Metabolic Profiler

- A Fully-Integrated Solution for Metabolic Analysis

Innovation with Integrity

NMR | MS

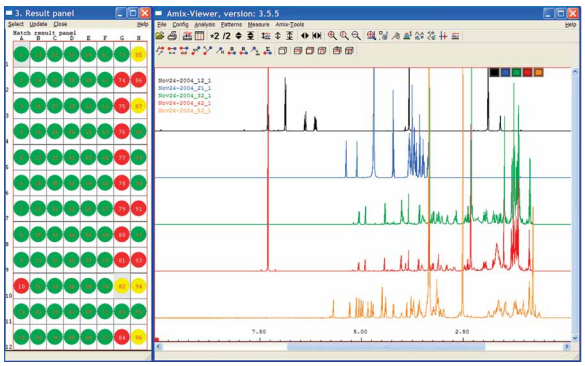
The Most Complete Solution for Your Metabolic Research

Metabolic profiling and finger printing is a key process in the pharmaceutical industry to study drug efficacy or toxicology. In clinical research, metabolic profiling helps identify biomarker compounds for early disease detection and monitoring, and allows studying the effects of drugs in biological systems in a rapid and robust method. Bruker offers a Metabolic Profiler, that combines the structural resolving power of NMR and intuitive software programs, giving you the most complete and highly automated system for metabolic research today.

Integrated Analysis

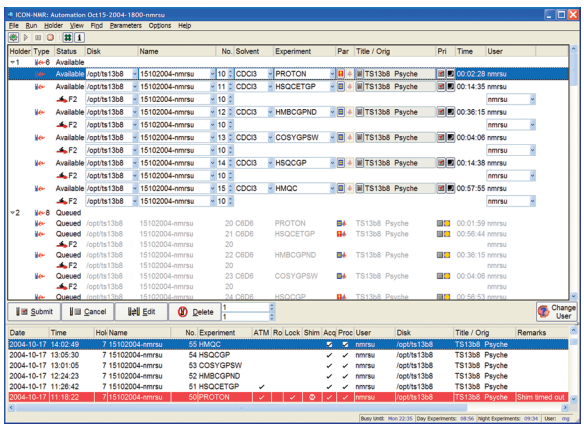
The Metabolic Profiler offers a unique integrated metabolic analysis solution. This system provides a simple, easy to use and inexpensive base system to acquire the spectroscopic data needed to do basic metabolic profiling. The system enables you to integrate your automated sample handling, acquire, collect and archive your data, and allows for comparative and statistical analysis needed for your research.

Analysis with AMIX



AMIX™ analyzes data and is linked to the Spectral Database for further comparative analysis.

Data Acquisition with Icon-NMR



Icon-NMR acquires data, collects and archives.

Register your samples with routine bar code scanners. SampleTrack™ inputs the sample data acquired.

Automated high-throughput screening

Software Features

Data Management

SampleTrack™ an Oracle based information system, which utilizes SQL tools for organizing, searching and archiving sample information, can be added to simplify experimental control of large sample sets.

Statistical Analysis

The AMIX program provides a collection of powerful tools that enable statistical and spectroscopic analyses of your NMR data. Below you'll find just a few of features AMIX offers:

- Pattern Match - Spectral patterns can be defined in multiple ways and projected to spectra (Figure 1a). Multi-Integration is also possible, which can be used to identify and quantify metabolites in complex mixtures (Figure 1b).

Pattern Match - Spectral Patterns using AMIX

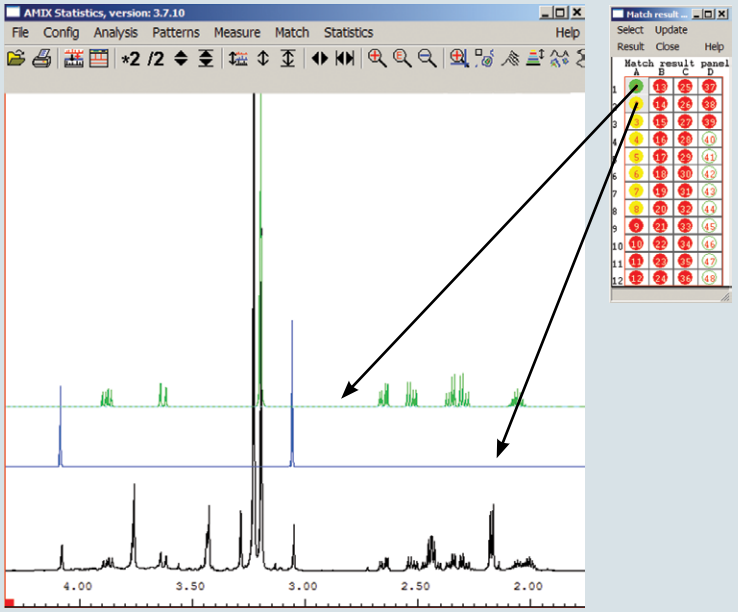


Figure 1a: Spectral matching of single compounds in a juice mixture. A data panel with color coding based on degree of match is directly linked to matching spectra.

Pattern Search - Multi-Integration using AMIX

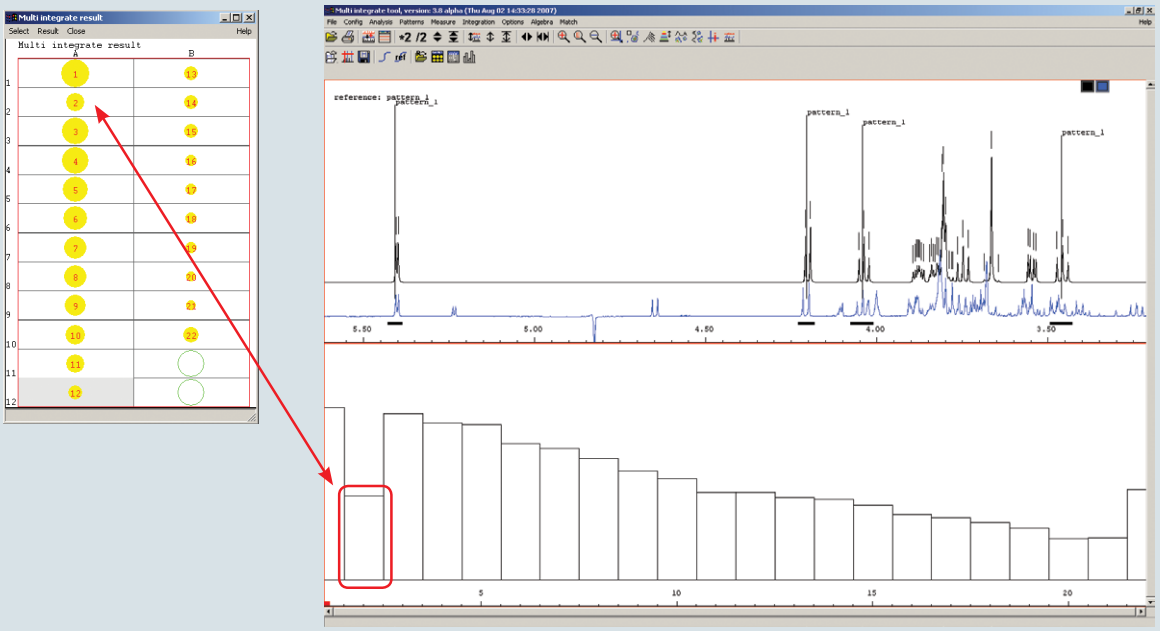


Figure 1b: Multi spectra integration results from a pattern search of sucrose content in spectra of different juice types. Intensity based data panels or histograms visually represent the sucrose content.

- Principal Component Analysis (PCA) can be applied to bucket tables for visualization and interpretation of results. Spectra are selected from either scores, hotelling or influence plots, each visualized with the multiple linked cursor (Figure 2). You are able to build PC models save them as classes and use them for classification. Refining or building models within the PCA module can describe an ensemble of normal spectra.

- Interactive Visualization between loadings plot covariance matrix and the real NMR spectra allow rapid visualization of chemical shifts of interest (Figure 3a).

- Partial Least Squares fitting (PLS) - With the AMIX PLS feature (or discriminating analysis; PLS-DA) you are able to find the maximum correlation between a bucket table and other tabulated data (Figure 3b).

PCA using AMIX

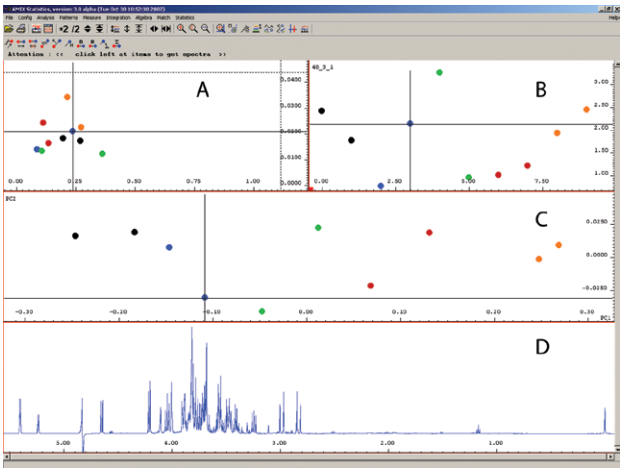


Figure 2: Multilinked cursor shows the plotted position in the (a) influence, (b) Hotelling and (c) scores plots. The acquired NMR spectra (d) are accessible from all plots by clicking on the representative symbol.

Bucketing Identification using AMIX

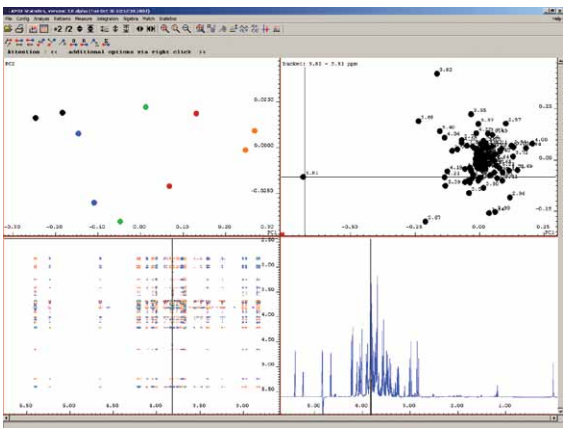


Figure 3a: Identifying individual buckets can be used to match spectra which have a similar chemical shift.

Visualization using AMIX

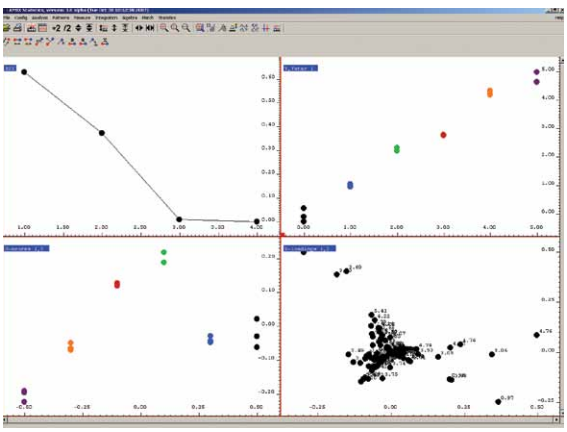


Figure 3b: Supervised methods can be used to visualize samples of model space, describe residual variance, and scores and loadings variations.

Reference Compound Spectral Database

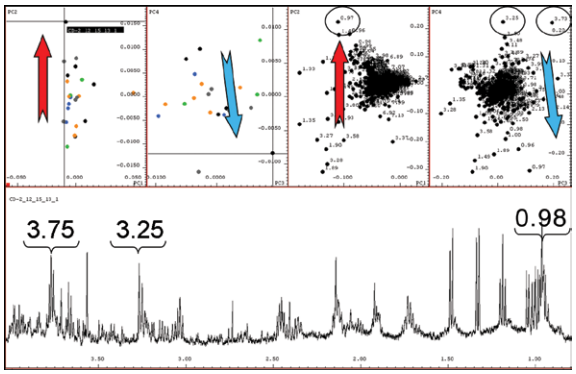
Our metabolite spectral database contains 17,000 spectra of the most common endogenous metabolites. The most complete NMR spectral database allows the assignment of metabolites in biofluids, cell extracts and tissues in a unique and unambiguous way; by taking into account the effects of pH, field strength and by using one as well as two dimensional NMR data.

The database is linked to AMIX and allows automatic investigations like matching to mixture spectra. Direct integration into statistical data evaluation is also possible.

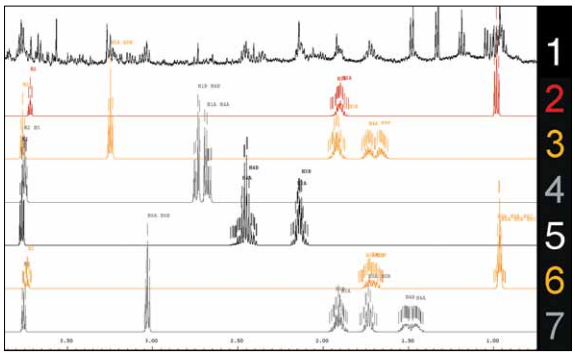
Common spectra available include:

- 1D NOESY
- 2D TOCSY
- 2D J-Resolved
- 2D COSY
- 2D HSQC
- 1D Carbon

Spectral Database

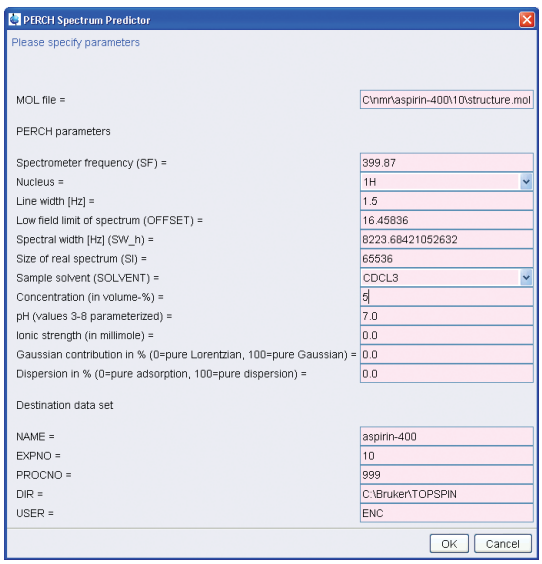


Scores and 2D loadings plots indicating buckets at 0.98 (Red vector) and 3.75 (Blue vector).



Spectral Base search results of bucket loading at 3.75 (±0.02) ppm. Data are: 1) water flea hemolymph, 2) 2-aminobutyric acid, 3) arginine, 4) dithiothritol, 5) glutamine, 6) leucine, 7) lysine.

PERCH



PERCH prediction tool set up window

NMR Prediction

PERCH Solutions and Bruker BioSpin have teamed up to bring you advanced NMR Prediction, which uses realistic descriptors based on the 3D molecular structure and its flexibility to predict NMR parameters including solvent effects, pH and with full stereochemistry (distinguishing diastereomers). It predicts ^{1}H and ^{13}C NMR spectra using higher order effects and applies a user defined linewidth.

Applications

Clinical Research

Metabolic profiling is used in clinical research for disease detection. For example, NMR has demonstrated capabilities in successfully distinguishing more than 80 inborn errors with a single ^{1}H spectrum. A significant advantage to using the NMR method is that the sample requires no modification prior to analysis. The rapid analysis by NMR enables physicians to quickly respond to the patient's medical issue and limit the harmful effects of the disease.

Toxicity Screening in Drug Development

Drug toxicity is a major reason for the failure of a drug to successfully achieve a new drug application status. As a result, a successful drug discovery program identifies the presence of toxic drug metabolites early in the discovery process. Studies on drug toxicity may utilize rapid screening using statistical methods on biofluids or be conducted to identify individual metabolites resulting from treatment with pharmaceutical candidates. Studies done on intact biofluids and individual metabolite require highly sensitive NMR probes, such as CryoProbes™ or MicroProbes. The system can be extended to allow substrate isolation using hyphenated techniques such as LC-(SPE)–NMR-MS.

Additional applications that can be researched with our fully integrated analyzer:

- Systems Biology
- Drug Discovery & Development
- Plant Science
- Food Screening
- Public Health Studies

Combining NMR and MS

This information-rich approach combines the strengths of both NMR and time-of-flight (TOF) mass spectrometry (MS) into an integrated data acquisition, data evaluation and statistical model building solution for drug development.

The combination of NMR and q-TOF-MS, the most widely used techniques for metabolic profiling, together with an integrated operating and processing software platform, which includes statistical analysis tools, make the Metabolic Profiler the most complete system for metabonomics research available today.

Our software solution allows operation of the system by a non-spectroscopist while still allowing full integration of the many hardware options. Data analysis brought together with one unified user interface allowing one software module that does not require you to jump around between software programs. Along with the integrated hardware, the Metabolic Profiler provides easy to use software for system control and integrated data evaluation tools from statistics to structure elucidation. NMR and MS spectral databases of reference compounds from all types of bio-fluids can be integrated to allow automatic verification of the presence of specified metabolites.

Bruker BioSpin

info@bruker-biospin.com
www.bruker.com/metabolomics