PHENOTYPE CONTROL AND ELIMINATION OF VARIABLES IN BOOLEAN NETWORKS

A REVIEW

1. Overview

The paper under review is a well designed study of behavior of Boolean networks under a particular type of network reduction, when a node without self loop is removed from the network. In particular, first the effect of such reduction on attractors and trap spaces is examined. Second, then the effect of three different approaches to network control (attractor-based control, value propagation and control of minimal trap spaces) is examined. Both types of effects are examined for synchronous, asynchronous and generalized asynchronous update schemes.

Since the main motivation for reduction of networks is the simplification of a network that would have no (or perhaps minimal but predictable) effect on the network dynamics, the article provides a guide that informs users when they can employ such a reduction, depending on what characteristics of dynamics and/or control they are interested in. This is helped by a large number of counterexamples that illustrate how the desired goal of preservation of dynamics and control can fail.

2. Strengths

- The definition of a mediator node whose regulators are not regulating its targets, allows stronger conclusions about what is preserved during network reduction, as is shown for instance in Theorems 3.3, 4.3 and 4.9.
- The list of counterexamples is extensive and Figures are very informative.
- A nice message from the paper is that trap spaces are better behaved than attractors since they do not depend on the update scheme and they are preserved under reduction
- I found the example 4.7 very informative since when shows that if control by value propagation exists for reduction, it may not exist for the original network

3. Weaknesses

- The title can be perhaps a little more specific where instead of "and" connecting two clauses there is more specific description of the work:
  "Effect of elimination of variables in Boolean networks on phenotype control" But this is just a personal preference.

- There are two statements on page 6 close to each other that seems to say very similar things (if not, this should be explained):
  (1) In light of this latter remark, we restrict the analysis of control strategy behaviour under reduction to the removal of components that are free in the control strategy.
  (2) ... it is reasonable to limit the control strategies under consideration to subspaces that do not fix any component that is fixed in the target phenotype.
- . The concept of "linear components" on page 10 at the end of section 3.1 was defined and it was advertised that it will be used, but as far as I can tell, it was never used in the subsequent text.

4. Suggestion

The results seem to suggest that the trap spaces may be conceptually better objects than attractors, since they behave better under reductions. Trap sets (as opposed to more restricted trap spaces) have an analog in theory of dynamical systems where they are called attracting neighborhoods [1]. It is known that these sets form a lattice and that this lattice contains all the information about the global structure of the invariant sets.

Although trap spaces are natural objects in the Boolean networks, it may be that the results for persistence of trap sets under network reduction may be stronger than or the trap spaces. In particular, I am curious if lattice of trap spaces is preserved under network reduction studied in this paper.

References

[1] W.D. Kalies, K. Mischaikow, and R.C.A Vandervorst. Lattice structures for attractors I. *Journal of Computational Dynamics*, I:307–338, 2014.