

Patrick F. SuthersLaboratory of John Yin
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University of Wisconsin-Madison***Modeling the regulation of ribosomal
synthesis: in vivo insights from in vitro data*****Abstract:**

All living cells depend on energy-rich nutrients to grow and maintain their essential functions. The molecular mechanisms by which their metabolic and biosynthetic functions are coordinated and controlled, particularly in response to changes in the availability of nutrients, are not fully understood. In vitro experiments that elucidate fundamental biochemical interactions often have to be performed under non-physiological conditions. The construction of mechanistic mathematical models can enable a comparison of in vitro and in vivo data that lead to new insights. We demonstrate this approach by examining the transcription of ribosomal RNA in *Escherichia coli*. Unlike traditional transcription regulation by protein activators or repressors that bind DNA, the ribosomal promoters are modulated by the levels of small-molecule effectors that interact with RNA polymerase. Parameter estimation and local sensitivity analysis were performed and highlighted the need for precise measurements of key steps. We also generated various candidate models for activities of the protein factor DksA. The rival models were compared using relative posterior probabilities that penalized overparameterization. We compare the model with experimental data for cells responding to changes in the environment such as amino acid starvation or shifts to higher nutrient content. These data demonstrate both a fast and slow response, the latter of which the model is only able to capture once translation is incorporated. The model also suggests further experiments which can improve its predictive capability.

**Tuesday, February 22nd, 2005
4:00 p.m.**Genetics/Biotechnology Center Auditorium
425 Henry Mall