GCxGC-HRMS:
Combining Multidimensional GC with Ultra High Resolution Time-of-Flight Mass Spectrometry for Comprehensive Analysis of Complex Samples

Overview
The recent advancements in GC-HR-TOFMS based on the Folded Right Flight™ (RPF) mass analyzers for improving sensitivity and capacity of the complex mixtures analysis are presented.

Introduction
Gas Chromatography coupled to mass spectrometry provides the best analytical tool: combining selectivity, sensitivity, reliability, and information capacity for targeted or non-targeted methods of environmental analysis. The GC-MS identification of knowns (by matching against standard and user spectral libraries) and structural elucidation of unknowns becomes considerably more reliable if complemented by accurate mass measurements while using High Resolution Mass Spectrometry (HRMS). However, when analyzing real-life samples containing a very high number of compounds of interest with a wide range of concentrations present in complex matrix, a significant increase in chromatographic peak capacity is required, which can be provided only by using multidimensional GC. Therefore, GCxGC coupled to a high resolution mass spectrometer is becoming a powerful tool for comprehensive analysis of complex samples (Figure 1).

Figure 1: The Concept of GCxGC coupled with High Resolution TOFMS with high speed Data Acquisition System.

Duty Cycle is a critical parameter affecting the sensitivity of analysis by Time-of-Flight Mass Spectrometry with an Orthogonal Accelerator (OA-TOFMS). The Duty Cycle for an OA-TOFMS is defined as the ratio between the time to fill the acceleration region with the largest mass/range ions and the time-of-flight (TOF) through the mass analyzer of these ions: Duty Cycle = LY/TOF.

LECO has implemented Encoded Frequent Pushing™ (EFP), a method of pushing an orthogonal accelerator multiple times per transient with unique time intervals between each push pulse. This method is particularly well suited for improving the duty cycle of a TOFMS with FFP, where the highly resolved ion peaks are sparsely populated across the TOF spectrum. The key concept is that within overall mass spectra produced by the multiple pushes, some overlaps are likely to occur between peaks of various ions. However, if the time intervals between the ion pushes are unique, the overlaps will not be systematic. In addition, the decoding method departs from a traditional “inverse method” used in mass/charge space which is responsible for creating mass spectral artifacts. Instead, a novel decoding method uses a logical and statistical analysis of spectral overlaps to prevent the production of those spectral artifacts. With EFP, the duty cycle is improved proportionally to the increased pushing frequency, meaning that the continuous ion beam is sampled much more efficiently. For example, if the typical non-multiplexed operation of the GC-MS mass spectrometer uses 2 kHz pushing frequency, a multiplexed acquisition with 20 push pulses per transient will increase the pushing frequency to approximately 20 kHz, and in EFP mode the sensitivity will also grow by up to 10 times (Figure 2).

Figure 2: The Concept of the Encoded Frequent Pushing.

Figure 3: The total ion chromatograms of the sample.

Figure 4: Addressing peak interferences with GCxGC enhanced separation.

Figure 5: Peak finding and identification improvements with GCxGC EFP runs.

Methods
The GCxGC system is comprised of the Agilent 7890B GC equipped with Thermal Modulator. The ultra high resolution mass spectrometer was a LECO Pegasus HR™ prototype with EFP capabilities and modified to provide a resolving power up to 50,000 at full mass range (10-1500 m/z). The data acquisition rate is 200 spectra/s, in order to match sampling speed requirements for GCxGC peaks (~50 ms). The environmental samples – Arctic ice – were obtained from Prof. A. Lebedev (Moscow State University) and prepared according to EPA Method 8270. The data were collected in three modes: 1D GC runs with EFP; GCxGC runs with EFP and GCxGC runs without EFP.

Results and Discussion
The obtained data shows that even such relatively simple samples as Arctic ice include very large numbers of analytes, including chemicals introduced during sample preparation and GC column and septa bleed (Figure 3). There were multiple examples in the data when 2D data revealed the presence of the lower concentration analytes coeluting with higher concentration analytes (Figure 4). The GCxGC with EFP analysis allows to discover more analytes and provide better mass accuracy mass spectra, especially for the low level components, due to improved ion statistics in the peaks (Figure 5).

Conclusions
• Using GCxGC with EFP mode of operation (GC-HR MS 4D prototype) we were able to detect and identify more than 320 analytes in the environmental sample of Arctic ice.

• The novel Encoded Frequent Pushing (EFP) technique provides multiple benefits for the analysts focused on comprehensive analysis of real life samples improved detection limit and dynamic range, full mass range of analysis, improved mass accuracy for low level analytes, etc. GCxGC using EFP was considered to be a valuable tool in the arsenal of the environmental scientists who are interested in comprehensive, accurate and detailed analysis of the samples of interest.

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