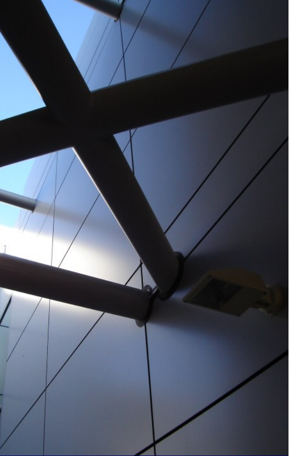

MECHANICAL ENGINEERING

DISSERTATION DEFENSE

The Department of Mechanical Engineering presents:

The Ph.D. Dissertation Defense of

Christian Cuba

Tuesday, May 23, 2017, 12-2PM
in Winston Chung Hall 205/206

The application of feedback control theory in synthetic biology

Doctor of Philosophy, Graduate Program in Mechanical Engineering
University of California, Riverside, May 2017
Dr. Elisa Franco, Chairperson

Synthetic biology promise to provide solution to many challenges in energy, agriculture, and health by reprogramming cells to execute new tasks in the host organism. In order to do that, it requires (1) the understanding of the design principles that underlie complex dynamics in biology, (2) the development of computational tools that support the identification those principles and (3) the use of those principles and computational tools to guide the experimental implementation of novel biomolecular programs. The main motivation of this thesis is to describe my current progress and future plans to expand (1)-(3).

We incorporate a new design principle, known as ultrasensitivity response, to design robust biomolecular dynamical system. We show that molecular titration in the context of feedback circuits enhance the emergence of oscillations and bistable behavior in the parameter space. We also propose and analyze a new molecular network, termed Brink motif, which exhibits an ultrasensitive input-output response similar to a zero-order ultrasensitive switch. We discuss the Brink motif in the context of robust feedback circuits as a suitable mechanism to build (1) reliable circuits, oscillatory and bistable dynamical behaviors, under parameters uncertainty, downstream load effects and shared resources and (2) robust closed loop controllers that overcome the limitation of unidirectional action controllers. Ultrasensitivity is achieved by combining molecular titration and an activation/deactivation cycle and requires fast titration and switching rates. Additionally, the response of the Brink motif has a precisely tunable threshold, which can be determined by an external input to the motif. We assess the robustness of feedback circuits with numerical simulations and mathematical analysis.