

MS-Xelerator™: Advanced Algorithms for LC/MS Data Processing applied to Impurity/Degradation Profiling, Differential Analysis and Isotope Pattern Recognition

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Introduction

The amount of data from LC/MS experiments, coming from Impurity Profiling, Degradation Profiling, Metabolite Profiling and Biomarker Discovery studies, has increased extremely.

In the case of **Impurity and Metabolite Profiling** often long processing times are necessary to find **significant and relevant** peaks in complex samples. Searching specific drug metabolites in samples containing thousands of peaks is a difficult and time-consuming task.

In the area of **Differential Analysis, Biomarker Discovery and Metabonomics** more advanced chemometric and bioinformatic techniques are needed to find specific peaks or combinations of peaks to discriminate between different classes of samples, e.g. healthy versus diseased. In general, multiple steps are necessary to solve these difficult problems (binning, alignment, peak picking and the choice of the proper classification algorithms). Due to many possible pitfalls, advanced knowledge of specialized algorithms and methods will be necessary in order to arrive at valid conclusions.

MS-Xelerator™ is a software program dedicated to all of the above tasks. It contains a large number of powerful modules and algorithms which will even help the inexperienced user to solve all of the above problems. MS-Xelerator contains the following modules:

Modules:

- MBrowser:** Powerful interactive graphical environment specialized for Impurity Profiling and in-depth analysis of single samples
- MPeaks:** Fast and easy-to-use module for Peak Picking, Conversion of Peaks to Components, Differential Analysis and Metabolite Identification
- IPeaks:** State of the art algorithms for finding components having specific Isotope Patterns (Cl, Br, labeled amino acids/drugs, user defined patterns)
- MS Viewer:** Specialized plots of mass chromatograms and mass spectra (overlay – matrix – line, in combination with external signals)
- MS Compare:** Comparison of series of LC/MS samples, Biomarker Discovery, PCA, Clustering, Data Mining and Explorative Search

Features:

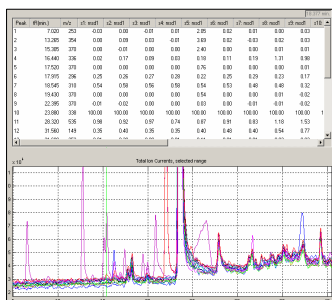
- Ultra sensitive fast Peak Detection (4 seconds/sample)
- Co-correlation with external signals (UV, ELSD)
- Run 100 samples in less than 5 minutes
- High Res. Mass Defect Filters, Data Mining & Filter Modules
- Baseline Correction, De-Spiking, Alignment (MS ↔ UV)
- Search results based on predefined m/z list

Impurity Profiling: Drug Stress Testing & Batch Comparison

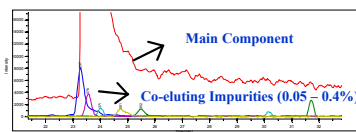
Data: 13 samples from a stress testing study using different treatments (oxidation, light, etc.)

- Goals:** i. find and identify the impurities in all samples simultaneously
ii. compare different treatments using Multivariate Analysis (Clustering or PCA)

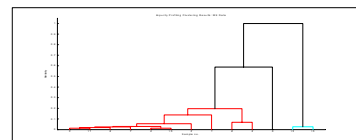
Total time needed to complete full analysis: about 10 min.



Peak Picking Result Table & overlay of TIC's

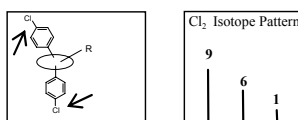


Peak Picking: 5 Co-eluting Impurities Detected in 1 Sample

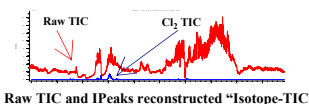


Sample Comparison using Clustering: some samples show up as having very different profiles

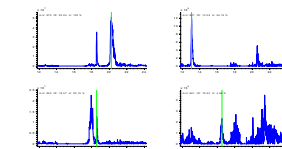
Peak Detection using Isotope Pattern Recognition



Mpeaks → 731 peaks (7 sec.)
IPeaks → 16 peaks (24 sec.)



Raw TIC and IPeaks reconstructed "Isotope-TIC"



Sensitive detection of Cl₂ containing peaks

Introduction

Pesticides very often contain chlorine or bromine. The specific isotopic pattern of the active compounds, degradation products and metabolites can be very helpful to discriminate compound related material against background peaks or other peaks having no relationship with the sample.

IPeaks contains 5 very powerful and very sensitive peak detection algorithms based on the presence of specific isotopic patterns.

Chlorine Example: the example on the left shows a compound containing two chlorines. MPeaks finds 731 peaks in the complex sample (red TIC). Using IPeaks and the Cl₂ pattern only 16 peaks were detected, all related to the pesticide being studied (blue TIC).

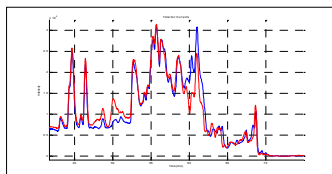
Differential Analysis between Sample/Control

Data: Sample/Control or Sample/Reference

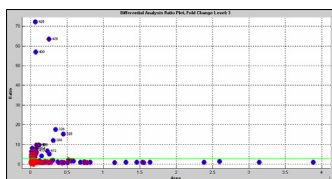
Goal: find all peaks in Sample which are not present in the Control

Workflow: 2 Samples → MPeaks → convert to components → Differential Analysis → Visualize

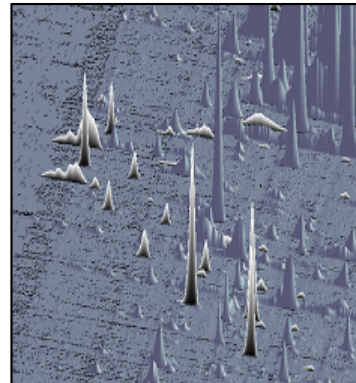
Total time needed to complete Differential Analysis: about 20 seconds



Overlay of very similar Total Ion Currents



Differential Analysis: Area - Ratio Plot: a large number of very small peaks are not present in the control

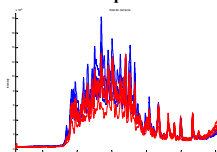


3D LC/MS Plot showing marked differential peaks present in the Sample but not in Control

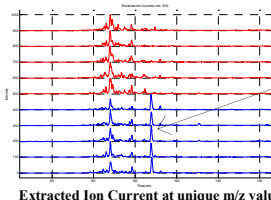
Biomarker Discovery

Data: urine samples of controls and patients

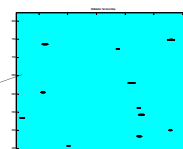
Goal: find unique peaks discriminating both classes using non-peak-detection methods



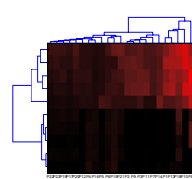
Overlay of TIC's



Extracted Ion Current at unique m/z value



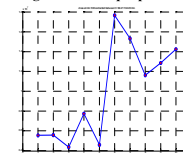
BioMarker Surface Map of aligned and unique peaks



Double Cluster Map (Samples & Peaks)



Principal Component Analysis (PCA)



EIC Concentration Profile

MS-Xelerator has been designed to be extremely fast, easy-to-use and is independent of instrument vendor. The software offers a multitude of algorithms and modules to solve a large number of complex problems in LC/MS Data Processing and Profiling studies.