The Number of Different Binary Functions
Generated by $NK$-Kauffman Networks
and the Emergence of Genetic Robustness

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Abstract

We determine the average number $\vartheta(N, K)$, of $NK$-Kauffman networks that give rise to the same binary function. We show that, for $N \gg 1$, there exists a connectivity critical value $K_c$ such that $\vartheta(N, K) \approx e^{\varphi N}$ ($\varphi > 0$) for $K < K_c$ and $\vartheta(N, K) \approx 1$ for $K > K_c$. We find that $K_c$ is not a constant, but scales very slowly with $N$, as $K_c \approx \log_2 \log_2 (2N/\ln 2)$. The problem of genetic robustness emerges as a statistical property of the ensemble of $NK$-Kauffman networks and impose tight constraints in the average number of epistatic interactions that the genotype-phenotype map can have.

Short title: $NK$-Kauffman networks and Genetic Robustness

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1. Introduction

NK-Kauffman networks, also known as NK-Kauffman cellular automata, were proposed in 1969 as models for the study of gene regulation. Since then, their rich dynamical behavior has motivated many studies, and as very general models with few parameters their applications have been extended to several complex systems. Of particular interest in this work is their application for modeling the genotype-phenotype map. For an excellent review on several applications see also Ref. 4.

An NK-Kauffman network consists of $N$ Boolean variables (or bits) $S_i(t) \in \{0, 1\}$, with $i = 1, \ldots, N$, that evolve deterministically in discretized time $t = 0, 1, 2, \ldots$ according to Boolean functions on $K$ of these variables (the inputs) at the previous time $t - 1$. For every $S_i$, a Boolean function $f_i$ is chosen at random and independently from a given distribution in all the possible Boolean functions with $K$ inputs. Also, for every $S_i$, $K$ inputs are randomly selected from a uniform distribution among the $N$ Boolean variables of the network. The selection process may be done with allowed repetitions; this is to say, some inputs might be identical and $K$ could be bigger than $N$. Or without repetitions; namely, all inputs are different and $K \leq N$. In this work we adopt the latter alternative, because it is more natural from the biological point of view, and it suits better for our calculation purposes. It is important to bear in mind this distinction (repetition vs. no repetition) when contrasting our results with those from other approaches.

Once the $K$ inputs and the function $f_i$ for each of the $N$ variables have been selected, a particular NK-Kauffman network has been constructed, and evolves deterministically in discrete time $t$ according to the rules

$$S_i(t + 1) = f_i(S_{i_1}(t), S_{i_2}(t), \ldots, S_{i_K}(t)), \quad i = 1, \ldots, N,$$

(1)

where $i_\alpha \neq i_\beta$, for all $\alpha, \beta = 1, 2, \ldots, K$, with $\alpha \neq \beta$, because all the inputs, while random, are different.

Let's denote $L_{NK}^N$ the set of different NK-Kauffman networks that might be built up with the aforementioned process, for given $N$ and $K$. Since each element of $L_{NK}^N$ is a deterministic dynamical system evolving in a finite phase space, with $2^N$ states, its dynamics eventually settles into a cycle. One can think the system as composed of attraction valleys, each with one cycle (or attractor), whose number might go from just 1 to $2^N$, and with cycle lengths varying from 1 for a punctual attractor, to $2^N$ when a single cycle traverses the whole phase space. The behavior of a typical NK-Kauffman network is in between these two extreme cases.

Determining the distribution in $L_{NK}^N$ of the number of attractors and their size for general $N$ and $K$, is a difficult and challenging problem. Several
numerical simulations and analytical methods have been used to approach it \(^5\)–\(^10\). However, significant advances have been obtained only for the so-called \textit{random map model}; i.e., when the Boolean functions are taken from a uniform distribution and \(K = N\) \((K = \infty\) in Ref. \(5\), since they permit repetition in the inputs). The first results obtained from this model go as far as the 50’s, when accurate formulas were found for the distribution of attractors in the context of \textit{random functional graphs} \(^{11}\). Decades later, Derrida and Flyvbjerg studied it in the context of statistical mechanics with an interest on its applications to cellular automata \(^5\). We recently have founded an asymptotic formula for the statistical distribution of the number of connected components in the random map model, deriving it from a new combinatorial expression \(^{12}\). In Ref. \(13\) we also, furnished both: exact and asymptotic formulas, for several measures that help to understand the connectivity of random functional graphs; such as cycle and trajectory lengths, expected number and size of attraction valleys, and the like.

The general case \(K < N\) were treated by mean field analysis taking \(N \to \infty\) \(^{10}\). The results indicate that when the Boolean functions are extracted from a distribution such that \(f_i\) is 1 or 0 with probability \(p\) or \(1 - p\), respectively, there is a bifurcation of the dynamics of the elements of \(\mathcal{L}_K^N\) at the critical connectivity value

\[
K^* = \frac{1}{2p(1 - p)},
\]  

(2)

with \(p = 1/2\) corresponding to the uniform distribution considered in this paper. For \(K < K^*\); there is an ordered phase, where small perturbations die out. When \(K > K^*\), the phase is chaotic and small perturbations spread exponentially through the network. While, in the critical case \(K = K^*\), the evolution is mainly governed by fluctuations and has been qualified of being neither ordered, nor chaotic \(^4\).

The extreme cases \(K = 1\) and \(K = 2\) have been approached analytically for \(p = 1/2\). The former was first studied by Flyvbjerg and Kjaer \(^6\), and it has been recently founded that, when the constant functions \textit{tautology} and \textit{contradiction} are excluded from consideration, the number of attractors and their length grow super polynomially (faster than any power law) in \(N\) \(^7\). In the case of \(K = 2\) a super polynomial behavior for the number of attractors was also founded \(^8\).

In this work we calculate; for given \(N\) and \(K\), the exact value of the average number \(\vartheta(N, K)\) of different \(NK\)-Kauffman networks that give rise to the same binary function. For that scope, we define the function \(\Psi: \mathcal{L}_K^N \to \mathcal{G}_{2^N}\); where \(\mathcal{G}_{2^N}\) is the set of binary functions in \(N\) binary variables. Then, we calculate the values of the cardinalities \(#\mathcal{L}_K^N\) and \(#\Psi(\mathcal{L}_K^N)\); of \(\mathcal{L}_K^N\) and the set of binary functions, \(\Psi(\mathcal{L}_K^N) \subseteq \mathcal{G}_{2^N}\) that they generate, respectively.
Our findings, show that, for \( N \gg 1 \) the asymptotic formula for \( \vartheta(N, K) \), behaves so that there exists a critical value \( K_c \) of the connectivity, such that: \( \vartheta(N, K) \approx e^{\varphi(K)N} \) for \( K < K_c \), with \( \varphi(K) > 0 \); so that many \( NK \)-Kauffman networks generate the same binary function. And, \( \vartheta(N, K) \approx 1 \) for \( K > K_c \), indicating that almost any binary function is generated by a different \( NK \)-Kauffman network. Furthermore, the value of \( K_c \) turns out to be not a constant, but to grow very slowly as the double logarithm of \( N \). Important to remark, is the fact that, \( K_c \) does not signal a transition from a regular to a chaotic behavior for the elements of \( L_N^N \); as \( K^* \) given by (2) does. Instead, it shows an abrupt change in the injectivity of the map \( \Psi : L_N^K \rightarrow \Psi (L_N^K) \subseteq G_{2N} \).

\( NK \)-Kauffman networks play an important roll in applications to genetics for modeling the genotype-phenotype map, represented by \( \Psi \). The genotype, carries all the necessary information to create a living organism; the phenotype. The genotype is mainly composed of DNA that is a double chain of base-pares (Adenine-Thymine and Cytosine-Guanine) which in turn constitutes the genes. In this context, an \( NK \)-Kauffman network, represents the genotype, while their attractors in \( \Psi (L_N^K) \); the phenotype of the alternative cells types. A conspicuous observation in the theory of natural selection is the robustness of the phenotype against mutations in the genotype. Natural radiation in the environment changes the genotype by making mutations on DNA-bases. Random mutations and recombination of the genotype by mating, constitute the essential engine of species evolution. The effect of random mutations range from having no effect at all, to complete damage in the phenotype. The reasons of this phenomena are still not completely understood. One hypothesis is that it provides selective advantages to the phenotype since an organism with a damaging mutation will be at disadvantage in evolution. So, natural selection must have favored organisms with a mechanism that prevents mutations from accumulating in the gene, ensuring that useful genes remain in the genome.

A mechanism proposed to explain genetic robustness is due to the finding of the existence of genetic redundant material. This implies that not all genes are essential. Experiments to estimate how many genes are actually essential were carried out by induced mutations. The results varied among the different organisms under study, but in all cases; the estimates showed that more than 50% of the genes are not essential. However, recent studies on gene-deletion at genome-scale, revealed that thousands of genes whose deletions had no detectable effect in the phenotype were single-copy i.e. they had no duplicate in the genome. Other mechanism is the discovery by modern genetics of the epistatic effects. This refers to effects that a gene may have on the phenotype, that strongly depend on the levels of expression of other unrelated genes in the genotype. For example, studies in yeast...
revealed that up to 50% of mutations, almost do not affect their fitness due to the epistatic compensations. Today there is some agreement that genetic robustness, emerges as a mixture, between genetic redundancy and epistatic buffering.

As we shall see, our mathematical findings show that genetic robustness emerges in the genotype-phenotype map modeled by NK-Kauffman networks, as a consequence of their statistical properties: with the \( K \) connections playing the role of the average number of epistatic interactions among the genes. Our calculations impose tight restrictions on the values that \( K \) may have when \( N \) attains values in the range of the known number of genes that living organisms have.

The paper is organized as follows: In Sec. 2 we establish a mathematical correspondence between binary functions and functional graphs through a bijection \( \phi_N \). This allows us to define the function \( \Psi \) and show that \( \vartheta(N, K) = \#L_N^K/\#\Psi(L_N^K) \). The exact computations of the cardinalities \( \#L_N^K \), and \( \#\Psi(L_N^K) \); are carried out by combinatorial methods in Sec. 3. In Sec. 4 the asymptotic behavior of \( \vartheta(N, K) \) is studied and expressions for \( K_c(N) \) and \( \Delta K_c(N) \) (the width of the transition) are found. Finally, in Sec. 5 we set our conclusions showing that: the asymptotic behavior of \( \vartheta(N, K) \) imposes the restriction \( K \leq 3 \), in the average number of epistatic interactions, in order that, genetic robustness emerges in the ensemble of NK-Kauffman networks.

2. Mapping NK-Kauffman Networks into Binary Functions

Binary functions can be represented by means of functional graphs. For a given positive integer \( n \), an \( n \)-functional graph is composed: by the set \( P_n = \{1, \ldots, n\} \), whose elements are called nodes or vertices, and a function \( g : P_n \to P_n \).

Functional graphs can be represented graphically, and it is this graphical representation that helps to understand many of their properties. Each node is indicated by a point, and an arrow from node \( i \) to node \( j \) is drawn whenever \( g(i) = j \). As an example, Figure 1 shows a 12-functional graph with three connected components (i.e., three attractors). For clarity, nodes are depicted here as small disks.
Figure 1: A 12-functional graph with three connected components.

Note that, in an $n$-functional graph, although exactly one arrow goes out from each of its nodes, several arrows might be directed towards any of them. Denote $G_n$ the set of all possible $n$-functional graphs; its cardinality is well known and given by $\# G_n = n^n$. The problem of determining in $G_n$ the distribution of cycle lengths and number of connected components (number of attractors) has been undertaken by several authors since the early 50’s.

Let $\Omega_N = \{ S = (S_1, \ldots, S_N) \mid S_i = 0, 1, \text{ for } i = 1, \ldots, N \}$ be the set of $2^N$ binary vectors with $N$ components which is mapped by NK-Kauffman networks $(f : \Omega_N \rightarrow \Omega_N)$ through (1). There is a well-known bijection $\phi_N : \Omega_N \rightarrow P_{2^N}$ given by:

$$\phi_N (S) = 1 + \sum_{i=1}^{N} 2^{i-1} S_i.$$  \hspace{1cm} (3)

Clearly, $S$ is nothing else than the binary decomposition of $\phi_N (S) \in P_{2^N}$. Now, the following diagram commutes:

$$\begin{array}{ccc}
\Omega_N & \xrightarrow{f} & \Omega_N \\
\downarrow{\phi_N} & & \downarrow{\phi_N} \\
P_{2^N} & \xrightarrow{g} & P_{2^N}
\end{array}$$

and assigns to each binary function $f$ the functional graph $g = \phi_N \circ f \circ \phi_N^{-1}$. This defines the function

$$\Psi : \mathcal{L}_K^N \longrightarrow \Psi (\mathcal{L}_K^N) \subseteq G_{2^N}.$$  \hspace{1cm} (4)
In the case $K = N$ we get from (1) that $\mathcal{L}_N^N$ coincides with the set of all possible binary functions from $\Omega_N \to \Omega_N$. So, from the commuting diagram it happens that $\mathcal{L}_N^N \cong \mathcal{G}_{2N}$.

The average number of $NK$-Kauffman networks that $\Psi$ maps to the same binary function is directly expressed in terms of the cardinalities of the inverse image sets $\Psi^{-1}(g) = \{ f \in \mathcal{L}_K^N \mid \Psi(f) = g \}$ as

$$\vartheta(N, K) = \frac{1}{\# \Psi(\mathcal{L}_K^N)} \sum_{g \in \Psi(\mathcal{L}_K^N)} \# \Psi^{-1}(g),$$

(5)

where

$$\Psi^{-1}(g) \cap \Psi^{-1}(g') = \emptyset \quad \forall \ g \neq g'.$$

(6)

Furthermore $\mathcal{L}_K^N$ may be decomposed as

$$\mathcal{L}_K^N = \bigcup_{g \in \Psi(\mathcal{L}_K^N)} \Psi^{-1}(g)$$

so that, due to (6)

$$\# \mathcal{L}_K^N = \sum_{g \in \Psi(\mathcal{L}_K^N)} \# \Psi^{-1}(g).$$

Substituting back into (5) we obtain

$$\vartheta(N, K) = \frac{\# \mathcal{L}_K^N}{\# \Psi(\mathcal{L}_K^N)},$$

(7)

for the average number of $NK$-Kauffman networks that give rise to the same binary function.

3. The Cardinalities of $\mathcal{L}_K^N$ and $\Psi(\mathcal{L}_K^N)$

For each of the $N$ Boolean variables there are $2^{2K}$ different Boolean functions with $K$ connections; moreover, as there are $\binom{N}{K}$ different ways to make the connections without replacement, the total number of $NK$-Kauffman networks is

$$\# \mathcal{L}_K^N = \left[ 2^{2K} \binom{N}{K} \right]^N.$$

(8)
Now, let $A_K = \{A_K(m, i)\}$ denote the $2^K \times K$ binary matrix whose $m$-th row encodes the binary decomposition of $m \in P_{2^K}$, that is,

$$m = 1 + \sum_{i=1}^K A_K(m, i) 2^{i-1}.$$  

As an example, $A_3$ is shown in Figure 2, at left.

$$A_3 = \begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & 1 \\ 0 & 1 & 0 \\ 0 & 1 & 1 \\ 1 & 0 & 0 \\ 1 & 0 & 1 \\ 1 & 1 & 0 \\ 1 & 1 & 1 \end{bmatrix}$$  

$$T^{(11)}_2 = \begin{bmatrix} 0 & 0 & 0 \\ 0 & 1 & 1 \\ 1 & 0 & 0 \\ 1 & 1 & 1 \end{bmatrix}$$  

$$T^{(12)}_2 = \begin{bmatrix} 0 & 0 & 1 \\ 0 & 1 & 1 \\ 1 & 0 & 0 \\ 1 & 1 & 1 \end{bmatrix}$$  

$$T^{(13)}_2 = \begin{bmatrix} 0 & 0 & 0 \\ 0 & 1 & 0 \\ 1 & 0 & 1 \\ 1 & 1 & 1 \end{bmatrix}$$

**Figure 2.**

There are $\binom{N}{K}$ possible $K$-connection sets

$$C^{(\alpha)}_K = \{i_1, i_2, \ldots, i_K\} \subseteq P_N, \text{ with } \alpha = 1, \ldots, \binom{N}{K} \tag{9}$$

and hence without loss of generality we can take $i_1 < i_2 < \cdots < i_K$. To each $C^{(\alpha)}_K$ we associate a $K$-connection map $C^{(\alpha)}_K : \Omega_N \to \Omega_K$, such that

$$C^{(\alpha)}_K(S) = C^{(\alpha)}_K(S_1, \ldots, S_N) = (S_{i_1}, \ldots, S_{i_K}). \tag{10}$$

A $K$-Boolean function

$$b_K : \Omega_K \to \Omega_1, \tag{11}$$

is completely determined by a $K$-truth table $T_K$, that consists of a $2^K \times (K + 1)$ binary matrix of the form

$$T_K = [A_K \ b_K], \tag{12}$$
where the vector
\[ b_K = [\sigma_1, \sigma_2, \ldots, \sigma_{2^K}] \] (13)
is expressed in column form in (12), and its entries correspond to the \(2^K\) images of the function (11).

As any \(K\)-truth table (12) has \(2^K\) rows there are as much as \(2^{2^K}\) possible \(K\)-truth tables, i.e., the total quantity of binary vectors (13). The Boolean functions (11) have been classified by Wolfram's notation according to their decimal number \(\mu\) given by
\[ \mu = 1 + \sum_{s=1}^{2^K} 2^{s-1} \sigma_s. \] (14)

Let us number the vectors (13) as well as the \(K\)-truth tables (12) according to (14) by adding the superscript \((\mu)\), i.e., \(b^{(\mu)}_K\) and \(T^{(\mu)}_K\), with \(\mu = 1, \ldots, 2^K\). Thus, for instance, the 2-truth tables \(T^{(11)}_2\), \(T^{(12)}_2\), and \(T^{(13)}_2\) in Figure 2.

The connection function (10) projects \(\Omega_N\) on \(\Omega_K\), enabling us to define projected \(N\)-Boolean functions \(b^{(\mu)(\alpha)}_N = b^{(\mu)}_K \circ C^{(\alpha)}_K\), that are completely defined through their \(N\)-truth tables
\[ T^{(\mu)(\alpha)}_N = \left[ A_N \ b^{(\mu)}_K \circ C^{(\alpha)}_K \right]. \] (15)

Within this notation, an \(NK\)-Kauffman network consists of a set
\[ \left\{ T^{(\mu_i)(\alpha_i)}_N \right\}_{i=1}^N, \]
and an evolution rule (equivalent to (1)):
\[ S_i (t + 1) = b^{(\mu_i)}_K \circ C^{(\alpha_i)}_K (S(t)), \]
where some of the indexes \(\alpha_i\) and \(\mu_i\) may be the same for different values of \(i\); and a \(2^N\)-functional graph \(g \in \mathcal{G}_{2^N}\) is associated through \(\Psi\) in (4).

An example is in point. Let \(N = 3, K = 2\), and consider the 2-connection sets \(C^{(1)}_2 = \{1, 2\}, C^{(2)}_2 = \{1, 3\}, C^{(3)}_2 = \{2, 3\}\), and the 2-truth tables \(T^{(11)}_2\),
We can construct an $NK$-Kauffman network consisting of the projected tables $\{T_{2}^{(11)(1)}, T_{3}^{(12)(2)}, T_{3}^{(11)(3)}\}$, that gives rise to an 8-functional graph with two connected components as in Figure 3. Note that taking the projected tables $\{T_{3}^{(13)(3)}, T_{3}^{(12)(2)}, T_{3}^{(11)(2)}\}$ the same 8-functional graph appears.

Figure 3. The nodes are labelled here in binary form, according to (3).

Now, for $\alpha = 1, \ldots, \binom{N}{K}$, let $B_{N}^{K}(\alpha)$ denote the $2^{N} \times 2^{2K}$ binary matrix whose $\mu$-th column results from the application of the projected $N$-truth table $T_{N}^{((\mu)(\alpha))}$ given by (15), that is:

$$B_{N}^{K}(\alpha) = \left[ b_{K}^{(1)} \circ C_{K}^{*}(\alpha) \quad b_{K}^{(2)} \circ C_{K}^{*}(\alpha) \quad \ldots \quad b_{K}^{(2^{2K})} \circ C_{K}^{*}(\alpha) \right].$$

To clarify how matrices $B_{N}^{K}(\alpha)$ are built up, consider for example $N = 3$ and $K = 2$. There are $2^{4} = 16$ truth tables, numbered according to (14), and shown below in compact form.

|   | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 |
|---|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|
| 00| 0 | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 1  | 0  | 1  | 0  | 1  | 0  |
| 01| 0 | 0 | 1 | 1 | 0 | 0 | 1 | 1 | 0 | 0  | 1  | 1  | 0  | 1  | 1  |
| 10| 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 0 | 0  | 0  | 1  | 1  | 1  | 1  |
| 11| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0  | 1  | 1  | 1  | 1  | 1  |

Moreover, there are $\binom{3}{2} = 3$ possible ways to choose two columns of $A_{3}$. Thus, assuming that columns 1 and 2 of $A_{3}$ form the connection set number 1 we get $B_{2}^{3}(1)$:
Taking columns 1 and 3 of $A_3$ as the connection set number 2 yields matrix $B_3^2(2)$:

\[
\begin{array}{cccccccccccccccc}
A_3 & 1 & 2 & 3 & 4 & 5 & 6 & 7 & 8 & 9 & 10 & 11 & 12 & 13 & 14 & 15 & 16 \\
000 & 0 & 1 & 0 & 1 & 0 & 1 & 0 & 1 & 0 & 1 & 0 & 1 & 0 & 1 & 0 & 1 \\
001 & 0 & 1 & 0 & 0 & 1 & 1 & 0 & 1 & 0 & 1 & 0 & 1 & 0 & 1 & 0 & 1 \\
010 & 0 & 0 & 0 & 1 & 1 & 0 & 0 & 0 & 1 & 1 & 0 & 0 & 1 & 1 & 0 & 1 \\
011 & 0 & 0 & 1 & 1 & 0 & 0 & 1 & 1 & 0 & 0 & 1 & 1 & 0 & 1 & 0 & 1 \\
100 & 0 & 0 & 0 & 0 & 1 & 1 & 1 & 1 & 1 & 0 & 0 & 0 & 0 & 1 & 1 & 1 \\
101 & 0 & 0 & 0 & 0 & 0 & 1 & 1 & 1 & 1 & 0 & 0 & 0 & 0 & 1 & 1 & 1 \\
110 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 1 & 1 & 1 & 1 & 1 & 1 \\
111 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 1 & 1 & 1 & 1 & 1 & 1 \\
\end{array}
\]

Finally, matrix $B_3^3(3)$ results from columns 2 and 3 of $A_3$:

\[
\begin{array}{cccccccccccccccc}
A_3 & 1 & 2 & 3 & 4 & 5 & 6 & 7 & 8 & 9 & 10 & 11 & 12 & 13 & 14 & 15 & 16 \\
000 & 0 & 1 & 0 & 1 & 0 & 1 & 0 & 1 & 0 & 1 & 0 & 1 & 0 & 1 & 0 & 1 \\
001 & 0 & 0 & 1 & 1 & 0 & 0 & 1 & 1 & 0 & 0 & 1 & 1 & 0 & 0 & 1 & 1 \\
010 & 0 & 1 & 0 & 1 & 0 & 1 & 0 & 1 & 0 & 1 & 0 & 1 & 0 & 1 & 0 & 1 \\
011 & 0 & 0 & 1 & 1 & 0 & 0 & 1 & 1 & 0 & 0 & 1 & 1 & 0 & 0 & 1 & 1 \\
100 & 0 & 0 & 0 & 0 & 1 & 1 & 1 & 1 & 1 & 0 & 0 & 0 & 0 & 1 & 1 & 1 \\
101 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 1 & 1 & 1 & 1 & 1 & 1 \\
110 & 0 & 0 & 0 & 0 & 1 & 1 & 1 & 1 & 1 & 0 & 0 & 0 & 0 & 1 & 1 & 1 \\
111 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 1 & 1 & 1 & 1 & 1 & 1 \\
\end{array}
\]

Let 

\[\Xi_K^N = \{B_K^N(\alpha)\}_{\alpha=1,...,\binom{N}{K}}.\]

The number $\#\Psi\left(\mathcal{L}_K^N\right)$ of different functional graphs that can be generated by the $NK$-Kauffman networks, equals the $N$-th power of the number
c of different columns belonging to the matrices of $\Xi^N_K$. Moreover,
\[ c = 2^{2^K} \binom{N}{K} - r, \] (16)
where $r$ is the number of ‘redundant’ columns (that is, the ones that are repeated) in the elements of $\Xi^N_K$. As no two columns of $A_N$ are the same, redundant columns arise solely from the following functions:

- The tautology: $b_K(C^*_K(S)) = 1$, for any $S \in \Omega_N$. As there is one tautology (column 16 in the last example) in each of the $\binom{N}{K}$ matrices, we get as much as $\binom{N}{K} - 1$ redundant columns.

- The contradiction: $b_K(C^*_K(S)) = 0$, for any $S \in \Omega_N$. With one contradiction (column 1 in the last example) in each matrix, we come also to $\binom{N}{K} - 1$ redundant columns.

- The identity: $b_K(S_{i_1}, \ldots, S_{i_K}) = S_{i_l}$, for $l = 1, \ldots, K$. Observe that no two columns of $A_N$ are the same. Hence, for each $j = 1, \ldots, N$, one replica of column $j$ of $A_N$ can be found in precisely $\binom{N-1}{K-1}$ matrices, yielding $\binom{N-1}{K-1} - 1$ redundant columns. Hence there is a total of $N \left[ \binom{N-1}{K-1} - 1 \right]$ redundant columns accounting for the identity function, (in the last example, columns 11 of $B_2^3(1)$ and 13 of $B_2^3(3)$ replicate column 2 of $A_3$).

- The negation: $b_K(S_{i_1}, \ldots, S_{i_K}) = 1 - S_{i_l}$, for $l = 1, \ldots, K$. This function leads also to $N \left[ \binom{N-1}{K-1} - 1 \right]$ redundant columns, because one complement of column $j$ of $A_N$ can be found in each of $\binom{N-1}{K-1}$ matrices.

Summing up we get
\[ r = 2 \binom{N}{K} - 2 + 2N \binom{N-1}{K-1} - 2N, \]

as the total number of redundant columns in $\Xi^N_K$. Substituting in (16) and using the identity $\binom{N-1}{K-1} = \frac{N}{K} \binom{N}{K}$, yields $c = \left(2^{2^K} - 2 (K + 1)\right) \binom{N}{K} + 2 (N + 1)$. Thus, the number of different functional graphs generated by $N$-$K$-Kauffman networks amounts to
\[ \#\Psi(L^N_K) = \left[ \left(2^{2^K} - 2 (K + 1)\right) \binom{N}{K} + 2 (N + 1) \right]^N. \] (17)
4. The Asymptotic Expansion of $\vartheta(N, K)$

From equations (7), (8) and (17) we get for the reciprocal of $\vartheta(N, K)$ that:

$$\vartheta^{-1}(N, K) = \{1 - \varphi(K)[1 - \xi_N(K)]\}^N,$$

where

$$\varphi(K) \equiv \frac{K + 1}{2^{2K-1}},$$

and

$$\xi_N(K) \equiv \frac{N + 1}{K + 1} \binom{N}{K}^{-1}.$$

The function $\xi_N(K)$ is unimodal on the interval $1 \leq K \leq N$, where it attains its maximum at $K = N$, yielding $\xi_N(N) = 1$, and its minimum at $K = N/2$, where $\xi_N(N/2) \sim \mathcal{O}\left(\sqrt{N/2}\right)$.

For fixed $N$, though $N \gg 1$, we obtain the following:

By means of Stirling’s approximation in the factorials involved in $\binom{N}{K}^{-1}$, it happens that $\xi_N(K) \sim \mathcal{O}(1/N^{K-1})$ for $K \sim \mathcal{O}(1)$, and $\xi_N(N - m) \sim \mathcal{O}(1/N^m)$ for $m \sim \mathcal{O}(1)$. Thus, $\xi_N(K) \sim o(1)$ over $1 < K < N$. Hence, since $\varphi(K) \ll 1$ for $K > 1$, $\vartheta^{-1}(N, K)$ exhibits the following asymptotic behavior

$$\vartheta^{-1}(N, K) \approx \{1 - \varphi(K)\}^N \approx e^{-N\varphi(K)}.$$  \hfill (20)

Figure 4 shows an excellent agreement for the functions (18) and (20) for just $N = 10$. There are two main asymptotic regimes:

i) $\vartheta^{-1}(N, K) \approx 1$ for $N\varphi(K) \ll 1$, \hfill (21.a)

and

ii) $\vartheta^{-1}(N, K) \approx 0$ for $N\varphi(K) \gg 1$, \hfill (21.b)

The critical point $K_c$ defining the transition region, where the regime changes is given by setting $\vartheta^{-1}(N, K_c) = 1/2$ in (20), yielding the transcendental equation

$$2^{K_c} \ln 2 - \ln(K_c + 1) = \ln\left(\frac{2N}{\ln 2}\right),$$

with solution

$$K_c \approx \log_2 \log_2 \left(\frac{2N}{\ln 2}\right) + \mathcal{O}\left(\frac{\ln \ln N}{\ln N}\right).$$

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Figure 4: The graph of $\vartheta^{-1}(N,K)$ as a function of $K$ and its asymptotic approximation (dashed); for $N = 10$.

The leading term corresponds to the solution obtained by neglecting the second term in the left hand side of (22). Equation (23) gives $K_c$ as a very slowly growing function on $N$. To estimate the width of the transition region let us expand $\vartheta^{-1}(N,K)$ in Taylor series up to the first order in $K - K_c$. From (20) we obtain:

$$\vartheta^{-1}(N,K) \approx \frac{1}{2} \left[ 1 - N \varphi'(K_c) (K - K_c) \right], \quad \text{for} \quad |K - K_c| \ll 1. \quad (24)$$

The width $\Delta K_c$ of the transition region is then given by:

$$\Delta K_c \equiv K_1 - K_0 = \frac{2}{N \varphi'(K_c)},$$

where $K_0$ and $K_1$ are such that $\vartheta^{-1}(N,K_0) = 0$ and $\vartheta^{-1}(N,K_1) = 1$, in (24). From (19) we get

$$\Delta K_c = \frac{2 (K_c + 1)}{2^{K_c} (K_c + 1) (\ln 2)^2 - 1} \ln 2 \sim \mathcal{O} \left( \frac{1}{\ln N} \right), \quad (25)$$
that is smaller than the absolute error in (23).

Summing up the results from (20) and (21) we have, for the asymptotic regimes outside of the transition region (of width $\Delta K_c$), that:

$$\vartheta (N, K) \approx \begin{cases} e^{\varphi(K)N} \gg 1 & \text{for } K < K_c - \Delta K_c \\ 1 + \varphi(K)N \approx 1 & \text{for } K > K_c + \Delta K_c \end{cases}.$$  \hspace{1cm} (26)

5. Conclusion

We have calculated an exact formula (18) for the average number $\vartheta (N, K)$ of $NK$-Kauffman networks, that are mapped by $\Psi$ [defined by (4)] onto the same binary function. The asymptotic expression (26) for $\vartheta (N, K)$ shows an abrupt change of regime at the critical value $K_c$ (23), that grows with $N$ as a double logarithm. The width of the transition $\Delta K_c$ (25), becomes small as $O (1/ \ln N)$.

In genetics $\Psi : \mathcal{L}_K^N \rightarrow \Psi (\mathcal{L}_K^N) \subseteq \mathcal{G}_{2^N}$ may be used for modeling the genotype-phenotype map $^3$. The genotype is represented by a $NK$-Kauffman network with $N$ Boolean variables; $S_i (t)$ representing the expression of the $i$-th gene at time $t$ within some developmental process. While a gene’s expression, could be much more complex than just to be described by binary values; $NK$-Kauffman networks have enough mathematical richness for a first approximation to the problem $^2,16$. The binary values $+1$ and $0$ correspond to an expressed or not expressed gene, respectively. Boolean functions $f_i$, and the $K$-connection sets $C_K^{(\alpha)}$ (9) represent the epistatic interactions among the genes $^6$. The phenotype and/or its metabolic regulation is represented by the different attractors, that the dynamics of the $NK$-Kauffman network generates, each of them, playing the role of an alternative cell in the organism. So, the different states in the attractor represent the metabolic process $^1,2,15$.

Changes in the $f_i$ and the $C_K^{(\alpha)}$ mimic random biological mutations, and so, $\vartheta (N, K)$ represents the average number of genotypes giving rise to the same metabolic process in the phenotype by means of mutations. From the asymptotic formula (26) for $\vartheta (N, K)$, it follows that, in order that $\Psi$ represents a robust genotype-phenotype map; it must be a many-to-one map, which implies that $K < K_c - \Delta K_c$. The number of genes that living organisms have, ranges from $6 \times 10^3$ in yeast, to less than $4 \times 10^4$ for the $H. sapiens$ $^{14}$. Substitution of these figures in (23) and (25) shows that, in both cases: for $NK$-Kauffman networks, to exhibit genetic robustness; it must happen that $K \leq 3$ for the average number of epistatic interactions.
Our results are in well concordance with the fact that, the existence of an ordered phase representing cycles on cells, requires the emergence of attractors whose length grows not faster than a power of \( N \); otherwise the cycle length will be too long to represent a metabolic process\(^2\). From the mean field analysis result (2) for \( K^* \), done by Derrida et. al.; that happens for \( K \leq 2 \) (in the case \( p = 1/2 \))\(^4,10\). To remark also, is that since the 70’s, the case \( K = 2 \) has been used as a model for cell differentiation\(^1,22\) and the mitotic cycle\(^23\).

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