Northeastern University
College of Engineering

Please join us for a
Special Chemical Engineering Seminar

Wednesday, February 19, 2014
320 Shillman Hall
11:45 a.m. – 1:00 p.m.

"Using Dynamical Measurements and Kinetic Models to Yield Biological Insights in Gene Regulation"

NARENDRA MAHESHRI, Ph.D.

Assistant Professor, Department of Chemical Engineering
Massachusetts Institute of Technology

ABSTRACT

Genetic regulatory networks play a central role in cellular information processing. Both the understanding of their dynamics and function and the engineering of even small gene circuits with predictive behavior are major goals of systems and synthetic biology. Bottom-up approaches to this problem rely on models of single genes and recurring network motifs embedded within the larger network. We have been particularly interested in whether common equilibrium thermodynamic models of gene expression are even sufficient to *qualitatively* predict the dynamics of single genes and simple gene networks. I describe several examples in budding yeast using synthetic gene circuits that suggest this is not the case. Second, I will discuss the importance of accounting for the fact that gene expression is an inherently stochastic process, with potentially large number fluctuations in associated chemical species. This "noise" in gene expression can lead to paradoxical consequences. Furthermore, predictions from stochastic kinetic models depend on the statistics of this noise. We are finding that the large population variability seen at the mRNA level, which has previously been attributed to random and intermittent periods of promoter activity, is largely driven by a heretofore unappreciated cell-cycle dependent difference in transcription before and after DNA replication. This may be essential to consider in future models that aim to predict the behavior of natural or synthetically engineered gene networks. Understanding its mechanistic basis may open new connections between replication, chromatin, and gene expression. The inadequacy of current models is just one reason why engineering synthetic regulatory networks with prescribed dynamical behavior is challenging. Tuning such networks by introducing genetic variability has proven to be an effective engineering strategy. Similar approaches are taken for metabolic and signaling networks. I'll briefly describe our efforts in developing a method to selectively mutagenize multiple genes *in vivo*. This method could be applied for the directed evolution of any multigenic phenotype or behavior.

BIOGRAPHY: Dr. Maheshri holds a PhD in Chemical Engineering from the University of California, Berkeley and is currently heading up a research group at MIT that conducts fundamental studies aimed at understanding the in vivo dynamics of eukaryotic gene expression and regulation using budding yeast as a model organism.

Refreshments will be served.