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Modelling the oscillatory component of forward locomotion in C. Elegans

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Abstract:
In this study we provide a simplified model of the forward oscillatory locomotion neural circuit of the worm C. Elegans. Based on available connectome but lacking electrophysiological data on neurons and synapses we fill this gap by fine-tuning the electrophysiological parameters of the model so that it achieves oscillations.
We observe that without electrical synapses the motor neurons are not active synchronously, thus hindering movement patterns observed in live worms. After the introduction of electrical synapses into the model, motor neurons work in synchrony.
Worm C. Elegans is still the only organism with a completely mapped connectome. This makes it a popular system for computational modelling. C. Elegans hermaphrodite has 302 neurons. The number of chemical and electrical synapses is in the thousands but is not yet definitively mapped. A seminal study by White et al.(1986) provided the first description of C. Elegans connectome and is continually updated.
In spite of its relatively simple nervous system, C. Elegans is capable of a whole range of behaviours. The locomotory system of C. Elegans comprises of 95 wall muscles and 75 ventral cord motor neurons. Motor neurons are regulated by motor command interneurons. A worm moves by propagating bends along its body. C. Elegans is capable of moving forward and backward with differing speed. It can also realise U-turns to abruptly change the direction of its movement.
Using Animatlab2 software we specified a set of neurons. We built two pairs of artificial motor neurons, representing VB and DB class and a single artificial neuron representing the PVC interneuron. Parameters of neurons and synapses were set by the software and fine-tuned by the authors to mimic processes described in theory.
The first step was to build an oscillatory circuit that would enable the undulatory movement of the animal. We set up the PVC neuron with 100 nA tonic stimulus that would simulate incoming impulses that drive the forward movement. We also added 0.1 mV tonic noise to all neurons simulating noise inherent in neural systems. The initial threshold of the PVC neuron was -40mV; the resting potential was -60mV. Accommodation time constant was set to 10 ms, AHP conductance to 1 microS and AHP time constant to 3 ms. Relative accommodation was set to 0.3, relative size to 1 and time constant to 5 ms.
We then set up DB1, DB2, VB1 and VB2 neurons with the same parameters: the initial threshold of neurons was -40mV, and the resting potential was -60mV. The accommodation time constant was set to 1 ms, the AHP conductance to 1 microS and the AHP time constant to 30 ms. The relative accommodation was set to 0.3, the relative size to 1 and the time constant to 5 ms.
In the next step we introduced four depolarising IPSP synapses from PVC to DB and VB neurons. The equilibrium potential of each synapse was set to -30 mV, the decay rate to 10 ms and the facilitation decay to 100 ms. The relative facilitation was set to 1 and the synaptic conductance to 5 microS.

Then we built two pairs of mutually inhibitory synapses; between DB1 and VB1 and between DB2 and VB2. These reciprocal inhibitory synapses together with the threshold adaptation enable oscillation of activity alternating between DB and VB neurons. The parameters of inhibitory (hyperpolarising IPSP synapses) were set as follows: the equilibrium potential of each synapse was set to -70 mV, the decay rate to 10 ms and the facilitation decay to 100 ms. The relative facilitation was set to 1.5 and the synaptic conductance to 0.5 microS.
There are more ways to achieve oscillation in a neural circuit. We do not know yet what mechanism is used in C. Elegans as we have very little information on the electrophysiology of C. Elegans neurons. Oscillation can happen because of a rhythmically bursting pacemaker neuron or by mutual inhibition of neurons with adaptation of either neural threshold or the synapses.
In our study we provide a possible mechanism of oscillatory synchronised activity necessary for C. Elegans locomotion. We show that without the electrical synapses muscle, contraction would not be synchronous and forward movement would not happen.

Keywords:
C. Elegans. Locomotion. Computational modelling.

Introduction

Worm C. Elegans is still the only organism with a completely mapped connectome. This makes it a popular system for computational modelling. C. Elegans hermaphrodite has 302 neurons. The number of chemical and electrical synapses is in the thousands but is not yet definitively mapped. Seminal study by White et al. (1986) provided the first description of C. Elegans connectome and is continually updated (Varshney et al., 2011; wormwiring.org).

In spite of its relative simple nervous system, C. Elegans is capable of a whole range of behaviours. The locomotory system of C. Elegans comprises of 95 wall muscles and 75 ventral cord motor neurons. Motor neurons are regulated by motor command interneurons. A worm moves by propagating bends along its body. C. Elegans is capable of moving forward and backward with differing speed. It can also realise U-turns to abruptly change the direction of its movement.

We still do not know how the motor circuit operates, although many models have been proposed (e. g. Bryden, Cohen, 2008; Majmudar et al., 2012).

In this study we look at the question of how the oscillatory pattern that could cause movement in C. Elegans could be generated.

Method

Using Animatlab2 software (www.animatlab.com) we specified a set of neurons. Studies (Goodman, 2006; Olivares et al., 2017, Wen et al., 2012) show that PVC interneurons play a crucial role in forward locomotion in C. Elegans. PVCL and PVCR neurons run across the body of the worm and innervate (among others) the VB and DB class of motor neurons (Figure 1).

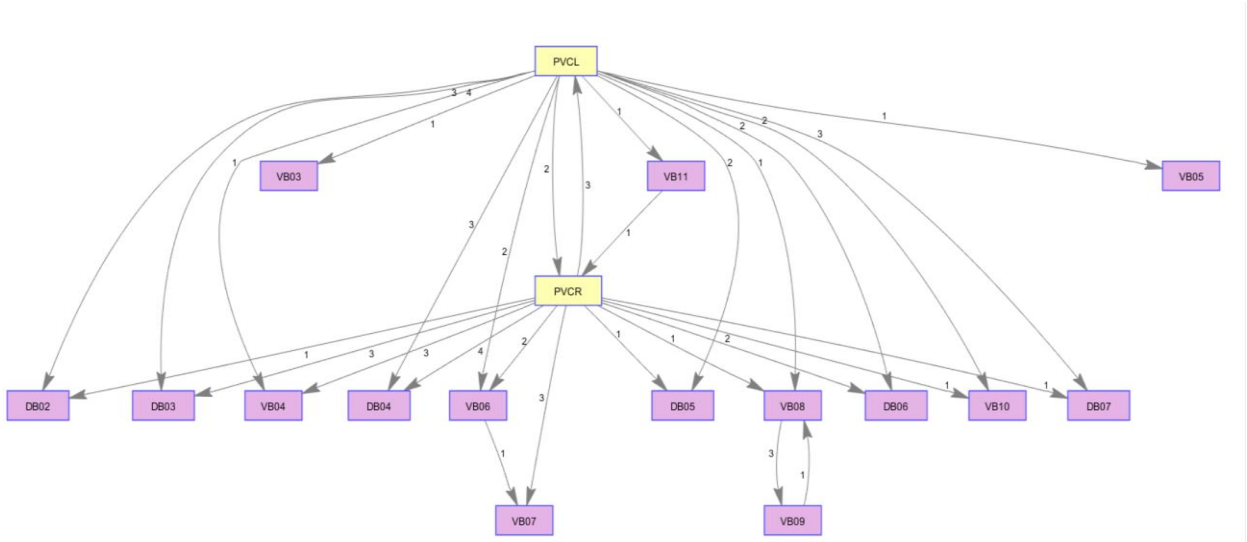

Figure 1: Connectome of PVC, DB and VB neurons - chemical synapses. Reconstructed from data from White et al. (1986) and Varshney et al. (2011).

We built two pairs of artificial motor neurons, representing the VB and DB class and a single artificial neuron representing the PVC interneuron (Figure 2). The parameters of neurons and synapses were set by the software and fine-tuned by the authors to mimic processes described in the theory.

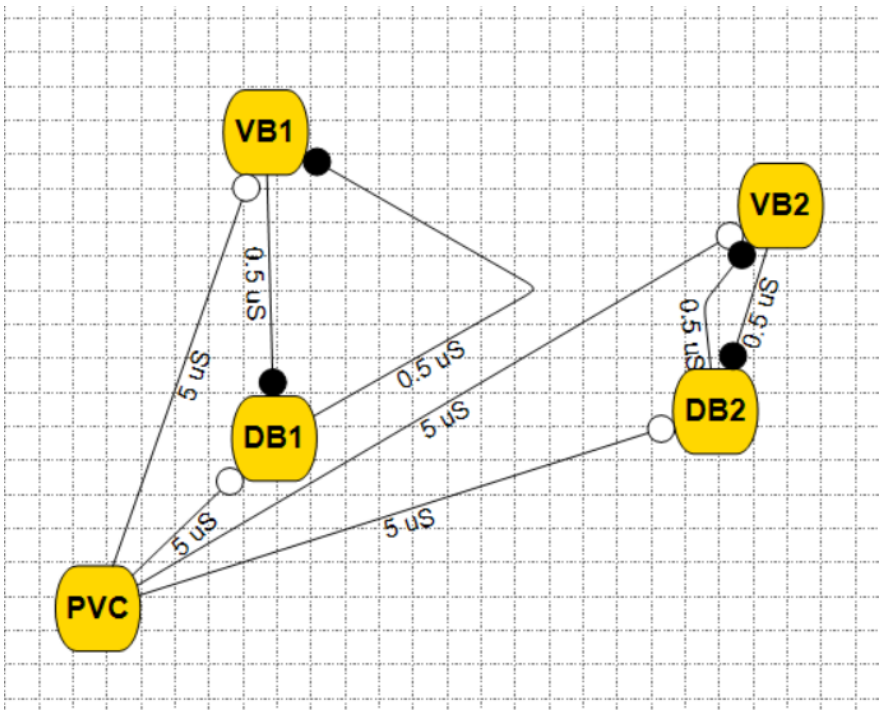

Figure 2: A simplified model of the oscillatory circuit in C. Elegans. White dots = excitatory synapses. Black dots = inhibitory synapses.

The first step was to build an oscillatory circuit that would enable undulatory movement of the animal. We set up the PVC neuron with 100 nA tonic stimulus that would simulate incoming impulses that drive the forward movement. We also added 0.1 mV tonic noise to all neurons simulating noise inherent in neural systems. The initial threshold of the PVC neuron was -40mV, the resting potential was -60mV. The accommodation time constant was set to 10 ms, the AHP conductance to 1 microS, and the AHP time constant to 3 ms. The relative accommodation was set to 0.3, the relative size to 1 and the time constant to 5 ms.

We then set up DB1, DB2, VB1 and VB2 neurons. Their parameters were the same; the initial threshold of neurons was -40mV, and the resting potential was -60mV. The accommodation time constant was set to 1 ms, the AHP conductance to 1 microS, and the AHP time constant to 30 ms. The relative accommodation was set to 0.3, the relative size to 1 and the time constant to 5 ms.

In the next step we introduced four depolarising IPSP synapses from PVC to DB and VB neurons. The equilibrium potential of each synapse was set to -30 mV, the decay rate to 10 ms and the facilitation decay to 100 ms. The relative facilitation was set to 1 and the synaptic conductance to 5 microS.

We then built two pairs of mutually inhibitory synapses between DB1 and VB1, and between DB2 and VB2. These reciprocal inhibitory synapses together with the threshold adaptation enable the oscillation of activity alternating between DB and VB neurons. The parameters of inhibitory (hyperpolarising IPSP synapses) were set as follows: the equilibrium potential of each synapse was set to -70 mV, the decay rate to 10 ms and the facilitation decay to 100 ms. The relative facilitation was set to 1.5 and the synaptic conductance to 0.5 microS.

Results

When running a simulation, we can observe an oscillatory pattern of activity in DB and VB neurons (Figure 3). In a random pattern, either neuron starts being active and via inhibitory synapse inhibits the activity of its counterpart. After the neural threshold adapts, the neuron's activity ceases, inhibition stops and the opposite neuron starts to be active. The process repeats, forming oscillations.

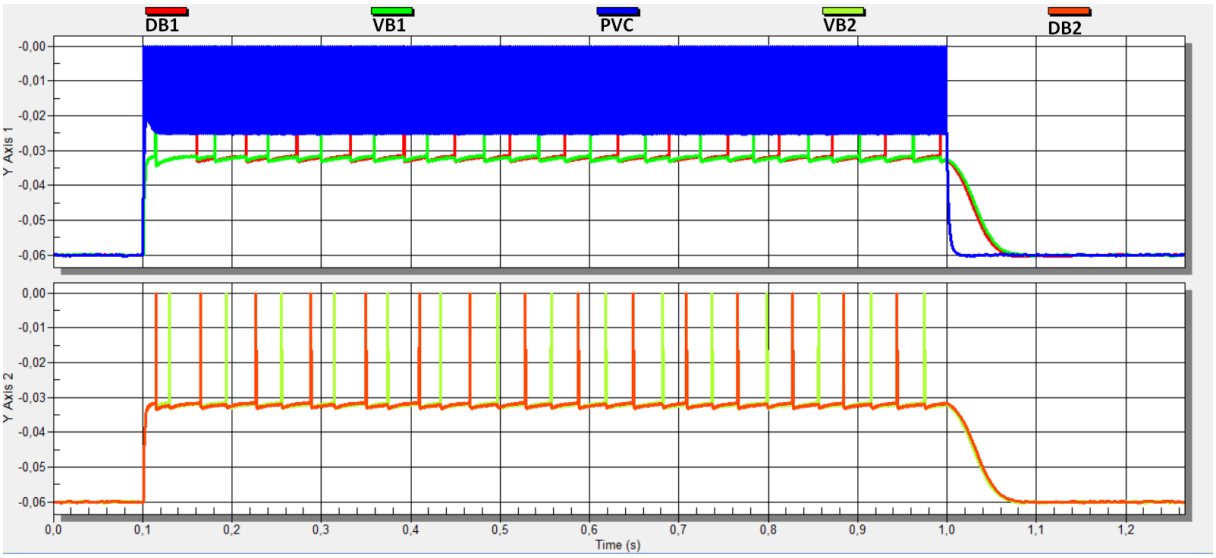

Figure 3: Oscillatory activity of DB and VB neurons. Y-Axis 1 and 2: membrane voltage in mV.

However, after closer inspection we can see that the activity of DB1 and DB2 neurons (as well as the activity of VB1 and VB2 neurons) is not synchronised. Such behaviour would in practice lead to uncoordinated muscle activity in the worm, seriously impairing its movement. This is when electrical synapses come into play. We introduced electrical synapses following the data from White et al., 1986, Varshney et al., 2011 and wormwiring.org that connect classes of motor neurons. In Animatlab we used non-rectifying electrical synapses between DB1 and DB2 neurons and VB1 and VB2 neurons (Figure 4). Both low coupling and high coupling was set to 0.2 microS.

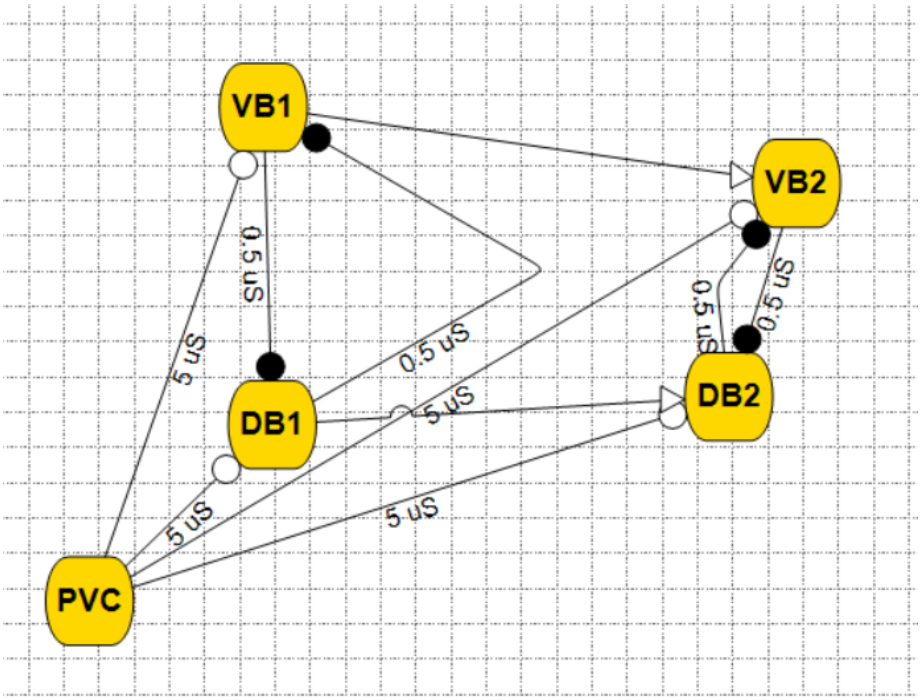

Figure 4: Extended model with electrical synapses. White dots = excitatory synapses. Black dots = inhibitory synapses. Arrows = electrical synapses.

After the introduction of electrical synapses we can see that the activity of pairs of motor neurons belonging to the same class is synchronised (Figure 5).

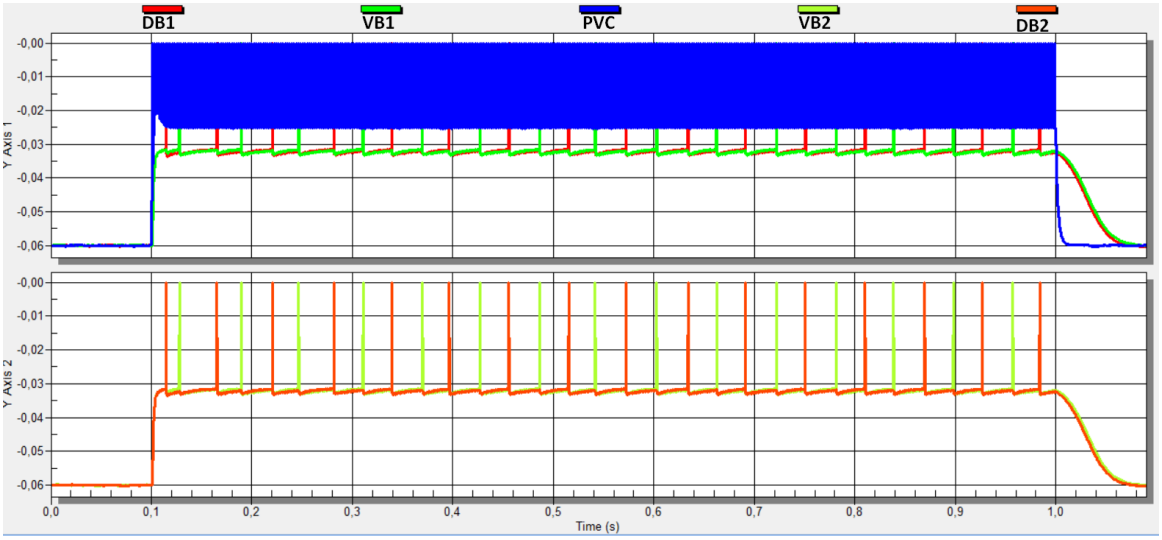

Figure 5: Synchronised oscillatory activity of DB and VB neurons. Y-Axis 1 and 2: membrane voltage in mV.

Discussion

There are more ways to achieve oscillation in a neural circuit. We do not know yet what mechanism is used in C. Elegans as we have very little information on the electrophysiology of C. Elegans neurons. Oscillation can happen because of rhythmically bursting pacemaker neuron or by mutual inhibition of neurons with the adaptation of either neural threshold or the synapses.

In our study we provide a possible mechanism of oscillatory synchronised activity necessary for C. Elegans locomotion. We show that without electrical synapses, muscle contraction would not be synchronous and forward movement would not happen.

References:

Bryden, J., Cohen, N. (2008). Neural control of Caenorhabditis elegans forward locomotion: the role of sensory feedback. *Biol Cybern, 98*(4), 339-351.

Goodman, M. B. (2006). Mechanosensation. *Wormbook,* 1-14. Online: http://www.wormbook.org/chapters/www_mechanosensation/mechanosensation.html. DOI: 10.1895/wormbook.1.62.1

Majmudar, T., et al. (2012). Experiments and theory of undulatory locomotion in a simple structured medium. *J R Soc Interface, 9*(73), 1809-1823.

Olivares, E. O., Izquierdo, E. J., & Beer, R. D. (2017). Potential role of a ventral nerve cord central pattern generator in forward and backward locomotion in Caenorhabditis elegans. *Network Neuroscience, 2*(3), 323-343. DOI: 10.1162/netn_a_00036

Varshney, L. R. et al. (2011). Structural Properties of the Caenorhabditis elegans Neuronal Network. *PLoS Computational Biology, 7*, 2.

Wen, Q. et al. (2012). Proprioceptive coupling within motor neurons drives C. elegans forward locomotion. *Neuron, 76*(4), 750-761.

White, J. G. et al. (1986). The structure of the nervous system of the nematode Caenorhabditis elegans. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences, 314*(1165), 1-340.

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