

XCMS Online

Metabolomics in the Clouds



H. Paul Benton

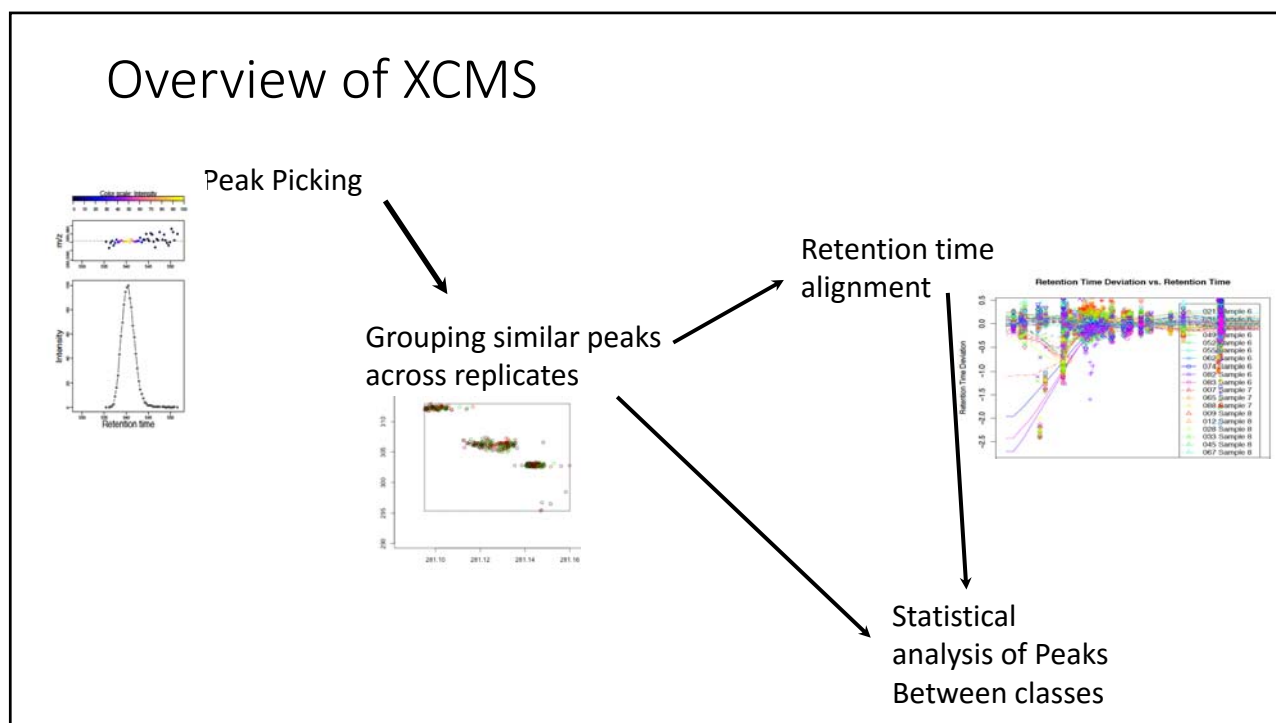
The Siuzdak Lab @ The Scripps Research Institute La Jolla, CA



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 13,500 users
 - Average 50 jobs a day
 - 75 Users logging in per day

Overview of XCMS



Peak detection choice

Peak Picking

matchedFilter

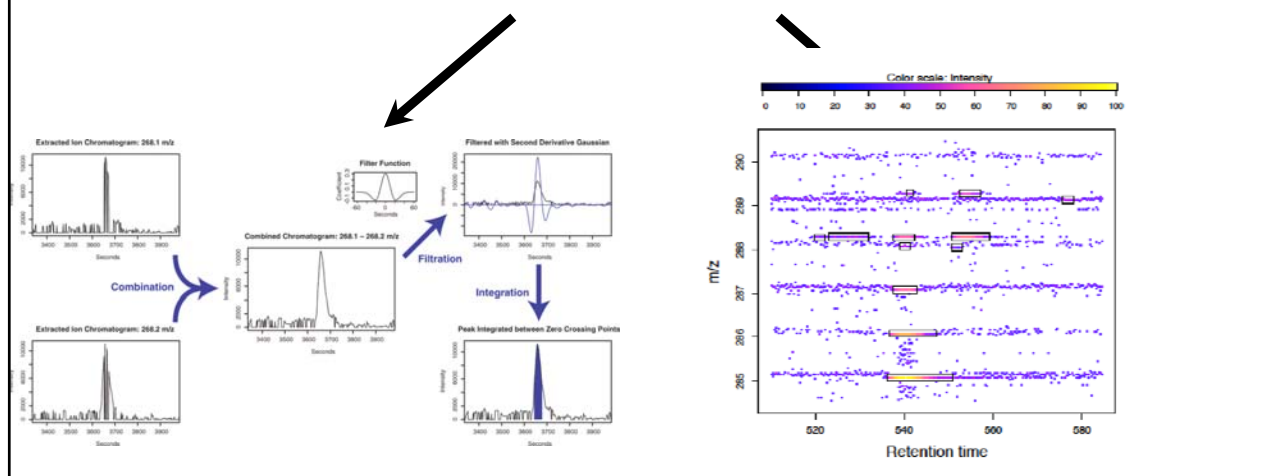
- Profile Data
- Low resolution data
- Original algorithm

centWave

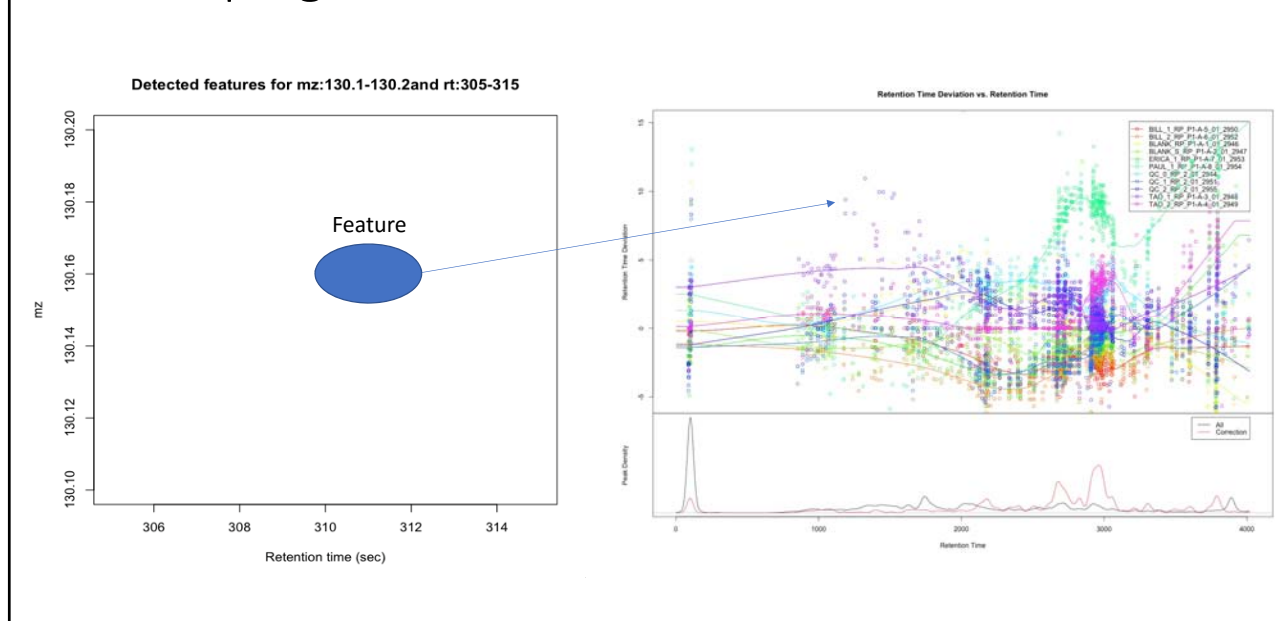
- Centroid data
- High resolution data
- Separately published algorithm

Peak detection choice

Peak Picking



Grouping and Retention time correction



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)

Home News Databases Create Job View Results XCMS Public XCMS Institute Stored Datasets Account Toolbox Help Logout [Hybridion]

XCMS

The original and most widely used metabolomic and lipidomic platform

Download on the 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 multigroup 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](#)

MetIn

MetIn was created in 2004 to facilitate metabolite identification and pathway analysis. MetIn includes 901,820 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 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 trusted, 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

View Results section

View Jobs

[Share Job\(s\)](#)
[Job Grouping](#)
[Resubmit Job\(s\)](#)
[Delete Job\(s\)](#)

Job Count: 12

Search Jobs [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"/>
<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)		<input type="checkbox"/>

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

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 19:58:53 - #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_stres (230089) *
- Salt_control (230090)

Total Ion Chromatograms (original)

PNG PDF

Retention Time Deviation vs. Retention Time

PNG PDF

Total Ion Chromatograms (corrected)

PNG PDF

Cloud Plot: 558 features with p-value < 0.01, fold change > 1.5

PNG PDF

Non-Metric Multidimensional Scaling

PNG PDF

PCA Scores

PNG PDF

v3.5.1

6

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

Quick Compound Search:

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

featureid	fold	pvalue	updown	mzmed	rtmed	maxint	dataset1_mear	dataset2_mear	isotope	adducts	peakgroup	usernotes
1	3.8	1.85209e-7	UP	412.2560	2.14	2.708	4.847	17.328		[M+H- ⁺ COOH]87		
2	3.8	4.35106e-4	UP	125.0190	34.42	5.091	26.240	90.061			41	
3	89.4	0.00003	DOWN	796.5530	2.30	3.179	11.282	109			80	
4	38.9	0.00004	DOWN	571.3829	2.00	16.769	133.168	3.420	[317]M-	[M-2H+Na]-55/91		
5	2.8	0.00004	DOWN	242.8751	36.67	1.399	10.848	3.920			42	
6	6.7	0.00006	DOWN	861.0270	21.81	2.484	19.610	2.912	[541]M+1-		24	
7	100.1	0.00007	DOWN	797.5553	2.30	2.228	6.908	0			60	
8	5.0	0.00014	DOWN	573.3806	2.01	2.139	13.481	2.875	[317]M+2-		91	
9	7.3	0.00017	DOWN	188.9401	36.22	11.058	327.350	44.735			202	
10	5.7	0.00019	DOWN	918.3967	1.94	1.203	3.620	916			145	
11	6.2	0.00021	DOWN	616.7667	32.04	1.793	2.901	453			110	
12	16.5	0.00021	DOWN	851.4037	13.21	1.117	3.105	153		[M+Cl]-816.43	18	
13	9.1	0.00026	DOWN	560.3820	2.20	1.060	4.034	426	[307]M+1-		31	
14	1.7	0.00027	UP	485.1368	57.89	2.144	4.078	7.008	[259]M-		87	
15	20.4	0.00028	DOWN	792.5330	1.92	6.85	2.816	121	[501]M+3-		145	
16	6.9	0.00037	DOWN	408.3014	1.95	1.823	8.891	1.251	[188]M+1-		145	
17	4.4	0.00040	UP	366.8748	37.00	969	1.393	6.174		[M+Cl]-331.90	219	
18	2.7	0.00046	UP	384.3187	2.80	8.114	3.999	8.930			210	
19	9.1	0.00047	DOWN	409.3305	2.44	367.425	1,190.430	130.244		[M+Cl]-374.35	25	
20	9.4	0.00047	DOWN	605.5123	1.90	1.316	7.703	821		[M+Cl]-770.54	15	
21	8.4	0.00048	DOWN	407.2884	1.95	6.881	31.079	3.718	[188]M-	[M+H-C8H10O2]	145	
22	9.4	0.00050	DOWN	791.5234	1.93	1.529	6.332	673	[501]M+2-		145	
23	5.8	0.00051	DOWN	901.8173	22.82	1.347	12.177	2.138		[M+H]-902.828	38	
24	6.1	0.00053	UP	633.4817	2.18	763	504	3,050		[2M-2H+K]-291	31	
25	5.6	0.00053	UP	415.9558	35.12	2.723	2.112	11.896		[M+Cl]-300.99	116	
26	5.1	0.00053	DOWN	388.1975	2.31	2.494	7.257	1,411	[171]M+1-		60	
27	8.4	0.00057	DOWN	410.3302	2.46	111.534	338.156	40.083	[188]M+1-		25	
28	6.8	0.00059	DOWN	971.6025	22.78	1.613	11.338	1,656	[604]M+1-		38	
29	13.8	0.00060	UP	650.1819	31.28	1.518	1.291	17.779		[M+H]-651.186	28	
30	28.3	0.00064	DOWN	409.3134	1.89	11.815	57.568	2,037	[187]M-		15	
31	9.5	0.00067	DOWN	236.8825	35.70	5.549	62.822	5,556		[M+H-COOH]2	107	

[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](#) [Shrink](#)

Main Panel Advanced

p-value: 1

fold change: 2807.731

[Regenerate Cloud Plot](#)

EIC_ABBR Box and Whisker Spectrum

Bubble Size Multiplier:

[Download Cloud Plot Manual](#)

Welcome to the Cloud Plot x

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.

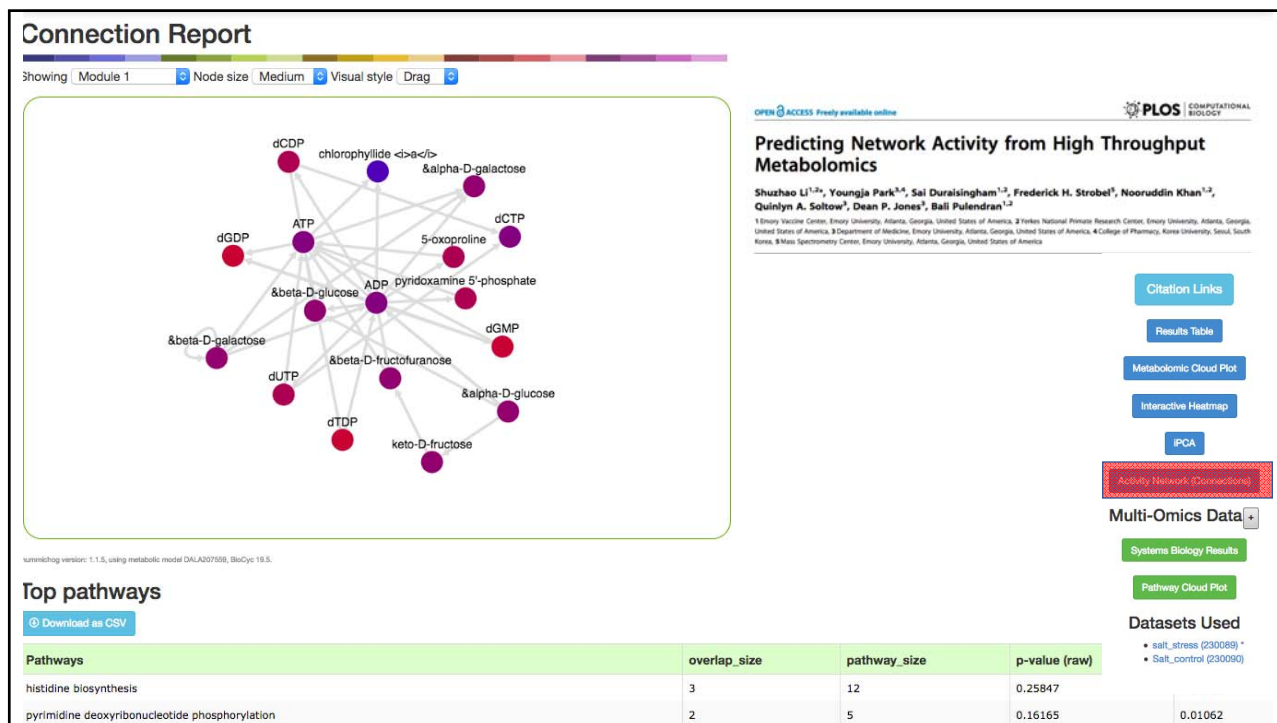
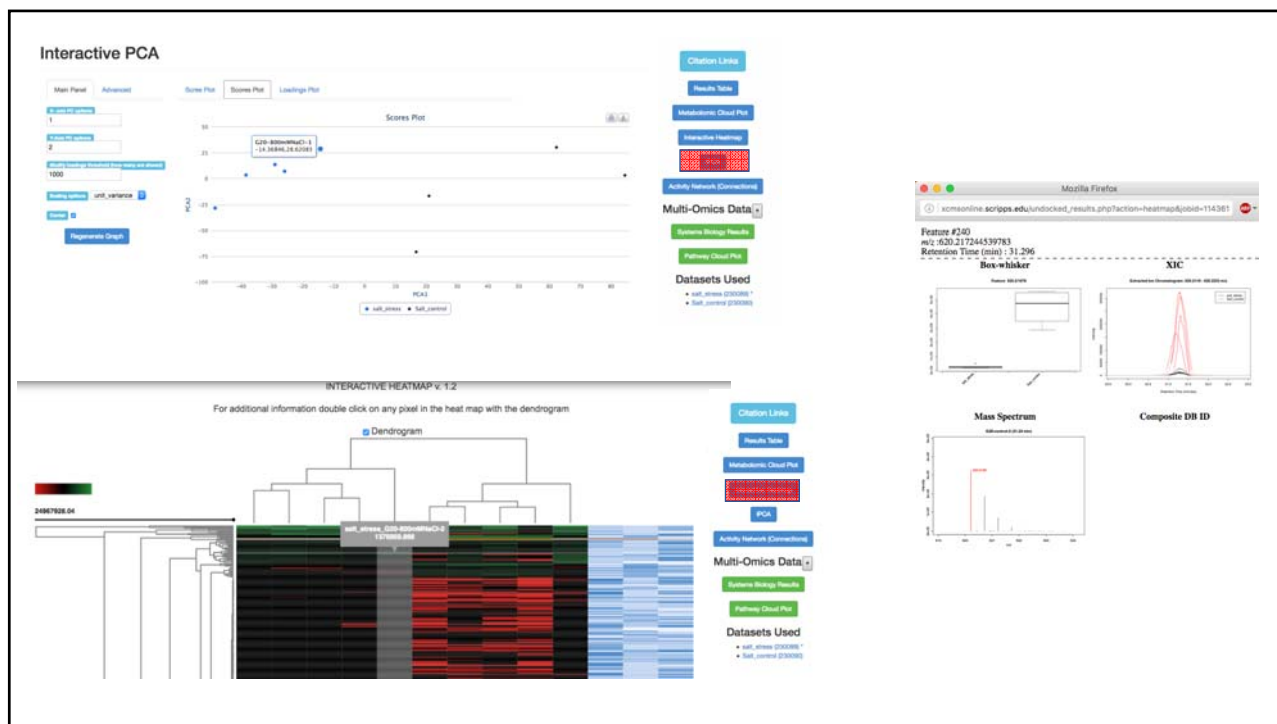
Toggle Upregulated
 Toggle Downregulated

p-Value: 0-0.01 | fold change: 1.5 - 2807.731 | m/z Range of 0 - 1099 | Retention Range of 0 - 45
 Radius Scale: Fold Change

[Table View](#)

- 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)



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
235.082800		M+CH3COO[-]	0.001000	
5-OXOPROLINE	5-oxoproline	8	129.0426	
	149.009700	M+Na-2H[-]	-0.000300	
	128.035900	M-H[-]	0.000600	
	164.011900	M+Cl[-]	0.000400	
	128.035800	M-H[-]	0.000500	
CHLOROPHYLLIDE-A	chlorophyllide a	6	614.238	
	613.230100	M-H[-]	-0.000600	
	659.238500	M+HCOO[-]	0.002900	
CPD-1130	3-ethylmalate	6	162.0528	
	161.046300	M-H[-]	0.000800	
	197.021200	M+Cl[-]	-0.000500	
UDP-MANNACA	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 | Search:

Pathway	Overlapping genes	All genes*	Overlapping proteins	All proteins*	Overlapping putative metabolites ¹	All metabolites*	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

[Citation Links](#)

[Results Table](#)

[Metabolomic Cloud Plot](#)

[Interactive Heatmap](#)

[IPCA](#)

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

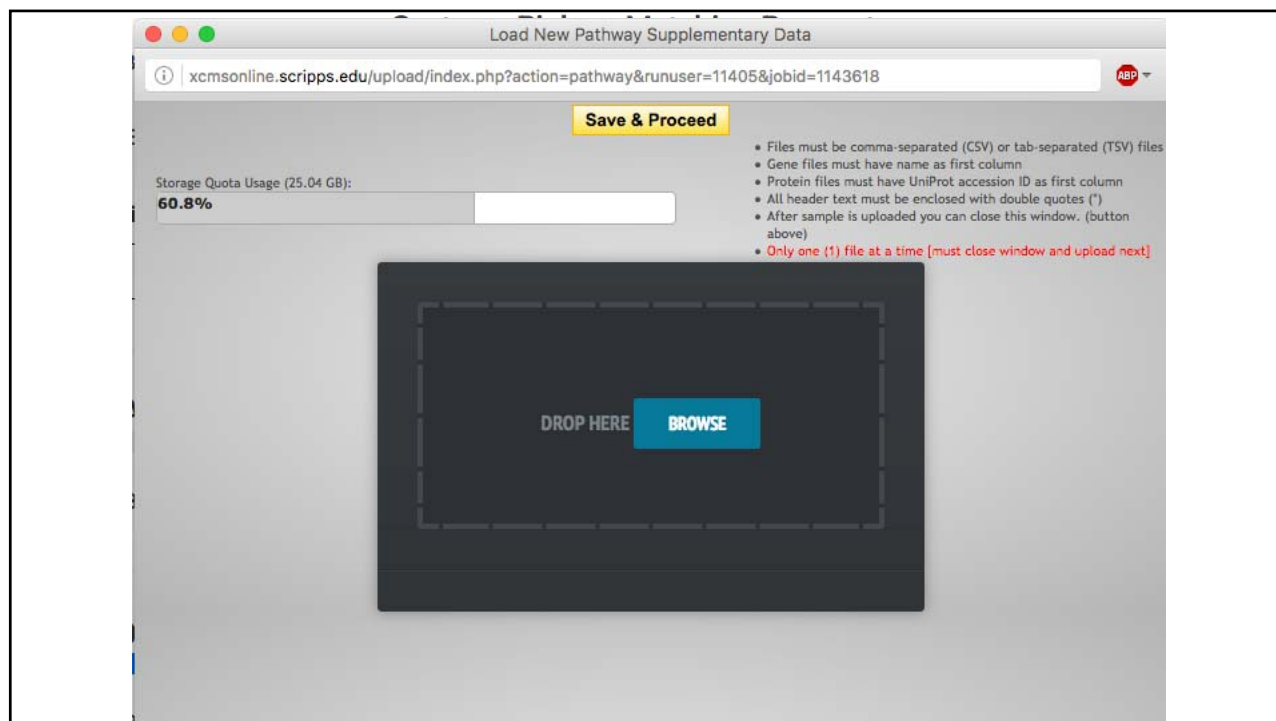
Multi-Omics Data +

[Systems Biology Results](#)

[Pathway Cloud Plot](#)

Datasets Used

- salt_stress (230089) *
- Salt_control (230090)



Systems Biology Matching Parameters

JOB ID:

JOB NAME:

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	<input type="button" value="View Results"/>	<input type="button" value="X"/>

Run matching subjob

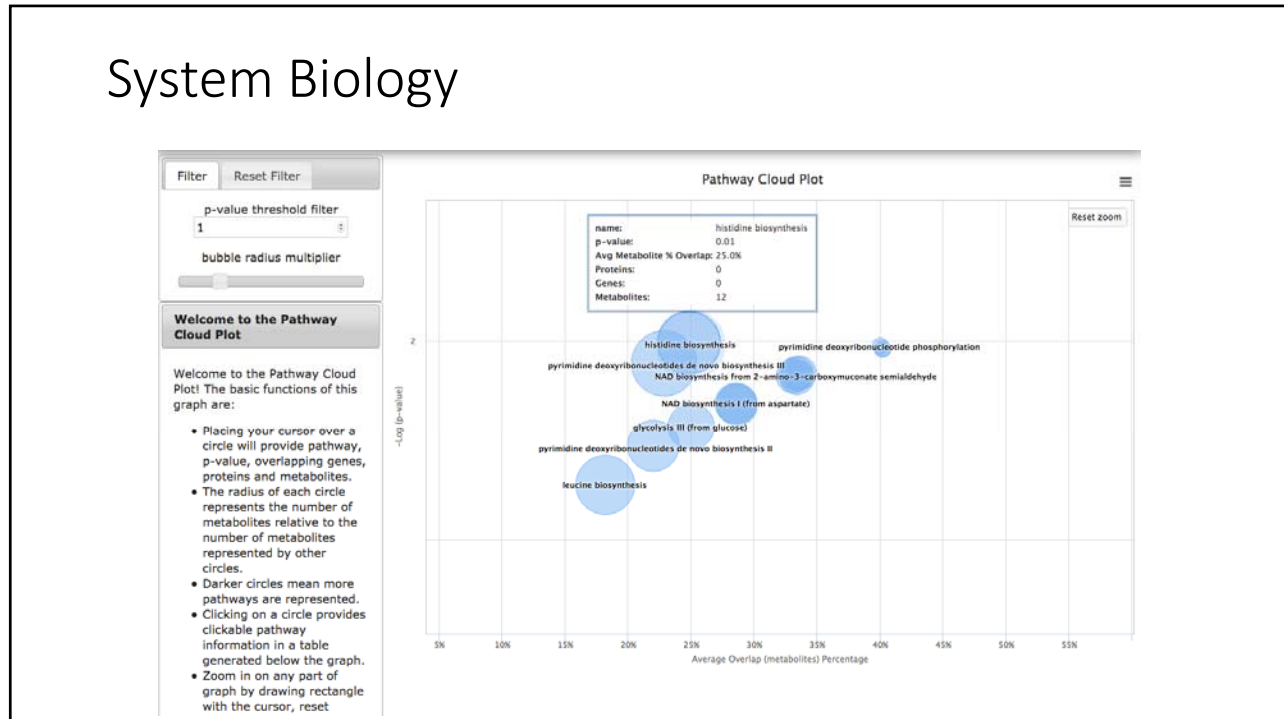
MATCHING PROGRESS (1%)

SUBJOB ID:

POPULATE TABLE PROGRESS (0%)

SUBJOB ID:

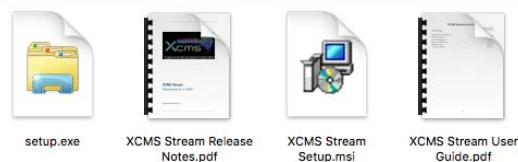
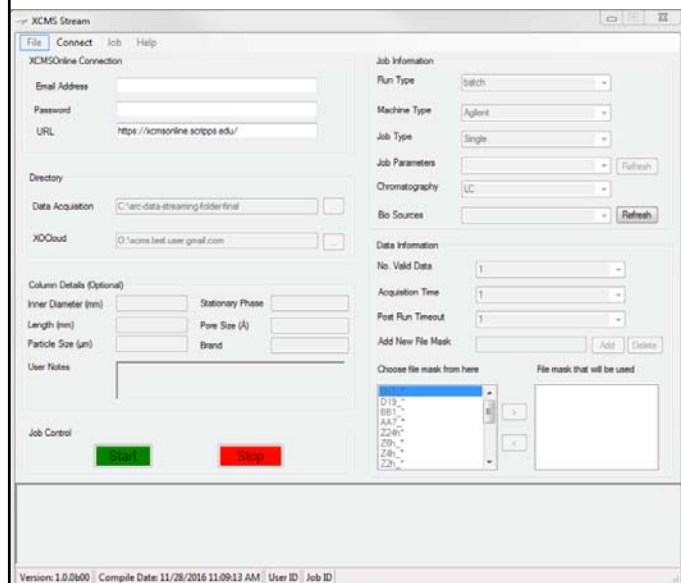
System Biology



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?

Steaming – upload to XCMS Online



XCMS Online Stream uploads data and starts the jobs on XCMS Online automatically. This highly reduces the dead time between instrument acquisition and can also be used in offline mode.

http://xcmsonline.scripps.edu/xcmsonline/XCMS_Stream-v1.0.0b00.zip

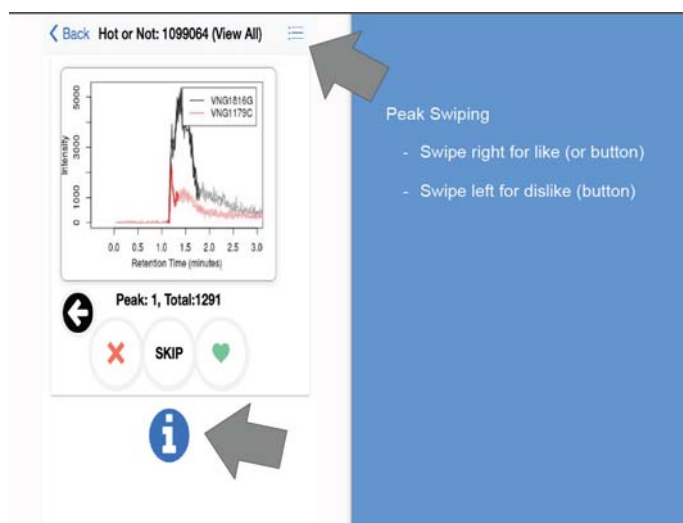
Job Sharing

View Public Job Shares

Show 10 entries Search:

Status	ID	Job Name	Author(s)	Publication	Notes
VIEW	1009445	r.jansen_2013-11-13_03:46:50	Jansen et al.	ABCC6 prevents ectopic mineralization seen in pseudoxanthoma elasticum by inducing cellular nucleotide release, PNAS 2013 110(50), 20206-11	Culture medium of HEK293/control vs HEK293/human ABCC6 cells
VIEW	1009444	r.jansen_2013-11-13_03:46:21	Jansen et al.	ABCC6 prevents ectopic mineralization seen in pseudoxanthoma elasticum by inducing cellular nucleotide release, PNAS 2013 110(50), 20206-11	Plasma of wildtype mice vs ABCC6 knockout mice
VIEW	128681	RPLC_SUP-T1 parental vs. Ramos parental			
VIEW	1027173	huangxi_2014-06-27_22:43:31	David G. Cotter, Baris Ercal, Xiaojing Huang, Jamison M. Leid, D. André d'Avignon, Mark J. Graham, Dennis J. Dietzen, Elizabeth M. Brunt, Gary J. Patti, and Peter A. Crawford	(currently) in revision JCI 76388-RG-RV-2	ASO-treated mouse liver, ex vivo perfusions
VIEW	1017901	Brain regions_HILIC	Julijana Ivanisevic, Adrian Epstein, Michael E. Kurczyk, H. Paul Benton, Winnie Uritboonthai, Howard S. Fox, Michael D. Boska, Howard E. Gendelman and Gary Siuzdak	Brain Region Mapping using Global Metabolomics	
VIEW	1004148	RPLC_Raji Empty Vector vs. Raji luciferase Puro	Johnson CH, Fisher TS, Hoang LT, Felding BH, Siuzdak G, O'Brien PJ.	Metabolomics. 2014 Jun 1;110(3):354-360.	lymphoblastic leukemia cell lines
VIEW	1004141	Fed_Raji Empty Vector vs. Raji luciferase Puro	Johnson CH, Fisher TS, Hoang LT, Felding BH, Siuzdak G, O'Brien PJ.	Metabolomics. 2014 Jun 1;110(3):354-360.	lymphoblastic leukemia cell lines

EIC hot or not





XCMS Developments

- Speed: Faster jobs and XCMS Online that can handle multi 100Gb's data files.
- Sub-jobs : Allows for custom PCA, PLS-DA, Bayesian Stats on selected features, custom normalisation per user
- System Biology workflow : Further developments including signaling networks
- Targeted MS studies using both full scan MS1 and triple Quad data (MRM).

Thank you ! Questions ?



Prof. Gary
Siuzdak



The Scripps Research Institute



Aries
Aisporna



Duane
Rinehart