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3- dimensional micro-gas chromatography device for rapid and sensitive indoor air chemical exposure assessment

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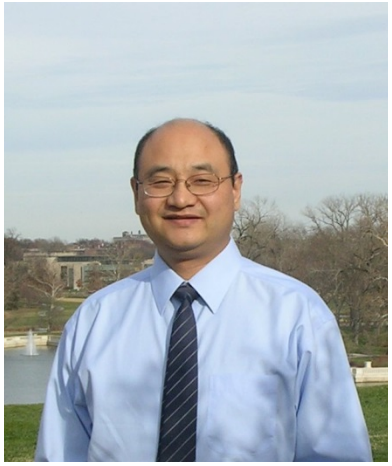


Outline

- **Challenges for indoor (S)VOC assessment**

- **Introduction**
  - Gas chromatography (GC)
  - Micro-GC (μGC)
  - Comprehensive 2-D GC/μGC (GC x GC or μGC x μGC)

- **Smart multi-channel multi-dimensional GC**
  - Concept
  - Comparison
  - On-column vapor detectors
  - 2-D smart GC
  - 3-D smart GC

- **Proposed project**

Challenges for indoor (S)VOC assessment

1. Large number of (S)VOCs to be quantified
   Cleaning products, pesticides, *etc*.
   Interference background

2. Temporal variations

3. Spatial variations

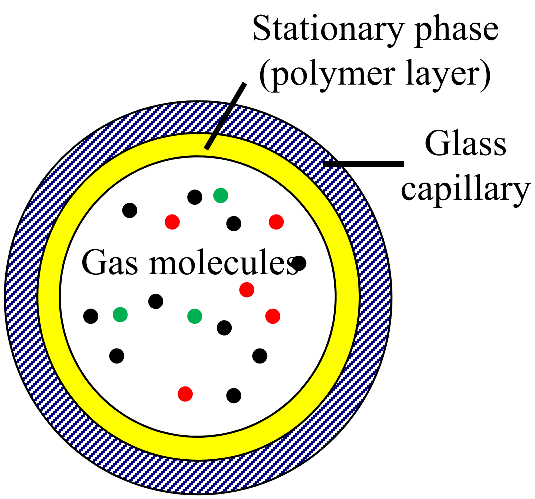
An instrument should be

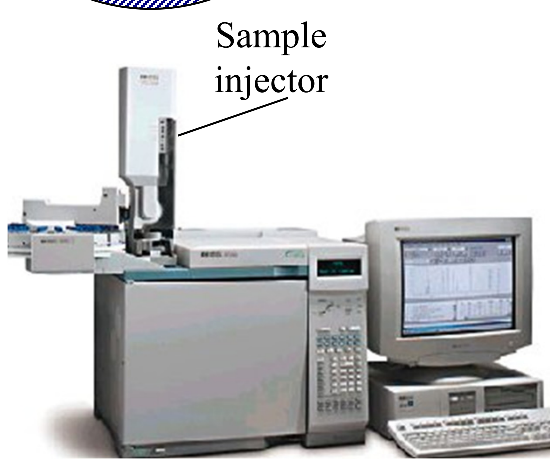
1. Able to analyze many (S)VOCs
   - qualitatively (type of molecule)
   - quantitatively (how much)
2. Portable (in-situ measurement)
3. Rapid (temporal measurement)

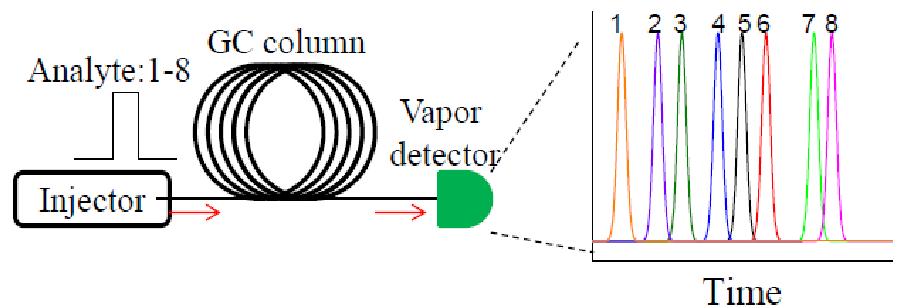
Introduction

Gas chromatography (GC) + Mass Spectrometer

- **Best analytical tool to analyze hundreds of volatile organic compounds (VOCs)**



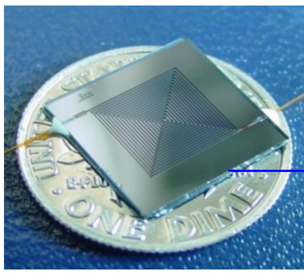


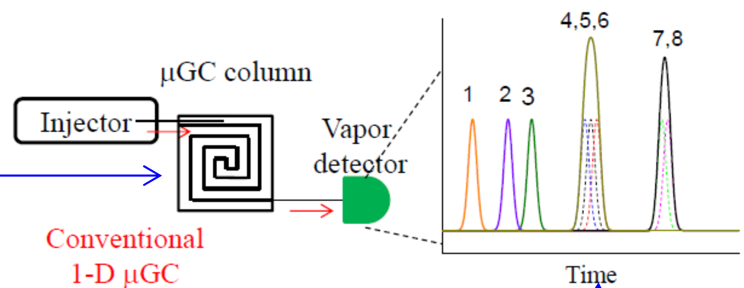


- High peak capacity
- Long analysis time
- Heavy and bulky
- Needs dedicated personnel
- High power consumption

GC on a chip
Micro-GC (μGC) or portable GC

- First demonstrated in 1979 (first lab-on-a-chip device)
  Terry et al., IEEE Trans Electron Devices, ED-26, 1880 (1979)

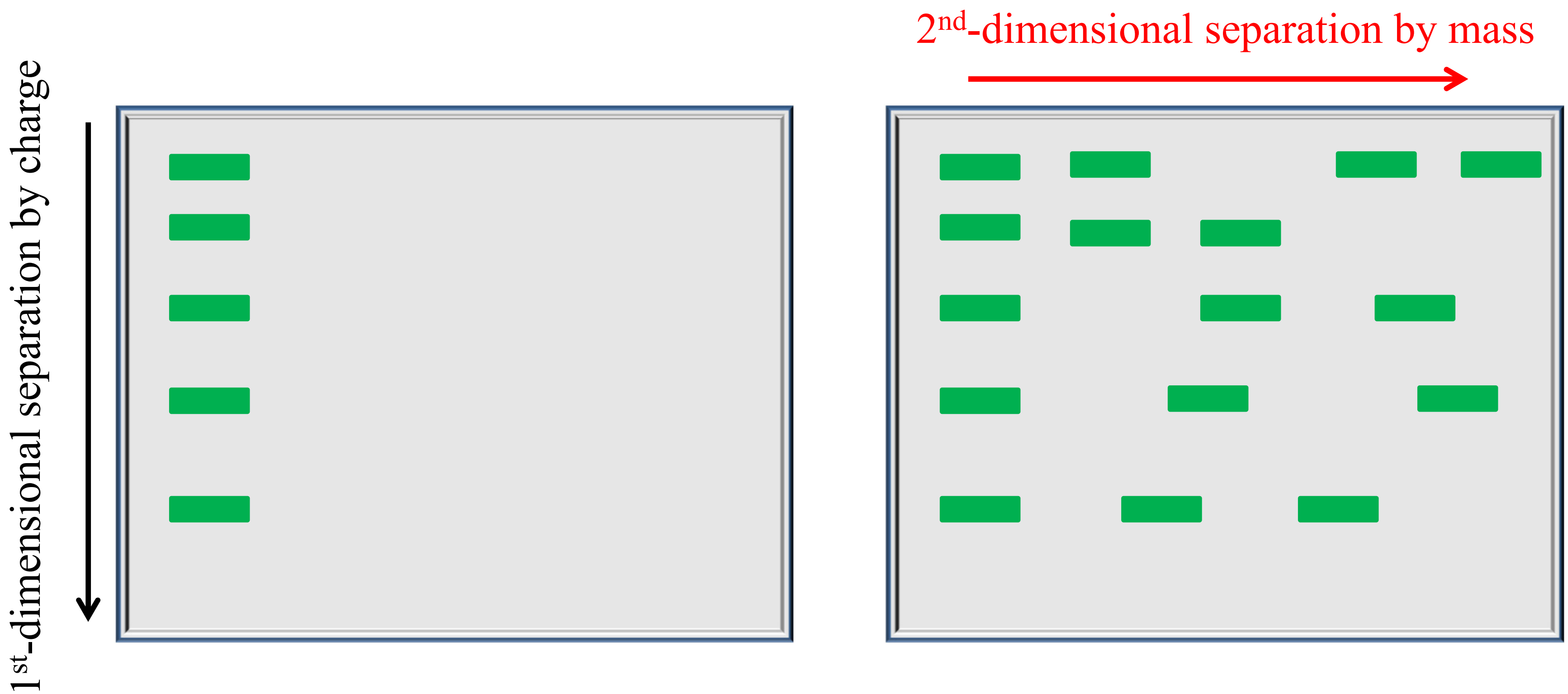




- Portable
- Rapid analysis
- Less power consumption
- Can be automated
- Low chromatographic resolution and peak capacity → co-elution

General concept of multi-dimensional separation

- 2-D gel electrophoresis as an example
- Two independent separations based on two distinct properties (*e.g.*, charge and mass)
- Enhanced separation capability or resolution



Total peak capacity = $N_1 \times N_2$

N_1: peak capacity for 1st separation

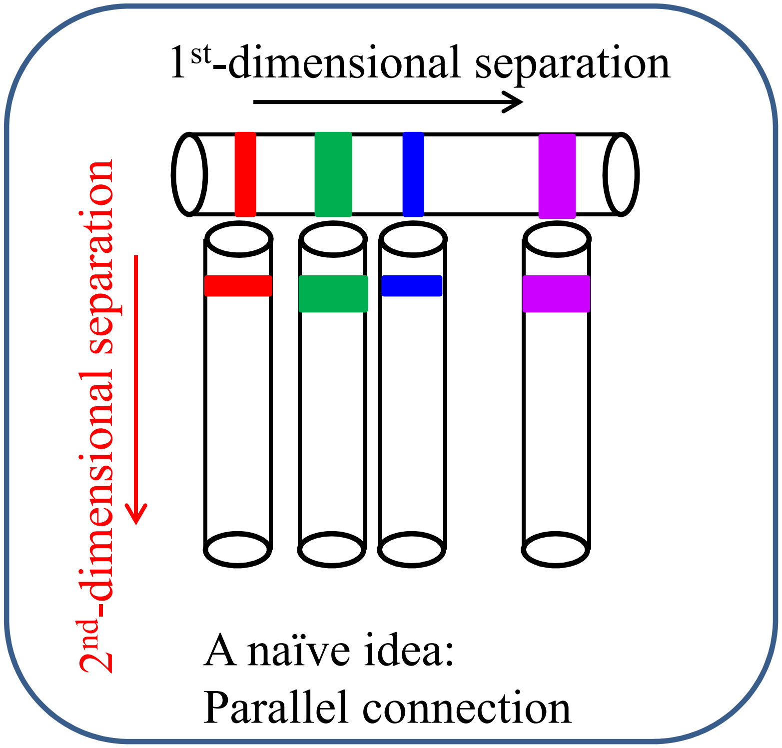
N_2: peak capacity for 2nd separation

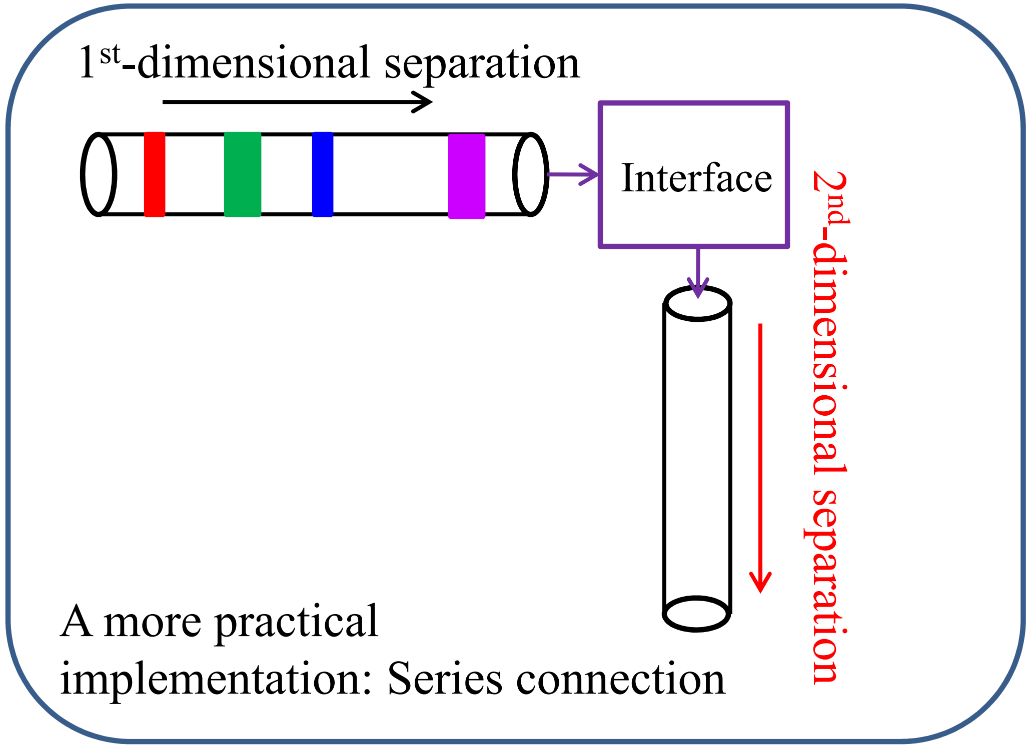
Multi-dimensional GC

How to translate the 2-D (or higher-dimensional) gel electrophoresis concept to 2-D GC?

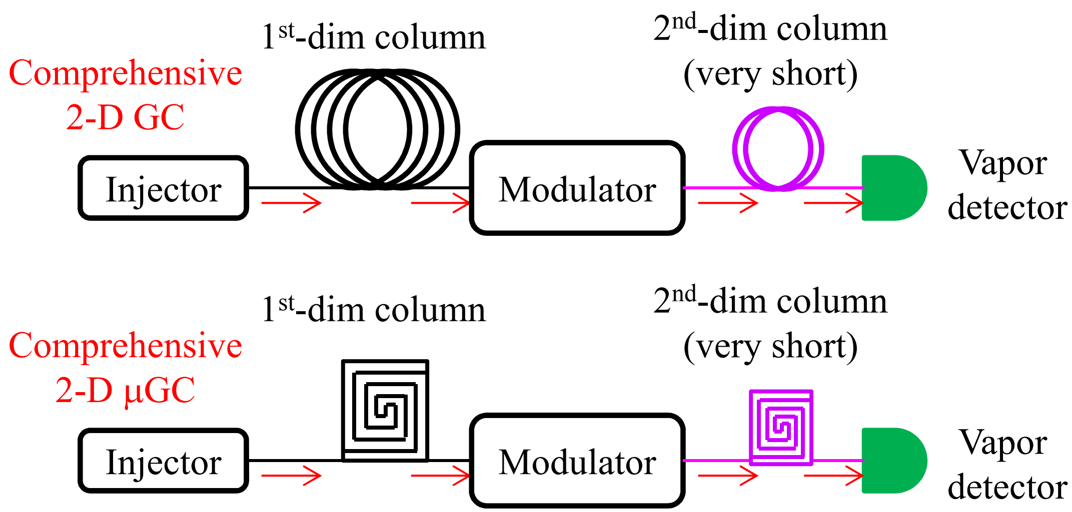
Difficulties:

- Vapors are difficult to be held in place





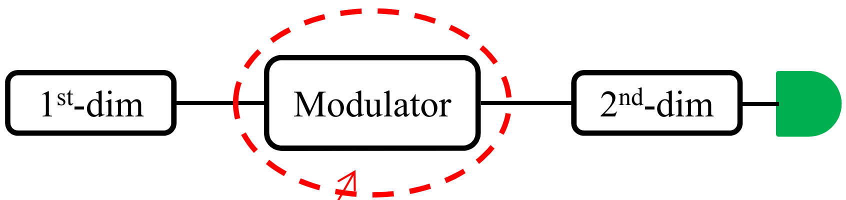
Comprehensive 2-D GC or µGC (GC x GC, µGC x µGC)



- 1st-dim column: long (5-30 m), coated **non-polar** stationary phase
- 2nd-dim column: **very short** (0.5-1 m), coated with **polar** stationary phase
- Vapor molecules undergo two separations by vapor pressure and polarity
- Total peak capacity = N_1 x N_2 (**ideally**)

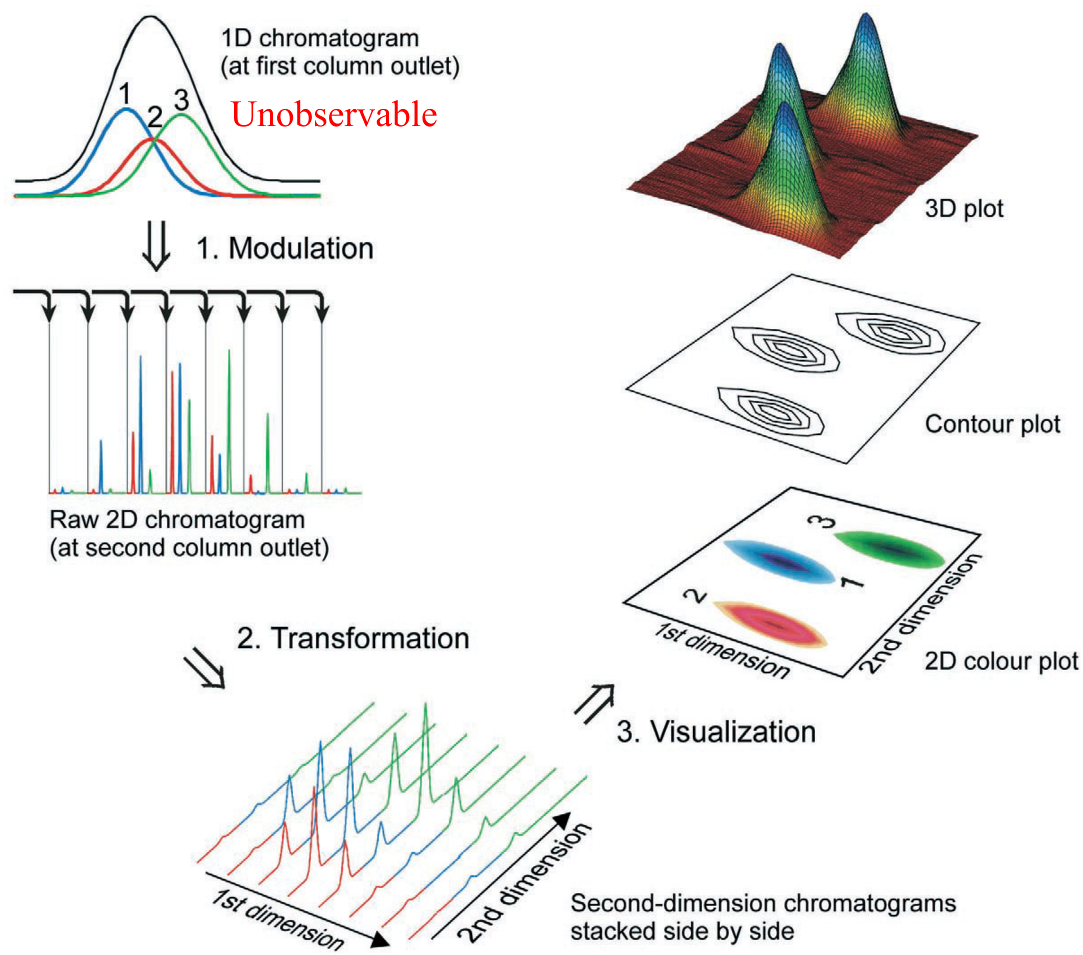
M. M. Bushey et al., Anal. Chem. **62**, 161 (1990).
Z. Liu et al., J. Chromatogr. Sci. **29**, 227 (1991).
Phillips et al., J. Chromatogr. A **703**, 327 (1995).
J. Dallüge et al., J. Chromatogr. A **1000**, 69 (2003).
J. V. Seeley et al., Anal. Chem. **85**, 557 (2012).

Working principle of GC x GC or μGC x μGC



- Pneumatic modulator
- Thermal modulator (more popular)

Modulator period: 1-10 seconds



J. Dallüge et al., J. Chromatogr. A **1000**, 69 (2003).

Comments on GC x GC (or μGC x μGC)

Advantages:

- Improved peak capacity ($N_{GCxGC} > N_{GC}$)

J. V. Seeley et al., J. Chromatogr. A **962**, 21 (2002).
L. M. Blumberg et al., J. Chromatogr. A **1188**, 2 (2008).

Drawbacks:

1. Reduction of n_1 by a factor of $\sqrt{1+0.5(P_M/\sigma_{1,0})^2}$ due to modulation (sampling theory)
   P_M: modulation period; $\sigma_{1,0}$: unmodulated peak width from the 1st-dim column

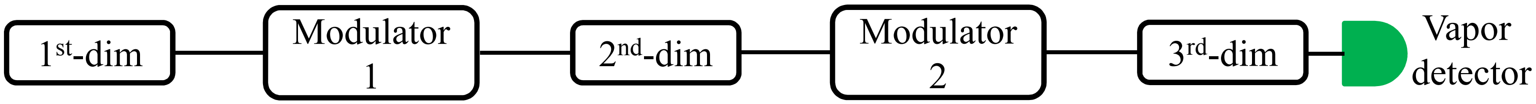
2. Insufficient 2nd-dimensional separation (low n_2)
   - Limited by the modulation period
   - Only a few seconds in order to avoid wrap-around issue

3. Peak capacity below theoretical prediction of N_1 x N_2.
   - N_{GCxGC} is only 5-10X better than N_{GC} (under optimal condition)

4. Complicated 2-D chromatogram re-construction
   - Has only one end-column detector

5. Difficult to scale up for higher dimensional separation

Scale up to GC x GC x GC



- 1st-dim column: long (25 m), coated **intermediate polar** stationary phase
- Modulation #1 period: **~5 seconds**
- 2nd-dim column: **shorter** (5 m), coated with **non-polar** stationary phase
- Modulation #2 period: **~0.2 seconds**
- 3rd-dim column: **shortest** (0.55 m), coated with **polar** stationary phase
- Peak capacity: N_1=175, N_2=5, N_3=4 → Total peak capacity = 3500 or 58/min

Comments:

1. Doable, but benefit is diminishing?
2. Very complicated hardware and 3-D chromatogram re-construction
3. More stringent requirements on higher-dimensional separation (*e.g.*, very short separation time)
4. Rarely explored

E. B. Ledford, Jr. et al., J. High Resol. Chromatogr. **23**, 205 (2000).
N. E. Watson et al., Anal. Chem. **79**, 8270 (2007).
W. C. Siegler et al., J. Chromatogr. A **1217**, 3144 (2010).

Some general thoughts on current GC^2 and GC^3

Problem: Information about the 1st-dim (or low dimension) separation is missing
Current solution: We rely on **a modulator** and a detector at the end and to figure it out
Re-construction of 1-dim requires sufficient 2-dim separation

Problem: 1st-dim and 2nd-dim separation are not completely independent. They are connected through **a modulator**
→ Conflicting requirements
- Short modulation period for better 1st-dim separation re-construction
- Long modulation period for better 2nd-dim separation

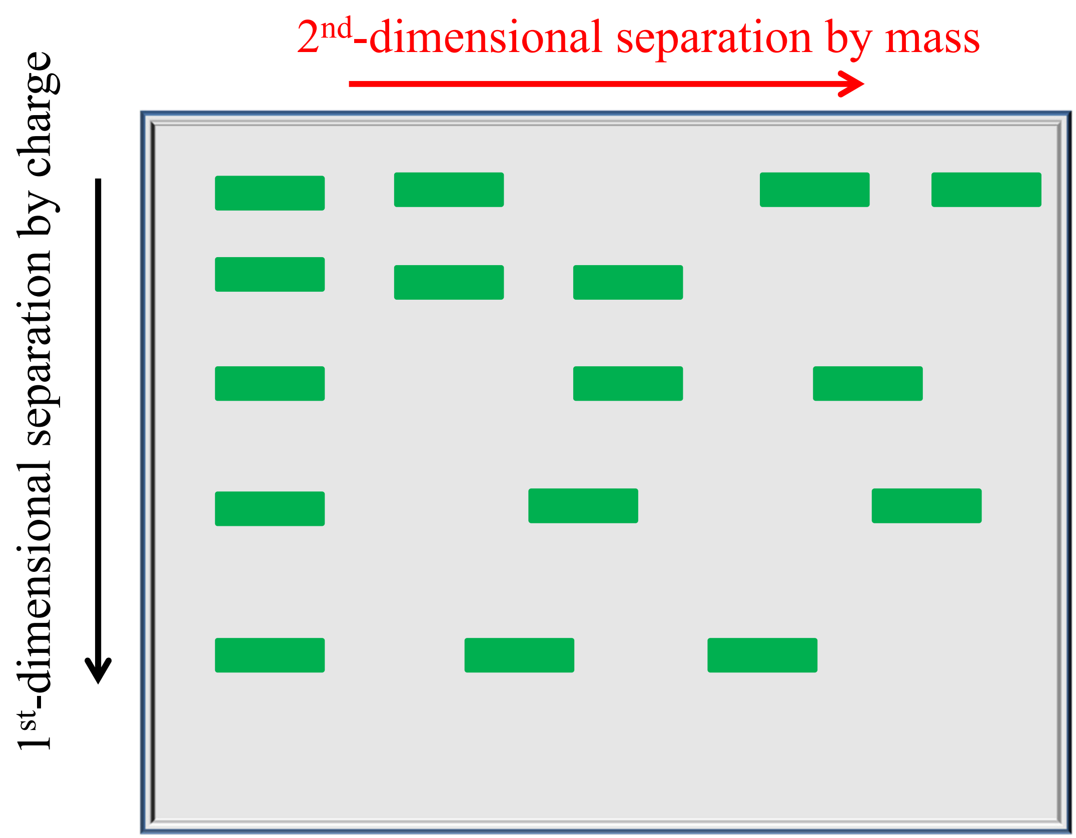
Current solution: We try to optimize or balance the 1st- and 2nd-dim separation

Why do we need a modulator?

- To sample the elution from the 1st-dim separation and provide the 1st-dim retention time

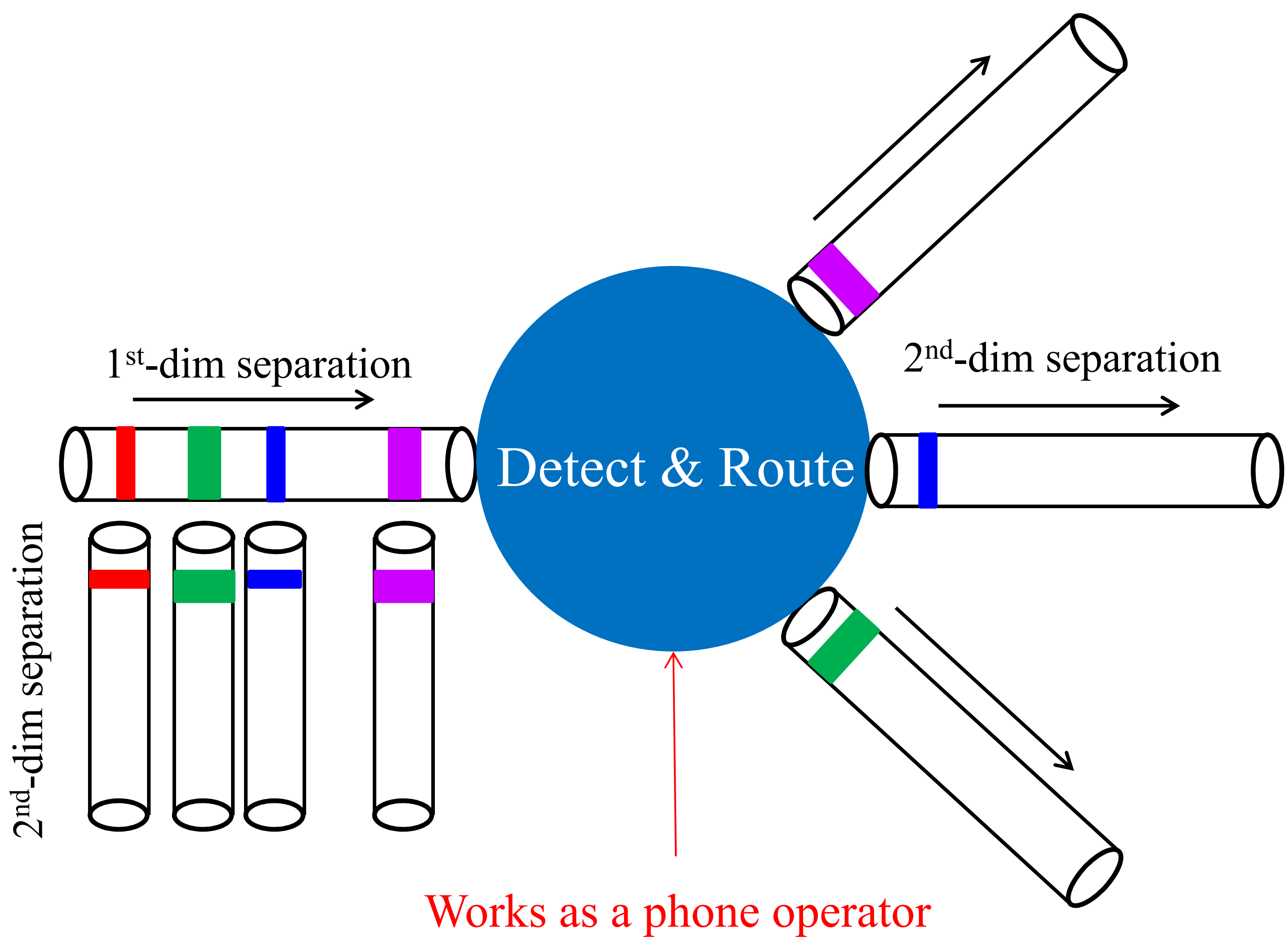
Is it necessary?

Revisit 2-D gel electrophoresis

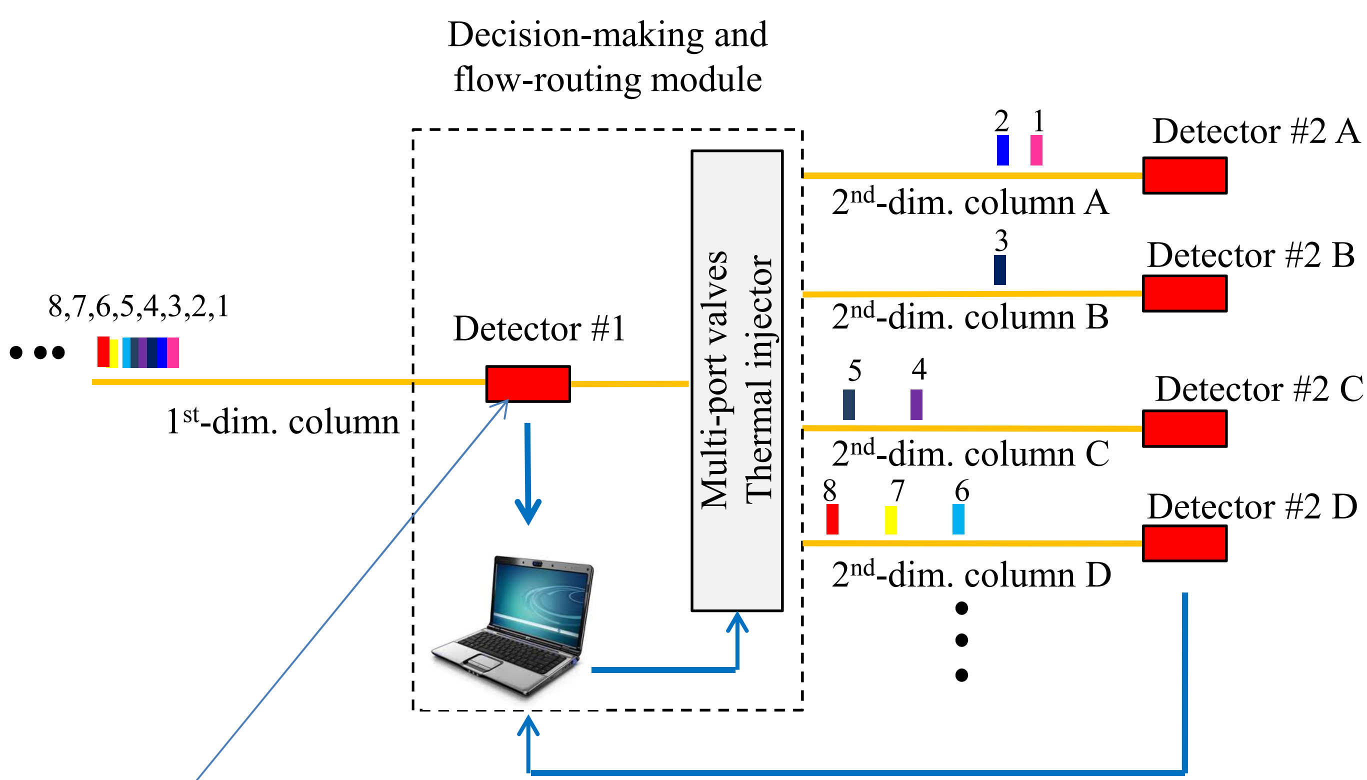


- 1st- and 2nd-dim separation are independent
- 1st-dim separation can be measured directly
- No modulator, no re-construction

Revisit the interface between two separations



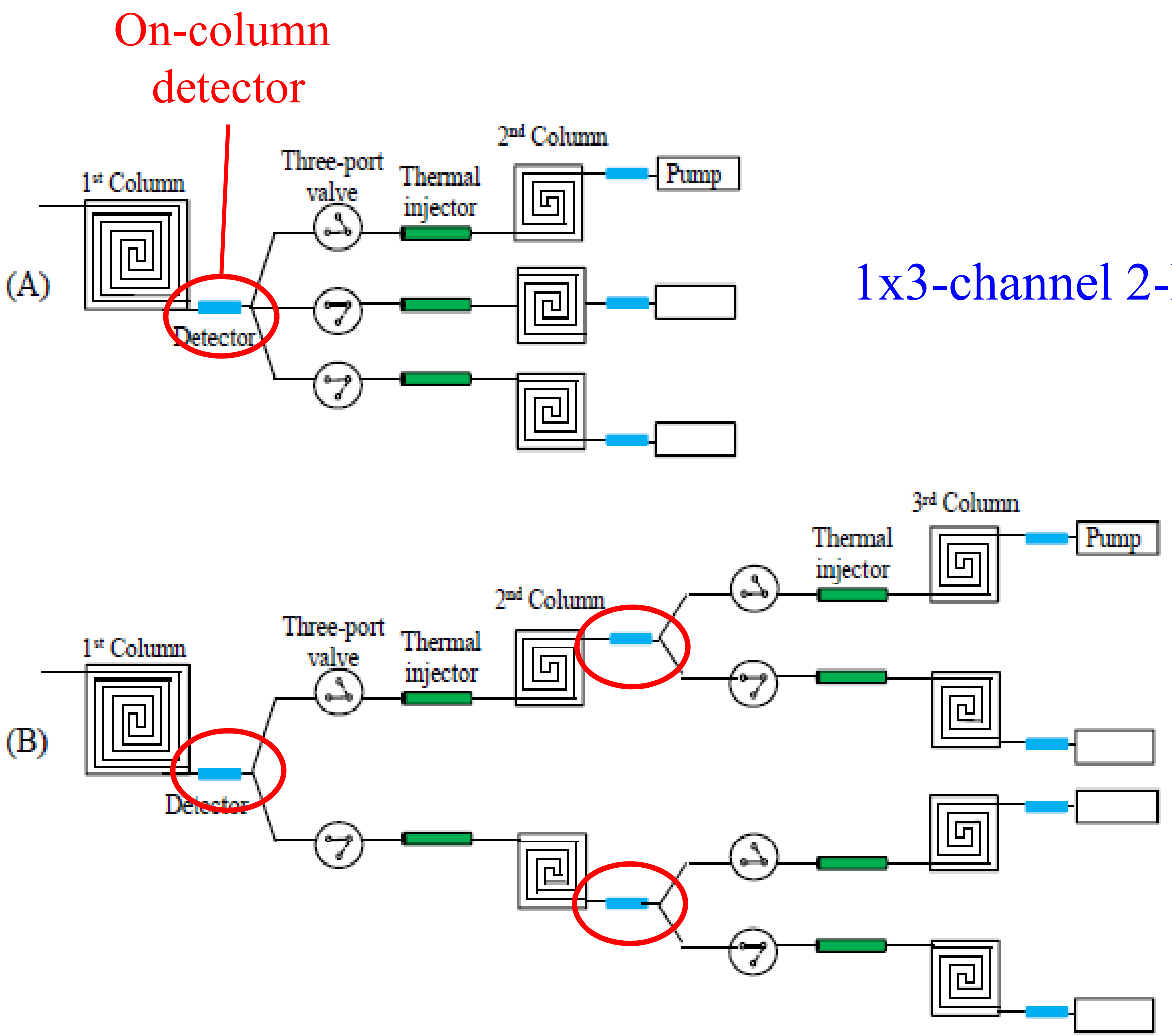
New concept of smart multi-channel multi-dimensional micro-GC



Non-destructive flow-through on-column vapor detector

- Rapid, sensitive, no interference with the flow
- Watch, but not touch
- No additional dead volume

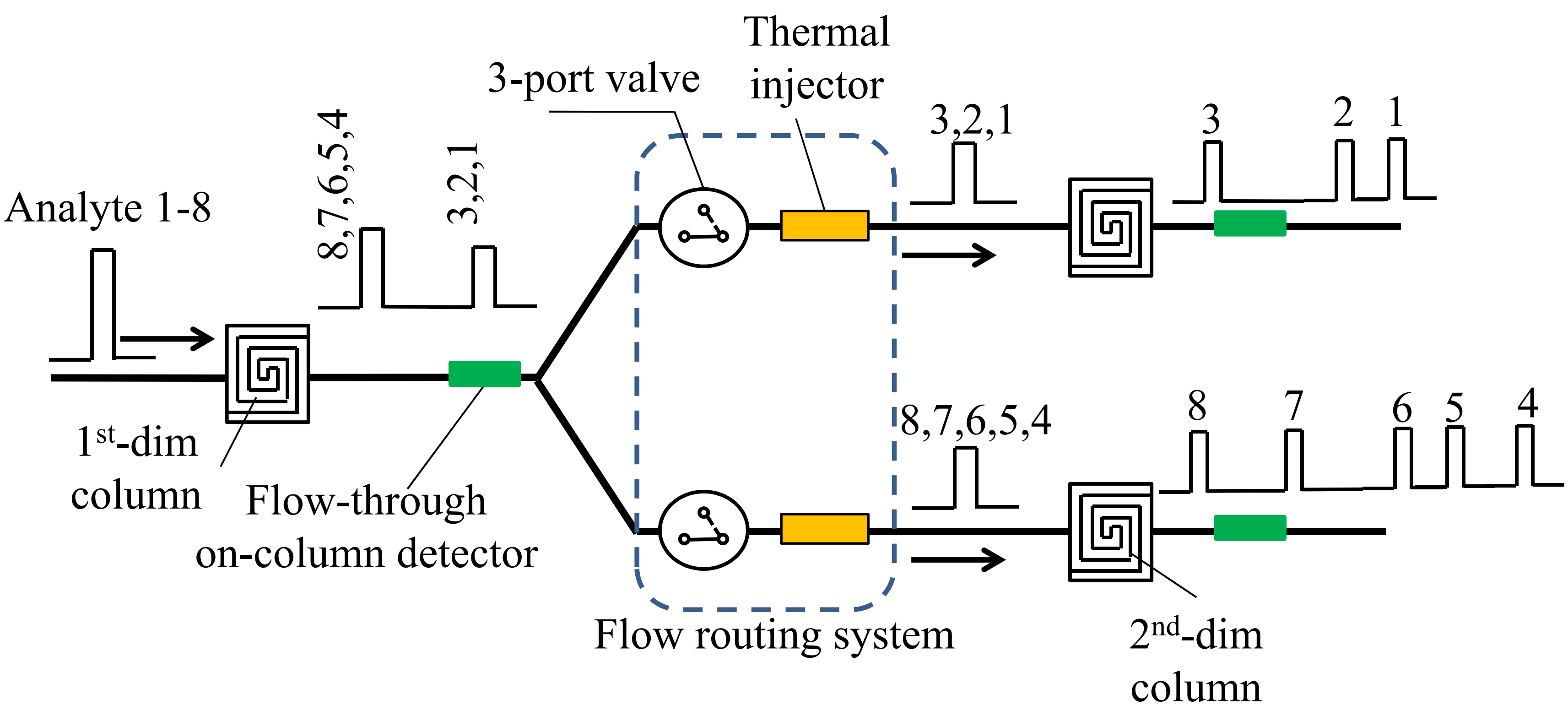
Examples of smart 2-D and 3-D GC architectures



1x3-channel 2-D micro-GC

1x2x4-channel 3-D micro-GC

Working principle



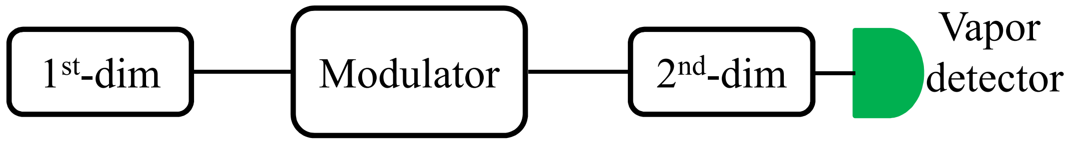
Using 1x2-channel 2-D micro-GC for illustration

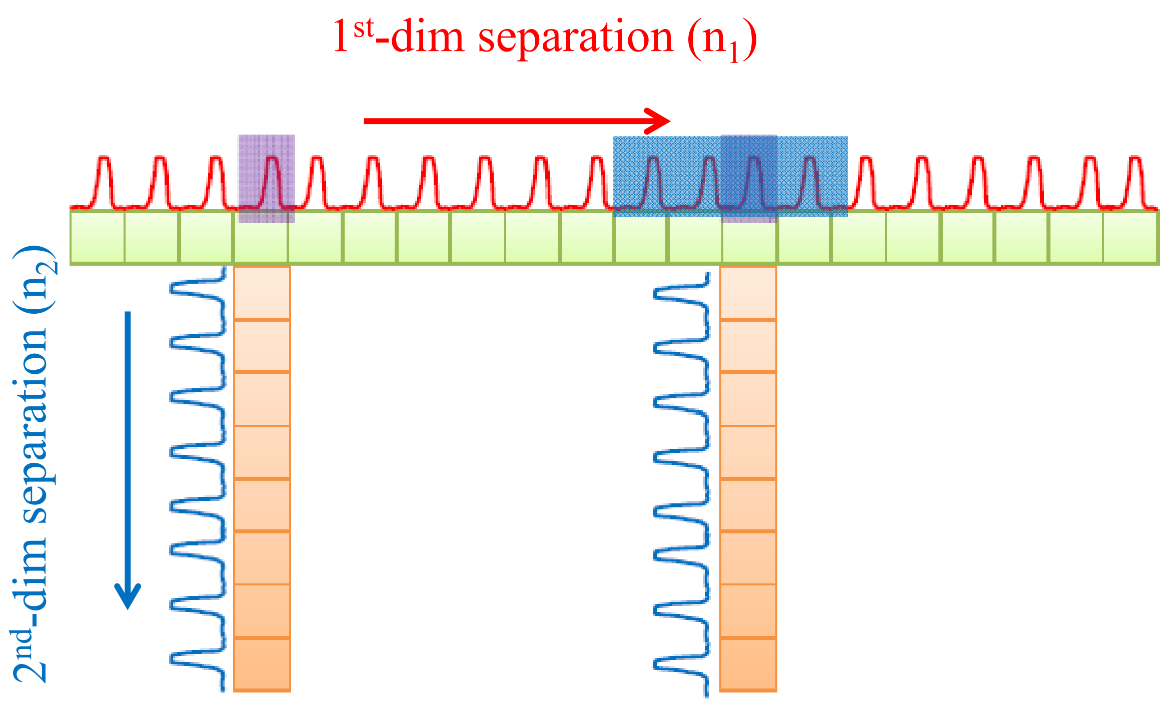
Advantages

1. No modulation on the low-dimension effluent
   - No broadening
   - Entire analyte (not just a slice of it) will be sent to the next separation (improved detection limit)
2. Long high-dimension separation (adjustable dynamically)
   - $N_{total} = N_1 \times N_2 \times N_3$ ….
   - N_2, N_3 can be large, not limited by the modulation period
   - Can do temperature ramping
3. No thermal modulator is needed. Only simple thermal injectors are needed.
   - Simple and robust, easy to fabricate, less power consumption
4. Easy construction of multi-dimensional chromatogram
   - Directly read from the vapor detectors
5. Cascadable
   - Can scale up to 3-D, 4-D, etc. by simply adding more columns to the preceding columns
   - Independent control of each dimension of separation
6. Versatile
   - General purpose instrument
   - Tailored for specific analytes

Comparison (1)

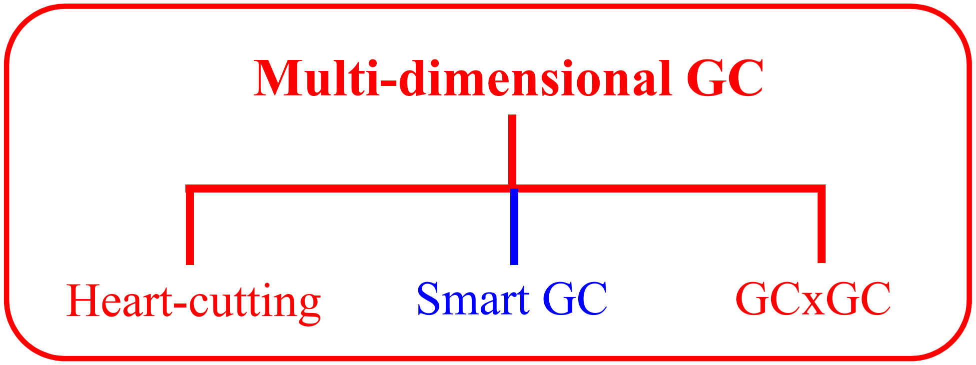
Heart-cutting technology





Total peak capacity = $N_1 + N_2 \times M$ (M: # of cuts)

Comparison (2)



	Number of cuts	**Time window selection**	**Window width**
Heart-cutting	A few times *Each cut contain multiple peaks*	Pre-determined	50-100 seconds *Depending on applications*
Smart GC	N_1 times *Each cut has one peak*	Informed decision *Made by the system*	Depending the peak width *Dynamically adjustable*
GC x GC	3 x N_1 times *Each cut has 1/3 peak*	Periodic window *Blindly, even without analyte*	~1-10 second

Comparison (3) - Comparison

Isothermal operation			
	Total peak capacity	**Total assay time**	**Peak capacity production**
Comp. GC^2	19968	100 min	200/min
Comp. GC^3	87360	100 min	874/min
1x2 smart GC^2	38828	100 min	388/min
1x2x4 smart GC^3	570000	108 min	5278/min

Temperature ramping operation			
	Total peak capacity	**Total assay time**	**Peak capacity production**
Comp. GC^2	11018	15 min	735/min
Comp. GC^3	79560	60 min	1326/min
1x2 smart GC^2	502600	100.8 min	4984/min

Development of flow-through on-column vapor detectors

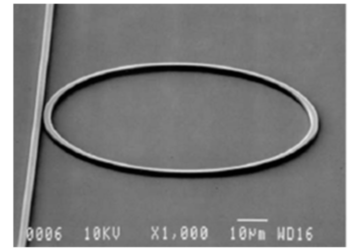
On-column flow-through vapor sensors (Overview)

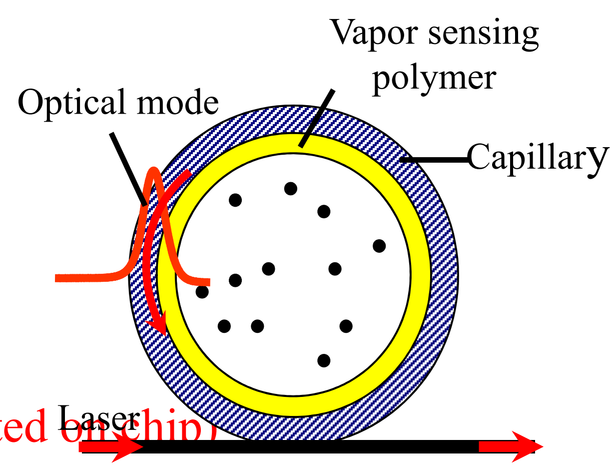
Requirements:

- Non-destructive
- No interference with gas flow
- No or minimal dead volume

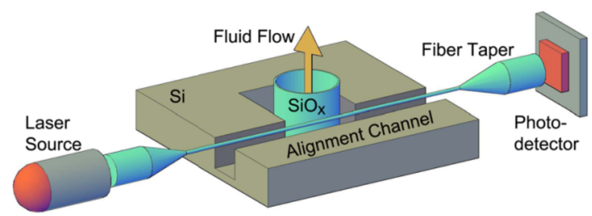
Possible candidates:

- TCD (thermal conductivity detector)
- SAW (Surface acoustic wave detector)
- Chemi-resistor
- Chemi-capacitor
- Nanoelectronics (graphene, nanotubes)
- Optical vapor sensors
  - Optical ring resonator (fabricated on chip)
  - Optofluidic ring resonator (capillary based or fabricated on chip)
  - Optical interferometric sensor (Fabry-Perot sensor)

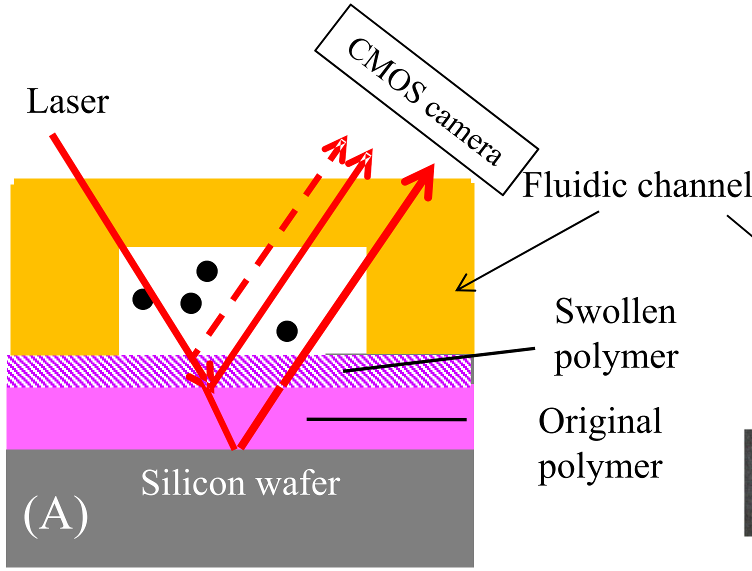




Shopova et al., Anal. Chem. **80**, 2232 (2007)
Sun et al., Opt. Express **16**, 10254 (2008)
Sun et al., Analyst **135**, 165 (2010)
Reddy et al., Lab Chip **12**, 901 (2012)
Scholten et al., Appl. Phys. Lett. **99**, 141108 (2011)
Scholten et al., Lab Chip **14**, 3873 (2014)
Kulkarni et al., Nature Commun. **5** 3779 (2014)



On-column flow-through vapor sensors (Optical)



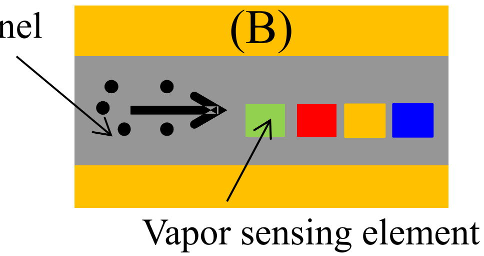
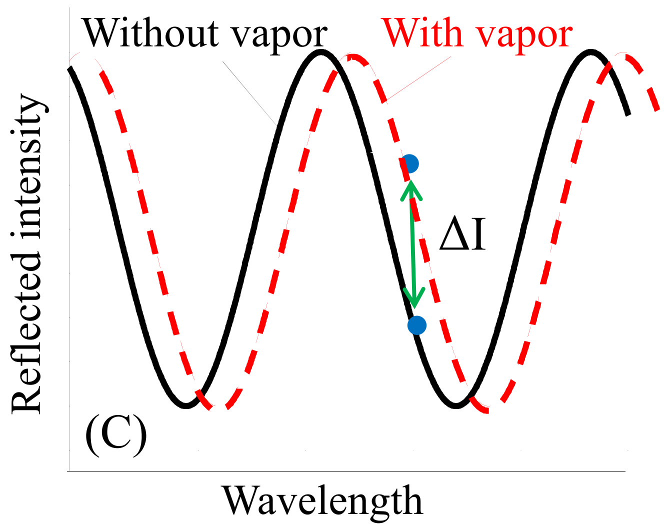
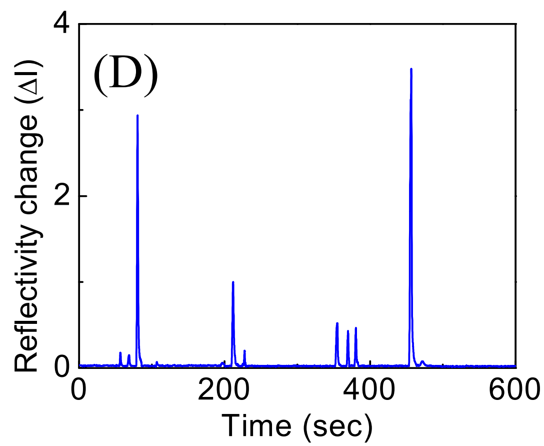


Photo of vapor sensor array

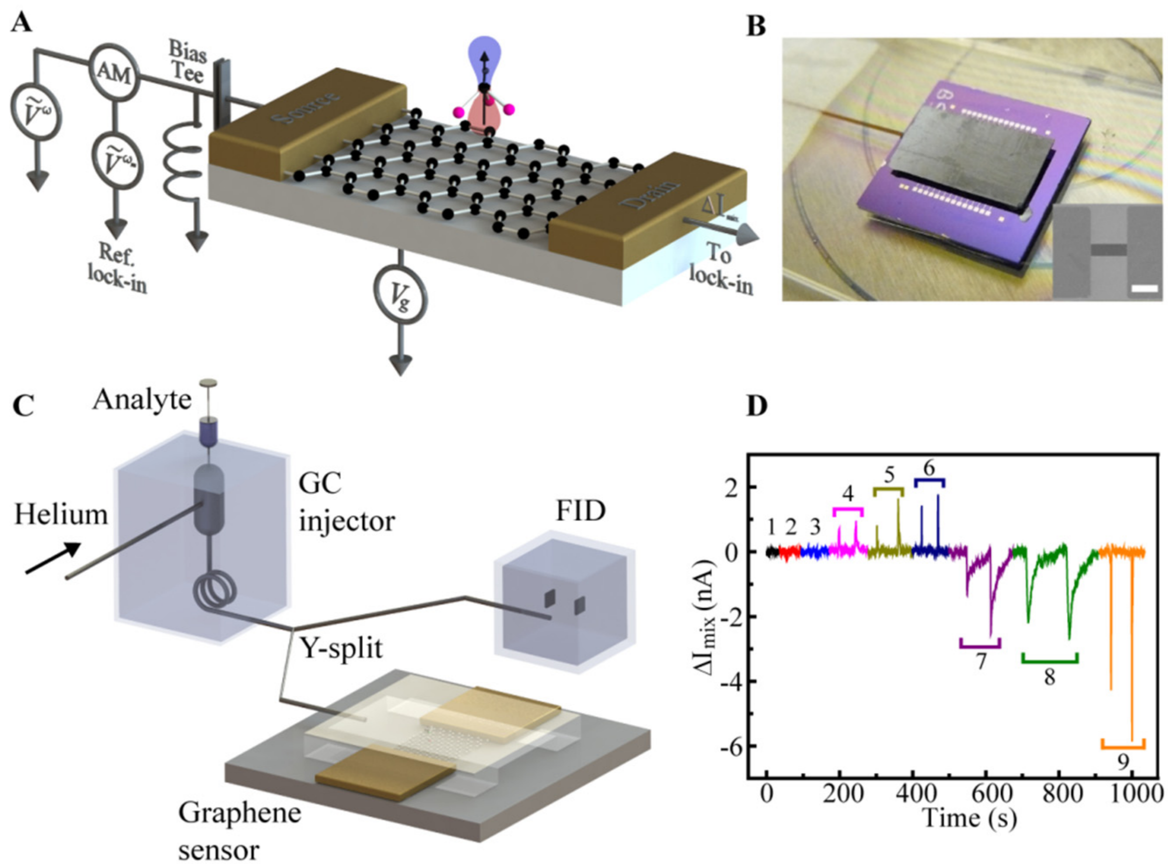




Response time: < 1 s
Detection limit: 1-10 pg
Array detection

Liu et al., Opt. Express **17**, 2731 (2009); Liu et al., Anal. Chem. **82**, 4370 (2010)
Reddy et al., Sens. Actuators B **159**, 60 (2011); Reddy et al., Lab Chip **12**, 901 (2012)
Reddy et al., Opt. Express **20**, 966 (2012); Reddy et al., IEEE JMEMS **22**, 1174 (2014)

On-column flow-through vapor sensors (Graphene)

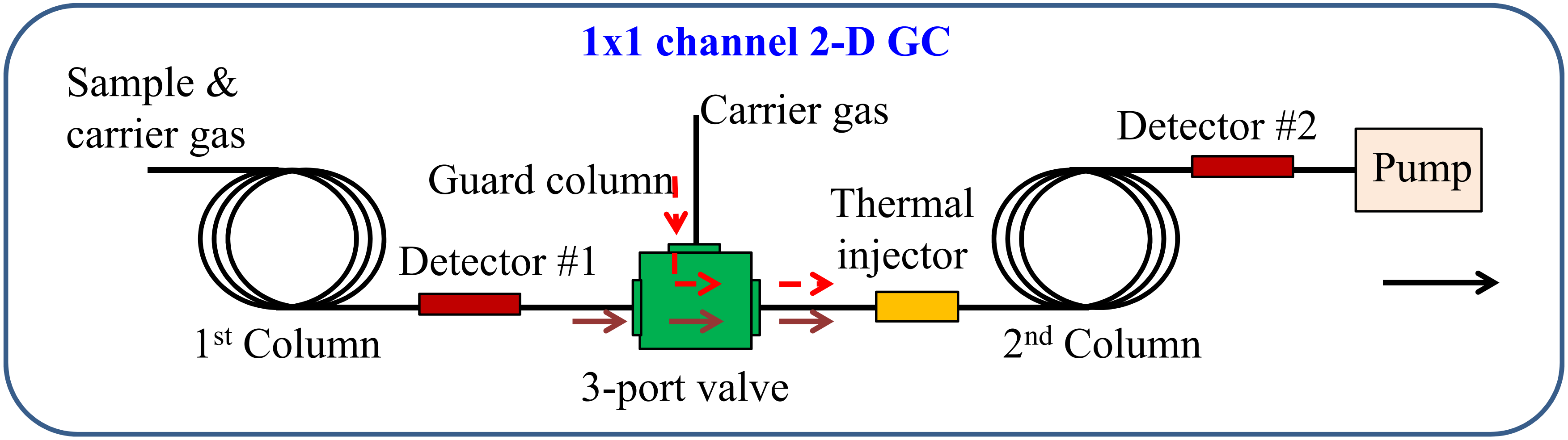


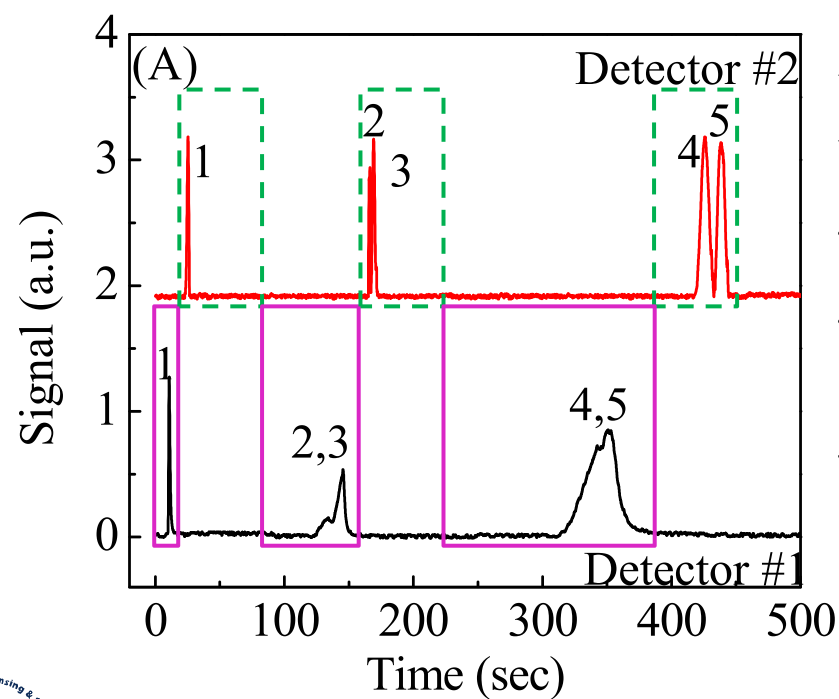
Response time: < 0.1 s
Detection limit: 1-10 pg (ppb)
Array detection

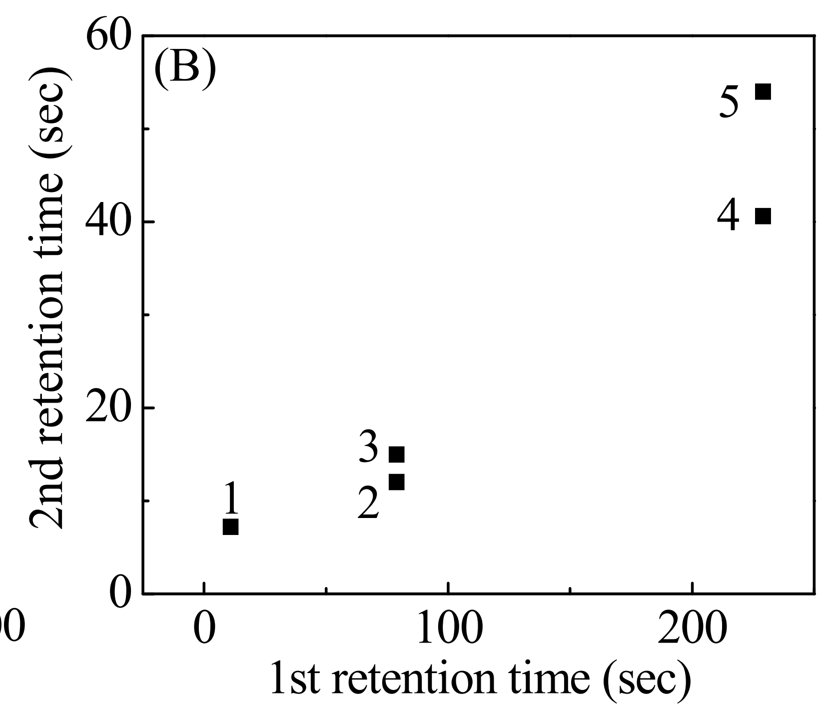
Kulkarni et al., Nature Commun. **5** 3779 (2014)

Smart 2-D GC

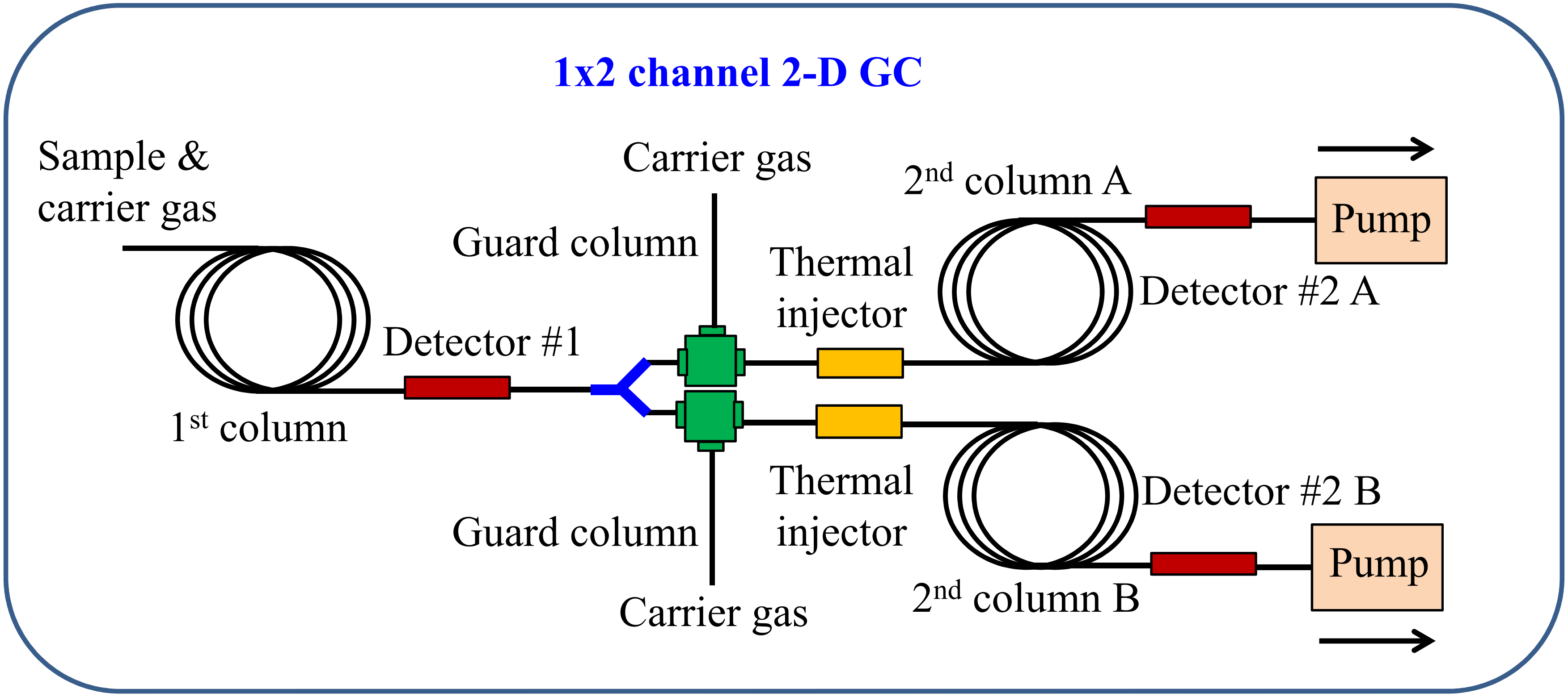
Simple example





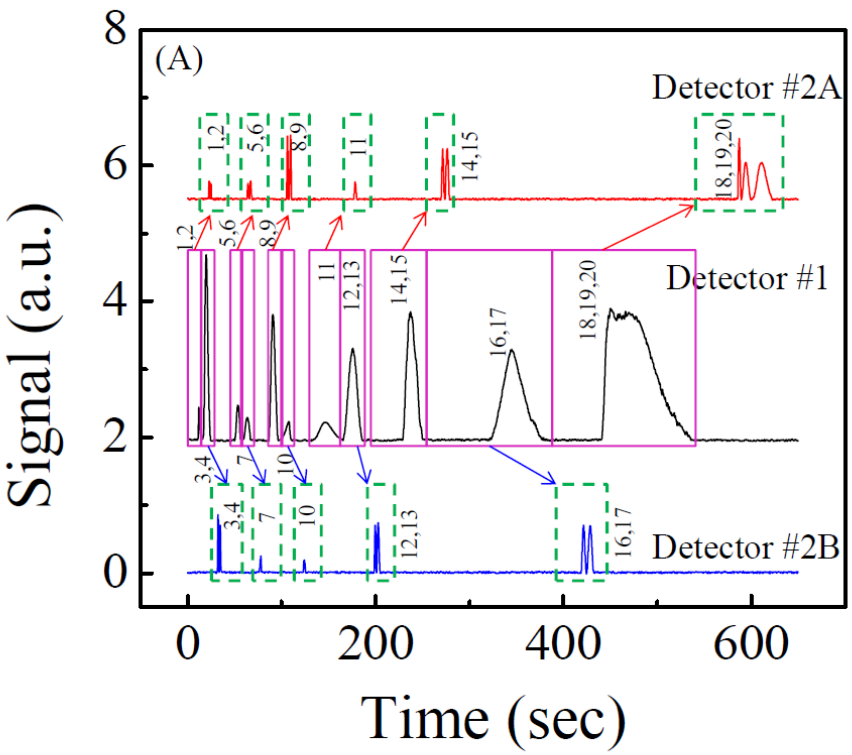


Scale up to more channels

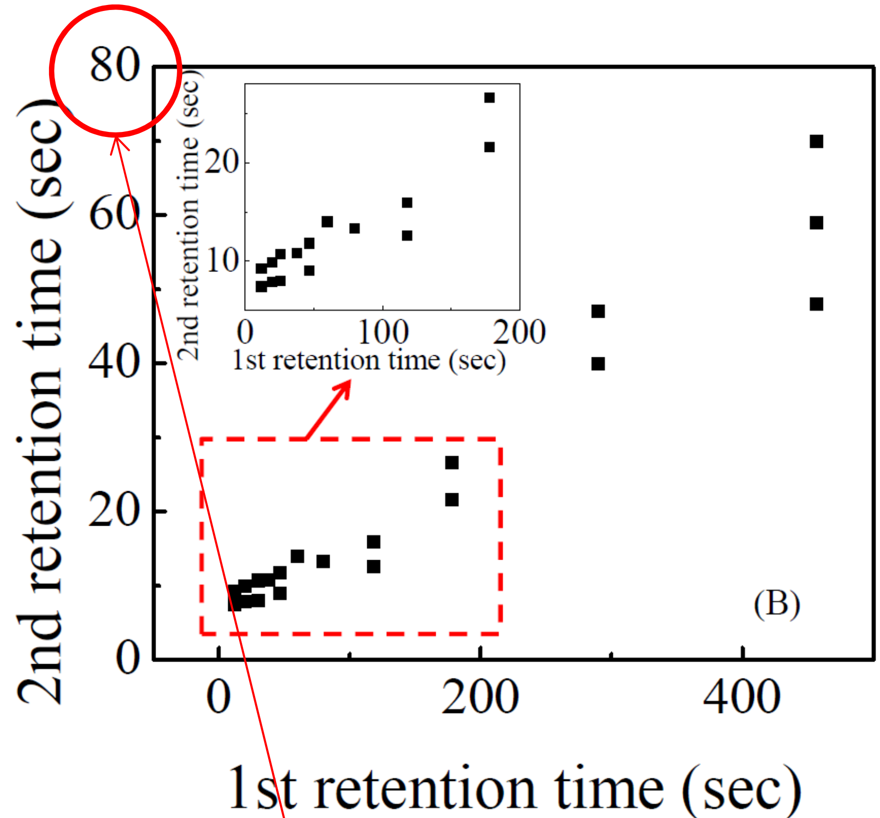


[1]D column: 2 m long, i.d. = 0.25 mm, RTX-1 coating
[2]D column: 0.8 m long, i.d. = 0.25 mm, Carbowax coating

Results



Thermal injector turned on/off only 13 times



Very long second-dimensional separation

Liu et al., Anal. Chem. **84**, 4214 (2012)

Analysis

	Nonane (#12)	Limonene (#15)
t_1	119 s	179 s
σ_1	4.36 s	4.95 s
n_1	20	31
t_2	12.9 s	26.5 s
σ_2	0.465 s	1.1 s
n_2	11	14
Total peak capacity (n_1 x n_2)	240	434
Total analysis time for analyte	200 s	276 s
Peak capacity production	72/min	94/min

Peak capacity $$n = \frac{\sqrt{N}}{4R_s}\ln\left(\frac{t}{t_0}\right) + 1$$

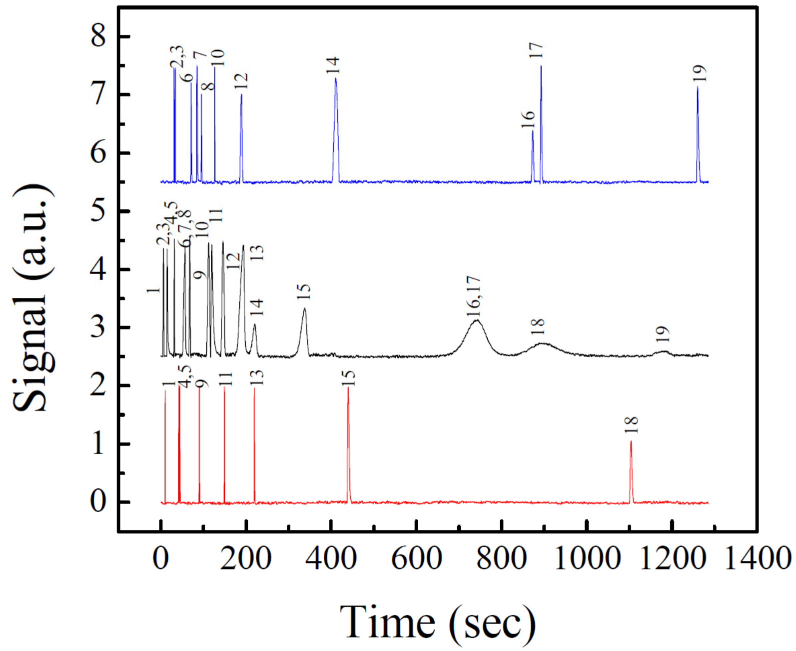
N: plate number

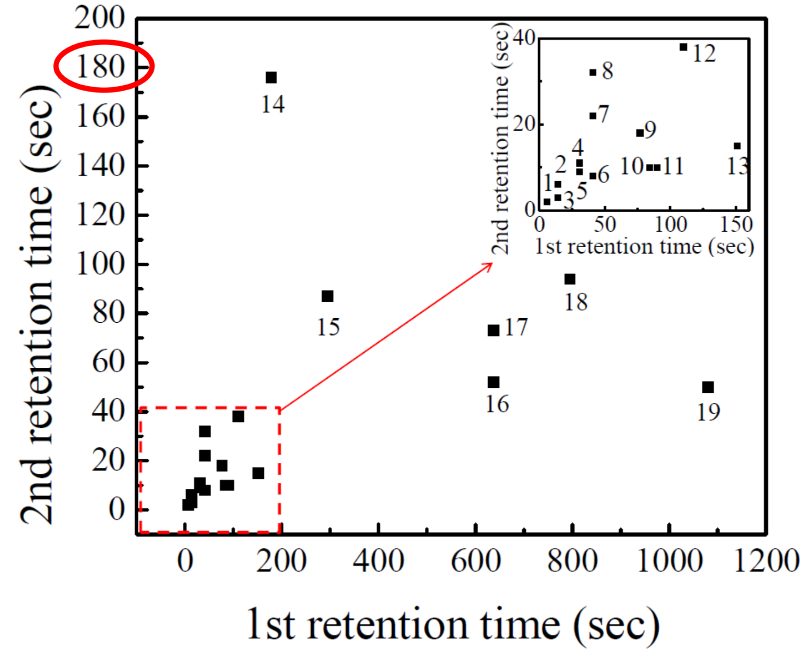
R_s: desired resolution (R_s=1 in the above table)

t: retention time

t_0: hold-up time

Temperature ramping





[1]D column: 2.7 m long, i.d. = 0.25 mm, HP-5 coating.

Temperature ramping:

Room temperature for 3 min and then heated up to 150 °C at a rate of 20 °C/min

[2]D column: 0.7 m long, i.d. = 0.25 mm, Carbowax coating. Room temperature

Assay time is much shorter

Liu et al., Anal. Chem. **84**, 4214 (2012)

Analysis

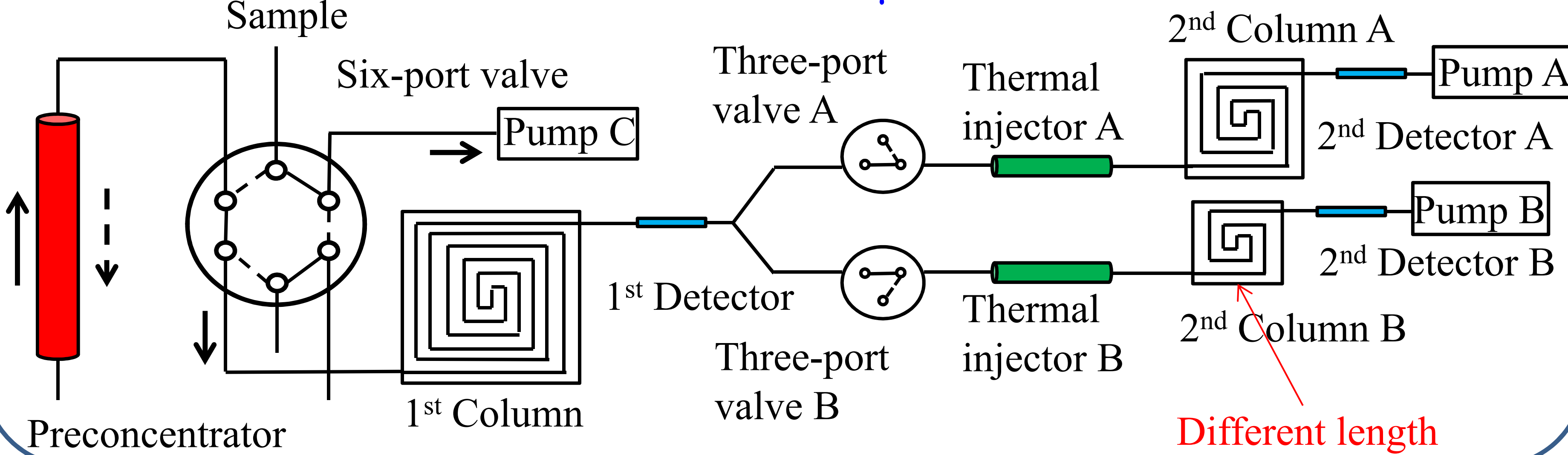
	Methyl salicylate (#14)	Jasmone (#17)	Caryophyllene (#19)
t_1	180 s	640 s	1,079 s
σ_1	9.1 s	46.9 s	34 s
n_1	37	36	92
t_2	175 s	72.7 s	50.1 s
σ_2	8.8 s	2.3 s	3.9 s
n_2	53	67	25
Total peak capacity (n_1 x n_2)	1,961	2,412	2,300
Total analysis time for analyte	410 s	894 s	1,260 s
Peak capacity production	287/min	162/min	110/min

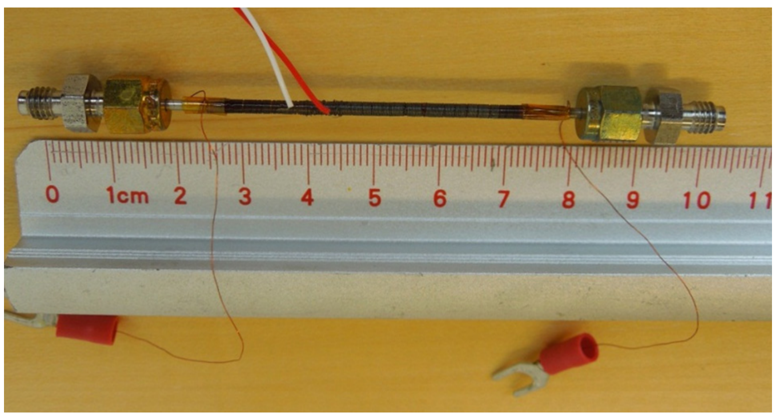
Higher peak capacity

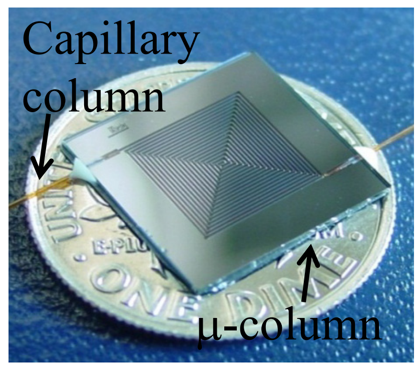
Higher efficiency

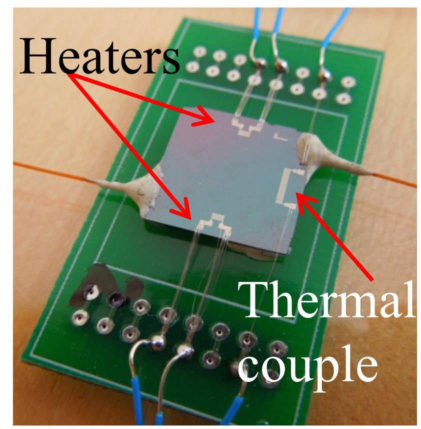
Move to μGC system

1x2 channel 2-D μGC



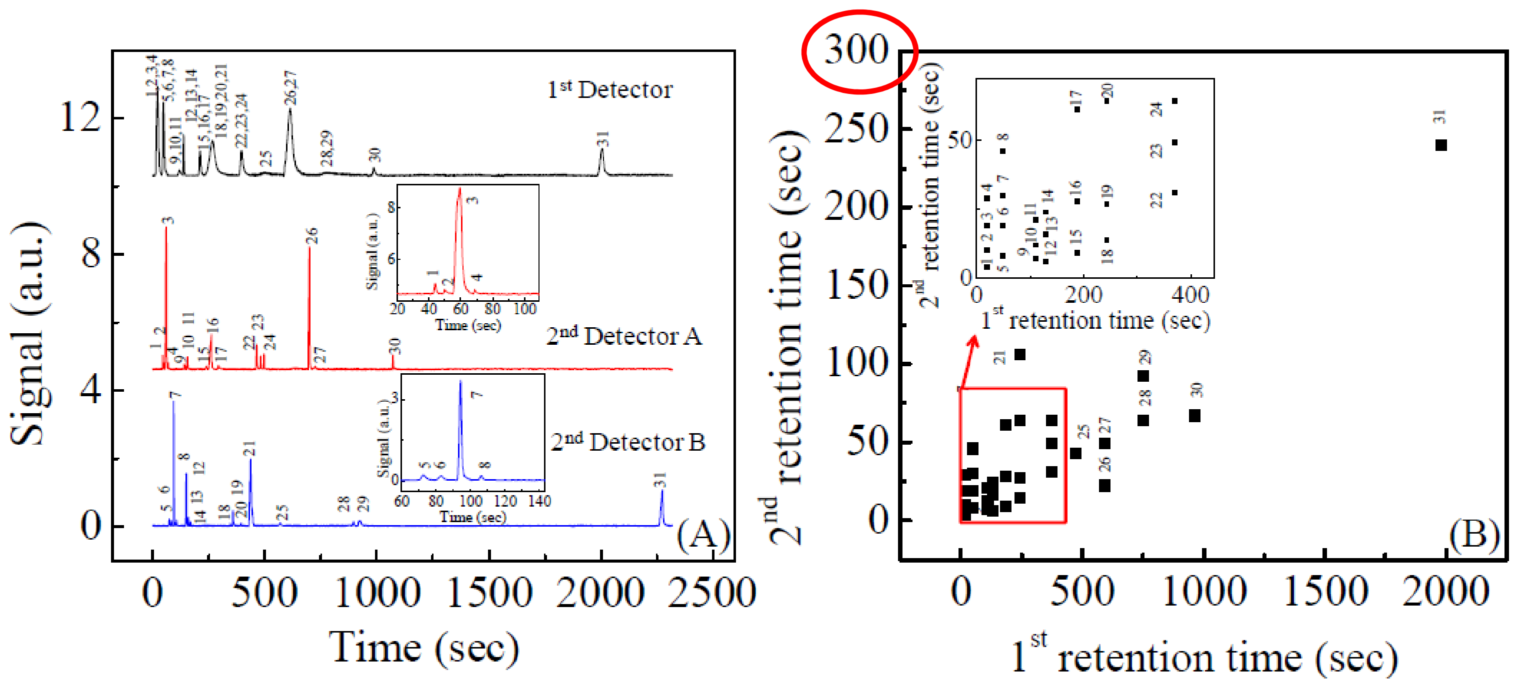






[1]D column: 1 m long, 0.24 mm x 0.15 mm cross section, OV-1 coating
[2]D column A: 0.5 m long, 0.24 mm x 0.15 mm cross section, OV-215 coating
[2]D column B: 0.25 m long, 0.24 mm x 0.15 mm cross section, OV-215 coating

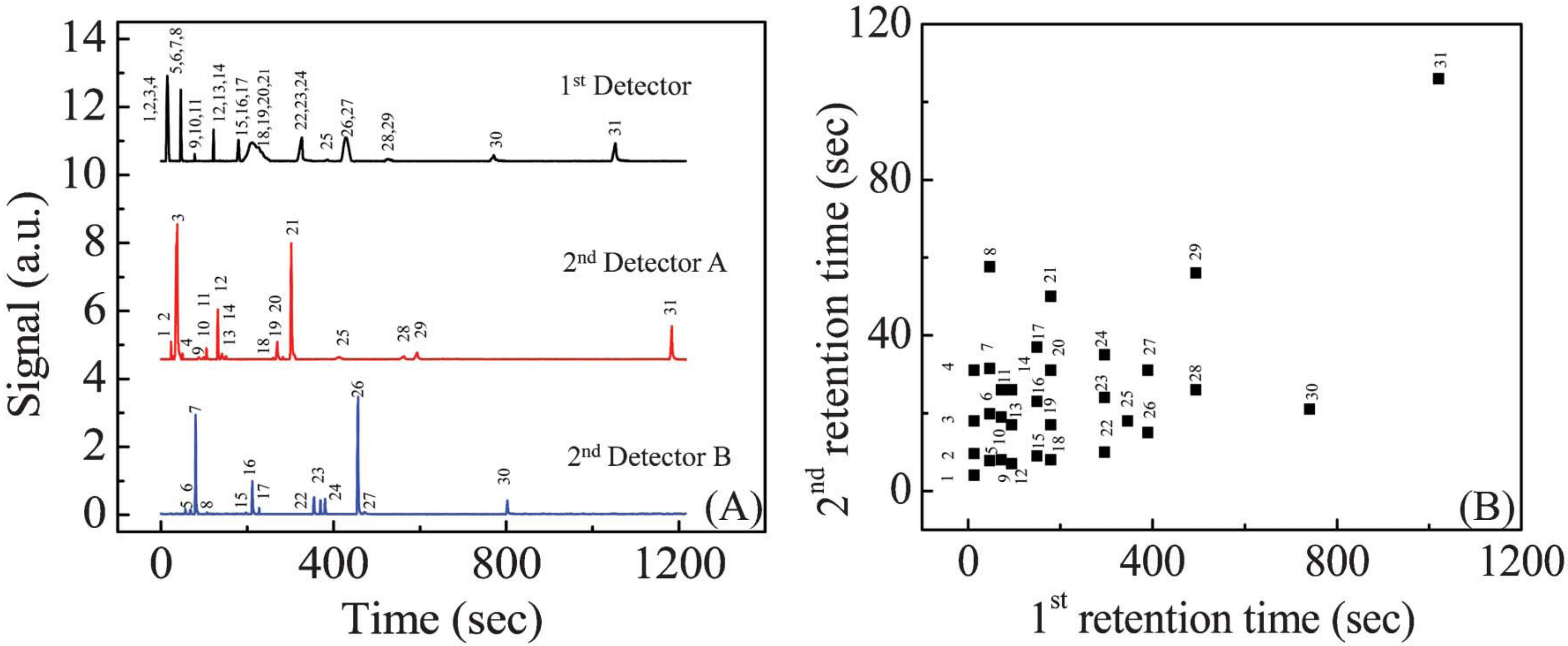
Results (Isothermal)



Separation of 31 workplace hazardous volatile organic compounds reported by California Standard Section 01350 Specification

Liu et al., Lab Chip. **13**, 818 (2013)

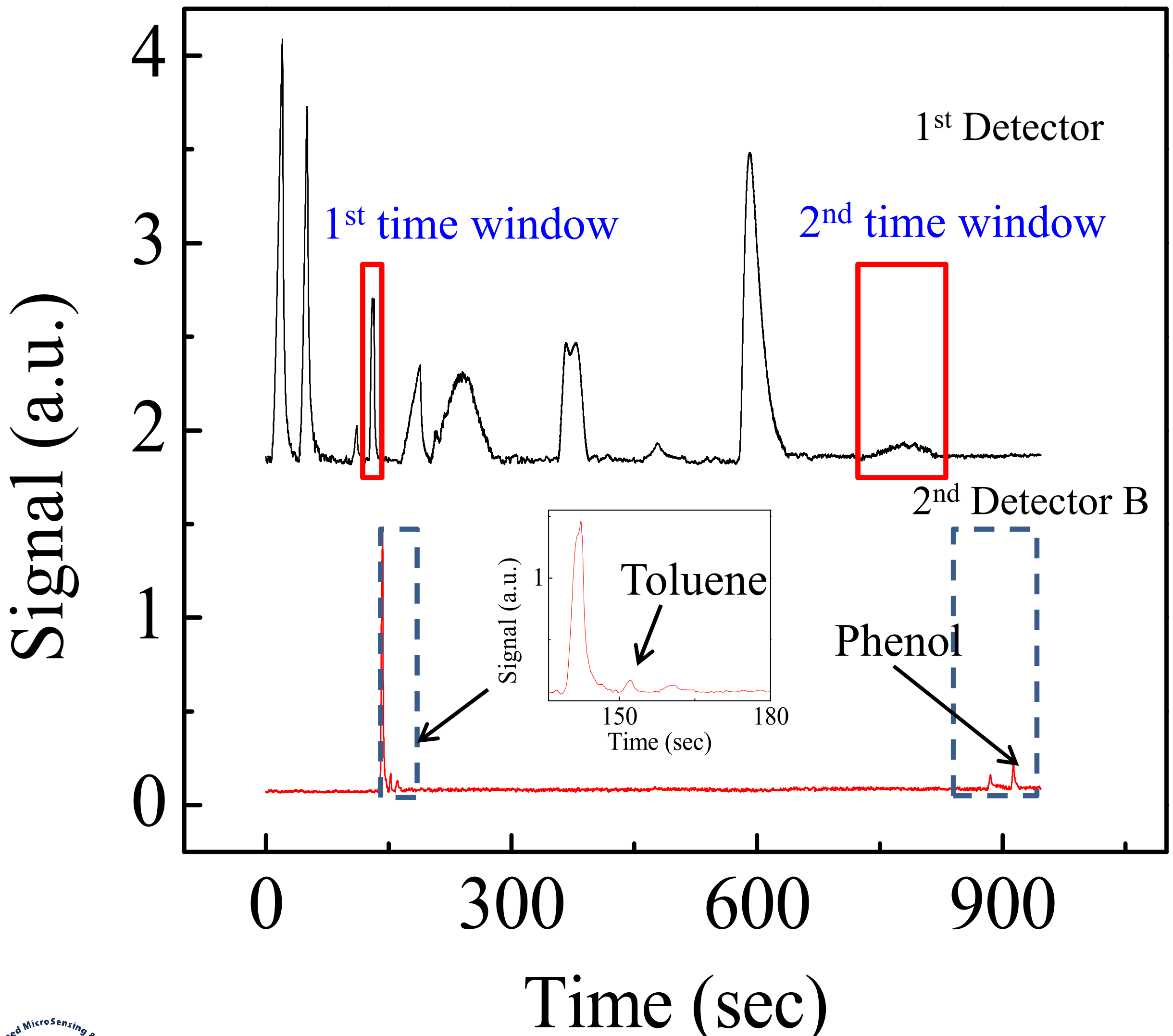
Results (Temperature ramping)



Analysis time is shortened

Liu et al., Lab Chip. **13**, 818 (2013)

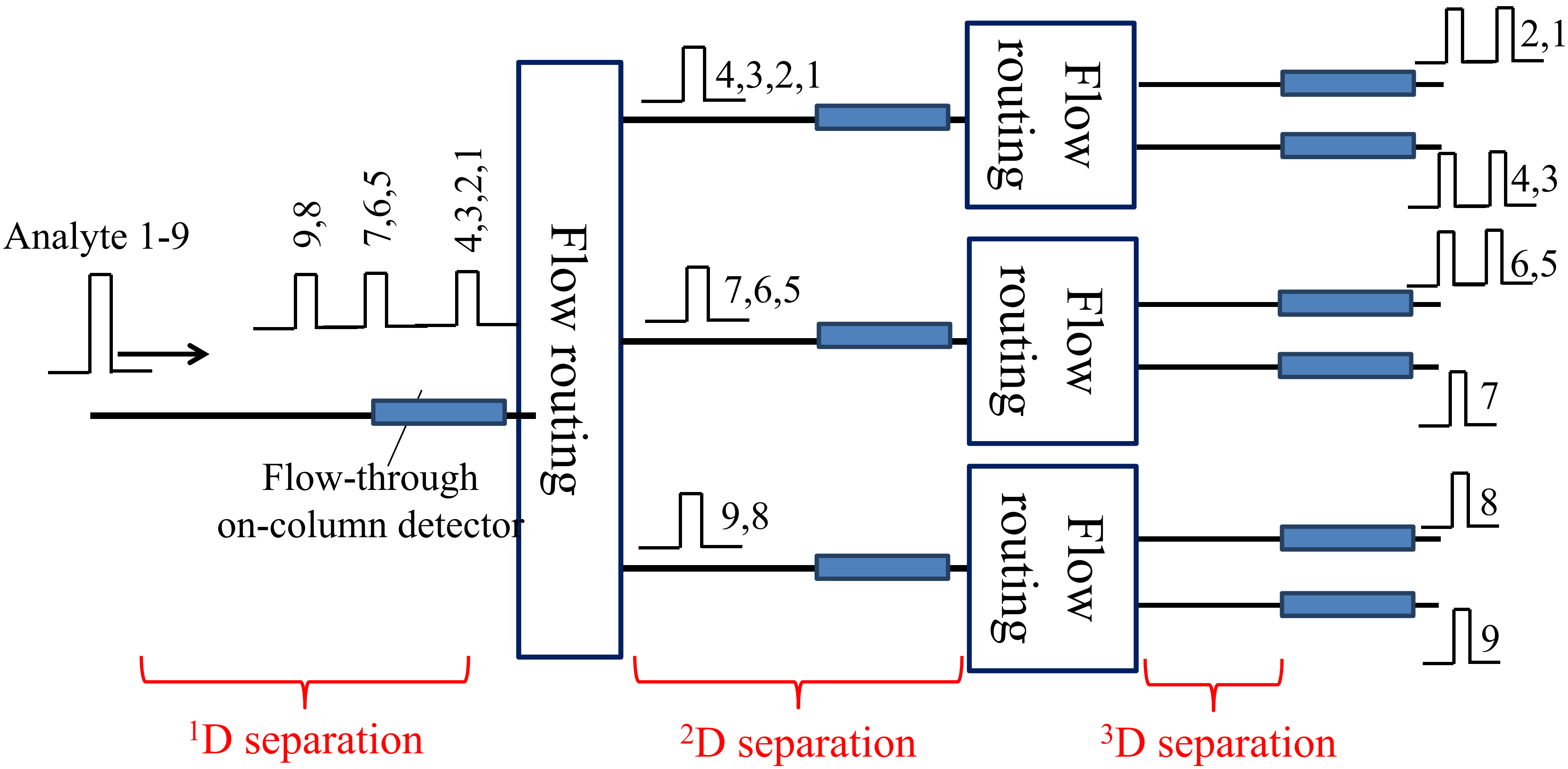
Selective detection (Heart-cutting detection)



1. Good for specific targets
2. Stand-by mode operation

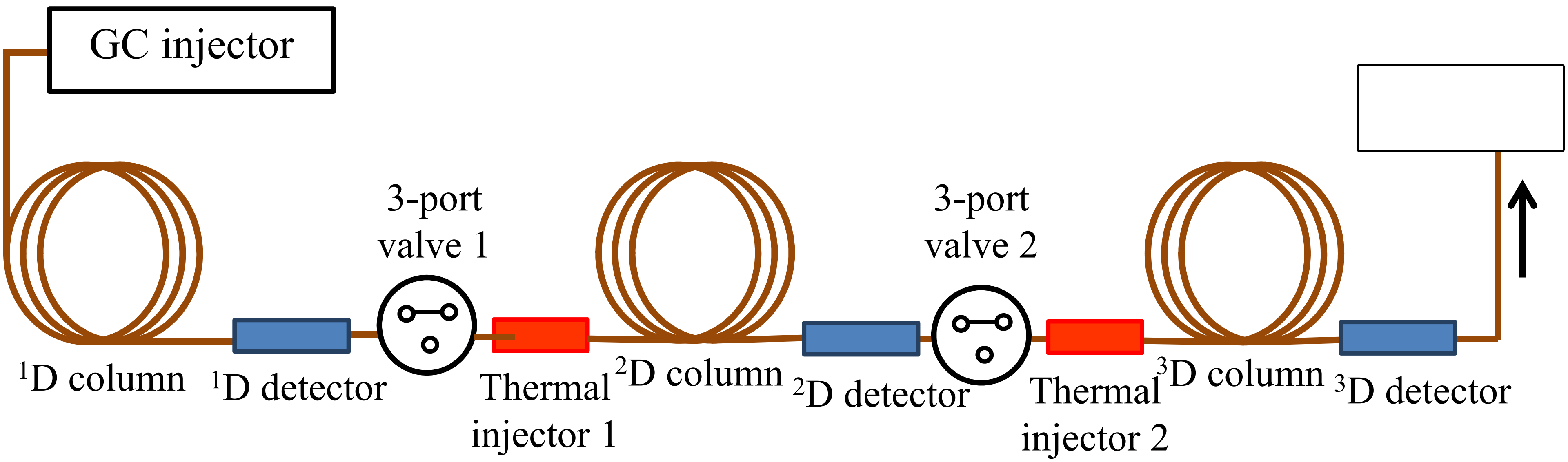
Liu et al., Lab Chip. **13**, 818 (2013)

Smart 3-D GC



Chen et al., Anal. Chem. DOI: 10.1021/ac401152v (2013)

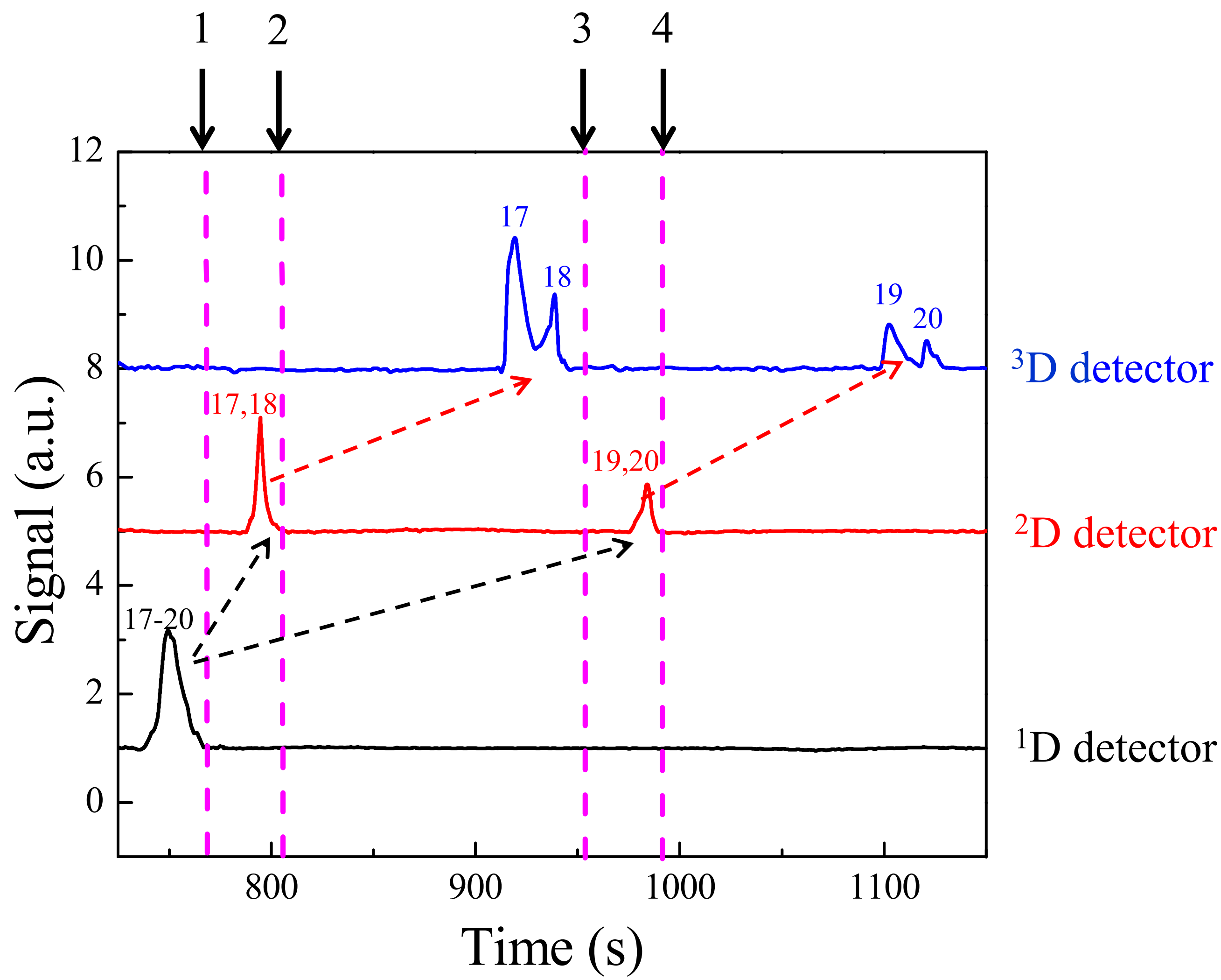
Setup



^{1}D column: 0.8 m long, i.d. = 0.25 mm, Rtx-5 ms coating
^{2}D column: 1 m long, i.d. = 0.25 mm, Rtx-1 coating
^{3}D column: 3 m long, i.d. = 0.25 mm, SUPELCOWAX-10 coating
Isothermal at room temperature
Flow rate = 6.5 mL/min

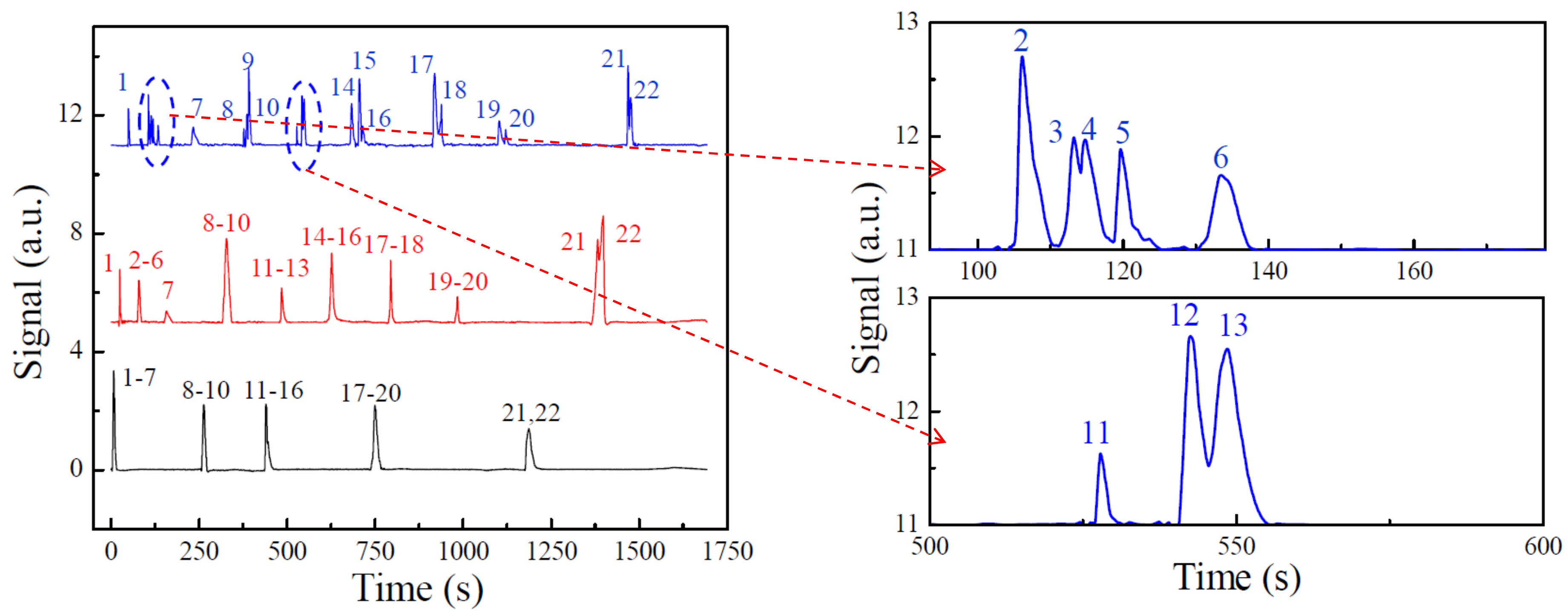
Chen et al., Anal. Chem. DOI: 10.1021/ac401152v (2013)

Simple example



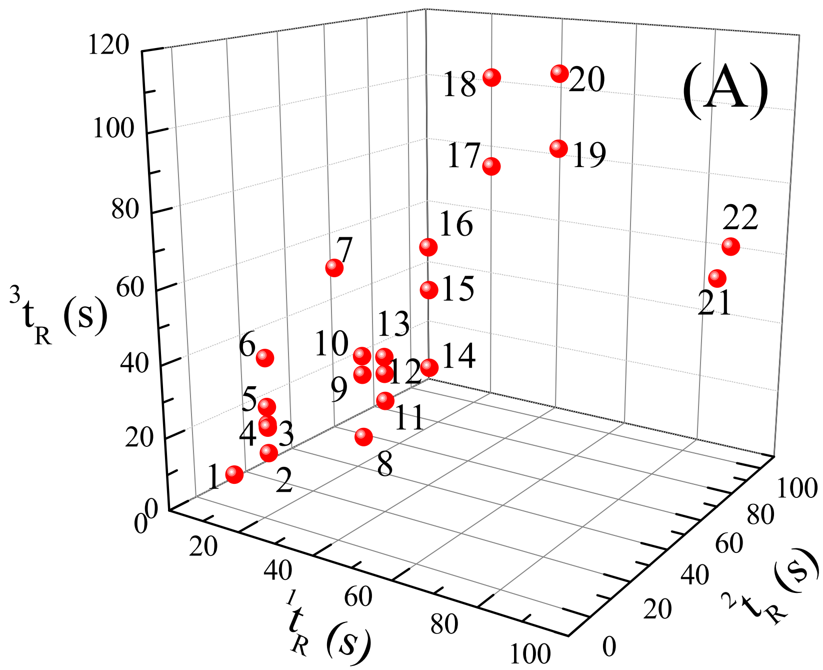
Chen et al., Anal. Chem. DOI: 10.1021/ac401152v (2013)

Isothermal separation of 22 analytes

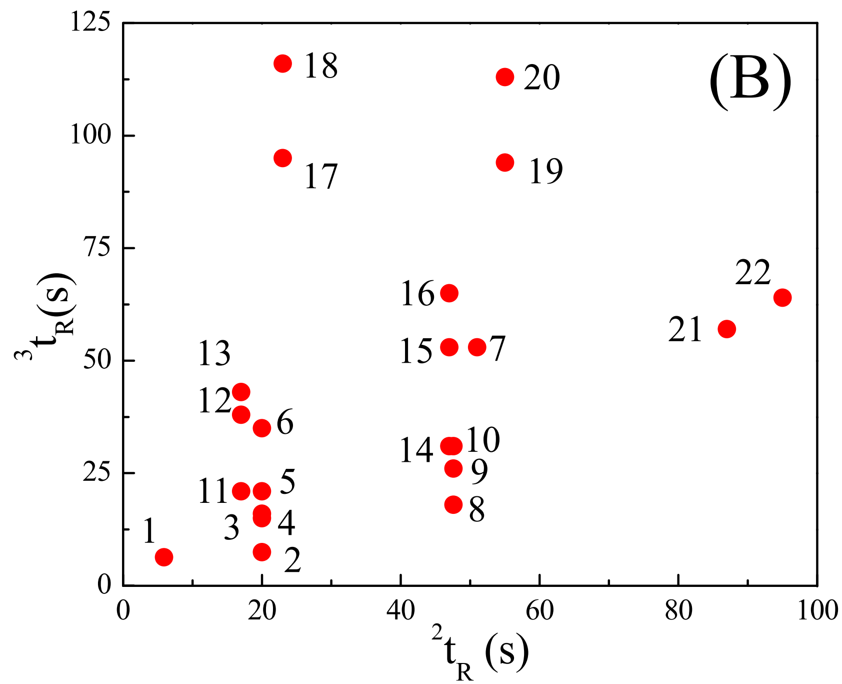


Chen et al., Anal. Chem. DOI: 10.1021/ac401152v (2013)

3-D chromatogram



3-D chromatogram



2-D chromatogram projected from 3-D chromatogram

Chen et al., Anal. Chem. DOI: 10.1021/ac401152v (2013)

Analysis

	Chlorobenzene (#18)	m-xylene (#22)
t_1	65.5 s	91.5 s
σ_1	4.5 s	6.4 s
n_1	19	20
t_2	23 s	95 s
σ_2	1.46 s	5 s
n_2	15	25
t_3	116 s	64 s
σ_3	1.35 s	1.35 s
n_3	76	24
Total peak capacity (n_1 x n_2 x n_3)	21,660	12,000
Total analysis time for analyte	937 s	1,476
Peak capacity production	1,336/min	488/min

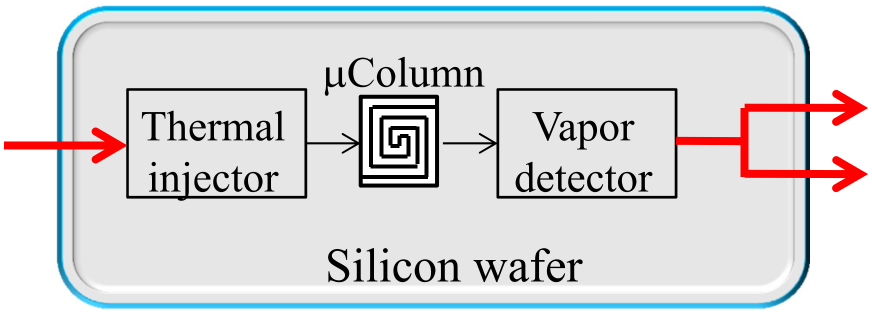
- 3-D starts to show the strength of high-dimension of separation
- With increased number of dimensions, total peak capacity increases

Proposed project

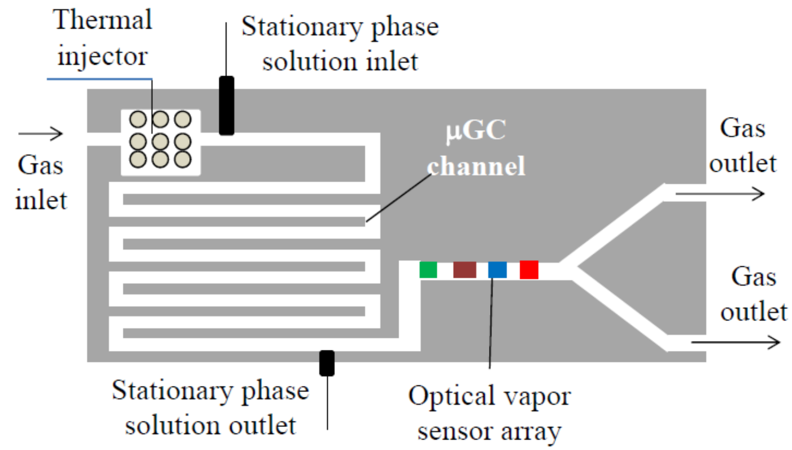
To develop an automated field-deployable multi-channel 3-dimensional micro-gas chromatography device capable of rapid (~20 minutes), sensitive (~ppb to sub-ppb), and *in-situ* analysis of >100 indoor (S)VOCs for human exposure assessment.

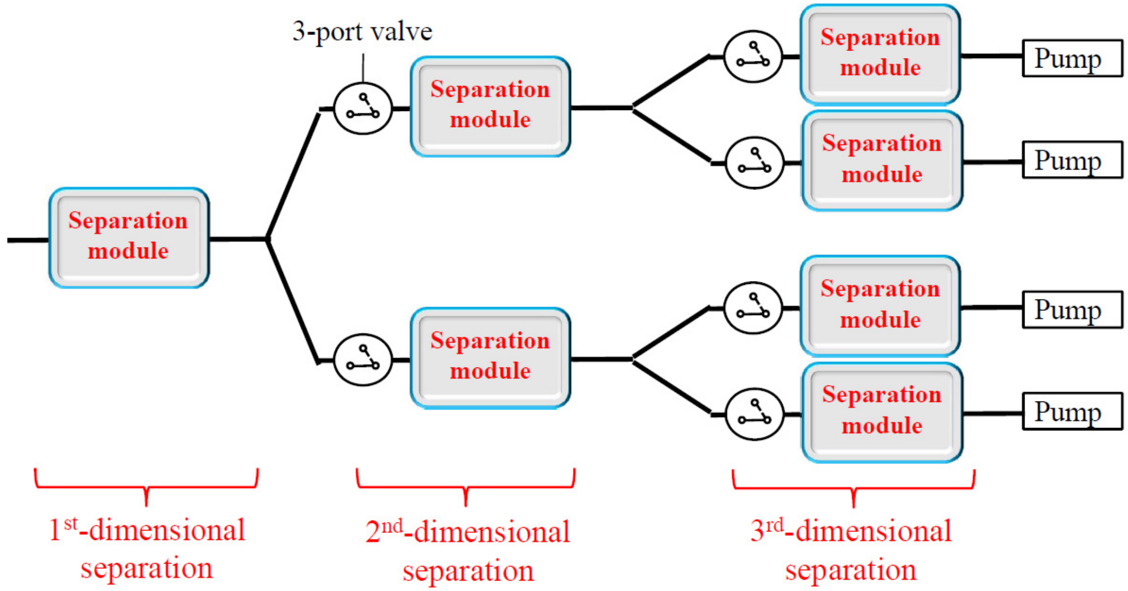
Proposed task #1 (Year 1)

1. Microfabrication to reduce the cost and system complexity
2. Modular design for ease of scale-up and re-configuration



Separation module

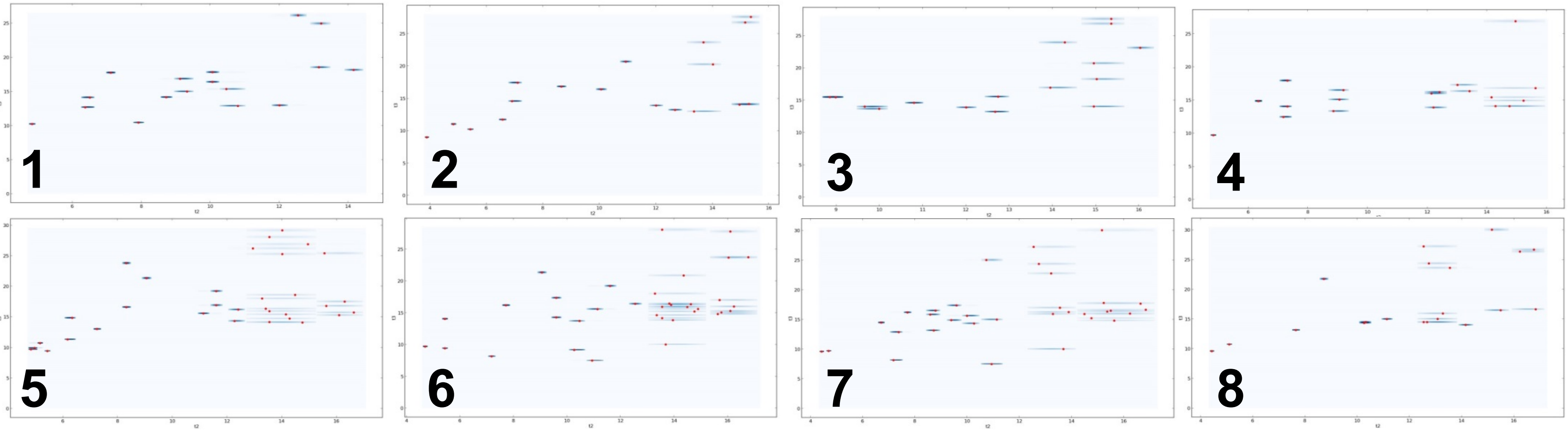




Proposed task #1 (Year 1)

1. Simulation to better understand the smart GC design
2. Algorithm for better peak detection
3. Algorithm to more efficiently use analysis time and peak capacity
   How to maximize the total peak capacity while minimizing the assay time

Simulation for smart 1x2x4 channel GC^3 (Most recent result)



- Isothermal operation for all 3 dimensions
- 150 VOCs
- Able to separate 94% of 150 VOCs in 6 minutes

Proposed task #2 (Year 2)

System assembly and testing

μGC	Weight	Size	Sensitivity	Automation	Total analysis time
3-D	2-3 kg	Desktop	1-10 pg	Yes	<20 min. for 150 VOCs

Proposed task #3 and #4 (Year 3)

3-D GC measurement of 150 (S)VOCs related to indoor environment

20 min analysis time
Quantification of >90% of 150 (S)VOCs
Building a 3-D chromatogram reference library
Benchmarking against standard GC-MS

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Post-doctors

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- IOS-0946735
- ECCS-0729903

University of Michigan: WIMS^2

Global Challenges for a Third Century

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Prof. Edward Zellers (University of Michigan)
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End of the presentation

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