



WAN 2021

WORKSHOP ON AUTOMATA NETWORKS

Marseille, 14–17 July 2021

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automata-wan-2021.lis-lab.fr

INTRODUCTION

Description

The workshop will be held on 14–17 July, starting with a day in common with Automata 2021, which will be the opportunity to celebrate Eric Goles's 70th birthday.

This workshop aims at bringing together, favoring exchanges and working together, through oral scientific presentations and joint thematic working sessions, the community that studies automata networks, from the perspective of mathematics and computer science. This will notably be the place to take stock of recent advances in the field, and to identify open questions and inspire the community with promising theoretical and applied research directions.

Scientific context

From a general point of view, automata networks are discrete dynamical systems informally defined as sets of entities (the automata) – whose local states are discrete – that interact with each other over discrete time. In that way, cellular automata are particular automata networks so that the automata (the cells) are distributed into a regular topology, namely a cellular space. From a more applied point of view, automata networks are often considered

and studied as finite dynamical systems. In this framework, they have been central in many works related to the modelling of complex systems, as communication networks, particle interaction networks, regulation networks, and social networks.

Whatever vision we have of automata networks, their study is a booming field, both in the most theoretical aspects and in those closer to applications. This is because they are fundamental for two reasons (mainly):

- their definition, and its intrinsic simplicity, which integrates the just necessary and allows you to focus on the essence of interactions (transmission of information);
- their ability to capture behavioral richness (and associated complexities) of the systems they model.

Among the central themes at the fundamental and applied levels are:

- links between static and dynamical characteristics;
- organisation of time and updating;
- importance of feedback and (non-)convergence;
- convergence time and behavioral optimization;
- simulation;
- modularity / compositionality.

Of course, this list is not exhaustive.

All oral contributions are made on the basis of invitations from the scientific committee.

Scientific committee

- Julio Aracena, Universidad de Concepción, Chile
- Pierre Guillon, CNRS, Marseille, France

- Kévin Perrot, Aix-Marseille Université, France
- Élisabeth Remy, CNRS, Marseille, France
- Adrien Richard, CNRS, Sophia Antipolis, France
- Lilian Salinas, Universidad de Concepción, Chile
- Sylvain Sené, Aix-Marseille Université, France
- Guillaume Theyssier, CNRS, Marseille, France

Organization committee

- Pablo Arrighi, Université Paris-Saclay, France
- Amélia Durbec, Aix-Marseille Université, France
- Nathanaël Eon, Aix-Marseille Université, France
- Guilhem Gamard, Aix-Marseille Université, France
- Pierre Guillon, CNRS, Marseille, France
- Etienne Moutot, Aix-Marseille Université, France
- Kévin Perrot, Aix-Marseille Université, France
- Antonio E. Porreca, Aix-Marseille Université, France
- Élisabeth Remy, CNRS, Marseille, France
- Sylvain Sené, Aix-Marseille Université, France
- Guillaume Theyssier, CNRS, Marseille, France

PROGRAM

Wednesday 14 July

- 14:00 – WAN introduction (**Sylvain Sené**)
- 14:30 – short: **Sara Riva**, Factorization of discrete dynamical systems
- 15:00 – short: **Antonio E. Porreca**, Dynamical systems and their algebra
- 15:30 – invited: **Matthew Macauley**, Algebraic structures hiding in automata networks
- 16:15 – Break
- 17:00 – tribute: **Jacques Demongeot**
- 17:30 – long: **Eric Goles**
- 18:15 – tribute: **Maurice Tchuente** (in French)
- 18:30 – tribute: **Michel Morvan**
- 19:00 – tribute: **Sergio Rica**
- 19:30 – Dinner

Thursday 15 July

- 09:30 – short: **Pierre Guillon**, On the simulation notion
- 10:00 – long: **Florian Bridoux**, Complete simulation in automata networks
- 10:45 – *Break*
- 11:15 – short: **Stéphanie Chevalier**, Automatic Boolean network synthesis to model cell differentiation from single-cell transcriptomics
- 11:45 – short: **Sergiu Ivanov**, Sequential reprogramming of biological network fate
- 12:15 – *Free time*
- 12:30 – *Lunch*
- 14:00 – **Working sessions** (complexity, combinatorial dynamics, updating modes, modelling...), only onsite
- 16:00 – *Break*
- 16:30 – invited: **Jorge G. T. Zañudo**, Model-dependent and model-independent control of biological network models
- 17:15 – short: **Martín Ríos Wilson**, On symmetry versus asynchronism: at the edge of universality in automata networks
- 17:45 – short: **Lilian Salinas**, Inverse block-sequential operator in conjunctive networks
- 18:15 – *Free time*
- 19:30 – *Dinner*

Friday 16 July

- 09:30 – invited: **Elisa Tonello**, Buffer extensions of Boolean networks
- 10:15 – short: **Brigitte Mossé**, Isometries of the hypercube: a tool for Boolean regulatory networks analysis
- 10:45 – *Break*
- 11:15 – long: **Guilhem Gamard**, Rice-like theorems for automata networks
- 12:00 – *Free time*
- 12:30 – *Lunch*
- 14:00 – **Working sessions** (complexity, combinatorial dynamics, updating modes, modelling...), only onsite
- 16:00 – *Break*
- 16:30 – long: **Adrien Richard**, Complexity of maximum and minimum fixed point problem in Boolean networks
- 17:15 – short: **Julio Aracena**, Complexity of limit-cycles in conjunctive Boolean networks
- 17:45 – short: **Kévin Perrot**, Complexities of block-sequential update modes
- 18:15 – *Free time*
- 19:30 – *Dinner*

Saturday 17 July (only onsite)

- 09:30 – **Working sessions** (complexity, combinatorial dynamics, updating modes, modelling...)
- 11:30 – **Working sessions restitution**
- 12:30 – *Happy formal ending and picnic*

ABSTRACTS

Julio Aracena • Complexity of limit-cycles in conjunctive Boolean networks

We address the complexity of the problem of determining if a given conjunctive Boolean network has a limit cycle for some block-sequential update schedule. We prove that this problem is NP-complete even in the case of only sequential schemes.

Florian Bridoux • Complete simulation in automata networks

An automata network is a finite graph where each node holds a state from some finite alphabet and is equipped with an update function that changes its state according to the configuration of neighboring states. More concisely, it is given by a finite map $f : A^n \rightarrow A^n$. In this presentation, we will show how some automata networks can or cannot be simulated by some other automata networks with a prescribed update mode. When we consider non-Boolean alphabets and for any network size, we show that there are intrinsically non-sequential transformations (i.e. which cannot be obtained as a composition of sequential updates of some network). We also conjecture that any network of size at least 3 with a Boolean alphabet can be computed

sequentially. Moreover, we show that there is no universal automaton network that can produce all non-bijective functions via compositions of sequential updates. Eventually, we show that there are universal automata networks for sequential updates if one is allowed to use a larger alphabet and then use either projection onto or restriction to the original alphabet.

Stéphanie Chevalier • Automatic Boolean network synthesis to model cell differentiation from single-cell transcriptomics

Our work addresses the synthesis of Boolean networks from constraints on their domain and emerging dynamical properties of the resulting network. The synthesis is expressed as a Boolean satisfiability problem, described as a logic program containing both the modelling formalism (Most Permissive Boolean network, MPBN) and the data on the biological process (static and dynamical knowledge : prior knowledge network, experimental measurement dynamics, observations on the reachable phenotypes depending on conditions...). We enable the modelling of processes implying bifurcations as in cell differentiation, thanks to the implementation of constraints in Answer-Set Programming that address the notion of trajectory (succession of changes in gene state), non-reachability (bifurcating event) and stability (differentiated cell). To illustrate the method, I present an application leveraging scRNA-seq data as dynamical knowledge for the modelling. This example notably shows that, by facing dynamical data with a large prior knowledge network, the method allows to retain the essential interactions to reproduce the behaviors.

Guilhem Gamard • Rice-like theorems for automata networks

In this talk, we'll show that testing properties on the transition graph of an automata network, given the network itself as input, is algorithmically hard as soon as the considered property is nontrivial. This echoes the Rice theorem: any property of the function computed by a Turing machine, given the machine itself as input, is algorithmically undecidable as soon as the considered property is nontrivial. Of course, a metric ton of fine print is missing here: I haven't said what is a "property", what is "algorithmically hard", and what is "nontrivial". Come to the talk, and you'll know.

Pierre Guillon • On the simulation notion

The concept of simulation between computational models appears in many works in computability, complexity, dynamics... with a heterogeneous level of explicitness. We will discuss some examples appearing in the literature, distinguish them according to some properties, and propose a general framework that can be refined into many such examples.

Sergiu Ivanov • Sequential reprogramming of biological network fate

Network controllability is a major challenge in network medicine. The problem is to rewire the molecular network for reprogramming the cell fate. The reprogramming action is considered as a control usually performed once. However, in some cases, a therapy has to follow a time-scheduled drug administration protocol. Furthermore, some diseases are induced by a sequence of mutations leading to a sequence of actions on molecules. In this paper, we extend the single control action method by investigating the

sequential control of Boolean networks. We present a novel theoretical framework for formal study of control sequences, leading to algorithms resolving the PSPACE-hard problem of inferring minimal parsimonious control sequences under the synchronous dynamics.

Matthew Macauley • Algebraic structures hiding in automata networks

I will begin this talk with a problem from dynamical algebraic combinatorics about toggling independent sets, and frame it as a finite asynchronous cellular automata using ECA rule 1. In analyzing the dynamics, we find two local invariants that define bijections of the “live entries” in the orbits. This defines a simply transitive action of an infinite abelian group. In other words, it endows the live entries with the structure of a Cayley diagram. By studying this action, and using the theory of covering spaces from algebraic topology (which I will not assume prior knowledge of), we are able to classify many combinatorial properties and relationships about the structure of the orbits. Happily, this is all a special case of a more general theory, applicable to other automata networks and combinatorial dynamical systems, which seems to be mostly unexplored. I will pose a number of interesting avenues for future research, in hopes to entice members of the audience. Though it will not be necessary to follow this talk, I or (most likely) a colleague will give a survey talk at AUTOMATA about the connections between dynamical algebraic combinatorics and cellular automata, which will give this problem more context and motivation. Both talks will be filled with lots of examples, colorful pretty pictures, and puns.

Brigitte Mossé • Isometries of the hypercube: a tool for Boolean regulatory networks analysis

Given S a Boolean finite dynamical system (FDS), and f an isometry of the hypercube, we consider the conjugated FDS $\phi = f \circ S \circ \text{inv}(f)$. This conjugate conserves all the dynamical properties of S . Moreover, the regulatory graphs of two conjugated FDS are similar: they have the same topology; edges may switch their signs, but signs of circuits remain unchanged. The logical rules may be modified; for example, logical operators OR and AND may be interchanged between two conjugated FDS, but not OR and XOR. The group of all the isometries of the hypercube then defines classes of Boolean FDS, gathering all the conjugates of a given Boolean FDS, in other words gathering all the isometric dynamics. Thus, we classify the set of Boolean FDS on the basis of those isometries. We can then restrict the dynamical analysis of all the Boolean FDS to one representative per class, and thereby considerably restrict the dynamical analysis of all the Boolean FDS. Relying on invariants properties, we propose a constructive method to provide, given a FDS, a representative regulatory graph of its class of FDS under isometries, that fits the addressed questions. We illustrate the efficiency of the method in concrete situations. For instance, the analysis of well-known motifs is strongly improved thanks to the reduction of the space to explore.

Kévin Perrot • Complexities of block-sequential update modes

Update digraphs are the convenient objects to discuss block-sequential update schedules (ordered partitions of the automata set). We will first see that counting update digraphs is $\#P$ -hard in general (with an introduction to counting classes), but can be done in polynomial time on graphs of treewidth 2 (series-parallel). Fixed points are invariant under block-sequential update schedules, but limit-cycles are not. We will see a related problem complete for NP^{NP} , one level above NP in the polynomial hierarchy.

Antonio E. Porreca • Dynamical systems and their algebra

Two natural operations to combine finite, discrete dynamical systems (or, from the opposite perspective, to decompose them into smaller ones) are their alternative and their synchronous execution. By choosing these two operations as sum and product, we obtain a commutative semiring structure. The resulting algebra is quite complex; for instance, most systems are irreducible, but those that are reducible sometimes admit multiple factorisations into irreducibles. We present some results related to the resolution of polynomial equations on the semiring of dynamical systems, which turns out to be undecidable in general, and NP-complete even for linear equations. Furthermore, we describe some recent research on the existence of prime dynamical systems; these are systems that, whenever they appear in the decomposition of a system, they necessarily appear in all the others as well, and are thus fundamental building blocks. We do not know yet if prime systems exist, or even if there exists a computable primality test, but several interesting classes of systems have been proved to be non-prime, including systems only consisting of limit cycles (which includes the asymptotic behaviour of any dynamical system).

Martín Ríos Wilson • On symmetry versus asynchronism: at the edge of universality in automata networks

An automata network (AN) is a finite graph where each node holds a state from a finite alphabet and is equipped with a local map defining the evolution of the state of the node depending on its neighbors. The global dynamics of the network is then induced by an update scheme describing which nodes are updated at each time step. We study how update schemes can compensate the limitations coming from symmetric local interactions. Our approach is based on intrinsic simulations and universality and we study both dynamical and computational complexity. By considering several families of concrete symmetric AN under several different update schemes, we explore the edge of universality in this two-dimensional landscape. On

the way, we develop a proof technique based on an operation of glueing of networks, which allows to produce complex orbits in large networks from compatible pseudo-orbits in small networks.

Adrien Richard • Complexity of maximum and minimum fixed point problem in Boolean networks

Given a fixed integer k , the maximum (minimum) fixed point problem is the following: given a signed graph G , is there a Boolean network with at least (most) k fixed points and with G as interaction graph? Firstly, we prove that the maximum fixed point problem is NP-complete if $k > 1$ and polynomial otherwise. Secondly, we prove that the minimum fixed point problem is NEXPTIME-complete for every k . We also present complexity results when k is a part of the input.

Sara Riva • Factorization of discrete dynamical systems

Boolean automata networks, genetic regulation networks, and metabolic networks are just a few examples of modeling by discrete dynamical systems (DDS). Unfortunately, in most cases, real phenomena modeled by DDS have very complex dynamics. However, it has been empirically observed that in many cases this complex behavior seems to be the result of the “cooperation” of many simpler systems. Equipping finite discrete dynamical systems with an algebraic structure of semiring provides a suitable context for hypothesis verification on the dynamics of DDS. Indeed, a hypothesis on the systems can be translated into polynomial equations over DDS (with a constant right-hand term). Solutions to these equations provide the validation to the initial hypothesis. The issue is that general equations over DDS are plagued by undecidability. In order to avoid the swamp of undecidability, we study the original equation through some abstractions of the problem (regarding different properties of the possible solutions such as cardinality of sets of states, asymptotic and transient behavior). We will show

how one can solve, simplify and intersect them to identify the possible solutions to validate or not an initial hypothesis.

Lilian Salinas • Inverse block-sequential operator in conjunctive networks

We address the problem of determining the dynamical behaviors of synchronous conjunctive networks which can be simulated by some conjunctive network with a block-sequential schedule. In particular, we show a polynomial algorithm that given a conjunctive network N and a scheme s , returns a conjunctive network N' (if it exists) such that N' updated with s has the same dynamical behavior that N synchronously updated.

Elisa Tonello • Buffer extensions of Boolean networks

Boolean networks are often used as modelling tools, for instance in the investigation of biological systems. Regulations between Boolean species are encoded in interaction graphs, and the resulting qualitative behaviours are captured in state transition graphs describing the possible dynamics according to different interpretations (e.g. synchronous or asynchronous). One drawback of adopting a Boolean approach is that regulation thresholds are inevitably “squashed”, and trajectories that are visible in multilevel or continuous modelling frameworks can be lost. In this talk, I will discuss some properties of a class of Boolean networks that can be obtained by adding “buffer” variables to separate the regulation thresholds. The asynchronous dynamics of these extended networks can recover many behaviours seen in more refined models. We will see how the associated state transition graphs relate to dynamics arising from other interpretations, e.g. generalised asynchronous or most permissive dynamics, and discuss some of their properties. We will see, in particular, that if all thresholds are separated and all cycles in the interaction graph admit at least one buffer, then the asynchronous attractors are in one-to-one correspondence with the minimal

trap spaces. I will conclude by outlining some open questions on buffer-extended Boolean networks.

Jorge G. T. Zañudo • Model-dependent and model-independent control of biological network models

Network models of cell signaling and regulation are ubiquitous because of their ability to integrate the current knowledge of a biological process and test new findings and hypotheses. An often asked question is how to control a network model and drive it towards its dynamical attractors (which are often identifiable with phenotypes or stable patterns of activity of the modeled system), and which nodes and interventions are required to do so. In this talk, we introduce two recently developed network control methods - feedback vertex set control and stable motif control - that use the graph structure of a network model to identify nodes that drive the system towards an attractor of interest (i.e., nodes sufficient for attractor control). Feedback vertex set control makes predictions that apply to all network models with a given graph structure and stable motif control makes predictions for a specific model instance, and this allows us to compare the results of model-independent and model-dependent network control. We apply these methods to various biological network models and discuss the aspects of each method that makes its predictions dependent or independent of the model. In addition, and if time permits, I will talk about some of the mechanistic models of oncogenic signaling I have worked on (the epithelial-to-mesenchymal transition in liver cancer and drug resistance in breast cancer) and the insights we have learned from them.

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