"Engineering Gene Networks: Integrating Synthetic Biology & Systems Biology"

J.J. Collins
Center for BioDynamics and Dept. of Biomedical Engineering Boston University

Many fundamental cellular processes are governed by genetic programs which employ protein-DNA interactions in regulating function. Owing to recent technological advances, it is now possible to design synthetic gene regulatory networks, and the stage is set for the notion of engineered cellular control at the DNA level.

Theoretically, the biochemistry of the feedback loops associated with protein-DNA interactions often leads to nonlinear equations, and the tools of nonlinear analysis become invaluable. In this talk, we describe how techniques from nonlinear dynamics and molecular biology can be utilized to model, design and construct synthetic gene regulatory networks. We present examples in which we integrate the development of a theoretical model with the construction of an experimental system. We also discuss the implications of synthetic gene networks for biotechnology, biomedicine and biocomputing. In addition, we present integrated computational-experimental approaches that enable construction of first-order quantitative models of gene-protein regulatory networks using only steady-state expression measurements and no prior information on the network structure or function. We discuss how the reverse-engineered network models, coupled to experiments, can be used: (1) to gain insight into the regulatory role of individual genes and proteins in the network, (2) to identify the pathways and gene products targeted by pharmaceutical compounds, and (3) to identify the genetic mediators of different diseases.