

OmicNet Tutorial: Starting from two lists of molecules

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

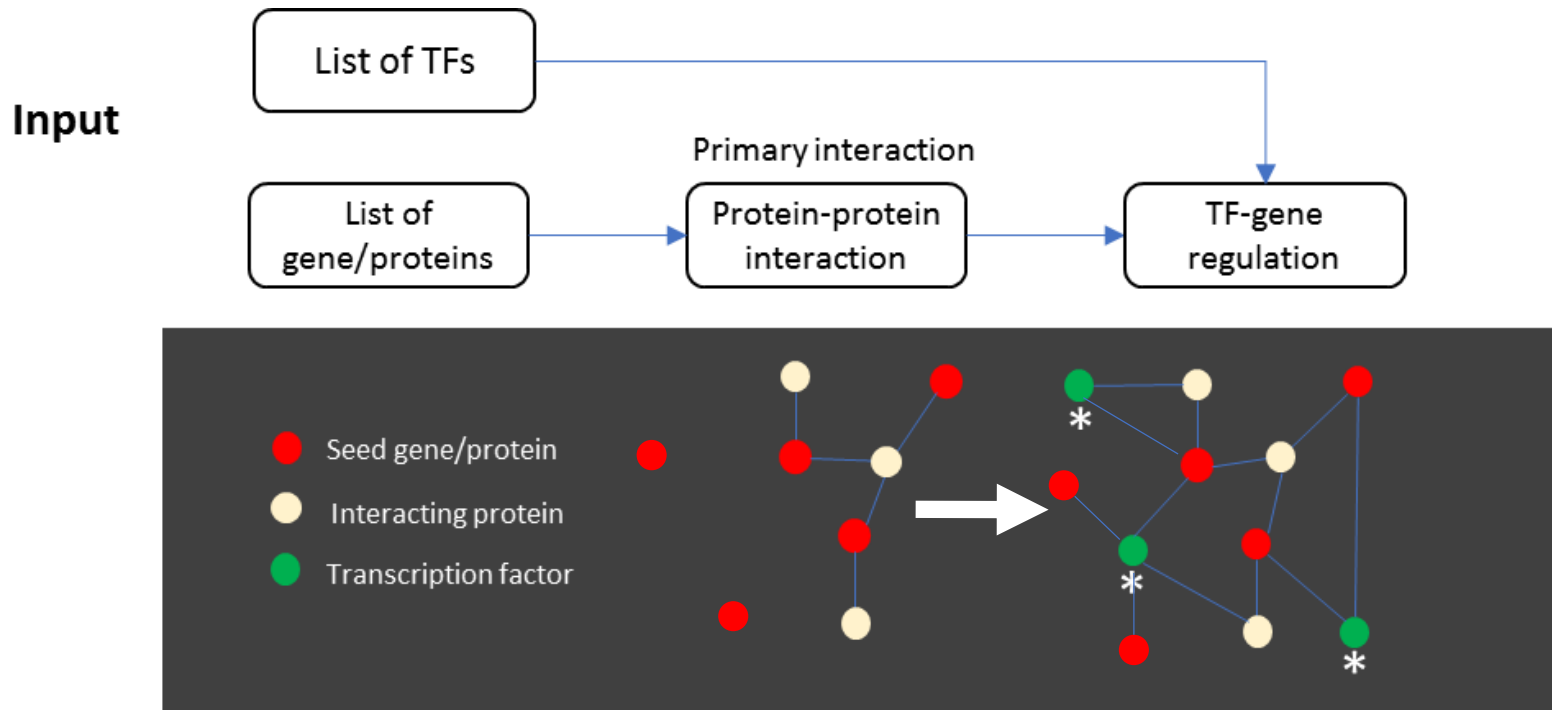
Motivation

- Explore the different interacting relationships between two list of molecules
 - Proteins
 - Metabolites
 - Transcription factor
 - miRNA
- Build composite network to visualize and analyze.
- Approach:
 - Search for interacting partners of seed molecules to build primary interaction network and expand on it to include seeds from the second list of molecules that directly interact with it.

Network Building Rules

- Primary interaction network is composed of seeds and its immediate interacting partners.
- Secondary and tertiary interaction will query for interactions against gene/proteins 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..

Case 1: Build transcriptional regulatory network



* From the input TF list.

This procedure identifies which TFs from input list interact with seed proteins or its direct interacting proteins

- It could expand the primary network to include previously unconnected seed gene/protein

Network Building

OmicsNet

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Network Builder

Network Building

By default, PPI will be selected for gene input, MPI for metabolites, MGI for miRNAs, and TGI for TFs. To build composite network containing more than one type of interactions, use numbers (1, 2, 3) to indicate the orders.

- If PPI is not the primary interaction, only edges will be added
- Duplicate numbers are not permitted

Orders	Interaction Types	Databases
1	Protein-protein interactions (PPI)	<ul style="list-style-type: none"><input checked="" type="radio"/> InnateDB Manually curated comprehensive PPI (human/mouse)<input checked="" type="radio"/> IntAct Manually curated experimentally validated PPI<input type="radio"/> STRING Comprehensive PPI containing both known and predicted PPI (set parameters)
--	miRNA-gene interactions (MGI)	<ul style="list-style-type: none"><input type="radio"/> miRNet Experimentally-validated miRNA targets information based on TarBase and miRDB
--	Metabolite-protein interactions (MPI)	<ul style="list-style-type: none"><input type="radio"/> KEGG Metabolite-protein interaction data based on KEGG reactions<input type="radio"/> Recon2 High-quality genome-scale metabolic reconstruction (human)
2	TF-gene interactions (TGI)	<ul style="list-style-type: none"><input checked="" type="radio"/> TRRUST TF-gene interactions constructed using text mining, followed by manual curation<input type="radio"/> ENCODE TF-gene interactions derived from ENCODE CHIP-seq data<input type="radio"/> JASPAR TF-gene interactions derived from transcription factor binding profiles

Submit

Input Summary

Type	Size
Gene List	48
TF List	6
miRNA List	0
Metabolite List	0

Network Tools

Network Result

Primary: Protein-protein (IntAct)
Secondary: TF-gene (TRRUST)
The current selection will be displayed by default.

Networks	Nodes	Edges	Seeds
● subnetwork1	250	266	25
● subnetwork2	14	13	1
● subnetwork3	12	11	2
● subnetwork4	5	4	1
● subnetwork5	4	3	1
● subnetwork6	4	3	2
● subnetwork7	3	2	2

Previous Proceed

Xia Lab @ McGill University (last updated 2018-04-28)

Callouts:

- Set PPI as primary interaction and select IntAct database
- Set TF-gene as secondary interaction and select TRRUST database
- Click on "Submit" button to generate the network

- When there are multiple input types, we suggest setting **protein-protein or metabolic network** as primary interaction
 - Generally, interaction confidence is higher than miRNA-gene and TF-gene
 - Setting miRNA or TF as primary could result in large quantity of target gene nodes due to promiscuity of certain TF and miRNAs (housekeeping TF for example).

Network Building Options

Network Building

By default, PPI will be selected for gene input, MPI for metabolites, MGI for miRNAs, and TGI for TFs. To build composite network containing more than one type of interactions, use numbers (1, 2, 3) to indicate the orders.

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Orders	Interaction Types		
1	Protein-protein interactions (PPI)	<input type="radio"/> InnateDB <input checked="" type="radio"/> IntAct <input type="radio"/> STRING	Manually c Manually c Comprehe
--	miRNA-gene interactions (MGI)	<input type="radio"/> miRNet	Experiment
--	Metabolite-protein interactions (MPI)	<input type="radio"/> KEGG <input type="radio"/> Recon2	Metabolite High-qualit
2	TF-gene interactions (TGI)	<input checked="" type="radio"/> TRRUST <input type="radio"/> ENCODE <input type="radio"/> JASPAR	TF-gene int TF-gene int TF-gene int

Network Building Options

Select an approach to expand the primary PPI network

	Option	Details	Notes
<input type="radio"/>	Target primary seed nodes only	Add interactors from your uploaded list that target seed nodes in primary network, do not consider non-seed nodes.	You can see your miRNAs/TFs /metabolites of interest that interact <u>only</u> with your genes of interest.
<input type="radio"/>	Target primary seed nodes and other nodes	Add interactors from your uploaded list that target both seed nodes and other nodes in primary network (i.e. add edges targeting non-seeds).	You can view your miRNAs/TFs /metabolites of interest that interact with both your genes of interest and other genes in the network.
<input checked="" type="radio"/>	Target any nodes in primary network	Add interactors from your uploaded list that target any nodes in the primary network.	You can view your miRNAs/TFs /metabolites of interest that interact with <u>any</u> genes in the primary network.

Proceed

Input Summary

Type	Size
Gene List	48
TF List	6
miRNA List	0
Metabolite List	0

Network Tools

Network Result

Primary: Protein-protein (IntAct)

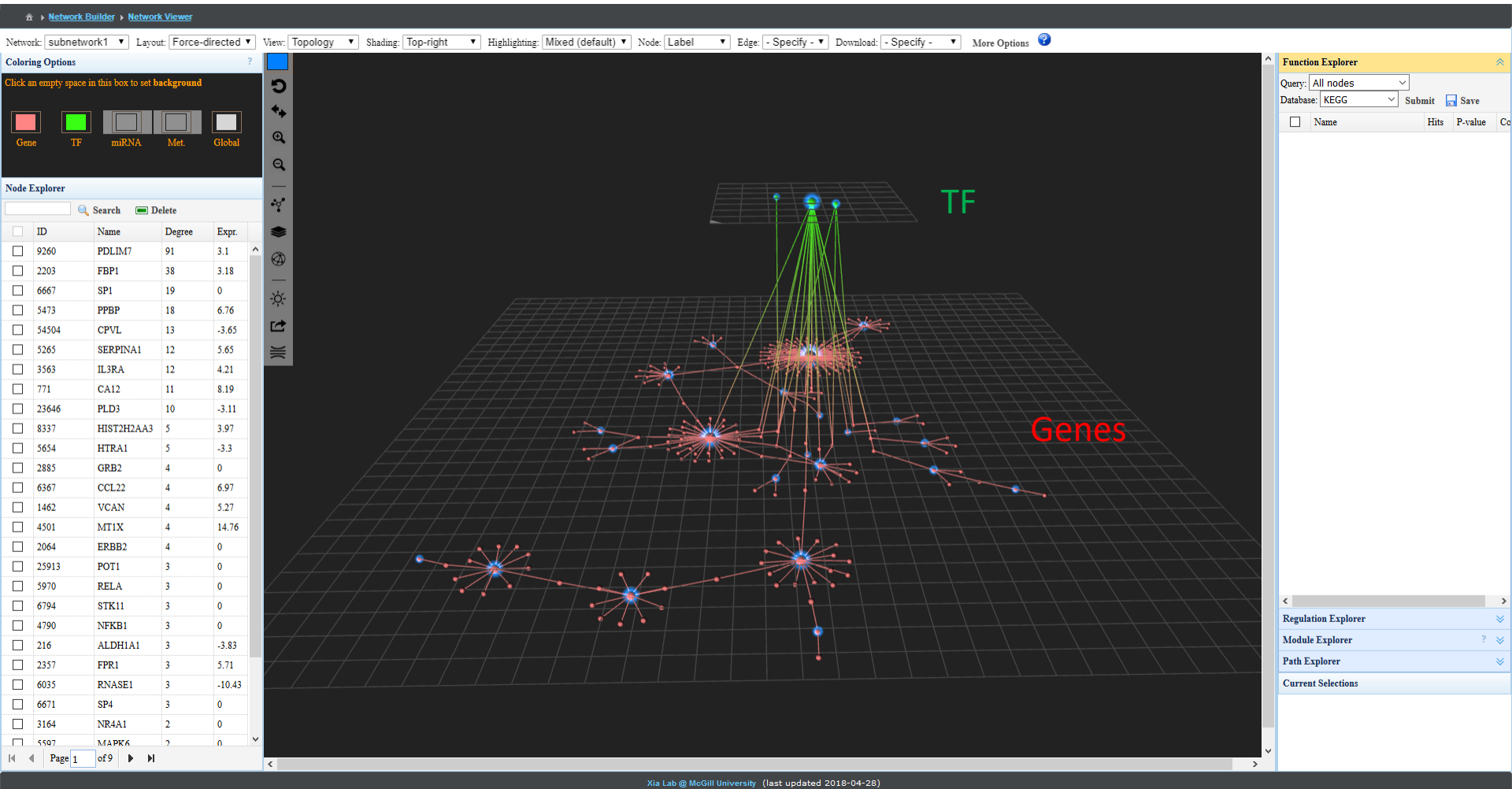
Secondary: TF-gene (TRRUST)

The current selection will be displayed by default.

	Networks	Nodes	Edges	Seeds
<input checked="" type="radio"/>	subnetwork1	250	266	25
<input type="radio"/>	subnetwork2	14	13	1
<input type="radio"/>	subnetwork3	12	11	2
<input type="radio"/>	subnetwork4	5	4	1
<input type="radio"/>	subnetwork5	4	3	1
<input type="radio"/>	subnetwork6	4	3	2
<input type="radio"/>	subnetwork7	3	2	2

Select "Consider all nodes" option to show all TFs/miRNAs having targets in our primary PPI network.

Network Visualization



2D perspective layered layout with seed nodes highlighted in blue

The End
