Evolving nature of

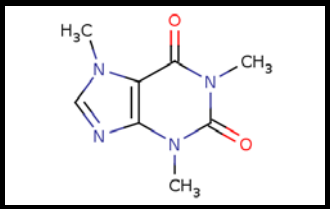
METLIN

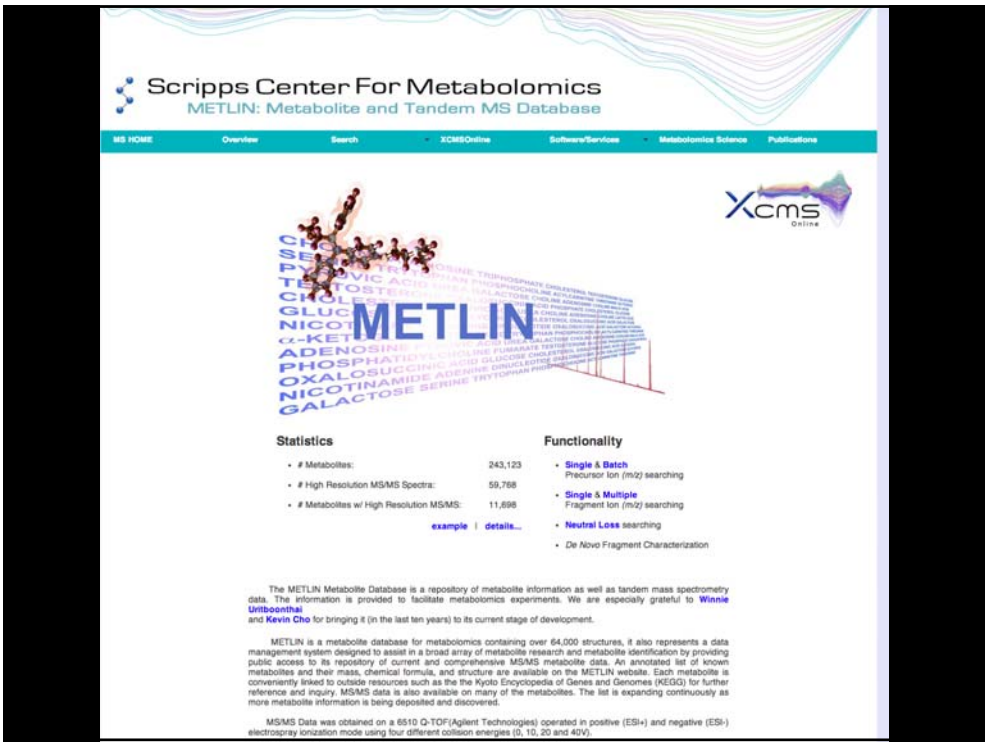
- interpretation of LC-MS data and other features

H. Paul Benton

What is METLIN

- Accurate mass database
  - Endogenous Metabolites - 243,123
- Tandem mass spectra - 11,698

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METLIN: Metabolite and Tandem MS Database
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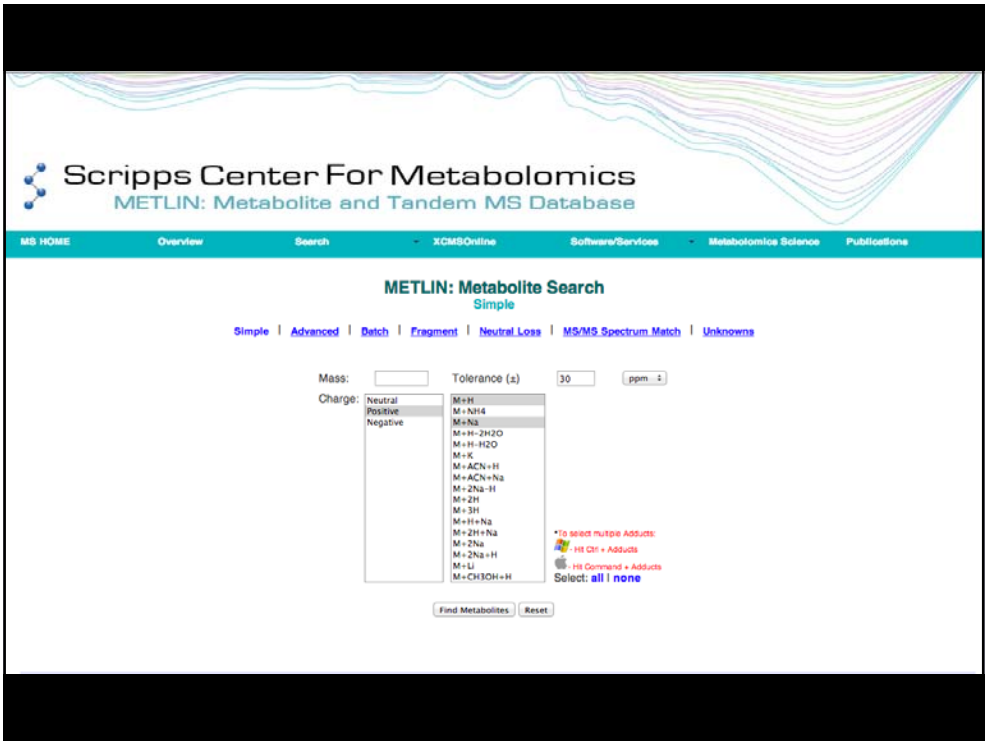
Statistics
Metabolites: 243,123
High Resolution MS/MS Spectra: 59,768
Metabolites w/ High Resolution MS/MS: 11,698
example | details...
Functionality
Single & Batch Precursor Ion (m/z) searching
Single & Multiple Fragment Ion (m/z) searching
Neutral Loss searching
De Novo Fragment Characterization
The METLIN Metabolite Database is a repository of metabolite information as well as tandem mass spectrometry data. The information is provided to facilitate metabolomics experiments. We are especially grateful to Winnie Uritboonthai and Kevin Cho for bringing it (in the last ten years) to its current stage of development.
METLIN is a metabolite database for metabolomics containing over 64,000 structures, it also represents a data management system designed to assist in a broad array of metabolite research and metabolite identification by providing public access to its repository of current and comprehensive MS/MS metabolite data. An annotated list of known metabolites and their mass, chemical formula, and structure are available on the METLIN website. Each metabolite is conveniently linked to outside resources such as the the Kyoto Encyclopedia of Genes and Genomes (KEGG) for further reference and inquiry. MS/MS data is also available on many of the metabolites. The list is expanding continuously as more metabolite information is being deposited and discovered.
MS/MS Data was obtained on a 6510 Q-TOF(Agilent Technologies) operated in positive (ESI+) and negative (ESI-) electrospray ionization mode using four different collision energies (0, 10, 20 and 40V).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Simple
Simple | Advanced | Batch | Fragment | Neutral Loss | MS/MS Spectrum Match | Unknowns
Mass:
Tolerance (±)
30
ppm
Charge:
Neutral
Positive
Negative
M+H
M+NH4
M+Na
M+H-2H2O
M+H-H2O
M+K
M+ACN+H
M+ACN+Na
M+2Na-H
M+2H
M+3H
M+H+Na
M+2H+Na
M+2Na
M+2Na+H
M+Li
M+CH3OH+H
*To select multiple Adducts:
- Hit Ctrl + Adducts
- Hit Command + Adducts
Select: all | none
Find Metabolites
Reset

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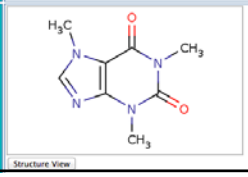
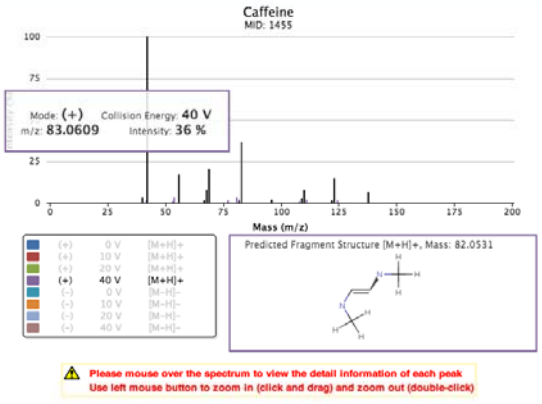
METLIN
Metabolite

Back To Result

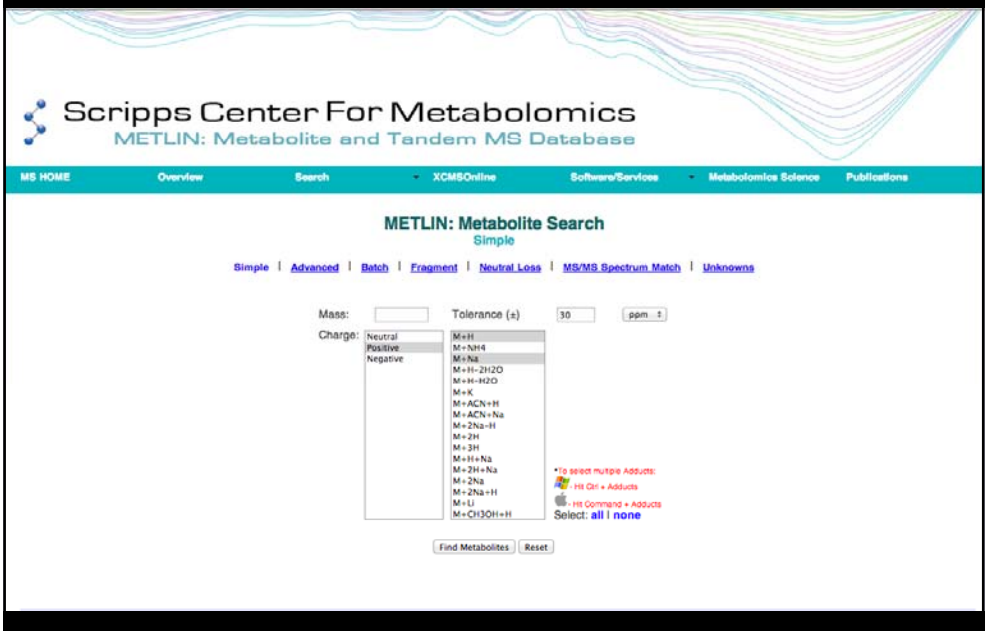
MID	1455
Mass	194.080376 m/z calculator
Name	Caffeine
Synonym	1,3,7-Trimethylxanthine; 7-methyl Theophylline; Thein; 1-methyl-Theobromine; Methylxanthine theophylline; 1,3,7-Trimethyl-3,7-dihydro-1H-purine-2,6-dione; Lanorinal; 1,3,7-Trimethyl-2,6-dioxopurine; 3,7-Dihydro-1,3,7-trimethyl-1H-purine-2,6-dione; Methyltheobromide; Guaranine; Anhydrous caffeine (JP15); Monohydrate Caffeine
Systematic Name	1,3,7-trimethylpurine-2,6-dione
Formula	$C_8H_{10}N_4O_2$
CAS	58-08-2
Purchase Option	Sigma-Aldrich: C1778 SIGMA-ALDRICH Chromadex: ASB-00003032-010 ChromaDex
LMID	
KEGG	C07481
HMDB	HMDB01847
PubChem	2519
Notes	naturally occurring alkaloid Dollery, Colin Therapeutic Drugs, 2nd Ed. 1999 p. C4
Updated	2013-06-15 16:24:26
Drug	N
Structure	 Structure View

Spectrum

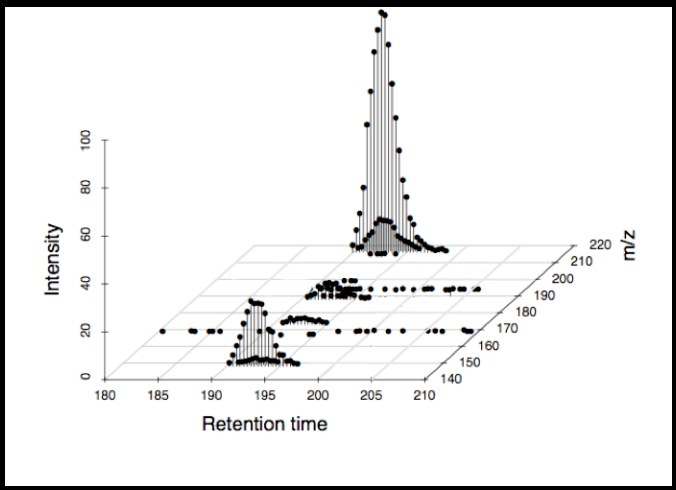


Please mouse over the spectrum to view the detail information of each peak
Use left mouse button to zoom in (click and drag) and zoom out (double-click)

Adducts

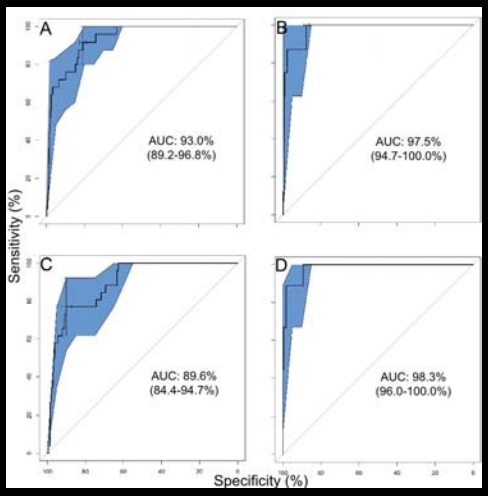


Explanation of adduct characterisation



How accurately can we find Adducts?

- Adducts were manually found for spiked in standards
- Across file correlation
- Lowest AUC 89.6%
  - very good!



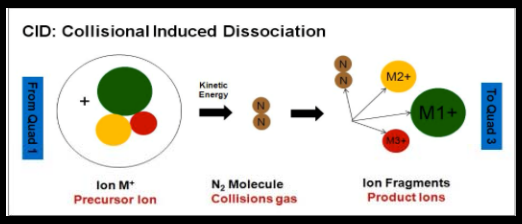
Software to do Automate

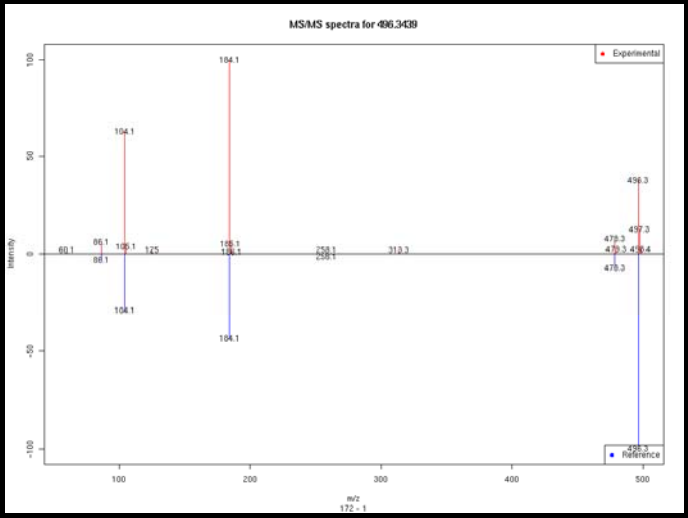
- CAMERA - R package - Steffen Neumann group
- AStream - R package - Sara Marsal group
- xcms Online - Also matches to Metlin hits

Understanding Fragmentation spectra

- Fragmentation spectra are complex
- Q: From this wheel can we tell that the car which smashed into the brick wall is a Ferrari or a Ford?
  - This is essentially what fragmentation spectra are!!

How CID works





x-rank algorithm

- Many different algorithms available
- X-rank is unique in that it ranks the peaks and uses the ranks not true intensity values
- A very good way to match spectra to reference spectra
- X-rank asks what is the probability that the experimental spectra is the same as the reference spectra given that a fragment is/is not in the reference spectra.

http://www.ncbi.nlm.nih.gov/pubmed/19702277

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MS/MS Spectrum Match

Simple | Advanced | Batch | Fragment | Neutral Loss | MS/MS Spectrum Match | Unknowns

m/z, intensity

Peaks:
(MAX: 30 peaks)

138.066, 10877
110.071, 2221
42.034, 644
69.045, 351
123.043, 350

EXAMPLE DATA
POSITIVE NEGATIVE

Mode:

Positive
Negative

M+H
M+NH4
M+Na
M+H-2H2O
M+H-H2O
M+K
M+ACN+H
M+ACN+Na
M+2Na-H
M+2H
M+3H
M+H+Na
M+2H+Na
M+2Na
M+2Na+H
M+Li
M+CH3OH+H

*To select multiple Adducts:
- Hit Ctrl + Adducts
- Hit Command + Adducts

Collision Energy (eV): 20eV
Tolerance MS/MS (Da): 0.01
Tolerance Precursor (ppm): 20
Precursor m/z: 195.0877

Find Metabolites | Reset

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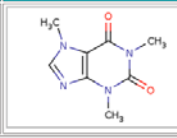
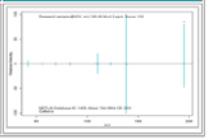
METLIN

Spectrum Search Result

Precursor *m/z*: **195.0877** MODE: **Positive** CE: **20** Tolerance MS/MS: **0.01** Tolerance Precursor: **20**

Change Query

METLIN ID	Name	METLIN Score (0-100)	precursor	precursor ΔPPM	Structure	Spectrum Matching
1455	Caffeine	100	M+H	0		

- If time permits show live demo of metlin batch search
- Also show getting data from tandem MS2 files

Upcoming features

- Save searches
- Similarity searching
- Integration with Online XCMS
- Predicted amino acid fragmentation spectra
- Isotope work