

# Enhanced separation capacity via Vapor Doping in Tandem Transversal Modulation IMS-MS

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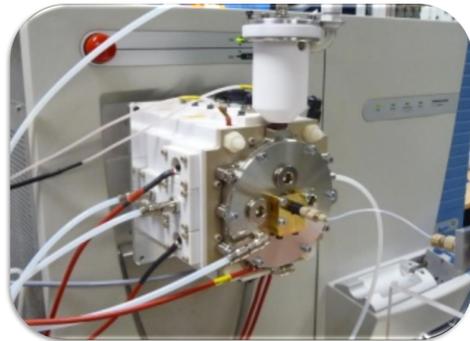
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## Overview

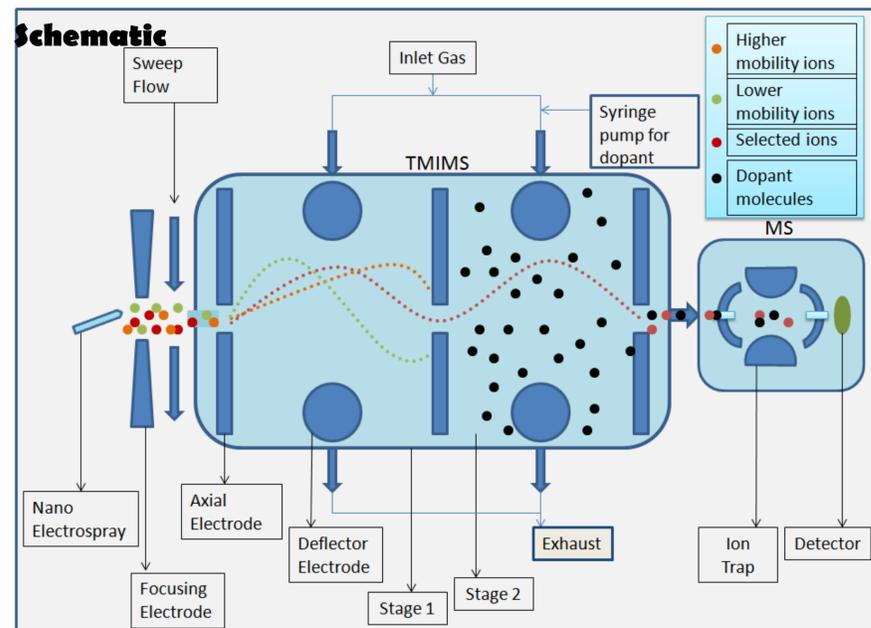
- The purpose of this work was to study the influence of vapor dopants on the ion mobilities of model peptide ions using a transversal modulation IMS-MS system.
- Transversal Modulation IMS (TMIMS) utilizes an axial electric field, which pushes the ions forward, and an oscillating transversal field, that deflects ion trajectories.
- When the period of the oscillating electric field equates to the residence time of the ions (which is inversely proportional to mobility), ions reach the outlet slit of the TMIMS. TMIMS thus provides a continuous beam of ions with mobilities  $nK_0$  ( $n = \text{integer}$ ).



## Introduction

- While ion mobility spectrometry-mass spectrometry (IMS-MS) enables some degree of two-dimensional separation, ion mobility and mass to charge often correlate with one another. To achieve improved separation capability in IMS, vapor dopants can be added, shifting the mobilities of ions to varying, chemical-structure-dependent extents. Vapor dopants can be ideally exploited in IMS-IMS-MS systems, in which the first IMS operates in the absence of dopant, and in the second dopant is introduced.

## Methods



- As depicted in the schematic, a two stage TMIMS was coupled with a Linear Ion Trap (LTQ XL, Thermo), with the 1st stage operating in transparent all ion transmission mode, and with isopropanol (2-propanol) dopant introduced in the 2nd stage.

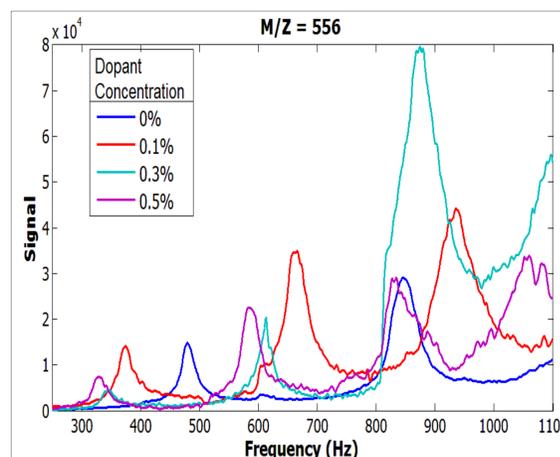
- The dopant introduction system consisted of a syringe pump supplying a constant flow rate of dopant (as a liquid) which flowed into a porous material. Dopant was introduced into the gas phase by passing Nitrogen gas flow at room temperature over the porous material.
- Positively charged ions were introduced into the TMIMS system via nanoelectrospray. As a test mixture, protonated ions of the polypeptides noted below were examined.

Peptide Name	m/z	Structure
Glycyl-L-tyrosine	238/1	
Val-Tyr-Val	380/1	
Leu Enkephalin	556/1	
Met Enkephalin	574/1	
Angiotensin II	1046/2	

## Results

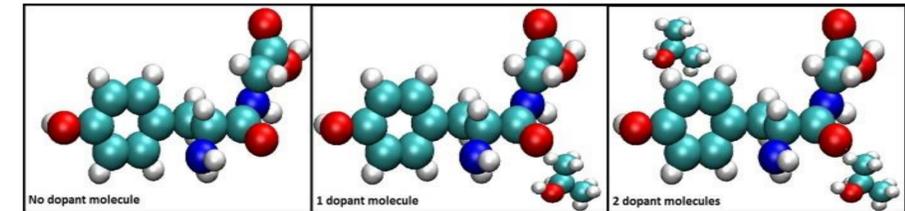
- Raw data from TMIMS-MS measurement take the form of measured ion signal intensity as a function of TMIMS modulation frequency, for a given m/z ion. As depicted in figure 1 for Leu Enkephalin (m/z = 556), the addition of dopant alters this spectrum, however, because of heating in the inlet of the mass spectrometer, the ion is detected at the same m/z (with no dopant bound).

**Figure 1.** Characteristic TMIMS-MS results for Leu-Enkephalin ions. Frequency (Hz) corresponds to the electric field modulation frequency, which is varied to control which ions are transmitted through the TMIMS. For a given frequency, ions not only of mobility  $K_0$  are transmitted, but also those of mobility  $nK_0$ , where  $n = 1, 2, 3$ , etc. Therefore, a given ion is transmitted at multiple resonant frequencies.

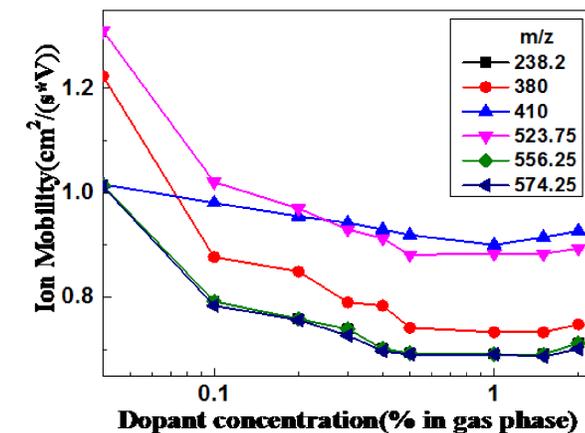


As observed in the plot, the addition of dopant leads to a shift in all peaks to the left, which indicates a decrease in ion mobility

**Figure 3.** Structures of Glycyl-L-Tyrosine predicted with 0, 1, and 2 isopropanol molecules bound (density functional theory, GAUSSIAN)



- The decrease in mobility appears to arise because of transient sorption of dopant molecules to ions as they migrate through the TMIMS, which operates close to the low field limit. As depicted in Figure 3, local energy minimum structures of ions with even 1-2 dopant molecules bound are noticeably larger in size than the base ion.
- At appreciably high dopant concentrations, dopant ion collisions may also increase the collision cross section, as dopant molecules are large and have appreciable dipole moments.



**Figure 3.** The ion mobility of observed peptide ion peaks as a function of dopant concentration (expressed as percent of molecules in the gas phase).

- As depicted in figure 3, as the dopant concentration is increased, initially, large shifts in the mobilities of peptide ions are evident when compared to shifts observed for the calibration ion, tetraheptylammonium<sup>+</sup> (m/z = 410). However, at higher concentrations, the mobility appears to be insensitive to dopant concentration.
- This behavior is not consistent with classical models of vapor uptake by ions, and is qualitatively similar to site-binding models (i.e. dopants appear to bind at specific sites on ions, and once sites are saturated no further dopants may bind).

## Conclusions

- The mobility of each peptide ion examined decreases steeply with dopant concentration and then becomes constant at higher concentrations (>0.5%). These significant mobility shifts provide an additional degree of freedom in gas phase separation and a very orthogonal IMS-IMS separation scheme could be developed with this approach.
- Further improvements to TMIMS, including improved resolution and determination of transmission functions, will enable further application of this technology.