

## SYSTEMS BIOLOGY OF GENETIC INTERACTIONS IN YEAST

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To what extent and why do the effects of mutations depend on the genetic background? What is the mechanistic basis of epistatic interactions between genes and how does it depend on the environment? Answers to these questions are relevant not only to functional genomics, but also to problems such as the evolution of mutational robustness and how deleterious mutations are eliminated from the population. Understanding the nature of epistasis in a systematic way has been hindered until recently by the presence of a huge number of gene combinations that could potentially interact. Recent developments in functional genomics now enable the mapping of genetic interactions in the model organism *Saccharomyces cerevisiae* at an unprecedented rate. At the same time, advances in computational systems biology provide a framework for simple *in silico* genetic experiments and interpretation of experimental results and hence pave the way for a mechanistic understanding of epistasis. In this presentation, we will ask i) how accurately genetic interactions can be predicted by genome-scale computational models of yeast metabolism, ii) to what extent genetic interactions depend on the environment and how they evolve, and iii) how high-throughput data on mutant phenotypes can be utilized to systematically improve the metabolic model and generate new hypotheses.