Detection Techniques for CW Agents and Related Compounds

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Outline

- **Instrumental Detection Techniques – User scenarios determine requirements**
  - Verification/compliance: Requirements = OPCW Proficiency Standards
  - Weapon demilitarization: Ensure material destruction
  - Personnel protection, military or civilian: "Detect-to-warn"

- **Portable instrumentation for Detect-to-Warn applications**
  - Requirements
  - Current technologies – strengths and limitations
  - Portable GC, GCxGC, and GC-MS development efforts

- **Opportunities for progress**
  - Performance of most GC instruments at present (even bench instruments) is degraded by poor sample injection.
  - Portable MS instruments: Vacuum pumps, not mass filters, determine system size, weight, and power. Explore mass spectrometry at higher P.
  - Portable GCxGC: Potential advantages and limitations.

Instrumental Detection Scenarios: Comparisons
(Based on GC- and GC-MS)

	Compliance verification	Weapon destruction	Detect-to-warn	Range of values
Time available	15 days 10^6 sec	Mins – hrs 10^2-10^3 sec	Sec – min 1-10^2 sec	10^6
Sample cleanup?	Yes	Sometimes	No	
Target analytes	>10^3	<10	<10^2	
Sample matrix	Very complex	Varies	Complex	
Instrument volume	> 2 m^3	< 0.1 m^3	10^{-1} - 10^{-3} m^3	10^4
Man-portable?	No	No	Yes	
Energy/analysis	10^6 - 10^7 J	100J (no MS) 10^5 J (w/MS)	100J (no MS) 10^5 J (w/MS)	10^5
LOD	Spikes 1-10 ppm[1]	Est. < 20 ppt[2]	Est. <1 ppb[3]	10^6
FAR (Type 1 error rate)	Zero [1]	Unknown	Varies, est. <10^{-7}	

1) V. Dubey, S. Velikeloth, M. Sliwakowski, G. Mallard, Accred Qual Assur **14**(2009)431
2) Based on 24hr GB exposure at 0.0001*LC_{t50} limit at http://www.fas.org/programs/bio/chemweapons/cwagents.htm
3) Based on 1 min GB exposure at 0.0001*LC_{t50} exposure limit, Federation of American Scientists, *ibid*.

Instrumental Detection Scenarios: Observations
(Based on GC- and GC-MS)

- **WHY is GC-MS considered the preferred instrumental technique?**
  - **"Chemical discrimination power" is large**
  - **Discrimination power can be quantified: $C_p/t * t_C * M/\Delta M *$ (Mass range)**
  - **Discrimination power ~ 1/FAR**

- **Range of instrumental requirements varies over many orders of magnitude**
  - Requirements for ***SPEED***, energy consumption, LOD, and size are all at the difficult end of the range for "Detect to warn" instrumentation

- **Energy/analysis estimates in the table are dominated by the mass spectrometer rather than the GC for man-portable instruments**
  - The whole ***system*** must be portable – vacuum pumps and the batteries to run them are usually bigger and heavier than the sample-wetted components of the instrument.

- **These factors are the drivers for development of current and future portable detection instruments.**

Examples of Available Portable Instruments

- A representative example: Smiths Detection LCD3.2E ion mobility spectrometer

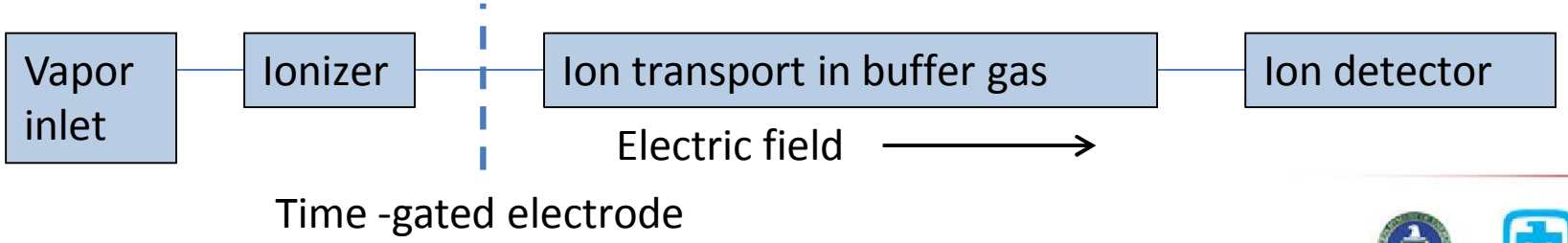
- Convenient SWAP (Size, Weight, and Power)
- Relatively fast, 30-120 sec/analysis
- Manufacturer's LOD claims meet specs for CW detection
- Manufacturer publishes detection limits for a wide range of TICs

But: No false alarm rate data are provided

- Manufacturer provides the following advice:

> It is not recommended that more than 10 TICs are programmed into the unit at any one time. Any more than this may increase the probability of false alarms.

i.e., the IMS used in the unit cannot reliably ***separate*** more than about 10 known compounds. Estimated Cp ~10-30, where Cp = (Ion transport time)/(peak width)



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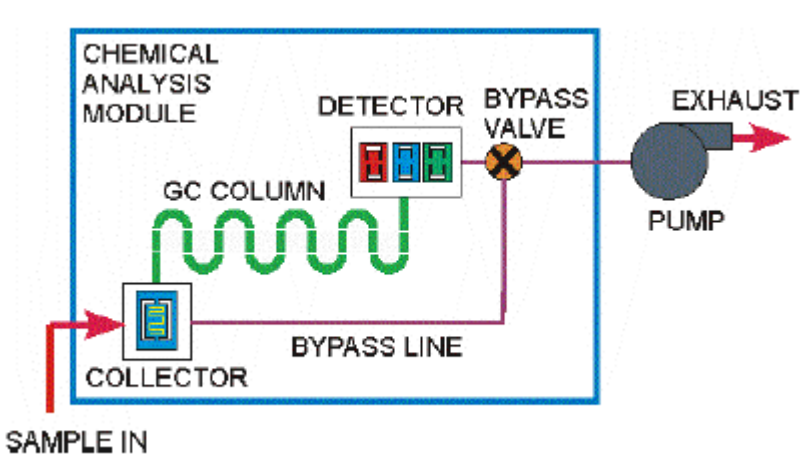
Commercially Available Portable GC: An Example

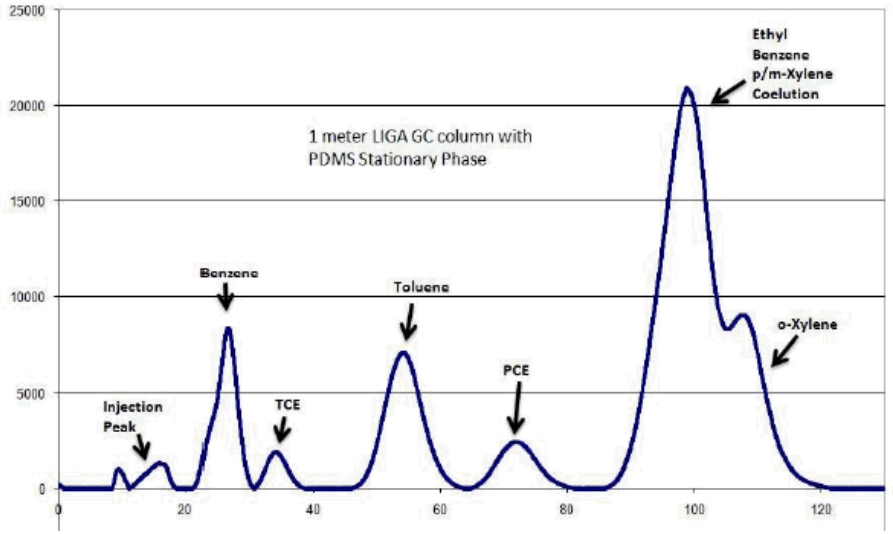
www.defiant-tech.com



- Air carrier gas, ambient inlet and vacuum outlet
- Thermal injector
- Polymer coated SAW detectors

- This system can still deliver usefully low false alarm rates because the sample preconcentrator and detector stages are chemically selective, unlike the IMS.

- This fact limits the range of target chemicals that can be analyzed.



Low Peak capacity production: W_b ~ 10 sec, so Peaks/sec ~ 0.1

Douglas R. Adkins and Patrick R. Lewis, Proc. Of SPIE Vol. 7304 73040S-1

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Commercially Available Portable GC-MS: Examples

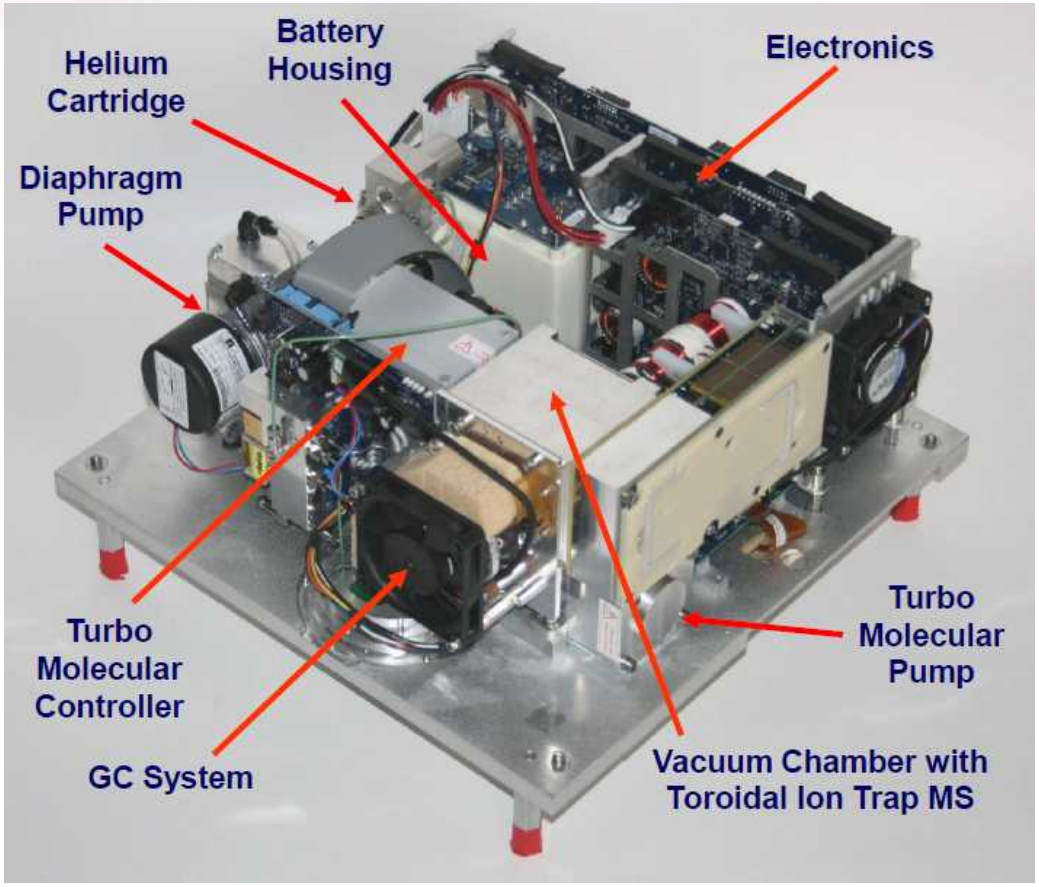
Griffon™ 460
www.flir.com/detection
GC-CITMS (MS/MS capable)
Turbomolecular pump
44.5 kg
600 W

Inficon HAPSITE™
www.inficon.com
GC-MS (now with GPS!)
Non evaporable getter pump
16 kg + 20 kg "service module"
30W average

Torion® Guardion
www.torion.com
GC- Toroidal ion trap MS
Turbomolecular pump
14.5 kg
60W average

GC-MS capability greatly exceeds IMS and PC-GC-SAW examples, but…
large, heavy, and slow.

A Look Inside One Portable GC-MS



A nicely engineered system, but the GC and ion trap are still only a small fraction of the total.

The vacuum pumps and the associated battery to run them are bigger than the GC and MS components.

Opportunity: How can we reduce vacuum pumping requirements?

1. Operate GC at higher efficiency with reduced carrier gas load.
2. Operate MS at higher pressure?

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A Closer Look at "Chemical Discrimination"

- **WHY is GC-MS considered the preferred instrumental technique?**
  - **"Chemical discrimination power" is large**
  - **Discrimination power can be quantified: $C_p/t * t_C * M/\Delta M *$ (Mass range)**
  - **Discrimination power ~ 1/FAR**

- **GC *separates* mixtures, mass spec *identifies* individual components by M+, cracking pattern, MS-MS.**

- ***Gedanken* experiment: IF GC could do a perfect separation of an arbitrary mixture, components could be identified by t_R alone.**

- **This is impractical because separation capacity required would be enormous. Statistical analysis: 90% probability of single peak separation in an arbitrary mixture requires 95% unused or "empty" peak capacity[1].**

- **BUT – a significant increase in GC peak capacity would still provide latitude for a decrease in detector selectivity – thereby reducing system MS (or other detector?) performance requirements.**

1) Davis and Giddings, Anal. Chem. **55**(1983)418.

A More Rigorous Definition for C_p

Peak Capacity for a 1D separation @ R_s=1:

$$C_p = {}^1n_{c,1D} = \frac{{}^1t}{{}^1w_b}$$

Where: t = elution time
W_b = peak width at baseline

Peak Capacity Production* for a 1D separation:

$$\frac{{}^1n_{c,1D}}{{}^1t} = \frac{1}{{}^1w_b}$$

This is intuitive: Narrower GC peaks mean more possible separate elutions per unit time.

* X. Wang, D. R. Stoll, P. W. Carr, P. J. Schoenmakers, *J. Chromatogr. A*, 2006, 1125, 177-181

Peak Widths from GC Theory. 1.

Longitudinal Diffusion

Resistance to Mass Transfer – Mobile Phase

Resistance to Mass Transfer – Stationary Phase

Plate Height (H): index describing the rate of band broadening along the separation path

$$H = \frac{B}{u} + C_g u + C_s u + H_{ext}$$

Injection
Detection
Electronics
Dead Volumes

u: average linear velocity of mobile phase

Golay Equation neglecting H_{ext}:

$$H = \frac{2D_{g,o} j f}{\bar{u}} + \frac{1 + 6k' + 11k'^2}{96(1+k')^2} \frac{d_c^2 \bar{u} f}{D_{g,o} j} + \frac{2k' d_f^2 \bar{u}}{3(1+k')^2 D_s}$$

D_g = gas phase diffusion coefficient
Ds = stationary phase diffusion coefficient
j = James-Martin compressibility factor
f = Giddings compressibility factor

u = gas flow velocity
k = analyte retention factor = $(t_R - t_M)/t_M = K_{eq}(V_s/V_g)$

Peak Widths from GC Theory. 2.

Analysis due to V. R. Reid and R. E. Synovec, *Talanta* 76 (2008) 703-717.

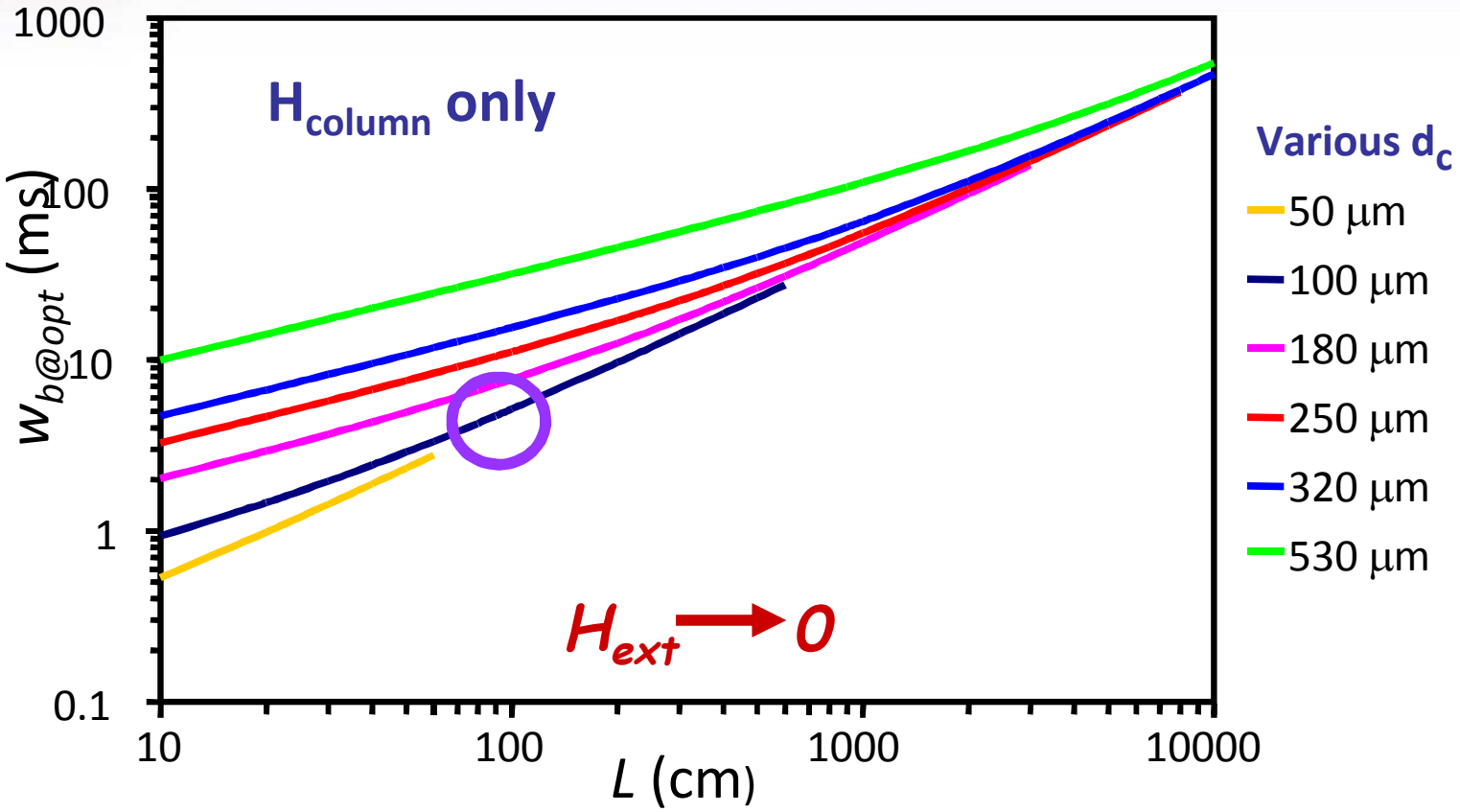
- **To find what the best possible peak widths would be under ideal temperature programming:**
  - **Take the derivative of the Golay equation to find optimal gas flow, u_{opt}**
  - **For a given set of column conditions (diameter, phase thickness, phase type) set $k_i = 0$ at the elution time t_{Ri} for each analyte (ideal T program).**
  - **Calculate H_{min} at those conditions**
  - **Calculate peak width at baseline from the relation:**

$$W_b = (4/u_{opt})(H_{min}L)^{1/2}$$

For standard, off the shelf commercial GC columns, the results are a bit surprising…

Peak Widths from GC Theory. 3.

V. R. Reid and R. E. Synovec, *Talanta* 76 (2008) 703-717



For a meter of standard 100 µm diameter GC column, W_b ***should*** be about 2 msec !

Most of our GC analyses have peak widths 1000X or greater than this! Why?

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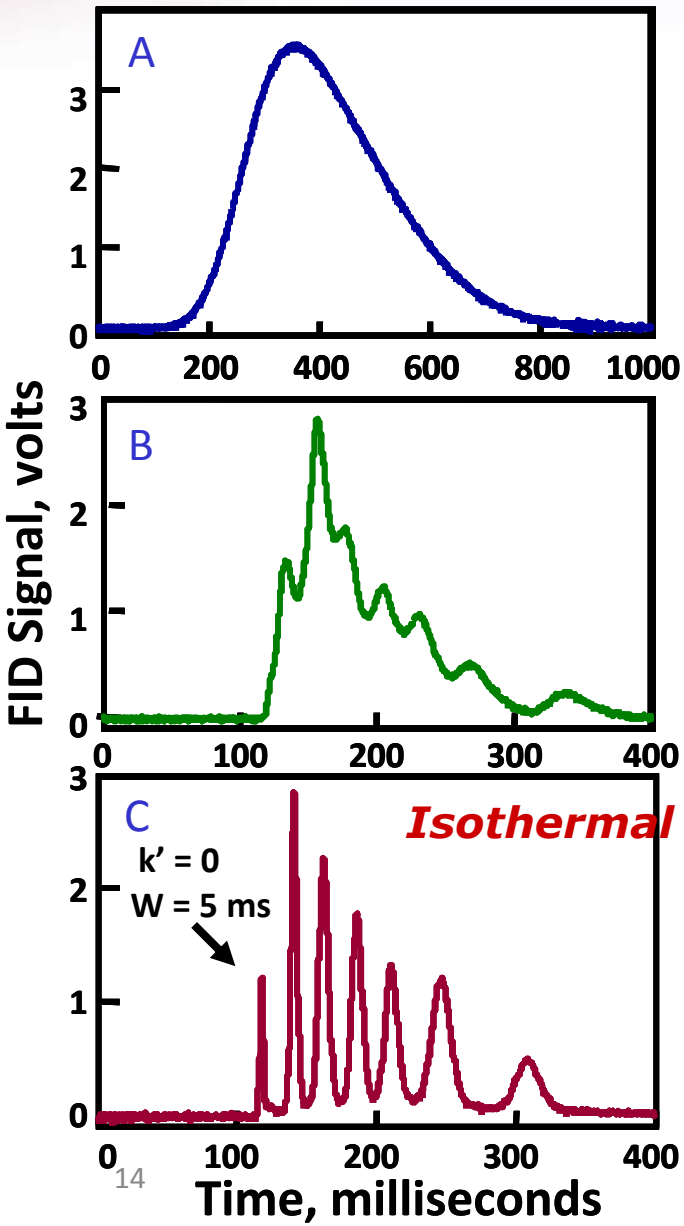
Currently, GC Capability is Lost to Poor Injections

This applies to *both* lab and portable GC!



- Three types of injection under identical separation conditions (1 m x 100 µm column)
- Same 7-component mixture injected. Retention order: methanol, benzene, octane, chlorobenzene, anisole, decane, butylbenzene

(A) standard primary autoinjector

(B) single valve sample injector (20 ms)

(C) synchronized dual valve injector (2.5 ms)

High-speed valves were used to achieve narrow injection pulses, but with large sample splits:

G.M. Gross, B.J. Prazen, J.W. Grate, R.E. Synovec, Anal. Chem. **76** (2004) 3517-3524.

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Golay Equation: The Extra-column Term

$$H = \frac{B}{u} + C_g u + C_s u + H_{ext}$$

Injection, Detection, Electronics, Dead Volumes: Experiment shows that for a fast detector, H_{ext} is dominated by injection.

$$H_{ext} = \frac{\Delta t^2 u^2}{L(k+1)^2}$$

[1]Where $\Delta t = \frac{\text{Volume of injector or interconnect, m}^3}{\textit{Local} \text{ gas flow rate, m}^3/\text{sec}}$

Only 1 term is quadratic in ū … so extra-column broadening dominates at high speeds!

L = column length, which cannot be increased without increasing the analysis time

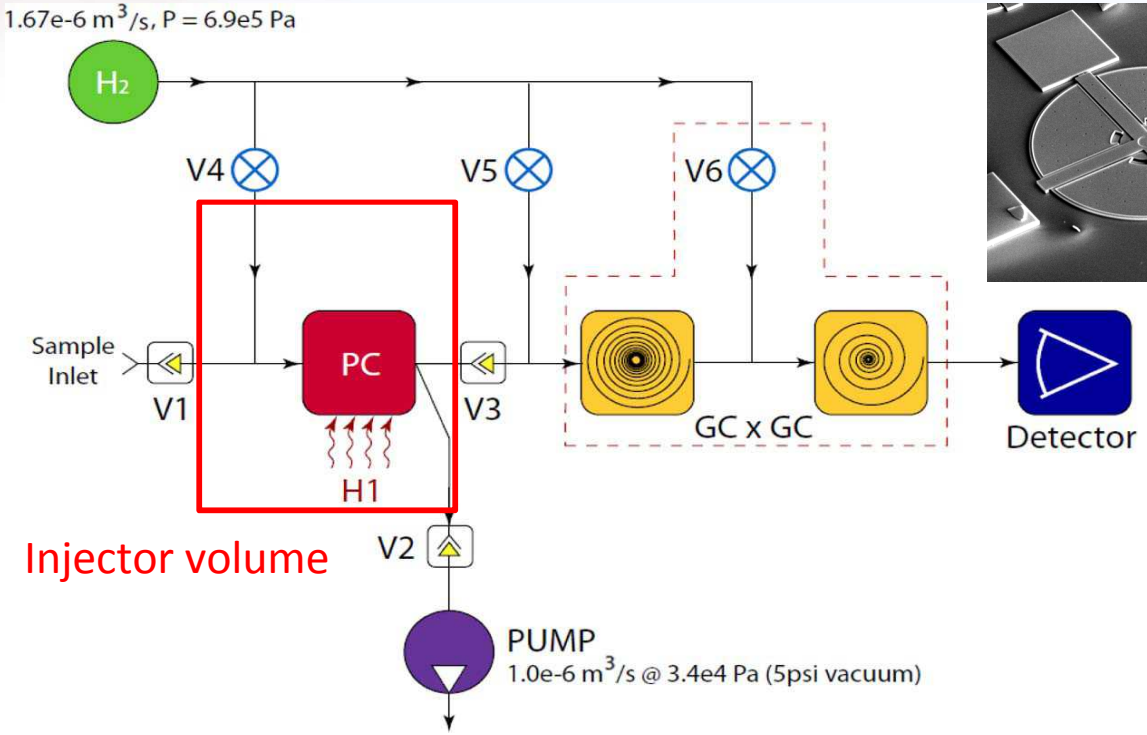
k = retention factor, determined by the analyte and stationary phase chemistries

Local gas flow rate is slowest at the front of the column, i.e., the sample injector!

If you don't split the volume (and thereby lose sample and increase LOD), you need a very small volume for the sample injector to achieve high speed GC performance.

1) H. Ahn and S. Brandani, AIChE Journal **51(7)** (2005) 1980-1990.

“Micro” Portable GC Instrument Efforts



Microfabricated valves define the volume of a splitless injector (~4 µL) for high speed flow-modulated GCxGC

P. Galambos, et al., Journal of Microelectromechanical Systems **20(5)** (2011) 1150 – 1161.

- Basic components have been demonstrated: Valves, sample trap/injector, GC columns, candidate detectors.
- Many engineering challenges remain before micro instruments will be commercially available.
- Similar efforts in many laboratories: Examples include Prof. Alistair Lewis (U. of York, UK), Professor E.T. Zellers (U. of Michigan, US), many others.

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Portable MS: Developmental Efforts

- **Extensive literature exists on miniaturizing mass spectrometers. Cf Z. Ouyang and R.G. Cooks, Annu. Rev. Anal. Chem. 2009. 2:10.1-10.28.**

- **Instrument portability is limited by vacuum pumping and associated power requirements. Therefore, consider means by which the vacuum requirements can be significantly reduced:**

1. **Reduce the radius of ion trap mass analyzers into the 100 – 1000 µm range**

    - As the radius decreases and trapping frequency increases, stable ion trajectories are smaller and scattering by ambient neutrals becomes less probable.

    - M/e scans of ~50-350 Da have been accomplished at ~ 1 Torr (~ 100 Pa)

    - Trap performance calculations: W. B. Whitten, Peter T.A. Reilly and J. Michael Ramsey, Rapid Commun. Mass Spectrom. **18** (2004) 1749-1752.

2. **Nondestructive ion trap mass analysis recently reported at >1mTorr by image current measurement rather than "scanning the trap" into an ion multiplier.**

    - W. Xu, et al., Anal. Chem. 83 (2011) 685-689.

High Pressure Portable MS: Engineering Challenges

- Smaller trap radius allows mass filter operation at elevated pressure, but…
- Frequency of trap operation increases, making impedance matching between RF power supply and the trap more difficult.
- Frequency stability must also improve as trap radius decreases.
- Trap charge capacity decreases due to space charge effects. Fewer ions can be trapped.
- Attempts to make parallel arrays of very small traps (to overcome charge capacity problems) result in increased parasitic capacitance, making the RF matching problem worse.
- Ionizers and ion detectors must also run at elevated pressures with useful device lifetimes.
- Note that if gas chromatography is optimized as discussed earlier, GC peak widths could decrease by 1000X, requiring an equivalent INCREASE in ion trap scan rates without loss of S/N. This puts high demands on ion detection and amplifier bandwidths.

Before Closing, a Disclaimer

- For “detect-to-warn” CW detection applications in particular, there are many alternative approaches not discussed herein. Just one example:

www.flir.com/detection

- “Reactive materials” detection methods hold promise, especially for improving possible optical/spectroscopic remote detection schemes.

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Summary

- GC- and GC-MS methods are dominant in “point detection” for CW because of the unparalleled qualitative analysis/identification capability.

- This arises because the physics of phase partitioning (GC separation) and mass/charge measurement (MS, MS-MS) are separate, leading to “orthogonal information axes” that span a wide space.

- Opportunities for improvement in GC-MS instrumentation:
  - In the short term, the biggest unused capability is in GC separations.
  - GC columns are capable of much better performance than we typically get from them, both in laboratory bench and portable applications.
  - Look for improvements in sample injection to enhance GC separations by ~100X. Cryofocused small-volume injection or fast-valve injection.
  - Note that mass spec scan rates must increase if GC peak widths are reduced.

- Improvements in portable GC-MS instrumentation for CW detection will be slower in coming to market.
  - Engineering constraints on portability are driven by vacuum pumping.
  - Mass analyzers running at >100 Pa are still research projects, not products.