5.12 Project: A Simple Neuron Model

Neurons are cells in the body that transmit information to the brain and the body by amplifying an incoming stimulus (electrical charge input) and transmitting it to neighboring neurons, then turning off to be ready for the next stimulus. Neurons have fast and slow mechanisms to open ion channels in response to electrical charges. The key quantities are the concentrations of sodium ions and potassium ions (both positively charged). A resting neuron has an excess of potassium and a deficit of sodium and a negative resting potential (an excess of negative ions).

Neurons use changes of sodium and potassium ions across the cell membrane to amplify and transmit information. *Voltage-gated channels* exist for each kind of ion, which open and close in response to voltage differences, which are closed in a resting neuron. When a burst of positive charge enters the cell, making the potential less negative, the voltage-gated sodium channels open. Since there is an excess of sodium ions outside the cell, more sodium ions enter, increasing the potential until it eventually becomes positive. Next a slow mechanism acts to block the voltage-gated sodium channels, and another slow process begins to open voltage-gated potassium channels. Both of these diminish the buildup of positive charge by blocking sodium ions from entering and by allowing excess potassium ions to leave. When the potential decreases to or below the resting potential these slow mechanisms turn off, and then the process can start over. If the electrical excitation reaches a sufficiently high level, called an *action potential* , the neuron fires and transmits the excitations to other neurons.

In order to describe a simple model for this process, we let the potential be v, scaled so that $v = 0$ is the resting potential. We let $v = a$ be the potential above which the neuron fires and $v = 1$ the potential at which sodium channels open ($0 < a < 1$). A model of the form

$$v' = -v(v-a)(v-1)$$

with asymptotically stable equilibria at $v = 0$ and $v = 1$ and unstable equilibrium at $v = a$ would explain part of the observed behavior. If the initial potential is above a, the potential increases to one and if the initial potential is below a, it decreases to zero. Thus, the model allows the signal amplification of the neuron but stops at $v = 1$. We must also build in a blocking mechanism.

Let w denote the strength of the blocking mechanism with $w = 0$ (turned off) when $v = 0$. As v approaches one, the blocking mechanism becomes stronger but remains bounded, and we assume an equation of the form

$$w' = \varepsilon(v - \xi w)$$

with a limiting value v/ξ for w if v is fixed. If $v=0$, then $w \to 0$, and if $v=1$, $w \to 1/\xi$ (the maximum strength of the blocking mechanism). The parameter ε influences the rate of

approach to equilibrium but does not affect the equilibrium value. We use a small value of ε to indicate a slow-acting mechanism.

In order to formulate a model that includes both v and w, we must also take account of the effect of the blocking mechanism on v. The model we shall examine is the two-dimensional system

$$v' = -v(v-a)(v-1)-w, \quad w' = \varepsilon(v-\xi w)$$

(5.43)

known as the *Fitzhugh–Nagumo* system. [Fitzhugh (1961); Nagumo, Arimato, & Yoshizawa (1962)] It is a simplification of the four-dimensional *Hodgkin-Huxley* model proposed in the early 1950s by Sir Alan Hodgkin and Sir Andrew Huxley [Hodgkin and Huxley (1952)], for which they received the 1963 Nobel Prize in Physiology and Medicine, and which is still being used in the study of neurons and other kinds of cells. Excitable systems occur in a large variety of biological systems, and the Fitzhugh–Nagumo and Hodgkin–Huxley models are prototypical models of excitable systems.

Question 1
Show that the only equilibrium of the Fitzhugh–Nagumo system (5.43) is $v = 0$, $w = 0$, and that this equilibrium is asymptotically stable.

Question 2
Use a computer algebra system to draw the orbit of the system (5.43) with $a = 0.3$, $\xi = 1$, $\varepsilon = 0.01$ and a starting point $(v_0,0)$ with $v_0 > a$, say $v_0 = 0.4$. You should observe that v grows quickly and then returns to zero. You should also note that after the neuron fires and the potential drops, it overshoots zero (this can also be observed experimentally).

Another experiment gives the cell a constant input of positive ions instead of a single pulse. If we apply a constant electrical current J, we add J to the rate of change of potential (taking units of current so that one unit of current raises the potential by one unit in unit time). Thus, we replace the system (5.43) by

$$v' = -v(v-a)(v-1)-w+J, \quad w' = \varepsilon(v-\xi w).$$

(5.44)

Question 3
Show that increasing J moves the equilibrium from (0,0) into the first quadrant of the (v, w)-plane. Show that this equilibrium is asymptotically stable for small values of J but becomes unstable for larger values of J.

Question 4
Use a computer algebra system to experiment with different values of J, taking $a =$

$0.3, \xi = 1, \varepsilon = 0.01$, and find a value for which the system (5.44) has a periodic orbit.

Question 5

Use a computer algebra system to graph v as a function of t for the periodic orbit found in Question 4. You should observe a "bursting" behavior, with potential rising close to one and dropping below zero (similar to observations in real neurons).

Question 6

Add a periodic term to the equation for u in the model and experiment using a computer algebra system with different amplitudes and periods to see the effects on the behavior of the model.