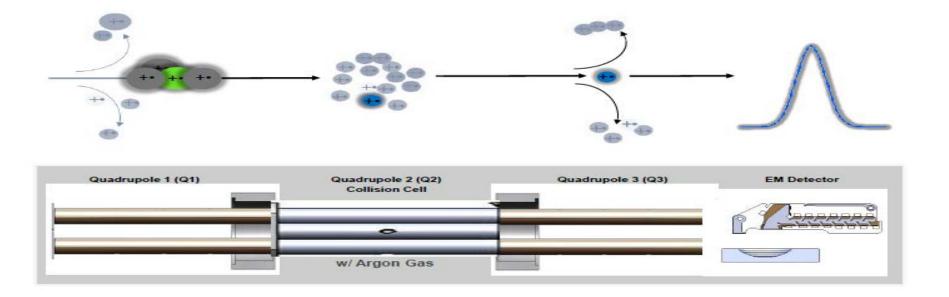
SIM Measurement in Heavy Matrix



- 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



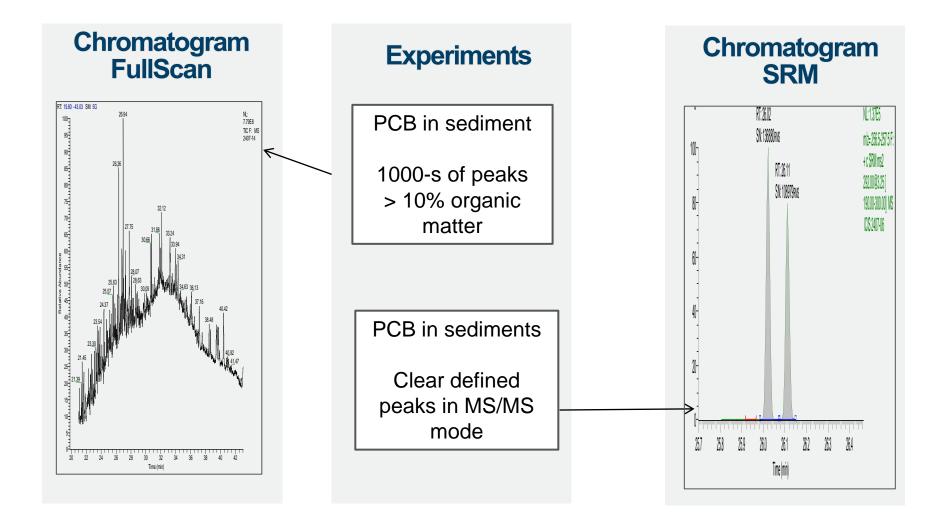
SRM or Triple Quad measurement in Heavy Matrix



- 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





SRM Method



- 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

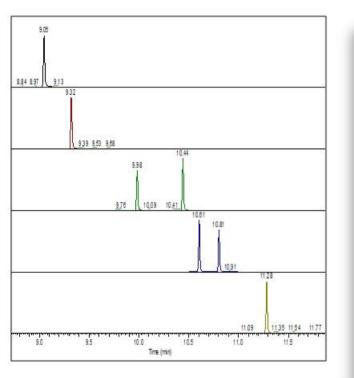


Timed SIM and Timed SRM

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



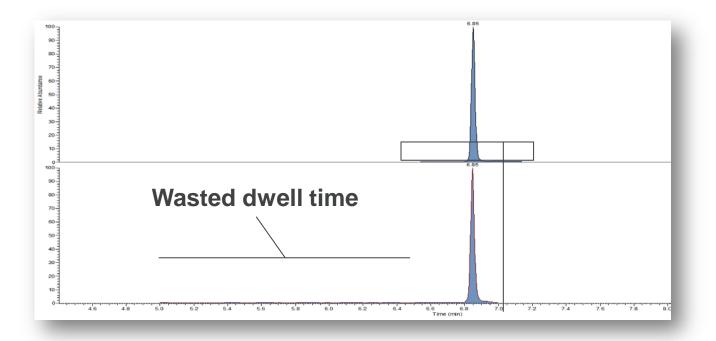
ISQ and TSQ 8000 GC-MS Series: Timed SIM and SRM

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

Name	RT	Width (min)	Mass	Product Mass	Collision Energy	Peak Width [sec]		analytes	analysi
Lutenum 1	4.60	0.30	175.99	120.99	Collion Energy 20				
Luterwoon 1	4.60	0.30	175.99	147.99	20				
Metaburan	4.64	0.30	190.08	82.03	20				
Metributin	4.54	0.30	198.00	110.05	20	5.00	6		
Butylate (Sutar)	4.67	0.30	174.12	146.1	10				
Butylate (Sutan)	4.67	0.00	217.15	156.11	5				
Olomephos	4.72	0.30	153.98	120.98	5	5.00			
Chlomephos	4.72	0.30	233.97	120.90	14	5.00			
Ebidiacole (Tena	4.78	0.30	210.93	00302	15	5.00			
Enidamie (Tena	4.28	0.30	210.33	182.94	15	5.00	2		
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		P Etridazole (Etridazole (Nizmephor	opetanghoo						

- 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

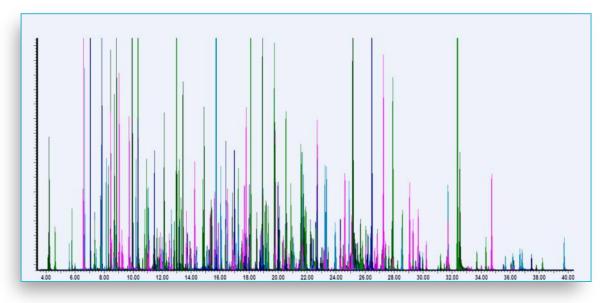


• Timed scanning: Overall higher dwell times, for more sensitivity

• 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



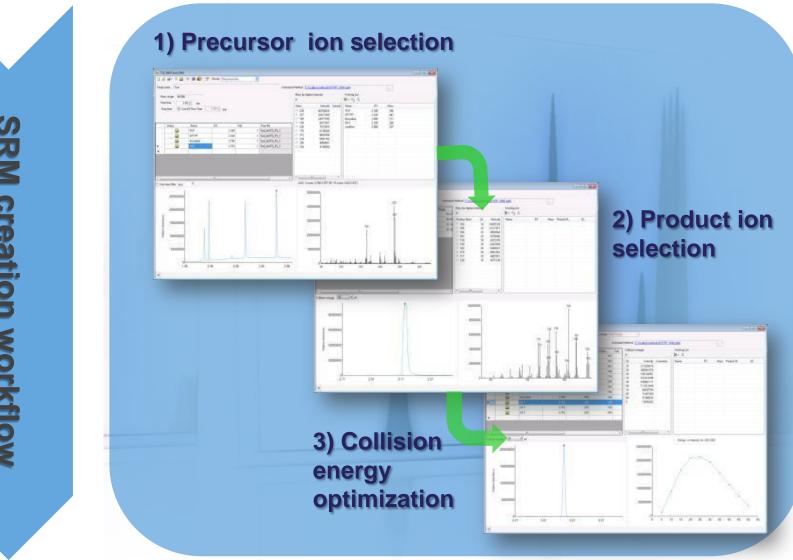
"Give a man a fish, feed him for a day. Teach a man to fish, feed him for a lifetime"

Lao Tzu circa 5th Century BC



AutoSRM Overview

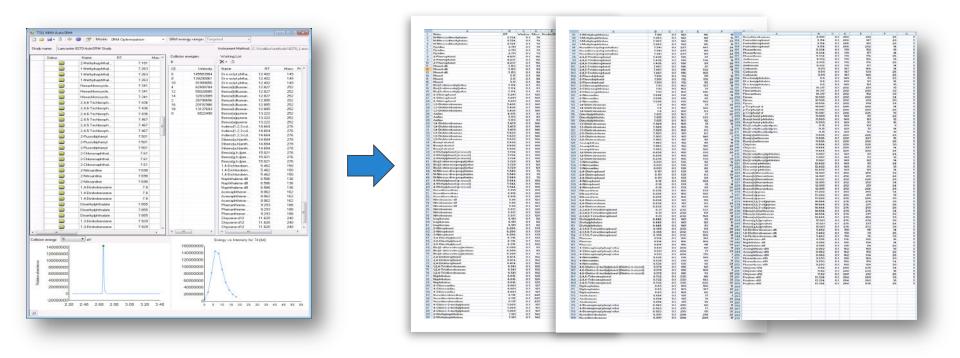
SRM creation workflow





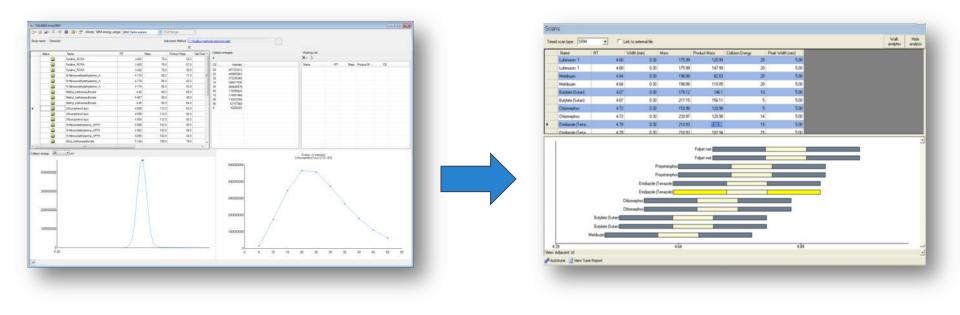
AutoSRM Use Case

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





Export form AutoSRM to Instrument Method





 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

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Your Main Benefits in One Slide

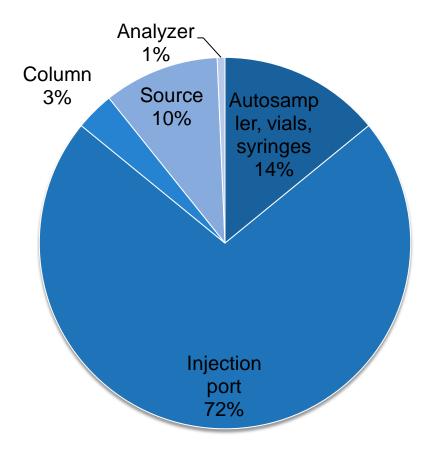
- Source replacement without venting the MS, including switch from EI to CI
- Wireless source
- Up and running again in 15 min



- 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

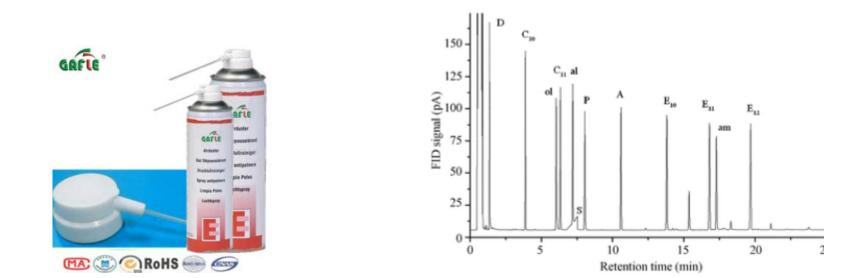




Two Troubleshooting Tools

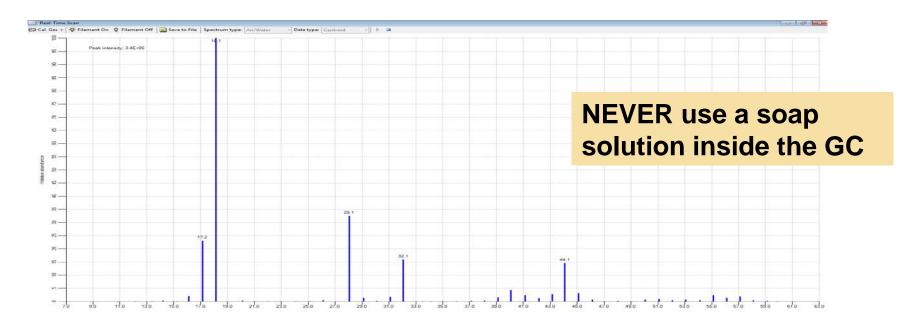
- Air duster spray with freon gas
- Check for m/z 69 and 83
- Cost 5-10 euro

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





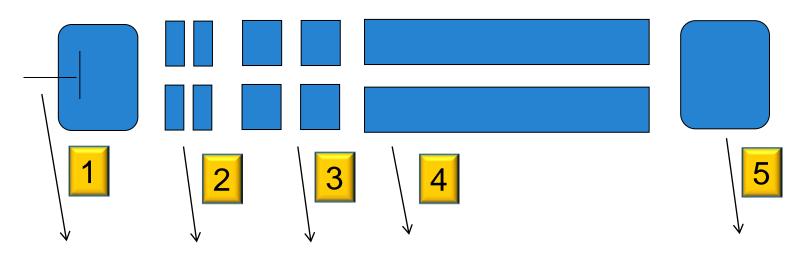
Air/Water Background



- 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



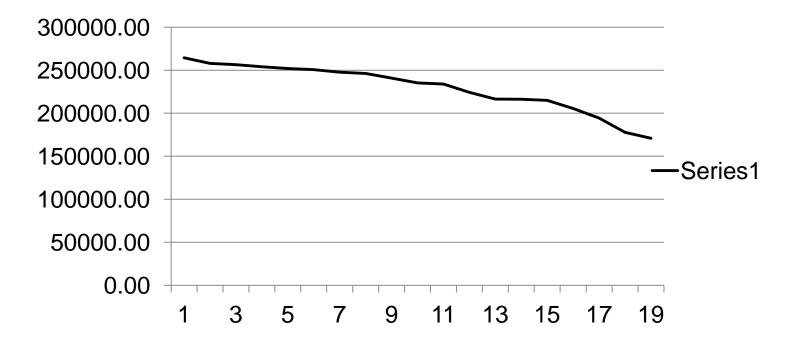
Tuning of the Mass Spec



- 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

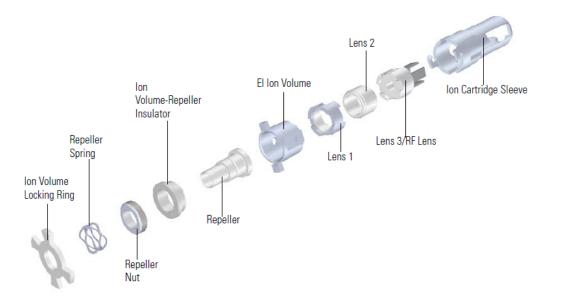


Dirty MS Source: What are the Consequences



- 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

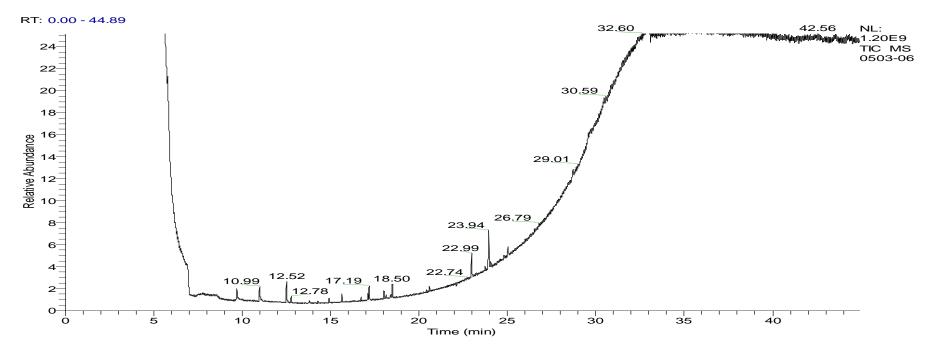
- Step 2: Rinse thoroughly under tap water
- Step 3: Put the parts in detergent and sonicate for 15 min, rinse again
- Step 4: Sonicate in MeOH for 15 min, let dry
- Step 5: Assemble wearing dust free gloves

Inspect the cleaned dry parts for "grey" hue. This means aluminium oxide 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.



Journal of Chromatography, 156 (1978) 1-20

COMPREHENSIVE, STANDARDISED QUALITY TEST FOR GLASS CAPILLARY COLUMNS

 2480
 J. Sep. Sci. 2007, 30, 2480–2492

 Jim Luong¹ Ronda Gras¹ Walter Jennings²
 Original Paper

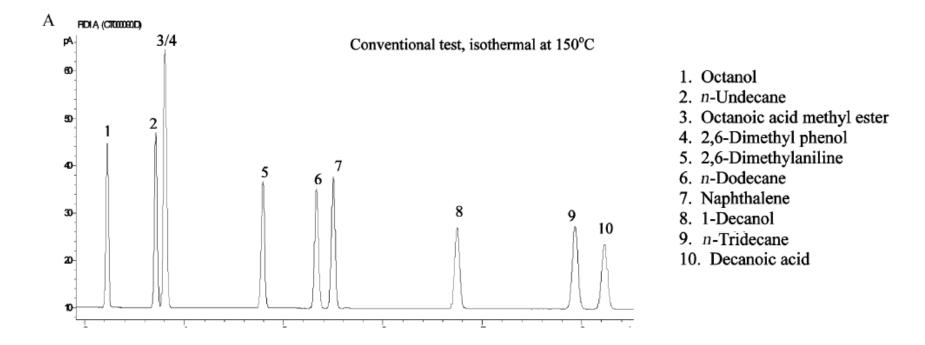
 ¹Dow Chemical Canada, Fort Saskatchewan, Alberta, Canada ²Professor Emeritus, University of California, Davis, CA, USA
 An advanced solventless column test for capillary GC columns

 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......



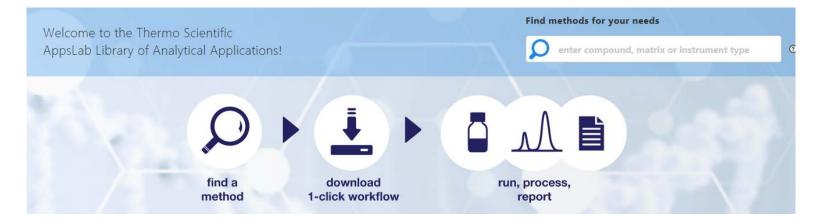
Grob test Mix for Repeatability and System Check



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%

- Liner selection guide
- <u>Chrom expert site</u>
- Downloadable applications







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

Please send an E-Mail to <u>analyze.eu@thermofisher.com</u> and we will get back to you.

