Improving Detection and Selectivity of PFAS Molecules Using Cyclic Ion Mobility Wideband Enhancement

Michael McCullagh [1], Yuriy Pyatkivskyy [2], Brian McCullough [1], Darren Hewitt [1], Zoltan Laszlko [1] and Chris Hughes [1]
[1] Waters Corporation, Stamford Avenue, Altrincham Road, Wilmslow, SK9 4AX. UK. [2] Waters Corporation, Milford, Massachusetts, USA.

Introduction

Polyfluorinated alkyl substances (PFAS) are emerging environmental contaminants that have been linked to increased risks of cancer and other diseases in humans. Monitoring PFAS concentrations in human biofluids is essential for understanding exposure levels and pathways. However, accurately identifying PFAS at extremely low concentrations (ng/L) remains challenging. To address this, a Cyclic™ IMS P20 Instrument equipped with Wideband Enhancement (WBE) can be programmed to target characteristic PFAS drift time trendlines and synchronize them with the time-of-flight (ToF) pusher (see Figures 1 and 2).[1] This acquisition mode improves the ToF duty cycle and lowers detection limits. Analysis using Cyclic ion mobility with WBE provides enhanced selectivity, sensitivity, and collision cross section (CCS) measurements, which serve as complementary descriptors for PFAS identification.[2,3]

Experimental

LC-Cyclic-IMS-MS analyses of a dilution series of Native PFAS: PFAC30PAR (Wellington laboratories) were performed using a quadrupole-Cyclic-IMS-time-of-flight mass spectrometer (Cyclic IMS resolution R ~65–145). Reversed-phase LC separation employed mobile phases of: A (95:5 water: methanol, with 2 mM ammonium acetate) and B (methanol with 2 mM ammonium acetate) using a 22 min gradient at 0.3 mL/min. An ACQUITY™ UPLC™ BEH™ C18 column (100 mm × 2.1 mm, 1.8 µm) at 35 ° C with a 10 µL injection volume was used. The modified ACQUITY i-Class System included a PFAS-free conversion kit and Atlantis™ Premier BEH C18 AX Isolator Column, 2.1 x 50mm, 5 µm.[4]

Results

The environmental impact of PFAS exposure is influenced by isomeric distribution, as both linear (L-PFAS) and branched (br-PFAS) forms have been associated with specific health risks, including increased infant burden during pregnancy. Enhanced sensitivity in the WBE analytical method for precursor ions, enables the detection of PFAS at lower concentrations compared to conventional HDMS^E acquisition. The WBE acquisition strategy allows targeting of mass/drift time trendlines, with potential to reduce false detections caused by isobaric biological interferences. PFAS molecules exhibit distinct ion mobility drift time trendlines due to their unique CCS-to-mass ratios, a result of their fluorinated structures. This property causes PFAS to appear “denser” than hydrocarbon-based molecules, shifting their drift time trendline downward relative to molecules of similar *m/z*.[5] For a dilution series of PFAC30PAR we compared LC-Cyclic-IMS-MS (HDMS^E) and WBE LC-Cyclic-IMS-MS, LC-Cyclic-IMS-MSMS, LC-Cyclic-IMS-DIA-MS responses for PFAS. The WBE mode was calibrated to optimize drift time alignment (See Figure 3) for PFAS constituents of PFAC30PAR, the improvement in sensitivity resulting from enhanced selectivity and ToF duty cycle is shown in Figure 4 and Figure 5. An RMS S/N 48 for 0.4 ng/L for the PFOS homologous series have been achieved as well as improved detection limits for branched PFOS byproducts, P5MHpS and P6MHpS, compared to using conventional HDMSE (see Figure 6).

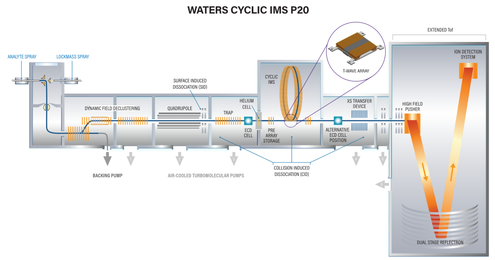
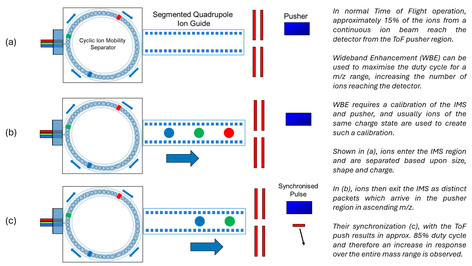


***Figure 1**. Cyclic IMS P20 System.*



In normal Time of Flight operation, approximately 15% of the ions from a continuous ion beam reach the detector from the ToF pusher region.

Wideband Enhancement (WBE) can be used to maximise the duty cycle for a m/z range, increasing the number of ions reaching the detector.

WBE requires a calibration of the IMS and pusher, and usually ions of the same charge state are used to create such a calibration.

Shown in (a), ions enter the IMS region and are separated based upon size, shape and charge.

In (b), ions then exit the IMS as distinct packets which arrive in the pusher region in ascending m/z.

Their synchronization (c), with the ToF push results in approx. 85% duty cycle and therefore an increase in response over the entire mass range is observed.

***Figure 2**. Schematic representation of WBE Cyclic ion mobility selectivity combined with ToF pusher synchronisation.*

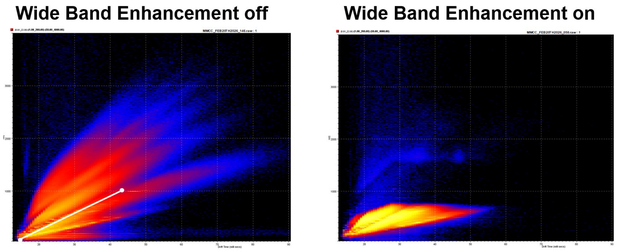


***Figure 3**. m/z versus drift time plots demonstrating WBE: (a) WBE off, showing selection of singly charged PFAS characteristic drift times for calibration; (b) WBE on, illustrating improved ion mobility mass spectrometry selectivity for PFAS detection.*

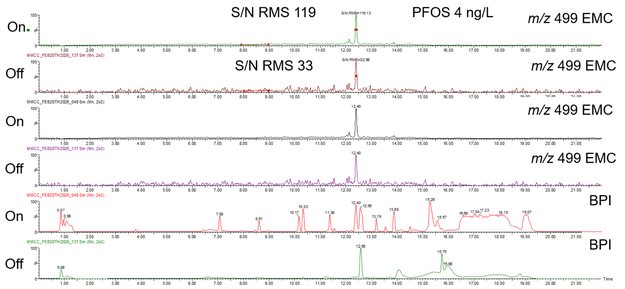


***Figure 4**. Comparison of WBE on/off conditions: base peak intensity (BPI) for PFAC30PAR (4 ng/L), and PFOS (m/z 499) assessed using extracted mass chromatograms (EMC) and RMS signal-to-noise (S/N).*

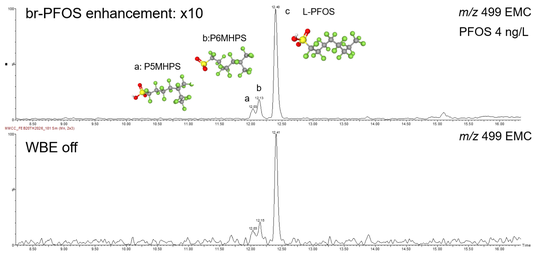


***Figure 5**. Comparison of br-PFOS and L-PFOS WBE responses on and off at 4 ng/L, demonstrating a ~10 × increase in signal intensity and improved branched isomer chromatographic peak fidelity.*

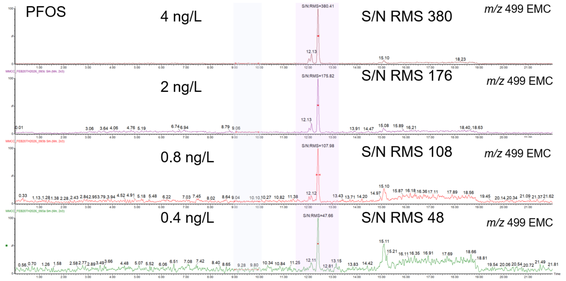


***Figure 6**. Detection limits and RMS S/N obtained for PFOS using HDMSMS with WBE.*

Conclusions

- **Integration of Cyclic ion mobility and WBE improves analytical selectivity and sensitivity for PFAS.**
- **Application of WBE with Cyclic ion mobility HDMSMS enabled PFOS detection at 0.4 ng/L.**
- **LC–Cyclic-IMS–MS with WBE provides a flexible platform for both targeted and non-targeted analysis of known and emerging PFAS in complex matrices.**

References
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Conflict of Interest Disclosure: Yuriy Pyatkivskyy, Brian McCullough, Darren Hewitt, Zoltan Laszlko. Chris Hughes and Michael McCullagh are employees of Waters Corporation and are presenting the poster on behalf of the company.

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