Computational Neuroscience

Project 2

Group 2

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1. Units chosen:
   Current/area -> microamps/cm2
   Voltage ->millivolts
   Time -> milliseconds
   Conductance/area -> millisiemens/cm2
   Capacitance/area -> microfarads/cm2

   To verify ohms law with respect to dimension,
   Current = conductance x voltage

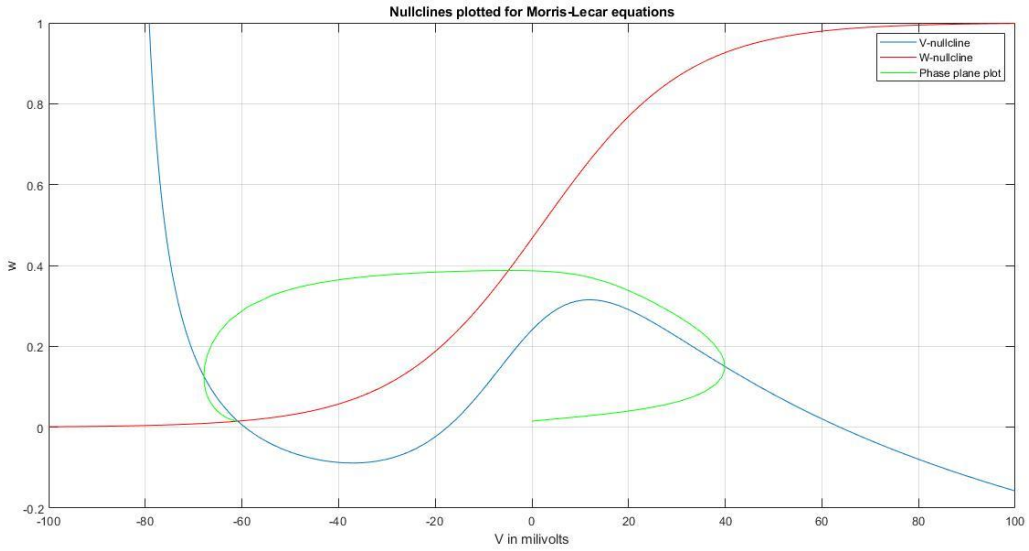
Millisiemens/cm2*millivolts = 10^-3 siemens/cm2 x 10^-3 volts = 10^-6 amps/cm2= 1 microamps/cm2

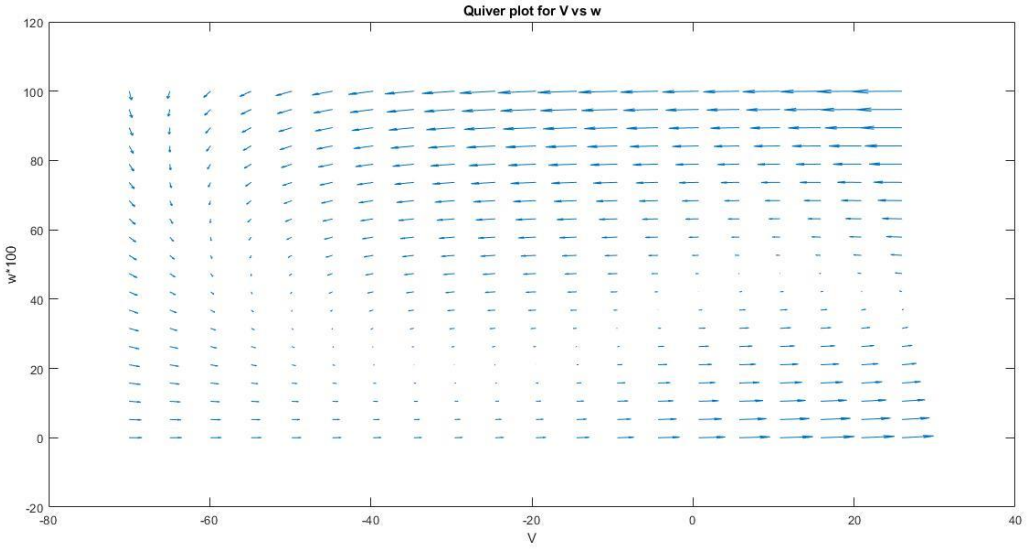
Units are consistent.
If conductance was microsiemens/cm2, voltage could be in volts and current in microamps/cm2 OR voltage in millivolts and current in nanoamps/cm2

The solution is not unique as any common factor in units involved in the Ohm's law will get cancelled.

2. Morris Lecar equations –
   dv/dt = -gCa x m_inf(V) x (V-VCa) / C - gK x w x (V-VK) /C – gL x (V-VL)/C + I/C ----- (1)
   dw/dt = phi x (w_inf(V) – w)/ tau_w(V) ------ (2)

   At equilibrium,
   dv/dt=dw/dt=0
   Solving the equation in Matlab, we get equilibrium at v=-60.8554 mV and w=0.01491





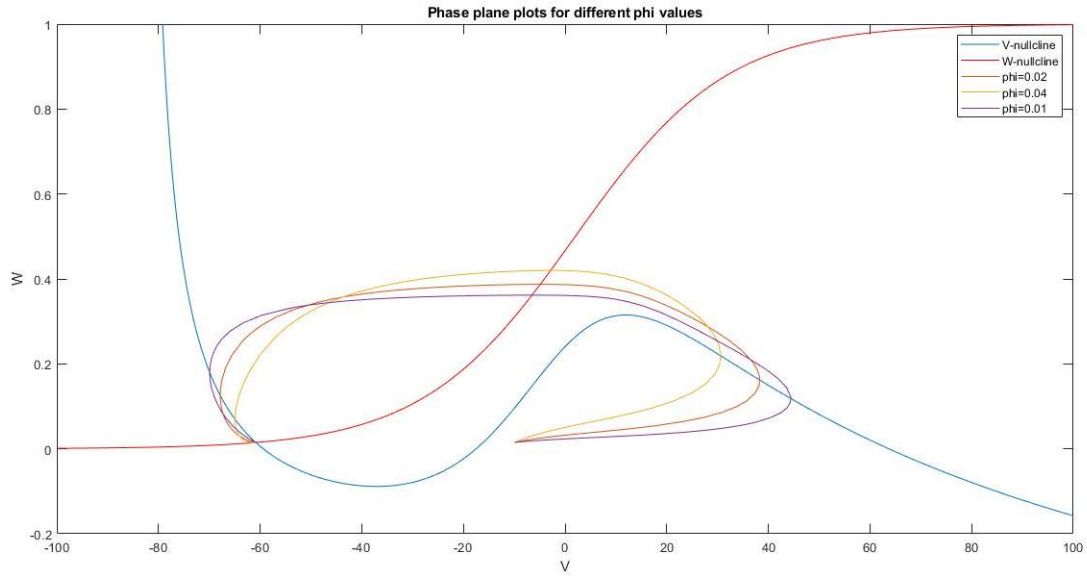
3. Eigenvalues from Jacobian matrix are (- 0.09146 + 0.0258i) and (- 0.09146 - 0.0258i). Stable equilibrium as real parts of eigenvalues are negative.

4. At each step of the ode45 or ode15s algorithm, an error is approximated. If yk is the approximation of y(xk) at step k, and ek is the approximate error at

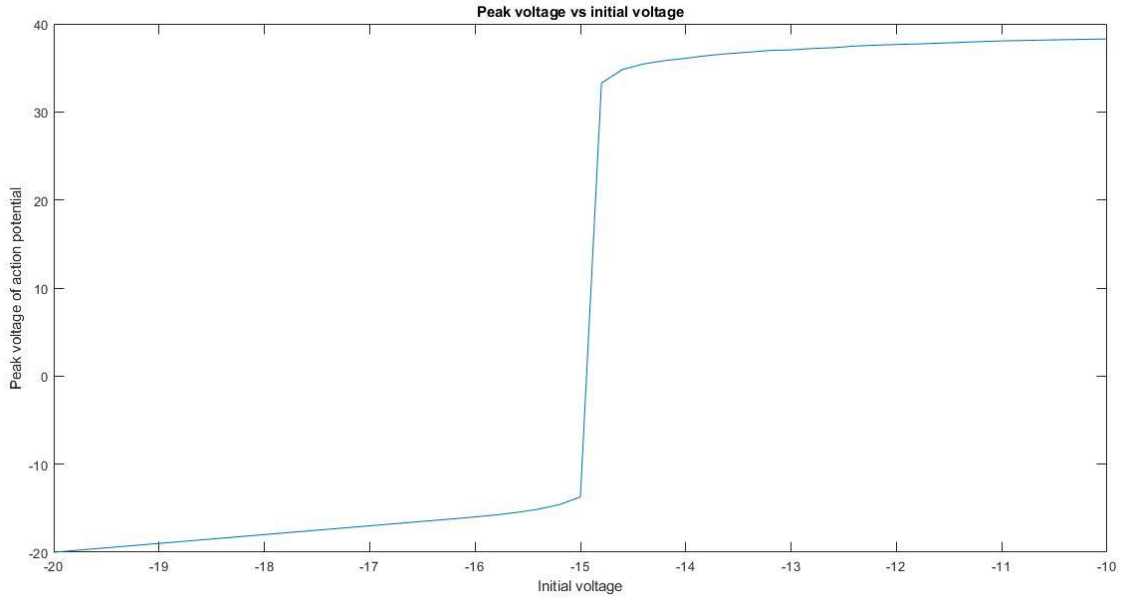
this step, then MATLAB chooses its partition to ensure ek ≤ max(RelTol · |yk|, AbsTol), where the default values are RelTol = 10−3 = 0.001 and AbsTol = 10−6 = 0.000001. Notice that with this convention, if the magnitude of the solution |yk| gets large then the error can be quite large and RelTol should be reduced. On the other hand, if the magnitude of the solution is smaller than 10−6 then AbsTol must be reduced. As the voltages are of the order of 100 mV, for sufficient precision in solutions of the MLE, these values are appropriate. If the value of voltage is changed to the order of Kilovolts, we need to make the AbsTol value much lower (changed to about 10^-12) because the voltages are of the order of few mV and say 60mV = 6*10^-5 kV. Now, precision of the order 10^-6 will produce larger errors especially as precise voltage values are needed for threshold calculations.

5. The phase plane plots in this case were started from the point (W=0.0149, V=-20mV). This is point is taken such that action potential is being generated for all three phi values as observed from the V-t plot. From the plot, we can see than on increasing the value of phi, the onset of action potential is faster, i.e., it occurs at a smaller positive value of V. This means that W becomes around 0.4 faster corresponding to faster potassium channel activation and spikes.

   The change in phi in the differential equations leads to change in the solution and therefore a new (higher) minimum Iext value at which action potential occurs. Physically phi is a temperature factor and this shows that the required current impulse magnitude for spiking changes with temperature.

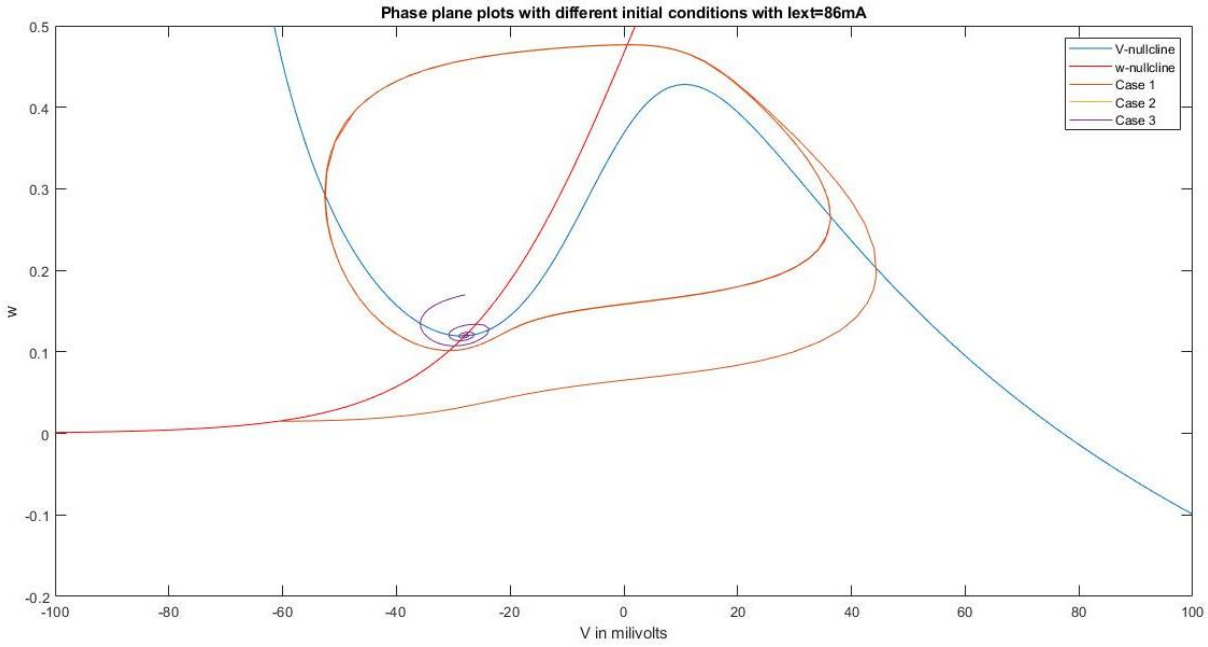


6. At around -15 mV of initial voltage V, we find there is a threshold and above this, spiking occurs as seen by a huge jump in peak voltage.



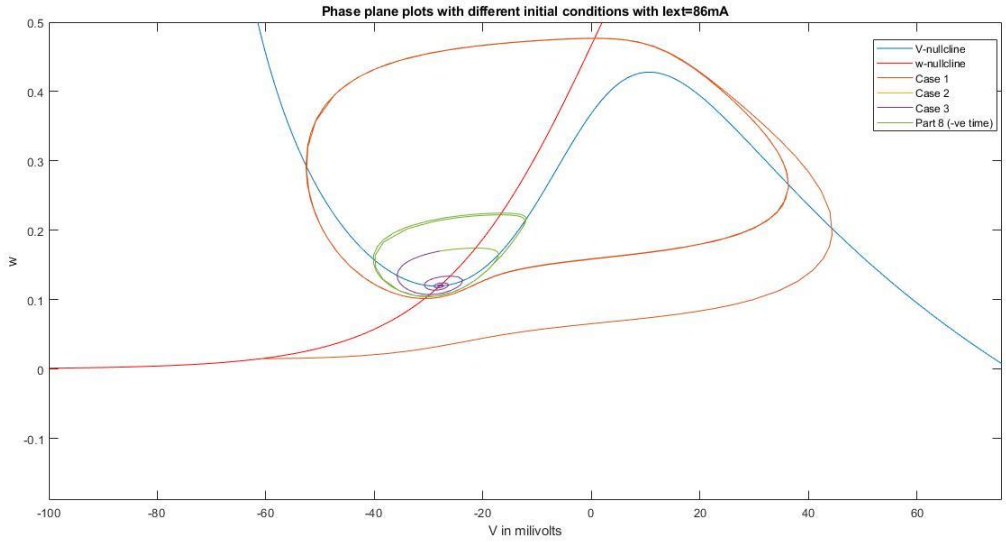
7. In the first case, on starting the new system from the equilibrium point of the initial system, it spirals and converges to a limit cycle. On starting the system at the new equilibrium point, a plot is not visible because it stays at

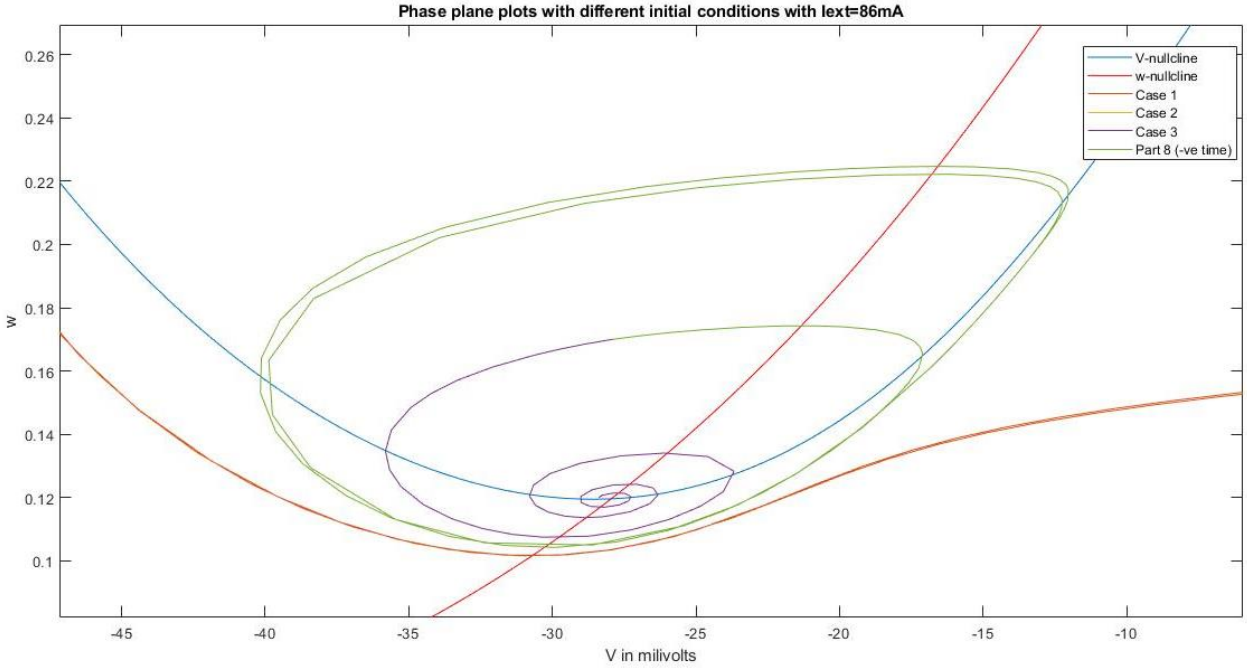
the equilibrium point and doesn't change. In the third and final case, the new system is started from a point that has same V value as the equilibrium and a larger w value. Here, the system has a converging spiral path that leads to the equilibrium point of the new system eventually. The difference between parts 1 and 2 is that on changing Iext, the equilibrium point of the system shifts. Therefore, only on starting the system at the newly found equilibrium point, it stays there. It is also observed that the new equilibrium point is also stable based on its eigenvalues (-0.011+0.067i) and (-0.011-0.067i).



8. On running the system backwards in negative time, we find a periodic unstable orbit shown by the green plot. In positive time period, any point outside of UPO ends up in a limit cycle and any point inside it converges to the stable equilibrium point in positive time. This can be seen by comparing cases 3 and the green plot for negative time in the zoomed in version of the plot around the equilibrium point. The UPO is a true threshold because on one side of the threshold which has no thickness, the phase plane plot converges to the equilibrium point implying there will not be an observed spike. On the other side of the UPO, there is a limit cycle showing spikes

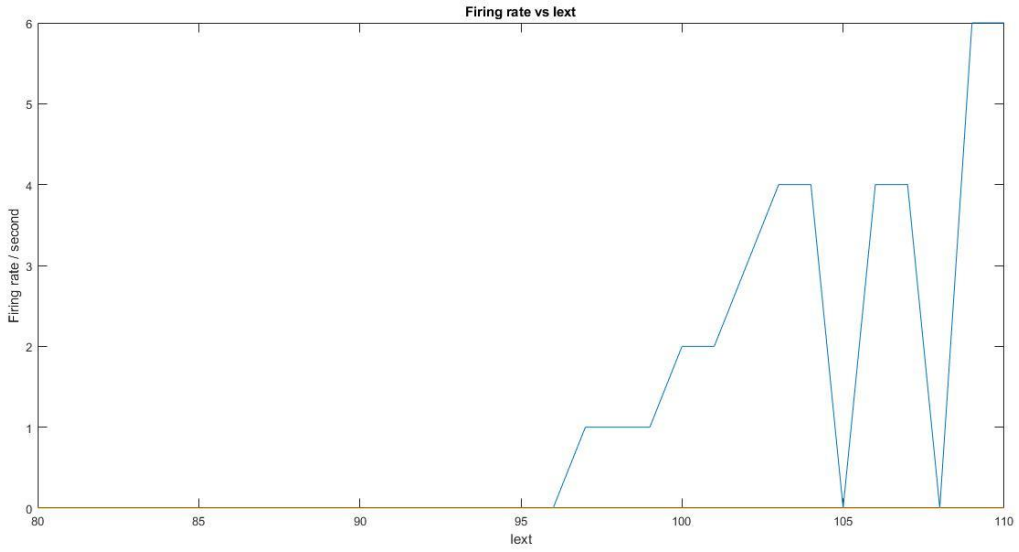
can occur. Since the UPO boundary does not have a middle ground, this is a true threshold signifying all or none events of spiking.





9. Eigenvalues corresponding to Iext =80mA, 86mA and 90mA are: (0.0225 + 0.0659i) and (0.0225 - 0.0659i) ; (-0.0109+0.06i) and (-0.0109-0.06i); (-0.0198-0.066i) and (-0.0198+0.066i). All these equilibrium points correspond to stable converging spirals.

For Iext ranging from 80mA to 96mA, there is no firing of action potentials as seen from the plot. In each case, the system has been started from the equilibrium point corresponding to that Iext value. Beyond that, it has rates of 1, 2, 4 or 6 spikes/second but sometimes drops to zero for intermediate values of Iext.



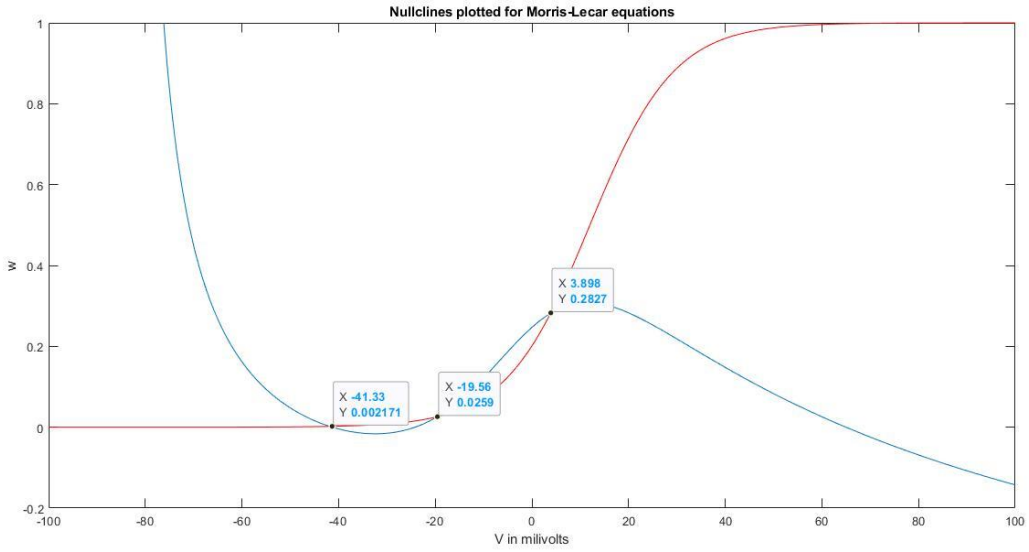
10. Corresponding to three equilibrium points,

eigenvalue 1 = -0.7336 ; -0.0689

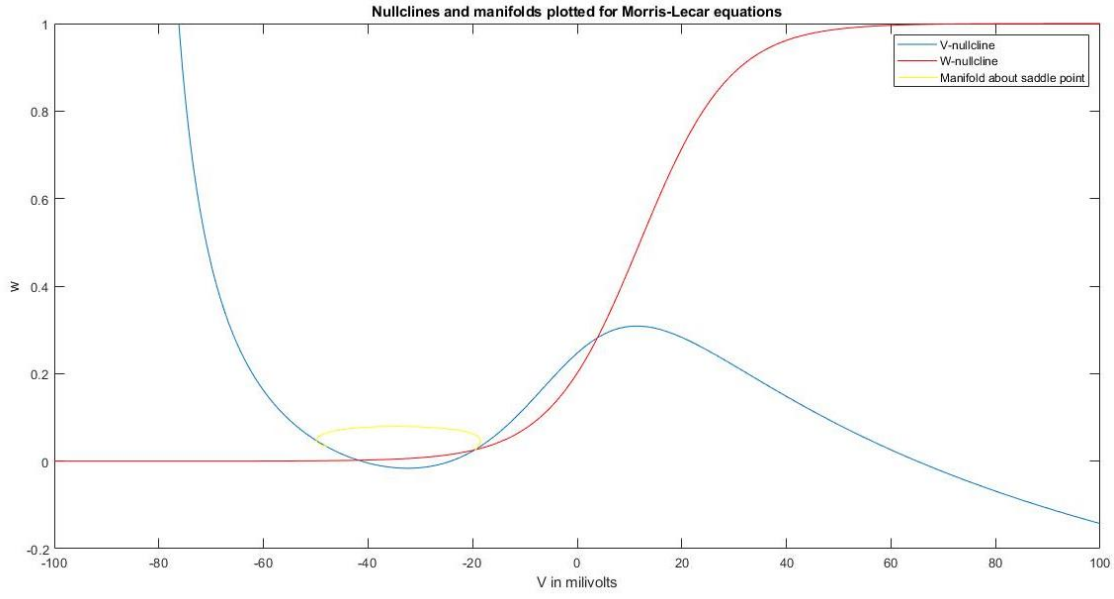
eigenvalue 2= -0.1648 ; 0.1373

eigenvalue 3= 0.0910 - 0.1827i ; 0.0910 + 0.1827i

Hence, the equilibrium points are stable node, saddle point and unstable spiral respectively.

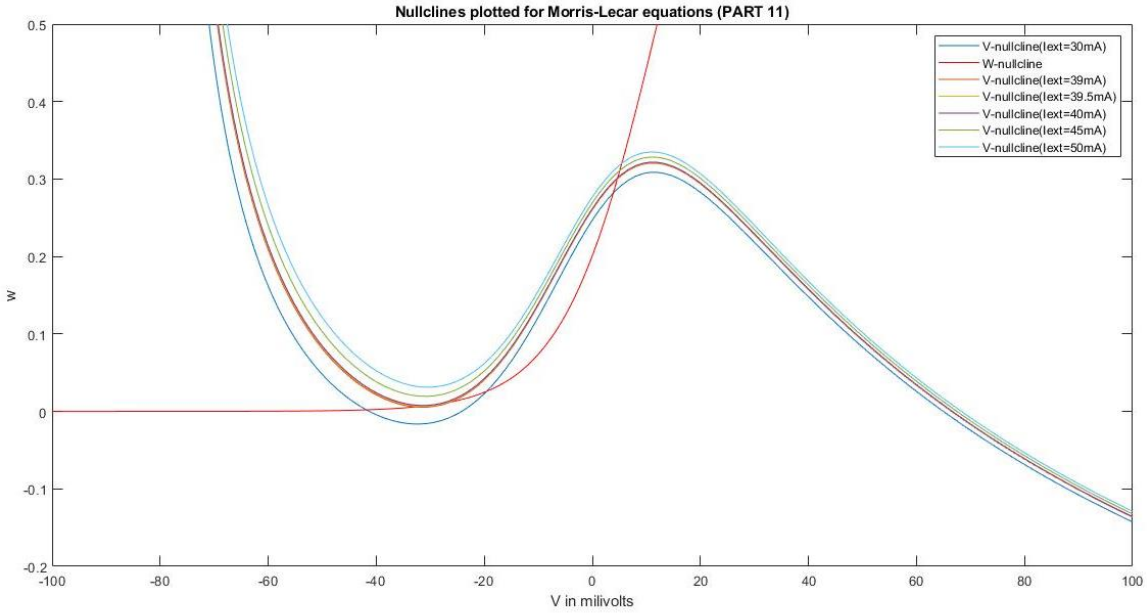


The manifold is plotted about the saddle point with slight variation in values of W and V from the equilibrium points.



11. The number of equilibrium points for this system changes on changing the value of Iext. For Iext=30 mA to 50mA, the V-nullcline moves up and results in changing the number of equilibrium points from 3 to 2 to 1 eventually. The firing action potential rate gets changed significantly as well due to

change in number and nature of equilibrium points.



Hodgkin Huxley model:-

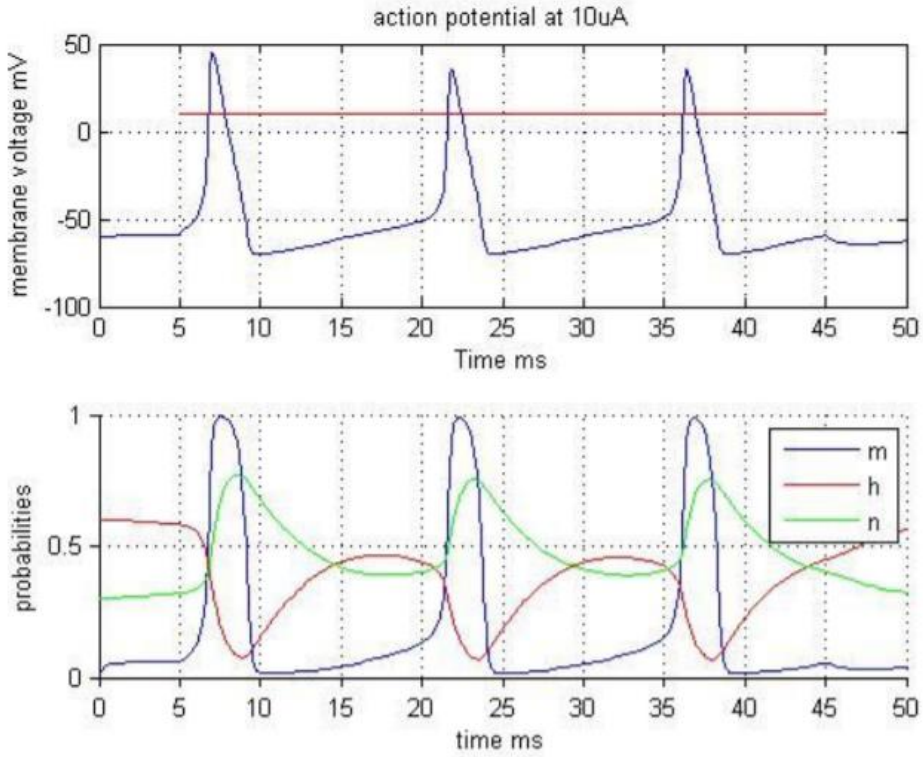
12. The 0/0 situation is handled by computing the limit at the voltage by using L'Hospital rule of differentiation.

13. To compute E_L where the resting potential is -60mV we take

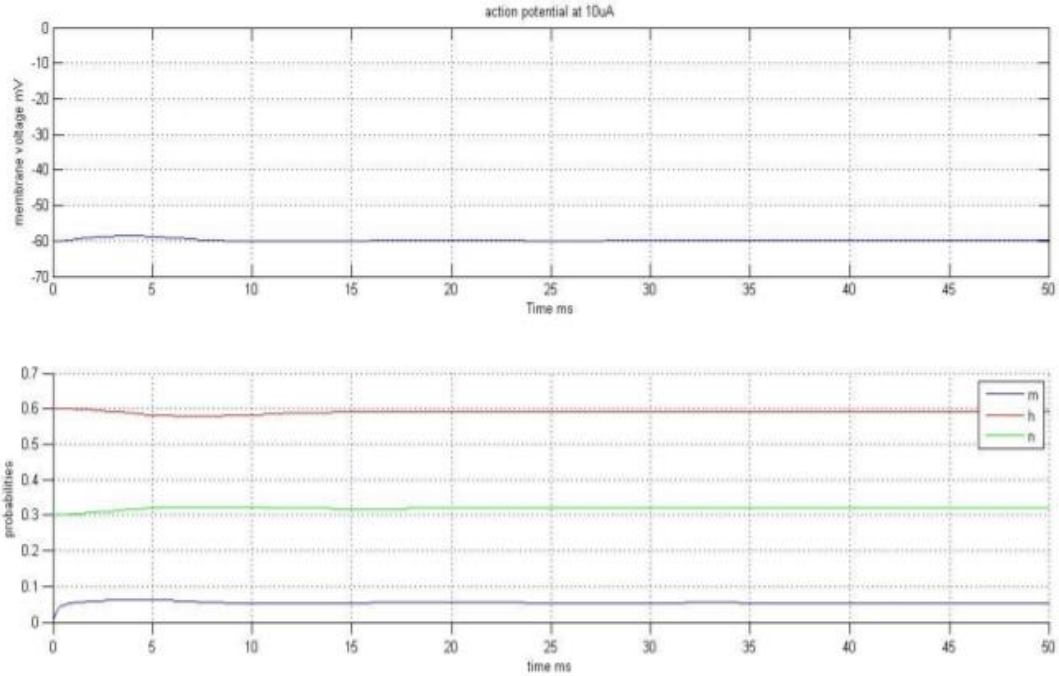
$$\frac{dm}{dt} = \frac{dn}{dt} = \frac{dh}{dt} = 0 \; at \; v = 60mV$$

We put these values into the $\frac{dV}{dt}$ equation and get the value of E_L as -49mV

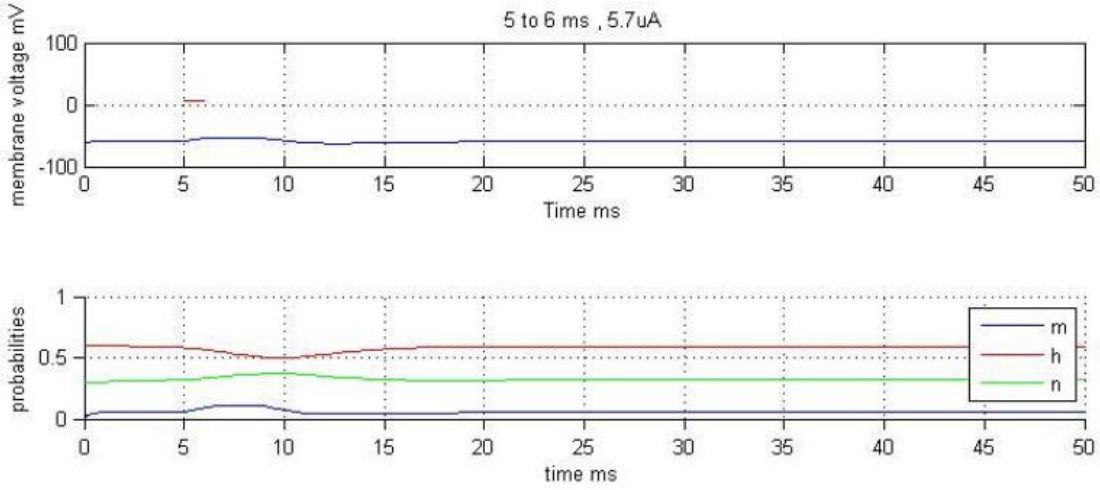
By fixing these values and current of 10μA we get the following plots:



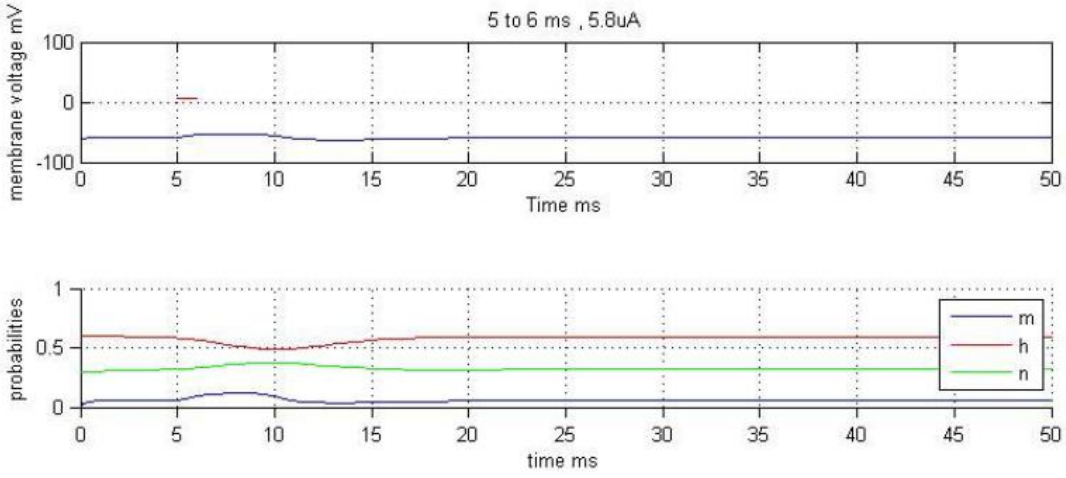
14. The following plot shows the stability of the model at $I_{ext} = 0$



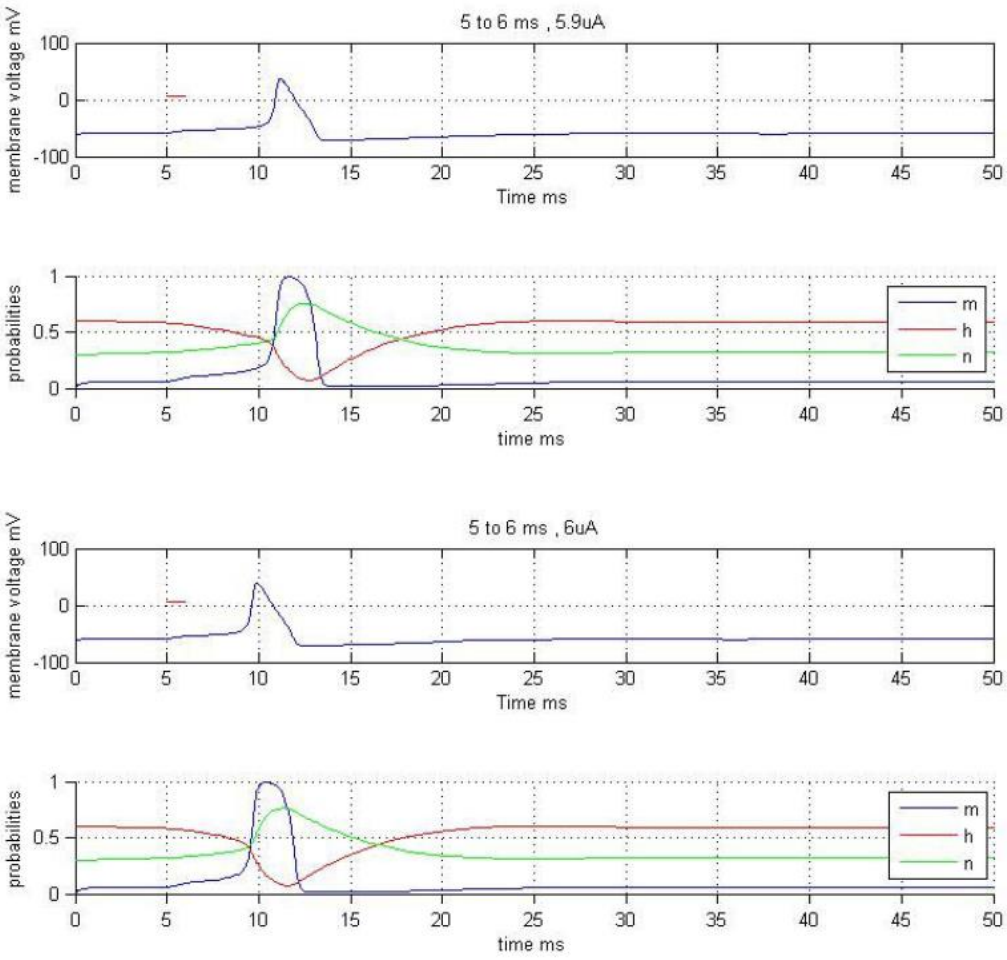
Now, current pulse of various amplitudes is applied for 1ms



At 5.7 µA and 5.8 µA no action potential can be seen



At 5.9 µA and above, action potential behavior is seen



15. The equilibrium points from 8 µA to 12 µA are as follows:-

    -55.3054 0.0905 0.4288 0.3914

    -54.9055 0.0946 0.4149 0.3978

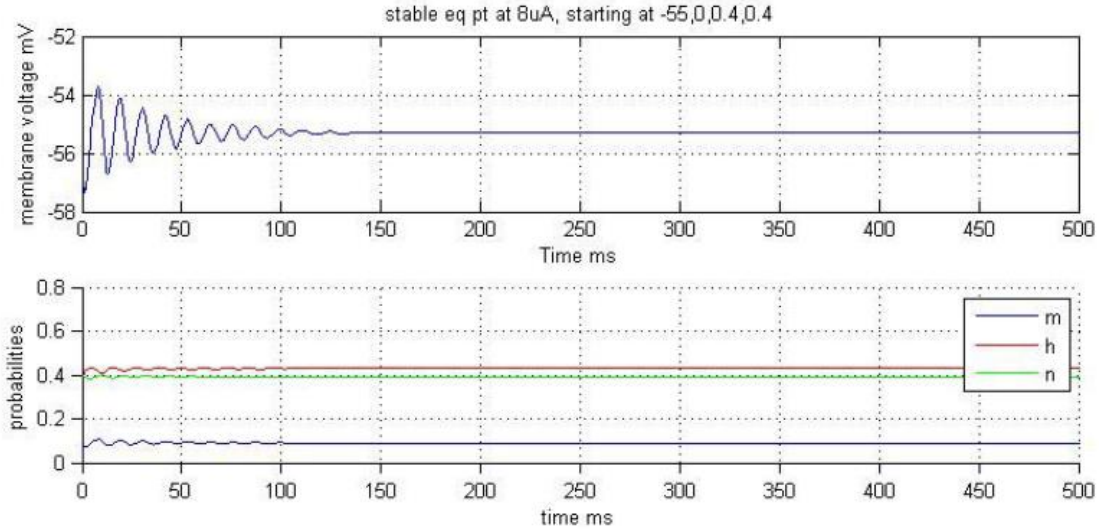
    -54.5278 0.0986 0.4019 0.4038

    -54.1696 0.1025 0.3897 0.4095

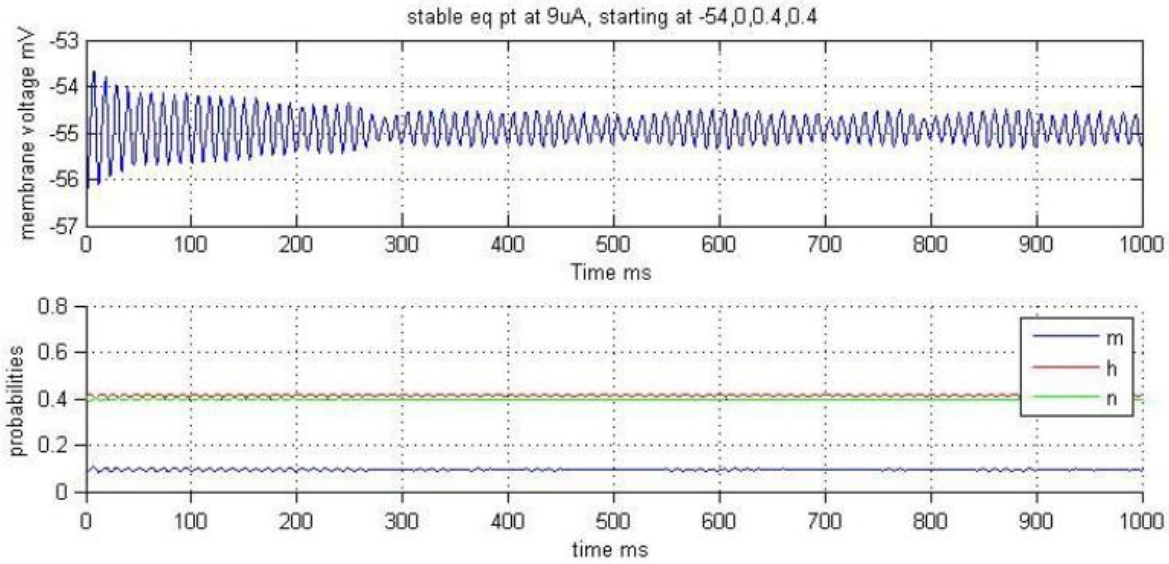
    -53.8290 0.1064 0.3783 0.4149

    To find the nature of equilibrium points, we run the model for the respective current values.

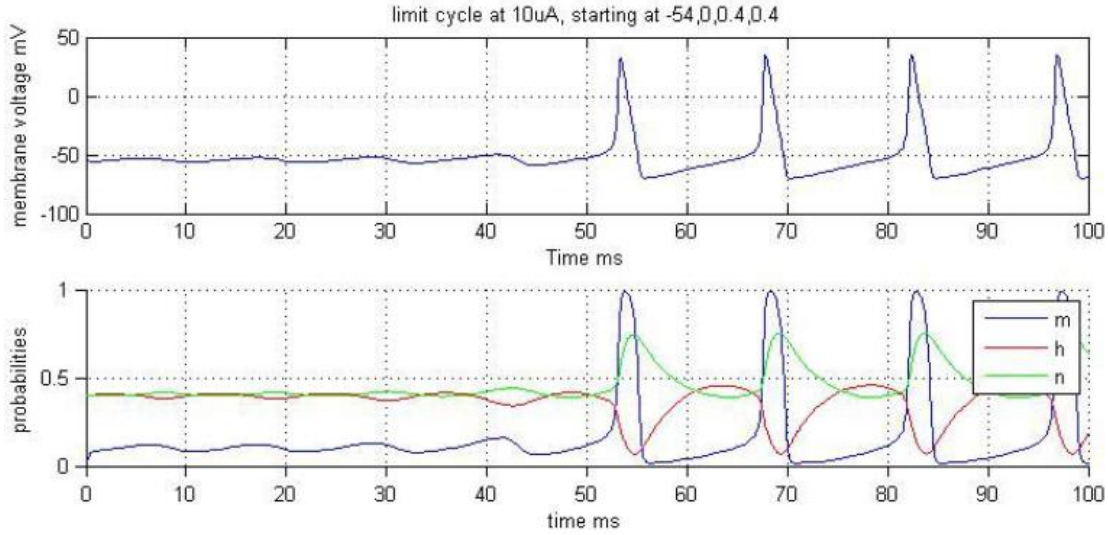
At 8 µA we have a stable equilibrium point



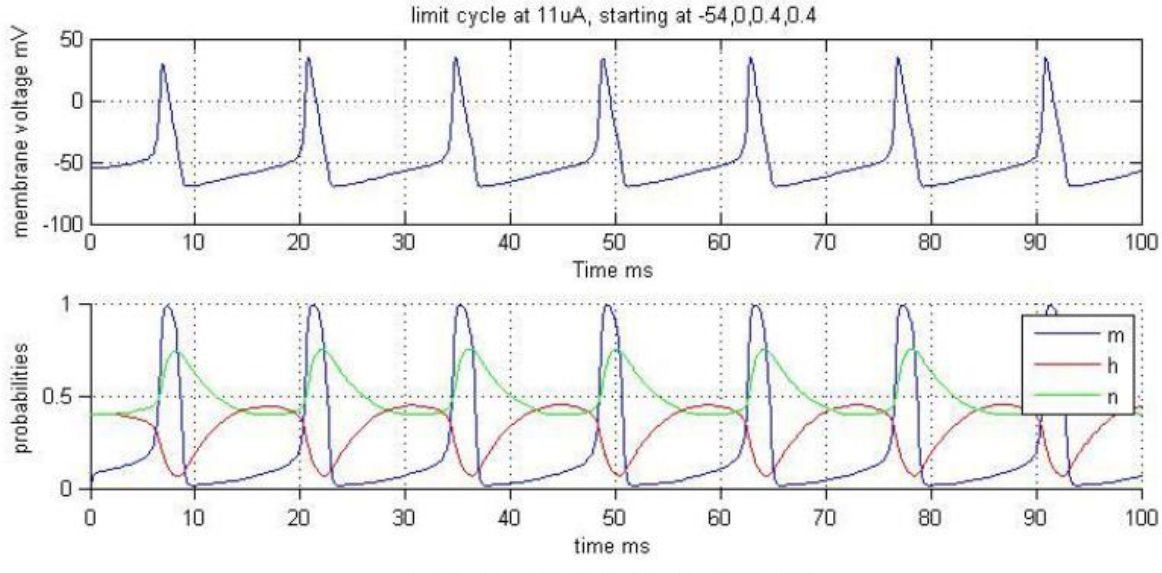
At 9 µA we have a stable equilibrium point but it takes longer time to decay



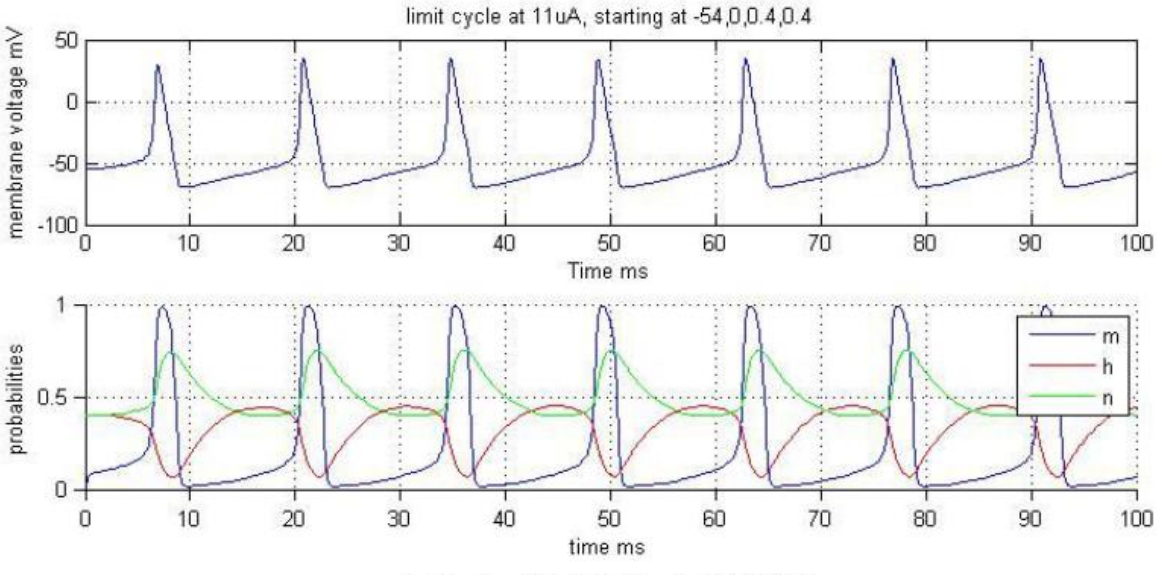
At 10 μA we have a limit cycle after some oscillations



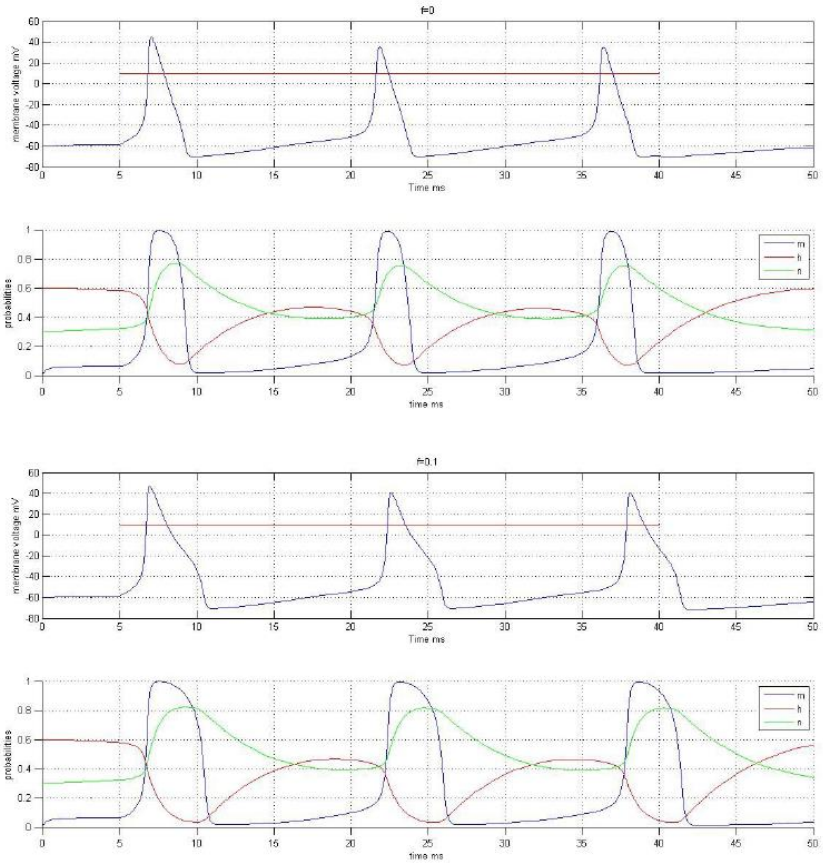
At 11 μA we have unstable equilibrium point and we get a full limit cycle



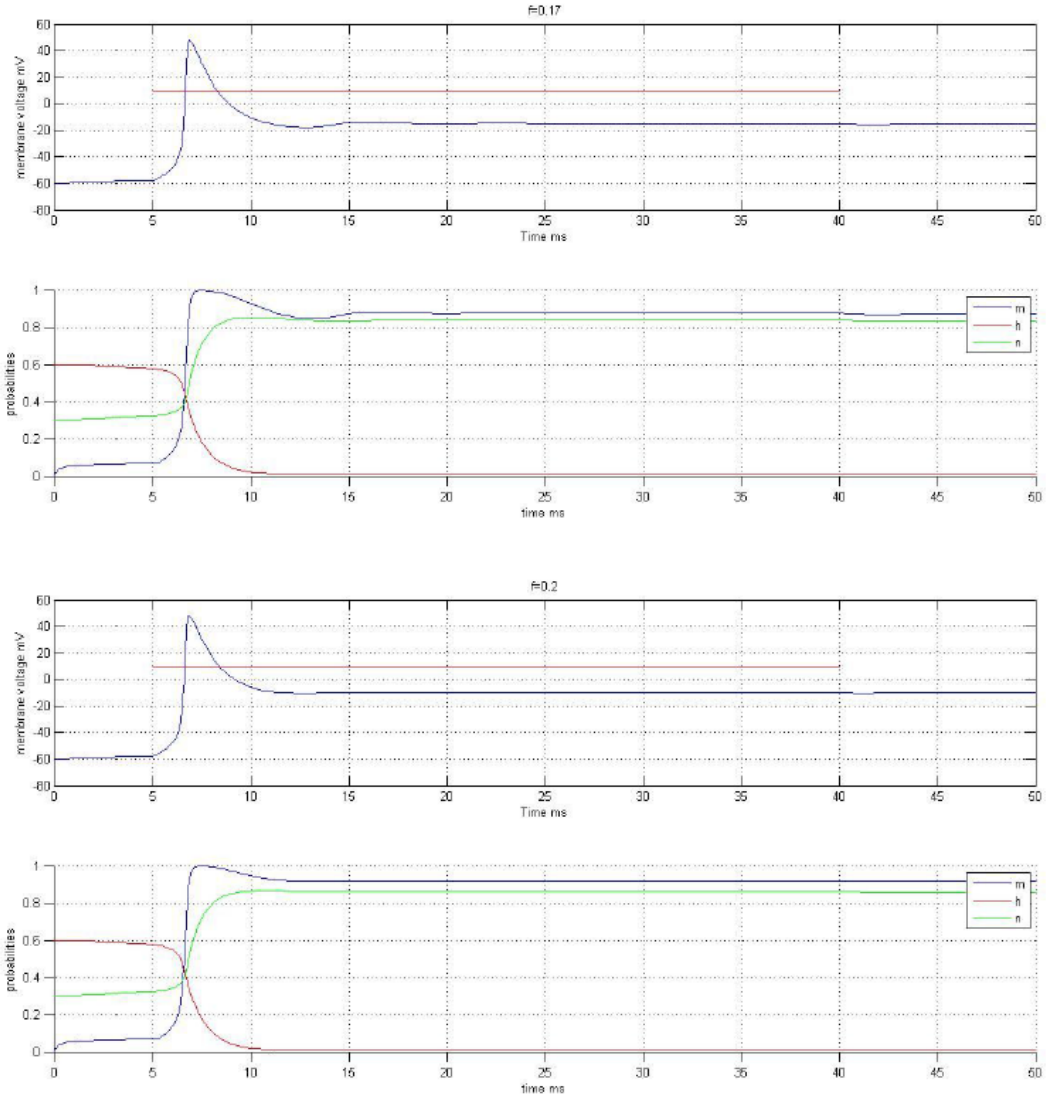
At 12 μA we have unstable equilibrium point and we get a full limit cycle



16. At f = 0 and f = 0.1, the action potentials are generated



At f = 0.17 and f = 0.2, action potentials are not generated

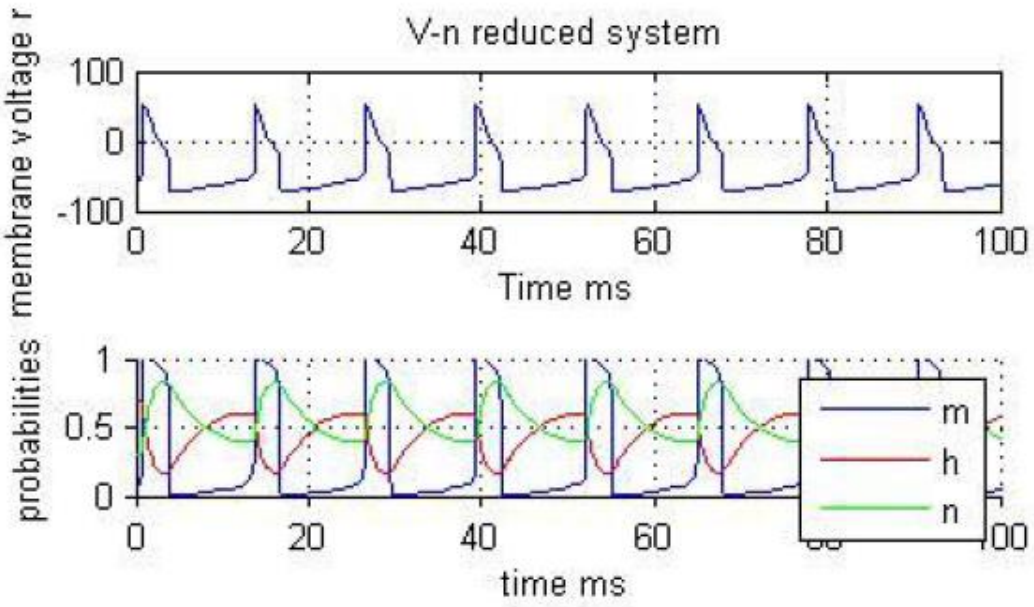


It can be observed that a fraction of Na channels replace their h variables with f and lose their inactivating behavior. This behavior is necessary for the absolute refractory period which brings down the cell to ground state and makes it ready for the next action potential

The above graph shows that the cell is not coming back to its ground state and thus not getting a stimulus, its not firing any action potentials.

17. The following assumptions have been made in the reduced model:-
    a) h and n roughly have similar behavior so h can be approximated as 1-n
    b) the decay time of m is very small as compared to h and n so m has been approximated as m_inf(V) where V is the changing membrane potential

we get the following plots using these assumptions:-



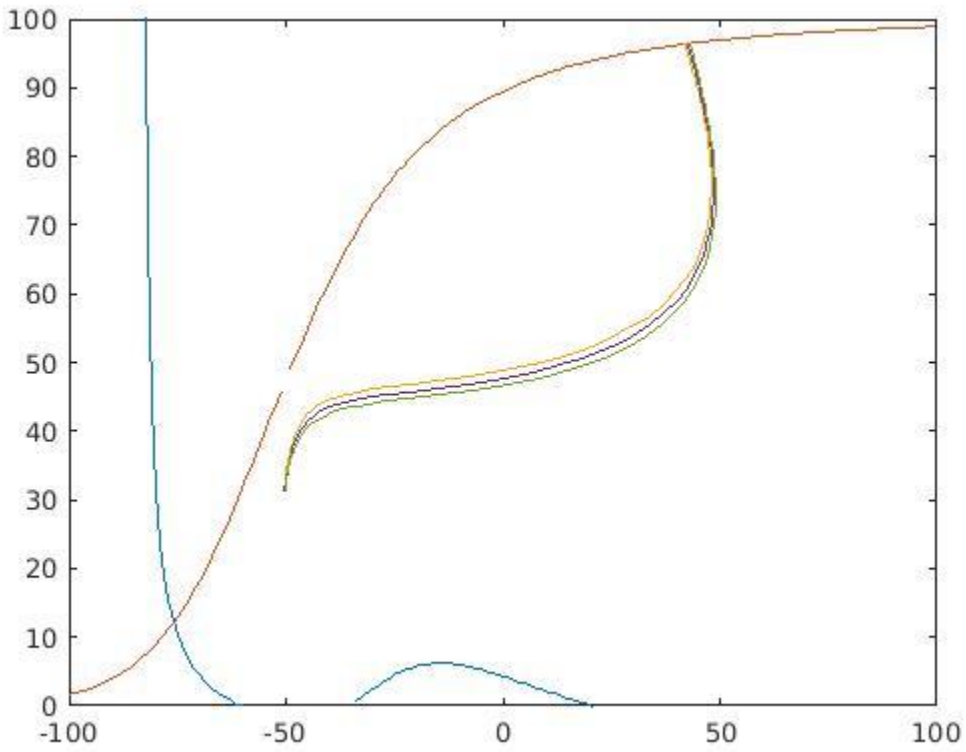
It can be seen from the images that the cell is firing action potentials like in 4 dimensions but the shape of action potential is changed since we consider m to be m_inf(V), the rising time for the action potential is almost zero and we have replaced h by 1-n so the shape drop i.e. shape of the refractory period has changed and is now dependent on h.

18.

Code for plotting the phase plane (n,v) for the reduced HH model.

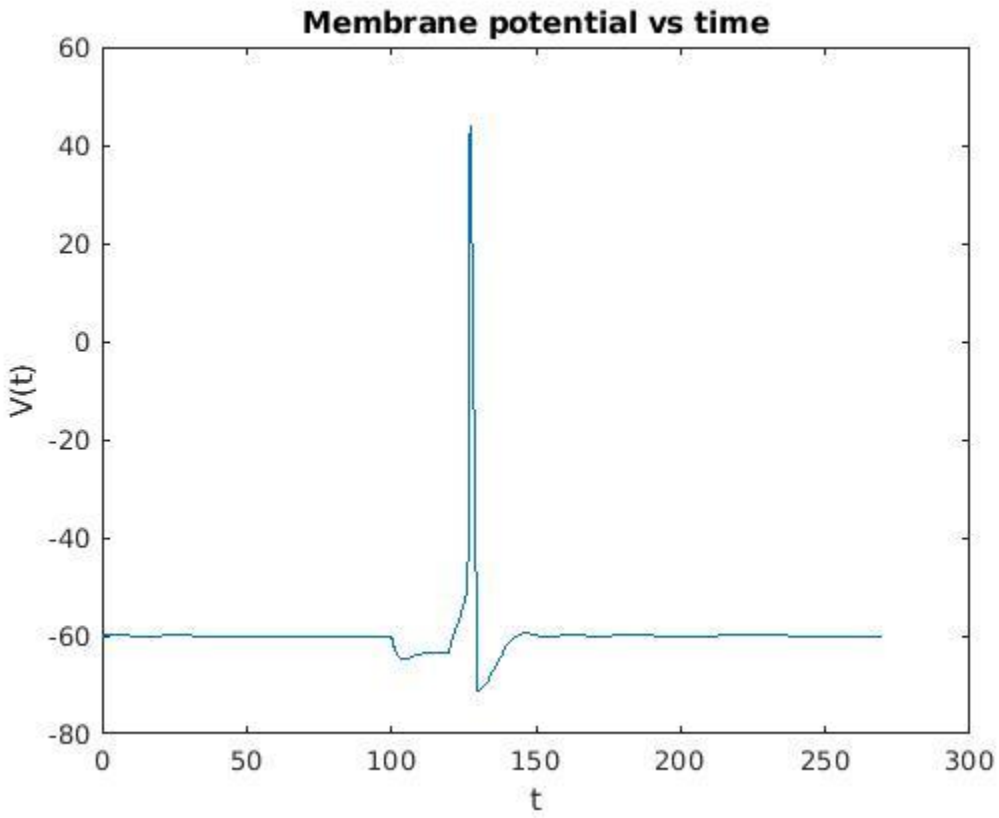
```
am = @(V) -0.1 * (35+V) ./ (exp(-0.1*(35+V)) - 1);
bm = @(V) 4 * exp(-(60+V)/18);
```

```
an = @(V) 0.01 * (-(50+V)) ./ (exp(-0.1*(50+V)) - 1);
bn = @(V) 0.125 * exp(-(60+V)/80);


nc1 = @(V)((Iext - Gk*equiPoint3(4)*((am(V))./((am(V))+(bm(V)))).^3.*(V-Vna) -
Gl*(V-Vl))./(Gk*(V-Vk))).^1/4;
nc2 = @(V) an(V)./(an(V)+bn(V));

V = -100:1:100;
plot(V,100*nc1(V)); hold on;

ylim([0 100])
xlim([-100 100])

plot(V,100*nc2(V));



for i = 0.2:0.1:0.4
    fni = i;
    equiPoint3 = fsolve(@hhPara,y_init,optionsfsolve);
    %plot(equiPoint3(1),100*equiPoint3(3),'b*')
    disp(equiPoint3)
    hinit = equiPoint3(4);
    equiPoint1 = zeros(2,1);
    equiPoint1(1) =  equiPoint3(1);
    equiPoint1(2) =  equiPoint3(2);
    equiPoint1(1) = equiPoint3(1) + 10 ;
    deltaT = [0,1000];
    [t, y] = ode45(@hhReducedPara4ode,deltaT,equiPoint1);
    plot(y(:,1),100*y(:,2)); hold on;
end
```



19. Anode-break excitation is the behavior of an excitable cell, like a neuron to fire an action potential when its membrane potential is allowed to return to its resting potential after being briefly held at a hyperpolarized potential.

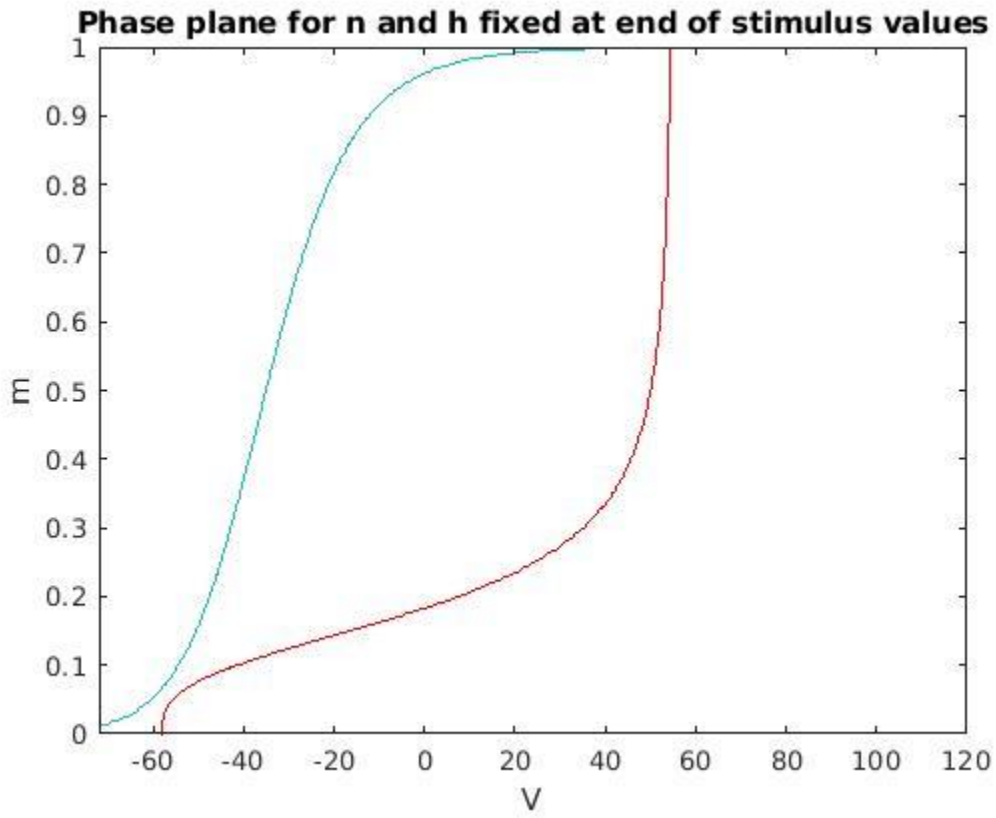
Using the HH reduced model the below graph shows the membrane potential vs time. We can easily observe firing of the action potential .

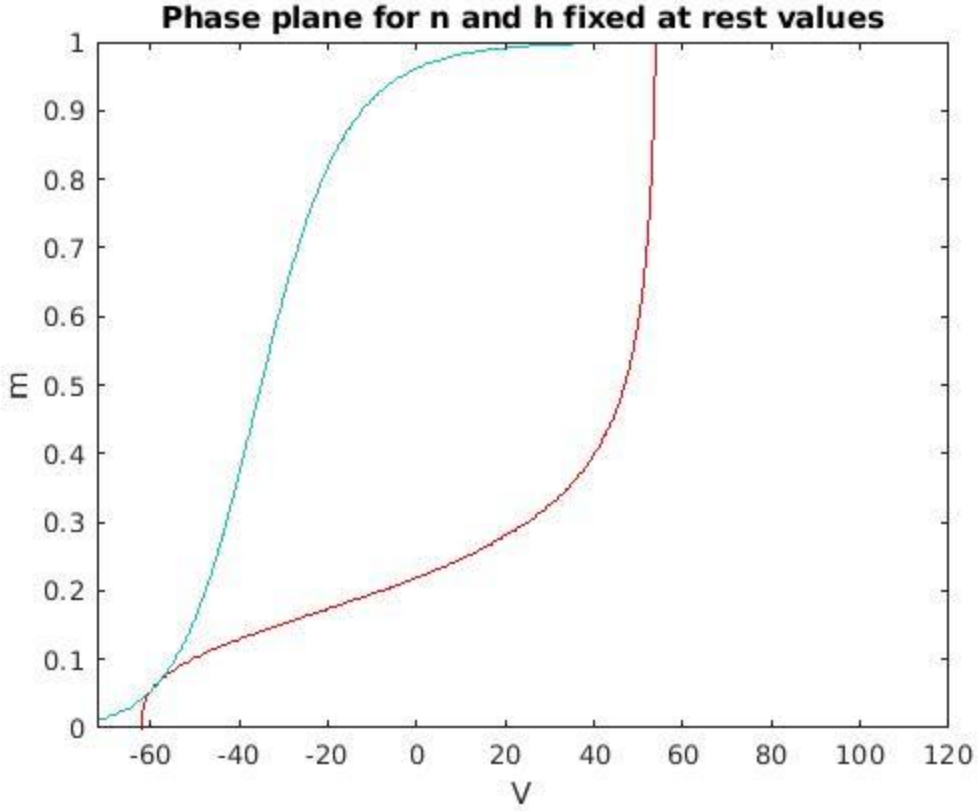


20. n and h are fixed to a constant value for this question

n = 0.26
h = 0.70

Using this the HH model is reduced to two state variable (V, m).
Phase plane for m, V is plotted below.





We have an equilibrium point in second case