Tracking perturbations in Boolean networks with spectral methods

Juha Kesseli,* Pauli Rämö, and Olli Yli-Harja
Institute of Signal Processing, Tampere University of Technology, P.O. Box 553, 33101 Tampere, Finland
(Received 21 March 2005; published 30 August 2005)

In this paper we present a method for predicting the spread of perturbations in Boolean networks. The method is applicable to networks that have no regular topology. The prediction of perturbations can be performed easily by using a presented result which enables the efficient computation of the required iterative formulas. This result is based on abstract Fourier transform of the functions in the network. In this paper the method is applied to show the spread of perturbations in networks containing a distribution of functions found from biological data. The advances in the study of the spread of perturbations can directly be applied to enable ways of quantifying chaos in Boolean networks. Derrida plots over an arbitrary number of time steps can be computed and thus distributions of functions compared with each other with respect to the amount of order they create in random networks.

DOI: 10.1103/PhysRevE.72.026137 PACS number(s): 05.70.Fh, 02.30.Nw, 05.45.−a

I. INTRODUCTION

Boolean networks are a class of simple discrete dynamical systems that have been used, e.g., in connection with studies on genetic regulatory networks [1] and evolutionary principles [2]. Boolean networks are interesting since they consist of simple deterministic parts, but yet they give rise to complex emergent phenomena. The phase transition from order to chaos in particular has been studied [3–8].

The parameter values at which the phase transition from order to chaos occurs in random Boolean networks (RBNs) were first derived using an annealed approximation [4]. In this approximation the connections between nodes and the update functions at each node are selected randomly after each time step. This is in contrast to quenched networks in which the network connections and update functions remain constant as the state of nodes is updated. The results for RBNs obtained using the annealed approximation can be seen to hold for quenched networks as well, hence the interest in this approximation.

The so-called Derrida plots were first discussed in the context of annealed approximation as mappings that describe the average distance between two points in the state space at time $t+1$ selected at different initial distances at time t [4,5]. It was found that the behavior of perturbations in random networks can be correctly predicted for RBNs using only this mapping iteratively. Numerical experiments with Derrida plots have since been performed [9,10]. The slope of the Derrida plot at the origin is often used as a chaoticity measure for network dynamics. It can be seen, however, that it provides only a first-order approximation of what happens as perturbations are studied in networks with update functions from arbitrary distributions. Better ways of quantifying chaos are therefore needed. One approach for doing this is presented in Ref. [11], in which influences of functions are used to study arbitrary distributions of functions with similar goals as in this paper.

Fourier analysis of Boolean functions has been used for decades and it has found applications in, e.g., switching theory [12,13]. These applications include logic design and fault detection [14]. Fault detection in particular has close relations with the Derrida plot since consequences of bit flips in the state are considered in both cases. In coding theory it is of interest to examine codes that are error correcting. In this application the so-called Krawtchouk polynomials are used [15]. These polynomials can be seen to arise also in the spectral decomposition of Derrida plots. In Ref. [12] the equivalent of the Derrida plot for single Boolean functions is called the generalized sensitivity. In this work we choose to use the terminology from Boolean networks.

Since the amount of points in the state-space grows exponentially with the network size N, numerical studies on Derrida plots typically use random sampling of the state-space. This gives rise to inaccuracies in the results and the amount of computation needed for a good approximation can be significant.

In Ref. [12] a special case of the current spectral result is presented in which the perturbations are computed over one time step only. In addition, only single functions, not networks, are discussed in that context. This result for Boolean networks along with a practical approximation is presented in Ref. [16]. In this paper similar methods are used to track the perturbations over an arbitrary number of time steps. Approximations that apply to large networks are utilized. Based on the result presented Derrida plots over an arbitrary number of time steps can be computed with a better accuracy than has been possible up to now.

II. THE ABSTRACT FOURIER TRANSFORM

Denote $\mathbb{B}=\{0,1\}$. The set $\mathcal{F}$ of all real functions on the hypercube $\mathbb{B}^N$, $\mathcal{F}=\{f:\mathbb{B}^N\rightarrow\mathbb{R}\}$, is a 2^N-dimensional real vector space with an inner product defined by

$$\langle f,g\rangle=\frac{1}{2^N}\sum_{x\in\mathbb{B}^N}f(x)g(x).$$

Denote the ith component of vector w by w_i and for each $w\in\mathbb{B}^N$ let $W(w)=\{i\in\{1,2,\ldots,N\}|w_i=1\}$. Denote $|w|$

*Electronic address: kesseli@cs.tut.fi

$=\Sigma_i w_i$. For each $w \in \mathbb{B}^N$ a Fourier transform kernel function $Q_w : \mathbb{B}^N \to \{-1,1\}$ is defined as the parity function over the corresponding subset $W(w)$ of variables,

$$Q_w(x) = (-1)^{w^T x} = (-1)^{\sum_{i \in W(w)} x_i}.$$

$\{Q_w | w \in \mathbb{B}^N\}$ is an orthonormal basis for $\mathcal{F}$ [12]. Let $f:\mathbb{B}^N \to \mathbb{B}$. The abstract Fourier transform (in this context also the name Walsh transform is used) of Boolean function f is the rational valued function $f^*:\mathbb{B}^N \to \mathbb{Q}$ which defines the coordinates of f with respect to the basis $\{Q_w | w \in \mathbb{B}^N\}$, i.e.,

$$f^*(w) = \langle Q_w, f \rangle = \frac{1}{2^N} \sum_x Q_w(x) f(x).$$

f can then be reconstructed from the coefficients as

$$f(x) = \sum_w f^*(w) Q_w(x).$$

The fast Walsh transform can be used to calculate the Fourier coefficients and thus also the Fourier spectrum efficiently [12,17].

III. ITERATIVE FORMULAS FOR PERTURBATION IN BOOLEAN NETWORKS

Boolean network $F:\mathbb{B}^N \to \mathbb{B}^N$ is a directed graph with N nodes. Each node is assigned a binary output variable and a Boolean function, whose inputs are the nodes from which there is an arc to the node in question. The network nodes are updated synchronously.

We study the effect of perturbations in the state of the network. At each time instant t denote by b_t the proportion of bits in the state that are equal to 1 and by ρ_t the proportion of bits in the state that are affected by the perturbation in the initial state at time $t=0$. Let

$$C_1 = C_1(b,\rho) = \binom{bN}{\frac{\rho N}{2}} \binom{(1-b)N}{\frac{\rho N}{2}},$$

$$C_2 = C_2(b) = \binom{N}{bN},$$

and

$$C = C(b,\rho) = \sum_{\substack{x: \\ |x|=bN}} \sum_{\substack{y:|y|=\rho N \\ |x\oplus y|=bN}} 1 = C_1(b,\rho) C_2(b).$$

For an infinite network the proportion of ones in the network updates according to the expected probability that inputs are selected such that we get an output of one,

$$b_{t+1} = E_f\left(\sum_{x \in \mathbb{B}^K} f(x) b_t^{|x|} (1-b_t)^{K-|x|} \right), \tag{1}$$

where the expectation is taken with respect to the function f and K is the effective in-degree of f.

We propose that the number of perturbed bits in the state is modeled as changing as follows:

$$\rho_{t+1} = E_f\left(\frac{1}{C} \sum_{\substack{x: \\ |x|=b_t N}} \sum_{\substack{y:|y|=\rho_t N \\ |x\oplus y|=b_t N}} f(x) \oplus f(x \oplus y) \right)$$
$$= \frac{1}{C} \sum_{\substack{x: \\ |x|=b_t N}} \sum_{\substack{y:|y|=\rho_t N \\ |x\oplus y|=b_t N}} E_f[f(x) \oplus f(x \oplus y)]. \tag{2}$$

That is, the number of bits in the perturbation changes as it would on average given that both the nonperturbed (x) and the perturbed $(x \oplus y)$ state have a proportion of ones given by iterative equation (1) but are otherwise selected randomly. Together formulas (1) and (2) can be used to model the spread of perturbations in time. Note that since exactly the same proportion of ones, b_t, is required for both states, for finite N only perturbations of sizes $\rho_t = 0/N, 2/N, \ldots$ are possible whereas b_t can take any of the values $0/N, 1/N, \ldots, N/N$.

The main simplifications in the model are twofold. First, we assume that the network is of infinite size or that the network model is annealed, which means that the connections between nodes in the network are generated randomly at each time t. This assumption enables us to compute b_t and ρ_t using a mean-field approach where the outputs of individual functions are replaced by distributions of outputs from distributions of functions. Whereas the resulting approximation can be used for large networks with random connections, this approach is not as such applicable, e.g., for cellular automata with regular topologies.

All kinds of regular structures in the topology can result in problems with the approximation. One way of describing these kinds of cases is considering local neighborhoods in which the values of the nodes will affect their own future value more than other nodes because of the connection structure of a part of the network. Mean-field approximation is thus only a first-order approximation of the dynamics of real genetic regulatory networks since the topology of regulatory networks is not likely to be without local structures. A way to quantify the difference between the annealed approximation and real networks would be to compare cell dynamics with the predictions of network dynamics obtained with the current method from the distributions of regulatory functions described in the literature. With suitable data this should be possible in the future. The difference observed between the predictions and the dynamics could be considered as evidence of topological regularities in the network.

As a second simplification, only expected values of b_t and ρ_t are studied. It turns out, however, that for the $N \to \infty$ cases considered here this limitation is not important. This is due to the fact that the distributions of b_t and ρ_t are typically rather close to the ones obtained with this assumption of independent nodes and the mean is enough to predict the propagation of perturbations. We do not know, however, if this holds for all cases. Evidence of the usability of the current approach is thus mainly based on numerous simulations with different kinds of functions. Only a part of these simulations is presented in this paper.

The model assumes that both the initial and the perturbed state have the same bias. If the initial state has an average

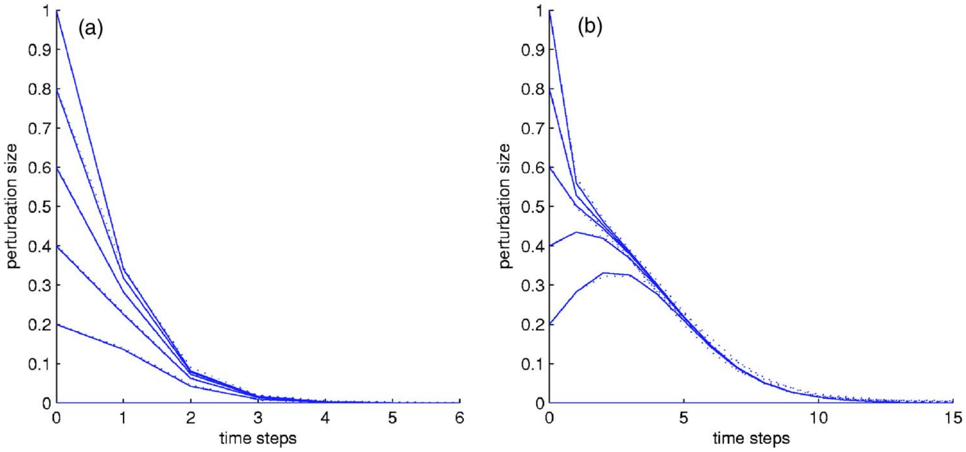

FIG. 1. (Color online) Spread of perturbations in two test cases. On the left-hand side, the network is created with function distribution taken from Ref. [18] and on the right-hand side with a mixture of the four functions given in the text. Solid lines denote the results computed with the spectral method and dotted lines the ones obtained by random sampling of the states and perturbations. Network size for the numerical experiment is $N=139$.

bias of one-half, as we have in the definition of ordinary Derrida plots, this condition holds on average. In general, if we study large perturbations from arbitrary initial state biases, the condition will not hold exactly and the predictions cannot be expected to be accurate unless the perturbations are created according to the bias requirements of the model. For the application of the current method to ordinary Derrida plots over several time steps discussed here this difference is thus not significant.

We have defined (2) as a model for spread of perturbations in time. In order to use this formula for computational purposes, we need to be able to do that efficiently. This is possible using the following result and the expected spectrum of the functions in the network. If $f:\mathbb{B}^N \mapsto \mathbb{B}$ is a Boolean function with K essential variables and f^* is the Fourier transform of f with redundant variables removed, then

$$\frac{1}{C}\sum_{\substack{x:\\|x|=bN}}\sum_{\substack{y:|y|=\rho N\\|x\oplus y|=bN}} f(x)\oplus f(x\oplus y) \to 2\sum_{w\in\mathbb{B}^K} f^*(w)(1-2b)^{|w|} - 2\sum_{w\in\mathbb{B}^K}\sum_{u\in\mathbb{B}^K} f^*(w)f^*(u)(1-2\rho)^{u^Tw}(1-2b)^{u\oplus w}$$

as $N\to\infty$. A proof for this result can be found in the Appendix.

Perturbations propagate in infinite networks according to what follows if we apply the previous result to (2),

$$\rho_{t+1} = 2\sum_{i=0}^{K} s_i(1-2b_t)^i - 2\sum_{i=0}^{K}\sum_{j=0}^{K} S_{i,j}(1-2\rho_t)^i(1-2b_t)^j, \tag{3}$$

where

$$s_i = E\left(\sum_{|w|=i} f^*(w)\right),$$

$$S_{i,j} = E\left(\sum_{\substack{(u,w):\\ w^Tu=i\\ |w\oplus u|=j}} f^*(w)f^*(u)\right),$$

K is the maximum in-degree of functions in the network, ρ_t is the size of the perturbation at time t, and b_t is the bias of the states at time t. This result can be used to compute the spread of perturbations in Boolean networks with any distribution of functions over an arbitrary number of time steps.

IV. APPLICATIONS

The model we have for the spread of perturbations can now be tested with any given distribution of functions. For finite networks average spectrum values should be used instead of the expectation. In the case of a finite network the results are not exact but the approximation is quite good. For comparison purposes we compute in each test case the spread of perturbations with simulations in quenched networks randomly generated with the same distribution of functions. Random states with bias $\frac{1}{2}$ and random perturbations of selected size are chosen and the network is run forward in time for the desired number of time steps. The average perturbation size resulting from a selected number of initial pairs of states is plotted as a dotted line in Figs. 1 and 2.

Figure 1 shows the spread of perturbations for two different networks. On the left-hand side, the perturbations are computed for a network with functions corresponding to the distribution of the 139 Boolean functions in Ref. [18]. These functions were found by studying publications containing information on genetic regulation and the resulting test network can thus be considered representative of real biological networks. From the figure it can be seen that the network is indeed stable as the perturbations vanish quite rapidly.

On the right-hand side, the network is created as a mixture of four updating rules, $f_1(x)=x_1(x_2\oplus x_3)+\overline{x_1}x_2x_3$, $f_2(x)=x_1\overline{x_2}+\overline{x_1}x_2x_3$, $f_3(x)=x_2x_3+x_1\overline{x_2}\,\overline{x_3}$, and $f_4=x_1(x_2\oplus x_3)+x_2x_3$. A numerical result is computed for comparison such that it has 35 nodes with f_1, 35 nodes with f_2, 35 nodes with f_3, and

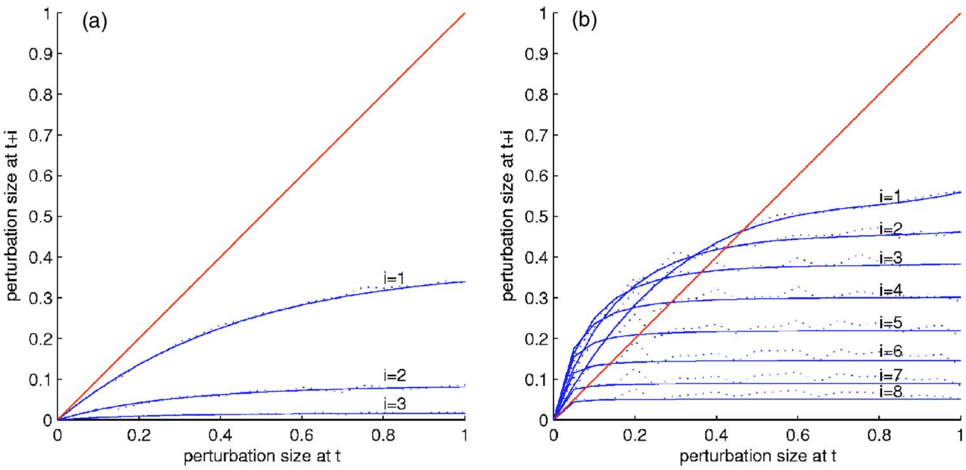

FIG. 2. (Color online) Derrida plots for the test cases of the preceding figure computed over i time steps. Solid lines denote the results computed with the spectral method and dotted lines the ones obtained by random sampling of states and perturbations. Network size for the numerical experiment is $N=139$.

34 nodes with f_4 for a total of 139 nodes. The results using the spectral method are computed using the corresponding weights on the spectrum. In this case, small perturbations tend to increase initially but since (1) converges to zero this is only temporary. For both cases the numerical results are close to the ones computed with the spectral method.

Figure 2 shows the results if we use the same networks to compute Derrida plots over several time steps. In the Derrida plots the initial bias is set to one-half. In the latter case it is of interest to note that as more time steps are taken, the slope at the origin increases initially but then approaches zero. This shows in practice how the slope of the ordinary Derrida plot with initial bias of one-half computed over one time step only is not a sufficient measure of chaos in general despite its common use. Derrida plots computed numerically over several time steps can be used for such purposes. In the computation of these Derrida plots over several time steps the method presented here can give superior accuracy with given computational resources. For the images shown here the numerical result, the dotted line, takes at least 10 times as long to compute as the spectral version and still has clearly too much variance to be useful.

The Derrida plots over several time steps can thus be easily computed for networks of any functions with a suitable in-degree and thus chaos in networks quantified with increased accuracy as compared with the previous measures like the slope of the standard Derrida plot. The fixed points of the iterative mappings from Derrida plots over several time steps can be used as improved approximations of the real fixed points and thus also the distinction between ordered and chaotic networks can be made with a greater accuracy [4]. As a first-degree approximation a network can be called ordered if the simple Derrida plot has a stable fixed point at the origin. If chaoticity is quantified with Derrida plots over several time steps there are networks that have a stable fixed point at zero even though the first-degree approximation would not suggest this. There are therefore cases in which the method gives a different classification of networks than simpler approximations and is consequently significant in practice.

The slope of the Derrida plot at the origin is related to the so-called average sensitivity of Boolean functions [16]. As discussed in Ref. [11] the bias at which the sensitivity of Boolean functions to perturbations is studied is significant. The choice of initial bias of one-half in the example cases here is made mainly for convenience of comparison with previous usage of the Derrida plot. If we want to study the long-term behavior that is decisive for chaoticity we need to study the sensitivity of Boolean functions for small perturbations at the fixed point of the bias. This is the limiting value of b_t that is obtained as $t \to \infty$. Note that there need not necessarily be such convergence for an arbitrary selection of functions but in practice there typically is such a fixed point. It can be verified numerically that the current approach can predict the long-term behavior of perturbations at bias fixed point with a good accuracy. The changing bias of the state can be seen to be highly relevant to Boolean network dynamics as the predictions are made more accurate for Derrida plots computed at the bias fixed point as compared with the Derrida plots at bias $\frac{1}{2}$.

V. DISCUSSION

The method presented enables the efficient prediction of spread of perturbations in a large network with arbitrary functions if the in-degree is bounded by a reasonably small K. Alternatively, results can be obtained for such classes of functions for which the expected values of spectrum parameters can be computed particularly easily. This is significant in at least two respects.

First, the Derrida plots over an arbitrary number of time steps presented in Sec. IV are an example of applications that enable an improved quantification of chaos in Boolean networks. New hypotheses on chaoticity of regulatory networks in nature can be tested as suitable data emerge. Since arbitrary classes of functions can now easily be compared with each other, the approach promises to enable more thorough analysis of different types of functions that have been proposed as the basis of large in-degree ordered networks found in e.g., biological systems in nature. The classes of functions under consideration include, e.g., canalyzing [19] and Post functions [9].

Second, the method could help in problems such as counting attractors in random networks or determining their average length. Relations between the spectral computation of spread of perturbations and attractors are an interesting focus of further work in this area. Our method has the benefit of easy application with any types of functions so that any advance towards the attractor problem would simultaneously give answers to questions on many different kinds of networks.

It can be seen that for ordinary RBNs [4] $S_{i,j}=0$ for $j>0$. Thus the perturbation mapping (3) reduces to the ordinary Derrida plot for RBNs. This is consistent with the fact that the Derrida plot in the original annealed approximation predicts perturbations in RBNs correctly. It should also be noted that for any function f $S_{i,j}=0$ if $i+j>K$, where K is the number of inputs of f.

Since the number of spectral coefficients goes up as 2^K with the in-degree K, there are still limits on the in-degree that can be used in the network, although in-degrees up to at least 10 are still quite efficient in all cases. In order to compute the spread of perturbations for networks with some number of nodes with larger in-degrees special techniques are needed. Since, e.g., scale-free networks have a significant number of nodes with a large in-degree it is of great interest to extend the current methods to these cases as well. Another area of further work will be in studying special cases of interesting functions for which the computation of the spectral parameters needed in the iterative equation (2) can be done efficiently.

APPENDIX: PROOF FOR THE SPECTRAL FORM OF THE ITERATIVE FORMULA

$$
\begin{aligned}
&\frac{1}{C}\sum_{\substack{x:\\|x|=bN}}\sum_{\substack{y:|y|=\rho N\\|x\oplus y|=bN}} f(x)\oplus f(x\oplus y)\\
&\quad=\frac{1}{C}\sum_{\substack{x:\\|x|=bN}}\sum_{\substack{y:|y|=\rho N\\|x\oplus y|=bN}}\frac{1}{2}(1-(2f(x)-1)[2f(x\oplus y)-1])\\
&\quad=\underbrace{-\frac{2}{C}\sum_{\substack{x:\\|x|=bN}}\sum_{\substack{y:|y|=\rho N\\|x\oplus y|=bN}} f(x)f(x\oplus y)}_{A_1}+\underbrace{\frac{1}{C}\sum_{\substack{x:\\|x|=bN}}\sum_{\substack{y:|y|=\rho N\\|x\oplus y|=bN}} f(x)}_{A_2}\\
&\quad\quad+\underbrace{\frac{1}{C}\sum_{\substack{x:\\|x|=bN}}\sum_{\substack{y:|y|=\rho N\\|x\oplus y|=bN}} f(x\oplus y)}_{A_3}
\end{aligned}
\tag{A1}
$$

With spectral decomposition the first double sum can be written as

$$
\begin{aligned}
A_1&=-\frac{2}{C}\sum_{\substack{x:\\|x|=bN}}\sum_{\substack{y:|y|=\rho N\\|x\oplus y|=bN}}\sum_{w\in\mathbb{B}^K}\sum_{u\in\mathbb{B}^K} f^*(w)f^*(u)\\
&\quad\times(-1)^{w^Tx}(-1)^{u^T(x+y)}\\
&=-\frac{2}{C_2}\sum_{w\in\mathbb{B}^K}\sum_{u\in\mathbb{B}^K} f^*(w)f^*(u)\\
&\quad\times\overbrace{\sum_{\substack{x:\\|x|=bN}}(-1)^{(u+w)^Tx}\frac{1}{C_1}\underbrace{\sum_{\substack{y:|y|=\rho N\\|x\oplus y|=bN}}(-1)^{u^Ty}}_{B_1}}^{B_2}.
\end{aligned}
\tag{A2}
$$

We will first compute B_1. Denote $c=u^Tx$ and $d=u^T(1-x)$, $c+d=|u|$. $(-1)^{u^Ty}$ will be one when an even number of ones in y overlap ones in u and minus one otherwise. By dividing the ones of y into those that overlap with ones in x and those that do not we obtain the number of even u^Ty's,

$$
\begin{aligned}
&\sum_{j\text{ odd}}\sum_{i\text{ odd}}\binom{c}{i}\binom{d}{j}\binom{bN-c}{\frac{\rho N}{2}-i}\binom{(1-b)N-d}{\frac{\rho N}{2}-j}\\
&\quad+\sum_{j\text{ even}}\sum_{i\text{ even}}\binom{c}{i}\binom{d}{j}\binom{bN-c}{\frac{\rho N}{2}-i}\binom{(1-b)N-d}{\frac{\rho N}{2}-j}.
\end{aligned}
$$

We can approximate the product of the two binomial coefficients containing N if we take the constant C_1 from B_1,

$$
\begin{aligned}
&\frac{1}{C_1}\binom{bN-c}{\frac{\rho N}{2}-i}\binom{(1-b)N-d}{\frac{\rho N}{2}-j}\\
&\quad=\frac{(bN-c)!}{(bN)!}\frac{[(1-b)N-d]!}{[(1-b)N]!}\\
&\quad\quad\times\frac{\left(\frac{\rho N}{2}\right)!}{\left(\frac{\rho N}{2}-i\right)!}\frac{\left[\left(b-\frac{\rho}{2}\right)N\right]!}{\left[\left(b-\frac{\rho}{2}\right)N-c+i\right]!}\\
&\quad\quad\times\frac{\left(\frac{\rho N}{2}\right)!}{\left(\frac{\rho N}{2}-j\right)!}\frac{\left[\left(1-b-\frac{\rho}{2}\right)N\right]!}{\left[\left(1-b-\frac{\rho}{2}\right)N-d+j\right]!}.
\end{aligned}
$$

As $N\to\infty$ we have

$$\frac{1}{C_1}\binom{c}{i}\binom{d}{j}\binom{bN-c}{\frac{\rho N}{2}-i}\binom{(1-b)N-d}{\frac{\rho N}{2}-j}$$
$$\to \binom{c}{i}\binom{d}{j}\left(\frac{\frac{\rho}{2b}}{1-\frac{\rho}{2b}}\right)^i\left(\frac{\frac{\rho}{2(1-b)}}{1-\frac{\rho}{2(1-b)}}\right)^j$$
$$\times\left(1-\frac{\rho}{2b}\right)^c\left(1-\frac{\rho}{2(1-b)}\right)^d.$$

In order to sum these over odd or even i and j, note that the z transform for a sequence of the form $s_i=\binom{A}{i}a^i$ is

$$S(z)=\sum_i s_i z^i=(1+az)^A. \tag{A3}$$

The sums for odd and even indices can now be easily computed,

$$\sum_{i\text{ even}} s_i=\frac{1}{2}[S(1)+S(-1)] \tag{A4}$$

and

$$\sum_{i\text{ odd}} s_i=\frac{1}{2}[S(1)-S(-1)]. \tag{A5}$$

Applying these to the above limit formulas, and noting that we can get the result by multiplying the number of even u^Ty's by 2 and subtracting the total number of y's to sum over C_1, we obtain

$$B_1=\frac{1}{C_1}\sum_{\substack{y:|y|=\rho N\\ |x\oplus y|=bN}}(-1)^{u^Ty}$$
$$\to\frac{1}{2}\left[1-\left(1-\frac{\rho}{b}\right)^c\right]\left[1-\left(1-\frac{\rho}{1-b}\right)^d\right]$$
$$+\frac{1}{2}\left[1+\left(1-\frac{\rho}{b}\right)^c\right]\left[1+\left(1-\frac{\rho}{1-b}\right)^d\right]-1$$
$$=\left(1-\frac{\rho}{b}\right)^c\left(1-\frac{\rho}{1-b}\right)^d=\left(1-\frac{\rho}{b}\right)^{u^Tx}\left(1-\frac{\rho}{1-b}\right)^{|u|-u^Tx}.$$

Substituting this to the latter part of formula (A2) and summing over all x with constant $g=u^Tx$ at a time we get

$$\sum_{\substack{x:\\ |x|=bN}}(-1)^{(u+w)^Tx}\frac{1}{C_1}\sum_{\substack{y:|y|=\rho N\\ |x\oplus y|=bN}}(-1)^{u^Ty}$$
$$=\left(1-\frac{\rho}{1-b}\right)^{|u|}\sum_g\left(\frac{\frac{\rho}{b}-1}{1-\frac{\rho}{1-b}}\right)^g\underbrace{\sum_{\substack{x:|x|=bN\\ x^Tu=g}}(-1)^{w^Tx}}_{B_3}.$$

We will next compute B_3, the summation over x in this formula. For x with given $|x|=bN$ and $u^Tx=g$ we will have an even w^Tx for any choice of x such that i ones of x are from the u^Tw bits that are one in both u and w, j ones of x are from the $|w|-u^Tw$ bits which are one in w and zero in u, and that both i and j are odd or both are even. In addition, the other ones of x will have to be selected such that the two given conditions for b and g both hold. In this way the summation can now be written as

$$B_3=\sum_{\substack{x:|x|=bN\\ x^Tu=g}}(-1)^{w^Tx}$$
$$=2\sum_{i\text{ even}}\sum_{j\text{ even}}G(i,j)+2\sum_{i\text{ odd}}\sum_{j\text{ odd}}G(i,j)-\sum_i\sum_j G(i,j), \tag{A6}$$

where

$$G(i,j)=\binom{u^Tw}{i}\binom{|u|-u^Tw}{g-i}\binom{|w|-u^Tw}{j}$$
$$\times\binom{N-|u|-|w|+u^Tw}{bN-g-j}.$$

We can again use an approximation as $N\to\infty$, since

$$\frac{1}{C_2}\binom{N-|u|-|w|+u^Tw}{bN-g-j}$$
$$=\frac{(N-|u|-|w|+w^Tu)!}{N!}\frac{(bN)!}{(bN-g-j)!}$$
$$\times\frac{[(1-b)N]!}{[(1-b)N+g+j+w^Tu-|u|-|w|]!}$$
$$\to\left(\frac{b}{1-b}\right)^g\left(\frac{b}{1-b}\right)^j(1-b)^{|u|+|w|-w^Tu}.$$

Using this and summing over j in (A6) we get

$$B_2=\frac{1}{C}\sum_{\substack{x:\\ |x|=bN}}(-1)^{(u+w)^Tx}\sum_{\substack{y:|y|=\rho N\\ |x\oplus y|=bN}}(-1)^{u^Ty}$$
$$\to\left(1-\frac{\rho}{1-b}\right)^{|u|}(1-b)^{|u|+|w|-w^Tu}\sum_g\left(\frac{\rho-b}{1-b-\rho}\right)^g$$
$$\times\left\{\sum_{i\text{ even}}H(i)\left[\left(1+\frac{b}{1-b}\right)^{|w|-u^Tw}+\left(1-\frac{b}{1-b}\right)^{|w|-u^Tw}\right]\right.$$
$$+\sum_{i\text{ odd}}H(i)\left[\left(1+\frac{b}{1-b}\right)^{|w|-u^Tw}-\left(1-\frac{b}{1-b}\right)^{|w|-u^Tw}\right]$$
$$\left.-\sum_i H(i)(1-b)^{|w|-u^Tw}\right\},$$

where

$$H(i)=\binom{u^Tw}{i}\binom{|u|-u^Tw}{g-i}.$$

We can now change the order of summation and sum over g if we in addition to (A3) note that the z transform of $s'_n = s_{n+m}$ is

$$S'(z)=S(z)z^m.$$

We now get

$$\begin{aligned}B_2 \to{}& (1-b-\rho)^{|u|}\left(1+\frac{\rho-b}{1-b-\rho}\right)^{|u|-u^Tw}\\ &\times\Bigg\{\sum_{i\ \text{even}}\binom{u^Tw}{i}[1+(1-2b)^{|w|-u^Tw}]\left(\frac{1-b-\rho}{\rho-b}\right)^i\\ &+\sum_{i\ \text{odd}}\binom{u^Tw}{i}(1-(1-2b)^{|w|-u^Tw}]\left(\frac{1-b-\rho}{\rho-b}\right)^i\\ &-\sum_i\binom{u^Tw}{i}\left(\frac{1-b-\rho}{\rho-b}\right)^i\Bigg\}.\end{aligned}$$

By summing over i we have

$$\begin{aligned}B_2 \to{}& (1-b-\rho)^{|u|}(1+q)^{|u|-u^Tw}\\ &\times\Bigg\{\frac{1}{2}[1+(1-2b)^{|w|-u^Tw}][(1+q)^{u^Tw}+(1-q)^{u^Tw}]\\ &+\frac{1}{2}[1-(1-2b)^{|w|-u^Tw}][(1+q)^{u^Tw}\\ &-(1-q)^{u^Tw}]-(1+q)^{u^Tw}\Bigg\},\end{aligned}$$

where

$$q=\frac{\rho-b}{1-b-\rho}$$

so that

$$\begin{aligned}B_2 &\to (1-2b)^{|u|}(1-2b)^{|w|-u^Tw}\left(\frac{1-2\rho}{1-2b}\right)^{u^Tw}\\ &=(1-2\rho)^{u^Tw}(1-2b)^{|u\oplus w|}.\end{aligned}$$

This means that we can now write the entire sum of (A2) as

$$A_1 \to -2\sum_{w\in\mathbb{B}^K}\sum_{u\in\mathbb{B}^K} f^*(w)f^*(u)(1-2\rho)^{u^Tw}(1-2b)^{|u\oplus w|}.$$

We still need to compute the other two sums in (A1). Similar approximations as previously used can be applied again. In the first one y only occurs in the indices,

$$\begin{aligned}A_2 &= \frac{1}{C}\sum_{\substack{x:\\|x|=bN}}\ \sum_{\substack{y:|y|=\rho N\\|x\oplus y|=bN}} f(x) = \frac{1}{C_2}\sum_{\substack{x:\\|x|=bN}} f(x) = \sum_{w\in\mathbb{B}^K} f^*(w)\frac{1}{C_2}\sum_{\substack{x:\\|x|=bN}}(-1)^{w^Tx} = \sum_{w\in\mathbb{B}^K} f^*(w)\left(2\sum_{i\ \text{even}}\frac{\binom{|w|}{i}\binom{N-|w|}{bN-i}}{\binom{N}{bN}}-1\right)\\ &\to \sum_{w\in\mathbb{B}^K} f^*(w)\left[2(1-b)^{|w|}\sum_{i\ \text{even}}\binom{|w|}{i}\left(\frac{b}{1-b}\right)^i-1\right] = \sum_{w\in\mathbb{B}^K} f^*(w)\left\{(1-b)^{|w|}\left[\left(1+\frac{b}{1-b}\right)^{|w|}+\left(1-\frac{b}{1-b}\right)^{|w|}\right]-1\right\}\\ &= \sum_{w\in\mathbb{B}^K} f^*(w)(1-2b)^{|w|}.\end{aligned}$$

For the last sum remaining we need to sum by using variable g as in the double sum,

$$\begin{aligned}A_3 &= \frac{1}{C}\sum_{\substack{x:\\|x|=bN}}\ \sum_{\substack{y:|y|=\rho N\\|x\oplus y|=bN}} f(x\oplus y) = \frac{1}{C}\sum_{w\in\mathbb{B}^K} f^*(w)\sum_{\substack{x:\\|x|=bN}}(-1)^{w^Tx}\sum_{\substack{y:|y|=\rho N\\|x\oplus y|=bN}}(-1)^{w^Ty}\\ &\to \frac{1}{C_2}\sum_{w\in\mathbb{B}^K} f^*(w)\sum_{\substack{x:\\|x|=bN}}(-1)^{w^Tx}\left(1-\frac{\rho}{b}\right)^{w^Tx}\left(1-\frac{\rho}{1-b}\right)^{|w|-w^Tx} = \frac{1}{C_2}\sum_{w\in\mathbb{B}^K} f^*(w)\left(1-\frac{\rho}{1-b}\right)^{|w|}\sum_g\left(\frac{\frac{\rho}{b}-1}{1-\frac{\rho}{1-b}}\right)^g\sum_{\substack{x:|x|=bN\\w^Tx=g}}1\\ &= \sum_{w\in\mathbb{B}^K} f^*(w)\left(1-\frac{\rho}{1-b}\right)^{|w|}\sum_g\left(\frac{\frac{\rho}{b}-1}{1-\frac{\rho}{1-b}}\right)^g\frac{\binom{|w|}{g}\binom{N-|w|}{bN-g}}{\binom{N}{bN}} \to \sum_{w\in\mathbb{B}^K} f^*(w)(1-b-\rho)^{|w|}\sum_g\binom{|w|}{g}\left(\frac{\rho-b}{1-b-\rho}\right)^g\end{aligned}$$

$$= \sum_{w \in \mathbb{B}^K} f^*(w)(1-b-\rho)^{|w|}\left(1+\frac{b-\rho}{1-b-\rho}\right)^{|w|} = \sum_{w \in \mathbb{B}^K} f^*(w)(1-2b)^{|w|}.$$

Thus we have the result,

$$\frac{1}{C}\sum_{\substack{x:\\|x|=bN}}\sum_{\substack{y:|y|=\rho N\\|x\oplus y|=bN}} f(x)\oplus f(x\oplus y) \to 2\sum_{w\in\mathbb{B}^K} f^*(w)(1-2b)^{|w|} - 2\sum_{w\in\mathbb{B}^K}\sum_{u\in\mathbb{B}^K} f^*(w)f^*(u)(1-2\rho)^{u^T w}(1-2b)^{|u\oplus w|}$$

as $N\to\infty$.

[1] S. A. Kauffman, *The Origins of Order* (Oxford University Press, New York, 1993).

[2] M. D. Stern, Evolution (Lawrence, Kans.) **96**, 10746 (1999).

[3] M. Aldana, S. Coppersmith, and L. P. Kadanoff, in *Perspectives and Problems in Nonlinear Science*, edited by E. Kaplan, J. E. Marsden, and K. R. Sreenivasan (Springer, New York, 2003), pp. 23–89.

[4] B. Derrida and Y. Pomeau, Europhys. Lett. **1**, 45 (1986).

[5] B. Derrida and D. Stauffer, Europhys. Lett. **2**, 739 (1986).

[6] B. Luque and C. Blanc, Santa Fe Institute working paper 97-11-084, 1997.

[7] B. K. Sawhill and S. Kauffman, Santa Fe Institute working paper 97-05-038, 1997.

[8] I. Shmulevich and S. A. Kauffman, Phys. Rev. Lett. **93**, 048701 (2004).

[9] I. Shmulevich, H. Lähdesmäki, E. R. Dougherty, and W. Z. Jaakko Astola, Proc. Natl. Acad. Sci. U.S.A. **100**, 10734 (2003).

[10] A. Wuensche, Santa Fe Institute working paper 98-11-101, 1998.

[11] A. Moreira and L. Amaral, Phys. Rev. Lett. **94**, 218702 (2005).

[12] A. Bernasconi, Ph.D. thesis, University of Pisa, 1998.

[13] R. J. Lechner, *Recent Developments in Switching Theory* (Academic, New York, 1971), Chap. Harmonic Analysis of Switching Functions, pp. 122–229, Electrical Science Series.

[14] M. G. Karpovsky, *Spectral Techniques and Fault Detection* (Academic, Orlando, FL, 1985).

[15] F. J. MacWilliams and N. J. Sloane, *The Theory of Error-Correcting Codes* (North-Holland, Amsterdam, 1977).

[16] J. Kesseli, P. Rämö, and O. Yli-Harja, Physica D **206**, 49 (2005).

[17] J. L. Shanks, IEEE Trans. Comput. **C18**, 457 (1969).

[18] S. E. Harris, B. K. Sawhill, A. Wuenche, and S. Kauffman, Complexity **7**, 23 (2001).

[19] S. A. Kauffman, C. Peterson, B. Samuelsson, and C. Troein, Proc. Natl. Acad. Sci. U.S.A. **100**, 14796 (2003).