Vacuum-Ultraviolet Detection

a Completely new Detection Technique for GC

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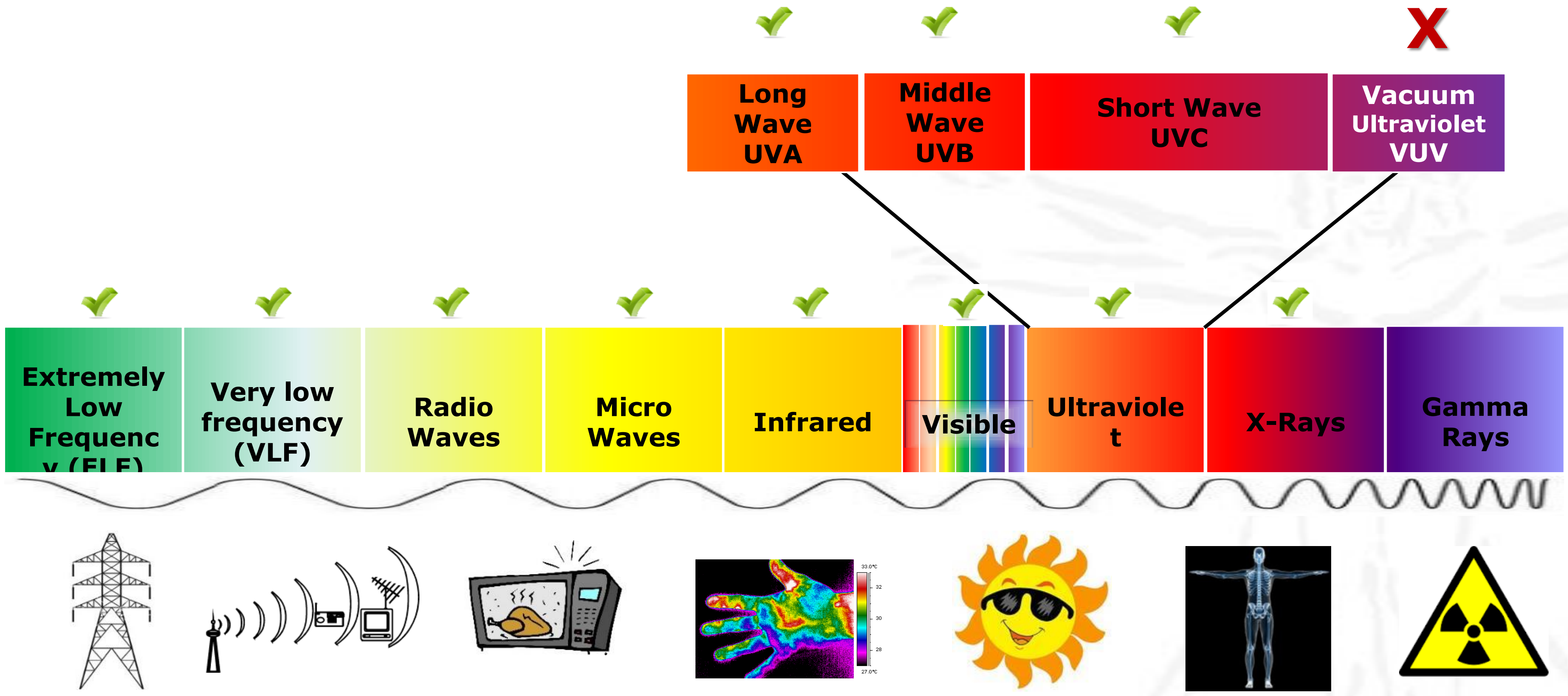
Product Manager Advanced Detections
Da Vinci Laboratory Solution

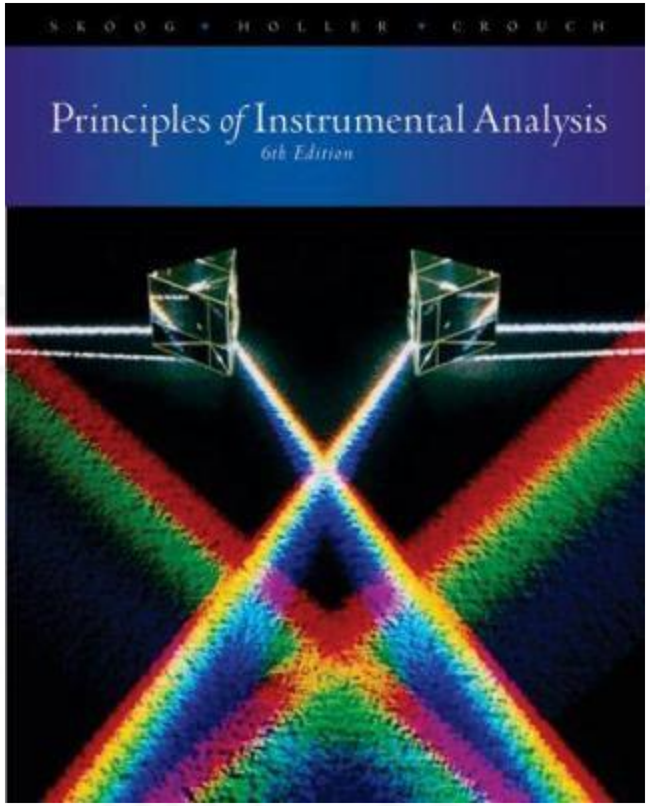
The Electromagnetic Spectrum



- The Vacuum Ultraviolet (VUV) portion of the ultraviolet spectrum is a region of short wavelength, high energy absorbance that provides unique spectral fingerprints of nearly every compound
- He, Ar, H_2 are the exceptions
- Photons in this region can induce electronic transitions, especially ground state to excited state transitions such as $\sigma \rightarrow \sigma^*$ and $\pi \rightarrow \pi^*$
- Compound identification is unambiguous due to the unique nature of the absorbance

Teached at school

- Principals of Instrumental Analysis, by Douglass Skoog, Sixth Edition, 2006
  - *"The excitation* ***energies associated with*** *electrons forming* ***most single bonds are*** *sufficiently high that absorption by them is* ***restricted to the*** *so-called* ***vacuum ultraviolet*** *region (λ<185nm), where components in the atmosphere also absorb strongly.* ***The experimental difficulties*** *associated with the vacuum ultraviolet* ***are significant; as a result*** *……* ***no further discussion will be devoted to this*** *type of absorption."*



It has been taught to be instrumentally too difficult.

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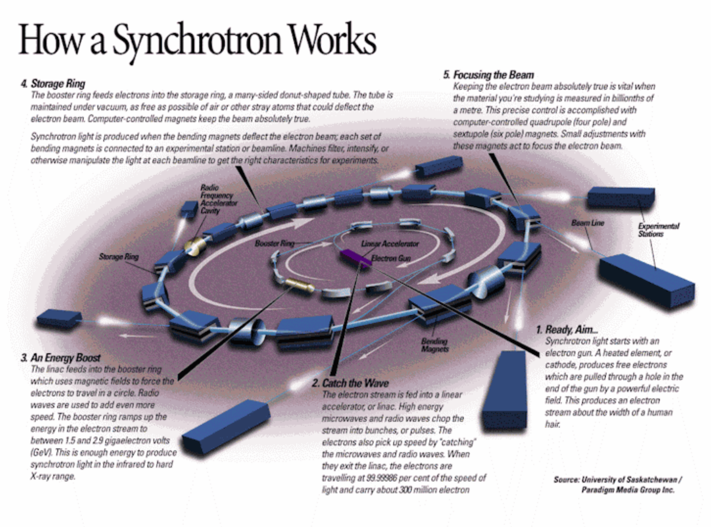
Only in synchotron



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World's First GC—VUV Detector

- Vacuum Ultraviolet (VUV) Absorption from 120nm to 240nm
  - VGA-101 extends this capability out to 430 nm
- Enables powerful detection capabilities
  - Unique selectivity
    - Unambiguous compound identification
    - Easily deconvolve co-eluting analytes
    - Clear and easy isomer differentiation
  - Excellent sensitivity
    - Low picogram
  - Non-destructive analysis
    - No ionization required
  - Excellent temporal resolution
    - Up to 100Hz Sampling
  - Predictable linear response
    - 1st principle detection reduces calibration burdens
  - Reliable & Easy to use
    - No vacuums pumps

VUVision

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How does it work

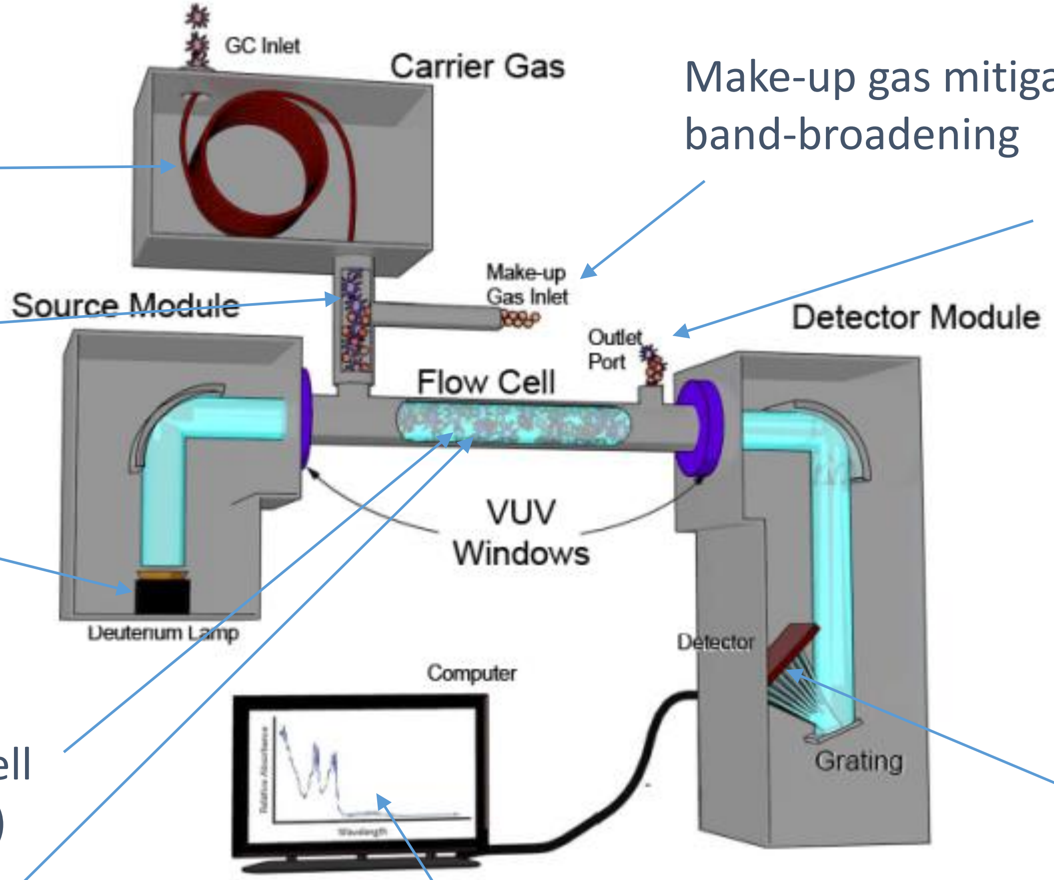
Carrier and make-up gases (He, H_2, N_2, Ar) largely VUV transparent.

Make-up gas mitigates/alleviates band-broadening

Nondestructive

Heated transfer line (up to 320 °C (420 °C))

VUV/UV source lamp (D_2); stable signal and robust



Thermostatted flow cell (up to 320 °C (420 °C))

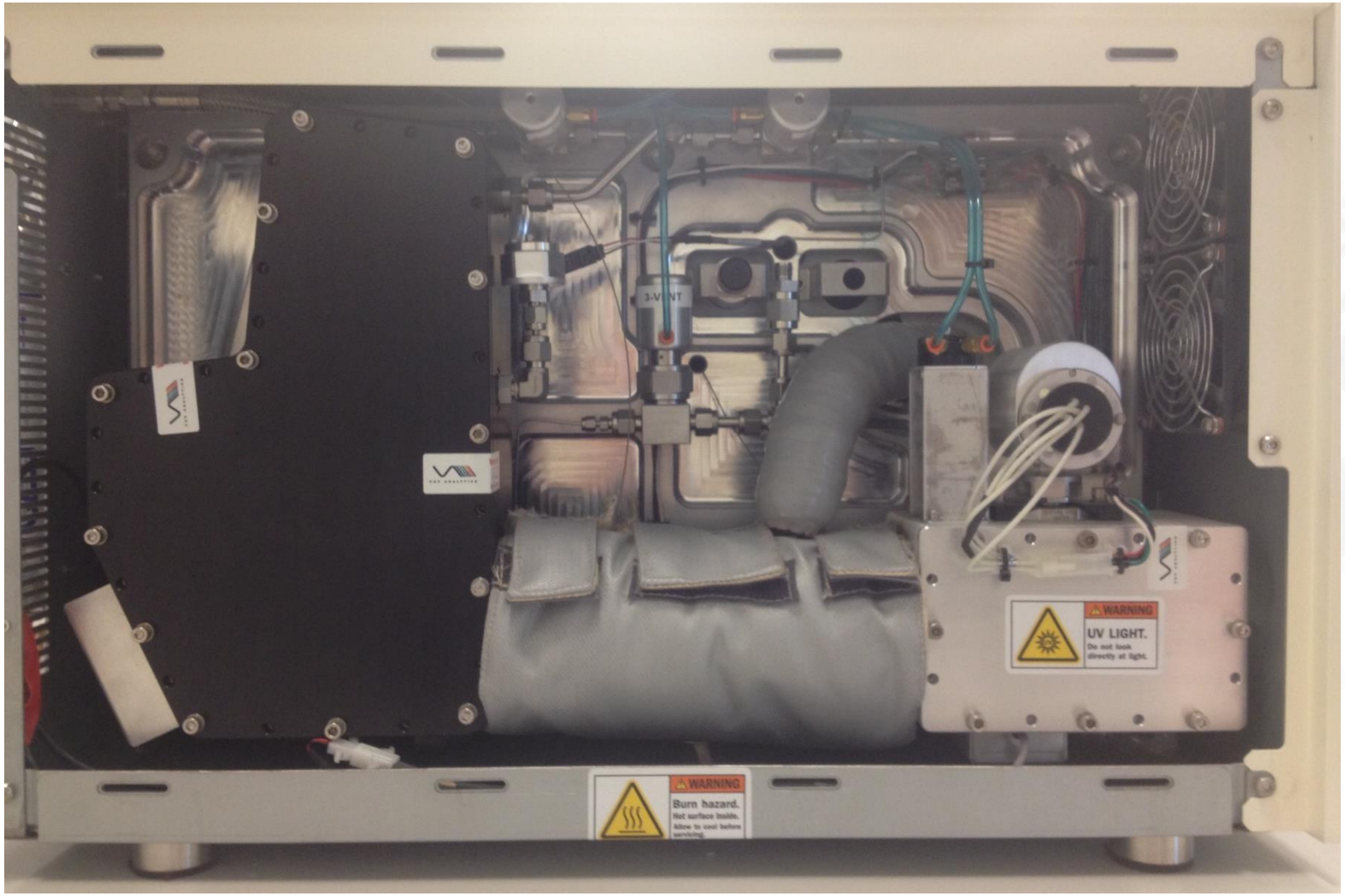
Full range 120 – 240 nm (430 nm) data acquisition at up to 100 Hz

Post-run processing for universal or selective detection; library spectral matching; etc.

Analyte-specific absorption based on Beer's Law principles; Qualitative and quantitative analysis (wide linear range)

Schug et al., *Anal. Chem*. **2014**, *86*, 8329-8335.

How does it work



Easy Spectral Quantitation

Governed by Beer's Law:

$A = \epsilon bC$

- A = absorbance
- ϵ = extinction coefficient ($M^{-1}.cm^{-1}$)
- b = path length (cm)
- C = molar concentration ($mol.dm^{-3}$)

Peak area of an analyte depends on:

- Concentration of analyte (the number of molecules or mass)
- Cross-section (ability of a molecule to absorb a photon)
- Total flow rate through the flow cell (residence time)
- Flow cell geometry (length and volume)

Spectral quantitation is robust and repeatable

- Identity not dependent on retention time or baseline resolution
- Compound % Mass is directly proportional to sum of its absorbance
- No special integration tools required
  - All fitting and quantitation is performed by the software
- VUV absorbance is an inherent property unique to every compound

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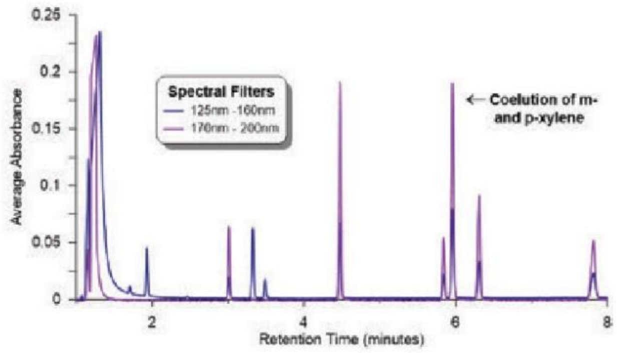
GC—VUV Data is 3D

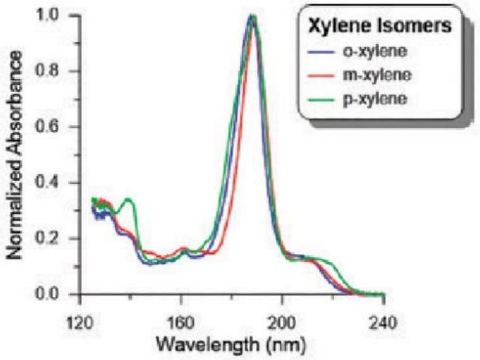
GC-VUV absorbance data contains both chromatographic & spectral information

(VUV absorbance, time, and wavelength)

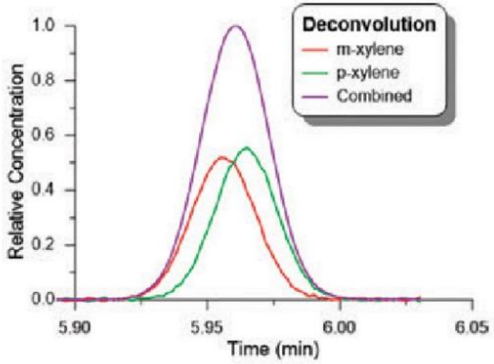
Spectral deconvolution of m&p Xylene



GC-VUV chromatogram showing the co-elution of m- and p-xylene



VUV absorbance spectra of overlapping xylene isomers



Deconvolution of the overlapping chromatographic signals for m- and p-xylene

Chromatographic baseline resolution is not necessary

Co-eluting analytes and isomers can be spectrally deconvolved and quantitated

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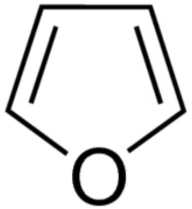
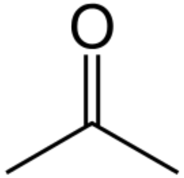
Some applications

Factory exhaust

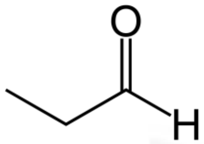
Compounds of interest



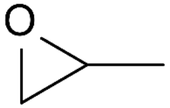
Furan



Acetone



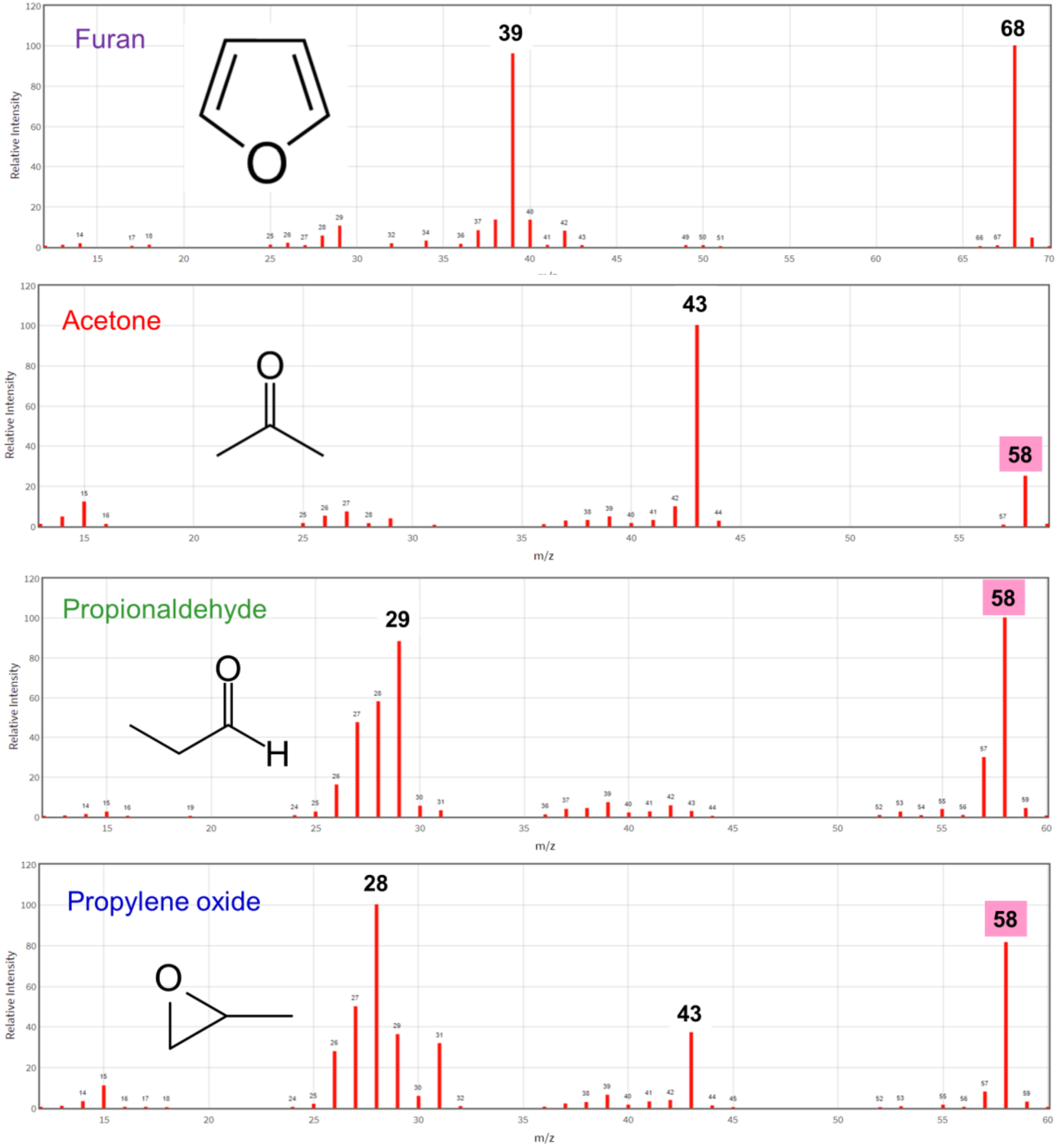
Propionaldehyde



Propylene oxide

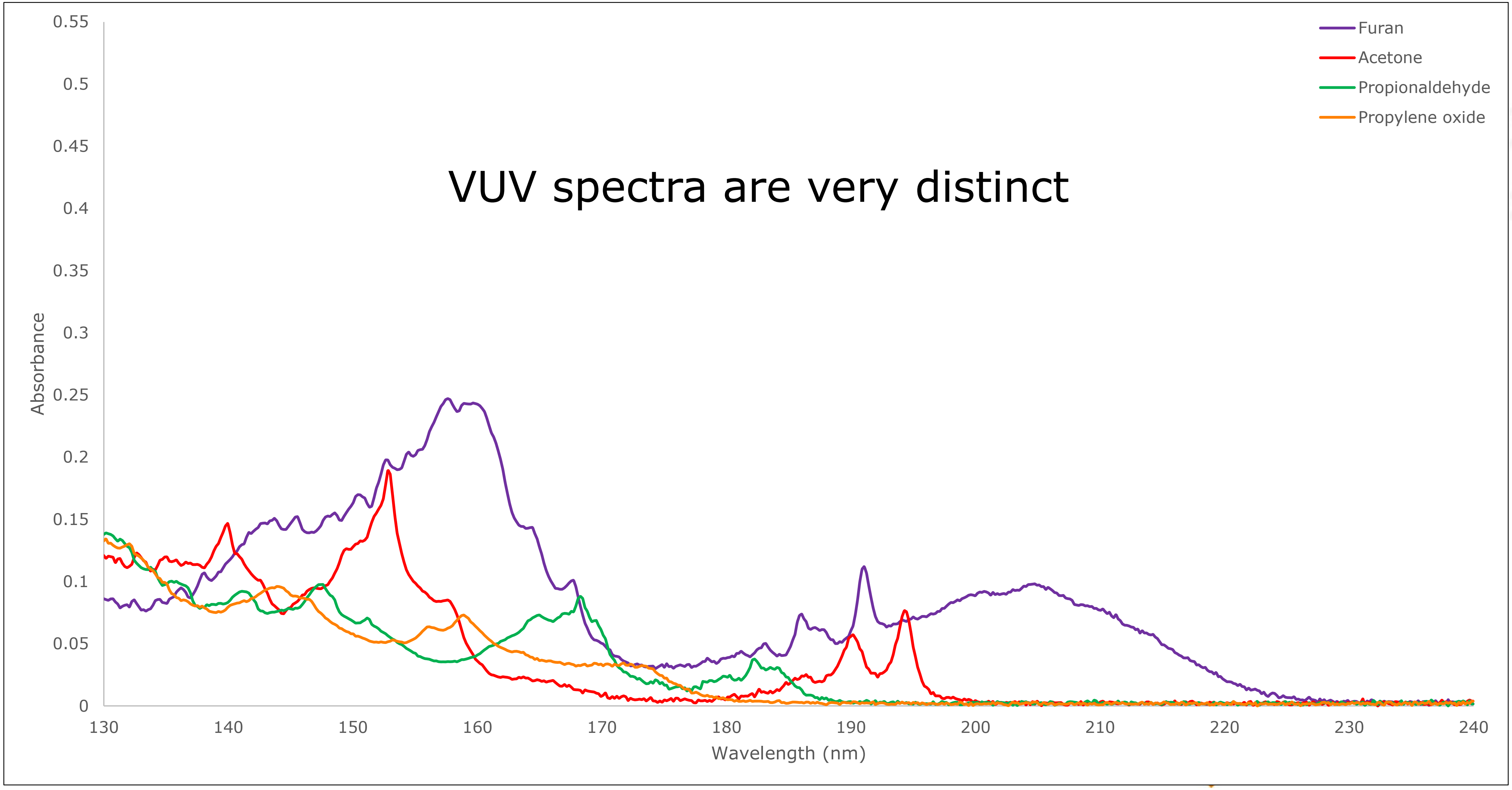
- Small molecules
- Coelute under many GC conditions
- Mostly cannot be differentiated by electron ionization MS
- Can they be analyzed successfully using GC-VUV?

MS spectra



MS spectra are closely related

VUV spectra

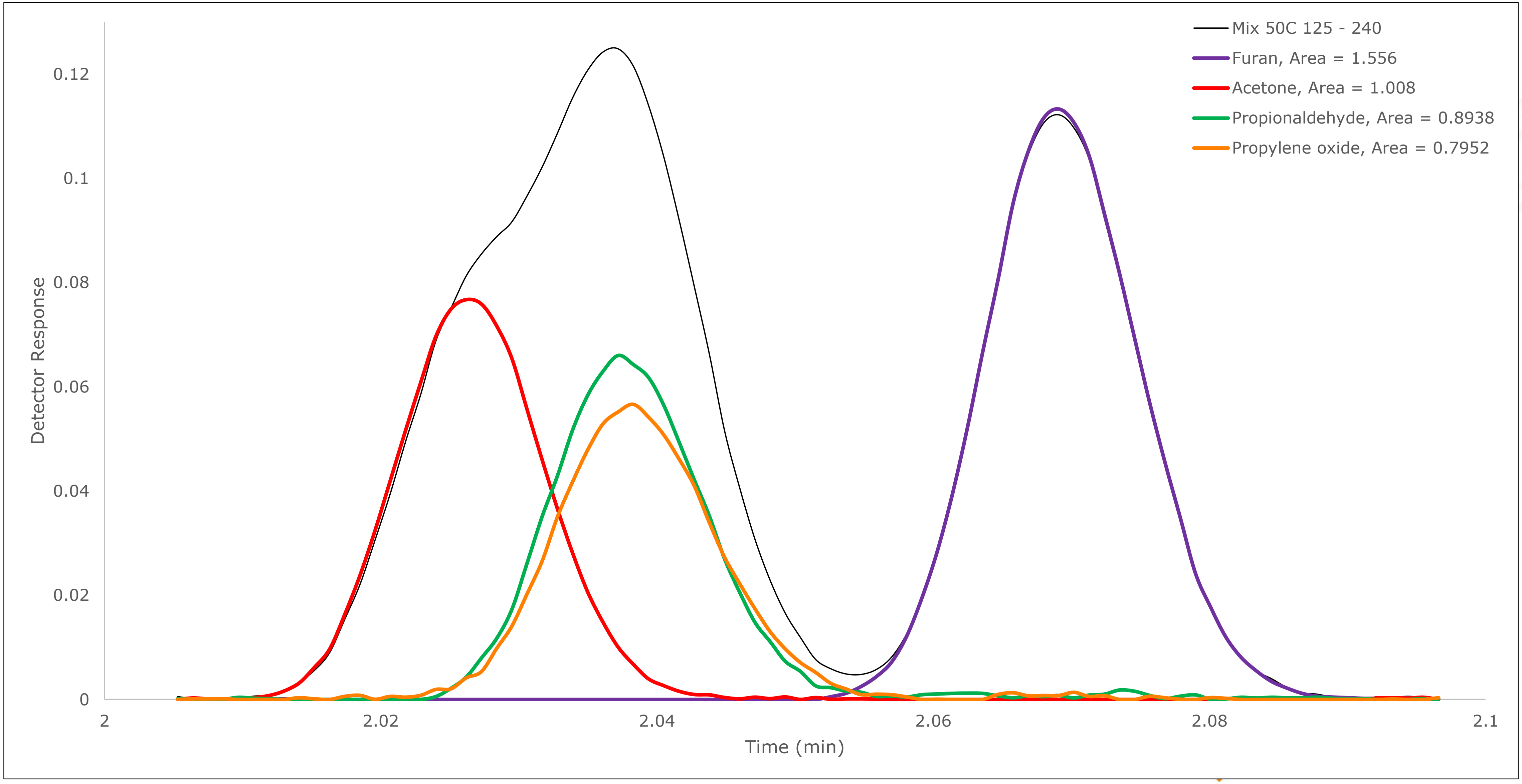


VUV spectra are very distinct
Absorbance
0.55
0.5
0.45
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
130
140
150
160
170
180
190
200
210
220
230
240
Wavelength (nm)
Furan
Acetone
Propionaldehyde
Propylene oxide

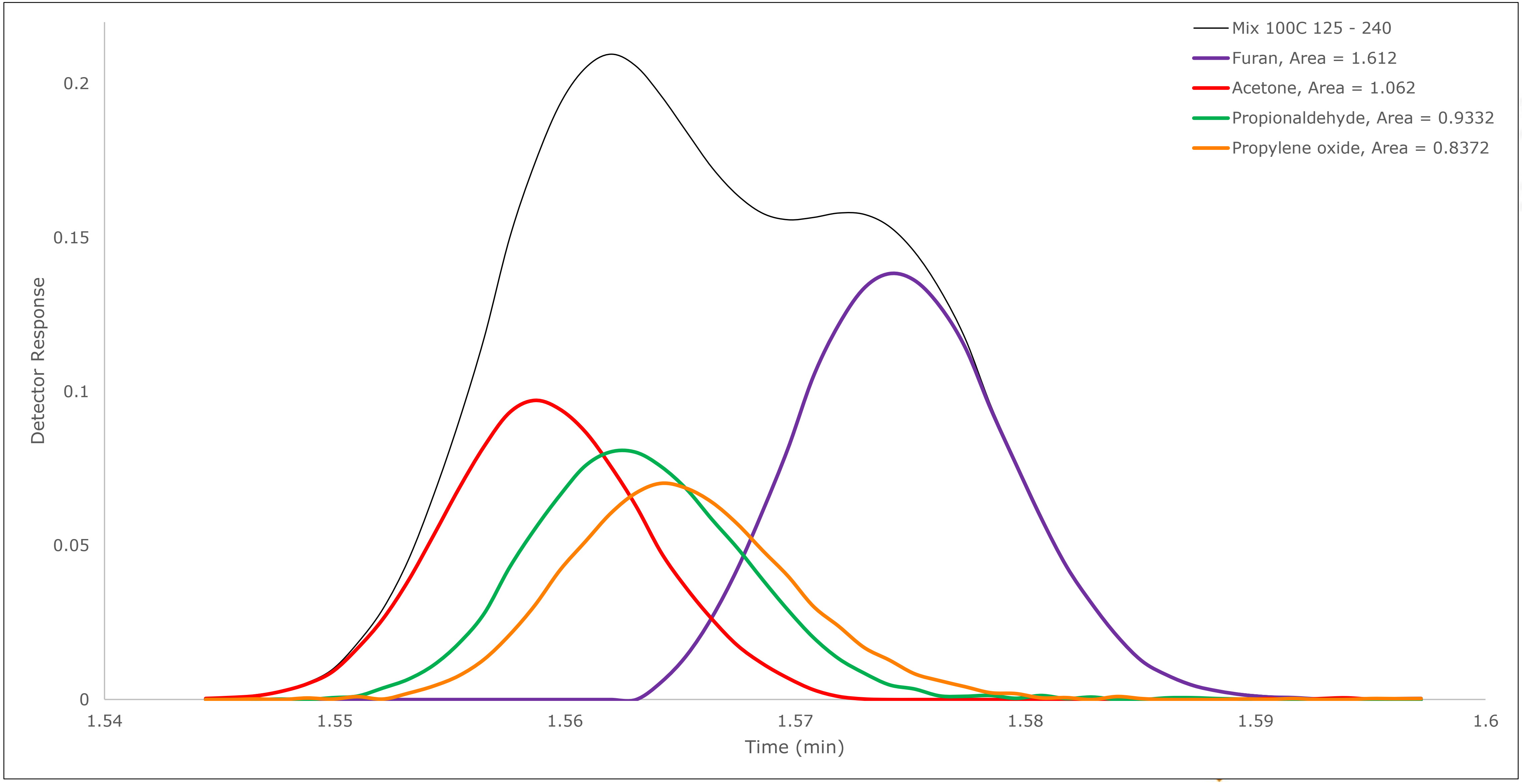
GC—VUV Conditions

- Agilent 6890 GC
  - 30m x 0.25mm x 0.50µm Rxi-5ms
  - Column Flow: 2 mL/min He
  - Oven: Isothermal (various temperatures), hold 3 min
  - Inlet: 200° C
  - Split Ratio: 495:1
  - Injection Volume: 0.2 µL
- VUV Analytics VGA-100
  - Transfer Line and Flow Cell Temperature: 275° C
  - Makeup Gas: 2.83 psi N_2
  - Acquisition Rate: 15 spectra/sec

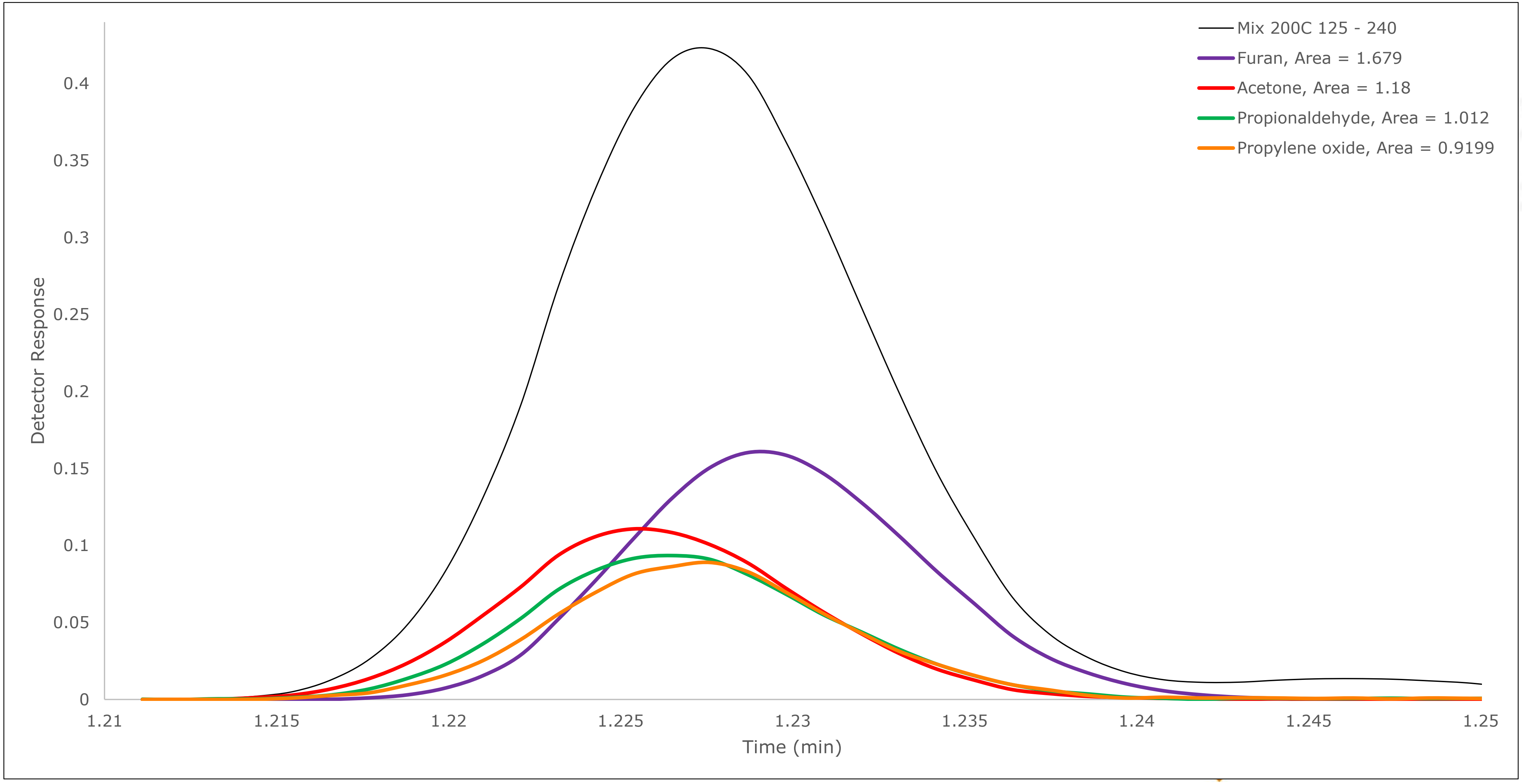
GC Oven Isothermal 50˚ C



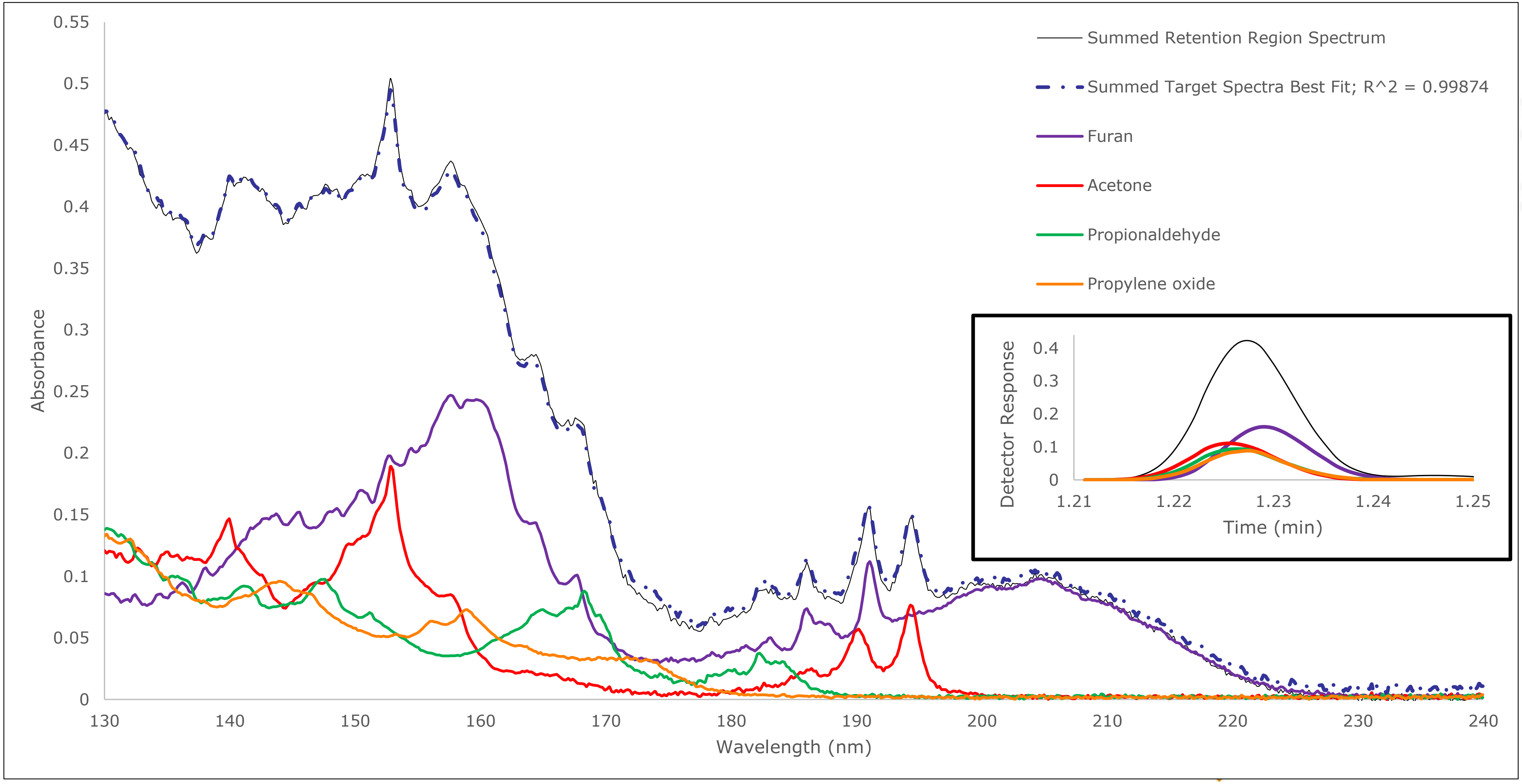
GC Oven Isothermal 100° C



GC Oven Isothermal 200˚ C



Summed and Individual VUV Absorbance Spectra



Residual Solvents in Pharmaceuticals

Residual Solvents in pharmaceuticals are defined as volatile organic compounds used in or generated from the manufacture of drug substances, pharmaceutical additives, or drug products

Pharmaceutical Regulatory Agencies

- A scientific organization that sets standards for the identity, strength, quality, and purity of medicines, food ingredients, and dietary supplements manufactured and consumed worldwide.

- USP's drug standards are enforceable in the United States by the Food and Drug Administration

- The International Council for Harmonisation (ICH) of Technical Requirements for Pharmaceuticals mission is to achieve greater harmonisation worldwide to ensure that safe, effective, and high quality medicines are developed and registered in the most resource-efficient manner.

USP Static Headspace Conditions

Pharmaceutical product for analysis dissolved in water or another suitable solvent in a headspace vial.	Headspace Operating Parameter Sets		
	1	2	3
Equilibration temperature (°)	80	105	80
Equilibration time (min.)	60	45	45
Transfer-line temperature (°)	85	110	105
Carrier gas: nitrogen or helium at an appropriate pressure			
Pressurization time (s)	30	30	30
Injection volume (mL)	1	1	1

https://www.usp.org/sites/default/files/usp_pdf/EN/USPNF/generalChapter467Current.pdf

USP 467 GC Conditions

- Flame ionization detector (FID) 250°C
- GC inlet 140°C, split ratio 5
- 30m x 0.32mm x 1.80µm G43 (624- or 1301-type phase)
- Or… 30m x 0.53mm x 3.00µm G43
- Nitrogen or helium 35 cm/sec
- GC oven: 40°C (20 min), 10°C/min to 240°C (20 min)

- Run time: 60 min

https://www.usp.org/sites/default/files/usp_pdf/EN/USPNF/generalChapter467Current.pdf

Can GC—VUV Do Better?

- **Absorbance spectra to identify solvent**
  - Flame ionization detector is non-specific
- **Combine Class 1 and Class 2 solvents in one run**
  - Good detectability and linear range for VUV
- **Faster GC runs for higher sample throughput**
  - Higher GC flow rates which may be unsuitable for other detection platforms
- **Spectral filters provide specificity**
  - 170-240 nm for benzene, for example
- **Spectral deconvolution for coeluting solvents**
  - VUV Vision

VUVision

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GC—VUV Experimental Conditions

VUV Analytics VGA-100

- Transfer line & Flow Cell temperature: 275°C
- Makeup gas pressure: ~0.36 psi
  - GC column flow is 4 mL/min
  - So really just represents flow cell pressure
- Acquisition range: 125 to 240 nm
- Acquisition rate: 4.5 Hz

GC Conditions

- Agilent 6890 GC
- 30 m x 0.25 mm x 1.40 µm Rxi-624Sil MS GC Column
- GC oven: 35°C (1 min), 30°C/min to 245°C
- Run time: 8 min

Gerstel MPS2

- Syringe temperature: 90°C
- Incubation temperature: 80°C
- Incubation time: 10 min
- Agitator: 250 rpm
  - 10 sec on, 1 sec off
- Injection volume: 250 µL
- Injection speed: 200 µL/se

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GC conditions

- Agilent 6890 GC

- Topaz 2 mm ID Straight Inlet Liner (Restek)
- 250°C
- Split ratio 2.5
- 30m x 0.25mm x 1.40µm Rxi-624Sil MS GC Column (Restek)
- Helium 4 mL/min (constant flow)
- GC oven: 35°C (1 min), 30°C/min to 245°C
- Run time: 8 min

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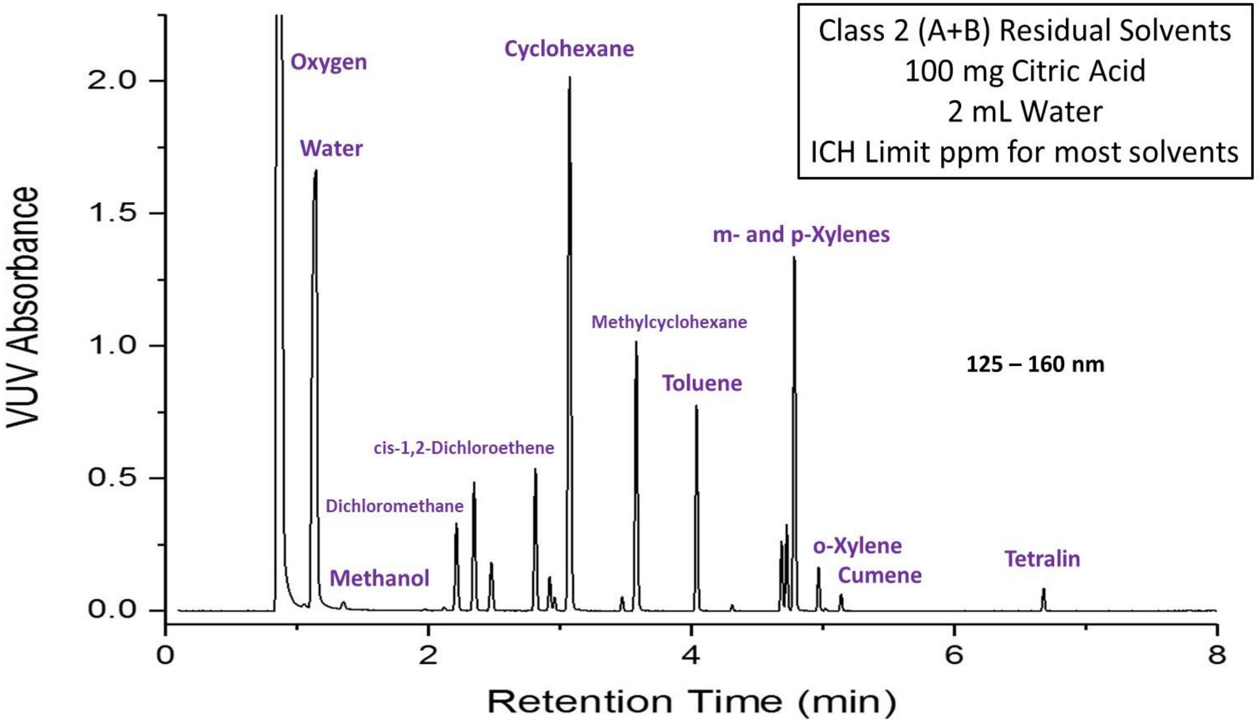
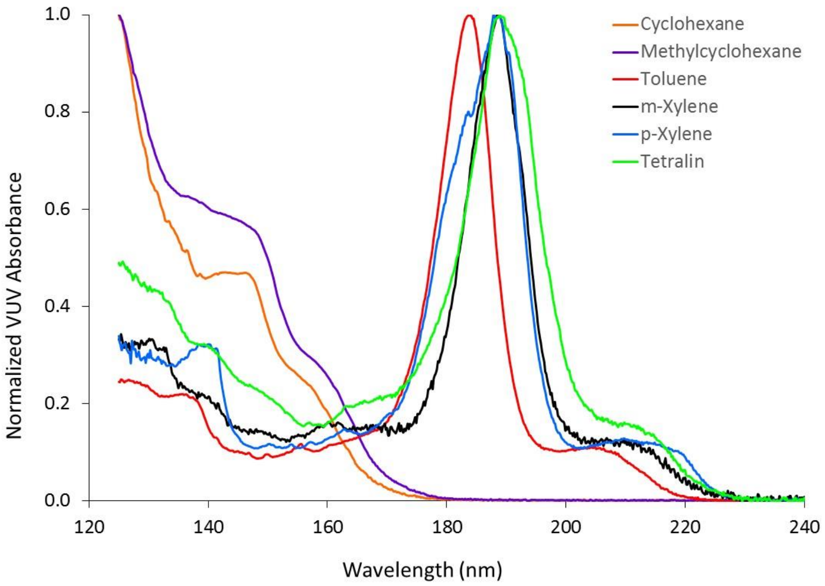
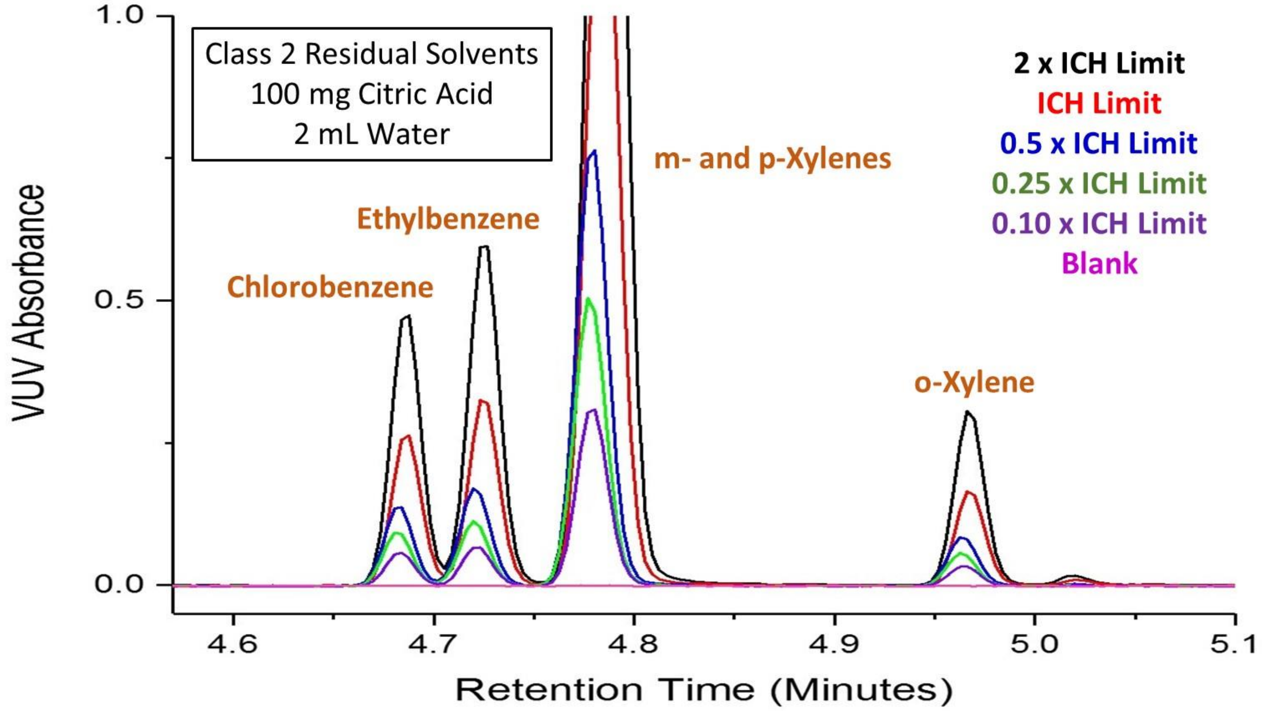
GC-VUV Analysis of Class 2 Residual Solvents

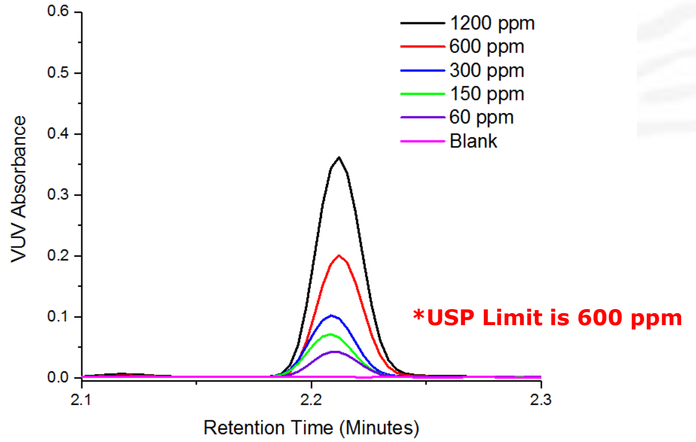


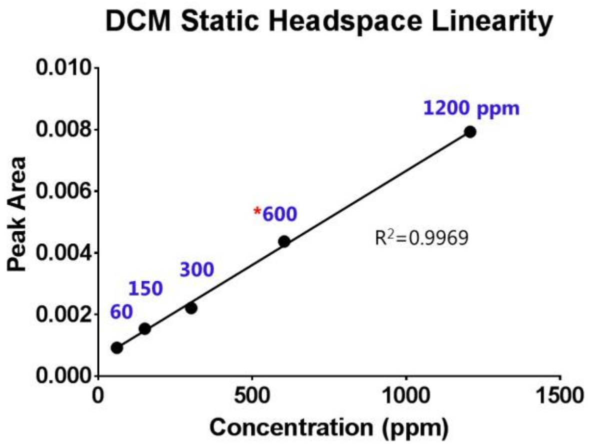


Chromatographic Linearity Above & Below ICH Limits



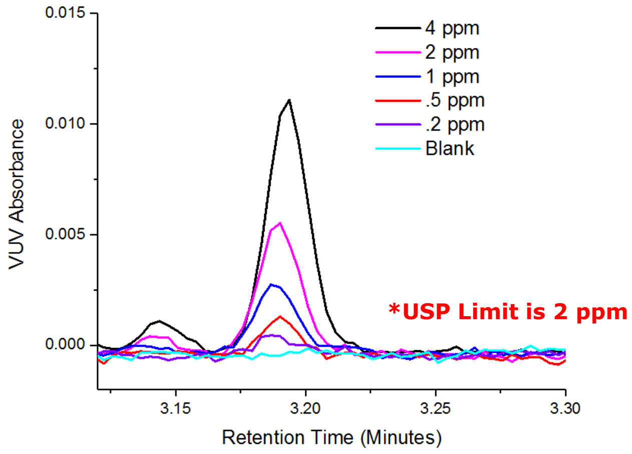
Dichloromethane



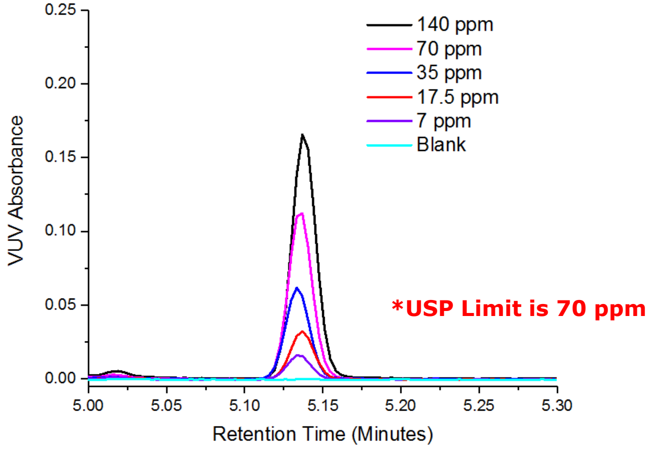


Linearity of Class 1 & 2 Solvent Mix Spiked into Throat Spray

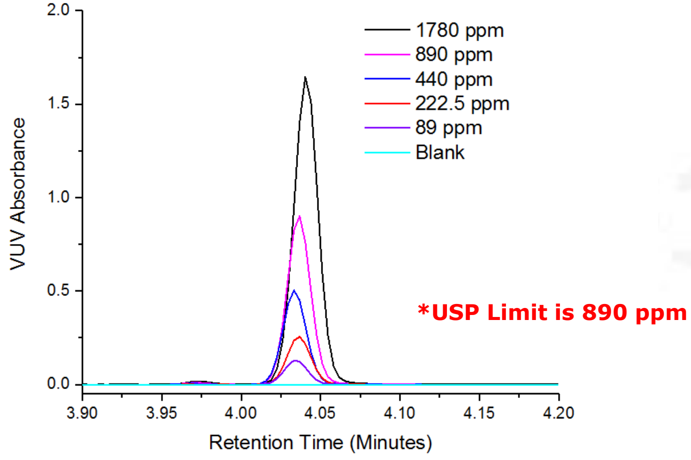
Benzene



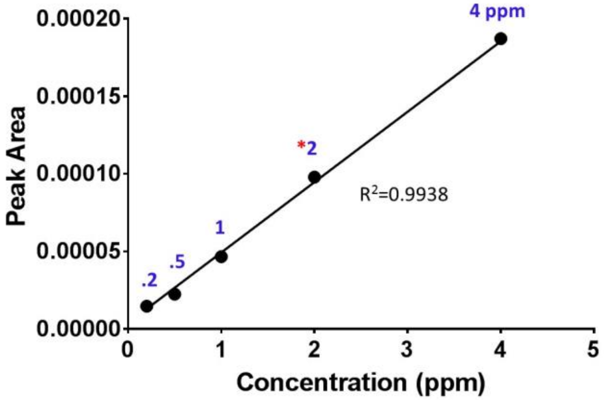
Cumene



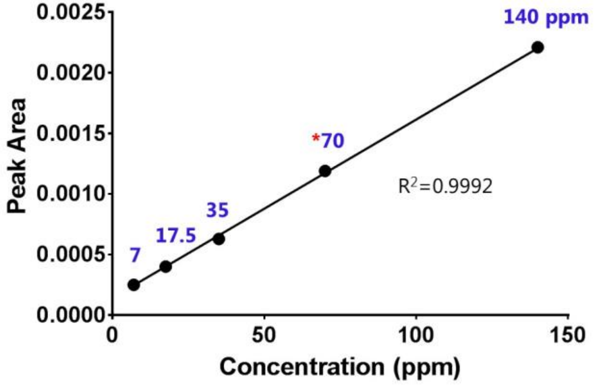
Toluene



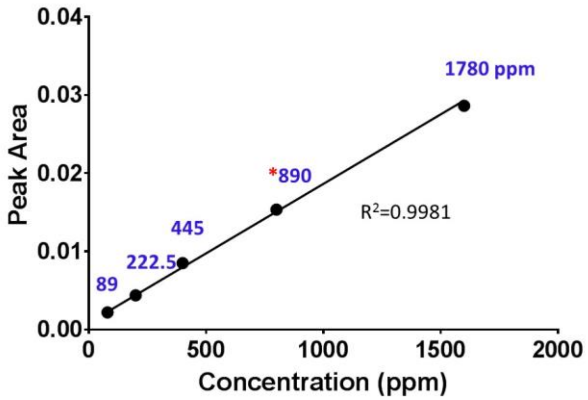
Benzene Static Headspace Linearity



Cumene Static Headspace Linearity



Toluene Static Headspace Linearity



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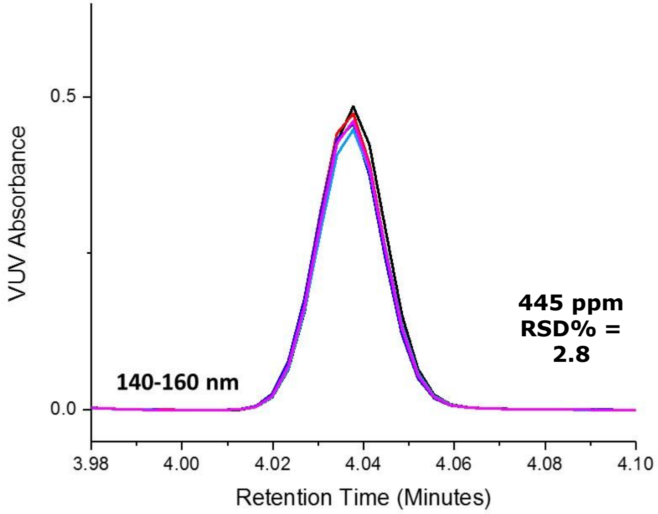
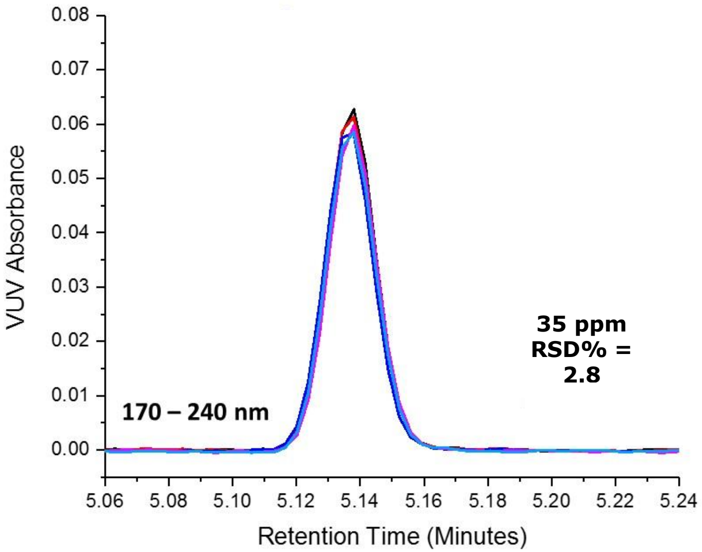
Reproducibility of Class 1 & 2 Solvent Mix Spiked to Throat Spray

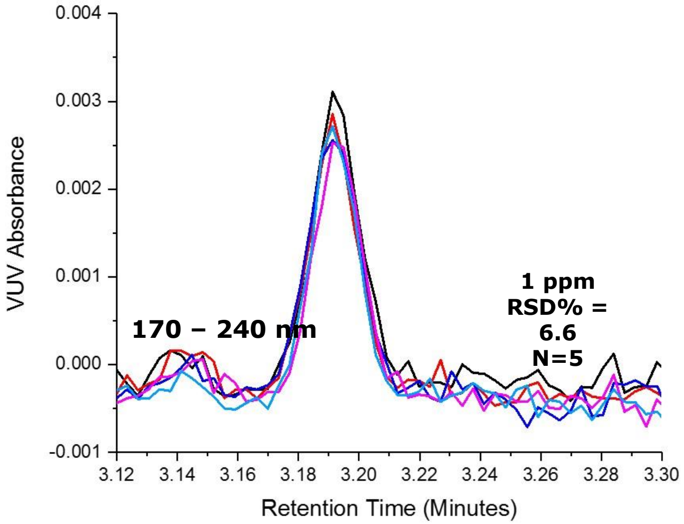
Toluene



Cumene

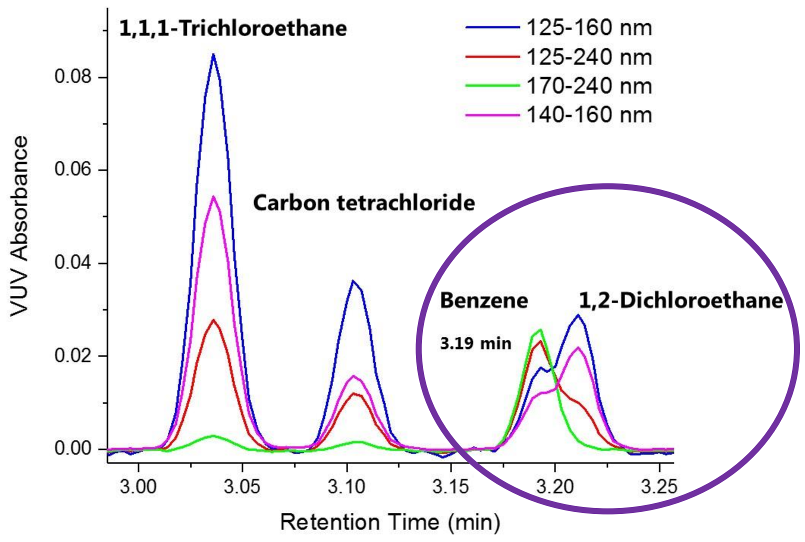


Benzene

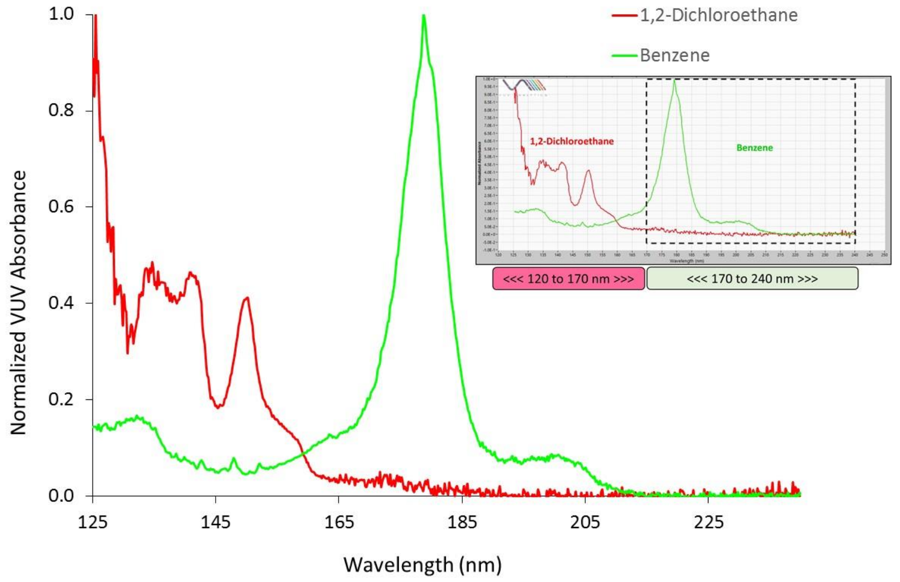


Co-elution & Deconvolution of Class 1 Residual Solvents

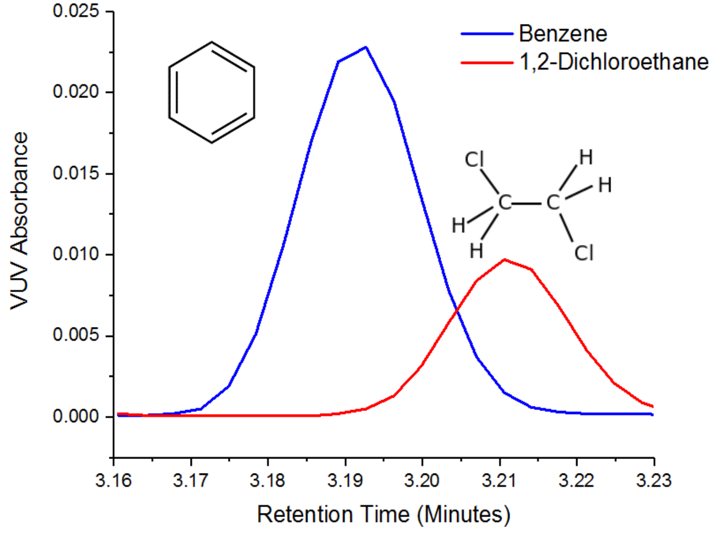
Chromatogram Zoomed-in on Class 1 Co-Elution



Spectral Comparison of Co-Eluting Analytes



Deconvolution of Co-Eluting Analytes



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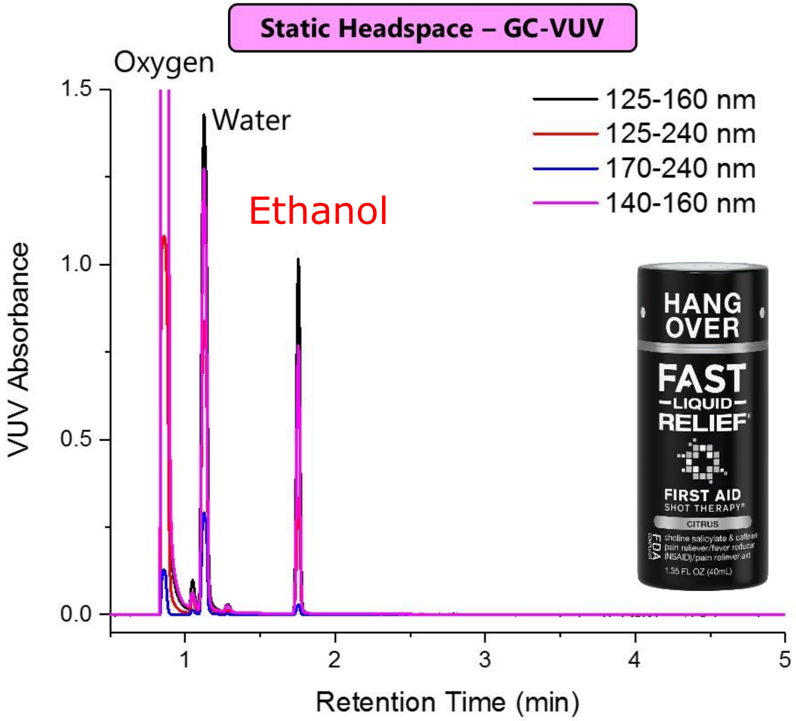
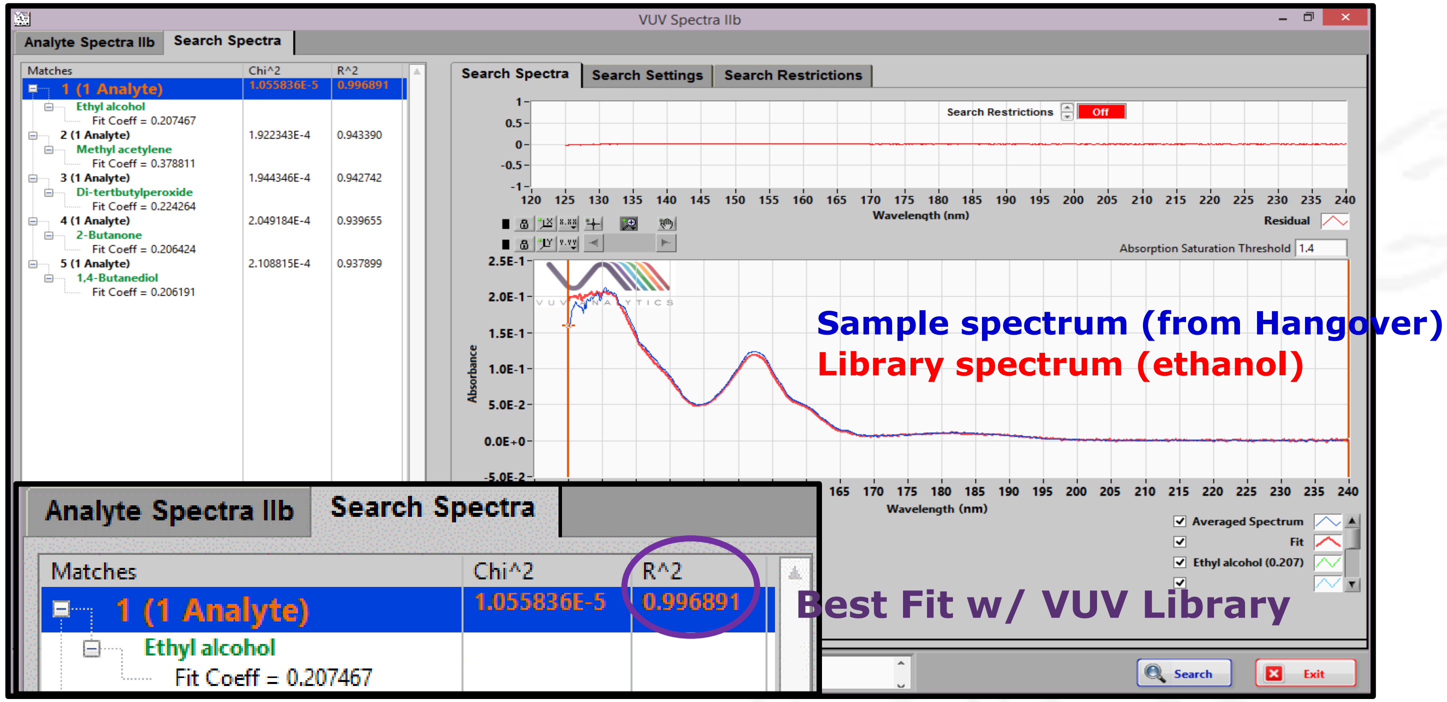
Analyzing Untargeted Unknowns by GC-VUV: Hangover Pain Relief





GC—VUV Key-features

- Universal and selective detection
- Unique, class similar spectra
- Complementarity to MS
- Deconvolution of coeluting analytes
- Automated classification and speciation of mixtures
- Good quantitative performance
- Theoretical computations

Acknowledgements

- Jack Cochran – VUV Analytics
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- Lindsey Shear – VUV Analytics
- Kevin Schug – University of Texas at Arlington

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