Modelling and Verifying Properties of Biological Neural Networks

School of Electrical Engineering and Computer Science, University of Ottawa, Canada

Abstract -

In this talk, I present a formal model of biological neural networks and discuss the use of model checking and interactive theorem proving to verify some of their properties. Having a formal model can increase our understanding of the behavior and properties of such networks, as well as provide insight into their response to external factors such as disease, medicine, and environmental changes. We focus on neuronal micro-networks, considering properties of single neurons as well as properties of slightly larger ones called archetypes, which represent specific computational functions. Archetypes, in turn, represent the building blocks of larger more complicated neuronal circuits. I first present work by colleagues on a model checking approach, and then present our joint work on a newer theorem proving approach. Using interactive theorem proving allows us to generalize the kinds of properties that we can prove. This work is joint with Abdorrahim Bahrami and Elisabetta De Maria.

2012 ACM Subject Classification Theory of computation \rightarrow Logic and verification; Applied computing \rightarrow Systems biology

Keywords and phrases Neuronal networks, Model checking, Theorem proving, Coq

Digital Object Identifier 10.4230/LIPIcs.ITP.2022.1

Category Invited Talk

1 Summary

Formal verification has become increasingly important in a variety of areas such as providing important guarantees for software systems, and building an increasingly large library of formalized mathematics. In our work, we consider the application of such formal techniques in the area of biological systems; in particular, we consider human neural networks. This talk reports on our past [1, 5, 6] and current work in this area.

It would be extremely difficult to use real biological experiments to prove the results that are expected from the biological theory that we are working with. Our main goal is to contribute to this area via modelling and verification. A longer term goal is to be able to apply what we learn to treat medical disorders. As an example, we hope that continuing this line of work will lead to an ability to detect inactive regions of the human brain and to treat mental disorders. Furthermore, our approach can be generalized to the verification of other kinds of networks, such as regulatory, metabolic, or environmental networks.

We focus on human neuronal networks, which can be viewed as the micro level of human neural networks, where a node represents a single neuron. Archetypes group several neurons together in a circuit that performs a specific function. To model archetypes, we adopt boolean spiking neuron models [3], where a leaky integrate-and-fire (LI&F) model is used to describe the electrical properties of the neurons. Neuronal archetypes are represented as weighted directed graphs whose nodes are neurons and whose edges represent synaptic connections. Time is modelled as discrete steps, where at each time unit, the neurons of the network compute their membrane potential from various parameters such as the current input signals and a leak factor that expresses signals degrading over time in a given temporal window.

1:2 Modelling and Verifying Properties of Biological Neural Networks

Two examples of basic neuronal archetypes of our model [8] include a simple linear series of neurons and two neurons forming a loop where the output of one feeds into the input of the other, and this input either activates or inhibits the other neuron. Such archetypes represent primitives that can be composed in various ways to form larger networks. We prove some basic properties that have been identified in discussions with neurophysiologists. For example, the delayer effect is a property that states that under certain conditions, a single neuron or a series of neurons has an output which is the same as the input after a certain amount of delay. As another example, the filter effect also applies to a single or a series of neurons, and expresses that under certain conditions two spikes are never emitted in two consecutive time steps. Furthermore, we show that every neuron always exhibits either the delayer or filter effect.

In the work of De Maria et. al. [7, 8], the synchronous reactive language Lustre is used to represent neuronal networks and express their properties, which are then checked automatically by the Kind2 [4] model checker. To do so, various parameters must be given fixed values, such as the number of neurons in a series, the number of time steps, the specific input sequence, the value of the leak factor, as well as other parameters used to compute the membrane potential. In our work [1, 6], we use the Coq Proof Assistant [2], express such properties generally so that they hold for any values of these parameters, and prove them interactively with the help of some limited automation. Neurons and archetypes are modelled using dependent records, and we rely on Coq's powerful mechanisms for carrying out proofs by structural induction and case analysis, as well as on its standard libraries for reasoning about a variety of basic data types such as lists and rational numbers. Our work also includes a comparison of the two approaches on a fixed set of properties (see [5]).

- References

- Abdorrahim Bahrami, Elisabetta De Maria, and Amy Felty. Modelling and verifying dynamic properties of biological neural networks in Coq. In *Ninth International Conference on Computational Systems-Biology and Bioinformatics (CSBio)*, pages 12:1–12:11, 2018.
- Yves Bertot and Pierre Castéran. Interactive Theorem Proving and Program Development—Coq'Art: The Calculus of Inductive Constructions. Springer, 2004.
- 3 Wulfram Gerstner and Werner M. Kistler. Spiking Neuron Models: Single Neurons, Populations, Plasticity. Cambridge University Press, 2002.
- 4 George Hagen and Cesare Tinelli. Scaling up the formal verification of Lustre programs with SMT-based techniques. In 2008 Formal Methods in Computer-Aided Design (FMCAD), pages 1–9, 2008.
- 5 Elisabetta De Maria, Abdorrahim Bahrami, Thibaud L'Yvonnet, Amy Felty, Daniel Gaffé, Annie Ressouche, and Franck Grammont. On the use of formal methods to model and verify neuronal archetypes. Frontiers of Computer Science, 16(3), 2022. Article No: 163404.
- 6 Elisabetta De Maria, Joëlle Despeyroux, Amy Felty, Pietro Lió, Carlos Olarte, and Abdorrahim Bahrami. Computational logic for biomedicine and neurosciences. To appear as a chapter in an ISTE-Wiley book, 2020.
- 7 Elisabetta De Maria, Thibaud L'Yvonnet, Daniel Gaffé, Annie Ressouche, and Franck Grammont. Modelling and formal verification of neuronal archetypes coupling. In Eighth International Conference on Computational Systems-Biology and Bioinformatics (CSBio), pages 3–10, 2017.
- 8 Elisabetta De Maria, Alexandre Muzy, Daniel Gaffé, Annie Ressouche, and Franck Grammont. Verification of temporal properties of neuronal archetypes modeled as synchronous reactive systems. In *Fifth International Workshop on Hybrid Systems Biology (HSB)*, pages 97–112, 2016.