Canalization in the Critical States of Highly Connected Networks of Competing Boolean Nodes

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Canalization is a classic concept in Developmental Biology that is thought to be an important feature of evolving systems. In a Boolean network it is a form of network robustness in which a subset of the input signals control the behavior of a node regardless of the remaining input. It has been shown that Boolean networks can become canalized if they evolve through a frustrated competition between nodes. This was demonstrated for large networks in which each node had $K = 3$ inputs. Those networks evolve to a critical steady-state at the boarder of two phases of dynamical behavior. Moreover, the evolution of these networks was shown to be associated with the symmetry of the evolutionary dynamics. We extend these results to the more highly connected $K > 3$ cases and show that similar canalized critical steady states emerge with the same associated dynamical symmetry, but only if the evolutionary dynamics is biased toward homogeneous Boolean functions.

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I. INTRODUCTION

Boolean networks were originally proposed as models of genetic regulatory networks and are now widely used as models of self-regulatory behavior in biological, physical, social, and engineered systems \cite{1,4}. They are designed to capture essential features of the complex dynamics of real networks by “course-graining” that assumes that dynamical state of each node is Boolean, or simply on/off \cite{5}. For example, in a model of a genetic regulatory system each node corresponds to a gene and its Boolean dynamical state refers to whether or not the gene is currently being expressed. The regulatory interactions between nodes are described by a directed graph in which the Boolean (output) state of each node is determined by a function of the states of the nodes connected to it with directed in-links. It has been shown that, despite their simplicity, Boolean networks capture many of the important features of the dynamics of real self-regulating networks, including biological genetic circuits \cite{6,9}.

Perhaps the most notable feature of Boolean networks is that they have two distinct phases of dynamical behavior. These two phases are called “frozen” and “chaotic”, and in random Boolean networks there is a continuous phase transition between them \cite{10,12}. The two phases can be distinguished by how a perturbation in the network spreads with time: in the frozen phase a perturbation decays with time, while in the chaotic phase a perturbation grows with time \cite{11,13}. In networks in which the states of the nodes are updated synchronously, the two phases can also be distinguished by the distribution of network’s attractor periods \cite{11,14}. When the updates are synchronous the system always settles onto a dynamical attractor of finite period. In the frozen phase the distribution of attractor periods is sharply peaked with a mean that is independent of the number of nodes $N$. In the chaotic phase the distribution of attractor periods is also sharply peaked, but with a mean that grows as $\exp(N)$. In the “critical” state, at the boundary between the two phases, the distribution of attractor periods is broad, described by a power-law \cite{14,17}.

Many naturally occurring, as well as engineered, self-regulating network systems develop through some sort of evolutionary process. Motivated by this fact, a number of models that evolve the structure and dynamics of Boolean networks have been studied \cite{17,32}. These evolutionary Boolean network (EBN) models generally seek to determine the properties of networks that result from the evolutionary mechanism being considered. For example, some studies have explored evolutionary mechanisms that result in networks that have dynamics that are robust against various types of perturbations, or that result in networks that are in a critical state.

One example of an EBN is the model of competing Boolean nodes first introduced in Ref. \cite{17}, and later studied in Refs. \cite{23,23,26}. In this model, the Boolean functions of the nodes evolve through a frustrated competition for limited resources between nodes that is a variant of the Minority game \cite{33}. In the original paper on the model, it was shown that the network self-organizes to a nontrivial critical state with this evolutionary mechanism. Later it was discovered that this critical state is highly canalized \cite{23}. Canalization is a type of network robustness, and is a classic idea in developmental biology. Recently, experiments have demonstrated its existence in genetic regulatory networks \cite{35,37}. It occurs when certain expression states of only a subset of genes that regulate the expression of a particular gene control the expression of that gene. Canalization is thought to be an important property of development biological systems because it buffers their evolution, allowing greater underlying variation of the genome and its regulatory interactions before some deleterious variation can be expressed phenotypically \cite{38}. Critical net-
works are thought to be important for gene regulation because they can store information in a way that encourages the evolution of more homogeneity. This competition between canalization and homogeneity is reflected in the frequency at which the Boolean functions are biased. For $p = 1/2$ the choice of functions is unbiased and $p$ is near 0.5 to 1. There is a continuous phase transition between these phases at the so-called "edge of chaos." The critical value $p_c$ where this transition occurs satisfies the expression \[ 1 = 2Kp_c(1 - p_c) \] (4)

We will refer to the networks that are critical because they satisfy Eq. 4 by construction as "non-evolutionary" networks, since such networks have no evolutionary dynamics associated with them.

B. Evolutionary Game of Competing Nodes

The process for evolving the Boolean functions in the network is:
1. Start with an RBN constructed with a bias \( p \), and choose a random initial state \( \Sigma(0) \).

2. Update the state of the network using Eq. 1, and determine the attractor of the dynamics. (The attractor can be found using the algorithm discussed in the Appendix of Ref. [23].)

3. For each update on the attractor, determine which Boolean value is the output state of the majority of the nodes, and give a point to each node that is part of the majority.

4. Determine the node with the largest number of points; that node “loses”. If two, or more, nodes are tied, pick one at random to be the loser.

5. Replace the function of the losing node with a new randomly chosen Boolean function with bias \( p \).

6. Return to step 2.

The essential features of the game are (1) frustration [33, 40], since most nodes lose each time step, (2) negative reinforcement, since losing behavior is punished, and (3) extremal dynamics [41], since only the worst performing nodes Boolean function is changed.

Note that previous studies of this evolutionary model have always replaced the function of the losing node with an unbiased, \( p = 0.5 \) random Boolean function. Thus, the evolutionary game we study here differs from previous work only at step 5.

If the attractor period is longer than some limiting time, \( \Gamma_{\text{max}} \), then the score is kept only over that limited time. In our simulations, \( \Gamma_{\text{max}} = 10^4 \) was used. Each progression through the game is called an “epoch”.

In this evolutionary process only the Boolean functions evolve; the directed network describing the regulatory interactions between nodes does not change. However, as we will see, canalization effectively removes interactions from the network. Thus, as the Boolean functions evolve and canalization increases the directed network of regulatory interactions effectively changes [39]. Thus, effectively, both the structure of the network and the dynamics of the nodes simultaneously evolve, making the model effectively a co-evolving adaptive network model [23, 42].

III. CANALIZATION AND SYMMETRY

A. Canalization and Ising Hypercubes

As mentioned above, for large networks with \( K = 3 \), it has been found [23, 24] that the 256 = 2^{2K} possible Boolean functions of three variables organize into 14 different classes in which the functions belonging to each class occur with the same frequency in the critical steady-state that results from the evolutionary game. Moreover, all the functions in a class are equally canalizing, and, in the steady state, functions in classes that are more canalizing occur with higher frequency. Thus, for \( K = 3 \) the game causes networks to evolve to a critical steady state that is highly canalized. Canalization occurs in Boolean networks when the Boolean functions assigned to the nodes are canalizing. A Boolean function is canalizing if its output is fully determined by a specific value of one, or more of its inputs, regardless of the value of the other inputs. The canalization of a function can be quantified by a set of numbers \( \mathbf{P}_k, k = 0, 1, ..., K - 1 \), which are defined as the fraction of the different possible sets of \( k \) input values that are canalizing [23].

Canalization can be further understood by mapping Boolean functions of \( K \) inputs onto configurations, or “colorings”, of the \( K \)-dimensional Ising hypercube [39]. The Ising hypercube is a hypercube which has each vertex labeled, or colored, either ‘0’ or ‘1’ (“black” or “white”). In this representation, each of the \( 2^K \) possible sets of input values corresponds to coordinates on a given axis of the hypercube. The color of each vertex represents the output value of the function for the associated input values. The mapping of a Boolean function of \( K \) inputs to a configuration of the \( K \)-dimensional hypercube is one-to-one.

This representation of Boolean functions as colorings of Ising hypercubes facilitates quick recognition of canalizing functions. For a \( K \)-dimensional hypercube, the fractions of canalizing inputs \( \mathbf{P}_k \) of a Boolean functions are the fraction of its \( K - k \) dimensional hypersurfaces that are homogeneously colored.

B. Symmetry of Evolutionary Dynamics

This Ising hypercube representation is particularly helpful for understanding the role of symmetry in the evolutionary dynamics. The fourteen (14) different classes that were observed empirically in the original \( K = 3 \) study were later recognized as being those Ising hypercube colorings that are related by cubic symmetry plus parity [39]. Parity in this case refers to simultaneously inverting the Boolean values associated with each vertices. An underlying symmetry of the evolutionary dynamics was therefore reflected in this symmetry of the evolved steady-state. Furthermore, this symmetry preserves the canalization values \( \mathbf{P}_k \) of functions in each class, since neither cubic nor parity operations change the percentage of homogeneously colored hypersurfaces.

In mathematical terms the different classes correspond to the group orbits of the “Zyklenzeiger” group, which is the hyper-octahedral symmetry group \( O_n \) (where \( n = K \)) combined with parity [39]. A group orbit is the set of configurations that map into each other through applications of a group’s symmetry operations. The number of orbits \( P_G \) can be calculated analytically using Pólya’s theorem [42]:

\[
P_G = \frac{1}{|G|} \sum_{g \in G} |X^g|
\]  

(5)
where $G$ is the symmetry group acting on the $K$-dimensional Ising hypercube, $|G|$ is the number of operators $g \in G$, $X$ is the set of hypercube colorings, $X^g$ is the set of colorings that are left invariant by $g$, and $|X^g|$ is the size of set $X^g$.

To apply this theorem, one must construct all the operators of the group, sum the number of functions left invariant by each operator, and divide by the total number of symmetry operators. The hyper-octahedral group $O_n$ has $n!2^n$ operations. Including parity operations doubles this number.

A given symmetry operator $g$ can be written as a permutation of the vertex numbers on a given hypercube. As a result, each operator $g$ can be expressed in terms of its cycle structure $x_1^{b_1}x_2^{b_2}...x_m^{b_m}$, where $\sum_{i=0}^{m}i b_i = 2^k$. This notation indicates that $g$ contains $b_1$ cycles of length 1, $b_2$ cycles of length 2, etc. The complete cycle representation of the hyper-octahedral group for an arbitrary dimension $K$ is given by a known recursion relation $|G| = n!2^n/K!$. For $K = 3$ the complete cycle relation is:

$$x_1^8 + 13x_2^4 + 8x_1^2x_3^2 + 8x_2x_6 + 6x_1^4x_2^2 + 12x_4^2$$

where the coefficients of this polynomial indicate the number of operators with a particular cycle structure.

Without parity, the number of functions left invariant is equal to $2^{N_c}$, where $N_c = \sum_{i=1}^{m} b_i$ is the total number of cycles in the operator. Parity must be treated separately; no functions are left invariant by the parity operator with any hyper-octahedral operator containing at least one cycle of length 1. Thus there are $2^{N_p}$ functions left invariant for the operators which include parity, where $N_p = (1 - \Theta(b_1)) \sum_{i=1}^{m} b_i$ and $\Theta$ is the Heaviside step function.

Thus, applying Polya’s theorem to the $K = 3$ case, we arrive at

$$P_G = \left(\frac{1}{96}\right)(2^8 + 13(2)^4 + 13(2)^4 + 8(2)^4 + 8(2)^2 + 8(2)^2 + 6(2)^2 + 12(2)^2 + 12(2)^2) = 14$$

This is precisely how many function classes were found empirically in the $K = 3$ case [23, 39]. Similarly, the complete cycle representation for the $K = 4$ is

$$x_1^{16} + 12x_1^8x_4^4 + 51x_6^6 + 12x_1^4x_2^2 + 32x_1^4x_3^2 + 48x_1^2x_2x_3^2 + 84x_2^2 + 96x_1^2x_6^2 + 48x_6^2$$

Using this result, accounting for parity, and applying Polya’s theorem we calculate $P_G = 222$ for a 4-dimensional hypercube under rotation plus parity symmetry. (Note that an erroneous value of $P_G = 238$ was reported in Ref. [39].) This is how many classes of functions should be observed in a critical steady state of $K = 4$ networks undergoing the evolutionary dynamics. Below we show that results from numerical simulations are consistent with this prediction. Moreover, the frequencies that these functions occur show a preference for canalization.

**IV. RESULTS**

**A. Critical States of K=4 Networks with Competing Nodes**

We have performed exhaustive simulations of ensembles of networks with $K = 4$ playing the game of competing Boolean nodes. All of the simulation results reported in this subsection are for networks with $N = 999$ nodes. Simulations were run for evolutionary processes with biases of $p = 0.5$, $p = 0.65$, and $p = 0.75$. The frequency that each of the $2^{2K}$ = 65536 different functions occurred in the evolved steady state was measured by simulating, for each $p$, an ensemble of 13,000 independent network realizations. Each realization was initialized with an independent random network with random links and different random functions biased with the associated $p$ value. The simulation of each realization was run for $10^4$ epochs to allow the network to reach a steady state. At the end the simulation of each realization, the functions of each node were recorded and then used to calculate the average frequency of each function for the ensemble of realizations.

Figure 1 shows a graph of the attractor period vs. epoch for a simulation of a $K = 4$ network realization with an evolutionary bias of $p = 0.65$. Notice that neither short periods nor long periods dominate the behavior after the steady state is reached at $\approx 10^5$ epochs.
non-evolutionary works is significantly different than the critical state of which each of the $2^{10} \approx 1024$ of $P$ network an average homogeneity of all Boolean function in the $p$ing to Eq. 4. This value of bias of the evolutionary process is within a range. Thus, critical steady states evolve only when the is no longer critical but instead remains in the frozen $p$ values of $p$ functions occur in the evolved steady state, for bias pa-

This indicates that the increased complexity of the more highly connected network disrupts the networks ability to self-organize with unbiased functions.

These results indicate that a phase transition occurs in the evolutionary dynamics as $p$ is increased. At values of $p$ below the transition value the evolutionary dynamics do not produce a critical steady state, while at values of $p$ above the transition, a critical steady state evolves. In fact, a second transition occurs at higher values of $p$. At values of $p$ above this second transition, the evolved state is no longer critical but instead remains in the frozen state. Thus, critical steady states evolve only when the bias of the evolutionary process is within a range.

Note that non-evolutionary $K = 4$ RBNs are constructed with a critical bias of $p_c \approx 0.85355$, according to Eq. 4. This value of $p_c$ produces networks with an average homogeneity of all Boolean function in the network $P \approx 0.85358$. However, the steady state value of $P$ for networks evolved with a bias of $p = 0.65$ is $\approx 0.71$ Clearly, the critical state of $K = 4$ evolved networks is significantly different than the critical state of non-evolutionary $K = 4$ RBNs.

Figure 2 shows the ensemble averaged frequency at which each of the $2^{24} = 65536$ different $K = 4$ Boolean functions occur in the evolved steady state, for bias parameters $p = 0.65$ and $p = 0.75$. The Boolean functions were ordered by first grouping them by their membership to a particular class under hyper-octahedral plus parity symmetry. Then the classes were ordered in descending order by how canizing the functions in the class are, as measured by the sum of their $P_k$ values. As expected, the graph shows that functions belonging to the same class occur with the same probability, at least to within the resolution allowed by statistical fluctuations. This confirms the hypothesis that the underlying symmetry of the evolutionary dynamics is hyper-octahedral plus parity.

Clearly, certain classes of functions occur with a higher probability than others. In general, functions on the left side of the graph (higher canization) occur much more frequently than functions on the right (lower canization). However, unlike in the $K = 3$ case, certain function classes with higher canization occur less frequently than function classes with lower canization. This occurs because, unlike in the previous $K = 3$ studies, the evolutionary process here is biased toward homogeneity. In this case, the drive for canization caused by the evolutionary dynamics is competing against the bias toward homogeneity for certain classes of functions. See Fig. 3. Nonetheless, the evolved critical steady state of these biased networks still shows a preference for canization and is strikingly different than a critical state of a non-evolutionary RBN where homogeneity entirely dominates the relative frequency of functions.

Analogous results presumably hold for even larger values of $K$. However, because the number of Boolean functions for a given $K$ goes as $2^{2^K}$, accurately measuring the frequency that each function occurs at in the critical steady state becomes unfeasible for values of $K$ greater than 4.
tractor periods are found. At too high a value of $p$, the evolved steady state is a chaotic state and only long at-

FIG. 4: (Color online) Critical state evolution order param-
eater $\Psi$ as a function of evolution bias parameter $p$ for networks
of size $N = 999$ with $K = 3$ (black straight line), $K = 4$ (red
dotted line), $K = 5$ (green dashed line), and $K = 8$ (blue
dashed-dotted line).

B. Criticality as a function of $p$ and $K$

Our results for $K = 4$ indicate that canalized critical
states evolve only when the bias $p$ of the evolutionary
game is within a range. At too low a value of $p$, the
evolved steady state is a chaotic state and only long at-
tractor periods are found. At too high a value of $p$, the
evolved steady state is a frozen state and only short at-
tractor periods are found. Only in an intermediate range
of $p$ does a critical steady state evolve. In order to quan-
titatively find the approximate range of $p$ for which
critical steady states evolve, we define an order parame-
ter $\Psi$ as the percentage of steady state attractor periods
that occur that are less than $\Gamma_{\text{max}}$. Then, when $\Psi = 0$
the networks are assumed to be in the chaotic state, when
$\Psi = 1$ the networks are assumed to be in the frozen state,
and when $0 < \Psi < 1$ the networks are assumed to be in
a critical state.

Figure 4 shows a graph of the order parameter $\Psi$ as
a function of the evolution bias parameter $p$ for network
connectivities $K = 3, 4, 5,$ and $8$. This data was produced
using networks of size $N = 999$, using an equilibration
time to reach the steady state of $10^4$ epochs, and then
computing $\Psi$ over $3 \times 10^4$ epochs. The $\Psi$ values were
also then averaged over 140 network realizations for each
value of $p$ and $K$. (Sixteen realizations were used for
$K = 8$). A period cutoff value of $\Gamma_{\text{max}} = 10^4$ was used
in these simulations.

For $K = 3$ the network already evolves to a critical
state at $p = 0.5$, the smallest possible value of $p$, and
stops evolving to a critical state at $p \approx 0.82$. This is con-
sistent with previous results [17] that unbiased $K = 3$
networks evolve to critical states. This is not the case,
however, for networks with $K > 3$. As shown in Fig. 4,
the onset of evolution to criticality for these more highly
connected networks occurs at a value $p > 0.5$. At least

for $K = 4, 5,$ and $8$, and presumably for all finite values
of $K$, evolution to a critical state occurs only for a finite
range of $p$. For example, for $K = 4$, this range is from
$p \approx 0.60$ to $p \approx 0.83$. The width of this range appears to
decrease, and both the minimum and median values of $p$
appear to increase, as $K$ increases. The findings from the
results shown in Fig. 4 vary quantitatively, but remain
qualitatively consistent if 1) the equilibration time is in-
decrease, and both the minimum and median values of $p$
appear to increase, as $K$ increases. The findings from the
results shown in Fig. 4 vary quantitatively, but remain
qualitatively consistent if 1) the equilibration time is in-
dered, 2) the value of $\Gamma_{\text{max}}$ is varied, or 3) the number
of nodes $N$ nodes is changed.

Figure 5 shows the value of $p$ when $\Psi = 0.5$, which
approximates the median value of $p$ in the range of the
evolution of a critical state, as a function of $1/K$ for
$K = 4, 5,$ and $8$. Unfortunately, simulating networks
with $K \gg 8$ is computationally unfeasible with our
methods, and we are thus restricted to predict the asymp-
totic behavior of these evolutionary random Boolean net-
works using these relatively small values of $K$. The three
points fall roughly on a straight line. If we extrapolate
the linear fit of the data points, the value of $p$ tends to-
ward a value slightly larger than $1$ in the limit of large $K$.
However, this is physically unrealizable since $p$ cannot be
larger than $1$. Therefore, we expect that as $K \to \infty$, the
width of the range of $p$ for which criticality occurs goes
to $0$, while the median value of the range goes to $1$.

It is important to note that the range of evolution bias
parameter $p$ for which critical state evolves is, at all stud-
ied values of $K$, less than the critical bias value $p_c$ for non-
evolutionary RBNs given by Eq. 1. Therefore, the critical
steady state that results from evolutionary process is dif-
ferent than the critical state of non-evolutionary RBNs.
From previous studies of $K = 3$ networks, and from the
results shown in Fig. 2 that were discussed above, the
difference is that the evolved critical steady states are
more canalized.
V. DISCUSSION

In this paper we have extended previous work on an EBN model in which the nodes compete in a frustrated game that causes the Boolean functions of the nodes to evolve. The previous studies of this model found that the game causes the system to evolve to a critical steady state that is highly canalized. Canalized states and their evolutionary mechanisms are important in Developmental Biology because of the usefulness of the robustness against diliterous phenotypic expression that canalization in the genome provides. The previous studies also found that the evolutionary dynamics of the $K = 3$ model has the symmetry of the 3-dimensional Zyklensgeizer group, which is the combination of parity and the cubic symmetry group.

The previous studies of this EBN, however, only considered networks with $K = 3$ in-links per node. Here we extended the study the more highly connected networks with larger $K$. Real self-regulatory systems, both biological and engineered, typically have nodes with a range of $K$ inputs [3]. Thus, it is important to understand how larger regulatory connectivity effects evolutionary mechanisms.

For networks with $K > 3$, we find that the game as previously studied does not cause the network to evolve to a critical steady state. Instead, it will evolve to a chaotic steady state. This occurs because the unbiased game, which was studied previously, replaces the Boolean function of nodes that lose the game with randomly selected new functions that are chosen unbiasedly from the set of all possible Boolean functions. Apparently, for networks with $K > 3$, unlike what happens for networks with $K = 3$, if they are composed largely of nodes with random Boolean functions with an unbiased distribution, then the evolutionary game is not “strong enough” to induce a shift in the distribution of the nodes’ Boolean functions sufficient to have critical state dynamics.

However, we have shown that for networks with $K > 3$ if the game replaces the Boolean function of the losing nodes with functions biased toward homogeneity, then a critical steady state can evolve. We studied the range of evolutionary bias that will cause critical state evolution and found that it narrows and that its median increases with $K$. We have also shown that the critical steady states that evolve for $K > 3$ are highly canalized, although there is also a competing bias toward more homogeneous Boolean functions. All functions in an orbit of the $K$-dimensional Zyklensgeizer group have both equal canalization and equal homogeneity and occur with equal frequency in the steady state. Thus, the symmetry of the evolutionary dynamics of the EBN with $K$ regulatory links per node is that of the $K$-dimensional Zyklensgeizer group.

This study illustrates the importance of symmetry in self-regulatory networks and of evolutionary processes. It would be interesting to analyze other self-regulatory network systems, both real and model systems, with the methods we have used. This would allow the importance of symmetry in evolutionary processes to be understood and become better appreciated.

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