



Life Engineering Symposium


University of California, San Francisco, Mission Bay Campus - August 19-20, 2005

Engineering the Outputs

Re-wiring Metabolic Circuitry

Edward M. Marcotte

Associate Professor, Center for Systems and Synthetic Biology, Department of Chemistry and Biochemistry, & Institute for Cellular and Molecular Biology
University of Texas

Please click on the link above to watch the presentation – both slides and audio. This presentation file (noted by ) require the [Flash Player](#), available free online.

Abstract:

Metabolic enzymes control cellular metabolite concentrations dynamically in response to changing environmental and intracellular conditions. This real-time enzymatic feedback regulation suggests that the global metabolome should sample distinct dynamic steady states, forming “basins of stability” in the energy landscape of possible metabolite concentrations and enzymatic activities. I’ll describe our preliminary attempts to characterize these dynamic steady states using a combination of metabolite, protein and transcriptional profiling, as well as experiments to drive the cell to distinct states *via* modifying the metabolic network. We characterize three distinct dynamic steady states of the yeast metabolome that form in response to perturbing the synthesis of the universal methyl donor *S*-adenosylmethionine (AdoMet). Conversion between these states is driven by precise changes—either the replacement of serine with glycine+formate in the media, the loss of feedback inhibition control by the metabolic enzyme Met13, or both. The latter causes abnormal accumulation of methionine and AdoMet, accompanied by dramatic global compensatory changes in the metabolome, including differences in amino acid and sugar metabolism, and possibly in the global nitrogen balance, ultimately leading to a G1/S phase cell cycle delay. Global changes in the metabolome are not necessarily accompanied by global changes in the transcriptome, and metabolite-controlled post-transcriptional regulation of metabolic enzymes is clearly evident.