

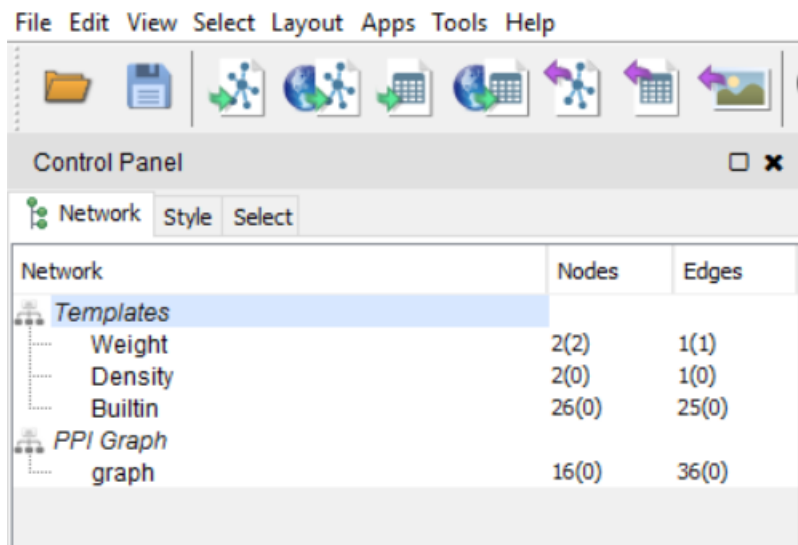
Walkthrough

Demo contents:

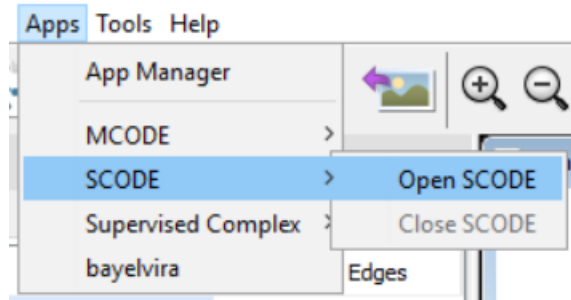
1. **DEMO.cys** : a session file containing a pre-loaded PPI graph and Bayesian template
2. **training.tab** : a tab-separated file containing the positive training data that will be used to train the network

Instructions:

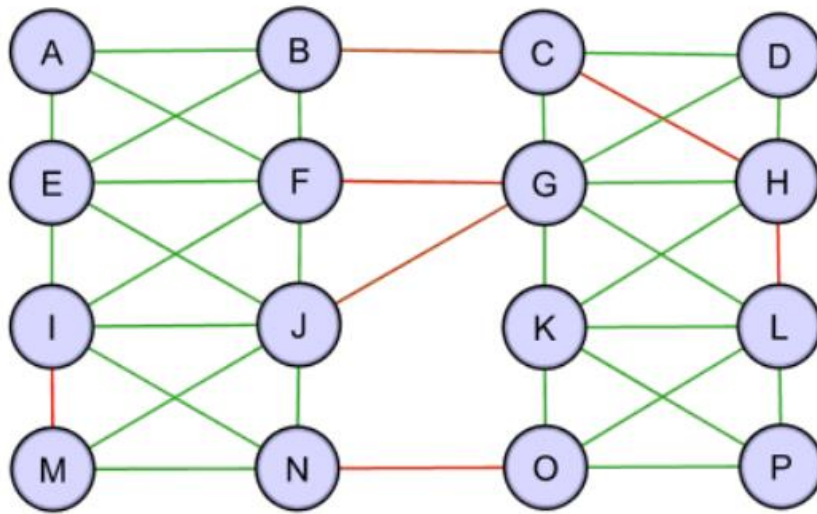
1. Open Cytoscape. In the welcome window, click the button to ‘**Open Session File**’ and select DEMO.cys. Alternatively, navigate to **File > New > Session** from the menu bar.
2. Once the session file has been read, you’ll notice two network collections in the ‘Control Panel’ on the left of the screen:
 - Templates: a collection of networks containing Bayesian templates that may be trained to score candidate complexes.
 - PPI Graph: a network collection containing the protein network that will be searched upon.



3. Open SCORE
In the top menu bar, select **Apps > SCORE > Open SCORE**.



4. Examining the PPI graph



In this simplistic model, we observe two edge weight ranges. Edges in green have weight 0.8, and edges in red range from 0.1 to 0.3.

With a Bayesian model that depends on the ‘Mean Weight’ feature, we would expect to identify complexes among connected nodes that all share weight values of 0.8. With a Bayesian model that depends on the ‘Density’ feature, we would expect to identify complexes among highly interconnected nodes.

The demo provides three sample templates to use for training the Bayesian model – Weight, Density, and Builtin. The third, Builtin, is provided for convenience in constructing other Bayesian networks. It directly matches the built-in option that is specified internally in the App.

5. Specify search parameters

A number of search parameters are hidden under the ‘Advanced Search Parameters’ button. After expansion, set the following search parameters (or alter them to your preference)

Searching for Complexes

Protein graph graph

Search Variant Greedy ISA

> Advanced Search Parameters

Search Limit 20

Initial Temperature 1.8

Temperature Scaling Factor 0.88

Overlap Limit 0.75

Minimum Complex Size 3

Use Seeds From File ☐ Seed File (.tab, .tsv)

Number of Random Seeds 16

Number of Results to Display 16

Select the appropriate PPI graph, and use “Greedy ISA” as the search type. Greedy ISA is the most thorough, examining every neighboring node to determine the best one to include in the expanding complex.

Using all nodes as starting seeds allows the program to exhaust the search space by expanding from every node possible.

6. Specify scoring parameters

Scoring Complexes

☐ Score with edge information (no learning)

☐ Train a Bayesian template to score complexes

☐ Provide a trained Bayesian model to score complexes

Minimum Complex Score 0

We’ll demonstrate the app using the ‘Weight’ Bayesian template. Selecting the second option: **‘Train a Bayesian template to score complexes’**, will allow the following additional parameters to appear:

☒ Train a Bayesian template to score complexes

Training the Bayesian Network

Select a Training Option:

☐ Train the built-in template

☐ Train a custom template

> Advanced Training Parameters

☐ Provide a trained Bayesian model to score complexes

Minimum Complex Score: 0

Then, clicking the second option under ‘Training the Bayesian Network’, ‘**Train a custom template**’, will allow you to specify which template you would like to use, as well as load the positive training file, **training.tab**

Training the Bayesian Network

Select a Training Option:

☐ Train the built-in template

☒ Train a custom template

Select Template: Weight

training.tab Training File (.tab, .tsv)

> Advanced Training Parameters

Click the ‘Advanced Training Parameters’ to ensure that the Cluster Prior is set to 0.5 (prior probability that a cluster is a true complex). For better results, increase the number of negative examples that are randomly generated to 20.

> Advanced Training Parameters

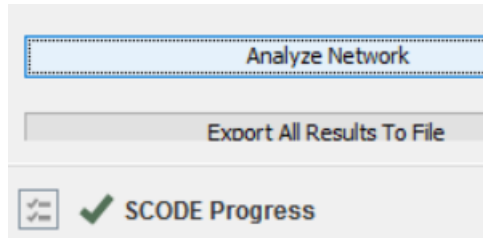
Cluster Probability Prior: 0.5

Generate # of Negative Examples: 20

Ignore Missing Nodes: ☒

7. Analyze Network

Click ‘**Analyze Network**’ to begin the training and search procedures. A progress bar may appear, depending on how quickly training and search are performed. When complete, a checkbox will briefly appear in the lower left corner of the window

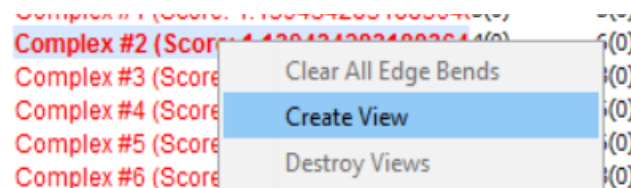


The list of discovered complexes will appear in the left control panel under the ‘Network’ Tab, along with the trained Bayesian network, which will be titled **Supervised Complex Model**

Network	Nodes	Edges
Templates		
Weight	2(2)	1(1)
Density	2(0)	1(0)
Built-in	26(0)	25(0)
PPI Graph		
graph	16(0)	36(0)
Complex #1 (Score: 1.139434283188364)	3(0)	3(0)
Complex #2 (Score: 1.139434283188364)	4(0)	6(0)
Complex #3 (Score: 1.139434283188364)	3(0)	3(0)
Complex #4 (Score: 1.139434283188364)	4(0)	6(0)
Complex #5 (Score: 1.139434283188364)	4(0)	6(0)
Complex #6 (Score: 1.139434283188364)	3(0)	3(0)
Complex #7 (Score: 1.139434283188364)	4(0)	6(0)
Complex #8 (Score: 1.139434283188364)	4(0)	6(0)
Complex #9 (Score: 1.139434283188364)	4(0)	6(0)
Supervised Complex Model		
Supervised Complex Model	10(0)	8(0)

Depending on the template used and based upon the training examples, we would expect returned complexes to feature either highly dense complexes or complexes featuring edges of value 0.8.

To examine each of the returned results, right click on the complex title and select **Create View**



The returned complexes should feature some of those provided as training in the positive complex file, as well as new complexes, such as:

