MAR09-2008-000179

Abstract for an Invited Paper
for the MAR09 Meeting of
the American Physical Society

Synthetic rescues and spontaneous cascades in metabolic networks[1]

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Using *in silico* experiments, I will show that organisms evolving to maximize growth rate, ATP production, or any other linear function of metabolic fluxes tend to significantly reduce the number of active metabolic reactions compared to typical non-optimal states. The reduced number appears to be constant across the microbial species studied and just slightly larger than the minimum number required for the organisms to grow at all. I will show that this massive reaction silencing is triggered by the irreversibility of a large fraction of the metabolic reactions and propagates through the network as a cascade of inactivity. Following these observations, I will introduce a network method to recover the loss of metabolic function due to mutations and other defects, which is based on bypassing rather than correcting the defective pathways. In particular, I will present predictions of *synthetic recovery*, in which the knockout of one enzyme-coding gene results in a non-viable phenotype while the concurrent knockout of a second enzyme-coding gene restores viability. In addition to their potential role in metabolic engineering and medical research, these results have puzzling implications for the recently observed temporary activation of latent pathways.

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