# Event based neuron models for biological simulation. A model of the locomotion circuitry of the nematode C.Elegans.

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*Abstract:* - C.Elegans is a nematode whose nervous system has 302 neurons. Its swimming motion is controlled by a subsystem of 80 neurons, which are able to generate both forward and backward locomotion at variable speed. We present both a model of this circuitry based upon event-driven models of neurons and a model of the nematode's body. We test its capability of generating forward/backward locomotion. The final aim of this work is to demonstrate the feasibility of using event-based models of neurons to reproduce the fundamental behaviour of circuits of neurons not only in locomotion but also in sensory signal processing.

*Key-Words*: - neuronal simulation, discrete simulation, C. elegans, locomotion

## 1 Introduction

C.Elegans is a nematode of small dimensions (1 mm long and 80 micrometers wide) which is found in soil. It lives on bacteria which it must locate and ingest. Despite the reduced size of its nervous system,with 302 neurons [1], it still has a relatively rich behaviour. Its locomotion is based on crawling, both forward and backward and its speed of propagation may be changed depending on stimulation from environment.It also bends in an elaborate manner when mating.

Several attempts have been made to model and simulate subcircuits of C.elegans' nervous system [2] [3] [4]. Functional data is presently limited to observation of behaviour due to difficulties in electrophysiological recordings.

In this paper we present a model of the locomotion neural circuitry which accounts for a variety of behaviours. We have extracted the relevant features of it and simulated a simplified version. A mechanical model for the nematode has been proposed [2]. We extend this model from two to three dimensions to allow the evaluation of the modeled nervous system at the behavioural level.

Different types of models have been used for the simulation of single neurons or small aggregates of neurons [5]. We have chosen an event-driven neuron model which combines the rich behaviour of real neurons with efficient simulation.

## 2 Event based simulation versus compartmental models

Traditionally, modeling of realistic circuits of neurons has been based on compartmental mod-

els. The simulation of these models usually involves the numerical solution of non-linear differential equations (due to the non-linearity of the Hodgkin-Huxley ion channel equations). In addition to the computational requirements of the simulation, compartmental models tend to be highly sensitive to the many parameters required. This makes them specially difficult to tune and difficult to use in simulating large aggregates of neurons. On the other hand, integrate and fire models use leaky capacitors and threshold functions. This solution reduces the computational requirements for simulation, allowing simulation of large aggregates, but limits the functionality of the neurons [6].

We use event driven models of neurons, whose computation requirements allow fast simulation but maintain a relatively high complexity in the functionality of each model neuron. Discrete simulation allows exploitation of latency in biological neurons to speed up simulation.

As an example, consider the simulation of integrate and fire versus event based. In an event driven model, the number of events depends on the number of action potentials. If no action potential is generated, the processor spends no time in that neuron whereas in integrate and fire models the membrane voltage is still updated for every time step.

The drawback of discrete models is their limitation in reproducing the neuron dynamics at the membrane voltage level. Our working hypothesis is that the behaviour of a neuron can be captured by pulse based models.

## 3 Event-driven neuron model

In Figure 1 the different blocks making up the model neuron are presented. It is an asynchronous system based on pulse modulation. Signals (pulses) are evaluated and propagated in the direction of the arrows in the diagram.

Signals originating in chemical synapses and electrical junctions (gaps) enter the neuron from the left hand side of Fig. 1. Blocks marked as gaps/synapses behave as monostable oscillators triggered by the incoming pulses (which model biological action potentials). They are stretched (thereby implementing a low pass filter) and a propagation delay is also introduced.

Delayed and stretched pulses reach the multifunctional block. This stage is responsible for evaluating different combinational functions with the inputs from the gaps/synapses. The specific function implemented depends on the functionality of the neuron.

For example, for a neuron working as a correlation detector, this stage would calculate the usual weighted sum of inputs and apply a thresholding function to it.

$$out = TH(\sum_{i=1}^{N} x_i * w_i) \qquad (1)$$

Where TH is the thresholding function, N is the number of synapses, $x_i$ is the value of input i (1 or 0) and $w_i$ is the weight of the synapse i. Negative weights account for inhibitory inputs whereas positive weigths account for excitatory inputs.

For a bypass neuron, the model behaves as a D flip-flop. Inputs are flagged with type ids therefore grouping input synapses into two classes (clocking synapses and D synapses setting the future state). When the neuron is in its asserted state, its output is a train of pulses. In the deasserted state its output is silent.

Both correlation detectors and bypass neurons are used in our model of the locomotion system in C.Elegans.

Two outputs drive the burst generator block from the multifunctional block. The line labeled "exc" is asserted when input activity is exciting the neuron. The " inh" line is asserted only when input activity gives rise to sufficient inhibition (as opposite to excitation). Both lines may be deasserted indicating that the input pulses do not force neither excitation nor inhibition.

To account for spontaneous activity an astable oscillator drives the bursting block. In our locomotion circuitry this block is only active for AVB and AVA inter neurons which control the speed of locomotion.

The last block, AP shaper, generates pulses of variable duty cycle when the output of the burst

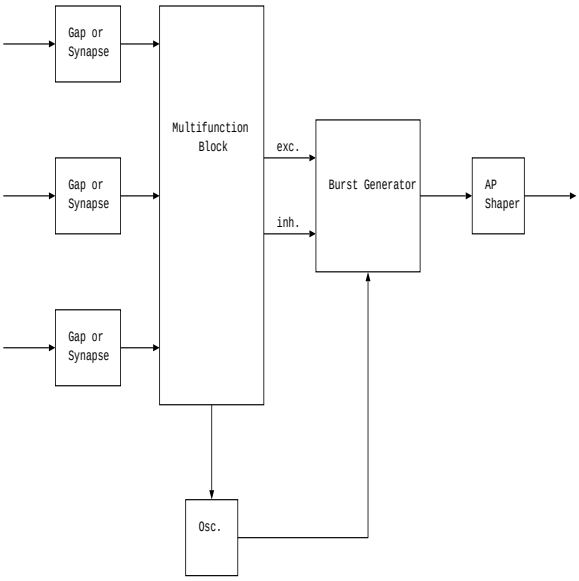


Figure 1: Blocks diagram of the neuron model.

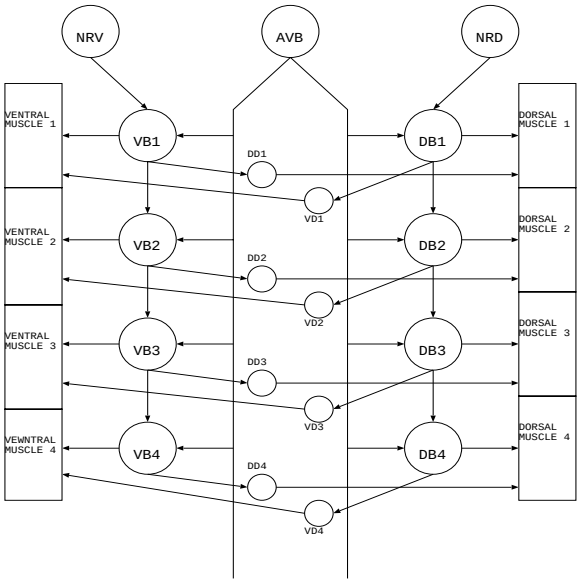


Figure 2: Locomotion circuit of C. elegans

block is asserted. The refractory period is modeled by silent periods between two pulses within which no action potential can be generated. This stage drives the output

# 4 Existing data about the locomotion circuitry

The nervous system of C. elegans has been mapped completely using electron microscopy [1]. In addition to this topological information, several techniques have provided insight to the functionality of specific neurons (immunochemistry allows staining cells which release a particular type of neurotransmitter, genetic studies allow identification of malfunctioning cells in mutants,and so on) [7].

Laser ablation allows the elimination of identified neurons and the study of the effect on locomotion [8].

Based on this data we propose the model presented in Fig. 2. Circles represent neurons and arrows represent synapses/electrical junctions.The top part of the diagram is closest to the head. On both sides square boxes represent body muscles. NRV and NRD stand for nerve ring ventral and dorsal excitation. AVB, DB and AVB generate and propagate contractions down the body while DD and VD inhibit antagonistic muscles.

Only a part of the forward locomotion circuit is included in the figure. The backward locomotion circuit uses a separate set of cells which is symmetrical to the forward locomotion circuit but rotated 180 degrees.

# 5 Mechanical model

To test the usefulness of the proposed neural circuit in the generation of forward and backward movement, it is advantageous to interface the control circuitry with the mechanical model, to allow the gross interaction of the system to be easily viewed. Our mechanical model is based on previous work on modeling the body movement of the nematode[2]. We have extended this model to three dimensions to allow further studies of the head movement (which has an extra degree of freedom when compared to the body). We have also simplified some force terms as explained below.

In summary, the model is based on an elastic cylinder made of an array of linear springs. Each point of the body mesh is connected to its four closest neighbours by a spring. The force acting on this point is the net contribution of all four springs. The resting length of the springs has

been set to force the mesh to be stable in cylindrical shape.

$$F_s = k * (d_i - d_0) * u_i \quad (2)$$

where k is the spring constant, $d_i$ the distance to the point i in the mesh, $d_0$ the ideal length and $u_i$ the unitary vector towards neighbouring point i.

To maintain its cylindrical shape, the nematode requires a high internal pressure [2]. The internal pressure term is calculated as,

$$F_p = k_p * n \quad (3)$$

where $k_p$ is a scaling factor and n is a unitary vector normal to the surface of the body.

The action of the environment is modeled as in Eq.4 Only inertial forces are considered; viscous forces are neglected as in [2].

$$F_e = -k_r * (v * n) * n \quad (4)$$

where $k_r$ is a scaling factor, n a unitary vector normal to the body and v is the velocity vector.

This force acts as a damping term to stop the mesh from oscillating in addition to provide the propulsion for body movement.

Finally, all types of forces acting on a point in the mesh are,

$$F_t = F_s + F_p + F_e \quad (5)$$

where $F_s$ is the force by neighboring point, $F_p$ the internal pressure and $F_e$ the resistance created by the environment.

Muscle contraction is simulated by changing the ideal length of the springs in the body wall (Eq. 2). Those springs located at the position where the contracted muscle is, will see their ideal lengths reduced until relaxation.

Fig. 3 shows the resulting body shape.

The cylindrical body of the nematode is covered by muscles which are organised in longitudinal stripes . Contraction of these muscles generates the bending of the body required for locomotion, mating, and so on.

In C.Elegans there are twelve muscles per row and eight rows in the body.

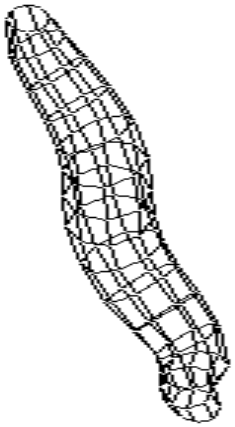

Figure 3: Screen shot of the mechanical model.

Sets of muscles are connected by electrical junctions and controlled by a single neuron. In our model, we have collapsed the body muscles into two rows (ventral and dorsal).

# 6 Simulation results

## 6.1 Normal forward/backward propagation

In Fig. 4 the results of the simulation of the forward locomotion circuit are shown. Only 4 muscles from the ventral side of the body have been included in the plot.

As mentioned before no electrophysiological experiments have been conducted so far on neurons from the locomotion system. Action potentials in mammalian neurons last for a few milliseconds. On the other hand, action potentials in pharyngeal muscle of C.Elegans has been shown to last hundreds of milliseconds and in Ascaris (a nematode similar to C. Elegans) pulse-like signals in neurons of up to a few hundreds of msec have been recorded [9].

In our model we have long pulses (action potentials) in muscles but we use pulses of a few msec in neurons.

The equivalent of the simulated circuit in the digital electronics domain would be a shift register. NRV and NRD act as inputs to the register, VB and DB behave as flip-flops making up the shift register and AVB takes the place of the

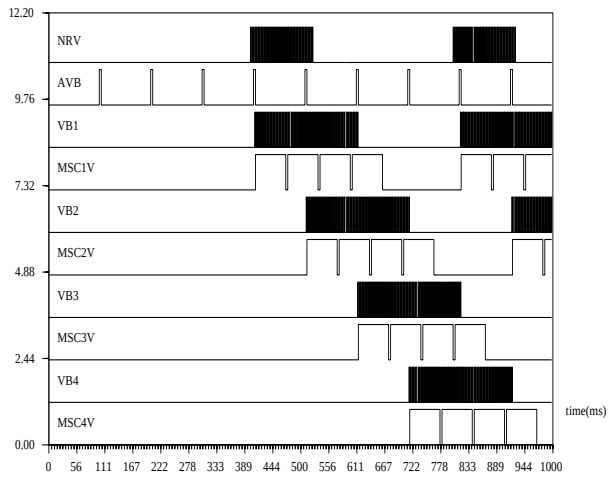


Figure 4: Simulation of forward locomotion circuit.

clock.

At t=0 all muscles in the body (labeled MSCxV) are relaxed and the animal remains still in a straight line. When it initiates forward locomotion, its muscles in the head contract forcing the bending of the tip of the body.

The head is driven by a neural circuit situated in the nerve ring which is independent from the forward/backward locomotion circuit. We have not simulated that circuit, hence, we assume that the head circuitry has forced the contraction of muscles in the head.

AVB is the inter neuron which controls the speed at which contraction propagates along the body. Each pulse generated by this inter neuron forces a displacement of the contraction pattern in the body muscles towards the tail.

Muscle cells close to the head (MSC1V and MSC2D) become active as a result of activity arriving from the AVB inter neuron and from the head (NRV and VRD). They generate a train of pulses and the muscle in the mechanical model contracts.

VB motor neurons behave as flip-flops making up the shift register. When AVB is asserted, the state of $VB_n$ is propagated to $VB_{n+1}$.

The output of the VB cell activates the adjacent muscle, creating a propagating wave of contraction.

The ability of the nematode to change speed can be accounted for by changing the frequency at which AVB works. An increase in frequency forces faster propagation of the contraction, increasing the speed of the animal through the medium.

VD and DD inhibitory neurons (not shown in Fig.4) will fire whenever the motorneuron they are connected to becomes active. Their output inhibits the muscle in the opposite side of the body preventing simultaneous contraction of two muscles in opposite positions (ventral and dorsal) in the same segment.

Backward locomotion follows the same mechanism. AVA is the inter neuron responsible for speed control and VA and DA are the bypass neurons which propagate contraction along the body muscles towards the head.

DD and VD act as inhibitory neurons preventing simultaneous contraction in antagonistic muscles in the same way they acted for forward locomotion.

### 6.2 Defective locomotion

Laser ablation of neurons in the locomotion circuit generates nematodes with locomotion defects.

When the AVA inter neuron is laser ablated [10] , backward locomotion is never observed. AVA is also required in our model to trigger the propagation of contraction down the body. If it is forced to be silent, though the head muscles contract, no contraction wave propagates in the body and backward locomotion is impossible.

When the AVB inter neuron is ablated, the effect in both animal and model is the opposite; no forward locomotion is seen though backward locomotion is possible.

The ablation of the VB and DB neurons also perturbs normal locomotion in the nematode. If these motor neurons are forced to be silent, contraction cannot be propagated correctly and normal locomotion is impaired.

## 7 Conclusions and future work

The presented work is part of ongoing research studying the possibility of using event-driven models of neurons in simulations of biological neural circuits. If the behaviour of biological neural nets can be captured by a set of event driven neuron models, the simulation of aggregates of hundreds of thousands of neurons would become feasible. In the case of the locomotion system, correlate detector neurons were not enough to generate the locomotion pattern. Bypass neurons (VB, VA, DA and DB) had to be added.

It is likely that more complex functionality will have to be added to the model neuron as more complex neural circuits are simulated.

C.Elegans has been chosen as the first target system. The simulation of the locomotion circuitry is being currently extended to other neural circuits. In particular, ongoing work is focusing on thermo taxis. C.Elegans is able to steer its locomotion towards a suitable temperature. Once the ideal temperature zone has been reached, the nematode ensures it does not move out of that region.

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