Analysis of autocatalytic networks in biology

Gentian Buzi, Ufuk Topcu, John C. Doyle

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Background and motivation

Specific question / knowledge gap

Background and motivation

Solution

Results

Significance and broader implications

Autocatalytic networks, in particular the glycolytic pathway, constitute an important part of the cell metabolism. Changes in the concentration of metabolites and catalyzing enzymes during the lifetime of the cell can lead to perturbations from its nominal operating condition. We investigate the effects of such perturbations on stability properties, e.g., the extent of regions of attraction, of a particular family of autocatalytic network models. Numerical experiments demonstrate that systems that are robust with respect to perturbations in the parameter space have an easily "verifiable" (in terms of proof complexity) region of attraction properties. Motivated by the computational complexity of optimization-based formulations, we take a compositional approach and exploit a natural decomposition of the system, induced by the underlying biological structure, into a feedback interconnection of two input-output subsystems: a small subsystem with complicating nonlinearities and a large subsystem with simple dynamics. This decomposition simplifies the analysis of large pathways by assembling region of attraction certificates based on the input-output properties of the subsystems. It enables numerical as well as analytical construction of block-diagonal Lyapunov functions for a large family of autocatalytic pathways.

While this abstract has all the different elements of an abstract, it does not follow the hourglass structure guidelines. The specific question or knowledge gap the research aims to address is in the middle of the background/motivation section. As a result, the reader has a difficult time distinguishing whether the background/motivation that follows the question/knowledge gap is background or results. Additionally, the significance section begins more broadly in scope and follows with a more specific implication (Lyapunov functions) when it should begin more narrow in focus and end more broadly (like the hourglass).

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Glycolytic Oscillations and Limits on Robust Efficiency

Fiona Chandra, Gentian Buzi, John C. Doyle

Science
Vol. 333, Issue 6039, pp. 187-192 (2011).

Background and motivation	Both engineering and evolution are constrained by trade-offs between efficiency and robustness
Specific question / knowledge gap	, but theory that formalizes this fact is limited.
Solution	For a simple two-state model of glycolysis, we explicitly derive analytic equations for hard trade-offs between robustness and efficiency with oscillations as an inevitable side effect.
Results	The model describes how the trade-offs arise from individual parameters, including the interplay of feedback control with autocatalysis of network products necessary to power and catalyze intermediate reactions. We then use control theory to prove that the essential features of these hard trade-off "laws" are universal and fundamental, in that they depend minimally on the details of this system and generalize to the robust efficiency of any autocatalytic network. The theory also suggests worst-case conditions that are consistent with initial experiments.
Significance and broader implications (omitted)	

This abstract starts off with a strong, broad motivation, but is too vague in its statement of the specific question/knowledge gap. The statement of the authors' solution to the problem is clear and understandable by an educated, non-expert audience. The rest of the abstract, however, summarizes results but fails to put those results in context by supplying their significance and the implications of the work.

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Linear control analysis of the autocatalytic glycolysis system

Fiona Chandra, Gentian Buzi, John C. Doyle

American Control Conference, 2009.

Background and motivation	Autocatalysis is necessary and ubiquitous in both engineered and biological systems
	but can aggravate control performance and cause instability.
Specific question / knowledge gap	We analyze the properties of autocatalysis in the universal and well studied glycolytic pathway.
Solution	A simple two-state model incorporating ATP autocatalysis and inhibitory feedback control
Results	captures the essential dynamics, including limit cycle oscillations, observed experimentally. System performance is limited by the inherent autocatalytic stoichiometry and higher levels of autocatalysis exacerbate stability and performance.
Significance and broader implications	We show that glycolytic oscillations are not merely a "frozen accident" but a result of the intrinsic stability tradeoffs emerging from the autocatalytic mechanism. This model has pedagogical value as well as appearing to be the simplest and most complete illustration yet of Bode's integral formula.

This abstract is refreshingly accessible to a wide audience: it uses clear, short sentences, present tense, active verbs, and no jargon. The question / knowledge gap is indeed specific, and the authors' solution is clearly stated. Only the major results are highlighted and adequate attention is paid to the significance and broader implications of the work.

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