Dynamics of Boolean Networks with Scale-Free Topology

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The dynamics of Boolean networks (the N-K model) with scale-free topology are studied here. The existence of a phase transition governed by the value of the scale-free exponent of the network is shown analytically by analyzing the overlap between two distinct trajectories. The phase diagram shows that the phase transition occurs for values of the scale-free exponent in the open interval (2, 2.5). Since the Boolean networks under study are directed graphs, the scale-free topology of the input connections and that of the output connections are studied separately. Ultimately these two topologies are shown to be equivalent. An important result of this work is that the fine-tuning usually required to achieve stability in Boolean networks with a totally random topology is no longer necessary when the network topology is scale-free.

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The study and characterization of the statistical properties of complex networks has received renewed attention in the last few years [2, 21]. In particular, it has been recently shown by A. L. Barabási, M. Newman, R. Solé and many other authors that a great variety of real networks exhibit a scale-free topology, including the WWW and the Internet [1, 3], social networks [4, 5], metabolic and protein networks [6, 7, 18], ecological networks [8, 14], and genetic networks [9, 17], to mention just a few examples (for more references see [2, 6]). A scale-free topology means that the probability $P(k)$ that an arbitrary element of the network is connected to exactly $k$ other elements has the form $P(k) = Ck^{-\gamma}$, where $\gamma$ is usually called the scale-free exponent. Scale-free networks have the key property that a small fraction of the elements are highly connected whereas the majority of the elements are poorly connected. The ubiquity of scale-free networks has led to a systematic study of the structural properties that characterize the wiring diagram of the network. Nevertheless, the dynamics generated by a scale-free network topology when the elements are provided with some kind of dynamic interaction rule, remain essentially unexplored.

An interesting dynamical network in which the scale-free topology has important implications is the N-K model proposed by Stuart Kauffman in 1969 to describe generically the dynamics involved in the processes of gene regulation and cell differentiation [13]. In this classic model, the genome of a given organism is represented by a set of $N$ genes, each being a binary variable describing the two possible states of gene-expression: either the gene is expressed (1) or it is not (0). Since the expression of a gene is controlled by the expression of some other genes, Kauffman assumed the genome as a directed network in which a link from a given gene $A$ to another gene $B$ means that $A$ controls the expression of $B$. In view of the complexity exhibited by real genetic networks, Kauffman made three simplifying assumptions: (a) every gene is connected (is controlled) by exactly $K$ other genes; (b) the $K$ genes to which every gene is connected are chosen randomly with uniform probability from the entire system; (c) each gene is expressed with probability $p$ and is not expressed with probability $1-p$, depending upon the configurations of its $K$ controlling genes.

Even with these simplifying assumptions, a very rich and unexpected behavior of the model was found (for references see [3]). In particular, in 1986 Derrida and Pomeau showed analytically the existence of a dynamical phase transition controlled by the parameters $K$ and $p$ [14, 20]. For every value of $p$ there exists a critical value of the connectivity, $K_c(p) = \left[2p(1-p)^{-1}\right]$, such that if $K < K_c(p)$ all perturbations in an initial state of the system die out (ordered phase). For $K > K_c(p)$ a small perturbation in the initial state of the system propagates across the entire system over time (chaotic phase). According to Kauffman, Stuaffer, and other authors, only when $K = K_c(p)$ (the critical phase) does the N-K model have the required stability properties compatible with the order manifest in the genetic networks of living organisms [14, 20]. This fact made Kauffman coin the term “life at the edge of chaos”.

Although the N-K model qualitatively points in the right direction, it fails to account for a quantitative description of what actually is observed in genetic networks. One of the main problems is that the critical connectivity $K_c(p)$ is very small for most values of $p$ (see Fig. 1). In contrast, it is well known that real genetic networks exhibit a wide range of connectivities. For example, the expression of the human $\beta$-globine gene (expressed in red blood cells) or the even-skipped gene in Drosophila (playing an important role in the development of the embryo), are each controlled by more than 20 different regulatory proteins [14]. Analogously, both the the fibroblast growth factor (FGF) activation and the platelet-derived growth factor (PDGF) activation in mammalian cells, result in the cascade activation of over 60 other genes [6]. On the other side of the spectrum is the $\text{lac}$ operon in $E.\text{coli}$, which is regulated by only two proteins: the $\text{lac}$ re-
compressor protein and the catabolite activator protein (CAP).

These observations are contrary to the Kauffman model since high connectivities imply either chaotic behavior or almost constant boolean functions ($p$ very close to 0 or 1). To achieve stability with moderate high connectivities in the $N$-$K$ model, it is necessary to fine-tune the value of $p$. In order to have ordered dynamics when the critical connectivity is $K_c = 20$, the value of $p$ should be in the interval $0 < p < 0.026$ (or $0.974 < p < 1$). As far as we can tell, there is neither a theoretical nor an experimental reason justifying why the parameters $K$ and $p$ should “live” in the shaded area of Fig. 1.

The above suggests that the random network topology upon which the Kauffman model is based, is inadequate. In view of the ubiquity of scale-free networks and of the fact that some genes in real genetic networks are highly connected whereas others are not, it is reasonable to replace assumptions (a) and (b) mentioned above by the assumption that the connectivity $k$ of every gene in the network follows a scale-free distribution, $P(k) \sim k^{-\gamma}$. It was not until very recently that the dynamics of the $N$-$K$ model with a scale-free topology were studied numerically [8]. Nevertheless, the values of $\gamma$ and $p$ at which the phase transition occurs, if it does occur at all, were unknown in these previous works and the results may have to be reinterpreted. In this letter we show analytically that the $N$-$K$ model with a scale-free topology undergoes a phase transition controlled by the scale-free exponent $\gamma$ and the parameter $p$, and provide the phase diagram that fully identifies the ordered, critical, and chaotic phases.

The model which we will be working with is the following. The network is represented by a set of $N$ boolean variables (or elements), $\{\sigma_1, \sigma_2, \ldots, \sigma_N\}$. Each element $\sigma_i$ is controlled by $k_i$ other elements of the network, where $k_i$ is chosen randomly with probability $P_\Sigma(k_i)$. Let $\{\sigma_{i_1}, \ldots, \sigma_{i_{\nu_i}}\}$ be the set of the controlling elements of $\sigma_i$. We then assign to each $\sigma_i$ a boolean function $f(\sigma_{i_1}, \ldots, \sigma_{i_{\nu_i}})$ such that for each configuration of the controlling elements, $f_i = 1$ with probability $p$ and $f_i = 0$ with probability $1-p$. Once the controlling elements and the boolean functions are assigned to every element in the network, the dynamics of the system is given by

$$\sigma_i(t+1) = f_i(\sigma_{i_1}(t), \ldots, \sigma_{i_{\nu_i}}(t)).$$

We denote as $\Sigma_t$ the state of the entire system at time $t$, $\Sigma_t = \{\sigma_1(t), \sigma_2(t), \ldots, \sigma_N(t)\}$.

To show the existence of the phase transition we consider the overlap $x(t)$ between two distinct configurations $\Sigma_t$ and $\tilde{\Sigma}_t$ (the temporal evolution of these two configurations is governed by the same set of boolean functions). The overlap is defined as the fraction of elements in both configurations that have the same value, and is given by

$$x(t) = 1 - \frac{1}{N} \sum_{i=1}^{N} |\sigma_i(t) - \tilde{\sigma}_i(t)|. \quad (1)$$

If $\Sigma_t$ and $\tilde{\Sigma}_t$ are totally independent, then $x(t) \approx 0.5$ whereas if they are almost equal $x(t) \approx 1$. In the limit $N \rightarrow \infty$ the overlap becomes the probability for two arbitrary but corresponding elements, $\sigma_i(t) \in \Sigma_t$ and $\tilde{\sigma}_i(t) \in \tilde{\Sigma}_t$, to be equal. The stationary value of the overlap, defined as $x = \lim_{t \rightarrow \infty} x(t)$, can be considered as an order parameter of the system. If $x = 1$, the system is insensitive to initial perturbations (all differences between configurations die out over time). In this case the system presents an ordered behavior. On the other hand, if $x \neq 1$, the initial perturbations propagate across the entire system and do not disappear. In this case the system exhibits a chaotic behavior.

By generalizing the annealed computation carried out by Derrida and Pomeau in Ref. [8] to the case in which each element receives $k$ inputs with probability $P_\Sigma(k)$,
one finds that the overlap obeys the dynamical equation

\[ x(t + 1) = F(x(t)), \]

where the mapping \( F(x) \) is given by

\[ F(x) \equiv 1 - 2p(1 - p) \left\{ 1 - \sum_{k=1}^{\infty} x^k P_2(k) \right\}. \quad (2b) \]

In the limit \( t \to \infty \), Eq. (2) becomes the fixed point equation \( x = F(x) \) for the stationary value of the overlap. Note that \( x = 1 \) is always a fixed point of Eq. (2). Nonetheless, this solution may be stable or unstable depending on \( P_2(k) \). Note also that \( F(x) \) is a monotonically increasing function of \( x \) with the property that \( F(0) = 1 - 2p(1 - p) \) and \( F(1) = 1 \). Therefore, Eq. (2) will have a stable fixed point \( x^* \neq 1 \) only if \( \lim_{x \to 1^-} dF(x)/dx > 1 \) (chaotic phase). In contrast, if \( \lim_{x \to 1^-} dF(x)/dx < 1 \) the only fixed point is \( x = 1 \) (ordered phase). The situation is illustrated in Fig. 2. The phase transition between the ordered and chaotic regimes occurs when \( \lim_{x \to 1^-} dF(x)/dx = 1 \). From Eq. (2b) it follows that

\[ \lim_{x \to 1^-} \frac{dF(x)}{dx} = 2p(1 - p) \sum_{k=1}^{\infty} k P_2(k) \]

\[ = 2p(1 - p) \langle k \rangle_x, \quad (3) \]

where \( \langle k \rangle_x = \sum_{k=1}^{\infty} k P_2(k) \) is the first moment of \( P_2(k) \). The phase transition is then determined by the condition

\[ 2p(1 - p) \langle k \rangle_x = 1. \quad (4) \]

In the standard \( N-K \) model all the elements have the same connectivity, \( k_i = \langle k \rangle_x = K \), and Eq. (4) reduces to the result obtained by Derrida and Pomeau in Ref. 8. (Luque and Solé derived Eq. (4) in Ref. 13 by considering the set of relevant elements of the system—the elements that do not reach a constant value over time.)

It is interesting to note that the phase transition is governed only by the first moment of \( P_2(k) \). Nevertheless, for the scale-free distribution \( P_2(k) = Ck^{-\gamma} \), the first moment is not necessarily a meaningful parameter to characterize the network topology. For instance, if \( 2 < \gamma \leq 3 \), the second moment of the distribution is infinite even when the first moment has a finite value, which means that the fluctuations around the first moment are much larger than the first moment itself. Therefore, rather than characterizing the phase transition using the first moment of the distribution, we will do it by means of the scale-free exponent \( \gamma \), which is the only natural parameter that determines the network topology.

For the scale-free distribution to be normalizable, it is necessary to have \( \gamma > 1 \). Under such conditions, the probability function \( P_2(k) \) is given by

\[ P_2(k) = \frac{1}{\zeta(\gamma)} k^{-\gamma}, \quad (5) \]

where \( \zeta(\gamma) = \sum_{k=1}^{\infty} k^{-\gamma} \) is the Riemann Zeta function.

The first moment of this distribution is then expressed as a function of \( \gamma \) as,

\[ \langle k \rangle_x = \begin{cases} \infty & \text{if } 1 < \gamma \leq 2 \\ \frac{\zeta(\gamma-1)}{\zeta(\gamma)} & \text{if } \gamma > 2 \end{cases}. \quad (6) \]

From Eqs. (3)-(6), it follows that the fixed point \( x = 1 \) is unstable if \( 1 < \gamma \leq 2 \). In this case Eq. (2) has a stable fixed point \( x^* \neq 1 \), and the system is in the chaotic phase for any value of \( p \) in the open interval \((0, 1)\). The only way in which the overlap between two distinct configurations can converge to 1 is if all the boolean functions are constant, namely, if either \( p = 0 \) or \( p = 1 \). On the other hand, when \( \gamma > 2 \) the first moment of the distribution is finite. In this case, the value \( \gamma_c \) of the scaling-free exponent at which the phase transition occurs is determined by the transcendental equation,

\[ 2p(1 - p) \frac{\zeta(\gamma_c-1)}{\zeta(\gamma_c)} = 1. \quad (7) \]

The values \( \gamma_c \) and \( p \) for which this equation is satisfied are plotted in Fig. 3. As can be seen, \( \gamma_c \in [2, 2.5] \) for any value of \( p \). Actually, \( \gamma_c \) reaches its maximum value \( \gamma_{c, \text{max}} = 2.47875 \) at \( p = 0.5 \). Above this maximum value the system is always in the ordered phase regardless of the value or \( p \). It is interesting to note that \( \gamma \in [2, 3] \) for the majority of the real scale-free networks that have been analyzed.

An important characteristic of the \( N-K \) model is that it is a directed graph: if \( \sigma_i \) is an input of \( \sigma_j \), the opposite does not necessarily occur. Every element \( \sigma_i \) is regulated by \( k_i \) elements. But \( \sigma_i \) can in turn regulate the value of a number of other elements, say \( l_i \). The distribution \( P_2(k) \) of input connections is not necessarily
equal to the distribution $P_o(l)$ of output connections. Up to now we have assumed that $P_T(k)$ is a scale-free distribution. But as the example of the fibroblast growth factor (FGF) suggests, it is also possible for the network of output connections to present a scale-free topology. To apply our previous results to the case in which $P_o(l)$ is known instead of $P_T(k)$, we should find how these two distributions are related.

Suppose that an arbitrary element $\sigma_i$ of the network has $l_i$ outputs with probability $P_o(l_i) = l_i^{-\gamma}/\zeta(\gamma)$. (We assume that $\gamma > 2$ so that the first moment of the distribution is well defined.) When the $l_i$ outputs of every element are chosen randomly with uniform probability from the entire system, the input probability distribution $P_S(k)$ is given by

$$P_S(k) = \frac{N^k}{K^N} \left( \frac{\langle l \rangle_o}{N} \right)^k (1 - \frac{\langle l \rangle_o}{N})^{N-k},$$

(8)

where $\langle l \rangle_o$ is the first moment of $P_o(l)$. In the limit $N \to \infty$, the above expression transforms into the Poisson distribution:

$$P_T(k) = e^{-\langle l \rangle_o} \frac{\langle l \rangle_o^k}{k!}.$$  

(9)

This result shows that the first moment of the input distribution $P_T(k)$ is equal to the first moment of the output distribution $P_o(k)$, $\langle k \rangle_T = \langle l \rangle_o$. Therefore, Eq. (8) and the phase diagram shown in Fig. 3 are still valid if we substitute $\langle l \rangle_T$ by $\langle l \rangle_o$.

A consequence of the scale-free network topology is the constraint of having a very low connectivity for every element (or a high connectivity with almost constant functions) in order to be in the ordered phase, is no longer valid. The scale-free topology eliminates the necessity of fine-tuning the parameters $K$ and $\gamma$ to achieve stable dynamics. Furthermore, the fact that the phase transition occurs for values of $\gamma$ in the interval $(2, 2.5)$, allows the existence of elements with a wide range of connectivities in the critical and ordered phases, which is required to describe the observed behavior of real genetic networks. Now that the human genome, as well as the genome of some other organisms, have been thoroughly sequenced, it will be possible to determine experimentally if the topology of real genetic networks is scale-free or not [22]. More work is called for to fully characterize the statistical properties of Boolean networks with scale-free topology, such as the distribution of the number of different orbits, the distribution of the orbit lengths, and the stability of the dynamics in the three different phases of the $N$-$K$ model. We believe that the phase diagram shown in Fig. 3 will be a useful guide for further studies.

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connectivity rather than the scale-free exponent.