NIMBioS Seminar

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"Programming Gene Regulation:

From Synthetic Gene Networks to Cell Differentiation"

Synthetic gene networks can be constructed from bottom up with desired properties. However, constructing predictable gene networks with desired functions remains a challenge. It is because of unpredictability of the assembled networks and the lack of well-characterized components.

Here I present the bottom-up and diversity-based approaches that combine promoter synthesis and mathematical modeling to quickly construct gene networks with desired properties. In the bottom-up approach, a hybrid promoter is engineered to allow the study of gene regulation under increasingly complex conditions. We develop a stochastic model that quantitatively captures the means and distributions of the expression from the engineered promoter, and show that the model can be extended to reveal some counterintuitive predictions that are confirmed experimentally. In the diversity-based approach, promoters with random strength diversities are synthesized and characterized in parallel. When coupled with mathematical modeling to simulate the network at a whole system level, promoters that are optimal for the intended functions can be selected before the actual network assembly, without the need for post-hoc modifications. This approach will first be demonstrated in yeast by constructing negative feedforward loop networks. Then the method will be used to produce a synthetic gene network that acts as a timer, tunable by component choice. We utilize this network to control the timing of yeast flocculation phenotype, to illustrate a practical application of our approach. The construction of a synthetic cellular counter will also be presented.

Finally, ongoing research on gene regulation networks that are responsible for cell fate determination will be presented. Stem cell differentiation from a pluripotent state to one of many different cell fates is a very important biological manifestation of *multistability*, the property of having two or more mutually exclusive states over time. Recent works have indicated that this multistability arises from inherently nonlinear dynamical systems. We develop the algorithm to screen for highly connected transcription factor regulation networks that show several stable steady states. Such networks are studied in detail to uncover design principles of gene regulation and roles of stochasticity in cell differentiation. Potential construction of synthetic biology prototypes will also be discussed.

Date: Thursday, January 28, 2010

Location: 223-224 University Center

Time: Refreshments will be served at 1:00pm and Seminar at 1:15pm