Manual for DAVID and STRING network analysis via Matlab.

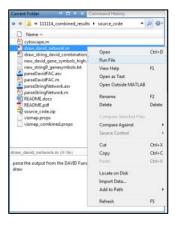
The published code should contain the following files

draw_david_network.m	Sup. Figure 1: Matlab script that parses a DAVID functional annotation clustering file and displays it in Cytoscape
draw_string_david_combination_network.m	Main Figure 1B: Matlab script that parses both a DAVID function annotation clustering file and a STRING network file, merges them as network and displays the result in Cytoscape
new_david_gene_symbols_high.txt	Example DAVID functional annotation clustering file (tab separated txt file, downloaded from http://david.abcc.ncifcrf.gov/summary.jsp)
new_string9_genesymbols.txt	Example STRING network file (tab separated txt file, downloaded from http://string-db.org/)
cytoscape.m	Matlab function that locates your cytoscape executable, and imports a network and its attributes from Matlab into Cytoscape.
parseDavidFAC.m	Matlab function to read in downloaded DAVID Functional Annotation Clustering files.
parseStringNetwork.m	Matlab function to read in a downloaded STRING 9 network file.
vizmap.props	Cytoscape vizualisation properties file for "draw_david_network.m" demo.
vizmap_combined.props	Cytoscape vizualisation properties file for "draw_string_david_combination_network.m" demo.

List of files included in the source code directory (excluding this readme file)

To run the code: demo mode

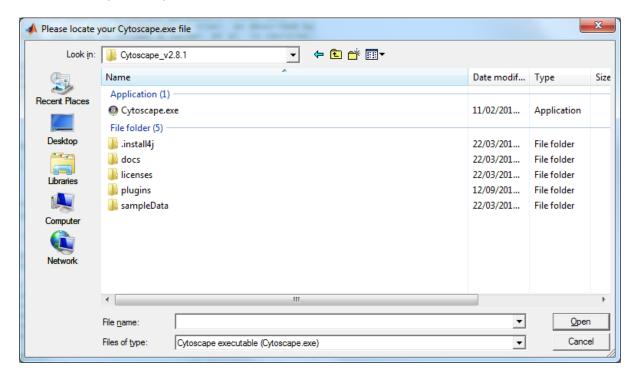
Using MATLAB (http://www.mathworks.ch/products/matlab/index.html), either run "draw_david_network.m" or "draw_string_david_combination_network.m". Running the code



in Matlab can be done for instance by changing the "Current Folder" from Matlab to the directory containing the downloaded published code, and then right-clicking either file in the "Current Folder" window and selecting "Run File" (see figure on the left). Alternatively, you can double click the .m files in Windows Explorer or Finder on Mac to open it in the Matlab editor, and run them by pressing F5 (on PCs) in the Matlab environment.

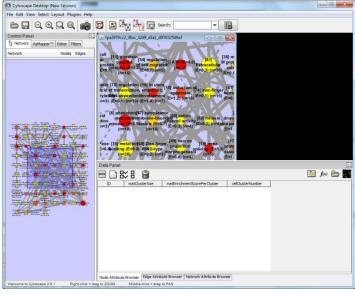
Make sure Matlab can see and write into the contents of the directory that contains the published code, by either adding it to your Matlab path or by changing the home directory to the directory containing the code.

The first time you run either of these scripts, you will (likely) be asked you to locate the Cytoscape executable on your computer:

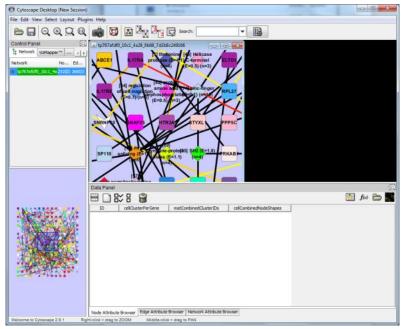


Cytoscape is a general tool for the visualization and manipulation of networks, and it's free. If you do not have it installed, you can go to http://www.cytoscape.org to install the latest version. On PCs the executable is the "Cytoscape.exe" file in the Cytoscape directory usually present in your Program Files directory, and on Macs it is "cytoscape.sh" in the Cytoscape directory in your Applications folder.

When the functions run successfully in demo mode, Cytoscape should start and you should see either of the following results:

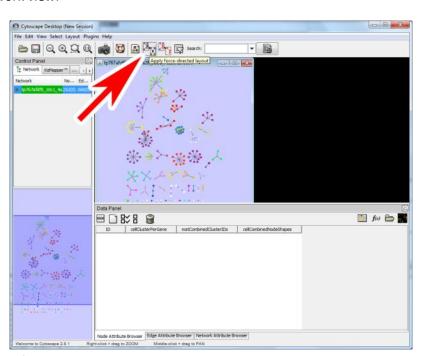


draw_david_network.m demo output



draw_string_david_combination_network.m demo output

Next, select the "Apply force-directed layout" button () within Cytoscape to get a nicer formatted network view:



Nicely formatted draw_string_david_combination_network.m demo output

See the Cytoscape help, manual and website (http://www.cytoscape.org) for further instructions on how to work with Cytoscape.

Note that minor differences between the manuscript figures (Mercer, Snijder, et al) and the demo figures generated by the Matlab code occur do to gene annotation mapping errors that were manually corrected for the manuscript.

To run the code with your own DAVID and STRING files

Open either script file in the Matlab editor and change the following lines in either "draw_david_network.m" or "draw_string_david_combination_network.m":

boolRunDemo = true;

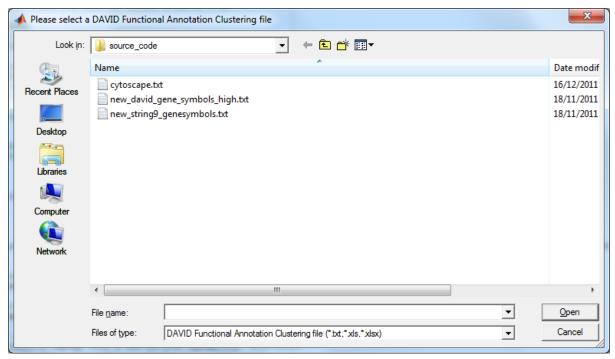
to

boolRunDemo = false;

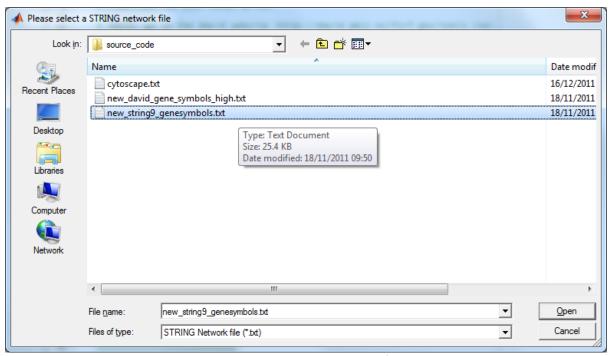
```
Editor - D:\VV_DG\11114_combined_results\source_code\draw_david_network.m
 🛅 🚰 💹 | 🔏 🖣 🖷 🦈 🤨 | 🚱 🔁 • | 🙌 🦛 🔷 🎉 | 💌 • 🗗 🛍 🖷 🛍 🖷 🛍 🕮 Stack: | Base 🗸 || 🎉
 × %, %, 0
                + ÷ 1.1
       % parse the output from the DAVID Functional Annotation Clustering and draw
       % it in a Cytoscape network.
      % see for DAVID: http://david.abcc.ncifcrf.gov/summary.jsp
      % see for CYTOSCAPE: http://www.cytoscape.org
      \% This is an example david file (passing gene symbols). If the file is not \% found, parseDavidFAC will ask the user to locate a valid file.
10
      11
      14
      % draw all overlap edges above the first threshold
15
       intPrimaryThreshold = 0.75;
16 -
17
       % and add the single highest edge for all unconnected nodes
       intSecondaryThreshold = 0.1;
19
       % wether to run demo mode, or ask the user to locate the files..
20
      boolRunDemo = true;
21 -
       % boolRunDemo = false;
22
```

Edit the .m files to switch demo mode off.

Running the code with "boolRunDemo = false" will result in the code asking you to locate your downloaded DAVID and / or STRING files, as shown in the figures below. See the manual further below for instructions on how to get DAVID and STRING files for your own data.



Select your DAVID functional annotation clustering file

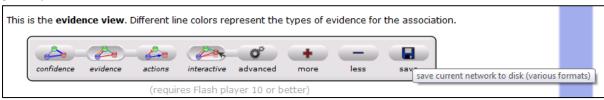


Select your STRING network file

How to obtain the STRING and DAVID input files

String (http://www.string-db.org) and DAVID (http://david.abcc.ncifcrf.gov/tools.jsp) are different web-services that analyse properties of genes and gene-lists. Both have their own manuals, which you can find on the websites. However, below is a short set of instructions aimed to get you started. Please use gene symbols in DAVID, as STRING returns the gene symbols for each mapped gene, which we use to connect the network. Note that mismatches can occur, and can be manually tweaked in the input files.

STRING: go to the String website (http://www.string-db.org), click multiple names, enter your list of gene symbols, click save (disk icon below network),



and save the "Text Summary (TXT - simple tab delimited flatfile)" on your local drive.



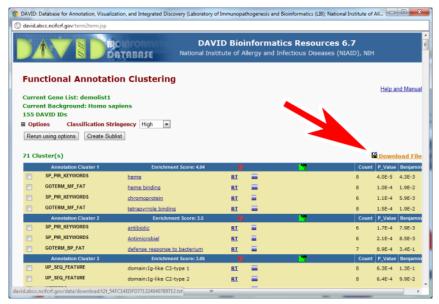
DAVID: go to the DAVID website (http://david.abcc.ncifcrf.gov/tools.jsp) (If you go to the DAVID



home page, click on the shortcut to "Functional Annotation"), select "upload" on the left panel, (step 1) paste your list of gene symbols into the field,

(step 2) select "official_gene_symbol" as gene identifier, (step 3) click on "gene list", and (step 4) submit list. On the left, be sure to select the correct species, and click the "Select Species" button. Next, click on the "functional annotation clustering" link, and click on the "functional annotation clustering" button. Set the classification

stringency to "high" and press "rerun using options". Now click the "Download File" link (see below), and save the file as text file to your local drive.



Download the DAVID Functional Annotation Clustering file as text file.