Optimal regulatory strategies for metabolic pathways in Escherichia coli depending on protein costs.

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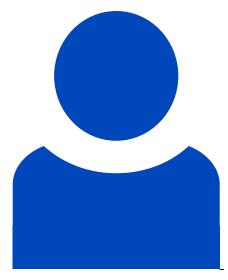
Abstract

While previous studies have shed light on the link between the structure of metabolism and its transcriptional regulation, the extent to which transcriptional regulation controls metabolism has not yet been fully explored. In this work, we address this problem by integrating a large number of experimental data sets with a model of the metabolism of Escherichia coli. Using a combination of computational tools including the concept of elementary flux patterns, methods from network inference and dynamic optimization, we find that transcriptional regulation of pathways reflects the protein investment into these pathways. While pathways that are associated to a high protein cost are controlled by fine-tuned transcriptional programs, pathways that only require a small protein cost are transcriptionally controlled in a few key reactions. As a reason for the occurrence of these different regulatory strategies, we identify an evolutionary trade-off between the conflicting requirements to reduce protein investment and the requirement to be able to respond rapidly to changes in environmental conditions.

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