Exploring the figures of merit of differential mobility spectrometry (DMS) cells of varied geometries

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OVERVIEW

- Differential mobility spectrometry (DMS) has enjoyed success in terms of its ability to remove isobaric chemical noise from mass spectrometry (MS) workflows, as well as its ability to separate closely related structures (including isomers). When considering the overall performance of a DMS system, it is worthwhile examining the influence of the geometry of a DMS cell, which has significant impact on the system's analytical figures of merit.
- A previous study (Schneider et al., 2015) demonstrated that increasing the DMS gap height (i.e., the separation between the two planar electrodes) can provide a proportional increase in the compensation voltage (CoV) spread for ions of interest. An increase in this CoV spread for a given group of ions can provide a proportional increase in the system's peak capacity, but only if the ionogram peak widths remain constant.
- Here, we have systematically explored the impact of cell gap height (1.0 vs 1.5 mm), width (10 vs 20 mm) and length (30 vs 65 mm) on a variety of performance metrics, including ion transmission, residence times, and resolving power.

MATERIALS AND METHODS

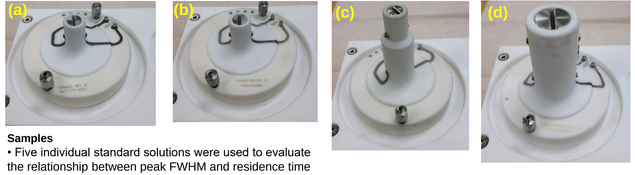
DMS-MS Instrumentation

A modified hybrid quadrupole linear ion trap mass spectrometer was used for these experiments with a custom DMS power supply that can deliver separation voltages (SV) in excess of 6500 Vp-p. A standard ESI source generated ions from solutions (see below) delivered at 10 µL/min using a syringe pump. The instrument used a standard orifice plate (0.6 mm ID), but employed different curtain plates based upon the geometry of the DMS cell being tested.

Ion residence times in the DMS cells were determined by calculating the volumetric flow rate through each of the cells as a function of their geometries and the added flow of DMS throttle gas (DR) added to the terminus of the DMS cell (Figure 2). The DR flow rates were measured by a flow meter (Cole-Parmer) at the DR gas line's exit from the coil box, and a baseline flow rate of 2.8 LPM was measured at the orifice of the MS.

Figure 1. Geometries of the four (4) DMS cells that were tested (dimensions are gap height x width x length):

(a) 1.0 x 10 x 30 mm (b) 1.5 x 10 x 30 mm (c) 1.5 x 10 x 65 mm (d) 1.5 x 20 x 65 mm

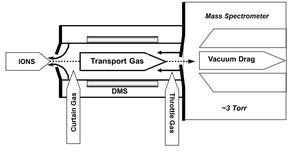


Samples

• Five individual standard solutions were used to evaluate the relationship between peak FWHM and residence time for each of the DMS cells: 10 pg/µL reserpine, 10 pg/µL minoxidil, 250 pg/µL proline, 500 pg/µL 5-fluorouracil, and 200 pg/µL taurocholic acid.

• One mixed standard solution was used to evaluate the thermal equilibration time (i.e., time to establish a stable CoV shift for a compound, +/- 0.4 V with modifiers and +/- 0.3 V without modifiers) from room temperature initial state to a final state (DT = 150° C) for each of the DMS cells: 100 pg/µL each of safranin orange, clenbuterol, haloperidol, and morphine. These stability tests were performed with only nitrogen in the curtain gas, as well as with 1.5% (v/v ratio) isopropanol in the curtain gas.

Figure 2. Schematic diagram of the DMS system configuration, displaying pertinent gas flows



RESULTS

Determining optimal residence times as a function of DMS cell geometry

It was of interest to determine the residence time that would be necessary for a 1.5-mm gap height device to match ionogram peak widths provided by the 1.0-mm gapped DMS cell.

For each of the DMS cells examined, we adjusted the FWHM of each ion by altering the DR value – the amount of throttle gas added to the terminal end of the DMS cell – which changed the residence times of the ions inside the DMS cell (Table 1).

Table 1. Calculated residence times for ions being transmitted though each of the four (4) DMS cells as a function of cell geometry and DR (throttle gas setting). The cell dimensions are provided in the following format: gap height x width x length. Volumes are reported in Litres.

	Ion Residence Times (all ms)			
	V (1.0x10x30mm) (L)	V (1.5x10x30mm) (L)	V (1.5x10x65mm) (L)	V (1.5x20x65mm) (L)
DR	0.0003	0.00045	0.00097	0.00195
0	6.4	9.6	20.9	41.8
2	7.7	11.5	25.0	50.0
4	8.4	12.6	27.2	54.5
6	8.9	13.4	29.0	58.1
8	9.5	14.2	30.8	61.5
10	10.1	15.1	32.7	65.4
12	10.7	16.0	34.7	69.5
14	11.4	17.1	37.1	74.2
16	12.2	18.3	39.7	79.5
18	13.1	19.6	42.5	85.1
20	14.1	21.1	45.7	91.4
22	15.1	22.7	49.1	98.2
24	16.3	24.5	53.1	106.2
26	17.7	26.6	57.6	115.2
28	19.5	29.2	63.2	126.5
30	21.5	32.3	69.9	139.8

Increasing the DR reduces the volumetric gas flow through the DMS cell, resulting in longer residence times. For the largest cell and the highest DR value examined, ions could encounter a residence time of almost 140 ms. A benefit of increased residence time is narrower peaks in the ionograms (smaller FWHM in the CoV dimension). The FWHM values for reserpine peaks could be narrowed to ~ 0.4 V. However, excessively long residence times can result in signal loss and long pause times between CoV switching.

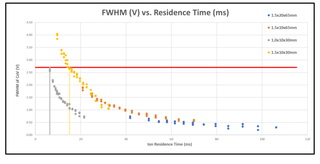


Figure 3 (left) shows a plot of reserpine FWHM versus residence time for a series of DMS cell geometries, including the 1.0-mm gapped DMS cell (data shown in grey) and 3 variants with 1.5-mm gap height. Referring first to the data from the 1.0-mm gapped cell, the reserpine FWHM was ~ 2.7 V (horizontal red line) when no throttle gas was provided. Curves generated from the 3 different 1.5 mm gapped cells generally overlay (as expected) for the data presented in Figure 3.

The 1.5-mm gapped DMS cells (yellow, orange, and blue data points) align to present a trend between FWHM and residence time; from these data we can determine the necessary residence time to match the FWHM provided by the 1.0-mm gapped cell. The data presented in Figure 3 suggest that a residence time on the order of ~15 ms would provide the desired FWHM (golden vertical line).

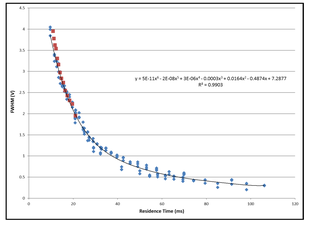


Figure 4 shows an overlay of the 1.5 mm gap height data from Figure 1 (blue markers) with additional data collected using a 1.5 x 10 x 65 mm DMS cell with vacuum suction on the throttle gas port (red markers). Since the relationship between FWHM and residence time is independent of how the gas flow is generated, this approach provided further corroboration for the results of Figure 3. The suction approach was necessary to achieve residence times less than 21 ms with the 1.5x10x65 mm DMS cell. All of the 1.5 mm gap height DMS data presented in Figure 3 was fit to a curve as shown in the inset. From the curve fitting, it was possible to determine the residence time that would be required to achieve a FWHM of 2.7 V using a 1.5 mm gap height DMS cell - 15.18 ms.

RESULTS

Monitoring relative ion transmission as a function of DMS cell geometry

For each DMS cell, we measured the signal height and peak width (full width at half maximum – FWHM) of each of the five standard compounds. These outputs were monitored as a function of DR applied to each DMS cell, with higher DR levels providing longer residence times for the ions in the DMS cell, with some signal losses due to diffusion of ions.

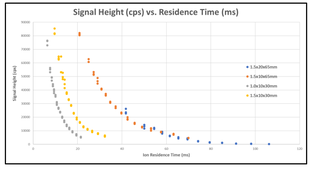
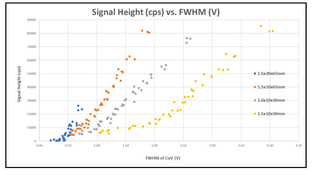


Figure 5 (left) displays the results obtained for the analyses of reserpine, with the other compounds tested displaying similar behaviors (data not shown). Concomitant with the increased residence time is opportunity for ion signal to be lost via diffusion during transport in the DMS cell.

However, differences in the performance of the DMS cells is apparent. For example, to achieve an ion residence time of 20 ms, the 1.5x10x65 mm cell (Figure 5, orange data) could transmit almost 4x the ion signal than the shorter 30-mm long cells (yellow data).

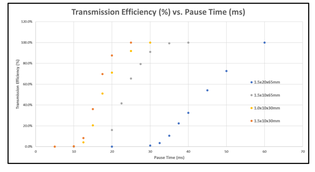


The FWHM for CoV peaks produced by each DMS cell for reserpine also had varying effects on the overall signal height (Figure 6). Generally, as the FWHM increased (i.e., wider peaks), so did overall signal height. To achieve a given FWHM (e.g., 1.50 V), the shorter (30-mm long) cells required the use of higher DR flow rates, which are deleterious to signal levels relative to the longer (65-mm long) cells.

Measuring the necessary pause times needed for each DMS cell geometry

As ions enter the DMS cell, they will have a finite "time-of-flight" as they traverse the DMS cell. These flight times must be taken into consideration to allow for transit of the ions through the DMS cell before switching CoVs to a different ion. This avoids unwanted signal loss or potential cross talk between related chemical MRM transitions.

To establish a minimum pause time for each DMS cell to allow clearance of ions before CoV switching, we monitored two MRMs: (1) a 5-ms dwell time for the analyte monitored at its optimal CoV at a 3500 V/mm p-p field strength and (2) a "dummy" MRM that was set to transmit Q1 and Q3 m/z values of 100 and 100 at a CoV of -100V (a voltage at the extreme edge of the power supply providing CoV to the DMS cell).



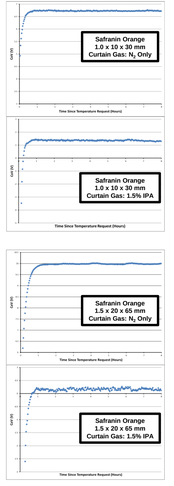
If the pause time were too short, little to no analyte signal should be detected, until a pause time of sufficient duration allowed ion beam transport ("flight").

As displayed in Figure 7 (left), the pause times needed to accommodate transmission of at least 80% of the maximum ion signal increased with increasing DMS cell volume.

RESULTS

Thermal equilibration times for DMS cells of different geometries

When any DMS cell left at ambient temperature is installed (i.e., after cleaning or installation), there is a recommended "thermal equilibration time" before the DMS cell can reach a thermally equilibrated state that can achieve consistent CoV shifts for a given compound.



To establish the thermal equilibration times for the different DMS cell geometries, we installed each DMS cell at ambient temperature and immediately began acquiring CoV profiles for each compound.

As the temperature of each DMS cell increased from ambient to a requested 150° C, the characteristic CoV shift of each ion would change until thermal equilibrium was achieved. These studies were performed using nitrogen only, as well as 1.5-% (v/v ratio) isopropanol in the transport gas. These results are displayed in Figure 8 (left).

To determine the equilibration time and the ultimate stability of the compounds' CoVs for each DMS cell, each experiment ran for ~16 hours. The experiments involved ramping the compensation voltage over a range of -30 V to +10 V (for nitrogen) or -40V to +10 V (for isopropanol), while monitoring the MRM signals for the four (4) test compounds.

To determine the time required to establish thermal equilibration for a DMS cell, we measured the time required for a cell to transmit each test compound at its overall average stabilized CoV value. For example, for the 1.0x10x30 mm DMS cell (Figure 8, top two plots), the optimal CoV for an MRM for safranin orange was monitored for >14 hours and its ultimate stable CoV was established as 6.73 V after ~48 min. However, for the physically larger 1.5x20x65 mm DMS cell, this time to equilibration is somewhat longer (Figure 8, bottom two plots).

However, when isopropanol modified was added to the transport gas flows, CoV equilibration was achieved in ~1 hour for each DMS cell regardless of size.

CONCLUSIONS

Based upon studies such as this one, where we have systematically explored the impact of cell gap (1.0 vs 1.5 mm), width (10 vs 20 mm) and length (30 vs 65 mm) on a variety of DMS performance metrics, including ion transmission, residence times, and resolving power, we gain a better understanding of the analytical performance that can be achieved with different gap height cells.

REFERENCES

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TRADEMARKS/LICENSING

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