Introduction to GC Method Development

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Q & A

Please submit any questions you have for Kirsty via the questions tab

Avantor Introduction to GC method development

Kirsty Ford

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November 2023

avantor™

Agenda

01

Establish objectives, tools and selectivity

02

Goals of optimizing GC parameters

03

Standard GC method development, split and splitless

04

What is Fast GC

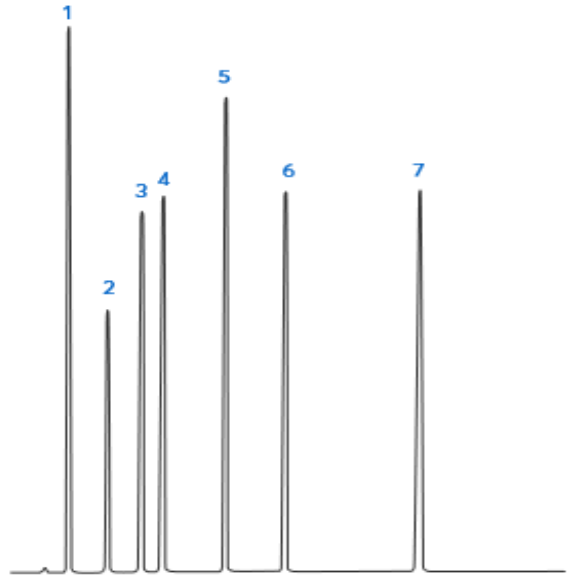
05

Method transfer from standard to Fast GC

Where to start with GC method development

Establish objectives, tools and selectivity

1. Analytes of interest
2. Aim of analysis/Application
3. GC configuration
4. GC column phase
5. Sample mixture



Separation of organophosphate pesticides using the HI-1701 - https://av.cmd2.vwr.com/pub/apl/chrom/main?key=C-12999

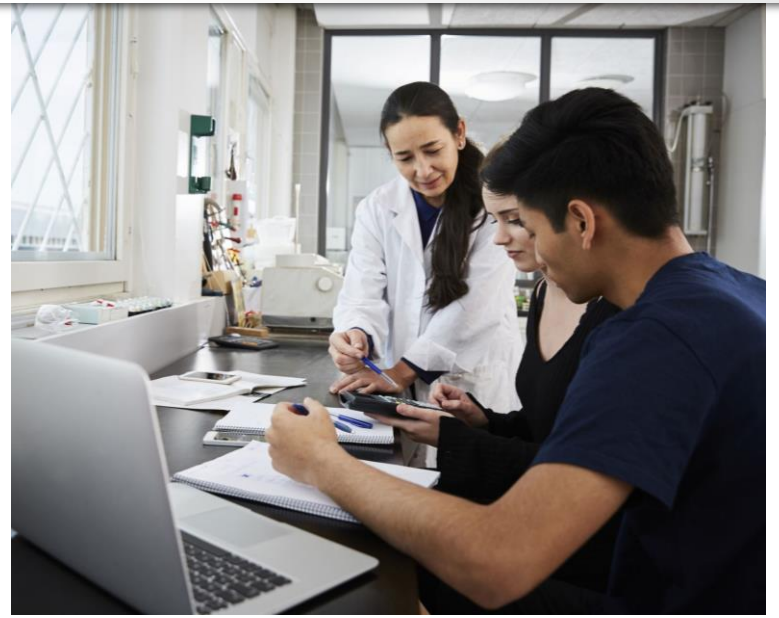
1. Analytes of interest

What are the analytes of interest?

Are they suitable for GC?

What physiochemical properties will influence the GC parameters?

- Analytes of interest



1. Analytes of interest suitable for GC?

Volatiles, semi volatiles & permanent gases = GC

- Low BP (<400 °C)
- Easily vaporised/Volatile
- Low molecular weight (Approx 800 Da)
- Stable at high temp.
- High vapour pressure
- Organic compounds

Non volatiles & volatiles = HPLC

- Usually higher BP, or decomposes before BP
- Soluble in a liquid phase
- Low to high molecular weight (<500,000 Da)
- Denatures at higher temp/stable at lower
- Contains salts, can carry a charge
- Organic and Inorganic compounds

Example - Essential oils

Which is more suitable, GC or HPLC?

1. Analytes of interest suitable for GC?

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- Denatures at higher temp/stable at lower
- Contains salts, can carry a charge
- Organic and Inorganic compounds

Essential oils

- Low BP, approx 100-200°C
- Easily vaporised/Volatile
- MW usually <500 Da
- Thermally stable, decompose >400°C
- High vapour pressure
- Organic compounds
- Soluble in liquid phase

1. Analytes of interest – Physiochemical properties

Properties influence method direction

Polarity – Column phase selection.

Boiling point – Inlet temperature and oven temperature.

Similar or different boiling points of analytes – Column phase selection.

Structural isomers – If separation wanted, mid to high polarity phase required.

Non labile or labile compounds - Labile compounds "Softer" conditions needed, lower initial temperatures.

Sample matrix, clean or dirty – Column dimensions, liner choice, sample prep process.

2. Aim of analysis/Application

What is the analysis to achieve?

What application notes suit the aim of analysis?

Are there application specific columns available?

- Analytes of interest
- Aim of analysis/Application

2. Aim of analysis/Application

What information is required from the results?

- New method or established method?
- Is the analysis of a simple or complex sample?
- Do all analytes need to be detected and separated?
- High level or low-level resolution required?
- Are application notes available?
- What level of sensitivity is required?

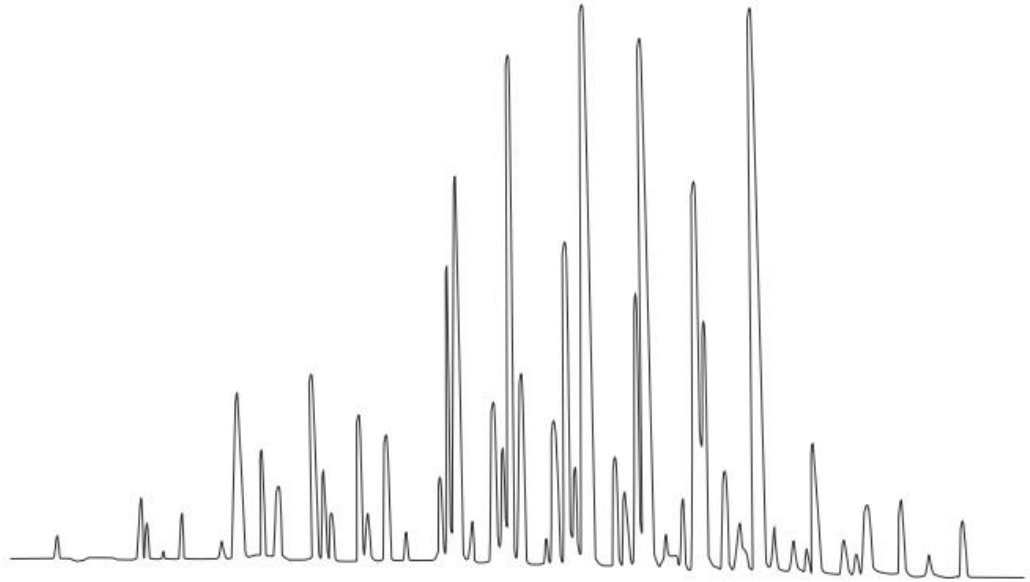

Figure 1: Quick screening of the Aroclor 1254 PCB mixture using the Avantor® Hichrom HI-SE54 phase.

https://av.cmd2.vwr.com/pub/apl/chrom/main?key=C-13114

Drives decisions on products and GC configuration suitability

2. Aim of analysis/Application

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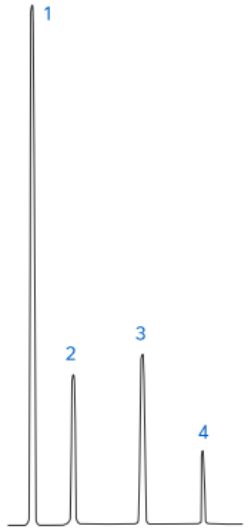


1. Cyclohexane
2. Cycloheptane
3. Cyclooctane
4. n-Decane

Figure 1: Analysis of cyclic hydrocarbons using the Avantor® Hichrom HI-1 phase.

https://av.cmd2.vwr.com/pub/apl/chrom/main?key=C-13098

Drives decisions on products and GC configuration suitability

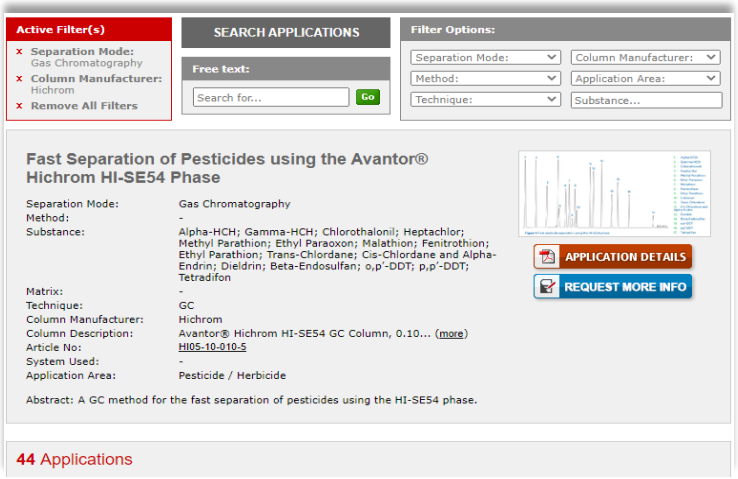
2. Aim of analysis/Application - Monographs

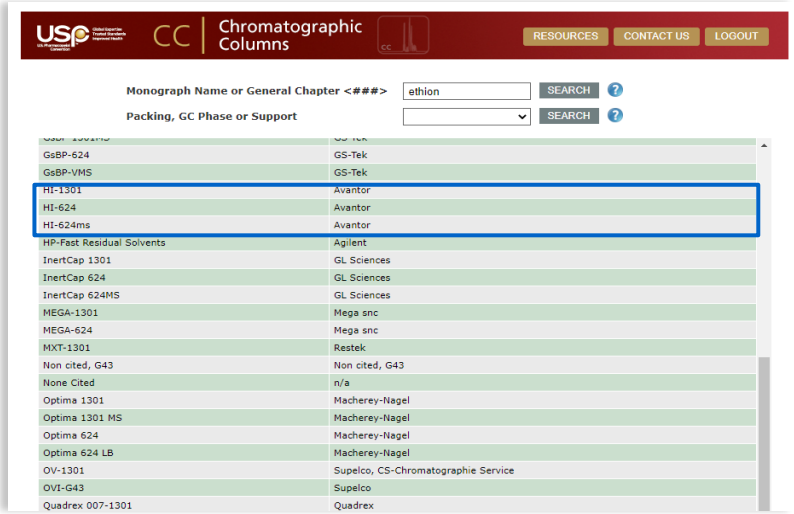
Check available resources -

1. Avantor GC phase document and cross reference document.

2. Check application notes, check what are the trends of columns used - https://uk.vwr.com/cms/chromatography_chrom_library

3. Check similar monograph/analyte or similar monograph of interest in USP databases - https://www.uspchromcolumns.com/





Phase	Functional group	Max. Temp.*	Crossbond	Application areas	Methods
APOLAR					
HI-1	100% Methyl Polysiloxane (100% Dimethylpolysiloxane)	350 °C	Yes	General purpose apolar phase - Solvent impurities, PCBs, Simulated Distillation, drugs, natural gases, hydrocarbons, essential oils, semivolatiles, pesticides, phenols	EPA: 504.1, 505, 551, 606, 612, 8141A/B USP: G1, G2, G9, G38
HI-1 HT	100% Methyl Polysiloxane (100% Dimethylpolysiloxane) - High Temperature	400 °C	Yes	High Molecular Weight Waxes, Motor Oils, Polymers/Plastics, Simulated Distillation	USP: G1, G2, G9, G38
HI-1 MS	100% Methyl Polysiloxane (100% Dimethylpolysiloxane) - low bleeding	350 °C	Yes	Low Bleed general purpose column for GC-MS. Solvent impurities, PCBs, Simulated Distillation, drugs, natural gases, hydrocarbons, essential oils, semivolatiles, pesticides, phenols	EPA: 504.1, 505, 606 USP: G1, G2, G9, G38
HI-1 PONA	100% Methyl Polysiloxane (100% Dimethylpolysiloxane) - optimized for hydrocarbon analysis	350 °C	Yes	Optimized for DHA (Detailed Hydrocarbons Analysis), PONA, PIANO and PNA analysis	ASTM D6730-01
HI-JXR	100% Methyl Polysiloxane	350 °C	Yes	General Purpose Apolar Column	USP: G1, G2, G9, G38
HI-SE30	100% Methyl Polysiloxane	350 °C	Yes	General Purpose Apolar Column	EPA: 504.1, 505, 606, 8141A USP: G1, G2, G9, G38
HI-PS255	1% Vinyl, 99% Methyl Polysiloxane	350 °C	Yes	Apolar phase to analyze solvents, alcohols, volatiles, suited to high film thicknesses	-

3. GC configuration

What is the GC configuration, inlet, detector, samplers, GC type?

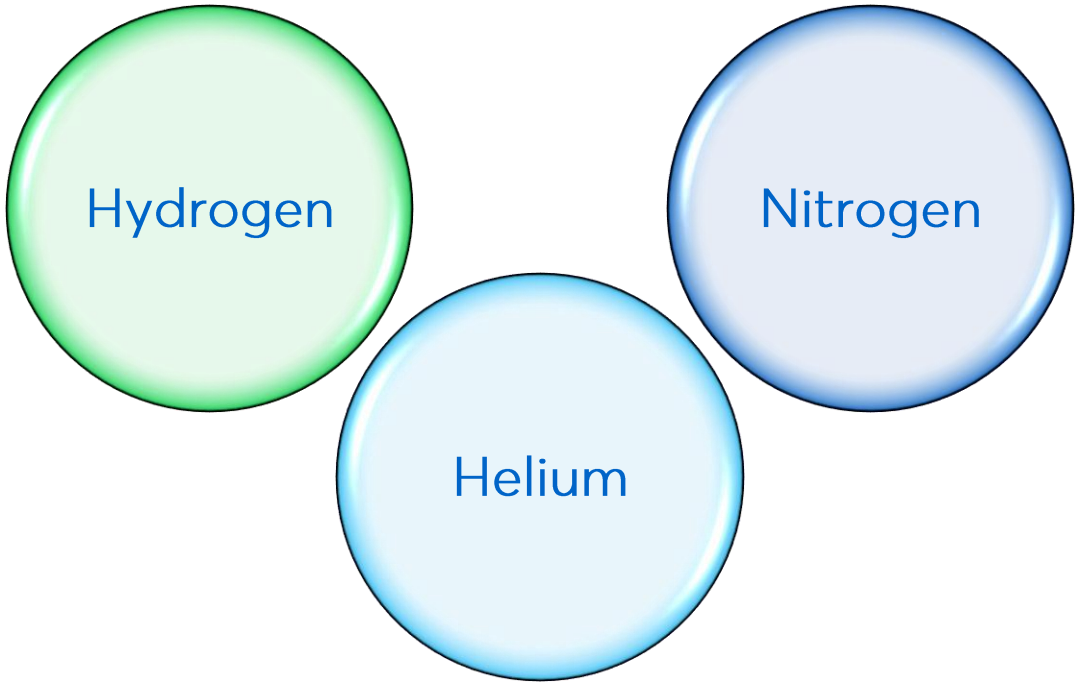
Is the GC configuration suitable for aim of analysis?

- Analytes of interest
- Aim of analysis/Application
- GC configuration

3. GC configuration – choice of carrier gas

Air is not suitable as a carrier gas!

- Most efficient carrier gas
- Least viscous
- Highest diffusivity of the 3 gases



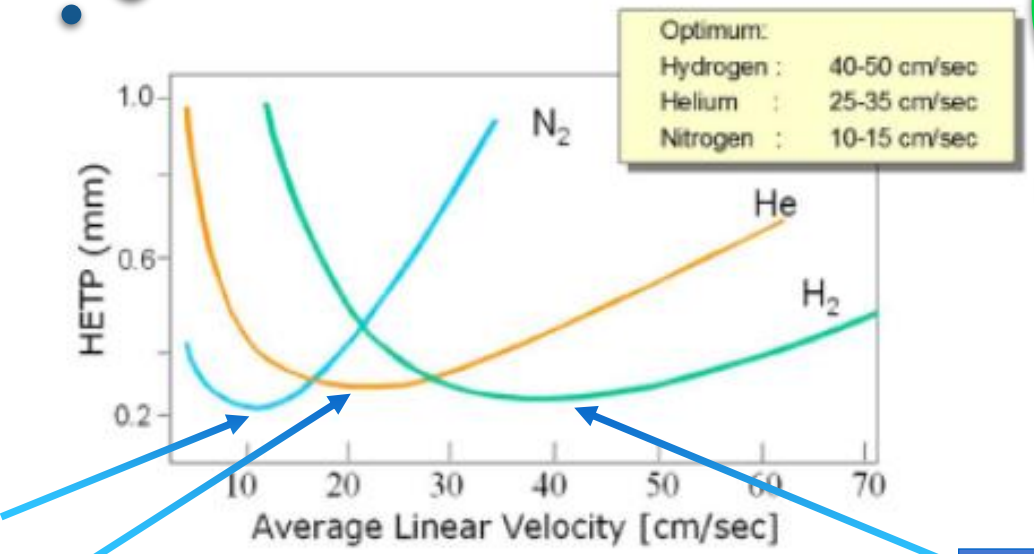
- Originally used with packed GC columns
- 2nd most viscous
- Low diffusivity

- Most popular carrier gas
- Most viscous of the 3 gases
- Higher diffusivity than nitrogen

Gas qualities such as viscosity and diffusivity affect gas speed and pressure.

3. GC configuration - Carrier gas linear velocity

Why does carrier gas linear velocity (speed cm/sec) matter?



Van Deemter equation*

*https://www.restek.com/globalassets/pdfs/literature/Impact-of-GC-Parameters_Part6.pdf

HETP (height equivalent to a theoretical plate)
A theoretical way to measure column efficiency, lower the better.

The faster the gas travels, gas linear velocity (speed cm/sec), the shorter the RT i.e. shorter analysis time. But HETP is affected…

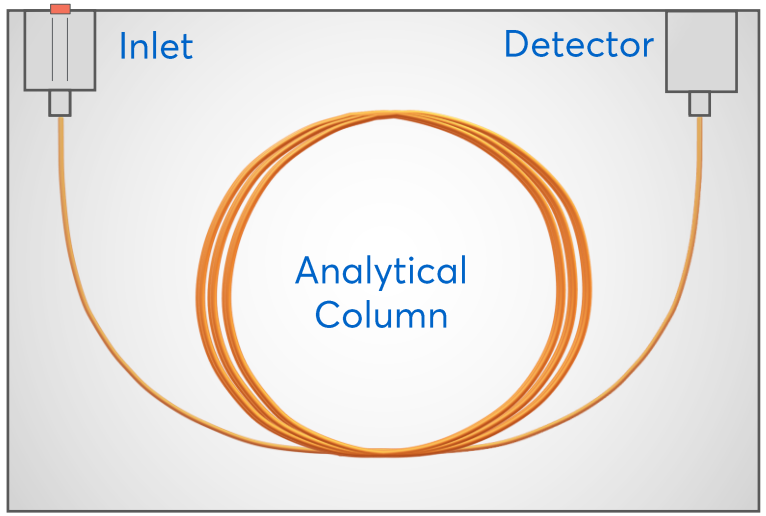
Carrier gas linear velocity
Too high = rapid RT but less resolution
Too low = long RT but more resolution

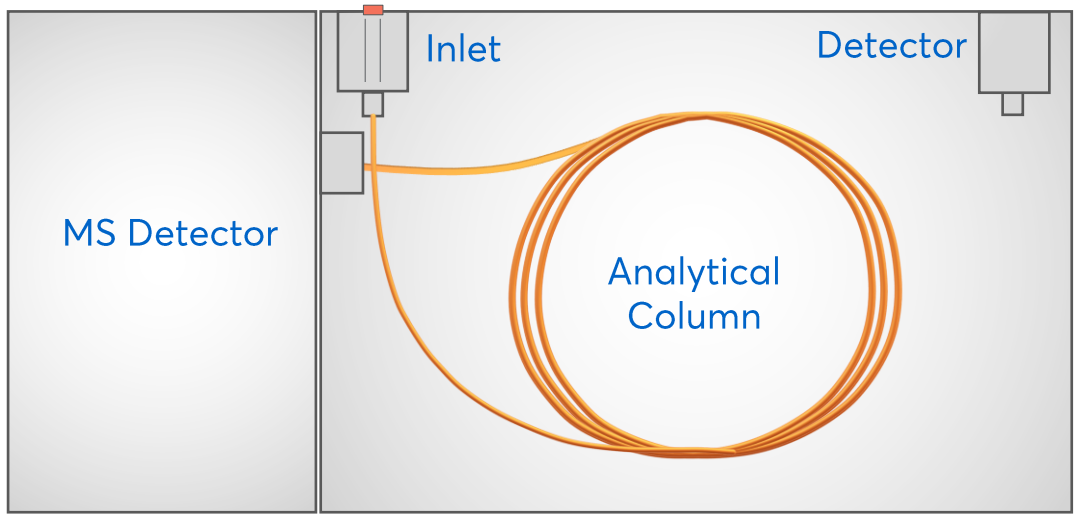
The optimum gas velocity is the balance between fast RT and good resolution.

3. GC configuration – Check what your GC config. is.

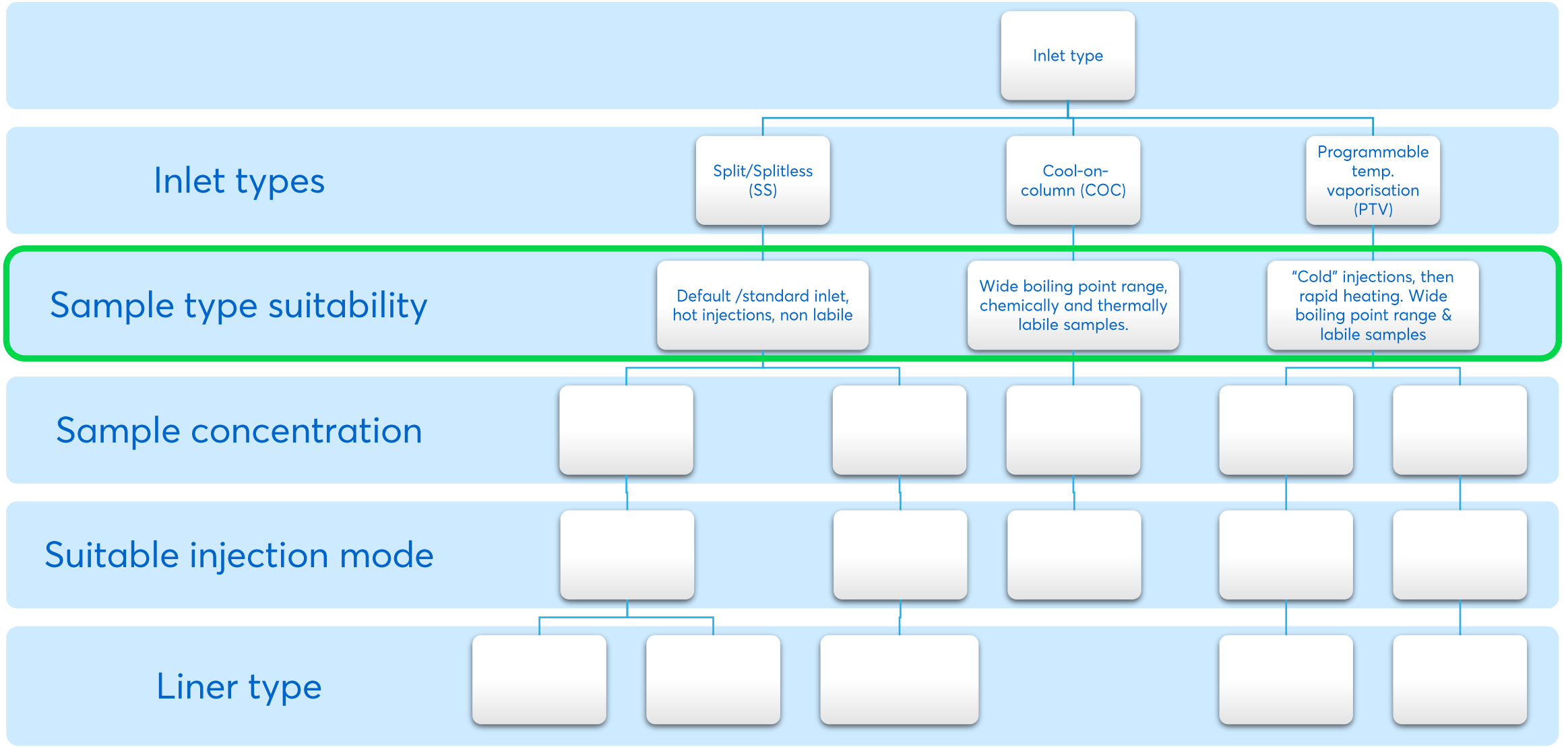
- Split/Splitless (SS)
- Cool-on-column (COC)
- Programmable Temperature Vaporization (PTV)
- Multimode inlet (MMI)
- Volatiles Interface (VI)

- Flame ionization detector (FID)
- Thermal conductivity detector (TCD)
- Flame photometric detector (FPD)
- Electron capture detector (ECD)
- Sulfur chemiluminescence detector (SCD)
- Mass Spectrometry (MS)





3. GC configuration – Inlet type



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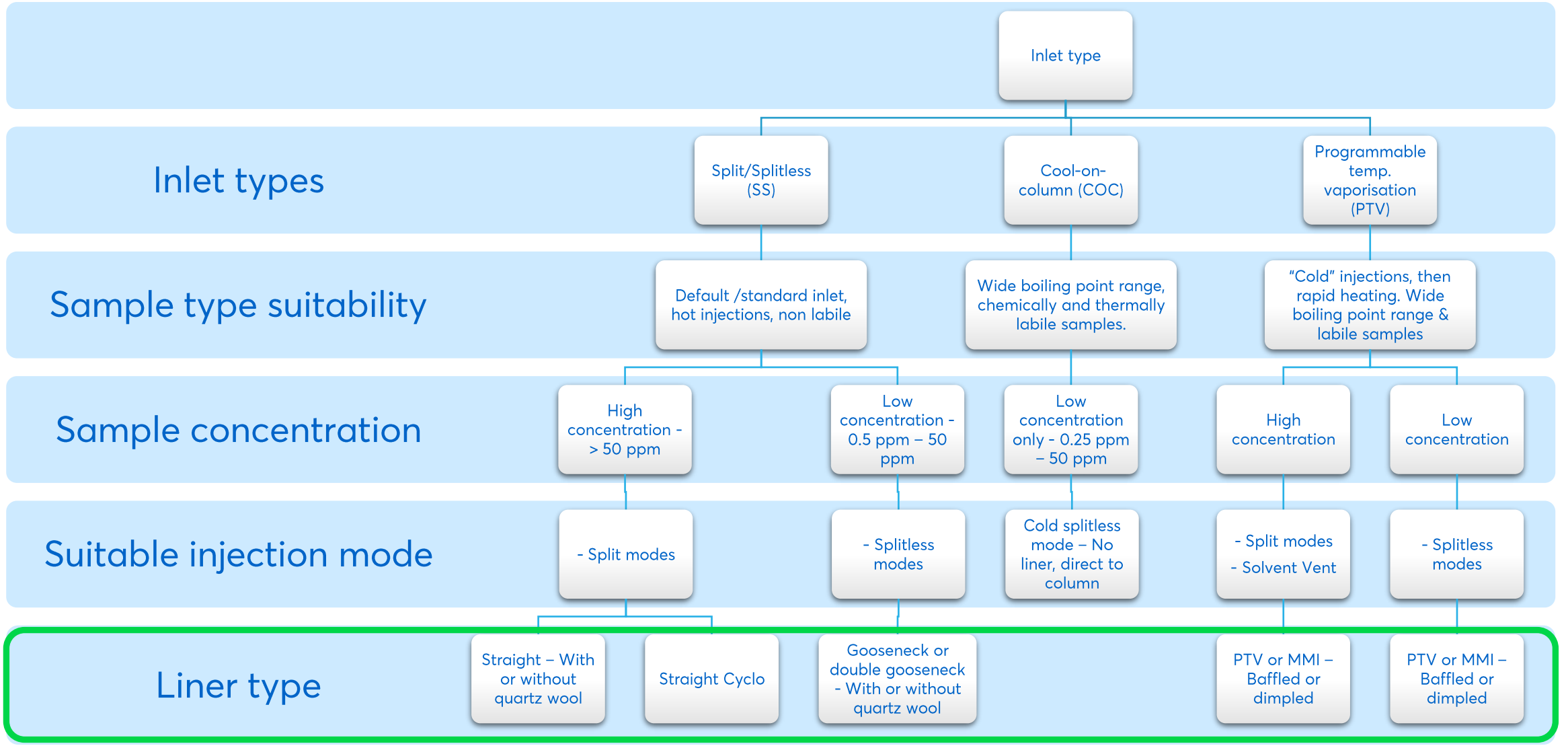
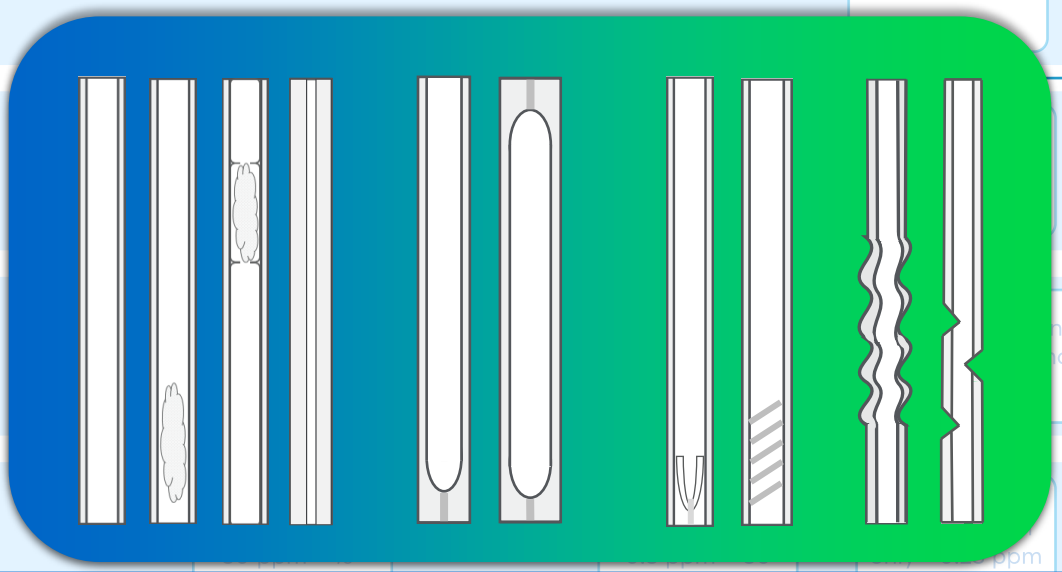


3. GC configuration – Inlet type and liners



Ensure the liner is suitable for sample, inlet and sampler.
Consider vapour volume of solvent/sample.

Inlet type

Inlet types

Programmable temp. vaporisation (PTV)

Sample type suitability

"Cold" injections, then rapid heating. Wide boiling point range & labile samples

Sample concentration

High concentration

Low concentration

Suitable injection

- Split
- Solvent Vent

- Splitless

Liner type

Straight – With or without quartz wool

Straight Cyclo

Gooseneck or double gooseneck - With or without quartz wool

PTV or MMI – Baffled or dimpled

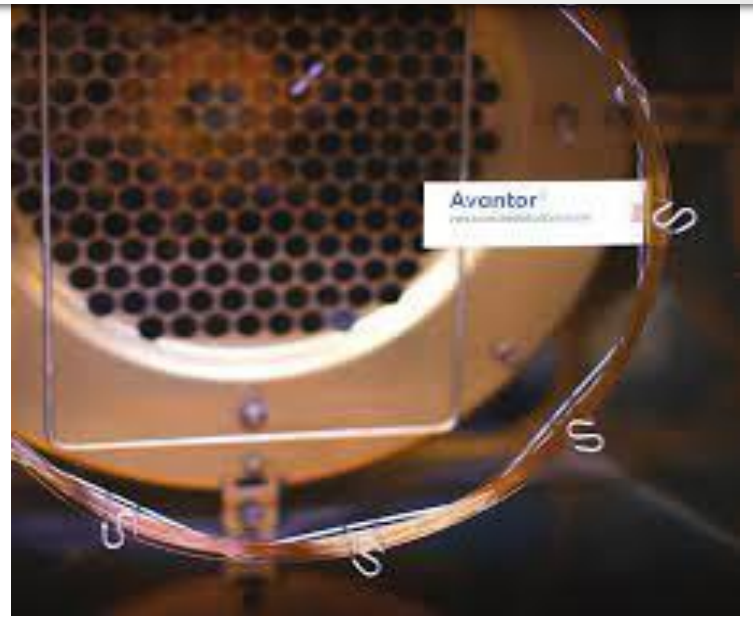
PTV or MMI – Baffled or dimpled

4. Column Phase

What column phase will retain and separate the analytes to fit the desired results?

What dimensions will be most suitable for my sample?

- Analytes of interest
- Aim of analysis/Application
- GC configuration
- GC column phase

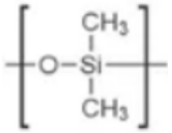


4. Column Phase - Most common column phase chemistries

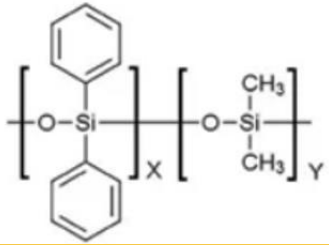
Stationary phase is a liquid coating of Polysiloxanes or Polyethylene glycol with various substituent groups.

To increase the polarity, the polysiloxane phase methyl groups are replaced by phenyls, cyanopropyl or other groups.

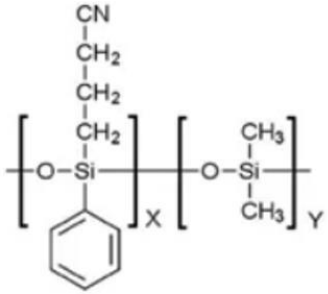
100% Dimethylpolysiloxane



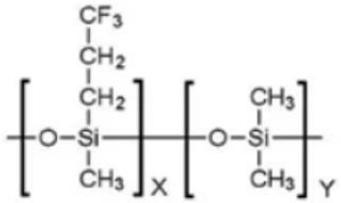
5% Phenyl, 95% Methyl Polysiloxane



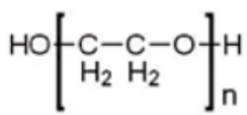
6% Cyanopropylphenyl, 94% Methyl Polysiloxane



Trifluoropropyl Methyl Polysiloxane



Polyethylene glycol (PEG) or wax



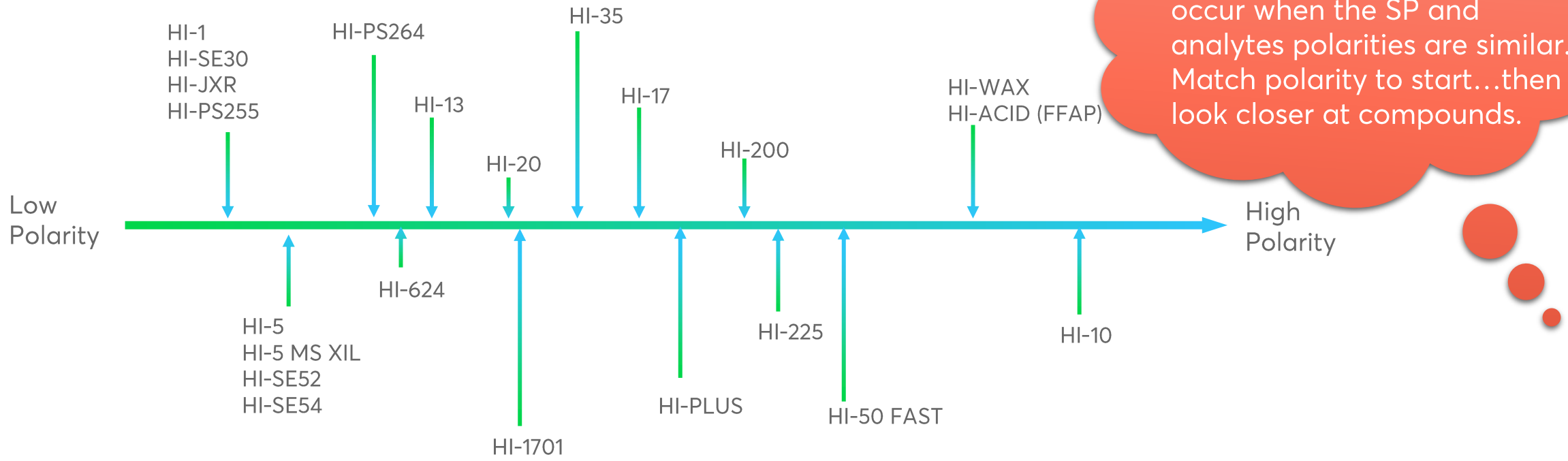
Stationary phase coating

Nonpolar → Polar/high polarity

4. Column Phase - Polarity and separation mechanisms

Apolar/Nonpolar/100% Dimethylpolysiloxane

Mid to High Polarity/6-50% Cyanopropyl or trifluoropropyl and/or more variants



As like attracts like, the strongest interactions occur when the SP and analytes polarities are similar. Match polarity to start…then look closer at compounds.

Low Polarity/5% Phenyl and/or variants

Polar/High Polarity Polyethylene Glycol/Wax and/or variants

BP influences elution order

Phase interaction influences elution order

4. Column selection - Resolution

Carrier gas, length, column ID

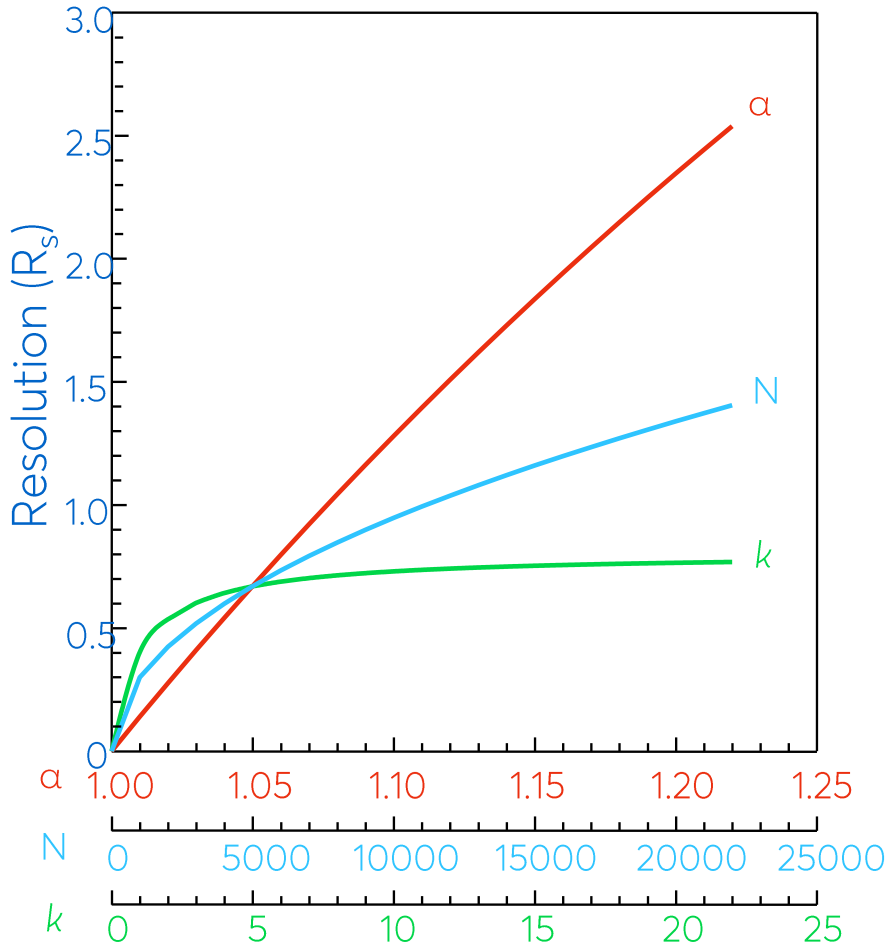
Phase design, temperature etc

FT, column ID, temperature etc

$$R_s = \frac{1}{4}\sqrt{N_2}\left(\frac{\alpha - 1}{\alpha}\right)\left(\frac{k_2}{1 + k_2}\right)$$

N - Efficiency α - Selectivity k - Retention factor

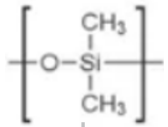
Purnell, J.H. (1960). "The correlation of separating power and efficiency of gas-chromatographic columns". *J. Chem. Soc.*: 1268–1274.



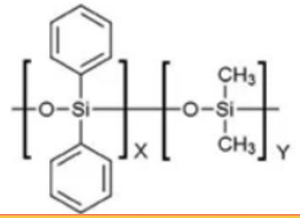
- **Selectivity is the most influential on Rs.**
- **Choose selective phase for your compounds** – use retention indices and/or application notes.

4. Column Phase – Separation mechanisms/interactions

Apolar/Nonpolar interactions	Low Polarity interactions	Mid to High Polarity interactions	High to Polar interactions
– Strong Dispersive – No Dipole – No H Bonding – Compound Types – C and H atoms only, C-C bonds – Alkanes – **Boiling point order**	– Strong Dispersive – No Dipole – Weak H bonding – Compound Types – Similar to nonpolar – Aromatic compounds – Boiling point order – Slightly more selective	– Strong Dispersive – Strong Dipole for Cyanopropyl – Moderate Dipole for trifluoropropyl – Moderate H bonding – Compound Types – Contain O for Cyanopropyl – Contain halogens for trifluoropropyl	– Strong Dispersive – Moderate Dipole – Weak H bonding – Compound Types – C and H atoms – Contain Br, Cl, F, N, O, P and/or S – Alcohols, amines, carboxylic acids, diols, esters, ethers, ketones, thiols.



100% Dimethylpolysiloxane



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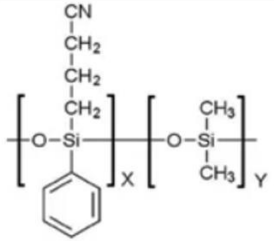

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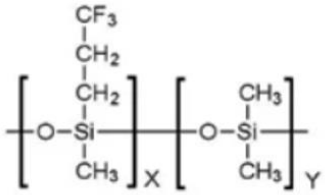
94% Methyl Polysiloxane



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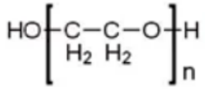


Polyethylene glycol (PEG)

Nonpolar → Polar/high polarity

4. Column Phase - Polarity and separation mechanisms

Apolar/Nonpolar/100% Dimethylpolysiloxane

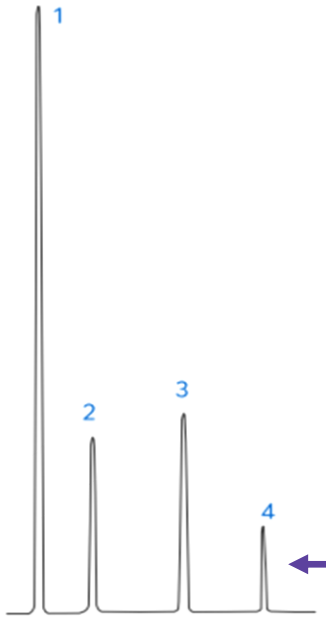
HI-1
HI-SE30
HI-JXR
HI-PS255

Application note # C-13098

1. Cyclohexane – Non-polar, BP 80.75 °C
2. Cycloheptane – Non-polar, BP 118.4 °C
3. Cyclooctane - Non-polar, BP 149 °C
4. n-Decane - Non-polar, BP 174.1 °C

BP influences elution order

Analysis of Cyclic Hydrocarbons using the Avantor® Hichrom HI-1 Phase

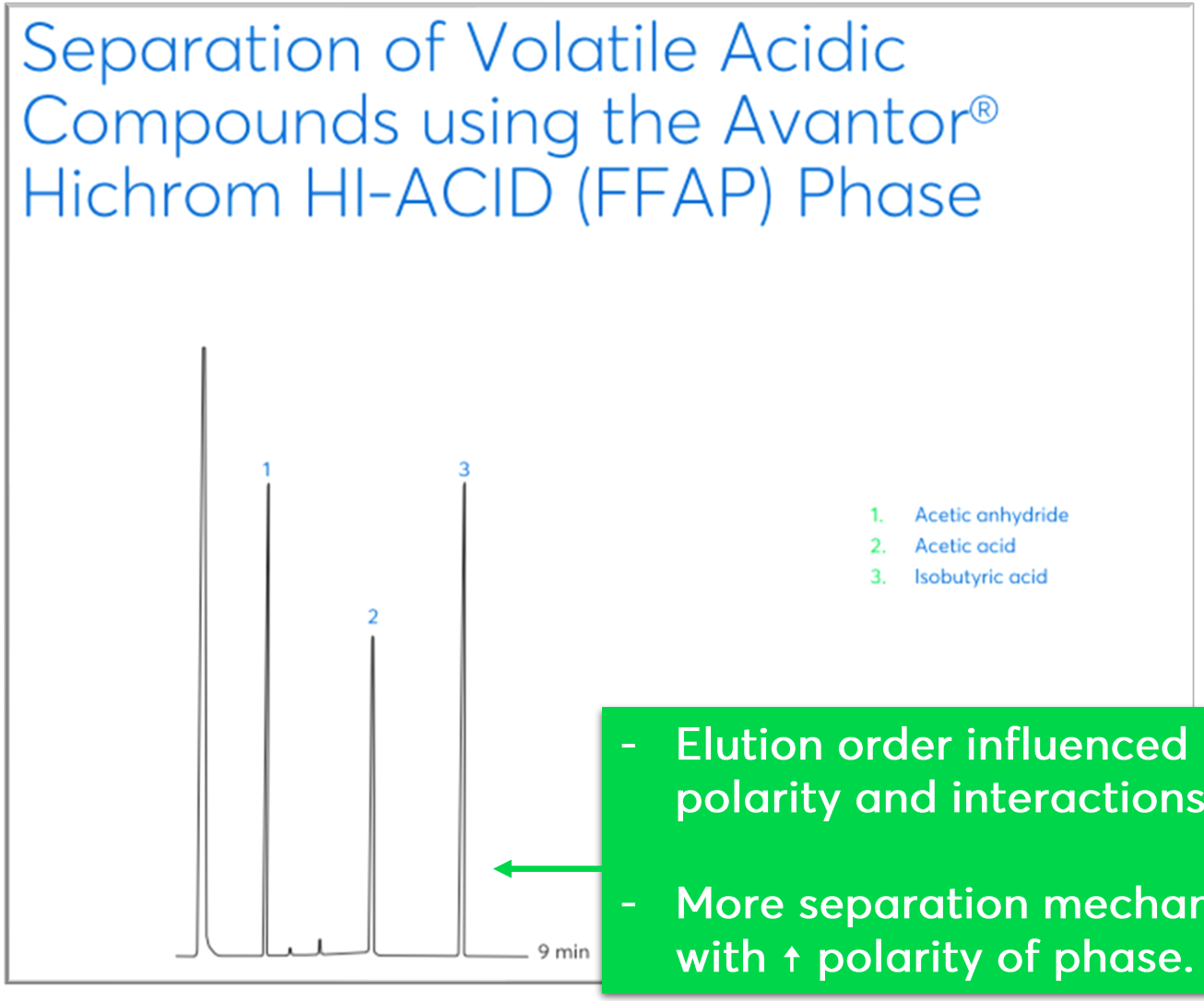


1. Cyclohexane
2. Cycloheptane
3. Cyclooctane
4. n-Decane

- Elution in order of BP's.
- Higher BP, larger compounds = Higher retention.

Figure 1: Analysis of cyclic hydrocarbons using the Avantor® Hichrom HI-1 phase.

4. Column Phase - Polarity and separation mechanisms



Polar/High Polarity
Polyethylene Glycol/Wax and/or variants

HI-WAX
HI-ACID (FFAP)

Application note # C-13009

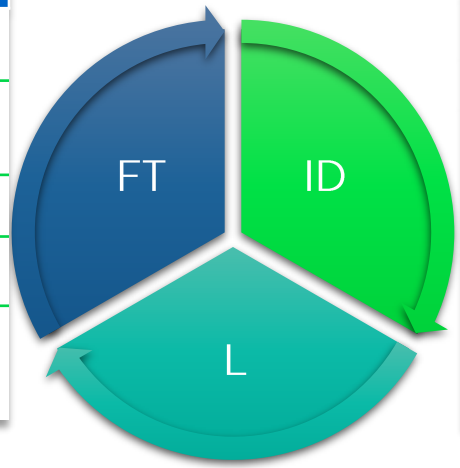
1. Acetic Anhydride – Polar, BP 139.5 °C
2. Acetic Acid – Polar, BP 118 °C
3. Isobutyric Acid – Polar, BP 155 °C

- Elution order influenced by polarity and interactions.
- More separation mechanisms with ↑ polarity of phase.

Phase interaction influences elution order

4. Column Phase – Column dimension considerations

Film Thickness	
Thin FT 0.10–0.50 µm	Thick FT 1–10 µm
Decreased retention and short RT	Increased Retention and longer RT
Lower sample capacity	Higher sample capacity
Higher temperatures	Lower Temperatures
Low column bleed	High column bleed
Medium to high molecular weight compounds	Volatiles and low molecular weight compounds



Column ID		
0.10-0.18 mm	0.25-0.32 mm	0.40-0.53 mm ID
Short RT	Moderate RT	Long RT
Low flow	Moderate flow	High flow
Lower sample capacity, <50 ng (based on 0.25 µm FT)	Medium sample capacity, <200 ng (based on 0.25 µm FT)	Higher sample capacity, < 2000 ng (based on 0.25 µm FT)
Split mode, Fast GC, GCMS, highly complex samples	Complex samples, split, splitless, DI, HS and on-column modes, broad conc. range.	Split, splitless, DI, HS and on-column modes.

Column Length		
Short <15 m	Medium 20-30 m	60-100 m
Lower resolution	Medium resolution, suits broad range	Increased Resolution
Short RT	Moderate RT	Long RT
Lower cost	Medium cost, more popular, general use length at 30 m	Higher cost, consider other options before increasing length
A few compounds in sample, high boilers, Fast GC, GCMS	Medium complexity of samples, GCMS	Very complex samples, low boilers

5. Sample mixture

What is in the sample mixture?

Is there a sample preparation protocol ready?

Is the sample solvent/diluent compatible with the column?

- Analytes of interest
- Aim of analysis/Application
- GC configuration
- GC column phase
- Sample mixture

5. Sample mixture - GC sample solvent/diluent selection

Lower polarity sample analytes and columns

- Low polarity solvent, e.g. n-hexane.

Mixture of polarities and/or mid polarity columns

- An intermediate polarity solvent may be used to compromise, e.g. ethyl acetate.

Polar sample analytes and more polar columns

- Higher polar solvent, e.g. Methanol.

Other considerations

- Sampler type and detectors need to be considered.
- Solvent needs a lower boiling point than compounds in sample mixture, for basic injection techniques.

Objectives, GC setup and aims established

1. Analytes of interest
2. Aim of analysis/Application
3. GC configuration
4. GC column phase
5. Sample mixture

Scout run

Avoid changing all parameters at once!

1st Approach – Application note located

- Acquire suitable test mix/external standard.
- Application note available – Use method parameters if applicable.
- Adjust parameters to suit GC config.
- Run injection, assess results.
- Set up more runs with adjusted parameters - E.g. Oven ramp 20°C, 30°C, 40 °C and 50 °C/min. Select best oven ramp, then adjust another parameter and run more injections.
- Parameter by parameter if possible.

2nd Approach - Set up method (default method or manually)

- Acquire suitable test mix/external standard.
- Set up method.
- Adjust parameters to suit GC config.
- Run injection, assess results.
- Set up more runs with adjusted parameters - E.g. Oven ramp 20°C, 30°C, 40 °C and 50 °C/min. Select best oven ramp, then adjust another parameter and run more injections.
- Optimize parameters and set up more runs, adjust one by one.
- Parameter by parameter if possible.

First run, split injection

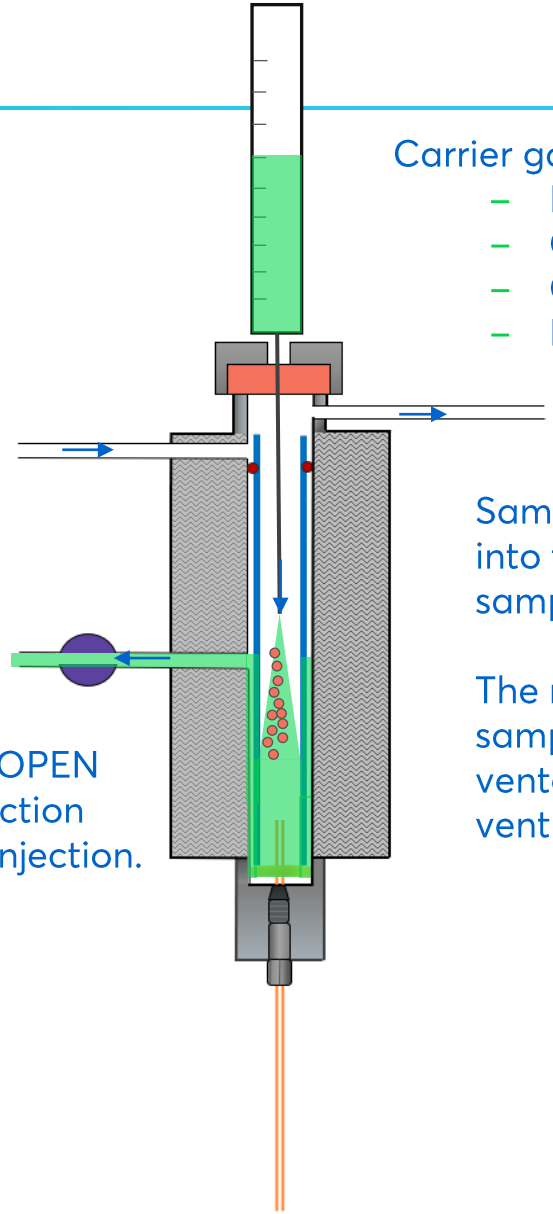
Method starting point with 0.32 mm X 25 m column using SS inlet

Split injection starting parameters	
Column capacity	50 – 150 ng per analyte, use higher end of capacity, 0.32 mm X 25 m
Injection volume	1 µL, e.g. 150 ng/µL
Inlet temp	250 °C
Column flow	1 mL/min (0.9 - 1.8 mL/min)
Column flow mode	Constant flow
Split ratio	50:1
Initial temp	40 °C
Initial hold time	NA
Oven ramp rate	10 °C/min
Final temp	Max operating temp of column if needed e.g. 360 °C, - 10 - 20 °C
Final hold time	10 min

GC inlet – Split injection

Used when the sample **concentration is too high**.

Splits off the majority of the volatilized sample and adjusts the amount of sample transferred to the column.



Carrier gas flow –
- Into inlet
- Out of septum purge
- Out the split vent
- Into column

Sample is introduced into the inlet and liner, sample is vaporised.

The majority of the sample and vapour is vented out the split vent line.

Split vent line/valve OPEN during injection and after injection.

Optimized split injection – Adjust flows and inlet 1st

Split injection starting parameters		Optimize - run more injections with a number of adjusted parameters
Column capacity	50 – 150 ng per analyte, use higher end of capacity, 0.32 mm X 25 m	+/- 50 ng, as needed, see below first before adjusting sample concentration.
Injection volume	1µL, e.g. 150 ng/µL	Overload = Dilute sample if increasing split flow does not help. Low response = + 0.5 µL steps if decreasing split flow does not help.
Inlet temp	250 °C	+/-25°C steps up to 300°C, if needed, choose best temp (Too high = degradation).
Column flow	1 ml/min (0.9 - 1.8 mL/min)	+0.2 mL/min (0.9 - 1.8 mL/min) or increase linear velocity to by + 5 cm/sec steps.
Column flow mode	Constant flow	
Split ratio	1:50	Split of 1:75, 1:100, 1:150, 1:200 (can go higher if needed). Ensure enough sample is transferred to the column.

What do you see after first run?

Overload

Retention time issues

Low Response

Peak degradation

Optimized split injection – Adjust oven ramp/temps. 2nd

What do you see after first run?

Poor resolution

Coelutions

Retention time issues

Not all peaks eluting

Initial oven temp	40 °C	Calculate T(i) (oven temperature of 1st eluting peak) T initial = T(i) – 45 °C.
Initial oven hold time	NA in split	Add hold for mid eluters, If needed, hold temperature over coeluting analytes.
Oven ramp rate	10 °C/min	Optimum Ramp Rate = 10 °C per t_0. Steps of + 20 °C, 30 °C, 40 °C and 50 °C/min.
Final temp	Max operating temp of column if needed e.g. 360 °C, - 10 - 20 °C	Check T(f) (final analyte elution temp), then calculate final temp/T (final) = T(f) + 20 °C, as long as it does not exceed max temperature of column.
Final hold time	10 min	Reduce or remove (only needed if all analytes not eluted and max temp reached)

First run, splitless injection

Method starting point with 0.32 mm X 25 m column using SS inlet

Splitless injection starting parameters	
Column capacity	50 – 150 ng per analyte, use higher end of capacity, 0.32 mm X 25 m
Injection volume	1 µL, e.g. 150 ng/µL
Inlet temp	250 °C
Column flow	1 mL/min (0.9 - 1.8 mL/min)
Column flow mode	Constant flow
Splitless hold time	**1 min (2 min is usually the maximum time), or time for the above.**
Splitless purge flow	**Common default is 50 mL/min**
Initial temp	**20 °C below BP of the solvent or as low as possible.**
Initial hold time	**Match to splitless hold time (up to 2 minutes)**
Oven ramp rate	10 °C/min
Final temp	Max operating temp of column if needed e.g. 360 °C, -10-20 °C
Final hold time	10 min

Splitless is different to split in oven parameters

Initial temp is 20 °C below BP of the solvent or as low as possible to allow -

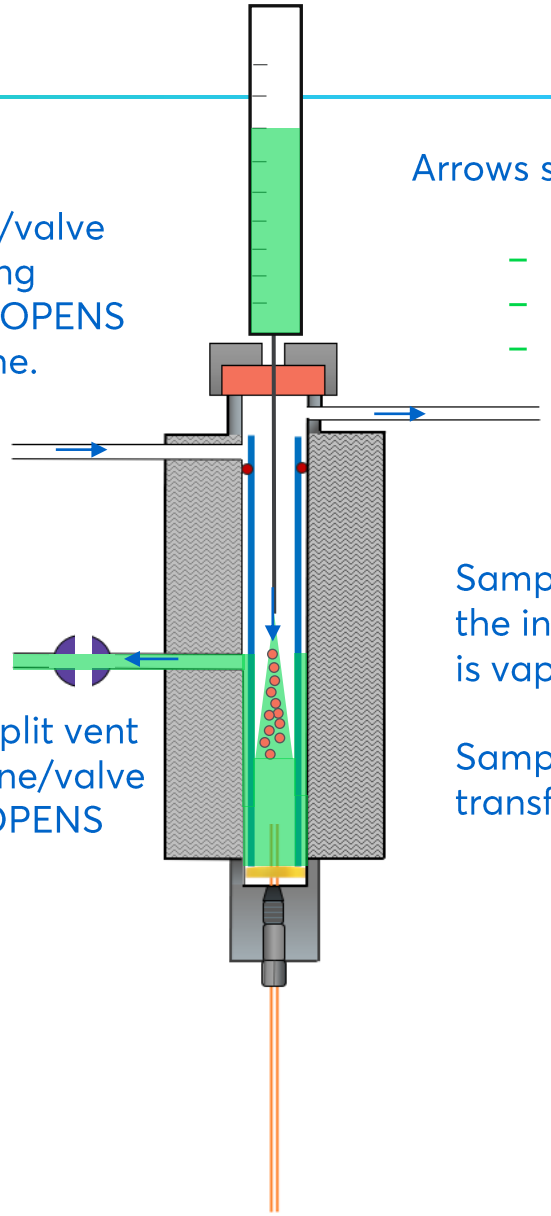
1. Solvent focusing
2. Cold trapping

GC inlet – Splitless injection

All of the sample is transferred to the column and suitable for low concentration samples.

Transfer of sample vapour is much slower, up to 2 min.

Split line opens at an optimized purge time to clear the inlet of any residual vapours.



Split vent line/valve CLOSED during injection and OPENS after a set time.

Arrows show carrier gas flow –

- Into inlet
- Out of septum purge
- Into column

Split vent line/valve OPENS

Sample is introduced into the inlet and liner, sample is vaporised.

Sample vapour is transferred to the column.

Optimize splitless injection– Adjust flows and inlet 1st

Splitless injection starting parameters		Optimize parameters for more runs based on results of scout run
Column capacity	50 – 150 ng per analyte, use higher end of capacity, 0.32 mm X 25 m	+/- 50 ng, as needed, see below first before adjusting sample concentration.
Injection volume	1 µL, e.g. 150 ng/µL	Overload = Dilute sample or reduce the sample volume. Low response = + 0.5 µL steps
Inlet temp	250 °C	+/-25°C steps up to 300°C, if needed, choose best temp (Too high = degradation)
Column flow	1 ml/min (0.9 - 1.8 mL/min)	+0.2 m L/min (0.9 - 1.8 mL/min) or increase linear velocity to by + 5 cm/sec steps.
Column flow mode	Constant flow	
Splitless hold time	1 min (2 min is usually the maximum time), or time for the above.	Adjust 1.5 to 2 times carrier gas sweep of the total inlet, up to 2 min.
Splitless purge flow	Common default is 50 mL/min	+ steps 10 mL/min, but only adjust as a last resort if there is issues with carryover.

What do you see after first run?

Overload

Carryover

Low Response

Retention time issues

Peak degradation

Optimize splitless injection - Adjust oven ramp/temps. 2nd

What do you see after first run?

Peak widening and resolution issues

Coelutions

Retention time issues

Not all peaks eluting

Initial temp	20 °C below BP of the solvent or as low as possible.	Reduce if peaks widening. Reassess after another run. Check bp of solvent is suitable for splitless injection.
Initial hold time	Match to splitless hold time (up to 2 minutes)	Match to splitless hold time (up to 2 minutes), add hold for mid eluters, If needed, hold temperature over coeluting analytes.
Oven ramp rate	10 °C/min	Add temp. holds, adjust ramp rate steps of + 20 °C, 30 °C, 40 °C and 50 °C/min.
Final temp	Max operating temp of column if needed e.g. 360 °C, - 10 - 20 °C	Check T(f) (final analyte elution temp), then calculate final temp/T (final) = T(f) + 20 °C, as long as it does not exceed max temperature of column.
Final hold time	10 min	Reduce or remove (only needed if all analytes not eluted and max temp reached).

Goals of optimizing parameters

01

– Transfer enough sample onto column for detection -

02

– See all peaks elute –

03

– Reduce retention time –

04

– See good peak shape and resolution of peaks -

05

– See a good response to enable concentration calibration –

06

– Achieve reproducible results –

Goals of optimizing parameters

01

- Transfer enough sample onto column for detection – Adjust split ratio, splitless hold time, injection volume.

02

- See all peaks elute – Adjust Splitless hold time, see the above.

03

- Reduce retention time – Increase flow and/or carrier gas velocity, increase temperature ramp.

04

- See good peak shape and resolution of peaks – Adjust column flow, split ratio, lower inlet temp if early eluters not resolved, add temp hold over mid-coeluters.

05

- See a good response to enable concentration calibration – See the above, check detection limits and adjust detector temperatures.

06

- Achieve reproducible results – Once RT reduced, resolution is good, all peaks elute with decent responses, then run further injections to test reproducibility.

Fast GC

What is Fast GC?

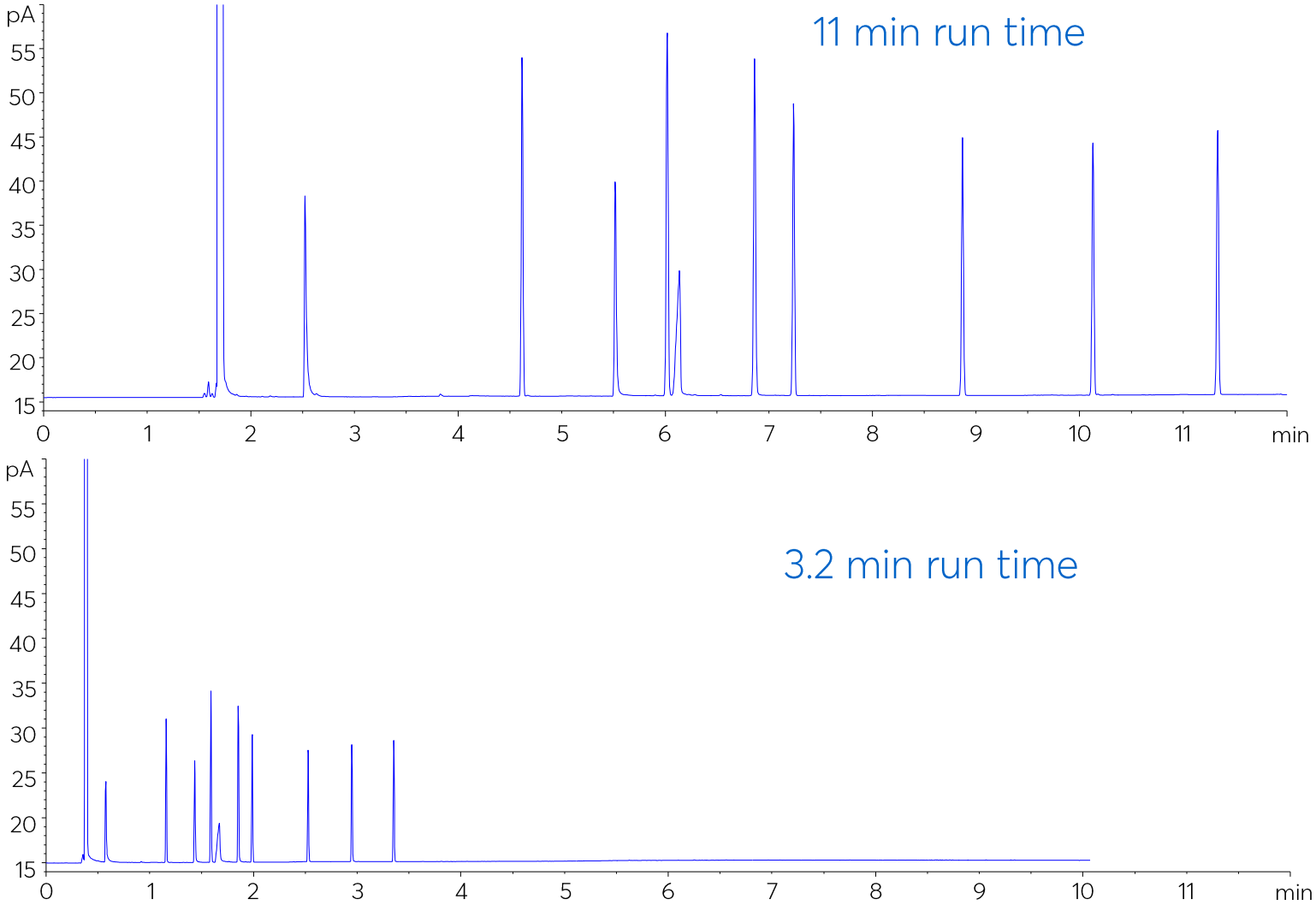
It is a technique that allows you to reduce the analysis time while keeping an adequate resolution power, thus increasing your throughput.

Can be applied to medium-to-high complexity mixtures analysis.

Provides 3–10 times faster analysis compared to conventional GC. Great for screening analysis.

Increases productivity by reducing dimensions to reduce analysis time, whilst maintaining or improving resolution.

Standard vs Fast GC results



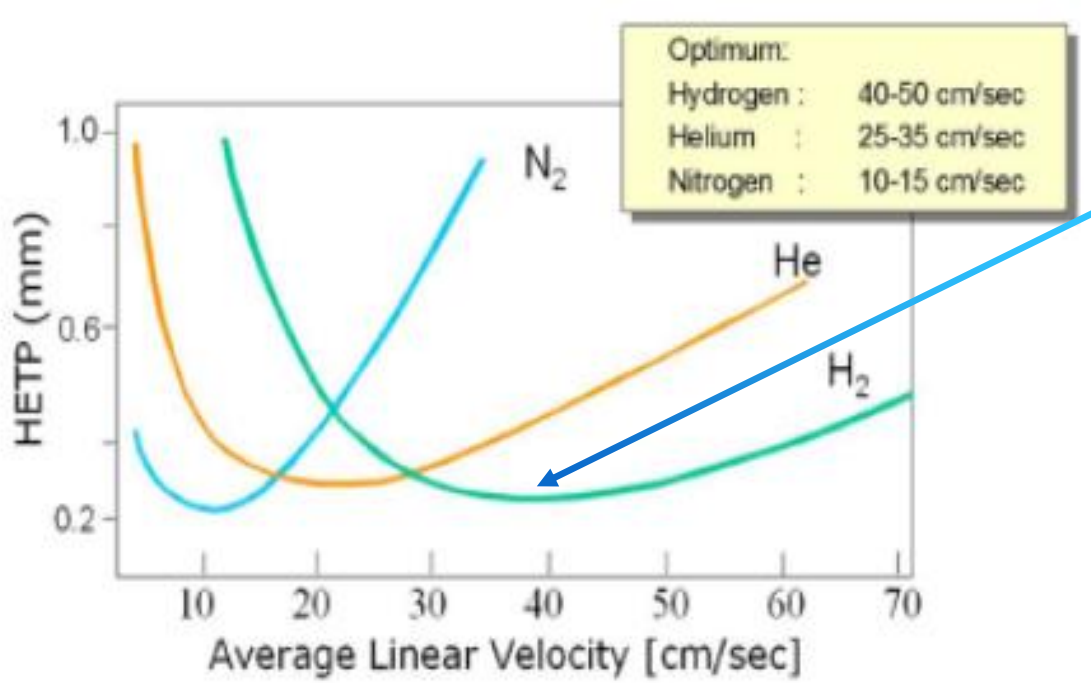
Teknokroma Fast GC FID FAMEs analysis, HI-5, 0.25 mm x 0.25 µm x 30 m

Standard Column	HI-5 0.25 mm x 0.25 µm x 30 m
Sample	Teknokroma Grob mix
Flow rate	1.2 mL/min
Linear velocity	35.7 cm/s
Injection volume	1 µL
Split ratio	75:1
Temp. program	60 to 220 °C @10 ° C/min
Hold time	10 min

Fast GC Column	HI-5 0.10 mm x 0.10 µm x 10 m
Sample	Teknokroma Grob mix
Flow rate	0.47 mL/min
Linear velocity	55.0 cm/s
Injection volume	0.5 µL
Split ratio	1:200
Temp. program	60 to 220 °C @30 °C per min
Hold time	10 min

Fast GC – What is required?

What you need to make FAST-GC…..



*https://www.restek.com/globalassets/pdfs/literature/Impact-of-GC-Parameters_Part6.pdf

<u>To reduce retention time -</u>

- Length - Shorter column 5 - 10 m.
- High temperature ramp (usually more than 15°C/min).
- Higher gas linear velocity.

<u>To accommodate for faster/shorter retention times -</u>

- Use H_2 carrier gas – optimum gas velocity (fastest).
- ID - Smaller ID, usually 0.10 mm.
  - ID and H_2 maintains resolution
- FT - 0.05 - 0.20 µm.

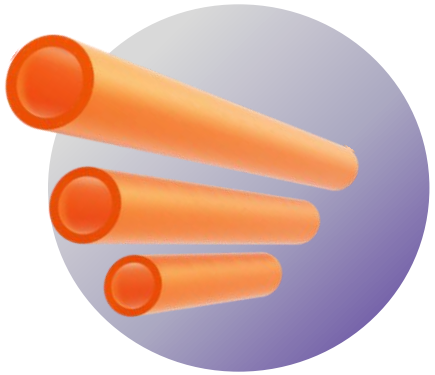
<u>Also requires -</u>

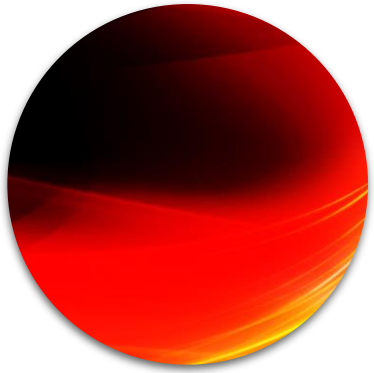
- Fast acquisition rates - frequency of at least 50Hz.
- Fast injections and split mode injections.

<u>Additional information -</u>

- Old MS systems may not be able to handle Hydrogen as a carrier gas.

Method transfer from standard to Fast GC





Walk through of transfer from standard to Fast GC method

Fast GC – How to select column dimensions

Ratio of film thickness and column internal diameter

β value = how retentive the FT and ID combination is.

Use the Phase Ratio/β

Choose similar phase ratio when changing column dimensions, achieves similar retention.

Higher β = decreased retention

Increasing retention

Lower β = increased retention

Column diameter, d_c (mm)	Film thickness, d_f (µm)										
	0.15	0.18	0.25	0.5	1	1.4	1.5	1.8	2.65	3	5
0.15	250	208	150	75	38	27	25	21	14	13	8
0.18	300	250	180	90	45	32	30	25	17	15	9
0.25	417	347	250	125	63	45	42	35	24	21	13
0.32	533	444	320	160	80	57	53	44	30	27	16
0.53	883	736	530	265	133	95	88	74	50	44	27

Fast GC – Selecting Fast GC dimensions

Use similar values and reduce the ID and FT to enable a faster analysis time

Use the Phase Ratio formula

$$\beta = \frac{d_c}{4d_f} \qquad \beta = \frac{\text{Column ID } (\mu m)}{4 \text{ x Film thickness } (\mu m)}$$

>400 for high molecular weight analytes <100 for highly volatile/low molecular weight analytes.

Increasing retention

Column diameter, d_c (mm)	Film thickness, d_f (µm)										
	0.15	0.18	0.25	0.5	1	1.4	1.5	1.8	2.65	3	5
0.15	250	208	150	75	38	27	25	21	14	13	8
0.18	300	250	180	90	45	32	30	25	17	15	9
0.25	417	347	250	125	63	45	42	35	24	21	13
0.32	533	444	320	160	80	57	53	44	30	27	16
0.53	883	736	530	265	133	95	88	74	50	44	27

Fast GC – Selecting Fast GC dimensions

Example – phase ratio of a 0.25 mm ID x 0.18 µm ID column?

Use the Phase Ratio formula
β of 0.25 mm ID x 0.18 µm ID column…

$$\beta = \frac{d_c}{4d_f} \rightarrow \beta = \frac{250}{4 \times 0.18} \rightarrow \beta = \frac{250}{0.72}$$

$$\beta = \frac{d_c}{4d_f} \qquad \beta = \frac{\text{Column ID (µm)}}{4 \times \text{Film thickness (µm)}}$$

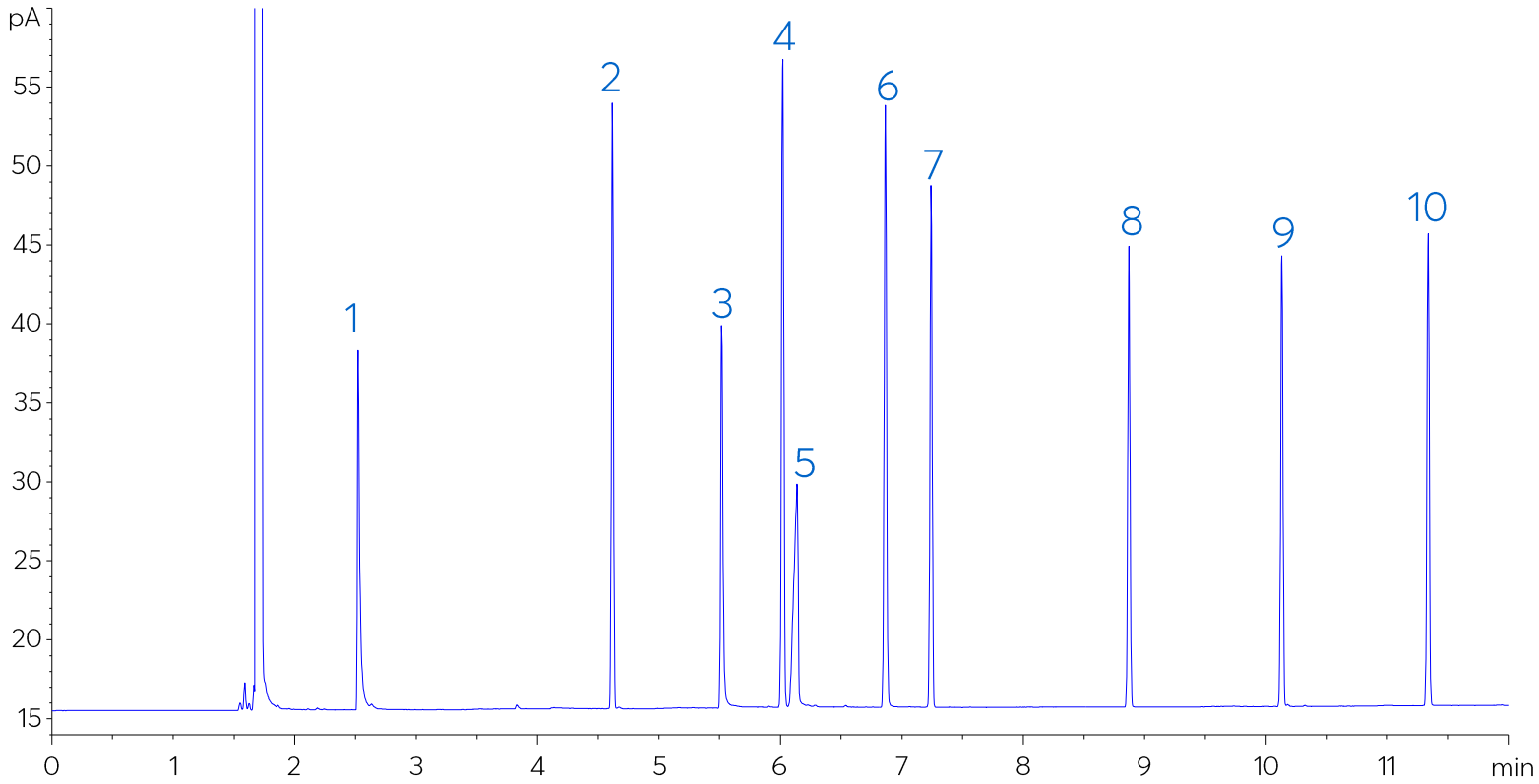
$$\beta = 347.22$$

Close to >400 for high molecular weight analytes

Increasing retention

Column diameter, d_c (mm)	Film thickness, d_f (µm)										
	0.15	0.18	0.25	0.5	1	1.4	1.5	1.8	2.65	3	5
0.15	250	208	150	75	38	27	25	21	14	13	8
0.18	300	250	180	90	45	32	30	25	17	15	9
0.25	417	347	250	125	63	45	42	35	24	21	13
0.32	533	444	320	160	80	57	53	44	30	27	16
0.53	883	736	530	265	133	95	88	74	50	44	27

Standard GC - run test mix & peak IDs

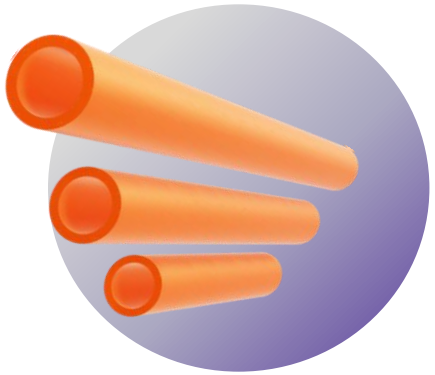


Teknokroma Fast GC FID FAMEs analysis, HI-5, 0.25 mm x 0.25 µm x 30 m

Column	HI-5, 0.25 mm x 0.25 µm x 30 m
Sample	Teknokroma Grob mix
Flow rate	1.2 mL/min
Linear velocity	35.7 cm/s
Injection volume	1 µL
Split ratio	75:1
Temp. program	60 to 220 °C @10 ° C/min
Hold time	10 min

1. 2,3-Butanediol
2. Decane
3. 1-Octanol
4. 2,6-Dimethylphenol
5. 2-Ethylhexanoic acid
6. 2,6-Dimethylaniline
7. Dodecane
8. C10:0 FAME
9. C11:0 FAME
10. C12:0 FAME

Fast GC column selected – First adjustments



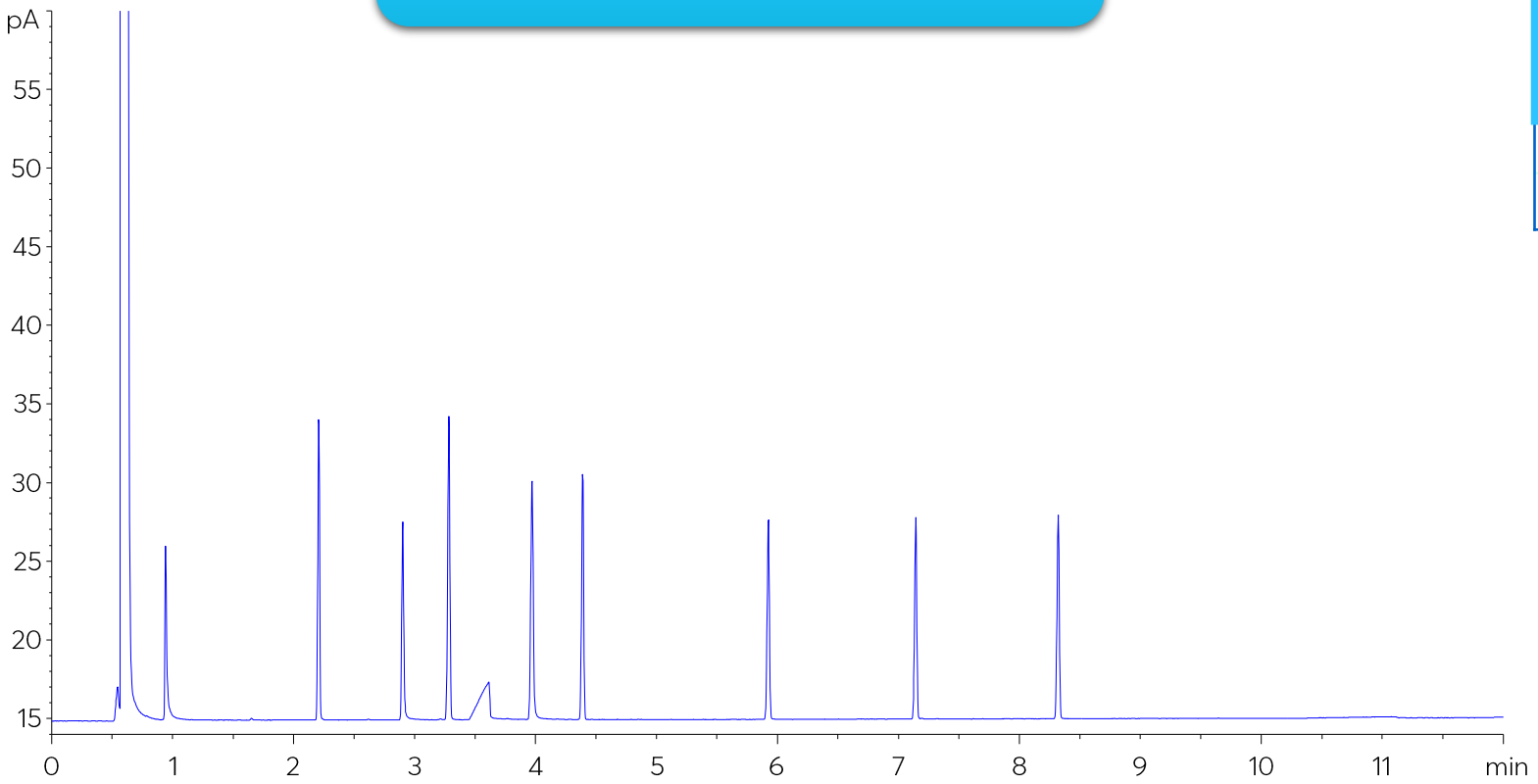
Standard column	HI-5, 0.25 mm x 0.25 µm x 30 m	HI-5, 0.10 mm x 0.10 µm x 10 m
Sample	Teknokroma Grob mix	
Flow rate	1.2 mL/min	
Linear velocity	35.7 cm/s	
Injection volume	1 µL	0.5 µL
Split ratio	75:1	1:100
Temp. program	60 to 220 °C @10 ° C/min	
Hold time	10 min	

1. Adjust split ratio/flow and sample volume – to suit smaller dimensions

- *Reconfigure column dimensions and carrier gas in software*
- Reduce sample volume.
- Use standard method carrier gas linear velocity.
- 1:100 - 1:400 (10x less sample conc. to standard GC).
- Use constant flow or constant velocity.
- -/+ 25 - 50 to adjust split ratio as needed….

Initial Fast GC run Fast GC Column dimensions

1. Adjust split ratio/flow and sample volume – to suit smaller dimensions



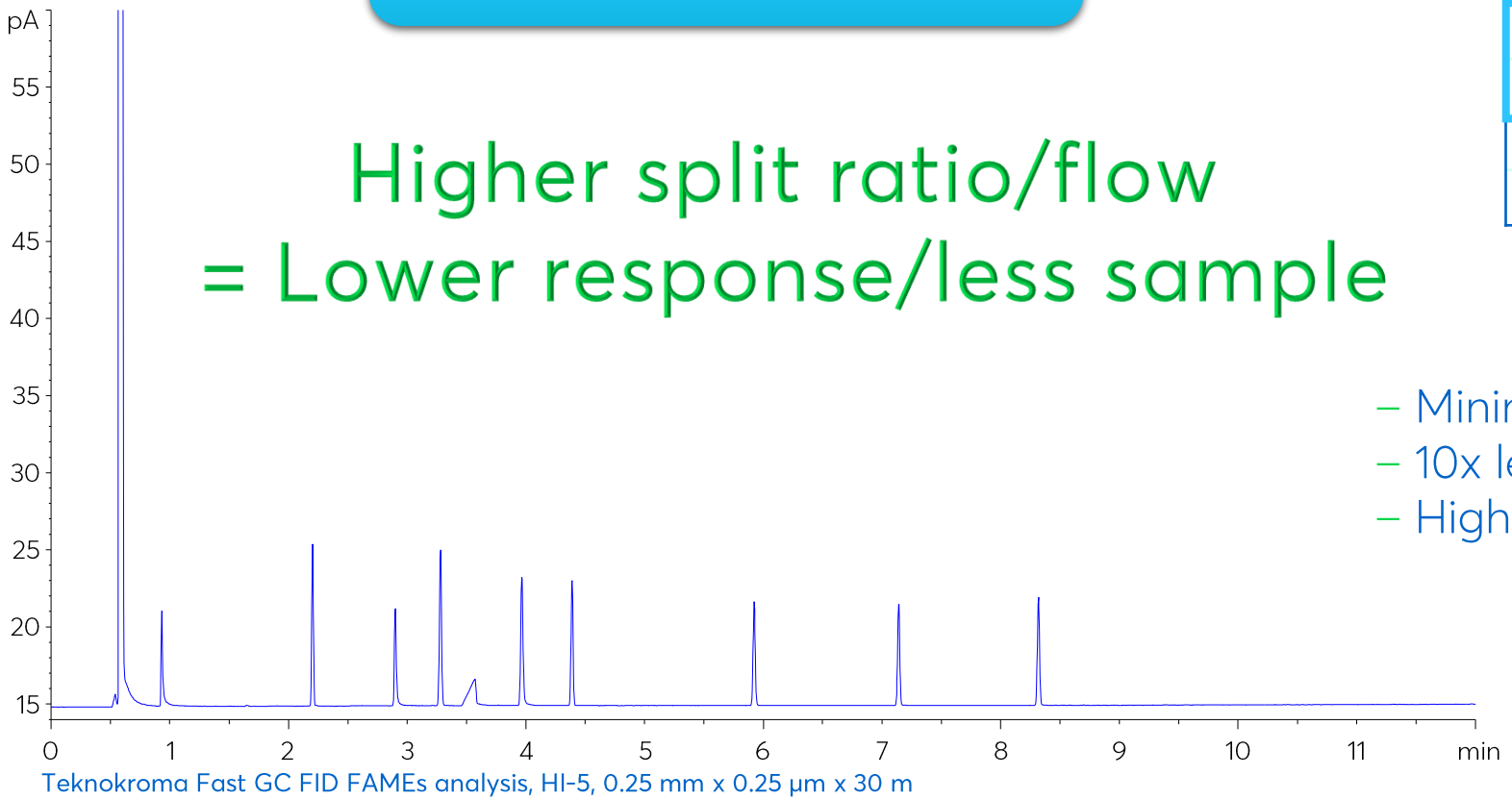
Teknokroma Fast GC FID FAMEs analysis, HI-5, 0.25 mm x 0.25 µm x 30 m

Column	HI-5, 0.10 mm x 0.10 µm x 10 m
Sample	Teknokroma Grob mix
Flow rate	0.245 mL/min REDUCED
Linear velocity	35.7 cm/s
Injection volume	0.5 µL
Split ratio	1:100
Temp. program	60 to 220 °C @10 ° C/min
Hold time	10 min

2nd Fast GC run - Split ratio increase from 1:100 to 1:200

1. Adjust split ratio/flow and sample volume – to suit smaller dimensions

Column	HI-5, 0.10 mm x 0.10 µm x 10 m
Sample	Teknokroma Grob mix
Flow rate	0.245 mL/min
Linear velocity	35.7 cm/s
Injection volume	0.5 µL
Split ratio	1:200
Temp. program	60 to 220 °C @10 ° C/min
Hold time	10 min

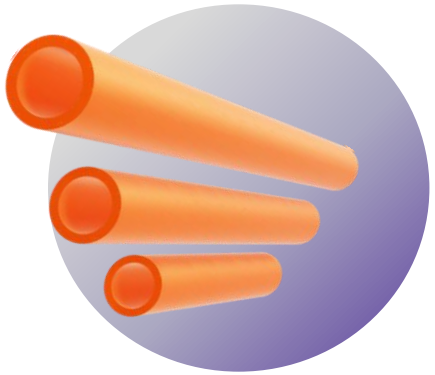


Teknokroma Fast GC FID FAMEs analysis, HI-5, 0.25 mm x 0.25 µm x 30 m

Higher split ratio/flow
= Lower response/less sample

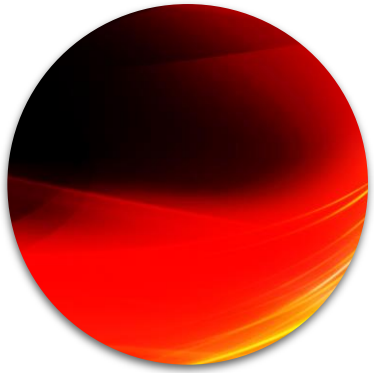
- Minimum split ratio 1:100.
- 10x less sample conc. to standard GC.
- Higher splits are okay to use.

Adjust carrier gas linear velocity



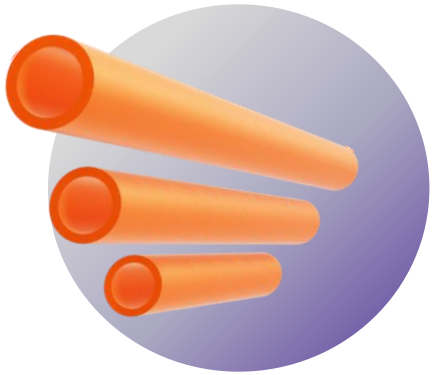
1. **Adjust inlet flow and sample volume** – to suit smaller dimensions

2. **Increase carrier gas velocity**



- Increase carrier gas velocity to ↓ the RT.
- -/+ 10 cm/sec steps, 30, 40, 50 cm/sec.

Adjust carrier gas linear velocity - Optimize



1. Adjust inlet flow and sample volume – to suit smaller dimensions

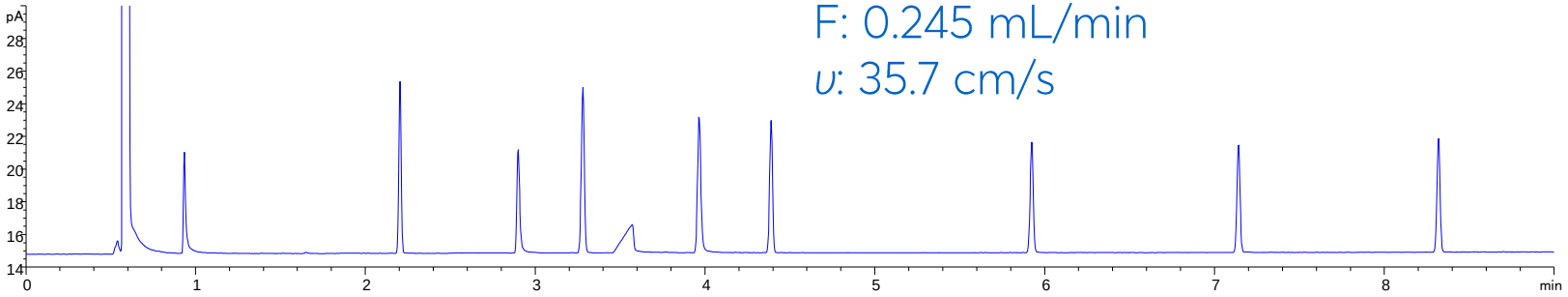
2. Increase carrier gas velocity

Adjust split ratio/flow

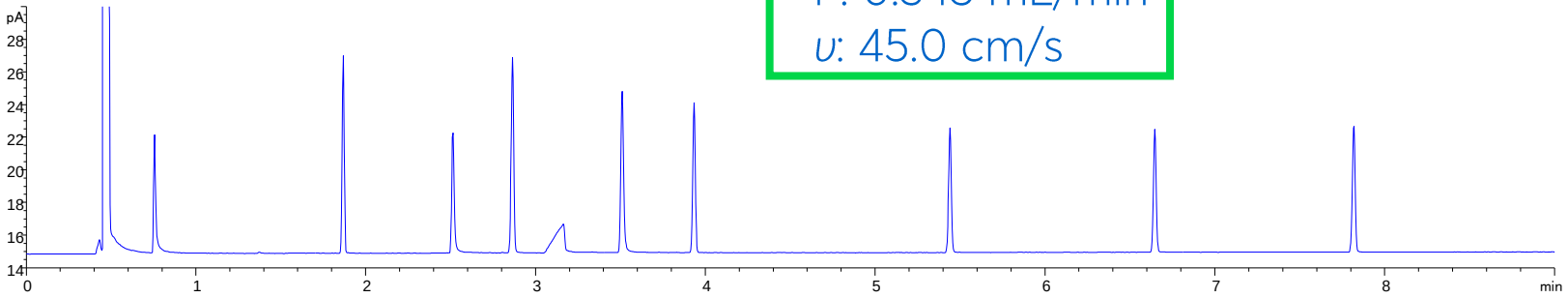
- Increase carrier gas velocity to ↓ the RT.
- -/+ 10 cm/sec steps, 30, 40, 50 cm/sec.
- Velocity ↑ = RT ↓, column flow ↑ and split flow ↑
- Poor peak shape due to overload = Split ratio too low.
- Poor response and peak loss = Split ratio too high.

Optimize if needed

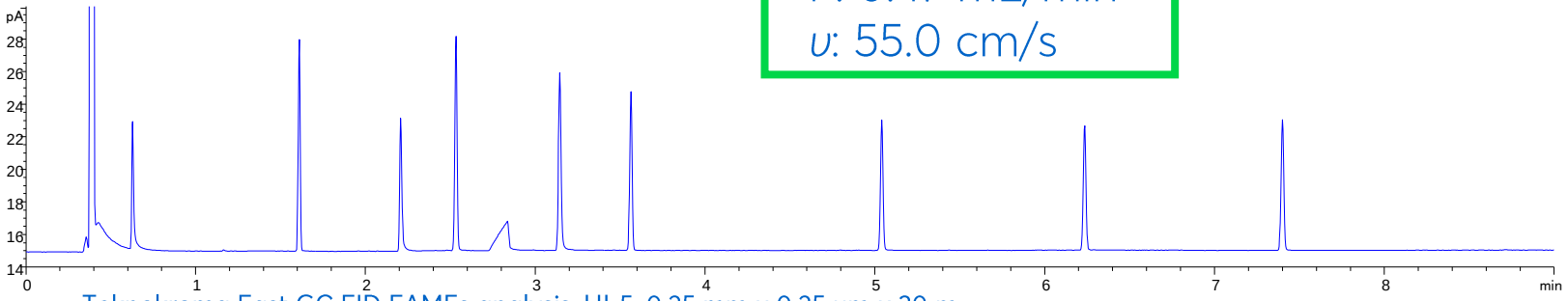
3rd and 4th run, increase linear velocity



F: 0.245 mL/min
u: 35.7 cm/s



F: 0.345 mL/min
u: 45.0 cm/s



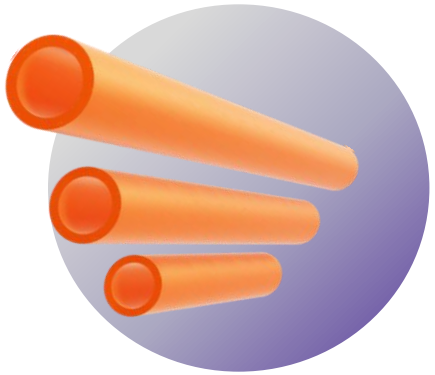
F: 0.47 mL/min
u: 55.0 cm/s

Teknokroma Fast GC FID FAMEs analysis, HI-5, 0.25 mm x 0.25 µm x 30 m

Column	HI-5, 0.10 mm x 0.10 µm x 10 m
Sample	Teknokroma Grob mix
Flow rate	Various
Linear velocity	Various
Injection volume	0.5 µL
Split ratio	1:200
Temp. program	60 to 220 °C @10 ° C/min
Hold time	10 min

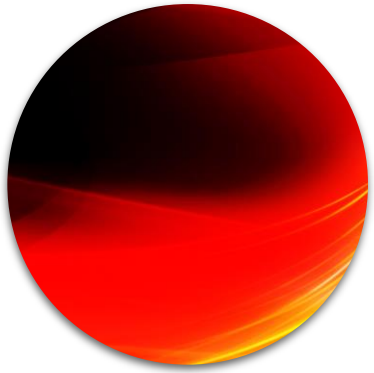
Set up a few runs in steps 10 cm/s to reduce run time.

Temperature ramp/Oven ramp rate



1. Adjust inlet flow and sample volume – to suit smaller dimensions

2. Increase carrier gas velocity



3. Adapt oven ramp rate

- + 10 °C, 20°C, 30°C, 40 °C /min (or ↑).
- Too high, peaks may elute close together.
- Calculate optimum ramp rate = 10 °C per t_0.
- Can use calculations for oven ramp rate and isothermal temps.

Temperature ramp/Oven ramp rate. calculations

1. Oven ramp rate

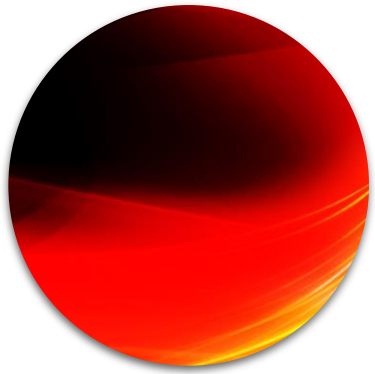
$$t_{g2} = t_{g1} \frac{\nu_2}{\nu_1} \frac{\beta_2}{\beta_1} \frac{l_1}{l_2}$$

2. Isothermal hold time

$$T_2 = T_1 \frac{\nu_1}{\nu_2} \frac{\beta_1}{\beta_2} \frac{l_2}{l_1}$$

Where;
t_{g1}, t_{g2} – temp. gradient for orig. & new conditions
ν_1, ν_2 - linear velocity of gas for orig. & new conditions
T_1, T_2 - Isothermal hold time for orig. & new conditions
β_1, β_2 - Phase ratio for orig. & new conditions
l_1, l_2 - Length of column for orig. & new conditions

Optimisation of Column Parameters in GC- Peter Morgan, Anila Khan, Tony Edge – Thermo Scientific, Runcorn, UK



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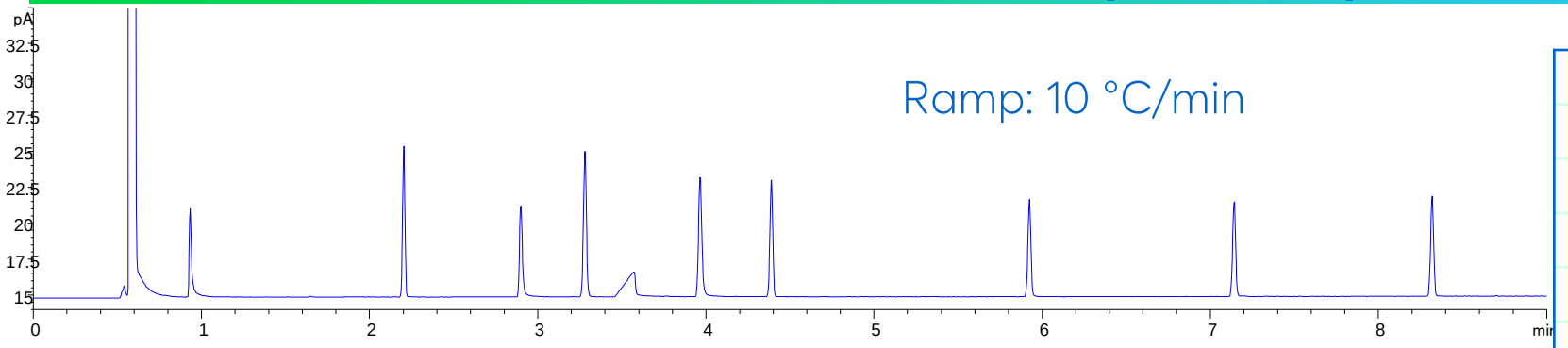
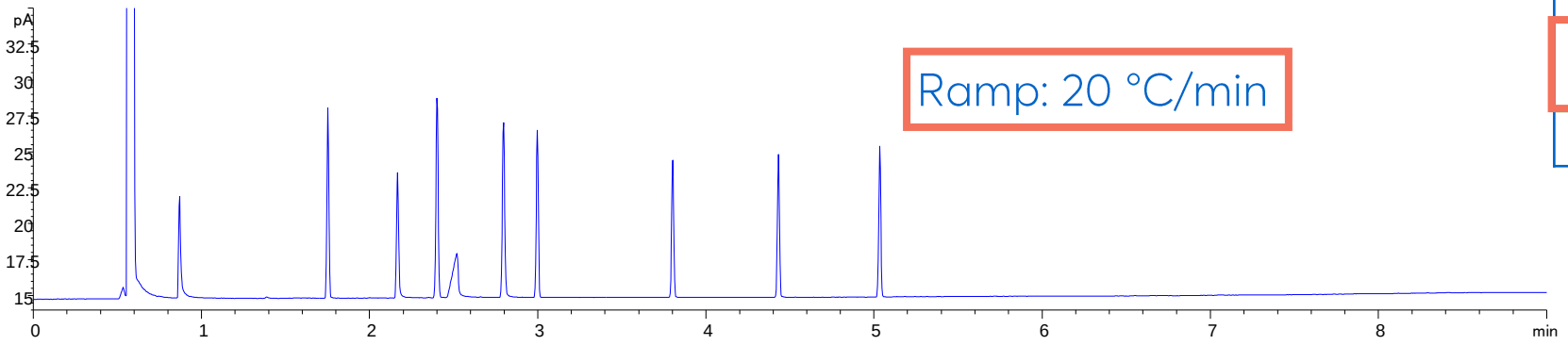
- Too high, peaks may elute close together.
- Calculate optimum ramp rate = 10 °C per t_0.
- Can use calculations for oven ramp rate and isothermal temps.

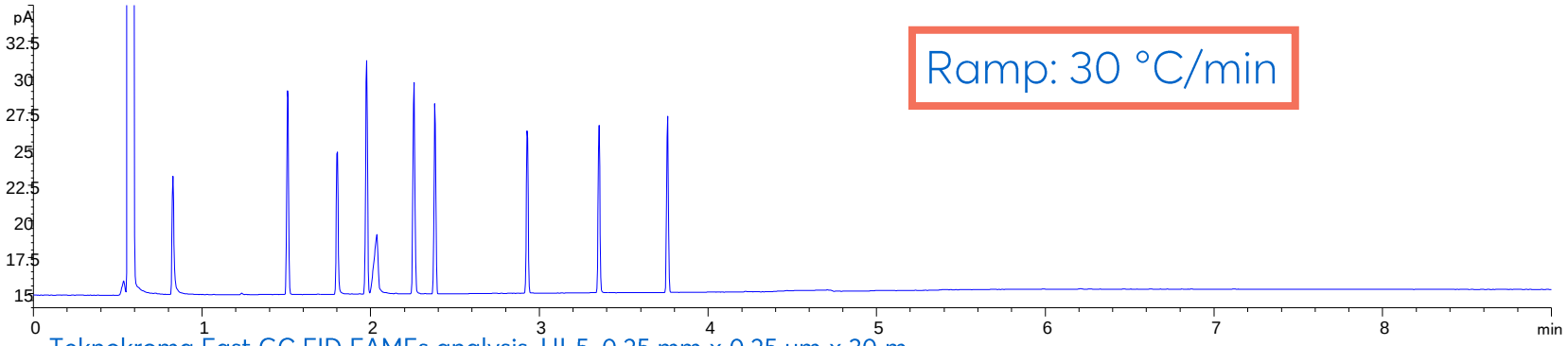
5th and 6th runs, increase temp. ramp/Oven ramp rate



Ramp: 10 °C/min



Ramp: 20 °C/min



Ramp: 30 °C/min

Teknokroma Fast GC FID FAMEs analysis, HI-5, 0.25 mm x 0.25 µm x 30 m

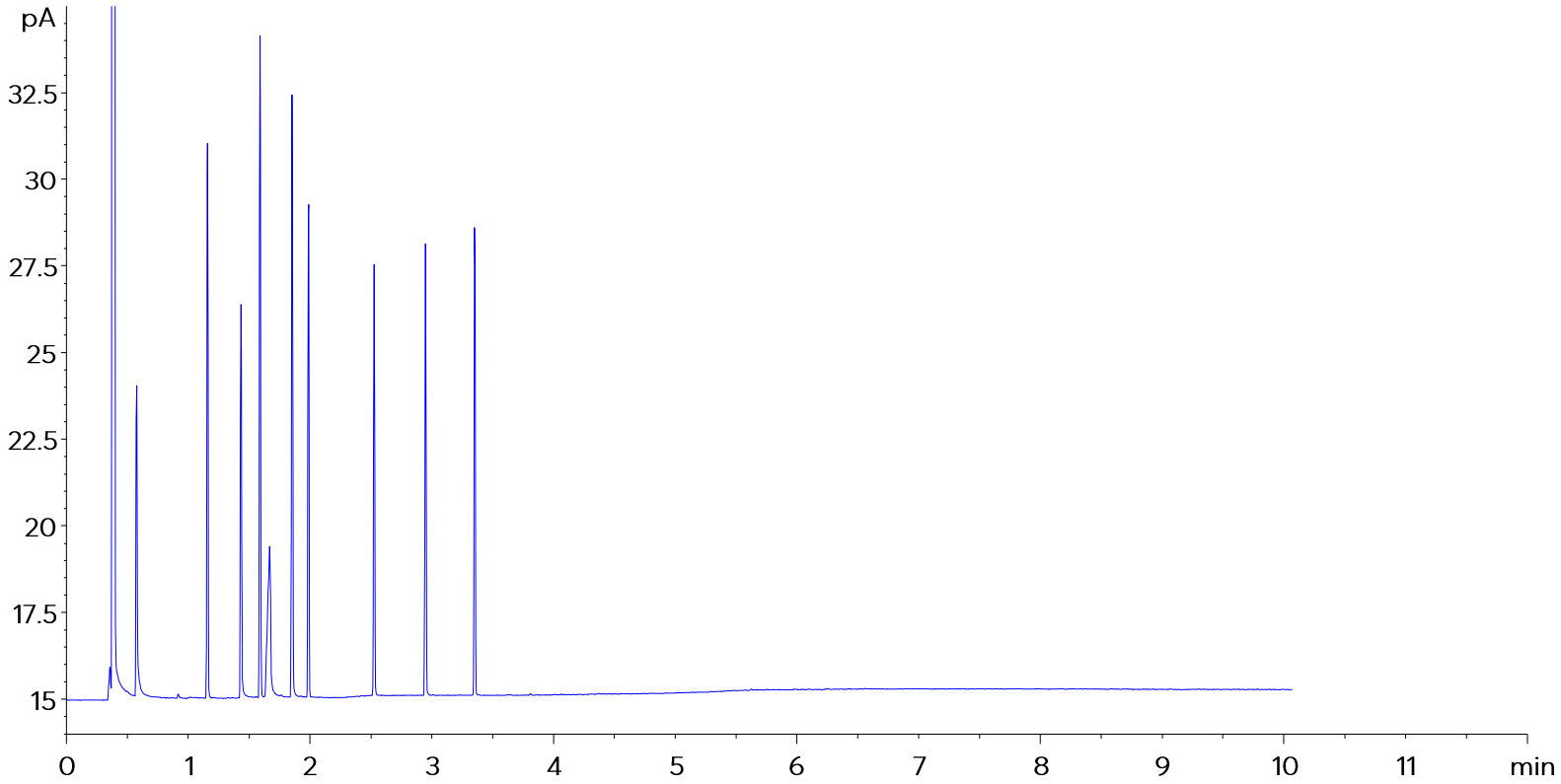
Column	HI-5, 0.10 mm x 0.10 µm x 10 m
Sample	Teknokroma Grob mix
Flow rate	0.245 mL/min
Linear velocity	35.7 cm/s
Injection volume	0.5 µL
Split ratio	1:200
Temp. program	60 to 220 °C @10°C, 20°C and 30 °C per min
Hold time	10 min

Set up a few runs in steps 10 °C per min to reduce run time.

Velocity was not adjusted at this point.

Oven ramp can be adjusted before or after linear velocity changes.

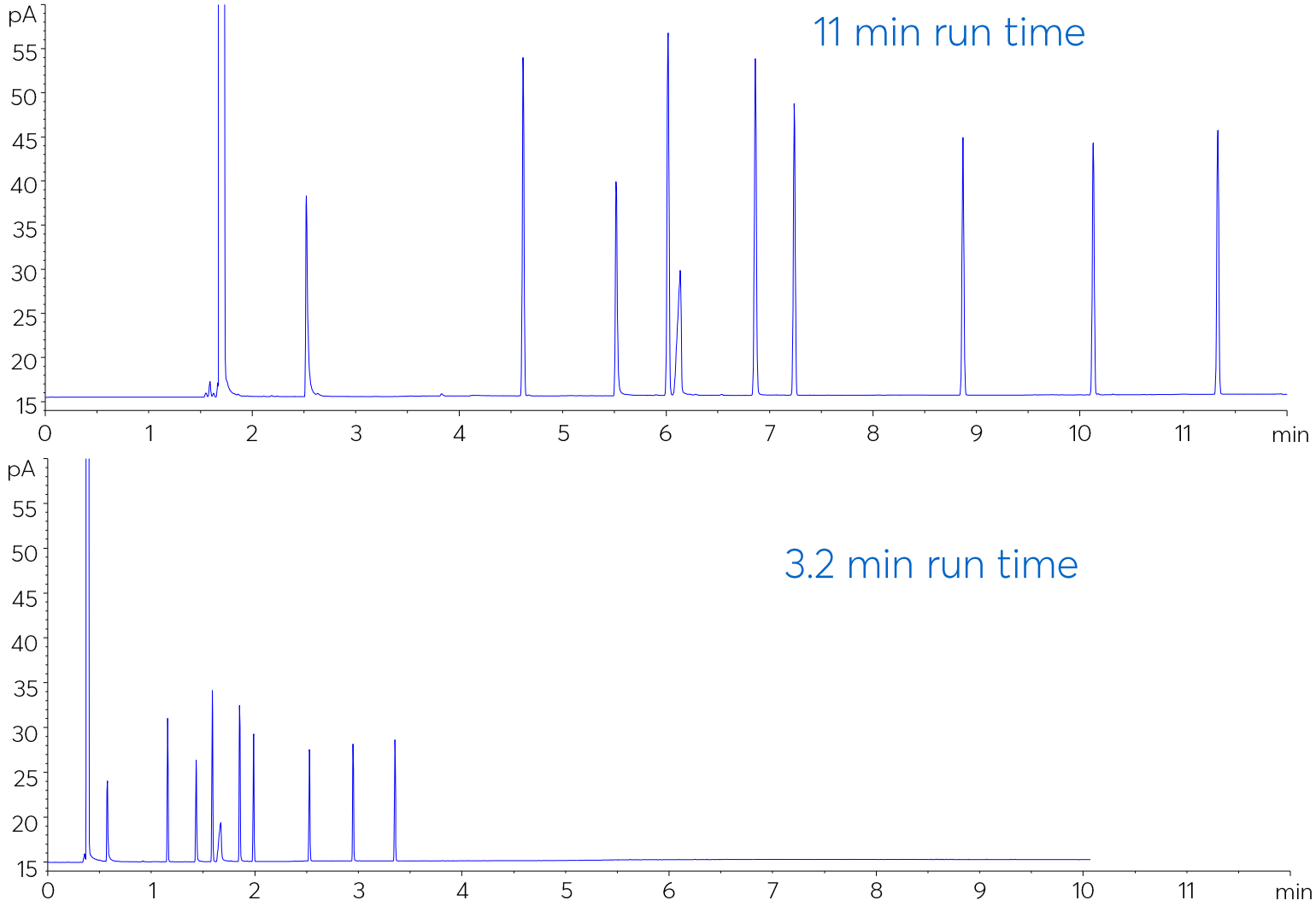
7th run, ramp rate 30 °C/min, linear velocity at 55 cm/s



Teknokroma Fast GC FID FAMEs analysis, HI-5, 0.25 mm x 0.25 µm x 30 m

Column	HI-5, 0.10 mm x 0.10 µm x 10 m
Sample	Teknokroma Grob mix
Flow rate	0.47 mL/min
Linear velocity	55.0 cm/s
Injection volume	0.5 µL
Split ratio	1:200
Temp. program	60 to 220 °C @30 °C per min
Hold time	10 min

Standard vs Fast GC results

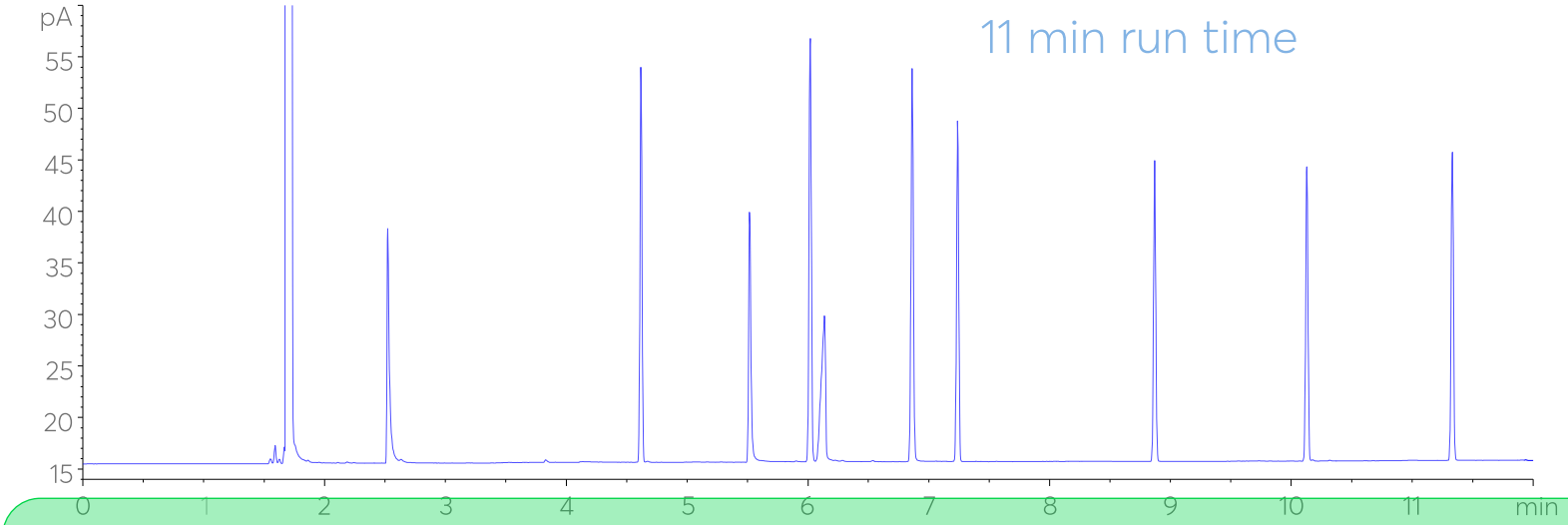


Teknokroma Fast GC FID FAMEs analysis, HI-5, 0.25 mm x 0.25 µm x 30 m

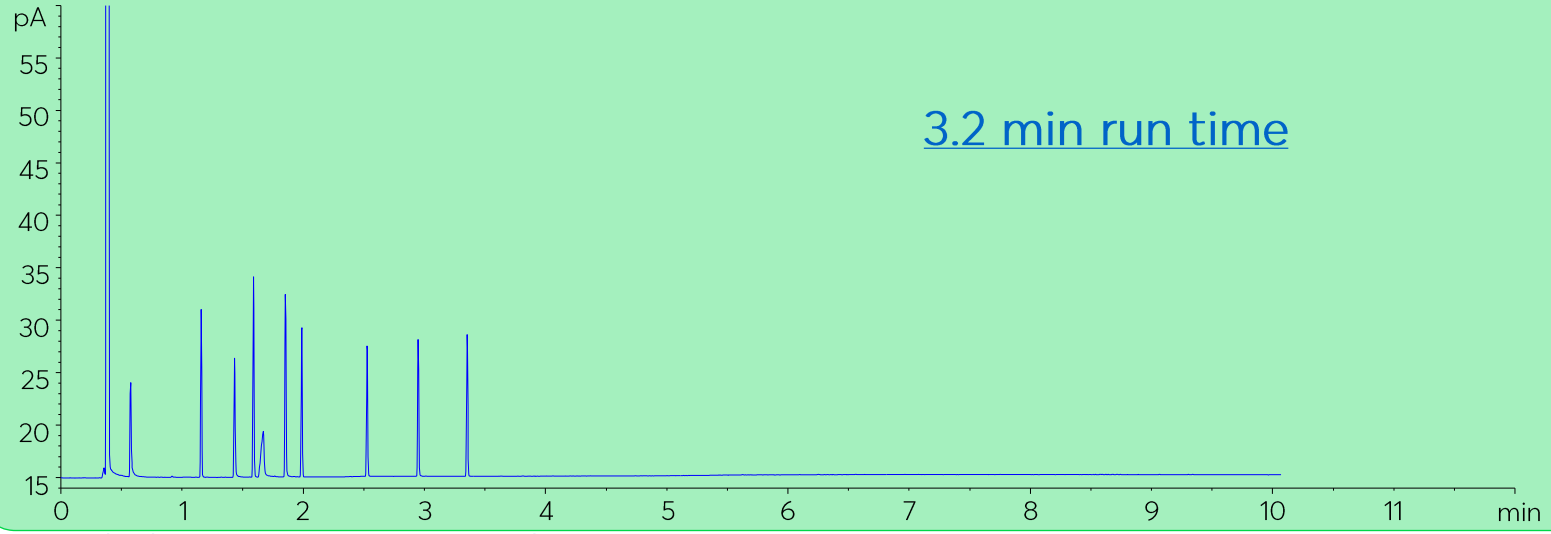
Standard Column	HI-5 0.25 mm x 0.25 µm x 30 m
Sample	Teknokroma Grob mix
Flow rate	1.2 mL/min
Linear velocity	35.7 cm/s
Injection volume	1 µL
Split ratio	75:1
Temp. program	60 to 220 °C @10 ° C/min
Hold time	10 min

Fast GC Column	HI-5 0.10 mm x 0.10 µm x 10 m
Sample	Teknokroma Grob mix
Flow rate	0.47 mL/min
Linear velocity	55.0 cm/s
Injection volume	0.5 µL
Split ratio	1:200
Temp. program	60 to 220 °C @30 °C per min
Hold time	10 min

Standard vs Fast GC results



Standard Column	HI-5 0.25 mm x 0.25 µm x 30 m
Sample	Teknokroma Grob mix
Flow rate	1.2 mL/min
Linear velocity	35.7 cm/s
Injection volume	1 µL
Split ratio	75:1
Temp. program	60 to 220 °C @10 ° C/min
Hold time	10 min



3.2 min run time

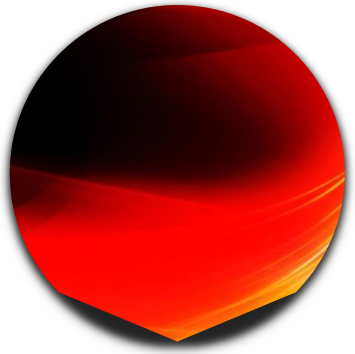
Fast GC Column	**HI-5 0.10 mm x 0.10 µm x 10 m**
Sample	Teknokroma Grob mix
Flow rate	0.47 mL/min
Linear velocity	55.0 cm/s
Injection volume	0.5 µL
Split ratio	1:200
Temp. program	60 to 220 °C @30 °C per min
Hold time	10 min

Teknokroma Fast GC FID FAMEs analysis, HI-5, 0.25 mm x 0.25 µm x 30 m

Fast GC method transfer summary

Smaller column dimensions, flows and sample dilution

Faster carrier gas linear velocity



Faster oven ramp rate

To achieve Fast GC

Thank you for your attention