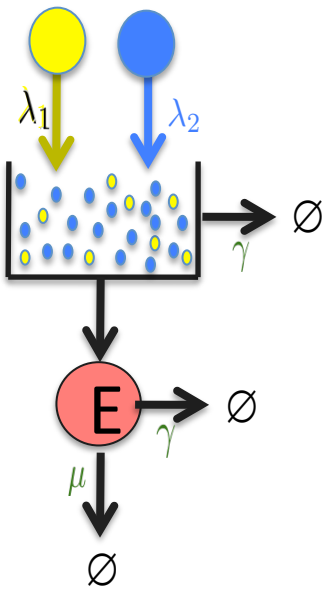
QUEUEING UP FOR ENZYMATIC PROCESSING

THEORY



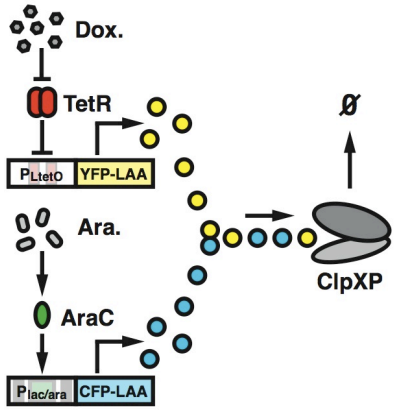
A major challenge for systems biology is to deduce the interactions that underlie correlations observed between concentrations of different molecular species inside a cell. Of particular interest is obtaining an understanding of such effects when biochemical pathways share common elements that are limited in capacity.

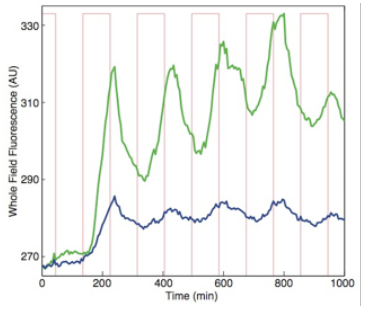
In this project, we used a stochastic model and accompanying experiments to explore correlations between expression levels of proteins degraded by a common enzyme.

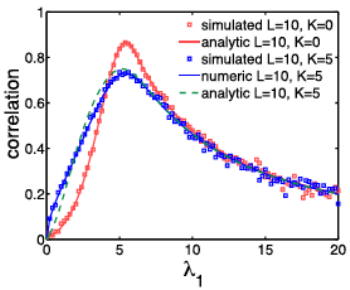
Analysis of the stochastic model predicted a significant increase in correlations as the system transitions from having excess capacity to being overloaded: a type of correlation resonance.

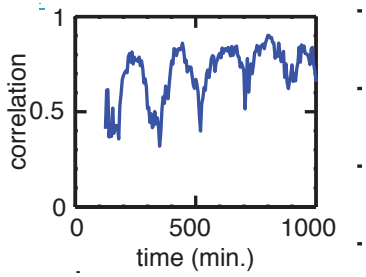
Experiments inspired by the theory were conducted with a synthetic genetic network in E. Coli using the enzymatic degradation machinery of ClpXP. Consistent with expectations from the theory, dynamic modulation of the production rate of one protein effected a response in the level of the other protein.

EXPERIMENT









References

1. Correlation Resonance Generated by Coupled Enzymatic Processing, W. H. Mather, N. A. Cookson, J. Hasty, L. S. Tsimring and R. J. Williams, Biophysical Journal, 99 (2010), 3172-3181.

2. Queueing up for enzymatic processing: correlated signaling through coupled degradation, N. A. Cookson, W. H. Mather, T. Danino, O. Mondragon-Palomino, R. J. Williams, L. S. Tsimring and J. Hasty, Molecular Systems Biology 7:561 (2011).