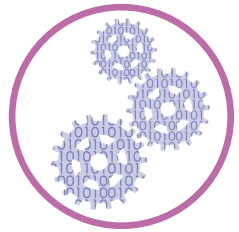
4 Software Solutions to Master Mass Spectrometry



ACD/Labs

CONTENTS

Why Mass Spectrometry Software?

The expectation to detect and identify compounds with greater efficiency, despite increasing sample complexity and shrinking analytical group sizes, are modern-day challenges faced by mass spectrometrists.

Traditional MS data analysis and interpretation workflows, using native instrument software, can struggle to address these challenges, requiring experts to augment experimental approaches with powerful third-party software.

Analytical Data Management Survey Results

SOURCE: C&EN BRANDLAB Survey, July 2018

80%

of scientists surveyed stated that **data integrity** was important or **very important**

63%

were looking to **improve** their ability to **search, share, and report** data

Advanced informatics solutions benefit mass spectrometrists by ensuring:

MS data from all instruments can be extracted & then analyzed together

Components are seamlessly distinguished, identified & characterized

MS results can be integrated with other relevant project data

Analytical information is easily accessible & shareable

Benefits of Advanced Informatics

Multi-Technique, Vendor Agnostic Data Analysis

Unite data from various instrument vendors and examine all together for improved data management.

Integrate mass spectral information with other analytical results, i.e., NMR, LC, GC, UV, etc., in one interface for enhanced analytical efficiency.

Seamless Component Extraction & Identification

Efficiently extract all relevant components from GC and LC experiments, including co-eluting peaks.

Easily assign structures to experimental data, and quantitatively assess the accuracy of these assignments.

Simple & Straight-Forward Data Management

Archive MS data in easily storable and readily accessible formats to help support data integrity.

Master Mass Spectrometry

Your Need:

Comprehensive MS Analysis
Import, extract, & interpret all MS data

Seamless Structure Assignment
Identify and characterize components

Streamlined Results Interpretation
Compile & analyze data in a single environment

Complete Databasing Capabilities
Database all relevant analytical data together to simplify collaboration & reporting

Our Solution:

1. IMPORT

Integrated, vendor-neutral data import

Unique ion thread technology (*IntelliXtract* algorithm) to extract components

2. IDENTIFY

Screening of spectral databases & chemical structure libraries

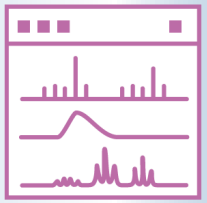
Ion fragmentation predictions

3. INTEGRATE

Consolidation of MS results with all other relevant project data

Complimentary NMR dereplication

4. INFORM



Streamlined reporting

Comprehensive databasing

Import

Comprehensive software solutions are required to interpret the vast amounts of analytical data generated during chemical characterization.

ACD/Labs offers feature-rich MS processing and analysis packages to provide seamless import and extraction of all MS information, regardless of instrument vendor or data format.

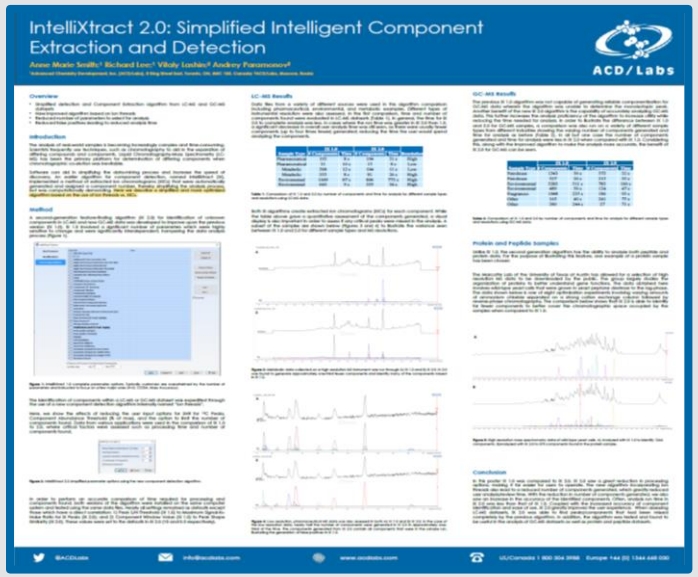
Unite Outputs from Virtually All Instruments

- ☑ Import and process MS data from all major instrument vendors, unifying disparate information in one software platform

Extract all GC/MS & LC/MS Data

- ☑ Extract all relevant peaks for efficient LC/MS and GC/MS component identification
- ☑ Detect all key components, including co-eluting peaks using our *IntelliXtract* algorithm to process GC and LC separations
- ☑ Visualize all GC/MS or LC/UV/MS data together in one interface

Simplifying & Optimizing Chromatographic Component Extraction


IntelliXtract 2.0: Simplified Intelligent Component Extraction and Detection

ACD/Labs

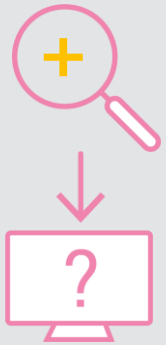
The Challenge

The original version of *IntelliXtract* automatically generated extracted ion chromatograms with component numbers but was computationally demanding. Thus, an opportunity existed to improve its user-input requirements and data processing capabilities.

The Solution

An updated version of *IntelliXtract* (2.0) was developed to expedite component identification through a new proprietary algorithm using ion threads. This optimized algorithm significantly reduced the number of user inputs required, decreased manual analysis times, and was able to reliably extract LC/MS, GC/MS, and peptide data.

Results



Fewer component false positives identified, shorter analysis times

Lower number of required user inputs

Identify

ACD/Labs provides a range of analytical MS solutions to seamlessly assign structures. Component characterization follows extraction, via structure assignment for knowns and unknowns.

Known

A component known to the investigator.

IntelliTarget

Scan experimental LC/MS & GC/MS data via *IntelliTarget* algorithm to specify *known* target ions (name, mass, etc.).

Identify expected components in complex samples or even at low concentrations.

Unknown

A component known in the chemical literature but unknown to the investigator.

IntelliXtract Compound Recognition (IXCR)

Screen LC/MS & GC/MS mass spectra for *known unknowns* via the *IXCR* workflow.

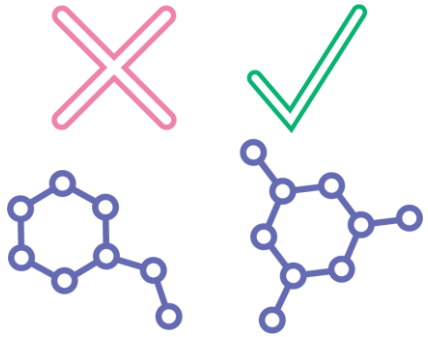
Perform spectral searches in proprietary or commercial databases for MS1/MS2 (LC/MS) and MS1 (GC/MS) data to compile structure hits in the Table of Components.

Compare experimental and candidate mass spectra via mirrored plots.

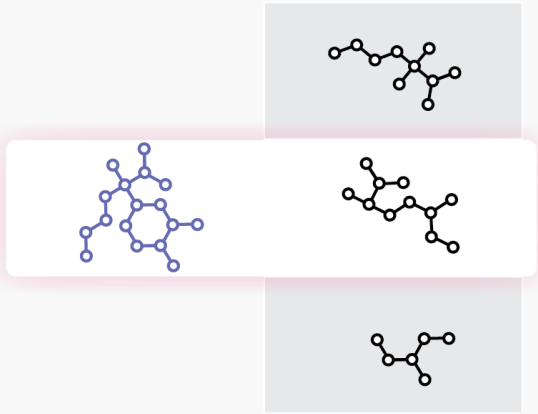
Identify

For *known unknowns* not identified by spectral searching, employ MS Structure ID Suite.

Screen PubChem to compile structure hits using a component's accurate parent mass and predicted molecular formula.



Filter structure candidates using include and exclude fragment lists.



Use the AutoAssignment tool to further interrogate top structure candidates and determine the best structural matches for experimental data.

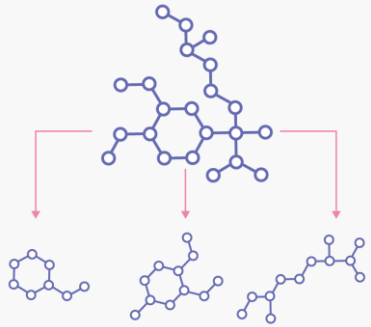
Accurately Predict MS Fragmentation

Achieve accurate structure verification by predicting fragmentation of ions by evaluating assignment quality through comparison of experimental vs. predicted masses.

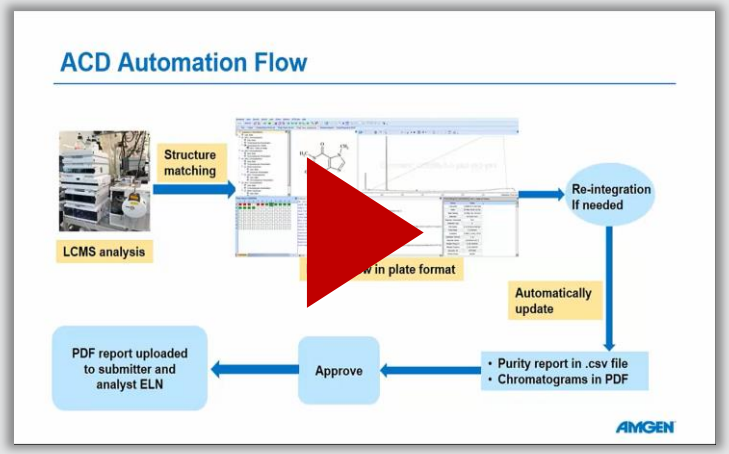
- ☑ Ions are predicted based on established MS fragmentation rules from scientific literature, which can be readily reviewed to understand the results for a given target molecule more clearly
- ☑ Individual fragment rules can also be selected or deselected based on user preference

Draw a structure

Select an ionization technique & polarity



Generate fragmentation pathways



Results

Automatic updates to purification projects

Elimination of manual printing, scanning & uploading of reports

Automating LC/MS Analysis

The Challenge

Small molecule drug discovery at Amgen relies on isolating high purity compounds prior to biological testing. Inefficiencies observed during this process were attributed mainly to the time-consuming process of post-purification analysis and data processing. Manual data review, report updating, and data dissemination were identified as the key contributors.

The Solution

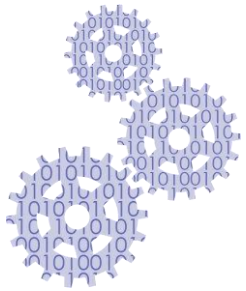
ACD/Labs had already assisted Amgen with NMR automation and were able to provide an LC/MS strategy that supported a plate-based framework for data visualization, flexible peak integration, automatic updates to purification reports, and elimination of manual report dissemination (printing, scanning, uploading).

Integrate

ACD/Labs' data processing and interpretation applications are multi-technique and vendor-neutral, enabling MS data to be integrated alongside additional information in a single software package.

Process and Interpret *All* Data

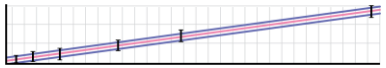
Import multi-technique data from virtually all instrument vendors, and readily perform collective processing and interpretation functions.



Perform routine processing including, smoothing, peak picking, and baseline correction

Assign a structure to easily view its consistency with MS data, and/or verify alignment with NMR Spectra

Create macros to automate repetitive tasks



Perform quantitative analysis of LC/UV/MS data and create a calibration curve and line of best fit with error bars

Query analytical databases for experimental spectra and overlay results with project data

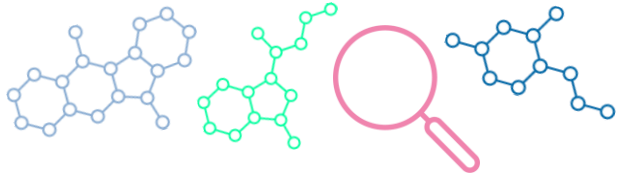
ACD/Labs' applications perform routine processing functions for complementary molecular characterization analyses, including NMR, FTIR, UV, Raman, and more.

Expand Deformulation Activities

Enhance mixture analysis by easily integrating NMR data; resolve any uncertainties from MS structure identification for known unknowns.

Clarify ambiguous MS structural information with NMR data for target compounds. Screen ^{13}C NMR spectra against predicted ^{13}C signals of ~98 million known structures collected in open chemistry databases (e.g., PubChem) via the known structure search workflow.

Using combined MS and NMR data, ensure conclusive structure identification for *known unknowns*



Identify possible candidates for further structure elucidation if an NMR spectral match is not found

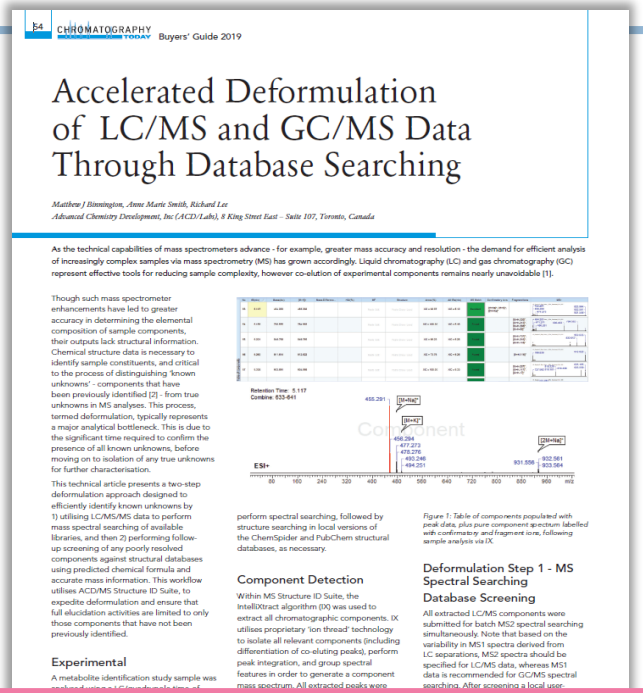
Accelerating Deformulation

The Challenge

During analysis of complex MS samples, chemical structure information is critical to differentiating known unknowns from unknowns in order to prioritize characterization of undiscovered targets. The process of separating and identifying components—termed deformulation (for formulated products), dereplication, and/or mixture analysis—typically requires a significant time investment and can delay further analyses.

The Solution

ACD/Labs offers multiple complementary tools to simplify component identification in complex mixtures. Our recent article in *Chromatography Today* discusses these solutions in detail, explaining how the combination of mass spectral searching via IntelliXtract Compound Recognition with accurate mass & molecular formula screening via MS Structure ID Suite accelerates the identification of known unknowns.



CHROMATOGRAPHY TODAY Buyers' Guide 2019

Accelerated Deformulation of LC/MS and GC/MS Data Through Database Searching

Matthew J Binnington, Anne Marie Smith, Richard Lee
Advanced Chemistry Development, Inc (ACD/Labs), 8 King Street East – Suite 107, Toronto, Canada

As the technical capabilities of mass spectrometers advance - for example, greater mass accuracy and resolution - the demand for efficient analysis of increasingly complex samples via mass spectrometry (MS) has grown accordingly. Liquid chromatography (LC) and gas chromatography (GC) represent effective tools for reducing sample complexity, however co-elution of experimental components remains nearly unavoidable [1].

Though such mass spectrometer enhancements have led to greater accuracy in determining the elemental composition of sample components, their outputs lack structural information. Chemical structure data is necessary to identify sample constituents, and critical to the process of distinguishing 'known unknowns' - components that have been previously identified [2] - from true unknowns in MS analyses. This process, termed deformulation, typically represents a major analytical bottleneck. This is due to the significant time required to confirm the presence of all known unknowns, before moving on to isolation of any true unknowns for further characterisation.

This technical article presents a two-step deformulation approach designed to efficiently identify known unknowns by 1) utilising LC/MS/MS data to perform mass spectral searching of available libraries, and then 2) performing follow-up screening of any poorly resolved components against structural databases using predicted chemical formula and accurate mass information. This workflow utilises ACD/MS Structure ID Suite, to expedite deformulation and ensure that full elucidation activities are limited to only those components that have not been previously identified.

Experimental

A metabolite identification study sample was

perform spectral searching, followed by structure searching in local versions of the ChemSpider and PubChem structural databases, as necessary.

Component Detection

Within MS Structure ID Suite, the IntelliXtract algorithm (IX) was used to extract all chromatographic components. IX utilises proprietary 'ion thread' technology to isolate all relevant components (including differentiation of co-eluting peaks), perform peak integration, and group spectral features in order to generate a component mass spectrum. All extracted peaks were

Figure 1: Table of components populated with peak data, plus pure component spectrum labelled with confirmatory and fragment ions, following sample analysis via IX.

Deformulation Step 1 - MS Spectral Searching

Database Screening

All extracted LC/MS components were submitted for batch MS2 spectral searching simultaneously. Note that based on the variability in MS1 spectra derived from LC separations, MS2 spectra should be specified for LC/MS data, whereas MS1 data is recommended for GC/MS spectral searching. After screening a local user-

> "This workflow utilizes MS Structure ID Suite, to expedite deformulation and ensure that full elucidation activities are limited to only those components that have not been previously identified."
>
> Chromatography Today, Buyers' Guide 2019

ACD/Labs provides valuable tools to effortlessly communicate and collaborate on MS projects.

Produce Comprehensive Reports

Perform straightforward reporting that clearly communicates experimental parameters, analytical findings, and interpretations.

- ☑ Capture all project information in one document, ensuring data traceability & providing comprehensive evidence of rational data analysis
- ☑ Configure report templates to a logical format that aligns with organizational goals
- ☑ Readily choose from various report elements
- ☑ Easily export to Microsoft Word, PowerPoint, or Adobe PDF

Ensure Effective Knowledge Management

Enable intuitive databasing of multi-technique results, along with their interpretation(s), to preserve critical knowledge and support collaboration.

- ☑ Search databases by numerous spectral, structural & text-based parameters
- ☑ Generate comprehensive experimental databases that can be readily configured to include all desired experimental information

Successfully Managing MS Data

The Challenge

Drs. Peter Bellstedt and Nico Ueberschaar oversee analytical techniques at the FSUJ Faculty of Chemistry and Earth Sciences. They were keen to consolidate analytical data management across the department, and reduce the experimental costs, time, and effort of analyses that were inefficiently distributed across multiple instruments in different laboratories.

The Solution

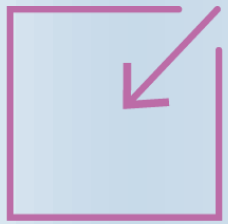
Implementation of various ACD/Labs tools provided access to a centralized database for housing all experimental methods, data, and analyses, eliminating a major data distribution bottleneck. New findings can now be seamlessly incorporated into ongoing projects, and previously stored data is readily available for reexamination and reinterpretation.

> “Whereas prior to software implementation key analytical technique knowledge was isolated in different working groups… now all methodologies and data are housed in a centralized server environment for easy sharing between individuals and laboratories.”
>
> Drs. Bellstedt and Ueberschaar

Next Steps

ACD/Labs has a variety of tools designed to fit the needs of any mass spectrometrist and is ready to help you with all stages of your mass spectrometry projects:

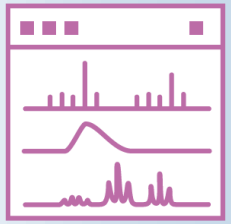
1 Import



2 Identify

3 Integrate

4 Inform



Is your organization ready to save time and effort on method development strategies? Do you want to:

- Support consolidated, vendor-neutral analysis of any MS data?
- Seamlessly distinguish, identify, and characterize all components?
- Unite MS results with additional relevant project data?
- Ensure that previous projects are easily accessible and shareable?

To learn more about how ACD/Labs can help you achieve this, contact us to get more information.

Contact Us