The combination of a chromatographic and spectral method.
Exploits advantages of each

**Chromatograph** - produces ‘pure’ fractions from your sample.

**Spectral method** - yields qualitative information about a ‘pure’ component.

Combination results in 3-D data providing both quantitative and qualitative information.

One critical aspect of GC-MS and LC-MS is the interface.
Both chromatographic approaches have relatively large flows.
GC - 1 - 50 ml / min
LC - 0.1 - 5 ml / min
- 50-5000 ml/min as a gas

The mass spec requires a vacuum of about $10^{-5} - 10^{-6}$ torr - gas phase.

**Gas Chromatography**
- Mass Spectrometry - GC-MS
- Infrared Spectrometry - GC-FTIR
- Atomic Emission - GC-AES

**Liquid Chromatography**
- Mass Spectrometry

For LC, the other two methods are not practical due to the solvent.

**Goals of an interface**
- Quantitatively transfer all analyte
- Reduce pressure/flow from chromatograph to level MS can handle
- Not cost an arm (or a leg)

No interface meets all of these requirements.
GC interfacing is a bit easier than for LC. The sample is already in the gas phase. Major goal is to remove most of the carrier gas - its the majority of the effluent.

**Interfaces we’ll cover**
- Molecular separator
- Open split
- Capillary direct

Most popular approach when packed columns must be used.

Based on concept that larger molecules will diffuse more slowly so more will reach the MS entry jet.

Relative simple and inexpensive approach.

**Molecular Separator**

- from GC
- to MS

Vacuum source

**Disadvantages**
- Rate of diffusion is MW dependent
- selectivity based on MW

If jet becomes partially plugged, you end up with an excellent carrier gas detector

**Open split interface**

- He in
- He out

from GC

liner

flow restrictor

to MS

Somewhat similar to a jet separator. The MS pulls in about 1 ml/min through the flow restrictor. If column flow is above that - excess is vented. If flow is <1 ml/min, He from external source is pulled in. Best for sources that have flows close to 1 ml/min like capillary columns.

**Advantages**
- Any gas producing source can be used.
- Relative low cost and easy to use.

**Disadvantages**
- Sample leaves column in split.
- Split changes as flow changes.
If we limit interface to capillary columns, the MS can actually use all column effluent.

Now that we have an interface, how do we justify having a detector that costs more than the chromatograph?

This is not a course in MS so we'll limit our discussion to using the MS as a chromatographic detector.

I'm assuming you know the basics of MS instrumentation and interpretation.

If your scan rate is too high, you don't obtain enough scans to properly define your peak. This results in a loss in precision.
Maximum sensitivity and precision is obtained under conditions when minimum qualitative information is collected.

We need some way to maximize both types of information

- Do multiple runs
- Target compound analysis

A simple approach to obtain both quantitative and qualitative analysis.

Works best if you are only dealing with a limited number of analytes.

You also want to have an isotope labeled internal standard.

**Line selection**
For each compound, identify at least three spectral lines
- **quantitation ion** - largest line.
- two or more **qualifying ions** - also should be larger lines resolved by at least 20-50 M/e from each other.

If a labeled internal standard is used, the selected lines must contain the label.

Add the internal standard to your sample.
Set MS to SIM for all 6 lines.

Basis for qualification
- Proper retention time
- Proper ions
- Proper ion ratios
- Internal standard agreement

Good enough to hold up in court!
**Target compound analysis**

Example Analysis of a drug in urine

*trideutrated internal standard*

145 179 214

142 176 211

**Sample**

**LC-MS**

Relative new method.

Much harder to interface due to
1. Volumes are much larger
2. Samples are in liquid phase
3. Sample components usually have a larger MW - more fragmentation
4. Current interfaces result in 'atypical' mass spectra

We'll just quickly look at two interfaces.

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**Thermospray interface**

- Sample is heated and allowed to rapidly expand into a vacuum.
- Solvent is quickly pulled from component drops and a ‘static’ charge is produced.
- Charged particles enter into the MS via a skimmer.

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**Electrospray interface**

A charge is transferred to the droplets.

They are then sprayed into a vacuum chamber where the volatile solvent is ‘pulled off’.

At some point, sample ions are ejected from the drop and enter the MS.
Thermospray and Electrospray both result in a solvent mist that is electrostatically charged.

As the drops are pulled towards the skimmer, solvent is evaporated.

This increases the charge density, causes the drop to further disperse and ultimately transfer the charge to the analyte.

Interfaces are still quite developmental. So is the data.

Since ions are produced by transferring a charge to the sample components, multiple charge ions are quite common.

You get unusual spectra, low fragmentation, extended effective MS range.

A lot of work is being done in data interpretation.
Other hyphenated methods

We’ll only look briefly at two other GC-XX methods

**GC-FTIR**
**GC-AES**

Interfacing of each is relatively straightforward - both can use direct interfacing.

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**GC-FTIR**

Two types of data are produced
IR spectra for each scan
Gram-Schmidt Chromatogram

Full FT transformation of data is slow whereas GS calculation is fast - it only results in one point per scan.

This permits real time display of your data.

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**GC-FTIR**

You can control some of the same operational parameters as with GC-MS.

**Full scan** - collect spectra over a fixed wavelength range

**Selected range(s)** - only collect over specific, small regions.

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**GC-FTIR**

One limitation at this point is a lack of standard spectra.

MS offers 250,000+ standard spectra
IR offers only a few thousand.

**Why?** Most IR spectra are for liquid or solid phase samples - gas phase spectra are different.

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**GC-AES**

This approach relies on doing plasma emission on your sample.

Hewlett-Packard offers a small plasma emission detector based on a microwave plasma source.

Relative expensive and sensitivity is very dependent on element and lines used.
• Produces emission spectra for each element.
• A reagent gas may be needed to insure proper atomization and excitation.
• Can obtain elemental analysis and empirical formula.
• Limited at this point - can only look at a limited number of lines (due to small range of photodiode).