

***ZDOG: a Cytoscape app for zooming in on dominating mutated genes in cancer pathways***

User manual

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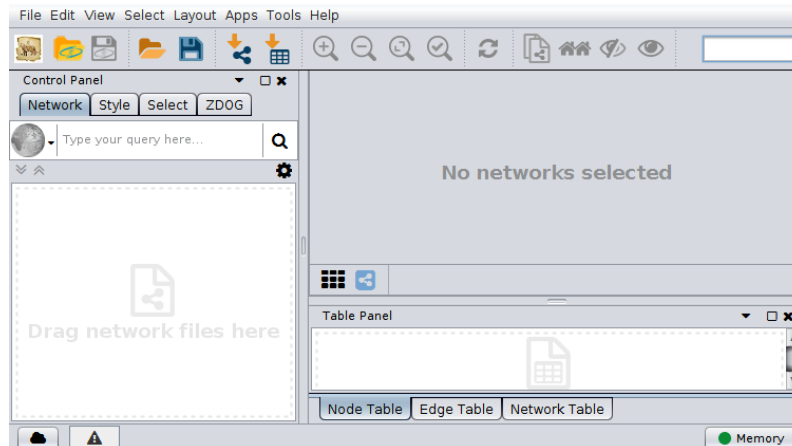
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## Cytoscape installation

ZDOG is an app running in Cytoscape. ZDOG is known to run in Cytoscape versions 3.0.1, 3.6.1 and 3.7.1. Probably it runs in many other versions  $\geq 3.0.0$ .

To install Cytoscape, download it from <http://www.cytoscape.org>, install it and start it. The program looks like this:



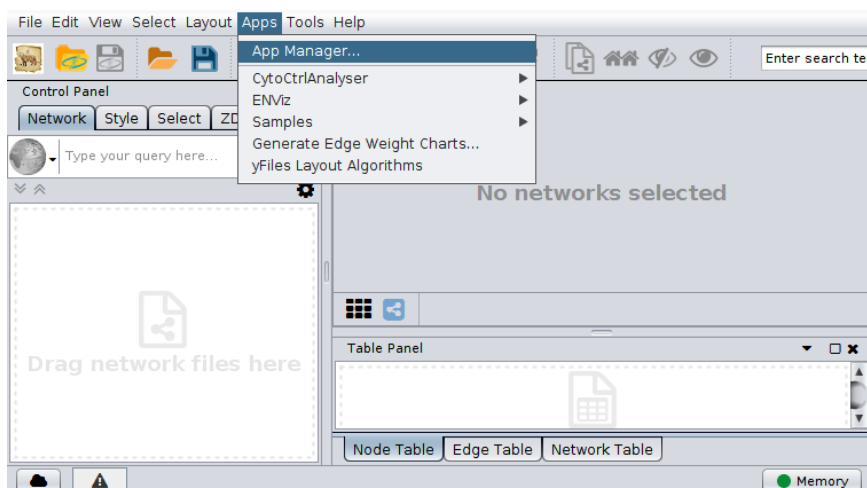
## ZDOG installation

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

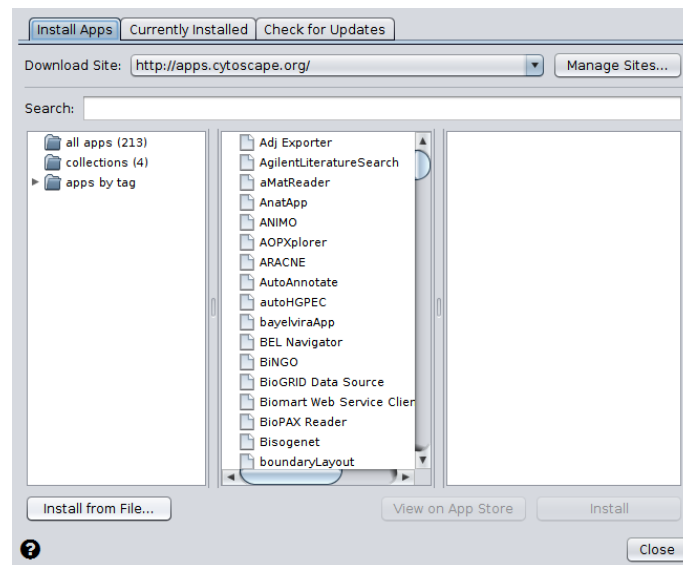
This is the Github page: <http://github.com/rudi2013/ZDOG>

This is a direct link to the jar file: <http://github.com/rudi2013/ZDOG/ZDOG-1.0.jar>

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

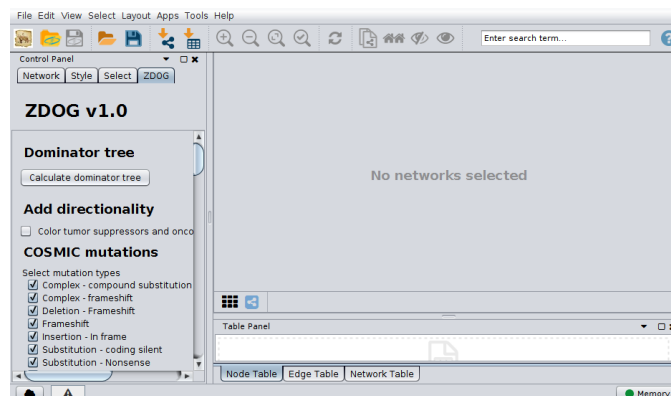


Under the tab “Install Apps”, click “Install from File...”



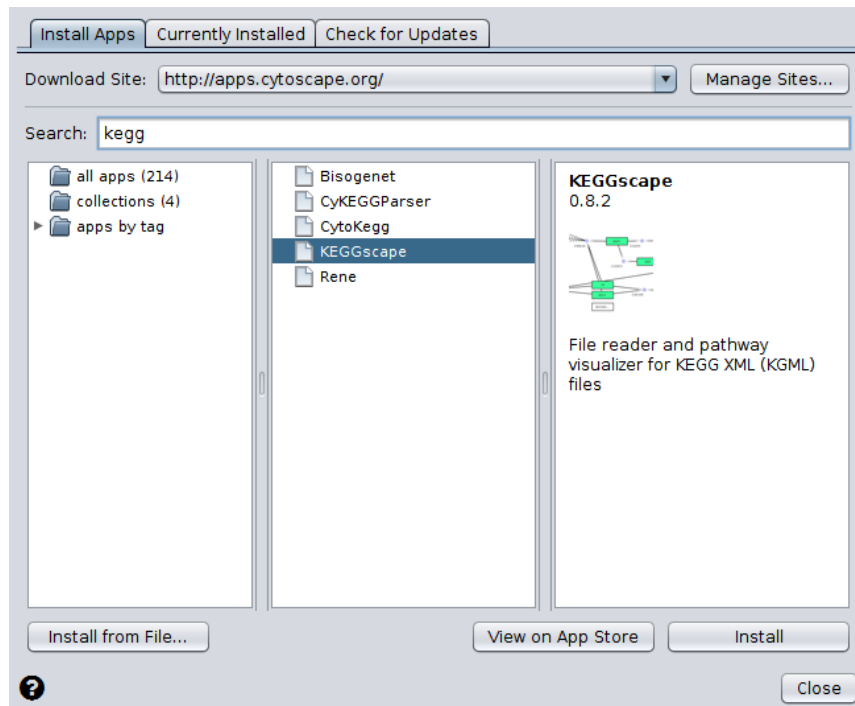
Browse to the downloaded ZDOG-1.0.jar file, select it and click “Open”.

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



ZDOG uses the yFiles tree layout in Cytoscape. Install the yFiles layouts by clicking Layout – Install yFiles layout algorithms and click the Install button in the internet browser window that opens.

To load a pathway, please use the KEGGscape app. To install KEGGscape, open the App manager in Cytoscape, search for kegg, select KEGGscape and click Install and after installation click close.



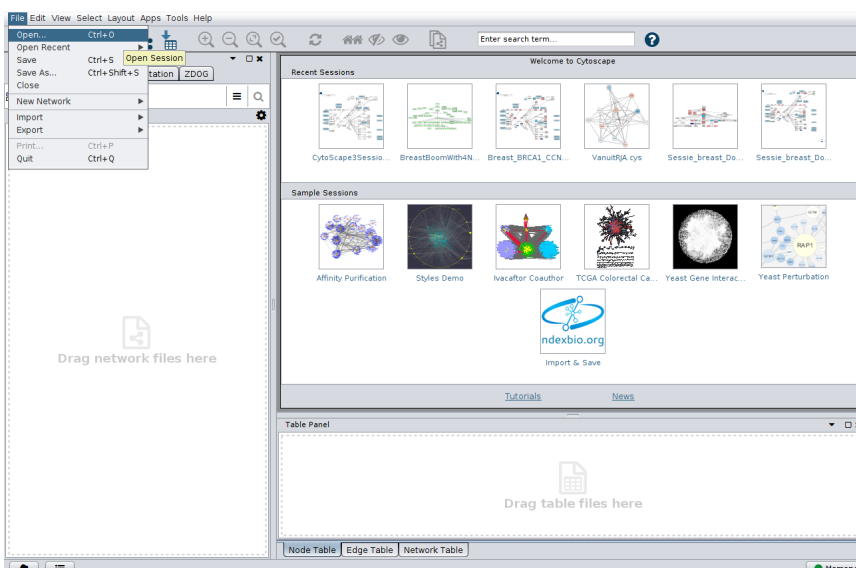
## Loading the PI3K-Akt pathway

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.

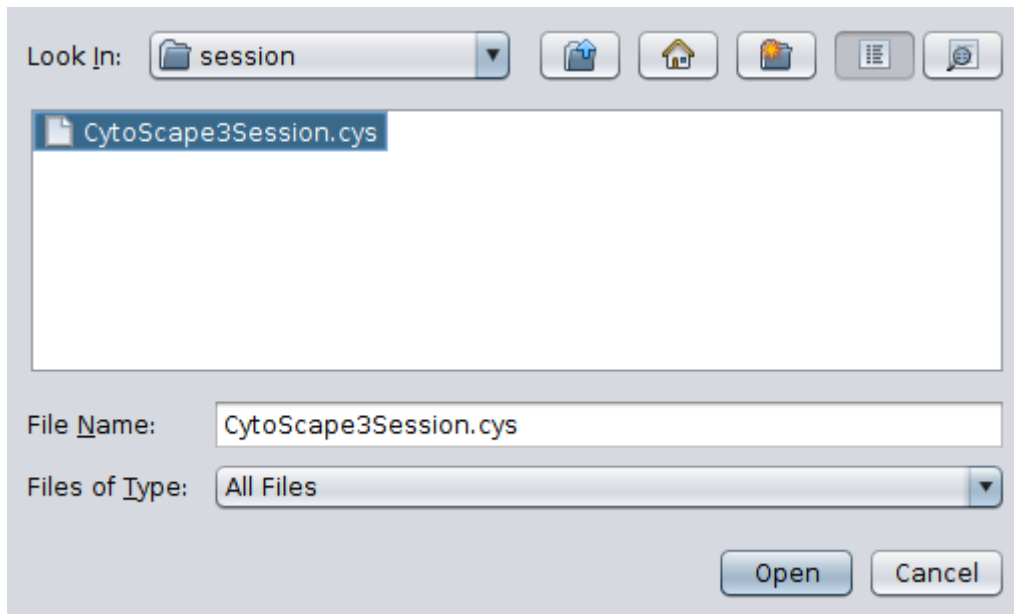
This is the Github page: <http://github.com/rudi2013/ZDOG>

This is a direct link to the session file: <http://github.com/rudi2013/ZDOG/CytoScape3Session.cys>

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

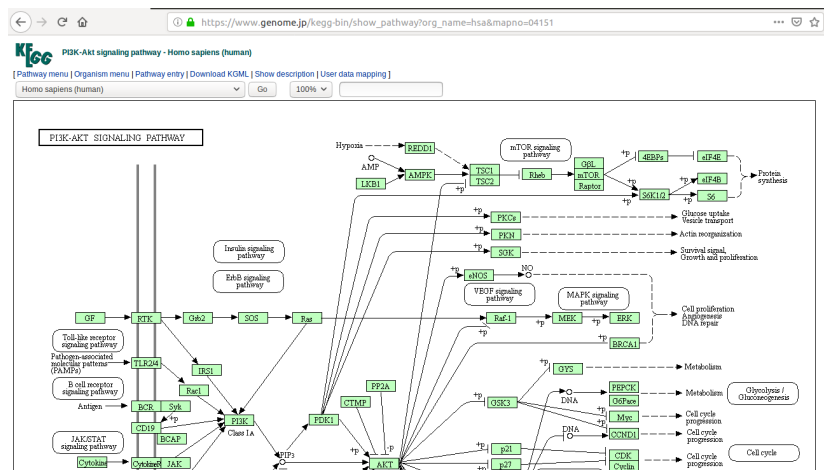


Then Browse to the CytoScape3Session.cys file, select it and click Open.

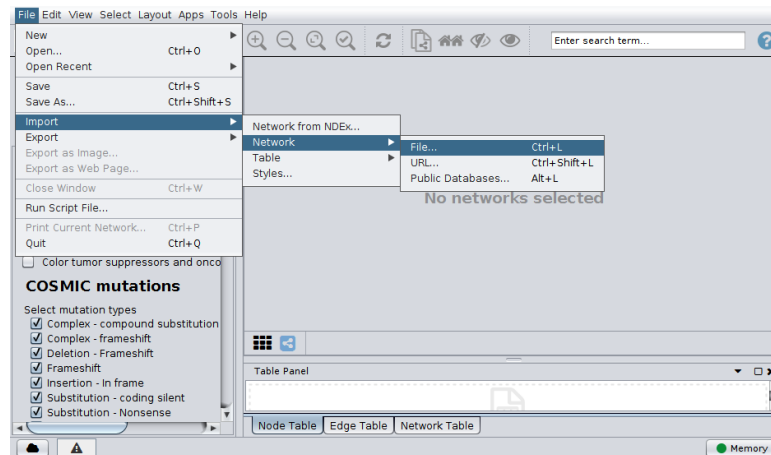


## Loading other pathway files

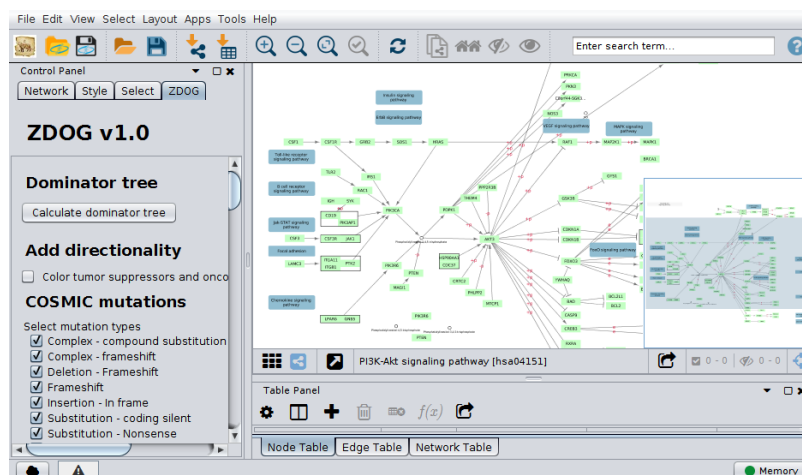
Pathway files can also be downloaded from KEGG. Browse online to a KEGG PATHWAY and download the KGML file by clicking “Download KGML” above the pathway. For example, the homo sapiens PI3K/AKT pathway can be downloaded here: [https://www.genome.jp/kegg-bin/show\\_pathway?org\\_name=hsa&mapno=04151](https://www.genome.jp/kegg-bin/show_pathway?org_name=hsa&mapno=04151)



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



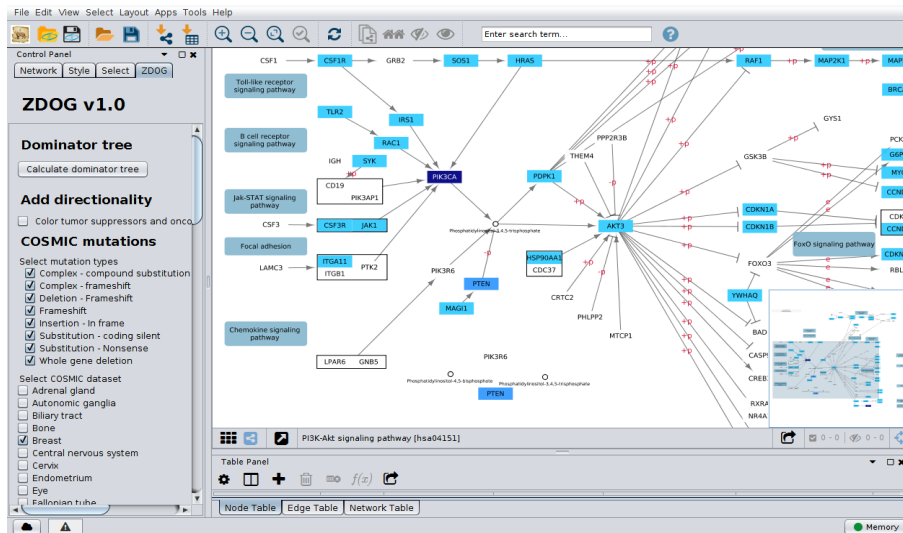
Browse to the downloaded KGML file (with extension .xml) and open it.



The original KEGG PI3K Akt pathway file can also be found on the ZDOG Github page:  
This is the Github page: <http://github.com/rudi2013/ZDOG>  
This is the file: [http://github.com/rudi2013/ZDOG/KEGG\\_PI3K\\_Akt\\_pathway.xml](http://github.com/rudi2013/ZDOG/KEGG_PI3K_Akt_pathway.xml)

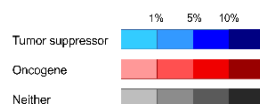
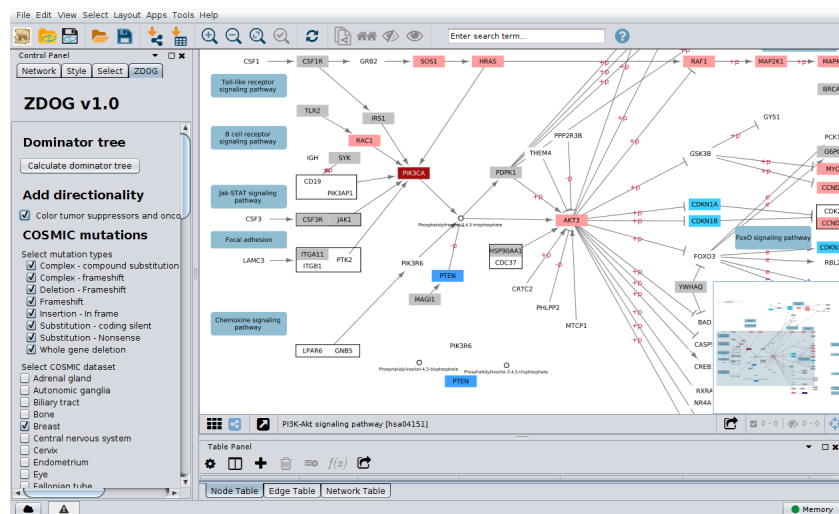
## Colouring mutations in COSMIC

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.



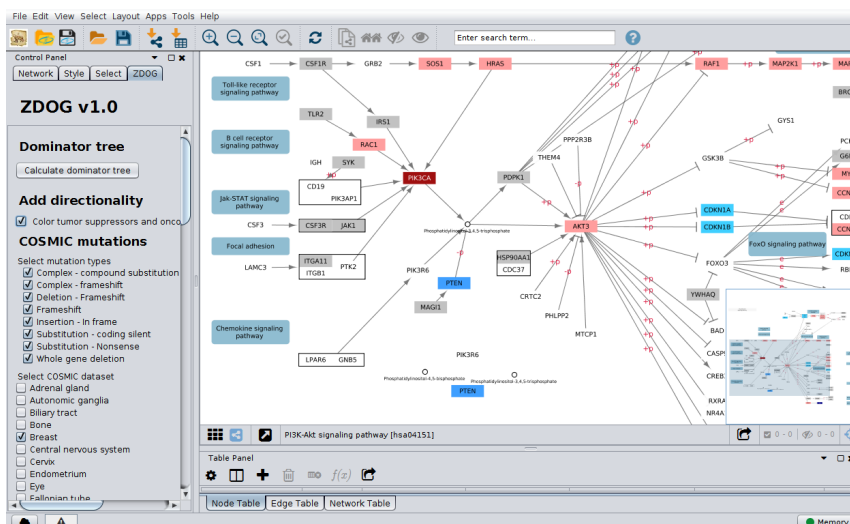
## Discriminating oncogenes and tumor suppressors

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



## Colouring mutations in TCGA

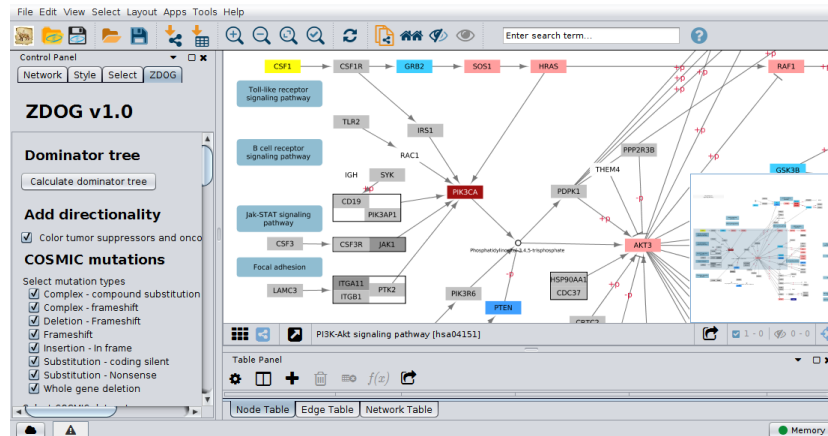
Scroll down the scroll bar on the right of the graphical user interface of ZDOG until “TCGA mutations”. Here, mutation types and TCGA datasets can be selected in the same fashion as above.





## 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).

