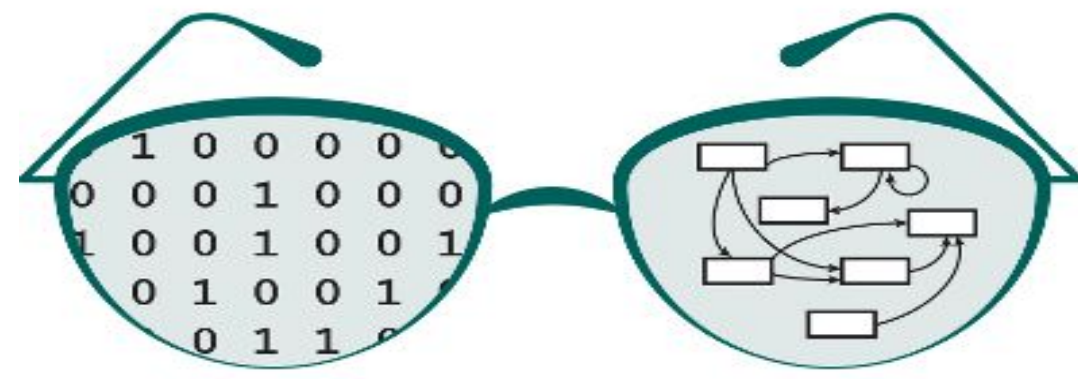


More Robust Testing of Data and UI for GRNsight: a Web Application for Visualizing Models of GRNs

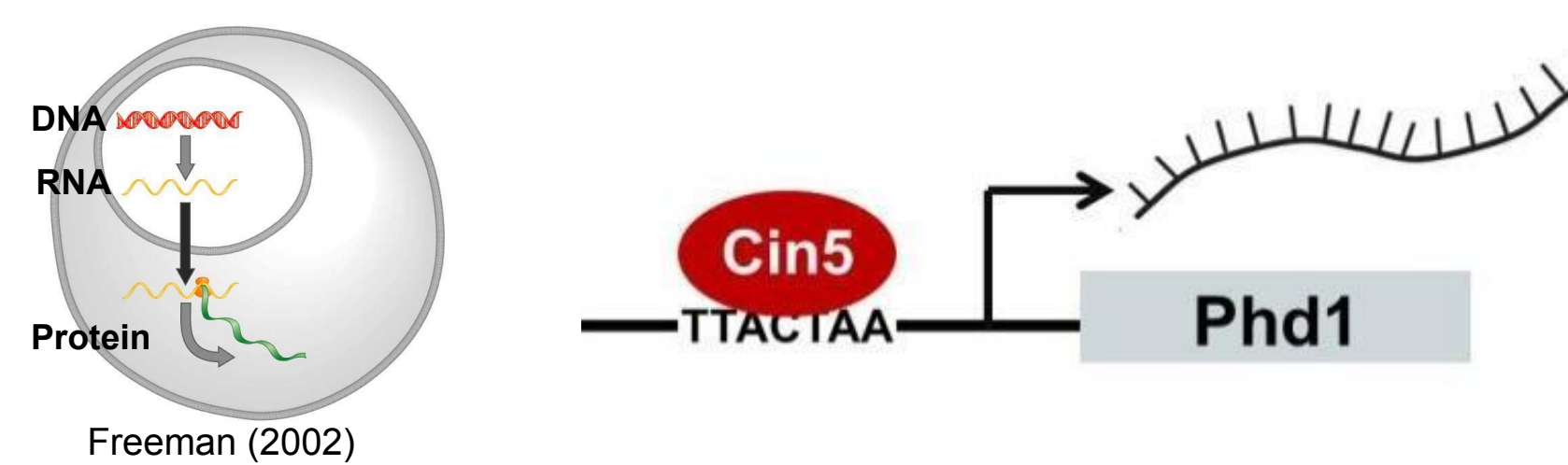


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 *Department of Computer Science, **Department of Biology Loyola Marymount University, 1 LMU Drive, Los Angeles, CA 90045
<http://dondi.github.io/GRNsight/>

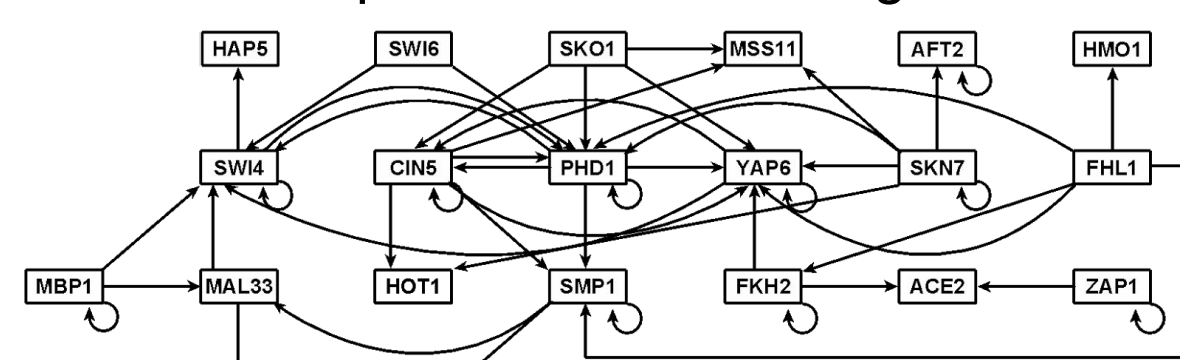


Gene Regulatory Networks Can Be Illustrated by Directed Graphs

- The central dogma of molecular biology describes the flow of information in a cell during gene expression from DNA to RNA to protein.
- Transcription factors control gene expression by binding to regulatory DNA sequences.
- Activators increase gene expression.
- Repressors decrease gene expression.
- Transcription factors are themselves proteins encoded by genes.



- A gene regulatory network (GRN) consists of genes, transcription factors, and the regulatory connections between them, which govern the level of expression of mRNA and proteins from those genes.

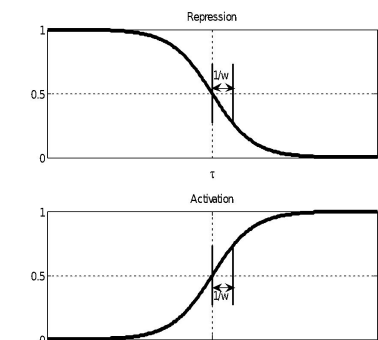


- Each node represents the gene, the mRNA, and the protein expressed from the gene.
- Each edge represents a regulatory relationship.
- All the nodes are transcription factors themselves.

GRNmap: Gene Regulatory Network Modeling and Parameter Estimation

- The MATLAB model is available at <http://kdahlquist.github.io/GRNmap/>

$$p(\bar{x}) = \frac{P_i}{1 + \exp\left(\sum_j -w_{ij}x_j + b_i\right)}$$



- GRNmap is a differential equations model of the changes in gene expression over time for a gene regulatory network (Dahlquist et al. 2015).
- Each gene (node) in the network has an equation.
- The parameters in the model are estimated from laboratory data.
- The weight parameter, w , gives the direction (activation or repression) and magnitude of the regulatory relationship.
- GRNmap produces an Excel spreadsheet with an adjacency matrix representing the network.

regulator	target	weight	direction
ACE2	ASH1	0	0
ACE2	CIN5	0	0
ACE2	GCR2	0	0
ACE2	GLN3	0	0
ACE2	HAP4	0	0
ACE2	HMO1	0	0
ACE2	MSN2	0	0
ACE2	SFP1	0	0
ACE2	STB5	0	0
ACE2	SW4	0	0
ACE2	SW5	0	0
ACE2	YHP1	0	0
ACE2	YOX1	0	0
ACE2	ZAP1	0	0
ASH1	ACE2	1	0
ASH1	ASH1	0	0
ASH1	CIN5	0	0
ASH1	GCR2	0	0
ASH1	GLN3	0	0
ASH1	HAP4	0	0
ASH1	HMO1	0	0
ASH1	MSN2	0	0
ASH1	SFP1	0	0
ASH1	STB5	0	0
ASH1	SW4	0	0
ASH1	SW5	0	0
ASH1	YHP1	0	0
ASH1	YOX1	0	0
ASH1	ZAP1	0	0
CIN5	ACE2	0	0
CIN5	ASH1	0	0
CIN5	CIN5	0	0
CIN5	GCR2	0	0
CIN5	GLN3	0	0
CIN5	HAP4	0	0
CIN5	HMO1	0	0
CIN5	MSN2	0	0
CIN5	SFP1	0	0
CIN5	STB5	0	0
CIN5	SW4	0	0
CIN5	SW5	0	0
CIN5	YHP1	0	0
CIN5	YOX1	0	0
CIN5	ZAP1	0	0
GCR2	ACE2	0	0
GCR2	ASH1	0	0
GCR2	CIN5	0	0
GCR2	GCR2	0	0
GCR2	GLN3	0	0
GCR2	HAP4	0	0
GCR2	HMO1	0	0
GCR2	MSN2	0	0
GCR2	SFP1	0	0
GCR2	STB5	0	0
GCR2	SW4	0	0
GCR2	SW5	0	0
GCR2	YHP1	0	0
GCR2	YOX1	0	0
GCR2	ZAP1	0	0
GLN3	ACE2	0	0
GLN3	ASH1	0	0
GLN3	CIN5	0	0
GLN3	GCR2	0	0
GLN3	GLN3	0	0
GLN3	HAP4	0	0
GLN3	HMO1	0	0
GLN3	MSN2	0	0
GLN3	SFP1	0	0
GLN3	STB5	0	0
GLN3	SW4	0	0
GLN3	SW5	0	0
GLN3	YHP1	0	0
GLN3	YOX1	0	0
GLN3	ZAP1	0	0
HAP4	ACE2	0	0
HAP4	ASH1	0	0
HAP4	CIN5	0	0
HAP4	GCR2	0	0
HAP4	GLN3	0	0
HAP4	HAP4	0	0
HAP4	HMO1	0	0
HAP4	MSN2	0	0
HAP4	SFP1	0	0
HAP4	STB5	0	0
HAP4	SW4	0	0
HAP4	SW5	0	0
HAP4	YHP1	0	0
HAP4	YOX1	0	0
HAP4	ZAP1	0	0
HMO1	ACE2	0	0
HMO1	ASH1	0	0
HMO1	CIN5	0	0
HMO1	GCR2	0	0
HMO1	GLN3	0	0
HMO1	HAP4	0	0
HMO1	HMO1	0	0
HMO1	MSN2	0	0
HMO1	SFP1	0	0
HMO1	STB5	0	0
HMO1	SW4	0	0
HMO1	SW5	0	0
HMO1	YHP1	0	0
HMO1	YOX1	0	0
HMO1	ZAP1	0	0
MSN2	ACE2	0	0
MSN2	ASH1	0	0
MSN2	CIN5	0	0
MSN2	GCR2	0	0
MSN2	GLN3	0	0
MSN2	HAP4	0	0
MSN2	HMO1	0	0
MSN2	MSN2	0	0
MSN2	SFP1	0	0
MSN2	STB5	0	0
MSN2	SW4	0	0
MSN2	SW5	0	0
MSN2	YHP1	0	0
MSN2	YOX1	0	0
MSN2	ZAP1	0	0
SFP1	ACE2	0	0
SFP1	ASH1	0	0
SFP1	CIN5	0	0
SFP1	GCR2	0	0
SFP1	GLN3	0	0
SFP1	HAP4	0	0
SFP1	HMO1	0	0
SFP1	MSN2	0	0
SFP1	SFP1	0	0
SFP1	STB5	0	0
SFP1	SW4	0	0
SFP1	SW5	0	0
SFP1	YHP1	0	0
SFP1	YOX1	0	0
SFP1	ZAP1	0	0
STB5	ACE2	0	0
STB5	ASH1	0	0
STB5	CIN5	0	0
STB5	GCR2	0	0
STB5	GLN3	0	0
STB5	HAP4	0	0
STB5	HMO1	0	0
STB5	MSN2	0	0
STB5	SFP1	0	0
STB5	STB5	0	0
STB5	SW4	0	0
STB5	SW5	0	0
STB5	YHP1	0	0
STB5	YOX1	0	0
STB5	ZAP1	0	0
SW4	ACE2	0	0
SW4	ASH1	0	0
SW4	CIN5	0	0
SW4	GCR2	0	0
SW4	GLN3	0	0
SW4	HAP4	0	0
SW4	HMO1	0	0
SW4	MSN2	0	0
SW4	SFP1	0	0
SW4	STB5	0	0
SW4	SW4	0	0
SW4	SW5	0	0
SW4	YHP1	0	0
SW4	YOX1	0	0
SW4	ZAP1	0	0
SW5	ACE2	0	0
SW5	ASH1	0	0
SW5	CIN5	0	0
SW5	GCR2	0	0
SW5	GLN3	0	0
SW5	HAP4	0	0
SW5	HMO1	0	0
SW5	MSN2	0	0
SW5	SFP1	0	0
SW5	STB5	0	0
SW5	SW4	0	0
SW5	SW5	0	0
SW5	YHP1	0	0
SW5	YOX1	0	0
SW5	ZAP1	0	0
YHP1	ACE2	0	0
YHP1	ASH1	0	0
YHP1	CIN5	0	0
YHP1	GCR2	0	0
YHP1	GLN3	0	0
YHP1	HAP4	0	0
YHP1	HMO1	0	0
YHP1	MSN2	0	0
YHP1	SFP1	0	0
YHP1	STB5	0	0
YHP1	SW4	0	0
YHP1	SW5	0	0
YHP1	YHP1	0	0
YHP1	YOX1	0	0
YHP1	ZAP1	0	0
YOX1	ACE2	0	0
YOX1	ASH1	0	0
YOX1	CIN5	0	0
YOX1	GCR2	0	0
YOX1	GLN3	0	0
YOX1	HAP4	0	0
YOX1	HMO1	0	0
YOX1	MSN2	0	0
YOX1	SFP1	0	0
YOX1	STB5	0	0
YOX1	SW4	0	0
YOX1	SW5	0	0
YOX1	YHP1	0	0
YOX1	YOX1	0	0
YOX1	ZAP1	0	0
ZAP1	ACE2	0	0
ZAP1	ASH1	0	0
ZAP1	CIN5	0	0
ZAP1	GCR2	0	0
ZAP1	GLN3	0	0
ZAP1	HAP4	0	0
ZAP1	HMO1	0	0
ZAP1	MSN2	0	0
ZAP1	SFP1	0	0
ZAP1	STB5	0	0
ZAP1	SW4	0	0
ZAP1	SW5	0	0
ZAP1	YHP1	0	0
ZAP1	YOX1	0	0
ZAP1	ZAP1	0	0

- 0 represents no relationship.
 - Initially, 1 represents a regulatory relationship where the gene specified by the column controls the gene specified by the rows.
 - After the parameters have been estimated, a positive weight value indicates activation and a negative weight value indicates repression.
 - The magnitude of the weight defines the strength of the relationship.
- However, GRNmap does not generate a visual representation of GRNs.**

GRNsight Accepts Microsoft Excel Files (.xlsx) in the Proper Format

- Excel workbooks need a "network" sheet (for unweighted graphs) or a "network_optimized_weights" sheet (for weighted graphs).
- The adjacency matrix can be symmetrical or asymmetrical.
- GRNmap input and output workbooks are accepted without adjustment.
- Adjacency matrices generated from other databases, such as YEASTRACT (Miguel et al., 2014), can be used with some modification.

Testing Suite can test Import and Export functionality

Warning

There were 4 warning(s) detected in this file. The graph will be loaded, but may not be displayed accurately. We recommend you review your file and ensure that it is formatted correctly. To view the details of the warning(s), please click on the "Warnings List" below.

Warnings List

The data in row 8 column B of the optimization_diagnostics sheet, is not a number. Please ensure that your MSE data is correct and only contains numbers.

The data in row 11 column F of the optimization_diagnostics sheet, is not a number. Please ensure that your MSE data is correct and only contains numbers.

The data in row 18 column D of the optimization_diagnostics sheet, is not a number. Please ensure that your MSE data is correct and only contains numbers.

2 more warning(s) like this exist.

GRNsight
 Web app and service for visualizing models of gene regulatory networks.

Beta v4.0.30

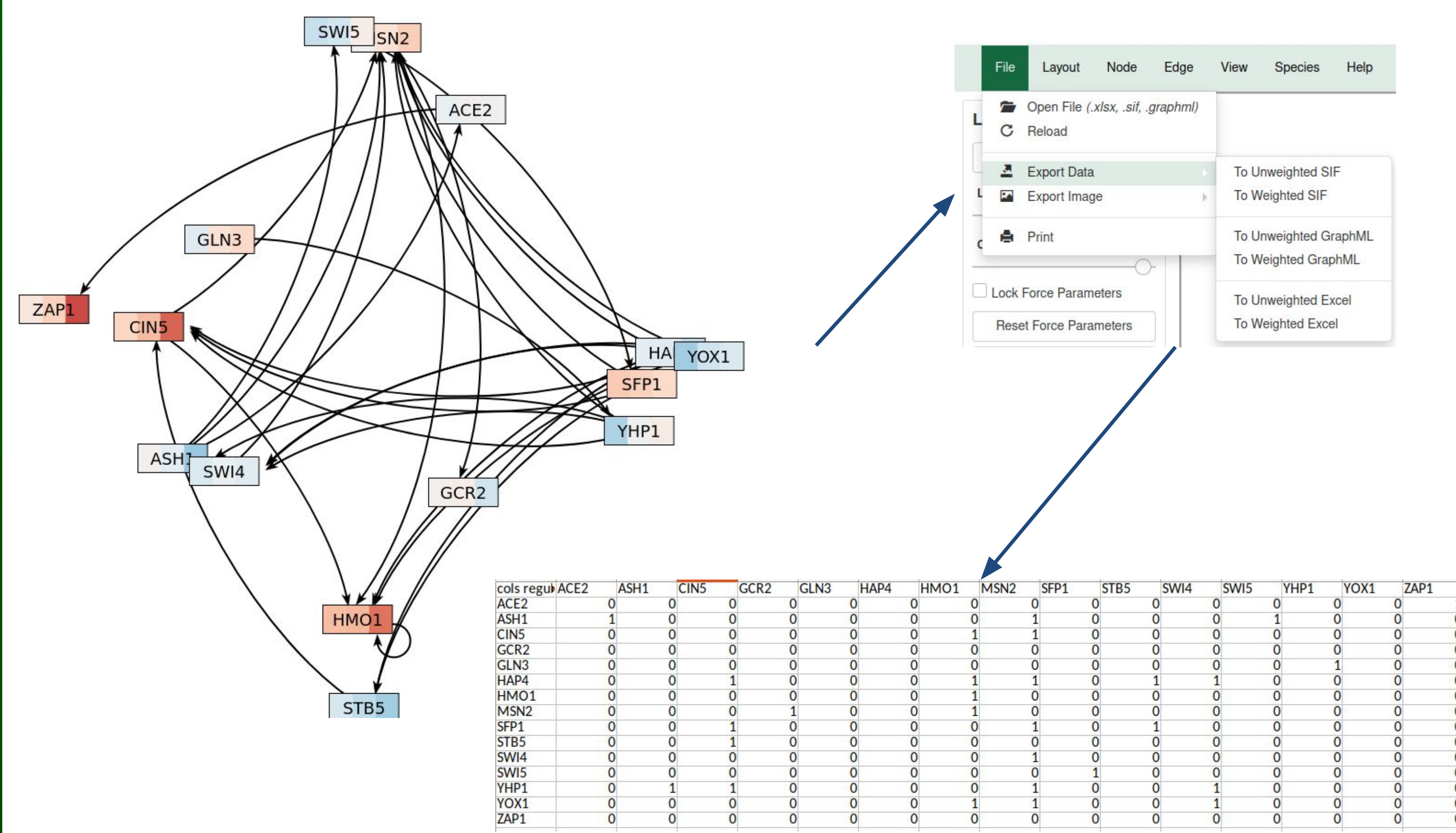
Disclaimer: This is the beta version of GRNsight for the testing of new functionality. For the most stable version, please go to the GRNsight home page.

File | Layout | Node | Edge | View | Species | Help

Open File (.xlsx, .xlsx_graphml)
 Reload
 Export Data
 Export Image
 Print
 Lock Force Parameters
 Reset Force Parameters

Layout: Force Graph, Grid Layout
 Line Distance (0-1000): 100
 Change (0-1000): 100
 Lock Force Parameters
 Links: Show
 Click here in order to view warnings

Node: Create Node Coloring
 Select from non-equivalent expression data, or use data from our Expression Database
 Top Downer
 Use Log Expression
 Average Replicate Values
 Brown Default



- Refactored Existing GRNsight import test, and expanded export tests**
- Refactored existing GRNsight code to consolidate error and warning messages, as well as added new tests for additional sheets in a GRNsight workbook.
 - Updated test to reflect additional features that GRNsight recently developed.
 - Expanded export tests to increase user visibility on possible errors that occurred during the import process.
 - Fixed bugs within the existing GRNsight export functionality and created a system to automatically fix minor issues within a workbook, alert the user of issues within a file that they must fix, or send an error message that something went wrong with the export process.

The Client Side Testing Documents Streamlines Testing of Frontend

Update Client Side Test Generator Script

- Client Side tests are generated for a subset of features by permuting all possible combinations of feature states, creating steps for the user to follow.
- These features are listed in JSON files, separated by their location in the user interface. These JSON files are read by the script and the requested features are used to generate the tests
- Each feature is given a unique static ID that is used to reference it easily.
- The generator script can include features based on an activation state in the features JSON, by command line arguments, or by a separate JSON file created by the tester.
- The client side testing document was updated so that the features include their ID and the wiki was updated.
- Client side features' descriptions were updated to better reflect the features intentions.

Test 17

Instructions:

- Sidebar Menu: Grid Layout - Click Grid Layout Button
- Dropdown Menu: Node -> Enable Node Coloring - Uncheck
- Dropdown Menu: View -> Viewport Size - Check "Medium"
- Dropdown Menu: View -> Restrict Graph to Viewport - Check

Results:

- The graph should change to grid layout
- Node coloring should become disabled, and Node Coloring Toggle Button text in sidebar menu should toggle off, if expression data sheets are present in input workbook
- The viewport size should be set to medium
- The viewport should always be contained within the viewport.

```

{
  "title": "Format Menu",
  "text": "The edge weight should",
  "options": {
    "select": {
      "show": "show With Mouse Over": "display when user mouses over an edge.",
      "select": "Always Show Edge Weights": "always be visible.",
      "select": "Never Show Edge Weights": "not be displayed."
    }
  },
  "included": true, // Includes this interaction group when generating tests.
  "availability": { "NoGraphLoaded": true, "WeightedGraphLoaded": true, "UnWeightedGraphLoaded": true }
}
    
```

GRNsight Client Side Testing Overview

ID	Included in Testing Protocol	GRNsight Option	User Action	Result
e1	NO	Dropdown Menu: Edge -> Enable Edge Coloring Based on Weight Value	Check	GRNsight should enable edge coloring and set the sidebar menu "Enable Edge Coloring" to checked

Library Updates

- Updated Dependencies**
- Dependencies had grown out of date and were updated
 - Issues arose with outdated dependencies and Firefox versions above 80 as a result of increased privacy controls and protections
 - Security vulnerabilities were identified within the dependencies as a result of outdated versions

- Began Migration of Deprecated Dependencies**
- Some dependencies, notably Jade, have been deprecated, threatening future iterations of GRNsight.
 - Migration of these libraries to their contemporary versions has begun to address this problem.