



Colloquium

*Mechanical Engineering Lecture in
Controls, Instrumentation, and Robotics*

Control Theory for Synthetic Biology: From Fundamentals to Application



Domitilla Del Vecchio

Assistant Professor, Department of Mechanical Engineering
Massachusetts Institute of Technology

Friday October 13, 4:00PM, 3-270

Synthetic biology has tremendous potential for tackling pressing societal problems from energy, to environment, to medicine. The success of the field hinges on the critical ability to design genetic circuits that perform as intended once interacting with each other inside the cell. Today, this ability is still largely missing. Genetic circuits rarely perform as specified because they are poorly robust to context: a circuit's input/output behavior is affected by surrounding systems, in ways that can be very subtle.

In this talk, I will take a control theoretic approach to this lack of robustness and describe a mathematical framework, along with experimental validations, to predict and mitigate effects of context-dependence. I will address two main sources of context-dependence: direct connectivity of a circuit module to other systems and competition among different circuit modules for limited cellular resources, focusing mostly on the latter problem. In particular, I will propose a decentralized feedback control approach for decoupling circuit modules from the effects of resource competition. A key element of this strategy is a quasi-integral controller to reject disturbances. With this controller, experiments confirm mitigation of the effects of resource competition on genetic circuits in mammalian cells. Finally, I will transition to application and introduce our preliminary work towards establishing a control theoretic framework for gene-based stem cell reprogramming. Overall, our results contribute to the progress of synthetic biology by aiding designs that are sufficiently robust for practical use.