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Title: Context dependence of biological circuits: Predictive models and engineering solutions

Abstract: Engineering biology has tremendous potential to impact applications, from energy, to environment, to health. As the sophistication of engineered biological circuits increases, the ability to predict system behavior becomes more limited. In fact, while a system's component may be well characterized in isolation, its salient properties often change in surprising ways once it interacts with other systems in the cell. This context-dependence of biological circuits makes it difficult to perform rational design and leads to lengthy, combinatorial, design procedures where each component is re-designed ad hoc when other parts are added to a system. In this talk, I will overview some causes of context-dependence. I will then focus on problems of resource loading and describe a design-oriented mathematical model that accounts for it. I will introduce a general engineering framework, grounded on control theoretic concepts, that can serve as a basis for creating devices that are "insulated" from context. Example devices will be introduced for both bacterial and mammalian genetic circuits. These solutions support rational and modular design of sophisticated genetic circuits and can serve for engineering biological circuits that are more reliable and predictable.