Mammalian synthetic biology by controller design

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SPEAKER

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Abstract: The ability to reliably engineer the mammalian cell will impact a variety of applications in a disruptive way, including cell fate control and reprogramming, targeted drug delivery, and regenerative medicine. However, our current ability to engineer mammalian genetic circuits that behave as predicted remains limited. These circuits depend on the intra and extra cellular environment in ways that are difficult to anticipate, and this fact often hampers genetic circuit performance. This lack of robustness to poorly known and often variable cellular environment is the subject of this talk. Specifically, I will describe control engineering approaches that make the performance of genetic devices robust to context. I will show a feedforward controller that makes gene expression robust to variability in cellular resources and, more generally, to changes in intra-cellular context linked to differences in cell type. I will then show a feedback controller that uses bacterial two component signaling systems to create a quasi-integral controller that makes the input/output response of a genetic device robust to a variety of perturbations that affect gene expression. These solutions support rational and modular design of sophisticated genetic circuits and can serve for engineering biological circuits that are more robust and predictable across changing contexts.