Abstract

The small (1 mm) nematode *Caenorhabditis elegans* has become widely used as a model organism; in particular the *C. elegans* connectome has been completely mapped, and *C. elegans* locomotion has been widely studied (c.f. http://www.wormbook.org Corsi [1]). We describe a minimal reaction-diffusion model for the *C. elegans* central pattern generator (CPG) Xu *et al.* [2] and Wen *et al.* [3]. We use simulation methods to show that a small network of FitzHugh [4]-Nagumo *et al.* [5] neurons (one of the simplest neuronal models) can generate key features of *C. elegans* undulation (see Magnes *et al.* [6]), and thus locomotion. Compare the neuromechanical model of Izquierdo & Beer [7]. We also investigate dynamics and stability of the model.

A minimal reaction-diffusion neural model generates *C. elegans* undulation

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March 26, 2020

1 Introduction

The small (1 mm) nematode *Caenorhabditis elegans* (*C. elegans*) has become widely used as a model organism [1], and has been among the most widely studied biological models of neuronal development, locomotion and the central pattern generator [8]. The C. elegans connectome has been completely mapped [9] and, as described below, its locomotion has been widely studied. "When crawling on a solid surface, the nematode C. elegans moves forward by propagating sinusoidal dorso-ventral retrograde contraction waves. A uniform propagating wave leads to motion that undulates about a straight line." [10]. A different type of locomotion, often called swimming, occurs when nematodes are submerged in a liquid medium. The nematodes "switch" between these two gaits, under the regulation of particular serotonergic and dopaminergic neurons.

The purpose of this paper to describe a minimal reaction-diffusion model for the *C. elegans* central pattern generator (CPG) [2, 3]. We use simulation methods to show that a small network of FitzHugh [4]-Nagumo *et al.* [5] neurons (one of the simplest neuronal models) based on a skeleton model of the C. elegans CPG can reproduce key features of C. elegans undulation [6] and thus locomotion.

2 The model central pattern generator

A central pattern generator is a small neural circuit which generates and regulates the movement of complex organisms. This structure is present in different forms in many animals, and it regulates many types of periodic motion. Xu *et al.* [2] proposed an architecture for the CPG of *C. elegans* which is described below in figure 2 on the following page.

The central pattern generator has two principal components. First is the **head oscillator**. As described by Gjorgjieva *et al.* [11], the head oscillator consists of two "head neurons" with mutually inhibitory coupling. Oscillations are generated when this coupling destabilizes an excitable steady state.

Second is the **descending pathway**, which consists of pairs of coupled, excitable, dorsal

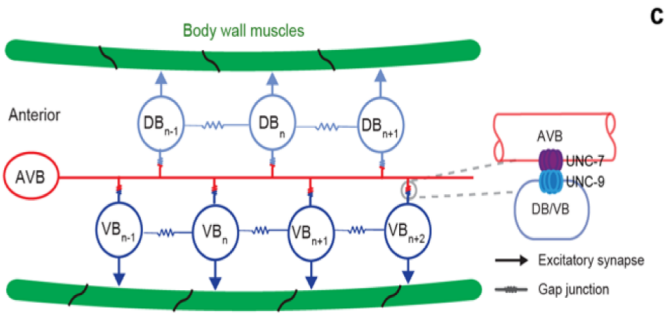

Figure 1: Pirated from Xu.

and ventral neurons. These follow the body of the worm, and are linked to motor neurons and muscles.

While *C. elegans* has twelve pairs of motor neurons, we have only used six pairs in our model. Figure 2 is a depiction of our simplified model as a graph, wherein neurons are nodes, and the arrows between them symbolize connections.

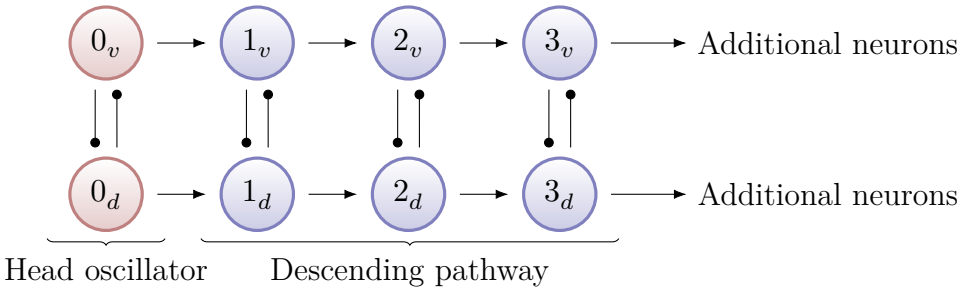

Figure 2: Our simplified central pattern generator model. Descending coupling (shows inhibitory connections, and potential flows through gap junctions, not necessarily symmetric)

3 The FitzHugh-Nagumo Neuron

In accord with the goal of this paper, we sought the simplest relevant neuronal model. The classical Hodgkin-Huxley[12] model of squid neurons has led to a variety of simpler conduction models, including the Morris-Lecar[13] and Fitzhugh-Nagumo models.

The FHN model consists of two dynamical variables; a fast activator variable v corresponding to the (rescaled) membrane potential, and a slow inhibitor variable w corresponding to a generalized gating variable.

$$\begin{aligned} dv &= f(v) + w - I_{\text{ext}} \\ dw &= \epsilon(a - bv) \\ f(v) &= \frac{v^3}{3} - v \end{aligned} \tag{1}$$

In this system, $f(v)$ can be any function which retains the appropriate dynamics, in that it has the same general shape as the cubic $f(v)$. In our analog implementation, we use

a piecewise linear approximation to the cubic, in order to simplify the circuit and avoid using expensive components.

Xu et al. used a simplified two-variable model consisting of a fast, cubic-like activator variable (see the V-nullcline) and a slow, non-linear inhibitor variable (see the n-nullcline). Both the Morris-Lecar model and the Fitzhugh-Nagumo model have similar activator nullclines.

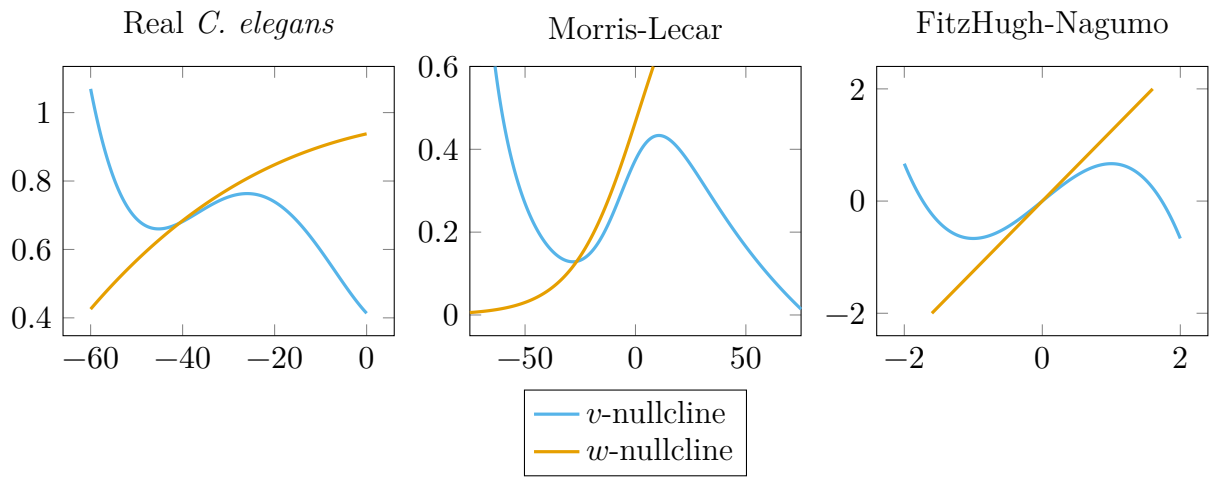

Figure 3: Nullclines of several different neuronal models; on the right is the biological model of Xu et al, in the centre is the Morris-Lecar model, and to the right is the FitzHugh-Nagumo model. These have been arranged in order of decreasing complexity.

The original system was meant to model one neuron only. We use diffusion to model a synapse. A positive coefficient would simulate a gap junction or an excitatory synapse; a negative coefficient would simulate inhibitory coupling (Collins & Richmond [14]).

The equations, when modified for synaptic connections, look like this:

$$\begin{aligned} dv &= f(v) + w - I_{\text{ext}} + D(\Delta v) \\ dw &= \epsilon(a - bv) \\ f(v) &= \frac{v^3}{3} - v \end{aligned} \tag{2}$$

4 Simulation

The simulation was performed in Python, using the standard SciPy ODE solvers.

4.1 Methods

See the appendix, or attached code, for how we simulated this motion. It should probably also be published on Github - I could make a Jupyter notebook with it.

We realize the network shown in Figure 2 on the preceding page into a system of ODEs, and solve it. The equations are integrated, giving a timeseries of neuronal potentials.

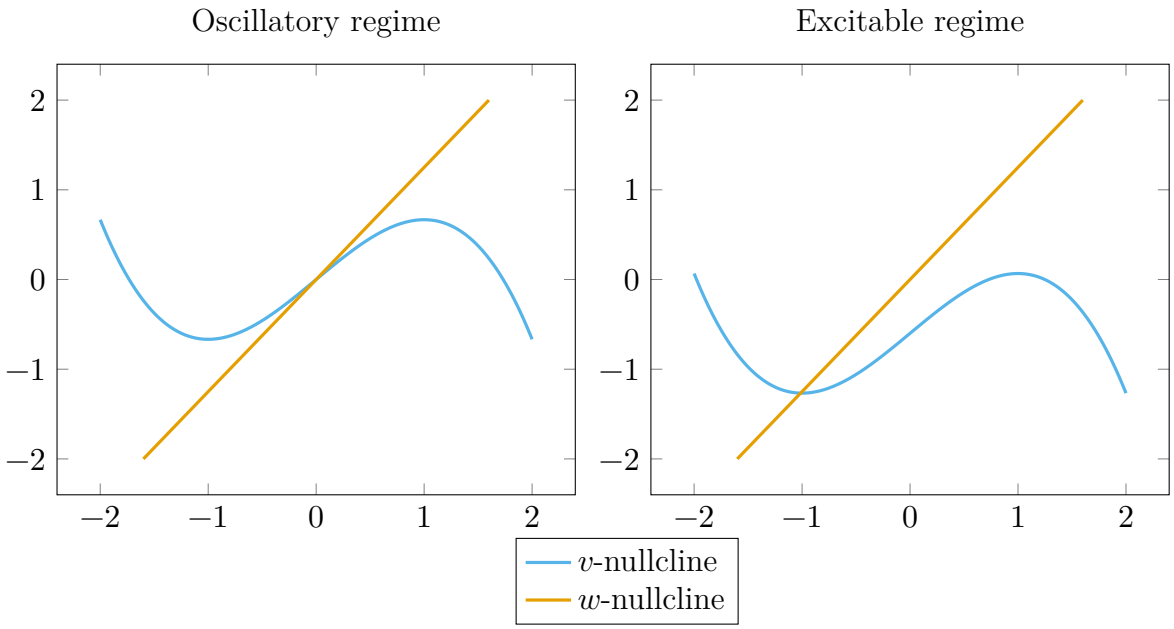

Figure 4: The nullclines of the FitzHugh-Nagumo neuron. Nullclines are isoclines where the derivative of a variable is zero. Here we show an oscillatory mode and an excitable one. In an oscillating cell, the stable equilibrium is replaced by an unstable equilibrium (open circle) around which it circles indefinitely. See Parsons & Huizinga [15] for a clear explanation of the dynamics of oscillatory biological systems.

These are passed through filters to simulate muscular movement and the resistance of the medium. we used Gaussian smoothing and B-splines for this purpose.

We generated a video by fixing the head of a worm to the origin, and re-normalized the coordinate output of the worm.

We achieved the undulatory effect by some to simulate the effect of real muscles.

4.2 Comparison to real worm

Cite the paper which Jenny sent here. It can be seen that our model closely approximates an unconstrained worm, specifically of the wild type.

While the angle which a worm crawling on agar subtends tends to be oblique, as the constraint on the worm decreases, the angle becomes more and more acute - consider the videos . It is not hard to see that a fully unconstrained worm might behave much like our model does.

5 Analog implementation

- Nagumo circuit, disadvantages

- Keener improved, op amps, why is that good - scalability, etc. Piecewise (N-shaped) linear approximation.

- Our modifications - diffusion, coupling mechanism. Some mention of mathematics involved

- Figures: circuits, circuit nullclines,

Nagumo *et al.* [5] proposed a circuit which could simulate the system which FitzHugh proposed. A depiction is included in Figure **??** on page ??. Howe

5.1 Comparison of analog and simulation

For this section, we will focus on the timeseries output of the neurons, and not on the end worm. Include the relevant figure here - you can see clearly that the effect is the same. There are some differences in the waveform because of the different activation function in the circuit (linear interpolation).

6 Conclusion

Mention the bullet points from the presentation. How could a system like this be used in applications? End with some future paths.

7 References

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