



Order or chaos in Boolean gene networks depends on the mean fraction of canalizing functions

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Abstract

We explore the connection between order/chaos in Boolean networks and the naturally occurring fraction of canalizing functions in such systems. This fraction turns out to give a very clear indication of whether the system possesses ordered or chaotic dynamics, as measured by Derrida plots, and also the degree of order when we compare different networks with the same number of vertices and edges. By studying also a wide distribution of indegrees in a network, we show that the mean probability of canalizing functions is a more reliable indicator of the type of dynamics for a finite network than the classical result on stability relating the bias to the mean indegree. Finally, we compare by direct simulations two biologically derived networks with networks of similar sizes but with power-law and Poisson distributions of indegrees, respectively. The biologically motivated networks are not more ordered than the latter, and in one case the biological network is even chaotic while the others are not.

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1. Introduction

The history of Boolean networks as models for gene networks started already in 1969 with the pioneering work by Kauffman [1]. Many interesting results within the realm of theoretical biology have come, see for example the overview by Kauffman himself [2]. However, more experimentally oriented people have often viewed these studies as irrelevant to biology due to their less clear coupling to the experiments. The situation changed somewhat with the advent in the late 1990s of new measurement technologies in molecular biology, such as microarrays, two-hybrid measurements on protein–protein interactions, genome-wide data for DNA binding proteins, etc. These large-scale measurement have inspired a renewed interest in simple network models, and many different approaches have been studied [3]. The Boolean networks belong to one extreme in this spectrum, by being able to contain very large numbers of nodes but very crude in their approximation of the biology. Parts of the studies have been on the reconstruction of the Boolean nets from experimental data, and reverse engineering algorithms specially suited for inferring Boolean networks from microarray data have been developed (see Ref. [4] for an overview and Ref. [5] for a very recent example). Other studies have

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concerned dynamical properties of the networks, and revealed an even more fascinating picture of Boolean networks than provided by Kauffman [2]. For instance, the number of the attractors grows faster than any polynomial with the number of nodes [6] and not as the square-root as earlier studies had indicated.

The use of a Boolean network as a model for a gene regulatory system contains many simplifying assumptions. Most obvious is the approximation of the state of a gene to be either “on” or “off”. Although this is a questionable assumption [7], it has indeed been shown not to be without some biological relevance [8]. Another commonly used approximation, which we also utilize here, is the synchronous updating. Depending on which properties one consider, the result can be that the choice of updating schemes hardly matter [9], or that they matter substantially [10]. An overview and introduction to random Boolean networks with respect to (artificial) life can be found in Ref. [11].

Here we focus on two recent results with respect to order in Boolean nets. The first is the result by Aldana from 2003 [12,13], which showed that networks with a power-law distribution of indegrees (sometimes called “scale-free”) provided a natural robustness and needed no fine-tuning, as networks with a Poissonian indegree distribution (sometimes called Erdős-Renyi networks) did. The other result was obtained by Kauffman et al. in 2004 [14] and concerned so-called canalizing functions. They proved that a network consisting only of such functions always are stable, regardless of topology of the net. In the present article, we show numerically that the dynamical order for nets with a uniform distribution of Boolean functions can to a large extent be explained by the fraction of canalizing functions. Further, we present simulations of two finite-size networks of different sizes (30 nodes and 56 edges, and 688 nodes and 1079 edges, respectively) inferred from the ordinary baker’s yeast *Saccharomyces cerevisiae*. The results from these simulations are compared with results from networks of the same mean indegree, but with a Poissonian and power-law distribution, respectively. The mean probability for canalizing functions turns here out to be a better indicator of order than the classical result. Similar studies of finite-sized networks with various topologies have been performed in, e.g., [15,16]. However, other measures for the order were utilized, and none of these studies considered any topology that were inferred from biological experiments.

The disposition of the present paper is as follows: First, in Section 2, we have some preliminaries where we introduce concepts and measures. In Section 3, we show how the mean probability for canalizing functions explains most of the stability regions found by Aldana [12] and Aldana and Cluzel [13]. The simulations of some biologically motivated nets are presented in Section 4. Finally, in Section 5, we conclude with a discussion of the results.

2. Preliminaries

2.1. Derrida plots

We will primarily utilize Derrida plots for measuring the degree of order the Boolean networks possess. The ideas behind the Derrida plot were introduced already in 1986 [17], and it has since then become a popular tool in this area (other measures used in the literature are, e.g., types of attractors, fraction of elements that are active, and length of period, as discussed in Ref. [15]). In short, two different initial states with a Hamming distance¹ of $D(T)$ are each evolved one time-step and the new Hamming distance $D(T + 1)$ is calculated. The Derrida plot is obtained by plotting the updated distance versus the original distance, and a network is considered ordered if the updated distance is less than or equal to the original one, i.e., if $D(T + 1) \leq D(T)$. For a more detailed description of the Derrida plot see Ref. [18].

2.2. Canalizing functions

Canalizing functions are Boolean functions where at least one of the inputs has the possibility to determine the outcome uniquely, regardless of the values of the other input variables.² It has been shown that they have

¹The Hamming distance between two states is the number of positions where the two states differ.

²In Ref. [16], a canalizing function was defined as one where the canalizing input solely determines the output. We follow instead the terminology from Ref. [2].

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