CS 304 : Introduction to Non-Linear Science The FitzHugh-Nagumo Model for Neuronal Excitability

Project Report

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1 Problem Statement

This report presents an analysis of the FitzHugh-Nagumo Model for modeling the electric signalling by individual nerve cells. The cell body of the neuron, also called *soma* receives the stimuli which is then conducted along the *axon*. The axon connects it to the other neurons via a collection of *synapses*. The nerve cell fires and is referred to as an action potential. A neighbouring nerve cell can sense the voltage change through chemical or electrical synapses and fires in response. This is the mechanism of the propagation of an action potential thorough the tissue.

2 Hodgkin-Huxley Model

Hodgkin and Huxley developed a model for the study of firing of nerve cells in a giant squid. The process of electrochemical transmission of neuronal signals along the cell membrane has been modelled using a simple circuit and has been described using a four-dimensional system of differential equations.

Let the positive direction of membrane current, I be outwards from the axon. $I(t)$ is made up of the current due to the individual ions that pass through the membrane and the contribution from the time variation in the transmembrane potential, also called the membrane capacitance contribution.

$$I(t) = C\frac{dv}{dt} + I_i \tag{1}$$

where C is the capacitance and I_i is the current contribution from ion movement across the membrane. Based on experimental observation,

$$I_i = I_{Na} + I_K + I_L = g_{Na}m^3h(V - V_{Na}) + g_K n^4(V - V_K) + g_L(V - V_L) \tag{2}$$

where V is the potential and I_{Na}, I_K, and I_L are sodium, potassium and 'leakage' currents respectively. Hence, I_L represents the contribution from all other ions. Here, g_{Na}, g_K, g_L represent the respective conductance values for the ions and V_{Na}, V_K, V_L are the corresponding equilibrium potentials. The values $0 < m, n, h < 1$ and are determined by the following differential equations:

$$\begin{aligned}\frac{dm}{dt} &= \alpha_m(V)(1-m) - \beta_m(V)m \\ \frac{dn}{dt} &= \alpha_n(V)(1-n) - \beta_n(V)n \\ \frac{dh}{dt} &= \alpha_h(V)(1-h) - \beta_h(V)h\end{aligned} \tag{3}$$

where α, β are given functions of V (determined by fitting results to data).

If an applied current $I_a(t)$ is imposed, the governing equation becomes

$$C\frac{dV}{dt} = -g_{Na}m^3h(V - V_{Na}) - g_K n^4(V - V_K) - g_L(V - V_L) + I_a \tag{4}$$

Equations (3) and (4) together constitute the Hodgkin-Huxley model.

3 Reduction to two-dimensional model

The equations of the four-dimensional Hodgkin-Huxley system are highly nonlinear in nature. Hence, the system is quite complex to analyze. FitzHugh and Nagumo produced a simpler mathematical model of the Hodgkin-Huxley model. An excitable nerve cell may have two stable rest states and an unstable rest state which is called the action potential pulse. The action potential consists of three phases - resting, depolarisation and repolarisation. If stimulated in a specific manner, the action potential will oscillate in time.

The two-dimensional FitzHugh-Nagumo model for an excitable neuron is based on the membrane potential v and the current variable w :

$$\frac{dv}{dt} = v - \frac{v^3}{3} - w + I \tag{5}$$

$$\frac{dw}{dt} = \frac{1}{\tau}(v + a - bw) \tag{6}$$

where a and b are constants satisfying :

$$0 < \frac{3}{2}(1-a) < b < 1$$

The typical values for the constants are taken as: $a = 0.7, b = 0.8, \tau = 13$.

FitzHugh called it the "Bonhoeffer-van der Pol model".The voltage v represents the excitability of the system, it allows regenerative self-excitation via a positive feedback and w captures a combination of other forces that tend to return the system to rest thus providing a slower negative feedback. Hence, w is called the recovery variable. I is the magnitude of stimulus current and a parameter that leads to the excitation of the system. v is the fast variable (responsible for the excitation of the system) and w is the slow variable (responsible for the relaxation).

The amplitude of τ, corresponding to the inverse of a time constant, determines how fast w changes relative to v. Because the nonlinear nature of these differential equations we can not derive closed-form solutions. However, we can deduce qualitative topological properties in the phase space spanned by v and w, just looking the phase portrait.

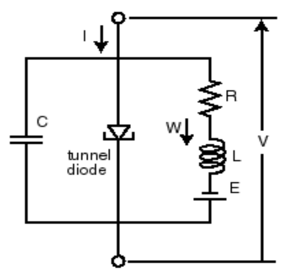


Figure 1: Circuit diagram for the nerve model (Nagumo et al.)

4 Modeling the behavior of the system

4.1 For a = b = I = 0

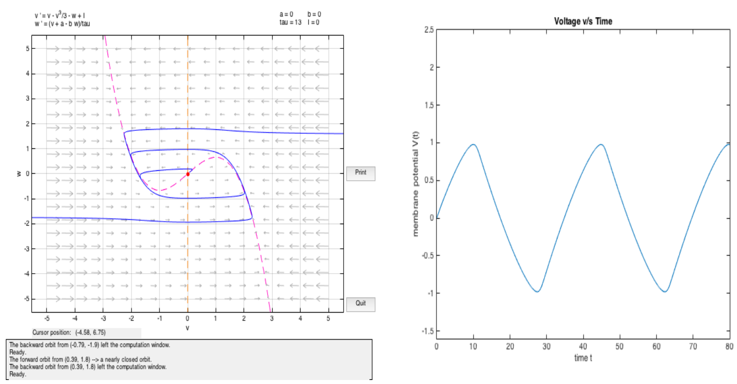


Figure 2: Graph for the case: a = b = I = 0

We observe relaxed oscillations in this case. The limit cycle consists of an extremely slow buildup followed by a sudden discharge, followed by another buildup and so on. We call this as relaxed oscillations because the stress accumulated during the slow buildup is relaxed during the sudden discharge.

4.2 Steady States

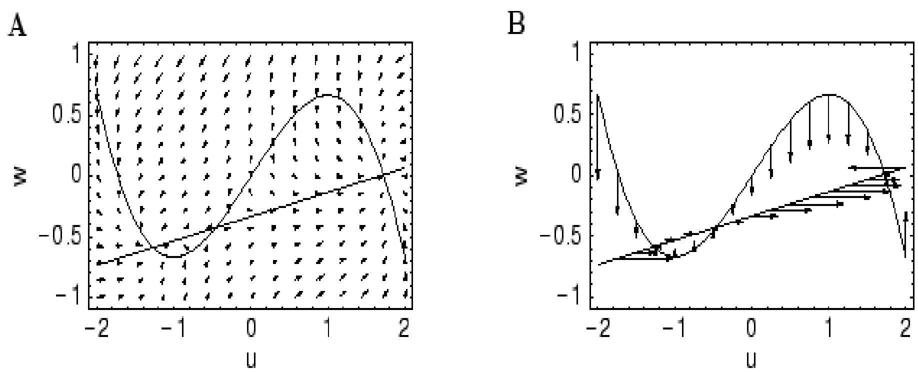
Consider I = 0. First we will determine the steady states of the system. The nullclines for our model are as follows:

$$v - \frac{v^3}{3} = 0 \qquad (\frac{dv}{dt} = 0) \tag{7}$$

$$w = \frac{v + a}{b} \qquad (\frac{dw}{dt} = 0) \tag{8}$$

We consider points located on the trajectories:

- For a point on the V-nullcine, its future trajectory would be pointing vertically upward ($w > 0$) or vertically downward ($w < 0$).
- For a point on the W-nullcline, it will point to the left ($v > 0$) or to the right($v < 0$).



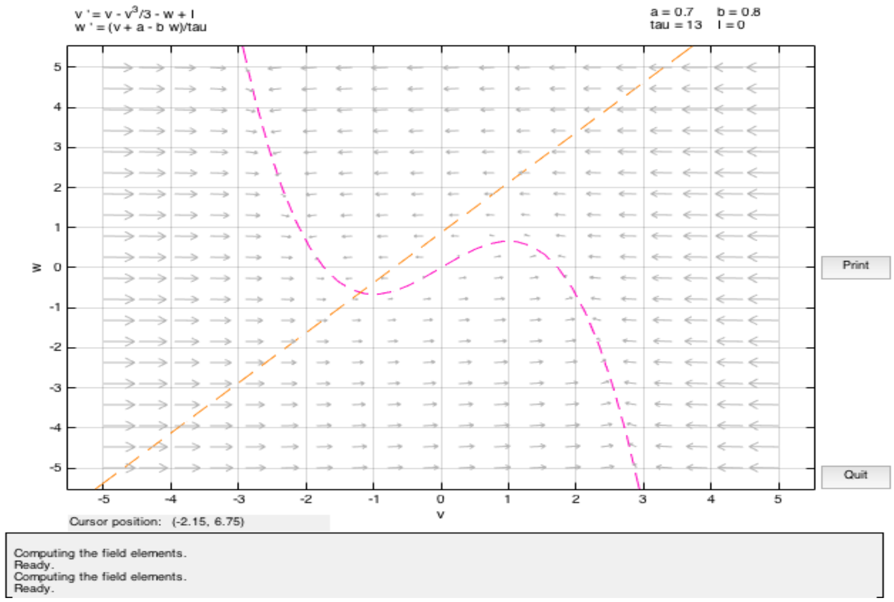


Figure 3: Nullclines

We determine the fixed points of the system which are the points of intersections of the nullclines. To check the stability of these points, we linearize arouund the equilibrium points and determine the corresponding eigen values.

$$\begin{pmatrix} \dot{x} \\ \dot{y} \end{pmatrix} = \begin{pmatrix} (1-x^2) & 1 \\ -1 & -b \end{pmatrix} \begin{pmatrix} x \\ y \end{pmatrix} \tag{9}$$

$$\begin{aligned} Tr(J) &= 1-b \\ \Delta &= -b+1 \\ Tr(J)^2 - 4\Delta &= (1-b)^2 - 4(1-b) \\ &= (1-b)(1-b-4) \\ &= (1-b)(-3-b) \\ &= (1-b)(b+3) \\ &= (b-1)(-3-b) \\ &= b^2 - 2b - 3 \\ -3 < b < 1 &\quad but \quad 0 < b < 1 \\ Tr(J)^2 - 4\Delta < 0 &\quad and \quad Tr(J) > 0 \end{aligned}$$

The roots of the equation ($\lambda_{1,2}$) are given by:

$$\lambda_{1,2} = \frac{-(1-b) \pm \sqrt{(1-b)^2 - 4(1-b)}}{2}$$

$$= \frac{-(1-b) \pm \sqrt{(1-b)(3+b)}}{2}$$

Solving for eigen values, if D is the discriminant and $\lambda_{1,2}$ are the roots, we observe that $D < 0$ and the roots are complex conjugate and $Re(\lambda_{1,2}) < 0$ .Hence, the fixed point is stable, it is a stable spiral and the system will oscillate before reaching the stable state.

On solving the system with $a = 0.7, b = 0.8, \tau = 13$, we observe that there is a spiral sink at (-1.1994,-0.62426) with $Re(\lambda_{1,2}) = -0.25006$. We observe a spiral sink at (1.2284,2.4105) with $Re(\lambda_{1,2}) = -0.28527$.

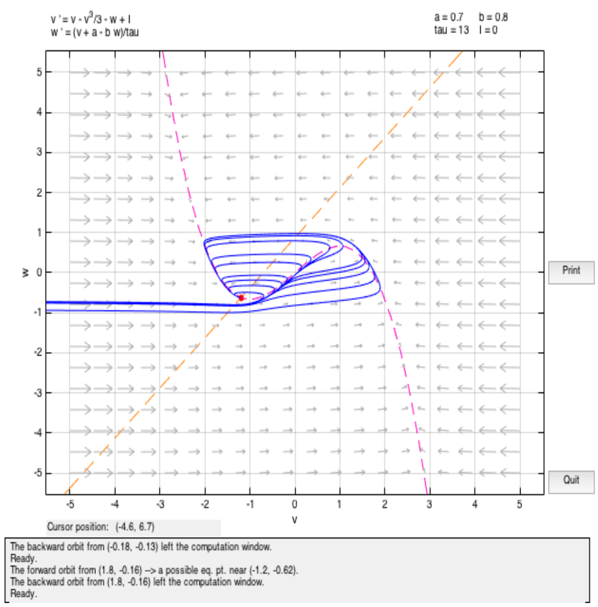


Figure 4: Spiral Sink

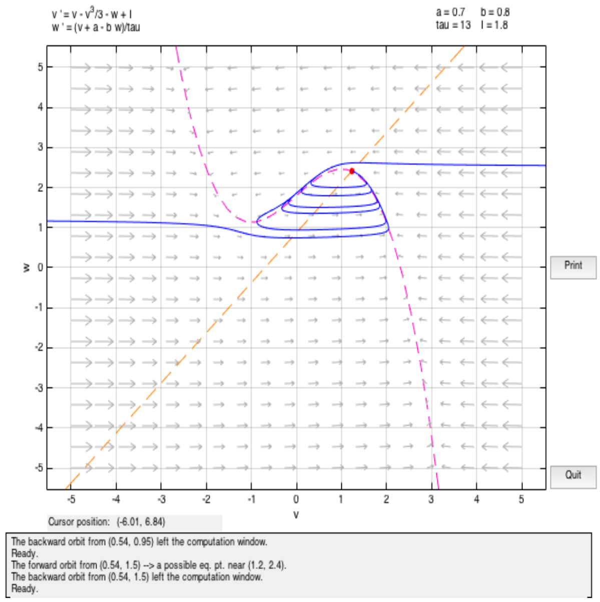


Figure 5: Spiral Sink

4.3 Bifurcations and Limit Cycles

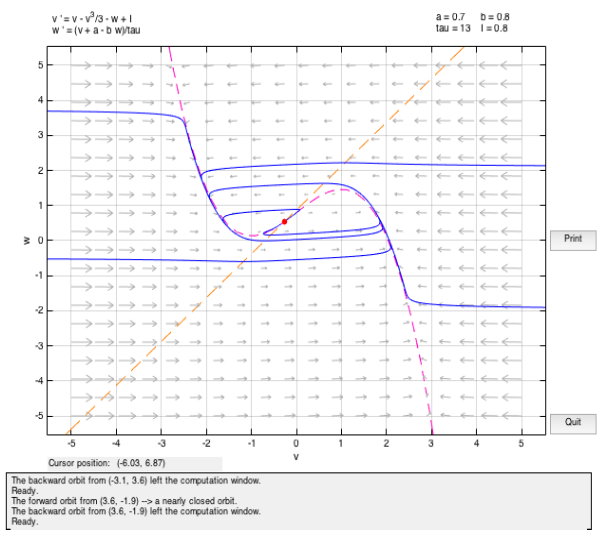


Figure 6: The limit cycle

If a current is applied to this system ($I \neq 0$), then the initial value of v will be different and accordingly move away from the fixed point considered above in the phase space. If the value of input current is small, the system will almost immediately return to rest following a trajectory about the equilibrium point. As the current value is increased, the system moves away from the v-nullcline and the trajectory excursion of the system before returning to the fixed point becomes larger.

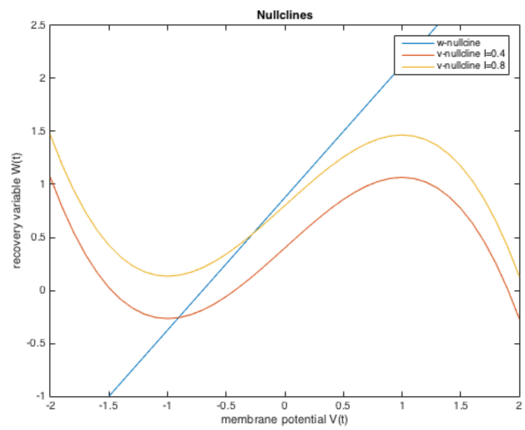


Figure 7: The v-nullcline moves as the value of I changes

Also, if the value of current is positive, the v nullcline shifts upward while the w nullcline remains at the same position. Hence, the fixed point being the point of intersection of the two nullclines, also moves upwards in the phase plane. Hence, its value may change. The fixed point will remain stable as long as the real part of both eigen values remains negative. As the real-values become zero and then positive, even small perturbations would cause the system to move away from the equilibrium point since it has become unstable now. It can be observed that the equilibrium point will remain stable whenever the w nullcline meets the v nullcline in its left or rightmost branches where the slope of the v nullcline is negative.

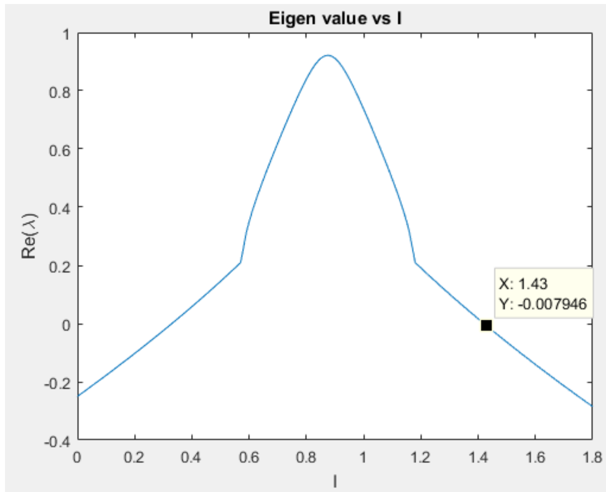


Figure 8: Eigen value plot

In the central region, the real-part of the eigen value becomes positive and the fixed point loses its stability. By plotting the eigen values at different points it is possible to determine the stability of the fixed point for a given set of values for the parameters. We determine where the real value of the fixed point changes from negative to positive causing a change in the stability. The point where the transition occurs is called the bifurcation point and I is called the bifurcation parameter. When the fixed point loses its stability, it is possible to construct a bounding surface around the unstable fixed point so from the **Poincare-Bendixon Theorem** we know that a limit cycle must exist. The imaginary solutions to the linearized system are of oscillatory nature. This scenario of loss of stability of the fixed point with an emerging oscillation is called a **Hopf bifurcation**. Hopf Bifurcation occurs when the both the eigen values cross the imaginary axis.

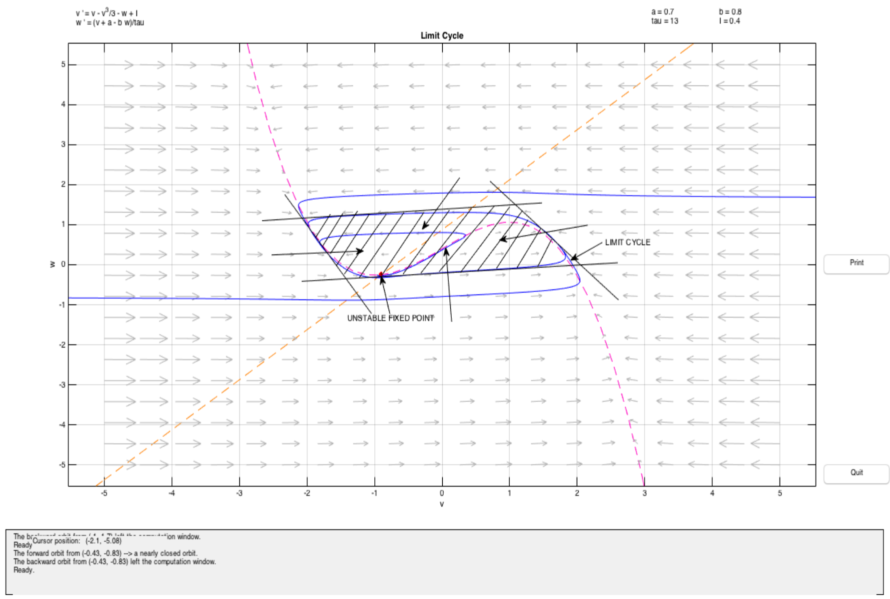


Figure 9: The limit cycle

In this case, the system is said to be in excitable state. The value of a in this case is the threshold. In the above diagram we observe a fixed point (source) at (-0.2729,0.53387) with $Re(\lambda_{1,2}) > 0$. The presence of w guarantees the eventual recovery of the rest state and hence it is called the recovery variable.

The model depicts the case of a Hopf bifurcation since a limit cycle surrounding the fixed point appears as the value of I varies. Furthermore, since the fixed point is unstable and surrounded by a stable limit cycle, it is a supercritical Hopf bifurcation.

4.4 Altering Parameter Values

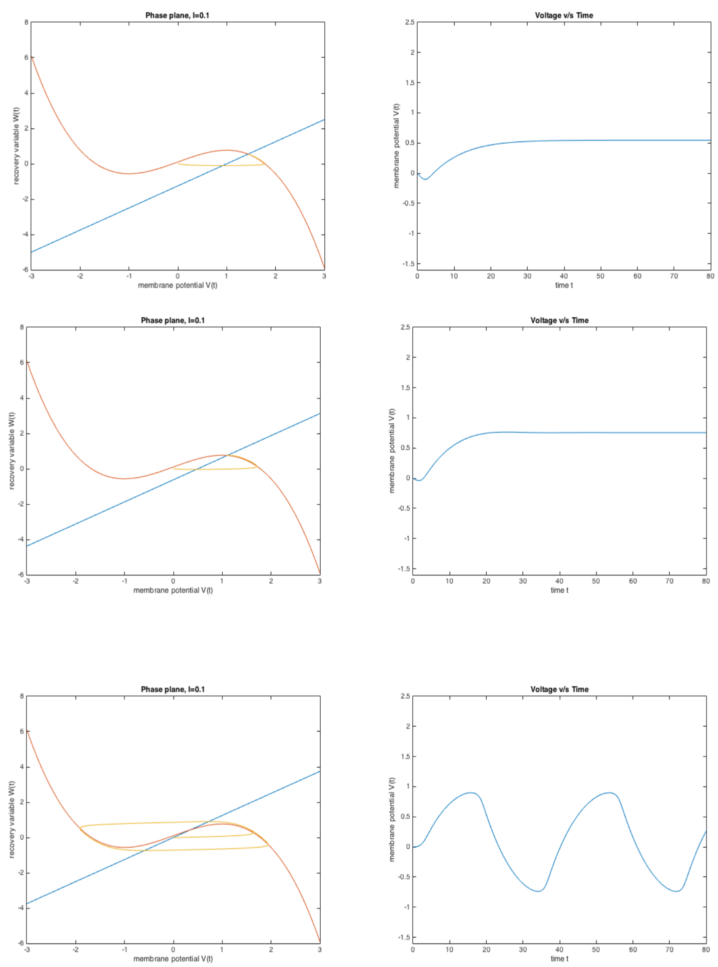
4.4.1 Altering the value of a

If we keep b and τ constant ($b = 0.8, \tau = 13$ and $I = 0.1$)and vary the value of a to observe the behavior of the system, the control parameter a plays the role of integrated stimulus of the neuron with larger negative values of a corresponding to stronger stimulus. Hence, the model can show stable fixed-point behavior or limit cycles depending on the value of the control parameter:

- Larger positive values of a represent a weak stimulus where the system has a resting potential and a single stable fixed point.
- As the stimulus increases with larger negative values of a, the system

converts from resting potential to a limit cycle representing **spiking**. This happens when the nullcline intersect in the region where the v-nullcline has a positive slope and on analysis it can be shown that this fixed point is unstable.

- As the value of the control parameter decreases further, the area of the limit cycle decreases continuously to a new fixed point. This conversion happens when w-nullcline crosses the local maximum of the v-nullcline.



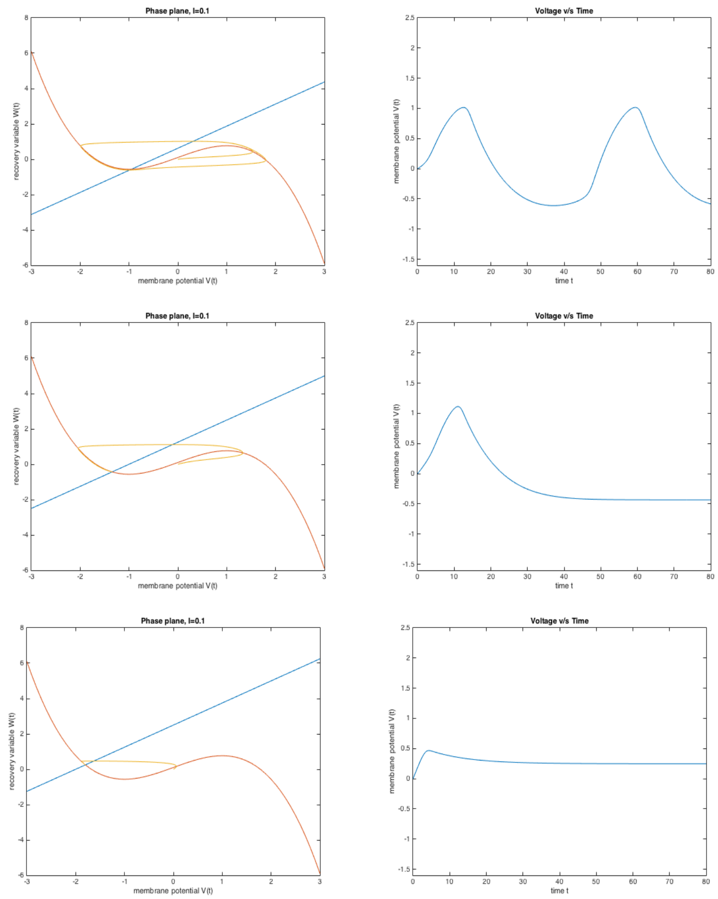
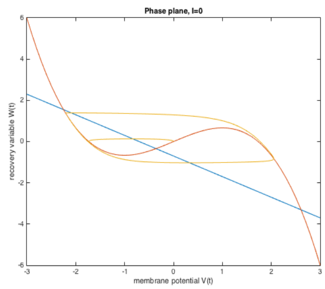


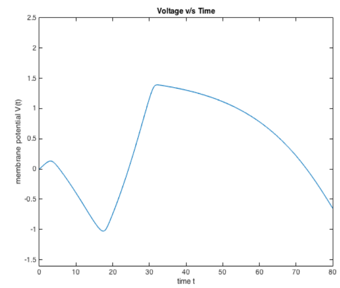
Figure 10: The effect of changing a on the system - a = -1, -0.5, 0, 0.5, 1, 2

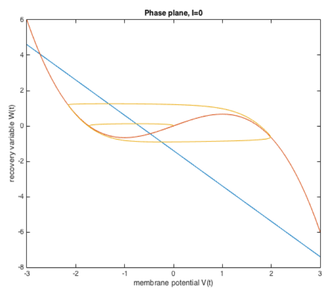
4.4.2 Altering the value of b

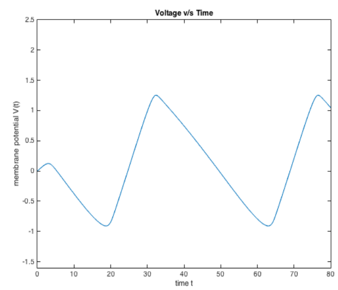
Keeping the value of a and τ constant, $a = 0.1, \tau = 13$ and $I = 0.1$ and altering the value of b we observe that it determines the slope of the w nullcline:

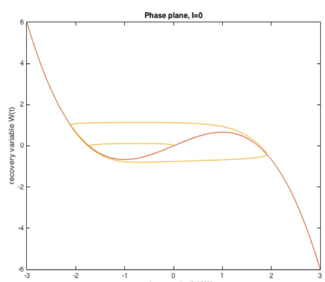
- For small values of b, it will intersect the v nullcline in two more places apart from the point of intersection as discussed in the previous sections. This means that there will be three steady states, two outer steady states representing the bistability in the system.
- Instead of approaching the previous point of intersection, the value of v now approaches one of the new steady values. From the biological point of view, this represents the depolarization block. The cell is dead and unable to depolarize.

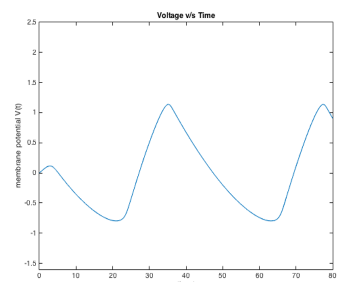

Phase plane, I=0
recovery variable W(t)
membrane potential V(t)

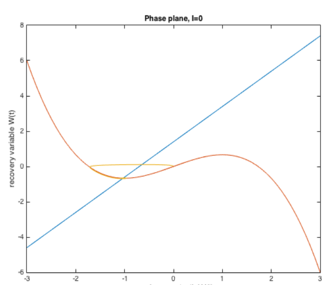

Voltage v/s Time
membrane potential V(t)
time t

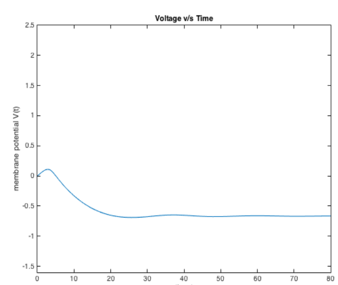

Phase plane, I=0
recovery variable W(t)
membrane potential V(t)


Voltage v/s Time
membrane potential V(t)
time t


Phase plane, I=0
recovery variable W(t)
membrane potential V(t)


Voltage v/s Time
membrane potential V(t)
time t


Phase plane, I=0
recovery variable W(t)
membrane potential V(t)


Voltage v/s Time
membrane potential V(t)
time t

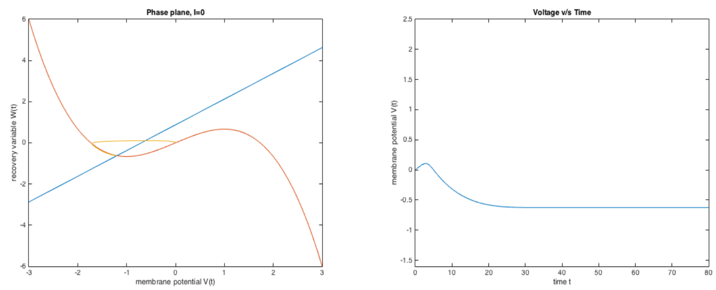


Figure 11: The effect of changing b on the system - b = -1, -0.5, 0, 0.5, 0.8

An interesting case is observed when we take $a = 0, I = 0$ and keep on varying the value of b ($\tau = 13$). Here, an unstable saddle node is formed between two stable saddle nodes:

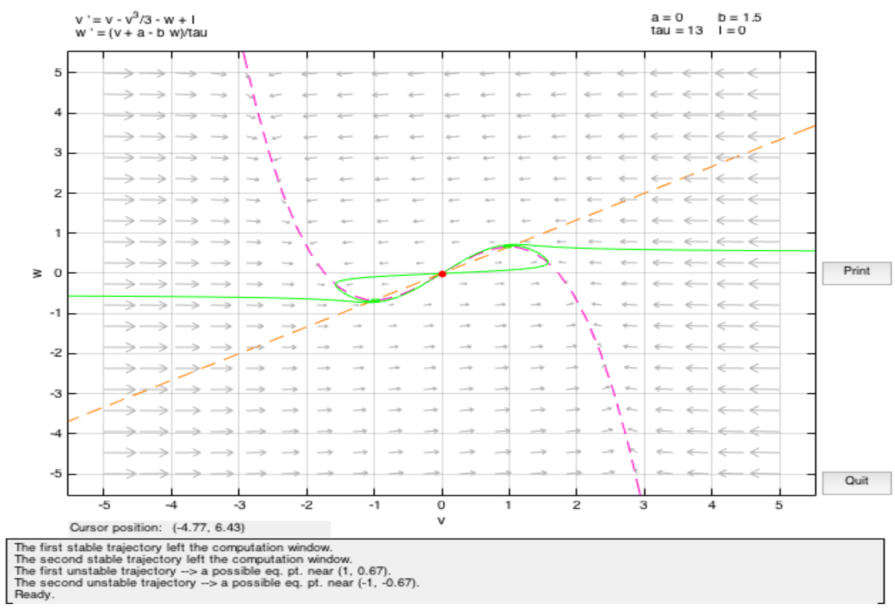


Figure 12: Observing saddle nodes by varying the value of b

4.4.3 Altering the value of τ

If we take a and b to be constants, $a = 0.1, b = 0.8$ and $I = 0.1$, we see that τ acts a scaling factor for w.Also, we observe a spiral type behavior of the system. Biologically, this corresponds to afterpolarisation where the potential of the cell membrane increases.

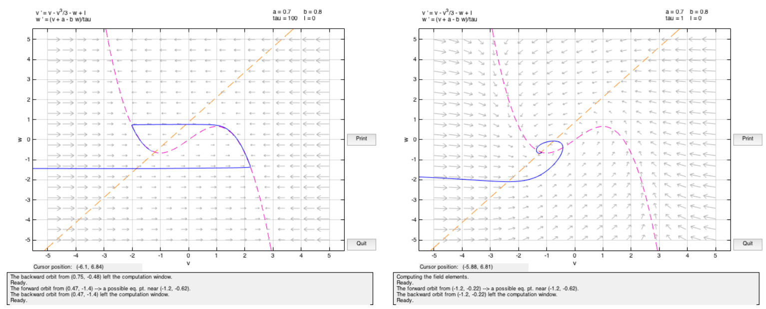
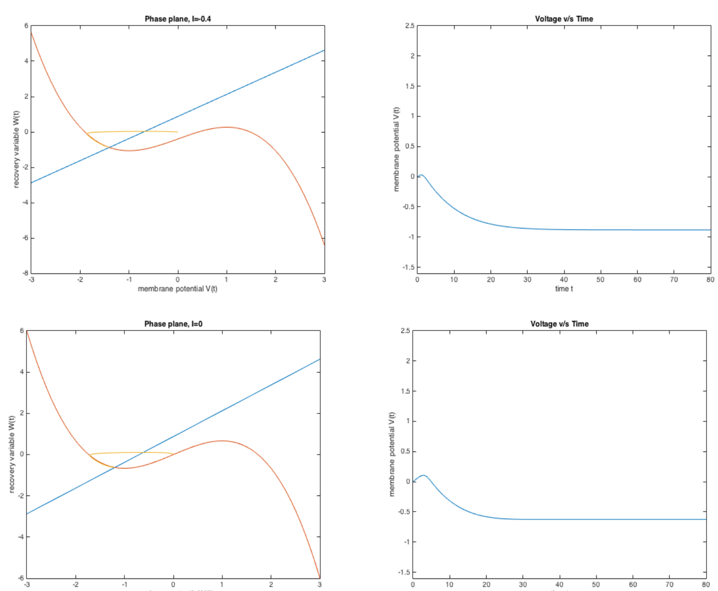


Figure 13: The effect of changing τ on the system - τ = 100, 1

4.5 Excitation Block

Hence, from the above discussion it can be concluded that the neurons may continuously experience electrical stimuli and hence there is no periodic behavior of the system. To capture this behavior we have added the value of I which represents the excitation block of the system which excites the system.

We alter the values of the different parameters of the system and then analyse the behavior of the system under these conditions.



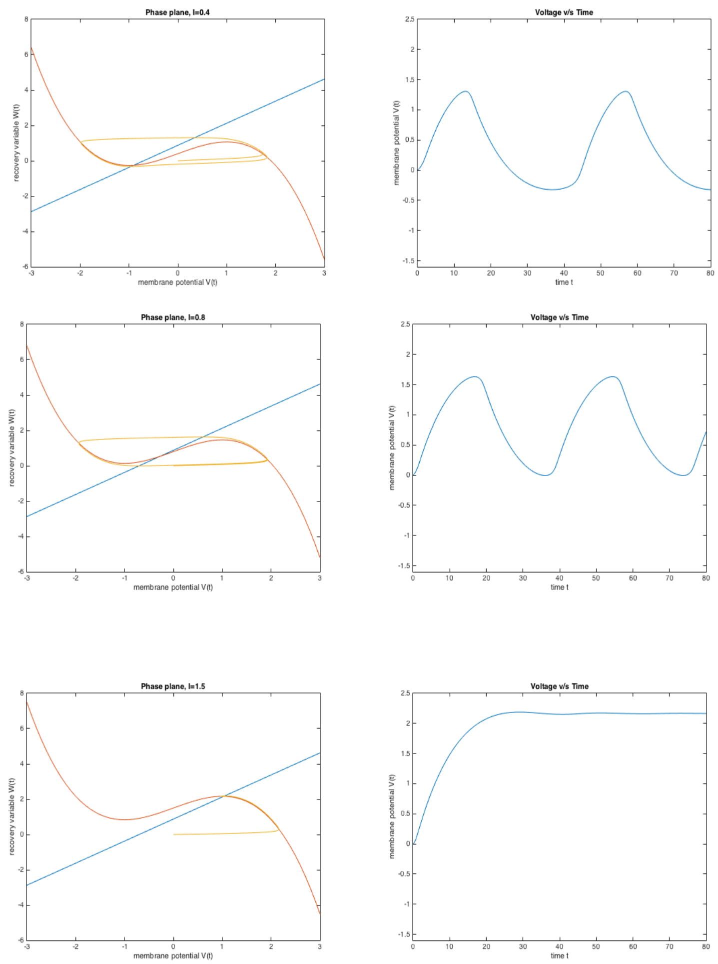


Figure 14: The effect of changing I on the system - I = -0.4, 0, 0.4, 0.8

Here, we observe periodic spiking at $I = 0.4$ when the Hopf bifurcation occurs, upto which periodic damping may be observed by varying the parameter values. At $I = 1.4$, three fixed points are observed, with a limit cycle around the middle fixed point and the outer two being unstable.

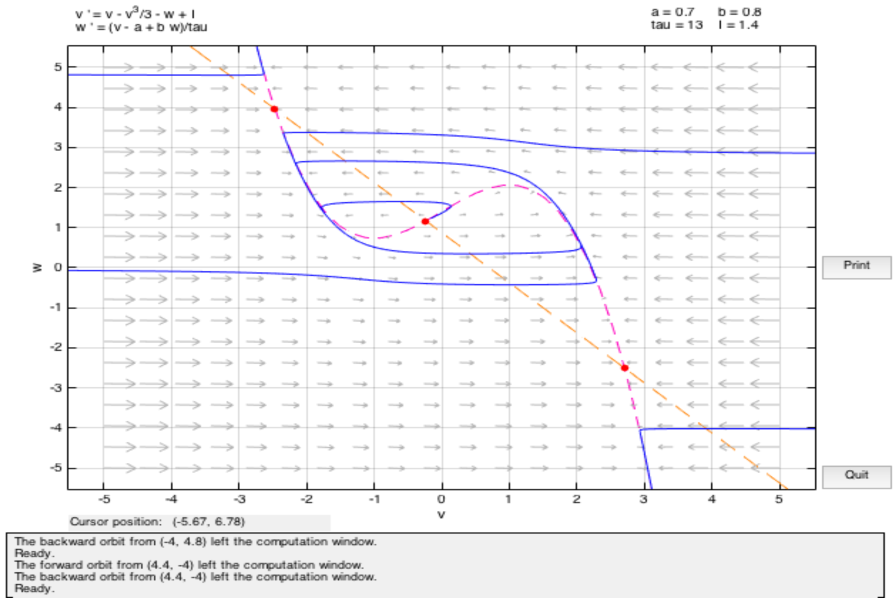


Figure 15: The effect of changing I on the system - I = -0.4, 0, 0.4, 0.8

5 Conclusion

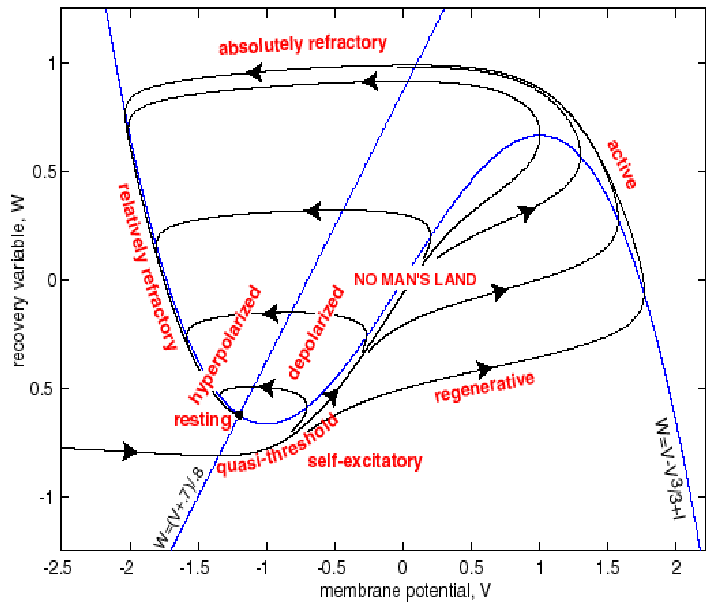


Figure 16: Phase Portrait

The phase portrait for this system shows how an excitable system works: the single equilibrium at the origin is locally stable, but a small perturbation causes the system to make a large excursion before returning to rest. This sort of phase portrait is typical of excitable systems. By varying a parameter such as I, the excitable system can be transformed into a bistable system in two variables. We have also seen that, by adjusting the parameters, the system can oscillate in a limit cycle.

- When I=0, there is only one stable fixed point.
- Hopf bifurcation is observed at $I = 0.33$. For $I < 0.33$, the fixed point remains stable and small damped oscillations are observed.
- This fixed point becomes unstable at $I = 0.33$ and sustained oscillations are observed on the limit cycle at Hopf-bifurcation with sustained periodic spiking.

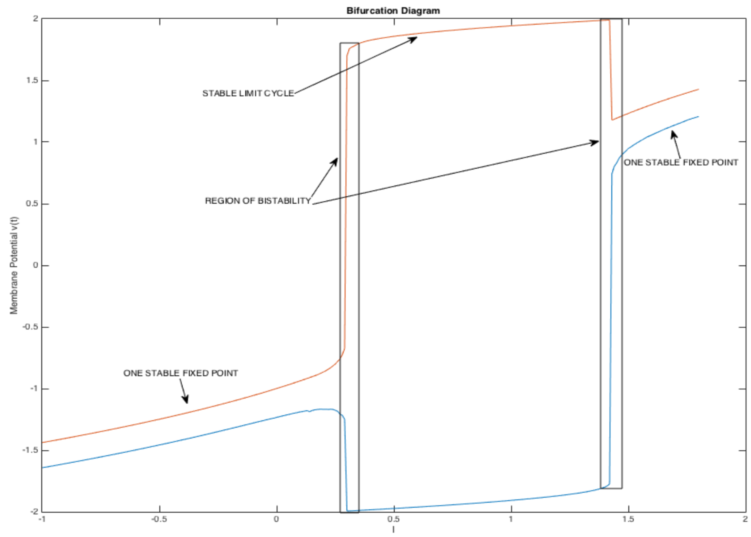


Figure 17: Bifurcation Diagram

From the above bifurcation diagram it can be seen that, The curve on the left before the first bifurcation represents the stable fixed point. The point at which we observe that the stable fixed point disappears into two branches - one above and the other below represents the bifurcation point. The value of I at that point is 0.33. A similar bifurcation point is present at the point where I = 1.4. The upper and lower curves correspond to oscillations. They represent the positive and negative peak values of one oscillation.

For small values of I, there is only one fixed point and moving to the larger values (I=0.3), there is a region of bistability. If the initial point lies within or outside the limit cycle it will move towards the limit cycle. As we move further to the right, we will observe a bistable region (I=1.4) after which there will only be one stable fixed point in the system.

The FitzHugh Nagumo model, in comparison to the Hodgkin-Huxley model hence allows more effective phase plane analysis. More complex dynamics are not considered by the model while still capturing the basic concept of neuronal activity.

6 Appendix

6.1 Matlab Program to observe the Phase Portrait

```
% this program is used to plot the nullclines and observe the phase
% portrait of the system

function nullclines()
    global a b tau I;
    % values of the parameters a, b, tau can be modified here
    a = 0.7; b = 0.8; tau = 13;

    % looping through different values of I to observe its effect as the
    % bifurcation parameter
    for I=[-1:0.01:1.5]
            hold off;
            % initial position - can be any value in the phase plane
            x0 = 0.2; y0 = 0;
            iv = [x0;y0];
            tspan = [0 80];
            % solving the system of diffrential equations using the ode45
            % solver
            [tspan, u] = ode45(@solve, tspan, iv);
            % plotting the nullines
            Y = [-3:0.1:3]; % Y represents voltage v
            X0 = (Y + 0.7) / 0.8;
            Y0 = Y - Y.^3/3 + I;
            plot(Y,X0,Y,Y0); hold on;
            % u contains the solution to the system of equations
            plot(u(:,1), u(:,2));
            axis([-2 2 -1 2.5]);
            xlabel('Mmebrane Potential v(t)');
            ylabel('Recovery Variable w(t)');
            title('Nullclines');
            legend('recovery variable w(t)','membrane potential v(t)');
            drawnow;
    end
end

% function called to solve the system of differential equations
function udot = solve(t,u)
    global a b tau I;
```

```
    x = u(1);
    y = u(2);
    xdot =  x - x.^3/3 - y + I;
    ydot = (x + a - b*y)/tau;
    udot = [xdot; ydot]; % create a matrix of the differential equations
end
```

6.2 Matlab Program to plot the Bifurcation Diagram

```
% this program is used to plot the bifurcation diagram. Here we find the
% fixed points of the system and calculate the max and min voltage values
% at each time instant starting from a given point. The plot of the voltage
% values represents the bifurcation diagram.

function bifurcation_diagram()
    global a b tau I;
    % values of the parameters a, b, tau can be modified here
    a = 0.7; b = 0.8; tau = 13;
    % initializing variables
    i = 1;
    V = zeros; Vmin = zeros; Vmax = zeros;

    % looping through different values of I to observe its effect as the
    % bifurcation parameter
    for I=[-1:0.01:1.8]
        % defining the system of equations
        f = @(t,y) [ y(1) - y(1).^3/3 - y(2) + I; (1/tau)*(y(1) + a - b*y(2)) ];
        g = @(y) f(0,y);
        % find the fixed points of the system
        fp = fsolve(g,[0 0]);
        % find the values of v and w at the fixed points
        v_fp = fp(1); w_fp = fp(2);
        tspan = [0 80];
        % solving the system of equations
        [tspan u] = ode45(f, tspan , [v_fp+0.2, w_fp]);
        V(i) = v_fp;
        % calculating the minimum and maximum voltage values at each time
        % step
```

```
        Vmin(i) = min(u(:,1));
        Vmax(i) = max(u(:,1));
        i = i + 1;
    end
      I = [-1:0.01:1.8];
      plot(I,Vmin,I,Vmax);
      title('Bifurcation Diagram');
      xlabel('I');
      ylabel('Membrane Potential v(t)');
end
```

6.3 matlab Program to observe the change in membrane potentialwith time

```
%This program is used to observe the change in the potential of the system
%over time. The phase plan is also plotted aling with it to understand the
%point in the phase plane being considered.

function voltage()
    global a b tau I;
    % values of the parameters a, b, tau can be modified here
    a = 0.7; b = 0.8; tau = 13;

    % looping through different values of I to observe its effect as the
    % bifurcation parameter
    for I=[-1:0.01:1.5]
        hold off;
        % initial position - can be any value in the phase plane
        x0 = 2; y0 = 0;
        iv = [x0;y0];
        tspan = [0 80];
        % solving the system of diffrential equations using the ode45
        % solver
        [tspan, u] = ode45(@solve, tspan, iv);
        % plotting the nullines
        Y = [-3:0.1:3]; % Y represents voltage v
        X0 = (Y + a) / b;
        Y0 = Y - Y.^3/3 + I;
        subplot(2,1,1);
        % u contains the solution to the system of
```

```
            equations
        plot(tspan,u(:,2)); %hold on;
        title(['Voltage v/s Time']);
        xlabel('time t');
        ylabel('membrane potential v(t)');
        axis([0 80 -1.6 2.5]);
        subplot(2,1,2);
        plot(Y,X0,Y,Y0); hold on;
        plot(u(:,1), u(:,2));
        title('Phase plane');
        xlabel('membrane potential v(t)');
        ylabel('recovery variable w(t)');
        drawnow;
    end
end

% function called to solve the system of differential
    equations
function udot = solve(t,u)
    global a b tau I;
    x = u(1);
    y = u(2);
    xdot =  x - x.^3/3 - y + I;
    ydot = (x + a - b*y)/tau;
    udot = [xdot; ydot]; % create a matrix of the
        differential equations
end
```

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