Variability in Gene Regulation due to Cold Shock Response in Wild Type Yeast

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BIOL 388/S19

Outline

- Previous research leads to interest in the cold shock response in yeast
- Analysis with ANOVA and STEM provided gene profiles which were used create gene maps
- An *in silico* experiment was performed to further test the data
- Comparison of results helped lead to conclusions and provided grounds for future experimentation

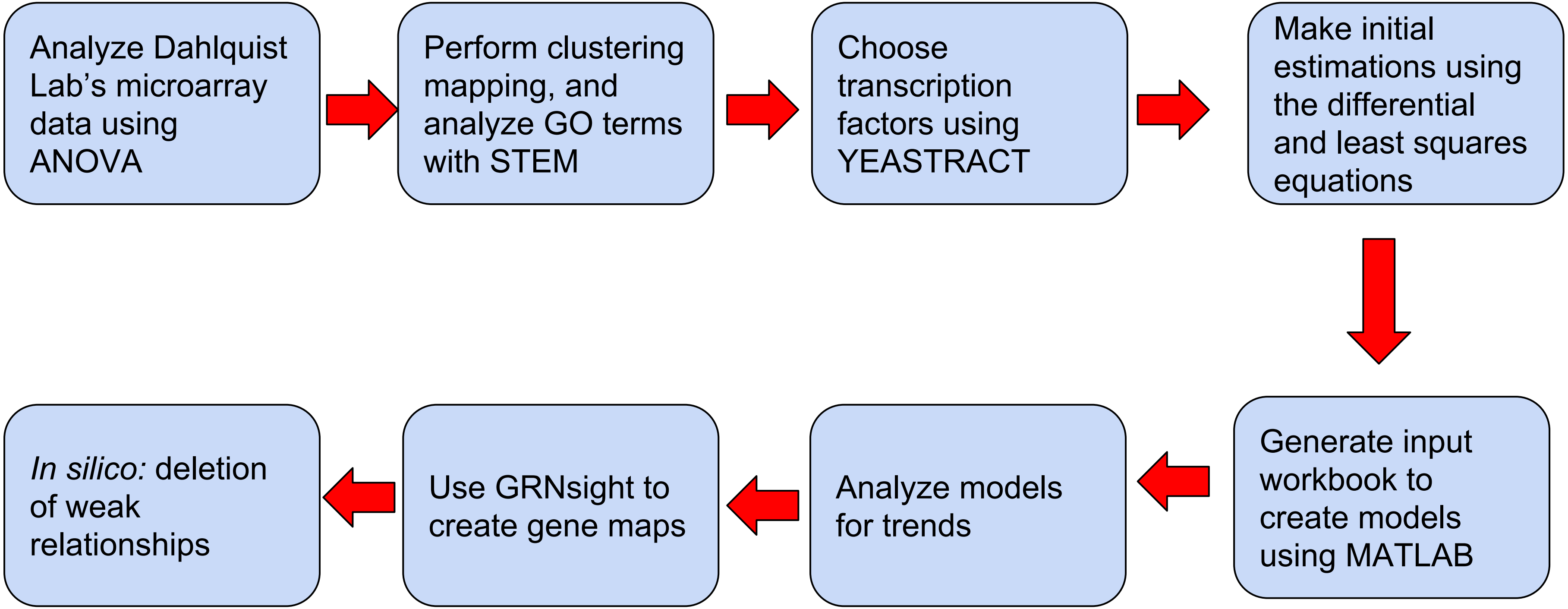
The specific transcription factors involved in regulation are not yet known

- Experiments have shown that in response to cold shock, yeast are able to change their gene transcription to adapt. However the specific transcription factors involved in early response and how they regulate each other is not yet clearly known.

- Dr. Dahlquist’s lab performed a cold shock experiment on yeast using different timepoints and different manipulations of certain genes (ex. deletion). This produced microarray data.

- With a focus on the wild type data, analysis were performed to ultimately create gene maps that would show the type of contribution each transcription factor has on other genes in the network.

Final results were achieved using the following:



Analyze Dahlquist Lab's microarray data using ANOVA

Perform clustering mapping, and analyze GO terms with STEM

Choose transcription factors using YEASTRACT

Make initial estimations using the differential and least squares equations

Generate input workbook to create models using MATLAB

Analyze models for trends

Use GRNsight to create gene maps

In silico: deletion of weak relationships

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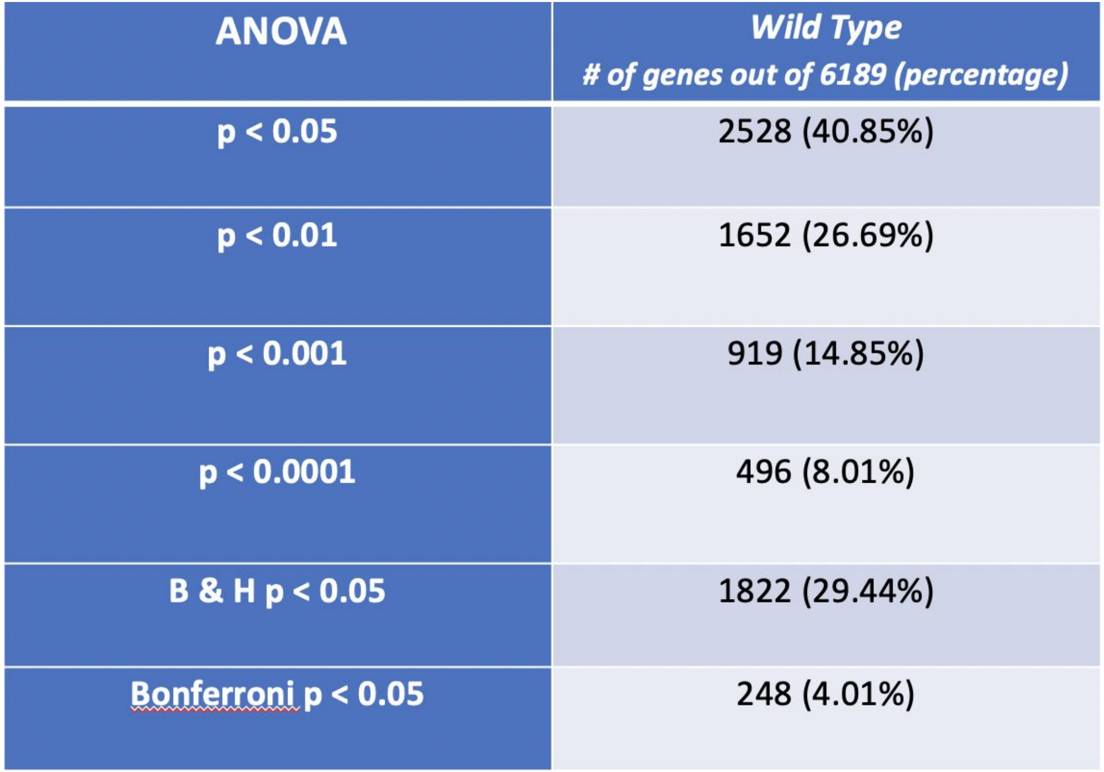
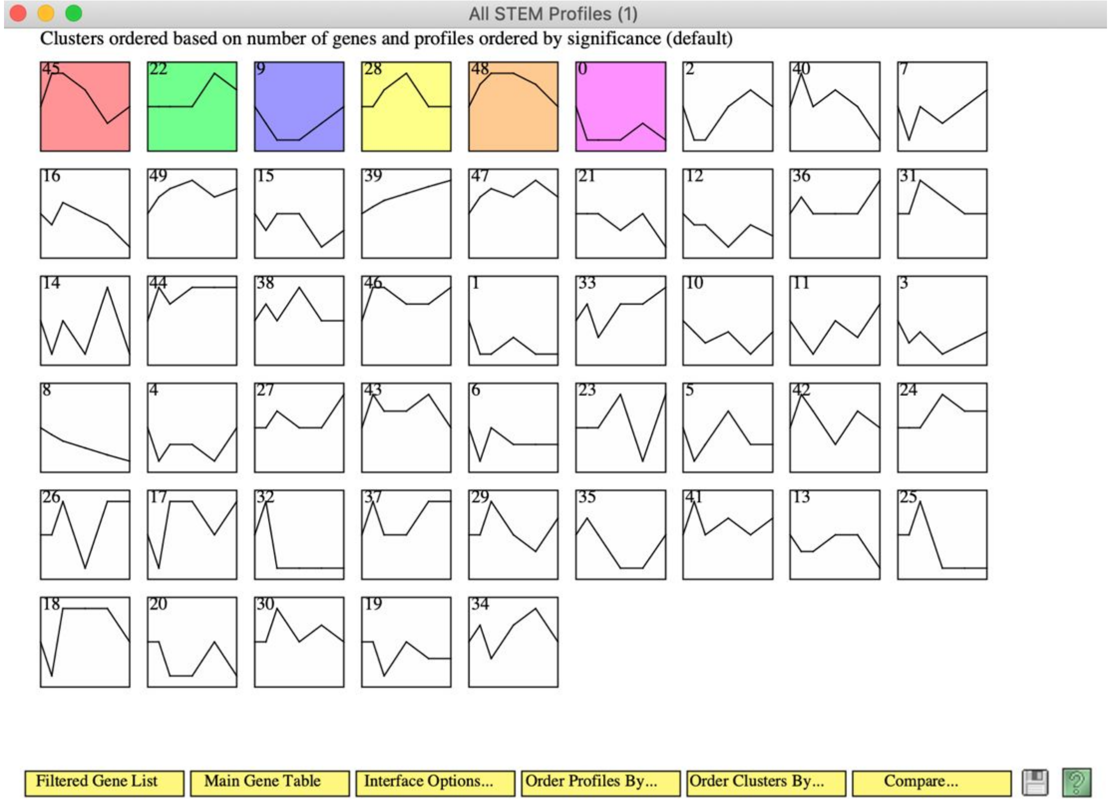
ANOVA Test on wild type shows presence in significant change except for Bonferroni correction



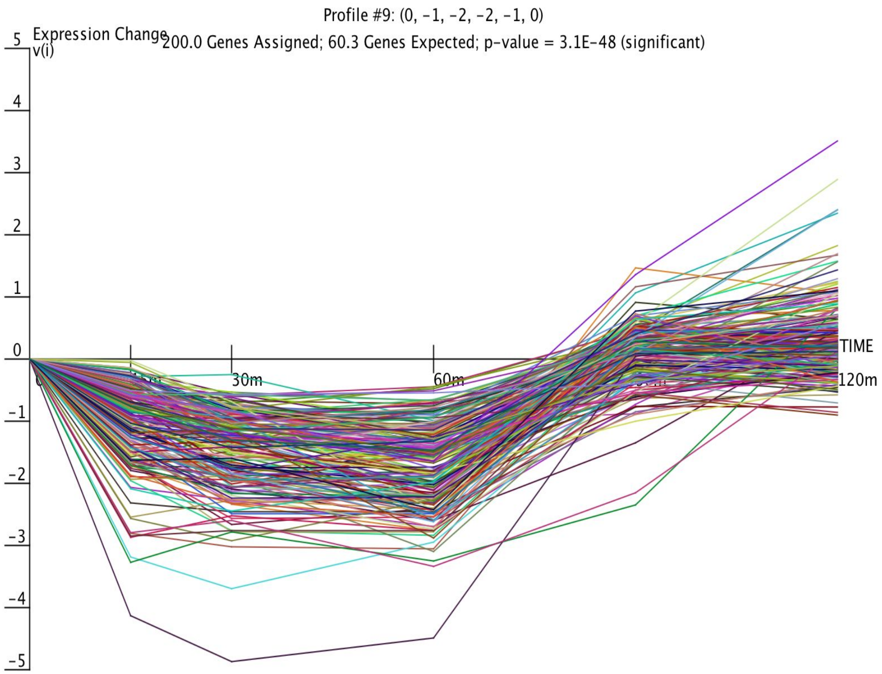
ANOVA	***Wild Type*** ***# of genes out of 6189 (percentage)***
$p < 0.05$	2528 (40.85%)
$p < 0.01$	1652 (26.69%)
$p < 0.001$	919 (14.85%)
$p < 0.0001$	496 (8.01%)
B & H $p < 0.05$	1822 (29.44%)
Bonferroni $p < 0.05$	248 (4.01%)

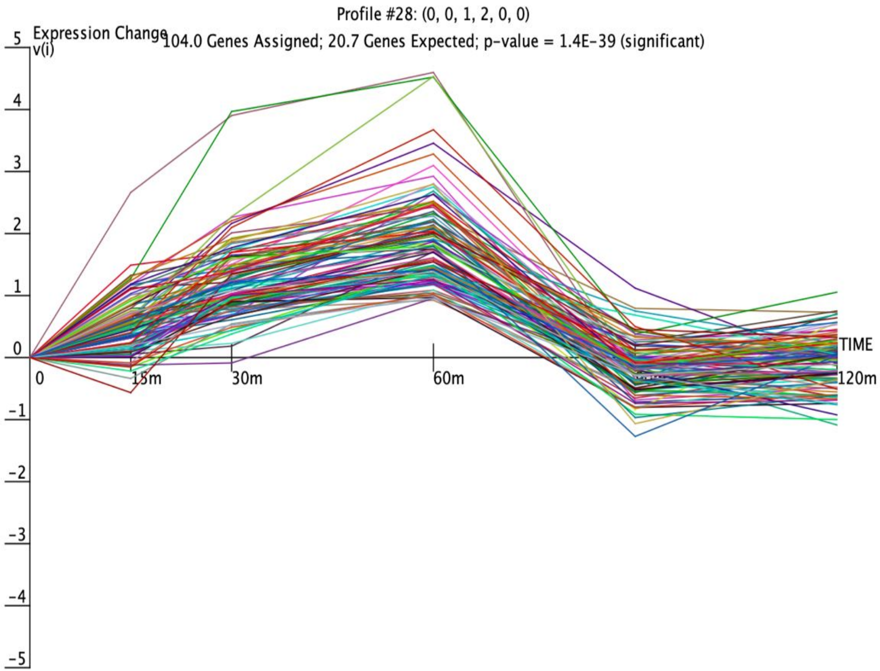
STEM analysis showed 6 significant profiles



Clusters ordered based on number of genes and profiles ordered by significance (default)

Profiles 9 and 28 were chosen for further analysis



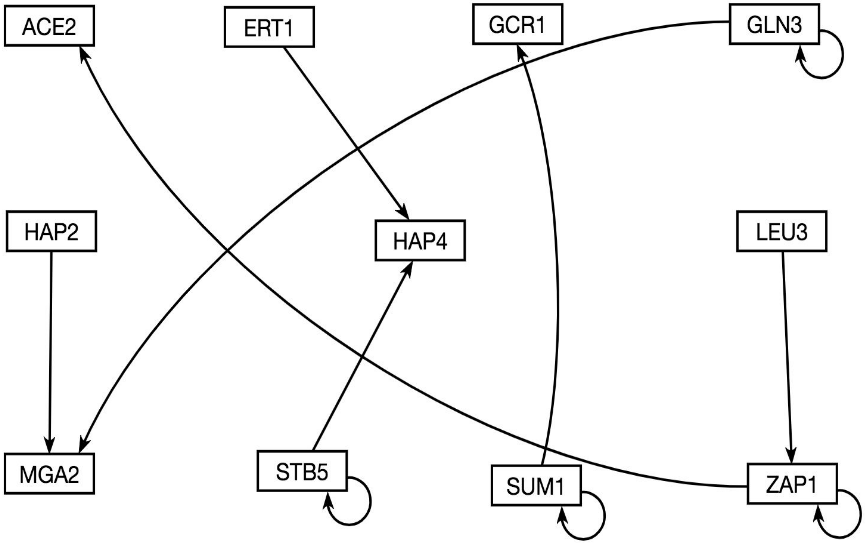


Each profile produced unique GO results

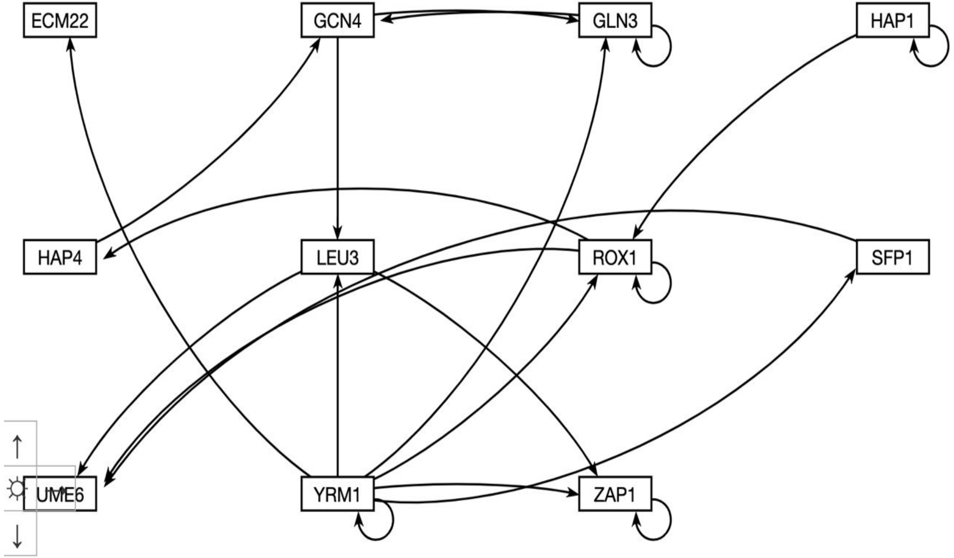
Profile 9	**Profile 28**
Small molecule catabolic process	Cellular amino acid biosynthetic process
Bounding membrane of organelle	DNA binding transcription factor activity
Endoplasmic reticulum to Golgi vesicle-mediated transport	Adenyl ribonucleotide binding
Protein transport	Response to stress
Vesicle-mediated transport	Active transmembrane transporter activity
Organelle subcompartment	Ligase activity

GRNsight was used to visualize these unweighted networks

Profile 9

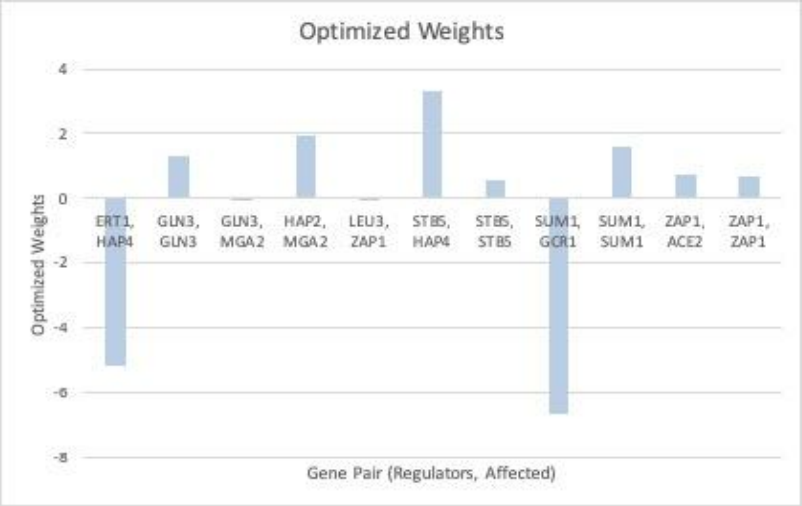


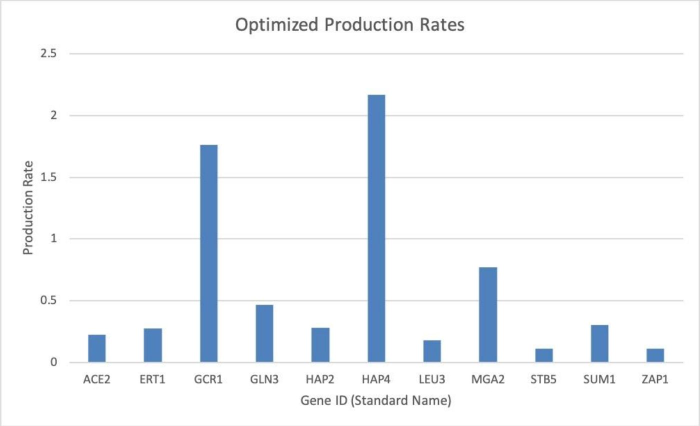
Profile 28

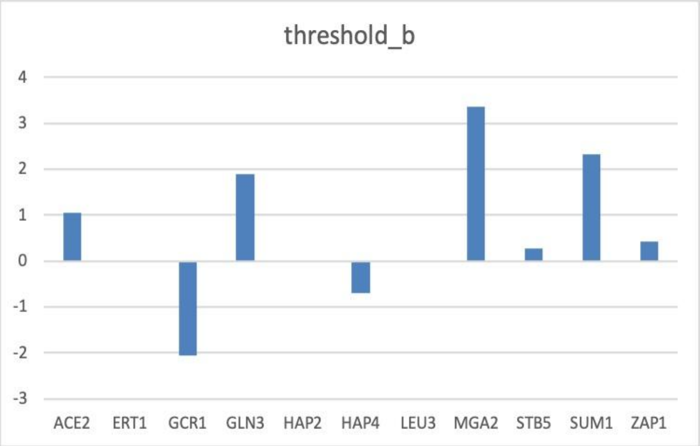


Graphs created using Excel output workbook from MATLAB

Profile 9 LSE:minSE Ratios
1.4244

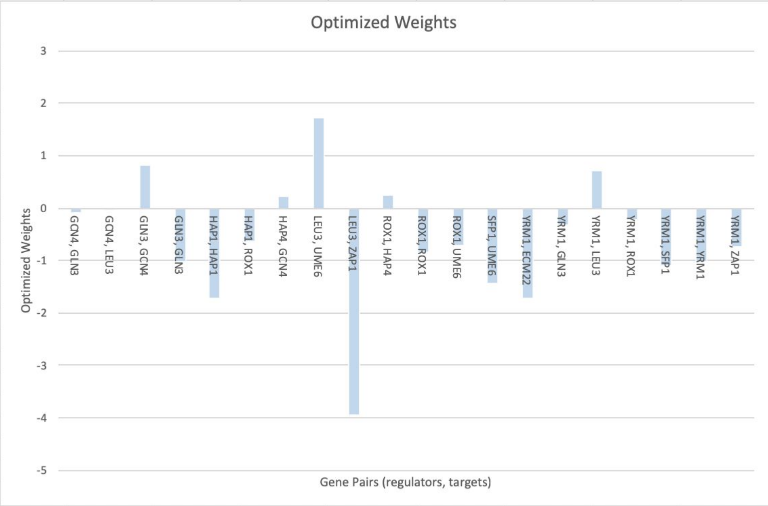


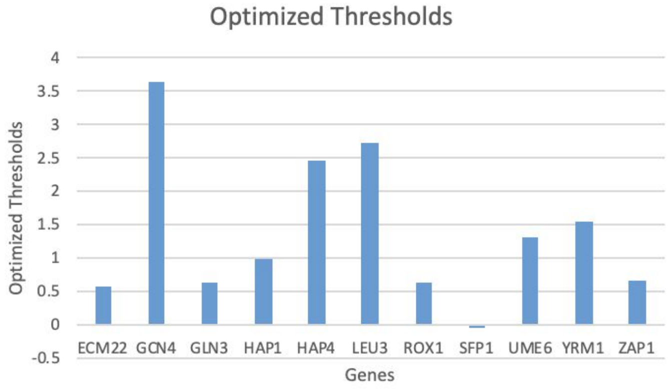


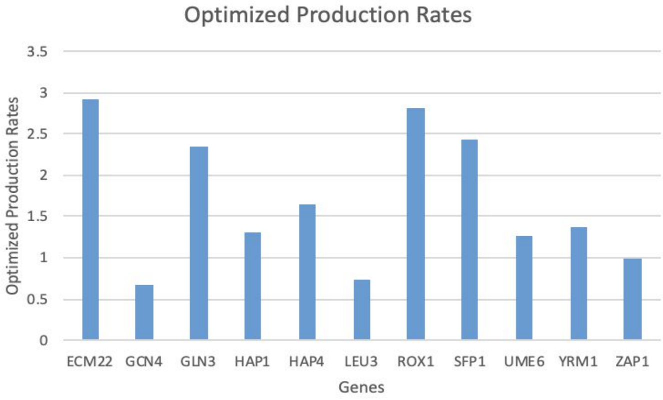


Graphs created using Excel output workbook from MATLAB

Profile 28 LSE:minLSE ratio:
1.5738

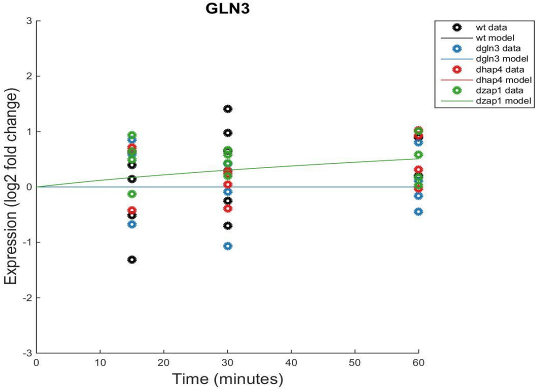


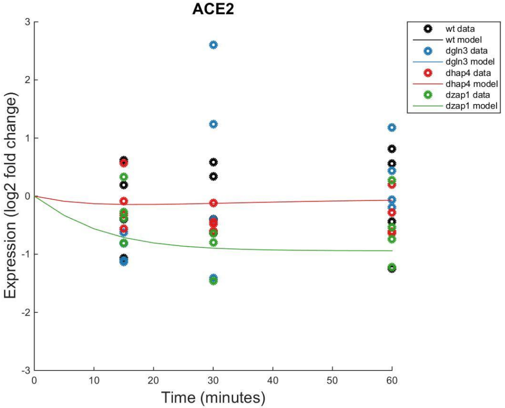




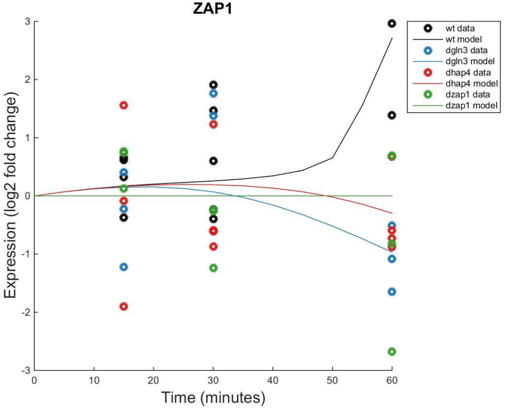
Expression plots show comparisons in gene activity

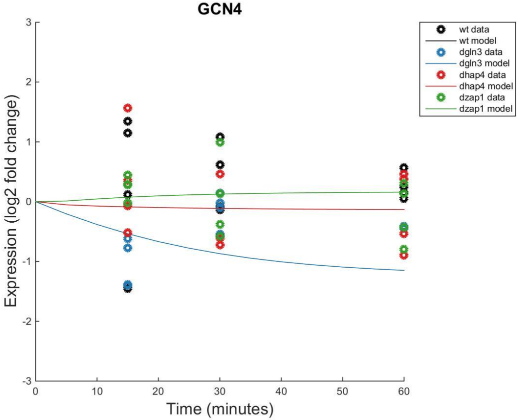
Profile 9



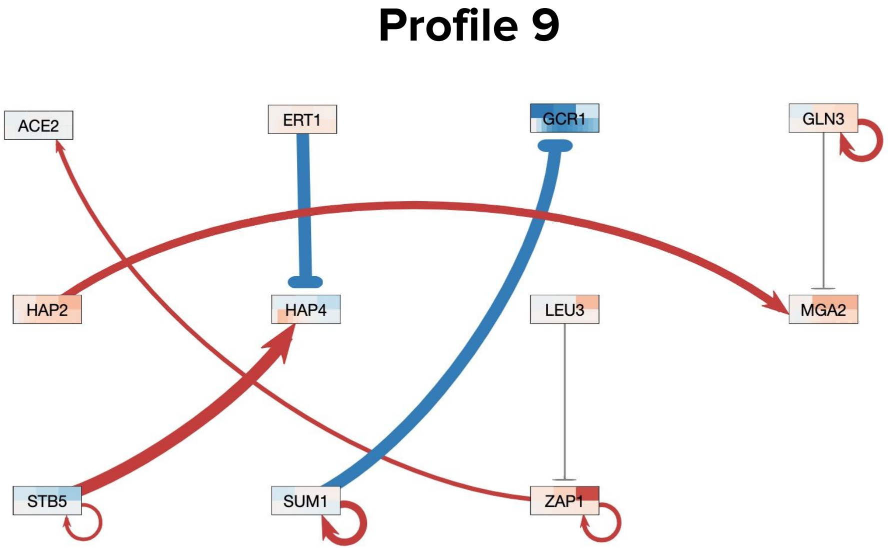


Profile 28

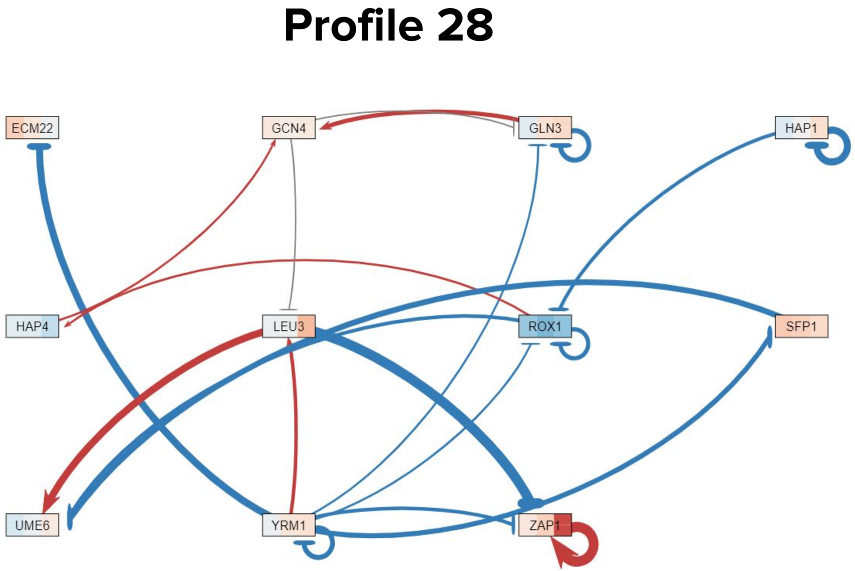




Weighted GRNsight networks show relationships between genes



Profile 9



Profile 28

Red: upregulation

Blue: downregulation

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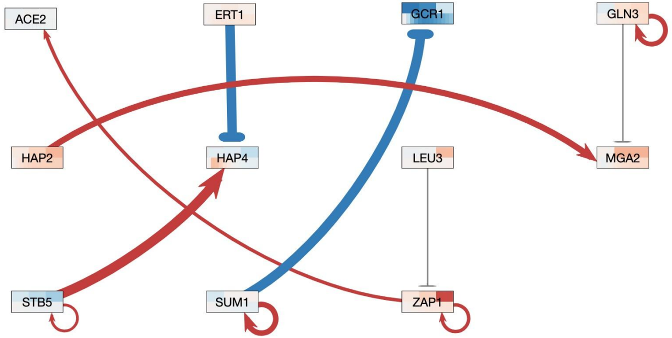
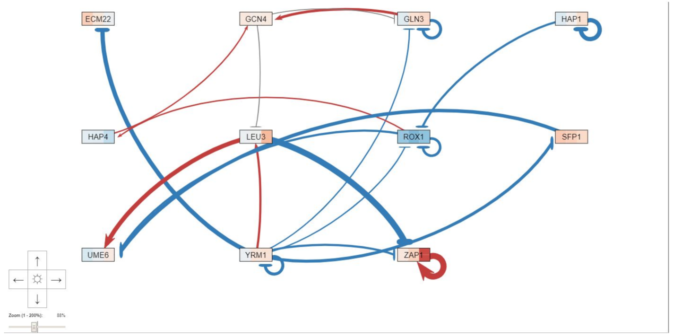
Deleting the ‘gray lines’ on the gene map can change the type of regulation

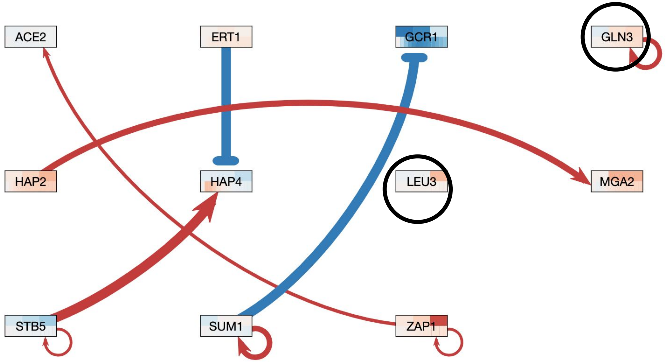
Profile 9

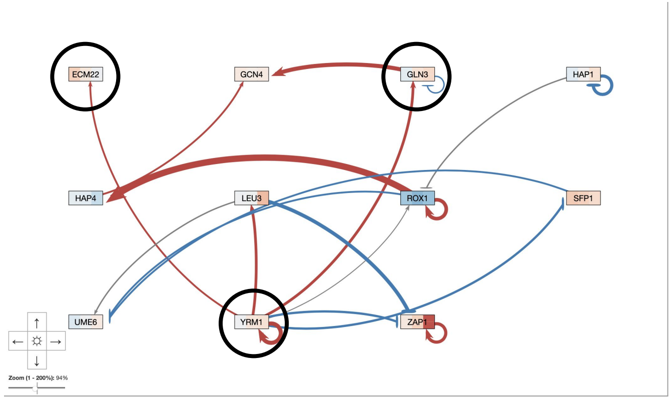
Profile 28





Before deletion





After deletion

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Conclusions & Future Directions

- Analysis of the microarray data of yeast in cold shock using ANOVA and STEM provided gene profiles which were used create gene maps.
- ‘Gray’ lines in the maps were removed to analyze any changes.
- In Profile 28, LEU3 and ROX1 are the factors that are most likely to regulate the cold shock response.
- In Profile 28, removing the relationship that GCN4 has with GLN3 and LEU3 changes the type of regulation that YRM1 has with ECM22 and GLN3.
- In the future, all of the significant gene profiles can be tested to see if the phenomena that occured in Profile 28 will repeat itself.

References

Week 7 Assignment:

Dahlquist, K., & Fitzpatrick, B. (n.d.). BIOL388/S19:Week 7. Retrieved from https://openwetware.org/wiki/BIOL388/S19:Week_7

Gene Ontology Resource. (n.d.). Retrieved February 20, 2019, from http://geneontology.org/

Acknowledgments

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