A biomimetic reaction diffusion network simulates C. elegans motion

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Abstract

The nematode *Caenorhabditis elegans* is a popular model organism, with a very simple, well-mapped neuronal structure (302 neurons). It moves using undulatory, quasi-sinusoidal motion, apparently generated by a simple central pattern generator (CPG). We aimed to simulate the dynamics of its CPG with a network of the simplest biomimetic model neurons, FitzHugh-Nagumo (FHN) neurons, using the SciPy ODE solver. The FHN model consists of two differential equations - membrane potential and a slow inhibitor. Gap junctions and inhibitory synapses were modeled with one-way diffusion, the latter with a negative diffusion constant. The network drove a simulated muscle structure which generated undulations resembling *C. elegans*. We also developed a prototype analog electronic implementation based on Keener's circuit, mimicking FHN dynamics, and found coupling mechanisms which reproduced key features of *C. elegans* dynamics. The next goal is to simulate *C. elegans* undulation with analog circuits. This work was performed at the Hastings lab (Simons Rock), collaborating with Jenny Magnes VAOL lab (Vassar).

The math

The FitzHigh-Nagumo equations have the form:

$$\frac{dv}{dt} = v - \frac{v^3}{3} - w + I$$
$$\frac{dw}{dt} = \epsilon(v - \gamma w + \beta)$$

where v is the membrane potential, and w is a slow inhibitor variable. D can be positive (excitatory synapses, gap junctions) or negative (inhibitory junctions). Implementation of diffusion coupling leads to the addition of a term $D \cdot \max(\Delta V,\ 0)$ to the membrane potential.

The worm

Caenorhabditis elegans is a small nematode with a well-known neuronal layout. Its central pattern generator can be sufficiently approximated by a network of only six neurons, arranged as such:

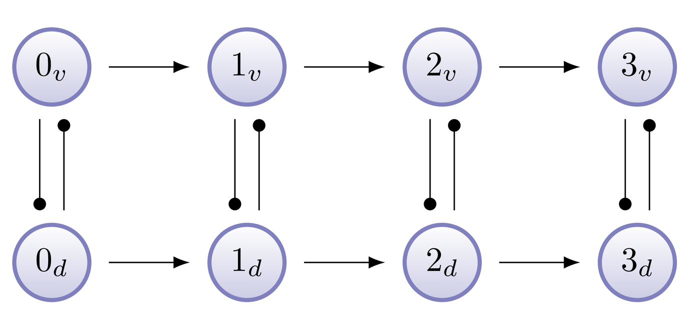

Fig. 1: Central pattern generator simplified

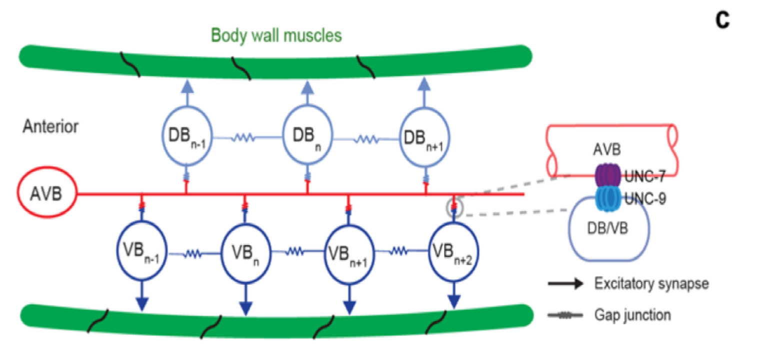

Fig. 2: CPG from Xu *et al*

wherein $0 \longrightarrow 1$ represents unidirectional diffusion coupling, and $0 \longleftrightarrow 1$ represents bidirectional diffusion coupling.

Simulations

We solved these differential equations with different parameter sets using SciPy's ODE solver.

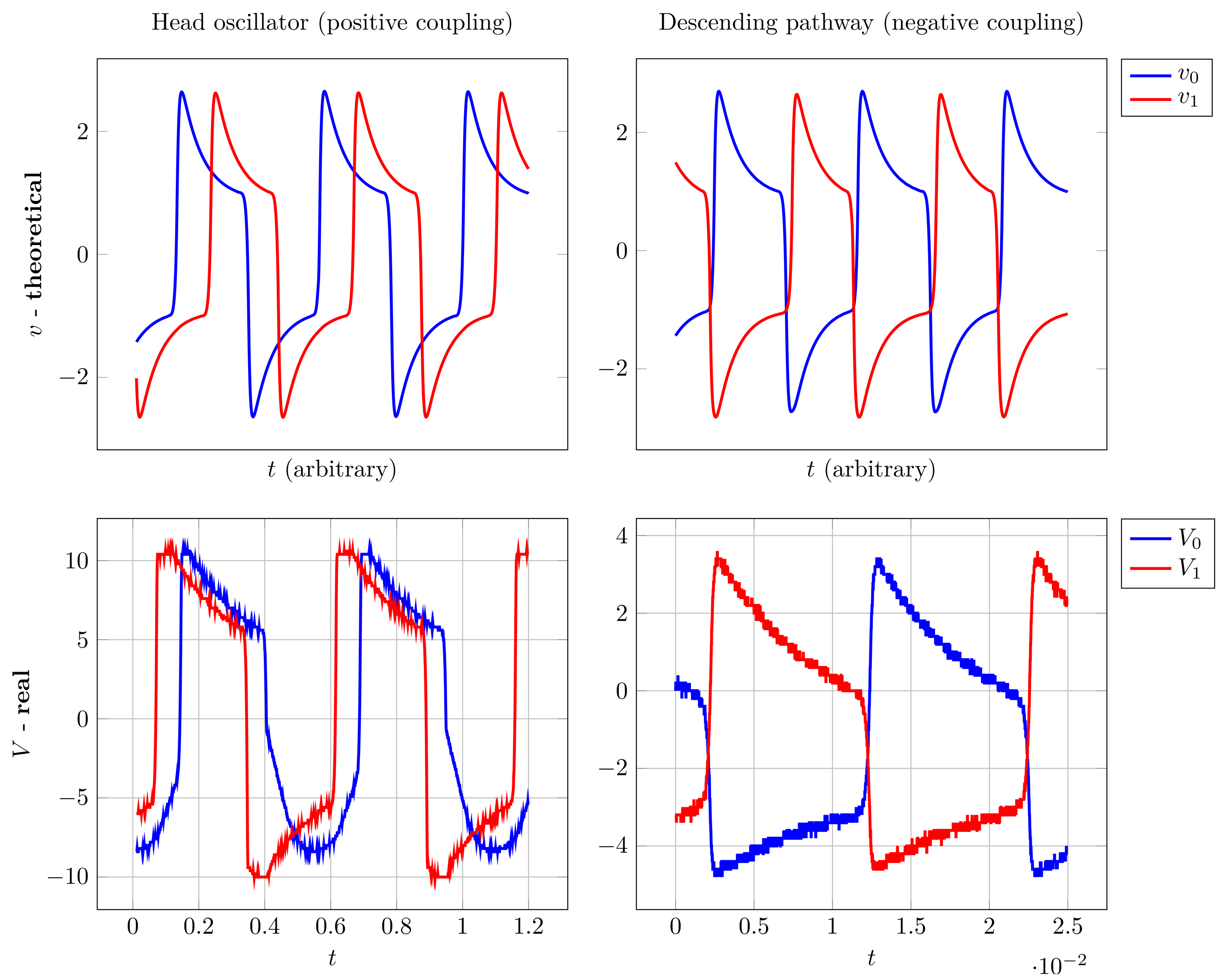

Fig. 3: Responses to coupling

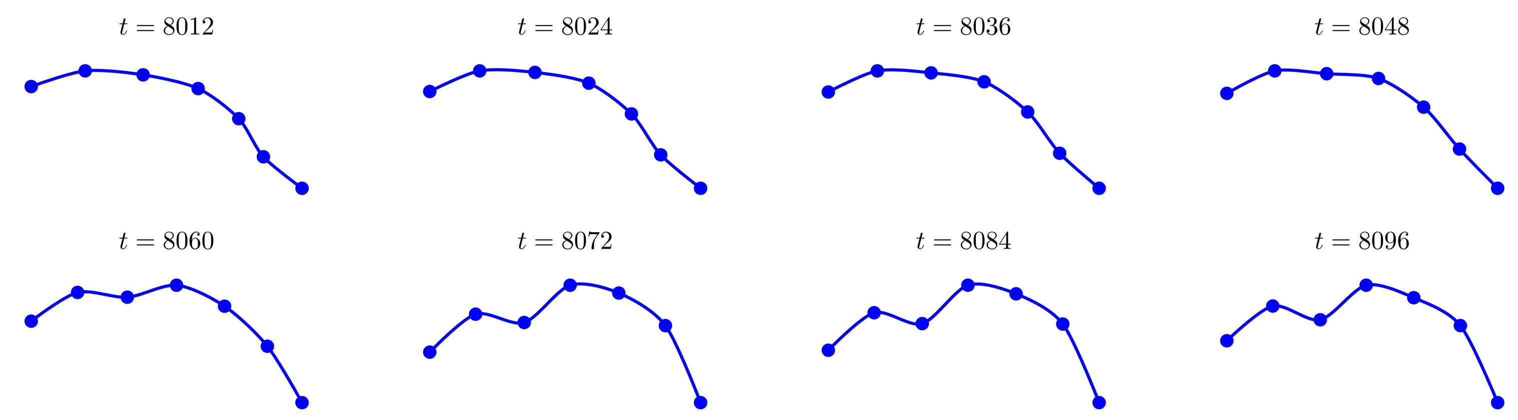

Fig. 4: Simulated worm motion

Minimal code example

```
# imports
import math
from scipy.integrate import odeint
# Initial conditions
dx0, dy0, vx0, vy0, dx1, dy1, ... = v0 \
= [1.0, −0.51, 1, −0.49, 1.0, 0.5, ...] # initial conditions
# etc. for other neurons up to #5; we break symmetry for n0 to start
# oscillation
def FHND(v, t):
    dx0, dy0, vx0, vy0, dx1, dy1, [...] = v  # variables
    # Parameters
    e0 = e1 = 0.08
    g = 0.8
    b0 = b1 = 0.46
    Dhead = −0.2  # diffusion constants
    Drest = −0.02
    Dgap  = −0.05
    return [
    vx0 − vx0 ** 3 / 3 − vy0 + Dhead * max(dx0 − vx0, 0),
    e0 * (vx0 − g * vy0 + b0),
    dx0 − dx0 ** 3 / 3 − dy0 + Dhead * max(−dx0 + vx0, 0),
    e0 * (dx0 − g * dy0 + b0),
    vx1 − vx1 ** 3 / 3 − vy1 + Drest * max(dx1 − vx1, 0),
    e1 * (vx1 − g * vy1 + b1),
    ...
    ] # return time derivatives

sol = odeint(FHND, v0, t)
```

The circuit

The FitzHugh-Nagumo equations translate directly into a circuit that uses inductors, as $L = \frac{dI}{dt}$; however, that is an expensive and impractical solution due to mutual inductance effects. Keener's circuit proposes a simulation of the inductors with operational amplifiers, which make the circuit considerably cheaper, stabler and allows for a linear piecewise voltage response rather than a cubic one, resolving the issue of long-term stability.

Frequency of oscillation changes with bias voltage, but is approximately 2 Hz with the circuit values here.

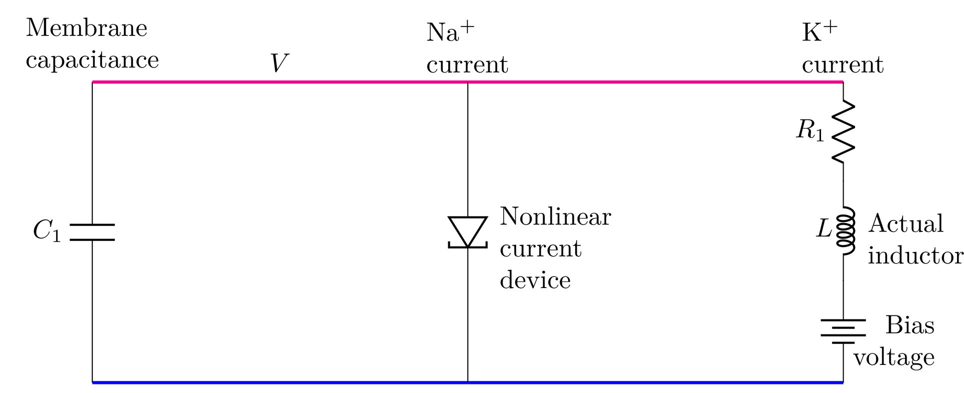

Fig. 5: Nagumo circuit layout

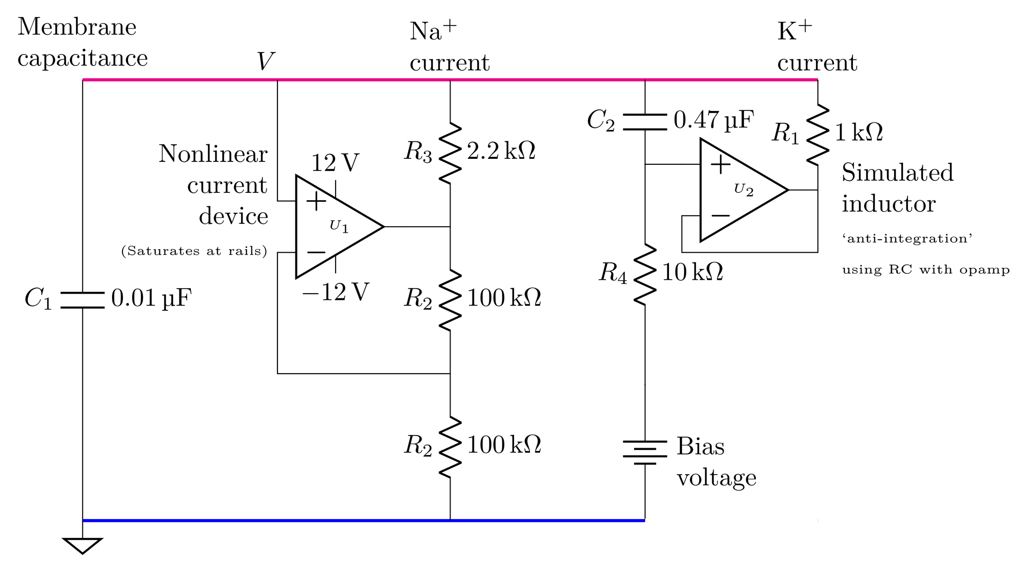

Fig. 6: Keener circuit layout

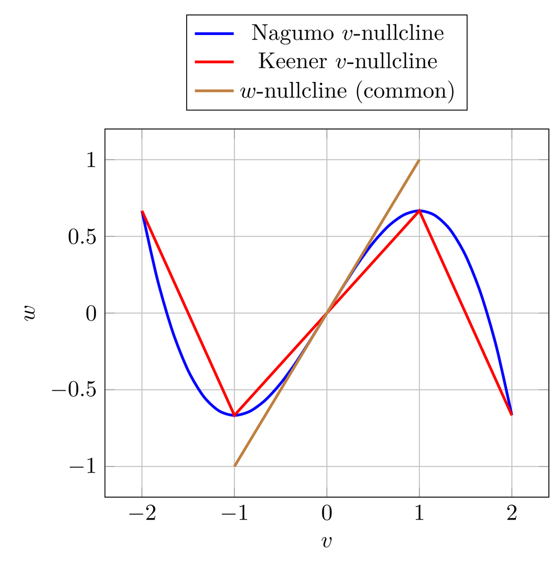

Fig. 7: Nullclines

This represents a single neuron.

We have implemented a time-delay unidirectional diffusion using an R-C circuit (to simulate diffusion of neurotransmitter across a membrane), as well as negative unidirectional diffusion coupling using an inverting amplifier:

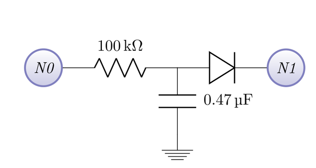

Fig. 8: Time-delay diffusion

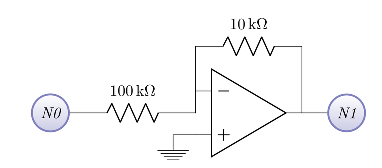

Fig. 9: Negative diffusion

Selected References

Gjorgjieva, Julijana, David Biron, and Gal Haspel. "Neurobiology of Caenorhabditis elegans Locomotion: Where Do We Stand?" In: (2014). DOI: 10.1093/biosci/biu058. URL: https://doi.org/10.1093/biosci/biu058.

Keener, James P. "Analog circuitry for the van der Pol and FitzHugh-Nagumo equations". In: (1983). DOI: 10.1109/tsmc.1983.6313098. URL: https://doi.org/10.1109/tsmc.1983.6313098.

Xu, Tianqi et al. "Descending pathway facilitates undulatory wave propagation in Caenorhabditis elegans through gap junctions". In: (2018). DOI: 10.1073/pnas.1717022115. URL: https://doi.org/10.1073/pnas.1717022115.