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Process-driven inference of biological network structure: feasibility, minimality, and multiplicity¹

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For a given dynamic process, identifying the putative interaction networks to achieve it is the inference problem. In this talk, we address the computational complexity of inference problem in the context of Boolean networks under dominant inhibition condition. The first is a proof that the feasibility problem (is there a network that explains the dynamics?) can be solved in polynomial-time. Second, while the minimality problem (what is the smallest network that explains the dynamics?) is shown to be NP-hard, a simple polynomial-time heuristic is shown to produce near-minimal solutions, as demonstrated by simulation. Third, the theoretical framework also leads to a fast polynomial-time heuristic to estimate the number of network solutions with reasonable accuracy. We will apply these approaches to two simplified Boolean network models for the cell cycle process of budding yeast (Li 2004) and fission yeast (Davidich 2008). Our results demonstrate that each of these networks contains a giant backbone motif spanning all the network nodes that provides the desired main functionality, while the remaining edges in the network form smaller motifs whose role is to confer stability properties rather than provide function. Moreover, we show that the bioprocesses of these two cell cycle models differ considerably from a typically generated process and are intrinsically cascade-like.

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