VITATOX 2021

Next level of targeted screening, which way to go: faster analysis or more certainty in the results?

Solutions Development – Applied Markets, Bruker, Bremen
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Bruker s.r.o.

QTOF Portfolio - Instruments

compact
30,000 res. FSR
1 ppm MS, MSMS
2 ppm MS, MSMS

impact II
60,000 res. FSR
0.8 ppm MS, MSMS
2 ppm MS, MSMS

maXis II
80,000 res. FSR
0.6 ppm MS, MSMS
2 ppm MS, MSMS

timsTOF
60,000 res. FSR
180 TIMS res with imeX™
0.8 ppm MS, MSMS

timsTOF Pro
60,000 res. FSR
0.8 ppm MS, MSMS
>100 Hz in PASEF mode
180 TIMS res with imeX™

timsTOF fleX
MALDI imaging with
SmartBeam3D laser
>100 Hz in PASEF mode
enable SpatialOMx

Improve identification in difficult matrix

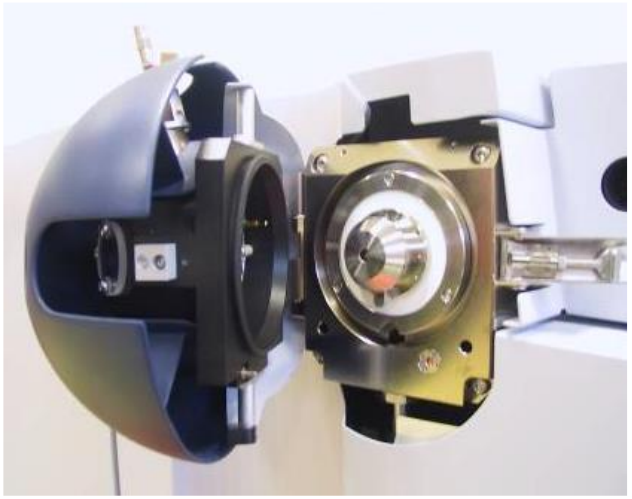
- Increase sensitivity due to VIP-HESI source
- Increase robustness by using active exhaust
- Decrease run time by using fast QTOF scans, 20 to 5 minutes
- Increase confidence by using tims technology
- Increasing separation power by using 4th dimension Ion Mobility

VIP-HESI

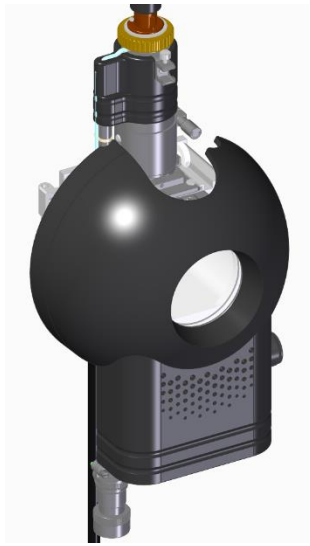
VIP-HESI Technology

Introduction

- A new Dual source design based on the Bruker EVOQ triple quadrupole source combines ESI and APCI
- The new source is compatible with Bruker timsTOF and QTOF systems and can replace the standard ESI and APCI sources



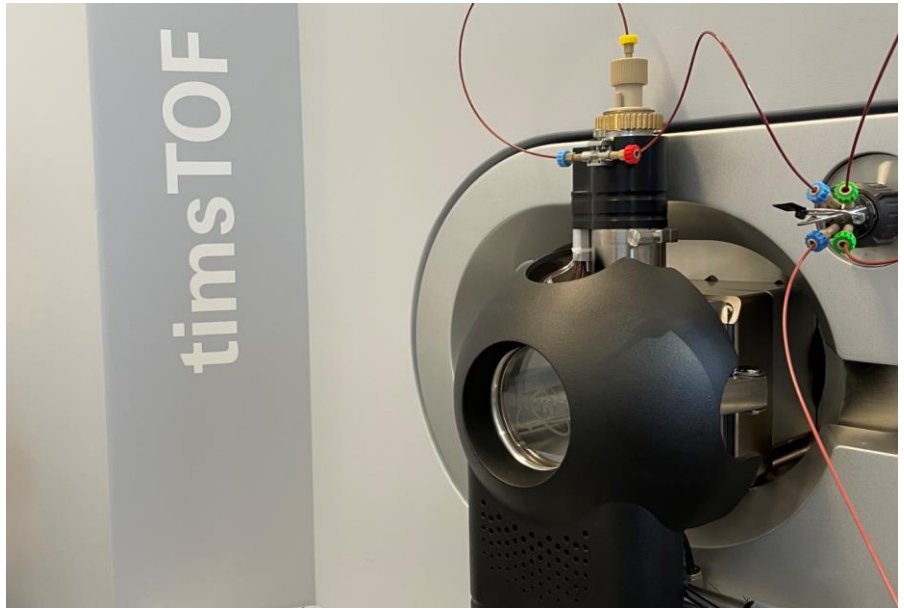
Standard ESI source



New VIP-HESI source

VIP-HESI @ impact II & timsTOF pro

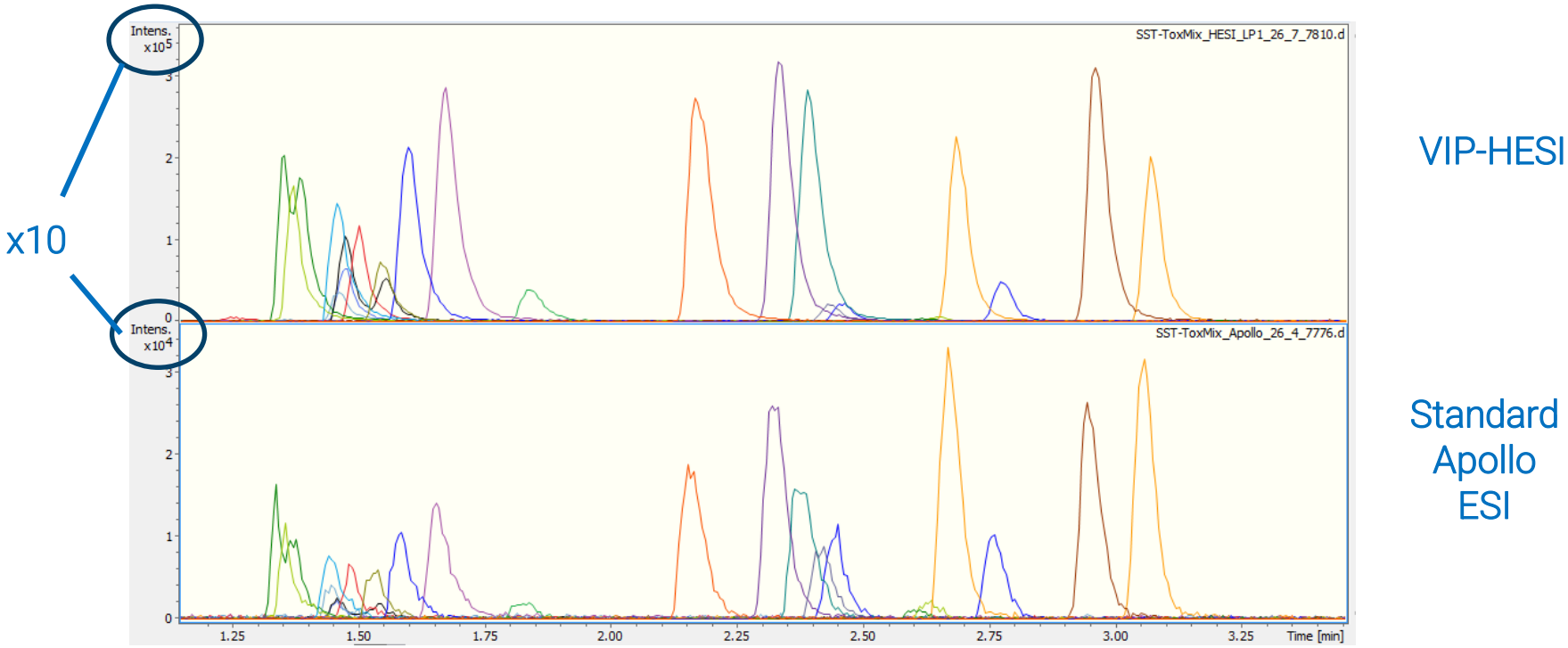
- Very sensitive and robust VIP-HESI source with active exhaust available for the timsTOF/QTOF product lines
- Well suited for high flow (1ml/min) applications with dirty matrices like urine, QuEChERS extracts or wastewater
- Average Gain > 5 times sensitivity
- VIP-HESI Technology:
  - No loss and fragmentation of compounds due to heat
- Active Exhaust reduces:
  - matrix effects
  - source contamination and memory effects in source



VIP-HESI @ timsTOF pro

VIP-HESI analytical data

Forensic Tox Mix (26 substances), (500-700) µL/min LC flow gradient, timsTOF Pro, TIMS off
MW Range 135 – 455 amu



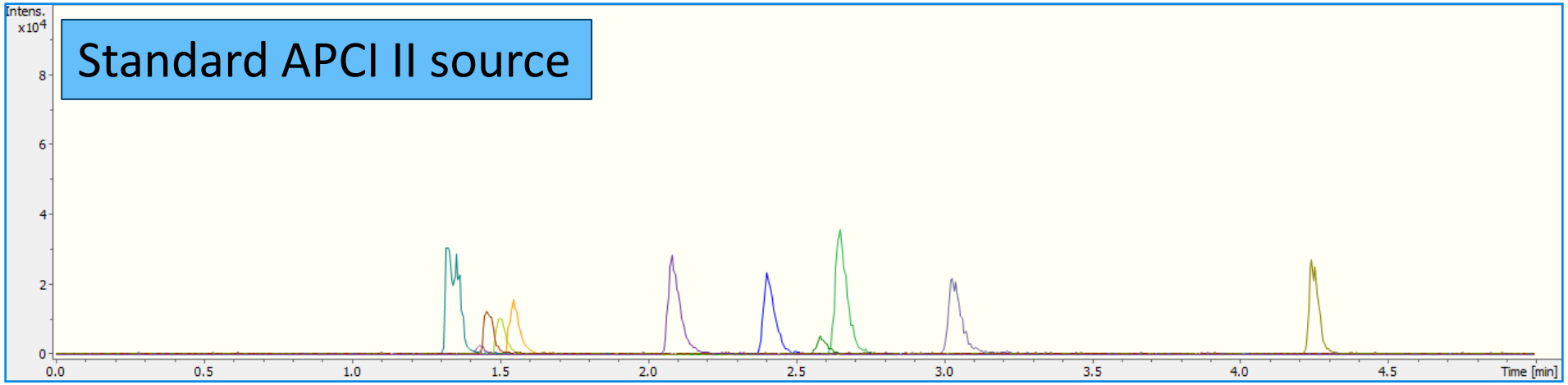
VIP-HESI

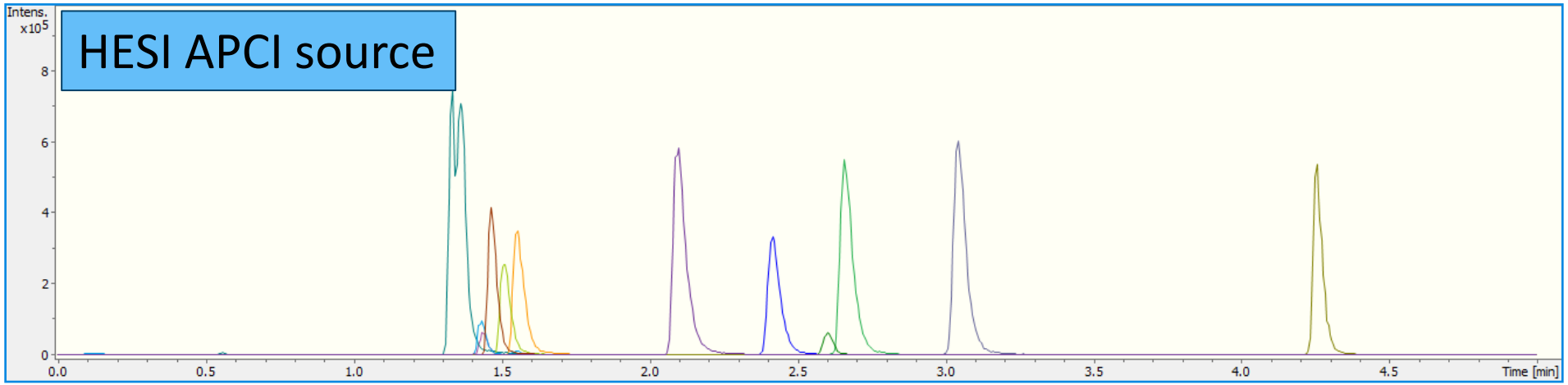
Standard Apollo ESI

- High intensity gains between VIP-HESI and standard ESI sources are reproducible, specification are at lower level. 50fg reserpine 1:200 S/N.

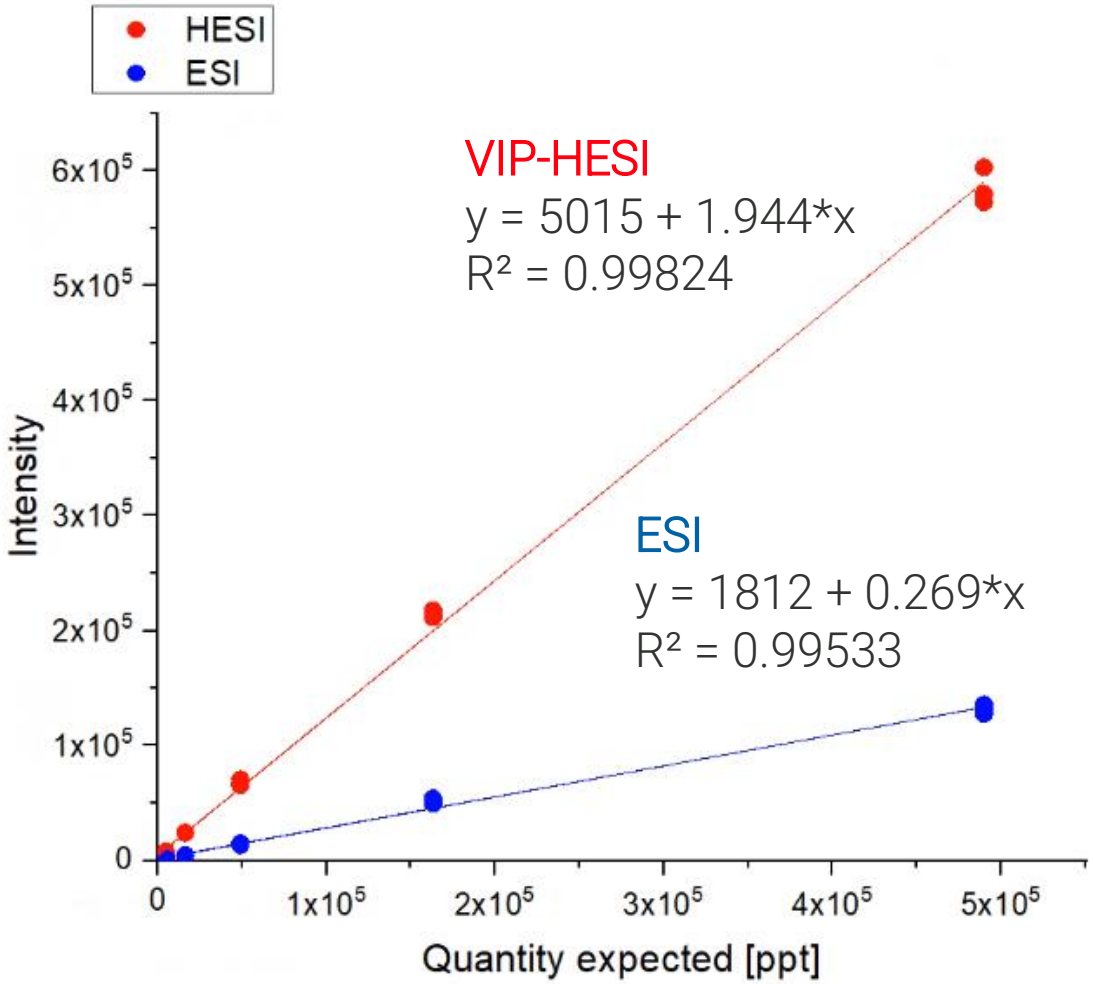
VIP-HESI APCI analytical data

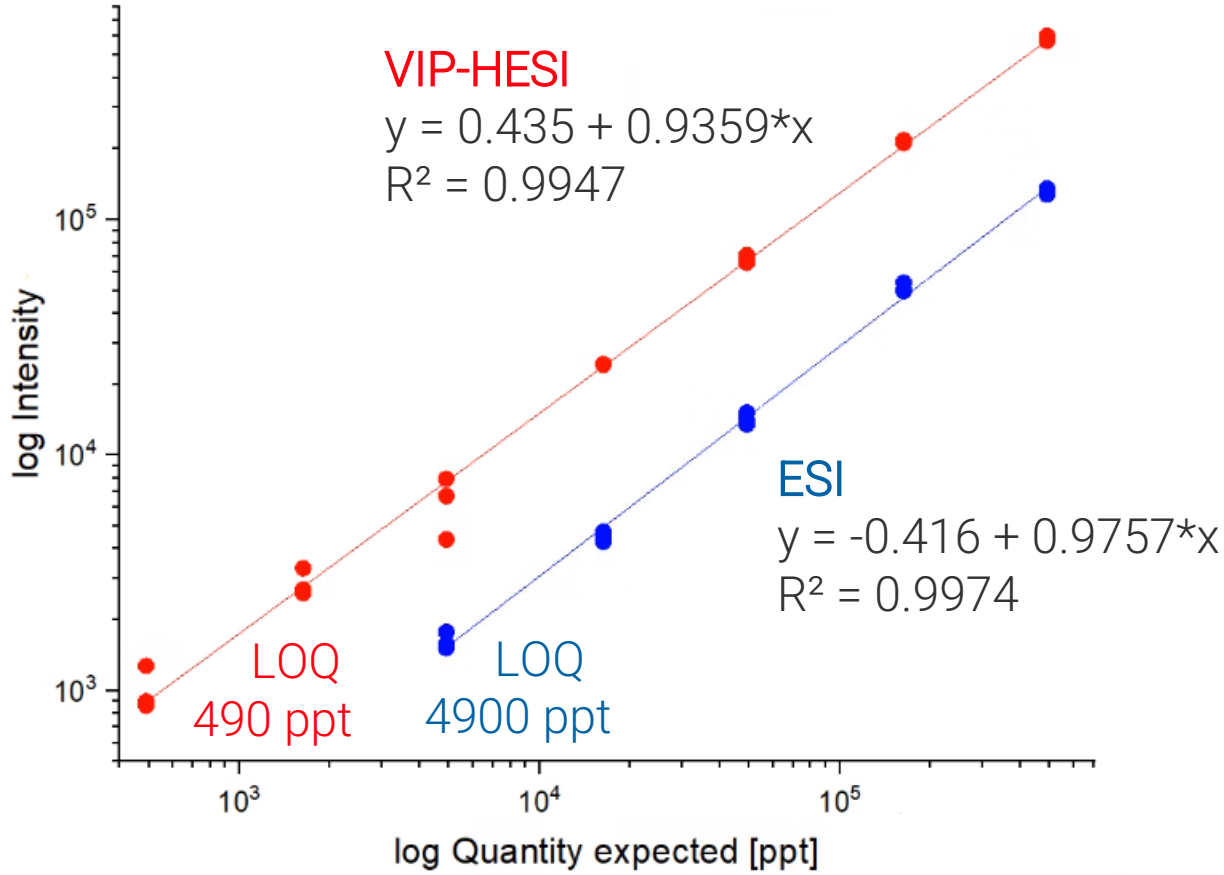
Forensic Tox Mix VIP-HESI APCI (26 substances), (500-700) µL/min LC flow gradient, timsTOF Pro, TIMS off
MW Range 135 – 455amu





Example calibration curve
Lyso PE 18:1 (d7) VIP-HESI vs. ESI negative mode





VIP-HESI source – Vacuum Insulated Probe

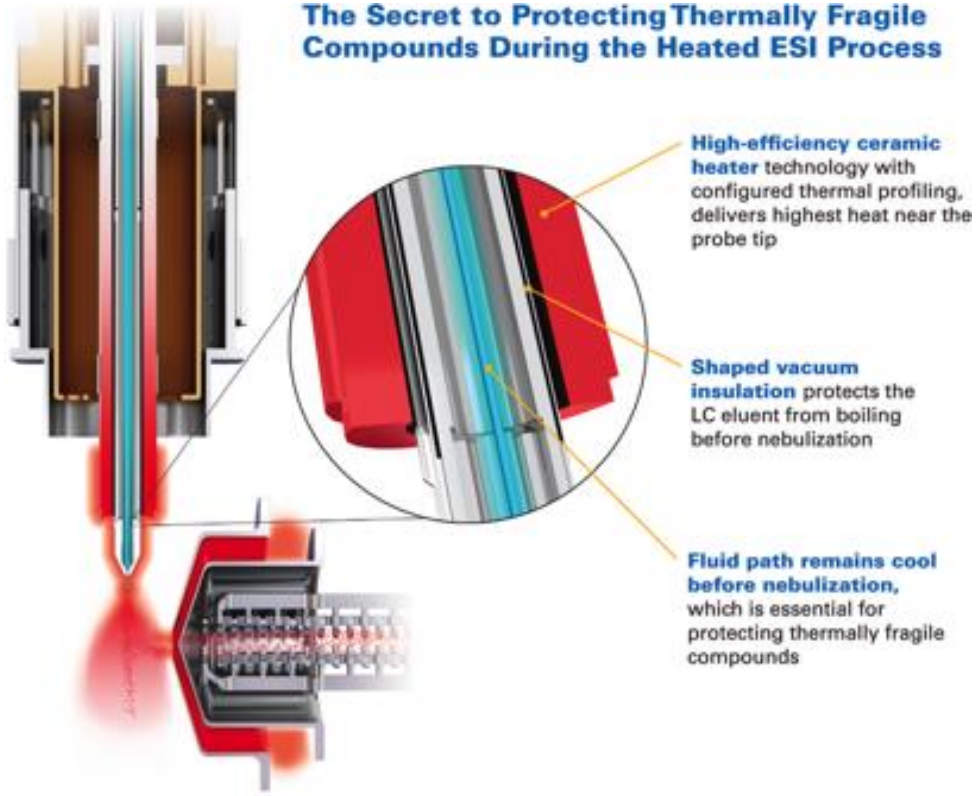
Problem of general heated ESI source:

- Low sensitivity because of thermal breakdown of thermally fragile compounds due to LC eluent ‘over-heating’ before the nebulization process.

Bruker’s technical solution:

Vacuum Insulated Probe Heated-ESI (VIP-HESI)

- A layer of vacuum between the ESI probe heater and the LC-eluent dramatically reduces heat transfer from the hot ceramic heater to the sample.



User benefit provided by Bruker:

- Less thermal degradation
- Higher sensitivity

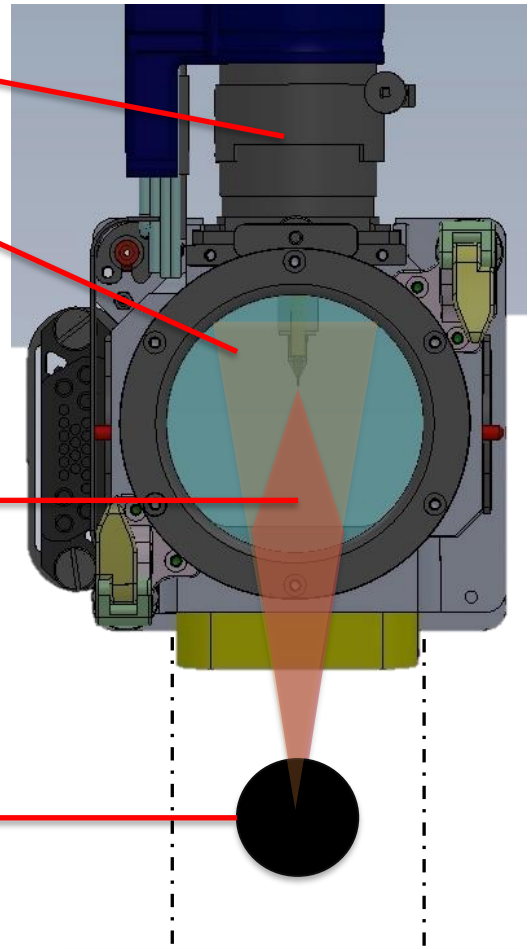
Active Exhaust

High wattage ceramic heater (1.5 kw) ensures complete desolvation

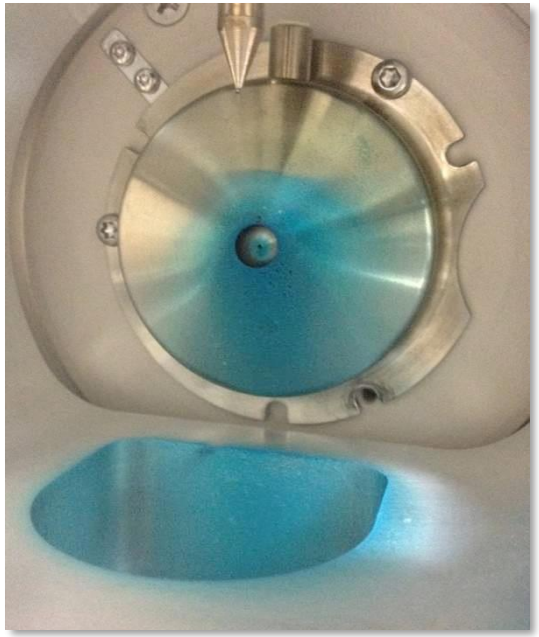
Source housing gases are streamlined and evacuated

Nebulized gas accelerates towards the low-pressure region of the Active Exhaust & exits the system

Low pressure region pulls all exhaust gases through the large exhaust opening and out of the mass spec



Exhaust opening sets new industry standard, allowing for unrestricted evacuation of nebulized gases.

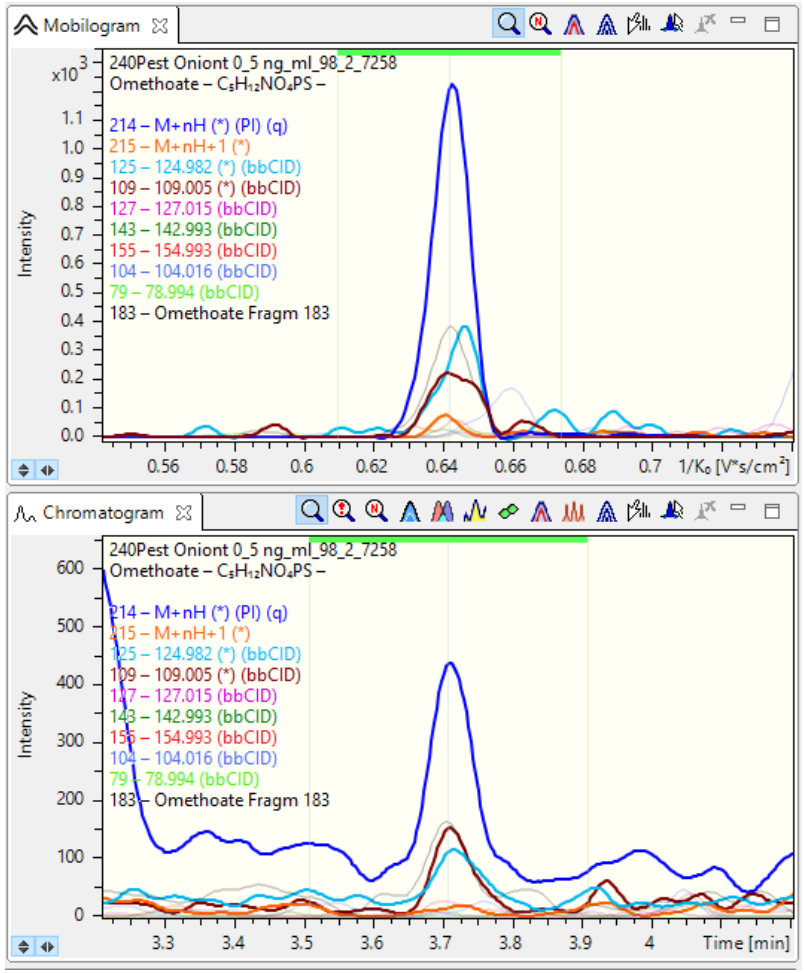


- 30 mL of blue food dye infused
- No accumulation anywhere inside the ion source chamber

➢ Successful elimination of recirculation of nebulized gases → More efficient ionization

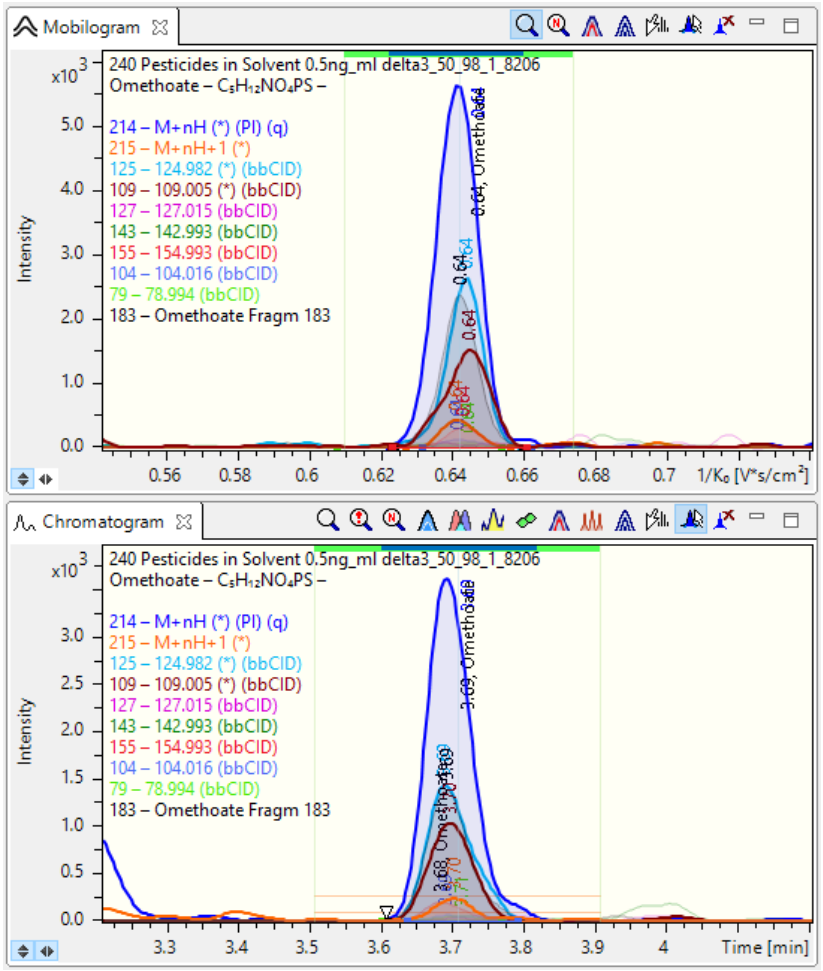
Omethoate: 0.5 ppb in Onion 20min method

Standard ESI

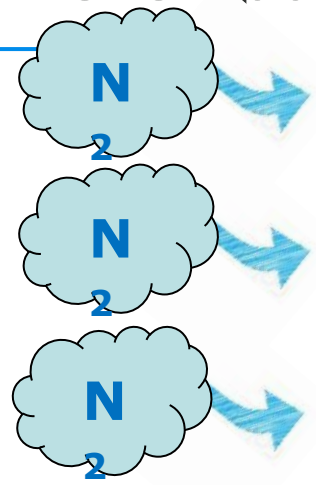


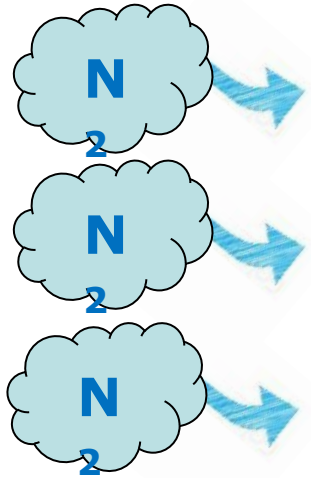
5X gain

VIP-HESI

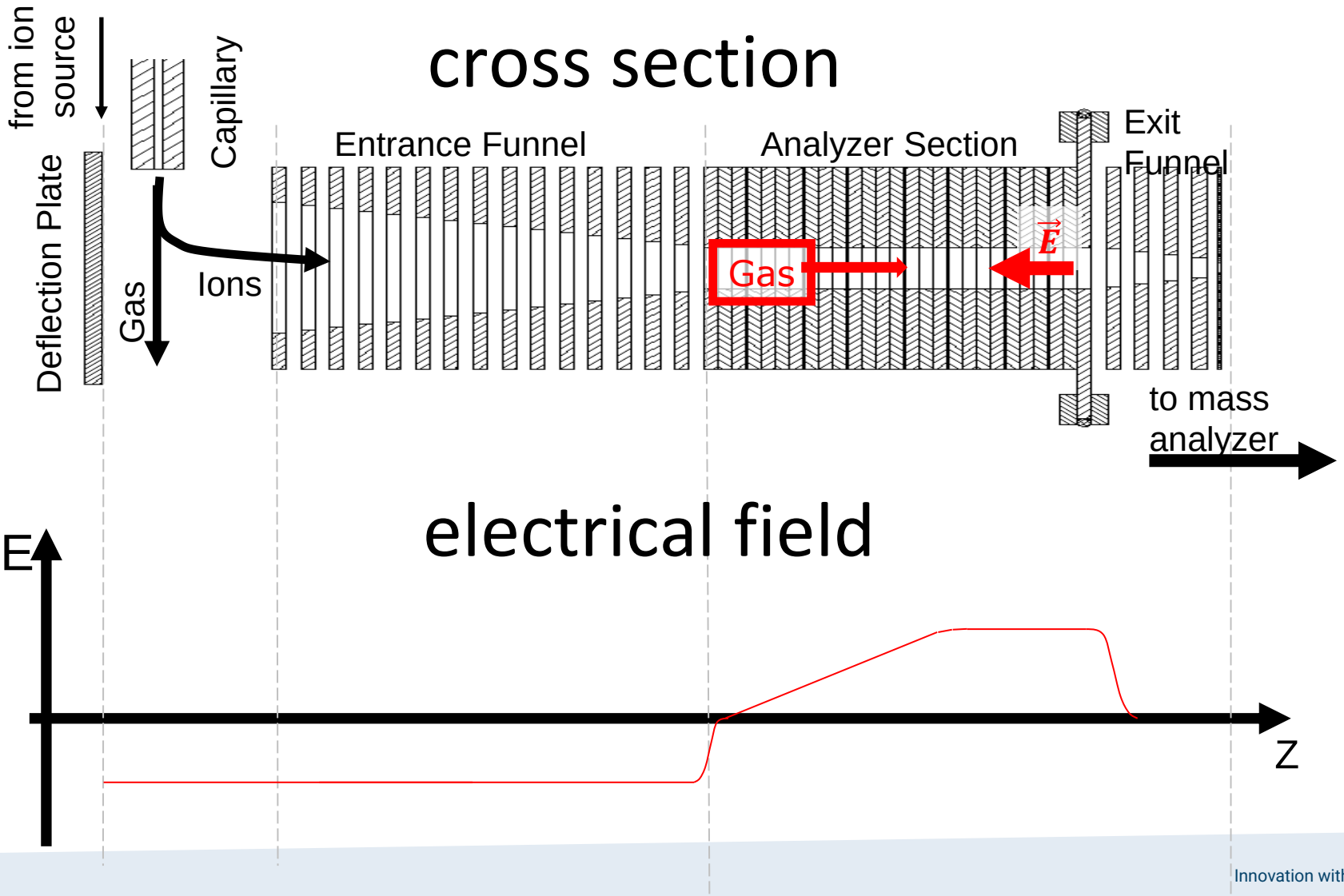


TIMS Separation Principle

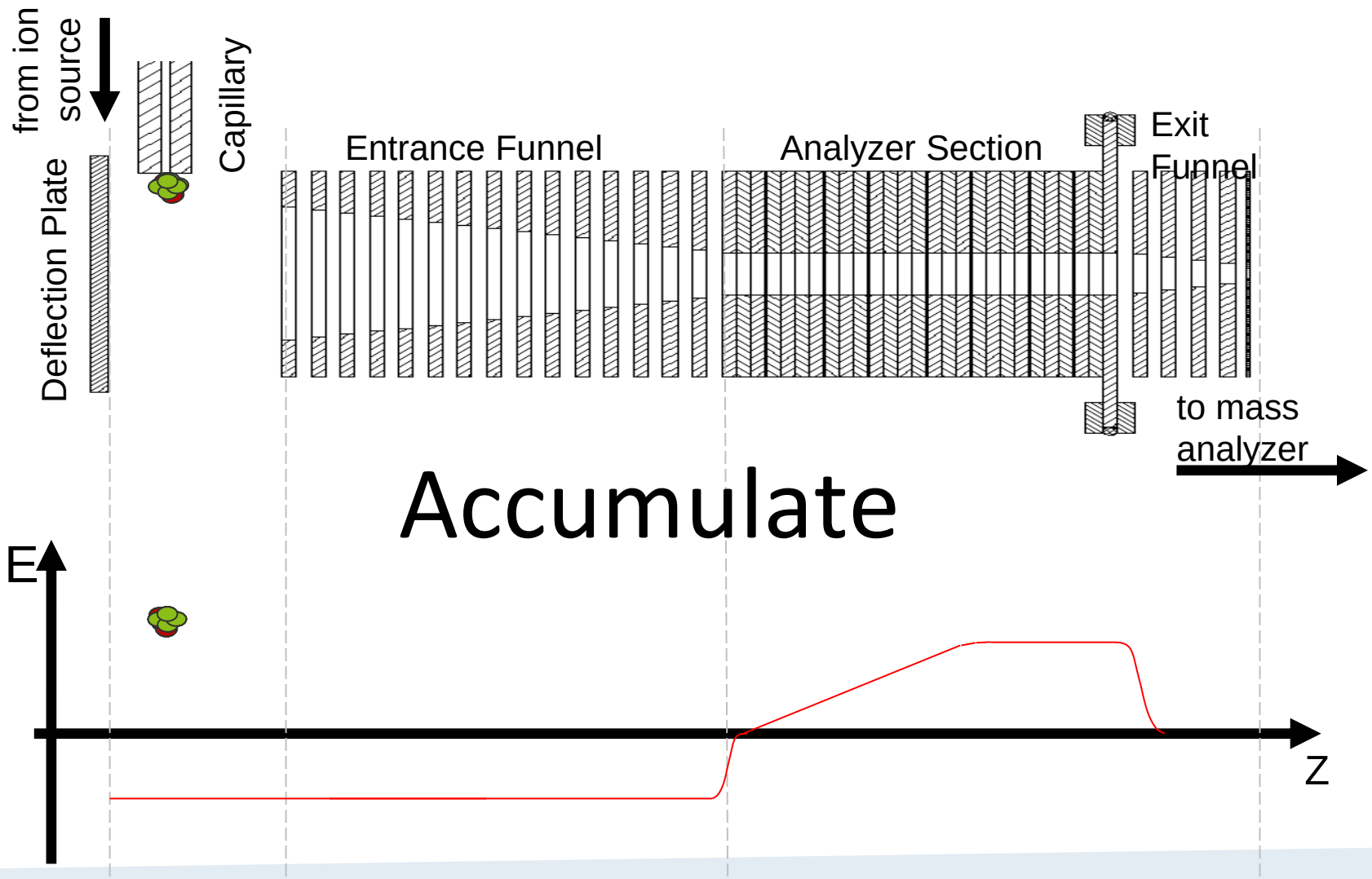




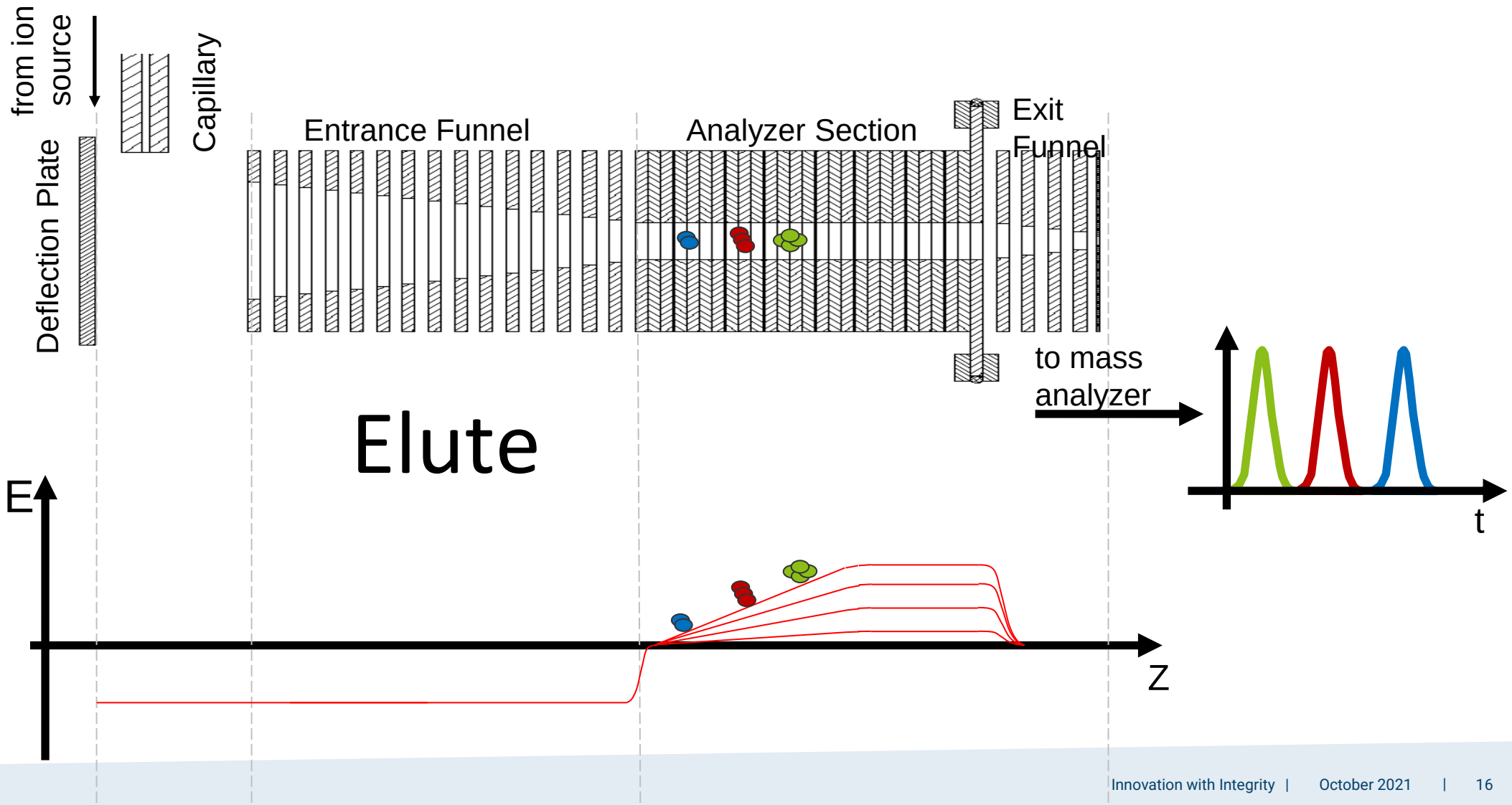
TIMS Separation Principle



TIMS Separation Accumulation



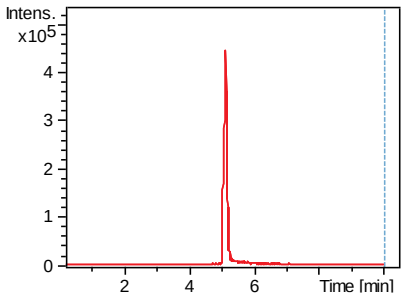
TIMS Separation Elution

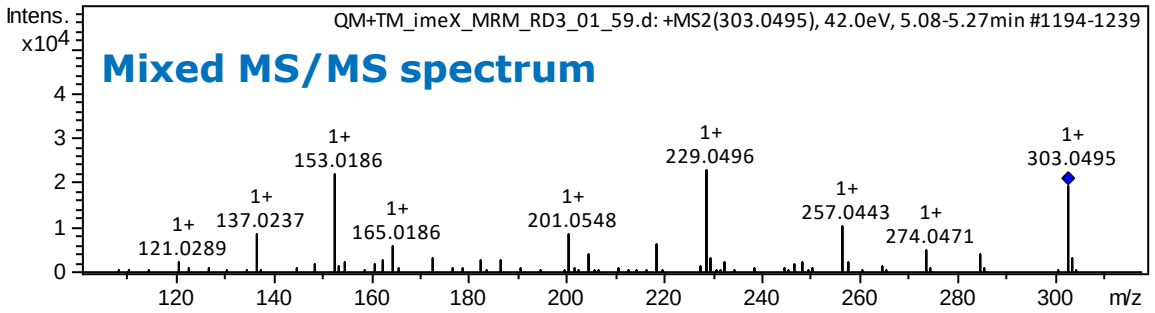


CCS values to differentiate isomers

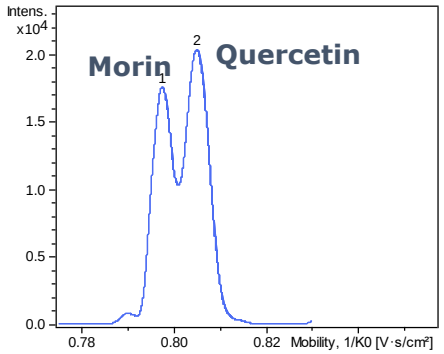
Example: IMS separation of flavonols Quercetin and Morin (MW 302) – generate individual MS/MS spectra of both analytes for increased confidence and structural information.

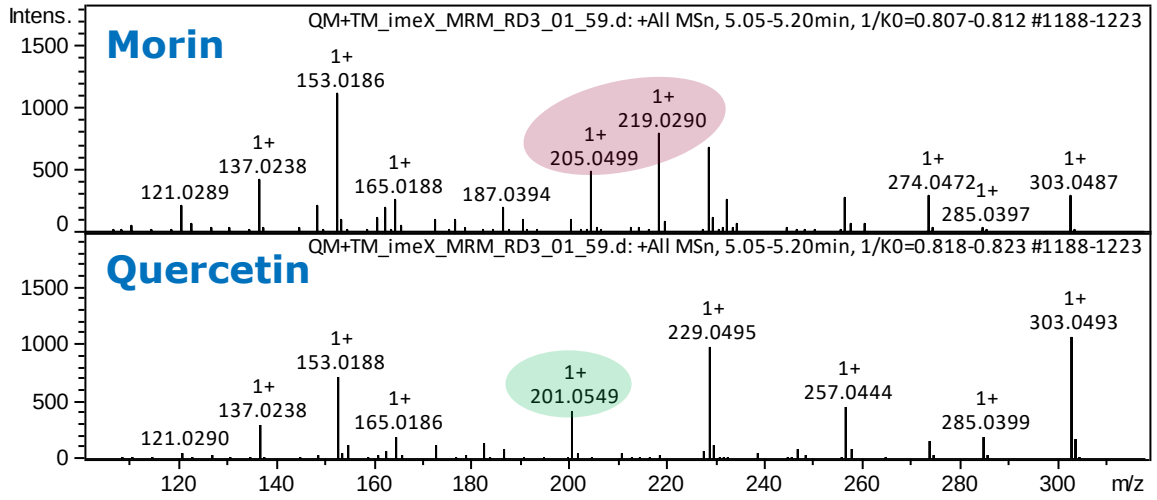
LC only:

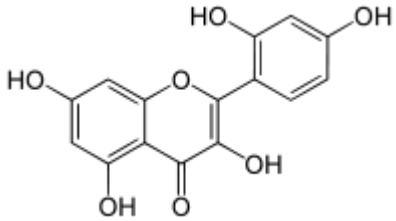


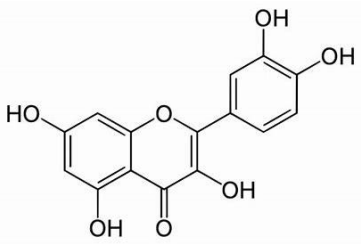


+ TIMS:





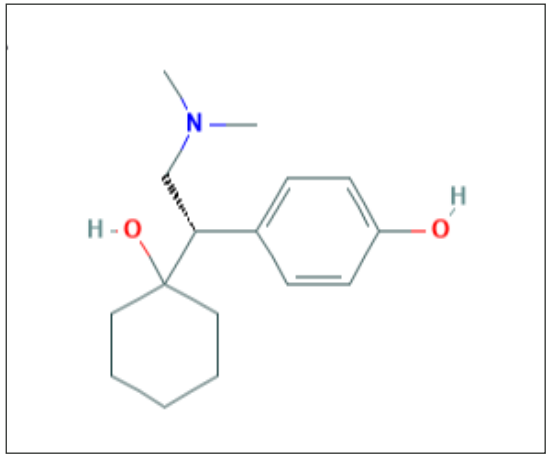




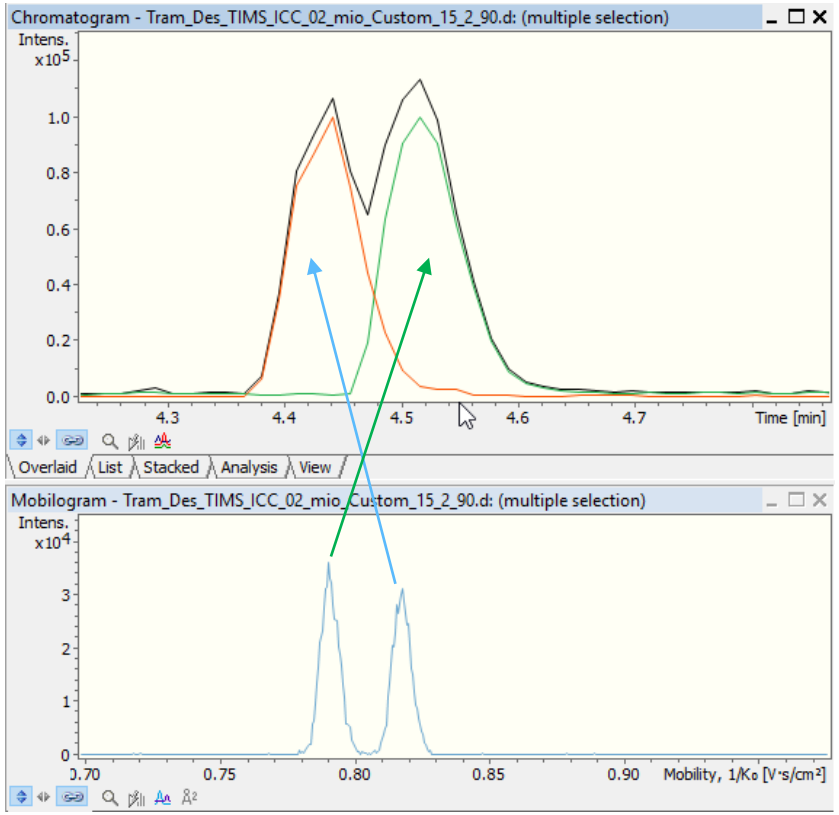
Separating Tramadol and O-Desmethylvenlafaxine using TIMS (they have nearly the same fragments)

XIC of 264.2 m/z
overlapping peaks

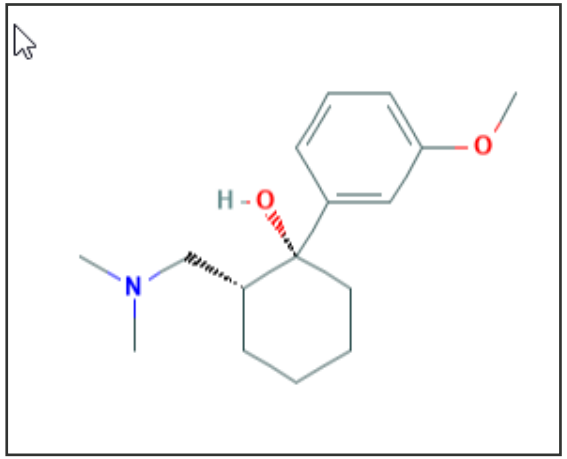
XIC using mobility of
Venlafaxine as filter



O-Desmethylvenlafaxine



XIC using mobility of
Tramadol as filter

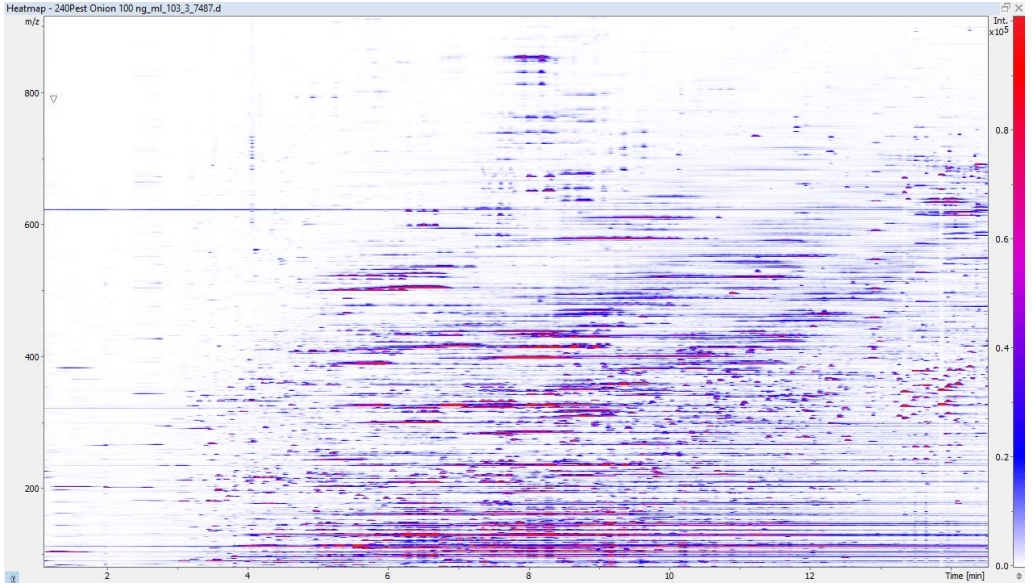


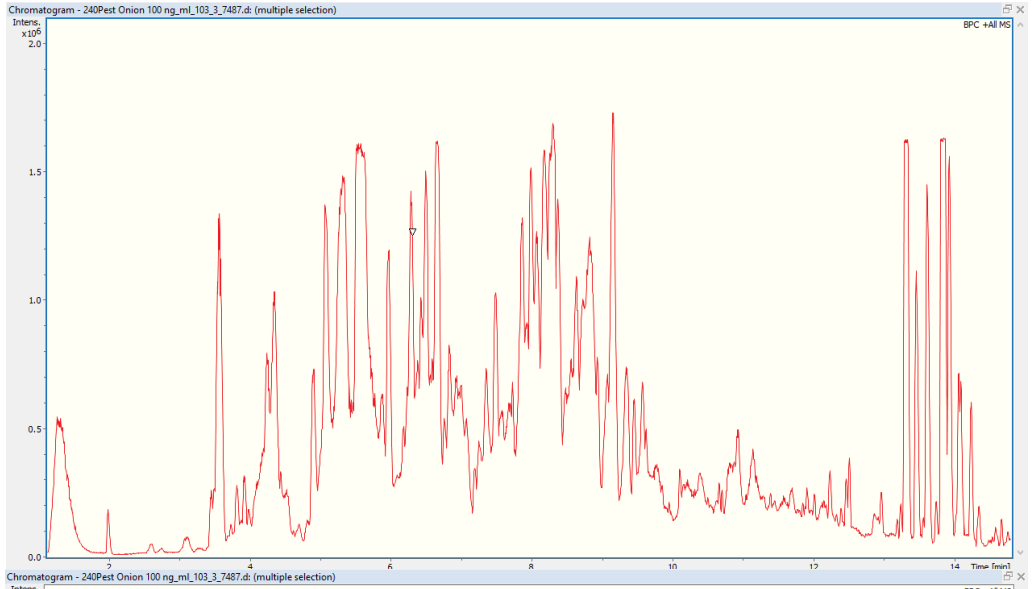
Tramadol

PESTICIDES @ TIMSTOF PRO

Pesticides in difficult matrix

Survey view and BPCs for 240 pesticides (100 ppb) in onion vs. solvent





Onion

Solvent

Pesticide screening in difficult matrix

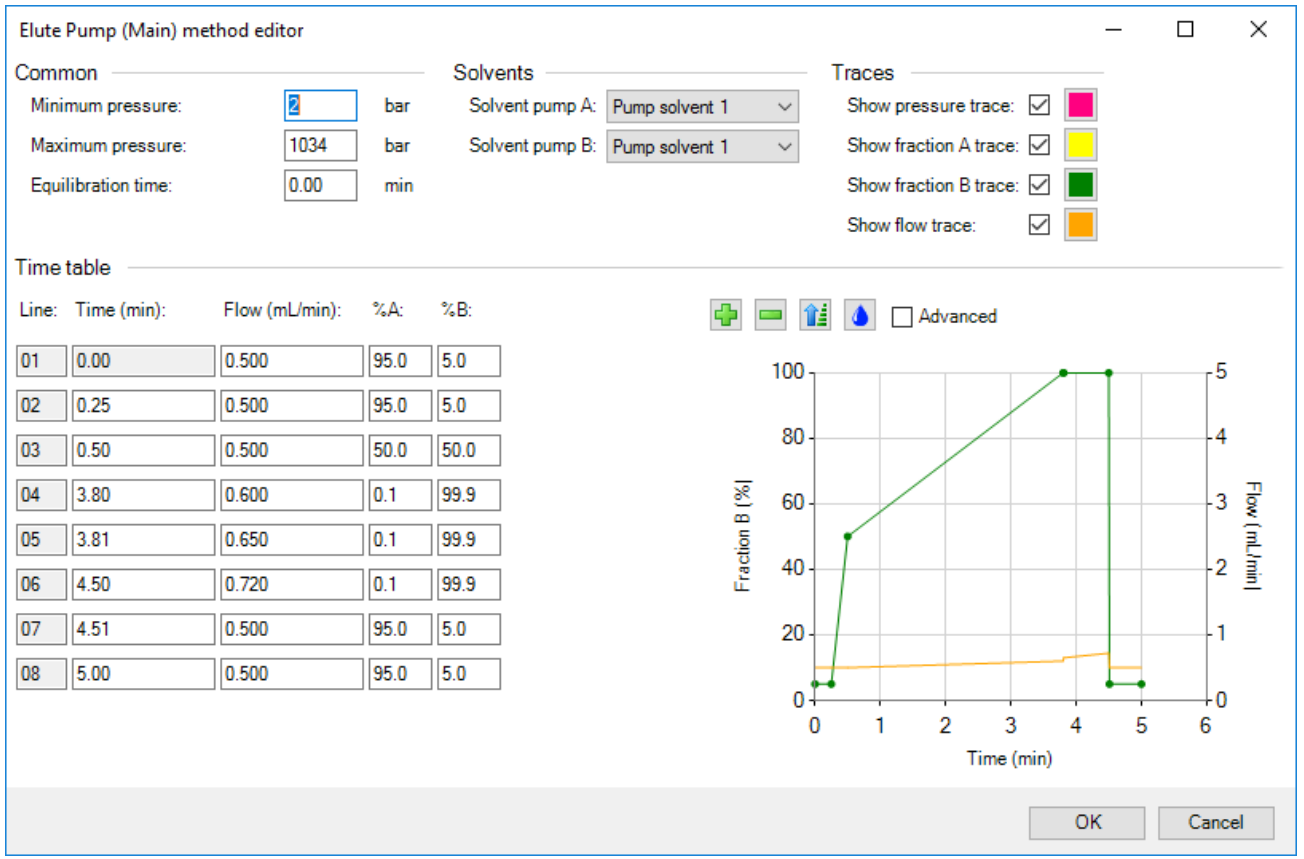
On the previous slide a “blank” sample was shown, within this matrix TargerScreener will have to detect a few hundred components on low level. This is done with data in depended acquisition to ensure no missing peaks (false negatives).

By using data in depending acquisition, a retrospective view is possible, more and more companies would like to look back if they find a new contamination in their samples.

The “standard” 20 minute method was long seen as the fastest possible reliable method, using a 5 minute fast method did show almost the same performance

By using VIP-HESI and additional timsTOF Ion Mobility separation this combination can create a 5 minute method with even better performance as the “conventional” 20 minute method. This new methods is currently under development.

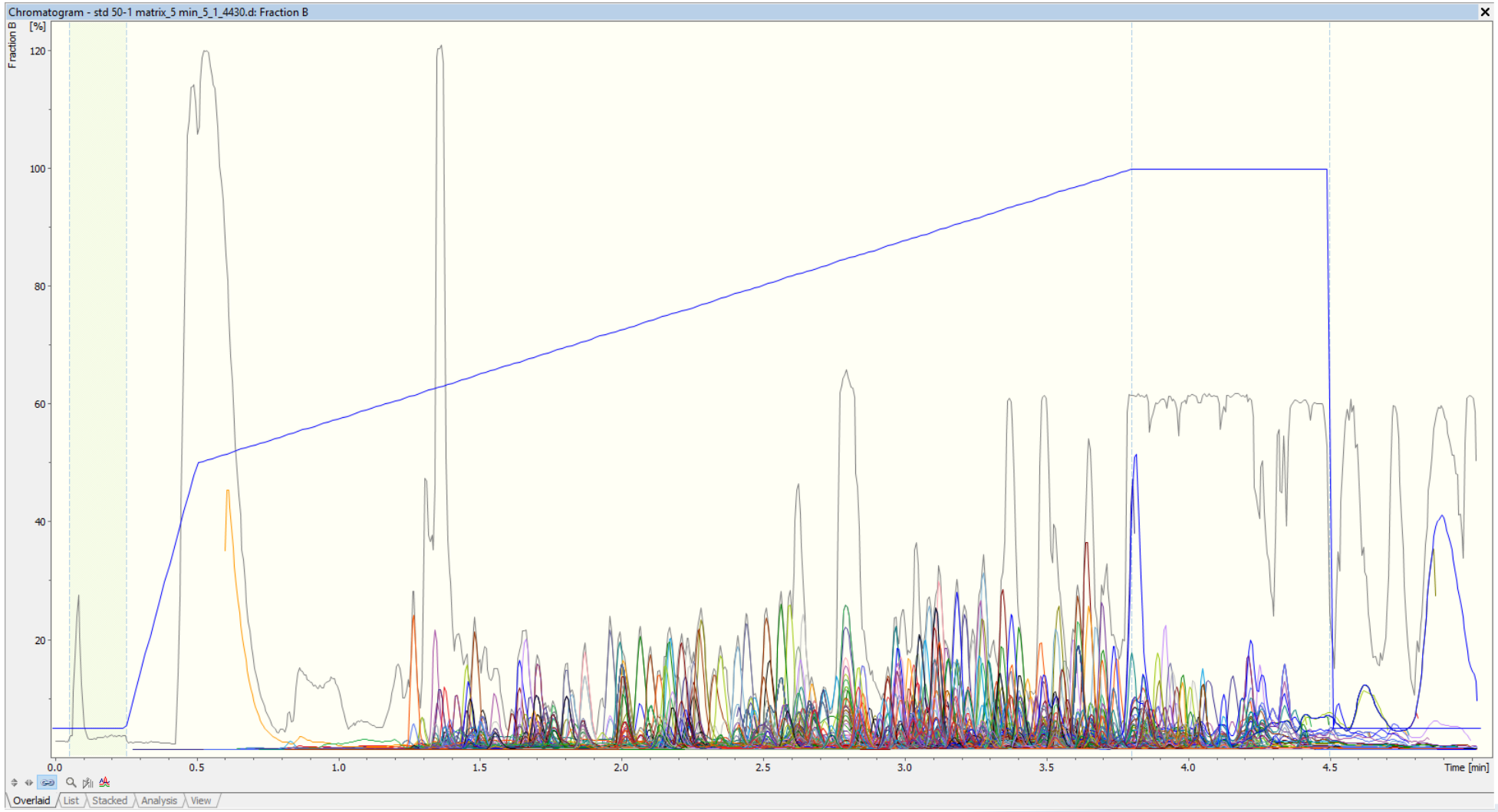
Faster method



- **Mobile phase solvents based on standard TargetScreener**
- Eluent A: Water/methanol (99T/1T)+ 5 mM NH4-formate + 0.01% formic acid
- Eluent B: Methanol + 5 mM NH4-formate + 0.01 % formic acid
- Column: Bruker IntensitySolo-2 (1.8 µm), 100 x 2.1 mm
- Oven *Temperature: 50°C*
- Injection volume: *2 µL*

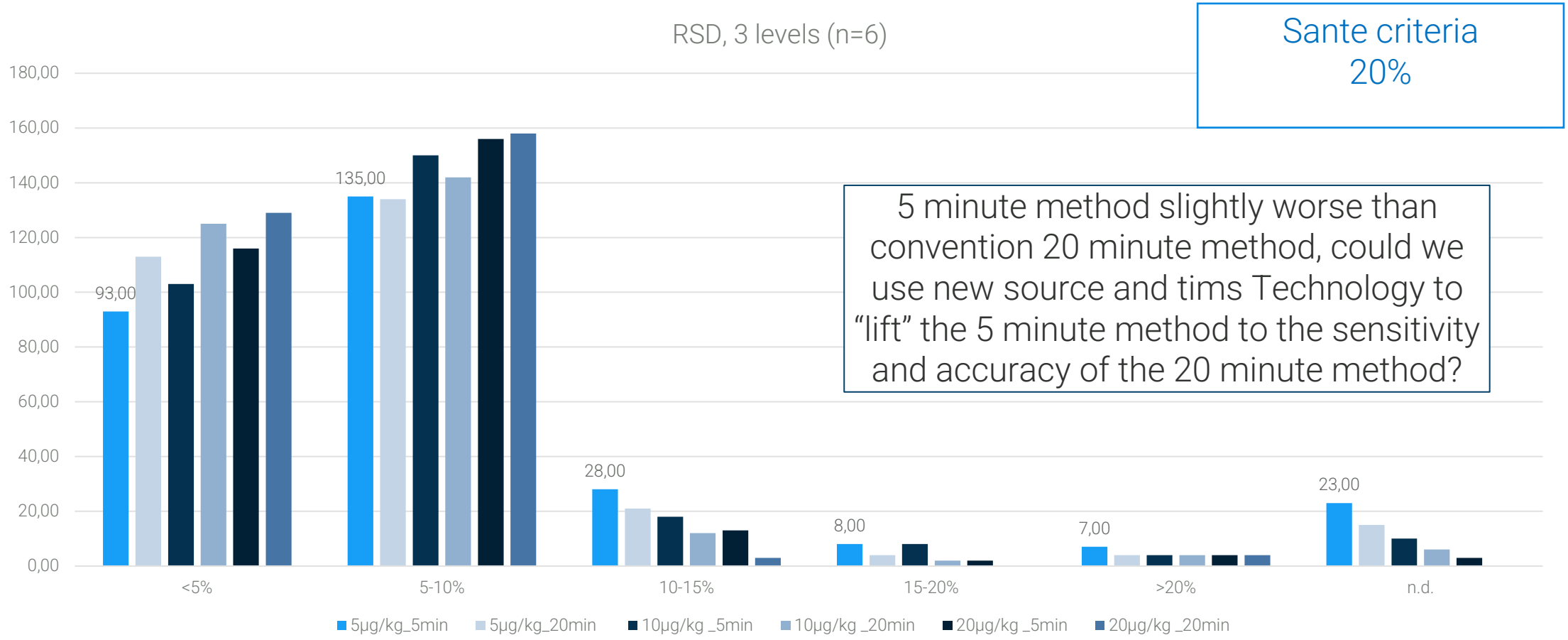
6Hz MS Method

Analyte distribution with the 5min method



5 min total runtime

RSD



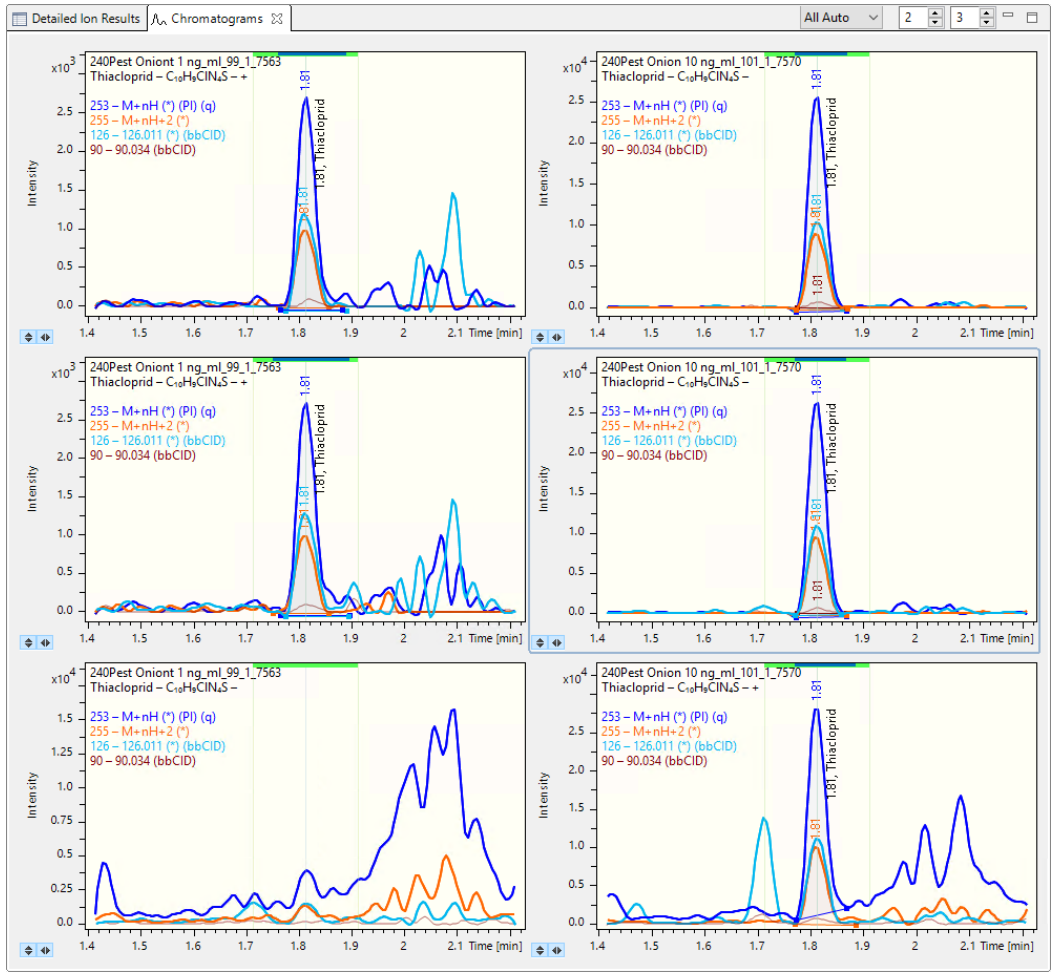
Sante criteria
20%

5 minute method slightly worse than convention 20 minute method, could we use new source and tims Technology to “lift” the 5 minute method to the sensitivity and accuracy of the 20 minute method?

Thiacloprid 5 min method, full scan on MS and Ion Mobility

1 ppb in Onion

10 ppb in Onion



Clean EICs
Target ion and all qualifier ions detected at 1 ppb

EIC 1/K0 = 0.01 V*s/cm2
Very narrow mobility filter

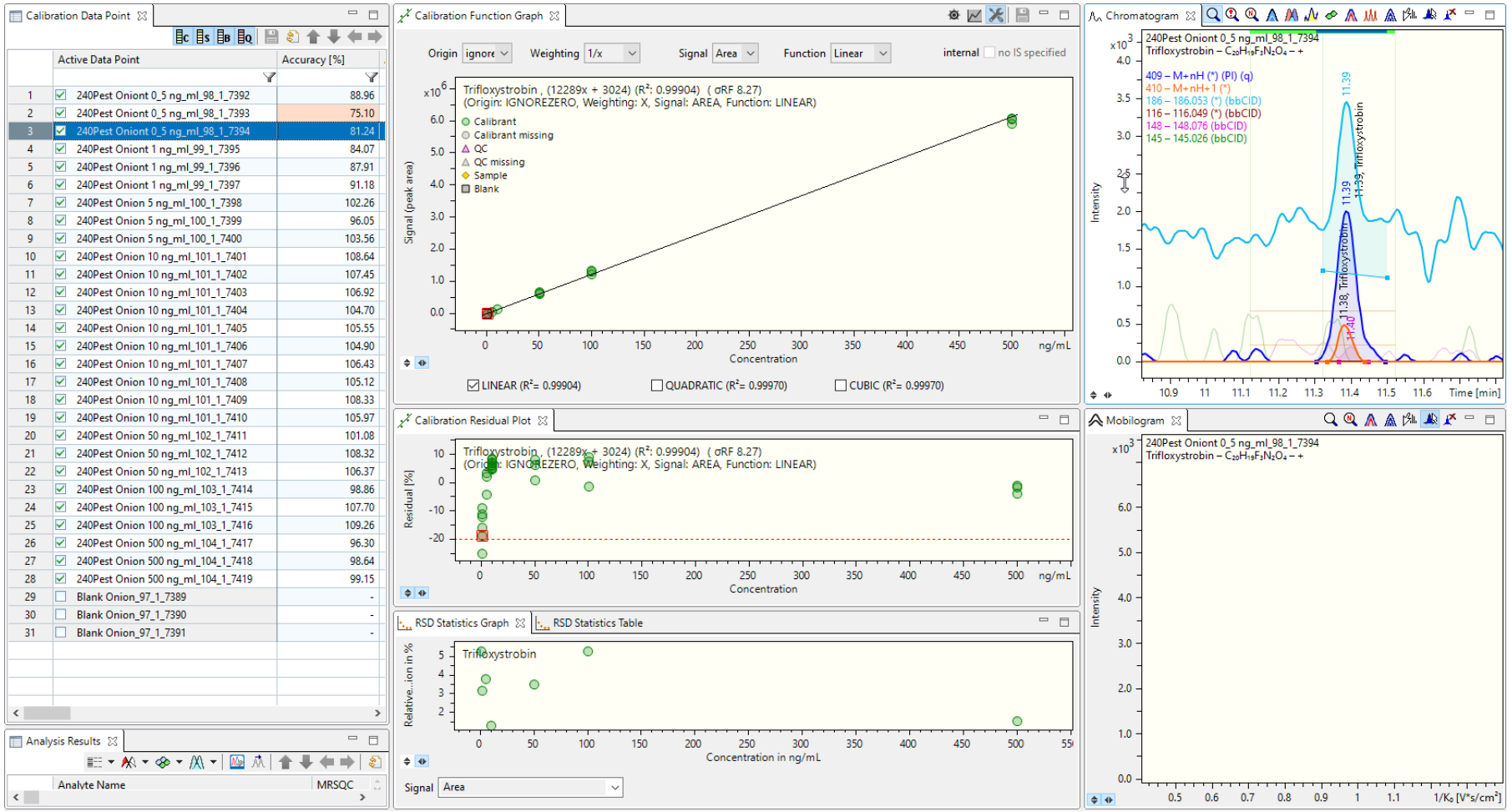
EIC 1/K0 = 0.02 V*s/cm2
Moderate mobility filter

Not detected at 1 ppb

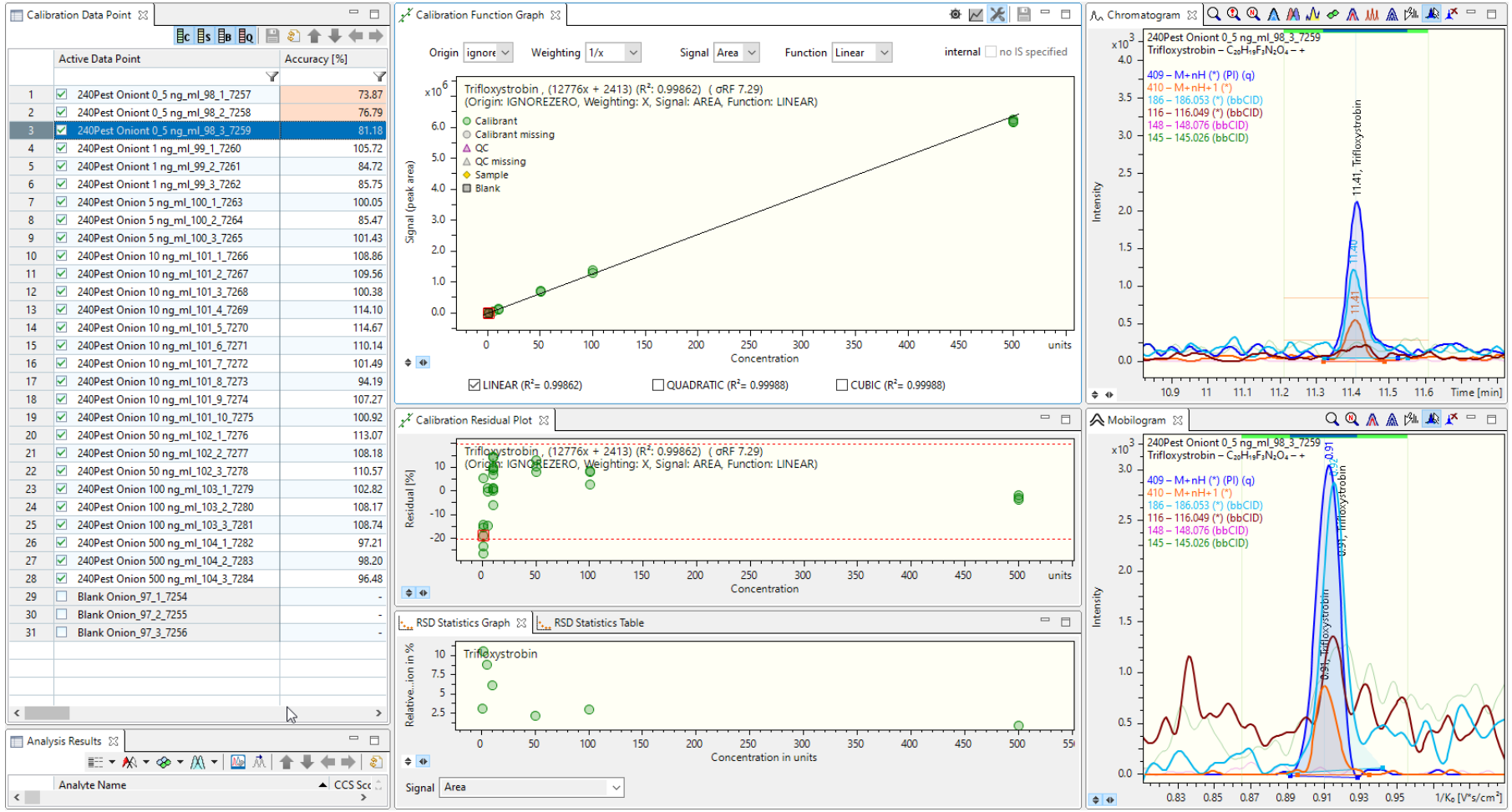
EIC 1/K0 = 1.00 V*s/cm2
No mobility filter

Filtering on CCS, all data is available

Trifloxystrobin in Onion : TargetScreener TIMS off



Trifloxystrobin in Onion: TargetScreener TIMS on



PESTICIDES @ TIMSTOF PRO

Pesticides in difficult matrix

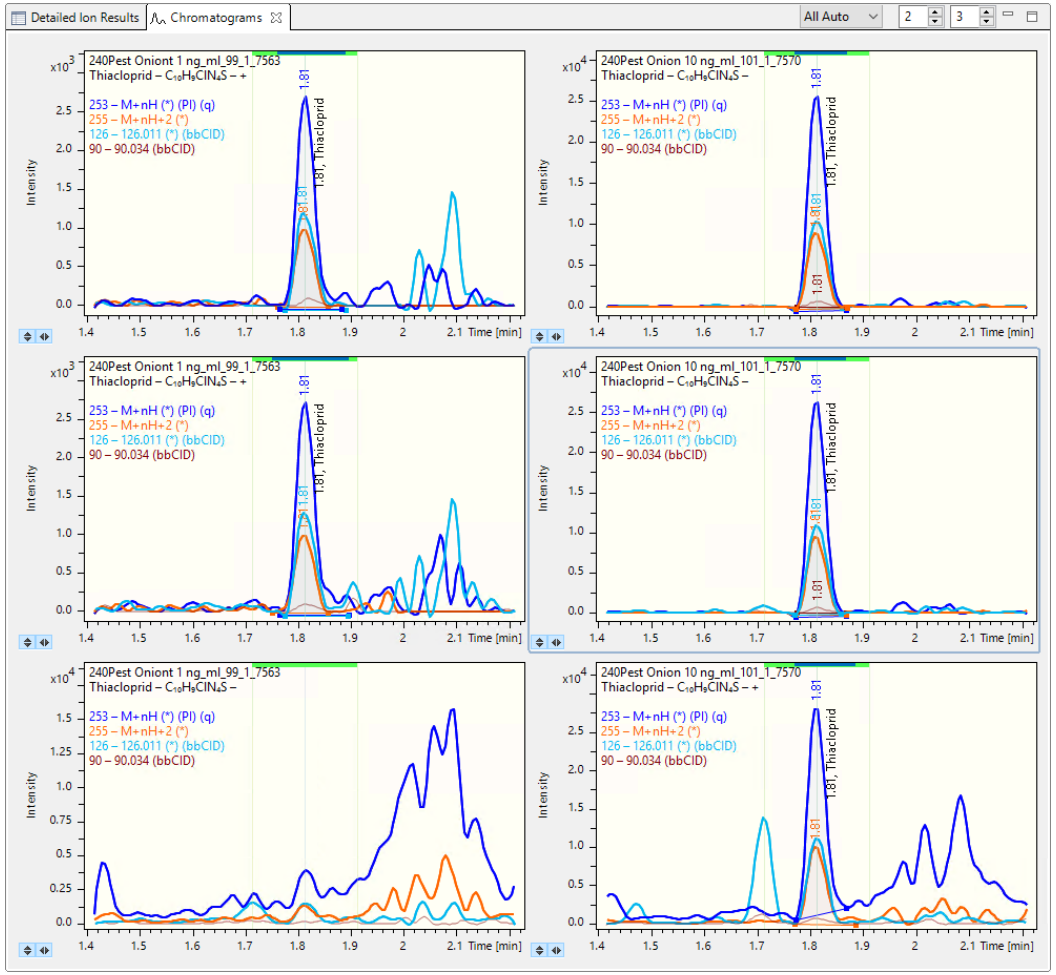
Thiacloprid 5 min method

Smaller CCS (Ion Mobility) filter used

Due to 100% duty cycle time technology the sensitivity of timsON and timsOFF is comparable, addition CCS separation increases signal to noise.

1 ng/ml in Onion

10 ng/ml in Onion



EIC 1/K0 = 0.01 V*s/cm2

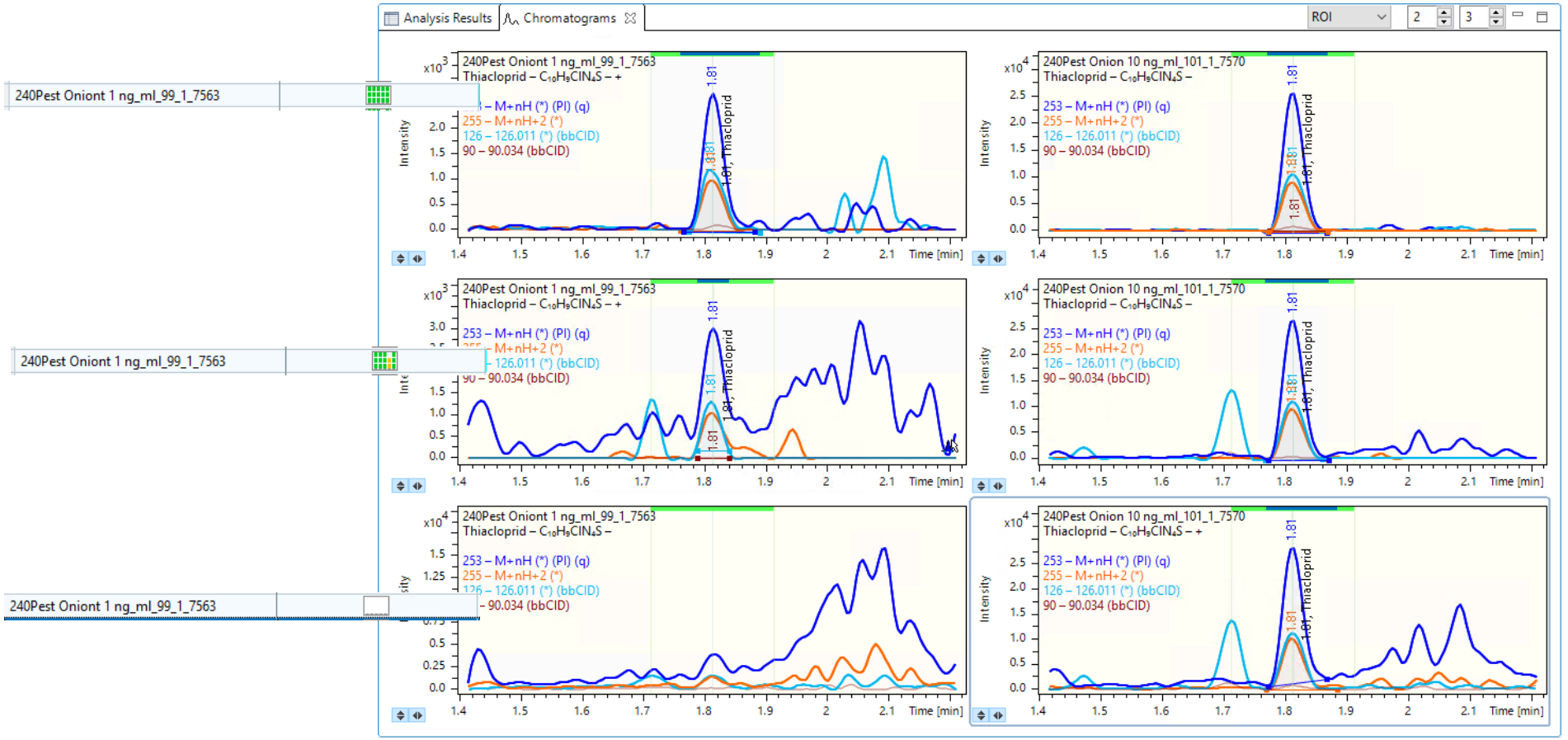
EIC 1/K0 = 0.02 V*s/cm2

EIC 1/K0 = 1.00 V*s/cm2 (no CCS filter)

Thiacloprid 5 min method and using Ion Mobility filter

1 ng/ml in Onion

10 ng/ml in Onion



EIC 1/K0 = 0.01 V*s/cm2

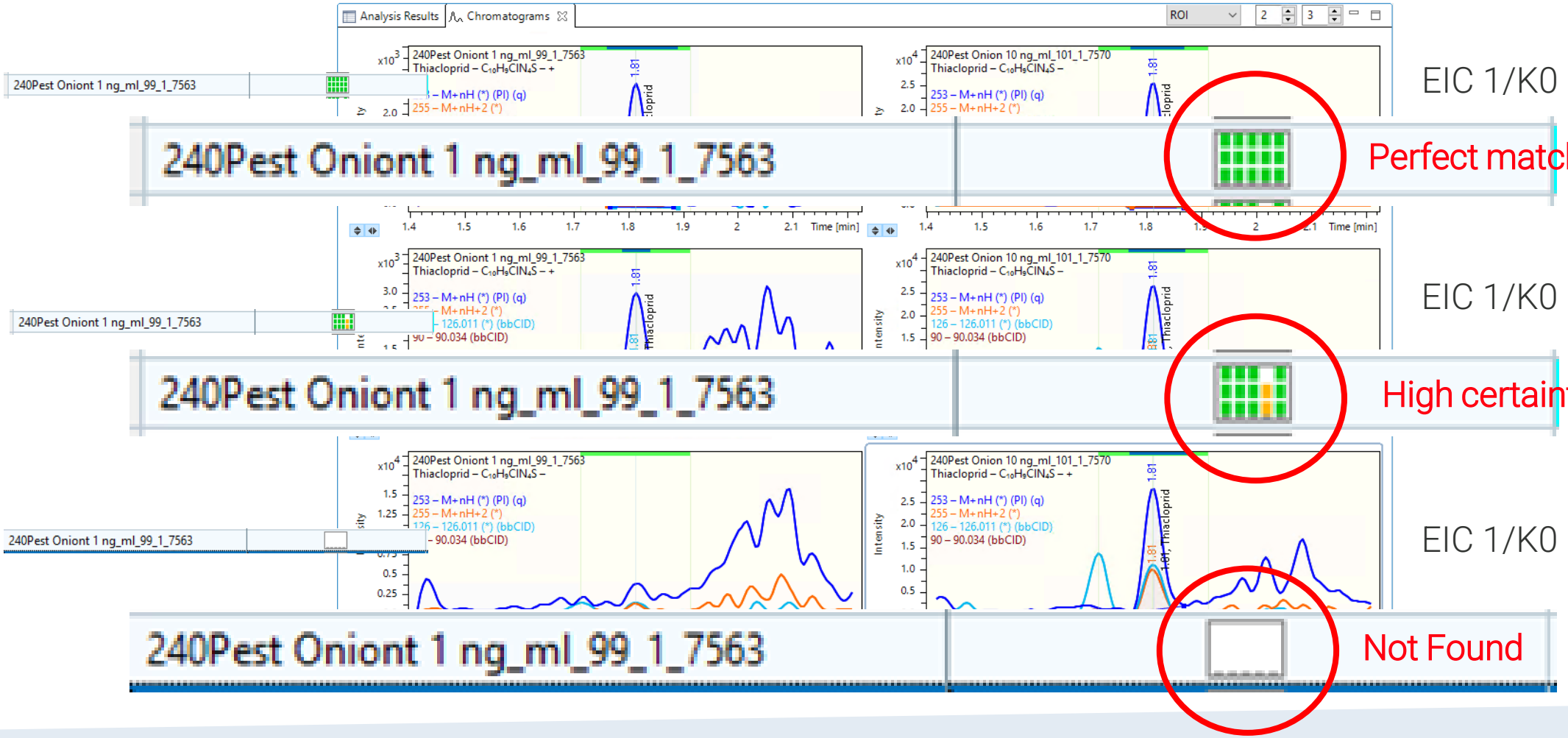
EIC 1/K0 = 0.05 V*s/cm2

EIC 1/K0 = 1.00 V*s/cm2
(no CCS filter)

Thiacloprid 5 min method and using Ion Mobility filter

1 ng/ml in Onion

10 ng/ml in Onion



EIC 1/K0 = 0.01 V*s/cm2

Perfect match

EIC 1/K0 = 0.05 V*s/cm2

High certainty

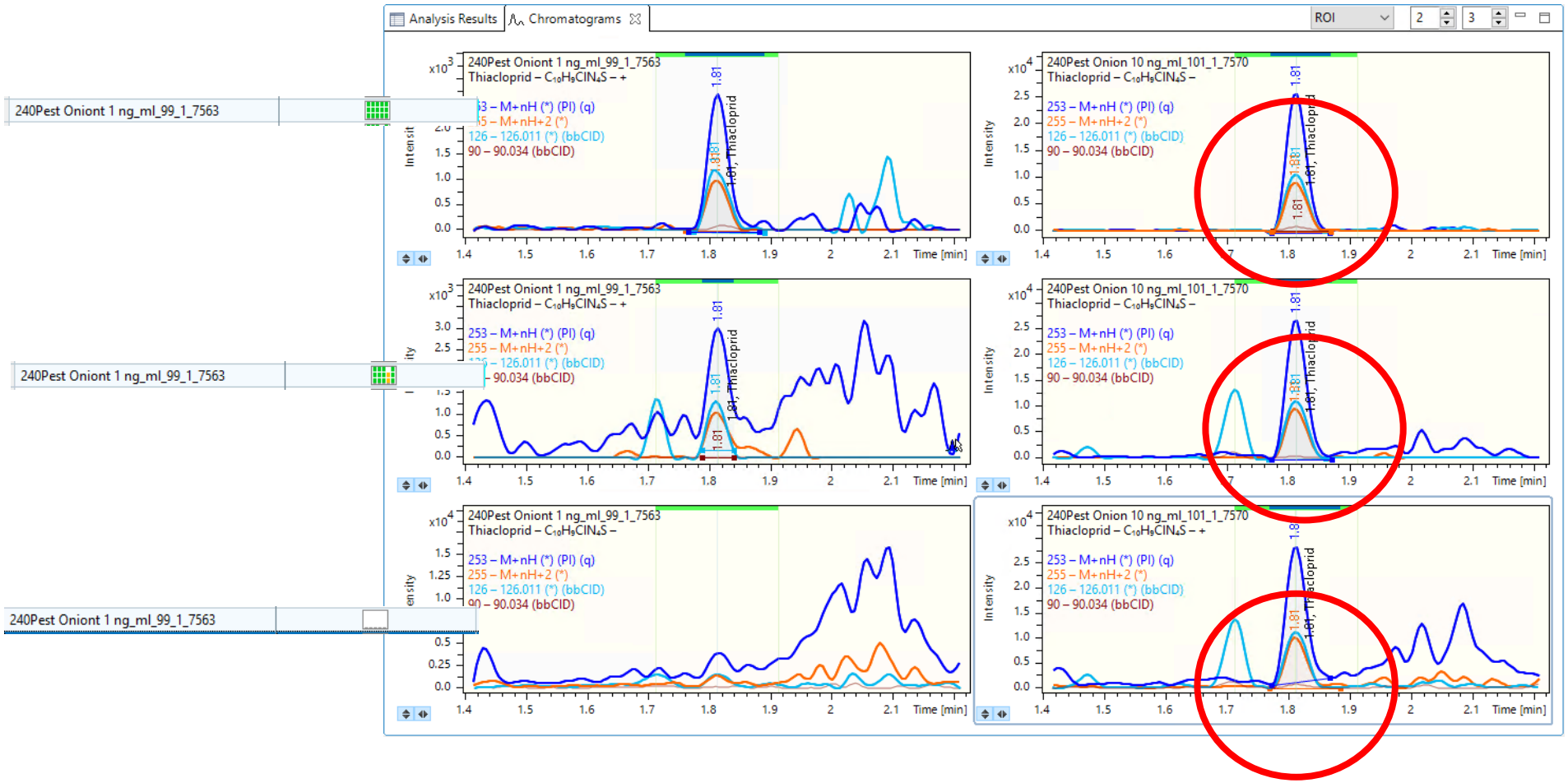
EIC 1/K0 = 1.00 V*s/cm2

Not Found

Thiacloprid 5 min method and using Ion Mobility filter

1 ng/ml in Onion

10 ng/ml in Onion



EIC 1/K0 = 0.01 V*s/cm2

Easy to integrate

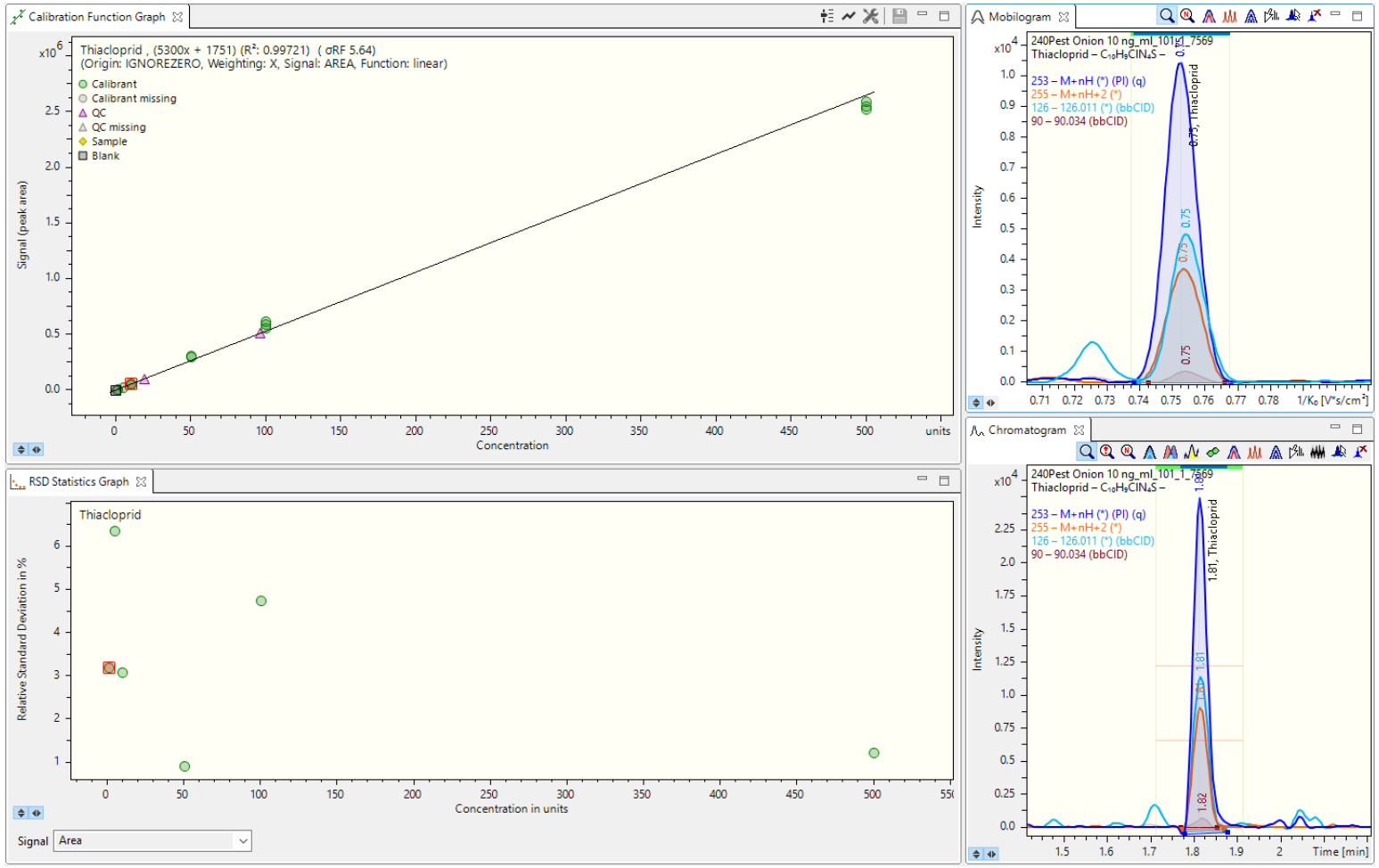
EIC 1/K0 = 0.05 V*s/cm2

Integration check needed on qualifier ion

EIC 1/K0 = 1.00 V*s/cm2

Manual integration needed

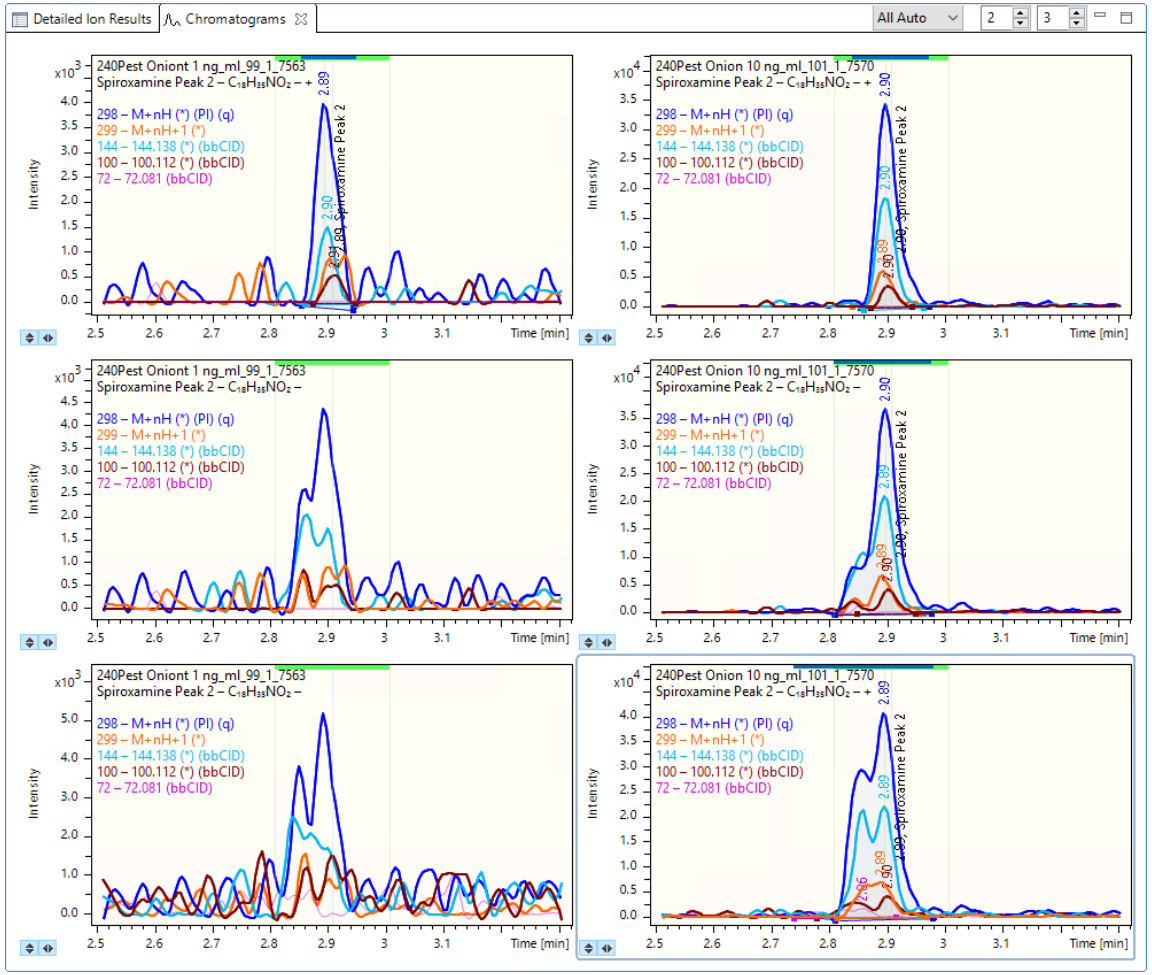
Thiachloprid Quant in Onion 1ng/ml - 500 ng/ml --- 5 min method !



Spiroxamine2 5min: Peak easier to integrate by using CCS filter

Dual peak, disturbing proper integration of component of interest

1 ng/ml in Onion | 10 ng/ml in Onion



EIC 1/K0 = 0.01 V*s/cm2

EIC 1/K0 = 0.02 V*s/cm2

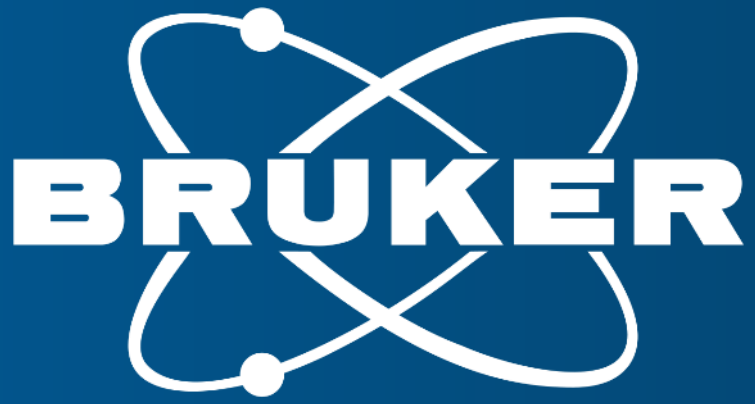
EIC 1/K0 = 1.00 V*s/cm2 (no CCS filter)

Conclusion

- Faster methods can be use with current technology
- Increased level of certainty can be obtained by current timsTOF technology

- The new combination of VIP-HESI and timsTOF needs to be validated, this is currently work in progress.
  - VIP-HESI is more sensitive, also in difficult matrix
  - CCS filter does increase signal-to-noise with proper settings
  - Ion Mobility does help to get better integration in difficult matrix
  - Fast QTOF scanning give the possibility to decrease run times

- Aim is to develop a validated 5 minute method which is faster and needs less manual interaction and less reviewing. This would result is lower cost per sample and higher throughput, increasing the quality of data.



Innovation with Integrity