The background features three overlapping circles in a medium blue color, arranged horizontally. The circles overlap in the center, creating a darker blue area. The overall background is a dark gray color.

OmicNet Tutorial: Omics Network Starting from MS Peaks

Computer Requirement

- Modern browser supporting **WebGL**
- Chrome 50+, Firefox 47+, Safari 10.1+ and Edge 12+
- Please make sure WebGL is enabled in your browser
 - Please consult this web page to verify: <https://get.webgl.org/>
- If not enabled, please consult our **FAQ** page for instructions
- For best performance and visualization, use:
- Latest version of **Google Chrome**
- A modern computer with at least 4GB of physical RAM
- A 15-inch screen or bigger (larger is better)
- Retina Display is supported

Motivation

- 1. Background :** Metabolomics based on Liquid Chromatography coupled with Mass spectrometer (LC-MS) has been extensively used for global detection on whole metabolome of a certain system;
- 2. Bottleneck:** Annotation of MS peaks usually laborious and require commercial standards for chemical identification;
- 3. Aim:** Comprehensively annotating the whole metabolomics peak set without tedious compound identification;
- 4. Approach:** Using biochemical/abiotic transformation network-based global annotation.

Data format for uploading

- **Uploading data should be a peak list with four required columns.**
- 1st column: m/z values;
- 2nd column: RT (retention time);
- 3rd column: intensity values of the peaks;
- 4th column: statistical p values of the peak intensities between different groups.

	A	B	C	D	
1	Mz	Rt	Int	Pvalue	
2	85.065	0.41	109023.1	0.486	
3	85.0843	2.79	2002051	0.197	
4	86.0602	0.62	623104.3	0.016	
5	86.0602	2.15	2304644	0.003	
6	86.0603	0.52	878208.6	0	
7	86.0966	0.98	1.14E+08	0.22	
8	86.0966	1.57	90493483	0.096	
9	86.0966	1.38	95475583	0.124	
10	86.0966	1.13	2.1E+08	0.053	
11	86.0966	1.87	1.92E+08	0	
12	86.3224	1.88	61372.2	0.029	
13	86.4142	1.66	74522.7	0	
14	86.9088	1.3	1365505	0.003	
15	86.9089	1.99	298156.1	0.754	
16	87.0555	2.09	1422187	0.114	
17	87.0807	0.4	16051646	0.092	
18	87.1	1.57	6070507	0.167	
19	87.1	1.37	5840515	0.092	
20	87.1001	0.99	8257790	0	
21	87.1001	1.87	11949551	0.063	
22	87.1001	1.14	11987004	0.038	
23	88.0396	1.97	2594988	0.117	
24	88.0634	2.69	11900171	0.087	
25	88.084	0.41	1087337	0.413	
26	88.5093	1.51	11359624	0.338	
27	88.5094	0.41	730502.2	0.83	

Example

Parameters for peak preprocessing

Multi-omics Integration via Biological Networks

Objective Click on a panel below to start

Explore networks in 2D or 3D space		A Graph File			
Annotate SNPs, taxa, or LC-MS peaks for network analysis		SNPs	Microbial Taxa	LC-MS Peaks	
Network analysis of one or more list(s) of molecules	Genes	Proteins	Transcription Factors	miRNAs	Metabolites

[Proceed](#) [Reset](#)

Click this module (LC-MS Peaks)

below

Upload and process peak list file

Data file  No file chosen

Ion Mode: 

Mass Tolerance (ppm):  (editable)

Specify organism: 

Use example data None [Malaria \(ESI+\)](#)

[Submit](#)

[Cancel](#)

From the uploading panel (as shown in the left side), user need to specify the Ion mode (polarity of ESI), mass tolerance and organism. Click 'Submit' to upload your data. Then click "Proceed" button from the home page to go the next.

Try to select the example for practice!

Database Selection

Database Selection

Databases are organized under different tabs. Please choose proper database(s) for network creation based on your analysis objectives. You can create multiple types of networks for one input types. They will be merged and customized in the next page

Metabolite-protein **Peak-metabolite** **Metabolite-metabolite**

[KEGG](#) KEGG compound database (16,908 compound).

[PubChem](#) PubChemLite Biopathway database (99,578 compound)

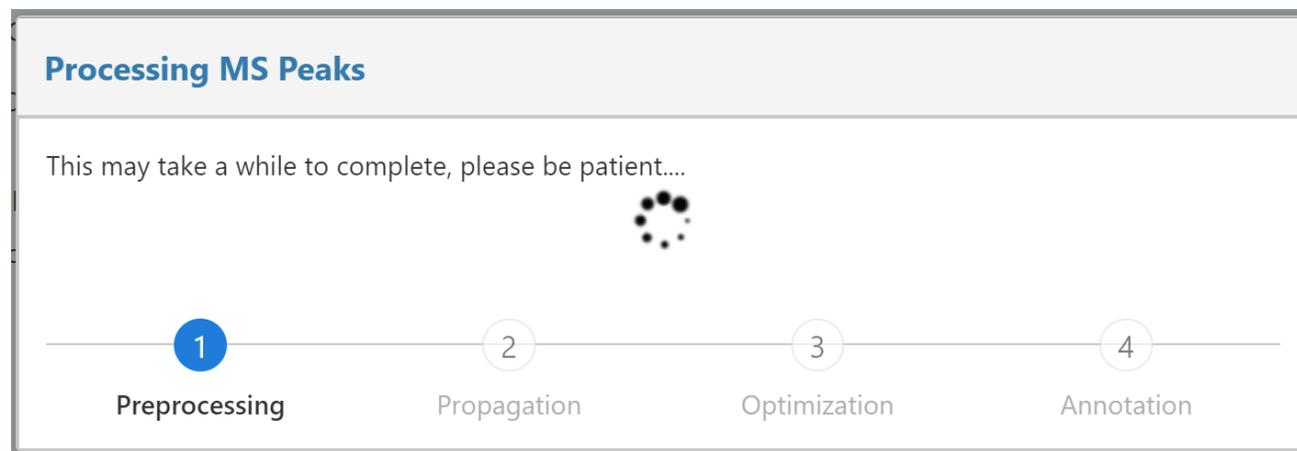
[HMDB](#) HMDB database (114,014 compounds).

Mapping from mass spectral (MS) peaks to (putative) metabolites and their corresponding chemical artifacts (adducts, isotopes, heterodimer, etc.). The network is established based on the bio-transformative/abiotic relationships among all MS peaks. Hover on help icon for more info. 

[▶ Submit](#)

There are three different compound databases (KEGG, PubChem Lite BioPathway and HMDB) provided for compound annotation. Different databases have different sizes. The smaller of the size, the faster annotation/processing will be.

Data Processing Steps



MS peak processing mainly includes 4 steps:

1. Processing: Seed compounds identification and structure base generation;
2. Propagation: Bio-transformative/abiotic propagation to cover the metabolome;
3. Network Construction: Optimal network construction with integer linear programming;
4. Annotation: Data organization and MS peak results output.

Peak to metabolite Network construction

- After uploading the peak list, the annotation will be executed automatically. Once the annotation and processing finished, user will be able to view the summary of the constructed network.
- Click “Proceed” to get the details of all subnetworks and click “Proceed” again to view the networks in 2D or 3D.

Network Results

Each network is created independently by searching input list against a selected database, which usually will form several (isolated) subnetworks. The **Sizes** are for those subnetworks combined together.

Input Type	Network Type	Sizes (node# - edge# - query#)	Download (edge list)	Delete
LC-MS peak	Peak-metabolite	260 - 371 - 128	Download	Delete

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Multi-omics Network Building

If more than one network was generated in the previous page, they are merged together to form multi-omics network through shared nodes. In some cases, the result will contain a larger subnetwork containing most of queries, and several smaller subnetworks containing one or a few queries. These subnetworks will be available for visual analysis in the next page.

If the network is too large, it is recommended to trim the network to a smaller size that is suitable for visual analytics (less than 2000 nodes), you can use network tools located on the left hand side for trimming and filtering.

Networks	Sizes (node# - edge# - query#)	Topology	Download (edge list)
subnetwork1	80 - 153 - 73	Details	Download
subnetwork2	51 - 90 - 4	Details	Download
subnetwork3	20 - 23 - 2	Details	Download
subnetwork4	16 - 27 - 2	Details	Download
subnetwork5	15 - 20 - 14	Details	Download
subnetwork6	8 - 8 - 1	Details	Download
subnetwork7	7 - 7 - 1	Details	Download
subnetwork8	6 - 5 - 1	Details	Download
subnetwork9	5 - 4 - 1	Details	Download
subnetwork10	5 - 4 - 1	Details	Download

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Metabolic reaction network expansion

- The peak-metabolite network can be extended according to the metabolic reactions from “Metabolite-metabolite” tab.
- Herein, user could select organism specific KEGG database or other metabolic databases.
- Click “Submit” to expand the network.

Database Selection

Databases are organized under different tabs. Please choose proper database(s) for network creation based on your analysis objectives. You can create multiple types of networks for one input types. They will be merged and customized in the next page

Metabolite-protein Peak-metabolite **Metabolite-metabolite**

- [KEGG \(organism-specific\)](#) Metabolite-metabolite interaction (metabolic reaction) data from KEGG databases (updated on 01/04/2022)
- [KEGG Generic](#) Non-organism specific Metabolites from KEGG metabolic network (updated on 01/04/2022)
- [Recon3](#) High-quality genome-scale metabolic reaction reconstruction (human) database (updated on 01/04/2022)
- [AGORA](#) High-quality genome-scale metabolic reaction reconstruction (microbial) database (updated on 01/04/2022)
- [EMBL](#) High-quality genome-scale metabolic reaction reconstruction (microbial) database (updated on 01/04/2022)

[▶ Submit](#)

Network Results

Each network is created independently by searching input list against a selected database, which usually will form several (isolated) subnetworks. The **Sizes** are for those subnetworks combined together.

Input Type	Network Type	Sizes (node# - edge# - query#)	Download (edge list)	Delete
LC-MS peak	Peak-metabolite	260 - 371 - 128	Download	Delete
LC-MS peak	Metabolite-metabolite	114 - 110 - 21	Download	Delete

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Metabolite-enzyme network construction

- The peak-metabolite network can be extended according to the metabolite-enzyme relationship from “Metabolite-protein” tab.
- Herein, user could select multiple databases and Click “Submit” to expand the network.

Database Selection

Databases are organized under different tabs. Please choose proper database(s) for network creation based on your analysis objectives. You can create multiple types of networks for one input types. They will be merged and customized in the next page

Metabolite-protein **Peak-metabolite** **Metabolite-metabolite**

- [KEGG \(Organism-specific\)](#) Metabolite-protein interaction data based on all KEGG reactions (updated on 01/04/2022)
- [Recon3](#) High-quality genome-scale metabolic reconstruction (human) (updated on 01/04/2022)
- [KEGG Generic](#) Non-organism specific metabolic reactions from KEGG metabolic network (updated on 01/04/2022)
- [AGORA](#) Agora based microbial metabolic reactions (updated on 01/12/2022)
- [EMBL](#) EMBL GEMs based microbial metabolic reactions (updated on 01/12/2022)

[▶ Submit](#)

Network Results

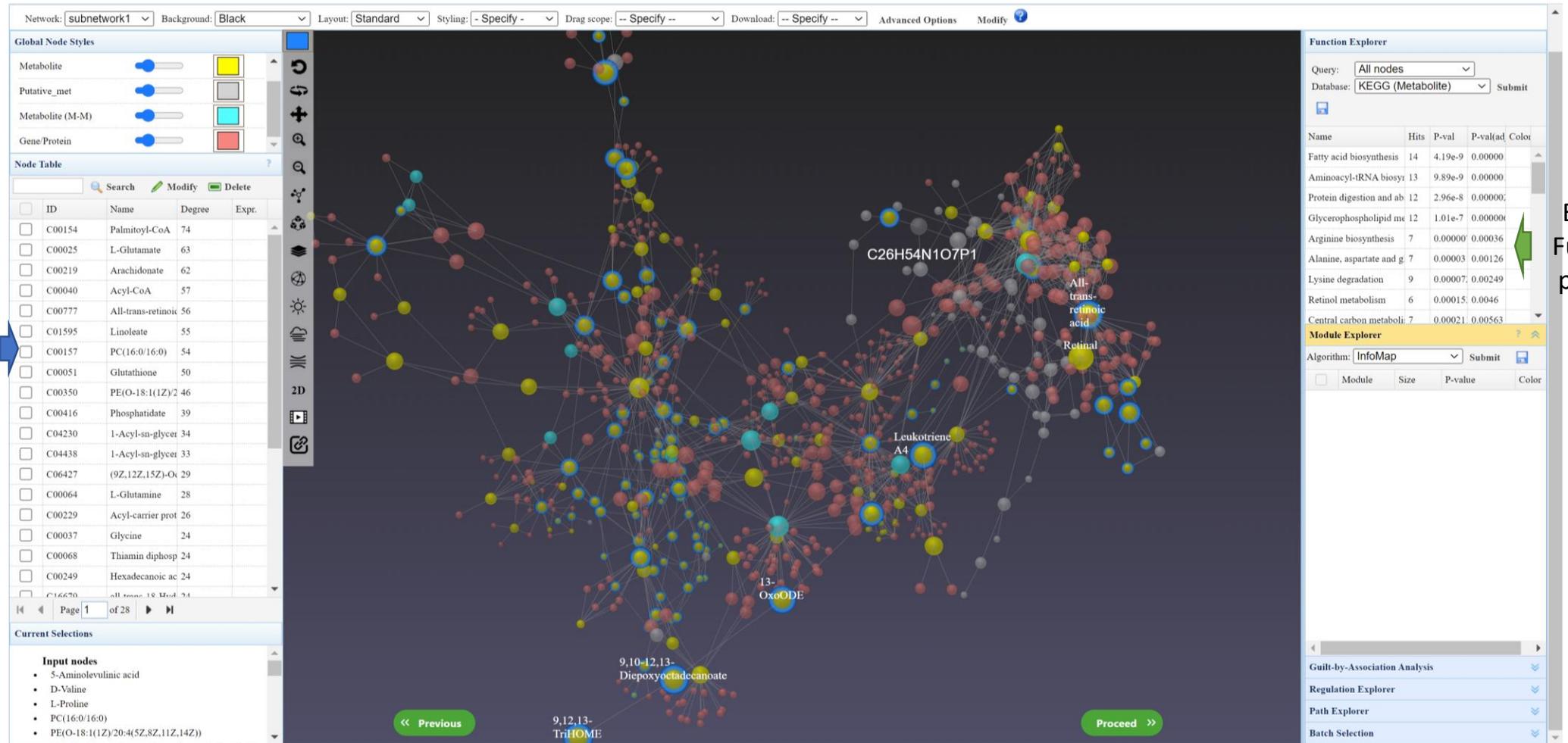
Each network is created independently by searching input list against a selected database, which usually will form several (isolated) subnetworks. The **Sizes** are for those subnetworks combined together.

Input Type	Network Type	Sizes (node# - edge# - query#)	Download (edge list)	Delete
LC-MS peak	Peak-metabolite	260 - 371 - 128	Download	Delete
LC-MS peak	Metabolite-metabolite	114 - 110 - 21	Download	Delete
LC-MS peak	Metabolite-protein	677 - 1287 - 27	Download	Delete

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Results of Omics Network



Enriched Functional pathways

Compound and genes (proteins) of the whole network

Constructed network

Result Explanation

- The MS peaks from LC-MS based metabolomics usually consists of many chemical artifacts, and as a result, only a small percentage of the MS matches to compounds;
- “Peak-metabolite” module allows to show the peak annotation network from NetID algorithms, with 20~90% of all peaks annotated as a certain chemical component;
- “Metabolite-metabolite” enhances the connection of the annotated metabolomics data by leveraging the metabolic reaction from knowledgebase (KEGG et al);
- “Metabolite-protein” further adds an extra layer to show the enzyme component of the corresponding metabolic network;
- In brief, the integration results originating from MS peaks intuitively display the (potential) complicated interaction within a metabolism-related system.

The End
