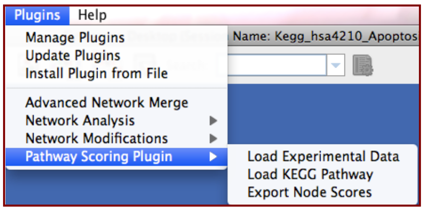
Cytoscape Pathway Scoring Plugin

This document has three parts:

1- Installation
2- Pathway construction
    a. <u>Manuel pathway generation</u>
    b. <u>KEGG pathway upload</u>
3- Execution
    a. <u>Input data file formats</u>
    b. <u>Calculated data export</u>

1-INSTALLATION

-Download Cytoscape from http://www.cytoscape.org/download.html (version must be 2.7 or above.)
-Download and un-pack installation files which are provided as supplementary electronic file (*Cytoscape_plugin_Setup_files.zip*)
-Copy all files in the "setup-files" folder provided under your Cytoscape/plugin folder.
-Open Cytoscape program, **Pathway Scoring Plugin** appear under ***Plugins*** menu bar.



2-PATHWAY CONSTRUCTION

The algorithm requires a pathway already in Cytoscape.

a. Manuel pathway generation:

A pathway can be manually generated by using Cytoscape editor.
Pathway <u>should have</u> the following node and edge attributes (case sensitive), which are assigned with the editor by the user.

Node attributes:
ID : Cytoscape ID assigned automatically by Cytoscape
ENTREZ_ID : Entrez unique identifier (UID)
NAME : HUGO gene symbol
NODE_TYPE : gene, group, compound, map (final activity process).
TARGET_PROCESS : if the node is final activity process assign “yes”. The other node types will have “no” value.
SCORE : Calculated activity enrichment score of the node, initially it is set to zero.

The edge attributes:
ID : Cytoscape ID
weight : Calculated edge flow score, initially it is set to zero.
interaction : The type of interaction, it would have only two values: inhibition or activation.

b. KEGG pathway upload:

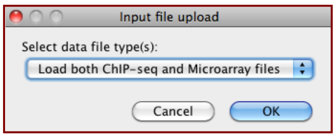
KEGG pathways can be uploaded from *Pathway Scoring Plug-in* menu using KEGG pathway identifier (e.g. path:hsa04210). The computer must be on-line for this operation, which may take some time since it uploads the pathway from KEGG database. Upon upload, be sure that all node and edge attributes are checked to be visible.
KEGG pathways may have orphan edges for some nodes user can link those nodes and assign their attributes.

3- EXECUTION

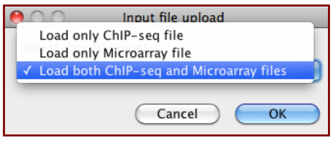
The score flow algorithm can be executed under *Pathway Scoring Plug-in* menu by loading experimental data.

Sample data and pathway execution:
-Open sample pathway named ***Akt_Pathway.cys*** using Cytoscape menu***.***
-Run the algorithm by clicking ***Load Experimental Data***.

-A dialog-box will appear for input files : ChIP-seq and/or microarray can be loaded.



Select data file type(s): Load both ChIP-seq and Microarray files



-Select the type of data to load and open sample data.
Be sure to provide the input score files in the correct format.

-Upon upload of data file the program executes automatically.

a. Input data file formats

The input file must contain tab-delimited 3 columns.
The first column indicates “Entrez UID” identifier corresponding to the ENTREZ_ID attribute of a node.
The second column indicates “HUGO gene name” corresponding to the NAME attribute of a node.
The third column is the floating-point input score of the gene/gene product, this number is the initial self score of each node.

Chip-seq input example:

```
18      ABAT    0.365495543
21      ABCA3   0.166754064
140     ADORA3  0.026743576
162     AP1B1   0.679077084
259     AMBP    0.704771893
```

In the current setup of algorithm, the input scores (i.e., the third column) of the ChIP-seq input file should be normalized between 0 and 1.
The most significant gene will have a score value, which is close to 0.

Microarray input example:

```
207     AKT1    8.95827657
471     ATIC    11.1768990
842     CASP9   5.58445703
1983    EIF5    9.85065037
9697    TRAM2   6.05300926
```

For the microarray score file, the input values must be log2 normalized gene expression value.

b. Calculated data export

The user can save the final activity scores of each node in a tab delimited text file under *Pathway Scoring Plug-in* menu by choosing “*Export Node Scores*”
A dialog-box will appear, provide a folder to save the output score files in tab-delimited text format.