# The Diffusion of Perturbations in a Model of Coupled Random Boolean Networks

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**Abstract.** Deciphering the influence of the interaction among the constituents of a complex system on the overall behaviour is one of the main goals of complex systems science. The model we present in this work is a 2D square cellular automaton whose of each cell is occupied by a complete random Boolean network. Random Boolean networks are a well-known simplified model of genetic regulatory networks and this model of interacting RBNs may be therefore regarded as a simplified model of a tissue or a monoclonal colony. The mechanism of cell-to-cell interaction is here simulated letting some nodes of a particular network being influenced by the state of some nodes belonging to its neighbouring cells. One possible means to investigate the overall dynamics of a complex system is studying its response to perturbations. Our analyses follow this methodological approach. Even though the dynamics of the system is far from trivial we could show in a clear way how the interaction affects the dynamics and the global degree of order.

**Keywords:** genetic network model, random Boolean network, cellular automaton, interaction, cell-criticality.

## 1 Introduction

One of the main goals of complex systems science is deciphering the influence of the interactions among the system components on the global dynamics. In this work we introduce a model in which another level of complexity is added: the system components are themselves well-know models of complex systems, i.e. random Boolean networks.

Random Boolean networks are a simplified model of genetic networks [1] and the statistical analysis of their dynamical properties has proven fruitful in the description of general emerging features of real networks [2,3,4,5,6].

The theme of interaction turns out to be deeply relevant when speaking of the so-called "criticality" of living organisms. The idea that evolution would drive living organism in a region of the space of parameters close to the boundary between order and chaos [2,7] is an intriguing general hypothesis to investigate

H. Umeo et al. (Eds): ACRI 2008, LNCS 5191, pp. 315–322, 2008.

and, since it applies to organisms as a whole rather than to their individual constituents, it makes particular sense to study the way by which the single elements constituting the whole system (i.e. single cells) interact and how their interaction affects the overall dynamical regime. Therefore, the aim of this work is to analyse the relationship between the dynamics of a single, isolated RBN (which has been extensively studied in the past) and that of a collection of interacting networks: the model we are going to present is a 2-D lattice cellular automaton in which of each cell (which is meant to simulate a biological cell) hosts a complete RBN. This model could be regarded as a simplified description of a tissue in a multicellular organism, or of a colony of unicellular organisms: at this level of modelling the two cases are rather similar, since all that matters is that neighbouring cells influence each other.[1] The particular kind of cell-to-cell interaction we want to represent implicates that the state of a cell is determined by both its own genetic network and the state and of its neighbouring cells. Cellular automata are particularly appropriate to simulate the evolution of phenomena that depends on local rules, since every entity of the system change its state taking into account what happens in its neighbourhood[12].

A particularly effective means to examine the dynamical regimes of complex systems is studying their response to perturbations. The analyses presented in this work follow this approach, in order to root out the different responses to small perturbation in case of either isolated or coupled networks.

## 2 Random Boolean Networks (RBN)

For an exhaustive description of the model of random Boolean networks please refer to [2,8,9]. Here we will only outline its main features.

A RBN is an oriented graph constituted of $N$ Boolean nodes, which represent the genes of a specific genetic network. A node is active (value = 1) if its corresponding gene synthesises its protein, inactive (value = 0) otherwise. The direct or indirect influences of genes on the expression of other genes in real networks are represented in the model by directed links (if the activation of gene $A$ influences the activation of gene $B$, node $A$ will be an input of node $B$). Therefore, the activation of a certain node depends on the value of its input nodes, according a specific Boolean function. The updating of the network is synchronous, the time is discrete and both the topology and the Boolean function associated to each node do not change in time (this is the so-called *quenched* model [9]. In "classical" RBNs each node has the same number of ingoing connections kin and its input nodes are chosen at random with uniform probability among the remaining $N - 1$ nodes (self-coupling and multiple connections are forbidden). The analysis of the dynamics that show up in RBNs reveals the presence of two typical dynamical regimes, which can be defined as "ordered" and "chaotic"

[1] Note that, according to the usual biological interpretation of RBNs, the attractor of a given network is associated to the cell type: therefore a tissue should be composed by cells which are all in the same attractor. This condition is not imposed in our model.

[2,9]. The dynamical regime of a RBN depends primarily on two parameters, the average connectivity of the network $K =< k_{in} >$ and the bias $p$.[2]

## 3 Multi Random Boolean Network (MRBN)

The model of *Multi random Boolean network* (MRBN) has been introduced in a previous work with different features and a different name [10]. In this section we will briefly describe its most important characteristics.

A Multi random Boolean network is a cellular automaton in each of whose cells is hosted a complete random Boolean network. In our case, we have a 2D square lattice automaton with $M^2$ cells. The neighbourhood we consider is of the von Neumann type (composed by the cell itself and its N, E, S, W neighbours) and the overall topology is toroidal. Every RBN of the MRBN is identical in

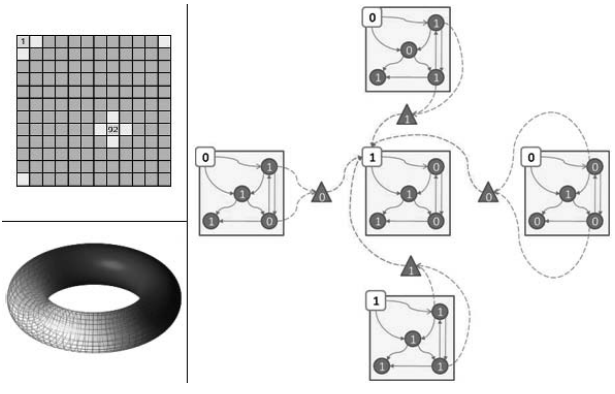

**Fig. 1.** (Left) The spatial shape of the CA is that of a torus, the neighbourhood is of the Von Neumann type. (right) The interaction mechanism for the central cell in the figure (nodes are numbered row by row from the top-left corner): nodes 2 and 5 of all the neighbouring cells can produce a specific signal molecule (triangle-shaped) according a specific Boolean function. If at least one of the neighbours of the central cell produces its signal molecule then the receptor of the central network (white-coloured) is active. Afterwards, the activation value of the receptor influences its output nodes, i.e. nodes 2 and 3 inside the central cell.

terms of number of Boolean nodes ($N$), topology (i.e. the ingoing and outgoing connections per node) and Boolean functions associated to each node, while the initial activation states of the genes are assigned randomly. The choice of homogeneous RBNs for all the cells of the automaton is due to the fact that the cells of a given multicellular organism or monoclonal colony share the same

[2] $p$ is the probability that the output of a certain Boolean function associated to a node is equal to 0. In this case we refer to the average value of $p$ for the whole set of $N$ nodes.

genetic material. In our model, the common structural features of the RBNs, i.e. number of nodes, topology and Boolean functions per node, define their common *genome*.

Real cells interact in many different ways. In this work we only consider the particular kind of interaction that occurs when certain molecules synthesized in a particular cell bind to specific membrane receptors of its neighbouring cells, so influencing the internal dynamic of the cells which host the receptors. In our model, every cell of the MRBN owns a certain number of nodes defined as *receptors*, whose ratio on the total number of nodes is defined as *interaction* strength, $f$. The activation state of a receptor is determined by the presence of a certain entity defined as *signal molecule*, produced by some genes in the neighbouring cells (according a specific Boolean function), but it is not affected by the presence of the signal molecule synthesized by the cell itself. The receptor has its own outputs and they can be either receptors or *internal* nodes of the network (Fig. 1). The interaction mechanism depends on the choice of an *interaction rule*. In this work we suppose that if at least one of the cells in the neighbourhood of cell A produces a signal molecule, then the correspondent receptor in cell $A$ is active (value = 1), inactive (value = 0) otherwise. Note that receptors are considered as actual nodes of the network (e.g. a network with $N = 100$ and $f = 10\%$ owns 90 internal nodes and 10 receptors).

It is important to specify that, in order to isolate the influence of the interaction strength, it is necessary to keep the other structural features of the MRBN fixed, i.e. dimension of the lattice $M$, topology of interaction, interaction rule and genome of each RBN.

## 4 Experiments

The simulations have been made on 100 distinct MRBNs, different in terms of the genome of their characterizing RBNs. All the MRBNs are 20*20 square lattices and the RBNs are composed of $N = 100$ nodes. [3] Past researches demonstrated how MRBNs whose RBNs are characterized by different genomes may show deeply different behaviours and this is the reason why it is important to make specific analysis on single MRBNs. The parameters of the RBNs in the cells are chosen in such a way to be "critical" [9], even though the dynamical behaviour of each single realization may be highly different from the average critical dynamics [11]. The networks are "classical" RBNs, with an equal number of incoming connections per node ($k_{in} = K = 2$). The input nodes are chosen at random with uniform probability excluding self-couplings and multiple connections. The Boolean functions are assigned with uniform likelihood on the set of all the possible functions. The initial states of the nodes are chosen at random for every RBN, independently from those of the other cells. In order to investigate the influence of the interaction strength on the dynamic, we analysed the differences

[3] Obviously, real networks are much larger in terms of number of nodes and interacting cells. Future researches will be aimed to study lager simulated networks and to investigate on possible scale properties of such systems.

in the behaviour of each single MRBN in presence of different values of the interaction strength.[4]

One possible method to investigate the dynamical regime of complex systems in general is to analyse their response to perturbation. A large sensitivity to the initial conditions of the system is usually related to disordered (or chaotic) systems, while, vice versa, a low sensitiveness (higher robustness) refers to ordered systems. For what concerns RBNs one possible means to discriminate the dynamical regimes is to observe the variation in time of the Hamming distance between a "control" network (wild type $WT$) and a perturbed network ($PN$). In our case the perturbation is the *flip* of one node chosen at random, i.e. the change of the activation value of one node in the initial condition of the network.[5] The variation of the Hamming distance in time is a relevant parameter since it provides a clear indication on how the dynamics of two systems diverge. In the case of a flip perturbation, a Hamming distance tending to 0 is peculiar of ordered networks, a value close to 1 is related to critical networks, while values higher than 1 refers to chaotic ones [9].In the simulations on MRBNs a node is chosen at random in a random cell and its initial activation value is flipped. It is then possible to calculate the variation of the Hamming distance of the whole automaton and the number of cell affected by the perturbations, i.e. the number of cells whose Hamming distance is higher than 0 after a certain transient.

## 5 Results

As clarified in the introduction, the primary aim of this research is deciphering the relation between the dynamical behaviour of a single random Boolean network and the emerging dynamics of a collection of coupled RBNs. We firstly analysed the variation of the Hamming distance in time of perturbed isolated RBNs with "critical" structural parameters. Although the average variation of the Hamming distance on the whole set of networks closely resembles the results of past studies of the same kind [9], there is an interesting aspect which is hidden by an analysis on average values. RBNs with identical structural parameters can indeed behave in a highly different way in response to perturbations and it is actually possible to group networks on the basis of the variation of the Hamming distance in time (Fig. 5(left)):

- *Ordered* behaviour: networks with average Hamming distance tending to values lower than 0.5
- *Chaotic* behaviour: networks with average Hamming distance tending to values higher than 1.5
- *Critical* behaviour: networks with average Hamming distance tending to values in the range 0.5 and 1.5.

[4] Every simulation on every MRBN is repeated 150 times. The simulation runs differ for the choice of the set of the receptors and for the initial condition of the nodes of the RBNs constituting the MRBN.

[5] Note that receptors and signal molecules also can be chosen for the flip.

Grouping the networks in the three classes above, we found out that: about 50% of the networks belong to the ordered group, 25% of the networks to the chaotic one and the remaining 25% belongs to the critical class. It is interesting to notice how the Hamming distance reaches its asymptotic value after a relatively small number of time steps for all the analysed RBNs. Coupling RBNs into MRBNs,

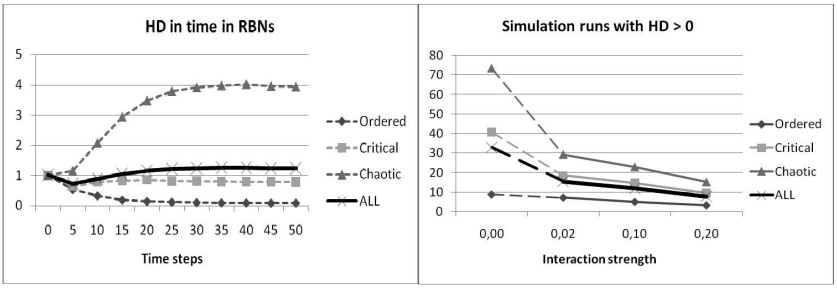


**Fig. 2.** (Left) Variation of the average Hamming distance in time for the three classes and for the complete set of 100 isolated RBNs (on 150runs). (right) Variation of the average simulation runs for the three classes and for the whole set of MRBNs in which the overall Hamming distance after 100 time steps is higher than 0, for different values of the interaction strength. The values in correspondence of $f = 0$ refer to the isolated RBNs.

we could study the changes of the dynamics in response to different value of the interaction strength. We focused our attention on some significant values of the interaction strength, i.e. 2%, 10%, 20%.[6] Once more it turns out to be fruitful to observe the behaviour of each MRBN separatedly; furthermore, we decided to keep the distinction in three groups on the basis of the dynamics of the isolated characterizing RBNs[7] (e.g. MRBNs whose characterizing RBNs have been signed as critical when analysed sigularly will be defined as *critical MRBNs*). Since for a certain number of MRBNs the Hamming distance reaches its asymptotic value after a large number of time steps, we decided to analyse the system after a precise transient (i.e. 100 time steps). In Fig. 5(right) we can notice how the number of runs in which the Hamming distance is higher than 0 after the transient (in other words, the number of runs in which the perturbation is not completely absorbed by the system) dramatically decreases when the RBNs begin to interact and, then, it diminishes monotonously as the interaction strength raises. The trend is analogous for all the three classes of MRBNs, even if the magnitudes are substantially different and coherent with the specific degree of order.

Apparently, the system would tend to more ordered states in correspondence of higher values of the interaction strength, for all the three classes of behaviour.

[6] Higher values of the interaction strength would entail a too large ratio of receptors over the number of internal nodes.

[7] Note that this classification of the MRBNs is possible because their characterizing RBNs are exactly those previously analyzed and grouped in three classes.

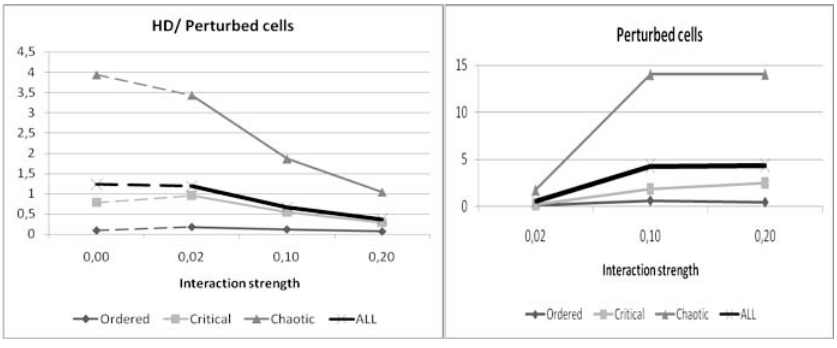


**Fig. 3.** (Left) Variation of the average ratio [Hamming distance/number of perturbed cells] after 100 time steps for the three different classes and for the whole set of 100 MRBNs (on 150 runs) for different values of $f$. The values in corrispondence of $f = 0$ refer to the average Hamming distance of the isolated RBNs. (right) Variation of the average number of perturbed cells after 100 time steps for the three different classes and for the whole set of MRBNs (150 runs) for different values of the interaction strength.

Nevertheless, the dynamics is far more complex. Figure 3 shows that if we consider an isolated RBN and we perturb it, the average Hamming distance reaches a value slightly higher than the critical value 1, while when the cells begin to interact within a MRBN the average value of the Hamming distance over the number of perturbed cells decrease and it continues to decrease as the interaction strength raises. On the other hand, in correspondence of higher values of the interaction strength the average number of cells involved in the perturbation plainly increases. Note that, even though the typical trends in the observed variables are analogous for the three classes, also in this case the differences in the magnitude are remarkable. Hence, the distinction in classes turns out to be robust also when RBNs interact and three distinct dynamical behaviours can indeed be identified.

From these results we can notice how a higher interaction strength may either contribute to brake the perturbation, or allow the diffusion of perturbations that hit a larger number of cells, although involving fewer nodes within each of them (on the average). We may ascribe this peculiar behaviour to the features of the specific interaction mechanism we adopted and, in particular, to the role of receptors in the overall dynamics. Nevertheless, further analyses on the model are needed to reach a definitive conclusion.

## 6 Conclusions

A first remark is about the intrinsic complexity of the model. The dynamical behaviour that shows up is far from trivial and so is its interpretation. Nevertheless, the analyses made on the model provided some interesting cues.

The approach that involves perturbations to examine the response of the system has proven to be effective for different reasons. First of all, it allows to

clearly discriminate three classes of RBNs on the basis of their actual dynamical regime, i.e. ordered, critical or chaotic. Once again, it is possible to demonstrate how networks with identical critical structural parameters can indeed show substantially different dynamic behaviours when analysed singularly. Besides, the dynamic behaviour of isolated RBNs is actually confirmed and enhanced when RBNs are coupled, even though we observe a general shift toward the ordered regime region in correspondence of a stronger interaction.

Yet, as we have shown, interaction leads to dynamic behaviours indeed hard to interpret. Therefore, further development of the model are needed, primarily aimed to grasp the relation among the features of the interaction mechanism and the overall dynamics: for instance, the study of the effect of different interaction rules, or the analysis of MRBNs whose RBNs are characterized by a constant number of internal nodes for different values of the interaction strength.

**Acknowledgments.** This work has been partially supported by the Italian MIUR-FISR project nr. 2982/Ric (Mitica).

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