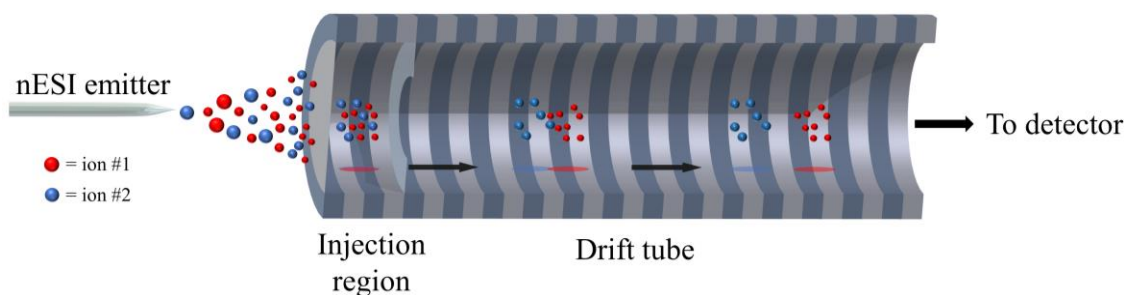


## Ambient Pressure Ion Mobility Spectrometry Using a 3D-Printed Ion Mobility Spectrometer

### Introduction

The emergence and sophistication of ion mobility spectrometry (IMS) has allowed researchers to probe the chemical structures of gas phase ions, both small and large, better than ever before [1,2]. Ion mobility is a particularly interesting separation technique because it can be used to separate gas phase conformational isomers on very short time scales (<1 s) [3]. This makes ion mobility ideal for coupling to mass spectrometry (MS) because conformer identification is difficult for the common, unaided mass spectrometer. The combination of IMS and MS offers unparalleled structural identification capabilities. The original IMS design was termed a drift-tube IMS (DT-IMS) because ions were separated based on the time they spent in a drift cell [4]. However, there are now several different kinds of ion mobility spectrometers which improve on aspects of the original IMS design, such as field-asymmetric waveform ion mobility spectrometers (FAIMS) and differential mobility spectrometers (DMS) with improved duty cycle [5], and traveling-wave ion mobility spectrometers (TW-IMS) with improved ion transmission efficiency [6].



**Figure 1.** Illustration of ions separating in an ambient pressure drift-tube ion mobility spectrometer.

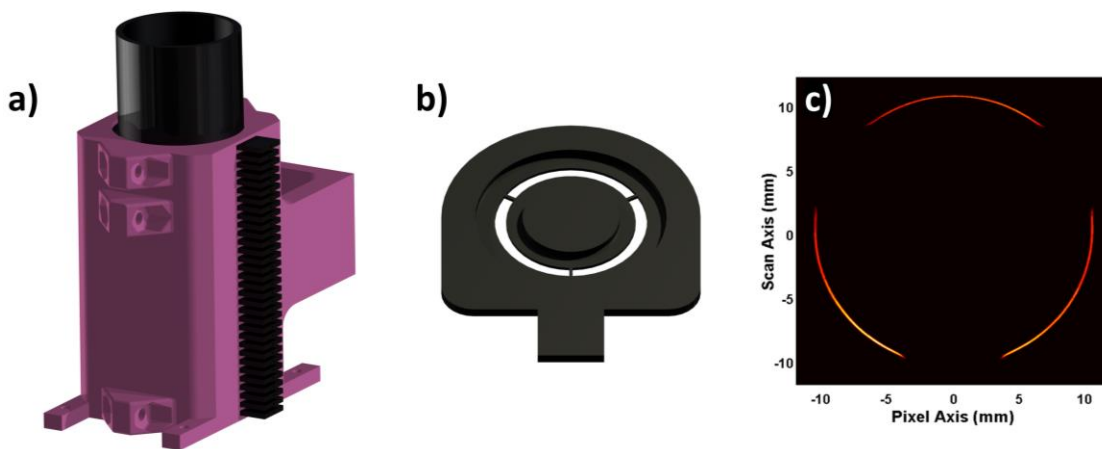
The fundamental operation of a DT-IMS is rather similar to that of a time-of-flight mass spectrometer (Figure 1). In a DT-IMS, ions are electrosprayed into a drift cell constructed of alternating conductive (dark) and nonconductive (light) rings. The rings can either all have the same diameter or can have incrementally decreasing diameters [3,7]. High DC or radiofrequency (Rf) voltages are then applied to the conductive rings order to generate a uniform electric field [8]. Before entering the drift tube, ions are collected in an injection region for a brief period of time before being ejected into the DT-IMS all at once. When ions enter the drift region, they encounter the uniform electric field and drift along the electric field lines towards the outlet of the IMS. The time it takes for an ion to reach the outlet is known as drift time ( $t$ ). During the course of their travel, ions collide with gas molecules residing in the DT-IMS, causing them to slow down and separate. The drift time of an ion is based on a number of factors, including the operating parameters of the DT-IMS, the ion's mass-to-charge, and the ion's collisional cross-section (CCS).

CCS is the 3D area around an ion that a background gas molecule needs to enter in order to cause a collision with the ion [9]. To put CCS into perspective, big elongated molecules have large collisional cross-sections and therefore experience more collisions with background gas molecules than small compact molecules. The background gas in an IMS is usually provided by flowing a gas counter to the direction that ions are moving. This gas aids in ion separation because ions with smaller CCSs usually experience less drag than ions with larger CCSs, assuming of course that both sets of ions have the same mass-to-charge [3]. Many DT-IMS systems operate at pressures around 1 torr when interfaced to mass spectrometers, though it is common to operate stand-alone IMS systems at atmospheric pressure (~760 torr) [10]. An ion's drift time can be described by the following equation:

$$\frac{1}{t} = \left( \frac{3q}{16N} \right) \left( \frac{2\pi}{kT} \right)^{\frac{1}{2}} \left( \frac{m+M}{mM} \right)^{\frac{1}{2}} \left( \frac{1}{\Omega} \right) \left( \frac{E}{L} \right)$$

where  $t$  is the drift time,  $q$  is the charge on the ion,  $N$  is the number density of the buffer gas,  $k$  is the Boltzmann constant,  $T$  is the absolute temperature in the IMS,  $m$  is the mass of the buffer gas,  $M$  is the mass of the ion,  $\Omega$  is the collisional cross-section of the ion,  $E$  is the electric field strength, and  $L$  is the length of the drift tube [3]. One will commonly see the variable  $K$ , or ion mobility constant, on the left-hand side of the above equation where  $K$  is simply the ion's velocity ( $\frac{L}{t}$ ) divided by the electric field strength. In addition to separating ions, IMS experiments can be performed to experimentally determine the CCS of an ion. This allows for structural information about the ion to be obtained via comparison to theoretical CCS values and stored in libraries for future use [11].

Many scientists are interested in the construction and optimization of IMS systems. Perhaps one of the most novel ways of constructing a DT-IMS has been by using a fused deposition modeling (FDM) 3D-printer [12]. 3D-printers are rapidly emerging as a key technology in laboratories because they can be used to construct needed items, including scientific equipment, quickly and cheaply. FDM 3D-printers create plastic structures by using gears to push plastic filament into a heated nozzle with a small diameter opening. The nozzle is heated until the plastic reaches a temperature at which it melts and flows easily out of the nozzle. Once commanded, the printer expels the molten plastic and will generate a plastic structure layer-by-layer until a completed structure emerges. Many types of plastics are available, including conductive plastic, which allows researchers to use 3D-printed model structures for a wide variety of applications, such as constructing a working IMS system (Figure 2a).



**Figure 2.** 3D-renderings of (a) a 3D-printed DT-IMS and (b) the ring electrodes used in the 3D-printed IMS. (c) Ions which have traveled through the DT-IMS are focused to a ring which corresponds to the shape of the electrode. However, the perimeter of the ring is  $\sim 200\mu\text{m}$  wide, which is much thinner than the 15mm slits in the electrodes with which the ions traveled through.

Under optimal conditions, the entire IMS housing and electrode set for the 3D-printed IMS can be printed in about 48 hours of continuous operation using one 3D-printer. The housing for the 3D-printed IMS was constructed out of nonconductive polylactic acid / polyhydroxyalkanoate (PLA/PHA) while the conductive ring electrodes were made from carbon nanotube-doped polyethylene terephthalate glycol-modified (CNT-PETG) polymer. The electrodes had 30 mm diameter openings and contained a 15 mm diameter central electrode held in place by three support bridges (Figure 2b). Ions passing through the IMS were focused to a 15 mm diameter ring with a 200  $\mu\text{m}$  line width (Figure 2c). This is a demonstration of a strong ion focusing effect in air. Developing tools for understanding how to focus and manipulate ions in air is of great interest to the Cooks lab [13,14]. Such developments are desirable because they would eliminate the need for cumbersome vacuum systems, which would greatly benefit miniature instruments. The 3D-printed IMS is a working example of how ions can be manipulated and focused in air using a device which costs less than one-hundred dollars to construct.

### Aims

Participants will be introduced to the concept of fused-deposition modeling (FDM) 3D-printing. The translation of a CAD model to an actual 3D-printed structure will be demonstrated and performed using a commercial 3D-printer. Various parameters relating to print quality will be discussed. While the 3D-printer is running, the performance of a 3D-printed ion mobility spectrometer will be demonstrated. A nanoelectrospray ionization source will be used to introduce a solution of quaternary ammonium cations into the 3D-printed ion mobility spectrometer. The separation of the compounds will be observed using a

current amplifier and an oscilloscope. Peak widths will be estimated from this data. The presentation will end with a discussion about manipulating and focusing ions in air using other 3D-printed devices.

### Experimental procedure

1. Introduction to FDM 3D printing.
  - Basic description of an FDM 3D-printer and the principle of fused deposition modeling (FDM).
  - Quickly produce a CAD model of an IMS electrode.
  - Translate the CAD file into a printable gcode file.
  - Use a 3D-printer to print an IMS electrode out of conductive plastic.
2. Introduction to IMS.
  - Basic description of the 3D-printed IMS, including the type of electrodes used, ion gates, detector, and housing.
  - Use nanoelectrospray to introduce a solution of quaternary ammonium ions into the 3D-printed IMS.
  - Use a current amplifier and oscilloscope combination to observe the separation of the quaternary ammonium ions.
  - Observe the changes in peak width when ion injection time is varied.

### References

1. Lanucara F, Holman SW, Gray CJ, Evers CE. The power of ion mobility-mass spectrometry for structural characterization and the study of conformational dynamics. *Nat Chem* **6**, 281-294 (2014).
2. Armenta S, Alcalá M, Blanco M. A review of recent, unconventional applications of ion mobility spectrometry (IMS). *Anal Chim Acta* **703**, 114-123 (2011).
3. Kanu AB, Dwivedi P, Tam M, Matz L, Hill HH. Ion mobility–mass spectrometry. *Journal of Mass Spectrometry* **43**, 1-22 (2008).
4. McDaniel EW, Martin DW, Barnes WS. Drift Tube-Mass Spectrometer for Studies of Low-Energy Ion-Molecule Reactions. *Review of Scientific Instruments* **33**, 2-7 (1962).
5. Kolakowski BM, Mester Z. Review of applications of high-field asymmetric waveform ion mobility spectrometry (FAIMS) and differential mobility spectrometry (DMS). *Analyst* **132**, 842-864 (2007).
6. Shvartsburg AA, Smith RD. Fundamentals of traveling wave ion mobility spectrometry. *Anal Chem* **80**, 9689-9699 (2008).
7. Hernandez DR, Debord JD, Ridgeway ME, Kaplan DA, Park MA, Fernandez-Lima F. Ion dynamics in a trapped ion mobility spectrometer. *Analyst* **139**, 1913-1921 (2014).
8. Allen SJ, Giles K, Gilbert T, Bush MF. Ion mobility mass spectrometry of peptide, protein, and protein complex ions using a radio-frequency confining drift cell. *Analyst* **141**, 884-891 (2016).
9. Santos ACF, Fröhlich A. Collision cross sections and the size of a coin. *Physics Education* **38**, 336 (2003).
10. Wu C, Siems WF, Asbury GR, Hill HH. Electrospray Ionization High-Resolution Ion Mobility Spectrometry–Mass Spectrometry. *Anal Chem* **70**, 4929-4938 (1998).
11. Campuzano I, Bush MF, Robinson CV, Beaumont C, Richardson K, Kim H, Kim HI. Structural characterization of drug-like compounds by ion mobility mass spectrometry: comparison of

**9<sup>th</sup> CAID Workshop: State-of-the-Art Mass Spectrometry for Point-of-Care and Other Applications**  
**Center for Analytical Instrumentation Development**  
**Discovery Park – Purdue University**  
September 18<sup>th</sup> – 19<sup>th</sup> 2016

- theoretical and experimentally derived nitrogen collision cross sections. *Anal Chem* **84**, 1026-1033 (2012).
12. Baird Z. Methods and instrumentation for the manipulation and characterization of electrosprayed ions under ambient conditions. Ph.D. Thesis, Purdue University (2015).
  13. Li A, Baird Z, Bag S, Sarkar D, Prabhath A, Pradeep T, Cooks RG. Using ambient ion beams to write nanostructured patterns for surface enhanced raman spectroscopy. *Angewandte Chemie International Ed.* **53**, 12528-12531 (2014).
  14. Baird Z, Wei P, Cooks RG. Ion creation, ion focusing, ion/molecule reactions, ion separation, and ion detection in the open air in a small plastic device. *Analyst* **140**, 696-700 (2015).