

ZDOG: Zooming in on Dominating Genes with Mutations in Cancer Pathways

User manual v1.0.3

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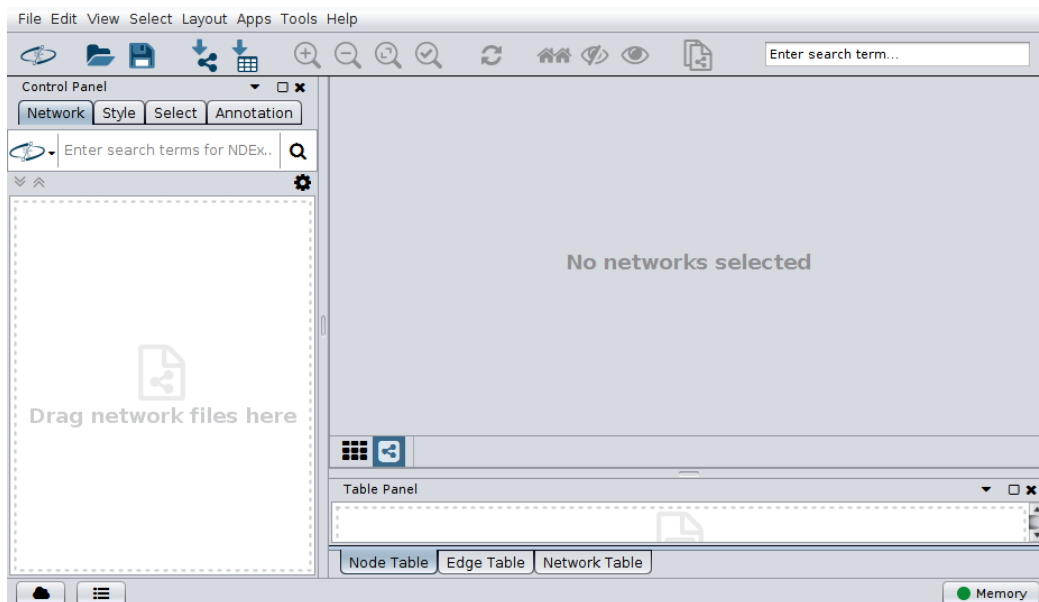
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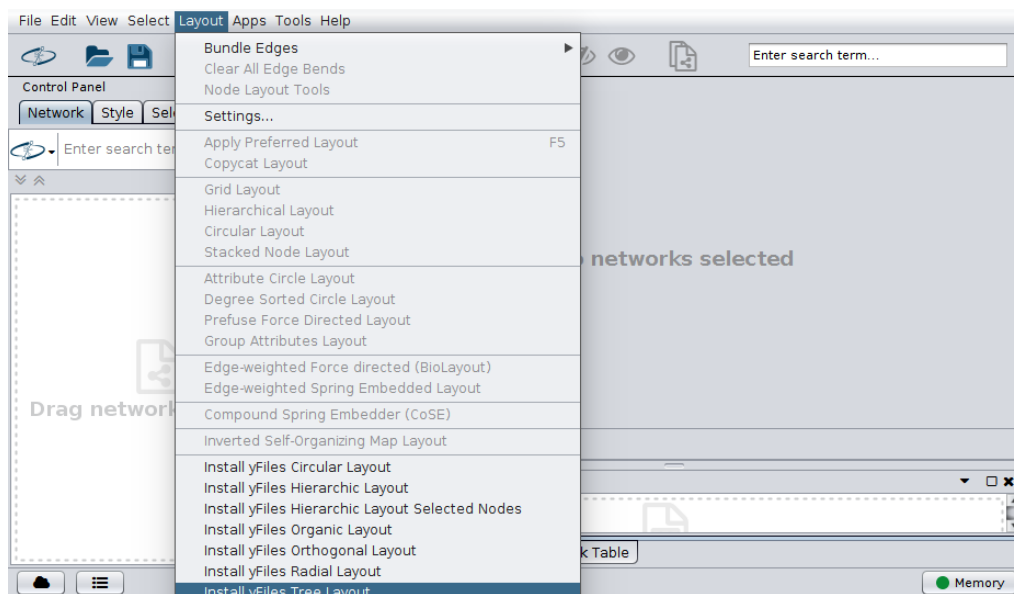
1 Cytoscape installation

ZDOG is an app developed for Cytoscape 3.7.1. ZDOG is known to run in Cytoscape versions 3.6.1 and 3.7.1. Cytoscape can be download from <http://www.cytoscape.org>. The interface of the program looks like this:

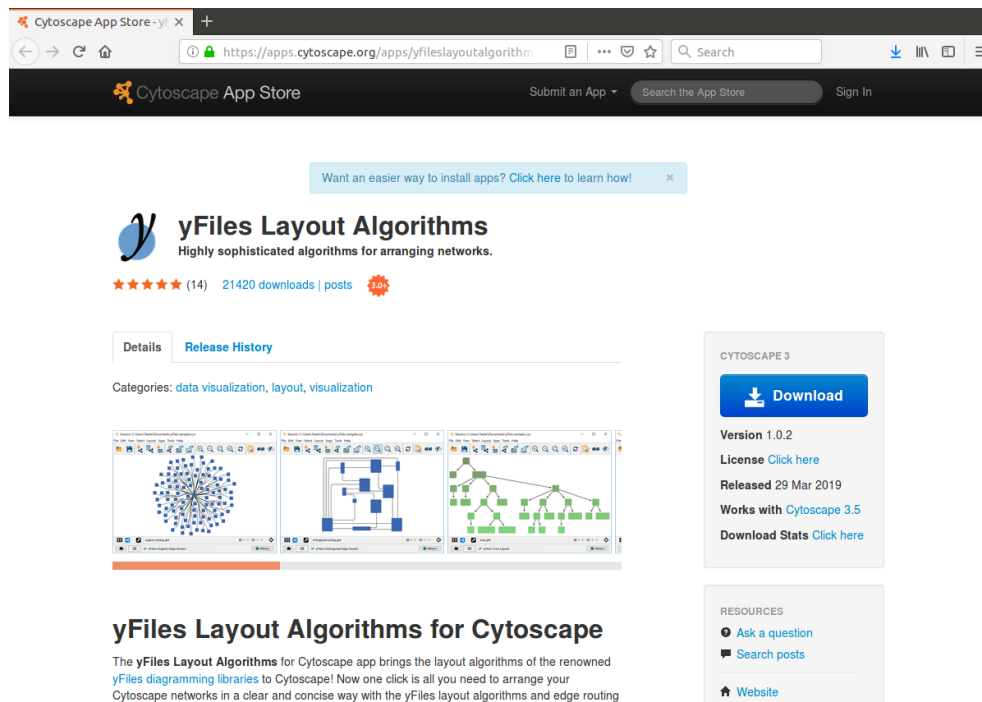


2 yFiles Tree Layout and KEGGscape installation

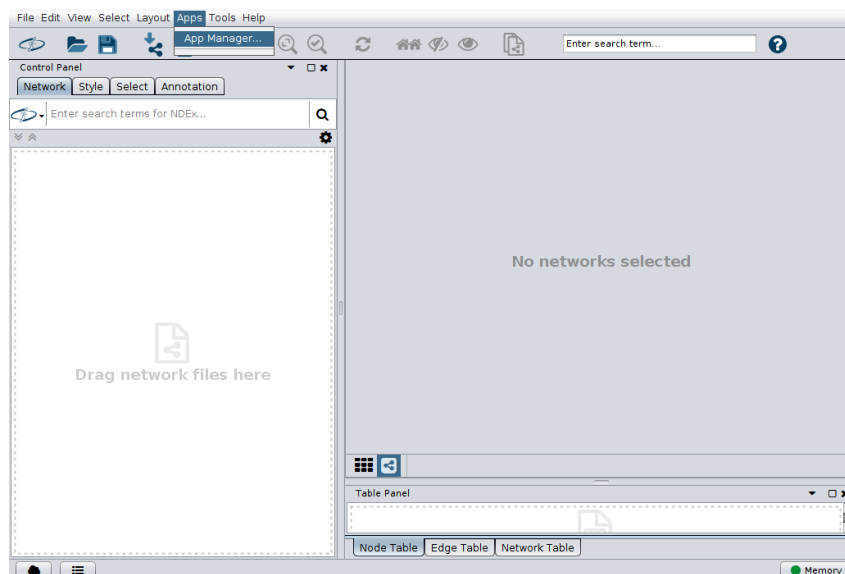
ZDOG makes use of yFiles Tree Layout and of KEGGscape. To install yFiles Tree Layout in Cytoscape, click on the “Layout” menu and then on “Install yFiles Tree Layout...”.



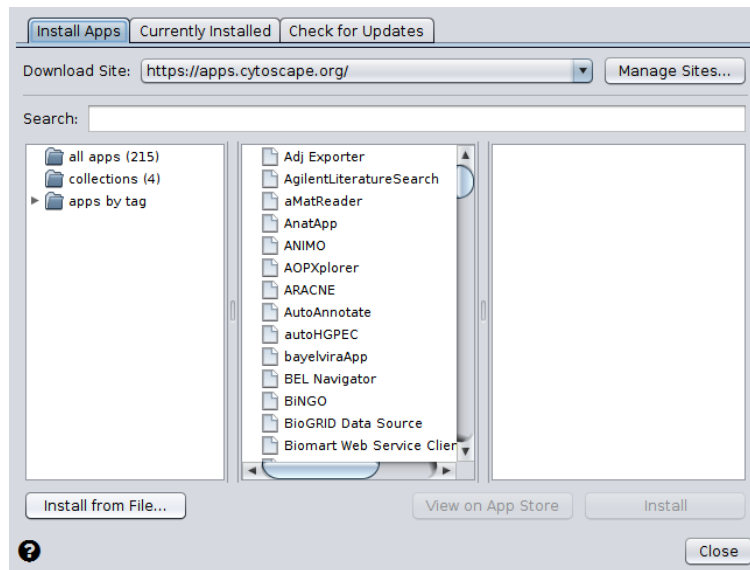
An internet browser such as Internet Explorer or Firefox will automatically open with the following webpage. On this webpage, click on the Download button on the right.



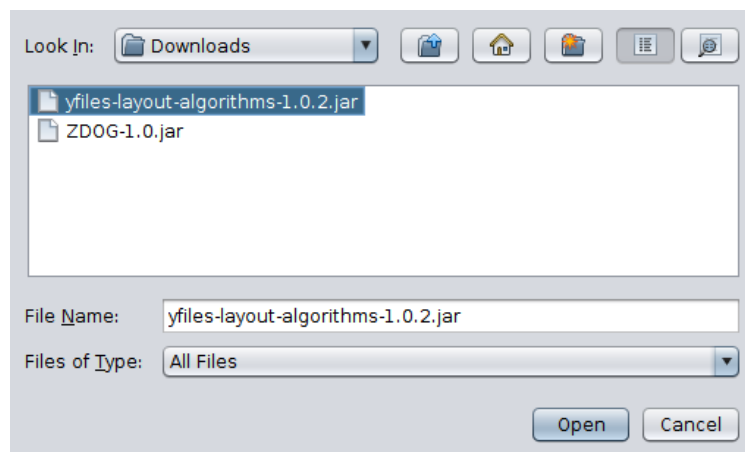
A file called yfiles-layout-algorithms.jar is now in your Downloads folder. Install this file in Cytoscape by clicking Apps – App Manager..



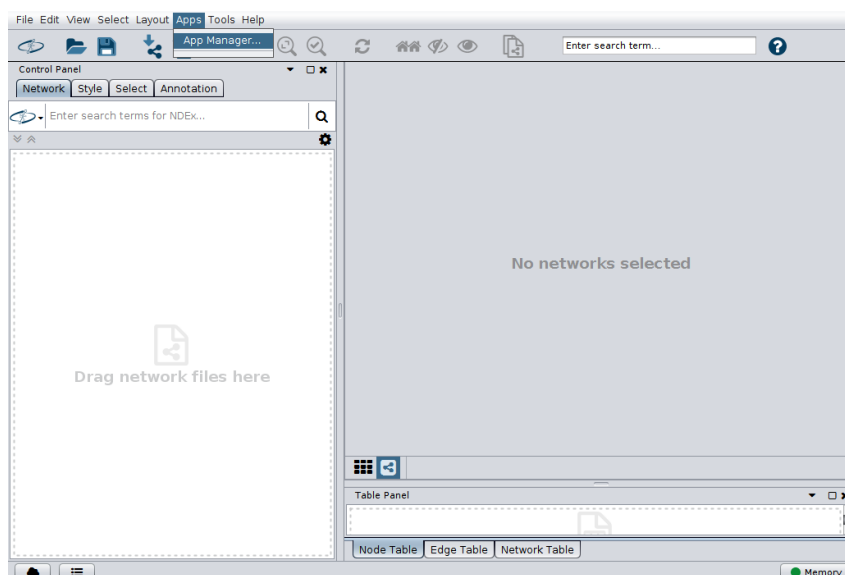
Click on the “Install from File...” button in the left bottom corner.



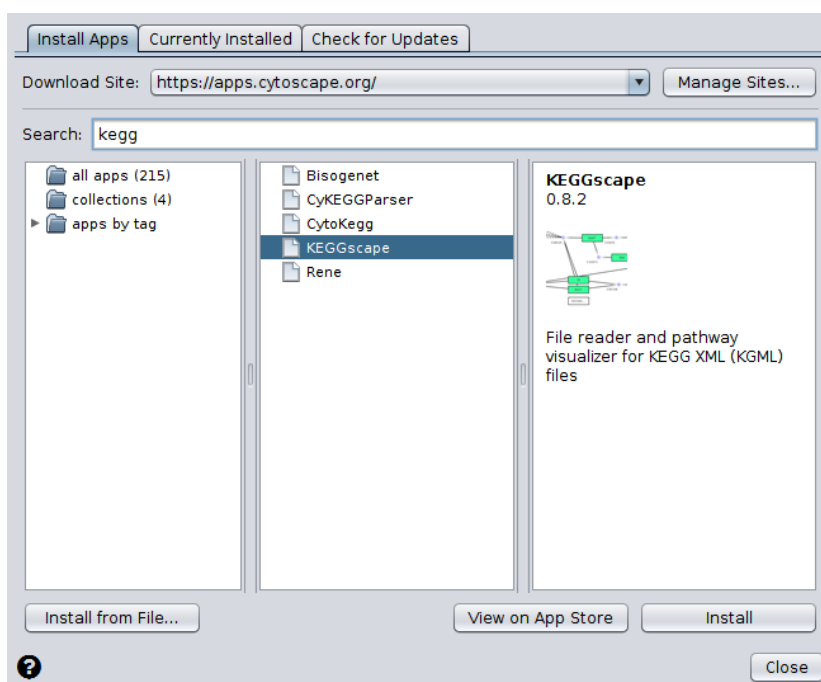
Select the file yfiles-layout-algorithms-version.jar and click “Open”. After installation click Close.



To install KEGGscape, open the App manager in Cytoscape.



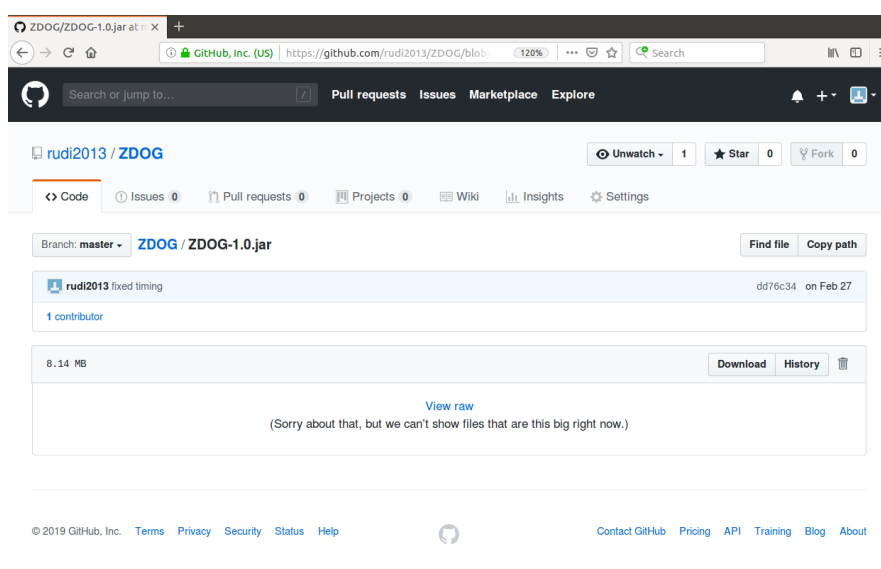
Next, search for kegg, select KEGGscape and click Install and after installation click close to close the App Manager.



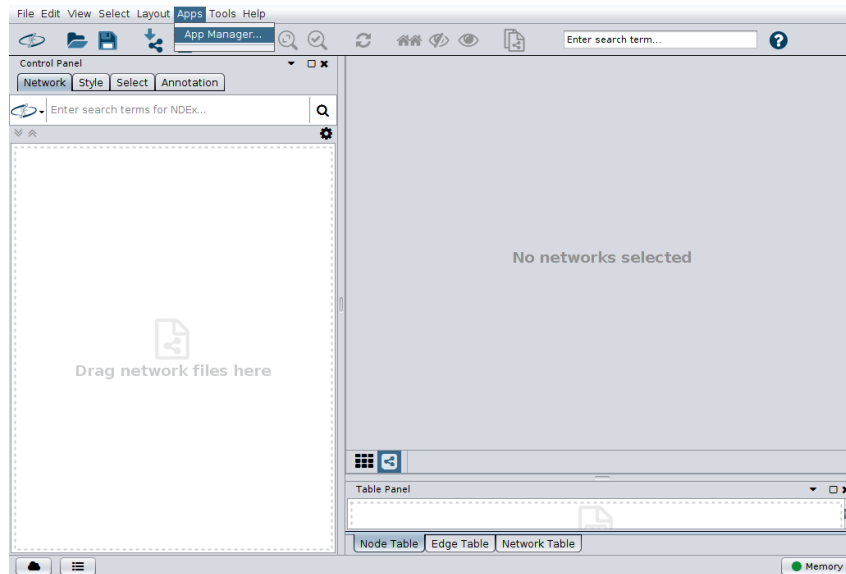
3 ZDOG installation

Install ZDOG by downloading the file ZDOG-1.0.jar from GitHub.

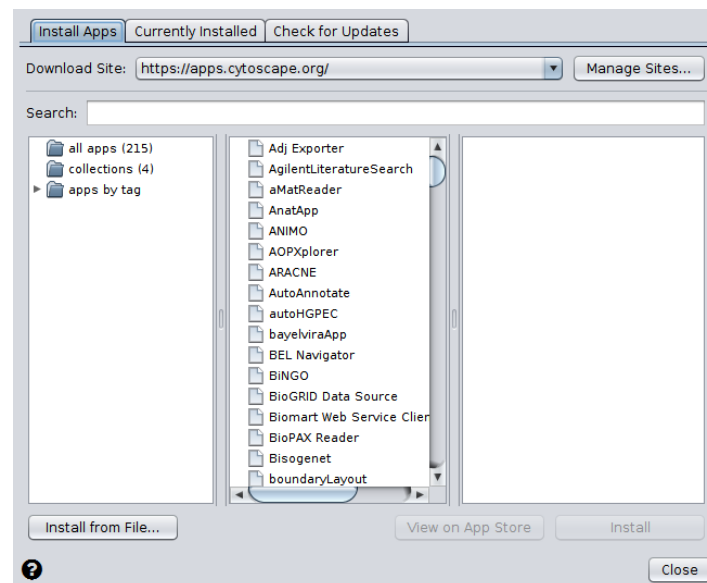
Go to the following page: <https://github.com/rudi2013/ZDOG/blob/master/ZDOG-1.0.jar> and click the “Download” button on the website.



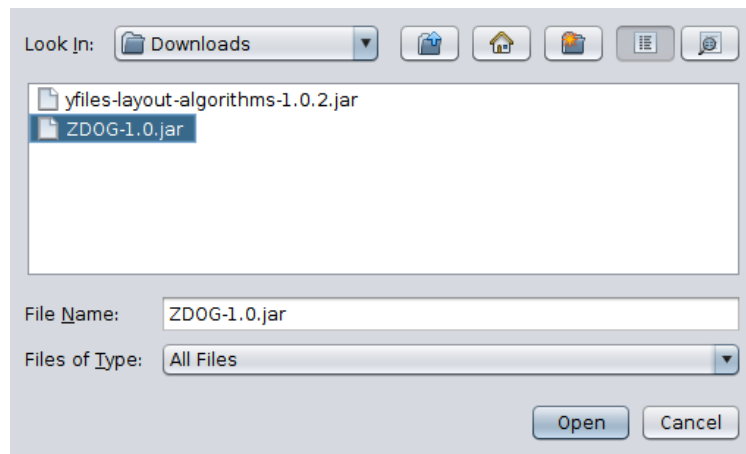
Next, start Cytoscape and install ZDOG by clicking Apps – App Manager...



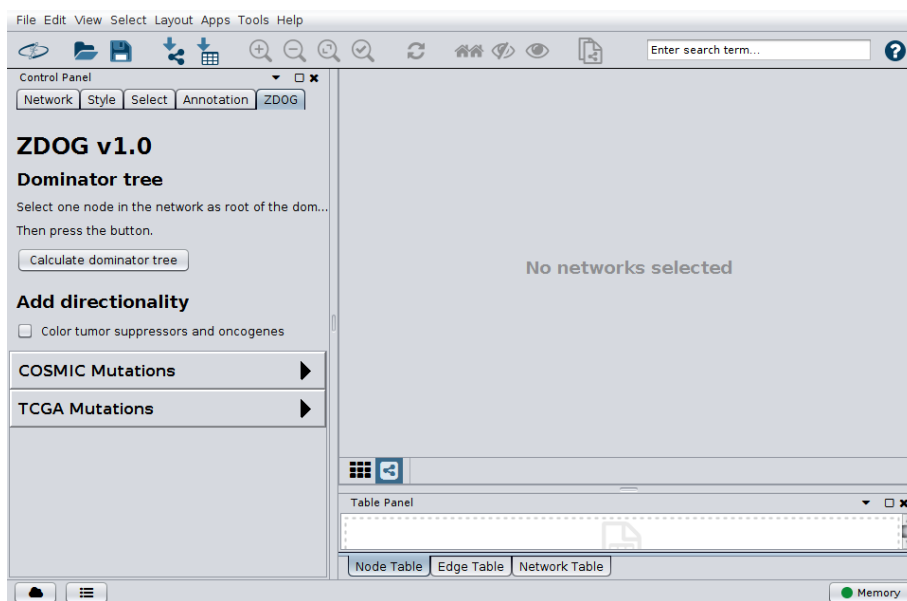
Under the tab “Install Apps”, click the button “Install from File...”.



Browse to the downloaded ZDOG-1.0.jar file and click “Open” to install the app.



Once installed, the ZDOG menu is added to the Control Panel in Cytoscape on the left.

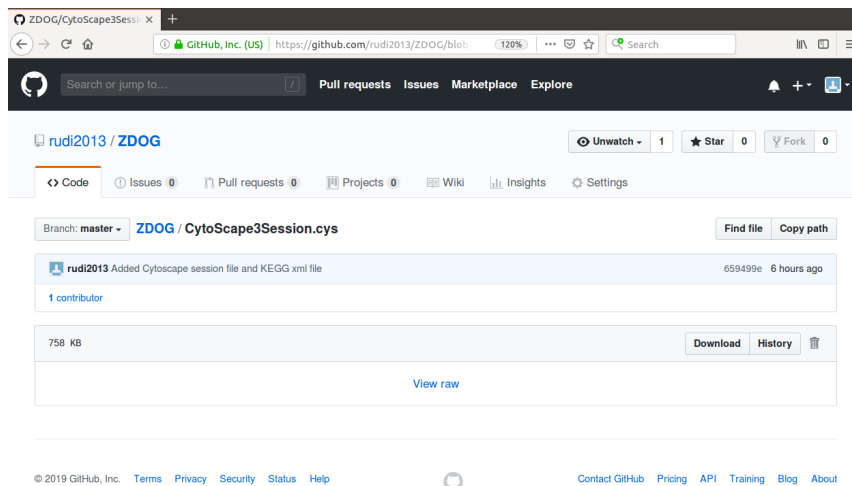


3 Loading the PI3K-Akt pathway

The PI3K-Akt pathway that we used in the paper can be downloaded as a Cytoscape 3 session file from GitHub and then opened in Cytoscape. Please browse here:

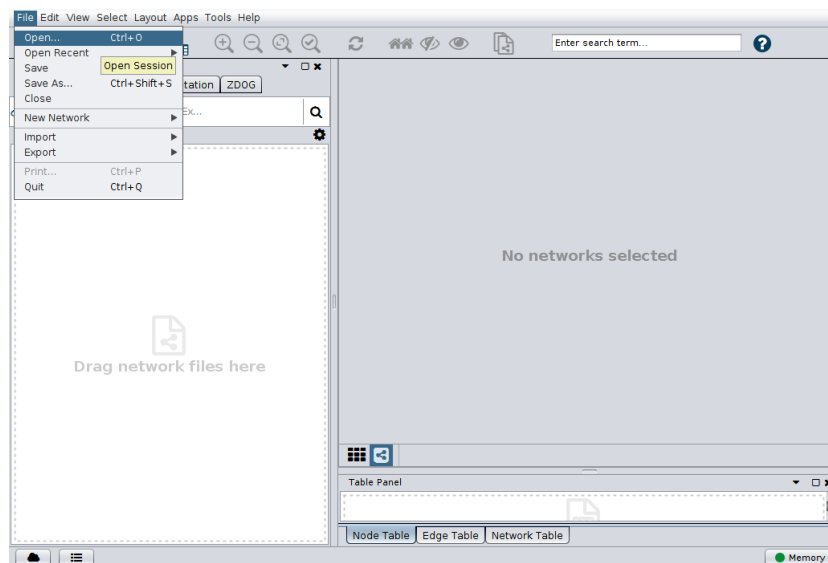
<http://github.com/rudi2013/ZDOG/blob/master/CytoScape3Session.cys>

and click the “Download” button on the website.

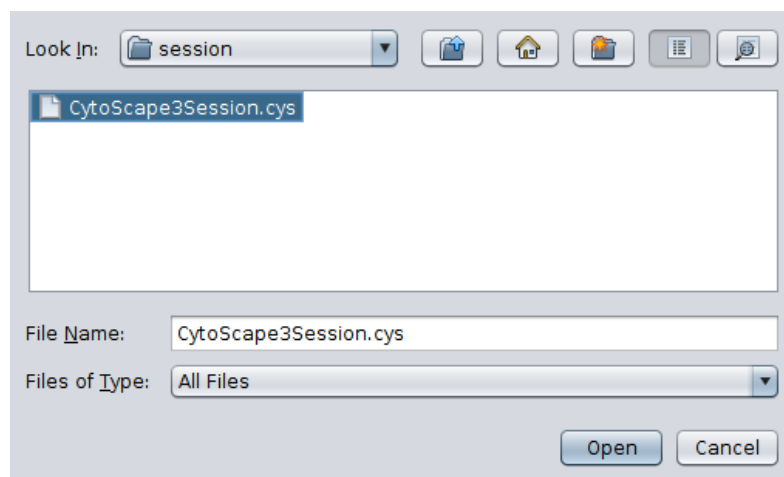


Alternatively, one can visit <https://github.com/rudi2013/ZDOG> and search the CytoScape3Session.cys file in the list. Click with the right mouse button on the file and choose “Save link as” to save the file to your computer.

Once the session file is downloaded, please start Cytoscape and click File – Open..



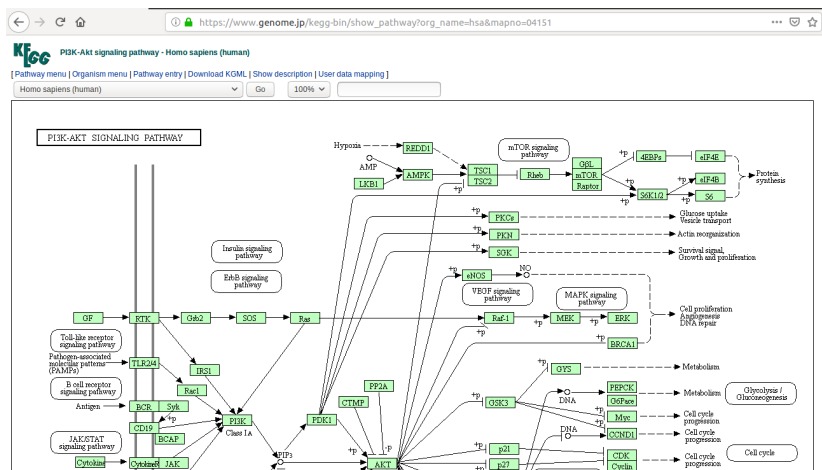
Then Browse to the CytoScape3Session.cys file, select it and click “Open”.



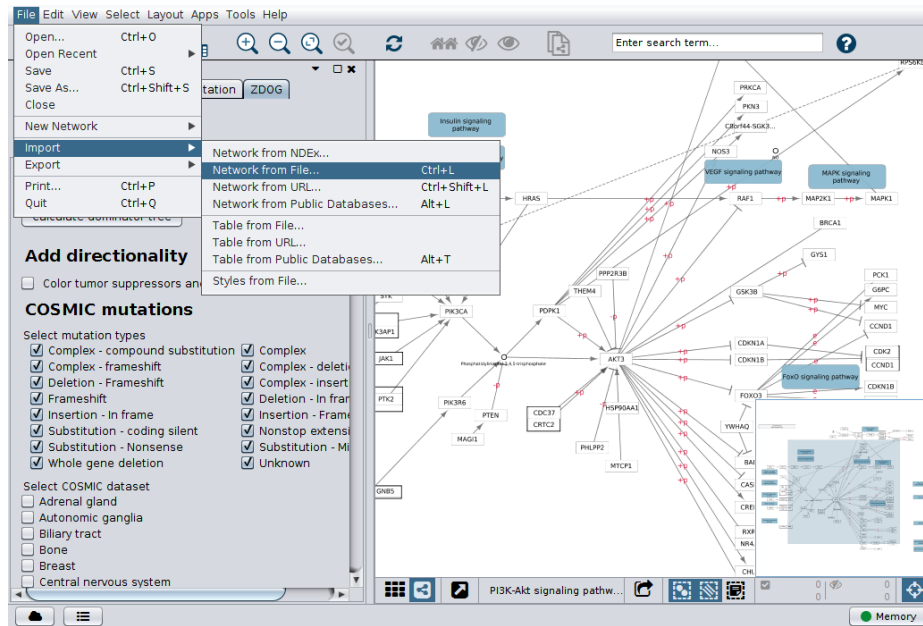
4 Loading other pathway files

Pathway files can also be downloaded from the KEGG website. One can browse online to a KEGG PATHWAY and download the KGML file by clicking “Download KGML” above the pathway. For example, the homo sapiens PI3K/AKT pathway can be downloaded here:

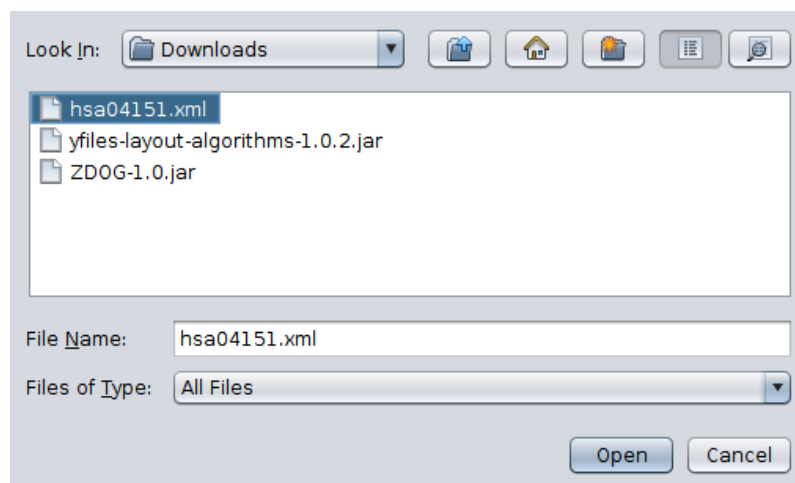
https://www.genome.jp/kegg-bin/show_pathway?org_name=hsa&mapno=04151



In Cytoscape, load the pathway by clicking File – Import – Network – File...



Browse to the downloaded KGML file (with extension .xml) and open it.



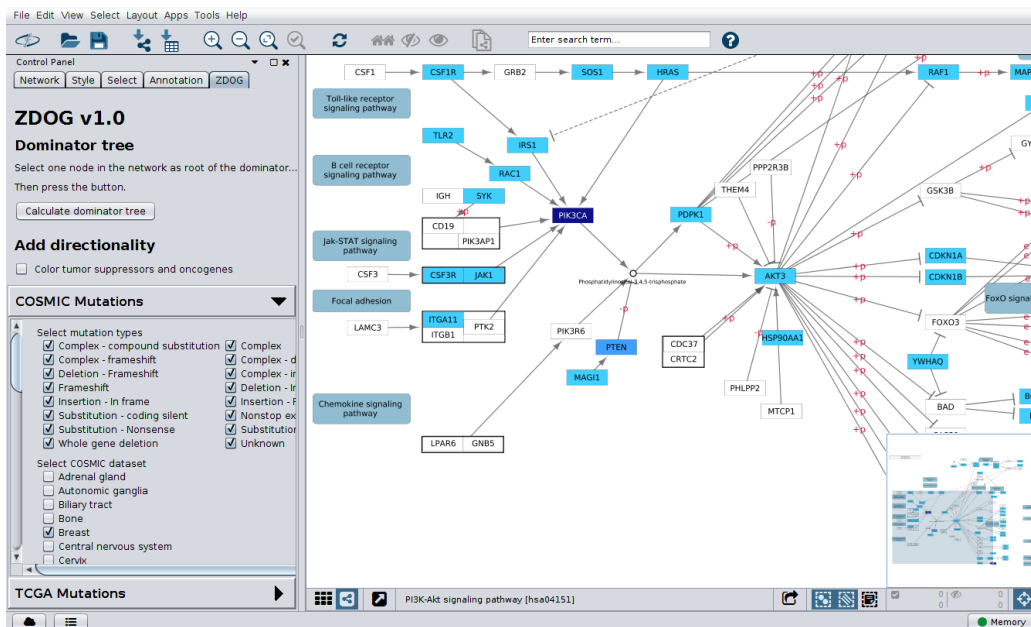
The original KEGG PI3K-Akt pathway file can also be found on the ZDOG GitHub page:

This is the GitHub page: <https://github.com/rudi2013/ZDOG>

This is the file: https://github.com/rudi2013/ZDOG/KEGG_PI3K_Akt_pathway.xml

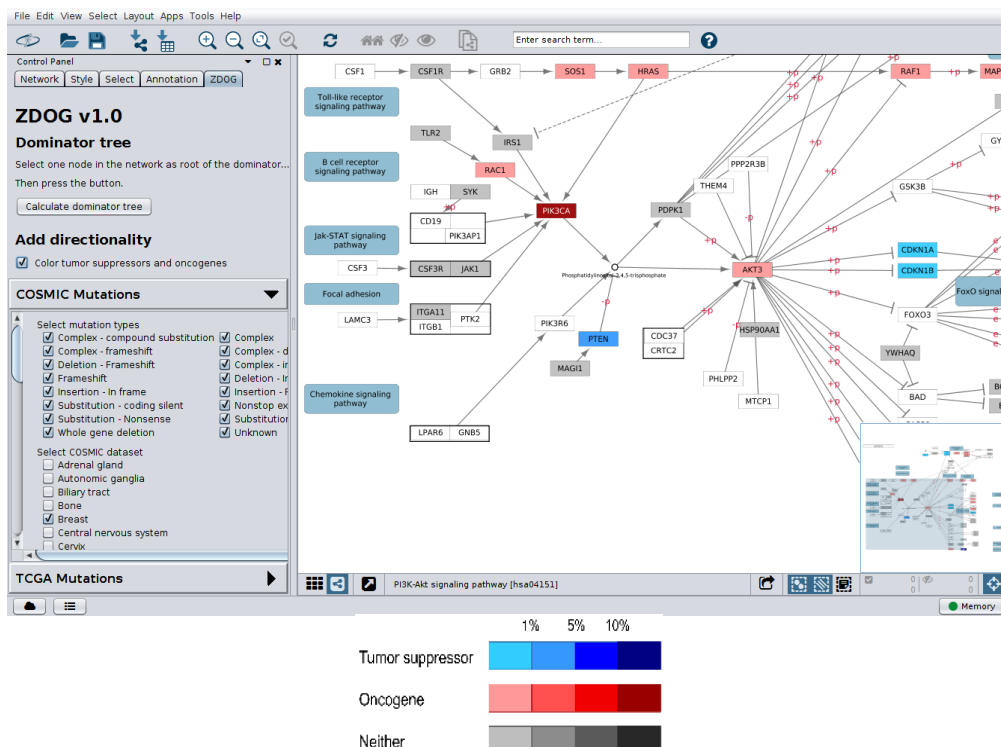
5 Colouring mutations in COSMIC

Under “COSMIC mutations” in ZDOG, select the wished mutation types and also one or several COSMIC datasets. Average mutation frequencies per gene will be instantly coloured on the pathway. All genes with mutations are coloured blue. Shades of blue indicate mutation frequency.



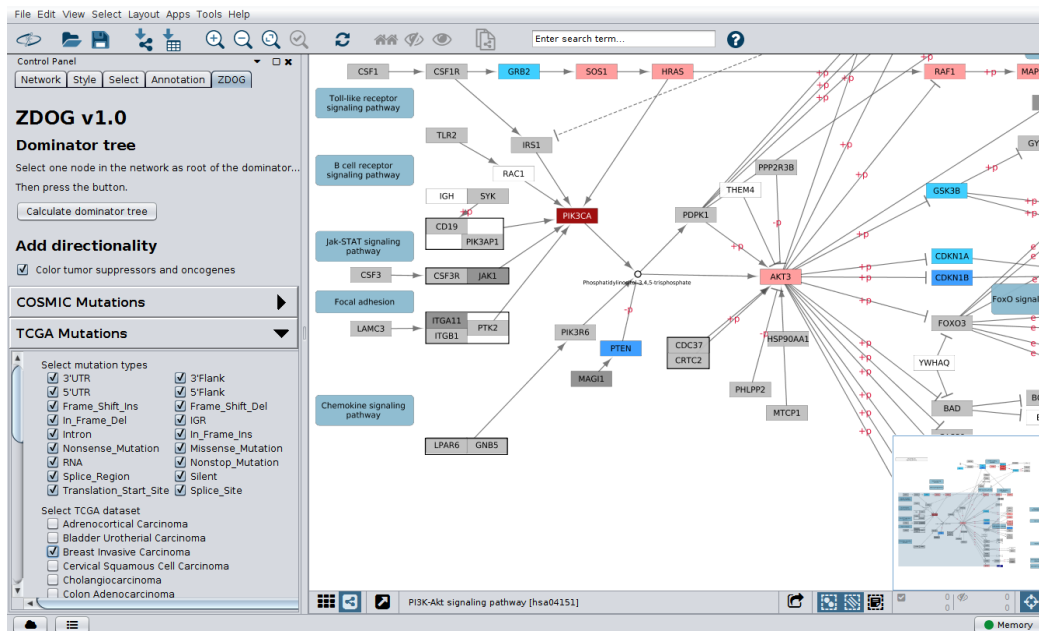
6 Discriminating oncogenes and tumor suppressors

Toggling the checkbox under “Add directionality” in ZDOG will colour oncogenes red and tumor suppressors blue and other genes grey.



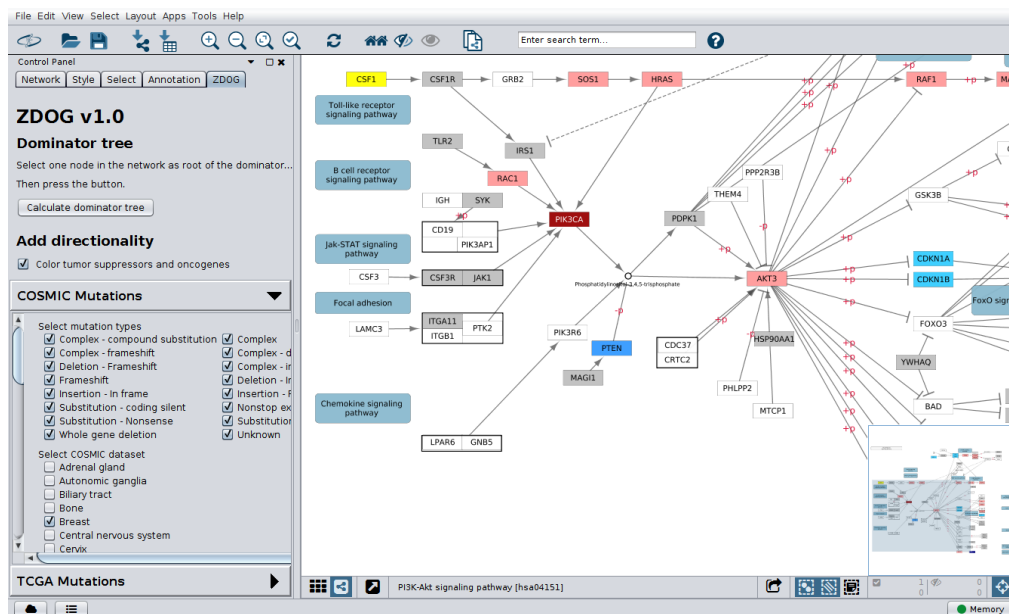
7 Colouring mutations in TCGA

Scroll down the scroll bar on the right of the graphical user interface of ZDOG until “TCGA mutations”. Here, mutation types and TCGA datasets can be selected in the same fashion as above.



8 Dominator tree calculation

Select one and only one node in the loaded pathway. Here we selected “CSF1”.



Click the “Calculate dominator tree” button to start the calculation. The tree will be presented in a new network window in Cytoscape (partially displayed).

