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Editorial

Boolean Networks Models in Science and Engineering

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As a generalization of other notions like cellular automata or Kauffman networks appeared in the last quarter of the twentieth century, the notion of Boolean networks has undergone a special development in recent decades. This is mainly due to their applications in science and engineering.

In this sense, several research groups of mathematicians have been working and obtaining relevant results in this area that can be applied in other fields. Thus, the purpose of this Special Issue was to collect novel and interesting papers, both theoretical and practical, related to the latest advancements on the study of Boolean network models. More specifically, we asked for new theoretical results, new algorithms and methods, as well as new models or applications in science and engineering.

In the call for papers, we included as potential topics: dynamics of Boolean network models; algorithms, methods and software for the study of Boolean network models; and, of course, Boolean network models applied in science and engineering.

In relation to this Special Issue, 10 submissions were received and peer reviewed by specialists in the area. Among them, seven papers were accepted for publication. This corresponds to an acceptance rate of 70%.

Next, we present a brief summary of the published works, following the order of their publication dates.

In [1], Shmulevich considers monotone Boolean networks whose updating rules are monotone Boolean functions and provides asymptotic formulas for the expected average sensitivity of a monotone Boolean function, depending on the parity of the number of variables of the Boolean function. Then, he shows that the logarithm of the expected average sensitivities can be directly interpreted as the Lyapunov exponent, which measures the state stability of the system under small perturbations. These results for almost all monotone Boolean networks suppose that the asymptotic formulas are valid with a probability of almost 1, when a monotone Boolean network is chosen randomly from the set of all such networks.

In [2], based on previous results for synchronously updated Boolean (directed) networks, Aledo et al. provide a more general class of fixed points systems by considering Boolean functions which are independent. That is, they deal with systems whose Boolean functions are not the restriction of a general one, usually known as non-homogeneous. They also get a more general class of (non-homogeneous) synchronously updated systems whose periodic orbits are either fixed points or 2-periodic orbits. In contrast with other previous studies, they show that, in these more general systems, fixed and 2-periodic points can coexist. Moreover, in contrast with the homogeneous case, they provide some examples showing that periodic points of a period greater than two can appear in this more general setting. In addition, the authors study the periodic structure of synchronously updated Boolean networks given by the composition of two of these systems, which are conjugated under an invertible map whose inverse is equal to the original map. In this context, they

check for updates

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demonstrate that, if the network is undirected, the composition of any homogeneous system induced by a maxterm (or minterm) Boolean function and its conjugate one by means of the complement map gives a fixed-point system as a result. However, this may not occur when the network is directed, since points of any period can appear, even for the simplest maxterm OR and the simplest minterm AND. In particular, it is demonstrated that, when a network is acyclic, the composition of OR and AND gives a fixed-point system as a result, proving that the cycles in the network are the reason for the appearance of periodic orbits which are not fixed points.

In [3], Mezzini and Pelayo present an algorithm for counting the fixed points in AND–OR symmetric positive Boolean networks which are synchronously updated. They use a greedy strategy and recursion to design such an algorithm and prove its correctness. Furthermore, they develop the algorithm obtained and provide another one which allows them to list all the fixed points in this kind of Boolean network.

In [4], Aledo et al. analyze the coexistence of periodic orbits in homogeneous Boolean (directed) networks induced by a maxterm or a minterm Boolean function. More specifically, they prove that any kinds of periodic orbits can coexist for both synchronously or asynchronously updated Boolean (directed) networks. This supposes an interesting breakdown in relation to the pattern found for systems over undirected networks, where fixed points cannot coexist with other kinds of periodic orbits. As an interesting point, this analysis completes the study of the periodic structure of homogeneous Boolean networks induced by a maxterm or minterm Boolean function.

In [5], Brim et al. deal with the control problem for parametrized Boolean networks with asynchronous semantics. Parametrized Boolean networks represent Boolean models with partially unknown updating Boolean functions. The idea of control consists in getting the stabilization of a system in a particular state, using as few interventions as possible. One-step control artificially drives a Boolean network into the desired state, instead of its natural behavior. In the parametrized setting, all possible controls are assigned parametrizations for which the control drives the network from the given source to the desired attractor. In particular, the authors propose a parallel efficient semi-symbolic method to compute the one-step control of parametrized Boolean networks.

In [6], Montalva-Medel et al. study the dynamical robustness of two Boolean models for the lac operon in *Escherichia coli* under any deterministic update schedule. In addition, alternative improvements consisting in biologically supported modifications are proposed for these two models. In particular, they show that the newly improved models are capable of reproducing the operon, being OFF, ON and bistable for different levels of lactose and glucose, as observed in real biological experiments.

In [7], Franco et al. use quantum Boolean functions to extend classical random Boolean networks. Specifically, they study the properties of the corresponding quantum Boolean networks and show that cycle lengths tend to be much longer for them. Although in random Boolean networks complex dynamics are restricted mainly to a connectivity close to a phase transition, they show that quantum Boolean networks can exhibit stable, complex and unstable dynamics, independently of their connectivity. In particular, it is found out that, on average, quantum Boolean networks tend to exhibit complex dynamics, while this is statistically rare in random Boolean networks.

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References

1. Shmulevich, I. On the Lyapunov Exponent of Monotone Boolean Networks. *Mathematics* **2020**, *8*, 1035. [CrossRef]
2. Aledo, J.A.; Barzanouni, A.; Malekbala, G.; Sharifan, L.; Valverde, J.C. On the Periodic Structure of Parallel Dynamical Systems on Generalized Independent Boolean Functions. *Mathematics* **2020**, *8*, 1088. [CrossRef]
3. Mezzini, M.; Pelayo, F.L. An Algorithm for Counting the Fixed Point Orbits of an AND - OR Dynamical System with Symmetric Positive Dependency Graph. *Mathematics* **2020**, *8*, 1611. [CrossRef]
4. Aledo, J.A.; Diaz, L.G.; Martinez, S.; Valverde, J.C. Coexistence of Periods in Parallel and Sequential Boolean Graph Dynamical Systems over Directed Graphs. *Mathematics* **2020**, *8*, 1812. [CrossRef]
5. Brim, L.; Pastva, S.; Šafránek, D.; Šmijáková, E. Parallel One-Step Control of Parametrised Boolean Networks. *Mathematics* **2021**, *9*, 560. [CrossRef]
6. Montalva-Medel, M.; Ledger, T.; Ruz, G.A.; Goles, E. Lac Operon Boolean Models: Dynamical Robustness and Alternative Improvements. *Mathematics* **2021**, *9*, 600. [CrossRef]
7. Franco, M.; Zapata, O.; Rosenblueth, D.A.; Gershenson, C. Random Networks with Quantum Boolean Functions. *Mathematics* **2021**, *9*, 792. [CrossRef]