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Growth induced instability in metabolic networks[1] SIDHARTHA GOYAL, Joseph Henry Laboratories of Physics, Princeton University, NED S. WINGREEN, Department of Molecular Biology, Princeton University — Networks of molecular interactions are essential for mass, energy, and information transport into and within cells. Thus, understanding the emergent physical properties of various network architectures is of fundamental interest in biology. One such architecture, product-feedback inhibition is widely used in the regulation of biosynthetic pathways of all organisms. Importantly, these biosynthetic pathways are often coupled both by the use of a common substrate and by stoichiometric utilization of their products for cell growth. We analyze networks having the following three essential features: all branches start from a common substrate, the product of each branch inhibits the first dedicated step towards its synthesis, and all products are essential for growth. We show that such a coupled network can have at most one steady state. However, the network may be unstable about this steady state, even if the branches are individually stable. In the unstable region, the network exhibits limit-cycle oscillations which arise via a Hopf bifurcation. In the oscillating regime, a two-branch coupled network can be mapped to a three-species frustrated system. Our results highlight new design principles essential for realizing robust biosynthetic pathways.

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