

The evolutionary dynamics of Gene Regulatory Networks (GRNs) in Yeast

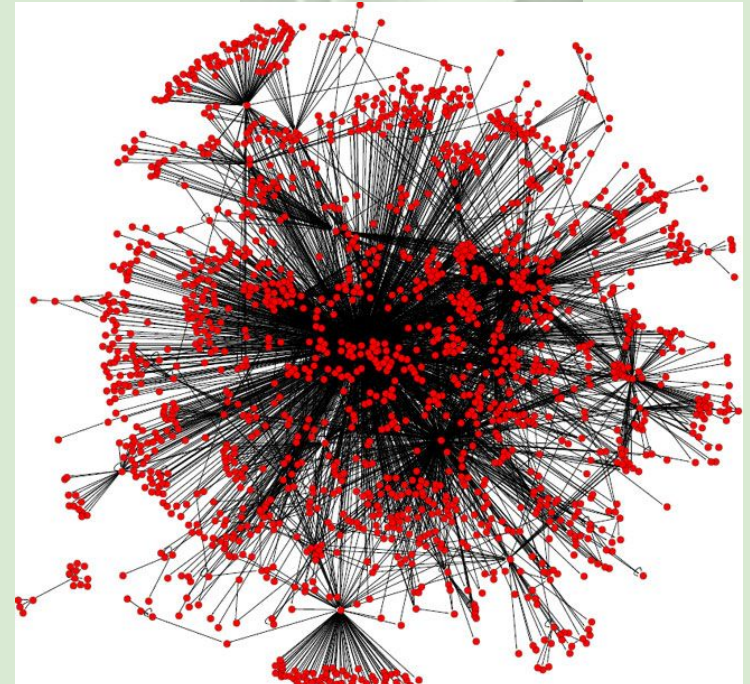
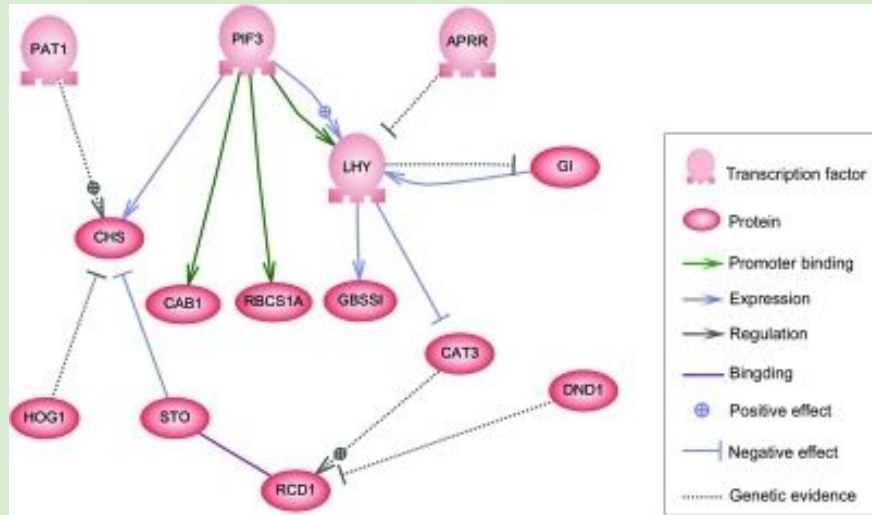
By Ellen Manders, Daan Stolker & Tjerk Swinkels

Introduction

- How does a code become an organism?
- Not just genetics, but gene regulation!
 - Epigenetics
 - *Cis*-regulatory elements
 - *Trans*-regulatory elements



Visualizing gene expression in a GRN



Short summary of yeast

Single celled eukaryote

Model organism for basal life processes

Budding Yeast (*Saccharomyces cerevisiae*) commonly used

Can be easily genetically modified



Method

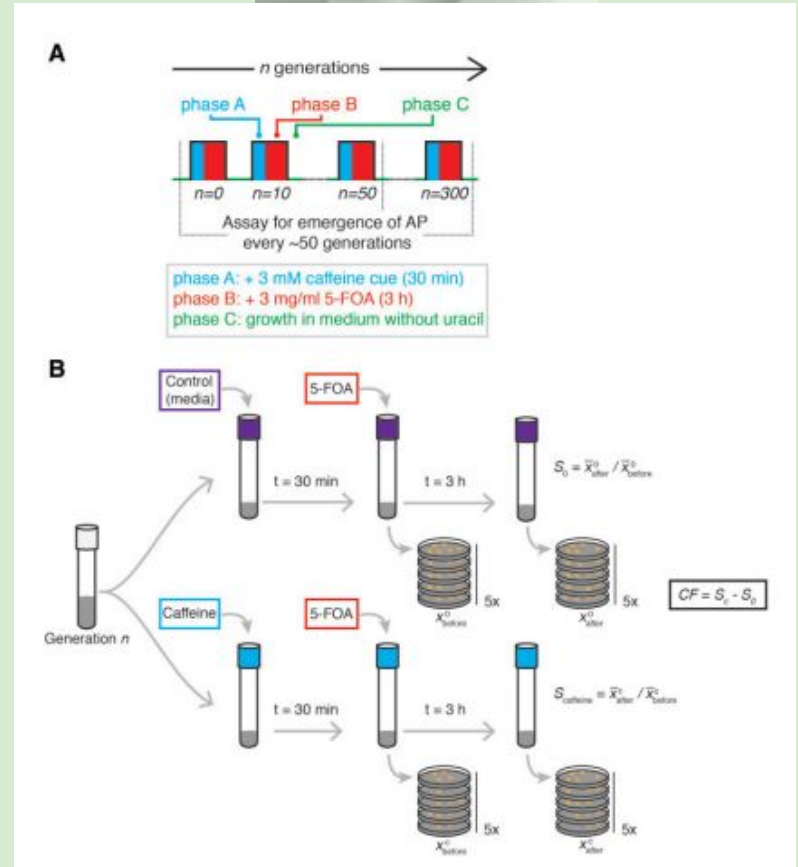
Lab experiment with modified Budding Yeast (*S. cerevisiae*)

“Pavlovian conditioning”

Cue: Caffeine or menadione

Sublethal 5-FOA-dose

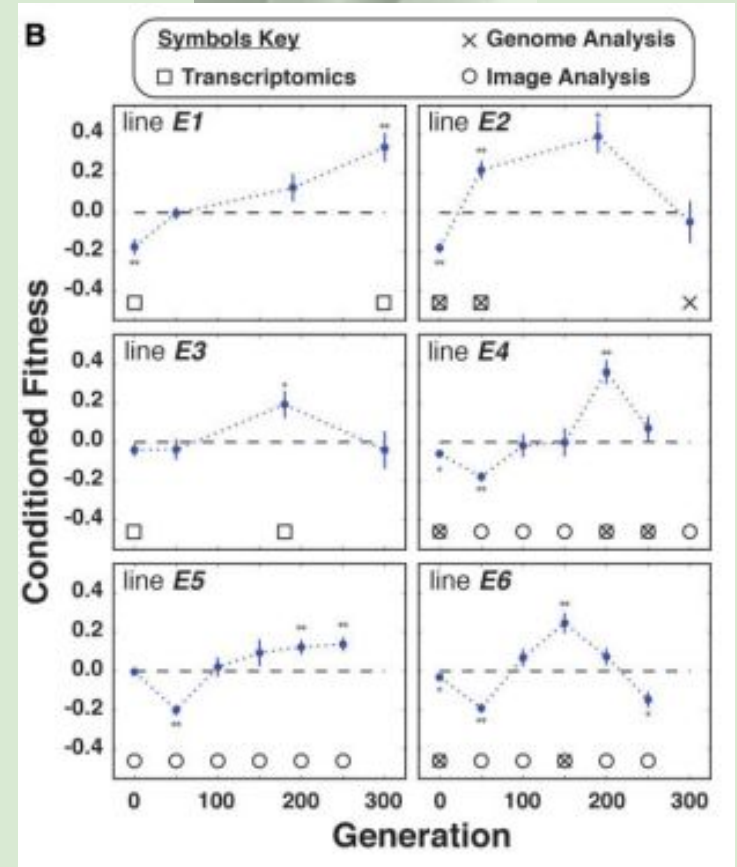
Repeated every ~50 generations



Adaptive Prediction?

Significant result in each cell line at least once

However, AP mostly does not persist



López García de Lomana *et al.* 2017

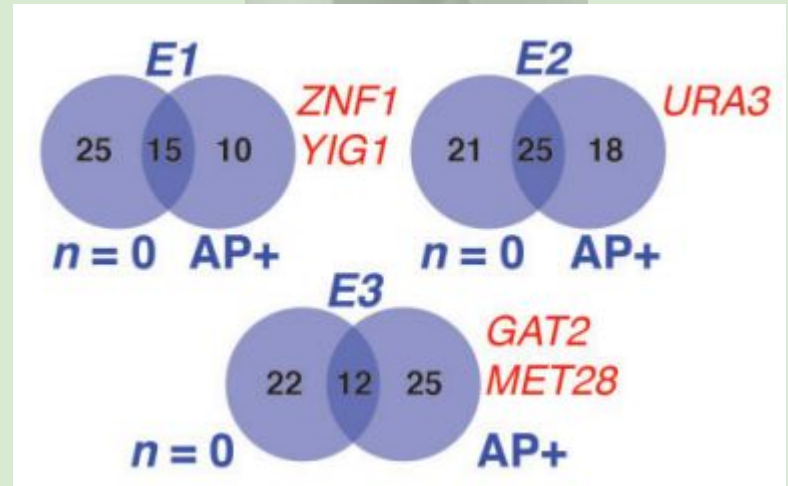
Possible explanation of AP

Rewiring of the gene regulatory network

Trans-regulatory factors differed between the population before and after AP

However...

the AP-lines cannot persist for a long generation span. A fitter mutant probably outcompeted the AP-yeasts



López García de Lomana *et al.* 2017

What does AP mean in a GRN

- Is comparable to evolution of evolvability
- Linking two parts of a GRN



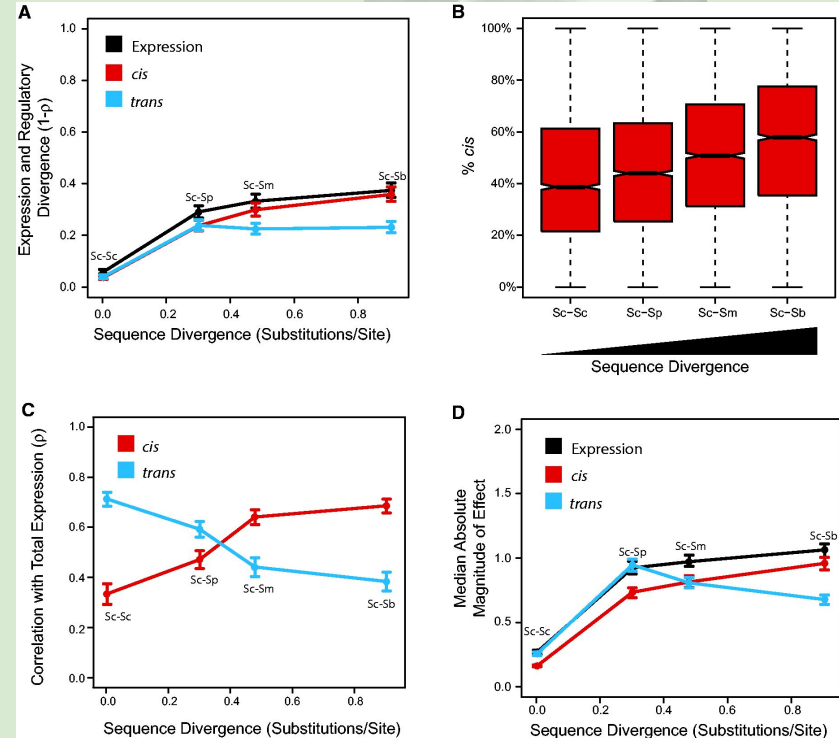
Regulatory changes and divergence of expression

- How much do *cis*- versus *trans*-regulatory elements affect the divergence of expression within and between species?
- Often large changes have been attributed to *trans*-regulatory elements. (Witkopp et al. 2004)



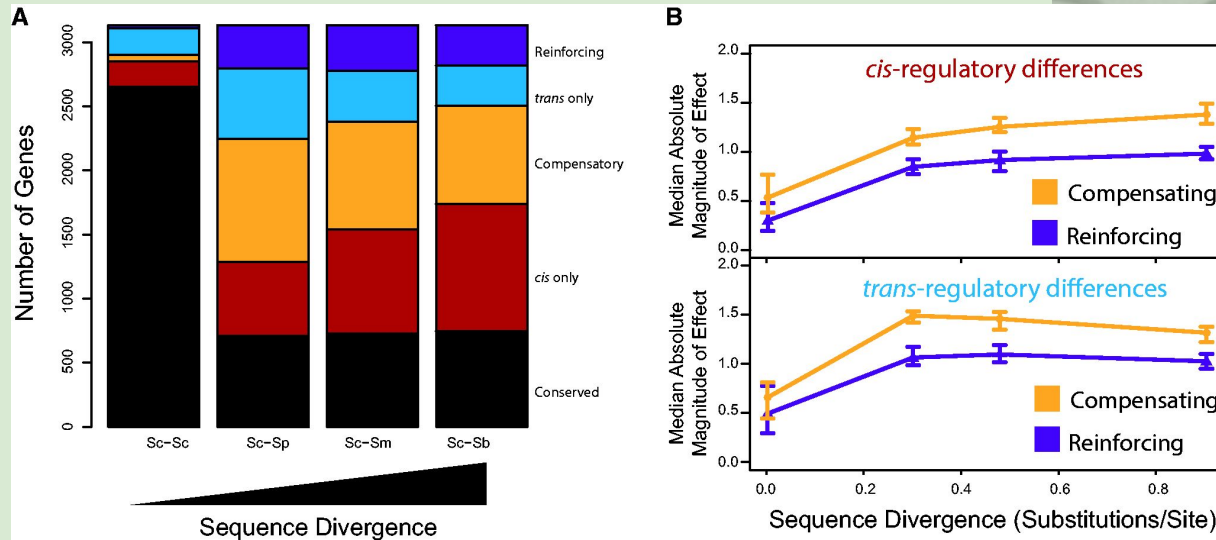
Metzger et al. say otherwise

- Two different types of *S. Cerevisiae* and three other types of *Saccharomyces*.
- Less *trans*-divergence, less *trans*-correlation.



Compensatory and Reinforcing

The differences in regulation of genes between less and more diverse sequences

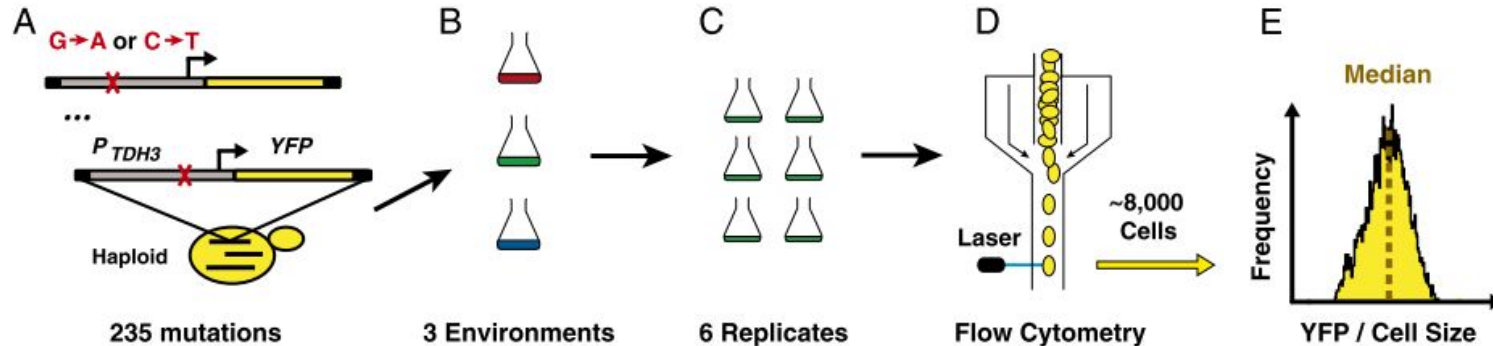


What about *trans-trans* compensation

- The calculation of divergence for *trans*-regulatory elements might be insufficient.
- This may downplay the role of changes due to *trans-trans* compensation.
- More sequence divergence also means more incompatibility.

Phenotypic plasticity

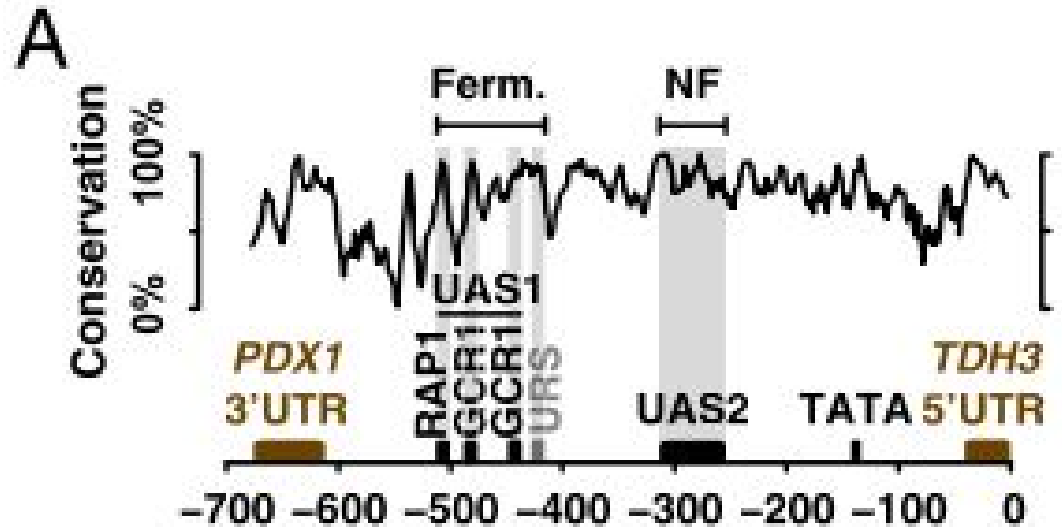
- *S. cerevisiae*
- Haplotype network
- Gene-by-environment



Duveau *et al.*, 2017 with glucose, galactose, or glycerol

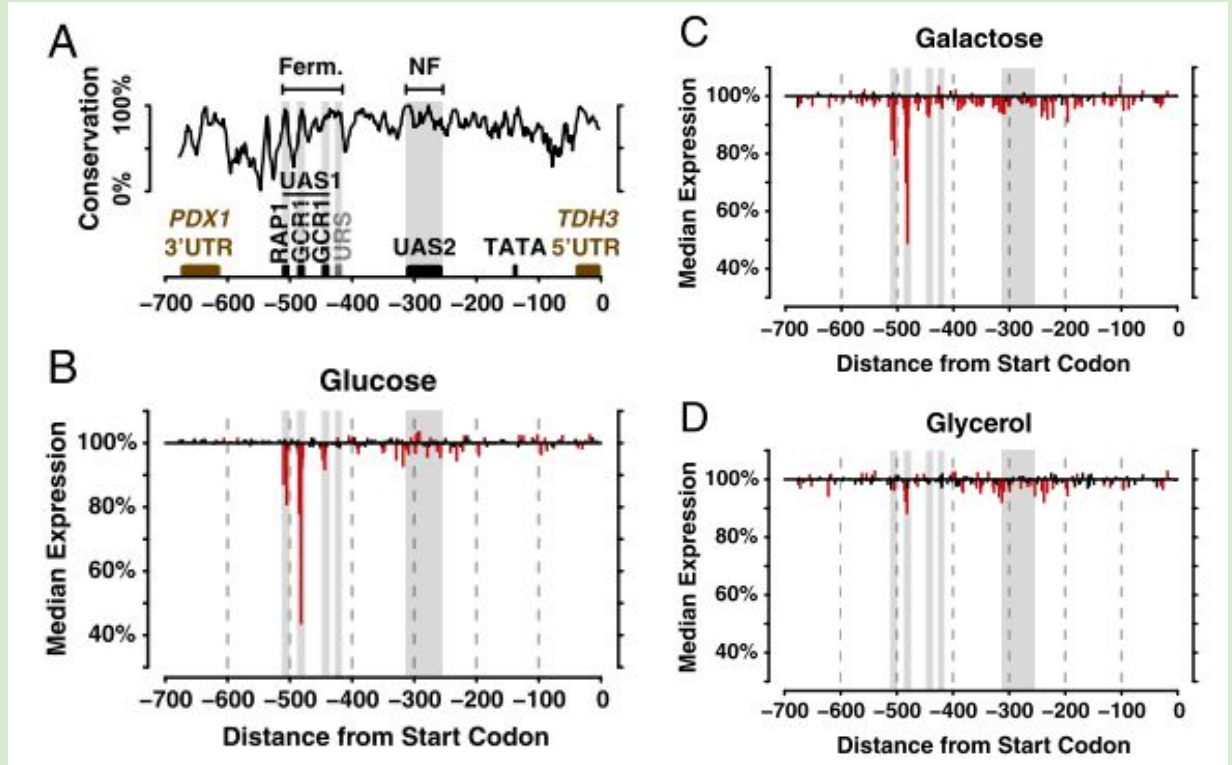
TDH3 promoter

- TDH3
- *Cis*-regulatory region
- RAP1
- GCR1
- UAS1
- UAS2



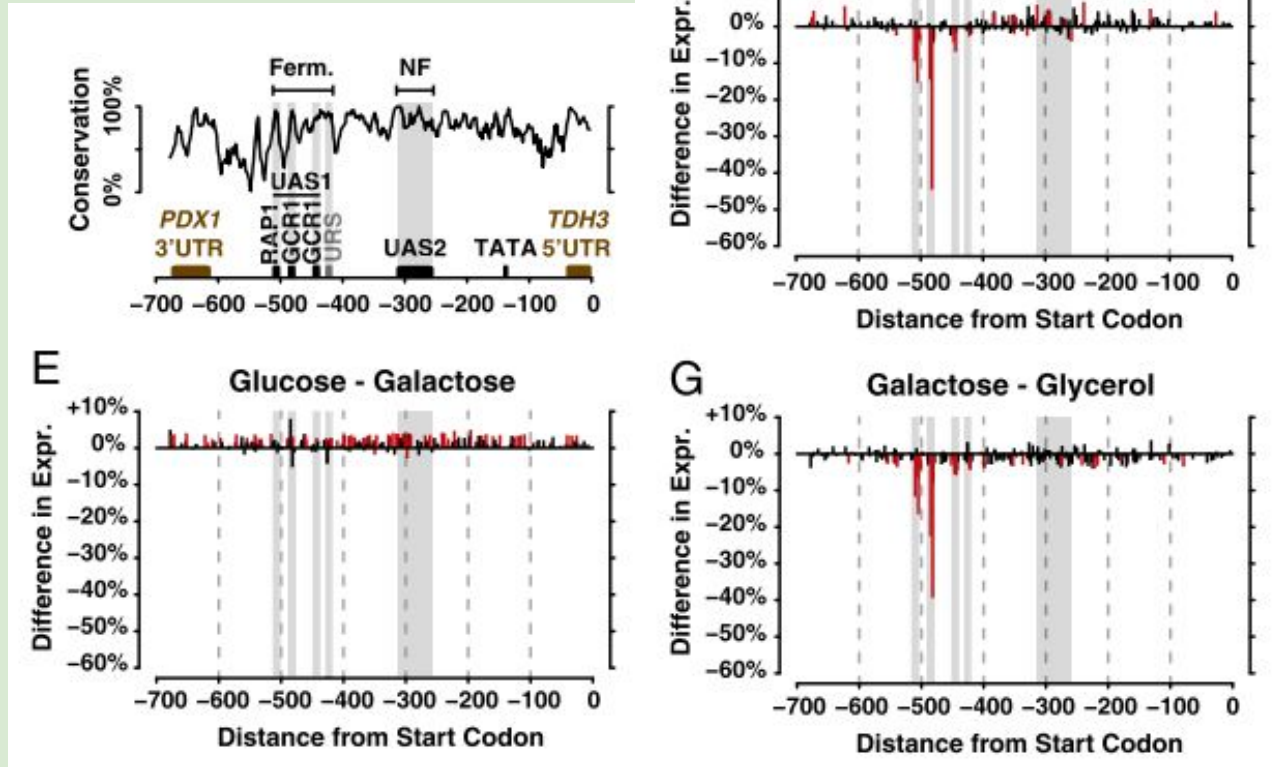
Effect of mutations

- USA1
 - Not limited
- USA2
 - Larger functional region
 - Not limited



Differences in mutational effects

- More widespread environment-specific chromatin structure
- Nucleosome-free region



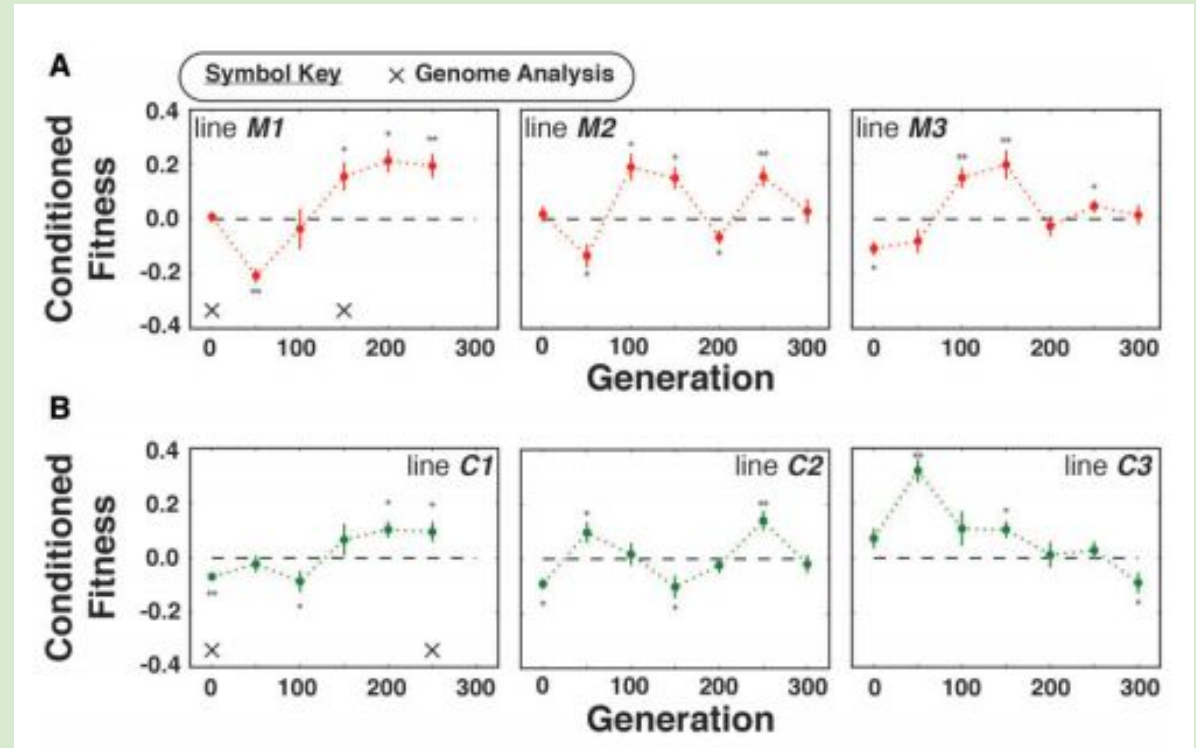
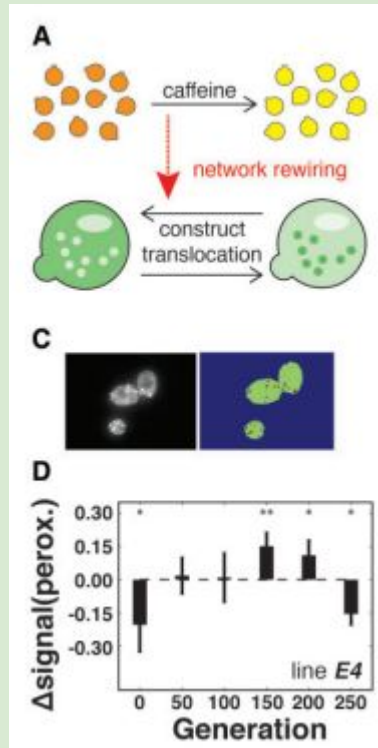
Conclusions

- Adaptive prediction can arise in yeast over short evolutionary time scales under specific conditions.
- *Cis*-regulatory elements are responsible for a larger part of divergence of regulation than *trans*-regulatory elements.
- Condition-dependent use of transcription factor binding sites regulates different TDH3 expressions.

Thank you for your attention
Are there any questions?



López García de Lomana *et al.* 2017



Metzger et al figure 3

