GFD-NET

Cytoscape Plug-in

GFD-Net is a Cytoscape plug-in designed to visualize and analyze the coherence of gene networks. GFD-Net can analyze a gene network based on Gene Ontology (GO) and calculate a quantitative measure of its functional coherence, i.e. a quantitative value of the degree of similarity between the connected genes in it. After the analysis, users can visualize the information retrieved from GO. For each gene the user can see its associated GO terms and its function (specified by a GO term) chosen as the most cohesive function in the set. For each edge the user can see the genes at its ends, the function chosen as the most cohesive function in the set for each one and the dissimilarity between them.

Juan José Díaz Montaña

juanjo.diazmo@gmail.com

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Introduction

This manual aims to provide basic knowledge for any user, regardless of their computer skills, to be able to use the Cytoscape plug-in GFD-Net.

GFD-Net is a Cytoscape plug-in that allows the user to analyze genetic networks. GFD-Net analyzes the networks based on Gene Ontology, calculates a quantitative measure of its consistency and provides additional information about the genes that form it and the interactions between them.

GFD-Net is distributed as a single file called GFDNET.jar.

What is it for?

GFD-Net provides a new approach to assessing the functional coherence of a gene network, i.e. the degree of similarity between genes forming it considering the relationships the network defines between them. This will reveal the quality or reliability of a network obtained from an experiment and see in which sense or with which function the genes are more consistent with each other since a gene may have more than one function in the body.

Consistency is measured from a repository of "real" biological information as the Gene Ontology (GO), which provides a controlled vocabulary that describes the gene and gene product attributes in any organism. Each gene is associated with multiple GO terms, and through them it is possible to compare the functional similarity.

It is important to note that GFD-Net is designed to analyze completely connected networks whose genes are all known in GO.

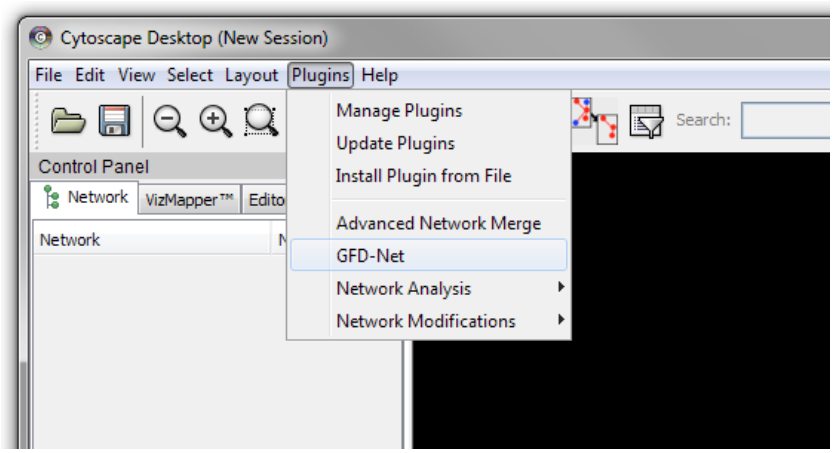
Requirements and installation

In order to run the plug-in, it is necessary to install an updated version of Java which can be downloaded from their website (http://www.java.com).

Furthermore, the current version of the plug-in is designed to Cytoscape 2.8.X. If you do not have this program, it can be downloaded from their website (http://www.cytoscape.org/). Once Cytoscape is installed, there are two ways to install the plugin:

Installing using the jar file through Cytoscape

Click on Plugins > Install Plugin. Select the file GFDNET.jar and it will be installed. Then, run Cytoscape. GFD-Net should already appear in the Plugins menu.



Installing through the Cytoscape Plugin Manager

Click on Plugins > Manage Plugins. The manager is displayed showing all the installed plugins and all the available plugins. GFD-Net can be found at Available for Install > Ontology analysis. Select it and click on the Install button to install it. Then, run Cytoscape. GFD-Net should already appear in the Plugins menu.

Uninstalling

Click on Plugins > Manage Plugins. The manager is displayed showing all the installed plugins and all the available plugins. GFD-Net can be found at Currently Installed > Ontology analysis. Select it and click on the Delete button to uninstall it.

Installing and Uninstalling Manually (Not recommended)

To install GFD-Net copy the file GFDNET.jar to the subfolder plugins in the Cytoscape folder. Cytoscape is installed by default at C:\Program Files\Cytoscape_v2.8.3. Then, run Cytoscape. GFD-Net should already appear in the Plugins menu.

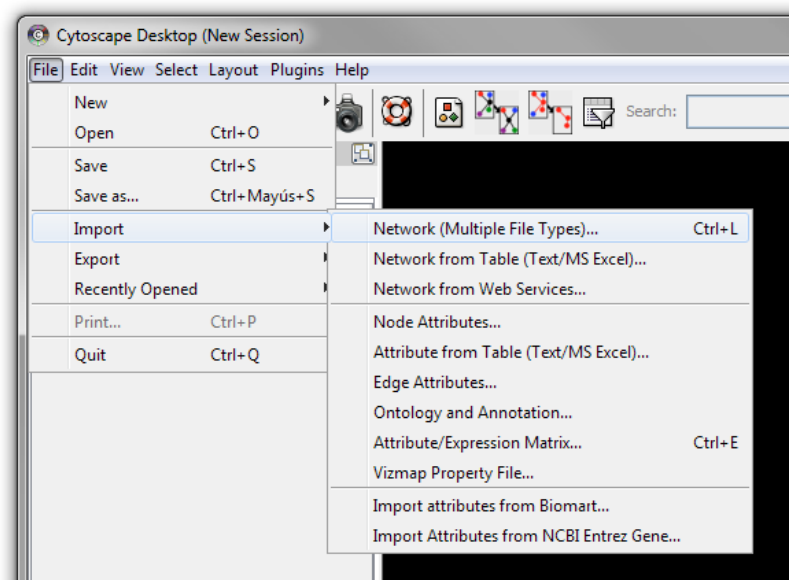
To uninstall GFD-Net just remove the jar from the folder. It is very important to note that this uninstalling system is only valid if the plugin was just copied into the folder. If the plugin was installed any other way, remove the jar may cause errors on Cytoscape.

Use of GFD-Net

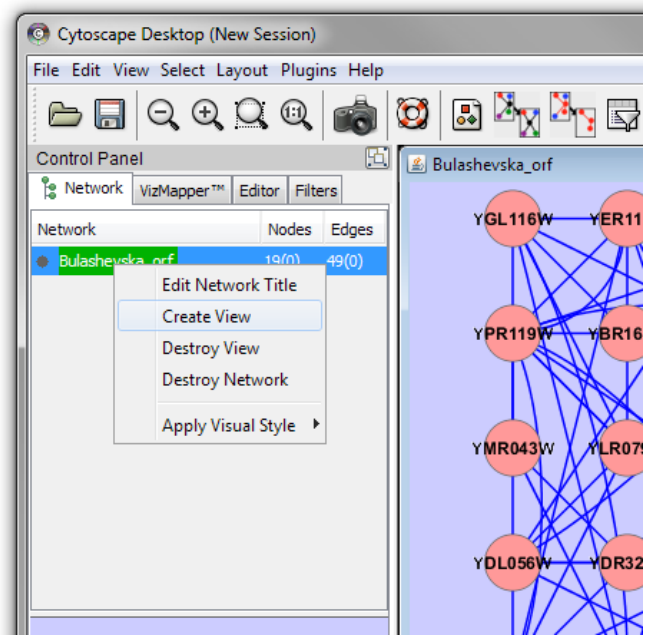
The following briefly describes how to use the plugin.

Launch the plug-in

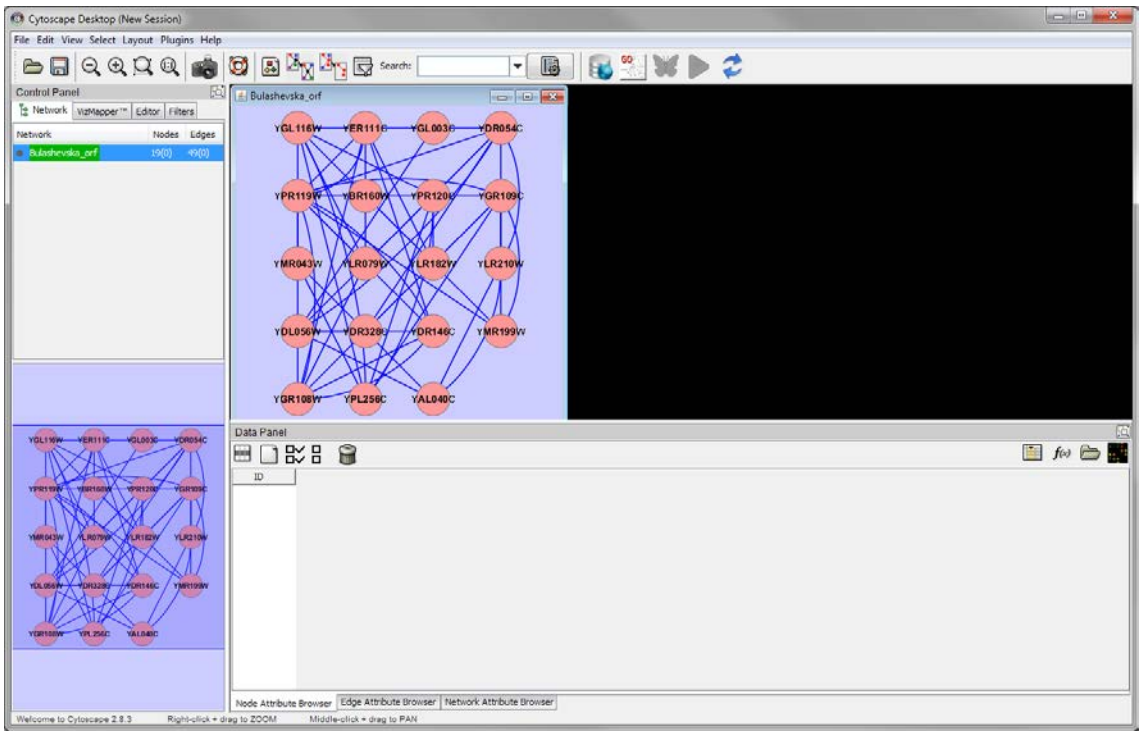
To launch the plugin you must load a network in Cytoscape. This can be done from the menu File> Import> Network (Multiple Files Types)... or through the keyboard shortcut Ctrl + L.



It must be taken into consideration that Cytoscape only creates a network view if you have less than 10000 nodes. If the network is greater, it must be created manually. This can be done by clicking the right mouse button on the network in the control panel to the left and clicking "Create View".



After correctly loading the network and its view, launch the plugin from the menu Plugins> GFD-Net. The GFD-Net buttons are then added to the toolbar but only "Configure DB Connection", "Set Ontology" and "Refresh" can be used.

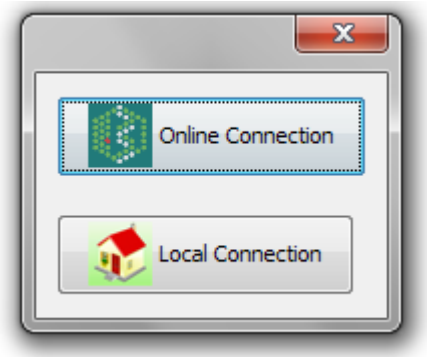


Configuration

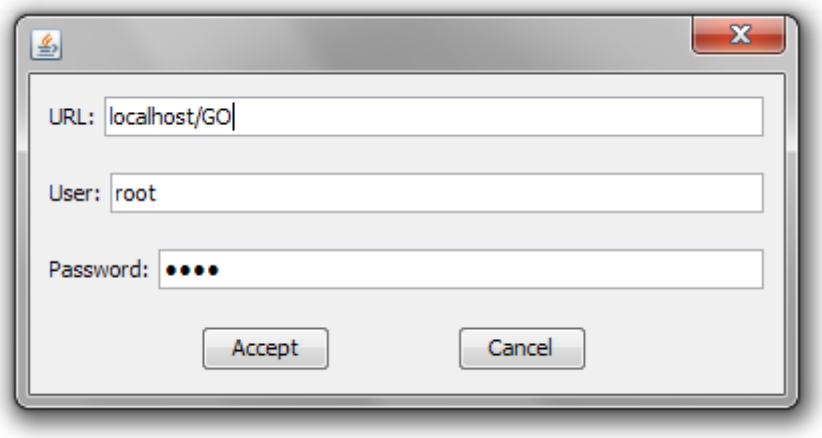
The first thing to do in order to run the GFD-Net approximation is to configure their parameters correctly. For this purpose the best way is to use the following steps.

Configure the BD

To set the connection to the database click the  *button. A dialog is displayed giving the user the option to connect to the online GO database provided online by the European Bioinformatics Institute (http://www.ebi.ac.uk) or to a local database (or not necessarily local; any address can be accessed). It is strongly advised to use a local database because of the extreme slowness of the online database, which makes it difficult to use.*



When choosing to use a local database, a form is displayed asking for the database address, user and password. This allows you to not only access databases in our local system but also in any other accessible address.

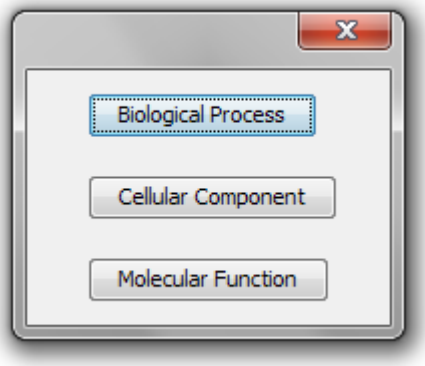


Once the database connection is successfully established, the "Set Organism" and "Execute GFD-NET" buttons are enabled.

To install a database locally, download the wanted GO database version from their website (http://www.geneontology.org) and follow the instructions they provide to install it. The simplest way is to use a MySQL server.

Set an ontology

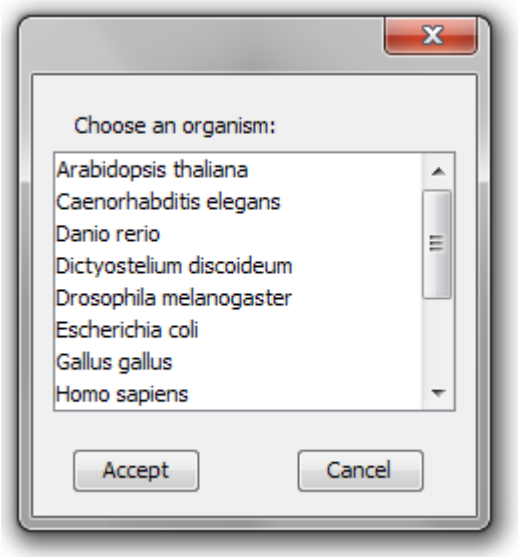
By default, GFD-Net runs on the biological processes ontology, but this can be changed by clicking on  *and choosing any other ontology.*



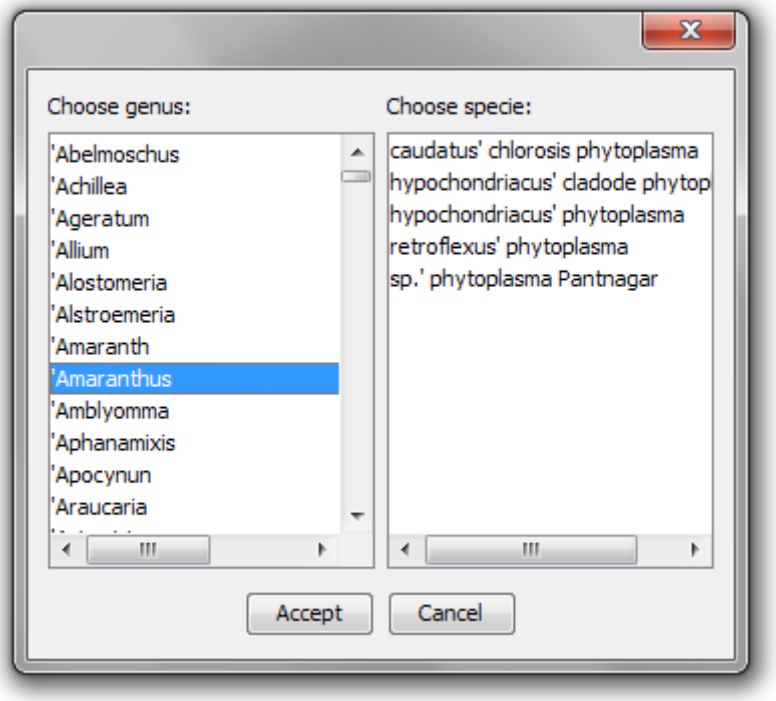
If GFD-Net has already been executed, setting a new ontology would restore the original network and lose the information obtained in the previous run.

Set an organism

It is not possible to execute GFD-Net without having an organism set. This can be done by clicking  *. A dialog is then displayed allowing the choice between the main organisms of GO. In case you want to use another organism, select "Other ...". Select the organism and click "OK" to set it.*



If choosing "Other ..." another dialog will be displayed showing a list of the genre contained in the database. Clicking on one of these genres will display a list of species that belong to it. With one genus and one species selected click "OK" to set the organism.



After choosing the organism, a panel is displayed on the right indicating that the organism is being loaded. The duration of the process depends on the information available on GO about this organism but will be much shorter if you load an organism which was loaded during the same session for the second time.

It should be noted that in GO the name of an organism is formed by its genre and specie put together. However, when extracting the genre and specie from the database, the first word is taken as the genre and the rest as specie.

If GFD-Net has been already executed, setting a new organism would restore the original network losing the information obtained in the previous run.

Refresh

If you want to change the network you are working on simply load a new one (it is advised to close the current one) and, having the view on the new network as current view, click on  *. This way the plugin returns to its initial state but is working on the new network.*

Execution:

Execute GFD-Net

To run GFD-Net, you must set the organism and the ontology as well as the database connection. Clicking on  *will display a panel on the right indicating that GFD-Net is running. The duration of the process depends on the size and complexity of the network introduced and on the amount of information about the organism that is contained in GO.*

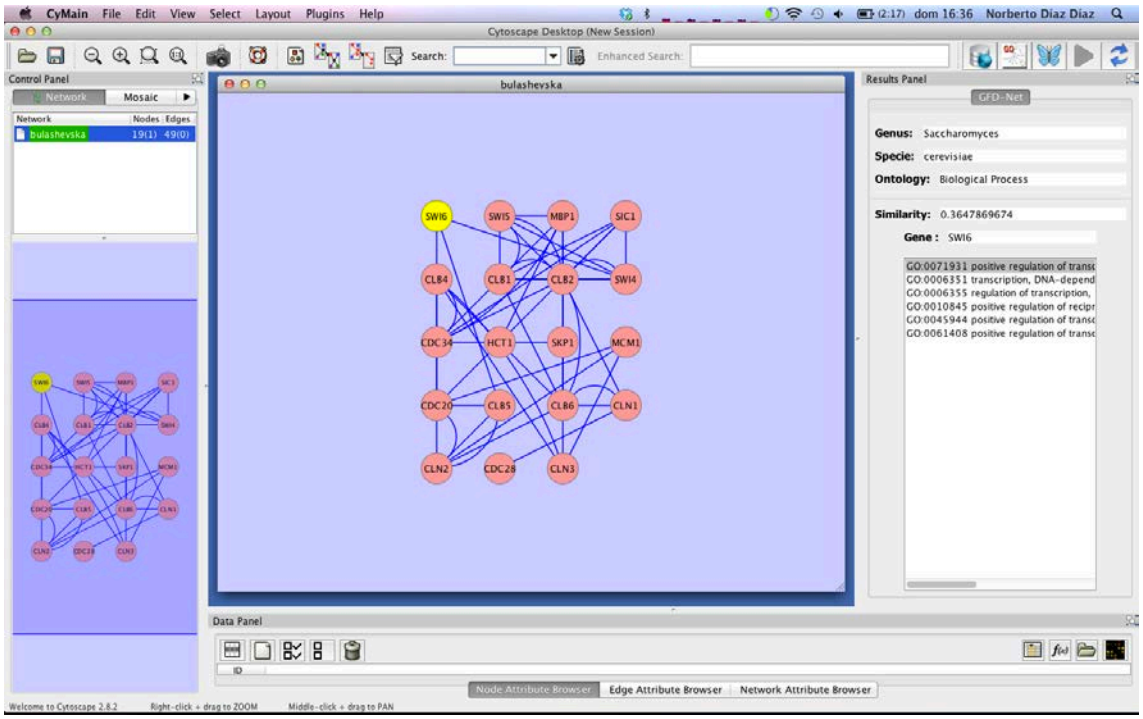
Once GFD-Net is executed, all nodes that were not found in GO are removed from the network, a panel is displayed on the right containing information about the results and the user is able to interact with the network.

Information Visualization

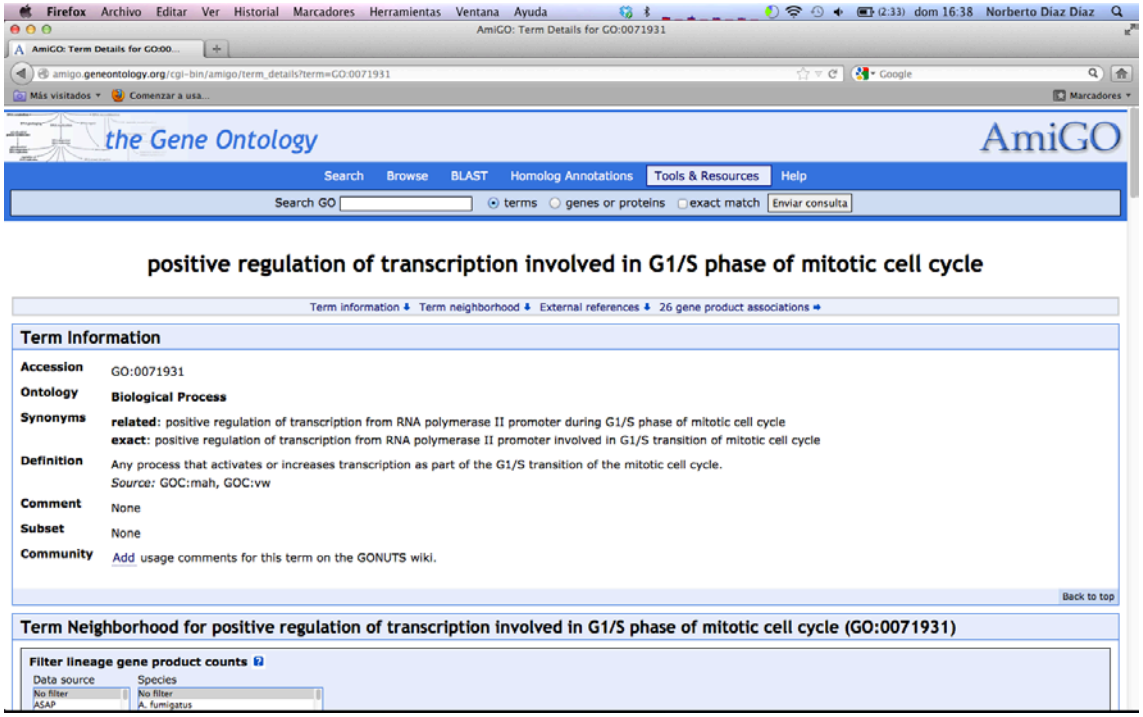
Once GFD-Net is executed, a panel is displayed on the right containing information about the results (ontology, genre, specie and value of dissimilarity). The user is able to interact with the network in order to visualize the information obtained for each node or edge.

Node Information

Clicking on a node adds information about it to the panel on the right, including its name and a list of its representations ("representations" is a GO term). The first representation of the list will be shaded indicating that is a representation chosen by GFD-Net. This means that the function indicated by the GO term is the most cohesive function for the gene in the network.

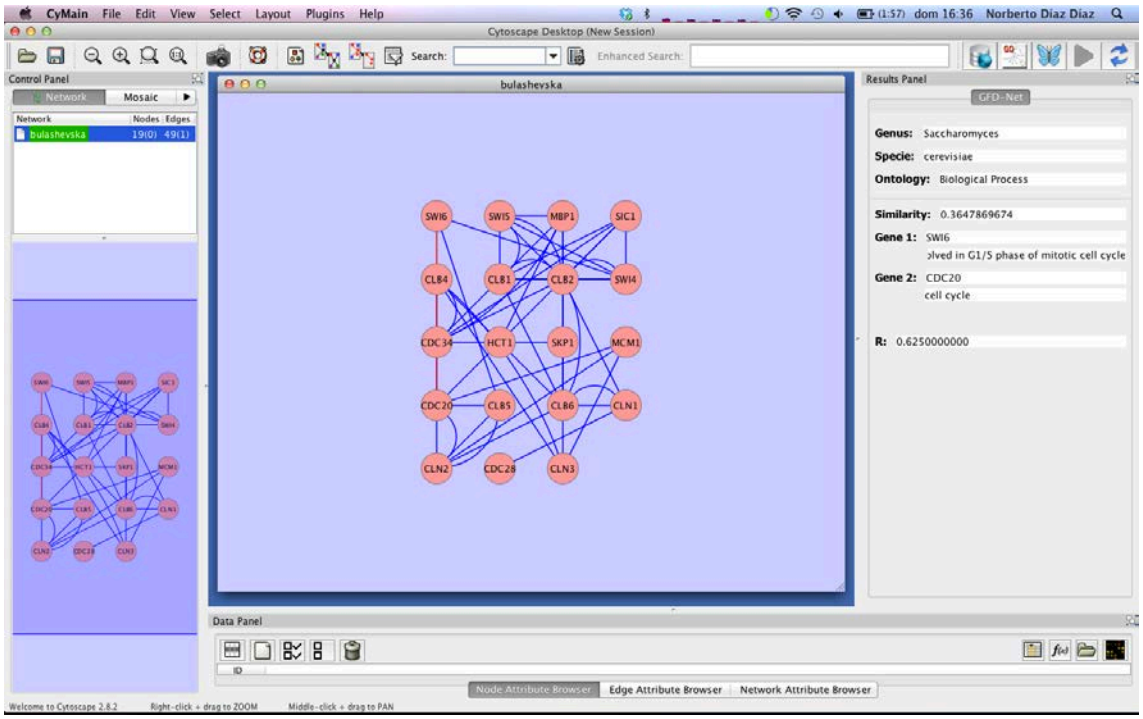


By double-clicking on one of the representations in the list, the browser will display the website for that GO term in AmiGO, a Gene Ontology online browser.



Edge Information

Clicking on an edge will show the names of the genes located at its ends, the representation chosen for each of them and the dissimilarity value between them.



Advanced User

For advanced users who want to use GFD-Net differently or independently of Cytoscape, it can be done using the existing API. Unfortunately, this API has not been released yet. Release date is pending.

Troubleshooting

Below is a list of common user mistakes when using the plugin as well as tips on how to avoid them.

- *Opening a new session keeps the plug-in loaded but eliminates the network. It should be loaded again, and the plugin must be refreshed to continue using it.*
- *Saving the session does not save the state of the plug-in or information obtained by it.*
- *Changing the network without refreshing causes malfunctions on the plugin.*
- *The best way to avoid errors is to work with only one network loaded into Cytoscape and having selected its view at all times.*
- *Trying to load very large or well-known organisms using the online database may not work. This is because it takes too long to retrieve all the information, and the database breaks the connection after a certain time.*