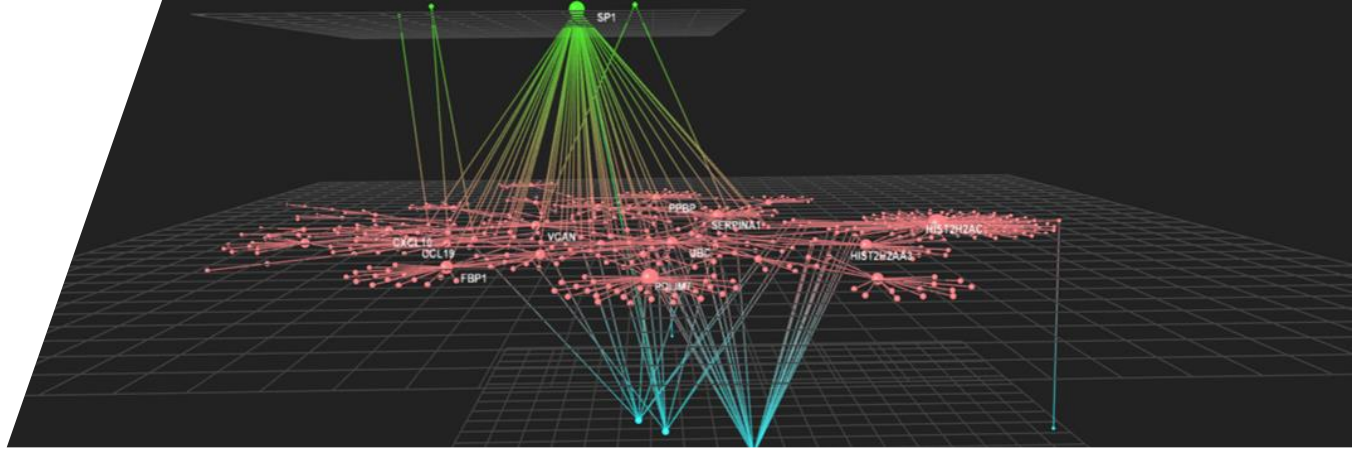
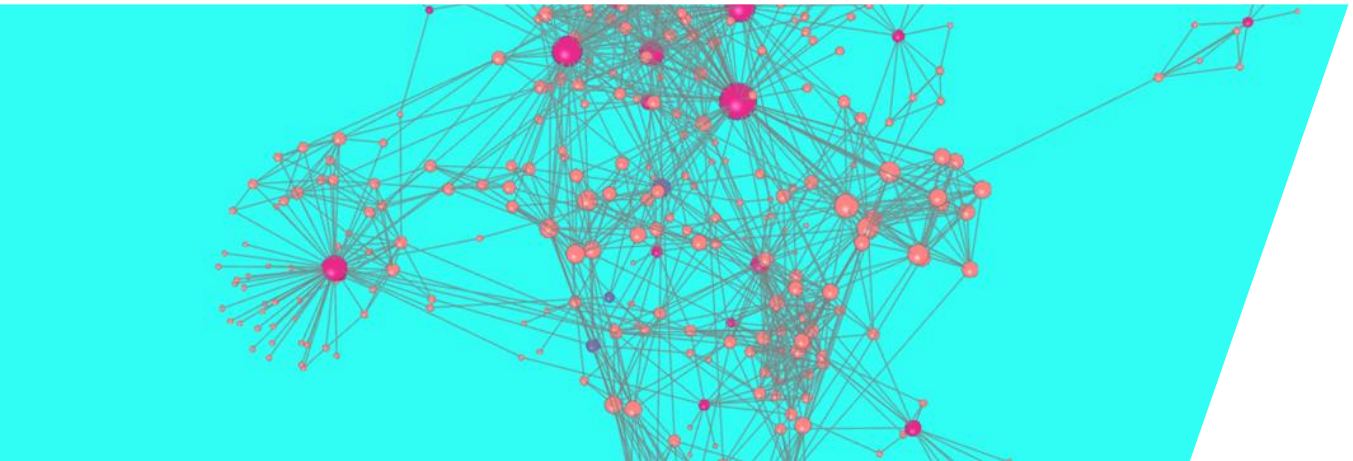


OmicsNet

---a web-based 3D visual analytics tool for biological networks

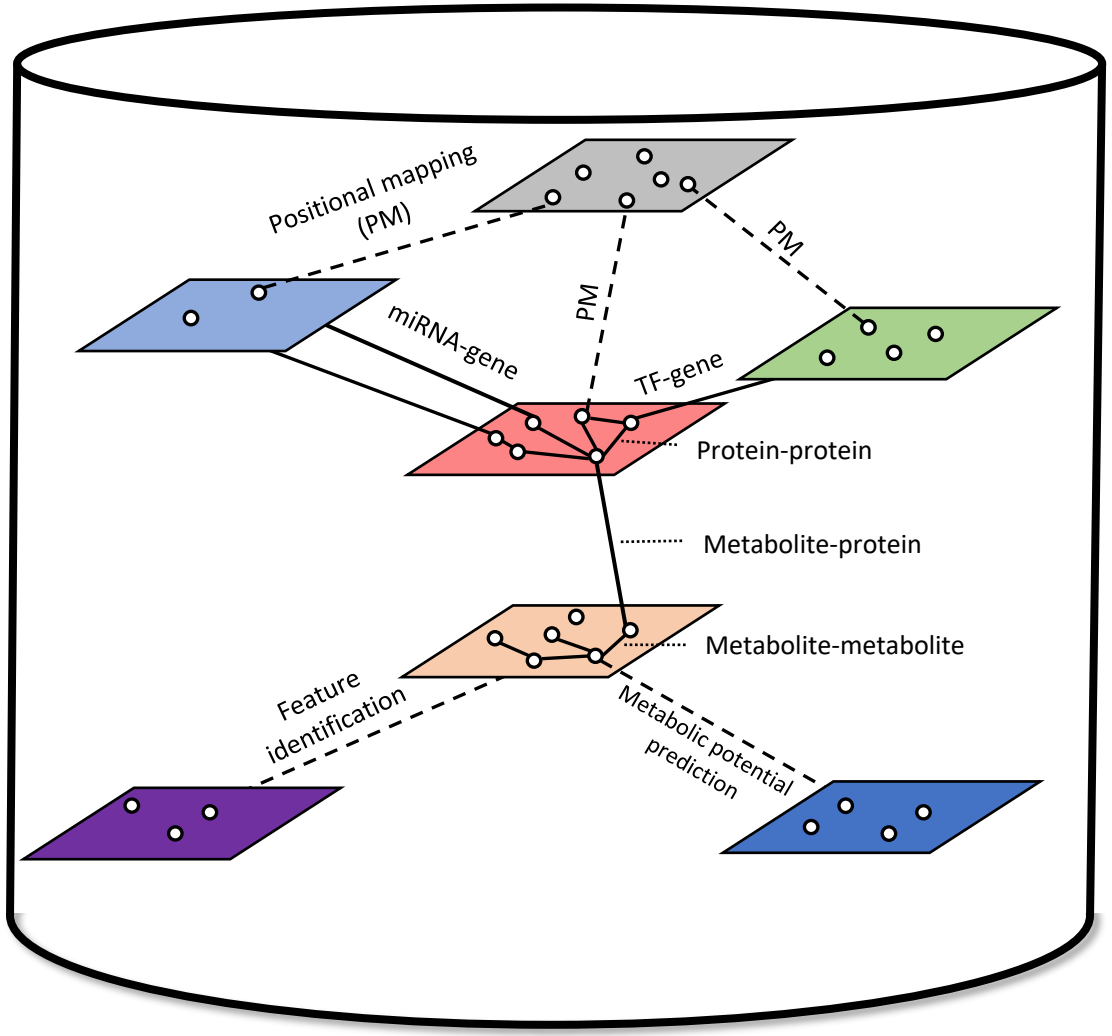


Requirement

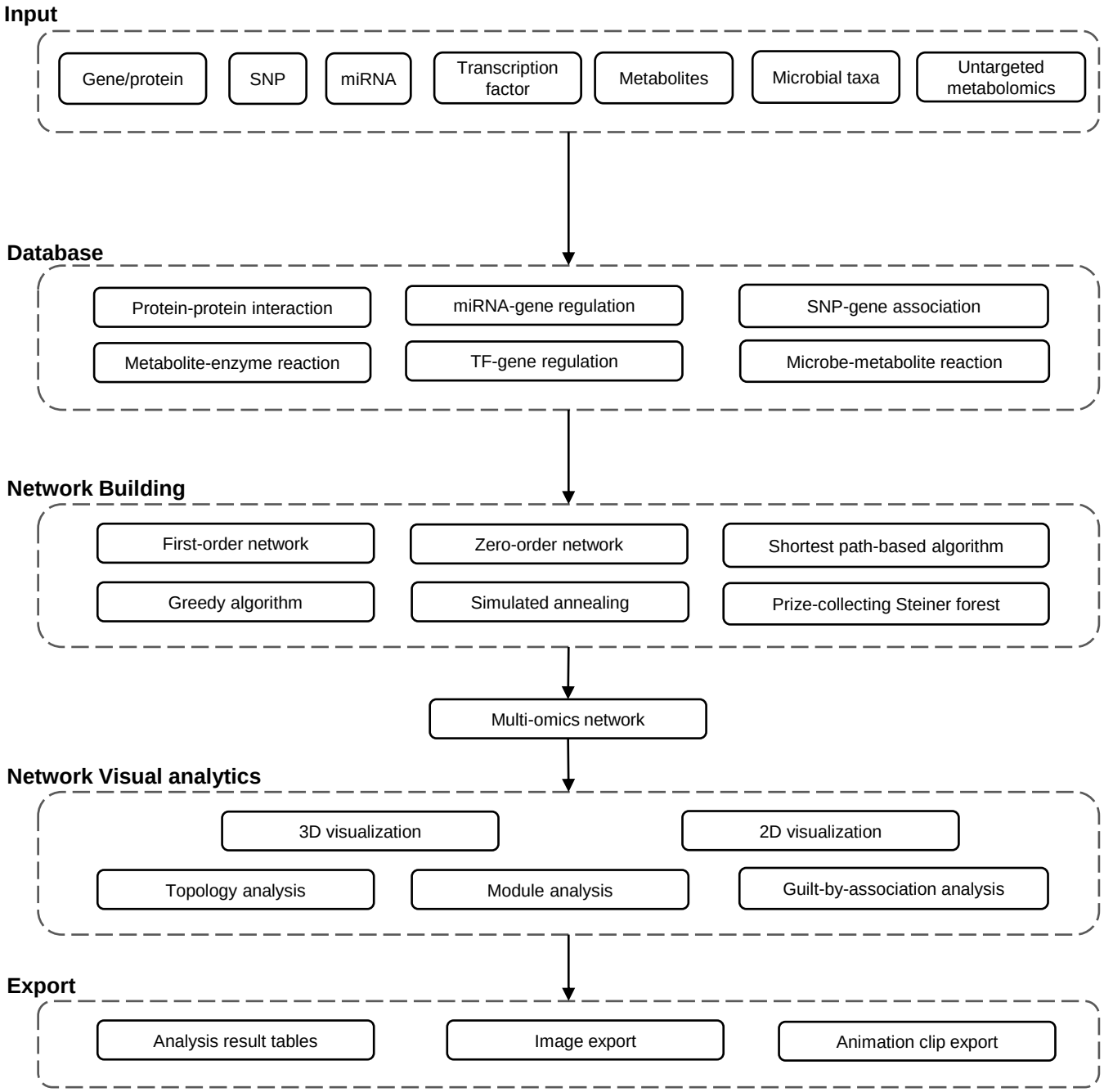
- Modern browser supporting **WebGL**
  - Chrome 50+, Firefox 47+, Safari 10.1+ and Edge 12+
- Please make sure WebGL is enabled in your browser
  - Please consult this web page to verify: https://get.webgl.org/
  - If not enabled, please consult our **FAQ** page for instructions
- For best performance 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

Overview

- Goal: Integration of different omics data in the current molecular interaction knowledge framework and visualization using 3D and 2D network.
  - Conventional molecular interaction networks
    - Protein-protein interaction
    - TF-gene regulation
    - miRNA-gene regulation
    - Metabolic reactions
  - Link untargeted MS peaks, SNPs and microbial taxa to knowledge framework
- Build composite network encompassing more than one interaction type

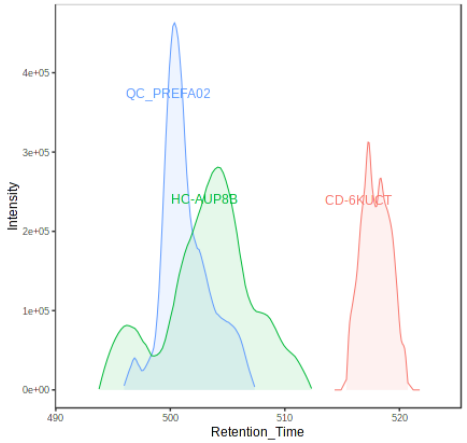


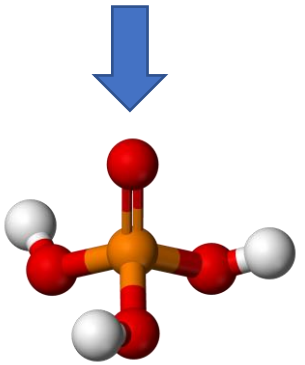
Workflow


Input
Gene/protein
SNP
miRNA
Transcription factor
Metabolites
Microbial taxa
Untargeted metabolomics
Database
Protein-protein interaction
miRNA-gene regulation
SNP-gene association
Metabolite-enzyme reaction
TF-gene regulation
Microbe-metabolite reaction
Network Building
First-order network
Zero-order network
Shortest path-based algorithm
Greedy algorithm
Simulated annealing
Prize-collecting Steiner forest
Multi-omics network
Network Visual analytics
3D visualization
2D visualization
Topology analysis
Module analysis
Guilt-by-association analysis
Export
Analysis result tables
Image export
Animation clip export

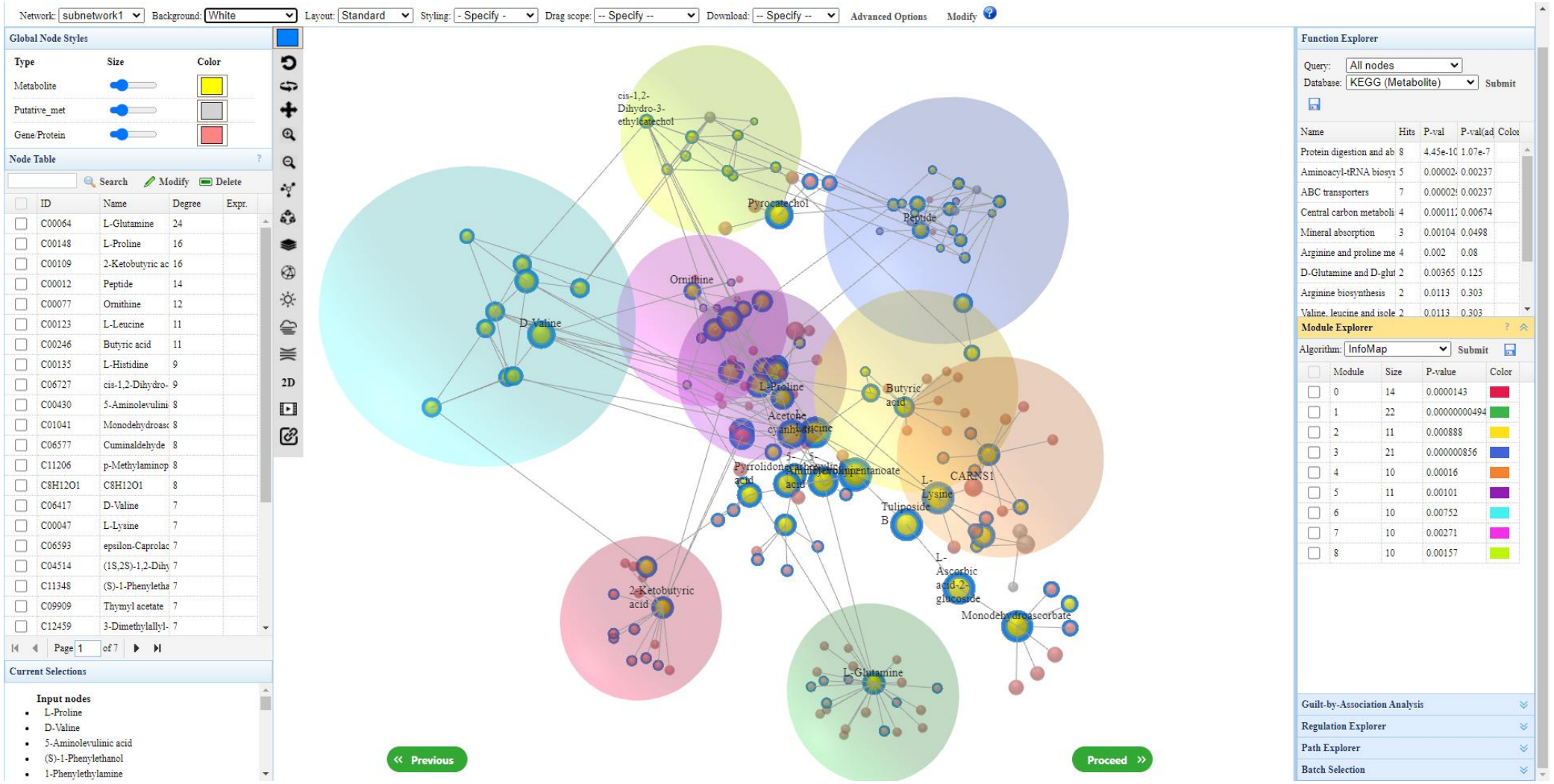
New features

- Integrate three new omics type in the molecular interaction framework
  - Use network optimization approach based from NetID algorithm to annotate metabolites from untargeted MS peaks
  - Use genome-scale metabolic models to predict metabolic potential
  - Link single nucleotide polymorphism (SNP) to genes using position-based mapping
- Support metabolite-metabolite network in the context of metabolic reactions.
- Heatmap visualization of metabolic potential of microbial taxa.
- Network-based guilt-by-association analysis using Random Walk with Restart (RWR) algorithm
- New 3D layout and alternative 2D network visualization



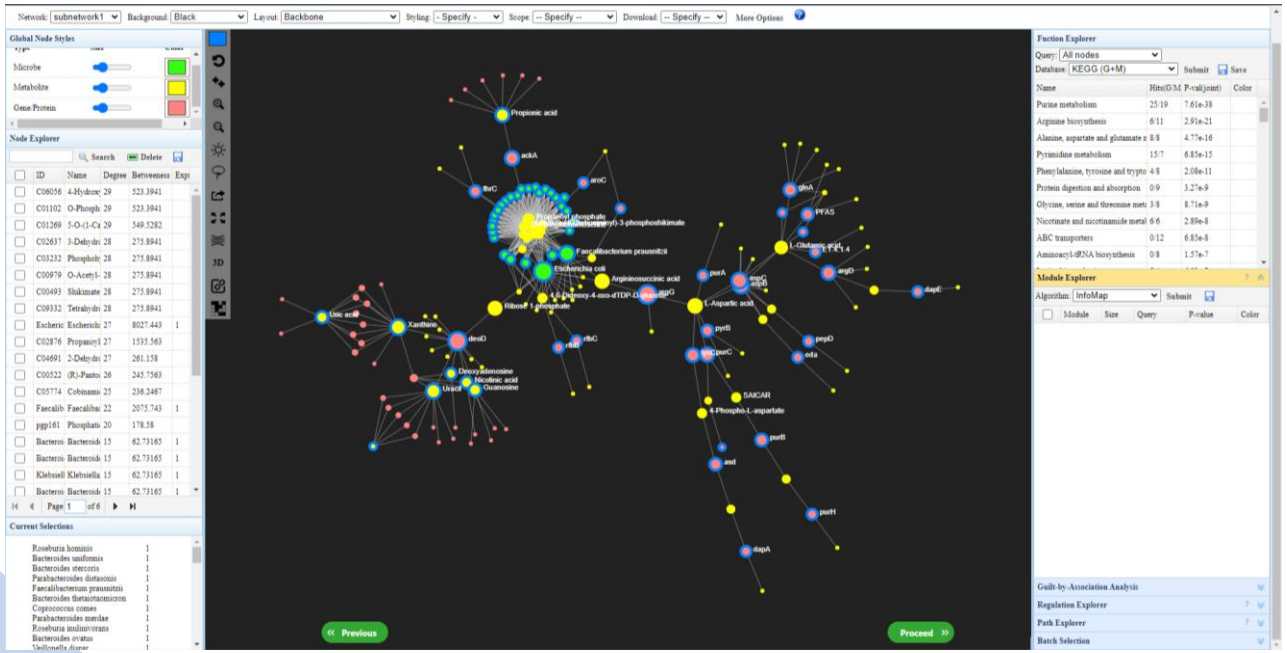


Integrating MS Peaks in metabolic network



The resulting network contains predicted metabolites (yellow), putative metabolites (grey) and enzymes (red).

Predicting microbial taxa’s metabolic potential



Integrating taxon-metabolite prediction in KEGG metabolic pathway. Metabolite are represented by yellow nodes. Size of metabolite

Heatmap showing metabolic potential of microbial taxa

Network building

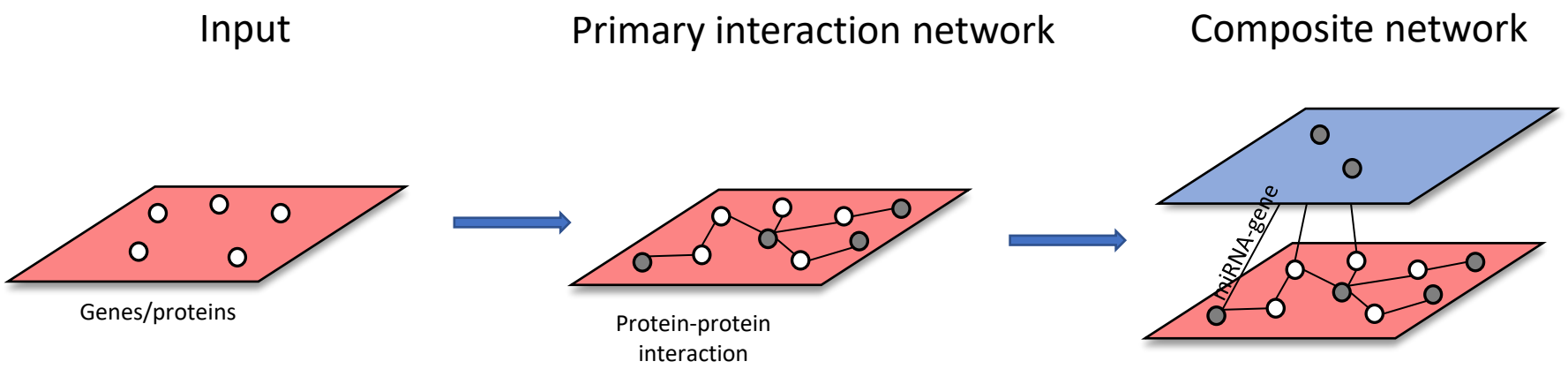
- OmicsNet supports two main cases of network building
  - Upload single omics list:
    - Identify interacting partners from its primary interaction type and expand the resulting network iteratively by adding other interaction types.
  - Upload multiple omics lists:
    - Build multi-omics network connecting the different omics features.

Network building for single list

- Primary interaction network is composed of seeds and its immediate interacting partners.

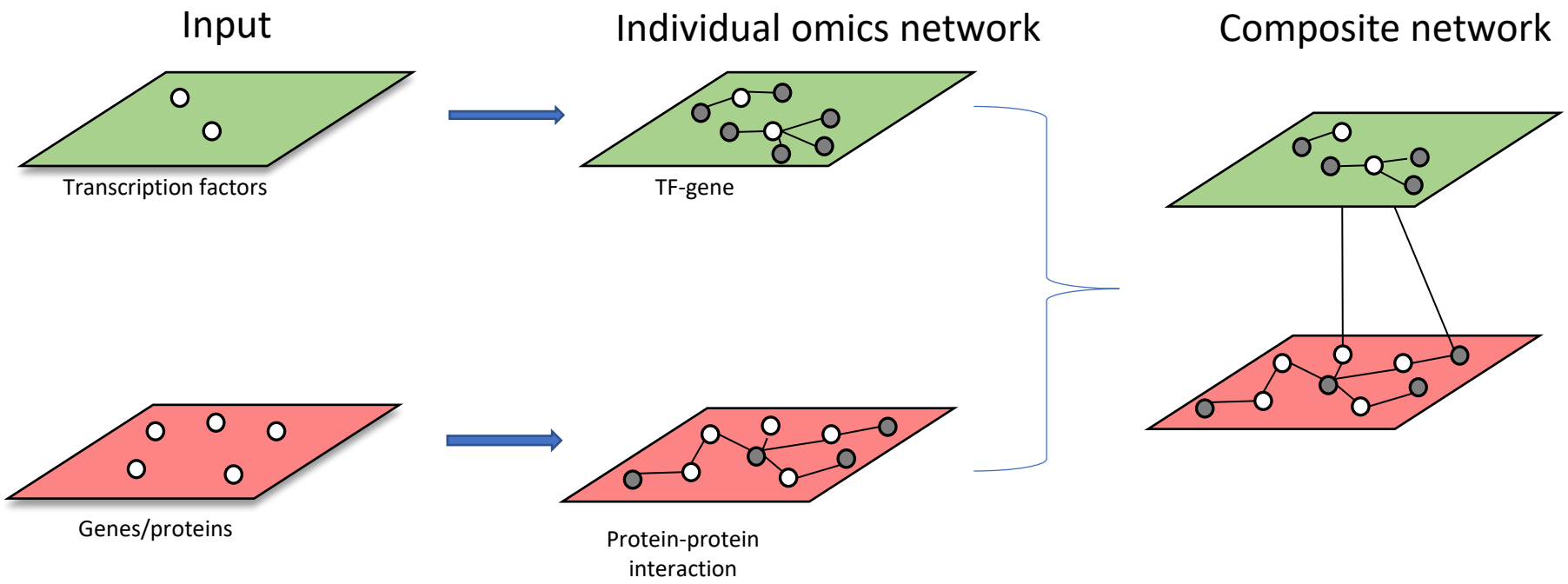
- Secondary interactions will query for interactions against molecules contained in the primary network.
  - **Add edges:** PPI as secondary or tertiary interaction will add edges to existing gene/proteins in the network
  - **Add nodes and edges:** All other interaction types

- If more than one input list is uploaded, the input list of secondary or tertiary interaction will serve as a constraint to filter out the nodes that are not seeds in the composite network.

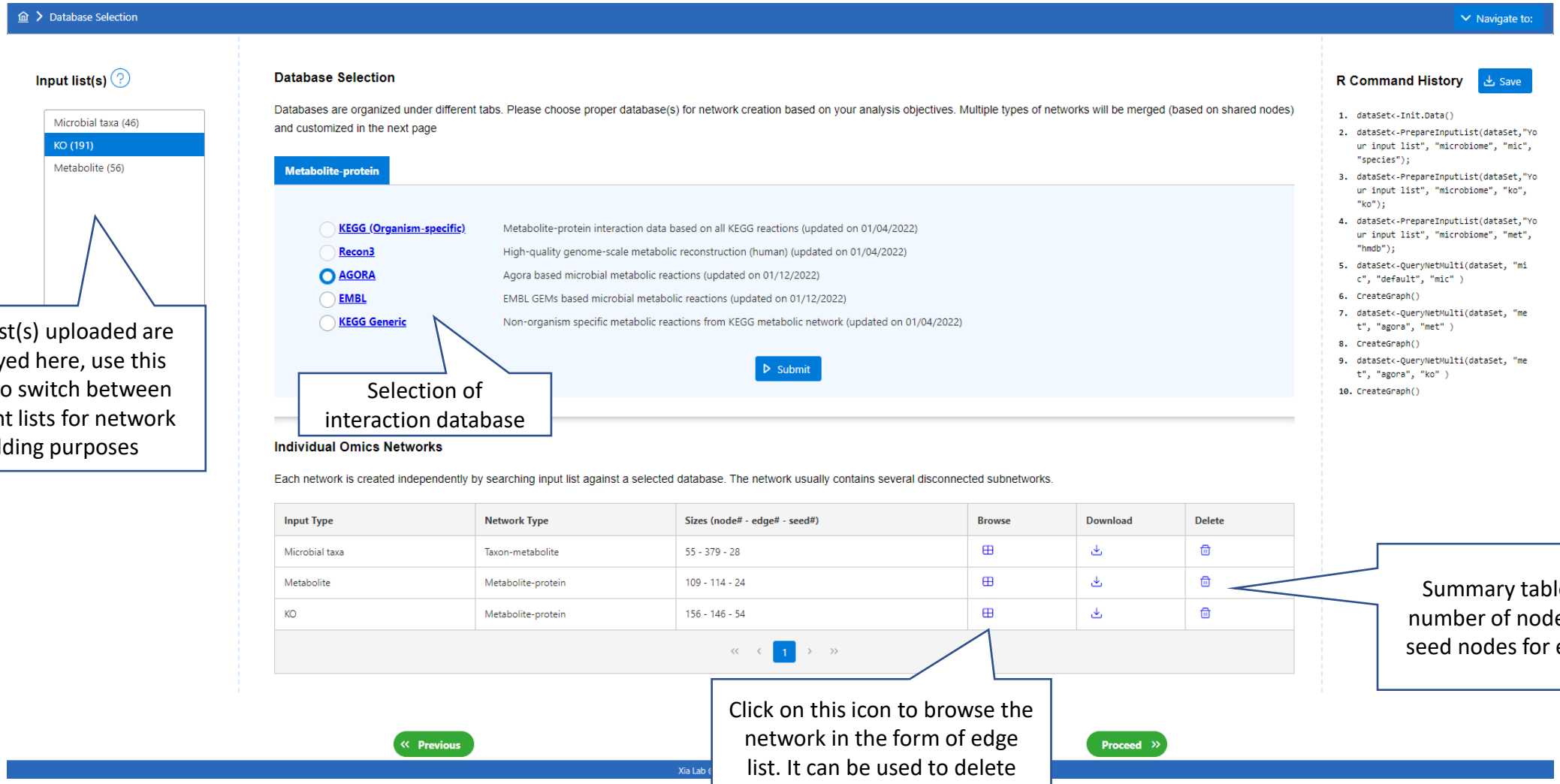


Network building for multiple lists

- Each list of molecules are used to build individual omics interaction network
- The individual omics networks are merged to form composite network through shared nodes.



Improved network building interface



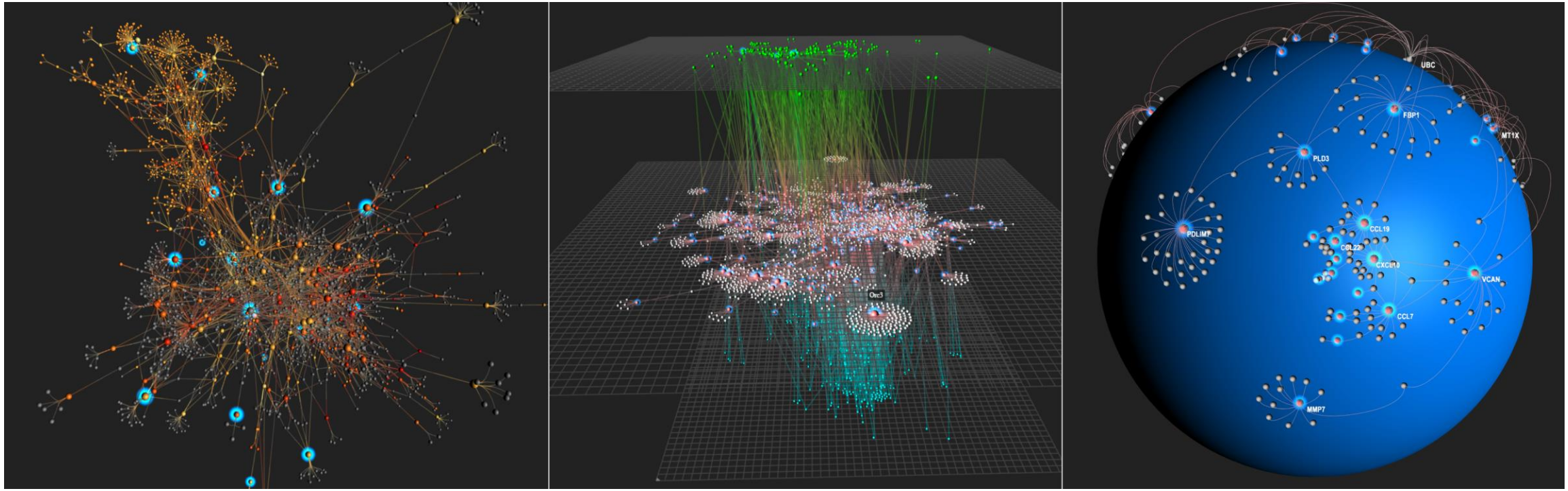
Input list(s) uploaded are displayed here, use this panel to switch between different lists for network building purposes

Selection of interaction database

Summary table displaying number of nodes, edges and seed nodes for each network

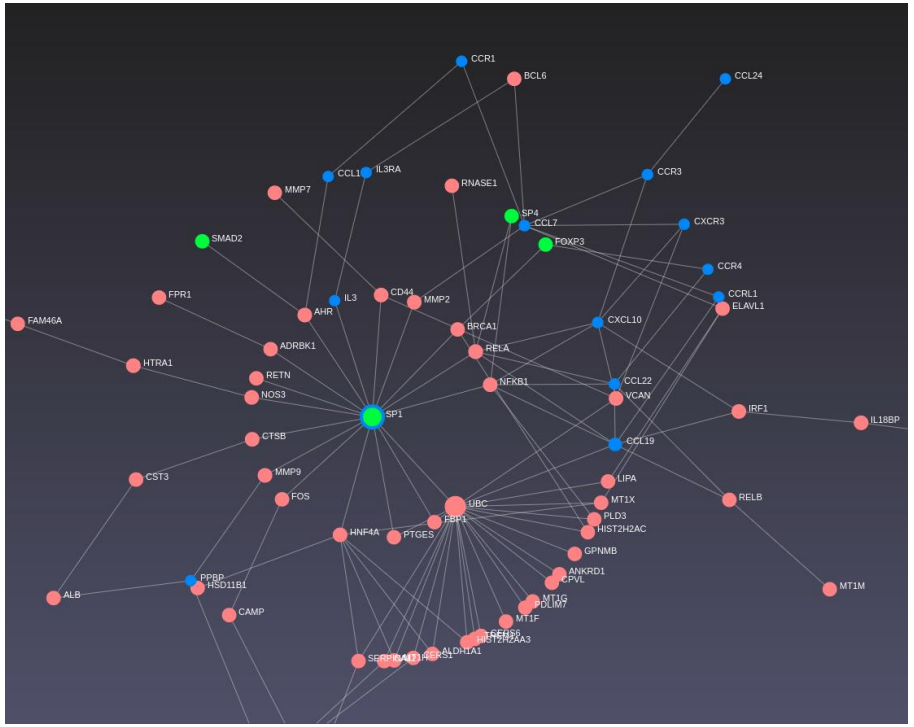
Click on this icon to browse the network in the form of edge list. It can be used to delete edges or nodes.

Different 3D layouts

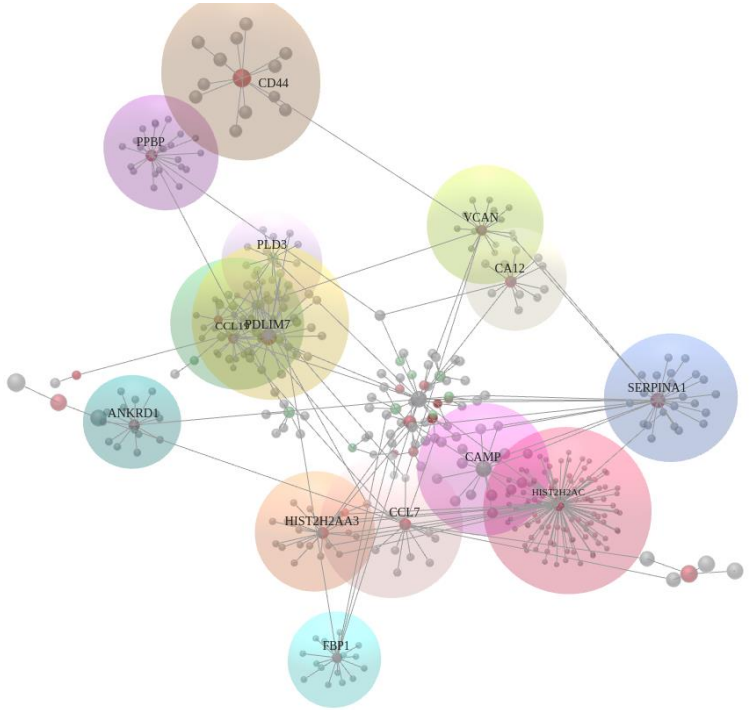


Left: force-directed layout (with edge bundling and halo effect); **Middle:** multi-layered layout (for multi-omics integration); **Right:** spherical layout (inspired by Google Earth)

New features in network visualization

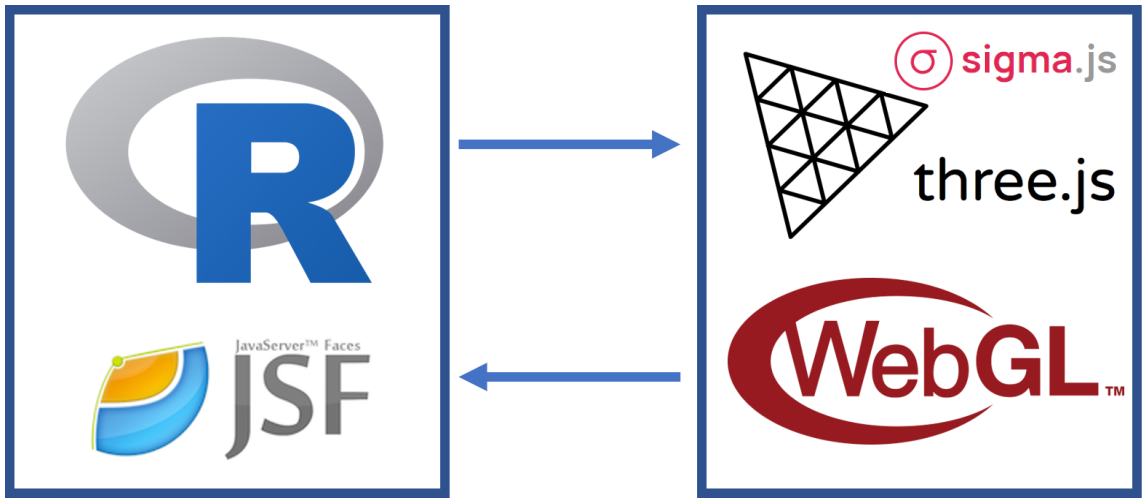


2D network visualization: concentric circle layout facilitates visualization of connection patterns of focal node with the rest of the network



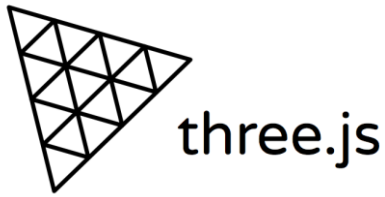
Module-based force-directed layout; Each bubble represents a graph community.

Implementation



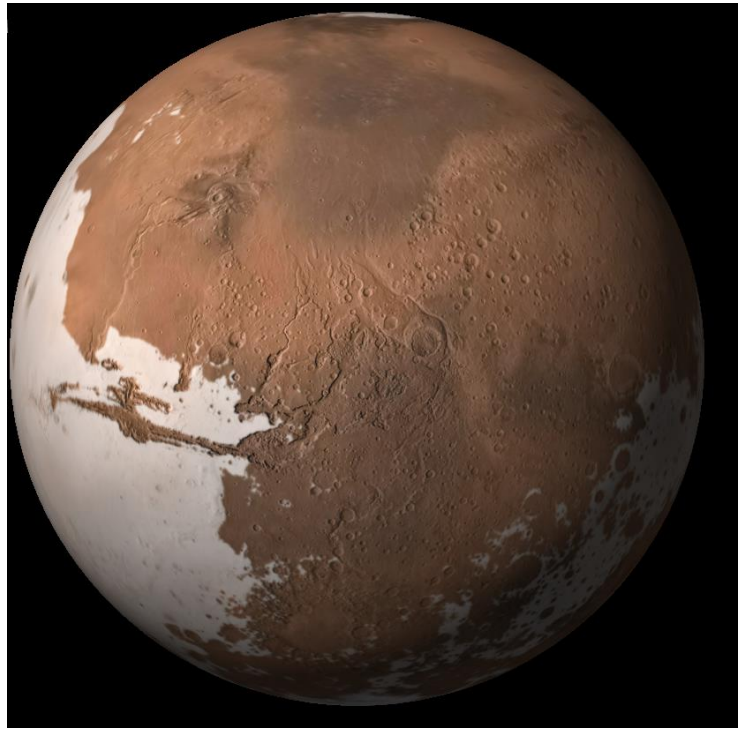
- Client-server framework that uses Java and R server for network construction and some analysis functions.
- Browser-based application using WebGL interfaced by Three.js to visualize 3D network interactively.
- Sigma.js, a canvas-based graphing library is used for 2D network visualization

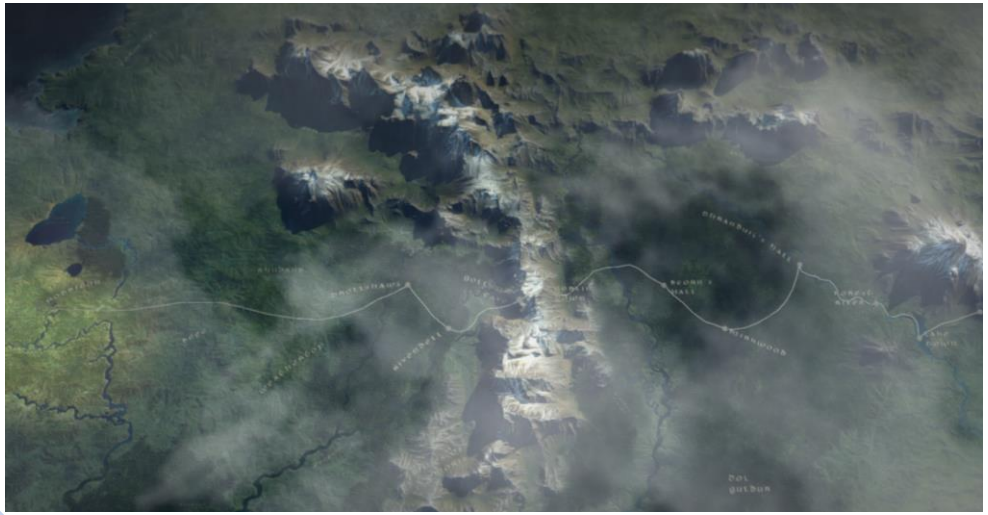
Core Technologies for 3D visualization



- WebGL
  - JavaScript API allowing the rendering of 3D graphics in web browser without plug-ins
  - High performance, GPU accelerated
  - Steep learning curve: requires developers to have extensive math knowledge about 3D, lighting and shading.
- Three.js
  - Framework interfacing with WebGL to display 3D graphics
  - Abstract away the difficulties of WebGL.

Three.js enables high quality 3D graphics

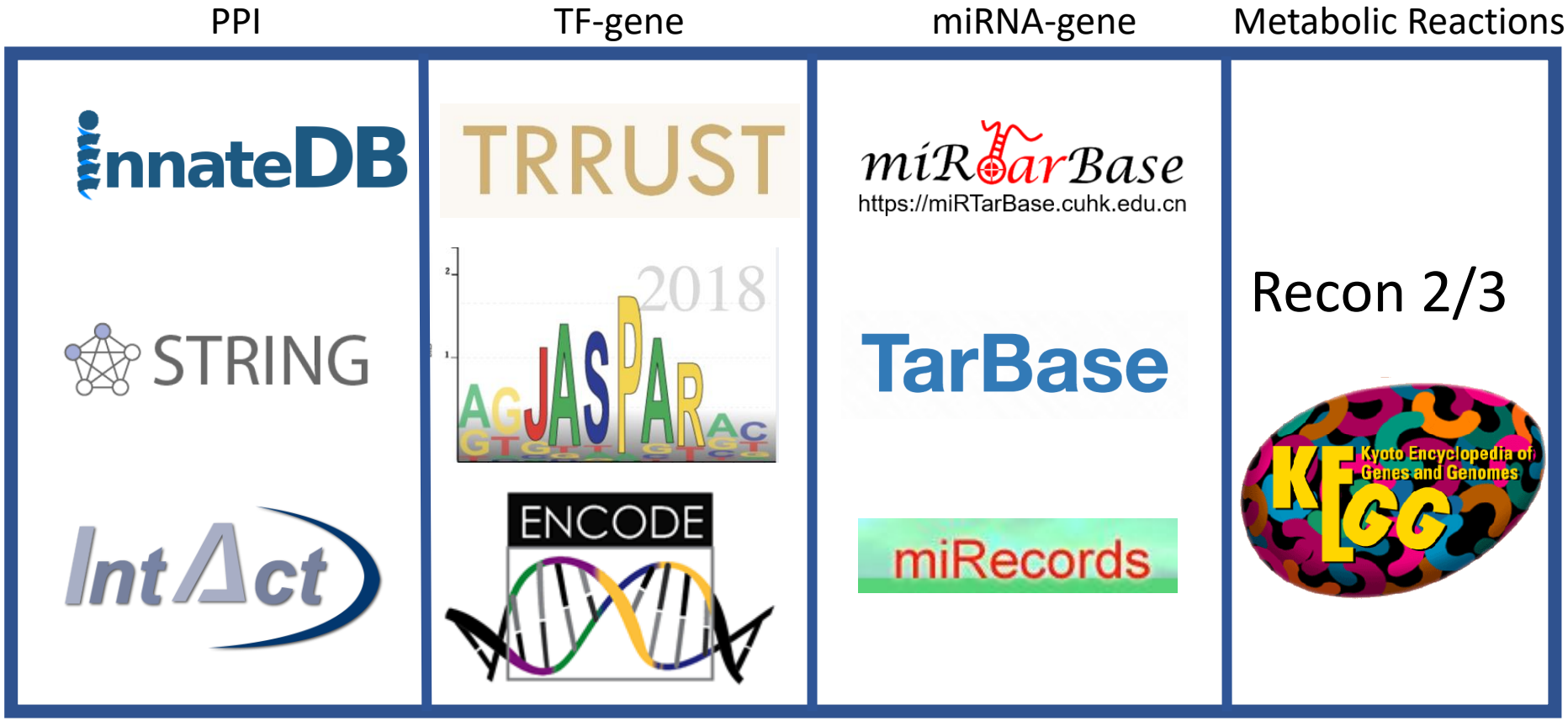




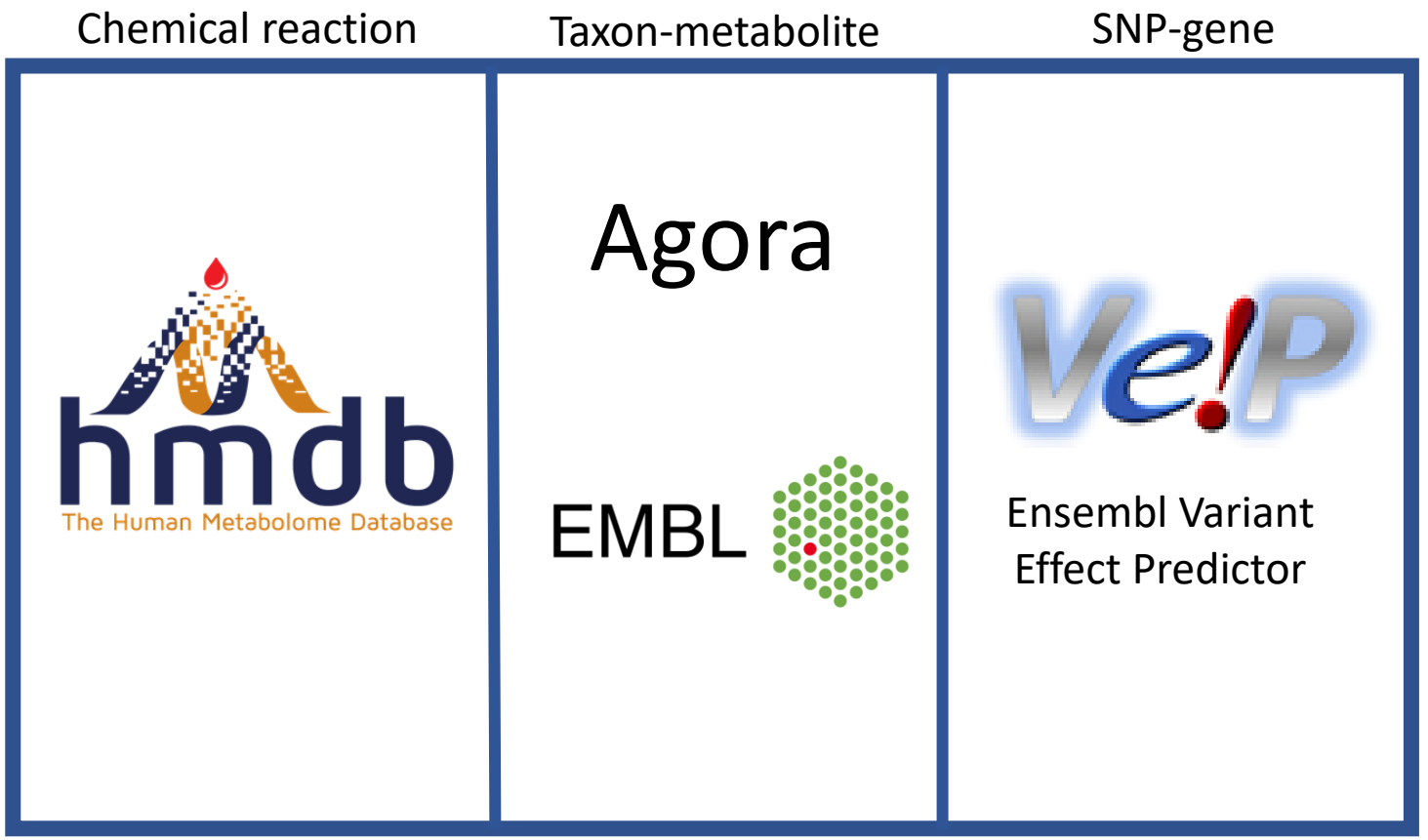
Key Features

- Interactive 2D/3D network visualization in web browser using canvas and WebGL technology
- Enable integration of multiple types of molecular interactions
- Built-in knowledgebase for network building
  - Protein-protein interaction
  - Transcription factor-gene regulation
  - miRNA-gene regulation
  - Metabolite-protein interaction
- Support integration of less well-established omics data types by using computational predictions
  - SNPs
  - Microbial taxa
  - Untargeted metabolomics MS peaks

Databases


PPI
TF-gene
miRNA-gene
Metabolic Reactions
InnateDB
TRRUST
miRTarBase
https://miRTarBase.cuhk.edu.cn
STRING
2018
JASPAR
TarBase
Recon 2/3
IntAct
ENCODE
miRecords
KEGG
Kyoto Encyclopedia of Genes and Genomes

Databases (2)


Chemical reaction
Taxon-metabolite
SNP-gene
hmdb
The Human Metabolome Database
Agora
EMBL
VeP
Ensembl Variant Effect Predictor

The End