Cracking the Complexity of Circuit-Host Interactions to Design Robust and Predictable Gene Circuits

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Abstract: Failure of modularity remains a significant challenge for assembling synthetic gene circuits with tested modules as they often do not function as expected. Hidden circuit-host interactions, such as growth feedback and resource competition, could significantly impair intended circuit function but are often overlooked. In this presentation, I will discuss our latest research to use mathematical modeling to quantitatively understand and predict the impact of network topology, host physiology, and resource competition on the functional behaviors of gene circuits. First, we will discuss how the interference of synthetic gene circuit function by growth feedback depends on circuit network topology and nutrient level. Second, we will demonstrate how resource competition redirected desired successive cell fate transitions following a 'winner-takes-all' rule. Third, we will highlight our control strategies against resource competition, including a division of labor using microbial consortia, and negatively competitive regulation (NCR) controllers. Lastly, we will discuss the effects of resource competition on circuit noise behavior. Overall, our work will help us in the understanding and control of circuit-host interactions toward engineering robust synthetic gene circuits.