Can You Hear Me, Mother? Signals in the Nervous System

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Introduction

Cell membranes are excitable media, as described by Hodgkin and Huxley in their classic series of papers in 1952[1], and in the axons of nerves the action potential can propagate, allowing signals to be passed through the nervous system. This biological system is highly nonlinear, and the signal propagation is very different from that found in linear systems such as sound in air or light in a vacuum. In fact, dependent on the system, it may be possible to propagate only travelling fronts or only pulses (see Figure 1).

[1] A L Hodgkin and A F Huxley. Currents carried by sodium and potassium ions through the membrane of the giant axon of *loligo*. *Journal of Physiology*, 116:449–472, 1952; A L Hodgkin and A F Huxley. The components of membrane conductance in the giant axon of *loligo*. *Journal of Physiology*, 116:473–496, 1952; A L Hodgkin and A F Huxley. The dual effect of membrane potential on sodium conductance in the giant axon of *loligo*. *Journal of Physiology*, 116:497–500, 1952; and A L Hodgkin and A F Huxley. A quantitative description of membrane current and its application to conduction and excitation in nerve. *Journal of Physiology*, 116:500–544, 1952

Continuum Model: Fronts

An example of a model which allows travelling fronts but not always travelling pulses is the bistable equation. This takes the form of a partial differential equation for the action potential V

$$\frac{\partial V}{\partial t} = \frac{\partial^2 V}{\partial x^2} + f(V),$$

where $f(V)$ is a nonlinear function of V. If $f(V)$ has zeros at $V = 0$, $V = \alpha$ and $V = 1$, where $0 < \alpha < 1$, the equation has two steady state values of $V = 0$ and $V = 1$. Three examples which are worth investigating are

$$f(V) = V(V-1)(\alpha - V) \tag{1}$$

$$f(V) = -V + \Theta(V - \alpha) \tag{2}$$

$$f(V) = \begin{cases} -V & \text{if } V \leq -\alpha/2 \\ V - \alpha & \text{if } -\alpha/2 < V < (1+\alpha)/2 \\ 1 - V & \text{if } V \geq (1+\alpha)/2 \end{cases} \tag{3}$$

(Theta is the Heaviside unit step function) and we shall investigate their properties.

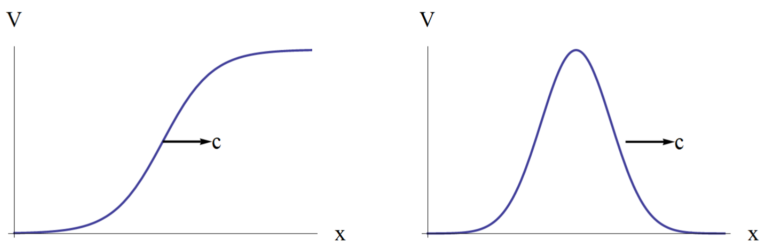

Figure 1: Characteristic shape of a moving front (left) and pulse (right)

Start by solving the bistable equation with the functions in Equation 1 or 2, for $\alpha = 0.1$ and $\alpha = 0.9$, using `NDSolve` over the range $-50 \leq x \leq 50$, $0 \leq t \leq 10$, taking boundary conditions $V(-50,t) = 0$, $V(50,t) = 1$, and $V(x,0) = \Theta(x)$. You should see the step propagate: compare the speed of propagation with the expected values for these two cases, which are $c = (2\alpha - 1)/\sqrt{2}$ and $(2\alpha - 1)/\sqrt{\alpha - \alpha^2}$. Also look at the shapes of the propagating fronts, and confirm that they resemble $1/(1+\exp(-\beta(x-ct)))$ and $1 + \tanh(\beta'(x-ct))$.

Your Own Code

The general-purpose `NDSolve` code is quite slow for solving this problem, so continue by constructing an explicit finite difference solver (although an implicit method would be more stable, the nonlinear terms make it harder to implement). The values of action potential will be held in a list, `V[n]`, representing the situation at time t, and the time-step is implemented using

$$\frac{\partial V(x,t)}{\partial t} \approx \frac{V(x,t+\delta t) - V(x,t)}{\delta t},$$

and if the values are spaced a distance δx apart spatially may write

$$\frac{\partial^2 V(x,t)}{\partial x^2} \approx \frac{V(x+\delta x,t) - 2V(x,t) + V(x-\delta x,t)}{\delta x^2}.$$

Investigate the stability of this approach (numerically rather than analytically) for the three forms of f, and try to confirm the results obtained with `NDSolve`.

Myelination

The finite-difference code can be used, with very little adaptation, to study the discrete bistable equation. The physiological model here is that nerve fibres are normally coated with myelin with periodic gaps (every 1 or 2 mm) in the sheath called the nodes of Ranvier (the gaps are about 1 μm wide). Signal propagation along the myelated sections is fast, so effectively the action potential jumps from node to node (*saltation*). Then the potential at node n varies according to

$$\frac{dV_n(t)}{dt} = f\left(V_n\right) + D\left(V_{n+1} - 2v_n + V_{n-1}\right).$$

What is different here is that whereas what appears as D here previously involved δx which was made small enough to get a good approximation to the derivative, here it is a constant coupling coefficient between nodes. Investigate what happens to the propagation of fronts as the coupling constant changes.

Travelling Pulses

Many nonlinear systems of the sort explored in this project can propagate pulses rather than just wavefronts. A simple example is the FitzHugh-Nagumo system[2] in which a cell membrane is modelled as a capacitor representing the membrane capacitance, a nonlinear current-voltage device representing the fast current, and a resistor-inductor-battery leg to represent the recovery current. Reduced to dimensionless terms, with v representing the membrane potential and i representing the recovery current, the governing equations are

$$\epsilon \frac{\partial v}{\partial t} = \epsilon^2 \frac{\partial^2 v}{\partial x^2} + f(v, i)$$
$$\frac{\partial i}{\partial t} = g(v, i),$$

where f and g represent any nonlinearities in the system.

[2] R FitzhHugh. Thresholds and plateaus in the Hodgkin-Huxley nerve equations. *Journal of General Physiology*, 43:867–896, 1960; R FitzhHugh. Impulses and physiological states in theoretical models of nerve membrane. *Biophysical Journal*, 1:445–466, 1961; J Nagumo, A Arimoto, and S Yoshizawa. An active pulse transmission line simulating nerve axon. *Proceedings of IRE*, 50:2061–2070, 1964; and R FitzHugh. Mathematical models of excitation and propagation in nerve. In H P Schwann, editor, *Biological Engineering*. McGraw-Hill, New York, 1969

Extend your finite difference equations to include two variables, v and i, and investigate solutions for the case

$$f(v, i) = \Theta(v - \alpha) - v - i$$
$$g(v, i) = v,$$

and study pulse propagation in this system. Typically, only certain pulse shapes will propagate, but a general initial pulse will evolve as it propagates by 'losing' the non-propagating components. Theory shows that for values of $\alpha < 0.5$ there are two different propagation speeds, with the faster one being stable, but for larger α pulses do not propagate. Confirm that the numerical model has these characteristics.

Possible Extensions

The project as described here is a numerical investigation of these nonlinear wave systems. A lot can also be discovered analytically, and a computer algebra program can be helpful in the necessary manipulations.

References

[1] R FitzhHugh. Thresholds and plateaus in the Hodgkin-Huxley nerve equations. *Journal of General Physiology*, 43:867–896, 1960.

[2] R FitzhHugh. Impulses and physiological states in theoretical models of nerve membrane. *Biophysical Journal*, 1:445–466, 1961.

[3] R FitzHugh. Mathematical models of excitation and propagation in nerve. In H P Schwann, editor, *Biological Engineering*. McGraw-Hill, New York, 1969.

[4] A L Hodgkin and A F Huxley. The components of membrane conductance in the giant axon of *loligo*. *Journal of Physiology*, 116:473–496, 1952.

[5] A L Hodgkin and A F Huxley. Currents carried by sodium and potassium ions through the membrane of the giant axon of *loligo*. *Journal of Physiology*, 116:449–472, 1952.

[6] A L Hodgkin and A F Huxley. The dual effect of membrane potential on sodium conductance in the giant axon of *loligo*. *Journal of Physiology*, 116:497–500, 1952.

[7] A L Hodgkin and A F Huxley. A quantitative description of membrane current and its application to conduction and excitation in nerve. *Journal of Physiology*, 116:500–544, 1952.

[8] J Nagumo, A Arimoto, and S Yoshizawa. An active pulse transmission line simulating nerve axon. *Proceedings of IRE*, 50:2061–2070, 1964.

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