Exploring Neural Principles with Si elegans, a Neuromimetic Representation of the Nematode Caenorhabditis elegans

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Abstract: Biological neural systems are powerful, robust and highly adaptive computational entities that outperform conventional computers in almost all aspects of sensory-motor integration. Despite dramatic progress in information technology, there is a big performance discrepancy between artificial computational systems and brains in seemingly simple orientation and navigation tasks. In fact, no system exists that can faithfully reproduce the rich behavioural repertoire of the tiny worm *Caenorhabditis elegans* which features one of the simplest nervous systems in nature made of 302 neurons and about 8000 connections. The *Si elegans* project aims at providing this missing link. This article is sketching out the main platform components.

1 INTRODUCTION

Caenorhabditis elegans, a soil-dwelling worm with a life span of a few days, 1 mm long and 80 µm in diameter, is one of the five best characterized organisms. It is multicellular and develops from a fertilized egg to an adult worm like any other animal. Although its genome is small (~ 10 M base pairs), there is about 40% homology to the human genome (3.2 G base pairs). The adult hermaphrodite is comprised of exactly 959 cells, including 95 body wall muscle cells and 302 neurons. Despite its simplicity, the nervous system of *C. elegans* does not only sustain vital body function, but generates a rich variety of behavioural patterns in response to internal and external stimuli. These include associative and several forms of nonassociative learning that persist over several hours (Hobert, 2003). Interestingly, many processes of learning and memory in *C. elegans* are highly conserved across evolution, which suggests that there are universal information processing mechanisms throughout the animal kingdom (Lin and Rankin, 2010). With all of this data, information and modern computer technology at hand, it is surprising that there is yet no comprehensive artificial *C. elegans* emulation system from which the principles of neural information processing underlying behaviour can be derived. The *Si elegans* project aims to fill this gap. It will do so by implementing completely reconfigurable neuronal models on FPGA modules representing individual neurons. Signals between neurons within the neural circuitry will be exchanged by light. Such optical free-space interconnection concept promises to be one of the most attractive solutions for overcoming the 'interconnectivity crisis', currently one of the most serious bottlenecks in upscaling neuromorphic network architectures. In a 3D configuration, a quasi-limitless number of connections between modules can be established due to the fact that light beams do not interfere with each other. It furthermore allows the easy reconfiguration of

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network connectivity by simply exchanging (or in case of active optical elements by reprogramming) the light distribution elements. Finally, due to the inherent scalability of the approach, more complex networks can be emulated.

2 THE *Si elegans* APPROACH

We currently develop a hardware-based computing framework that will accurately mimic *C. elegans* in real time and enable complex and realistic behaviour to emerge through interaction with a rich, dynamic simulation of a natural or laboratory environment. We initiated to replicate the nervous system of *C. elegans* on a highly parallel, modular, user-programmable, reconfigurable and scalable FPGA hardware architecture. It will be embodied in a virtual environment for behavioural studies. The virtualization will take the sensory-motor loop and realistic body physics into account. The resulting computational platform will be provided through an open-access web portal to the scientific community for its peer-validation and use (Figure 1).

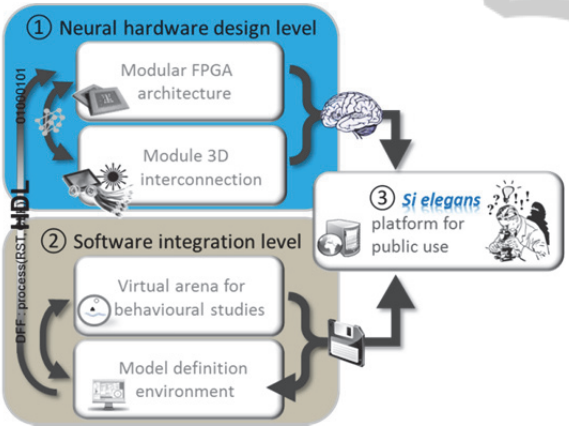

Figure 1: The three main elements of the *Si elegans* platform: 1. the hardware emulation of the *C. elegans* nervous system, which is 2. virtually embodied and interacting with an artificial environment that can 3. be defined by users.

Several innovative key concepts will ensure the accurate mimicry of the *C. elegans* nervous system architecture and function. Each of the 302 neurons will be represented by individual field-programmable gate array (FPGA) modules, each of them being independently and dynamically programmable with a user-specific and parame-terised neuronal response model through a user-friendly neuron model submission and configuration facility or through selection from a library of pre-defined and tested neuron models. Pioneering electro-optical interconnection schemes will allow dense module distribution and parallel, interference-free inter-neuron communication in a 3D space. In a closed-loop feedback design, this hardware blueprint of the *C. elegans* nervous system will control a biophysically correct virtual representation of the nematode body in a virtual behavioural setting. Instead of limiting its function and impact on science and technology by imposing pre-made models only, the *Si elegans* framework will be made available to the worldwide scientific community through an open-access web-portal. It will feature an intuitive and user-friendly remote configuration interface to define an unlimited number of neuron models and information processing hypotheses for automatic FPGA hardware configuration. This peer-participation concept will not only warrant the independent and unbiased functional validation of *Si elegans*, but permit the iterative optimization of neuron models and the asymptotical approach towards a holistic reproduction and understanding of the complete set of *C. elegans* behaviours and their underlying nervous system mechanisms through a set of reverse-engineering tools.

Two core aspects govern the project. The first addresses the technological design and assembly of the *Si elegans* hardware architecture accompanied by the development of the virtual arena and of the neural response model design and FPGA configuration interface followed by their integration into a user-friendly web-accessible platform. The second addresses its deployment to the scientific community for its independent peer-validation as a free-access tool and testbed for neurocomputational studies.

The hardware design includes individual neuron modules, each consisting of three elements in their simplest embodiment as sketched out in Figure 2: i) a synaptic/gap junction input array, ii) postsynaptic processing of synaptic/gap junction input based on the selected neuron-specific model that has been implemented on dynamically (re)programmable FPGA circuitry for the arbitrary definition of the type of neuron and its response behaviour, and iii) an axonal output line that distributes the neural response (*e.g.*, spikes, membrane fluctuations) simultaneously to individual synapses of one or many target neurons.

In a coarse comparison, i) represents individual synapses/gap junctions, ii) the soma and dendritic tree of a neuron, and iii) the axon with its axonal arbour. The spatial organization and assembly of the ***Si elegans*** nervous system will be based on the

published connectome (taking most recent and new findings or hypotheses published during project time into account (*e.g.*, (G. Haspel and O'Donovan, 2011)).

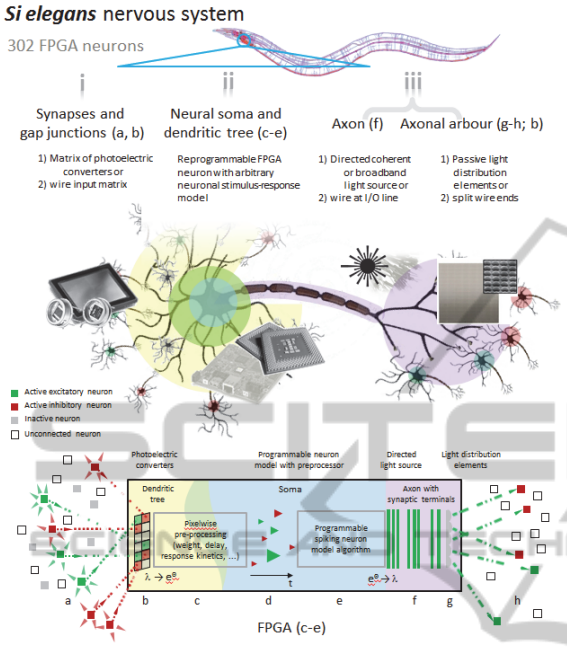

Figure 2: Concept and elements of an individual *Si elegans* FPGA neuron module and its comparison with a real neuron. Neural activity will arrive at individual input lines of an FPGA (i) and will be processed by the neuron-specific stimulus-response algorithm that the FPGA was programmed with (ii). Its output activity will be distributed in parallel through signal distribution elements (iii) to individual input lines (i) of the target FPGA neurons to which the neuron connects to. In case of signal propagation by light, incoming activity will arrive as spatially confined light pulses at individual pixels of photoelectric converters (synapses/gap junctions) being individually connected to the individual FPGA input lines. Neural response activity generated by the neural model residing on the FPGA will trigger a coherent light source at one of its output lines (axon). This light will pass through microoptical light-structuring elements to distribute activity onto selected pixels (synapses/gap junctions) of interconnected target neurons. In case of electrical signal transmission through wires, a split-wire bundle will transmit a digital signal pulse from the axonal output line of the FPGA to individual synapse/gap junction sockets of the target neurons.

2.1 FPGA Representations of *C. elegans* Neurons and Muscles

The *Si elegans* emulation framework is composed of distinct and independent modular components. To date, the majority of hardware-assisted simulation efforts have focused on mirroring a complete network of several neurons on a single FPGA chip or in ASIC/VLSI technology. *Si elegans*, in contrast, aims at dedicating a single FPGA module to a single neuron to emulate neuron-specific stimulus-response models at quasi arbitrary resolution. While from an engineering point of view this seems to be a waste of hardware resources at first glance, this approach will give room for implementing neural processing schemes of arbitrary complexity allowing for the consideration of all types of intracellular events (*e.g.*, signalling cascades *etc.*). This will allow biologists and computational neuroscientists to extend model complexity and fidelity to unimagined high degrees.

By means of dynamically reconfigurable field programmable gate arrays (drFPGAs) the inherent signal processing and response logic of each neuron will be reprogrammable. The need for dynamically reprogrammable somato-dendritic circuitry has several advantages: to stay flexible in defining the type and thus the response behaviour of a neuron, to implement any kind of synaptic or dendritic pre-processing algorithms, to freely adjust or upgrade the algorithms for emulating neural development (changes in neural response) or implementing upcoming neuroscience knowledge, and to emulate disease states (*e.g.*, Parkinson's, epileptic seizures) by temporarily modulating the response behaviour at run-time. drFPGAs thus offer the best ratio between hardware costs and performance, accuracy, and parameterization space. Since FPGA technology currently experiences fast technological advances, it will also be easy to exchange individual modules for more powerful or smaller ones at any time.

2.2 3D Interconnection of FPGA Modules to Replicate the *C. elegans* Connectome

In almost all hardware implementations of neural networks, the issue of inter-neuron connectivity is a major problem. Serial-type simulations introduce stochastic jitter in the timing of events and thus fail to accurately and reproducibly mimic parallel information flow between neurons. If a parallel inter-neuron connectivity is implemented on-chip instead (*e.g.*, by using ASIC technology), typically 90% of the chip is composed of interconnect and scaling networks becomes a major problem. In this project we are proposing to solve this problem by using optical or wire-based off-chip interconnects. Two complementary interconnection strategies will be pursued and compared for their ease of

implementation, reliability, functionality and scalability. They will be implemented by adding two elements to each FPGA neuron module: i) a synaptic/gap junction input field (pixel matrix for wire connection, optical fibre plugs or light-receptive pixels with light-to-charge conversion) and an axonal output line with distribution elements that communicate the neural response simultaneously to individual synapses of one or many target neurons.

For the optical information transmission among neurons, fast-switchable and intensity tuneable laser-diodes are the emission light source(s) of choice. They are triggered by the axonal output pin of an FPGA neuron module. Their light is structured and thus projected onto individual synaptic or gap junction inputs of those target neurons that the active neuron connects to. Any combination of reflective, refractive, diffractive and masking elements such as mirrors, micromirror arrays, microprism or microlens arrays, gratings, colour filters and etched shadow masks will be explored to ensure the correct addressing and optical information transfer between sending and receiving FPGA neurons. Synapses and gap junctions of the receiving neurons will be represented by arrays of photoelectric elements.

2.3 A Virtual Arena for Behavioural Studies

Several *C. elegans*-specific descriptors of its physiology, morphology and body mechanics exist, including a realistic representation of the body (*e.g.*, Virtual Worm Project, *neuro*Construct) and aspects of locomotion (Boyle, 2009; Bryden and Cohen, 2008; Gal Haspel, O'Donovan, and Hart, 2010; Mailler, Avery, Graves, and Willy, 2010; Niebur and Erdos, 1993; Stephens, Johnson-Kerner, Bialek, and Ryu, 2010; Wakabayashi, 2006). Based on these data, the *Si elegans* hardware nervous system of *C. elegans* will be embodied through a biophysically realistic virtual representation of the nematode in a virtual environment. The virtual body will share the shape, body-physics (*e.g.*, elasticity, friction) and cellular organization of *C. elegans* (including realistic spatio-functional representations of sensory cells). The interplay between active actuation through sensory-driven control circuits of its nervous system and passive actuation by environmental factors (material-properties, arena topology, gravity, air- or fluid-flow *etc.*) will be considered. The simulation of this virtual body being situated in a virtual arena will be running on standard PC hardware. The virtual arena can be freely configured to copy the 3D geometries and biophysical features of an experimental environment used in *in vivo* studies. It displays the native behaviour of the *C. elegans* representation, provides simulated environmental stimuli to its sensory neurons and shows stimuli-induced responses (*e.g.*, muscle actuation, secretory events). Information flow is channelled in real-time through a bi-directional interface between the computer and the *Si elegans* nervous system. Sensory neurons of the *Si elegans* nervous system receive their input from programmable light sources. *Si elegans*' motor neuron activity actuates associated muscles of the virtual body. Through a real-time closed-loop feedback, any resulting sensory experience (*e.g.,* change in posture, touch, change of chemical concentration gradients) is coded and transmitted to the *Si elegans* nervous system emulation as new sensory input.

2.4 Neural Model Definition User Interface and Network State Analysis

The modelling space shall allow for the definition of relevant neural processing parameters in a pictorial, object-oriented flow diagram (graphical drag-and-drop manner) or script. The desired network structure can be created by simply selecting various neuron, synapse or gap junction models from a library of available components and connecting them together. Alternatively, existing neural response models can be imported from other simulation engines (e.g., NEURON, BRIAN, NeuroML, ...) (Figure 3).

An assembly can be stored as a neuron-specific model to become a high-level, properly documented building block for other researchers. The modelling toolset provides all required design elements to address and freely combine all known features and events of neural signal transmission down to the synaptic level, possibly including even abstracted models of signalling cascades. These design elements can be altered, thus personalized and versioned by community members for experimental purposes. *E.g.*, the function of an individual synapse may include cable properties of the pre-synaptic axon and synapse to account for physiological and morphological boundary conditions that shape/affect signal properties such as signal transmission delays and attenuation. We furthermore implement a standard set of amplitude-invariant, self-terminating action potentials with stereotyped waveforms as well as graded regenerative potentials as the predominant signal type in *C. elegans* with amplitudes and

waveforms that are highly sensitive to the size, duration and waveform of the stimulus. Finally, the *Si elegans* platform will provide readout and storage tools for reverse-engineering nervous-system function.

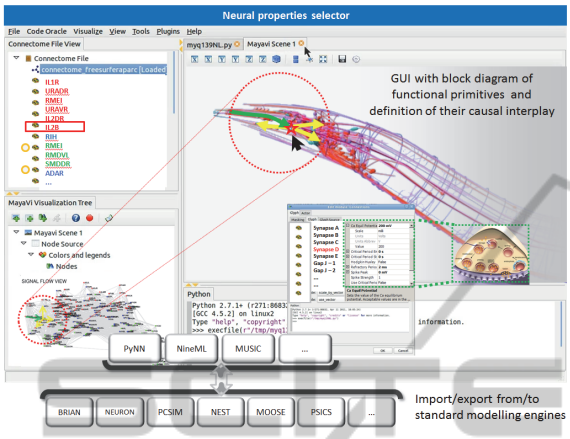

Figure 3: *Si elegans* GUI mock-up for model definition. We will provide users with a flexible GUI for the user-friendly and intuitive definition of neuron-specific response models for the efficient and fast design-to-FPGA prototyping of neural models. It will provide ready-made neuron models and sets of parameterisable components or functional primitives from which scientists can construct their own neural response models. The definition environment will contain a virtual representation of *C. elegans* including the locations and connections of individual neurons and muscle cells (and everything else). The user may zoom into the nervous system and click on a neuron, which will then show its incoming and outgoing connections within the nervous system along with their morphologically correct pathways from the source neurons (incoming) towards the target neurons/cells (outgoing). Upon double-click of elements in the GUI a dialog will open for defining the properties of individual input-output algorithms (neural response model - e.g., ion-channel response, synaptic integration *etc.*). A CAD-program-like tree lists all features/synapses/primitives of the particular neuron. A separate tab allows the definition of information flow among individual elements (blocks) within a particular neuron (*e.g.*, dendro-somatic kinetics, leakage …). Alternatively, these parameters may also be imported from other simulation engines or be defined by a Python/PyNN definition script.

2.5 Deployment of the *Si elegans* Platform for Public Access and Peer-Contribution

Given that there are over 300 laboratories worldwide working on *C. elegans*, a majority of them studying some aspect of nervous system function, there is considerable interest in modelling it. The seemingly trivial complexity of the nematode *C. elegans* has kept researches busy over the past 50 years without revealing a complete understanding of the functioning of its nervous system. The spirit and central mission of *Si elegans* as an 'open-science, peer-contribution' project is therefore the early involvement of the scientific community, particularly groups interested in behavioural and modelling aspects of *C. elegans*, but also the neuro-computation community at large. The *Si elegans* platform will therefore be made accessible to the scientific community (*e.g.*, in a shared-time, fair-use model) through a client/server-based remote access environment not only for the pursuit of scientific studies, but also for its independent validation and enhancement through extensions (*e.g.*, through plug-ins). Feedback from researchers will be shared through community outreach tools and be implemented into the public platform (Figure 4).

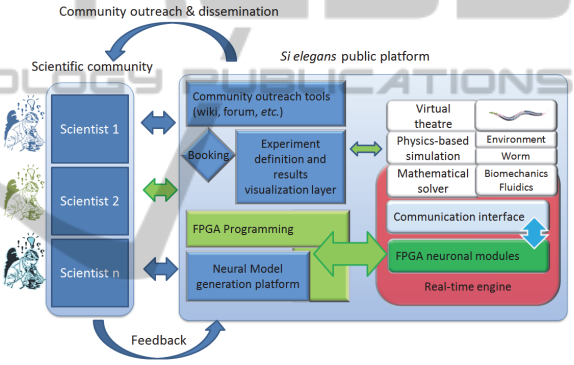

Figure 4: Schematic overview on the *Si elegans* platform elements and their accessibility by the scientific community.

3 CONCLUSIONS

While *Si elegans* restricts itself to the emulation of the *C. elegans* nervous system, the underlying design concepts have universal application. *Si elegans* will constitute a generalizable framework from which the universal working principles of nervous system function can be induced, and new scientific knowledge on higher brain function and behaviour can be generated. By being designed for open-source and peer-contribution, *Si elegans* promises to become a generalizable testbed for neurobiological signal processing hypotheses in healthy and disease-affected nervous systems in neuroscience, neurocomputation and neurology. It may also lay the foundation for exploring and refining new neuromimetic computational concepts

to provide a blueprint for the design of biologically inspired, brain-like parallel processing hardware architectures that are orthogonal to current von Neumann-type machines. If a holistic and verifiable understanding of *C. elegans* nervous system function could be achieved, a long-locked door would open to implement such knowledge in neuromimetic processing and control mechanisms in any technological field, be it robotics, medical assistance, decision-making devices, fraud-detection or surveillance.

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