How does Escherichia coli Allocate Proteome?

Background/Objective

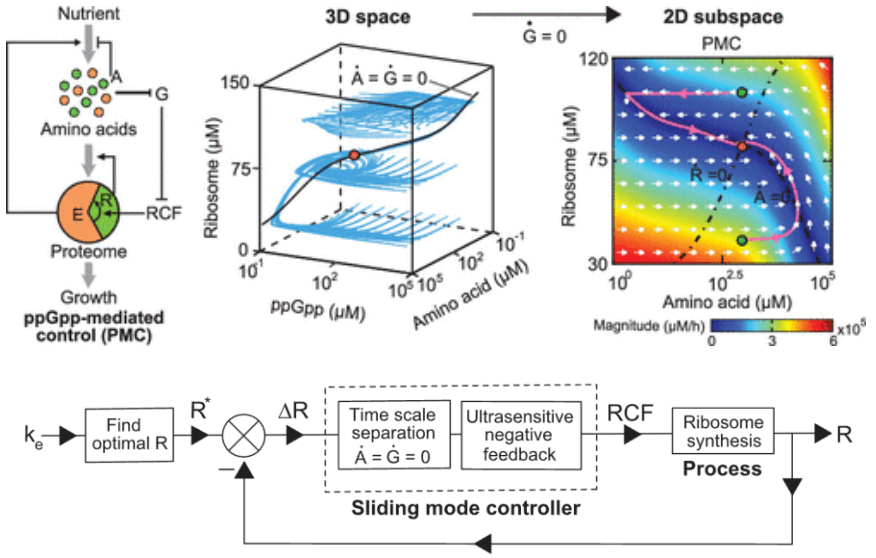
Microorganisms actively partition their cellular resources, such as proteins, for growth optimization. Recent experiments have identified some molecular components involved in partitioning; however, how the individual parts coordinate for robust and dynamic resource allocation is unclear quantitatively. Here, we developed a coarse-grained mathematical framework centered on guanosine pentaphosphate (ppGpp)-mediated regulation and used it to systematically uncover the design principles of proteome allocation in *Escherichia coli*.

Approach

We developed a minimal kinetic model of *E. coli* that focused on the central carbon flux, from extracellular nutrients to amino acids to proteins, and proteome partitions regulated by ppGpp. The model was validated with computational simulations and experimental data, and accurately predicted static and dynamic cell growth and proteome partitioning.

Results

The cell's ability to partition resources comes from a negative feedback-controlling system with zero-order amino acid kinetics and ppGpp-controlled ribosome synthesis. This mechanism, along with time-scale separation of ribosome synthesis, behaves similarly to the non-linear optimization strategy of artificial sliding mode control. Modeling investigation showed it was robust against parameter variations and molecular fluctuations, efficiently optimizing biomass production over time.



ppGpp-mediated control mimics a sliding mode control strategy.

Significance/Impacts

This work provides a mechanistic understand and control theory point of view of *E. coli* proteome allocation, thereby providing insights into quantitative microbial physiology and the design of synthetic gene networks.

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