Resolving noise-control conflict by gene duplication

Michal Chapal, Sefi Mintzer, Sagie Brodsky, Miri Carmi and Naama Barkai

Department of Molecular Genetics, Weizmann Institute of Science, Rehovot, Israel

Abstract

Background - Gene duplication promotes adaptive evolution in two main ways: allowing one duplicate to evolve a new function, and splitting ancestral functions between the duplicates. The second scenario may resolve adaptive conflicts that can rise when one gene performs different functions. In an apparent departure from both scenarios, low-expressing transcription factor duplicates commonly bind to the same DNA motifs and act in overlapping conditions.

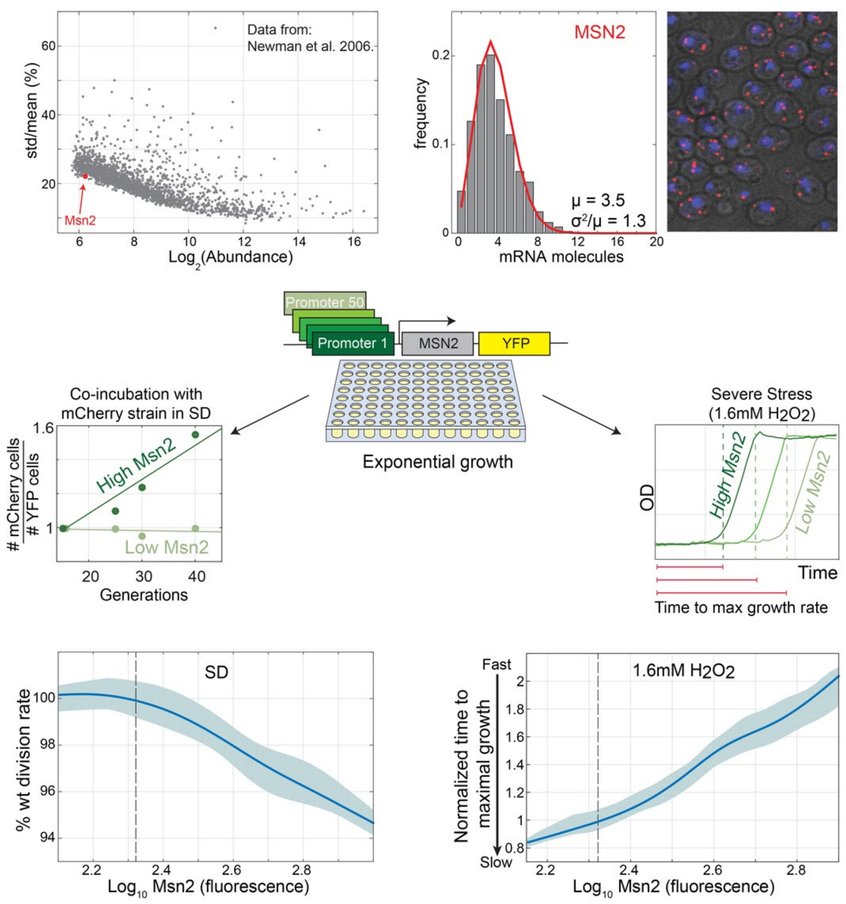
Motivation - Characterize the evolutionary forces and the possible benefits of the apparent duplicated TFs redundancy.

Strategy - We focused on Msn2 and Msn4, a pair of duplicated TFs which drives the general stress response in yeast. We studied their function and regulation.

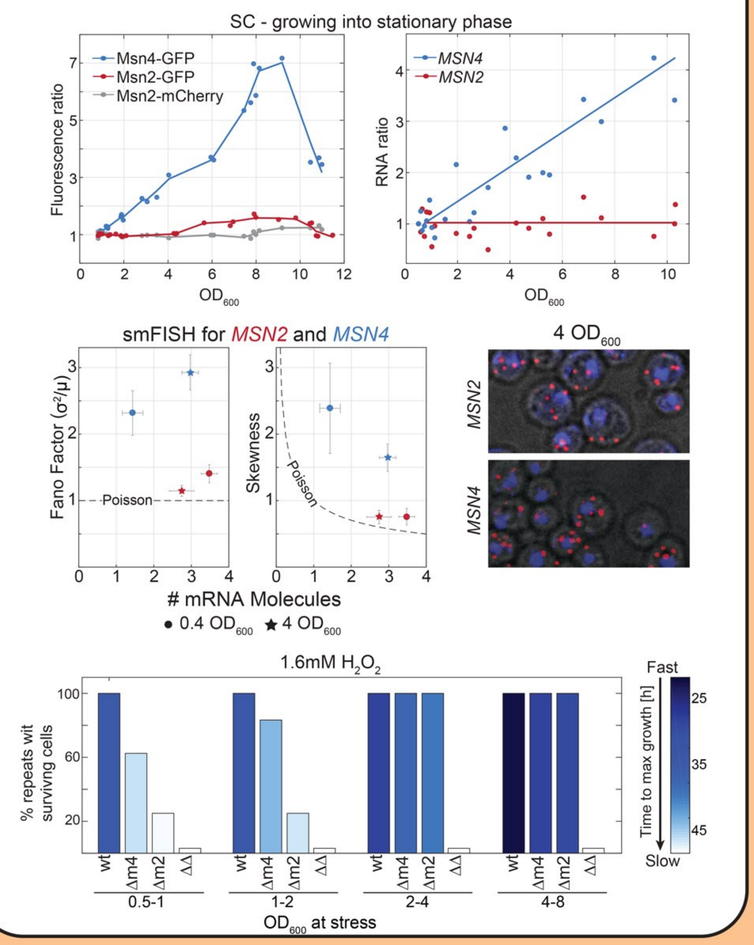
Results

- Msn2,4 function as one unit by inducing the same set of target genes in overlapping conditions.
- The two-factor composition allows this unit's expression to be both environmental-responsive and with low-noise, resolving an adaptive conflict that limits expression of single genes.

1. Low-noise tuning in Msn2 expression is adaptive and beneficial.

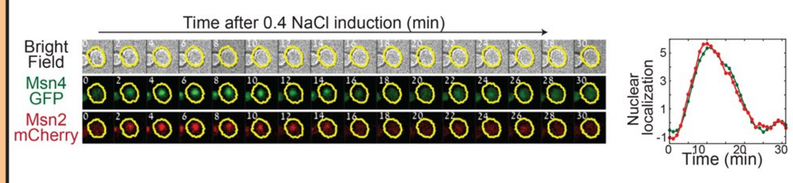


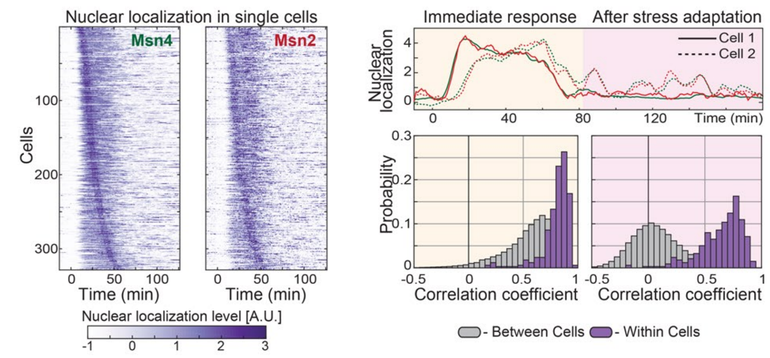
2. Msn4 expression is environmental-sensitive and of high noise.



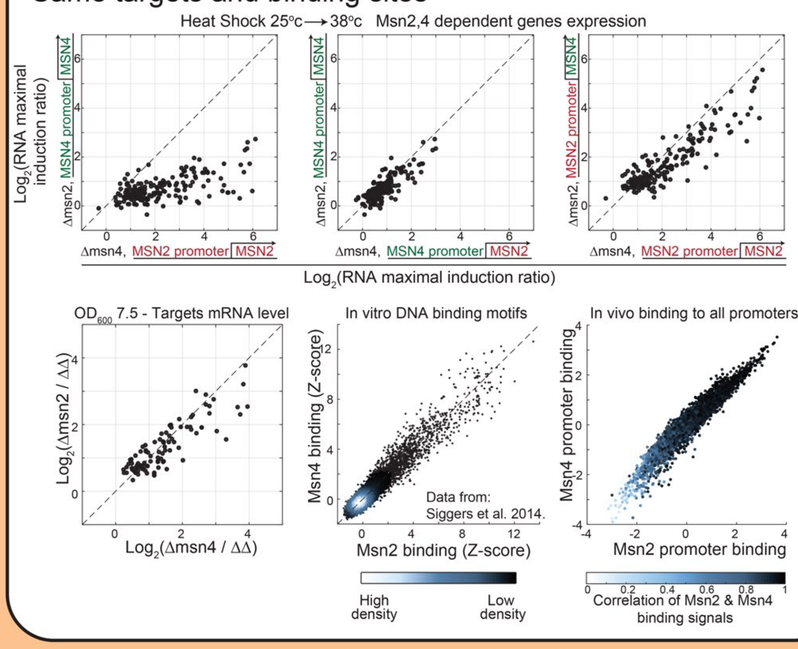
3. Redundancy in Msn2 and Msn4 activity.

Msn2 & Msn4 Co-localize to the nucleus

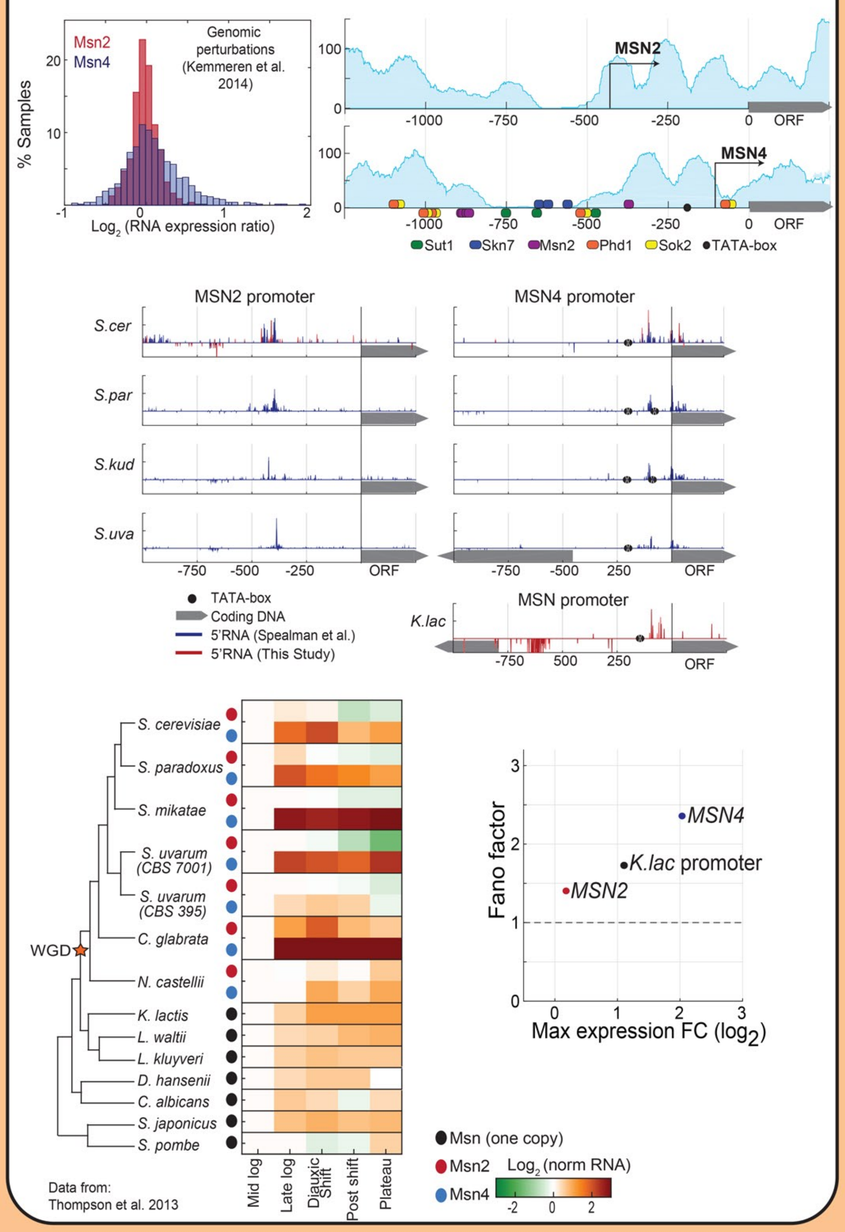




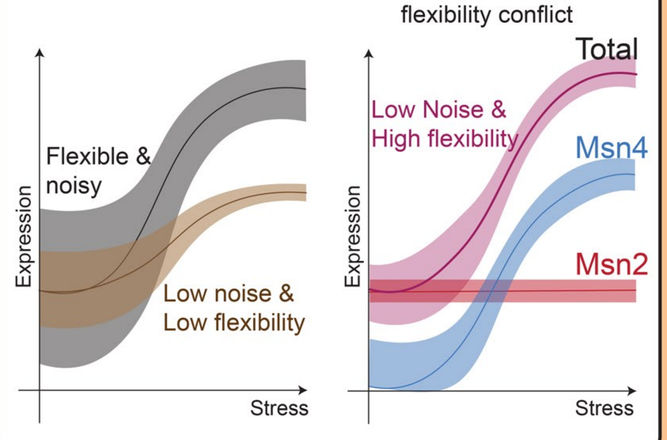
Same targets and binding sites



4. Msn2 shifted its TSS and gained a stable expression pattern after duplication.



5. Model



Conclusions

Msn2,4 function as one unit to regulate stress response genes: the two paralogs are translocated to the nucleus with the same kinetics, bind and regulate the same set of target genes, and contribute additively to stress-protection.

Msn2,4 differ in their expression characteristics: Msn2 provides the low-noise basal expression, whereas Msn4 is induced when additional amounts are needed.

Msn2,4 duplication solved an adaptive conflict by providing low-noise, yet highly flexible expression, that cannot be achieved with one promoter.