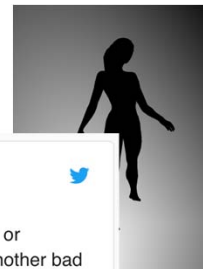


Capabilities of



H. Paul Benton
Scripps Research

What does the current software do?



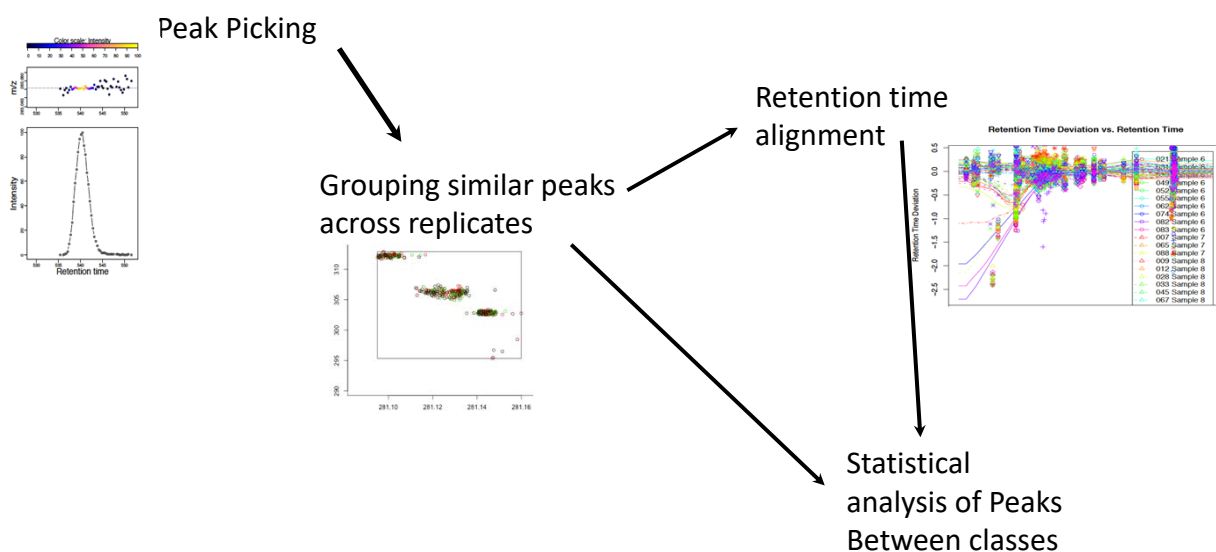
Hear Both Yanny and Laurel

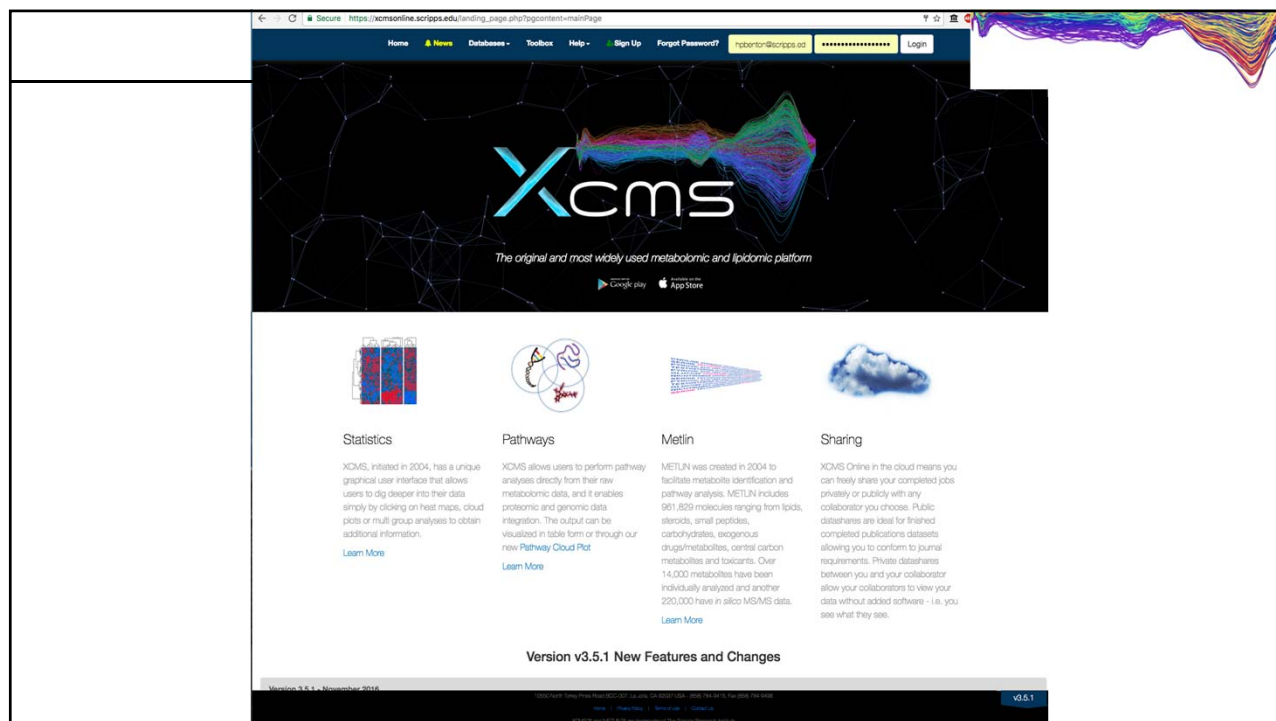


What is XCMS Online?

- The complete xcms system in a graphical web based system
- XCMS started in 2005
- First concept of XCMS Online was 2009 but production was started late 2011 (public mid 2012)
 - Approx. 25,000 users
 - Average 70 jobs a day
 - 150 Users logging in per day

Overview of XCMS





Home News Databases Toolbox Help Sign Up Forgot Password? ytdenr@scripps.edu ***** Login

XCMS

The original and most widely used metabolomic and lipidomic platform

Google play App Store

Statistics

XCMS, initiated in 2004, has a unique graphical user interface that allows users to dig deeper into their data simply by clicking on heat maps, cloud plots or multi group analyses to obtain additional information.

[Learn More](#)

Pathways

XCMS allows users to perform pathway analyses directly from their raw metabolomic data, and it enables proteomic and genomic data integration. The output can be visualized in table form or through our new Pathway Cloud Plot.

[Learn More](#)

Metlin

METLIN was created in 2004 to facilitate metabolite identification and pathway analysis. METLIN includes 991,829 molecules ranging from lipids, steroids, small peptides, carbohydrates, exogenous drugs/metabolites, central carbon metabolites and toxicants. Over 14,000 metabolites have been individually analyzed and another 220,000 have in silico MS/MS data.

[Learn More](#)

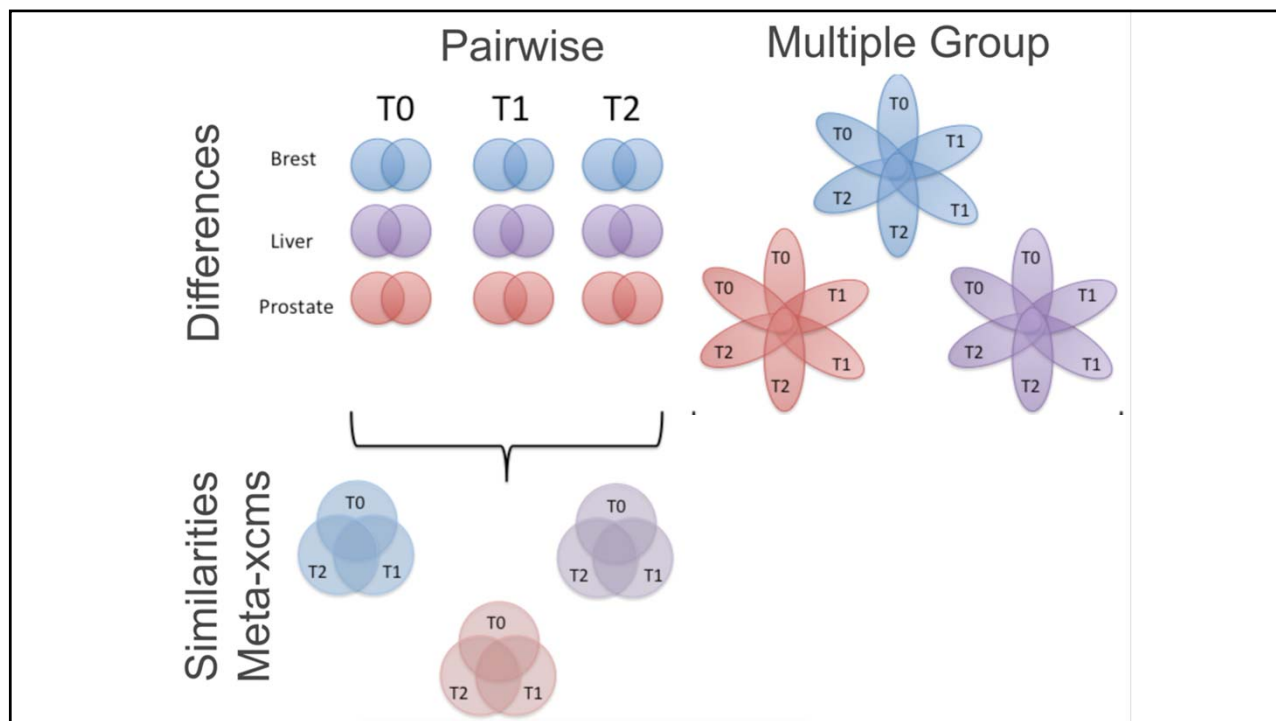
Sharing

XCMS Online in the cloud means you can freely share your completed jobs privately or publicly with any collaborator you choose. Public dashboards are ideal for finished completed publications datasets allowing you to conform to journal requirements. Private dashboards between you and your collaborator allow your collaborators to view your data without added software - i.e. you see what they see.

Version v3.5.1 New Features and Changes

Job types in XCMS Online

- Single Class Jobs – Either single file or single dataset (class or unknown classes)
- Pairwise analysis Jobs – Two class comparison, works best with KO –vs- WT type experiments
- Multigroup/class Jobs – Multiple classes including Quality control samples. Great for Time series jobs or multiple knockouts.
- meta-XCMS- Finds the overlap between many pairwise jobs. (Must have same control samples)
- MultiModal – Combining multiple polarities for better identification.



Running a job

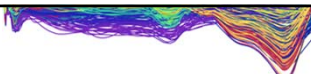
The screenshot shows the XCMS website interface. At the top, there is a navigation bar with links for Home, MRM, Databases, Toolbox, Help, Sign Up, and Forgot Password? Below this is a search bar and a login form with fields for email address and password, and a Login button.

The main content area features the XCMS logo and a large, colorful heatmap visualization. Below the logo, there are four columns of text describing different features:

- Statistics:** XCMS, initiated in 2004, has a unique graphical user interface that allows users to dig deeper into their data simply by clicking on heat maps, cloud plots or multi-group analyses to obtain additional information. [Learn More](#)
- Pathways:** XCMS allows users to perform pathway analysis directly from their raw metabolomic data, and it enables proteomic and genomic data integration. The output can be visualized in table form or through our new [Pathway Cloud Plot](#). [Learn More](#)
- Metlin:** METLIN was created in 2004 to facilitate metabolite identification and pathway analysis. METLIN includes 951,829 molecules ranging from lipids, steroids, small peptides, carbohydrates, exogenous drugs/metabolites, central carbon metabolites and toxins. Over 14,000 metabolites have been individually analyzed and another 226,000 have in silico MS/MS data. [Learn More](#)
- Sharing:** XCMS Online in the cloud means you can freely share your completed jobs privately or publicly with any collaborator you choose. Public databases are ideal for finished completed publications datasets allowing you to conform to journal requirements. Private databases between you and your collaborator allow your collaborators to view your data without added software - i.e. you see what they see.

At the bottom of the page, there is a footer with the text: **Version 3.7.1 New Features and Changes** and **Version 3.5.1 - November 2016**. The footer also includes copyright information: © 2004-2016 Scripps Institution of Oceanography, UC San Diego, CA 92037-0506. METLIN is a trademark of the Scripps Institution of Oceanography. XCMS and METLIN are trademarks of The Scripps Research Institute.

View Results section



View Jobs

Share Job(s) Job Grouping Resubmit Job(s) Delete Job(s)

Job Count: 12

Search Clear
View Public Shares

<input type="checkbox"/>	Exp Type	Status	ID	Progress	JobName	Datasets (ID#) [Control]	Created	Parameters (ID#)	Group	Shared
<input type="checkbox"/>	PAIR	VIEW	1143618	job complete 100%	pair_2017-01-31_16:29	salt_stres (#230089) Salt_contr (#230090)	2017-01-31 19:15:25	HPLC / UHD (6674)		✖
<input type="checkbox"/>	PAIR	VIEW	1143614	job complete 100%	pair_2017-01-31_16:29	set1 (#230082) set2 (#230083)	2017-01-31 16:29:20	Pauls-UAB_(26724)		✖

[Home](#) [News](#) [Databases](#) [Create Job](#) [View Results](#) [XCMS Public](#) [XCMS Institute](#) [Stored Datasets](#) [Account](#) [Toolbox](#) [Help](#) [Logout \[hpenton\]](#)

Pairwise Results Summary: pair_2017-01-31_16:29 (#1143618)

[Download Results](#)
hash: f28e713cb31c8cd95a48c053783fb5c7

Submit Date	Finish Date	Paired Samples	Total Aligned Features	Parameter ID#	Log	Shared
2017-01-31 19:21:26	2017-01-31 20:02:43	False	5773	HPLC / UHD Q-TOF (H) (6674)	View Log	NOT SHARED

The finished job has the following notes:
 2017-01-31 19:59:53 : #HeatMap data prep, memory requires limiting to top 1000 features <0.0349129 p-values

[Citation Links](#)

[Results Table](#)

[Metabolomic Cloud Plot](#)

[Interactive Heatmap](#)

[IPCA](#)

[Activity Network \(Connections\)](#)

Multi-Omics Data

[Systems Biology Results](#)

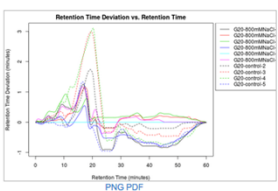
[Pathway Cloud Plot](#)

Datasets Used

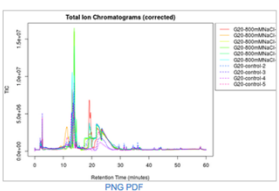
- salt_stress (230089)
- Salt_control (230090)



Total Ion Chromatograms (original)



Retention Time Deviation vs. Retention Time



Total Ion Chromatograms (corrected)



Cloud Plot 359 features with p-values < 0.01, fold change > 1.5



Non-Metric Multidimensional Scaling



PCA Biplot

v3.5.1

5

Citation Links

Results Table

Metabolomic Cloud Plot

Interactive Heatmap

IPCA

Activity Network (Connections)

Multi-Omics Data

Systems Biology Results

Pathway Cloud Plot

Datasets Used

- salt_stress (230089) *
- Salt_control (230090)

Quick Compound Search: Search

JOB#1143618 : PAIR_2017-01-31_16:29

featureidx	fold	pvalue	updown	mzmed	rtmed	maxint	dataset2_mear	dataset2_mear	isotopes	adducts	peakgroup	usernotes
1	3.6	1.85209e-7	UP	412.2580	2.14	2.708	4.847	17.328	[M-H+HCOO] ⁻	67		
2	3.8	4.35106e-6	UP	129.0199	34.42	5.091	26.249	99.061		41		
3	89.4	0.00003	DOWN	796.5530	2.30	3.179	11.262	109		60		
4	38.9	0.00004	DOWN	571.3829	2.00	16.769	133.188	3.420	[317] ⁺ [M] ⁻			
5	2.8	0.00004	DOWN	242.8751	36.87	1.386	10.848	3.926		42		
6	6.7	0.00006	DOWN	861.9270	21.81	2.484	19.619	2.912	[541] ⁺ [M] ⁻			
7	100.1	0.00007	DOWN	797.5553	2.30	2.226	6.908	0		60		
8	5.0	0.00014	DOWN	573.3896	2.01	2.139	13.481	2.675	[317] ⁺ [M] ⁻			
9	7.3	0.00017	DOWN	188.9401	36.22	11.058	327.350	44.735		202		
10	5.7	0.00019	DOWN	618.3867	1.94	1.203	3.626	616		145		
11	8.2	0.00021	DOWN	618.7867	32.04	1.793	2.901	453		110		
12	16.5	0.00021	DOWN	651.4027	13.21	1.117	3.106	163		110		
13	9.1	0.00026	DOWN	560.3820	2.20	1.080	4.034	426	[307] ⁺ [M] ⁻	31		
14	1.7	0.00027	UP	465.1368	57.99	2.144	4.078	7.009	[259] ⁺ [M] ⁻	97		
15	20.4	0.00028	DOWN	792.5330	1.92	585	2.816	121	[501] ⁺ [M] ⁻	145		
16	6.9	0.00037	DOWN	408.3014	1.95	1.923	8.891	1.251	[166] ⁺ [M] ⁻	145		
17	4.4	0.00040	UP	366.8748	37.00	968	1.393	6.174		210		
18	2.7	0.00045	UP	384.3167	2.80	6.114	3.599	9.830		210		
19	9.1	0.00047	DOWN	409.3305	2.44	367.425	1.180.430	130.244		145		
20	9.4	0.00047	DOWN	805.5123	1.90	1.316	7.703	821		145		
21	8.4	0.00048	DOWN	407.2984	1.95	6.681	31.079	3.716	[186] ⁺ [M] ⁻	145		
22	9.4	0.00050	DOWN	791.5234	1.93	1.529	6.332	673	[501] ⁺ [M] ⁻	145		
23	5.6	0.00051	DOWN	901.8173	22.82	1.347	12.177	2.138		145		
24	6.1	0.00053	UP	633.4817	2.16	763	504	3.658		97		
25	5.6	0.00053	UP	415.8658	35.12	2.725	2.112	11.896		97		
26	5.1	0.00053	DOWN	388.1976	2.31	2.494	7.257	1.411	[171] ⁺ [M] ⁻	60		
27	8.4	0.00057	DOWN	410.3302	2.46	111.534	338.156	40.083	[186] ⁺ [M] ⁻	25		
28	6.8	0.00059	DOWN	971.6025	22.78	1.613	11.338	1.858	[604] ⁺ [M] ⁻	38		
29	13.8	0.00060	UP	650.1819	31.26	1.518	1.291	17.779		97		
30	28.3	0.00064	DOWN	409.3134	1.89	11.815	57.568	2.037	[187] ⁺ [M] ⁻	107		
31	9.5	0.00067	DOWN	236.8825	35.70	5.549	52.822	5.556		145		

Return to Job Summary

Citation Links

Results Table

Metabolomic Cloud Plot

Interactive Heatmap

IPCA

Activity Network (Connections)

Multi-Omics Data

Systems Biology Results

Pathway Cloud Plot

Datasets Used

- salt_stress (230089) *
- Salt_control (230090)

Original Settings | Add New View | Remove Current View | Toggle Help Box

Main Panel | Advanced

p-value: 0 - 0-0.01 | 1

fold change: 0 - 1.5 - 2807.731 | 2807.731

Regenerate Cloud Plot

EIC_ABR | Box and Whisker | Spectrum

Extracted Ion Chromatogram: 163.582 - 165.076 min

Bubble Size Multiplier: 22

Download Cloud Plot Manual

Welcome to the Cloud Plot

Welcome to the Interactive

View 1

Retention Time vs m/z of 359 features

Click and drag in the plot area to zoom in

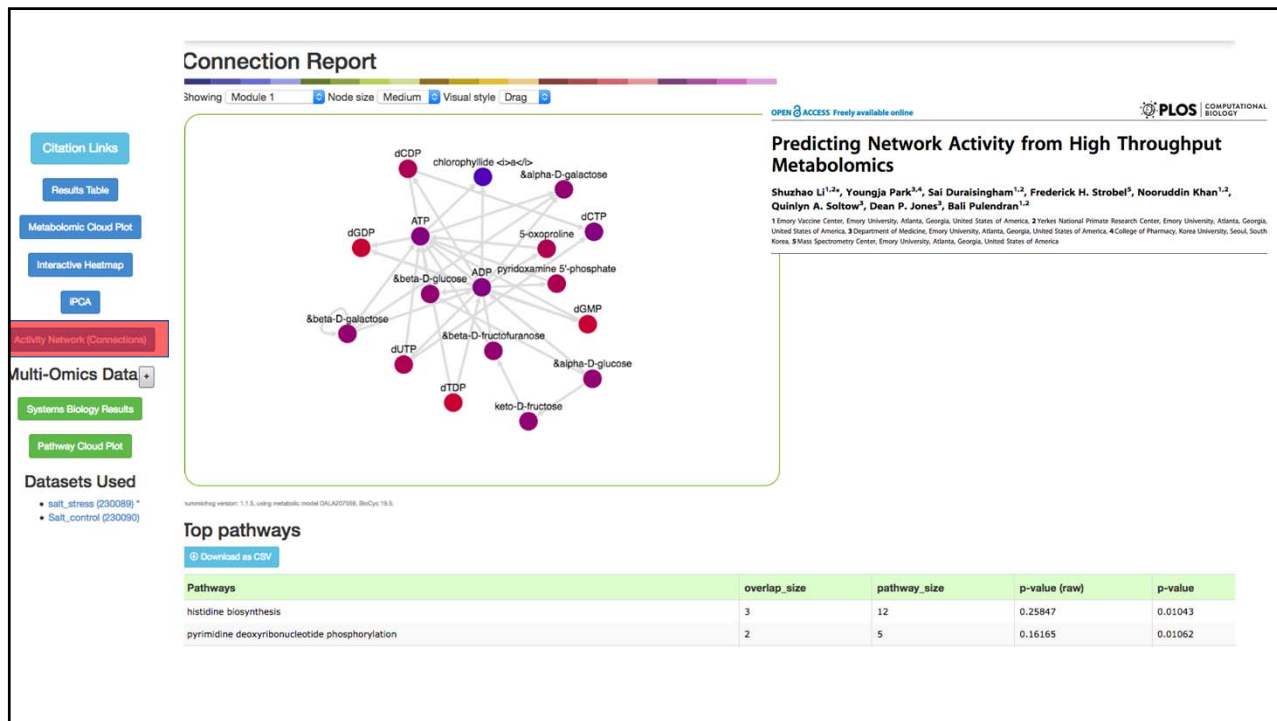
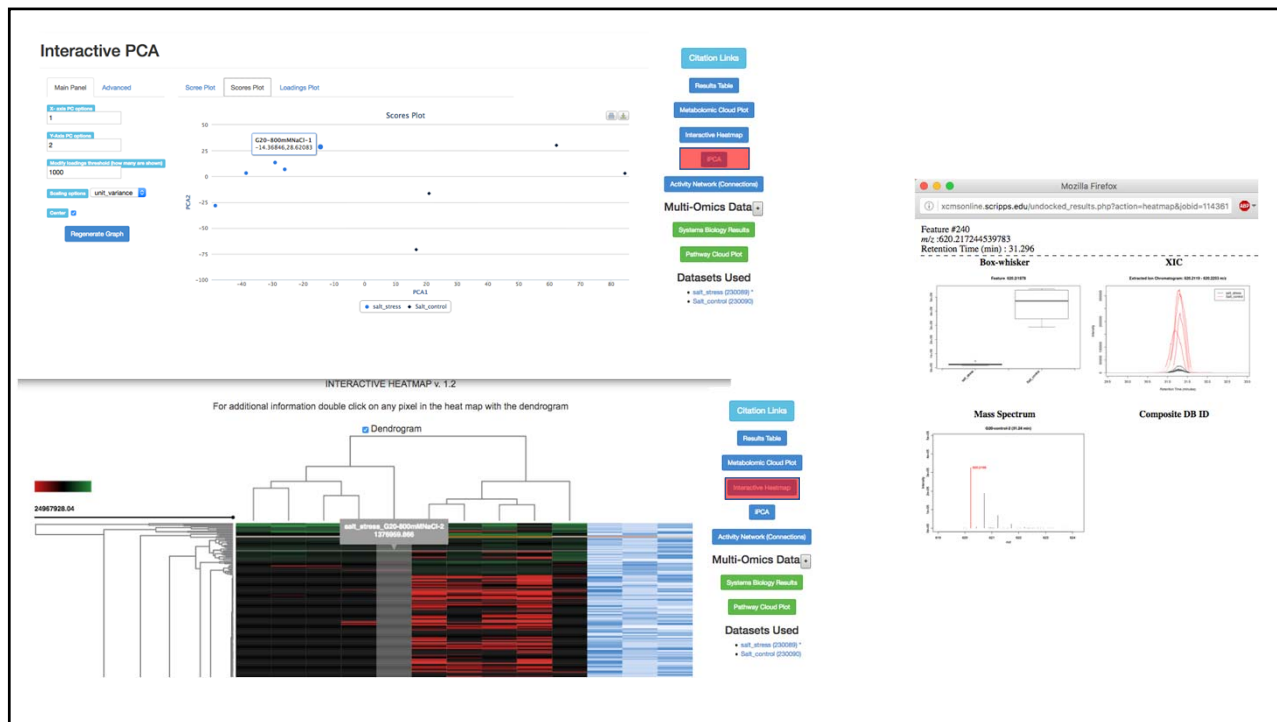
m/z : 940.571
retention time: 13.09 min
p-val: 0.00412
fold change: 28.641 (UP)
max intensity: 5265
0 matches found.

Toggle Upregulated | Toggle Downregulated

p-Value: 0-0.01 | fold change: 1.5 - 2807.731 | m/z Range of 0 - 1099 | Retention Range of 1-64 | max intensity: 0-6

Radius Scale: Fold Change

Table View



Top metabolite predictions

[Download as CSV](#)


Compound_ID	name(input_mz)	evidence_score(match_form)	MW(mz_diff)	
DCDP	dCDP	5	387.0233	
	386.017400	M-H[-]	0.001400	
	2-D-THREO-HYDROXY-3-CARBOXY-ISOCAPROATE	(2R,3S)-3-isopropylmalate	9	176.0685
	196.036600	M+Na-2H[-]	0.000700	
	175.061400	M-H[-]	0.000200	
5-OXOPROLINE	235.082800	M+CH3COO[-]	0.001000	
	157.051200	M-H2O-H[-]	0.000600	
	5-oxoproline	8	129.0426	
	149.009700	M+Na-2H[-]	-0.000300	
	128.035900	M-H[-]	0.000600	
CHLOROPHYLLIDE-A	164.011900	M+Cl[-]	0.000400	
	128.035800	M-H[-]	0.000500	
	chlorophyllide a	6	614.238	
	613.230100	M-H[-]	-0.000600	
CPD-1130	659.238500	M+HCOO[-]	0.002900	
	3-ethylmalate	6	162.0528	
	161.046300	M-H[-]	0.000800	
UDP-MANNACA	197.021200	M+Cl[-]	-0.000500	
	UDP-N-acetyl-α-D-mannosaminouronate	8	621.0608	

- Adding MS/MS checks to confirm the predicted metabolites.
- This will result in an increased/decreased score for the pathway

Systems Biology Analysis Results

Show 25 rows | VALUES <-> PERCENT | TSV | PDF | Print

Pathway	Overlapping genes	All genes*	Overlapping proteins	All proteins*	Overlapping putative metabolites ¹	All metabolites ^{2*}	p-values
histidine biosynthesis	0	0	0	0	3	12	1.0e-2
pyrimidine deoxyribonucleotide phosphorylation	0	0	0	0	2	5	1.1e-2
UDP-N-acetyl-α-D-mannosaminouronate biosynthesis	0	0	0	0	2	5	1.1e-2
NAD salvage pathway I	0	0	0	0	2	5	1.1e-2
pyrimidine deoxyribonucleotides de novo biosynthesis III	0	0	0	0	3	13	1.3e-2
NAD biosynthesis from 2-amino-3-carboxymuconate semialdehyde	0	0	0	0	2	6	1.5e-2
ethanol degradation II	0	0	0	0	2	6	1.5e-2

Multi-Omics Data 

Systems Biology Results

Pathway Cloud Plot

Datasets Used

- salt_stress (230089) *
- Salt_control (230090)

Load New Pathway Supplementary Data

xcmsonline.scripps.edu/upload/index.php?action=pathway&runuser=11405&jobid=1143618

Save & Proceed

Storage Quota Usage (25.04 GB): **60.8%**

- Files must be comma-separated (CSV) or tab-separated (TSV) files
- Gene files must have name as first column
- Protein files must have UniProt accession ID as first column
- All header text must be enclosed with double quotes (")
- After sample is uploaded you can close this window. (button above)
- Only one (1) file at a time [must close window and upload next]

DROP HERE **BROWSE**

Systems Biology Matching Parameters

JOB ID: 1143618

JOB NAME: pair_2017-01-31_16:29

FILES UPLOADED: **UPLOAD LIST**

FileID	Filename	Upload Date	List Type	Accession ID	Matches	Remove
297096	gene_list.	2017-02-01 00:32:38	Genes	Gene name	View Results	

Run matching subjob

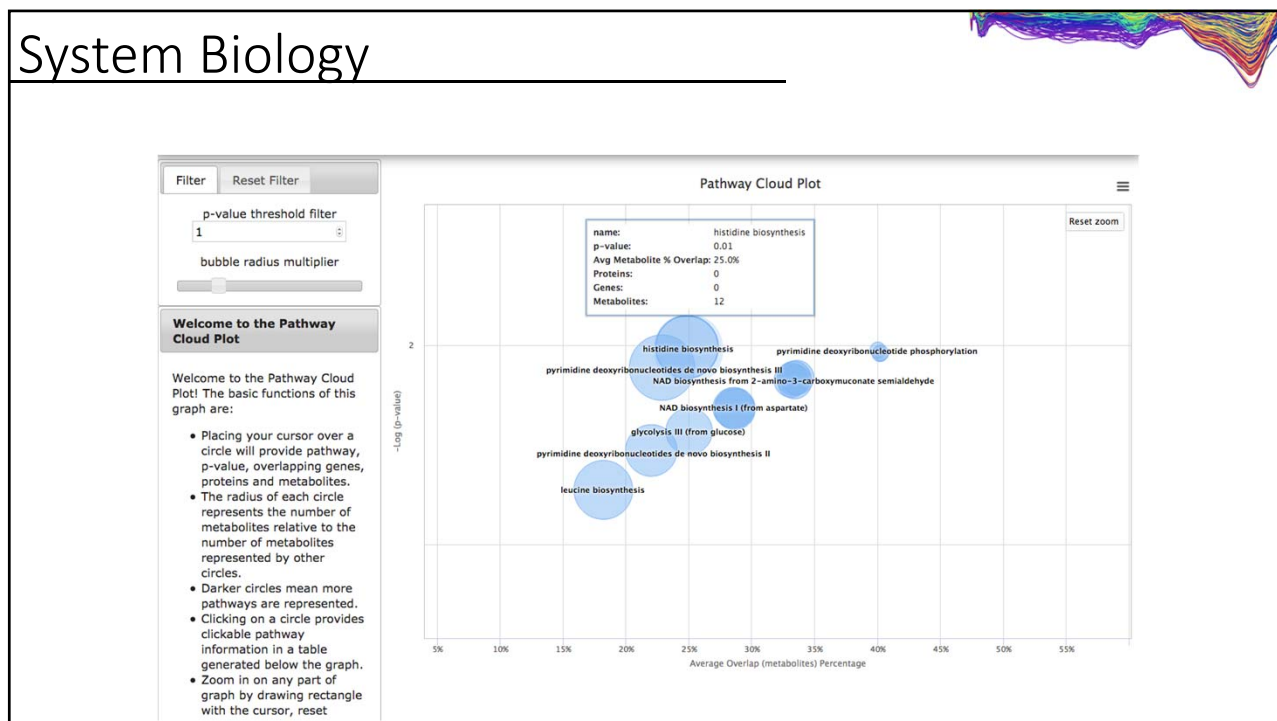
MATCHING PROGRESS (1%)

SUBJOB ID: 4973 **View Log**

POPULATE TABLE PROGRESS (0%)

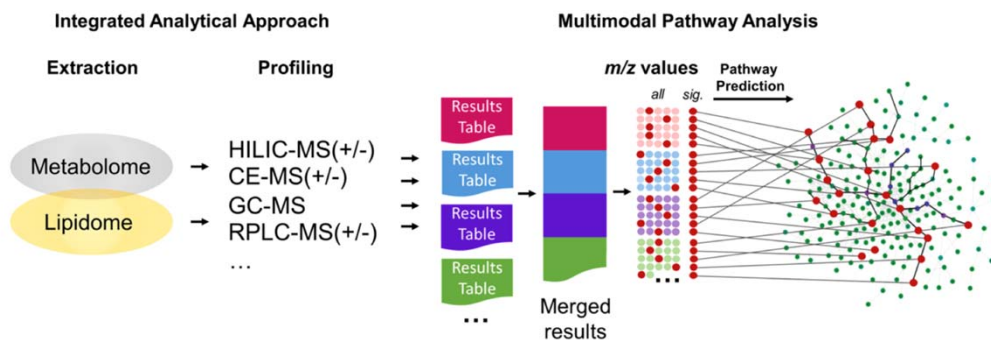
SUBJOB ID: 4970 **View Log**

System Biology

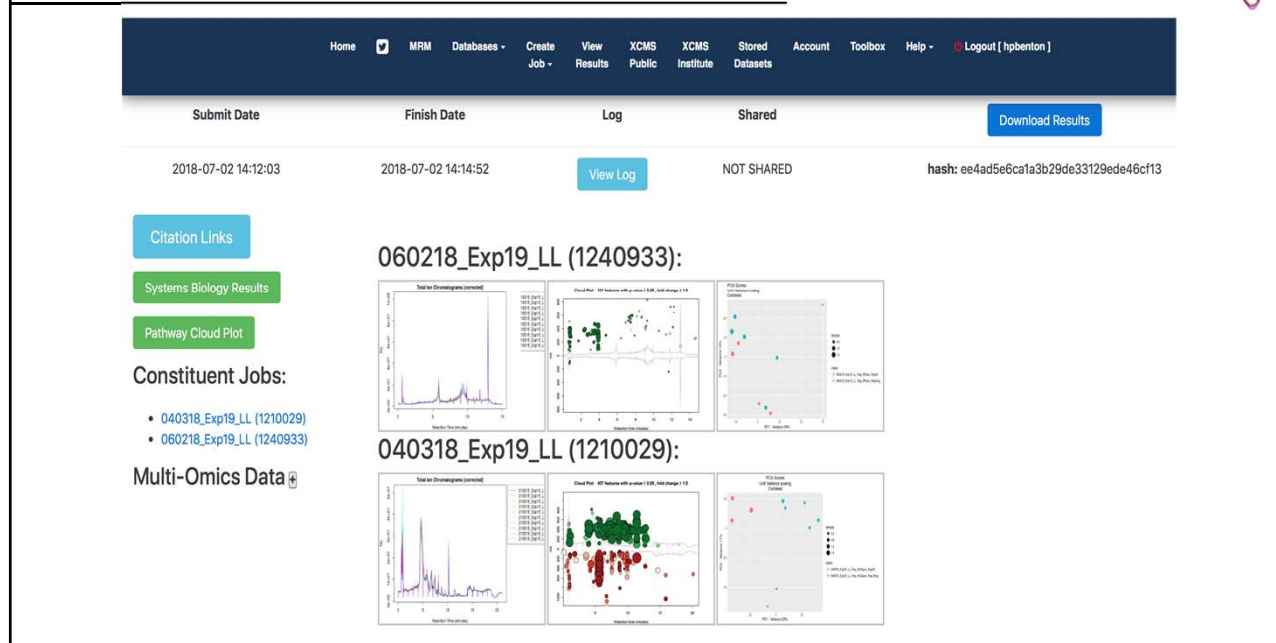


Multimodal metabolomics

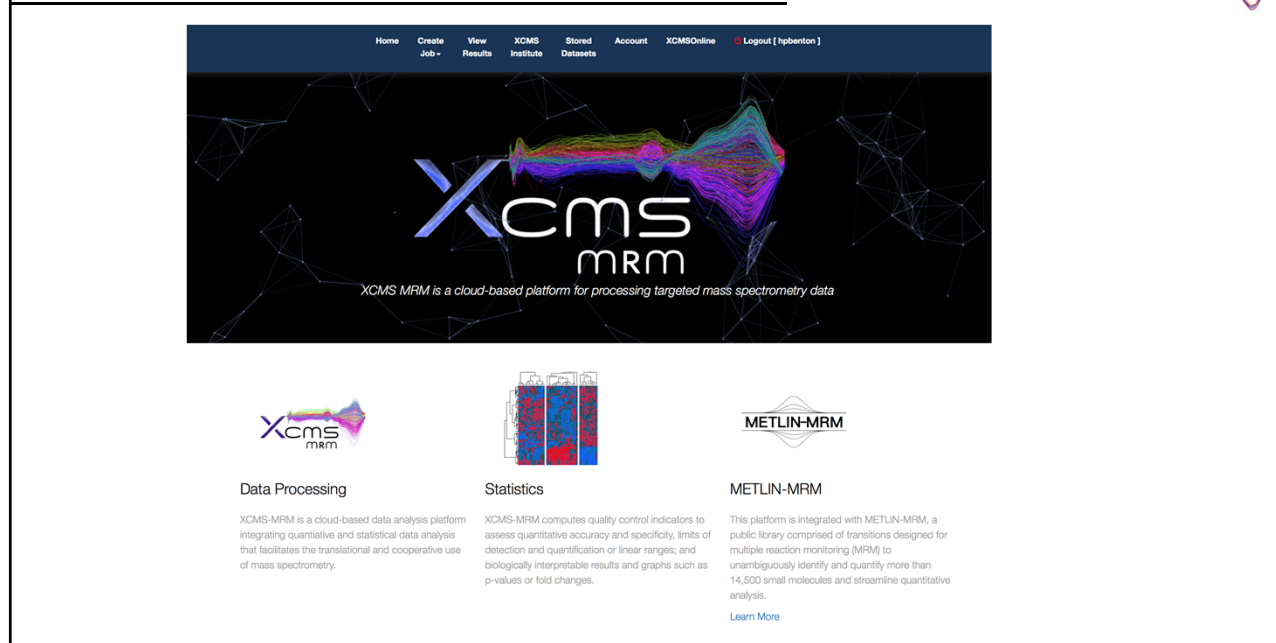
A. Multimodal Metabolomics Workflow



Multimodal metabolomics

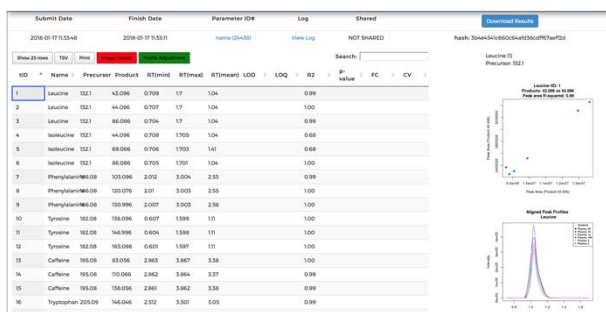


XCMS-MRM



XCMS-MRM

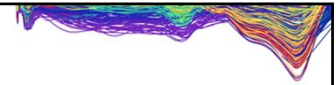
- XCMS – MRM – a central cloud based targeted analysis software
- With METLIN-mrm allows a standard for MRM analysis and optimization across multiple standards



Taking a step back

- We can automatically get to System level data quickly.
 - Where are the other dead time events?
- Sharing is caring : The future is sharing your data with others
- How can we make the data even better?

Thank you ! Questions ?



Prof. Gary
Siuzdak



The Scripps Research Institute



Aries
Aisporna



Duane
Rinehart