Tutorial:Introduction to Cytoscape

Slideshow Introduction to Cytoscape (about 30 minutes) [1]
Handout Introduction_to_Cytoscape.pdf (16 pages) [2]
Tutorial Sources Cytoscape Tutorial (Yeyejide Adeleye) [3]
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Cytoscape is an open source software tool for *integrating*, *visualizing*, and *analyzing* data in the context of networks. This tutorial will cover:

1. Navigating Cytoscape
2. Visualizing Data on Networks

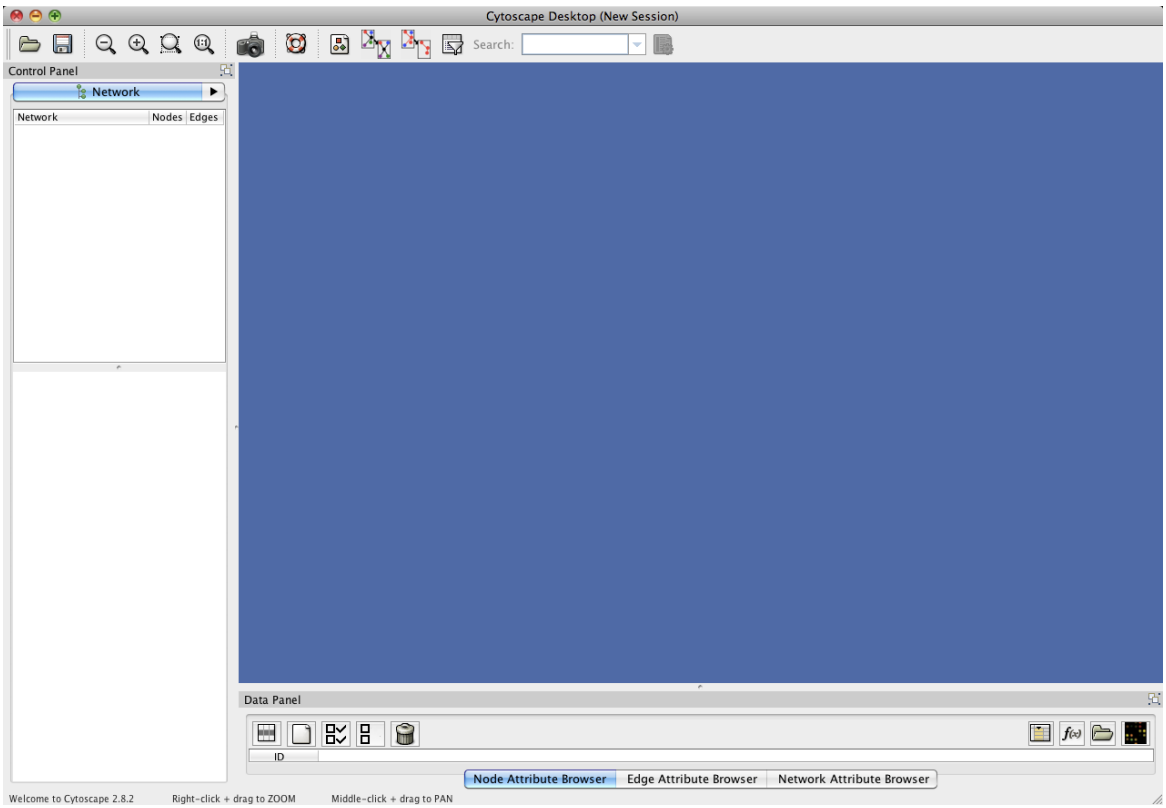
Part two of this tutorial can be found here

Navigating Cytoscape

This section will introduce the Cytoscape user interface. First of all we will look at the basic UI of Cytoscape. Then we will show all menu features of Cytoscape and the extended functionality provided by plugins.

Cytoscape Layout and User Interface

Launch Cytoscape. You should see a window that looks like this:



- At the top of the Cytoscape Desktop window is the toolbar, which contains the command buttons. The name of each command button is shown when the mouse pointer hovers over it.
- In the upper right is the Main Network View window, where network data will be displayed. This region is initially blank.
- At left is the Control Panel (Network Management) Panel. This lists the available networks by name and provides information on the number of nodes and edges.

- Immediately below the Control Panel is the Network Overview Pane
- At lower right is the Data Panel which can be used to display node, edge, and network attribute data

The Network Management and Data browser panels are dockable tabbed panels known as CytoPanels. You can undock any of these panels by clicking on the Float Window control in the upper-right corner of the CytoPanel. The Data Panel starts off with three tabs: **Node Attribute Browser**, **Edge Attribute Browser**, and **Network Attribute Browser**; the Network Management panel starts off with four tabs: **Network**, **VizMapper**, **Editor**, and **Filters**. Loaded plugins might add tabs to either of these CytoPanels.

Cytoscape Menus

We will briefly run through all the menus available in Cytoscape.

File

The File menu contains basic file functionality:

- **File → Open** for opening a Cytoscape session file
- **File → New** for creating a new network
- **File → Save** for saving a session file
- **File → Import** for importing data such as networks and attributes
- **File → Export** for exporting data and images.
- **File → Print** allows printing
- **File → Quit** closes all windows of Cytoscape and exits the program

Edit

The Edit menu contains:

- Undo and Redo functions which undo and redo edits made in the Attribute Browser, the Network Editor and the Layout.
- Options for creating and destroying views (graphical representations of a network) and networks
- Options for deleting selected nodes and edges from the current network.
- All deleted nodes and edges can be restored to the network via **Edit → Undo**.
- **Edit → Preferences → Properties** to edit preferences for properties and plugins

View

The View menu allows you to display or hide:

- The network management panel (Control Panel)
- The attribute browser (Data Panel)
- Results Panel
- VizMapper

Select

The Select menu contains:

- Options for selecting nodes and edges
- The **Select → Use Filters** option allows filters to be created for automatic selection of portions of a network whose node or edge attributes meet a filtering criterion (see below for the filters section).

Layout

The Layout menu has an array of features for visually organizing the network:

- Rotate, Scale, Align and Distribute are tools for manipulating the network visualization.
- The bottom section of the menu lists a variety of layout algorithms which automatically lay a network out.

Plugins

The Plugins menu contains options for managing your plugins (install/update/delete) and may have options added by plugins that have already been installed, such as the Agilent Literature Search or Merge Networks.

- Depending on which plugins are loaded, the plugins that you see may be different than what appear here.

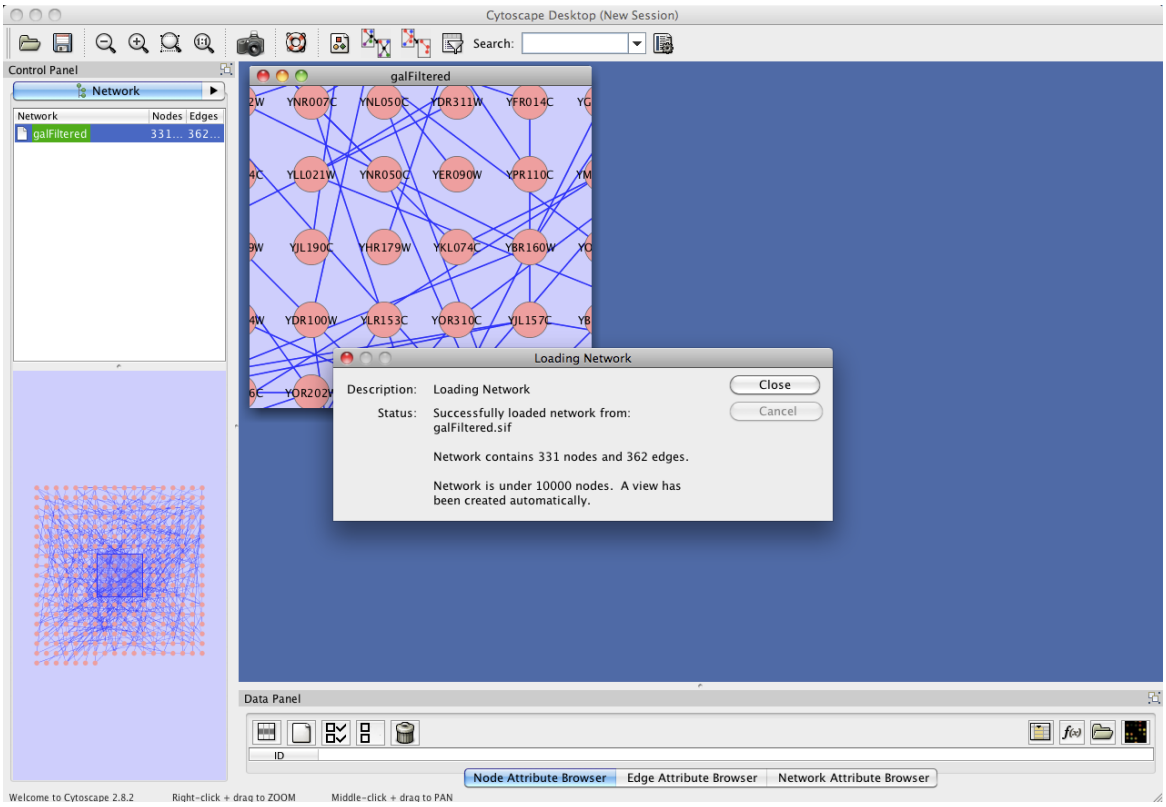
Help

- The Help menu allows you to launch the help viewer and browse the table of contents for this manual.
- The "About…" option displays information about the running version of Cytoscape.

Loading a Simple Network

- Go to **File-> Import -> Network (multiple file types)**
- You should see the Import Network File Dialog
- For Data Source Type select **Local** and then click **Select**
- Open the **sampleData** folder and select **galFiltered.sif** and then click on **Open** and then **Import**

You should see the following:



The SIF file format is about as simple as it gets. It consists of 3 columns: source, interaction type, and target. "Source" and "target" are gene/protein identifiers that are used to define nodes, while "interaction type" serves to label the edge connecting each pair of nodes.

Manipulating Your Network

Now that you have a network loaded, you can interact with it in a number of ways:

- Start by clicking on the node at the upper left corner of the network. The node with turn

yellow. If you hold your mouse down over the node and drag it around the node will move on the screen.

- Now add another node to the selection by holding down the Shift key and clicking on a node. Note that both nodes are now selected (yellow). Again, move the nodes around. Node that both nodes will move.
- To select a group of nodes, hold the mouse down in the upper left-hand corner and drag your mouse over a region of the network. Again, a group of nodes will be selected and can be moved around on the screen.
- To zoom in on the selected nodes, click on the  icon.
- To move the window around the network, you can either use the middle mouse button, or drag the small window outlined in blue around in the Network Overview Pane.
- Finally, zoom your network out by clicking on the  icon.

While useful, hand selecting nodes in dense networks can be error-prone and difficult. However, you can specifically search for a node by name or attribute:

- In the **Search:** box at the top of the screen, type in *ynr050c*. This will select that node and zoom the display to focus on it.

The **Search:** box will also allow you to select nodes by other attributes, but first, we need to import more attributes...

Visualizing Data on Networks

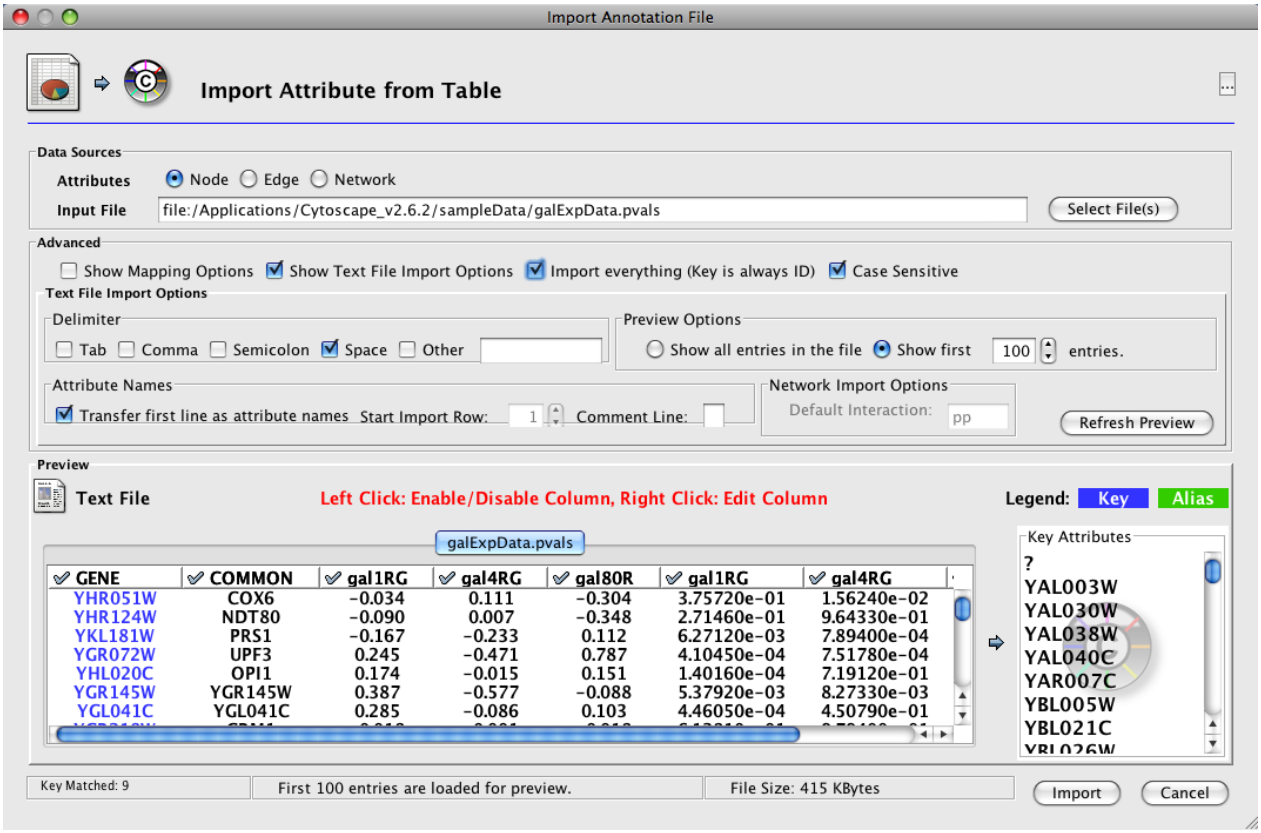
Cytoscape provides a number of features to load arbitrary data and visualize that data by mapping the attribute values to visual styles.

Importing Your Data

Cytoscape can read file structures that are delimited Text or Excel files.

- Go to **File-> Import->Attribute from Table (Text/MS Excel)**
- You should see the **Import Attribute from Table** Dialog Box
- Make sure the **Node** radio attribute button is selected in **Data Sources Attributes**
- In **Data Sources**, click on **Select File**
- Select **galExpData.pvals** from the **sampleData** folder and then click on **Open**
- In the **Advanced** section, select **Show Text File Import Options**
- By default, **Tab** is selected in the **Delimiter** section. Instead, select **Space**.
- In the **Attribute Names** section, select **Transfer first line attribute names**
- Also in the **Advanced** section, select **Import Everything**

*The 'Import Everything' option tells Cytoscape to load **all** of your data, not just the records that match currently loaded networks.*



If you were to click 'Import' now you would see a pop-up message complaining about duplicate attribute names. Notice that columns 6, 7 and 8 have the same names as 3, 4 and 5. The next steps show you how to fix column names without having to start over from Excel.

- Right click on the column header of the first duplicate name (column 6, gal1RG) to open the **Set Attribute Name and Type** dialog box
- Add the suffix 'sig' to the name (e.g, 'gal1RGsig') to distinguish the column as containing p-values (significance)
- Repeat these last two steps on columns 7 and 8 (gal4RG and gal80R)
- Now click **Import**

You've successfully loaded data! Now explore the **Data Panel** to confirm the mapping of the data to the network.

- Locate the **Select Attributes** button  in the **Data Panel**
- Select the data attributes: gal1RG, gal4RG, and gal80R
- Return to the **Data Panel** by click away from the attribute list
- Select some nodes in the network (ctrl-A selects all nodes) and see the associated data in the **Data Panel**

You now have access to your networked data and can begin playing with visualization.

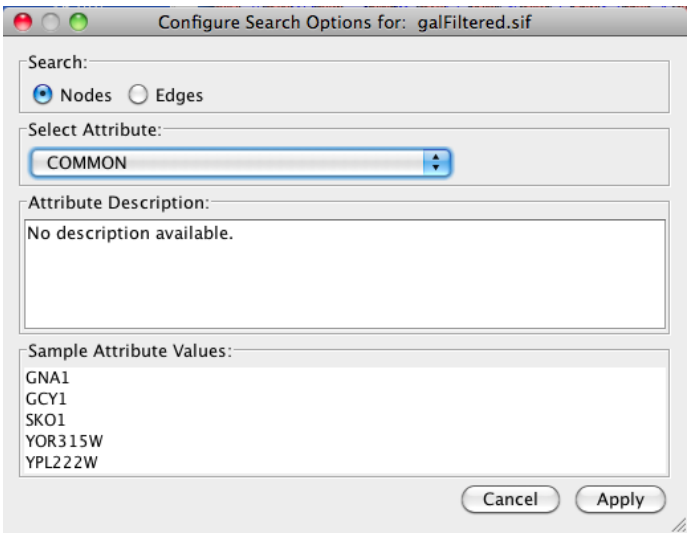
- Go to **Layout -> Cytoscape Layouts -> Force-Directed Layout**
- Go to the **VizMapper** tab in the **Control Panel** and select **Sample 1**

These are default visual styles. In the next section you will customize a visual style to highlight your data values.

Viewing Attributes

In the previous section, you were able to select a couple of attributes to display in the Data Panel. In this section, we will explore a little more about attributes and the Data Panel.

- First click on the **Configure search options** icon: .
- Change the **Select Attribute:** to **COMMON**. You should see this screen:



- Click on **Apply**
- Now type *mcm1* in the **Search:** box. This will select the node:*YMR043W*, and display the attributes for that node in the **Data Panel**.
- We're going add a new attribute for *MCM1*. Click on the icon and select **String Attribute**.
- Type in **pdb** for the name of the attribute -- this will define a new string attribute for nodes, and add it to the **Data Panel**.
- Now click into the empty cell for newly-created **pdb** attribute for **YMR043W** and type *1mnm*, which is the PDB ID for the yeast protein *mcm1*. You need to hit Return or Tab to enter that data.
- Move the **pdb** attribute to be the second column by dragging the column header to be behind the **ID** column
- Finally, select a number of nodes and note that the attributes for all of the nodes are shown in the **Data Panal**
- By clicking on the column header, you can sort the columns. Clicking again changes the order of the sort.

Visualizing Data with VizMapper

- Go to **File-> Open** (click 'Yes' to losing current session)
- You should see the Open a Session File Dialog
- Open the **sampleData** folder and select **galFiltered.cys** and then click on **Open**

Notice how the galFiltered Style maps multiple data and annotation values to:

- Edge Color
- Edge Line Style
- Node Border
- Node Color
- Node Label
- Node Size
- Node Tooltip

Modifying a Visual Style

Customising the way you visualize and manipulate networks is a key function of Cytoscape. This is achieved through the use of the VizMapper tool.

- To launch the VizMapper, either select the VizMapper tab on the Control Panel or click on the VizMapper icon  at the top of the tool bar
- Find **Node Color** in the **Visual Mapping Browser** and expand it by clicking on the triangle icon for expand/collapse
- Click on the value 'gal4RGexp' to select an alternative data value to map to node color: select 'gal80Rexp'. Notice the changes in the network display.
- Click on the gradient color mapping to open the **Gradient Editor**
- Control the values and colors of the mapping by means of triangular handles and endpoint markers
- Double-click on any handle or marker to change it's color: change green to blue and change red to yellow. Notice the immediate changes to the network
- Click-and-drag any handle to slide its value between the min and max
- To save your changes, close the editor
- Find **Edge Color** in the **Visual Mapping Browser** and expand it by clicking on the triangle icon
- Notice the discrete mapping of colors to values. Click on any color mapping to change the color.
- Close the editor to save your changes

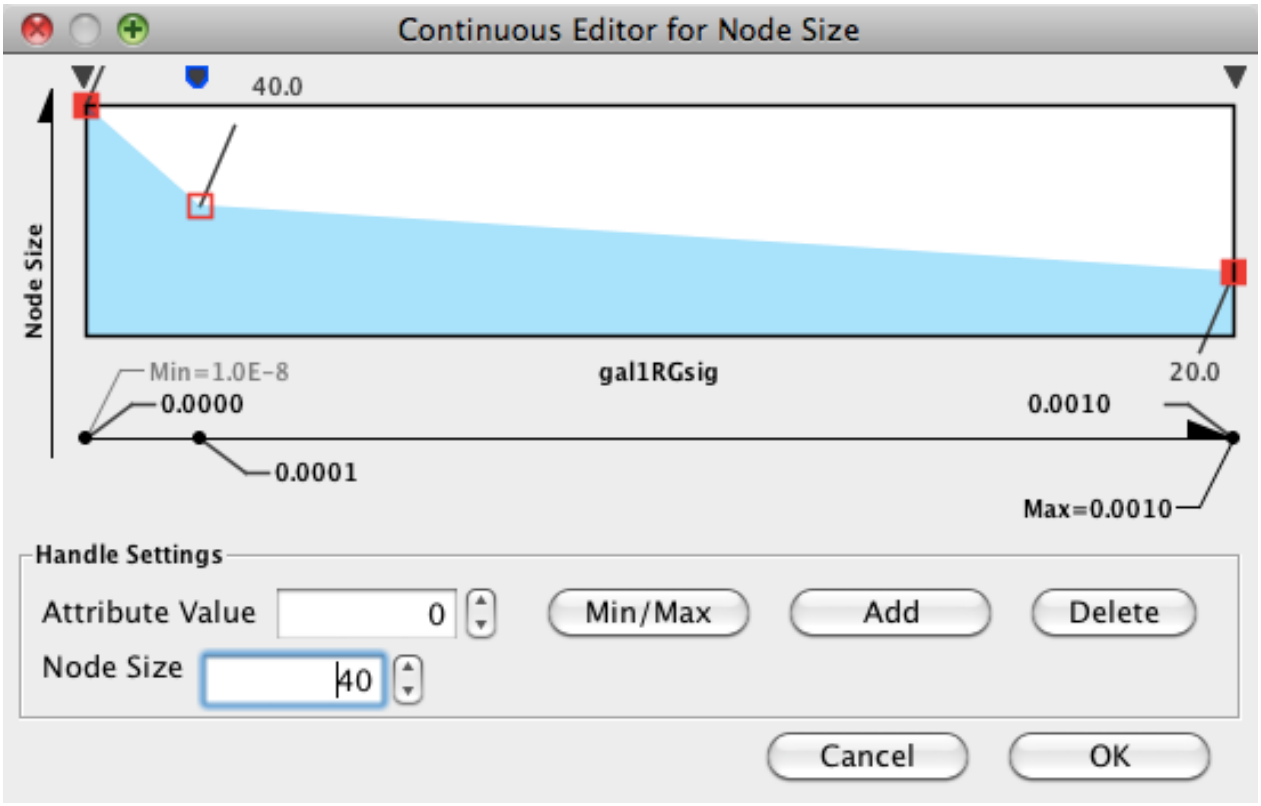
Creating a Visual Style (Advanced)

- In the **Current Visual Style** section, start a new visual style by clicking the **Options** button  and selecting **"Create new Visual Style"**
- Enter a name for your custom visual style when prompted, click on **OK**
- Find **Node Color** in the list of **Unused Properties** and double-click to activate
- For **Node Color** select the value 'gal1RGexp' to map expression fold values. For **Mapping Type** select 'Continuous'. For **Graphical View** click on the gradient to open the dialog:
  - Click on **Min/Max** button and set to -1 and 1, respectively
  - Double-click on gradient handles to set colors, e.g.
    - below -1.0 = green
    - -0.8 = green
    - 0.8 = red
    - above 1.0 = red
  - Click **Add** to add another gradient handle (added to max by default). Drag to center at 0.0. Leave as white color.
  - Close gradient dialog
- Next, activate **Node Size**. Select 'gal1RGsig' to map p-values. For **Mapping Type** select 'Continuous'. Click on gradient to open dialog:
  - Note: We want smaller p-values (more significant) to show as larger nodes
  - Click **Min/Max** to verify the correct values: 1.0E-8 and 1.0E-3, respectively.
  - Double-click on solid red box for p-values *below the minimum* (far left) to set the *maximum* node size. Set to 70.0
  - Double-click on solid red box for p-values *below the maximum* (far right) to set the *minimum* node size. Set to 20.0
  - Select handles along the top border to drag the x-position (p-value) of the gradient points. When selected, you can also set the Attribute and Node Size value by editing the **Handle Settings** field. You can also drag (or

double-click) the open red boxes to set the y-position (Node Size).

- Set the left open box to Node Size 70.0 and the right open box to 20.0. This defines the range of the gradient.
- Click 'Add' to add a new gradient handle. Set it to Attribute Value = 1E-4 and Node Size = 40.0.

This creates a pseudo-exponential gradient mapping:



- Click 'OK' in the gradient dialog and **explore** the visualization you've created!
- Zoom by selecting an area and clicking 
- Use the bird's-eye-view panel (bottom-left) to pan around network
- Return to VizMapper and switch mappings to another column of data:
  - For **Node Color** select 'gal4RG'
  - For **Node Size** select 'gal4RGsig'

Notice the change in the view of the network! You can reuse the mappings across multiple datasets. Now is a good time to save your Cytoscape session, to save the visual style you've created.

Laying Out Your Network

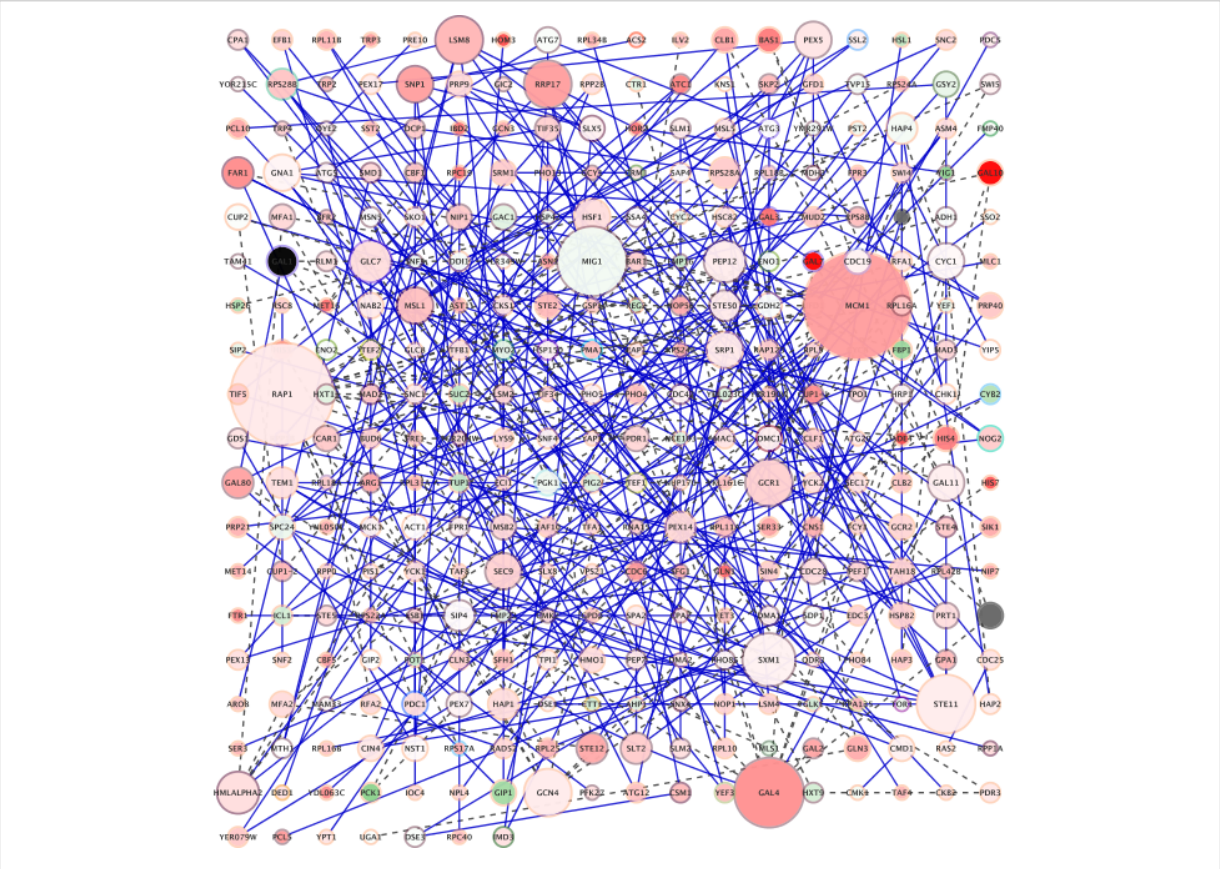
A network layout is a process that positions the nodes and edges for the network. There are a large variety of layouts in Cytoscape and plugins might add new layouts. All of the layouts will appear under the **Layouts** menu. In this section, we'll explore some of the layouts in the **Cytoscape Layouts** category, which are the core layouts supported by the Cytoscape team. All of the **Cytoscape Layouts** support the ability to only layout a portion of the network, and most expose parameters that can be used to tune the layout algorithm.

Simple Layouts

Grid Layout

The simplest layout that Cytoscape provides is the **Grid Layout**, which simply places all of the nodes in a grid arrangement.

- Using the network you loaded before, select **Layout->Cytoscape Layouts->Grid**. You should see the image below:

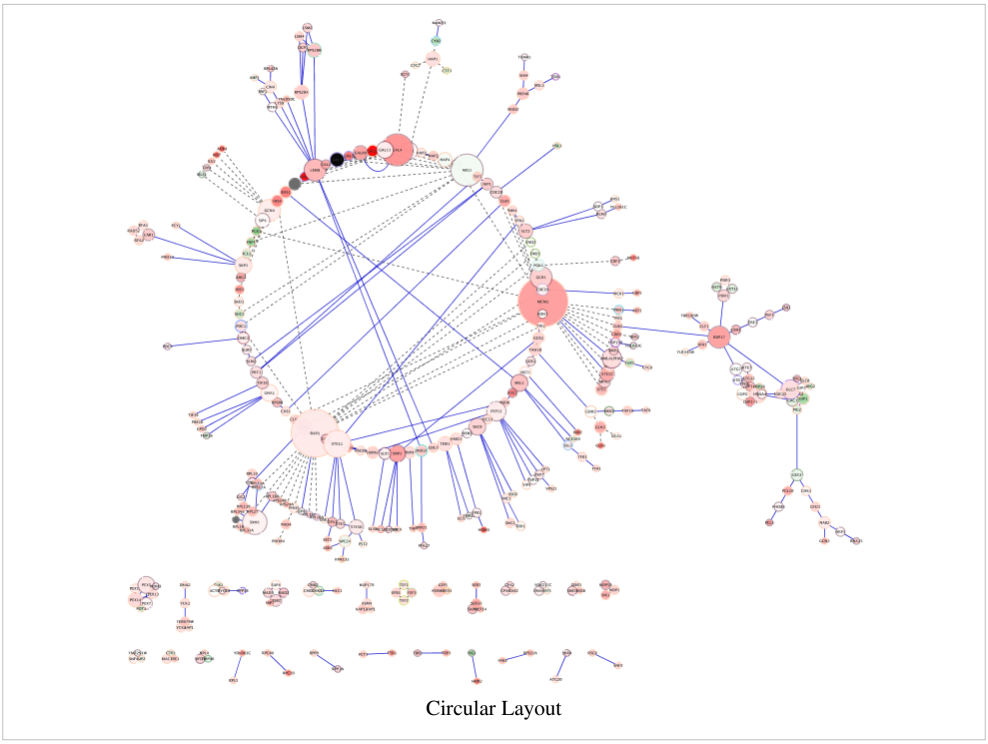


- Now, select **Edit->Undo Grid Layout Layout** and notice how your network reverts to the previous condition.
  - Many (but not all) of Cytoscape's actions may be undone.
- Select a group of nodes in your network and again select **Layout->Cytoscape Layouts->Grid**.
  - Notice that this now has a sub-menu with two options: **All Nodes** and **Selected Nodes Only**.
- Choose **Selected Nodes Only**.
  - Note that only the nodes you selected are changed.

Circular Layout

Grid is very fast, but often not very helpful. Alternatives:

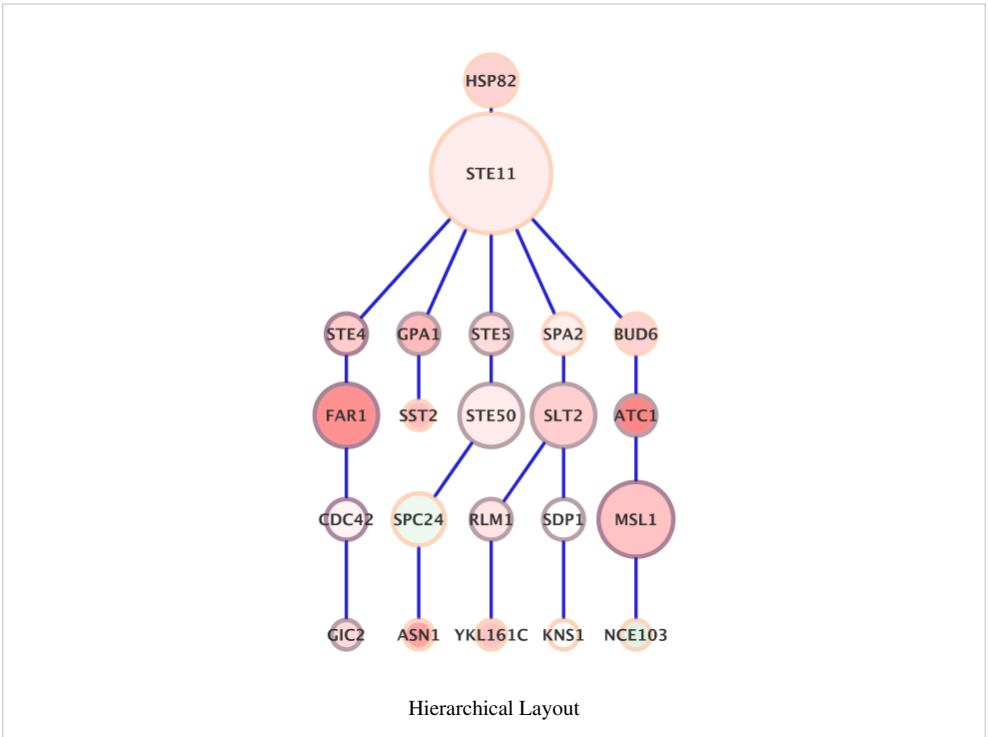
- **Circular Layout** places all of the nodes in a circular arrangement.
  - Very quick
  - Usually not very informative.
  - *Partitions* the network into disconnected parts and independently lays out those parts.



Circular Layout

Hierarchical Layout

- **Hierarchical Layout** forces the nodes into a tree structure.
  - Works best when the network is naturally tree-structured
  - Also works reasonably well when the network is mostly hierarchical.



Hierarchical Layout

Data-Driven Simple Layouts

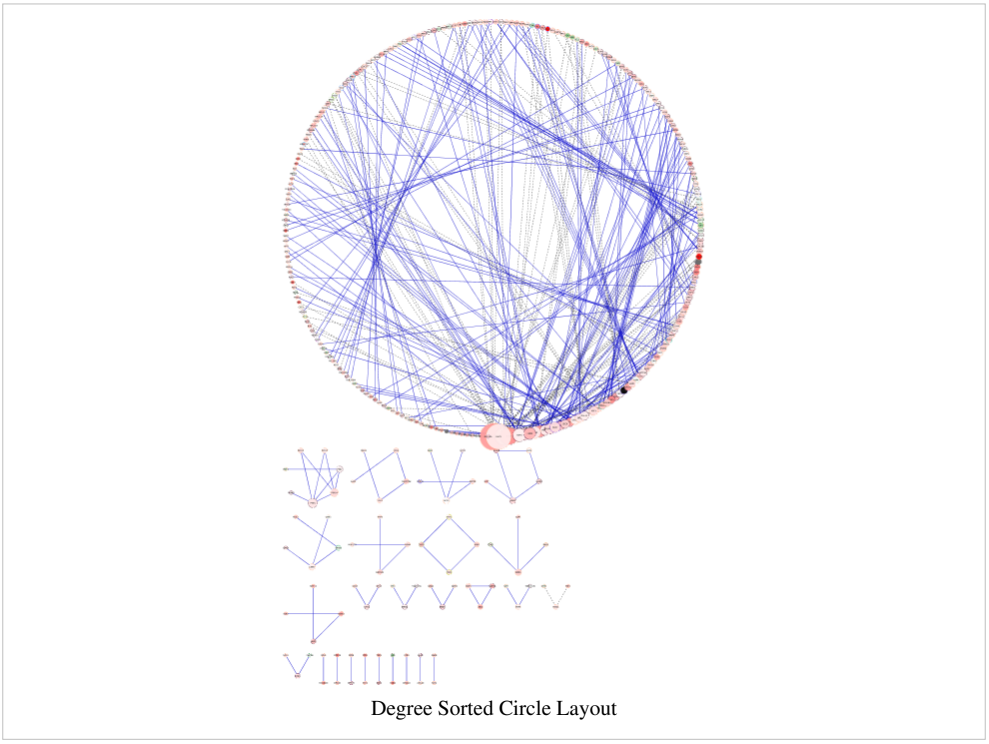
Often what is desired is to organize the nodes in space to reflect some data property of the nodes themselves. We'll look at three of the simple ones:

- **Degree Sorted Circle**: Orders the node around a circle based on node degree (number of edges)
- **Attribute Circule Layout**: Orders the node around a circle based on the value of some attribute
- **Group Attributes Layout**: Groups the nodes based on the value of some attribute

Degree Sorted Circle Layout

For example, assume you are interested in hubs (nodes with high degree):

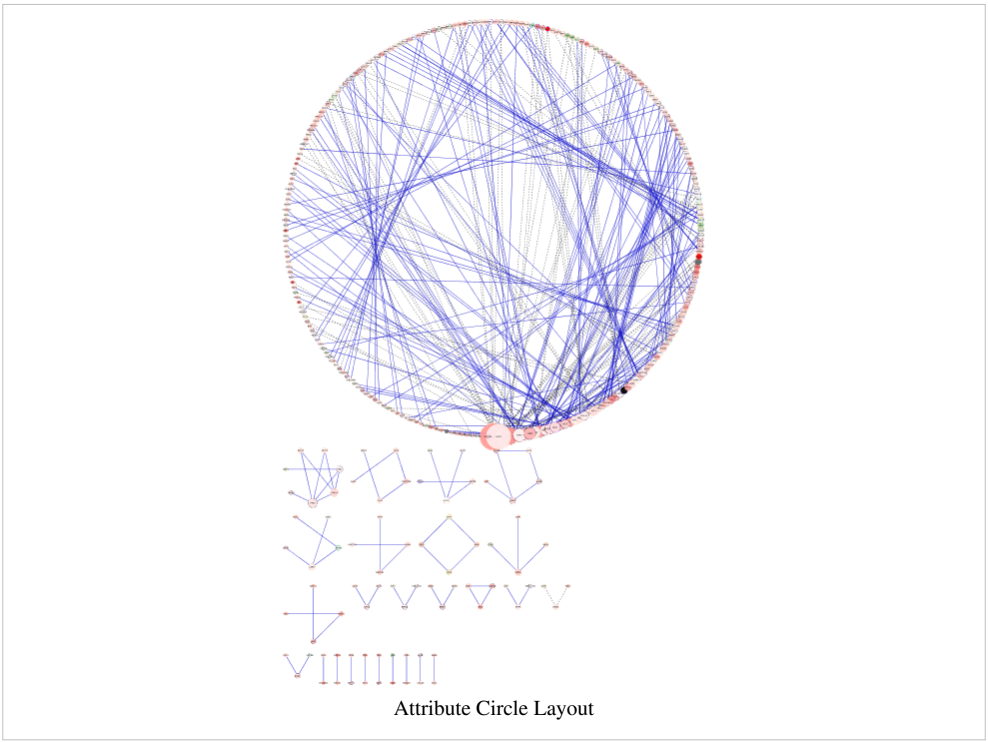
- Select **Layout->Degree Sorted Circle Layout**.
  - Note the highest degree nodes are in the same region of the circle and the degree decreases as you proceed counter-clockwise around the circle.
  - Also note that this layout supports partitioning of the network into disconnected components.



Degree Sorted Circle Layout

Attribute Circle Layout

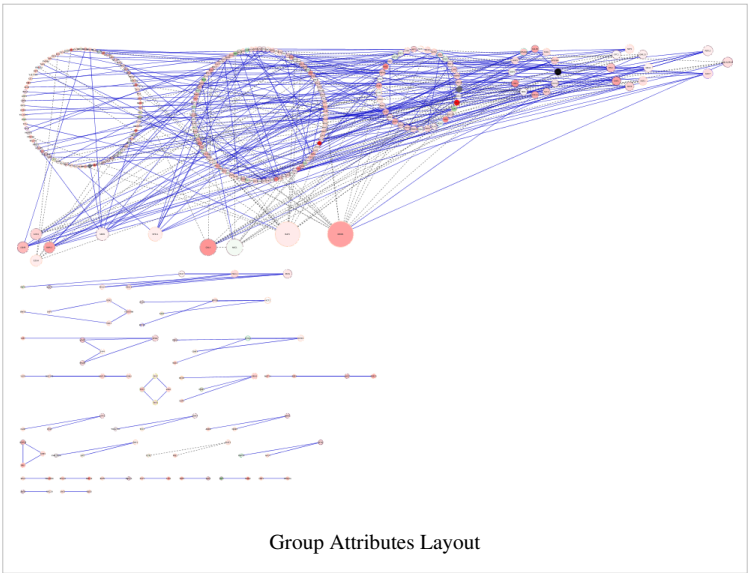
- Now try **Layout->Attribute Circle Layout->Degree**.
  - This should give you a very similar layout to the Degree sorted circle layout.
  - You should also try using other attributes to layout.



Attribute Circle Layout

Group Attributes Layout

- Finally, select **Layout->Cytoscape Layouts->Group Attributes Layout->Degree**.
  - Note that this layout organizes all of the nodes with the same degree into a circle and then positions the circles into a grid.
  - Partitions the graph before layouts.



Group Attributes Layout

These layouts are useful to represent data attributes associated with the nodes of a network, however, they don't provide much information about the network structure itself. For that, using more complicated layouts

are required.

Force-Directed Layouts

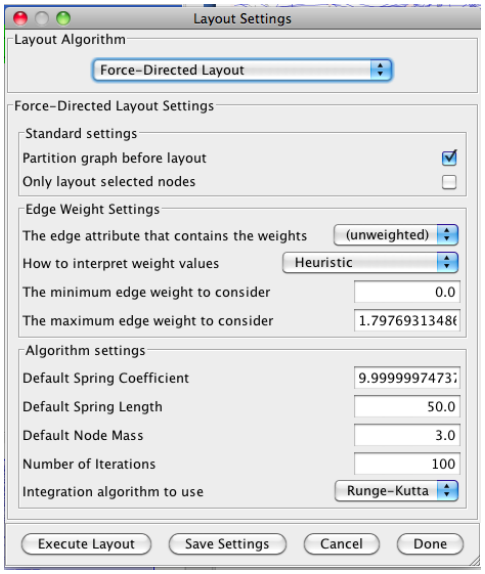
The force-directed methods for laying out graphs all use some kind of physical simulation that models the nodes as physical objects and the edges as springs connecting those objects together.

- Cytoscape provides 4 force-directed layouts:
  - Edge-weighted Force directed (BioLayout)
  - Edge-weighted Spring Embedded
  - Spring Embedded
  - Force-Directed

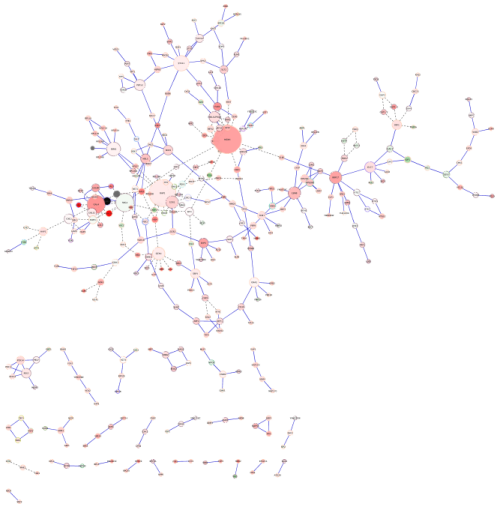
    In this exercise, we'll use the **Force-Directed Layout**, which is a port of the layout by the same name in the *prefuse* package (see [http://prefuse.org [4]]).

Force-Directed Layout

- We'll do all of our work from the Layout settings dialog, so bring up the dialog by **Layout->Settings...**
- In the **Layout Settings** dialog:
  - Select **Force-Directed Layout** under **Select algorithm to view settings**.
  - The result should look like the image on the right
- Lets start by creating a layout using the default parameters.
  - Select **Execute Layout**.
  - Note how this exposes more of the structure of the network than any of the previous layouts.



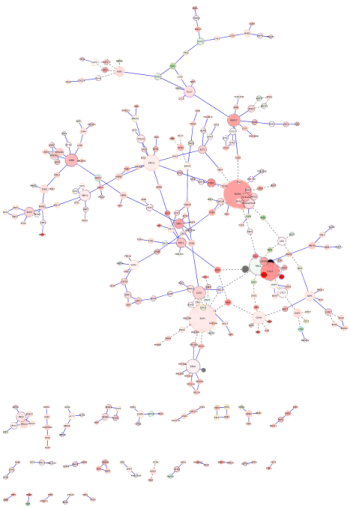
Force Directed Settings Dialog



Force Directed Layout

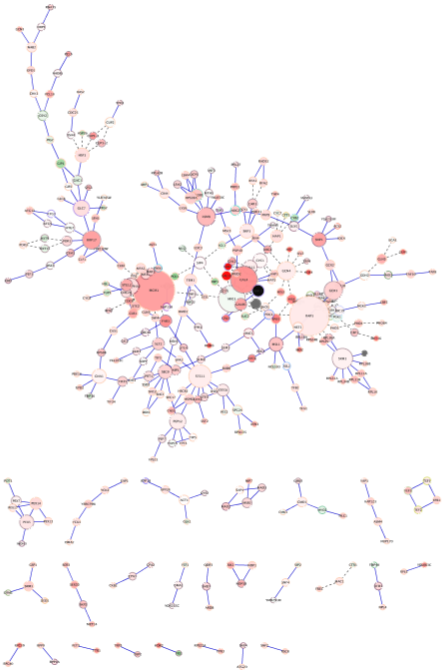
Now, let's see what the parameters do.

- Start by changing the **Default Spring Length** to **20**, and select **Execute Layout**.
  - The default spring length is the length of a spring (edge) with no forces exerted upon it. Essentially, it's the length of an edge connecting two nodes with no other connections.
- Note how the layout has changed.
  - The resulting network tends to be more closely packed in the denser regions.



Force Directed Layout (default spring length 20)

- Finally, lets change **Default Spring Length** back to **50** and the **Default Spring Coefficient** to **1E-3**.
  - The spring coefficient is a measure of the strength of the strength of the spring.
- Now click **Execute Layout**.
  - Note that the network remains pretty compact, even though we've reset the default spring length back to 50.



Force Directed Layout (default spring coefficient 1E-3)

Force-Directed Layout is also a good layout to use for circumstances when you want to have the length of your edges reflect some numeric weight on each edge.

- Select the attribute containing your edge weights from the menu **The edge attribute that contains the weights**.
- This often requires some tuning of the spring coefficient and the spring length to get an aesthetically pleasing layout.

References

[1] http://opentutorials.rbvi.ucsf.edu/index.php?title=Tutorial:Introduction_to_Cytoscape&ce_slide=true&ce_style=cytoscape
[2] http://opentutorials.rbvi.ucsf.edu/index.php/File:Introduction_to_Cytoscape.pdf
[3] http://cytoscape.wodaklab.org/wiki/CytoRetreat2007Tutorials
[4] http://prefuse.org

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Image:visualstyle.png *Source*: http://opentutorials.cgl.ucsf.edu/index.php?title=File:Visualstyle.png *License*: unknown *Contributors*: AnnaKuchinsky
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Image:DegreeSortedLayout.png *Source*: http://opentutorials.cgl.ucsf.edu/index.php?title=File:DegreeSortedLayout.png *License*: unknown *Contributors*: ScooterMorris
Image:GroupAttributesLayout.png *Source*: http://opentutorials.cgl.ucsf.edu/index.php?title=File:GroupAttributesLayout.png *License*: unknown *Contributors*: ScooterMorris
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Image:ForceDirected50Layout.png *Source*: http://opentutorials.cgl.ucsf.edu/index.php?title=File:ForceDirected50Layout.png *License*: unknown *Contributors*: ScooterMorris
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Tutorial:Introduction to Cytoscape-part2

Slideshow Introduction to Cytoscape (30 min) [1]
Handout Introduction_to_Cytoscape.pdf (9 pages) [2]
Tutorial Sources Cytoscape Tutorial (Yeyejide Adeleye) [3]
Tutorial Curators Anna Kuchinsky, Scooter Morris, Alex Pico

Cytoscape is an open source software tool for *integrating*, *visualizing*, and *analyzing* data in the context of networks. This tutorial is part two of the Introduction to Cytoscape tutorial and covers:

1. Plugin Manager
2. Network and Pathway Resources
3. Plugin Demos

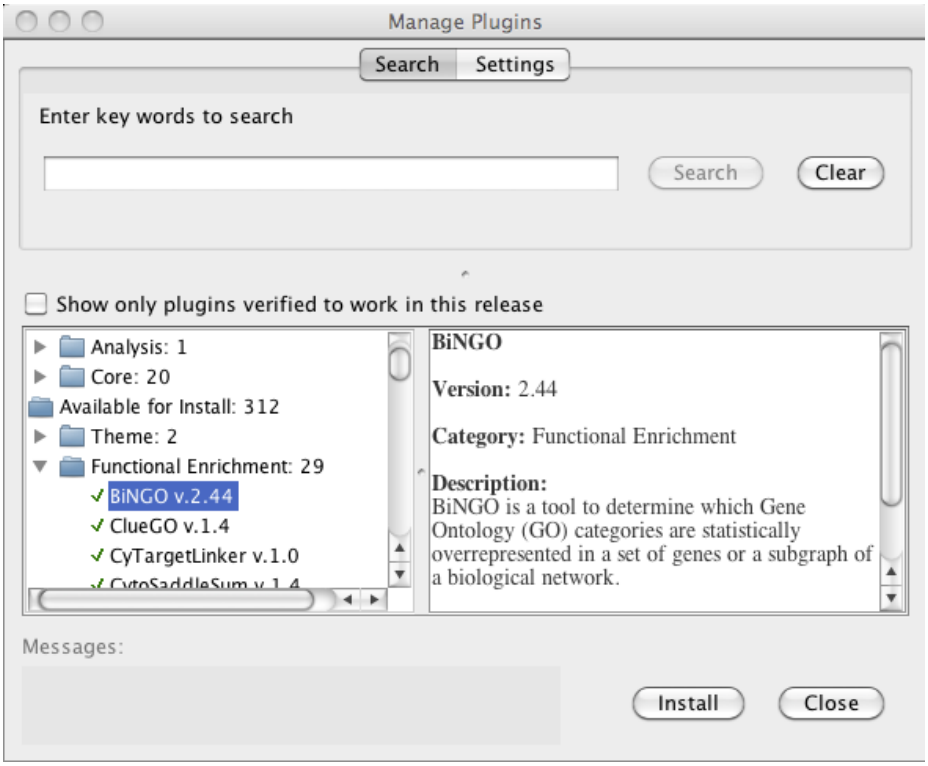
Plugin Manager

The Plugin Manager allows users to quickly and conveniently add extra features to Cytoscape directly from within Cytoscape, eliminating the need for manual searches through different websites to install and update plugins.

If you do not have Internet access enabled, you will not see the list of available plugins or be able to automatically update existing ones; however, you will still be able to view and delete previously installed plugins.

Install new plugins

- Go to the **Plugin Manager at Plugins -> Manage Plugins**. On the left side of the window that pops up, you will see plugin folders labeled **Currently Installed and Available for Install**. Double-clicking on these will show sub-folders, and then the plugins themselves. To find out more about a specific plugin, click on its name to display some basic information on the right-hand side of the window.



- **Currently Installed** folder contains a number of default plugins that are fully integrated in every copy of Cytoscape, as well as any additional installed plugins
- **Available for Install** folder displays plugins that may be installed.

- To install **jActiveModules**: Search for "jactive", expand the **Analysis** folder and then select **jActiveModules v2.23**. *Note: it may warn that it is not verified to work with this version. This simply means that a new version of Cytoscape was released after the plugin was release. Most plugins will continue to work after point releases.*
- Click on the Install button at the bottom of the window
- Click on close to exit the Plugin Manager
- Go to the **Plugins** menu and **jActiveModules** should appear in the list of plugins

To manually install a plugin

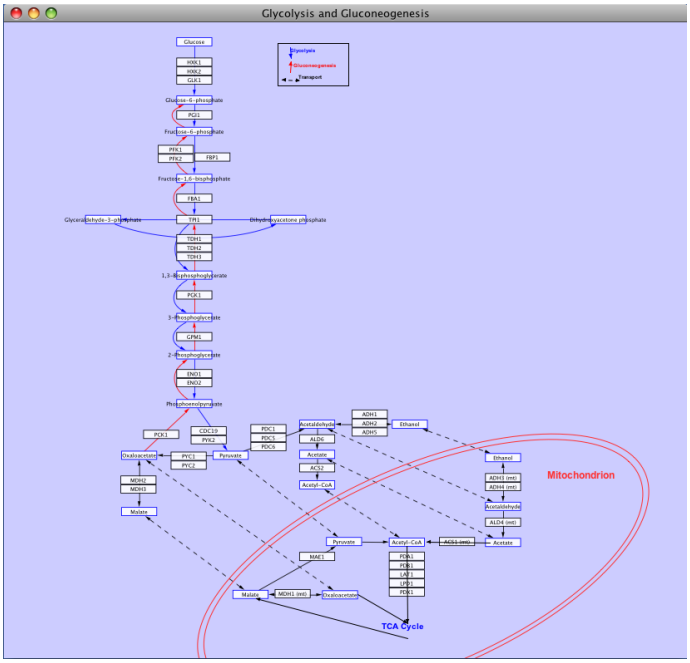
- Go to the Cytoscape plugins page (http://cytoscape.org/plugins.html),
- Scroll down to find the plugin
- Click on the appropriate link to download the file, and then save it in the Cytoscape_v#.#.#/plugins folder on your hard drive.
- Cytoscape will require a restart in order to load the manually installed plugin.

Network and Pathway Resources

But what if you don't have a network? In this section we will cover some of the ways you can retrieve, construct and infer networks and pathways from public sources using Cytoscape and selected plugins.

WikiPathways

- Begin by downloading the GPML-Plugin from the **Plugin Manager**, which can be found under the **Network and Attribute I/O** folder.
- Select **File-> Import -> Network from web services**
- From the drop-down menu, select the **WikiPathways Web Service Client**
- Enter a search term ('tca') and select a species ('Saccharomyces cerevisiae')
- A list of relevant pathways is returned
- Double-click on 'Glycolysis and Gluconeogenesis' to import the pathway

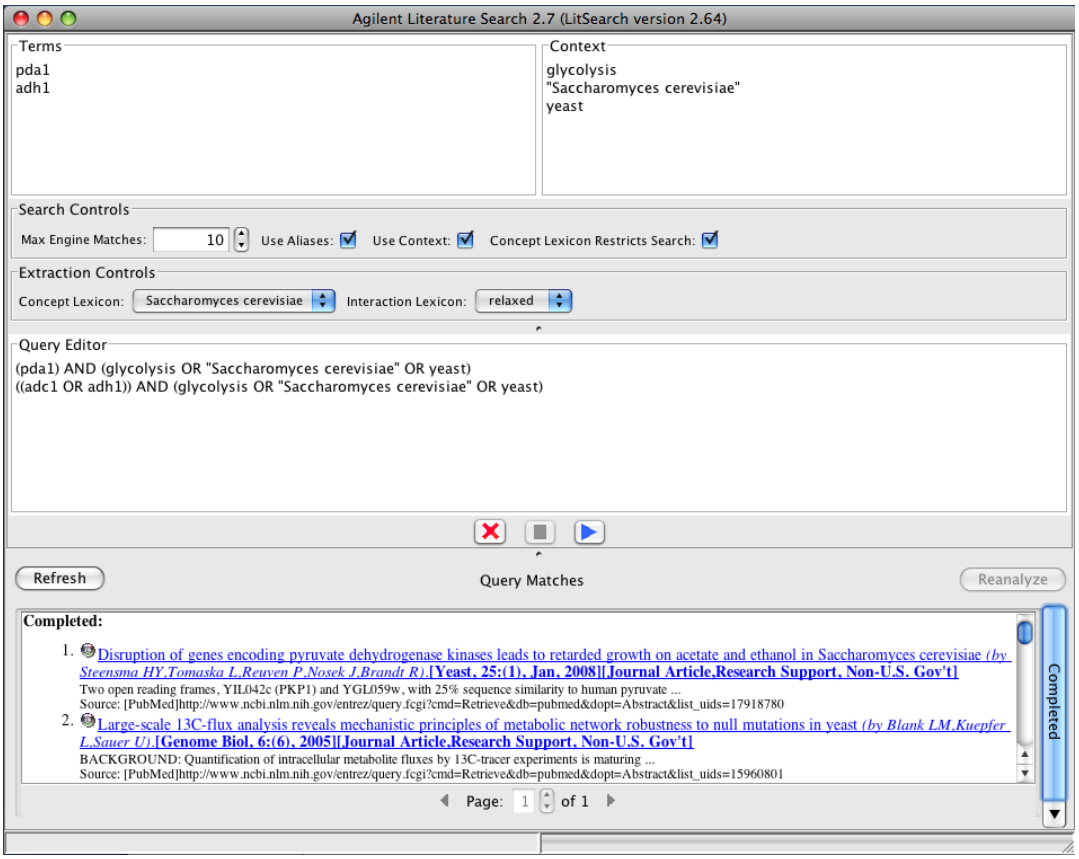


*WikiPathways uses the GPML data format, which includes curated coordinates, graphical annotations and labels, in addition to the node and edge network. You can hide the annotation layer using **View>Toggle GPML Annotations** and then treat the network like any other network in Cytoscape.*

Agilent Literature Search

Agilent Literature Search uses text mining technology to generate an "association" network from information extracted from the scientific literature. This can be useful in understanding how genes and proteins may interact in the context of a disease or other biological process.

- To open Agilent Literature Search, go to **Plugins->Agilent Literature Search**
- In **Terms**, enter "pda1" and "adh1"
- In **Context**, enter "glycolysis"
- Select **Use Aliases**. Notice the synonym for "adh1"
- Select **Concept Lexicon**: *Saccharomyces cerevisiae*
- Select **Interaction Lexicon**: "relaxed"
- Click the blue **Play button** to execute the search. Your results will appear in the Query Matches window.

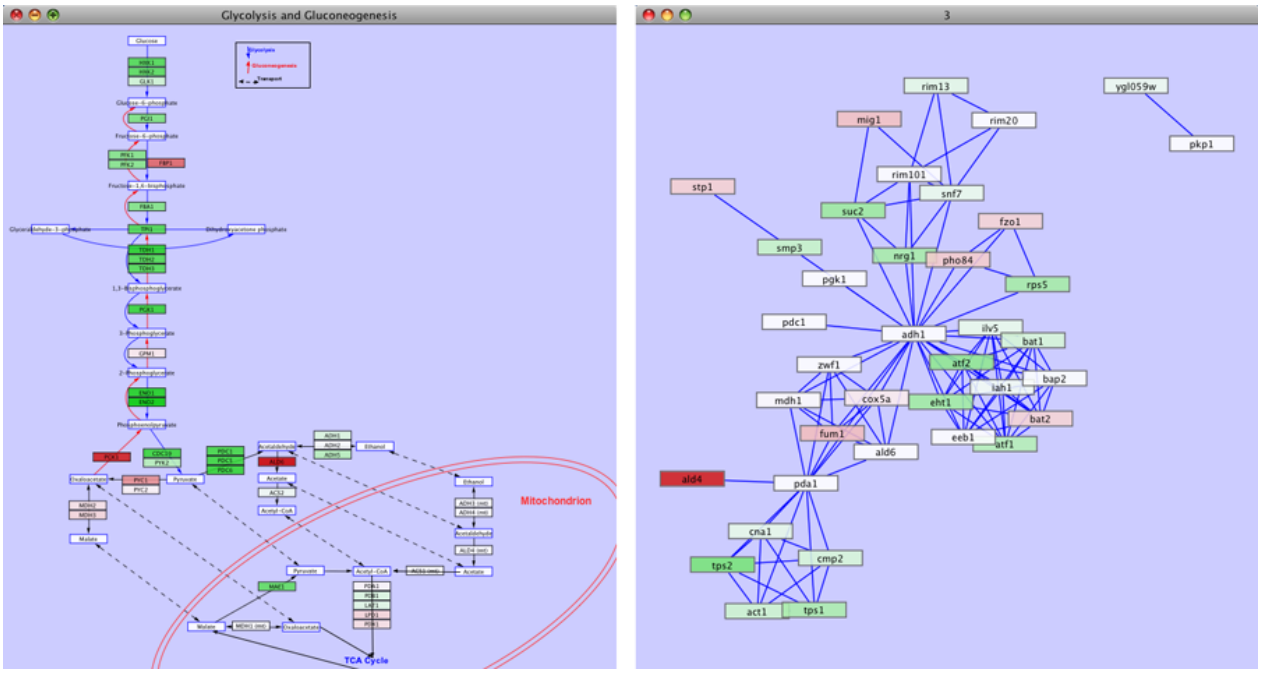


Non-default Data Mapping

When mapping data onto imported networks and pathways, you have to be aware of the key identifiers used in both your data and the imported network. The Attribute Importer provides advanced mapping options for such cases.

- Return to **File-> Import->Attribute from Table (Text/MS Excel)**
- Select **galExpData.pvals** from the **sampleData** folder and then click on **Open**.
- In the **Advanced** section, click **Case Sensitive** to deselect
- In the **Advanced** section, select **Show Text File Import Options**
- In the **Delimiter** section, select **Space**
- In the **Attribute Names** section, select **Transfer first line attribute names**
- Now select **Show Mapping Options**
- Change “GENE” to “COMMON”, and change “ID” to “canonicalName”

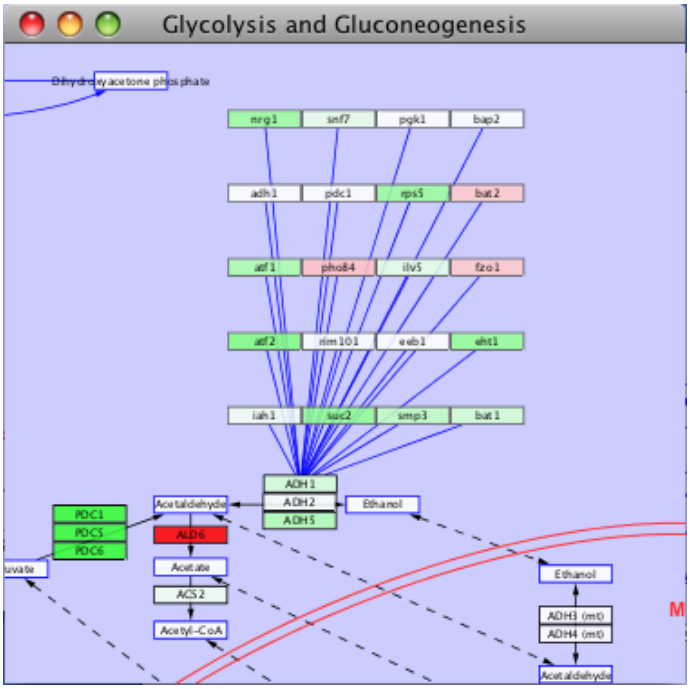
- Click on the headers of the second set of redundant columns in the **Preview** to simply exclude them from import, or rename them by right-clicking
- Click **Import**
- Now go to the **VizMapper** tab in the **Control Panel** and locate the **Node Color** property. Double-click to activate.
- Choose “gal1RG” and then choose “Continous”
- Click on the color gradient to open the **Gradient Editor**
- Set colors for end points and handles to create a color gradient
- Notice the visualization of data on all imported pathways and networks!



Extending Networks

This plugin also has an interactive feature that lets you expand a network using literature search results.

- Go to the imported pathway “Glycolysis and Gluconeogenesis” and use the **Search** box to find “ADH1”
- Right-click on the node and select **Evidence from Literature > Extend Network from Literature**
- Select and drag new nodes near ADH1, go to **Layout > CyLayouts > Grid > Selected Only**, reposition grid in available space near ADH1



- Notice the automatic data mapping
- Right-click on edges to new nodes to **Show Sentences from Literature**
- You can use this procedure to extend known pathways based on literature findings and your visualized data

More Plugin Demos

If continuing from the above tutorial, you may want to restart Cytoscape at this time to clean the slate of unused networks, nodes and attributes. The following plugins all use the same demo file:

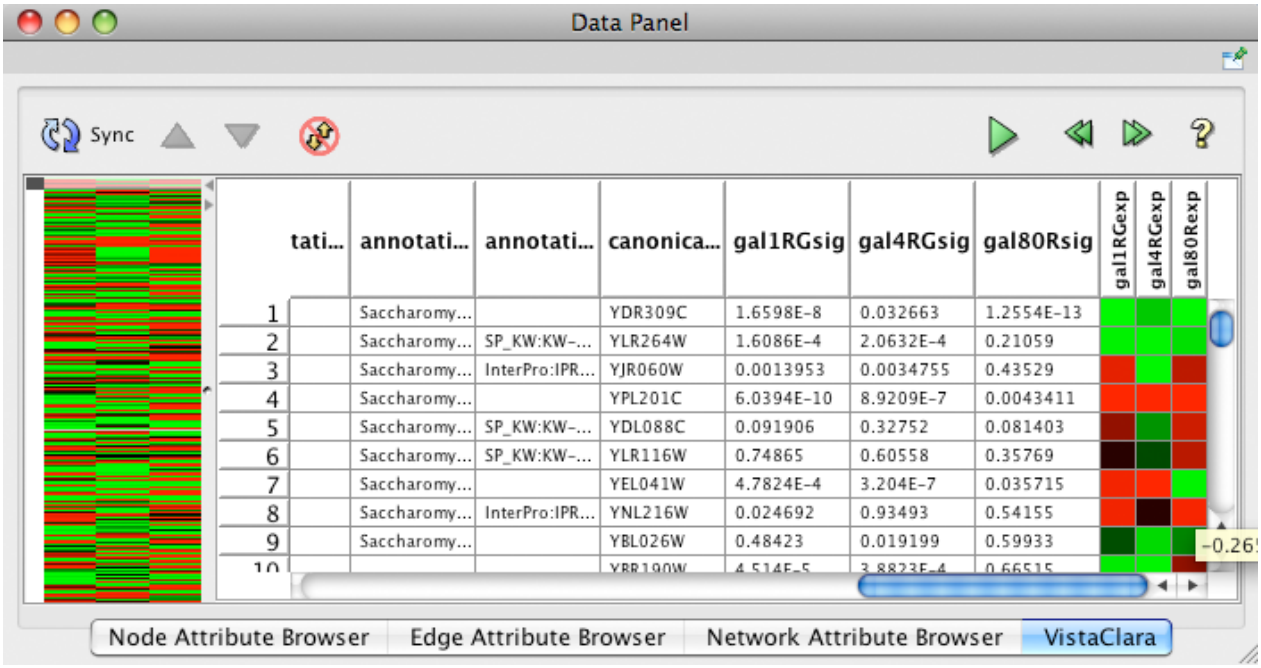
- Go to **File-> Open** (click 'Yes' to losing current session)
- You should see the Open a Session File Dialog
- Open the **sampleData** folder and select **galFiltered.cys** and then click on **Open**

Plugin 1: Vista Clara

Usage: explore data in an interactive, visual spreadsheet

The VistaClara plugin is available from the **Plugin Manager** (refer to Section 1.3)

- Select the **VistaClara** tab below the **Data Panel**
- Click **sync**
- It may be helpful to expand or undock the **Data Panel**



The first column on the left displays the automatically generated heatmap for all of your data. The last columns show the heatmap values for the selected range of data. Note: some columns of data may not be recognized (e.g., gal80R), or may not be properly formatted.

- To fix the formatting of any column of data, simply right-click on the column header, choose format and the correct value. Try 'log2 ratio' for all the fold values in the galFiltered dataset.
- Right-click on any column and select sort to sort by values
- Select or drag anywhere in the heatmap to scroll through the data values
- Select a column of heatmap data to visualize the data on the network
- Click the **play** button to cycle through all heatmap columns
- Notice that a 'VistaClara' visual style has been created in the **VizMapper**. You can select your previous visual styles to return to your custom view at any time

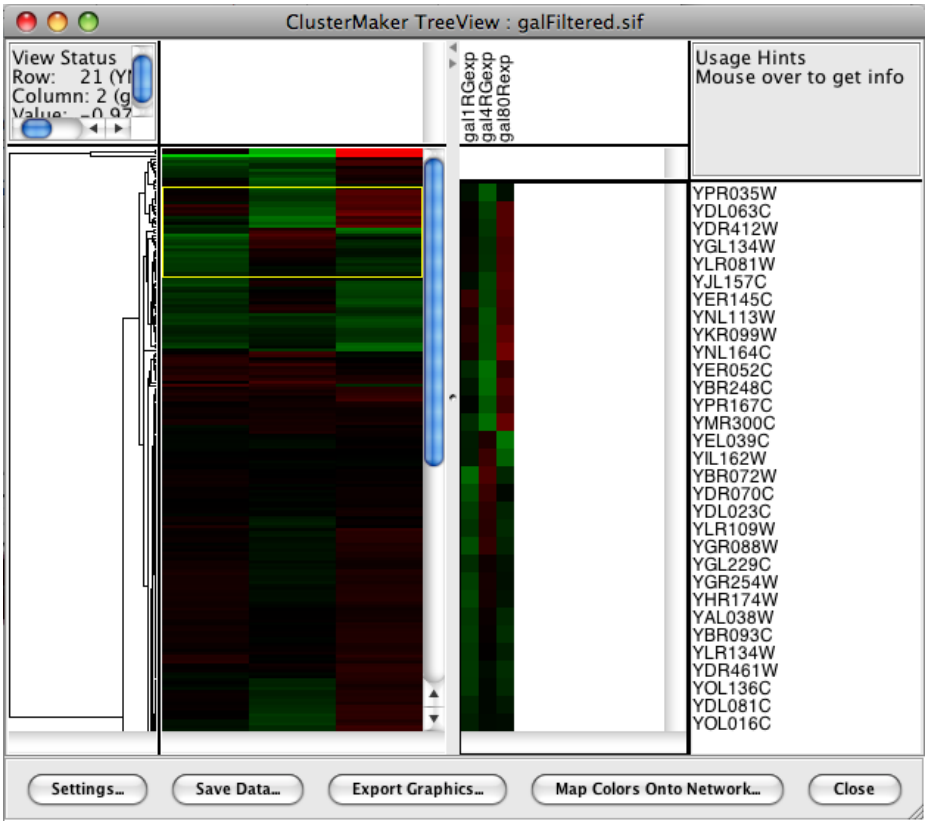
Plugin 2: Cluster Maker

The clusterMaker plugin provides a general framework for clustering and visualizing clusters of Cytoscape node and edge attributes. One of the primary use cases for clusterMaker is to support the analysis of expression data using either hierarchical or k-means clustering. Other uses include the analysis of epistatic mapping (E-MAP) data as well as clustering protein similarity networks to assign nodes to putative protein families.

Usage: perform and visualize cluster analyzes

The ClusterMaker plugin is available from the **Plugin Manager** (refer to Section 1.3)

- Select **Cluster->Hierarchical cluster** from the **Plugins** menu
- Use ctrl (or cmd on Macs) to select the three columns of fold value data (gal1RGexp, gal4RGexp, and gal80Rexp)
- Click **Only use selected nodes/edges for cluster** to deselect
- Click **Create Clusters**
- Click **Visualize Clusters**



This is a standard cluster view with the complete heatmap on the left, the selection heatmap in the middle and the gene names on the right.

- Click **Settings…** to adjust the **contrast, color gradient**, or **data range**
- Click and drag on the heatmap to select rows; Shift-click on heatmap to select individual columns
- Select a column and then click **Map Colors Onto Network…** to create a visual style from the cluster heatmaps, visualizing the data on your network
- If you select a row in the heatmap and then click **Map Colors Onto Network…**, a dialog will pop up asking which columns you want to use; select all three and click **Animate Vizmap**

*Now zoom out and watch your network come alive with data! You can use this view to identify "hot spots" in your network. Hit **Stop Animation** to end the cycle. And use VizMapper to switch back to any prior visual style.*

Plugin 3: BiNGO

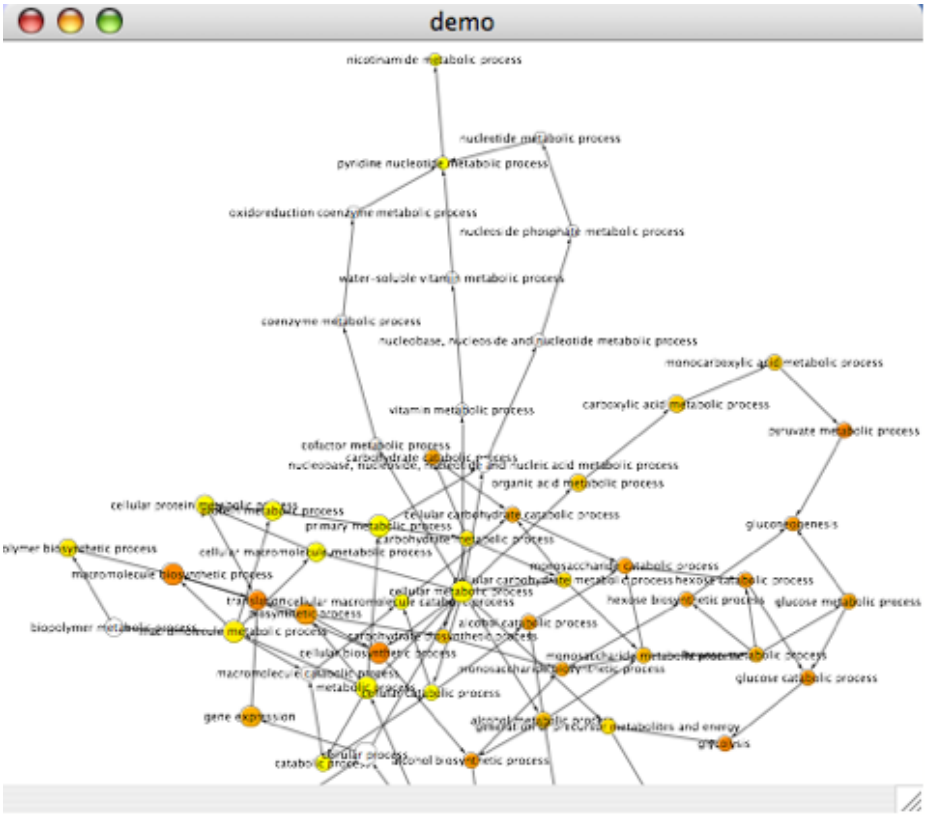
Usage: perform and visualize overrepresentation analyzes

The BiNGO plugin is available from the **Plugin Manager** (refer to Section 1.3)

- Select **BiNGO** from the **Plugins** menu
- Select a subset of nodes from the network, e.g.
  - Select a cluster from the **ClusterMaker** analysis
  - Select based on sorted or filtered data values in the **Data Panel**
- Provide a name for the cluster
- Review other settings (optional for this tutorial)
- Click 'Start BiNGO'
- You will be greeted with a table of ranked GO terms and statistics, and a network visualization of the GO terms colored by significance, and a legend window explaining the color gradient

*The long GO term names can make the network difficult to read. You can use **Force-directed** layout and **Layout>Scale** to increase the spacing between nodes. **Hierarchical** layout is also nice, though the names overlap*

even worse.



- Play with the cluster selection and BiNGO parameters to explore the analytical possibilities with your data.

References

[1] http://opentutorials.rbvi.ucsf.edu/index.php?title=Tutorial:Introduction_to_Cytoscape-part2&ce_slide=true&ce_style=cytoscape

[2] http://opentutorials.rbvi.ucsf.edu/index.php/File:Introduction_to_Cytoscape-part2.pdf

[3] http://cytoscape.wodaklab.org/wiki/CytoRetreat2007Tutorials

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Tutorial:Basic Expression Analysis in Cytoscape

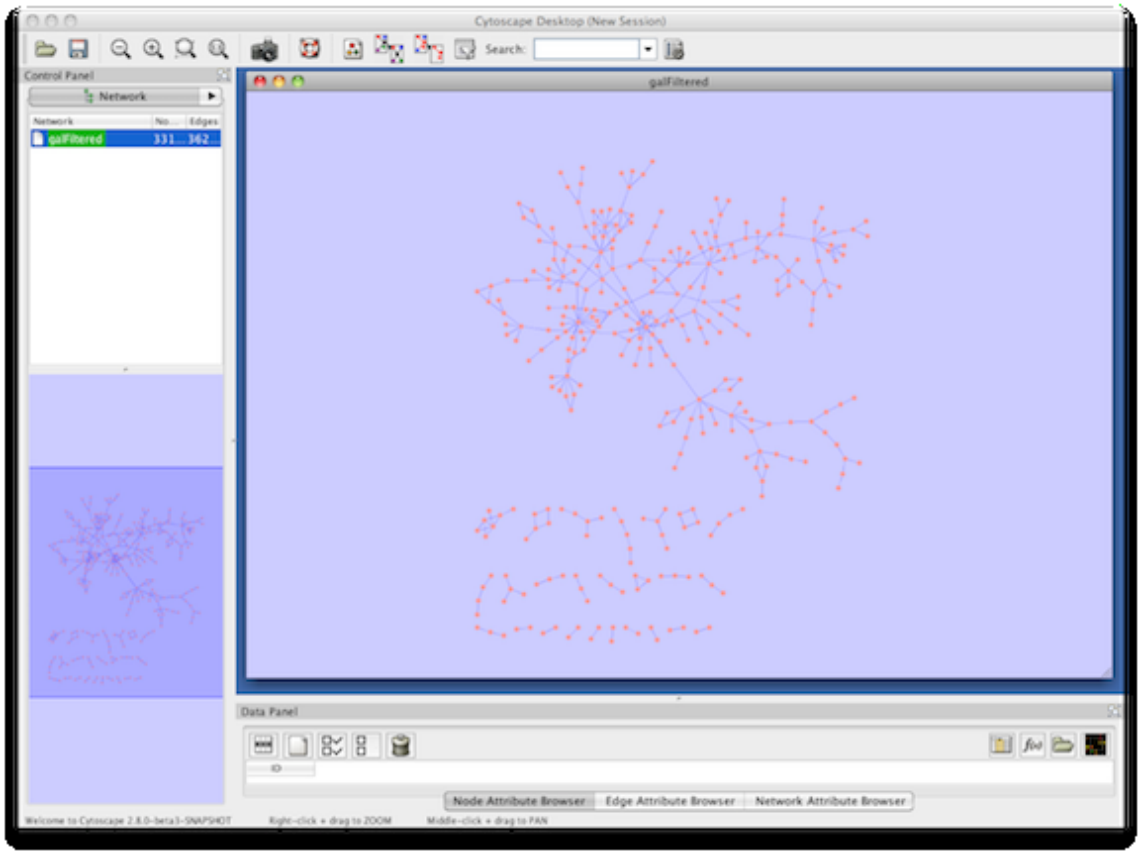
Slideshow Basic Expression Analysis in Cytoscape (30 min) [1]
Handout Basic_Expression_Analysis_in_Cytoscape.pdf (10 pages) [2]
Tutorial Sources Cytoscape Wiki (Natalie Yeung) [3]
Tutorial Curators Kristina Hanspers, Alex Pico, Mike Smoot

Cytoscape is an open source software platform for *integrating*, *visualizing*, and *analyzing* measurement data in the context of networks. This tutorial will introduce you to:

- Visualizing networks using expression data.
- Filtering networks based on expression data.
- Assessing expression data in the context of a biological network.

Loading Network

- Start Cytoscape and load the network galFiltered.sif.
- Apply the force-directed layout to organize the layout of the nodes. Select the "Layout->Cytoscape Layouts->Force-Directed Layout" menu.
- Cytoscape should now look similar to this:



Loading expression data

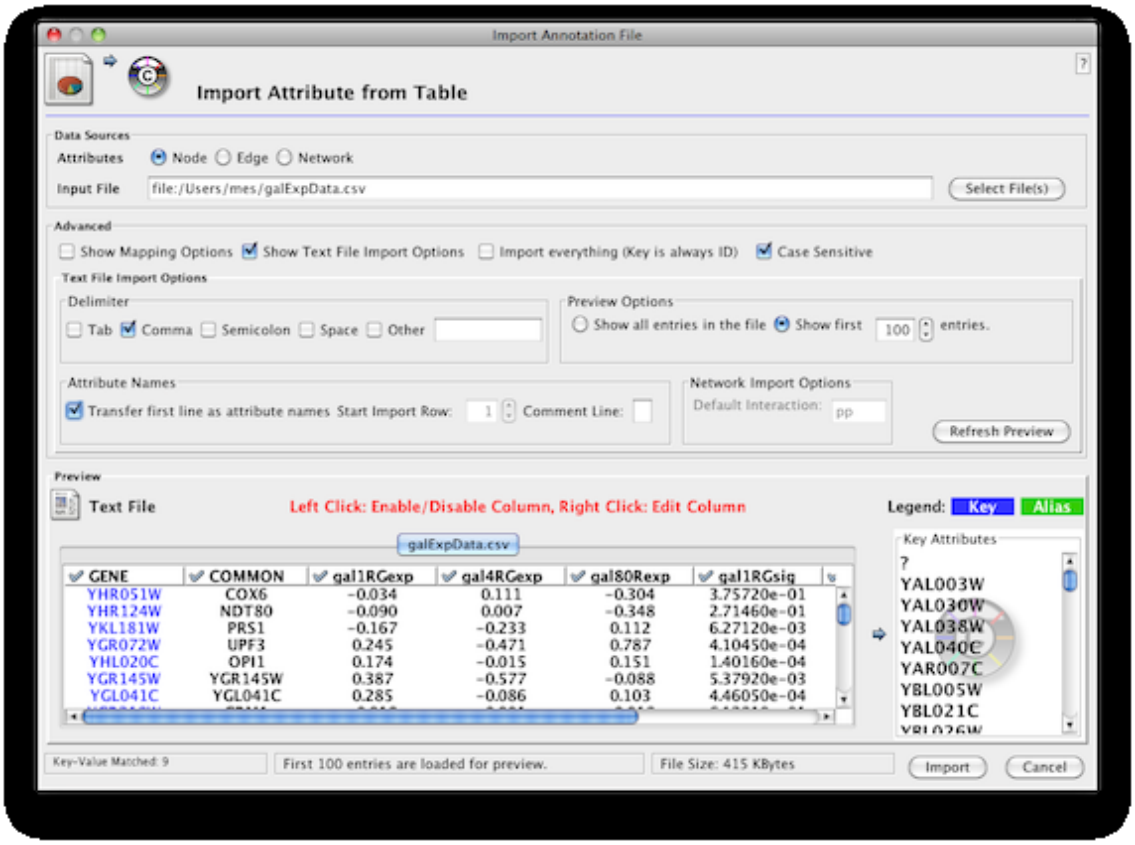
- Using your favorite text editor, open the file galExpData.csv. The first few lines of the file are as follows:

```
GENE,COMMON,gal1RGexp,gal4RGexp,gal80Rexp,gal1RGsig,gal4RGsig,gal80Rsig
YHR051W,COX6,-0.034,0.111,-0.304,3.75720e-01,1.56240e-02,7.91340e-06
YHR124W,NDT80,-0.090,0.007,-0.348,2.71460e-01,9.64330e-01,3.44760e-01
YKL181W,PRS1,-0.167,-0.233,0.112,6.27120e-03,7.89400e-04,1.44060e-01
```

You should note the following information about the file:

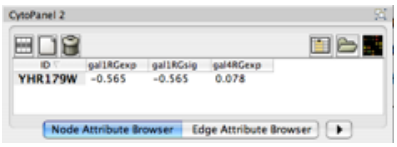
1. The first line consists of labels.
2. All columns are separated by a single comma character.
3. The first column contains node names, and must match the names of the nodes in your network exactly!
4. The second column contains common locus names. This column is optional, and the data is not currently used by Cytoscape, but including this column makes the format consistent with the output of many microarray analysis packages, and makes the file easier to read.
5. The remaining columns contain experimental data, two columns per experiment (one column represents the expression measurement and the second represents the significance value for that measurement), and one line per node. In this case, there are three expression results per node.

- Under the **File** menu, select **Import → Attribute from Table (Text/MS Excel)**.
- Click "Node" for the type of attribute to import.
- Select the file galExpData.csv.
- Click the "Text File Import Options" check box.
- Click the "Tab" check box in the "Delimiter" section to unselect Tab and click "Comma" instead. The preview should now indicate that it is importing multiple columns of data.
- Click the "Transfer first line as attribute names" check box in the "Attribute Names" section. The preview should now show be using the first row of the input file as column names and the import window should look like the image below.
- Click the "Import" button to import the attribute data.



Now we will use the **Node Attribute Browser** to browse through the expression data, as follows:

- Select a node on the Cytoscape canvas by clicking on it.
- In the **Node Attribute Browser**, click the **Select Attributes** button , and select the attributes gal1RGexp, gal4RGexp, and gal80Rexp by left-clicking on them. Right-click to close the menu.
- Under the **Node Attribute Browser**, you should see your node listed with their expression values, as shown.



Visualizing Expression Data

Probably the most common use of expression data in Cytoscape is to set the visual attributes of the nodes in a network according to expression data. This creates a powerful visualization, portraying functional relation and experimental response at the same time. Here, we will walk through the steps for doing this.

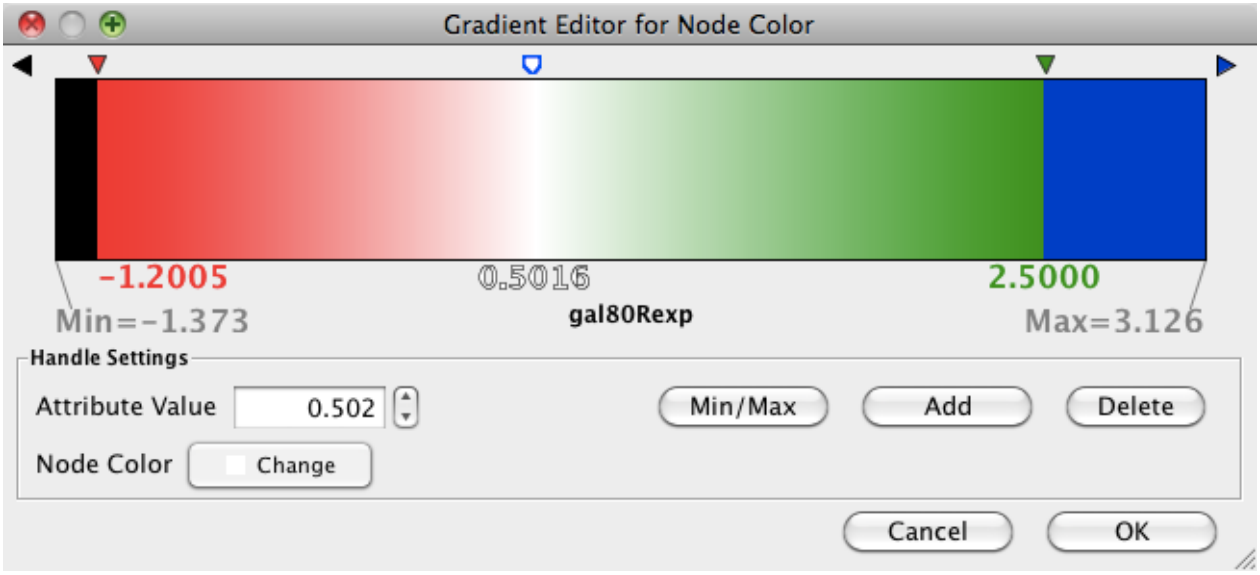
Label the Nodes

- Open the **VizMapper** by selecting its tab or by clicking on its icon: 
- Use the "Common" name attribute to give the nodes useful names.
- Zoom in on the network so that node labels are visible.
- Click the second column of the "Node Label" row in the **Visual Mapping Browser**.
- This should produce a drop-down menu of available attribute names. Select "Common".
- Verify that the node labels on the network have changed to their common names.
- Click the Triangle in the "Node Label" row of the "Visual Mapping Browser" to see the other visual properties.

Color the nodes

Define the node color of this visual style:

- Double-Click the **Node Color** row in the **Visual Mapping Browser** in the **Unused Visual Properties** Section.
- This action will move **Node Color** to the top of the **Visual Mapping Browser**.
- Click the "Please select a value!" cell in the **Node Color** section.
- This will produce a drop-down menu of available attribute names. Select "gal80Rexp".
- Click the "Please select a mapping" cell in the **Node Color** section.
- This will produce a drop-down menu of available mapping types. Select "Continuous Mapping".
- This action will produce a basic black to white color gradient.
- Click on the color gradient to change the colors. This will pop-up a gradient editing dialog.
- Drag the left-most, red handle along the top of the gradient. Drag it to an Attribute Value of approx. -1.2
- Drag the white handle to approx 0.5. You can type the Attribute Value in the Handle Settings section to be more precise.
- You can also change the color of each handle by double-clicking or using the Node Color selector button in the Handle Settings section.
- This should produce a Red-White-Green Color gradient like the image below, with min and max extremes colored black and blue, respectively.
- Click 'OK' to save the gradient adjustment dialog and verify that the nodes in the network reflect the new coloring scheme.



Set the default node color

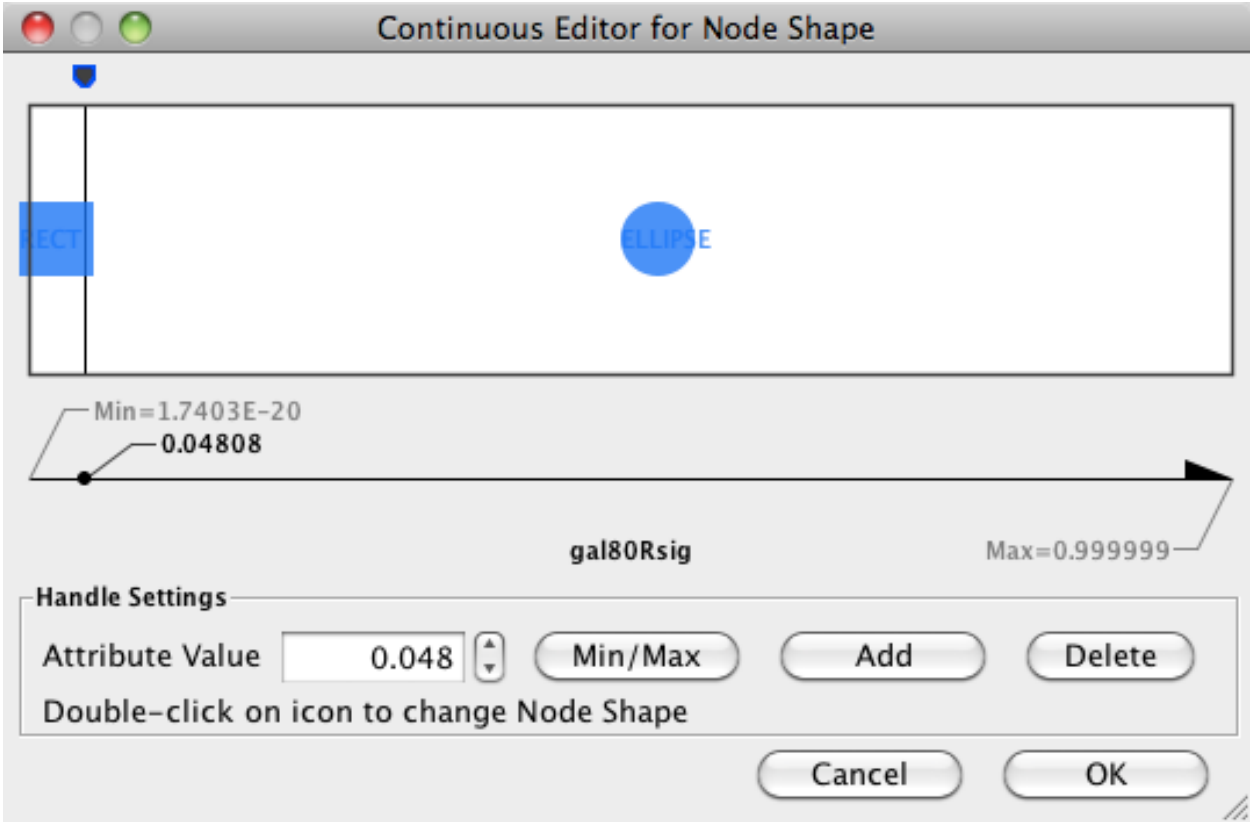
Note that the default node color of pink falls within this spectrum. A useful trick is to choose a color outside this spectrum to distinguish nodes with no defined expression value and those with slight repression.

- Click the **Defaults** network icon in the **VizMapper** panel.
- Click the **Node Color** entry and choose a dark gray color.
- Zoom out on the network view to verify that a few nodes have been colored gray.

Set the Node Shape

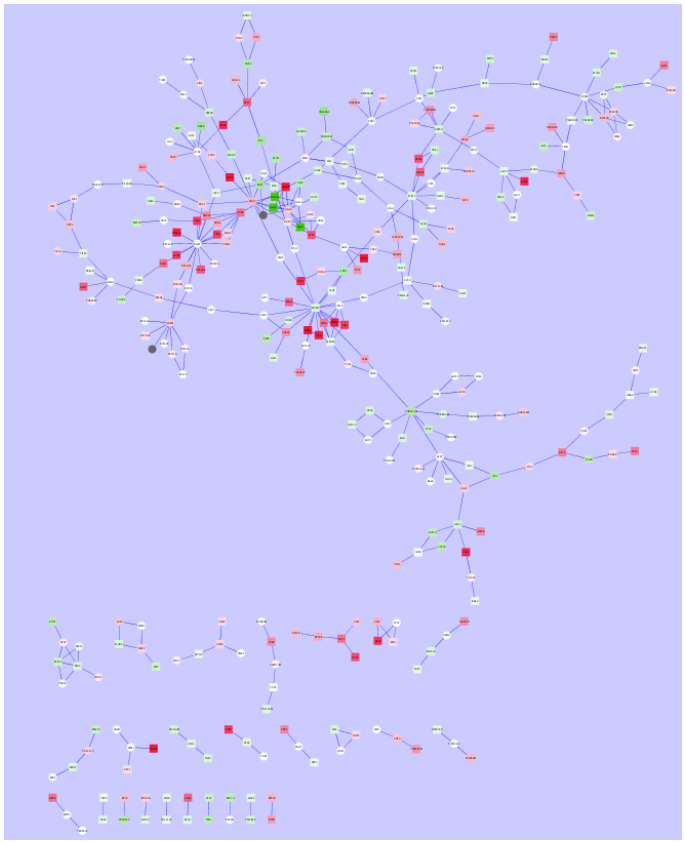
We imported both expression measurement values and significance values for those measurements. We can use the significance values to change the shape of the nodes so that measurements we have confidence in appear as squares while potentially bad measurements appear as circles.

- Double-Click the **Node Shape** row in the **Visual Mapping Browser** in the **Unused Visual Properties** Section.
- This action will move **Node Shape** to the top of the **Visual Mapping Browser**.
- Click the "Please select a value!" cell in the **Node Shape** section.
- This will produce a drop-down menu of available attribute names. Select "gal80Rsig".
- Click the "Please select a mapping" cell in the **Node Shape** section.
- This will produce a drop-down menu of available mapping types. Select "Continuous Mapping".
- This will create an empty icon in the "Graphical View" row of the **Node Shape** section. Click on this icon.
- This action will pop-up a continuous shape selection dialog.



- Click the **Add** button.
- This action will split the range of values with a slider down the middle with a node shape icon to either side of the slider.
- Double-Click on the left node icon (a circle).
- This will pop-up a node shape selection dialog.
- Choose the **Rectangle** shape and click the **Apply** button.
- The continuous shape selection dialog should now show both a square and a circle node shape icon.
- Click on the black triangle and move the slider to the left, to slightly lower that 0.05, our threshold for significance.
- Close the continuous shape selection dialog and verify that some nodes have a square shape and some nodes have a circular shape.

The network should now look like this:



A biological analysis scenario

This section presents one scenario of how expression data can be combined with network data to tell a biological story.

First, here is some background on your data. You are working with yeast, and the genes Gal1, Gal4, and Gal80 are all yeast transcription factors. Your expression experiments all involve some perturbation of these transcription factor genes. Gal1, Gal4, and Gal80 are also represented in your interaction network, where they are labeled according to yeast locus tags: Gal1 corresponds to YBR020W, Gal4 to YPL248C, and Gal80 to YML051W.

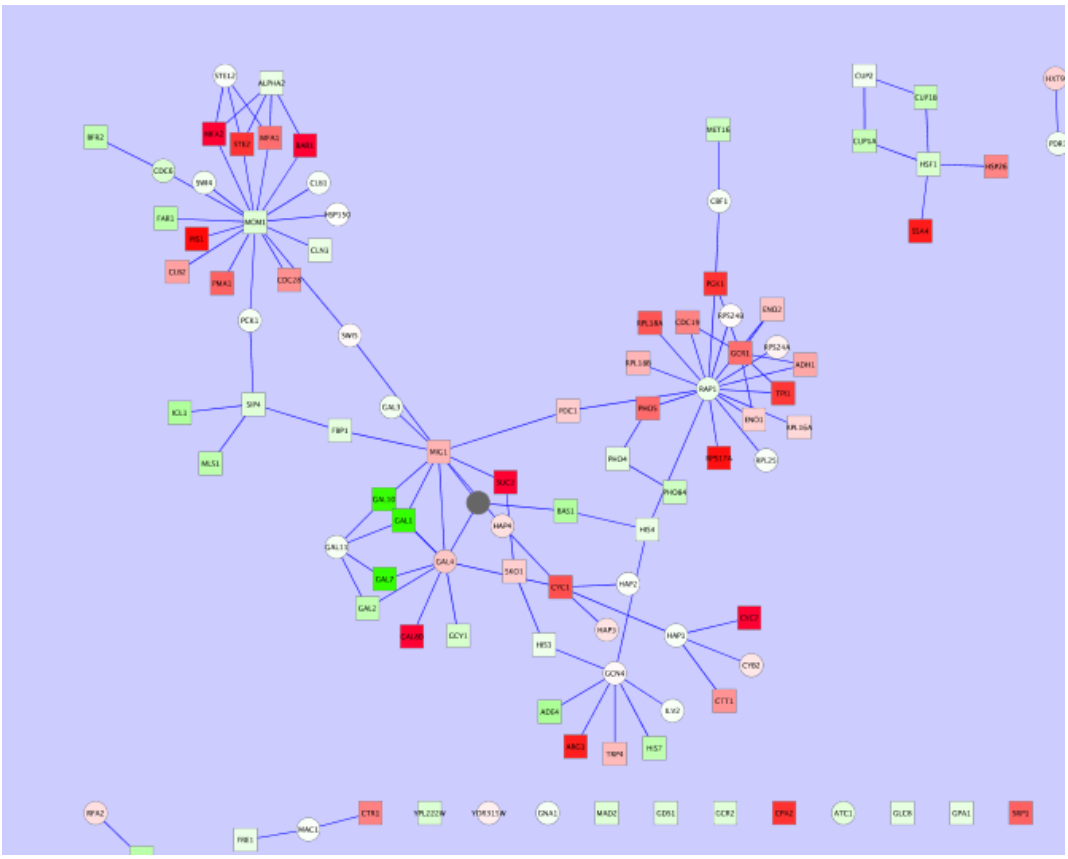
Filter Interactions

Your network contains a combination of protein-protein (pp) and protein-DNA (pd) interactions. Here, we shall filter out the protein-protein interactions to focus on the protein-DNA interactions.

- Click the **Filters** tab in the **Control Panel**.
- Click the **Attribute/Filter** chooser in the **Filter Definition** and choose "edge.interaction".
- Click the **Add** button in the **Filter Definition** section to add the selected attribute to the filter.
- This action will create a text search box entry in the filter.
- Type the letters "pp" into the text search box. This indicates that we're searching for all edge interaction attributes that match the string "pp".
- Click the **Apply Filter** button at the bottom of the Filters panel.



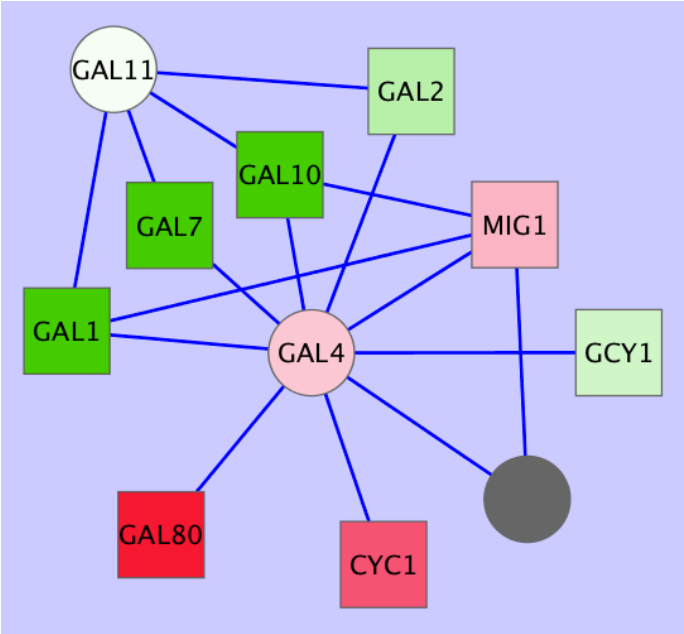
- You should now see many edges in the network selected (i.e. colored red).
- Since we're only interested in the protein-DNA edges, we can delete the protein-protein edges we've just selected.
- Select the menu **Edit → Delete Selected Nodes and Edge**. You should now see many unconnected nodes in the network.
- Select the menu **Layout → Cytoscape Layouts → Force-Directed Layout** to clean up the network visualization.
- The final filtered and cleaned up network should look like this:



Observe the Network

Notice that three bright green (highly induced) nodes are in the same region of the graph. Zoom into the graph to see more details.

- Notice that there are two nodes that interact with all three green nodes: GAL4 (YPL248C) and GAL11 (YOL051W).
- Select these two nodes and their immediate neighbors by selecting the menu **Select → Nodes → First Neighbors of Selected Nodes**.
- It is sometimes useful to create a new network from selected nodes. Do this by selecting the menu **File → New → Network → From Selected Nodes, All Edges**.
- With some layout and zooming, this new network should appear similar to the one shown:



Exploring Nodes

- Right click on the node GAL4.
- Select the menu **LinkOut → Entrez → Gene**.
- This action will pop-up a browser window and search the Entrez Gene database for the term "YPL248C", the id of the node.
- In the results in the browser the first entry should be labeled GAL4. Click on this entry.
- The description of GAL4 tells us that it is repressed by GAL80.
- Our data show precisely this:
  - Both nodes (GAL4 and GAL11) show fairly small changes in expression, and neither change is statistically significant: they are rendered as light-colored circles. These slight changes in expression suggest that the critical change affecting the black nodes might be somewhere else in the network, and not either of these nodes.
  - GAL4 interacts with GAL80 (YML051W), which shows a significant level of repression: it is depicted as a red square.
  - Note that while GAL80 shows evidence of significant repression, most nodes interacting with GAL4 show significant levels of induction: they are rendered as green squares.
  - GAL11 is a general transcription co-factor with many interactions.
- Putting all of this together, we see that the transcriptional activation activity of Gal4 is repressed by Gal80. So, repression of Gal80 increases the transcriptional activation activity of Gal4. Even though the expression of Gal4

itself did not change much, the Gal4 transcripts were much more likely to be active transcription factors when Gal80 was repressed. This explains why there is so much up-regulation in the vicinity of Gal4.

References

[1] http://opentutorials.rbvi.ucsf.edu/index.php?title=Tutorial:Basic_Expression_Analysis_in_Cytoscape&ce_slide=true&ce_style=cytoscape

[2] http://opentutorials.rbvi.ucsf.edu/index.php/File:Basic_Expression_Analysis_in_Cytoscape.pdf

[3] http://cytoscape.wodaklab.org/wiki/Presentations/04_Expression_Data

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