

Environmental Influence on Transcription Factors and Gene Regulation of Yeast Cells

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Course: BIOL 367

Loyola Marymount University

Predicting the DNA binding locations of transcriptional regulators

- Transcriptional regulators will influence gene expression when they bind to the DNA
- Phylogenetic conservation sequences have determined the genomic sequences for these yeast genes
- This data alone cannot determine where individual regulators will bind to them or the environmental conditions that are optimal for binding

Intro

Outline

1. Introduction
2. Main Results
3. Significance of the Work
4. Methodological Approach
5. Detailed Figure
6. Analysis
7. Summary and Conclusion
8. Acknowledgments
9. References

Yeast's Gene Regulation

- Introduced a basic model for Yeast's gene regulation
- Explores binding of regulators to cis-regulatory sequences
- Shows interaction changes with environmental shifts

Significant Expanse of Gene Regulatory System Knowledge

- Comprehensive study of gene regulation
- Analyzed over 6,000 DNA segments
- Diverse conditions
- Created an expanded map of the yeast transcriptional regulatory network

Limitations of Previous Studies

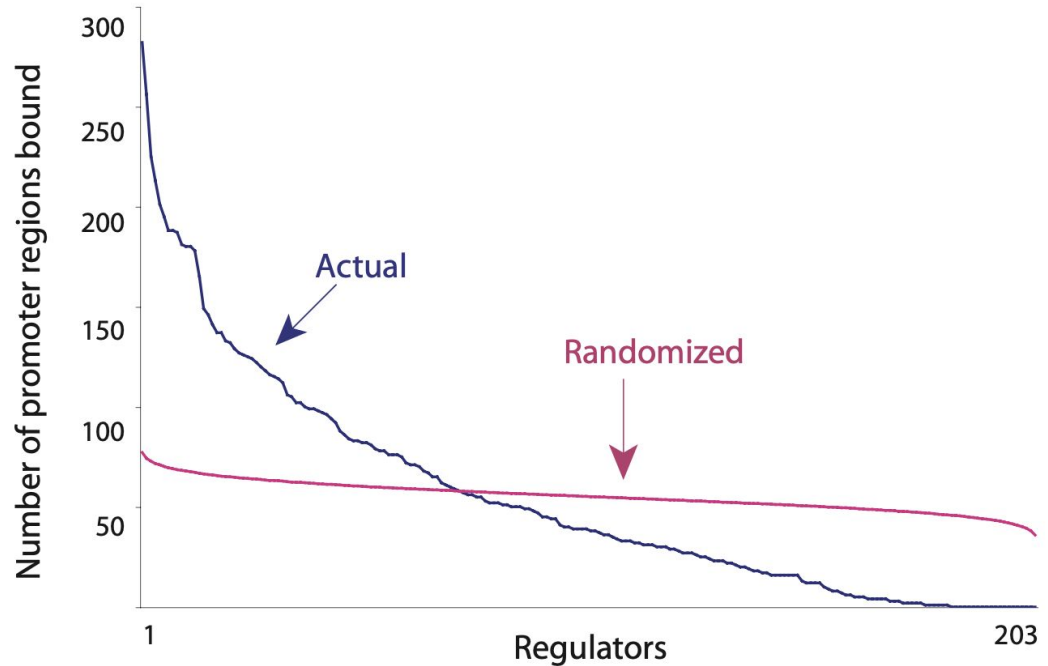
- Gaps in prior gene regulation models
- Limited regulatory sequence identification in previous studies
- Not enough environmental factors

Treating the Cells

- Performed a genome-wide location analysis
- Allowed them to determine where DNA-binding transcription regulators attach
- Different based on the environmental factors

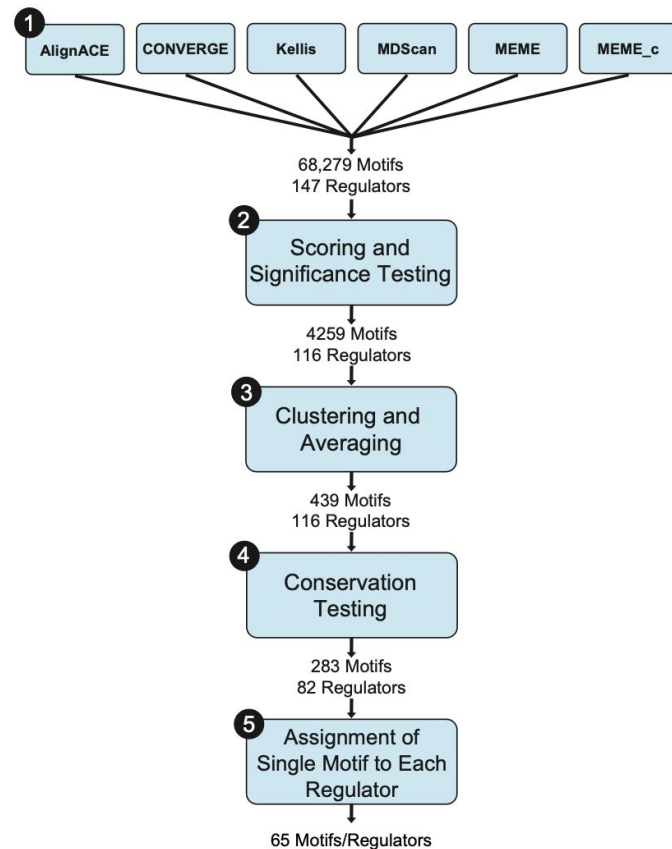
Supplementary Figure 1: The binding of regulators to promoters is selective

- The blue line suggests a few regulators bind to many proteins, most bind to a few
- The pink line suggests a more even distribution of binding across regulators if the process were random



Supplementary Figure 2: a large number of motifs were filtered in order to identify a smaller number of high-confidence motifs

- AlignACE, Converge, Kellis, MDScan, MEME, MEME_c: computational tools and algorithms used to identify potential motifs
- Scoring and Significance Testing: statistical methods are used to identify which motifs are biologically useful
- Clustering and Averaging: helps identify representative motifs for each group
- Conservation Testing: identified motifs are conserved across different species of strain to indicate biological importance
- Assignment of Single Motif to Each Regulator: one motif is selected for each regulator



Supplementary Figure 3: The newly discovered sequence is a better binding agent to the regulator (Gcn4)

- Figure to the right is a gel assay
- The left is a control in which the regulator is bound to a previously discovered sequence with dye
- Lanes 2-8 are the control group bombarded with a new sequence without dye
- Lanes 3-8 are the control group bombarded with the previously established sequence without dye

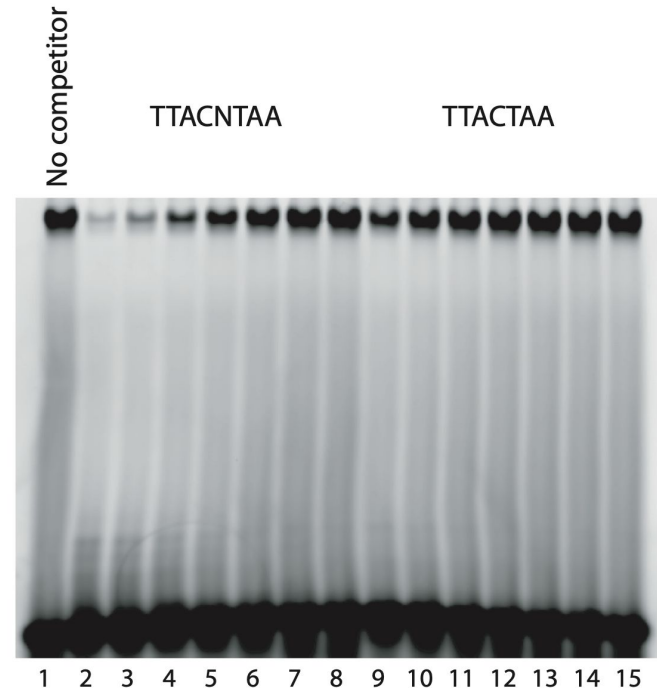


Figure 4: There are 4 patterns of DNA-binding behaviour of transcriptional regulators

- Colored Circle: transcriptional regulator
- Colored Boxes: gene promoters
- Lines: binding events

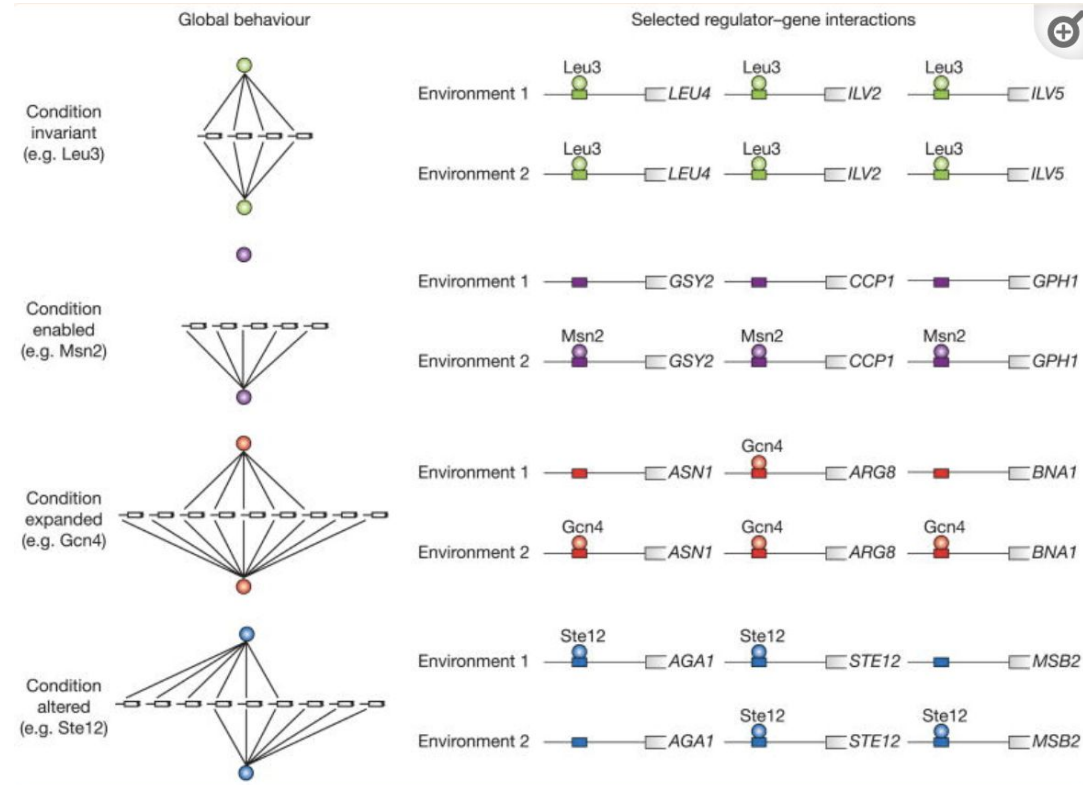
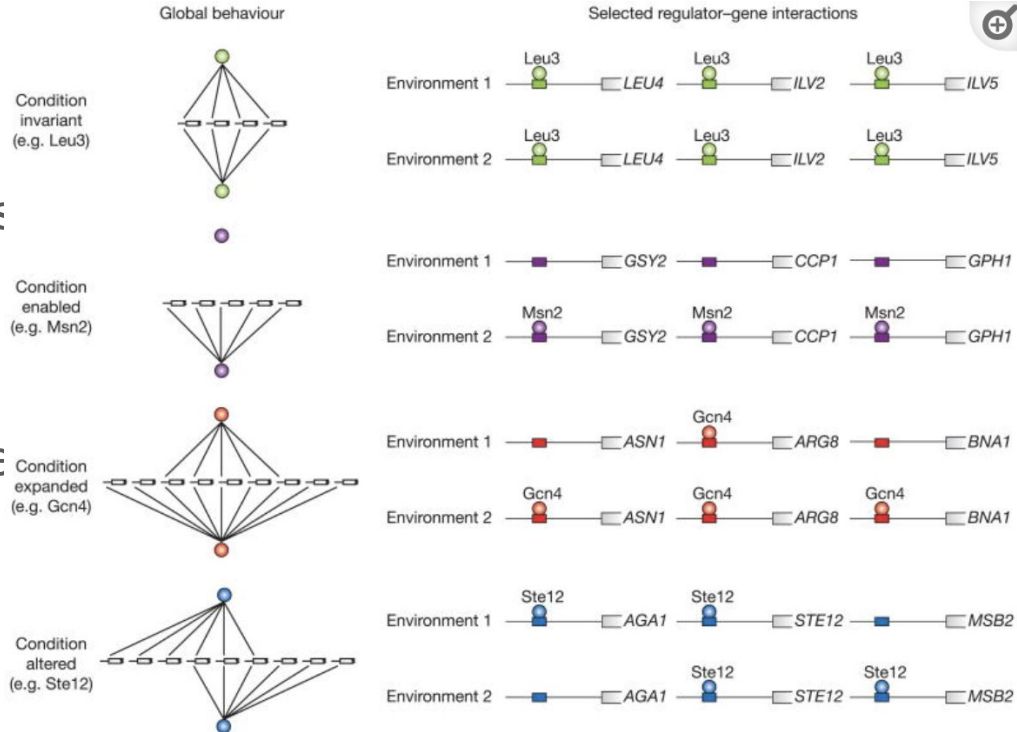


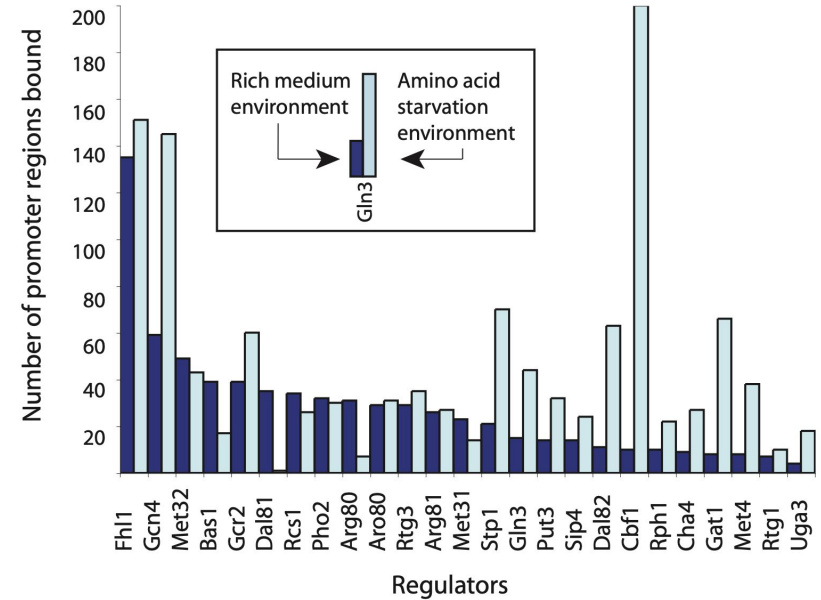
Figure 4: The role in gene expression in the same regulatory proteins can differ based on the cells environmental conditions

- Condition invariant: same regulator binds to the same target regardless of environment
- Condition enabled: a regulator binds to different targets depending on environment
- Condition expanded: a regulator binds to a basic set of targets in one condition and an expanded set in another
- Condition altered: a regulator changes binding targets based on environment



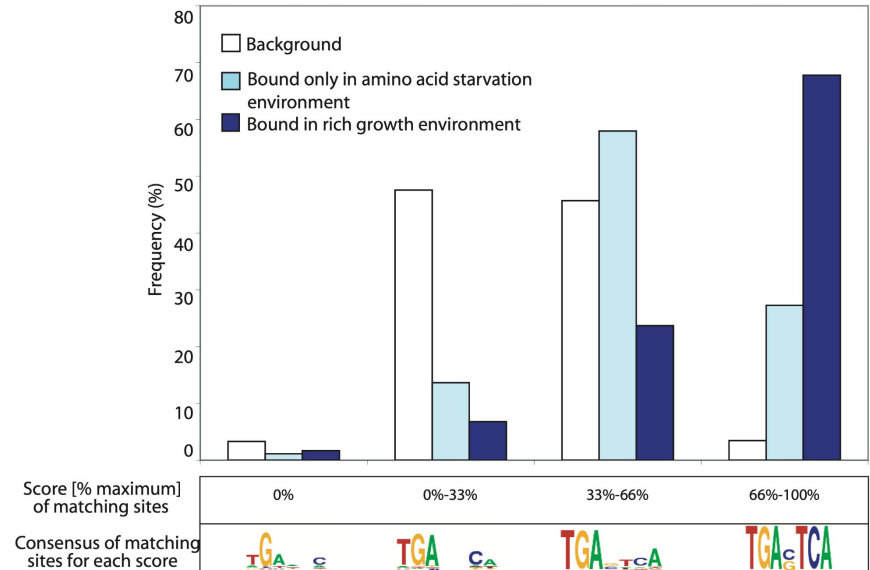
Supplementary Figure 4: Comparison of promoter regions in two different conditions

- Figure to the right is a bar graph comparing 25 regulators in 2 different environments
- Dark blue represents rich medium environment and light blue represents amino acid starvation
- Most of the regulators have some sort of environmental specificity



Supplementary Figure 5: Comparison of different quality binding sites with environmental conditions

- Figure to the right is a bar graph comparing the different environmental conditions
- X axis percentages is based upon strength of binding
- Y axis being the frequency it binds in that condition in that binding site
- The consensus of the matching site on the bottom represents the likely sequence



The study was very ambitious and was well done, but was not presented well in the paper

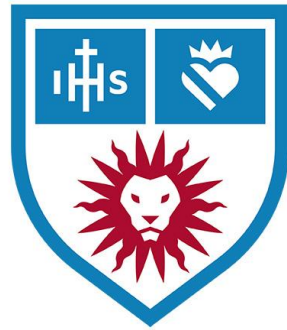
- The methods section of the paper was exceedingly short for the kind of information it was attempting to convey
- It was a very impressive experiment that combined several data types to determine very useful conclusions with high confidence rates
- However, the article was far too short to be explaining such complex experiments, and even left out very important information in some cases
- The supplemental methods were required to find what any of their environmental conditions were

The information was too difficult to understand

- Even when all of the methods and conditions and missing information has been found, it is still a very dense topic and hard to comprehend
- The methods section of the paper is quite cryptic and not reproducible based on what is given
- Also gives little to no scientific background for the methods that they used
- The figures were often not clear in what they were trying to convey and there were even some errors on them in some places
- The graphs also tended to use unconventional ways of displaying information, which is rather dense information, but it was sometimes overcomplicated

Thank you to all who made this presentation possible

Thank you to the Loyola Marymount University Biology department, as well as all of our classmates, group members, as well as our professor, Dr. Dahlquist.



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References

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<https://doi.org/10.1038/nature02800>
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