

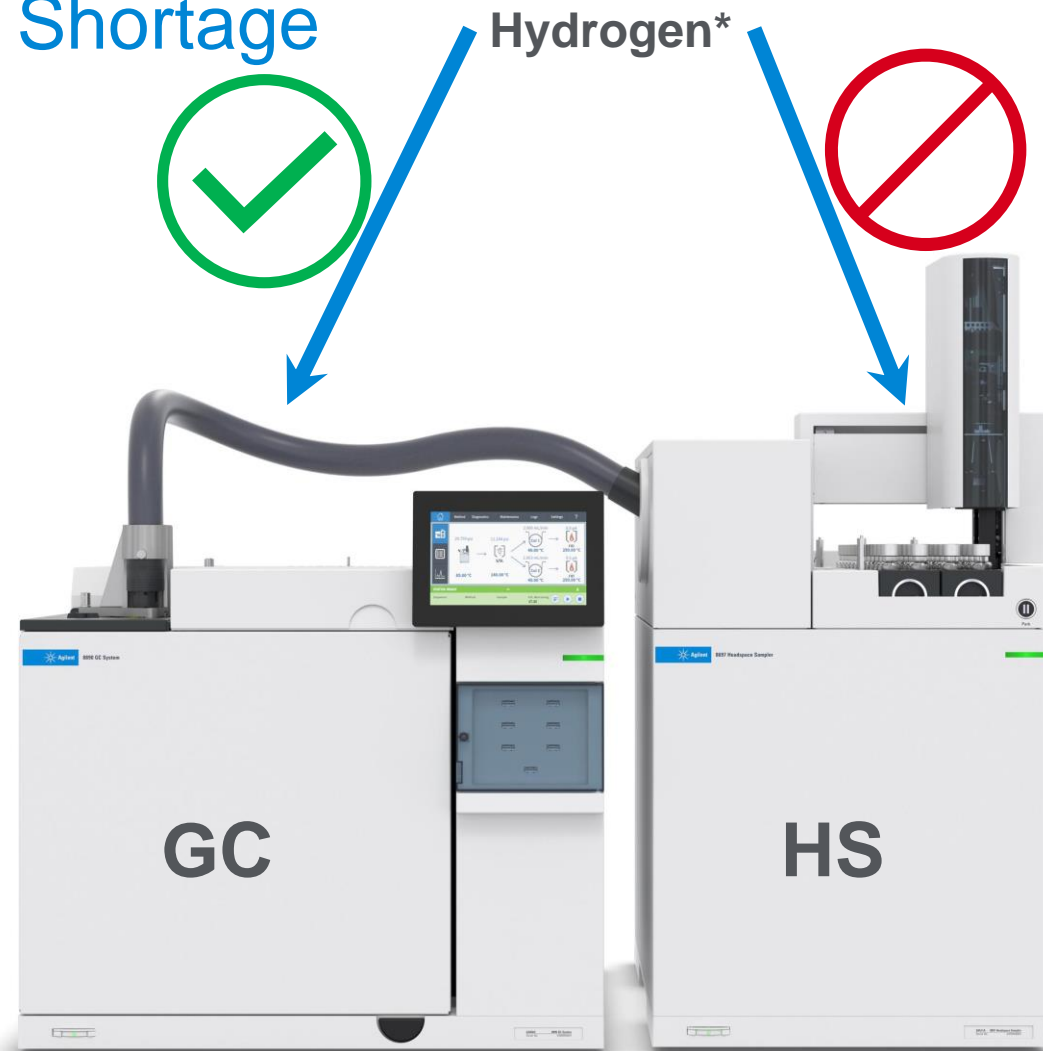
Scratching Your Head Over Headspace? We'll Help Make Things Simple

Method development, method
optimization, and troubleshooting

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GC Application Scientist
22 September 2022



Helium Shortage



***Consult safety guides linked below**

https://www.chem.agilent.com/Library/usermanuals/Public/5955-5398_030756.pdf

<https://www.agilent.com/cs/library/usermanuals/public/user-manual-gcms-hydrogen-safety-g7003-90053-en-agilent.pdf>

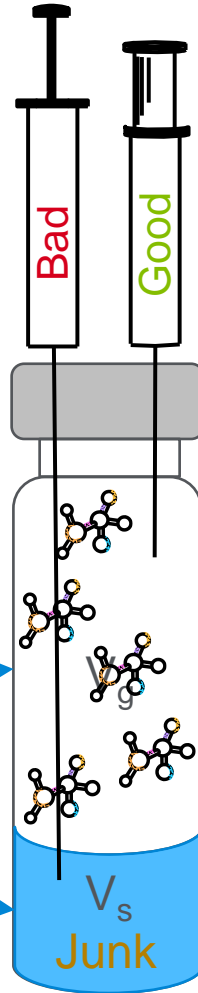
What Is Headspace?



$$\beta = \frac{V_G}{V_S}$$

$$K = \frac{C_S}{C_G}$$

$$C_S = \frac{W_S}{V_S}$$



Volatiles

Semi-Volatiles /
Salts, etc.

HEAT

$$C_G = \frac{C_0}{K + \beta}$$

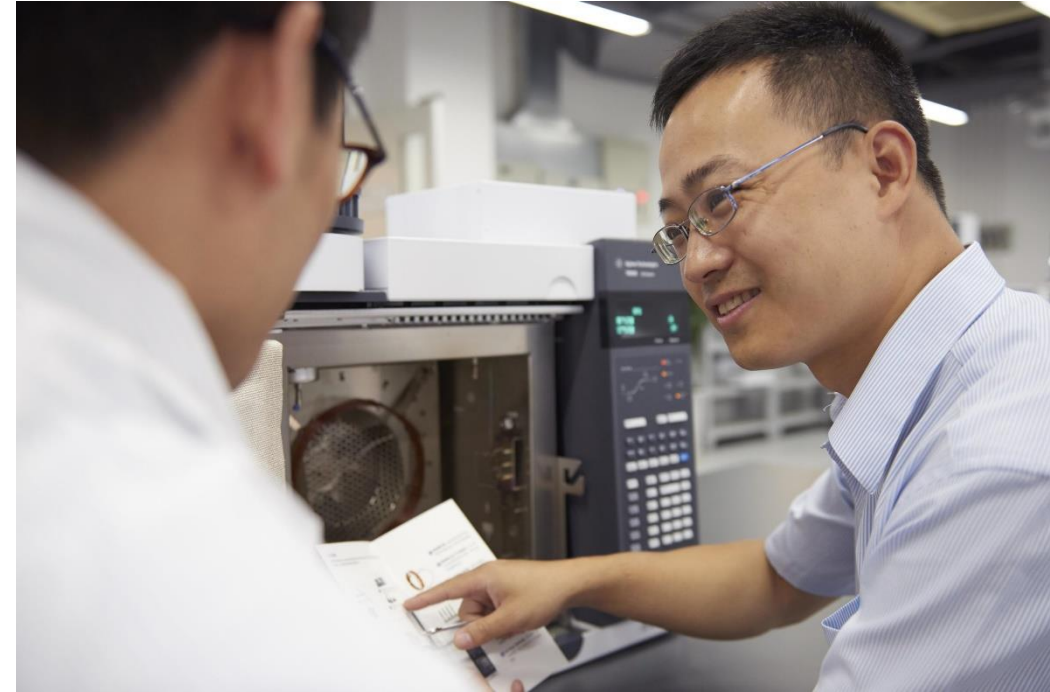
$$C_G = \frac{W_G}{V_G}$$

$$W_S + W_G = W_0$$

$$C_0 = C_G \left[\frac{K \times V_S}{V_S} + \frac{V_G}{V_S} \right] = C_G (K + \beta)$$

$$C_0 \times V_S = (C_G \times V_G) + (C_S \times V_S) = (C_G \times V_G) + (K \times C_G \times V_S) = C_G \times [K \times V_S + V_G]$$

$$A \propto C_G = \frac{C_0}{K + \beta}$$



Types of Headspace

Static versus dynamic

Dynamic – A continuous gas stream is passed through a sample that then elutes the compounds of interest onto a trap, where they are held and concentrated. At some point in the process, the trap is heated to desorb the analytes of interest onto the column to be chromatographed.

- Typically purge and trap
- Headspace trap

Static – The sample is placed into a closed vial, the vial is heated and shaken, and the sample is extracted and injected directly into the GC.

- Loop system
- Syringe
- Pressure balance

Why Headspace?

Offers clean injections into GC systems

- Less maintenance – only the volatile vapors are injected into the system

Less sample preparation

Ideal for analysis of volatile analytes in matrices that can't be directly injected into the GC.

*Not suitable for some applications

Types of Static Headspace Autosamplers

Gas tight syringes

- Not a 'true' closed system. A small amount of sample can be lost as the syringe moves from the vial to the inlet.

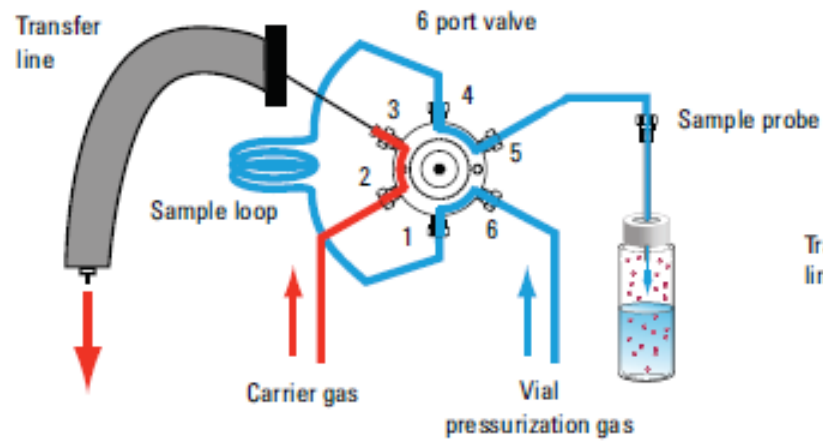
Balanced pressure

- The sample volume injection is regulated by time. Vial pressure is depressurized onto the column. The amount of sample injected is controlled by injection duration.

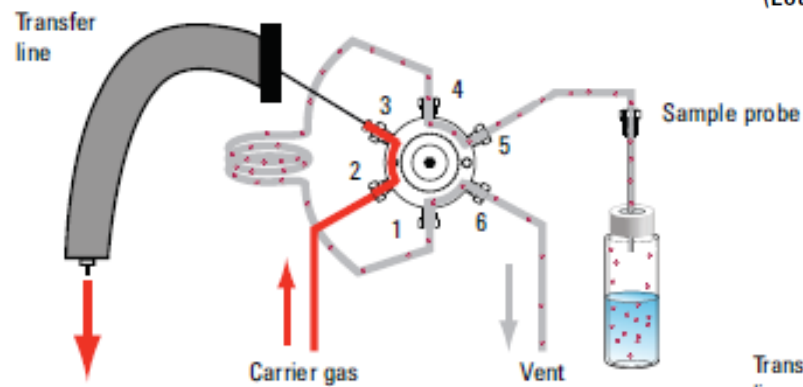
Pressure/loop systems

- Fixed loop size determines injected volume. The metal surface area is greater in the loop system.

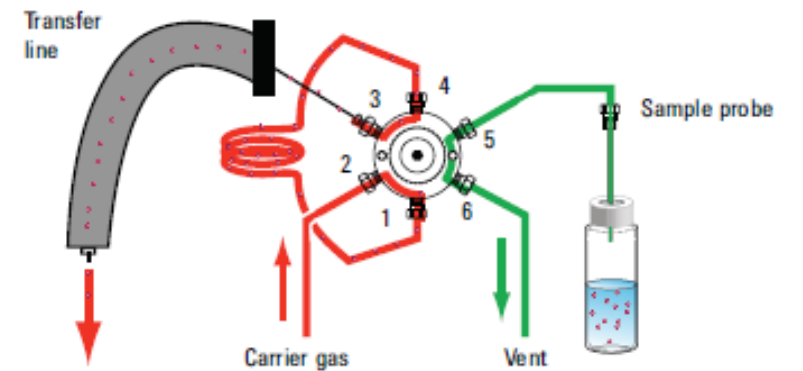
Agilent 7697A Loop System



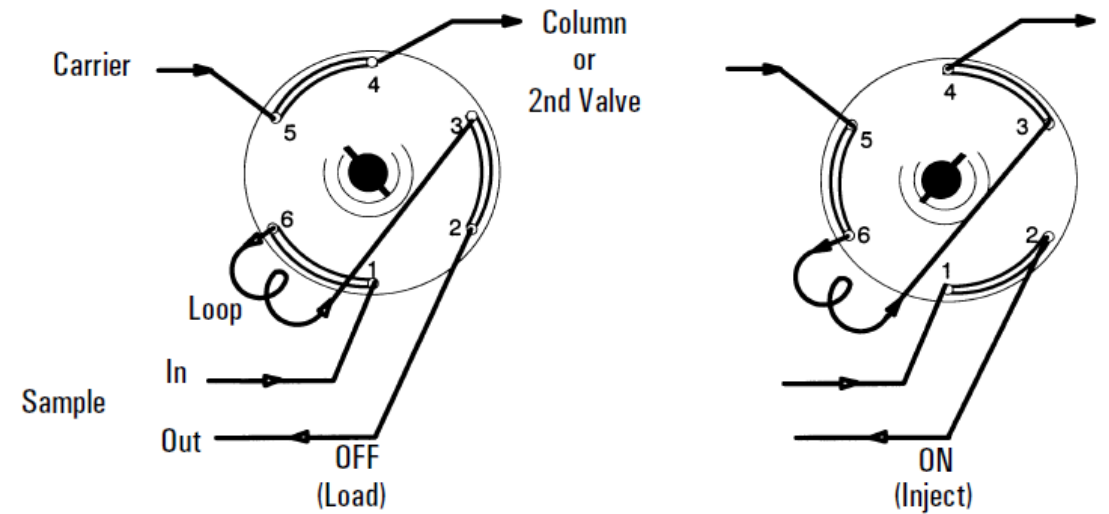
Vial pressurization



Loop fill



Injection



What Should We Focus On?

Partition coefficient: $K = \frac{C_s}{C_g}$

The smaller the “ K ”, the greater the concentration of the analyte in the gas phase.

Like dissolves like. The greater the solubility or affinity that an analyte has for the matrix, the larger the K .

What drives K ?

What Drives K ?

Temperature:

- Higher temperatures drive K down

Solubility:

- Add salt
- Add another solvent to the matrix

What Parameters Drive Success?

Incubation temperature

- Typically 20 °C below the solvent BP

Incubation time

Shaking

Efficient transfer of the sample from the vial to the column

Use of salts

Things to Consider

- You will need to have at least 5 mL of headspace in the vial.
- Keep the incubation temperature 10 to 20 °C below the BP of the solvent/matrix.
- Long incubation times 'generally' only delay the first sample.
- Higher split ratios help get the sample onto the column more efficiently; this results in sharper peaks.
 - Lower splits are 'OK' with larger id columns. Higher volumetric flow transfers sample faster.
- Shake, but try to keep the sample from touching the vial septum.
 - Sample can get into the sample probe and contaminate the loop
- Think about the temperature limitation of vial septa
 - Be considerate of sample/analyte degradation

Headspace Parameters

Temperatures

- Oven
- Sample loop
- Transfer line
- Transfer line interface

Times

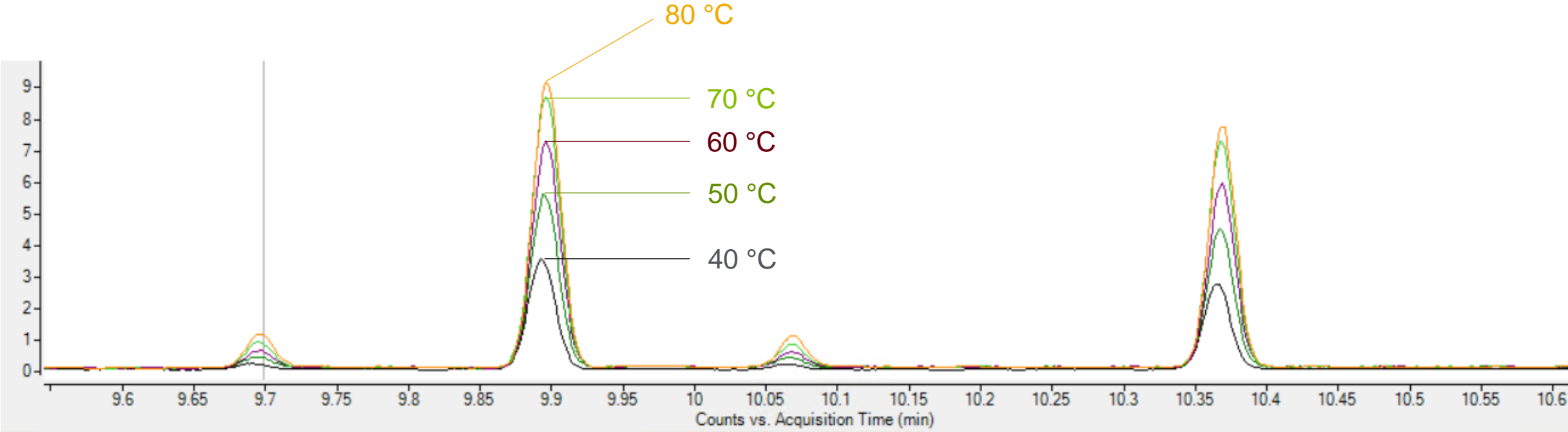
- Vial equilibration
- Injection duration
- GC cycle time

Vial and loop

- Vial size
- Shake vials while in oven
- Vial fill mode
- Loop fill mode

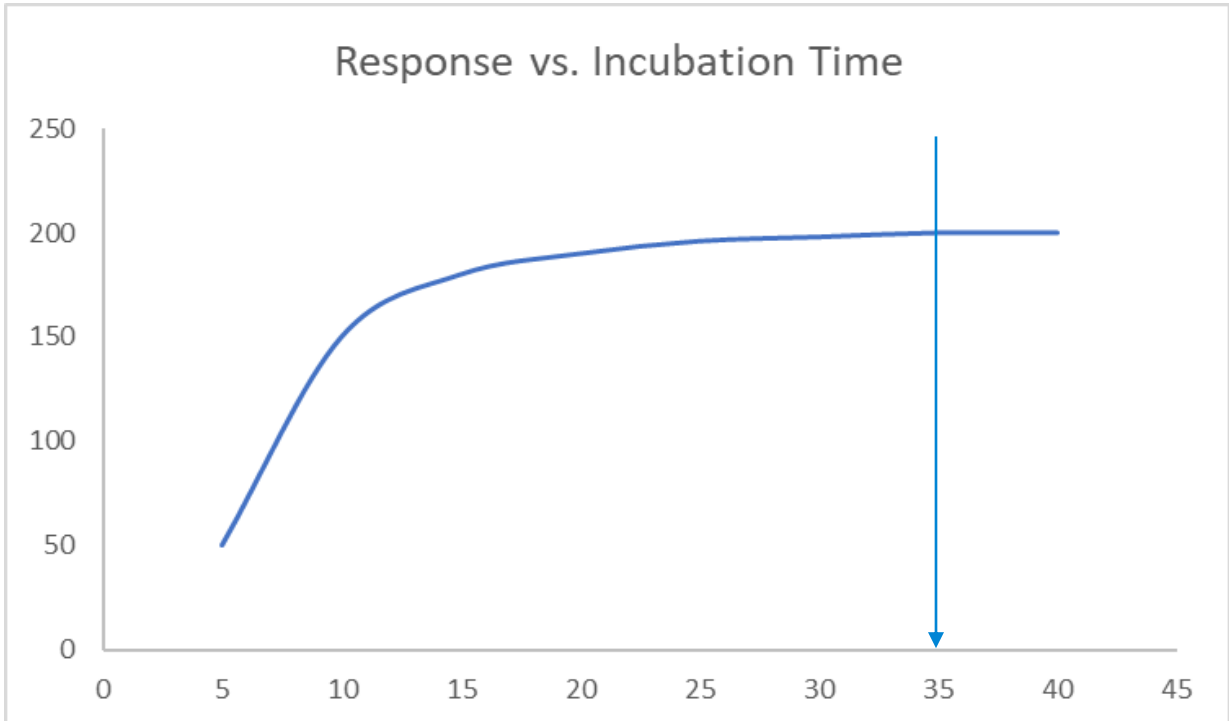
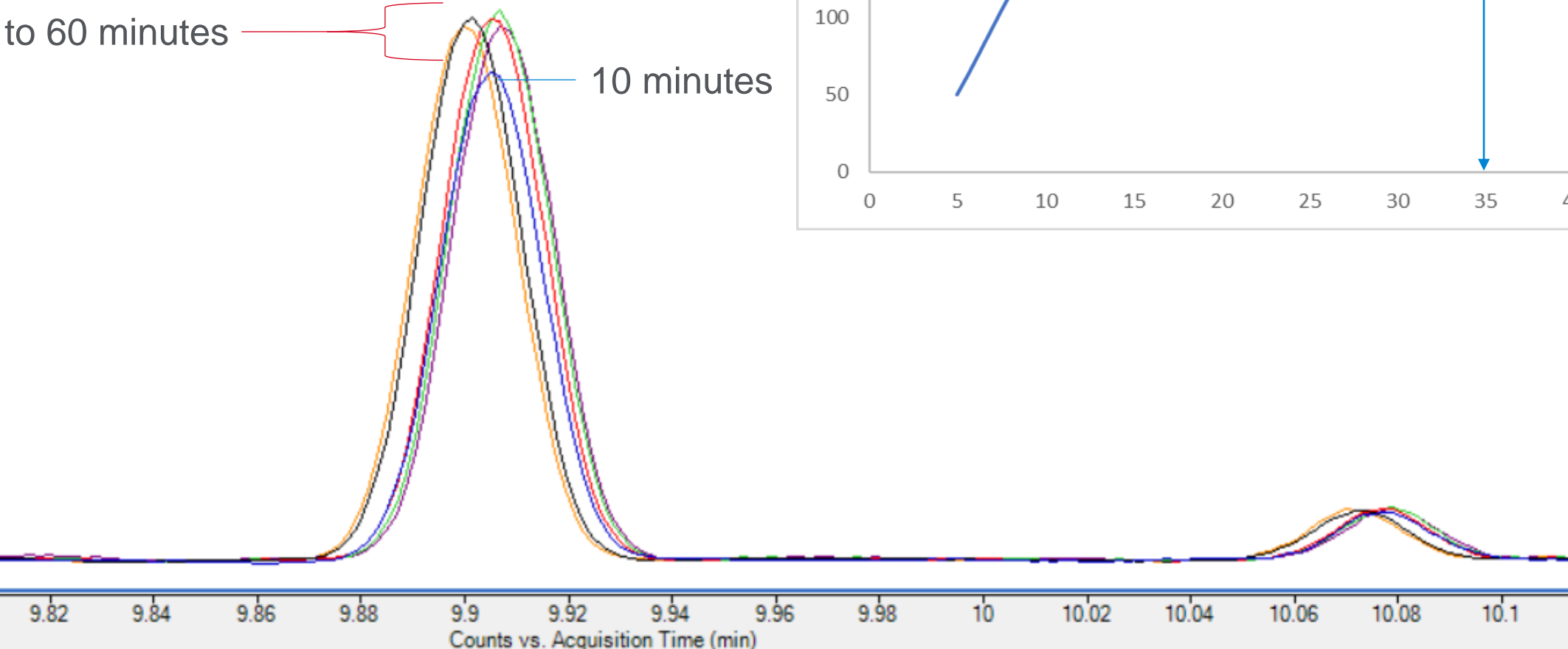
Incubation Temperature Increase

20 minutes
K decreases with T
Not equal for all analytes



Incubation Time

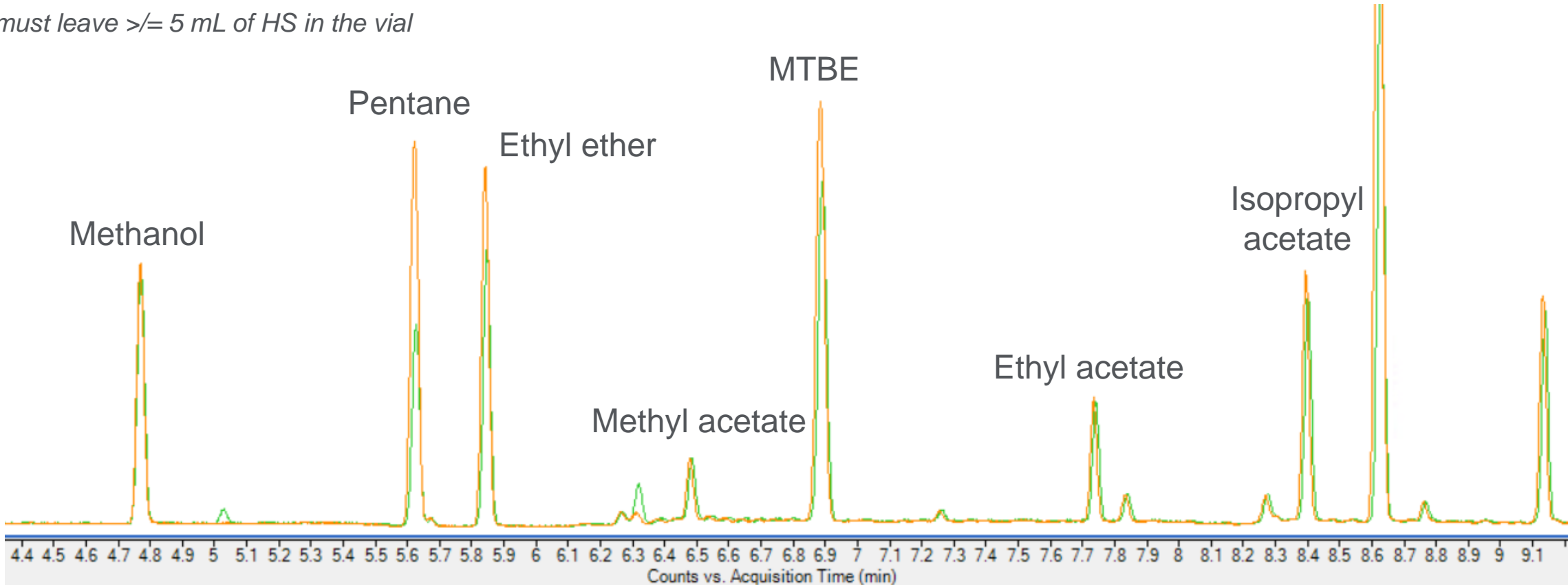
20 to 60 minutes
10 minutes



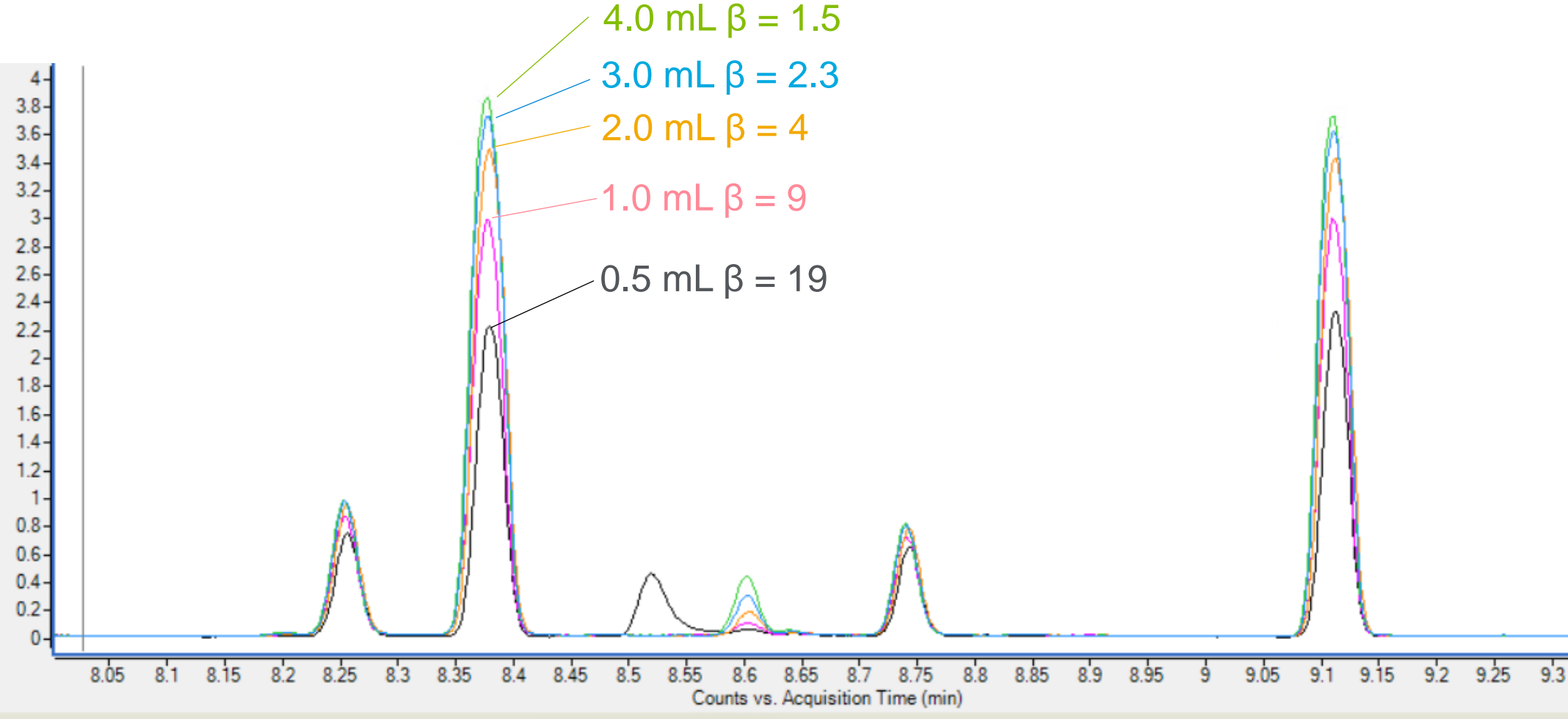
Change in Vial Size

4 mL sample, changing β^*
10 mL vial $\beta = 1.5$ (6 mL HS)
20 mL vial $\beta = 4$ (16 mL HS)

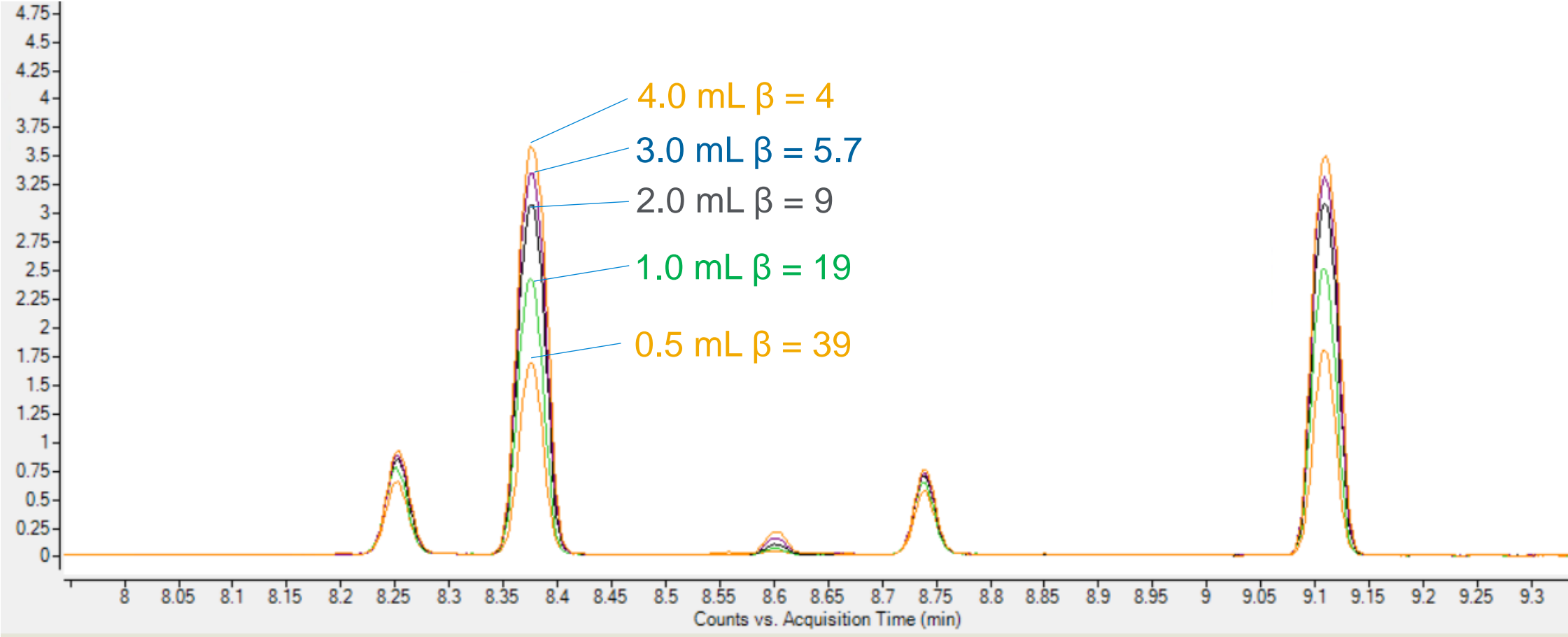
**must leave ≥ 5 mL of HS in the vial*



Change in Sample Volume in a 10 mL Vial



Change in Sample Volume in a 20 mL Vial



What Else Can Affect Signal?

Loop size

Loop pressure

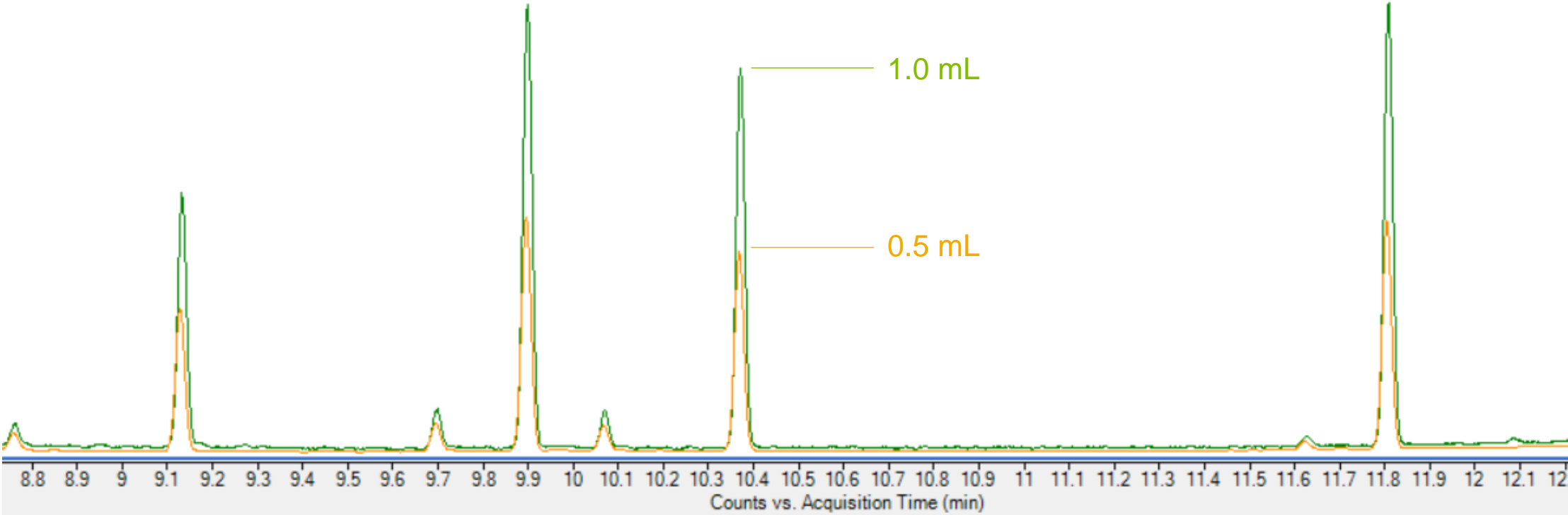
Split ratio

Liner type

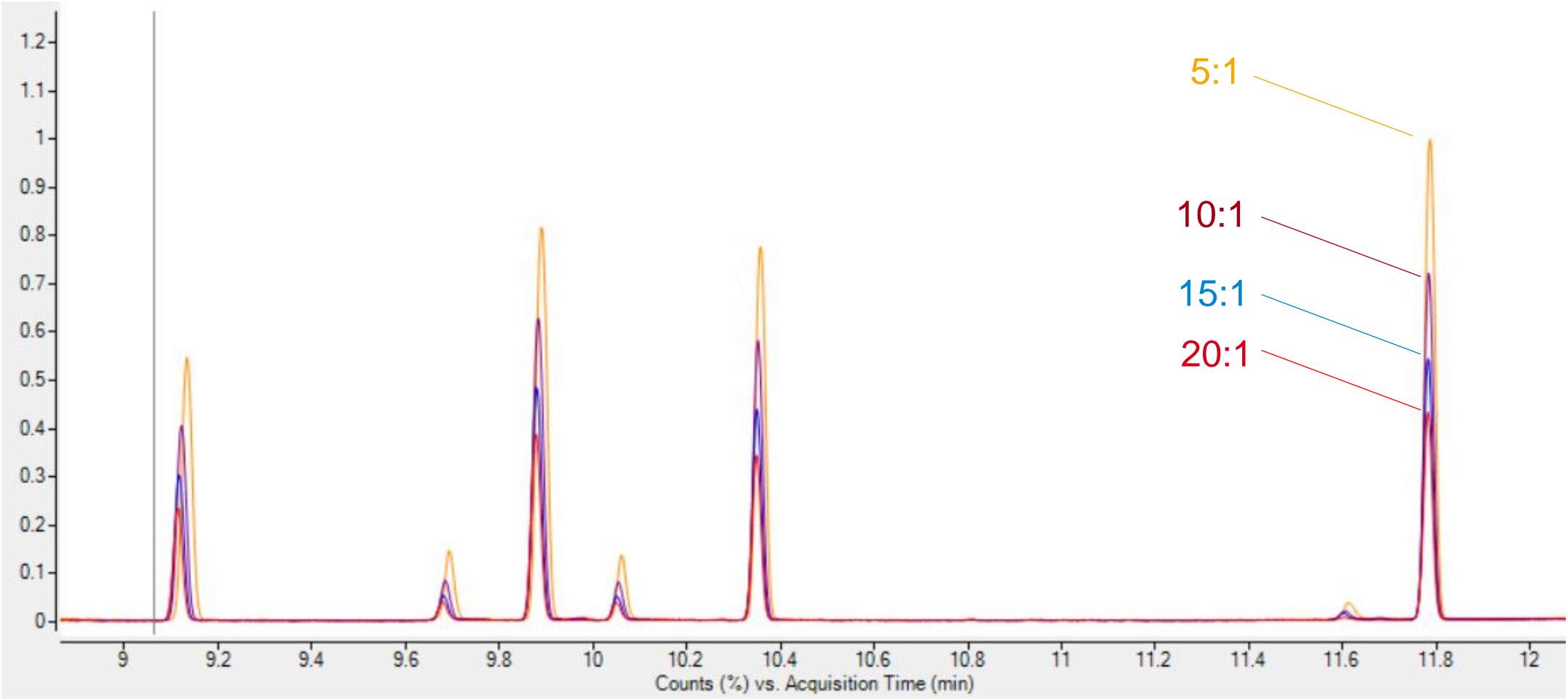
Using salt

Change in Loop Size

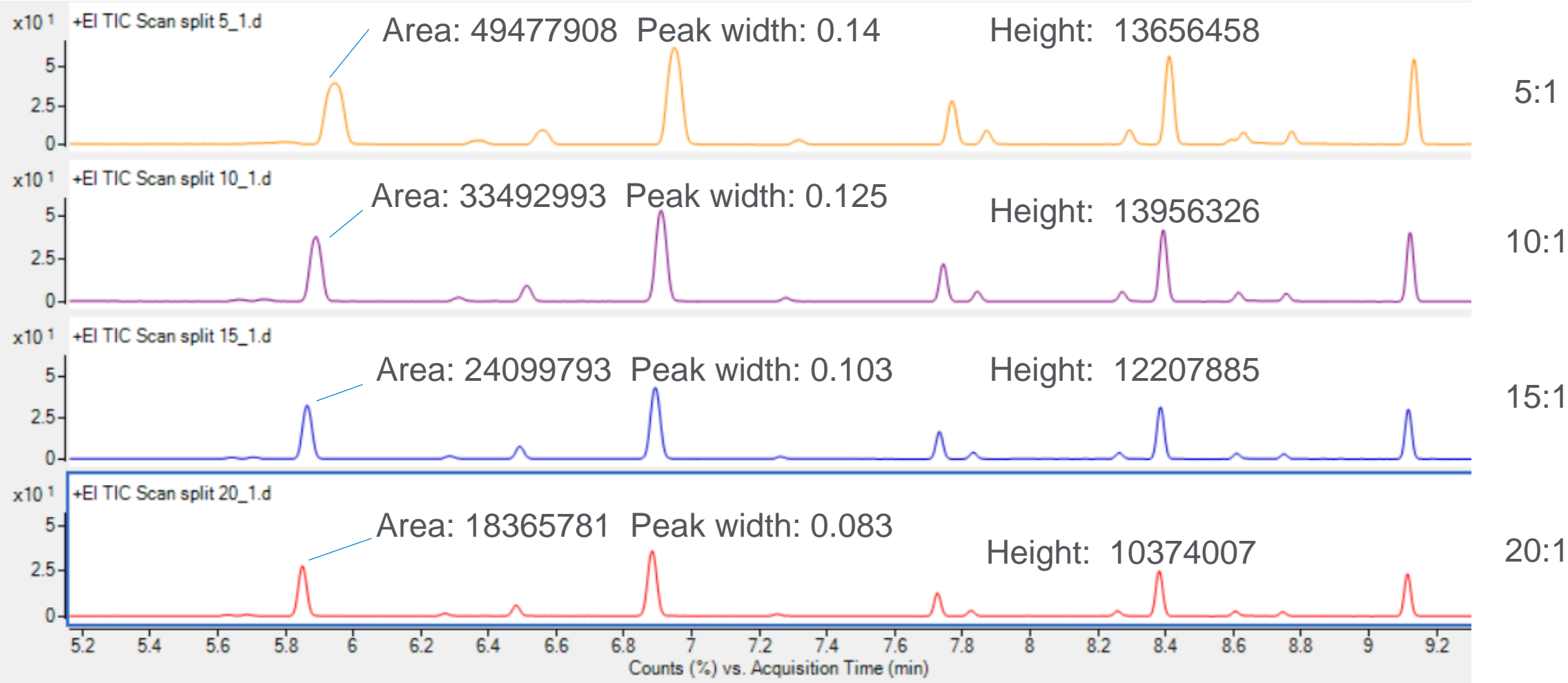
40:1 split (64 mL/min)



Change in Split Ratio



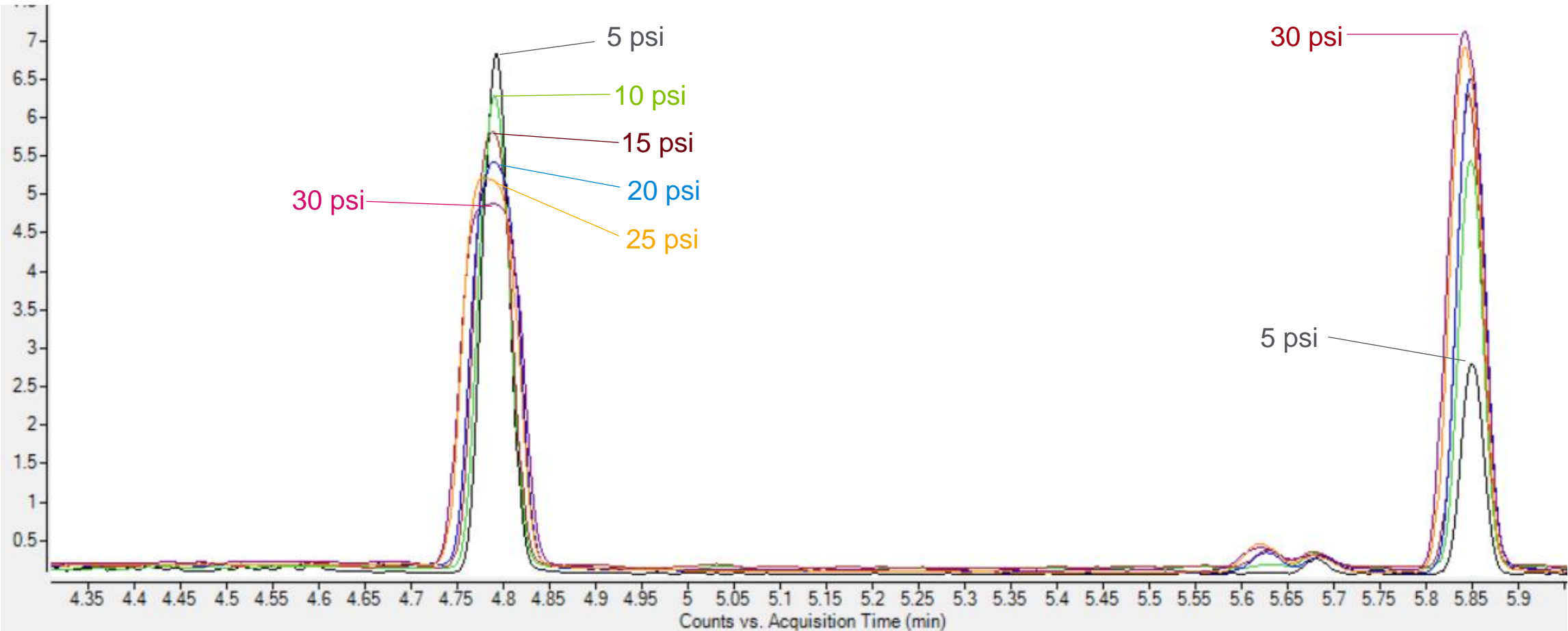
Change in Split Ratio



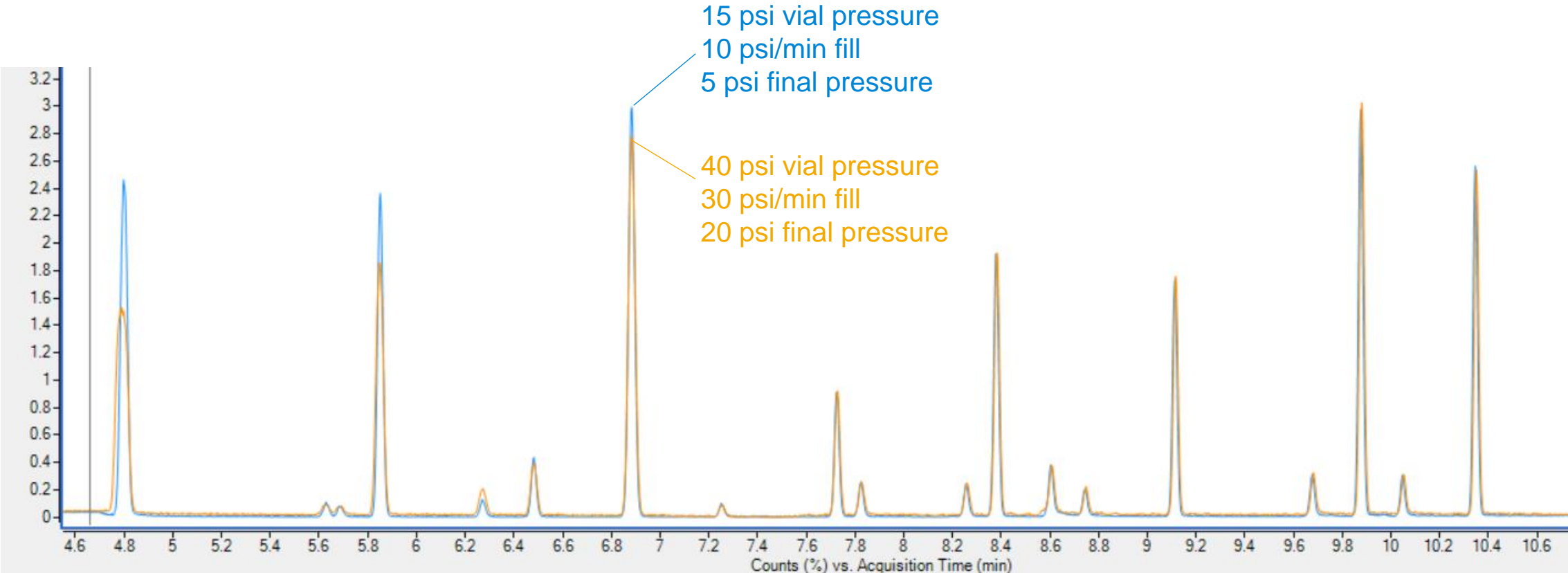
Change in Loop Pressure

First two eluting peaks

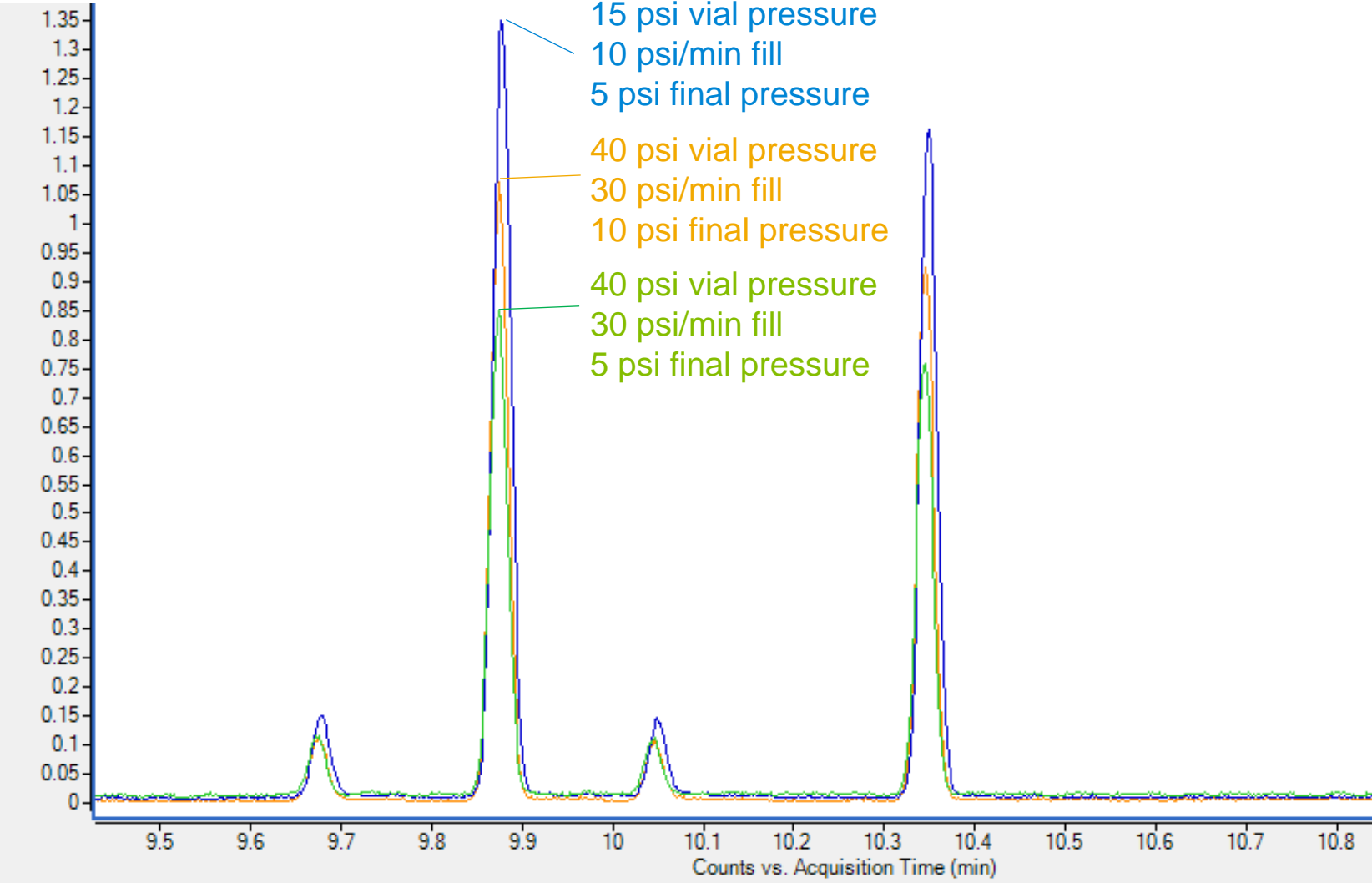
Vial fill pressure: 40 psi
Loop fill rate: 30 psi/min
Inlet pressure: 28.3 psi



Is That a Good Way to Increase Signal?

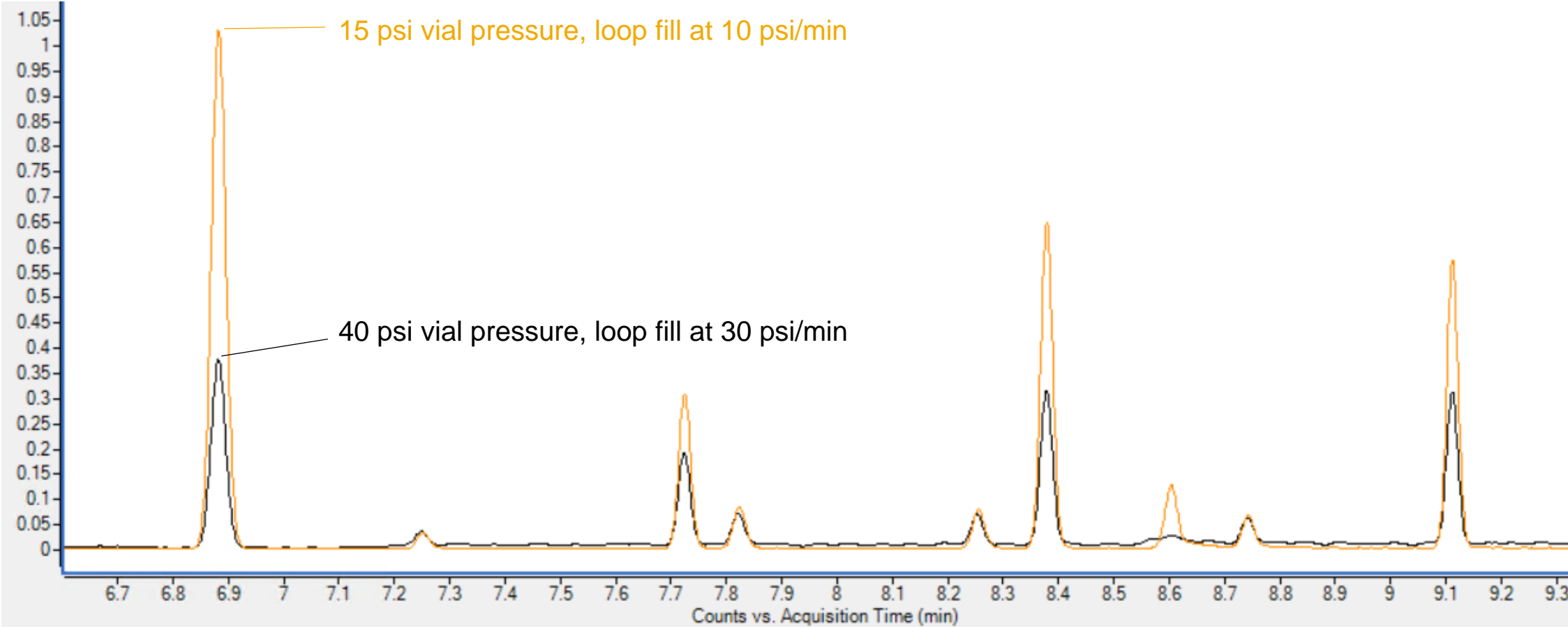


The Effect of Vial Pressure, Loop Pressure, and Fill Rate

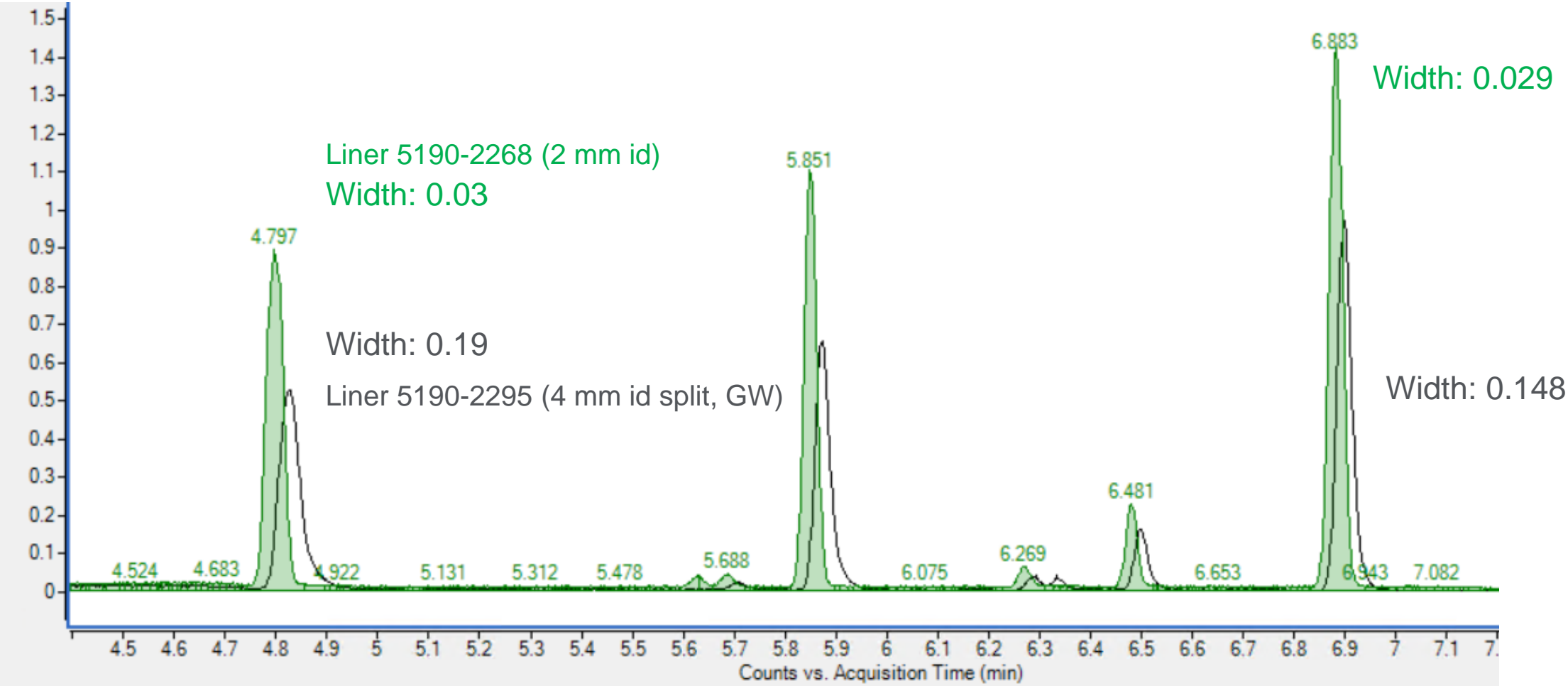


Changing Vial Pressure

5 psi final loop pressure



Liner Size and Type



Use of Salts

Decreases the solubility of polar analytes in aqueous samples

Decreases K , favoring the gas (headspace) phase

Potassium carbonate (K_2CO_3)

Ammonium chloride (NH_4Cl)

Ammonium sulfate ($(NH_4)_2SO_4$)

Sodium chloride ($NaCl$)

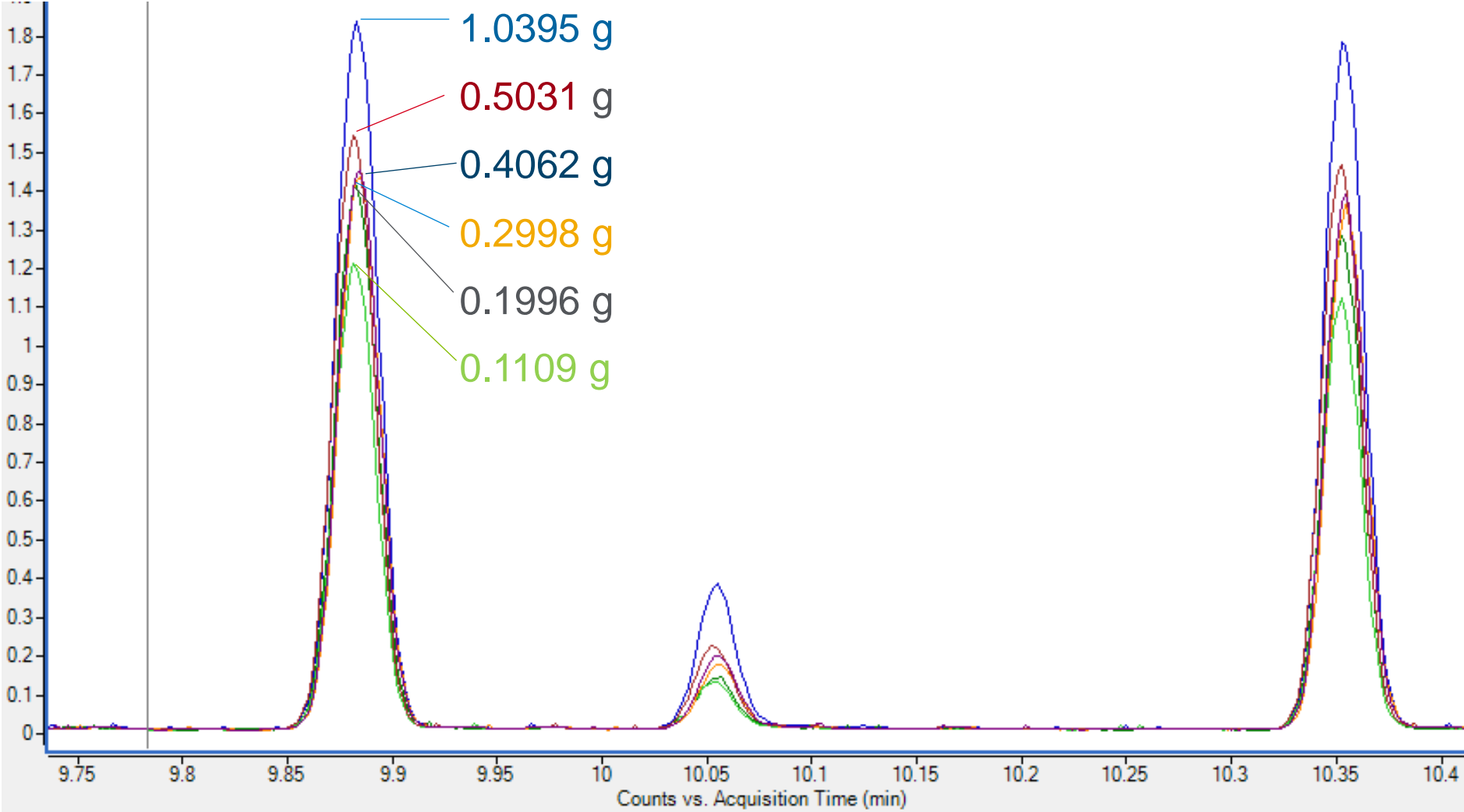
Sodium citrate ($Na_3C_6H_5O_7$)

Sodium sulfate (Na_2SO_4)

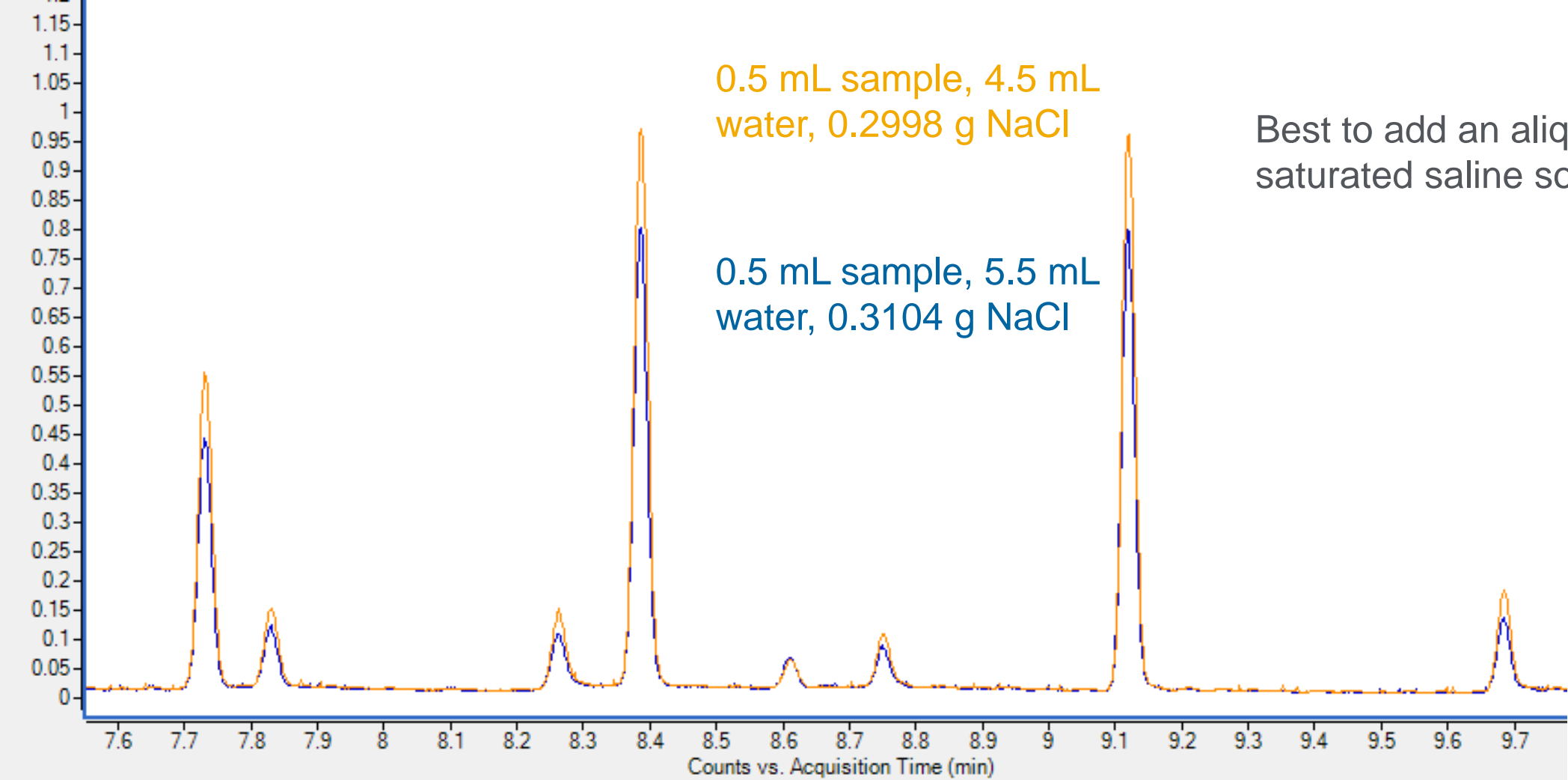
Use high quality, low impurity salts

How Much Salt Do I Add?

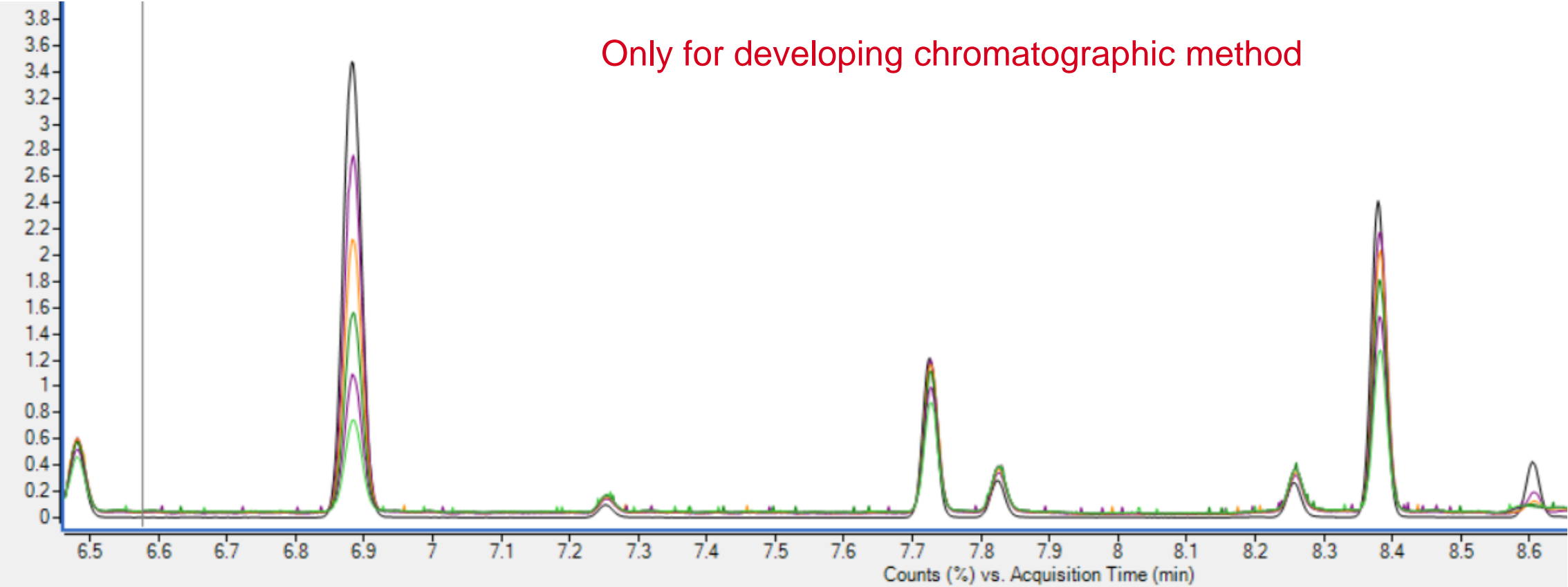
20 mL vial
80 °C oven temperature
20-minute incubation



Change in Matrix Volume with Salt



Can I Inject Multiple Times?



Headspace of Solid Matrices


Samples are ground to increase surface area


They are used for solvents in plastics or polymers


When a matrix match is not available, MHE – “multiple headspace extraction” is used


“Multiple Headspace Extraction for the Quantitative Determination of Residual Monomer and Solvents in Polystyrene” 5991-0974EN


Method Development Tools


 Edit Method Parameters


 Temperatures


 Times

 Vial and Loop

 Carrier

 Advanced Functions

 Sequence Actions

 Method Development

 Create method based on a specific application Convert an existing valve and loop Headspace method Convert an existing pressure transfer Headspace method

Standalone HS Method Development Viewer

Agilent 7697A Method Development Viewer

Time (min) for Headspace method **Total method run time: 40.63 min**

The chart displays a horizontal timeline from -12.50 to 18.75 minutes. A yellow bar labeled 'Vial Equilibration' spans from -12.50 to 0.00 minutes. A grey bar labeled 'GC Cycle' spans from 0.00 to 18.75 minutes. A tooltip for the GC Cycle indicates a run time of 25 minutes starting at 0 minutes.

Temperatures Times Vial and Loop Carrier Advanced Functions Sequence Actions **Method Development**

Method Development

Manual

Would you like to increment a method setting over subsequent runs?

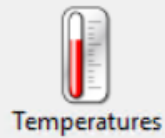
Assisted

- Convert an existing valve and loop Headspace method
- Convert an existing pressure transfer Headspace method

Export Print Exit

Method Development Tool

Edit Method Parameters



Temperatures



Times



Vial and Loop



Carrier



Advanced Functions



Sequence Actions



Method Development

Method Development

Manual

Would you like to increment a method setting over subsequent runs?

Temperature
None
Temperature
Vial Equilibration
Shaking

Temperature increment:

Maximum oven temperature:

Choose your setpoints

Choose what you want to increment

Assisted

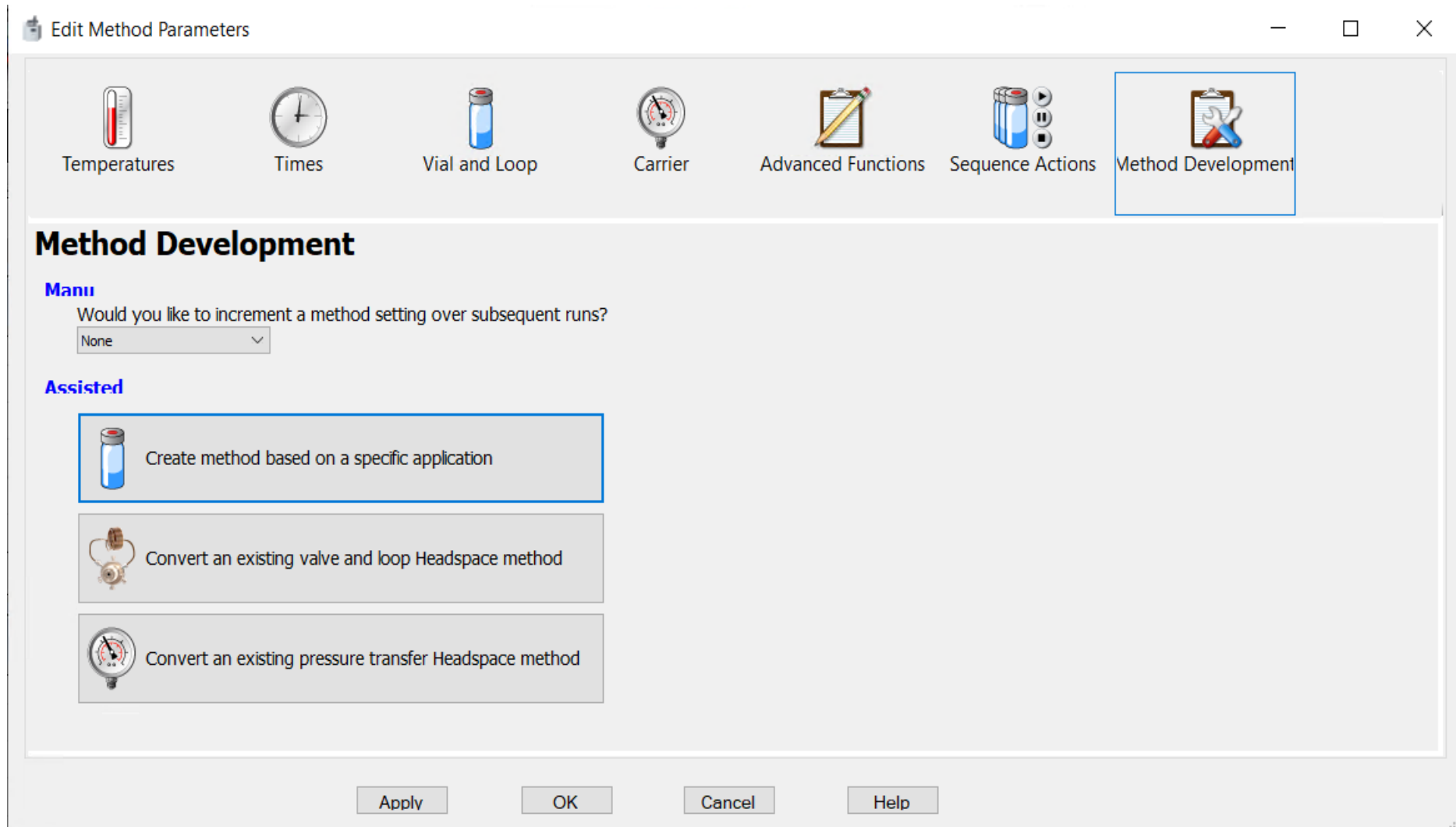


Create method based on a specific application

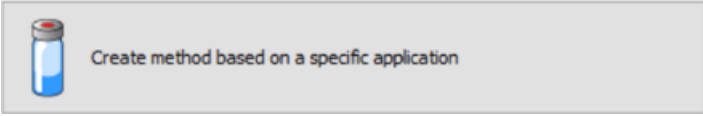


Convert an existing valve and loop Headspace method

Method Development Tool



Method Development Tools



Create method based on a specific application [X]

Sample Matrix

Matrix Type: Liquid Solid

Vial Size: 20 mL [v]

Sample Volume: 2 mL [input]

Solvent

Solvent: Hexadecane [v]

Boiling Point: 287 °C

Compound(s) of Interest

Highest Boiling Point: 160 °C [input]

Create Method Based on Specific Application

Red parameters are what will be change from the initial method.

Green parameters are the new settings.


Confirm method changes


Original Method	Modified Method
Temperature Settings:	Temperature Settings:
<i>Oven Temperature (°C):</i> 80	<i>Oven Temperature (°C):</i> 145
<i>Loop Temperature (°C):</i> 85	<i>Loop Temperature (°C):</i> 145
<i>Transfer Line Temperature (°C):</i> 120	<i>Transfer Line Temperature (°C):</i> 160
Timing Settings:	Timing Settings:
<i>Vial Equilibration (min):</i> 20.00	<i>Vial Equilibration (min):</i> 30.00
<i>Injection Duration (min):</i> 1.00	<i>Injection Duration (min):</i> 0.50
<i>GC Cycle Time (min):</i> 20.00	<i>GC Cycle Time (min):</i> 25.00
Vial and Loop Settings:	Vial and Loop Settings:
Vial Size: 20	Vial Size: 20
<i>Vial Shaking:</i> Level 3, 36 shakes/min <i>with acceleration of 125 cm/s²</i>	<i>Vial Shaking:</i> Level 1, 18 shakes/min <i>with acceleration of 60 cm/s²</i>
Fill Mode: Default	Fill Mode: Default
<i>Fill Pressure (psi):</i> 40	<i>Fill Pressure (psi):</i> 15
Loop Fill Mode: Custom	Loop Fill Mode: Custom
<i>Loop Ramp Rate (psi/min):</i> 30	<i>Loop Ramp Rate (psi/min):</i> 20
<i>Loop Final Pressure (psi):</i> 30	<i>Loop Final Pressure (psi):</i> 9
Loop Equilibration Time: 0.05	Loop Equilibration Time: 0.05
Carrier Settings:	Carrier Settings:
Carrier Control Mode: GC controls Carrier	Carrier Control Mode: GC controls Carrier
Advanced Settings:	Advanced Settings:
Extraction Mode: Single Extraction	Extraction Mode: Single Extraction
Vent After Extraction: ON	Vent After Extraction: ON
Post Injection Purge: Default, 100 mL/min for 1 min	Post Injection Purge: Default, 100 mL/min for 1 min
Acceptable Leak Check: Default, 0.2mL/min	Acceptable Leak Check: Default, 0.2mL/min
Sequence Actions:	Sequence Actions:
Vial Missing:: Skip	Vial Missing:: Skip
Wrong Vial Size: Continue	Wrong Vial Size: Continue
Leak Detected: Continue	Leak Detected: Continue
System Not Ready: Abort	System Not Ready: Abort

Print Accept Reject Help

Convert an Existing Pressure Transfer Method

Convert an existing pressure transfer Headspace method ✕

Temperatures		Timing	
	Setpoint		Setpoint
<input checked="" type="checkbox"/> Oven Thermostatting	80 °C	 GC Cycle	25 min
<input checked="" type="checkbox"/> Needle	80 °C	Thermostatting	15 min
<input checked="" type="checkbox"/> Transfer Line	120 °C	Pressurization	0.2 min
		Withdrawal	0.5 min
		Pre/Post Cryofocusing	0 min
		Inject	0.5 min

Pressure		Other Settings	
	Expected Value		
Carrier	28 psi	 Shaker	On ▾
Vial	15 psi		

[Preview Changes](#) [Cancel](#) [Help](#)

Convert an Existing Pressure Transfer Method

X

Confirm method changes

Original Method	Modified Method
Temperature Settings: Oven Thermostating Temperature (°C): 80 Needle Temperature (°C): 80 Transfer Line Temperature (°C): 120	Temperature Settings: Oven Temperature (°C): 80 Loop Temperature (°C): 80 Transfer Line Temperature (°C): 120
Timing Settings: GC Cycle Time (min): 25.00 Thermostating Time (min): 15.00 Pressurization Time (min): 0.20 Withdrawal Time (min): 0.50 Pre/Post Cryofocusing Time (min): 0.00 Injection Duration (min): 0.50	Timing Settings: Vial Equilibration (min): 15.00 Injection Duration (min): 0.50 GC Cycle Time (min): 25.00
Pressure Settings: Carrier (psi): 28 Vial (psi): 15	Vial and Loop Settings: Vial Size: 20 Vial Shaking: Level 5, 71 shakes/min with acceleration of 260 cm/s ² Fill Mode: Default Fill Pressure (psi): 15 Loop Fill Mode: Default
Advanced Settings: Vial Shaking: ON	Carrier Settings: Carrier Control Mode: GC controls Carrier
	Advanced Settings: Extraction Mode: Single Extraction Vent After Extraction: ON Post Injection Purge: Default, 100 mL/min for 1 min Acceptable Leak Check: Default, 0.2mL/min
	Sequence Actions: Vial Missing: Skip Wrong Vial Size: Continue Leak Detected: Continue System Not Ready: Abort

Print
Accept
Reject
Help

Common Issues

Carryover/contamination

- Too much sample in the vial
- Shaking is set too high
- Sample condensing in the loop

Contaminates the probe and loop

Septum or caps blowing off

- Oven temperature is too high creating too much pressure in the vial

High %RSD

- Vial leaks. Check vial crimping. Sequence actions and logbook.
- Condensation in the flow path.
- Check temperatures.
- Vial equilibration time too short

Can run leak check

Sequence makes it through first sample only

- GC cycle time is too short. Check sequence actions and logbook.

Change the Loop Purge Time and Flow

Carryover issues

Temperatures Times Vial and Loop Carrier **Advanced Functions** Sequence Actions Method Development

Advanced Functions

Extraction Mode

Single extraction Multiple extractions Concentrated extractions

Venting and Purging

Vent vial pressure after extraction

Post-injection purge: Purge flow: 100 mL/min Purge time: 1 min

Dynamic Leak Checking

Acceptable leak rate: Leak flow: 0.2 mL/min

Barcoding of Vials

Barcode symbology:

Vial barcodes include checksum

Vial Leaks

Temperatures Times Vial and Loop Carrier Advanced Functions Sequence Actions Method Development

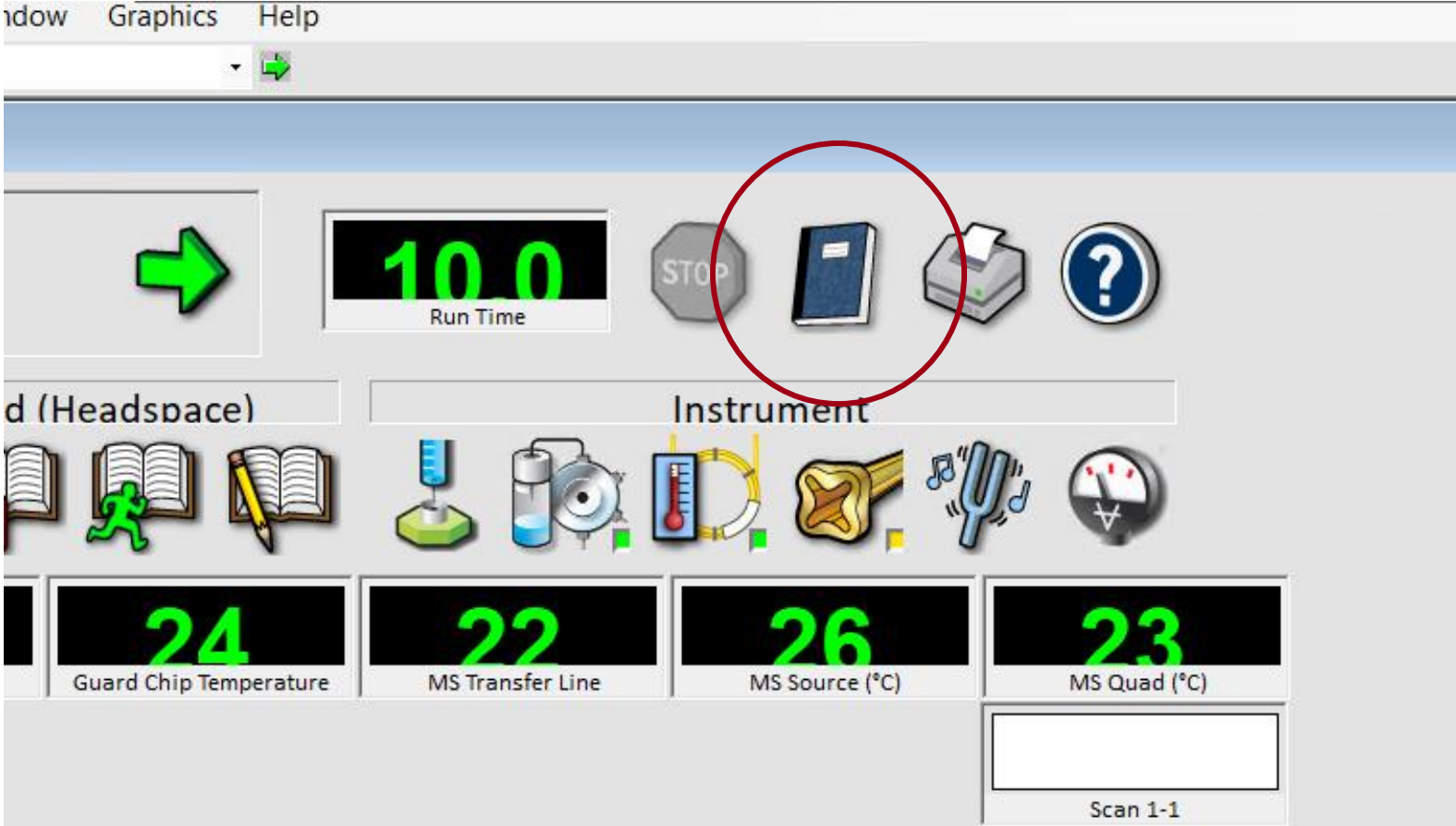
Sequence Actions

What should the sequence do if it encounters the following:

Vial Missing	Wrong Vial Size	Leak Detected	System Not Ready	Wrong Cooling Plate Temp
Skip	Continue	Continue	Abort	Continue

The system always logs detected issues and the action taken.

Logbook is in the Instrument Control Screen



Starting Parameters

Temperatures

- Oven **20 °C** below the BP of the matrix
- Sample loop **Same temp as oven**
- Transfer line **Hot enough not to have anything condense**
- Transfer line interface **Same as inlet**

Times

- Vial equilibration **10 minutes, but use method development**
- Injection duration **0.5 minutes**
- GC cycle time **Run time + cool down to ready**

Vial and Loop

- Vial size **20 mL**
- Shake vials while in oven **3 (low)**
- Vial fill mode **Default 15 psi**
- Loop fill mode **Default**

Types of Vials

Flat Bottom

Round Bottom
More ideal for certain autosamplers
(i.e. CTC/PAL)



5182-0838



5182-0837



5188-2753



5067-0226



5183-4474



5190-2239



Consumables



Good for SPME
8010-0139
(thinner septum)



Safety cap
(5183-4478)
Tears at 45 psi



Max temp 125 °C
Butyl/PTFE (5183-4479)



Max temp 180 °C
silicone/PTFE (5183-4477)

High-Performance Septa

Max temperature 300 °C

Reduced siloxane interferences at high temperature



8010-0428



5190-3987*

*High-power crimpers are required for steel crimp caps

A-line High-Power Crimper



- 5191-5624 (High Powered crimper with 20 mm jaw set)
- 5190-4062 (11 mm crimper jaws)
- 5190-4063 (11 mm de-capper jaws)
- 5191-5617 (Tool only + power supply; no jaws)



5190-4066 Base

<https://www.agilent.com/cs/library/usermanuals/public/manual-A-Line-crimper-high-power-5191-5627-en-agilent.pdf>

A-line Crimpers



5191-5615



5040-4669

How Tight is Right?



Good crimp



Too tight

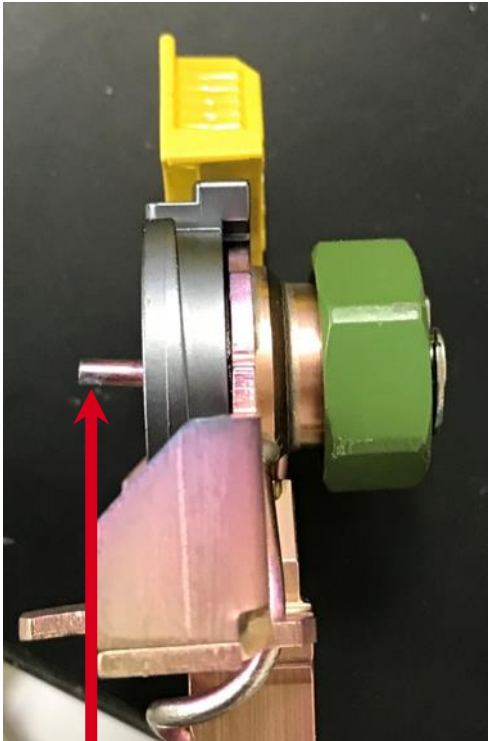
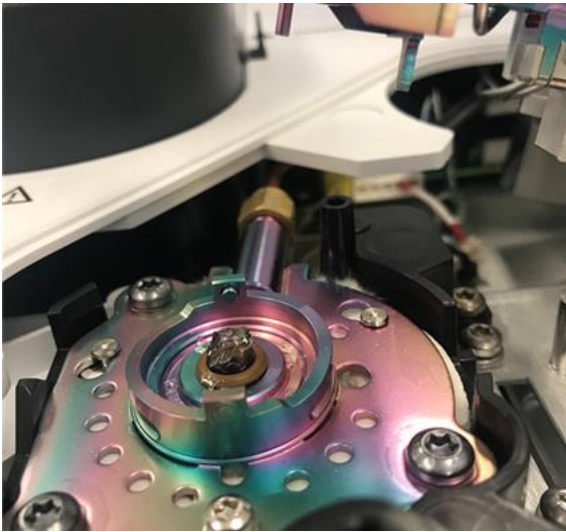
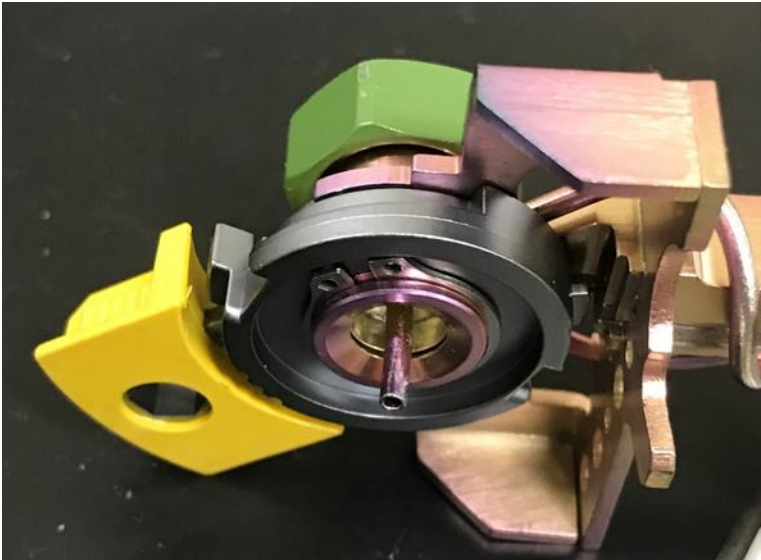


Too loose

Common Issues

Installation of liner

- 2 mm liner is ideal for HS applications for narrower peaks
- Standard 2 mm liner is too small to accept
- 5190-6168 has slightly large ID, but still a tight fit



Bent

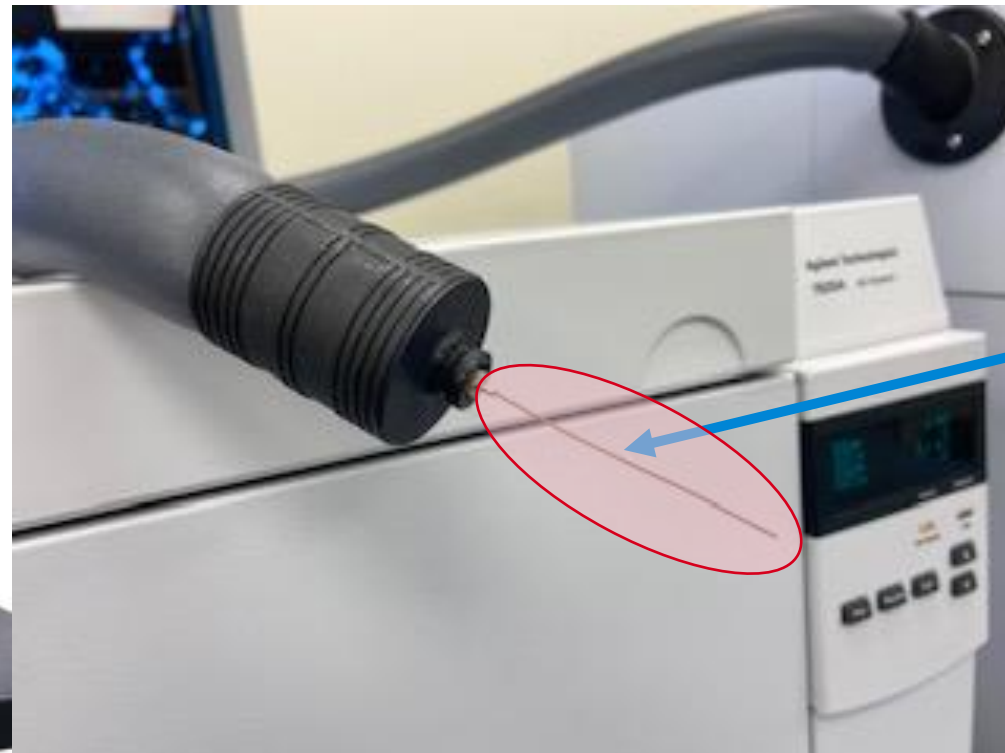
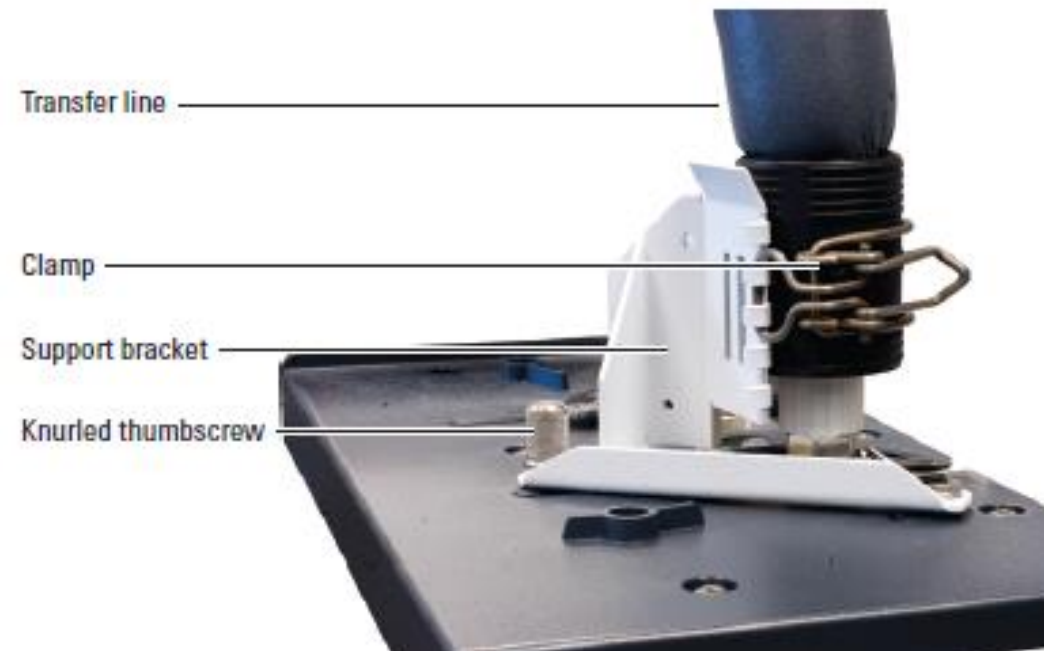
Common Confusion

Terminology

- Sample probe/needle
 - This is on the HS itself and probes the HS vial
- Transfer line “needle”
 - For 7697 and newer transfer line itself is the “needle”
 - No such needle when transfer line is plumbed laterally to the inlet



Figure 79 Sample Probe



This is not a needle but an extension of the fused silica xfer line that is inserted through the inlet septum

Sleeve for Pro-Steel Transfer Line

ProSteel Transfer Line Sleeve (4177-0607)

If you intend to use ProSteel and plan to operate the transfer line at temperatures 200 °C and higher, you must use the ProSteel protective sleeve (4177-0607). Without the protective sleeve, the ProSteel can permanently bind to the internal transfer line tubing.



Common Confusion

Terminology

- Sample probe/needle
 - This is in the HS itself and probes the HS vial
- Transfer line “needle”
 - For 7697 and newer transfer line itself is the “needle”
 - No such needle when transfer line is plumbed laterally to the inlet



Figure 79 Sample Probe

Summary

- Stay 10 to 20 °C below the boiling point of the solvent/matrix
- Keep a minimum of 5 mL of headspace in the vial
- Use the Method Development tools
 - Don't forget to turn off the function
- Try to maximize parameters based on compounds with highest K
 - Not every compound responds/reacts the same way
- Use 10 mL vials if appropriate
- Be consistent with crimping vials. Set the crimper properly so that every user is successful.
- When troubleshooting, think about what may or may not be causing the issues you are experiencing.
- Contact technical support

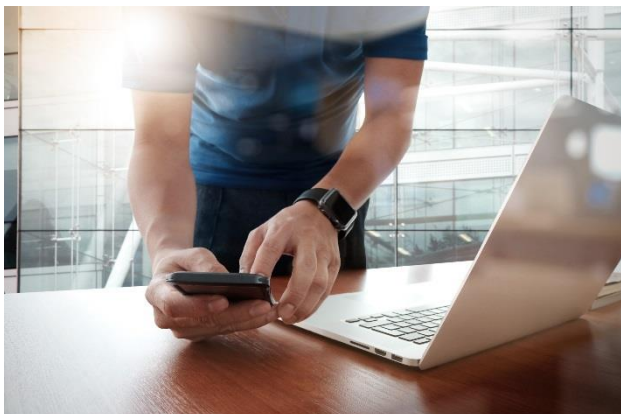
Additional Resources

[7697A Headspace Sampler Troubleshooting \(PDF\)](#) G4556-90018

[7697A Headspace Sampler Advanced Operation \(PDF\)](#) G4556-90016

[Search for 7697A Headspace Sampler on Agilent.com](#)

Contact Agilent Chemistries and Supplies Technical Support



1-800-227-9770 Option 3, Option 3:
Option 1 for GC and GC/MS columns and supplies
Option 2 for LC and LC/MS columns and supplies
Option 3 for sample preparation, filtration, and QuEChERS
Option 4 for spectroscopy supplies
Option 5 for chemical standards
Available in the USA and Canada 8–5, all time zones



gc-column-support@agilent.com
lc-column-support@agilent.com
spp-support@agilent.com
spectro-supplies-support@agilent.com
chem-standards-support@agilent.com