149f A Synthetic Gene-Metabolic Oscillator

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The *de novo* design approach in metabolic and gene circuits has provided a means to understanding and exploring complex biological behavior. In particular, autonomous oscillation, one of the most intriguing dynamics that occur at all levels in nature, has received much attention. While previous synthetic bio-oscillators were designed to function independently of metabolism, we aim to build an integrated gene-metabolic oscillator that resembles the natural biological oscillators.

Here we report the design and construction of a synthetic gene-metabolic oscillator in *Escherichia coli K12*. The circuit exploits the components of the acetate pathway but utilizing artificially rewired control loops. The system oscillates spontaneously when the glycolytic rate exceeds a critical value, where Hopf bifurcation occurs. On the other hand, the oscillation may be suppressed by addition of external acetate. Both of these control aspects are predicted mathematically and verified experimentally. Successful construction of this simple yet non-trivial oscillator demonstrates the importance of metabolism in regulation of cellular dynamics.