

# Natural selection on *cis* and *trans* regulation in yeasts

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## Abstract

Gene expression is regulated both by *cis* elements, which are DNA segments closely linked to the genes they regulate, and by *trans* factors, which are usually proteins capable of diffusing to unlinked genes. Understanding the patterns and sources of regulatory variation is crucial for understanding phenotypic and genome evolution. Here, we measure genome-wide allele-specific expression by deep sequencing to investigate the patterns of *cis* and *trans* expression variation between two strains of *Saccharomyces cerevisiae*. We propose a statistical modeling framework based on the binomial distribution that simultaneously addresses normalization of read counts derived from different parents and estimating the *cis* and *trans* expression variation parameters. We find that expression polymorphism in yeast is common for both *cis* and *trans*, though *trans* variation is more common. Constraint in expression evolution is correlated with other hallmarks of constraint, including gene essentiality, number of protein interaction partners, and constraint in amino acid substitution, indicating that both *cis* and *trans* polymorphism are clearly under purifying selection, though *trans* variation appears to be more sensitive to selective constraint. Comparing interspecific expression divergence between *S. cerevisiae* and *S. paradoxus* to our intraspecific variation suggests a significant departure from a neutral model of molecular evolution. A further examination of correlation between polymorphism and divergence within each category suggests that *cis* divergence is more frequently mediated by positive Darwinian selection than is *trans* divergence.

## Footnotes

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