

The background of the slide is a complex network visualization. It consists of numerous white circles of varying sizes, representing nodes, connected by a dense web of thin, light gray lines, representing edges. The nodes are distributed across the entire frame, with some appearing in clusters and others in isolation. The overall effect is a sense of interconnectedness and complexity.

NAViGaTOR

Network Analysis, Visualization, &
Graphing TORonto

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[HTTP://OPHID.UTORONTO.CA/NAVIGATOR/INDEX.HTML](http://ophid.utoronto.ca/navigator/index.html)

NAViGaTOR - Network Analysis, Visualization, & Graphing TORonto is a software package for visualizing and analyzing protein-protein interaction networks.

First release, February 2018



Contents

1	Getting Started	5
1.1	What is Navigator	5
1.2	Installation	5
1.3	Basic Introduction to Graph Theory	6
1.4	Creating a Network	7
1.5	Basic Network Handling	9
1.6	Basic Network Coloring	9
1.7	Open Network	10
1.8	Save Network	10
1.9	Subsets	11
2	Import, Export and Integration	13
2.1	Data Model	13
2.2	Read Network from file	14
2.3	Import data to Network	18
2.4	Divide and Merge Networks	20
2.5	Export Networks	22
3	Network Annotation	25
3.1	Manual Annotation	26

3.2	Annotation by File	26
3.3	Annotation by Database	26
3.4	Structuring Networks from Annotation	27
3.5	Visual Annotation	28
4	Visualization	33
4.1	Visualization Types	33
4.2	Network Layouts	36
4.3	Appearance of Network Components	41
5	Network Analysis	45
5.1	Add Dynamic Parameter	45
5.2	Topology	47
5.3	Clustering	48
5.4	Enrichment Analysis	50
5.5	Flow Analysis	50
5.6	Ontology tab	51
6	Tutorials	53
6.1	PPI Network Examples	53
6.2	World Network	54
6.3	Spokes Visualization	55
6.4	Importing Interaction Networks from the Internet	57
7	Troubleshooting	59
7.1	Common Problems	59
8	Dictionary	61
8.1	Menu	61
8.2	Panels	63
8.3	Layout Panels	70
9	Frequently Asked Questions	71



1. Getting Started

1.1 What is Navigator

NAViGaTOR - Network Analysis, Visualization, & Graphing TORonto is a software system for scaleable visualizing and analyzing networks.

The current version, NAViGaTOR 3, increases modularity, improves scaleability, extends input/output options, brings new network views and analysis algorithms.

Directed and undirected networks can be annotated by relevant online databases or local data sets, and analyzed by diverse algorithms, which in turn enable enrichment analysis and discovering relationship between network structure and function. In particular Gene Ontology, protein-protein interaction and pathway databases, and Human Disease Ontology are supported.

NAViGaTOR is an academic project under active development by members of Jurisica Lab of the Krembil Research Institute. The project has been funded by multiple grants, including Genome Canada, Ontario Research Fund - GL2, to extend its functionality and enhance data interchangeability with other tools (e.g. Cytoscape) for network analysis and visualization. Therefore, Navigator implements import and export functionality for the most common file formats, such as XGMML, PSI or text.

NAViGaTOR is freely available to academic research under the GNU General Public License (<https://www.gnu.org/licenses/gpl-3.0.en.html>).

1.2 Installation

1.2.1 System Requirements

- You must have downloaded and installed Java Runtime Environment (JRE) 8 to your computer in order to run the program.
- In order for the application to start and run properly, your machine must have the required Visual C++ runtime libraries. They can be installed here: <https://www.microsoft.com/en-us/download/details.aspx?id=30679>

- If there is an issue with file permissions in Windows versions, install the application in your user folder (rather than under C:Program Files), or run it as an administrator.

1.2.2 Windows

1. Download Navigator onto your Microsoft Windows system.
2. Open the downloads folder and run the program
3. Wait for Navigator setup wizard to open and click "next"
4. Select the folder in which you want Navigator to be installed
5. Select the start menu folder in which you want set up to create the program's shortcuts
6. NOTE: Please run the software as administrator, by right click "Run as administrator".

1.2.3 Linux

1. Download Navigator onto your Linux system.
2. Open the Terminal and go to the download folder.
3. Start the installation via:

```
$ chmod +x NAViGaTOR_...-sh
$ sudo NAViGaTOR_...-sh
```

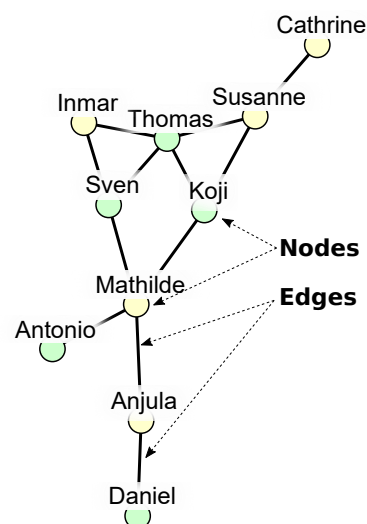
4. Follow the instructions in the opened installation window.
5. Chose the installation and symbolic links folder.
6. Click "Next" and wait until installation finished.
7. Switch to the installation folder.
8. Use the following command to start NAViGaTOR.

```
$ chmod +x navigator
$ ./navigator
```

1.3 Basic Introduction to Graph Theory

A network is an abstract conceptual model of a definite set of entities (e.g., humans, proteins, metabolites, neurons, species or non-biological objects such as cars or books), and the relationships between those entities (i.e., interactions among proteins in a protein protein interaction network or humans in a social network). In computer science and mathematics, a network is often referred to as a *graph*. Formally, the set of entities we seek to represent are the set of *nodes* in a graph, where the set of *edges* defines pair-wise relationships between members of nodes.

Objects such as proteins, genes, or humans can be represented by nodes, while their interactions, for instance, biological reactions, gene regulation, or the social interactions are represented by edges. In the example on the right side, the network visualizes the social interactions in a group of friends. Each person is depicted as node and the edges represents an interaction such as "friends with". This representation allows the analysis of structural features of a



network and reveals key components, for example, genes connected to certain cellular or disease mechanisms or highly connected influencers in a social network. It also allows one to apply a number of visualization techniques that enable the user to visually explore the data.

1.4 Creating a Network

To create a simple network, select menu **File** → **New...**, and select between an **Empty graph** or a **Random graph**. For more details on creating a manual network, see Section 1.4.2, while for a random graph see Section 1.4.3.

1.4.1 Node and Edge Types

In Navigator, Nodes and Edges have a specified type. A Type is a named category to which a node or edge belongs. For example, in a social network graph, a node could be of the type 'Person' while an edge could be 'Knows'. In a transportation network, nodes could be of the types 'City' or 'Town' while edges could be 'Road' or 'Railway'. By default, most nodes are set to the default type 'Node' and edges to the default type 'Edge' in Navigator, but very complex graphs and analyses can be produced by using multiple types instead of the default settings.

1.4.1.1 Node Types

A graph can contain different Types of nodes, for instance metabolites and enzymes that are processing them. In a network representing the structures of a company, node types can represent the different functions, such as sales representatives, IT-consultants, or engineers. Nodes can exist on their own or be connected by edges, and can have attributes associated with them. It can be created via **Graph** → **New Node Type ...**.

1.4.1.2 Edge Types

Edge Types can reflect different categories of interactions. Each edge is connecting a source node and a target node. Variations for protein protein interactions are for instance the covalent binding of proteins in a complex or regulatory activity or the enhancing influence of an enzyme. It can be created via **Graph** → **New Edge Type ...**.

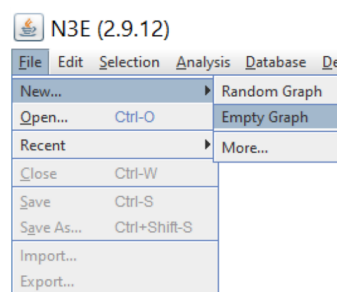
Functionally, edges can behave in different ways:

- Directed Edges allow traversal in one direction only; from source to target. This is relevant to algorithms and searches for which directionality is needed.
- Undirected Edges do not make a distinction when algorithms encounter them; the edge can be traversed from source to target or from target to source. Edges that are not explicitly Directed Edges are Undirected.
- Restricted Edges are edges that can only exist between specific types of nodes. This can be used to enforce rules when creating graphs.

Edges created with the 'neighbors' option maintain indexes of their nodes, allowing for faster traversals and searches. Like nodes, edges can have attributes associated with them.

1.4.2 Manual Creation of Networks

Before creating a new Network, an empty network file has to be created, using the Menu **File** → **New...** → **Empty Graph**.



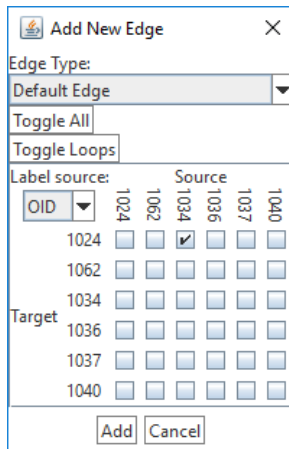
1.4.2.1 Create New Node

Adding a new Node to an open graph can be done by selecting menu **Graph** → **New Node**. If no Object Type is defined for nodes in the graph, you will be prompted to create one. Ensure that the name you use for your type is unique and descriptive.

When an Object Type is available, you can select it from the **Add New Node** dialogue, and a new node with that type will be created in the graph.

1.4.2.2 Create New Edge

Adding a new Edge to an open graph can be done by selecting the nodes you wish to connect and selecting **Graph** → **New Edge**. The message box that opens, requires to specify the type of edge you want to create and which nodes you want to connect with an edge. E.g. in the given example we want to create an edge from node 1024 to 1034. Therefore the square connecting the two is checked.



If no Object Type is defined for edges in the graph, you will be prompted to create one. Ensure that the name you use for your type is unique and descriptive, and refer to the documentation above for the significance of each setting. When an Object Type is available, you can select it from the Add New Edge dialog. A matrix will be generated that allows you to specify the source and targets for the edges to be generated. By default, all nodes will be identified by their OID, but this can easily be toggled to a more meaningful

attribute by using the Label Source combo box.

1.4.2.3 Remove Node

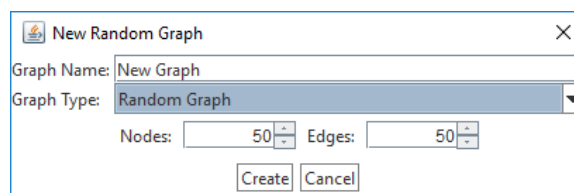
To remove one or several nodes, one can select the nodes and use the menu sequence **Edit** → **Delete Nodes**.

1.4.2.4 Remove Edge

To remove one or several edges, one can select the edges and use the menu sequence **Edit** → **Delete Edges**.

1.4.3 Create Random Network

To create a new random network, please use the menu sequence **File** → **New...** → **Random Graph**. When creating a random graph, a box will pop up allowing you to set a name for the new graph, select the type of random network and select the desired number of nodes and edges.



The following types of random networks are available:

Random Graph Randomly created nodes and randomly assigned edges.

Random Tree Graph Randomly created tree-like graph. A tree-like graph does not have any cycles.

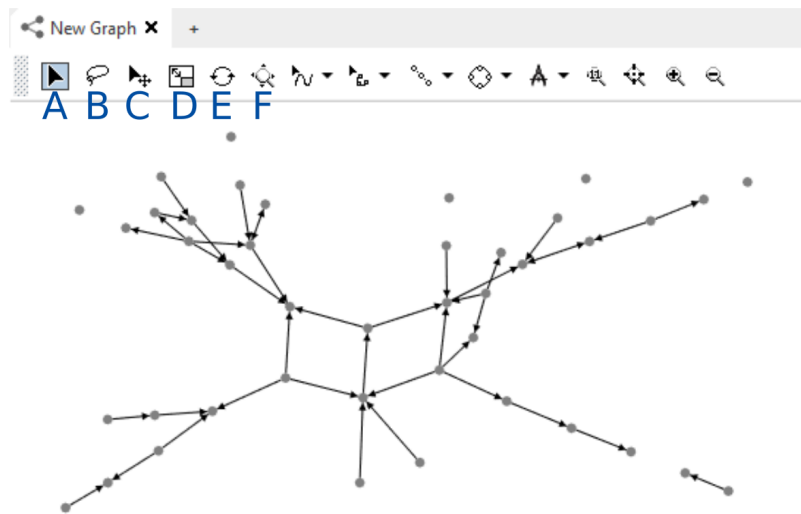
Complete Graph Randomly generated nodes, where each node is connected to each other node.

Random Directed Acyclic Graph Randomly generated nodes connected by directed edges. Again this algorithm ensures that the graph does not have any cycles.

Random Connected Graph Random graph as created by "Random Graph", with an additional requirement that all nodes belong to one connected component. That means, there is a path from each node to each other node.

1.5 Basic Network Handling

After creating a new network, it will be visible in the "Graph View" panel. The default graph layout in NAViGaTOR is the GRIP layout, see Chapter 4 "Network Visualization" for more details.

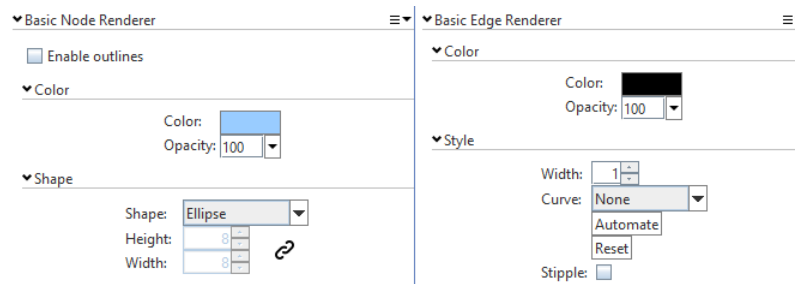


In the following we will describe a few basic functions in the NAViGaTOR graph view:

- A Selection Tool:** Use this tool to select single elements or objects. A mouse click on the targeted element selects it. The "Ctrl"-Key enables the selection of several elements.
- B Lasso Tool:** Use this tool to select a group of elements or objects. Draw a circle around the targeted elements.
- C Move:** Use this tool to move a selection of elements or the entire network.
- D Scaling:** Use this tool to scale a selection of elements or the entire network.
- E Rotation:** Use this tool to rotate a selection of elements or the entire network.
- F Navigate:** Use this tool to navigate through large networks.

1.6 Basic Network Coloring

The appearance of each component in the network (nodes, edges, node labels and edge labels) can be adjusted. The appearance panel provides different "Renderer" change attributes such as color or shape. Note: To manipulate the following features, ensure you select the objects in the network you wish to work on.



Color Change color of the node or edge respectively.

Opacity Change the opacity of the edge.

Node Shape Change the shape of the node.

Height Change the height of the node.

Width Change the width of the node.

Edge Width Set the width of the edge.

Curve Select the type of curvature of the edge.

Stipple Plot the edge as a dashed line.

To change node and edge labels, the "Basic Label Renderer" is required. Here you can change for instance:

Source Set the Variable shown as label.

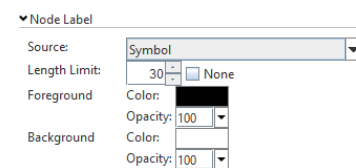
Length Limit Select the Label size limit.

Foreground Color Change color of the node or edge label.

Opacity Change the opacity of the node or edge label.

Background Color Change color of the background of the node or edge label.

Opacity Change the opacity of the background of the node or edge label.



1.7 Open Network

Opening a file in Navigator will create a new graph in the Workspace. Every file format has unique features and advantages. Here we give an overview of different file types supported by Navigator.

Plain Text Files Navigator is able to open any tab-delimited plain text file. A userfriendly wizard is guiding the user through the extraction of edges, source and target nodes, as well as their attributes. You can find a detailed description of the process in Section 2.2.3.

Network Files Specialized files dedicated to store all information required to mirror a network. Popular file formats supported by Navigator are XGMML, XML and PSI. You can find a detailed description of these formats in Section 2.

A listing of the all the formats and important information on their usage can be found below in Chapter2.

1.8 Save Network

In order to save or export information and analysis results from Navigator, a network can be stored in different file formats. The following list gives an overview of different export types supported by Navigator.

Text Information about the nodes, edges and subsets as well as the corresponding annotations and analysis results can be exported as tab deminited text files. This enables easy export to further analysis.

Network Files Specialized files dedicated to store all information required to mirror a network. Popular file formats supported by Navigator are XGMML, XML and PSI You can find a detailed description of these formats in Section 2.

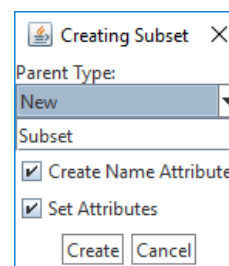
Figures Visualizations of the network and visual analysis results can be exported as image file such as BMP, GIF, JPG, PNG, SVG, TIF file. SVG is a vector graphics file format that can be handled by most modern graphical tools, such as Inkscape or Photoshop.

1.9 Subsets

1.9.1 Create Subsets

A network can be partitioned into sub-networks or sub-graphs. These can be used to structure a network. In NAViGATOR these partitions are called **subsets**. In the following we describe how to create them.

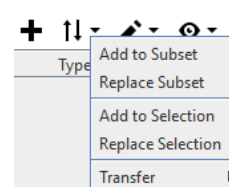
- Select the "Subsets" panel in the bottom part of the application.
- Select the nodes you want to combine into a partition.
- Chose the "Cross"-Botton in the "Subsets" panel.
- Enter the required fields:
 - Parent Type
 - Subset Name
- Click "Create"



The subset will appear in the subset panel, see section1.9.4, Subset Visualization.

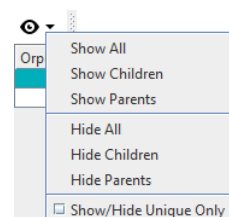
1.9.2 Edit Subset & Select Subset

A subset can be edited by adding nodes or replacing the whole subset by a new set of nodes. Open the "Arrow menu" and use "Add to Subset" or "Replace Subset" to add or replace nodes in a subset, respectively. The same menu is used to add nodes to a existing selection, "Add to Selection", or replace a current selection and selecting the nodes in the subset, "Replace Selection".



1.9.3 Hide Subset

Nodes also called here also Children and Parents the objects that represent the subset in the graph can be set to invisible by using the "Eye" menu: Select a subset and use the menu to hide or show "All", all "Children" or all "Parents" of a sub-network.



1.9.4 Subset Visualization

The following figures shows the subset panels in the bottom of the NAViGATOR framework: Subsets, Intersections and Nodes.

Subsets

OID	Type	Name	Degree
3072	Subset	Subset Subset A	0
3073	Subset	Subset Subset B	0
3074	Subset	Subset Subset C	0

The first panel on the left shows a list of all subsets created for this network including attached attributes, such as ID, type or name.

Intersections

Index	Set Type	Nodes	Edges	Total
3072	A	14	12	26
	A∩B	0	0	0
3073	B	7	7	14
	B∩C	11	12	23
3074	C	13	13	26
	C∩A	2	1	3
	A∩B∩C	0	0	0

The middle panel shows the number of nodes, objects and the sum, for all, selected subset (left panel) and intersections of these. The centre, shows bar plots for both nodes and edges in randomly assigned colours.

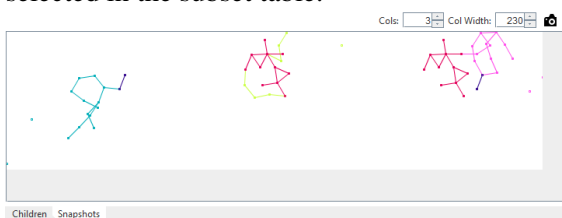
Nodes

OID	Type	Index	Name	Degree
1024	Default Node	44		1
1025	Default Node	45		2
1026	Default Node	46		1
1027	Default Node	47		1
1028	Default Node	48		2
1029	Default Node	49		0
1030	Default Node	50		0
1031	Default Node	51		0
1032	Default Node	52		0
1033	Default Node	53		0
1034	Default Node	54		0
1035	Default Node	55		0

The right panel shows the list of nodes that are member of the selected subsets. Each node is coloured according to the corresponding subset or subset intersection.

1.9.5 Snapshots View

The snapshot panel shows color coded representations of the children of the subsets that are presently selected in the subset table.

**1.9.6 Collapse Subsets**

In Navigator, subsets can be collapsed into multi-nodes, representing the group or subset. An example usage for this functionality is the representation of protein protein complexes and their connections in a protein protein interaction network. To collapse a subset do the following steps:

- Go to the "Graph Panel".
- Move the mouse into the panel and click right mouse button. The context menu opens.
- Select Visibility and Collapse, which shows a list of all Subsets.
- Select the subset to be collapsed.

1.9.7 Delete Subset

- Select the "Subsets" panel in the bottom part of the application.
- Select the subset to delete
- Chose the "Pen"-drop-down menu and select "Delete Subset".



2. Import, Export and Integration

Description of how data can be imported to and exported from Navigator, as well as which data formats are supported.

2.1 Data Model

The database backbone of the application is Sparksee graph database. In Sparksee, there can be multiple types of basic network types - nodes and edges. Multiple edges between two nodes are allowed, as well as loops (with the same node on both ends of the edge). Edges could be either directional or non-directional. Edge types can be set to be allowed to link only nodes of specific types. The data is stored as object attribute. Attributes are type-specific. Global type attributes can carry values for network objects, nodes and edges, regardless of their type. The data Types supported are Boolean, Integer, Long, Double, Timestamp, String, Text and OID. Attributes can be set to be unique and indexed. For more detailed description of Sparksee's data model, see General Concepts chapter of Sparksee User Manual at <http://www.sparsity-technologies.com/UserManual/GraphDatabase.html> For performance and flexibility reasons data model in NAViGaTOR 3 is extended by Graph Data objects. The data types that are supported by graph data are plugin specific and might have different ways to access and visualize information within.

2.1.1 Attributes Description

Attributes are values that are associated with Graph Objects. An attribute can either be Global (applying to all nodes and edges) or can be associated with a single type. For example, a node type called 'Protein' can have an associated attribute called 'UniProt ID'. If the graph contains another type called 'Gene', nodes of the 'Gene' type will not contain 'UniProt ID' attributes. If there is a global attribute called 'ID', both 'Protein' and 'Gene' nodes will have the 'ID' attribute.

The following list describes all possible attribute types:

Boolean A Boolean is a binary variable that can be either "TRUE" or "FALSE".

Integer Numeric variable that can represent discrete numbers (a 32-bit whole number, can be up to 2^{31} digits long).

Long Numeric variable that can represent discrete numbers (a 64-bit whole number, can be up to 2^{63} digits long).

Double Numeric variable that can represent continuous numbers (floating-point decimal, minimum value = 4.9E-324, maximum value = 1.7976931348623157E308).

Timestamp Variable that represents dates or times. Required for time series data. It works properly with timestamps in the range '1970-01-01 00:00:01' UTC - '2038-01-19 03:14:07' UTC.

String Variable that can store short text's or words (up to 2048 characters). Optimal for attributes like categories.

Text Variable that can store long texts (up to and beyond 2048 characters).

OID Object Identifier for Graph Objects.

In addition, attributes can have different features:

- Unique attributes have a unique value for every object they apply to. Two nodes, or two edges cannot have unique attributes with the same value.
- Basic attributes have no restrictions.
- Indexed attributes have no restrictions, but are special in that the graph database creates a fast-lookup table to make searching for them faster, at the expense of memory resources

2.2 Read Network from file

2.2.1 BioPAX Level 3 (.owl, .xml)

Biological Pathway Data (BioPAX) is a community standard data exchange format designed to enable integration, exchange, visualization and analysis of biological pathway data. Within NAViGaTOR, physical entities as well as some of the logical constructs of BioPAX are represented as nodes, but at the present time there is no 1:1 correlation between BioPAX and NAViGaTOR objects appearance.

BioPAX files can be loaded into NAViGaTOR using **File -> Open**. You must choose the "BioPAX Level 3 (.owl, .xml)" for file type.

For more information about the BioPAX file format, please visit <http://www.biopax.org/>.

2.2.2 DEX and DEX backup

DEX is the standard format of Sparksee (formerly known as DEX), NAViGaTOR's backbone. A DEX graph contains nodes and edges assigned to types (labels), supports directed and multiple edges and includes nodes and edges attributes. To open a file saved with this format, select **File -> Open** and choose DEX (.dex) or DEX backup (.dexb).

2.2.3 Import Tab-delimited file

Delimited Text Files are plain ASCII files in a row/column format, with a reserved character for separating columns. This file type is easily exportable from most spreadsheet programs, and many databases export 'flat' files of their data that can either be loaded in this format or translated to it. Data from Delimited Text Files can include graph objects and attributes, but does not support the creation of complex data structures such as XML. Each row defines a graph object or objects using columns in the row to identify objects and specify attribute values.

When you specify Delimited Text File as your file type and select a file from the Open dialog, you will be presented with a wizard interface, which will present you with a preview of the file, and options on how the file's rows and columns are to be interpreted.

- Import the Tab-delimited file via the Navigator menu **File-> Import**, select a file and Click **“Next”**.
- Set header size to 1 and click **“Next”**. Delimited text files often contain header rows, which describe the data in some way, but should not be loaded as data themselves. We can here specify the size of the header in rows, as well as to indicate a Title Row, which contains the names of each column generated. Though a Title Row doesn't need to be specified, it can be useful to automate some of the later steps in file loading. The Title Row will be indicated in the Data Preview panel by its darker blue color.
- For every imported tab-delimited file, two columns must be specified, whose contents indicate the unique ID's of the nodes. Each row defines an edge to join two nodes. Use the drop down fields above the columns to annotate the starting node as **source index** and the partner node as **target index**. The boxes (here indicated by A, B, and C) Enable the user to define node and edge Type. If the source and target nodes do not have the same type, remove the check from the "Same as source" field in box C and enter the required information. Click **“Next”**.

Set Node ID Columns

For every imported tab-delimited file, two columns must be specified, whose contents indicate the unique ID's of the nodes to join with edges in the graph. Use the column headers below to specify which columns should be used for ID's.

Source: Type: **New**, Index: **Index**, Attribute: **String**

Edge: Type: **New**, Index: **Index**, Attribute: **String**

Target: Type: **New**, Index: **Index**, Attribute: **String**, ☒ Same as source

Data Preview

Title Row	Query ID	Query UniProt	Partner UniProt	Query Symbol	Partner Symbol	Species	Evidence Type	Numeric/Variable
SNTA1	Q13424	P07148	SNTA1	FABP1	human	exp	5	
SNTA1	Q13424	P62993	SNTA1	GRB2	human	exp.ortho.pred	11	
SNTA1	Q13424	P09417	SNTA1	QDPR	human	pred	2	
SNTA1	Q13424	O60242	SNTA1	ADGRB3	human	exp	4	
SNTA1	Q13424	P12755	SNTA1	SIO	human	pred	6	
SNTA1	Q13424	Q01970	SNTA1	PLCB3	human	exp	7	
SNTA1	Q13424	P11801	SNTA1	PSKH1	human	exp	2	
SNTA1	Q13424	Q9V2H9	SNTA1	MAST1	human	exp.pred	8	

- If required for further analysis, attributes that are stored in the file can be associated to the source node, the target node or the edges. Each column corresponds to one attribute. Besides the corresponding type for each associated column we need to define the type of information (Text, numeric etc.) and whether it is a basic, indexed or unique variable.

Set Attribute Import Columns

Data can be imported by indicating the Attribute Type (Text, Double Number, etc), Attribute Object (Node A, Node B or Edge), and a unique Attribute Name by which to reference the imported Attribute.

Data Preview

Title Row	Query ID	Query UniProt	Partner UniProt	Query Symbol	Partner Symbol	Species	Evidence Type	Numeric/Variable
SNTA1	Q13424	P07148	SNTA1	FABP1	human	exp	5	
SNTA1	Q13424	P62993	SNTA1	GRB2	human	exp.ortho.pred	11	
SNTA1	Q13424	P09417	SNTA1	QDPR	human	pred	2	
SNTA1	Q13424	O60242	SNTA1	ADGRB3	human	exp	4	
SNTA1	Q13424	P12755	SNTA1	SIO	human	pred	6	
SNTA1	Q13424	Q01970	SNTA1	PLCB3	human	exp	7	
SNTA1	Q13424	P11801	SNTA1	PSKH1	human	exp	2	
SNTA1	Q13424	Q9V2H9	SNTA1	MAST1	human	exp.pred	8	
SNTA1	Q13424	P68133	SNTA1	ACTA1	human	pred	3	
SNTA1	Q13424	O94983	SNTA1	CAMTA2	human	pred	1	
SNTA1	Q13424	Q76619	SNTA1	POZD4	human	pred	1	
SNTA1	Q13424	Q16512	SNTA1	PKN1	human	pred	1	

- Finally, we need to manually define a unique name for each attribute or column. Alternatively, you can click the **“Copy Title Line”** to automatically fill the names. Note, the names have to be unique. Click **“Next”** to create the network.

The same procedure can be used to add nodes and/or edges to a pre-existing network.

2.2.4 GraphML

GraphML is an XML-based file format for graphs, used as a common format for exchanging graph structure data. It supports directed and undirected graphs as well as nodes and edges specific attributes. For more information on this file format, visit <http://graphml.graphdrawing.org/>. To open a graph in this format, use **File -> Open** and choose the "GraphML (.graphml, .xml)" file type.

2.2.5 KGML

The KEGG Markup Language (KGML) is the standard format used by KEGG PATHWAY database <http://www.genome.jp/kegg/pathway.html>. To open a file in this format use **File -> Open** and choose the "KGML File (.kgml, .xml)" type.

2.2.6 NAViGaTOR

NAViGaTOR's native format. Version 3 saves files with .n3e extension, but there is full compatibility with files generated using NAViGaTOR 2.x. To open a NAViGaTOR file, use **File -> Open** and choose either "N3E (.n3e)" - for files generated using NAViGaTOR 3 - or "NAViGaTOR 2.x XML (.xml)" - for files generated with any version of NAViGaTOR 2 - file type.

2.2.7 OBO

The Open Biological and Biomedical Ontology (OBO) is a file format designed to represent ontologies in a logically well-formed and scientifically accurate way. The ontology most frequently used in biology is Gene Ontology (GO). To open a file in this format, use **File -> Open** and choose the "OBO ontology (.obo)" file type.

2.2.8 PSI-MI Format

The Proteomics Standards Initiative - Molecular Interaction, (PSI-MI), is a community standard data exchange format for representing molecular interactions. For more information about the PSI-MI file format, please visit <http://www.psidev.info/index.php?q=node/60>. PSI-MI files can be loaded into NAViGaTOR using **File -> Open** and choosing the "PSI-MI (.xml)" file type.

2.2.9 SBML

Systems Biology Markup Language (SBML) was created as a language to describe biochemical reactions, describing it in a format exchangeable between different software packages. More information on SBML are available at <http://sbml.org/documents/>. To open a SBML file, use **File -> Open** and choose the "SBML (.sbml,.xml)" file type.

2.2.10 XGMML

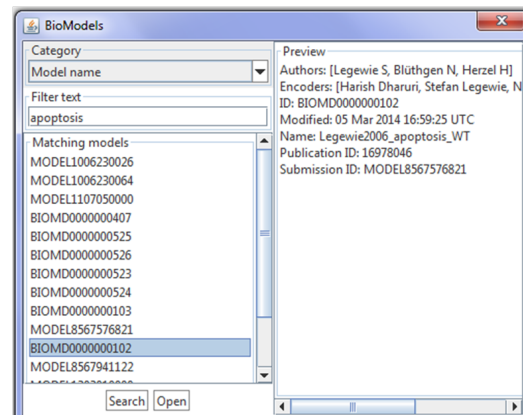
eXtensible Graph Markup and Modelling Language (XGMML) is an XML based format used for graph description. More info on XGMML file format is available at http://cgi5.cs.rpi.edu/research/groups/pb/punin/public_html/XGMML/. To open a XGMML file, use **File -> Open** and choose the "XGMML (.xgmml,.xml)" file type.

2.2.11 Import Network from Database

2.2.11.1 BioModels

BioModels is a central repository of mathematical models of biological/biomedical processes. Models described from literature are manually curated and enriched with cross-references. To know more about BioModels refer to <https://www.ebi.ac.uk/biomodels-main/>.

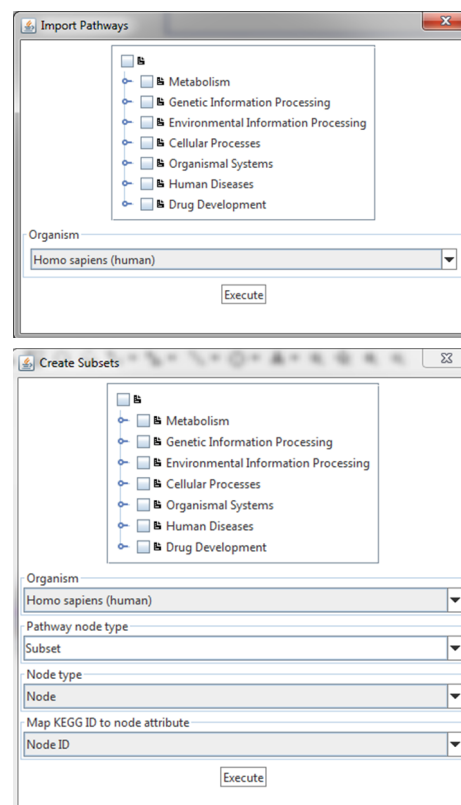
To upload a network from BioModels, select **Database -> BioModels**. A dialog window will open, where any model present in BioModels can be searched (using **Category** to select the type of search, and **Filter text** to perform the search) and retrieved. To upload the model of interest select the **Matching model** and click **open**.



2.2.11.2 KEGG

KEGG PATHWAY is a collection of manually drawn pathway maps including molecular interactions, reactions and relation networks. Specific details about KEGG query can be found at <http://www.kegg.jp/kegg/rest/keggapi.html>. To upload a network from KEGG PATHWAYS, select **Database -> KEGG**. A dialog window will open, where there are three possible searches:

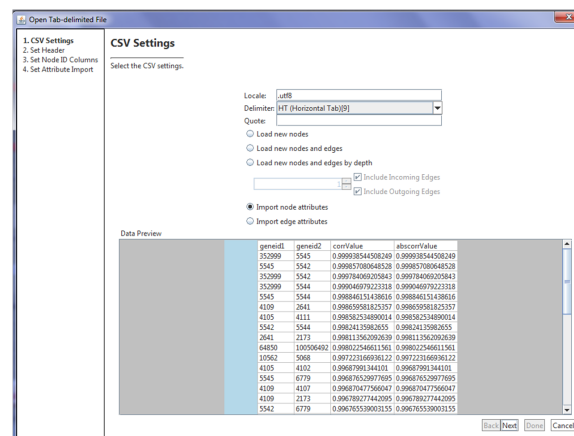
- **Build network from pathway.** It allows to import a pathway in NAViGaTOR from KEGG PATHWAY. The user can select any pathway from the ontology tree, and after specifying the **organism**, clicking execute the pathway will be imported in NAViGaTOR. This works only for the lowest level of the ontology.
- **Create subsets from pathways.** It allows to select a pathway from KEGG PATHWAY and to import it as a subset in the network. The user can select the pathway from the ontology tree on the left, and then select the **organism**, the **pathway node type**, the **node type** and what ID to **map to the node attribute**. **Execute** will import the pathway in NAViGaTOR.
- **Download conversion map.** Using this function it is possible to download two plain text files: **UniProt to HSA** and **HSA to UniProt** conversion maps, that map any KEGG ID to or from UniProt.



2.3 Import data to Network

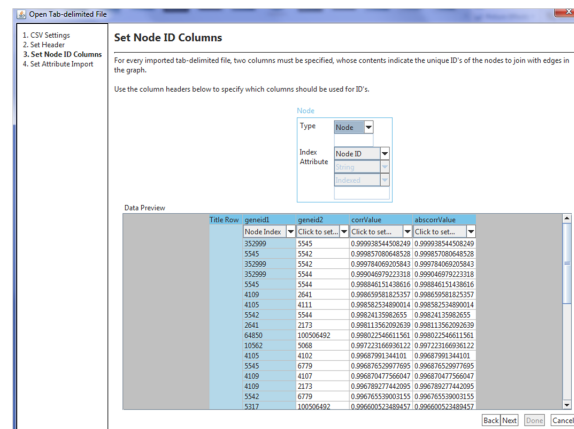
2.3.1 Delimited text

Importing data from a Tab-delimited file is very similar to reading a network from a text file. File formats included are .txt, .csv, .tab, .tsv. To import data, select **File -> Import** and then **delimited text**. This page allows you to specify the way in which your CSV data is loaded. **Locale** : The default locale (.utf8) will apply to most files, however, other formats are available as specified by the Data Import section of the Sparksee Manual. **Delimiter** : From here, you can select the ASCII character used to separate each row into columns (for example, horizontal tab, line feed...). **Quote** : For text or string type data, the column can be enclosed in quotations to ensure that characters in the column are not mistaken for delimiters. Any characters typed in this field will be used as quotes by the file loader.

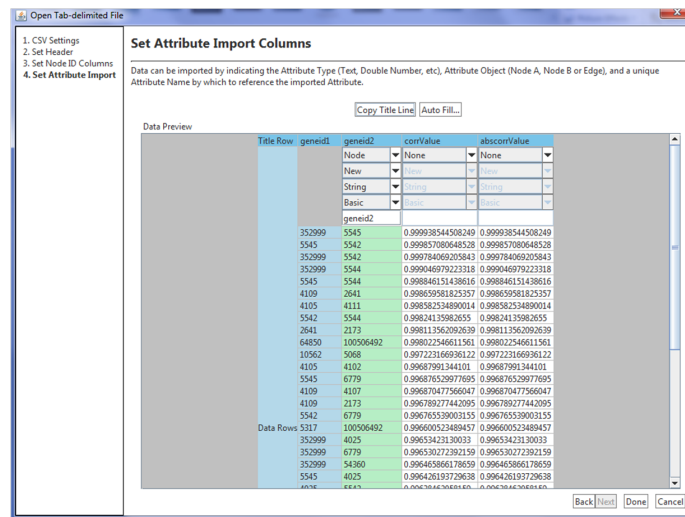


Set Header Information, as above.

Set Node ID Columns : The attribute will be used as node or edge identifier to associate data being imported to the specified graph entity.



Set Attribute Import Columns : For each column, you can specify what object that column refers to (Source, Target, or Edge), and define the Attribute you wish to use to represent that column. Ensure that the names you choose are unique and adequately describe the data in that column. If you previously selected a Title Row, you can automatically name each activated column (coloured green, after any type aside from None is selected) using the content of that row.

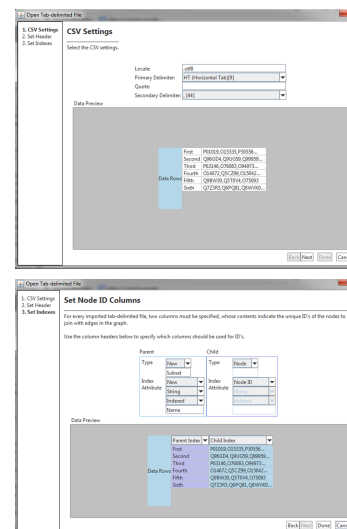


2.3.1.1 Delimited Text Subset File (.txt, .csv, .tab)

To automatically import subsets, the text file must include at least two columns, one that lists the name of the subset and one that lists the elements of the subset (it is important that the ID used for the elements of the subset coincide with an ID or annotation used for the elements of network). Moreover, the character used to separate the two columns must be different from the one used to separate the subsets elements.

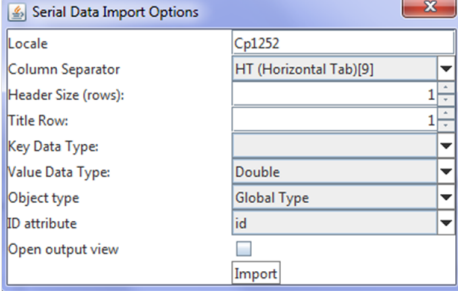
Once the file is correctly setup, select **Import -> Delimited Text Subset File (.txt, .csv, .tab)** and in the dialog window specify the primary delimiter (between columns) and the secondary delimiter (among elements), and click next.

Set then header information, as above, and click next. Finally, select a column for **parent index** (name of the subset) and **child index** (elements of the subset), and click done. The subsets will be automatically imported and created accordingly.



2.3.1.2 Serial Data Table (.txt, .csv, .tab)

This type of data is used to import repeated attributes for the same elements (for example, gene expression at different time points for each node). The text file for this task needs to be setup such as the first column of the file contains the series key (for example time points), while each consecutive column include data for each element (for example node). Columns headers have to include an attribute matching the attribute of the element in the network the data need to be assigned to. Once the file is correctly setup, select **Import -> Serial Data Table (.txt, .csv, .tab)** and a dialog window will open. In the window, select the **column separator** character, the **header** and **title size**, the **key** and **value data type**, to which object the values need to be assigned (**object type**), using which attributes (**ID attribute**). It is also possible to select **"open output view"** to see the imported data right away. Once clicked **Import**, serial data will be automatically imported.



Serial Data Import Options

Locale: Cp1252

Column Separator: HT (Horizontal Tab)[9]

Header Size (rows): 1

Title Row: 1

Key Data Type: Double

Value Data Type: Global Type

Object type: id

ID attribute: id

Open output view: ☐

Import

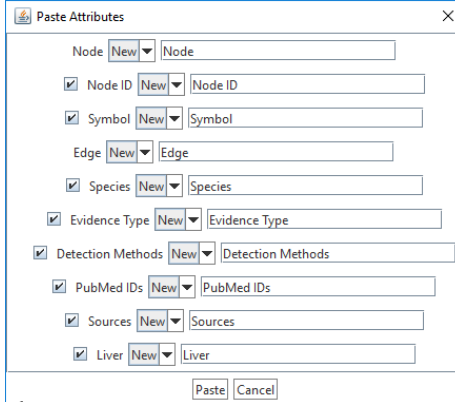
Time	A	C9	C9X	X	AC9X	AC9	C3	C3_star	C3_starX	C3_star	AC9_star	AC9_starX
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.01	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732
0.02	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732
0.03	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732
0.04	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732
0.05	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732
0.06	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732
0.07	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732
0.08	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732
0.09	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732
0.1	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732
0.11	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732
0.12	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732
0.13	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732
0.14	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732
0.15	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732
0.16	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732
0.17	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732
0.18	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732
0.19	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732
0.2	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732
0.21	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732
0.22	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732
0.23	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732
0.24	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732
0.25	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732
0.26	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732
0.27	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732
0.28	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732
0.29	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732	19.9030732

2.4 Divide and Merge Networks

2.4.1 Copy Sub-Networks

Copying a network or part of it:

- Mark the nodes and edges of interest
- Use the right click menu on one of the nodes and select "Edit"-> "Copy"
- Go the network file of interest (or create a new empty file).
- Use the right click menu and select "Edit"-> "Paste".
- A popup opens and requires you specify the attributes to be copied to the new network (see right side).
- For better visibility, we apply GRIP layout, set the colour of the nodes to blue and activate the node labels.



Paste Attributes

Node **New** Node

☒ Node ID **New** Node ID

☒ Symbol **New** Symbol

Edge **New** Edge

☒ Species **New** Species

☒ Evidence Type **New** Evidence Type

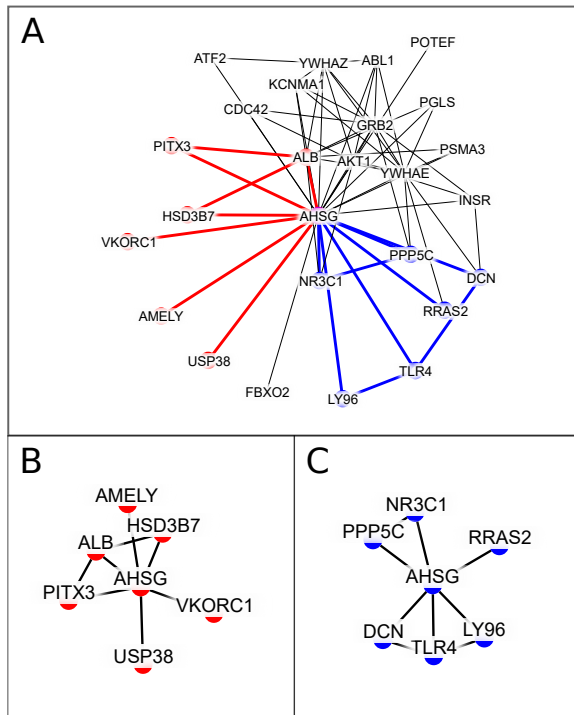
☒ Detection Methods **New** Detection Methods

☒ PubMed IDs **New** PubMed IDs

☒ Sources **New** Sources

☒ Liver **New** Liver

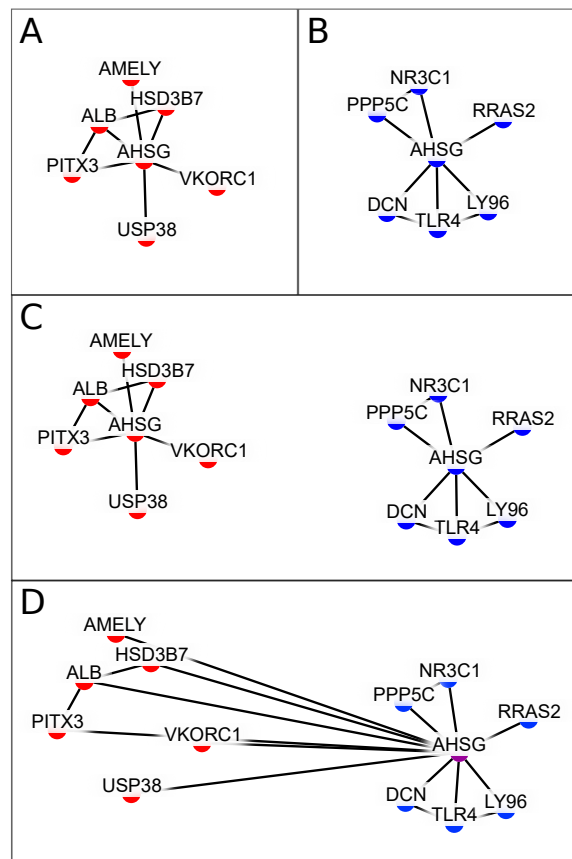
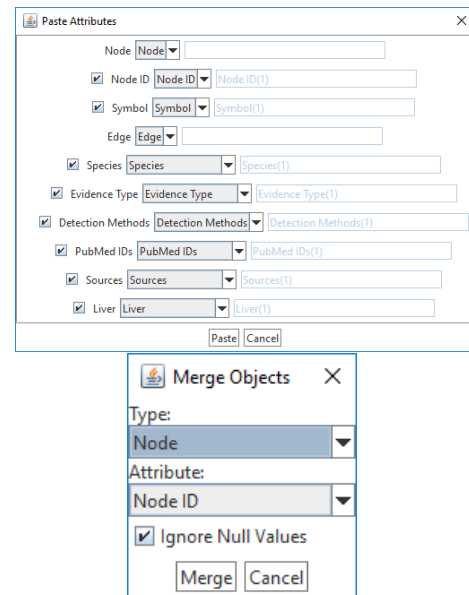
Paste Cancel



2.4.2 Merge Networks

Merging two networks:

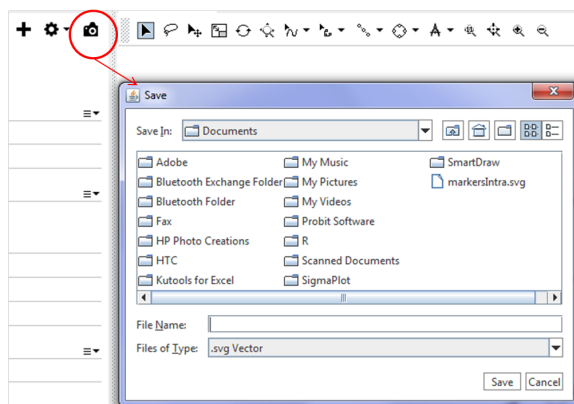
- Mark the nodes and edges of interest.
- Use the right click menu on one of the nodes and select "Edit"-> "Copy"
- Go the network file of you want to merge it with.
- Use the right click menu and select "Edit"-> "Paste"
- A popup opens and requires you match the attribute names of the copied network to the attribute names given network (See top right side).
- For better visibility, we apply GRID layout, set the color of the nodes to blue and activate the node labels.
- Finally, you need to merge the networks by using the right click menu and select "Edit"-> "Merge".
- Define the identifier to be used for the merging process (See bottom right side).



2.5 Export Networks

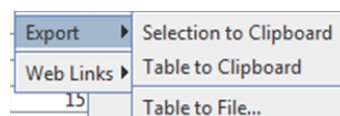
2.5.1 Image Export

You can export images from the Graph View in several formats. The preferred format for publication is SVG, as it is infinitely scalable and high-quality. For info on the SVG format, visit <http://www.w3.org/Graphics/SVG/>. However, for very large or graphically complex graphs, exported SVG files may be too large to edit or display in some software. In these cases, the following bitmap formats are available, which will export the graph View exactly as it appears on your screen: BMP, JPG, TIF, PNG, GIF. To export an image from a Graph View, first ensure that you have the Appearance Tab open in your Workspace. Once you have clicked on the graph view you wish to export, the Appearance Tab should show you the renderers in that view. From here, you can click on the camera icon to open a save dialog. Select your file format and name, and click on 'Save' to export the file.



2.5.2 Data Export

It is possible to export any data included as a table in NAViGaTOR. Right clicking on the table to be exported, select **export** and then choose among: **selection to clipboard**, where anything selected is copied to be pasted in any other text handling program, **table to clipboard**, where the entire table of interest is copied to be pasted in another program (note, if the table is very big, this command might take some time), and **table to file**, that opens a dialog window where the user can name the file and decide the location where to save it.



2.5.3 Whole Network Export

Note: some formats are repeated from Section 2.3

2.5.3.1 NAViGaTOR Format

When a graph is saved in .n3e format, it can be assumed that all information in the workspace pertaining to that graph will be saved, and can later be loaded into the workspace again without any losses. To save a network in NAViGaTOR format, select **Save** (if the first time) or **Save As**, and in the dialog window choose **N3E .n3e**, name the network and save it to a destination of choice.

2.5.3.2 DEX and DEX backup

DEX is the standard format of Sparksee (formerly known as DEX), NAViGaTOR's backbone. A network exported in this format will include nodes, edges and attributes, but not visual annotation or dynamic attributes. To save a network in DEX format, select **Save** (if the first time) or **Save As**, and in the dialog window choose **DEX (.dex)** or **DEX Backup (.dexb)**, name the network and save it to a destination of choice.

2.5.3.3 GraphML

GraphML is an XML-based file format for graphs, used as a common format for exchanging graph structure data. For more information on this file format, visit <http://graphml.graphdrawing.org/>. When saving on this format, only nodes/edges will be saved without any other feature. To save a network in GraphML format, select **Save** (if the first time) or **Save As**, and in the dialog window choose **GraphML, (.gml, .xml)**, name the network and save it to a destination of choice.

2.5.3.4 XGMML

XGMML is an XML based format used for graph description. More info on XGMML file format is available at http://cgi5.cs.rpi.edu/research/groups/pb/punin/public_html/XGMML/. When saving on this format, nodes, edges and attributes will be saved, but not visual annotations or dynamic attributes. To save a network in XGMML format, select **Save** (if the first time) or **Save As**, and in the dialog window choose **XGMML (.xgmml, .xml)**, name the network and save it to a destination of choice.

2.5.3.5 Delimited text

Tab-delimited files are plain ASCII files in a row/column format, with a reserved character for separating columns. As such, when saving a network in this format, only information about which nodes interact will be saved. On re-opening the network, no automatic upload will be performed and user will have to perform the same process as described in 2.2.3. To save a network in text format, select **Save** (if the first time) or **Save As**, and in the dialog window choose **Delimited text (.txt, .csv, .tab, .tsv)**, name the network and save it to a destination of choice.



3. Network Annotation

The visualization of large biological networks often results in an incomprehensible ‘hairball’, which is not directly interpretable. Therefore, it may be difficult to interpret and extract useful information with respect to biological meaning.

The integration of additional information about the entities represented in the network, may facilitate the organization and the analysis of the networks. These node or edge annotations can be included in the original data, such as network files, or imported from additional files or databases, see Chapter 2. We can categorize network annotation according to the type of data, quantitative and qualitative, respectively.

Qualitative annotations

Qualitative annotations can be visualized through qualitative visual attributes, such as colour, size, outline, and shape. Widely used sets of annotations are available from public biomedical databases and ontologies. An ontology formally names and defines the terms, properties, and relationships among the entities that exist in a particular domain. See Section 3.3 for examples.

Quantitative annotations

In contrast to qualitative information, quantitative annotations rely on continuous measures, that are determined analytically, calculated, or estimated by different techniques. Many databases collect quantitative data that can be used to annotate nodes, e.g., GEO (<https://www.ncbi.nlm.nih.gov/geo/>), ArrayExpress (<https://www.ebi.ac.uk/arrayexpress/>), The Protein Atlas (<http://www.proteinatlas.org/>), while very few databases include data that can be used to annotate edges - one example being COEXPRESdb (<http://coxpresdb.jp/>). Quantitative measures can be visualized through quantitative visual attributes such as size (node type and outline), transparency, or shades of colors

3.1 Manual Annotation

3.1.1 Adding a New Attribute

Select Graph -> New Attribute. Name the attribute in the "New Attribute Name" box. You can select an object type, value type, and constraints using the drop down menus for each. To use a default value, select the "use default value" box and manually enter the value.

3.1.2 Add Node Labels

Ensure you have highlighted the desired portion of the graph. Under the "basic label renderer" drop down, you can add and modify node labels. When selecting a source, you can choose from any of your created attributes, or "index" or "none" using the drop down menu. If you wish to add a length limit, deselect the "none" box and choose a numerical value with the up/down arrows. Foreground and background color and opacity can be modified using the respective scales. To reset colors, click "auto color". Label size, horizontal justify, vertical justify, and distance can be modified using the respective scales and drop down menus. By selecting only the "angled" box, you can modify the anchor point by dragging your cursor around the anchor point circle. From the anchor point, you can adjust by an increase or decrease of up to 10 units. Click "flip" to make the anchor point diametrically opposed. To center the anchor point, simply check the "center" box.

If selected, the same procedure will add labels to subset parent nodes as well.

3.1.3 Add Edge Labels

Ensure you have highlighted the desired portion of the graph. Follow the same instructions that apply to adding node labels, with the exception of angling and anchor point.

3.2 Annotation by File

This has already been described in Chapter 2 (importing data to network from tab separated file)

3.3 Annotation by Database

3.3.1 PathDIP

Click **Database -> PathDIP Enrichment**. Select a node type and node index attribute using the respective drop down menus. For the node ID entry, you can select between using the full graph or using graph selection by selecting the desired box. Choose an ID type from the drop down menu and select all the desired data sets. Choose a result node type, result name attribute, result source attribute and result P value attribute. Click search to view results. Then choose a max P-value to filter by using the up/down arrows and select the pathway(s) you wish to add. Pathways will be added as subsets.

3.3.2 Integrated Interaction Database (IID) Interactions

To complete an IID Protein-Protein search, select **Database -> IID Interactions**. Choose a node and edge type using the drop down menus. For a new edge or node type, it is possible to rename the output attribute. Select a node **Query ID attribute** and edge source attribute using the respective drop down menus. By clicking "**manual entry**" you can manually enter the node type, edge type, node index attribute and edge source attribute names, as well as a Node ID Entry. Otherwise it is possible to use the entire **Graph** or **Graph Selection**. It is moreover possible to select if the PPI of

interest need to be conserved in different species and/or in different tissues. Once clicked **Search** the retrieved interactions (and interactors) will automatically be added to the network.

3.3.3 UniProt

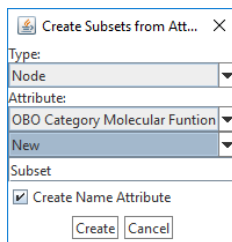
Select **Database -> Uni Prot Annotations**. Select a node type and UniProt ID attribute using the respective drop down menus. You can click the "use selection only" to narrow the search. You can select up to 3 available line parsers, and then select all of the databases/information platforms desired. Finish by clicking "add".

3.3.3.1 Gene Ontology

Querying UniProt provides the possibility to annotate nodes with data included in all the ontologies supported by UniProt (listed at <http://www.uniprot.org/database/>). Among these ontologies, the most widely used in biology is Gene Ontology (GO <http://www.geneontology.org/>). If selected, the plugin will add all the terms associated with each node. This will provide the base to automatically color nodes based on GO categories, with NAViGaTOR preset filters.

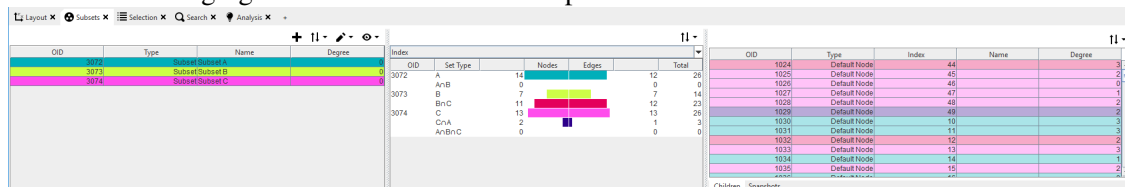
3.4 Structuring Networks from Annotation

Categorical annotations as described above, can be used to add structure to a network in the form of subsets. In the following we describe the process of creating subsets from categorical attributes.



- Select the "Subsets" panel in the bottom part of the application.
- Chose the "Pen"-drop-down menu and select "Create Subsets from Attribute".
- Enter the required fields:
 - Select Type
 - Select Categorical Attribute
 - Select type of Subset
- Click "Create".

The following figure shows the result subset panel in the bottom of the NAViGaTOR framework.

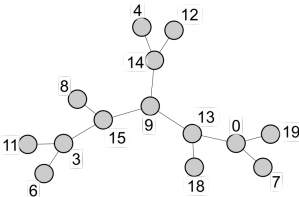
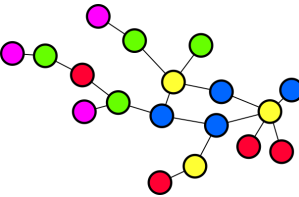
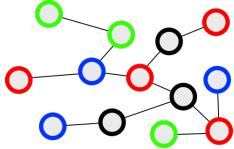
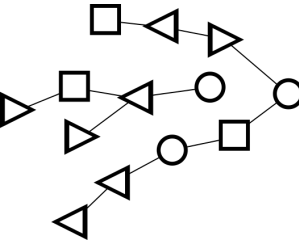


The first panel on the left shows a list of all subsets created for this network including attached attributes, such as ID, type or name. The middle panel shows the number of nodes, objects and the sum, for all selected subset (left panel) and intersections of these. The center shows bar plots for both nodes and edges in randomly assigned colours. The right panel shows the list of nodes that are member of the selected subsets. Each node is coloured according to the corresponding subset or subset intersection.

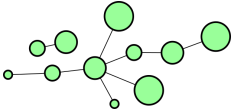
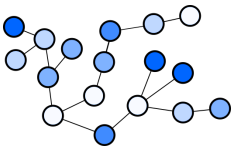
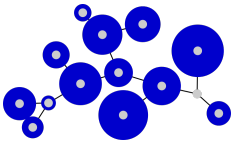
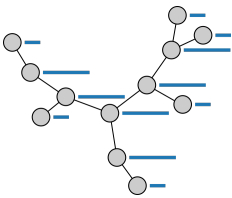
3.5 Visual Annotation

Incorporating this annotation information in the network visualization, by modifying the appearance of nodes and edges, can greatly increase the interpretability of the network. Note: To change the appearance of a node, edge or subset, the object has to be selected in the graph panel, see Chapter 4. As described previously, nodes and edges can be annotated by qualitative and quantitative parameters. In the following we will show different possibilities to visualize these attributes in a network with NAViGATOR.

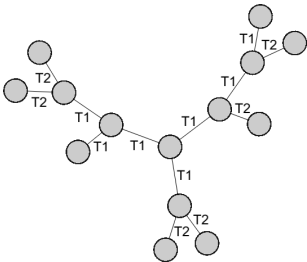
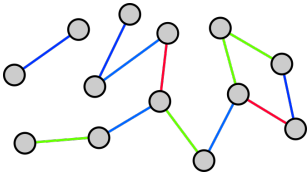
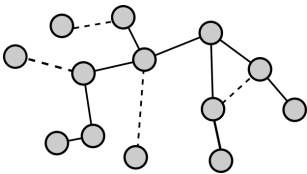
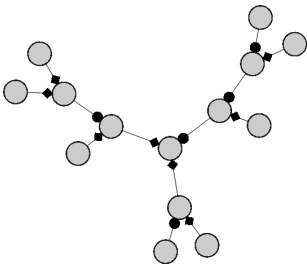
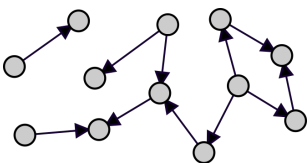
3.5.1 Visualization of Qualitative Node Attributes.

Visual	Description	Instructions
	<u>Node Label</u> : Annotating each node with a label/name. This can be for example an identifier, a gene symbol, name or role of the object represented by the node.	Navigator Appearance Panel; Open/Enlarge Basic Label Renderer and Node Label; Select the "Source" to be displayed as label and adjust other font parameter.
	<u>Coloured nodes</u> : This type of visualization is often used to indicate different categories, such as the ones obtained from biological process or molecular function Gene Ontologies.	Navigator Appearance Panel; Open/Enlarge Basic Node Renderer, Color; Select the nodes of one type. Click in the colored field and select the preferred colour in the color-selection pop-up.
	<u>Node highlighting</u> : Nodes that have special meaning or indications, such as drug targets or network hubs can be emphasized by highlights.	Navigator Appearance Panel; Open/Enlarge Basic Node Renderer, Highlight; Select the nodes of one type. Click in the colored field and select the preferred colour in the color-selection pop-up.
	<u>Shaped categories</u> : Similar to color, different shapes can indicate different groups or communities. In gene-regulatory or PPI networks, frequently a combination of both is used, where green and red, and up- and down-pointing arrows indicate up- and down-regulated genes, respectively.	Navigator Appearance Panel; Open/Enlarge Basic Node Renderer, Shape; Select the nodes of one type. Modify the shape by adjusting the corresponding drop-down field. Options are: Ellipse, Rectangle, Triangle (up), Triangle (down), Diamond, and Polygon. The height and width parameters specify the dimensions of the shape.

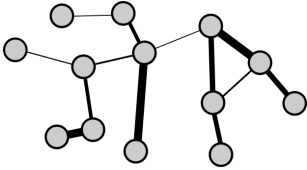
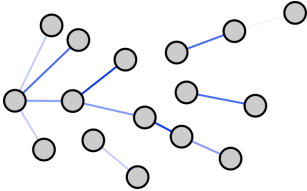
3.5.2 Visualization of Quantitative Node Attributes.

Visual	Description	Instruction
	<u>Node size:</u> Similar to the previous, it can be used to represent the importance of vertices with respect to a continuous feature. Both transparency and size can significantly increase the interpretability of a network by fading out or reducing unimportant information.	Navigator Appearance Panel; Open/Enlarge Basic Node Renderer and Filters; Use the Plus button to choose and add the Node Matrix Filter . Define a name and click OK . The new filter appears in the Filter section. The table of different numeric attributes (columns) and visual parameters (rows) is shown. By selecting the radial buttons for Width and/or Height , the size of the nodes will be set relatively to the corresponding node attribute.
	<u>Node transparency:</u> This technique can be used for instance to put emphasis on nodes that show a high range in a quantitative measure, such as expression, statistical significance, centrality, etc.	Navigator Appearance Panel; Open/Enlarge Basic Node Renderer and Filters; Use the Plus button to choose and add the Node Matrix Filter . Define a name and click OK . The new filter appears in the Filter section. The table of different numeric attributes (columns) and visual parameters (rows) is shown. By selecting the radial buttons for Transparency , the transparency of the nodes will be set relatively to the corresponding node attribute.
	<u>Node highlight:</u> This technique can be used for instance to indicate the importance of nodes. The highlight can increase in size, for instance, with respect to quantitative measures such as gene expression, statistical significance, centrality, etc.	Navigator Appearance Panel; Open/Enlarge Basic Node Renderer and Filters; Use the Plus button to choose and add the Node Matrix Filter . Define a name and click OK . The new filter appears in the Filter section. The table of different numeric attributes (columns) and visual parameters (rows) is shown. By selecting the radial buttons for Highlight size , the size of the highlight will be set relatively to the corresponding node attribute.
	<u>Spokes visualization:</u> Similar to color or shade, the spoke visualization can indicate numeric attributes. Each attribute is shown as a stacked level or bar plot attached to the outer side of each node. The advantage to this visualization is that multiple attributes can be shown at the same time. See Chapter 4 and 6 for more examples.	Use the Plus Button in the top right to add the Spoke Renderer to the Navigator Appearance Panel. Different parameter define the type of spoke, orientation, and maximal length. To add attributes, use the Plus button under Available Attributes . The attributes are added to the table and can be activated by the Show checkbox. To adjust the color you can use the corresponding color field and pop-up.

3.5.3 Visualization of Qualitative Edge Attributes.

Visual	Description	Instruction
	Edge Label: Annotating each edge with a label/name. This can be for example an identifier, name, or the type of connection or interaction, represented by the edge.	Navigator Appearance Panel; Open/Enlarge Basic Label Renderer and Edge Label; Select the "Source" to be displayed as label and adjust other font parameter.
	Edge colors: Different colors can indicate different categories of network relations, for instance, in PPI networks, the difference between protein complexes and regular interaction, levels of positive/negative co-expression, or PPI deregulation in normal vs cancer tissues.	Select the edges of one type. Go to Navigator Appearance Panel; Open/Enlarge Basic Edge Renderer, and open the Color section. Click in the colored field and select the preferred colour in the color-selection pop-up.
	Edge type: Similar to color, the type (stipple) of an edge can indicate different types of relations. This can be beneficial to visualize, for instance, train lines that are only in service for specific times of the day.	Select the edges of one type. Go to Navigator Appearance Panel; Open/Enlarge Basic Edge Renderer, and open the Style section. Use the parameters to adjust the appearance of the edges. E.g. Use the stipple checkbox to plot a dashed line for each edge.
	Edge arrow type: Similar to the edge type, the symbol at the beginning or end of an edge can indicate different types of relations.	Select the edges you want to activate the arrows. Go to Navigator Appearance Panel; Open/Enlarge Basic Edge Renderer, Head & Tail; Modify the shape by adjusting the corresponding drop-down fields for Head or Tail . Options are: Arrow, Circle, None. The height and width parameters specify the dimensions of the shape.
	Edge directionality: The arrows indicate the direction of the connection. For instance, trains or goods going from one city to another.	Navigator Appearance Panel; Open/Enlarge Basic Edge Renderer, Arrows; Select the edges you want to activate the arrows. Modify the shape by adjusting the corresponding drop-down fields for Head or Tail . Options are: Arrow, Circle, None. The height and width parameters specify the dimensions of the shape.

3.5.4 Visualization of Quantitative Edge Attributes.

Visual	Description	Instructions
	<p>Edge thickness: Similar to color and shade, the thickness of an edge can indicate different strength or type of relations. This can be beneficial to visualize, for instance, gene co-expression in a PPI or gene-regulatory network.</p>	<p>Navigator Appearance Panel; Open/Enlarge Basic Edge Ren- derer and Filters; Use the Plus button to choose and add the Edge Matrix Filter. Define a name and click OK. The new filter appears in the Filter section. The table of different numeric attributes (columns) and visual param- eters (rows) is shown. By selecting the radial buttons for Width, the width of the edges will be set relatively to the corresponding edge attribute.</p>
	<p>Edge transparency: Trans- parency can be used to indicate the strength of an interaction. In gene-regulatory networks it can be utilized to visualize the probability that a regulatory factor controls a certain gene.</p>	<p>Navigator Appearance Panel; Open/Enlarge Basic Edge Ren- derer and Filters; Use the Plus button to choose and add the Edge Matrix Filter. Define a name and click OK. The new filter appears in the Filter section. The table of different numeric attributes (columns) and visual param- eters (rows) is shown. By selecting the radial buttons for Transparency, the transparency of the edges will be set relatively to the corresponding edge attribute.</p>



4. Visualization

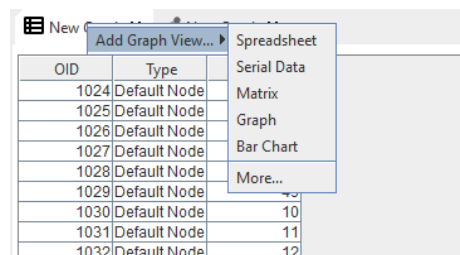
4.1 Visualization Types

NAVIGATOR supports different visualization types, so called **Graph Views**. They are special tabs in the center of the workspace that allow the user to interact with the graph structure, network attributes, and data in different ways. A graph view is bound to the graph for which it is created. When a graph is closed, graph views that are bound to it will no longer be available. When a graph is created, some views will be generated by default, while others can be added to the graph afterwards. The most commonly used views are:

- Graph Layout
- Spreadsheet
- Matrix View
- Bar Chart

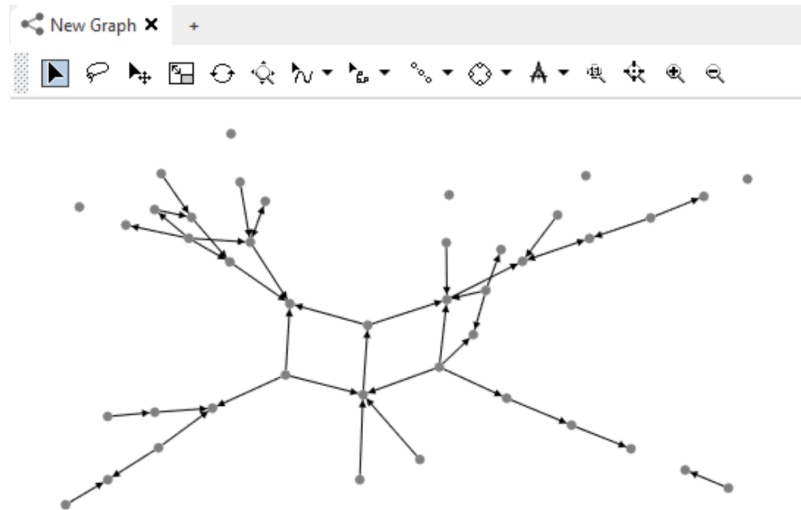
There are two ways to create new graph views for an existing graph:

1. From within an existing graph view tab, right click on the tab title. A drop-down menu will appear with a list of all the possible views that can be generated for that graph.
2. From the Workspace tab, expand your network, then **Graph Data**. Right click on **OGLGraphView** and select **Graph View**. From the menu it is possible to add a new view or show the selected graph.

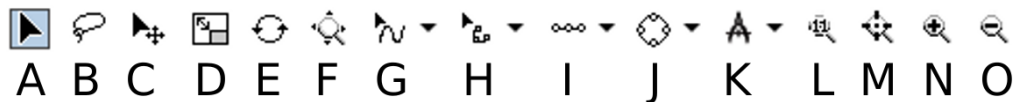


4.1.1 Graph Layout ("OpenGL")

After creating a new network, it will be first visualized in the "Graph View" panel. The default graph layout displayed is the GRIP layout. NAViGaTOR offers a variety of different layouts, see Section 8.3.6 "Network Layouts" for more details.



4.1.1.1 Graph Layout Menu Bar



In the following we will describe a few basic functions in the NAViGaTOR graph view:

- A Selection Tool:** Use this tool to select single elements or objects. A mouse click on the targeted element selects it. The "Ctrl"-Key enables the selection of several elements.
- B Lasso Tool:** Use this tool to select a group of elements or objects. Draw a circle around the targeted elements.
- C Move:** Use this tool to move a selection of elements or the entire network.
- D Scaling:** Use this tool to scale a selection of elements or the entire network.
- E Rotation:** Use this tool to rotate a selection of elements or the entire network.
- F Navigate:** Use this tool to navigate through large networks.
- G Curved Edges** Use this tool to curve the edges of your graph.
- H Curved Planar** Use this tool to arrange the nodes in a planar graph in a radial way.
- I Planar Layout** Use this tool to create a planar layout of the selected nodes.
- J Circular** Use this tool to create a circular layout of the selected nodes.
- K Node Swap** Use this tool to randomly or guided swap node locations.
- L Original Size** Use this tool to reset the network to it's original size.
- M Center** Use this tool to move the network to the center of the Graph View panel.
- N Zoom In** Use this tool to zoom in.
- O Zoom Out** Use this tool to zoom out.

4.1.2 Spreadsheet

The spreadsheet view contains three different tabs, showing the information for all nodes, edges and subsets, respectively. This comprises network attributes that are imported when loading the network, or while annotating edges and nodes with additional information. Additionally, it contains all dynamically generated properties, such as node degree, gene ontology function or the results of network analysis algorithms like community search.

OID	Type	Index	Name	Degree
1040	Default Node	0		3
1041	Default Node	1		2
1042	Default Node	2		1
1043	Default Node	3		3
1044	Default Node	4		1
1045	Default Node	5		1
1046	Default Node	6		2
1047	Default Node	7		2
1048	Default Node	8		2
1049	Default Node	9		2
1030	Default Node	10		3

OID	Type	Source	Target
2048	Default Edge	1049	1038
2049	Default Edge	1067	1050
2050	Default Edge	1058	1047
2051	Default Edge	1035	1025
2052	Default Edge	1065	1063
2053	Default Edge	1025	1064
2054	Default Edge	1037	1052
2055	Default Edge	1073	1041
2056	Default Edge	1030	1065
2057	Default Edge	1029	1055
2058	Default Edge	1073	1024

OID	Type	Name	Degree
3072	Subset	Subset A	0
3073	Subset	Subset B	0
3074	Subset	Subset C	0

4.1.3 Edge Matrix Layout

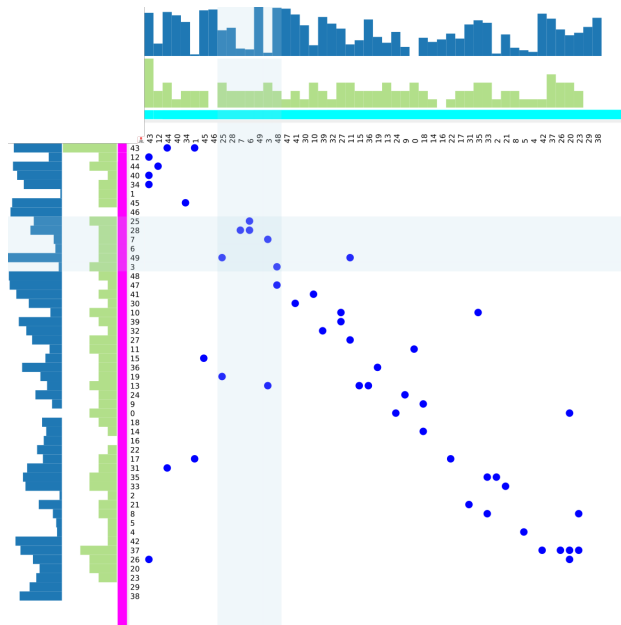
Edge-matrix or heatmap visualizations of networks, can be utilized to depict the edges and edge weights between the vertices in a network. Directed networks result in a non-symmetric matrix. This visualization can highlight densely connected subnetworks, by clustering the nodes according to a topological or content specific similarity.

Instruction Open the Matrix View panel in the central area of NAViGaTOR. The matrix view shows a dot for each edge. Additionally, labels can be added to the visualization. The matrix can be sorted via different attributes or algorithms, see ?? Sorting. Finally, several bar chart can be attached to each of the left or the top axis.

Add Label Use the right-click menu on one of the axis (left/top) and select "Labels"->"by Attribute" and the corresponding label.

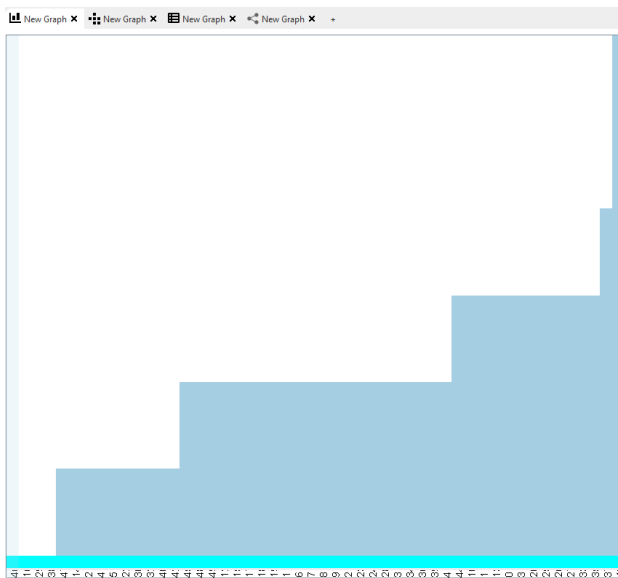
Sort Axis Use the right-click menu on one of the axis (left/top) and select "Order" and the corresponding sorting.

Add Bar Chart Use the right-click menu on one of the axis (left/top) and use "Charts" to add a selection of attributes as bar charts to the axis.



4.1.4 Bar Chart

This graph view displays graph attributes in a bar chart format. There are three tabs in this view, one each for Nodes, Edges, and Subsets, which can be selected in the lower left of the view. To add an attribute to the Bar Chart Graph view, right click anywhere on the tab, and select from the available attributes in the Charts sub-menu. To change the ordering of the objects in the bar chart, right click anywhere on the tab, and select from the available sorting methods in the Order sub-menu. To add a label for each object, right click anywhere on the tab, and select from the available attributes in the Labels sub-menu. The amount of space reserved for the label can be altered by clicking and dragging the border between the labels and the bar chart itself.



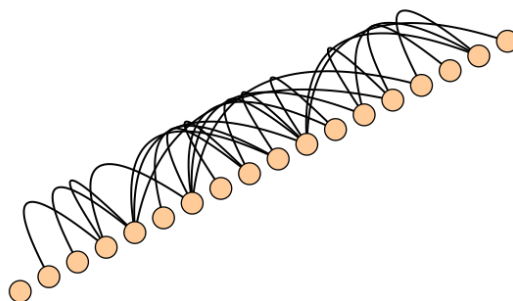
4.2 Network Layouts

4.2.1 Static Layouts

Static Layouts attempt to optimize all or a part of the graphs layout automatically. You can reach these layouts either using the "Layout" menu in the top-menu or using the "Graph View" menu bar.

4.2.1.1 Planar Layout

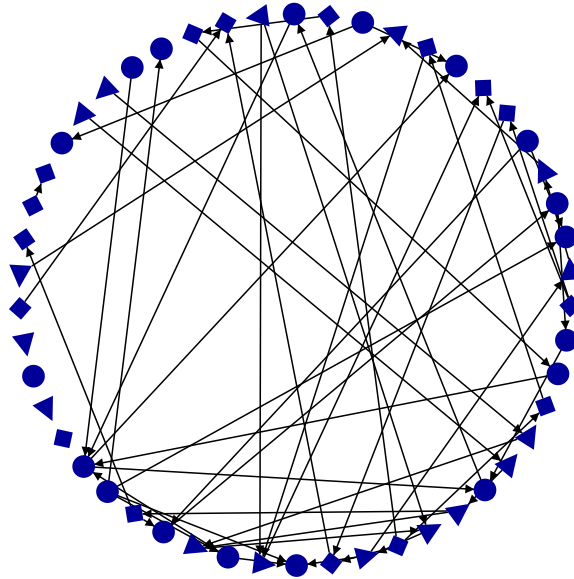
The planar layout is simple and easy to visualize for small and sparse networks. The main advantage is that individual nodes can be arranged with respect to any ordered node attribute, such as, node name, or biological features such as gene ontology and biological function. The edges are drawn as convex curves in one of the two half-planes separated by the line.



Instruction Select all nodes to be arranged by the planar layout. Use the "Graph View" menu and select the button for planar layouts **I**.

4.2.1.2 Circular Layout

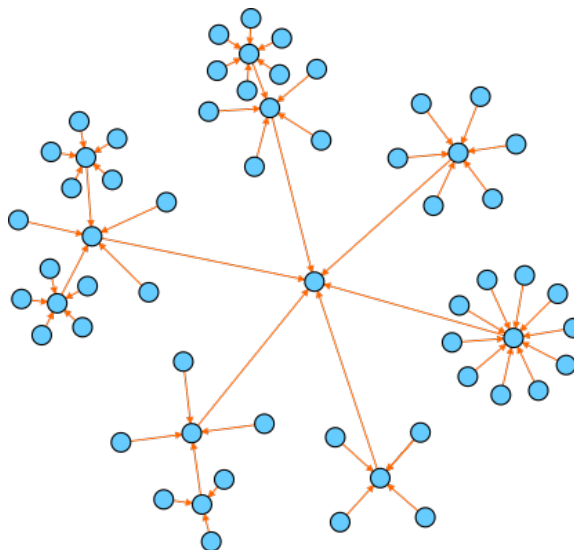
The nodes in the circular layout are placed equidistant from the graph, aiming to minimize overlapping nodes, see Figure ?? E. Despite its simplicity, the technique is widely used to visualize biological networks such as protein complexes, drug-protein, miRNA-gene and phylogenetic networks.



Instruction Select all nodes to be arranged by the planar layout. Use the "Graph View" menu and select the button for circular layouts **J**.

The radial layout or balloon layout are special tree-based visualizations incorporating the idea of circular layouts. The radial approach places the nodes onto concentric circles relative to their depth in the tree. The balloon view of a tree projects all sibling subtrees onto circles attached to the father node.

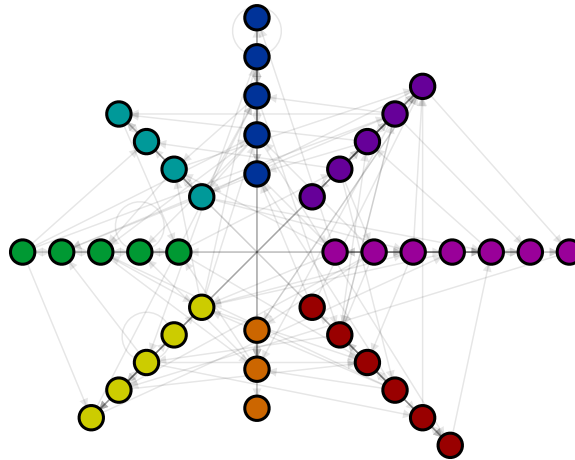
Radial Layout



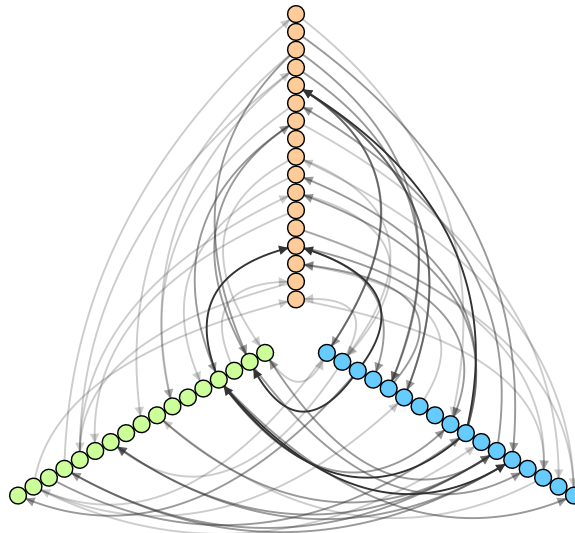
Instruction Move the root node in the center. Select all child nodes of root apply the circular layout. Move the root in the center of the circle. Repeat this approach iteratively.

4.2.1.3 Hive Plot (Spoke)

Similar to other approaches, the objective of a hive plot is to create rational, informative and reproducible layouts. The nodes are placed on multiple radially arranged straight lines originating in the center, representing linear axes with respect to a well-defined coordinate system. This creates a compact and reproducible layout with perceptual uniformity, where connections are easy to follow.

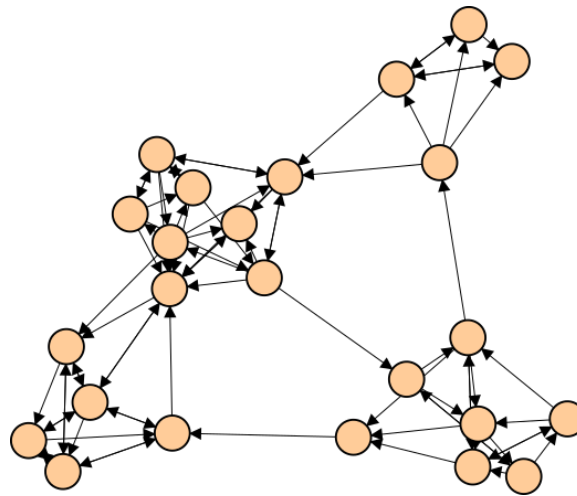


Instruction Create a subset for each group of nodes to be visualized as one of the axes. You can reach the hive plot layout using the "Layout" menu in the top-menu. It will request you to select the subsets to be used. When clicking the "OK" button, each group will be arranged as straight line originating in the center. The usage of the Curved Edges tool (G) can improve the visualization.



4.2.1.4 GRIP

Graph dRrawing with Intelligent Placement - GRIP - has been designed to effectively visualize very large graphs. It applies a multi-dimensional force-directed method in combination with a fast energy function minimization. Intelligent vertices placement ensures that the running time and space complexity of a network are near linear in the number of vertices.



Instruction Select the nodes to be arranged using the GRIP layout. When not selecting any node the entire network is used. You can reach the GRIP layout using the "Layout" - "Static Layout" menu in the top-menu.

4.2.2 Dynamic Layouts

Dynamic Layouts attempt to constantly optimize the layout of the graph, unlike a Static Layout, which will only execute the layout algorithm once. For example, the included Force Directed layout will attempt to bring interacting nodes a specified distance apart. If the user moves one of these nodes in a graph view, the dynamic layout will adapt to the change and push or pull the node back towards an ideal distance. By default, there are no Dynamic Layouts added to a graph.

Add To add a layout, click on the '+' button in the upper right of the tab. You will be given a list of possible layouts to choose from.

Remove To remove a Dynamic Layout, click on the menu arrow on the right side of the corresponding layout header, and select 'Delete Dynamic Layout'.

Start/Stop Dynamic Layouts can be stopped and started by toggling the Play arrow button in the upper right of the tab.

Lock Nodes From this tab, nodes can also be set to a 'locked' state. In this state, they will not respond to any attempts to be moved by a Dynamic Layout. To set nodes to locked or unlocked, select a set of nodes in a graph view, and click on the corresponding padlock icon at the top right of the Dynamic Layout tab.

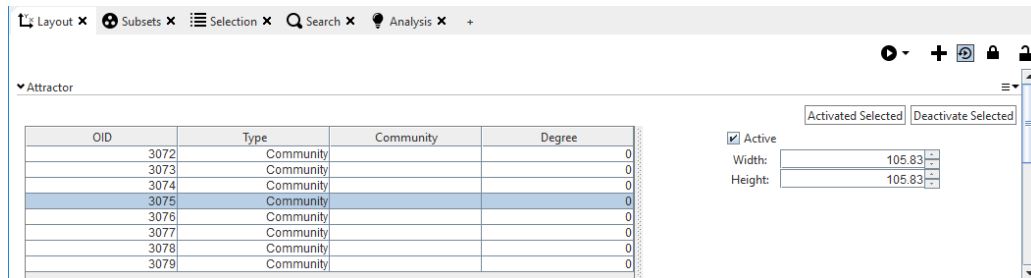
Multiple dynamic layouts can be added to a single graph to produce complex layout strategies. How they interact depends entirely on the layouts used, and some results may be unpredictable. If a combination of Dynamic Layouts turns out to be problematic, simply stop the layout process and perform a static layout.

4.2.2.1 Attractor

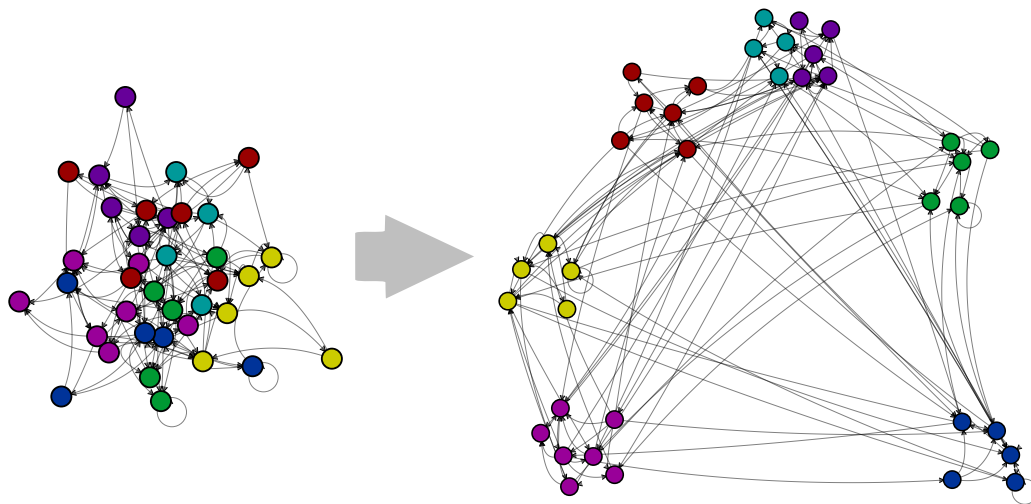
The Attractor Dynamic Layout constrains nodes within the same subset to the same area in the layout. Nodes in active subsets will be constrained to a single area surrounding the subset's parent node. The desired width and height of the area to be occupied by the subset can be set by the width and height controls. Deactivated nodes will not be affected by the layout.

Instruction Open the Layout panel in the bottom area of NAViGaTOR. Use the "PLUS" button to

add the attractor layout.



It shows a list of all subsets available for this network. Select all subsets to be arranged in separated areas and click "Activate Selection" or manually select each subset and use the "Active" check-box in the controls. The Width and Hight parameter can be used to refine the outcome. The following figure shows two networks, (1) network with detected communities in GRIP layout and (2) visualization of the network using the attractor layout.



4.2.2.2 Force Directed

The Force Directed layout attempts to move connected nodes to a set distance from each other, by applying a virtual force to each node from every edge connected to it. From Force Directed control panel, the distance between connected nodes can be set, as well as the level of force which will be applied to each node for every iteration of the algorithm.

Instruction Open the Layout panel in the bottom area of NAViGaTOR. Use the "PLUS" button to add the force directed layout.

4.2.2.3 GRID Variant

The GRID Variant is an optimization of the Force Directed Layout that divides the graph into a grid, and only performs layout tasks for nodes that exist in the same or adjoining grid sections. This layout has identical controls and analogous behaviour to the Force Directed layout.

Instruction Open the Layout panel in the bottom area of NAViGaTOR. Use the "PLUS" button to add the GRID variant layout.

4.2.2.4 Projector

The Projector layout translates node attributes into X or Y coordinates.

Instruction Open the Layout panel in the bottom area of NAViGaTOR. Use the "PLUS" button to add the Projector layout.

4.3 Appearance of Network Components

The appearance of each component in the network, namely nodes, edges, node labels and edge labels, can be adjusted. The appearance panel provides different "Renderer" change attributes such as color or shape. Note: To manipulate the following features, ensure you select the objects in the network you wish to work on. In the following we will describe how to change the appearance of different components. Note: To manipulate the following features, ensure you select the objects in the network you wish to work on.

4.3.1 Basic Node Appearance

The "Basic Node Renderer" enables to change various attributes of selected nodes:

4.3.1.1 Color

Color Clicking on the color button will open a color selection dialog with which to select a nodes color.

Opacity The node's transparency can be changed by using the slider dropdown beside the opacity value, or by manually entering a value between 1 and 100.

4.3.1.2 Shape

Shape Clicking on the node shape drop-down list will select between the available shapes for the node renderer.

Height & Width Node height and width can be manipulated using their respective controls, and may be locked to having the same height and width by clicking on the chain link icon.

Rotation Rotation can be altered by dragging your cursor around the rotation circle or using the numerical control.

Snap Edges to Midpoint You can "snap edges to midpoint" by selecting this box.

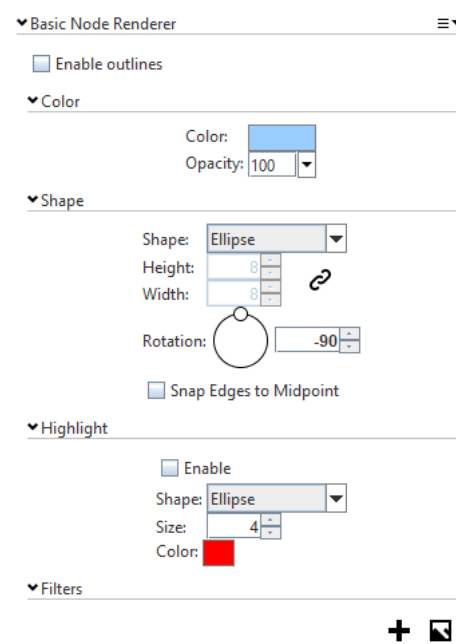
4.3.1.3 Highlight

Highlighting a node by clicking on the enable checkbox will draw a shape around the primary node shape.

Shape The highlight's shape can be altered through the shape dropdown list.

Size The size control will set the distance from the primary shape that the highlight will extend.

Color The color box will open a dialog to select the highlight color.



4.3.1.4 Filters

Click the filters drop down menu and select the "+" sign to add 1 of 6 default filters. You can choose from:

- Time Node Filter
- Rome Node Filter
- OBO Color Filter
- Node Matrix Filter
- Comparison Node Filter
- Color Scheme Filter

Click "add". You can change the name in the Graph Data Name box that appears. Select "OK". To change the features, click the drop down arrow to the left of the filter name. Each filter has different changeable features. Clicking on the arrow to the far right gives you the option to apply it to all objects, apply it to a subset, or to delete the filter.

4.3.2 Edge Appearance

The "Basic Edge Renderer" enables to change various attributes of selected nodes:

4.3.2.1 Color

Color Clicking on the color button will open a color selection dialog with which to select an edge's color.

Opacity The edge's transparency can be changed by using the slider dropdown beside the opacity value, or by manually entering a value between 1 and 100.

4.3.2.2 Style

Width To change the width, press the up or down arrow to select a number between 1 and 10.

Curve To change the curve, click the drop down menu and select "smooth curve" or "sharp curve" or none.

Automate You can automate and reset the edge curve by clicking the "automate" and "reset" buttons.

Stipple To give the edge a stipple (mark it with dashed specks), click to check off the stipple box.

▼ Basic Edge Renderer

▼ Color

Color:

Opacity: 100

▼ Style

Width: 1

Curve: None

Automate

Reset

Stipple: ☐

▼ Head & Tail

Head: Arrow

Width: 6

Length: 6

Tail: None

Width: 6

Length: 6

▼ Filters

+

4.3.2.3 Head & Tail

By clicking on the arrows drop down menu, you can change the shape, length, and width of the source and target arrows. Click the target and source drop down menus to select a shape, and click the up or down arrows to increase or decrease the length and width simultaneously.

4.3.2.4 Filters

Click the filters drop down menu and select the "+" sign to add 1 of 5 default filters. You can choose from:

- Time Edge Filter
- Rome Edge Filter
- Origin Edge Filter
- Edge Matrix Filter
- Comparison Edge Filter

Click "add". You can change the name by typing in the Graph Data Name box that appears. Select "OK". To change the features for each filter, click the drop down arrow to the left of the filter name. Each has different changeable features. Clicking on the arrow to the far right gives you the option to apply it to all objects, apply it to a subset, or to delete the filter.

4.3.3 Label Appearance

To change node and edge labels, the "Basic Label Renderer" is required. Here you can change for instance:

4.3.3.1 Node Label

Source Set the Variable shown as label.

Length Limit Select the Label size limit.

Foreground Color Change color of the node or edge label.

Opacity Change the opacity of the node or edge label.

Background Color Change color of the background of the node or edge label.

Opacity Change the opacity of the background of the node or edge label.

Auto Color Automatically sets color

Size Size of the label

Horizontal Justify Horizontal orientation of the label

Vertical Justify Vertical orientation of the label

Distance Distance from starting point of the label

Angled Activate rotation feature

Anchor Point Rotate label according to chosen angle

Flip Flip rotated label by 180 degree

Auto Angle Set angle automatically

▼ Basic Label Renderer

▼ Node Label

Source: Symbol

Length Limit: 30 ☐ None

Foreground: Color: Opacity: 100

Background: Color: Opacity: 100

Size: 14

Horizontal Justify: +

Vertical Justify: +

Distance: 0

Angled: ☐

Anchor Point: + Center

Flip: ☐ Auto Angle: +

▼ Edge Label

Source: NONE

Length Limit: 0 ☒ None

Foreground: Color: Opacity: 100

Background: Color: Opacity: 0

Size: 8

Horizontal Justify: +

Vertical Justify: +

Distance: 0

4.3.3.2 Edge Label

Source Set the Variable shown as label.

Length Limit Select the Label size limit.

Foreground Color Change color of the node or edge label.

Opacity Change the opacity of the node or edge label.

Background Color Change color of the background of the node or edge label.

Opacity Change the opacity of the background of the node or edge label.

Size Size of the label

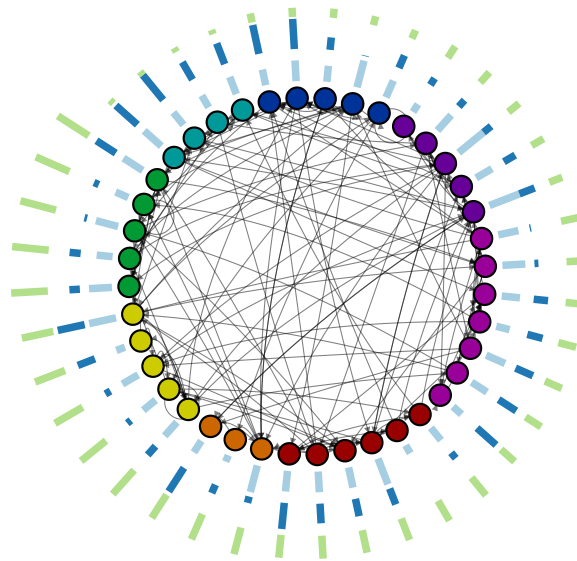
Horizontal Justify Horizontal orientation of the label

Vertical Justify Vertical orientation of the label

Distance Distance from starting point of the label

4.3.4 Spoke Visualization

Similar to color or shade, the spoke visualization can indicate numeric attributes. Each attribute is shown as a stacked level or bar plot attached to the outer side of each node. The advantage to this visualization is that multiple attributes can be shown at the same time. See Chapter 3 and 6 for more examples.



Use the Plus Button in the top right to add the **Spoke Renderer** to the Navigator Appearance Panel. Different parameter define the type of spoke, orientation, and maximal length. To add attributes, use the Plus button under **Available Attributes**. The attributes are added to the table and can be activated by the **Show** checkbox. To adjust the color you can use the corresponding color field and pop-up.



5. Network Analysis

The analysis menu includes several graph analysis methods that will be listed in Sections 5.1, 5.3, 5.4, 5.5 The Analysis Tab combines multiple methods of graph analysis into one interface and will be listed in Section 5.2, 5.6.

5.1 Add Dynamic Parameter

Dynamic parameters appear in the graph workspace as regular attributes, however, their values are determined by features of the graph, such as topology, and are not editable. Creating a dynamic parameter can be very useful for translating graph topology or complex combinations of graph attributes into visual properties in a rendering, or for sorting and selecting subsets of a graph that meet analysis criteria. Any dynamic parameter can be removed right clicking on it in the workspace area, under **graph data**, and selecting **Data -> Delete selected**.

5.1.1 Node Degree

The degree of a Node is defined as the number of edges touching that node. This function calculates degree (i.e. number of interactors) for each node. The output is a node attribute. Once selected **node degree**, it is possible to name the attribute or use the default "**degree**" name. Once clicked **create** the degree is added and it changes in real time every time there is a change in the network.

5.1.2 Subset Size

Subset Size calculates the number of nodes and edges present in a subset. The output is a numerical parameter added to each subset.

5.1.3 Subset Attribute Statistics

String attribute

Any node attribute in the string format can be used to calculate the average (**Average string length**), maximum (**Maximum string length**) and minimum (**Minimum string length**) length of such string

across all components of the subset. The output is a subset attribute.

Numeric attribute

Any numeric attribute can be used to calculate the **Maximum**, **Minimum**, **Mean**, **Median**, **Mode** and **variance** of such attribute in the subset. The output is a subset attribute. **Mode count** also provides the number of times the value identified in Mode is present in the subset. **Null count** identifies the number of empty cells for the attribute being tested in the subset.

Subset elements

Total returns the number of nodes that are present in the subset, while **Distinct** returns the number of nodes unique to the subset (based on a specified attribute). The output is a subset numerical attribute.

5.1.4 BFS Count

Centrality indices are widely used analytic measures for the importance of nodes in a network. Closeness centrality is very popular among these measures, and it sums the distances of a node to all other nodes. The currently best algorithms are based on breadth-first search (BFS) from every node. This function provides five options:

- BFS count directed, counts the number of directional BFS that pass through an object.
- BFS count undirected - counts the number of undirectional BFS that pass through an object.
- Closeness centrality incoming - provides ranking for each node based on the average length of incoming BFS paths.
- Closeness centrality outgoing - provides ranking for each node based on the average length of outgoing BFS paths.
- Closeness centrality undirected - provides ranking for each node based on the average length of any BFS path.

The output is an attribute.

5.1.5 All Pairs of Shortest Paths (APSP) Count

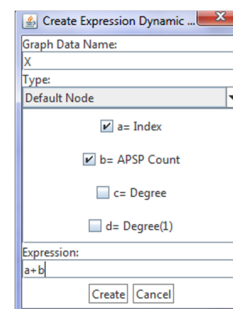
A path is a sequence of consecutive edges in a graph connecting a set of vertices. The length of a path is defined by the number of edges in such sequence. The path with minimal length between two vertices is a shortest path, and defines the distance between the two vertices. When clicking APSP Count, it is possible to select undirected (where the shortest path count increases with every shortest path passing through the object), directed source (where the shortest path count adds a value from 1.0 to 0.0 for each shortest path passing through the object, decreasing linearly as the path leaves the source node) and directed target (where the shortest path count adds a value from 0.0 to 1.0 for each shortest path passing through the object, increasing linearly as the path approached the target node). The output is an attribute.

5.1.6 Unweighted APSP Count

This analysis produces APSP as in Section 5.1.5, but uses an algorithm that counts approximate number of APSP. When clicking it is possible to select: Any (traverse the graph using any edge), Ingoing (traverse the graph using only incoming edges), Outgoing (traverse the graph using only outgoing edges). It is also possible to select one (or multiple) subsets and obtain only the count related to that subset. The output is an attribute.

5.1.7 Expression

Expression allows to perform any mathematical calculation using numerical attributes and dynamic parameters. Once selected **expression**, it is possible to name the graph data and select the type of graph element to use so that the attributes associated with it will automatically be shown with a letter associated to them. It is then possible to write any mathematical expression using these letters (i.e. $a+1$, $a+b/2$...). For more details see <https://docs.oracle.com/javase/8/docs/api/java/util/regex/Pattern.html>



5.1.8 OBO Category

Selecting OBO category allows to automatically add GO data to the graph using preset selections such as Molecular Function or Biological Process. The node IDs to obtain results must be in the UniProt ID format.

5.2 Topology

The combo box in the upper right corner of this tab selects which analysis method to use. Selecting a method will automatically begin analysis with default settings; the results will appear as a control panel with interactive components and methods for refining the analysis and manipulating the results. Clicking on the search button beside the combo box will run the analysis with the currently selected view, replacing any previous findings.

5.2.1 Biconnected Components

A biconnected component (also known as a block or 2-connected component) is a maximal biconnected subgraph).

After executing this analysis method, you will see a matrix.

The headers of the matrix represent individual biconnected components. The attribute used to label the objects represented by the headers can be changed by using the combo box in the upper left hand corner.

Matrix cells represent articulation points, or nodes that when removed would disconnect two biconnected components from each other. Right clicking on a component or an articulation point will give you options for copying that object to the current graph selection.

5.2.2 Shortest Path

The shortest path feature finder finds the least number of edges required to travel from one node to another in the graph.

Executing a shortest path search will automatically find shortest paths between all the nodes in the current selection. Be aware that on large graphs or selections, this may take some time to complete.

Once the shortest paths are found, they are displayed as a matrix. Each cell in the matrix represents a path, with the path length displayed as a number, and the corresponding column and row represent the source and target respectively. Right clicking on a path will give you options to copy that path to the current selection. The attribute used to label the objects represented by the headers can be changed by using the combo box in the upper left hand corner.

5.2.3 Inter-Subset Edges

This analysis allows you to find which edges provide connections between two subsets of nodes in the graph.

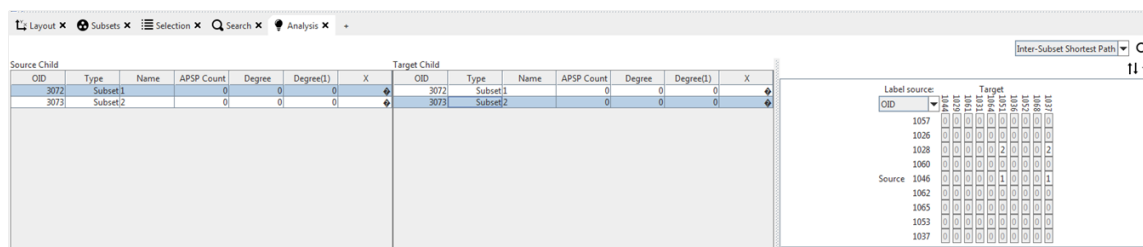
In the control panel for this feature, the source and target tables allow the selection of a single subset each. Any edges that provide connections between nodes in the selected subsets will be displayed in the table to the right. These edges can be copied to the current selection by using the transfer dropdown menu located in the top right corner of the control panel.

5.2.4 Inter-Subset Edge Count

Based on Section 5.2.3, this analysis count the number of edges that connect two subsets. The output is a matrix of subset ids in which each cell shows the number of edges connecting a subset (from row) to another subset (from column).

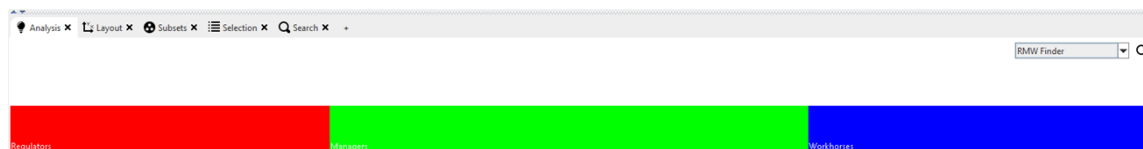
5.2.5 Inter subset shortest path

Similarly to what described in Section 5.2.2, this function identifies shortest paths between two subsets. When clicking on **Inter subset shortest path**, two panels will open (**Source** and **Target Child**) that list all the subsets. Upon selecting one subset from each of the two lists, a matrix will appear on the right including all shortest paths between one element of one subset and another element of the other subset. Right clicking on the matrix gives the possibility to use data for selection of graph elements or to export it to clipboard.



5.2.6 RMW finder

This function identifies upstream **Regulators** (red), downstream **Workhorses** (blue) and middle **Managers** (green). Right clicking one of the colors allow to **Add to selection** or **Replace selection** with the identified nodes.



5.3 Clustering

5.3.1 Clique search

Clique search tool searches for fully connected subgraphs (cliques) in the graph.

The options are:

- Exclude Objects - these objects will be removed from the search network

- Limit To Node Types - search network will be restricted to the nodes that match listed types
- Limit to Edge Types - search network will be restricted to the edges that match listed types
- Minimal Size - the output will be restricted to subgraphs of minimal size and above.
- Output Prefix - the prefix for the subset node type name.

Output: New subsets

5.3.2 Communities search

Communities search tool searches for dense subgraphs in the graph.

The options are:

- Exclude Objects - these objects will be removed from the search network
- Limit To Node Types - search network will be restricted to the nodes that match listed types
- Limit to Edge Types - search network will be restricted to the edges that match listed types
- Minimal Size - the output will be restricted to subgraphs of minimal size and above.
- Output Type - subgraphs can be output as subgraph index in a new attribute (the default option), or new subsets
- Output Prefix - the prefix for the new attribute name or the subset node type name.

Output: New attribute, or new subsets

The advanced community search gives options to exclude a set of objects

5.3.3 Connected components search

Connected components search tool searches for connected subgraphs in the graph.

The options are:

- Connectivity Type - Weak (default option) or Strong
- Exclude Objects - these objects will be removed from the search network
- Limit To Node Types - search network will be restricted to the nodes that match listed types
- Limit to Edge Types - search network will be restricted to the edges that match listed types
- Minimal Size - the output will be restricted to subgraphs of minimal size and above.
- Output Type - subgraphs can be output as subgraph index in a new attribute (default option), or new subsets
- Output Prefix - the prefix for the new attribute name or the subset node type name.

Output: New attribute, or new subsets

5.3.4 Context search

Context search tool searches for the nodes that are within specified distance from the starting node(s).

The options are:

- Node(s) - nodes from which the search starts.
- Maximal Depth - maximal depth of the search
- Exclude Objects - these objects will be removed from the search network
- Limit To Node Types - search network will be restricted to the nodes that match listed types
- Limit to Edge Types - search network will be restricted to the edges that match listed types
- Output Subsets - the result of the search will be output as a new subset
- Output Prefix - the prefix for the subset node type name.

Output: Active graph view selection and optionally new subset

5.4 Enrichment Analysis

The plugin allows to calculate enrichment of one specific subset compared to another. In the dialog window that pops up, **Node Set 1** and **2** needs to be filled with OID of subsets of interest. The output can be a **virtual** or a real **edge** between the two sets and the plugin can calculate **overlap**, **Fisher's p-value** and Monte Carlo (MC) **p-value**.

5.5 Flow Analysis

The plugin allows exploring the graph as a flow network. The analysis is based on the approach used for electrical circuits as explained at <https://www.allaboutcircuits.com/textbook/direct-current/chpt-10/node-voltage-method/>. The model uses linear relationship between edge resistance and the difference of potentials.

Flow analysis dialog. Flow analysis model is controlled through flow analysis dialog component. The top part of it has a table where variable requests are entered. The creation of a new request is started by pressing “**Add**” button to add new line in the table. The line is then changed to create a desired variable request. Unneeded line can be deleted by pressing “**Delete**” button. **Head** (start) and **Tail** (end) nodes should be specified using OID (it is possible to use a selected one right clicking and selecting **Paste from graph selection**) The plugin can calculate and output simple and aggregate variables.

Simple variables: Simple variables are **node variables (potential)** and **edge variables**. The latter include **flow** (current in the above chapter on electrical circuits), **absolute flow**, **potential drop** (difference between the potentials of tail and head nodes), **absolute potential drop**, **resistance** (ratio between flow and potential drop) and **conductivity** (inverse of resistance). Resistance and conductivity are output as new, virtual, edges.

Aggregate variables The collection of values can be aggregated, to produce a new value based on the **minimum**, **maximum**, **sum**, **sum of absolute**, **average**, **average of absolute** of the collection of values. Two types of aggregation are possible - simple aggregation and multi aggregation.

Simple aggregation. For a node, the results of the adjacent edges are aggregated, producing a node variable. For an edge, the results of the tail and head nodes are aggregated, producing an edge variable.

Multi aggregation and solution scopes. While the calculation of simple variables and simple aggregation is done over a single run for a pair of tail-head nodes, multi aggregation is performed over a composite scope - multiple simulations over multiple tail-head node pairs. Aggregation scope is generated based on the tail and head nodes. If head, or tail, or both nodes are subsets - containing collections of nodes - the scope of the aggregation will be made of all possible tail-head combinations between the two sets or between a single node and a set.

Source type and value. The source of the flow in the network can be either fixed flow from tail to head, or fixed potential at the tail node, assuming that the head node has the potential of 0. The value of the flow or potential difference is provided by the Value parameter.

Edge resistances. For the purpose of the simulation, all edges can be assumed to have equal resistance of 1 or be assigned a value based on an existing numeric attribute. Solver type selector decides which linear system solver is used. Available choices are direct solver which uses Cholesky factorization and iterative solver. Direct solver has guaranteed accuracy and efficiencies in multi-scope cases. Iterative solver has lower memory requirements. “Use Cache” checkbox - if the selected solver will use a hard drive to permanently store results.

Save mode selector tell the solver which results are supposed to be permanently saved to the hard drive - none, requested only or all, including the results for the variables that the requested results may be based on. The solution is activated by pressing the “Solve!” button.

Outputs. The results of the simulation are output to the graph as global attributes and, in the case of resistance and conductivity, virtual edges. The names of the attributes provide most of the information that went into producing the attribute. It is worth noting though that any addition or removal of graph objects or changing the value of the resistance attributes might make the computed variable values inaccurate for some or all graph objects.

5.6 Ontology tab

The OBO Ontology tab is designed to browse Open Biomedical Ontology data. The table on the left side of the tab shows the current selection of graph objects. If they contain OBO ontology information, obtainable using the ‘UniProt Annotations...’ database query, the relevant IDs will be displayed in a list on the right side of the tab.

OID	Type	Node ID	Uni	Gene Name	Degree	GO	OBO Category
1036	Node	Node1385	Q01955	COL4A3	4	basement memb...	Structural Molecu...
1036	Node	Node13043	Q9J9X3	TNR	0	apical plasma me...	Regulation of Mol...
1038	Node	Node4608	Q13203	MYBPH	2	M band, muscle ...	Structural Molecu...
1043	Node	Node80204	Q85X02	FBXO11	4	chromosome, cyt...	Binding
1044	Node	Node3672	P96199	FIGA1	1	acrosomal vesicle...	Binding
1045	Node	Node1268	P21554	CNRL	0	actin cytoskeleto...	Regulation of Mol...
1046	Node	Node54885	Q08M8	TBCLD8B	1	endomembrane s...	Enzyme Regulat...
1047	Node	Node5277	P31287	PIGA	2	endoplasmic reti...	Catalytic Activity
1049	Node	Node54383	Q9JUM8	HAO1	1	peroxisomal matr...	Binding
1050	Node	Node2688	P01241	GHI	0	endosome lumen...	Binding
1051	Node	Node1733	P46895	DIO1	4	endoplasmic reti...	Binding
1054	Node	Node238	Q9JUM73	ALK	0	intracellular enos...	Regulation of Mol...

Ontology: GO

basement membrane
collagen type IV trimer
endoplasmic reticulum
endoplasmic reticulum lumen
extracellular region
intracellular membrane-bounded organelle
intracellular matrix structural constituent
integrin binding
metalloendopeptidase inhibitor activity
structural molecule activity

6. Tutorials

6.1 PPI Network Examples

6.1.1 Loading a PPI Network from IID

- Acquire protein interactions by querying the IID database: “<http://iid.ophid.utoronto.ca/iid/>” with a set of genes. Click “Download results” and save the results into a file.

- Import the tab-delimited file via the Navigator menu **File-> Import**, select a file and Click “Next”. Set header size to 1 and click “Next”.
- Use the drop down fields to annotate the “Query UniProt” as source node and “Partner UniProt” as target node. Click “Next”.

- If required for further analysis, associate each of the other fields accordingly to source, target or edge and add names to the columns manually or by clicking “Copy Title Line”. Click “Next” to create the network.

6.2 World Network

6.2.1 MAP ATTRIBUTES TO NODE POSITIONS

The files included in this manual page were downloaded from <http://openflights.org/>. We are going to use airports.csv, routes.csv,

Select File->Open from the main menu and select Delimited Text (.txt, .csv, .tab) as your file type. Select the airports.csv file from the location you downloaded it to.

You will be presented with an Open Tab-Delimited File dialog. You should be comfortable using this interface; if you need to learn how to use it, you can explore the instructions in Section 2.2.3.

In the CSV Settings page, set the load type to Load new nodes. In the Set Header page, leave all settings at their default. In the Set Node ID Columns page, set the fifth column as your Node Index. In the Set Attribute Import page, set columns 7 and 8 as node attributes, with a Data Type of Double, and Attribute Kind of Basic. Name them Lat and Long Respectively.

At this point, you can associate other attributes with nodes, such as long form Airport names or countries. However, for the purposes of this example, we will only use the ones we just defined. Click on the Open button.

Your graph should now be a single node, which is actually all nodes mapped to a single point. To give these nodes a layout, select the Layout tab. From this tab, select the + button to add a new Dynamic Layout. From the dialog that pops up, select the Projector layout and click Add. You will be prompted to create a name, which you can leave as the default name 'Projector'. In the Layout tab, you should now see the projector control panel. We will now map node attributes to X and Y coordinates.

Map Node X Position to Long and Y Position to Lat. You will now see what looks like an inverted map. We can convert this to a familiar appearance by multiplying the Y Position by -1.

After changing the Y multiplier you should see a familiar map of the world's airports. We can make it cover a larger space by increasing the sizes of the X and Y multipliers. A value of 8 and -8 for X and Y respectively will make every node cover a degree of Latitude/Longitude, which isn't very precise, but when zoomed out, gives a clearer visualization.

At this point, all our mapping is done. If you wish to load air flight data into this graph, you can use the routes.csv file. Load new nodes and edges from Tab-delimited file. Specify a Header Size of 1. The Title Row will update automatically. Select the Type column, and set it to load as an Edge attribute, with the Attribute Type String, and the Attribute Kind as Basic. The Opened Graph

Once you have finished all these steps, you should see a graph in your Workspace, similar to what you see below. From here you can explore the contents of the graph, using different Graph Views, Searching, and Analysis.

Node X Position = Long Y Position = Lat





6.3 Spokes Visualization

6.3.1 Spoke Renderer

In this example, we will take a graph with existing Dynamic Attributes, add a Spoke Renderer, and then apply a sorted circular layout.

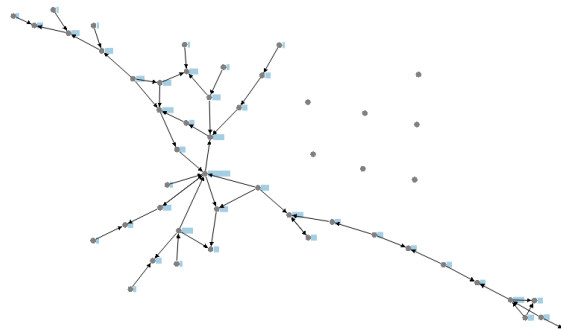
To begin, download Spoke Renderer Example.n3e [\[\[ToDo: link\]\]](#)

Open this file in N3E. You should see a plain graph visualization. To add a Spoke Renderer, in the top right of the Layers tab, click on the + button. This will open the 'Add Layers' dialog. From the available layers, select 'Spoke Renderer' and then click the 'Add' button. When queried for a name, use the default name provided.

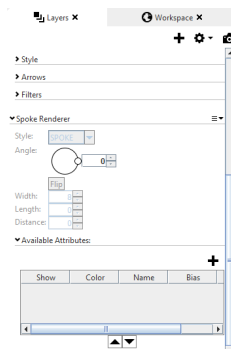
You should now see the Spoke Renderer in the Layers tab. You may have to scroll down to see it.

Nothing should have changed in the graph visualization. To quickly add spokes to the graph, use the Selection tool, or the Select menu to select all the nodes. When you have a selection of nodes, click the + button in the top right corner of the Available Attributes panel. A dialog will ask you which available attribute you would like to add. Select 'Degree' from the combo box and click the 'Add' button.

Your graph should now have a spoke on every selected node, similar to this:



Notice that each spoke is oriented in the same direction. This direction can be changed for selected nodes by using the Angle widget in the Spoke Renderer panel. The distance of the spoke



from the surface of the node, the width of the spoke, and the length of the spoke can also be changed manually. Feel free to play with these settings on your own to see how they affect the visualization.

In addition, you can turn the rendering of an attribute spoke on and off by selecting nodes and toggling the 'Show' checkbox in the Available Attributes table.

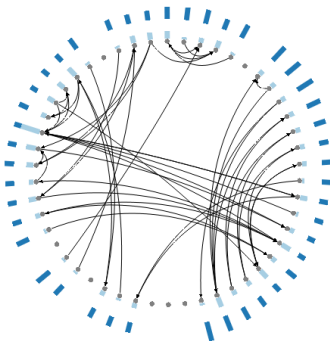
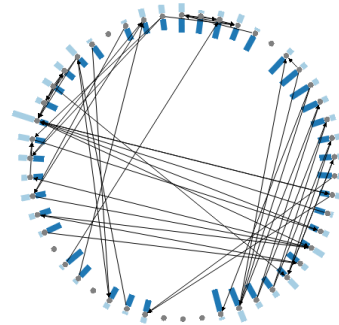
Now, add another Available Attribute to all the nodes using the same steps we used above, except this time select the 'Closeness Centrality (Undirected)' attribute.

Each node should now have two spokes, emerging from opposite sides of the node. This is the SPOKE Style for the spoke renderer, and is the renderer's default setting. As attributes are added, they will be distributed at regularly spaced intervals around the node. With just two attributes, this places them 180 degrees from each other. This is only useful if many attributes are to be compared in 'free' layouts such as grip. However, we can enhance the usefulness of our two spokes by combining a layout with one of the other two styles.

We then apply a Sorted Circular Layout. Select all the nodes in the graph using the Selection tool or the Select menu. From the Toolbar at the top of the OpenGL Graph View, select the drop-down menu to the right of the Circle Layout Tool. You will see a sorting menu. There are many sorting options available. One of the neatest for our purposes is the Hamming Sort. This sort will lay out the nodes by placing them closest to other nodes with which they share neighbors.

You should get a layout that looks something like the one below.

Notice that the angle for each spoke has been set by the layout algorithm. Though this is a good start, we can take several steps to make the graph more intelligible. First, we can set the Spoke Style to SPACED. This will stack the spokes on top of the node at regularly spaced intervals, and make them easier to compare. Secondly, we can better organize the edges by shifting their curve control points toward the center of the layout. To do this, select all the edges, and then switch to the Control tool. From the Control tool menu, select the 'Scale Selection' mode. Hold down the CTRL key and left click on any of the control points and gently adjust the curves of the selection until your graph looks something like the one below.



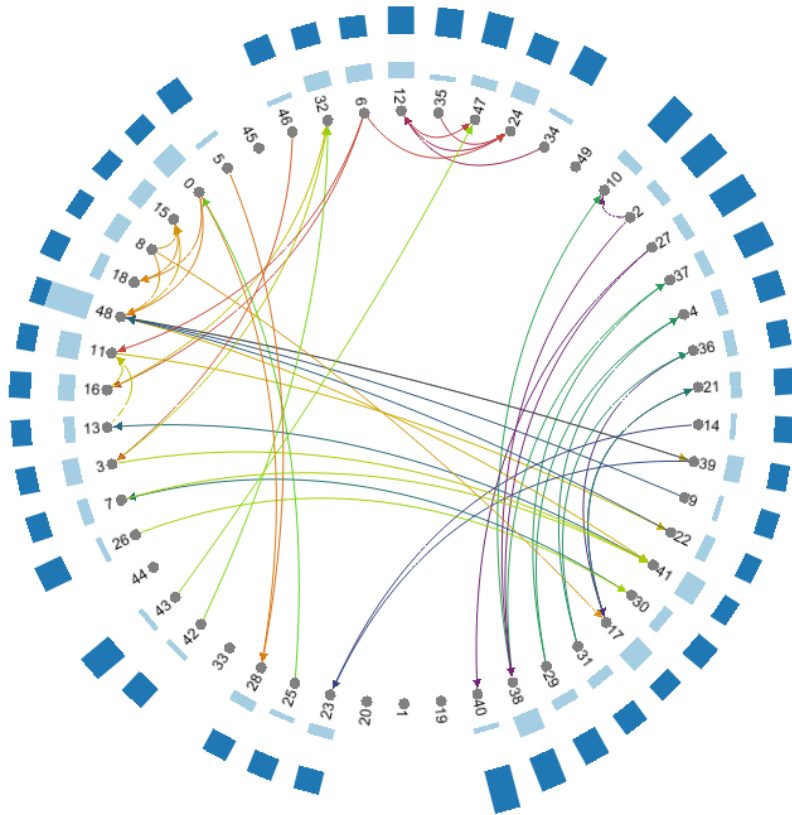
Notice that the edges are no longer intersecting as much with other edges and nodes. If you are not satisfied with the curvature, you can reset it at any time by double clicking on any control point in the selection. You can also edit the control points individually for any edge. Finally, we can further differentiate the edges by adding an origin edge filter. In the Basic Edge Renderer panel, expand the Filters panel. Click on the + in the upper right of the Filters panel. Select the 'Origin Edge Filter' in the dialog that appears, and click the 'Add' button. Use the default name for the new Filter. The resulting visualization will automatically color edges according to their point of origin in the layout, and the graph should look

something like the one below. With the graph topology and the spokes arranged to our liking, we may want to add labels to the nodes in the graph. To do so, first select all the nodes in the graph using the Selection tool or the Select menu. In the Basic Label Renderer panel, expand the Node Label panel. Select the Source as 'Index'. All the selected nodes should now have labels displayed on the outside edge of the node surface. You may have to zoom in to see them, as they overlap with the

spokes of the Spoke Renderer. This can be adjusted in the Spoke renderer by increasing the Distance setting. A setting of 12 should work for our graph, but you can change this to suit your tastes.

You should now have some idea of how to adjust the sizes and lengths of the spokes, as well as the label size to produce a legible graph. This can be subjective, and changes from graph to graph depending on the graph content and the desired size of the final illustration.

This is one possible visualization that can be produced by careful adjustment of each rendering layer:

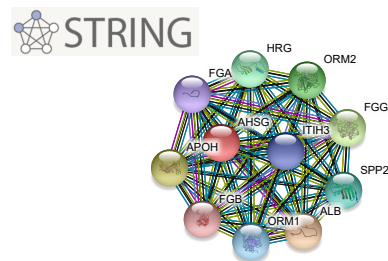


6.4 Importing Interaction Networks from the Internet

Many different types of interaction networks can be extracted from the internet (ex: social network). For example, the String framework (Search Tool for the Retrieval of Interacting Genes/Proteins) is a database and web resource of known and predicted protein-protein interactions.

The following instructions describe how to retrieve and visualize data from String:

- Go to string-db.org
- Click on "exports" and download the network as simple tabular text output
- Save the file, open downloads and rename the file as a tab file (filename.tab)
- Create an empty graph on Navigator by clicking File -> Empty Graph. Select File -> Import and select the network from your downloads file



- In the CSV Settings, select "load new nodes and edges"
- Some tab-delimited files have header lines reserved for describing the information contained within. Indicate how many lines are being used for this purpose. You may also indicate a 'title row', a tab-delimited line that contains the names of the columns you wish to import. Select 1 for header size.
- Set Node ID Columns. For every imported tab-delimited file, two columns must be specified, whose contents indicate the unique ID's of the nodes to join with the edges in the graph. Use the column header to select "source index" for column 1 and "target index" for column 2.
- Data can be imported by indicating the Attribute Type (text, double number, etc.), Attribute Object (Node A, B, Edge), and a unique Attribute Name by which to reference the imported Attribute. Select "source" for column 1 and "target" for column 2. For the desired column (ex: coexpression) select "double". When the title row boxes become red, rename the according columns.
- Select "done" and click the "new graph" tab to view your table.



7. Troubleshooting

If you are experiencing program errors in NAViGaTOR 3, check the Common Problems page to see if a solution already exists.

If this does not solve your problem, please start a topic regarding the problem in the NAViGaTOR 3 User Group. Describe the nature of your problem, and describe the steps required to recreate it in detail. We may ask you to attach copies of these two files:

error.log
output.log

These can be located in the directory in which NAViGaTOR 3 was installed.

We will not respond to problem reports that are vague or unhelpful, such as: ‘layout doesn’t work.’

7.1 Common Problems

1. Navigator Won’t Start.

If you start the Navigator application and a window doesn’t appear you may have a corrupt installation, or an unexpected configuration on your machine.

- **Cause:** You haven’t installed the correct version of Navigator

Solution: Verify that you have downloaded the correct installer for your operating system and system architecture.

- **Cause:** You have an incompatible version of Java

Solution: Ensure that you have a Java Runtime of 1.7 or higher.

- **Cause:** You are missing the Visual C++ Redistributable for Visual Studio 2012

Solution: You are missing the Visual C++ Redistributable for Visual Studio 2012. You can download a current version [here](#).

If you’ve checked all these possibilities, please report this as a bug.

2. I’ve opened a graph, but don’t see anything in the Workspace.

Ensure that the graph is loaded correctly. You can check this from the ‘Workspace’ tab.

By default, every graph created in Navigator should have an OpenGL view. You should be able

to see this view in the ‘Workspace’ tab under the subtree ‘Workspace->Your Graph->Graph Data’. If there is not a listing for ‘OGLGraphView’ under this subtree, you can create it by selecting your graph in the tree, then right-clicking and selecting ‘Graph View->New...->OpenGL View’.

If you have an OpenGL view, but it is displayed as a blank screen, there may be several causes. Check in the Layers tab to see if there are any layers in the graph. If there are none, you will have to select one or more layers to use in rendering the graph.

3. Navigator won’t open a file.
 - **Cause:** You’re using the wrong file loader.
Solution: Some file types, such as PSI-MI or BioPAX, have similar file extensions, and often cause confusion. Verify the type of file and ensure you are using the correct file loader.
 - **Cause:** The file is an XML file that doesn’t correctly follow an established schema.
Solution: XML files are sometimes generated to different standards of conformity with suggested schemas. This problem must be dealt with on a file-by-file basis.
If you’ve checked all these possibilities, please report this as a bug.
4. There are analyses missing from the Analysis panel
 - **Cause:** Your analysis panel is out of sink.
Solution: close the analysis panel and add it again using the plus sign above the panels. If you’ve tried and it doesn’t work, please report this as a bug.



8. Dictionary

8.1 Menu

The application menu allows quick access to some common functions of Navigator 3.
Further details in Chapter 1.

8.1.1 File

8.1.1.1 Preferences

The preferences dialog, available through selecting File->Preferences in the main application menu, allows the customization of some features of the Navigator application.

Types of editable preferences will be available in a list on the left side of this dialog. Selecting from this list will open relevant controls on the right side of the dialog.

8.1.2 Edit

The edit tab in the main menu allows for the use of commands such as copying, pasting, merging, and deleting nodes and edges.

8.1.3 Selection

The selection tab in the main menu allow you to perform functions such as selection and deselection of different types of nodes and edges, as well as copying and pasting of selected material.

8.1.4 Analysis

The Analysis Tab combines multiple methods of graph analysis into one interface. It allows you to perform various functions including adding dynamic attributes, selecting Cliques, COPASI, context, communities and connected components. It also allows for the merging of shared nodes, enrichment analysis, flow analysis and Petri Net. Further details in Chapter 5.

8.1.4.1 Subset

Subsets are subgraphs with common properties that are selected by the user according to the analysis interest. Further details in Chapter 1, 4 and 5.

8.1.4.2 BFS

Bredth First Search counts the number of BDF passing through an object (directed or indirected). Further details in Chapter 5

8.1.4.3 APSP

Counts number of all pairs of shortest paths passing though an object (directed or indirected).

8.1.4.4 Expression

Can be used to perform math calculations using any numerical attribute.

8.1.4.5 Cliques

This feature creates subsets with cliques identified using specific types of nodes or edge and size. Subsets created are with cliques of at least size n.

8.1.4.6 Context

This feature retrieves nodes at a specific distance from selected nodes and can be filtered by node or edge type. Retrieved nodes are at distance X from selected nodes.

8.1.4.7 Communities

This identifies dense subgraphs.

8.1.4.8 Connected Components

This identifies connected subgraphs in the graph.

8.1.5 Database

The Database tab allows you to search various databases including I2D, PathDIP and UniProt for protein sequences and functional information.

8.1.5.1 BioModels

BioModels plugin provides access to BioModels database.

8.1.5.2 KEGG

KEGG plugin provides access to KEGG pathway database. Creates new network based on one or more pathways.

8.1.5.3 IID Interactions

IID is an integrated protein-protein interaction database that can be queried through NAViGaTOR.

8.1.5.4 PathDIP Enrichment

PathDIP is an integrated pathway database that can provide pathway enrichment of the proteins present in the network.

8.1.5.5 UniProt Annotations

Through this plugin it is possible to query the entire set of ontologies and annotations included in UniProt (a reference database for proteins annotation).

8.1.6 Graph

The Navigator workspace supports the editing of many graphs. Each graph will have its own collection of graph objects, types, and attributes.

You can create new graphs, or open existing graphs. To create a new graph, select the File-> New -> Empty Graph menu item in the main menu. This will create an empty graph, with no graph objects or attributes.

To load an existing graph, select the File -> Open menu item from the main menu. This will open a dialog which will allow you to select different types of supported files to import into Navigator. You can find out which types of files are supported, plus information on their uses and features in the Importing Data section.

8.1.6.1 Graph Objects

Graph objects consist of nodes and edges.

8.1.7 Layout

The layout tab allows you to manipulate the visual presentation of your graph. You can easily center the graph, as well as select from four types of static layouts.

8.1.8 Help

The help tab provides two types of help (online help and "about N3E") to facilitate the user's use of the program.

8.2 Panels

The Navigator 3 Workspace is divided into customizable panels containing multiple tabs. Each tab is dedicated to a particular set of tasks in the Workspace (describing Graph Objects, searching for Graph Features, manipulating Graph Subsets, etc.).

You can customize panels by clicking on the '+' symbol next to the last tab header, or by clicking on an empty panel where prompted. This will open a popup menu with options for adding tabs or splitting and merging existing tabs. To add a tab, follow the 'Add Tab' menu item and select the type of tab you'd like to add.

To split the current panel into two new panels, follow the 'Split Tabs' menu item and select whether you'd like to split the panel horizontally or vertically. To merge the tabs from the neighbouring panel into the current panel, select the 'Merge Tabs' menu item.

To remove an existing tab from a panel, click the 'X' icon on that tab's header.

8.2.1 Appearance

8.2.1.1 Basic Node Renderer

The Node Renderer is used to define the appearance of a node on the graph canvas.

Node Label:

▼ Basic Node Renderer

☐ Enable outlines

▼ Color

Color:

Opacity: 100

▼ Shape

Shape: Ellipse

Height: 8

Width: 8

Rotation: -90

☐ Snap Edges to Midpoint

▼ Highlight

☐ Enable

Shape: Ellipse

Size: 4

Color:

▼ Filters

+

Color

Color	Variable shown as label
Opacity	Opacity of the edge

Shape

Shape	Shape of the node Ellipse, Rectangle, Triangle (Up), Triangle (Down), Diamond and Polygon.
Height	Height of the node
Width	Width of the node
Rotation	Rotation of the node Snap Edges to Midpoint.

Highlight

Enable	Enable the highlighting
Shape	Shape of the highlighting
Size	Thickness of the highlighting
Color	Color of the highlighting

Filters


Add filters


8.2.1.2 Basic Edge Renderer

The Edge Renderer can define the appearance of an edge. **Edge Renderer:**


▼ Basic Edge Renderer

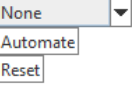
▼ Color


Color: 

Opacity: 100 


▼ Style


Width: 1 


Curve: 
 None
 Automate
 Reset


Stipple: 


▼ Head & Tail


Head: 
 Arrow

Width: 6 


Length: 6 

Tail: 
 None

Width: 6 

Length: 6 

▼ Filters

+ 

Color	
Color	Variable shown as label
Opacity	Opacity of the edge
Style	
Width	Width of the edge
Curve	Select the type of curvature of the edge. Options are "None", "Smooth Curve", and "Sharp Curve".
Automate	Set the curvature automatically.
Reset	Reset the settings.
Stipple	Plot the edge as a dashed line.
Head & Tail	
Head	Selection of the sign attached to the target of the arrow.
Width	Width of the target sign
Length	Length of the target sign
Tail	Selection of the sign attached to the source of the arrow.
Width	Width of the target sign
Length	Length of the target sign
Filters	

8.2.1.3 Basic Label Renderer

▼ Basic Label Renderer

▼ Node Label

Source: Symbol

Length Limit: 30 ☐ None

Foreground Color:

Opacity: 100

Background Color:

Opacity: 100

Auto Color ☐

Size: 14

Horizontal Justify:

Vertical Justify:

Distance: 0

Angled ☐

Anchor Point: ☐ Center 0

Flip ☐

Auto Angle ☐

▼ Edge Label

Source: NONE

Length Limit: 0 ☒ None

Foreground Color:

Opacity: 100

Background Color:

Opacity: 0

Size: 8

Horizontal Justify:

Vertical Justify:

Distance: 0

Node Label:

Source	Variable shown as label
Length Limit	Label size limit
Foreground Color	Color of the label
Opacity	Opacity of label
Background Color	Color of Background
Opacity	Opacity of Background
Auto Color	Automatically sets color
Size	Size of the label
Horizontal Justify	Horizontal orientation of the label
Vertical Justify	Vertical orientation of the label
Distance	Distance from starting point of the label
Angled	Activate rotation feature
Anchor Point	Rotate label according to chosen angle
Flip	Flip rotated label by 180 degree
Auto Angle	Set angle automatically

Edge Label:

Source	Variable shown as label
Length Limit	Label size limit
Foreground Color	Color of the label
Opacity	Opacity of label
Background Color	Color of Background
Opacity	Opacity of Background
Size	Size of the label
Horizontal Justify	Horizontal orientation of the label
Vertical Justify	Vertical orientation of the label
Distance	Distance from starting point of the label

8.2.1.4 Spoke Renderer

Spoke renderer lets the user map a quantitative attribute to bars for each node, that have a length proportional to the attribute.

To use it, open the Appearance Panel. Use the PLUS Button to add a Spoke Renderer. To chose a variable to be visualized as a spoke, use the PLUS button under Available Attributes. Select the nodes for which you would like to visualize the spoke and activate it via the show check box. The parameter in the tabel define the attributes of the Spoke: Color, Name, Bias, Length (of the largest value), and whether the values should be interpreted relatively. The parameter for the spokes renderer are Style, Angle, Width, Length, Distance. Note: To arrange the spokes in the Circular layout click the symbol for circular layout again after setting up all the parameter of the Spoke Renderer.

8.2.1.5 Minimal Renderer

The Minimal Renderer renders both nodes and edges using very primitive calls to OpenGL. The resulting visualization is less detailed than any of the other renderers, but uses fewer resources and is more responsive for large graphs.

8.2.2 Workspace

The workspace provides a concise visual summary of all of the nodes, edges, attributes and graph data in list format.

8.2.2.1 Graph

Allows exploration of the data model.

8.2.2.2 Nodes

Lists node types and respective object count.

8.2.2.3 Edges

Lists edge types and respective object count.

8.2.2.4 Attributes

Lists attributes with info on their types.

8.2.2.5 Graph Data

Lists graph data entries; options to delete graph data and restore OGLGraphView.

8.2.3 Documentation

The documentation tab provides a space to log your own notes, and a space that automatically saves your steps performed while working with a network (example, addition of rendering layers).

8.2.4 Layout

The layout space allows you to add various types of layouts to your graphs. It provides a space to track, modify and delete your layouts. Options include: static layouts (weighted grip, spoke, grip), dynamic layouts (projector, grid, force directed, attractor). Further details in Chapter 4.

8.2.5 Subsets

Subsets are groups of graph objects that are saved and labeled with a parent node. These are useful in creating logical groupings within your graph, and essential to creating hierarchical graphs, such as those used in BioPAX and KGML files. When a subset is created, a parent node is created by default. This node is used within hierarchical graphs to represent the subset. For example, if node A interacts with a complex containing nodes B and C, an edge could be used to represent this interaction connecting A to the parent node of the subset containing B and C. Parent nodes can be of any node type, and can have any attributes associated with that node type within spreadsheets and tables, their data is treated exactly the same as any other node. Subsets are generated by some file imports and can also be created and manipulated using the Subsets Tab.

8.2.6 Selection

For the highlighted portion of the graph, the selection space contains a table with the OID value, the type of node/edge, and the label number.

Changing settings within each rendering layer alters the visual properties of the objects rendered in the OpenGL Graph View. The objects affected by the changes are defined in the settings menu, accessible through the gear icon in the top right corner of the layers view. Based on the currently selected objects in the current OpenGL Graph View, you can change the settings for the selection,

the inverse of the selection, or the whole graph, depending on which option is selected from the menu.

Each rendering layer controls how the selection appears in the OpenGL graph, by outlining or otherwise indicating the objects selected. You can set the color used to do this by clicking on the 'Choose Selection Color...' item in the settings menu. In addition, the temporary selection color can also be set using the 'Choose Temporary Selection Color...' item.

8.2.7 Search

The search bar allows you to perform an attribute search, OBO search or XML search. It also provides the OID value and node/edge type when you input a label number into the search bar.

8.2.7.1 Attribute Search

Allows to search for nodes using any attribute. Selecting the type of object the attribute refers to will open a drop-down menu to select the attribute of choice. The choices for search include between, equal, greater or greater and equal than, less or less and equal than a value of choice for quantitative attributes. Once selected what to search for, the amount of reference needs to be specified. For qualitative attributes, it is possible to choose among equal, not equal, like, like case insensitive and regular expression. Some examples of regular expressions can be found at <http://www.regular-expressions.info/posix.html>. Once selected what to search for, it is important to specify the character that separate the texts being searched for.

8.2.7.2 OBO Search

The OBO Ontology tab is designed to browse Open Biomedical Ontology data.

The table on the left side of the tab shows the current selection of graph objects. If they contain OBO ontology information, obtainable using the 'UniProt Annotations...' database query, the relevant IDs will be displayed in a list on the right side of the tab.

8.2.8 Analysis

The analysis space allows you to visualize (and select) various graph features including the shortest path between source and target nodes, bioconnected components, and intersubset edges and shortest paths. It can also calculate attribute statistics, and provides an RMW Finder with which you can easily view the regulators, managers and workhorses on your graph. Further details in Chapter 5.

8.2.8.1 Bioconnected Components

Identifies maximal biconnected subgraphs.

8.2.8.2 RMW Finder

Identifies regulators, managers, workhorses in a graph.

8.2.9 Console

The console tab allows the user to view text feedback from the workspace, as well as execute console commands.

Text can come from individual graphs available in the Workspace, as well as from the workspace itself. Likewise written commands can be executed for the workspace or for individual graphs.

8.3 Layout Panels

The layout panels provide allow you to add, track and edit a variety of static and dynamic layouts on your graph.

8.3.1 Sorting

Allows you to sort nodes according to any attribute. Further details in Chapter 4.

8.3.2 Graph Layout

It lays out nodes and edges in an automatic way. Further details in Chapter 4.

8.3.3 Spreadsheet

A tabular visualization of all the data associated to the graph. Further details in Chapter 4.

8.3.4 Matrix Layout

A graph visualization where node to node relationships are shown as cells of a matrix where each row and each column represents a node. Further details in Chapter 4.

8.3.5 Serial Data Layout

This view summarizes repeated measurements for the same attribute for each node. Further details in Chapter 4.

8.3.6 Bar Chart

This graph view displays graph attributes in a bar chart format. There are three tabs in this view, one each for Nodes, Edges, and Subsets, which can be selected in the lower left of the view. Further details in Chapter 4.



9. Frequently Asked Questions

This chapter contains frequently asked questions with links to the corresponding section in the manual.

- a. How do I create a new network?**
Please refer to [Section1.4](#)
- b. Is it possible to merge networks?**
Yes, it is. Please refer to [Section2.4.2](#)
- c. How do I change the color of the nodes in a sub-network?**
Please refer to [Section3.5](#)
- d. How do I find connected components?**
Please refer to [Section5.3.3](#)



Glossary

Annotation Assigning values to an object. 25

APSP All Pairs of Shortest Paths. 46

Attribute Values associated with graph objects. 13, 26, 45, 47

BioModels Networks repository. 17

BioPAX Biological Pathway Data. 14

Boolean Binary variable that can be either true or false. 13

DEX Standard file format and previous name of Sparksee. 14, 23

Double Numeric variable that can represent continuous numbers (floating-point decimal). 14

Edge Edges or interactions, connect the objects in a network. 6, 8, 46, 48, 65

Global Applying to all objects in a graph. 13

GO Gene Ontology. 16, 27, 47

graph The network itself. 6

GraphML Graph format based on XML. 16, 23

IID Integrated Interaction Database. 26, 53

Integer Numeric variable that can represent discrete numbers (a 32-bit whole number). 13

KEGG Pathways repository. 17

KGML KEGG Markup Language. 16

Linux Linux is a family of free and open-source software operating systems. 6

Long Numeric variable that can represent discrete numbers (a 64-bit whole number). 14

Microsoft Windows Microsoft Windows is a family of graphical operating systems developed and marketed by Microsoft. 6

.n3e NAViGaTOR 3 file format. 16, 22

Node Nodes or vertices are representing the objects of a network. 6, 8, 45, 64

OBO Open Biological and Biomedical Ontology. 16

OID Object Identifier for Graph Objects. 14

PathDIP Database for pathway enrichment analysis. 26

PSI-MI Proteomics Standards Initiative - Molecular Interaction. 16

random network A random network consists of randomly generated nodes and edges. 8

Renderer Rendering or plotting the nodes, labels and edges on the graph canvas. 64, 65

SBML Systems Biology Markup Language. 16

serial Repeated attributes for the same element. 19

Sparksee NAViGaTOR backbone graph database. 13

String Variable that can store short text's or words (up to 2048 characters) Optimal for attributes like categories. 14

Subset Sub-graph. 11, 19, 27, 45, 48

Tab-delimited file A tab-delimited file is a text file with a table like structure Each row is represented by one line in the file and the columns in a line separate the columns. 14, 15, 18, 23, 54

Text Variable that can store long texts (up to and beyond 2048 characters). 14

Timestamp Variable that represents dates or times Required for time series data. 14

Type A type is a named category that an object, such as node, edge, or attribute belongs to. 7, 13, 15

XGMML eXtensible Graph Markup and Modelling Language. 16, 23