Overview

A new ESI-IMS-TOF MS was designed that incorporates electrodynamic ion funnels before and after the drift cell allowing the drift cell pressure to be increased from 4 to 12 Torr, providing increased IMS resolving power. A schematic of the ESI-IMS-TOF MS equipped with two electrodynamic ion funnels is shown in Figure 2. The instrument is comprised of six primary components:

1. ES source
2. High pressure gas ion funnel to focus and trap ions prior to ion injection
3. Ion mobility drift cell
4. Secondary high pressure ion funnel to focus the drift ion beam prior to IMS separation
5. Untargeted IMS MS is mass to charge ratio (m/z) of the sample
6. The drift cell used the same modular design concept with each modular unit placed at different voltages as previously reported in [1].

The ability of ion mobility separation coupled with drift cell (IMS-MS) to separate ions by conformation (Figure 1) has shown great potential for analyzing complex sample matrices. However, challenges posed by the extreme complexity of many biological sample matrices have demonstrated the need for IMS-MS with higher resolution and broader dynamic range.

Methods

Instrumentation

A new ESI-IMS-TOF MS was recently completed that incorporates electrodynamic ion funnels before and after the drift cell allowing the drift cell pressure to be increased from 4 to 12 Torr, providing increased IMS resolving power. A schematic of the ESI-IMS-TOF MS equipped with two electrodynamic ion funnels is shown in Figure 2. The instrument is comprised of six primary components:

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Compared to its predecessor the current platform features two primary modifications:

1. Increasing the length of the drift cell or the drift gas pressure can provide a significant increase in IMS resolving power, while maintaining comparable ion transmission.
2. Ions have already been separated in the drift cell before entering the mass analyzer.

The parent and fragment nested spectra for a 4 peptide mix with different charge states of fibrinopeptide A, neurotensin, angiotensin I and bradykinin are shown in Figure 4.

Results

Comparison of LC-MS and LC-IMS-MS

Figure 4 illustrates the nested spectra for a tryptic digest of 0.01 mg/mL BSA at 4 and 12 Torr. This work was supported by the PNNL Laboratory Directed Research and Development Program, and the NSF National Center for Research Resources (Grant 1R15RR025889-01A1), and the National Institute of Allergy and Infectious Disease (Grant 1R43AI058878). Pacific Northwest National Laboratory is operated by the Battelle Memorial Institute for the U.S. Department of Energy through contract DE-AC05-76RL01830.

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Conclusions

• Modifications to our previous ion funnel design allowed the ESI-IMS-TOF drift cell pressure to be increased from 4 to 12 Torr without substantially compromising sensitivity. An additional benefit of increasing the drift gas pressure was in increasing the resolving power from 517 to 80 at 12 Torr. A larger number of features were detected using the off-line fractionation of NanoMate™ compared to on-line fractionation of LC, likely because the solvent mixture could be varied for more efficient electrospray ionization.

• More features were found in the IMS-MS measurements than by just LC alone. Software is being developed to convert the NanoMate™-MS data to the AMT tag database so that the number of peptides and proteins observed can be quantified.

• The 12 Torr platform allowed greater sensitivity with increased resolving power, providing added information for laboratory scientists to make more informed decisions about their samples.

References