Biological Design Doctoral Defense

Emergent dynamics arising from the feedback between synthetic gene circuit and host cell growth

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Abstract

The mutual inhibition between synthetic gene circuits and cell growth produces growth feedback in the host-circuit system. Previous studies have demonstrated that the growth feedback has an marked impact on the molecular dynamics of the host-circuit system. However, the complexity of the growth feedback effect is not fully understood. A theoretical framework was developed to study the dynamics of the coupling between growth feedback and synthetic gene circuits. The study's results reveal three major points about the impact of growth feedback. First, a nonlinear emergent behavior mediated by growth feedback. The unexpected behavior depends on the dynamic ribosome allocation between gene circuit expression and host cell growth. Second, the emergence and loss of unexpected qualitative states on the host-circuit system generated by ultrasensitive growth feedback. Third, the growth feedback-induced cooperativity behavior in synthetic gene modules competing for resources. In addition, growth feedback attenuated the winner-takes-all rules on resource competition between the two self-activating modules. These results demonstrate that growth feedback plays an important role in the host-circuit system's molecular dynamics. Characterizing general principles from the effect of growth facilitates the ability to minimize or even harness unexpected gene expression behaviors derived from the effect of growth feedback.

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