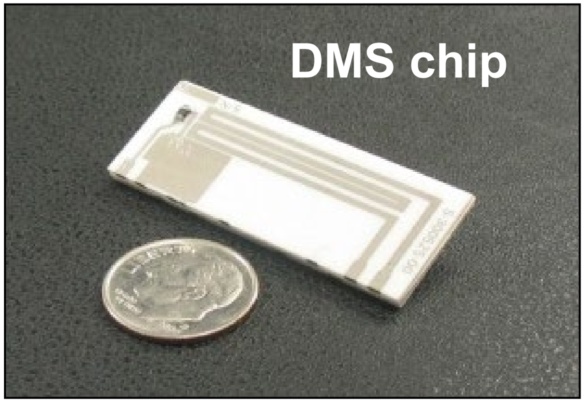
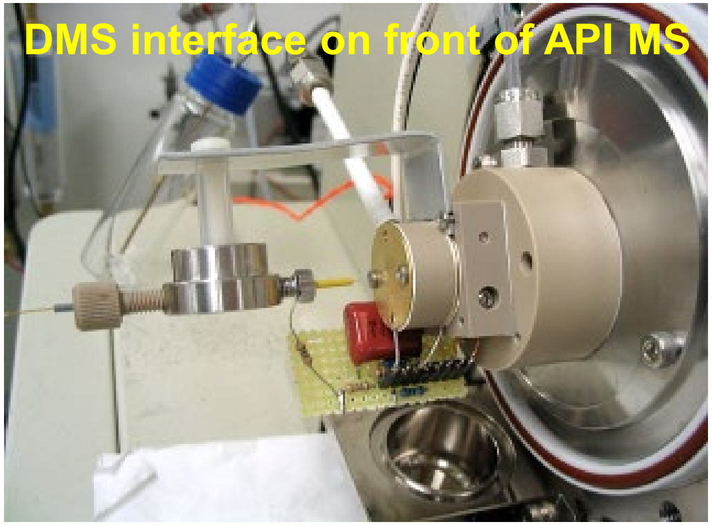
Planar Design Differential Ion Mobility Spectrometer (DMS) as a Prefilter for Portable Atmospheric Pressure Ionization Mass Spectrometers





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[2]GP Ionics, LLC, Las Cruces, NM, 88003
[3] SCIEX, Concord, ON L4K 4V8, Canada

For Motivation to Use DMS Interfaces on Front of API MS

AB Sciex, ThermoFisher Scientific, Waters, Agilent, ExcellIMS

Prof. Graham Cooks on ASMS 2013 made the following declaration:

"*If we will dedicate some addition resources on **managing ionic processes outside** MS **vacuum system**, **progress in mass spectrometry would be accelerated**.*"

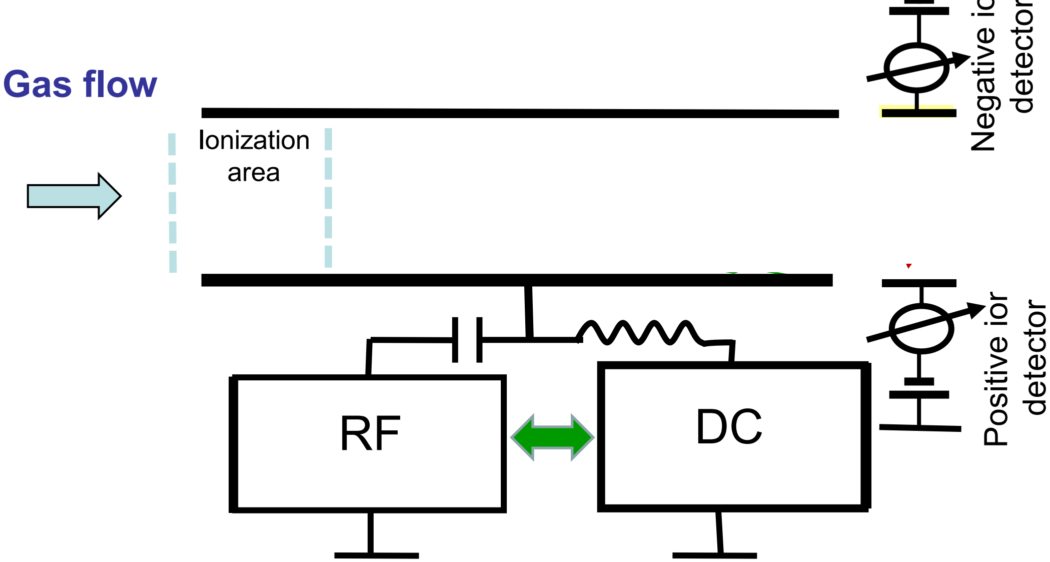
Possible system for Ion's pre-filtering :
IMS, FAIMS, DMS, DMA → API-MS

Outline

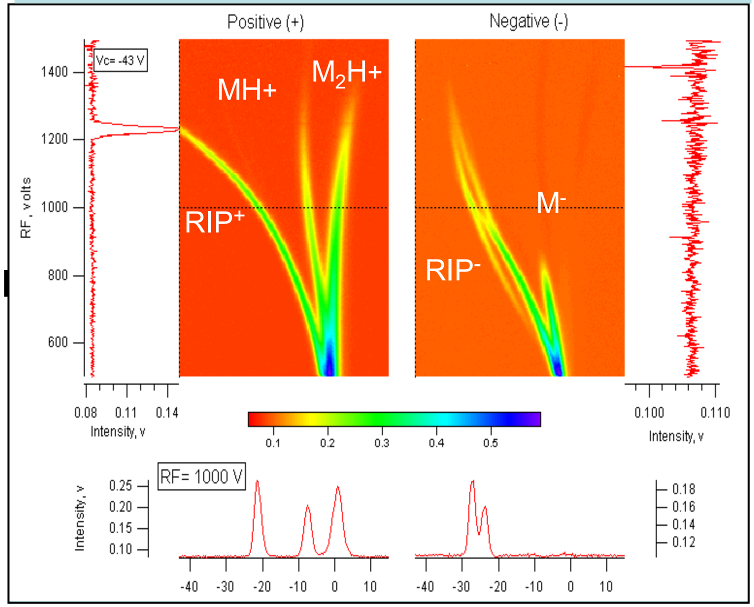
- Schematics, modeling, and regimes of planar DMS sensor operation.
- Physical-Chemistry Fundamentals for DMS sensor operation.
- Comparison DMS and MS techniques and clarify their output orthogonality.
- Examples of DMS spectra obtained in planar design sensor.
- Motivation to build a Tandem DMS-API MS.
- Experimental demonstration the advantages provided by DMS-API MS tandem system:
    a. Possibility in-situ provide MS identification DMS peaks,
    b. Decreasing chemical noise,
    c. Visualization kinetics of gaseous ions transformation (e.g., fragmentation).
- Design of DMS sensor for prefiltering ions on front of portable API MS.
- **Summary.**

Schematic and Operation Regimes of the Planar DMS Sensor

$$K_i(E/N) = K_i(0)[1 + \alpha_i(E/N)]$$



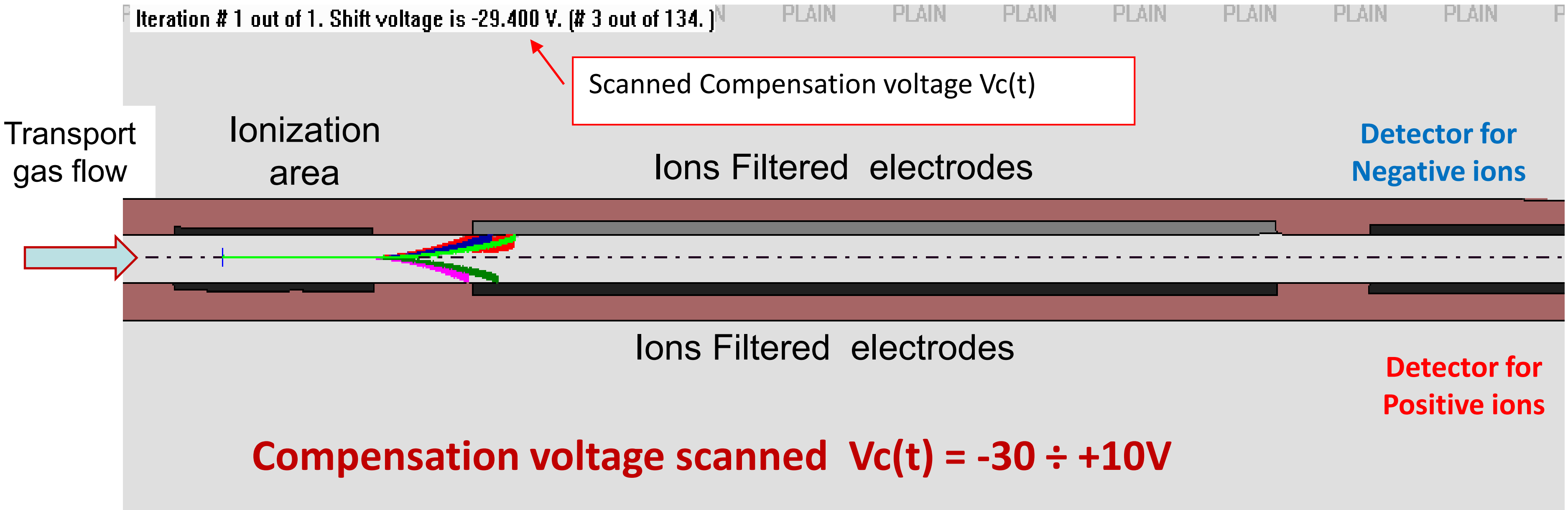
2D dispersion plots for DMMP



Four Regimes of operation DMS sensor:

1. **Transparent mode of operation** is realized when RF=0V, and DC=0V;
2. **Continuously filtration targeted ion species** occurs when RF is turn ON and DC voltage is adjusted to specific value for filtration only targeted ion species;
3. **Generation full DMS spectra** for specific RF realized when RF is set to needed value and compensation (**DC(t) voltage**) is scanned;
4. **Regime generation 2D dispersion plots** realized when RF(t) and DC(t) voltages are synchronized and scanned.

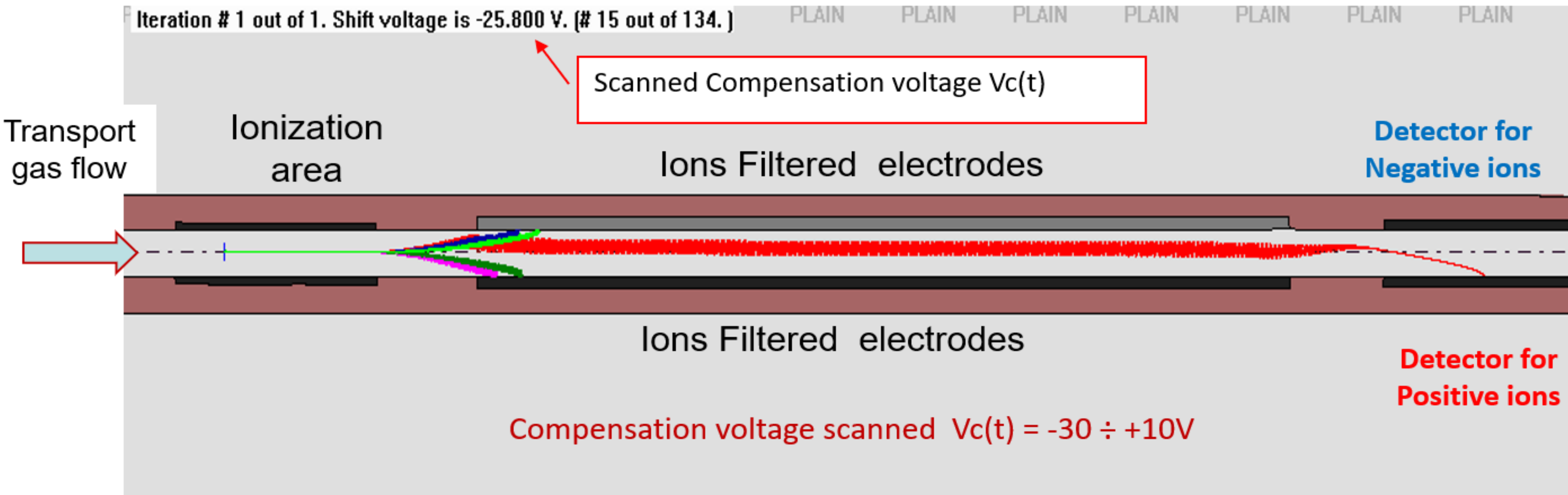
Modeling trajectories for 5 different positive and negative ion species when RF=1000V and Vc(t) is scanned



Tested Ion Species with different Ko and alpha parameters

Draw	K0	a2	a4	b2	b4	Weight	Charge	Diffusion	Color	V_C for filtration
Yes	3.00e+000	9.00e-006	0.00e+000	0.00e+000	0.00e+000	1.00e+000	1	No		-25.8V
Yes	2.50e+000	7.00e-006	0.00e+000	0.00e+000	0.00e+000	1.00e+000	-1	No		-21.3V
Yes	2.00e+000	5.00e-006	0.00e+000	0.00e+000	0.00e+000	1.00e+000	1	No		-17.7V
Yes	1.50e+000	3.00e-006	0.00e+000	0.00e+000	0.00e+000	1.00e+000	-1	No		-12.3V
Yes	1.00e+000	1.00e-006	0.00e+000	0.00e+000	0.00e+000	1.00e+000	1	No		-7.8V

Modeling trajectories for 5 different positive and negati ion species when RF=1000V.



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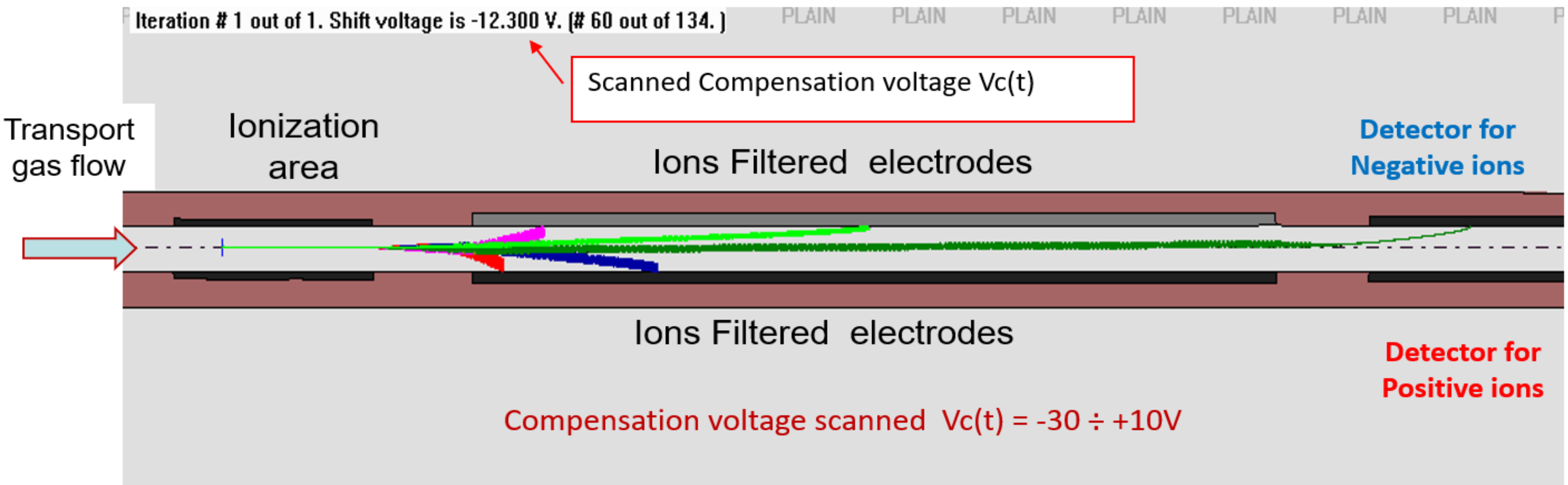
Yes	2.50e+000	7.00e-006	0.00e+000	0.00e+000	0.00e+000	1.00e+000	-1	No		-21.3V
Yes	2.00e+000	5.00e-006	0.00e+000	0.00e+000	0.00e+000	1.00e+000	1	No		-17.7V
Yes	1.50e+000	3.00e-006	0.00e+000	0.00e+000	0.00e+000	1.00e+000	-1	No		-12.3V
Yes	1.00e+000	1.00e-006	0.00e+000	0.00e+000	0.00e+000	1.00e+000	1	No		-7.8V

Modeling trajectories for 5 different positive and negativ ion species when RF=1000V.



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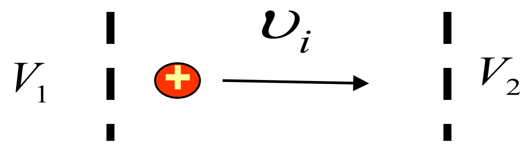
Yes	2.00e+000	5.00e-006	0.00e+000	0.00e+000	0.00e+000	1.00e+000	1	No		-17.7V
Yes	1.50e+000	3.00e-006	0.00e+000	0.00e+000	0.00e+000	1.00e+000	-1	No		-12.3V
Yes	1.00e+000	1.00e-006	0.00e+000	0.00e+000	0.00e+000	1.00e+000	1	No		-7.8V

IMS and DMS and MS Techniques Provide Complementary/Orthogonal Information for Ion Species



$$K_i(E/N) = K_i(0)[1+\alpha_i(E/N)]$$

In Mass Spectrometry (in vacuum)

$$\upsilon_i = \sqrt{2ez(V_2 - V_1) / m_i}$$

Ion **m/z** parameter

In IMS and DMS

In gases according Mason Schamp Equation

$$\upsilon_i = K_i(E) * E = K_i(E) * \frac{V_2 - V_1}{L}$$

$$K(E) = \frac{e}{\mu(E)\nu(E)} = \frac{3e}{16N}\left(\frac{2\pi}{\mu(E)kT_{eff}}\right)^{1/2}\frac{1}{\Omega^{1.1}(T_{eff})}$$

Ion reduce mass **Ions cross section**

MS, IMS and DMS characterize a different property of ions:

- *Mass-spectrometers provide the **m/z** parameters of ion species.*
- *Conventual time of flight IMS analyzers operates in low electric field conditions, therefore, provide a coefficient mobility of ions K(0) at low electric field **(E<1kV/cm)***
- *DMS in contrast to conventional IMS operates in high electric field **(E = up to 30kV/cm)** conditions. Therefore, DMS provides information (K(E)) related to transformation of ions conformation in strong electric field.*

Interrelation Between Ions' Characterized Parameters from Each Method

$$K(E) = K(0)[1 + \alpha_{eff}(E)]$$

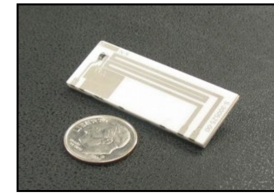
Provide IMS measurement

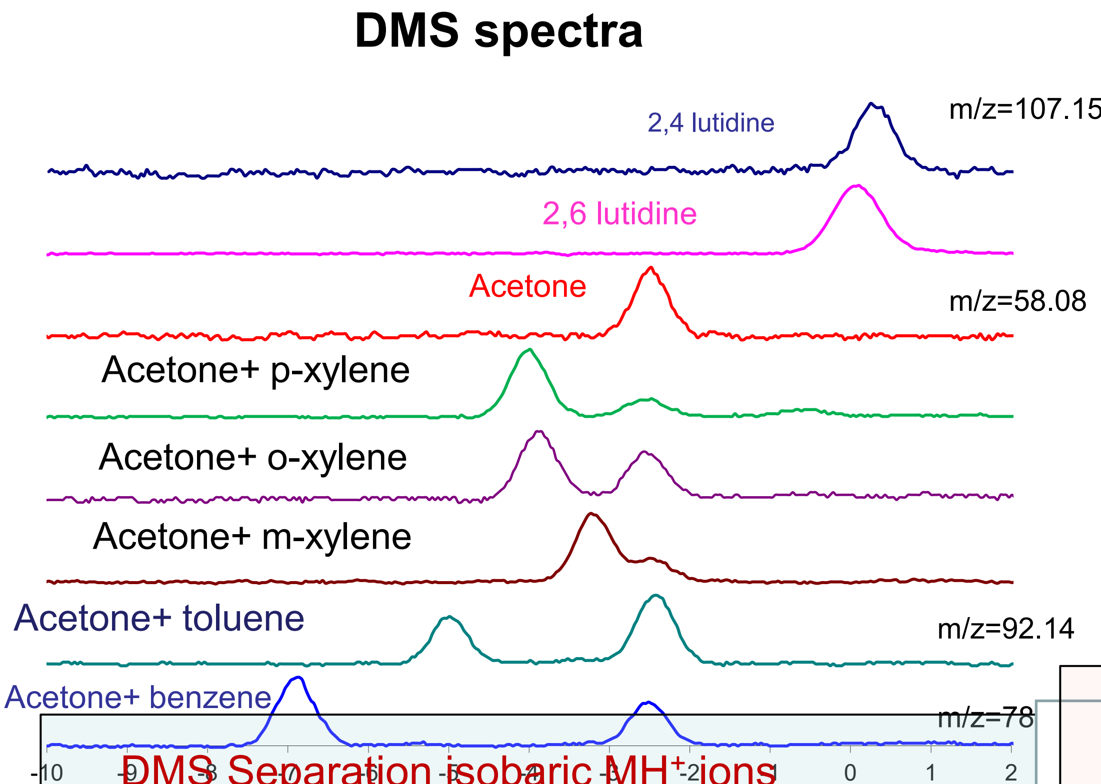
Provide DMS measurement

$$\alpha_{eff}(E) = \frac{K(E) - K(0)}{K(0)} = \frac{\Delta K(E)}{K(0)}$$

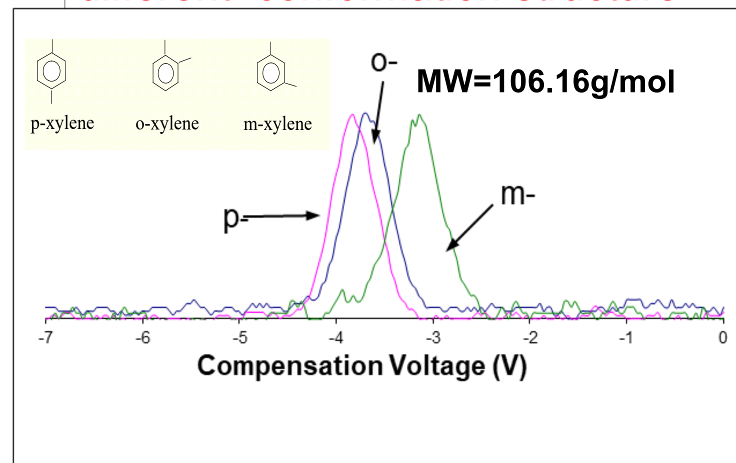
$$V_c \approx \frac{< \alpha E_s f(t) > d}{1 + < \alpha >}$$

Some Winning Examples of DMS spectra



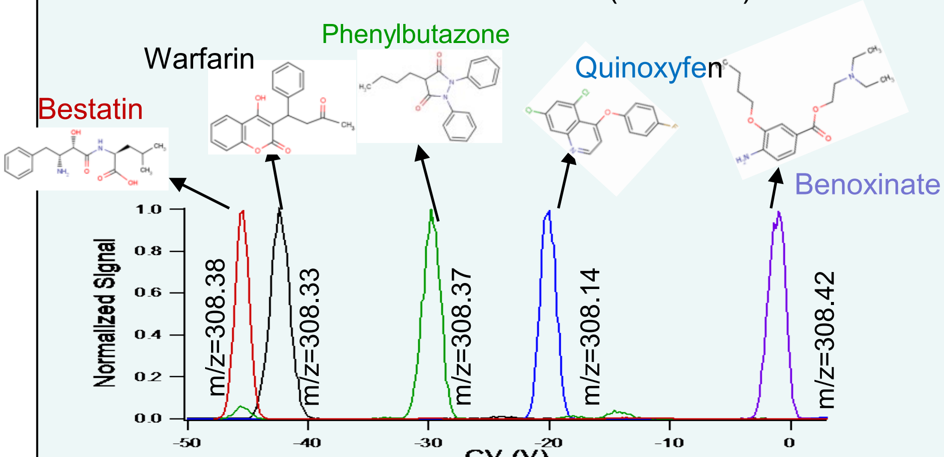


Separation Xylene isomers with different conformation structure



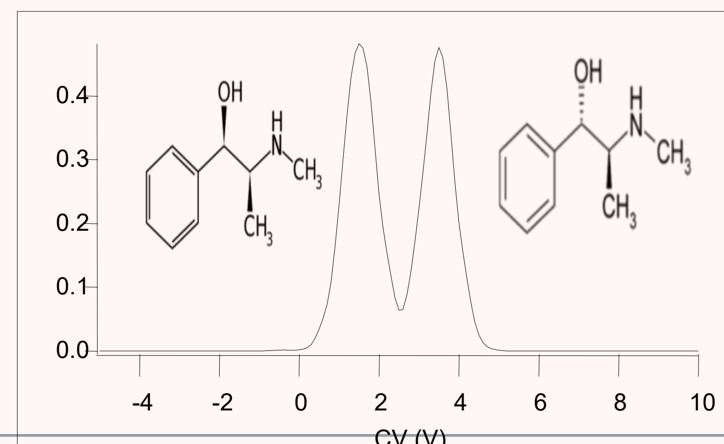
DMS Separation isobaric MH^+ ions

All 6 chemicals have close mass (m/z~309)



Separation **diastereoisomeric** molecules

Ephedrine and Pseudoephedrine have identical MW=165.11536.



Our statement: DMS pre-filtering on front of API-MS is a powerful adding to mass spectrometry

- As you can see the DMS generate a **low-resolution spectra** with ions resolving power between 10—15.
- A regular MS powerful device which provides significantly **higher resolution**; 100 – thousands.
- But, on another hand DMS able separate ion species with almost same molecular mass.

- Therefore, combination DMS with mass spectrometry (MS) offers **potential advantages over the use of mass spectrometry alone.**

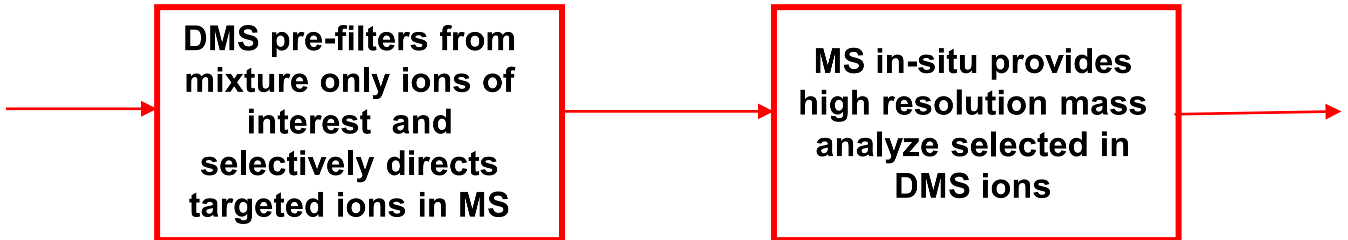
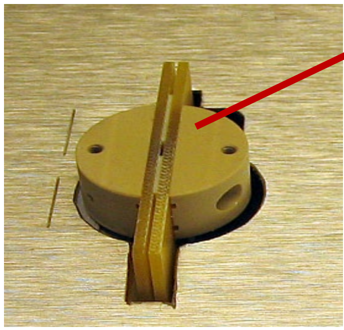


Image of Our First DMS Interface which was Mounted to Number Commercial Atmospheric Pressure Ionization Mass Spectrometers

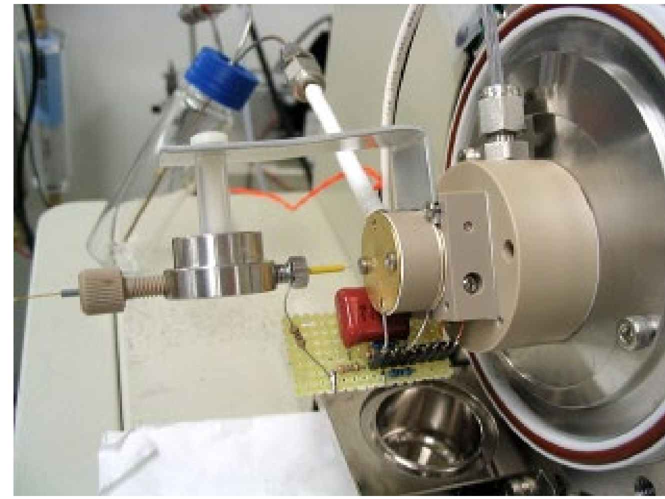


Low cost, small size, electromechanically simple, and robust DMS ions filter.

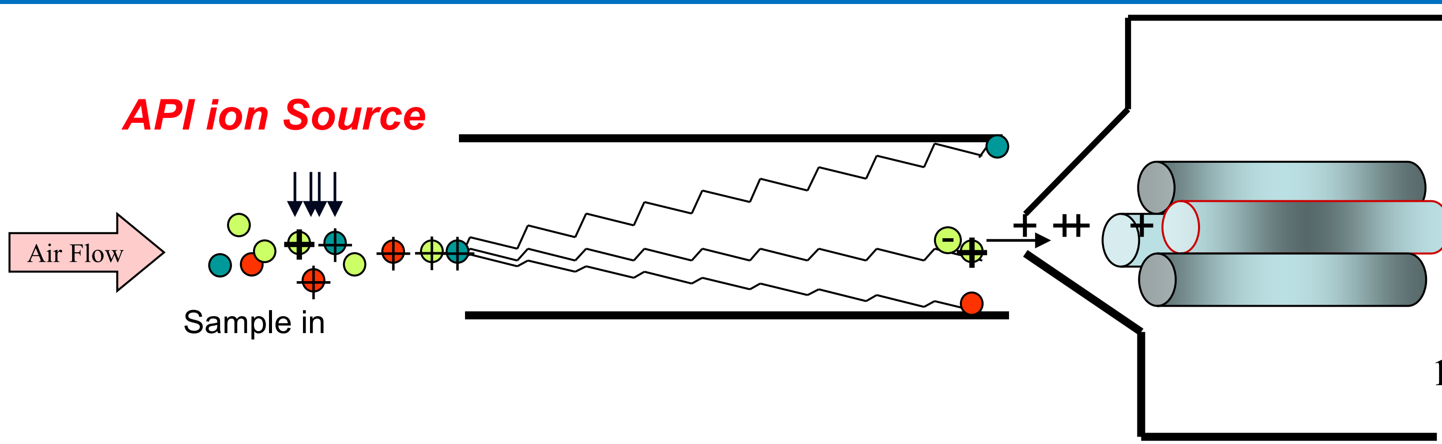
→ **DMS** → **API-MS** →

Cost DMS interface
$

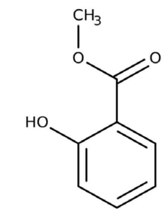
Cost of MS
$ $ $ $



In-line design for attaching DMS sensor to MS

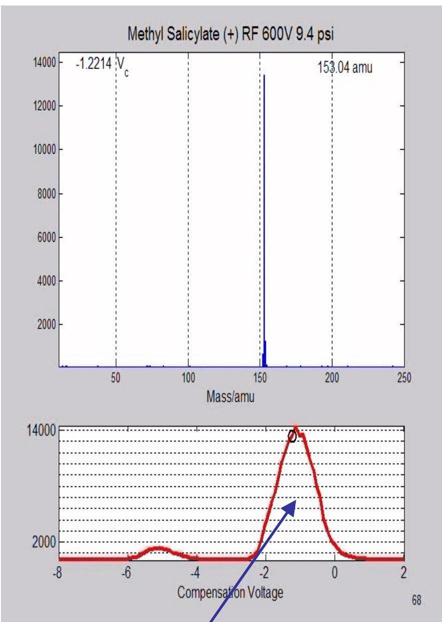


DEMO #1. DMS-MS System Provides in-situ Registration and MS Identification Ions in Regime of Fast DMS-MRM



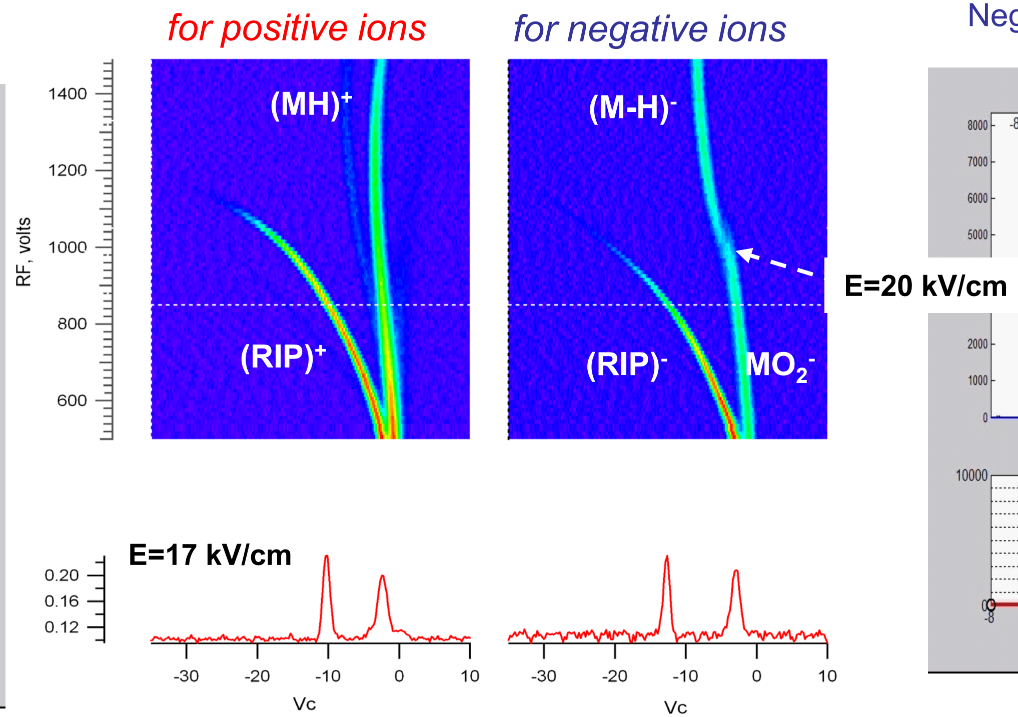
Dispersion plots for methyl salicylate*(1ppb)*.*(MW=152)*

Positive ions mass spectrum for Vc= -1.8V point

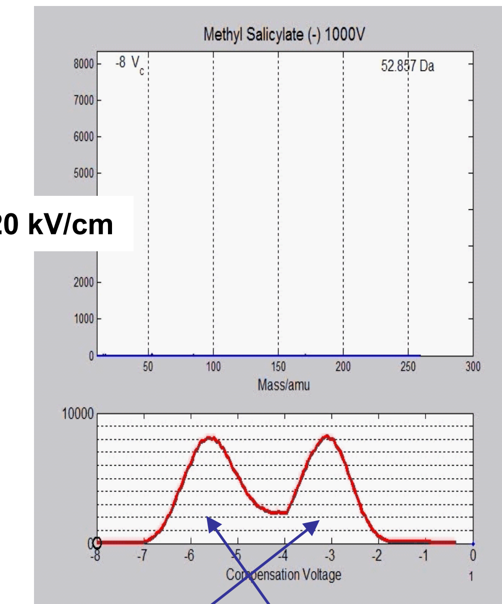


(MH)+

m/z= 153 Da



Negative ions mass spectra



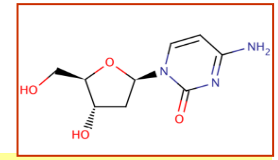
MO_2^- → $(M-H)^-$ + HO_2^*

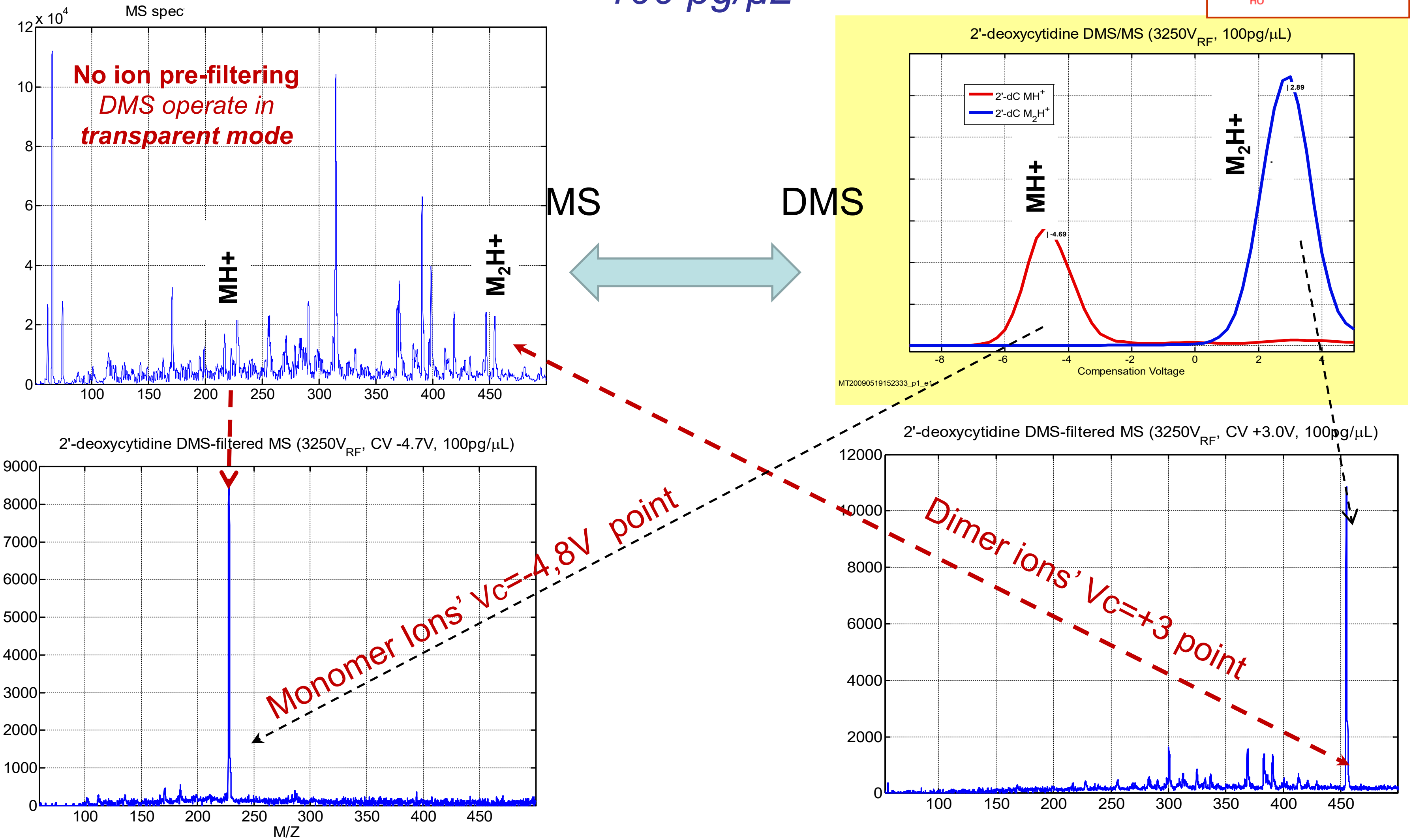
m/z = 184 Da   m/z = 151 Da

E. G. Nazarov, S. L. Coy, E.V. Krylov, R.A. Miller, GA. Eiceman. *Anal. Chemistry, 78, 7697-06. 2006.*

DEMO #2. Separation the Targeted Ions on Front of DMS-MS Helps to Reduce a Chemical Noise in recorded MS spectra

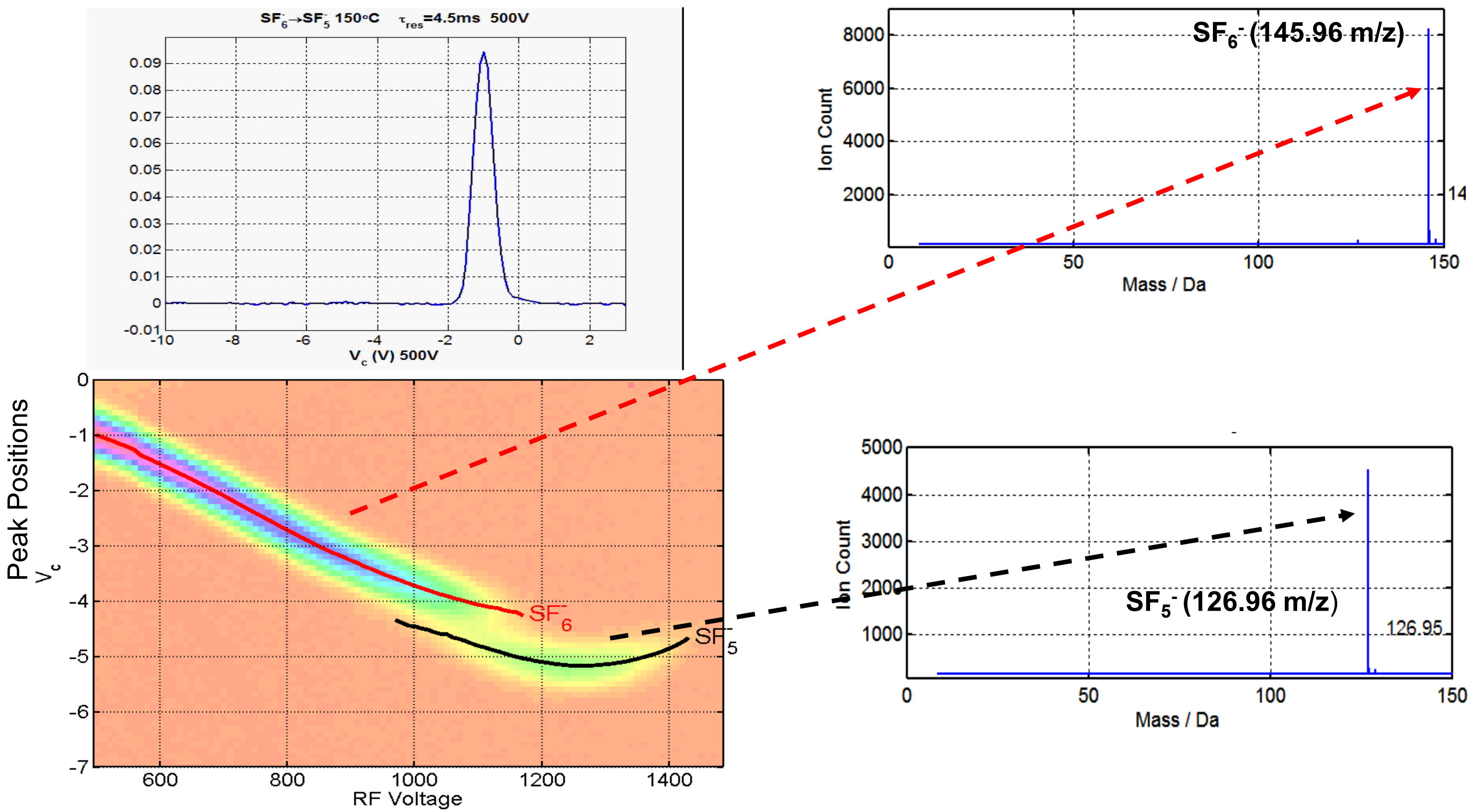
2'-Deoxycytidine Radiation Biomarker with MW 228, 100 pg/µL



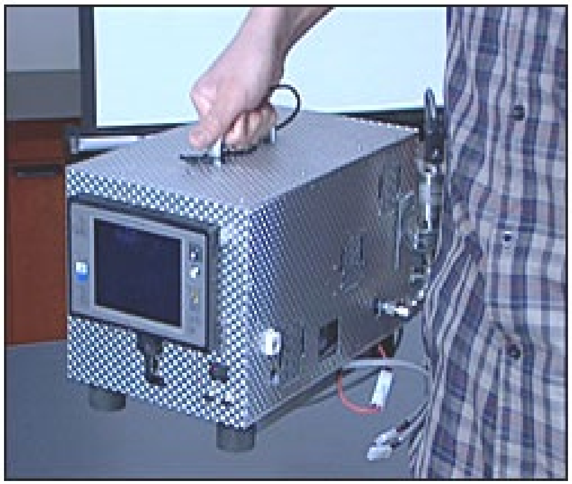


DEMO#3. Visualization the Kinetic of the SF6 Ions Fragmentation Under Effect of Strong RF Voltage

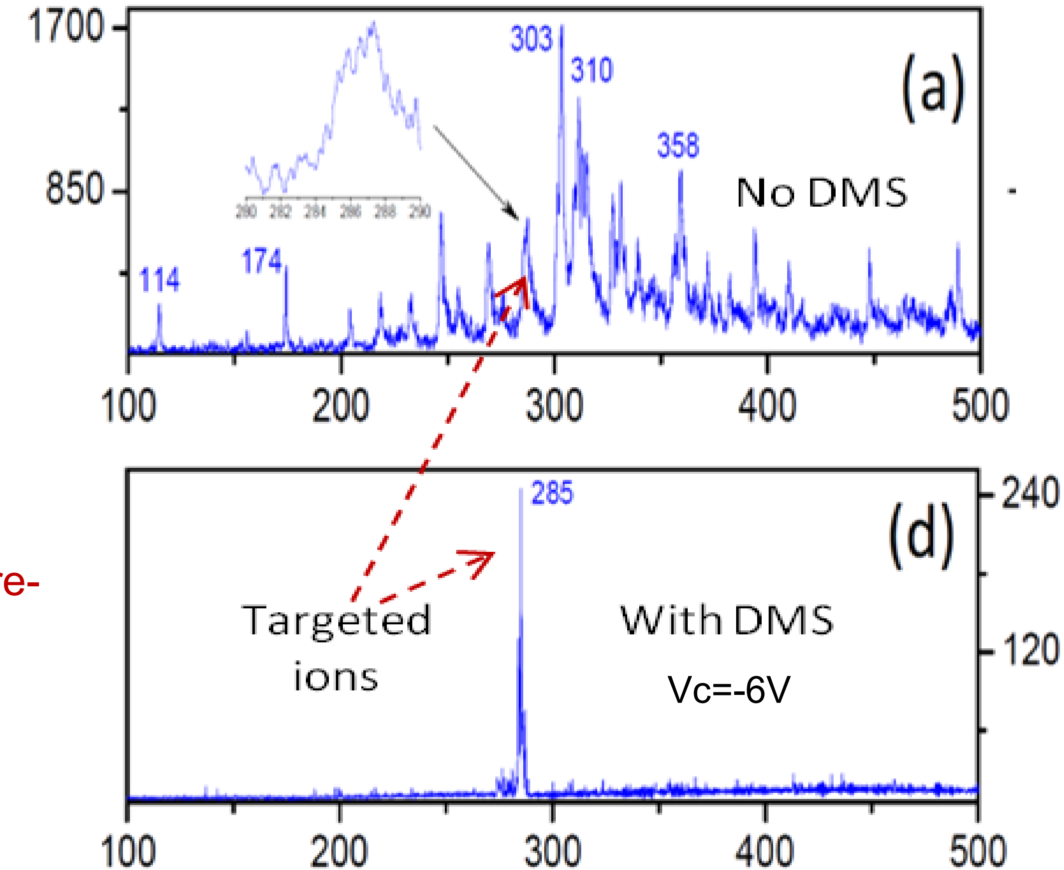
Transition under effect of strong electric field from SF_6^- to SF_5^-



Selective Detection and Identification Traces of Diazepam (m/z=285 Da) in Urine Samples in configuration when DMS Coupled to Mini10 Operated with DAPI



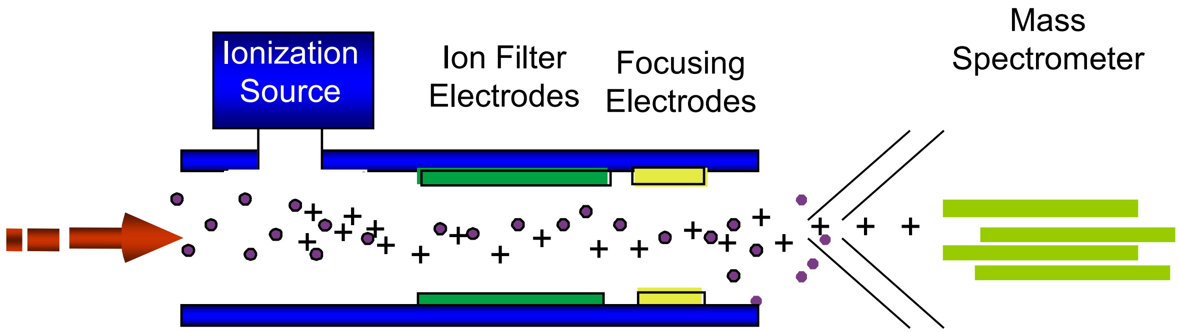
Mass spectra obtained with DMS pre-filtering on entrance of **Mini 10** operated in regime DAPI (samples introduction via a discontinuous atmospheric pressure interface)



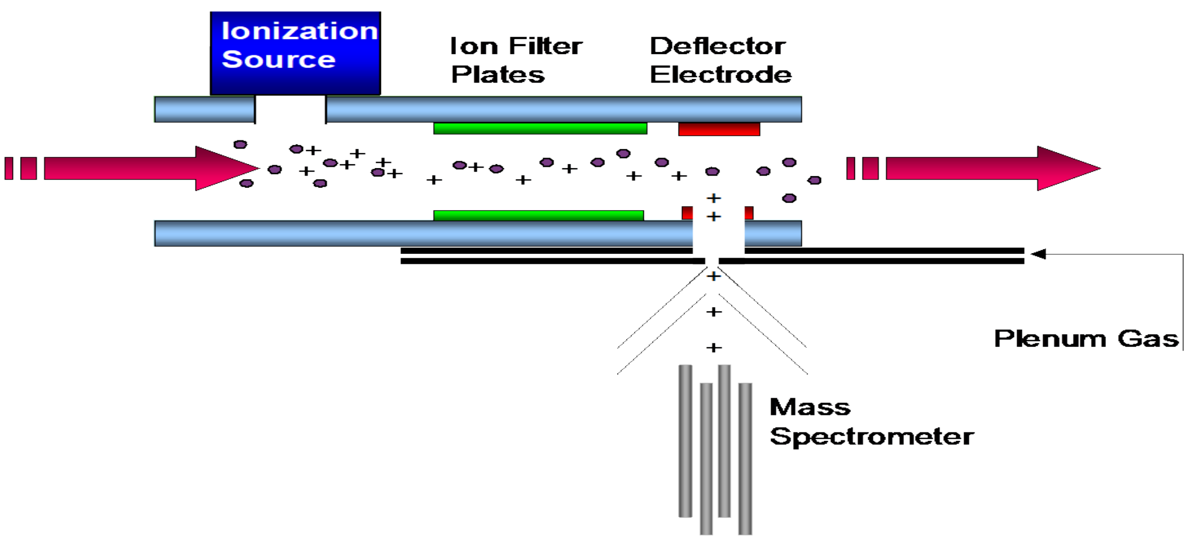
F. Kh. Tadjimukhamedov, A. U. Jackson, E.G. Nazarov, Z. Ouyang, and R. G. Cooks. Evaluation of Differential Mobility Spectrometer Coupled to a Miniature Mass Spectrometer. J Am Soc Mass Spectrum 2010, 21, 1477–1481

Planar DMS Designs for Ions Pre-separation in Front of Portable API MS(s) which have Limitation in Flow Rate for Samples Introduction.

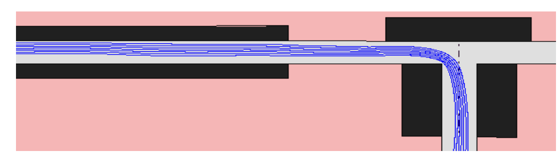
1) In-line design

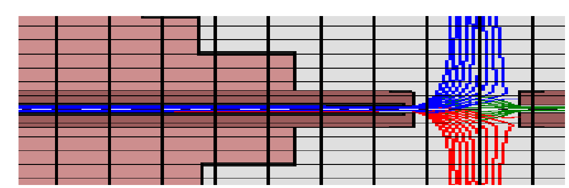


2) Right angel design for minimization flow rate introduction in API MS orifice.



No significant ion losses at right angle DMS exhaust





Summary: The interfacing DMS with mass spectrometry (MS) offers significant advantages over the use of mass spectrometry alone.

- Enriches chemicals' identification due to adding an additional ions characterization information

- It allows the in-situ comparison of mass spectra with and without ion pre-separation

- Provides detailed insight into ion gas-phase chemistry

- Reduces a chemical noise in MS spectra, which leads to enhancing sensitivity of a system

- We can claim that: Adding analyte ions pre-filtering especially valuable for portable MS(s) because additional information which provide a DMS can compensate the inevitably lost in the analytical performance of the portable MS systems in process of their miniaturization.