Towards an Electro-optical Emulation of the C. elegans Connectome

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Abstract: The tiny worm *Caenorhabditis elegans* features one of the simplest nervous systems in nature. The hermaphrodite contains exactly 302 neurons and about 8000 connections. The *Si elegans* project aims at providing a reverse-engineerable model of this nematode by emulating its nervous system in hardware and embodying it in a virtual world. The hardware will consist of 302 individual FPGAs, each carrying a neuron-specific neural response model. The FPGA neurons will be interconnected by an electro-optical connectome to distribute the signal at the axonal output or gap-junction pin of an FPGA neuron onto the respective synaptic input or gap-junction pins of those target FPGA neurons that a neuron interconnects with. This technology will replicate the known connectome of the nematode to allow for an as biologically meaningful as possible and truly parallel information flow between neurons. This article focuses on the concepts and first implementation steps of such optical connectome.

1 INTRODUCTION

Caenorhabditis elegans, a soil-dwelling nematode, is one of the best characterized organisms. The adult hermaphrodite is comprised of exactly 959 cells, including 95 body wall muscle cells, 302 neurons and about 8000 connections, of which about 2000 are electrical junctions. The seemingly low complexity of this worm has kept researches busy over the past 50 years without revealing a complete understanding of its nervous system and the rich behavioural repertoire emerging from its function. To fill this void, the *Si elegans* project aims at the development of a hardware-based computing framework that accurately mimics *C. elegans* in real time and enables complex and realistic behaviour to emerge through interaction with a rich, dynamic simulation of a natural or laboratory environment. We will replicate the nervous system of *C. elegans* on a highly parallel, modular, user-programmable, reconfigurable and scalable hardware architecture, virtually embody it for behavioural studies in a realistic virtual environment and provide the resulting computational platform through an open-access web portal to the scientific community for its peer-validation and use.

2 THE *C. eleg*ans CONNECTOME

In *C. elegans*, the spatial organization of neurons and their interconnectivity is largely known and almost fully mapped. The most up-to-date wiring information covers 279 neurons of the somatic nervous system, excluding 20 neurons of the pharyngeal system and three neurons that appear to be unconnected from the rest (Chen et al., 2006; Qian et al., 2011; Ruvkun, 1997). Every *C. elegans* neuron name consists of either two or three uppercase letters indicating class and in some cases a number indicating the neuron number within one class. If the neurons are radially symmetrical, each cell has a three-letter name followed by L (left), R (right), D (dorsal) or V (ventral). A complete list of *C. elegans* neurons, their lineage and descriptions can be found in the ‘individual neuron list’ of the WormAtlas (Altun, 2014). Neural location and connectivity maps are available through the 'Neuronal Wiring' section in the WormAtlas (Wormatlas, 2014). A highly compressed view on the overall connectivity matrix is given in Figure 1. Its data is based on work by Dmitry Chklovskii's group (Chen et al., 2006) that was modified by Nikhil Bhatla (Bhatla, 2009) for easier processing.

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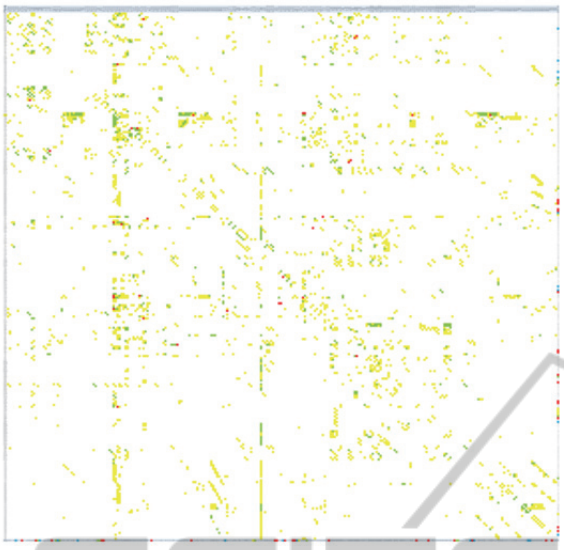

Figure 1: Connectivity matrix of currently 275 neurons extracted from the Neural Connectivity II dataset by Varshney *et al.* (Varshney et al., 2011). Pre-synaptic neurons listed in the row headers connect to their post-synaptic target neurons listed in the column headers via one or up to three simultaneous synaptic connections. Due to page size limitations, the names of the individual neurons are not legible. Colour codes for the number of synaptic connections: 1: yellow, 2: green, 3 red. Electrical gap junctions and neuromuscular junctions are not included in this matrix.

3 THE *Si elegans* CONNECTOME

One of the key challenges and features of the *Si elegans* computational platform is the development and implementation of the 3D electro-optical interconnectivity concept for the parallel processing and transmission of neuronal information. In current 2D interconnectivity designs based on static integrated circuitry-only schemes, network complexity is limited by 2D interconnectivity bottlenecks. Thus, inter-neuron connectivity is a major problem. To circumvent this limitation, other groups have deployed shared bus-based connectivity concepts and asynchronous address-based event-coding/event-representation systems (AES, AER, NoC, ..) to mimic parallel information transmission. But they are serial in nature. As long as processing rates are sufficiently high for a low number of synaptic connections (several thousands), their serial nature can be hidden and parallelism be pretended. However, a system may encounter communication bottlenecks when a high number of target synapses need to be addressed simultaneously. In that case, non-parallelism will become apparent. A more serious problem of serial-type simulations is their stochastic jitter in the timing of events that prevent the accurate and reproducible mimicry of parallel information flow between neurons.

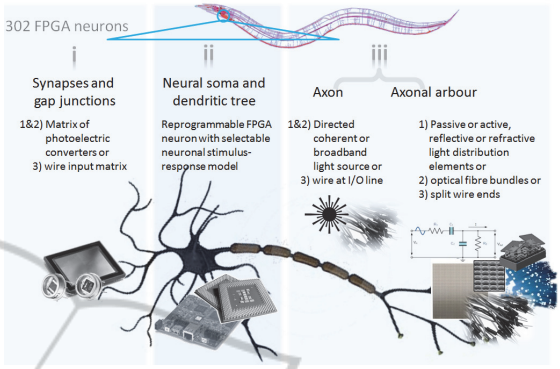

Figure 2: Concept and elements of an individual *Si elegans* FPGA neuron module and its comparison with a real neuron. Neural activity will arrive at individual input lines of an FPGA (i) and will be processed by the neuron-specific stimulus-response algorithm that the FPGA was programmed with (ii). 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 light distribution elements to distribute activity onto selected pixels (synapses/gap junctions) of inter-connected 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. Reproduced with permission from the *Si elegans* project consortium.

These limitations will be overcome through research into free-space communication technologies. This concept picks up on research into free-space optical computation and build on rapid progress in optical communication technology, be it for telecommunication or, more recently, on-chip and intra-chip optical interconnects (Assefa et al., 2010; Doany et al., 2012; Loughran, 2010; Orcutt et al., 2011). The *C. elegans* connectome will be replicated by connecting the individual FPGA neuron modules in a line-of-sight framework through light. This approach allows for the distribution of the signal at the axonal output or gap-junction pin of an FPGA neuron onto the respective synaptic input or gap-junction pins of those target

FPGA neurons that a neuron interconnects with. The involved elements and their biological counterparts in the *Si elegans* implementation are depicted in Figure 2, their respective arrangement in Figure 3. Because activity in the nervous system is temporally coded, light intensities will not require amplitude modulation.

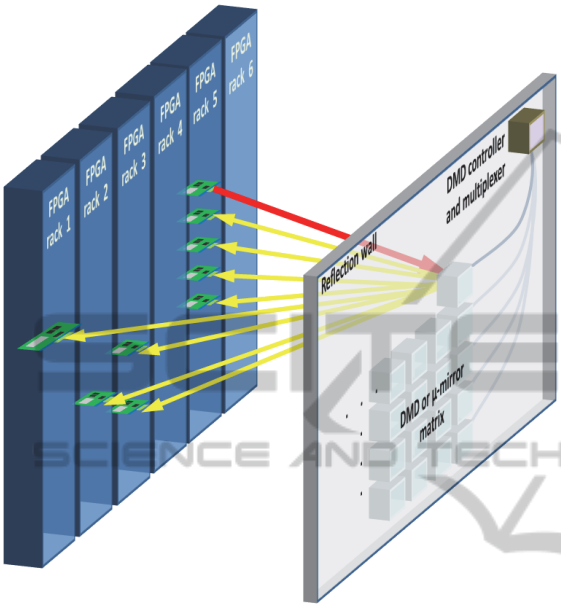

Figure 3: Sketch of one physical arrangement scenario for FPGA boards and optical line-of-sight interconnection pathways. An exemplary subset of 9 out of 302 FPGA boards and their interconnection by structured light beams is shown. The red arrow depicts the axonal output beam of a pre-synaptic sending FPGA neuron, which is spatially patterned by a neuron-specific reflective element at some distance opposite to the racks and thereby distributed onto the photoreceptive elements representing synapses or gap junctions of the post-synaptic target neurons (yellow arrows). The reflective optical light distribution elements can either be active (digital mirror device, DMD) or passive (µ-mirror arrays). 302 of these elements, one for each neuron, will be strategically arranged in a matrix on the 'reflection wall'.

4 OPTICAL LIGHT DISTRIBUTION ELEMENTS

Neuron-specific reflective microoptical arrays can be passive or active (Figure 4). They redirect the portion of an expanded LED or laser beam of fixed intensity towards different directions in space, corresponding to the virtual synapses or electrical junctions (optical receivers connected to the I/O lines) of the FPGA target neurons that the sending neuron connects to. Because each neuron connects to different target neurons or muscles, the microoptics of the individual neuron-specific arrays will be all different from each other. Therefore, a static connectome will require the fabrication of 302 passive micromirrors consisting of a reflective pixel pattern that projects incoming light to specific locations on the rack. An active connectome will be composed of 302 digital mirror devices (DMDs). In both cases, these reflective arrays will be installed opposite to the racks carrying the FPGA boards (Figure 3, right).

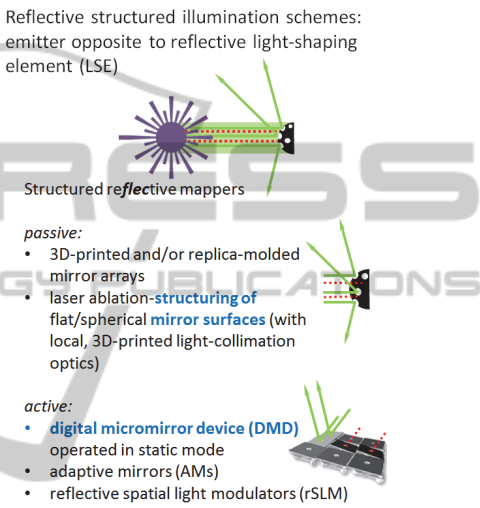

Figure 4: Examples of passive and active reflective light shaping elements (LSEs).

While the connectome of an organism like *C. elegans* is thought to not change over its lifetime, passive reflective devices, once aligned, will result in a robust interconnectivity matrix. Furthermore, no electrical power is needed to maintain a projection pattern. In case new insights on missing connections are published, individual mirrors with updated permissive pathways can be fabricated by standard (electron-beam) photolithography or laser ablation and replace obsolete mirrors.

A more flexible strategy is the use of active micromirror devices. They will allow an electronic re-programming of the connectome. Active micromirror devices find wide-spread application in video projectors. While various technologies for electronically programmable micromirrors exist, the most ubiquitous is the digital micromirror device (DMD) pioneered by Texas Instruments. In digital light processing (DLP) projectors, the image is created by microscopically small mirrors laid out in a matrix on a semiconductor chip. Each mirror represents one pixel in the projected image. The

number of mirrors corresponds to the resolution of the projected image. These mirrors can be repositioned rapidly between ±12 degrees to reflect light either through a projection lens or onto a heat sink (called a light dump). Rapidly toggling the mirror between these two orientations (essentially on and off) produces grayscales, controlled by the ratio of on-time to off-time. If no signal is applied, a mirror will be held electrostatically in its previous toggle state through three static memory elements underneath. This allows the creation of a quasi-static light distribution pattern that, upon demand, can be changed anytime on the fly by using a commercial DMD controller (*e.g.*, DLP® LightCrafter™, Texas Instruments) (Figure 5). Mirrors can be bundled (binned) to increase the light intensity at the projection screen at the cost of decreasing overall image resolution.

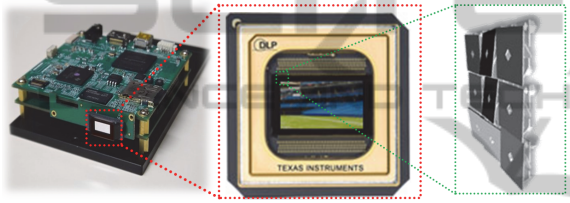

Figure 5: Example of a commercial DMD controller (left, Texas Instruments), a DMD (middle, Texas Instruments) and the three-state positioning of micromirrors (+12° light grey, -12° black, 0° dark grey; right).

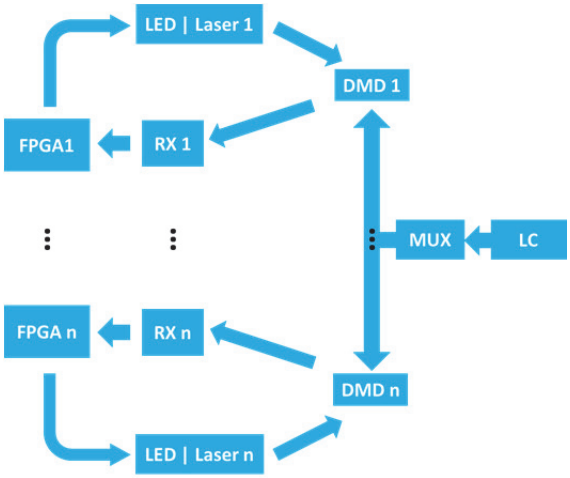

Figure 6: A general interconnection scheme based on multiplexing several (n = 302) DMDs for downloading individual neuron-specific and quasi-static, but re-programmable projection patterns (=synaptic/gap junction connections) onto them through a single DMD controller. Legend: DMD: digital mirror device; FPGA: field-programmable gate array; LC: LightCrafter (DMD controller by Texas Instruments); LED: light-emitting diode; MUX: multiplexer; RX: (photo) receptive matrix.

A general interconnection scheme is shown in Figure 6. The main limitation of the LightCrafter controller is its inability to control more than one DMD at a time. Considering that DMD mirrors will remain in the same position if no additional data is applied to the DMD (although it is suggested to reset the mirrors no less than 1 Hz to avoid mirror memory issues), we deploy a multiplexer board which permits a number of DMDs to share the same driver board.

5 CONCLUSIONS

Optical interconnection concepts have universal character and are not restricted to the layout chosen for the *Si elegans* platform. Once a convenient geometry for the emulation of a particular nervous system or any of its sub-circuits (*e.g.*, a cortical column) has been identified, neural emitters and receivers can be arbitrarily allocated in space, and network-specific optical light structuring and distribution elements be manufactured to implement a particular connectome. This approach also allows for the optical interlinking of several sub-circuits through dedicated optical ports, *e.g.*, to mimic cortical layers. In the simplest case, these can be holes in the support frameworks that are carrying the neuronal modules of different neural subassemblies. This free-scaling feature allows for the design of future generations of highly complex biomimetic computational architectures.

Ongoing work focuses on the physical implementation of the control electronics and the electro-optical components and on the development of an optimization algorithm for their strategic relative placement to each other.

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