

Reconciling a Biochemical Switch Catalog with Network Theories of Bistability

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Abstract

What characteristics of biochemical circuits endow them with potential for bistability? There have been two key approaches to answer this question. Classical network theories, e.g., Feinberg's deficiency theorems, Craciun-Feinberg species-reaction graphs, focus on specific classes of reaction networks and provide necessary/sufficient indicators for multi-stationarity/multi-stability. Catalog-based approaches, e.g., the CSPACE bistable catalog published by Ramakrishnan and Bhalla [2008], take a bottom-up strategy and, through numerical simulation and algebraic solution of polynomial systems of equations, enumerate reaction combinations that can exhibit bistability. An interesting question is to determine how well these approaches agree and, when they do not agree, what are the situational assumptions that lead to discordance. Our contributions are three fold. First, we conduct an exhaustive comparison of the CSPACE catalog with network theories and identify many sources of discordance. Second, by studying these discordances, we highlight the diverse assumptions under which a circuit can be modeled and which would affect its stability characterization. Finally, similar in spirit to standards for model reporting, such as MIRIAM, we propose a unifying framework to capture modeling assumptions that will serve to annotate bistable biochemical networks.