Project 2
Computational Neuroscience EC60007
1. Consistent units

1. Time – ms

current / area – $\mu A / cm^2$

Voltage – mV

Capacitance / area – $\mu F / cm^2$

Conductance / area – mS / cm^2

$$\left.\begin{array}{l} mV = 10^{-3} V \\ \mu A / ms = 10^{-3} A/S = 10^{-3} V \end{array}\right] \text{consistent}$$

charge = current x time = $\mu A \times ms = 10^{-9} C$

capacitance x voltage = $\mu F \times mV = 10^{-9} (FV)$

resistance = $k\Omega = 10^3 \Omega = \frac{1}{S \times 10^{-3}} = \frac{1}{\text{conductance}}$

These are a consistent set of units

Specify conductance /area as $\mu S / cm^2$

Then if we choose current = nA, area = cm^2

$$\text{voltage} = \frac{nA/cm^2}{\mu S / cm^2} = mV$$

time = ms

charge = $nA \cdot ms = pC$

conductance = μS

resistance = $10^6 \Omega$

capacitance = $\frac{pC}{mV}$ = nF

So,

$$\left.\begin{array}{l} ms \\ nA/cm^2 \\ mV \\ nF/cm^2 \\ \mu S / cm^2 \end{array}\right\} \text{are the new consistent set of units.}$$

* Solution is NOT unique

choose current as μA

area = cm^2

$$\text{Voltage} = \frac{\mu A / cm^2}{\mu S / cm^2} = \text{Volts (V)}$$

time = ms

$Q = \mu A \cdot ms = pC$

conductance = μS

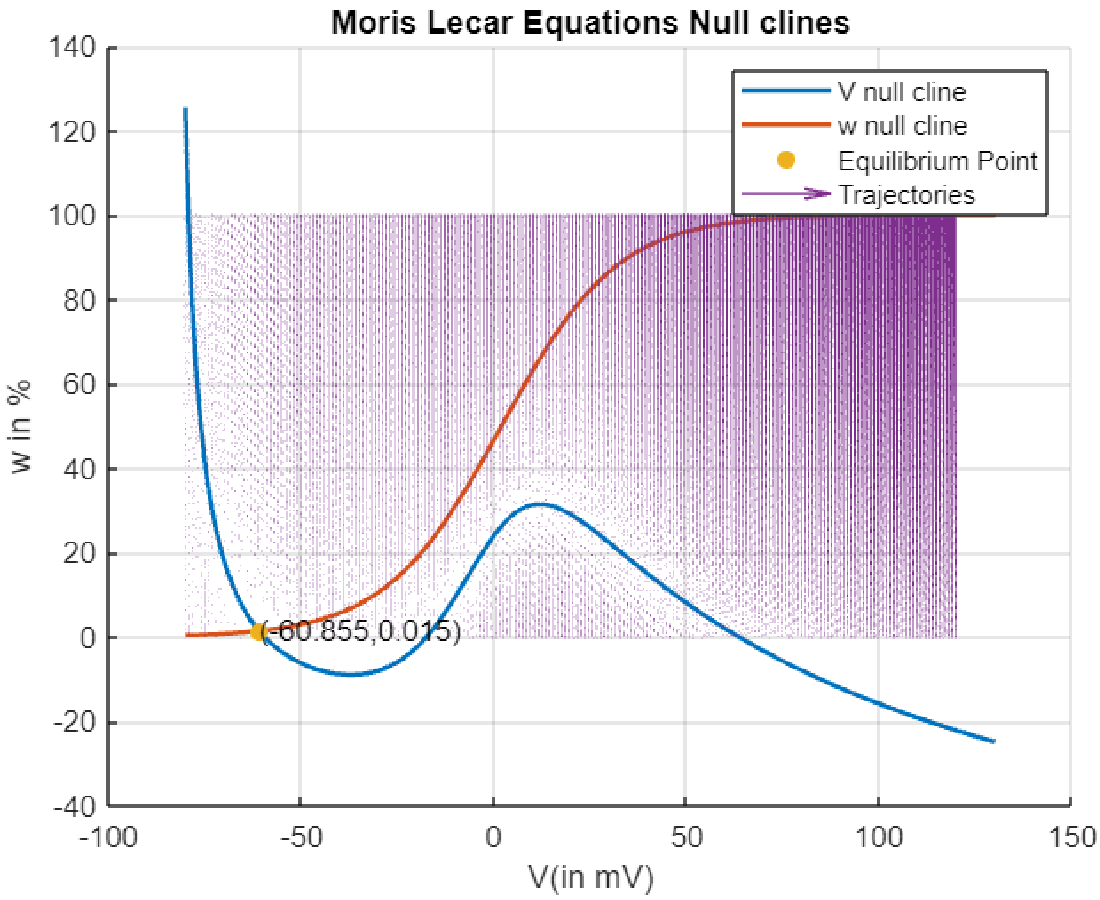
resistance = $G\Omega$

capacitance = $\frac{pC}{V} = pF$

area = cm^2

→ $$\left.\begin{array}{l} ms \\ \mu A / cm^2 \\ pF / cm^2 \\ \mu S / cm^2 \end{array}\right\} \text{is another set of consistent units.}$$

2. Equilibrium point calculated using intersection of the V null cline and w null cline

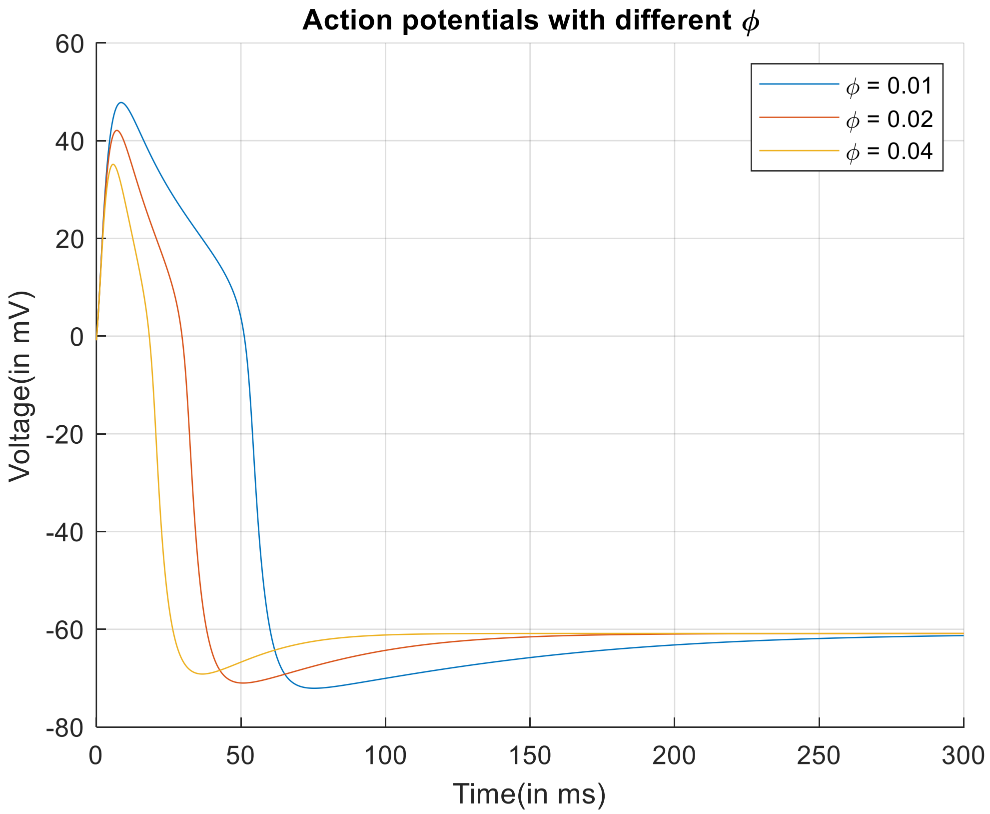


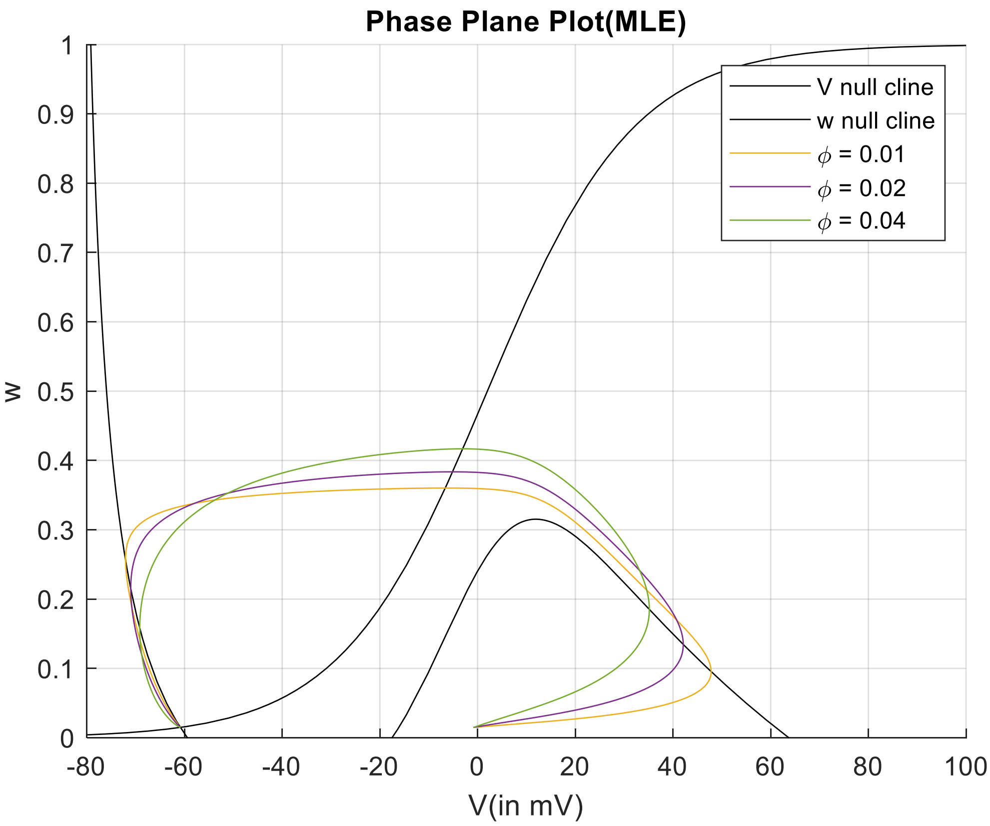
Equilibrium membrane potential : -60.855 mV
Equilibrium w : 1.5%

3. Stability analysis using Jacobian
The eigen values are -9.588030e-02 and -3.656140e-02
Both < 0 : stable

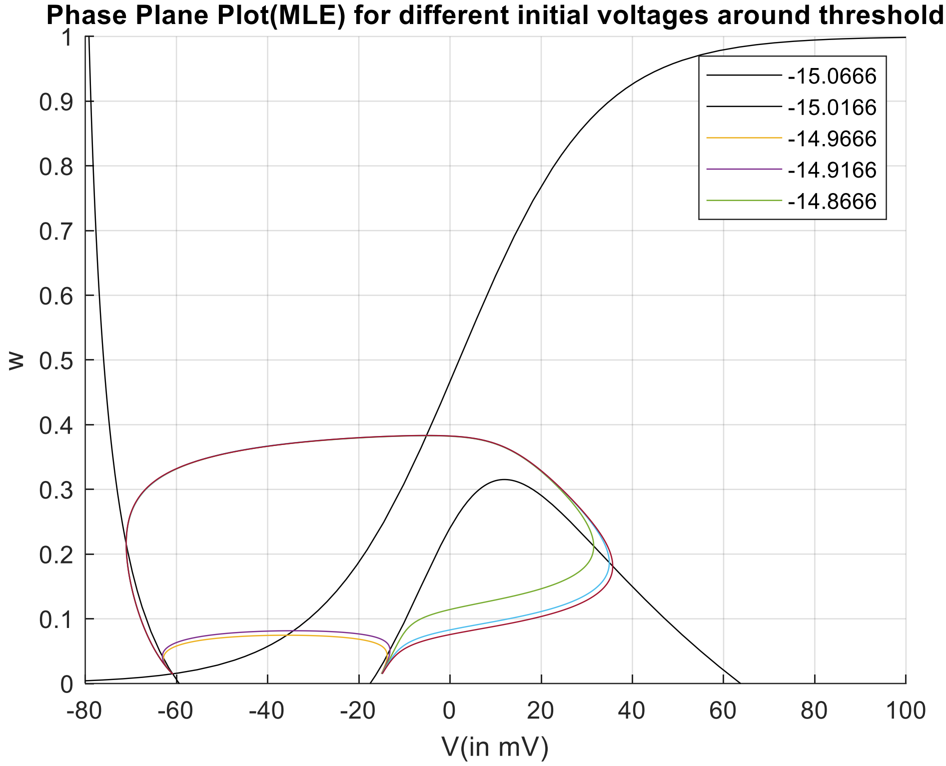
4. Absolute tolerance does not consider the actual value taken by the variables. Membrane potential is in mV so 10^-6 absolute tolerance = 1uV error. This is 0.1% error and acceptable. Relative tolerance of 10^-3 is the maximum ratio of error to value. 0.1% is acceptable. If voltage is measured in kV, then absTol needs to decrease by a factor of 10^9 to measure mV voltage with 0.1% maximum error. RelTol does not need to be changed since it considers the actual value taken by the variables.

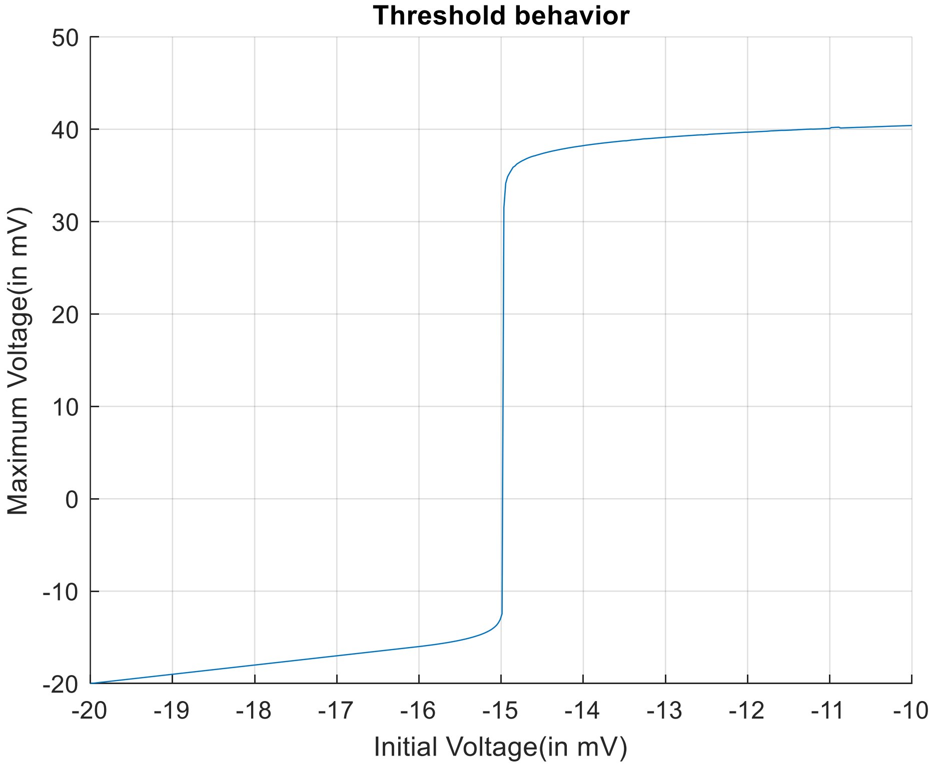
5. phi increases with temperature. dw/dt is proportional to phi. Increasing phi results in a slower relative increase in the membrane potential with increase in current injection. This agrees with the experimental result that the threshold behaviour becomes graded at higher temperatures, not true threshold behaviour. This explanation is confirmed by the spike being highest for lowest value of phi. (lowest temperature).



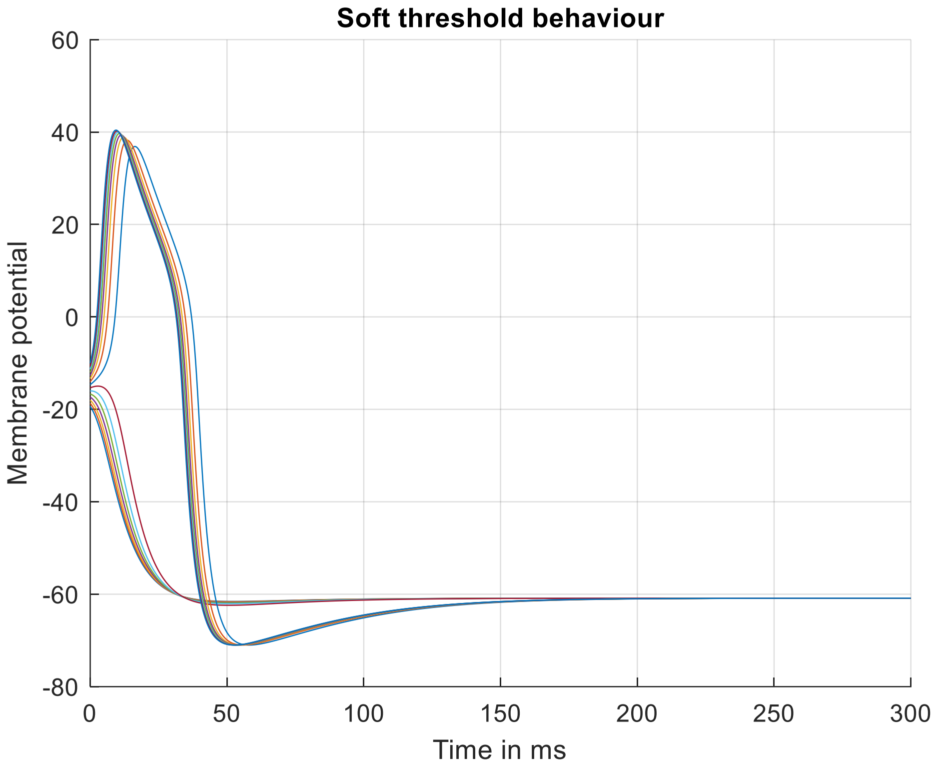


6. Threshold voltage is -14.966592 mV

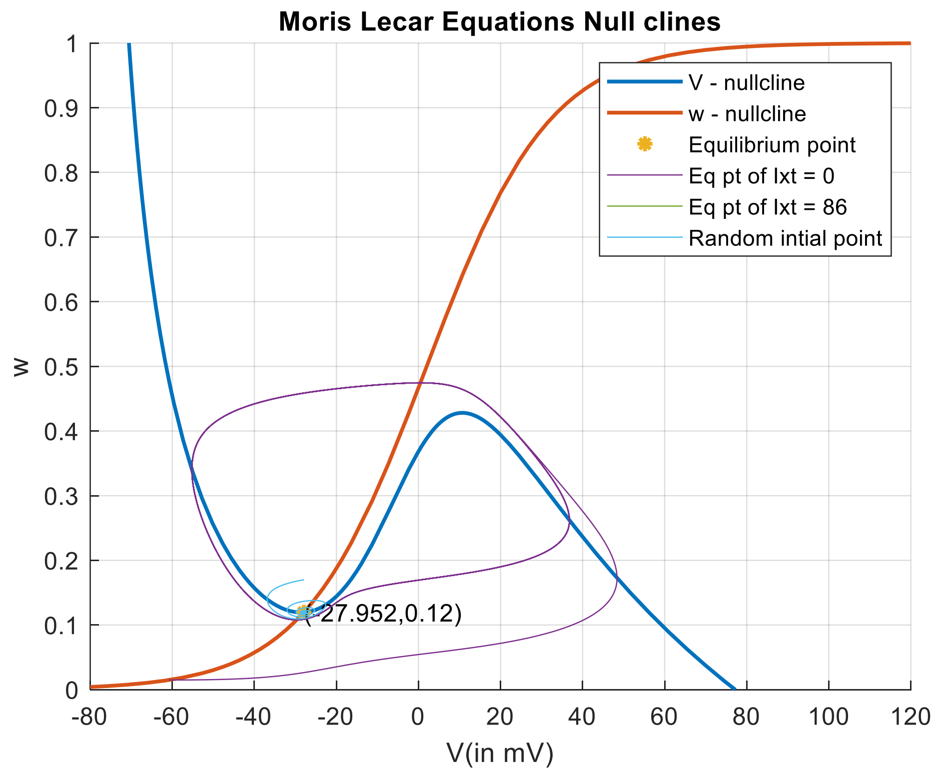




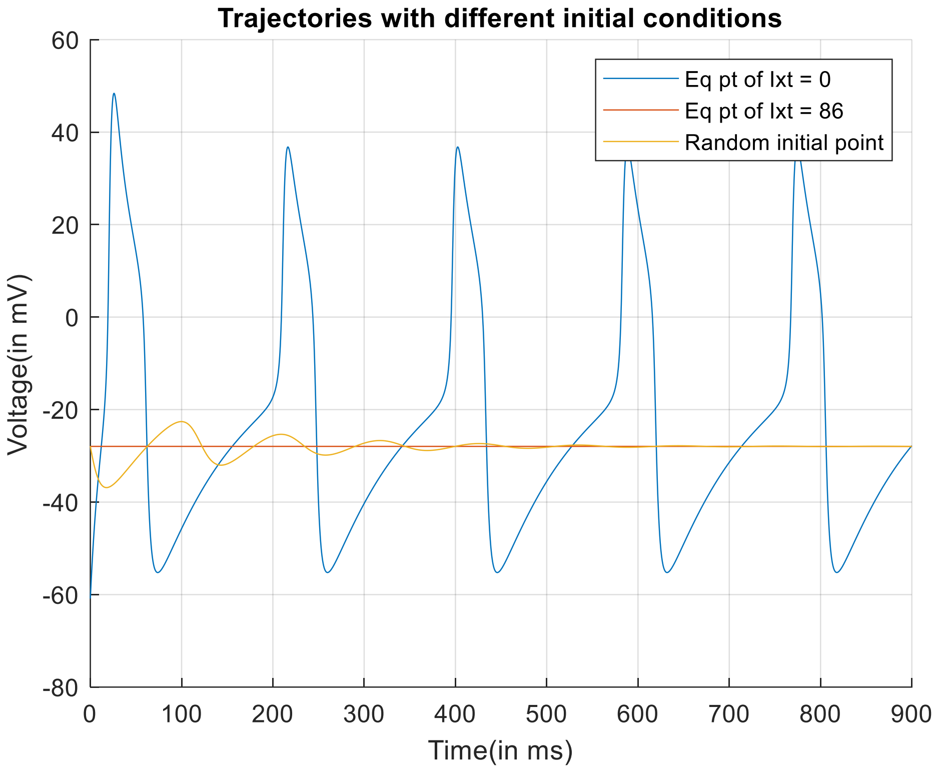
This is not a true threshold as the peak voltage continues to increase as depolarization is increased.



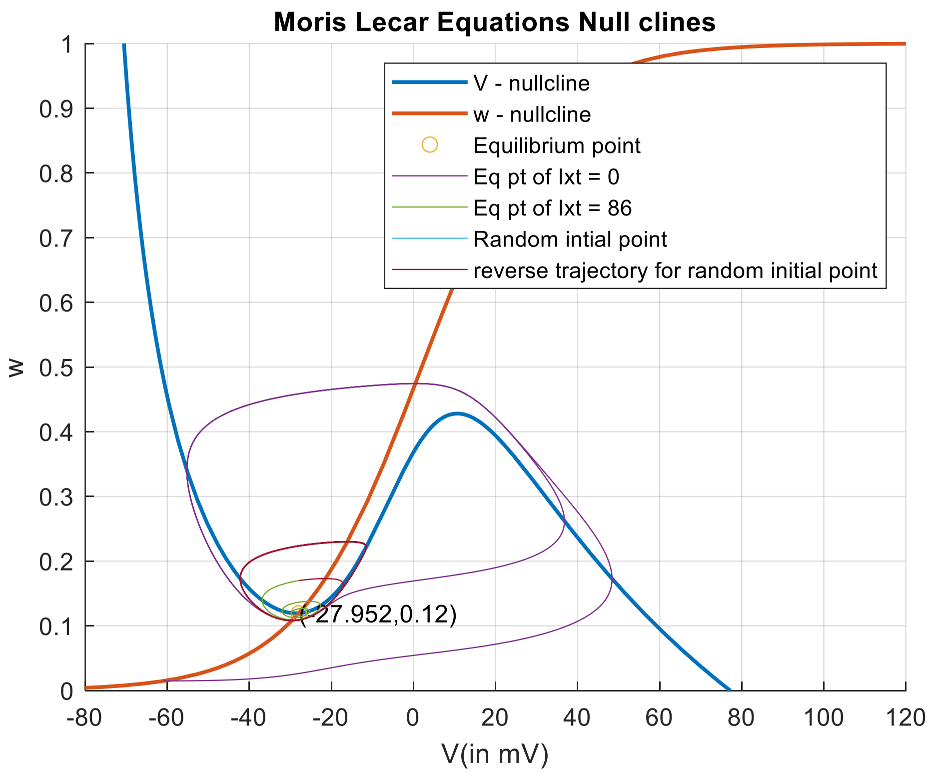
7. 86 uA/cm^2 dc current injection
The equilibrium point is located at (-27.95241 mV, 11.95364 %)
The real parts of eigen values are -6.784560e-03 and -6.784560e-03 : stable



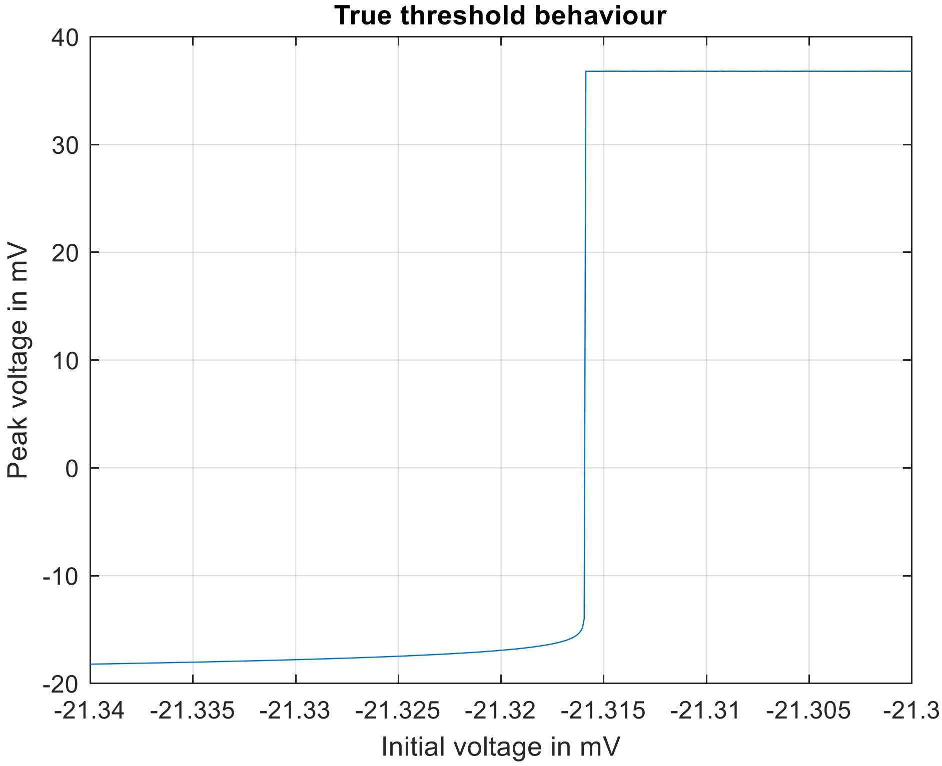
1. The initial condition is outside the unstable periodic orbit so in ends in a stable periodic orbit which is the limit cycle. (purple trajectory)
2. The initial condition is the equilibrium point so there is no change in state
3. The initial condition is inside the unstable periodic orbit so the state spirals inwards. (blue trajectory)



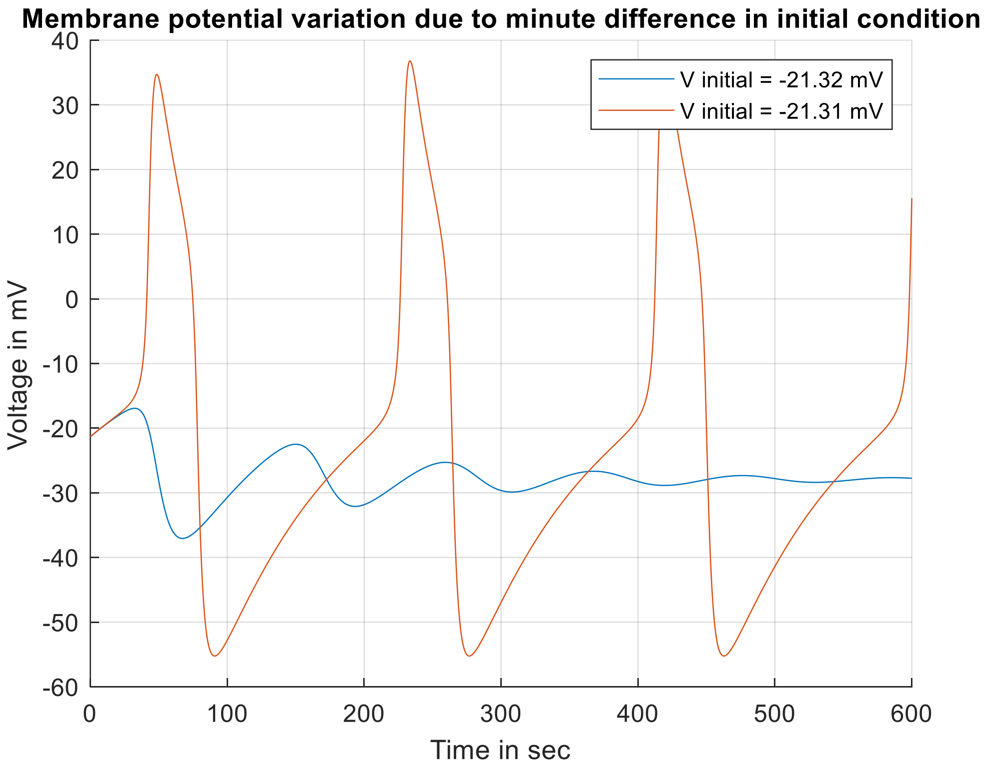
8. Unstable Periodic Orbit



The red loop is the UPO found by running the sim backwards in time.
It shows true threshold behaviour
Threshold: -21.31595 mV



The peak voltage increases sharply at the threshold then remains constant.



When time is reversed the stable points become unstable and vice versa. The null clines and hence the location of the equilibrium points remain unchanged. The unstable and stable manifolds at saddle nodes are exchanged.

9.

------------------------- Part 9 -> Iext = 80 uA/cm^2-------------------------

The equilibrium point is located at (-2.996618e+01,1.061127e-01)

The eigen values are -0.017784+0.055717i , -0.017784-0.055717i

Stable spiral

------------------------- Part 9 -> Iext = 86 uA/cm^2-------------------------

The equilibrium point is located at (-2.795241e+01,1.195364e-01)

The eigen values are -0.006785+0.057427i , -0.006785-0.057427i

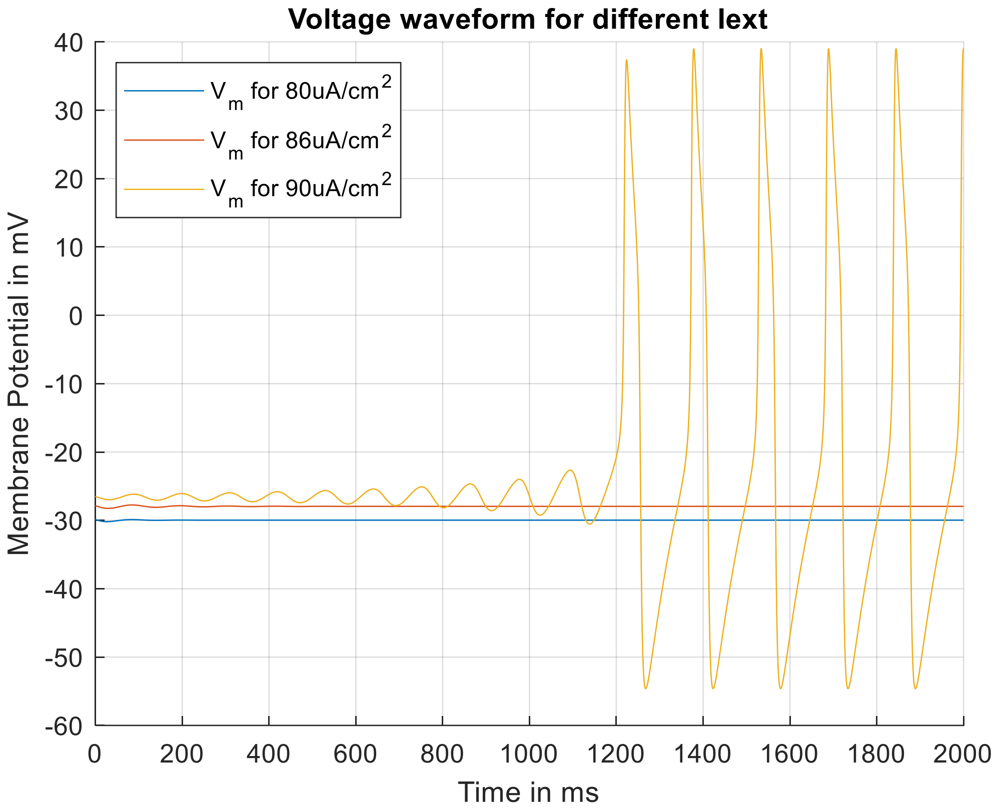
Stable spiral

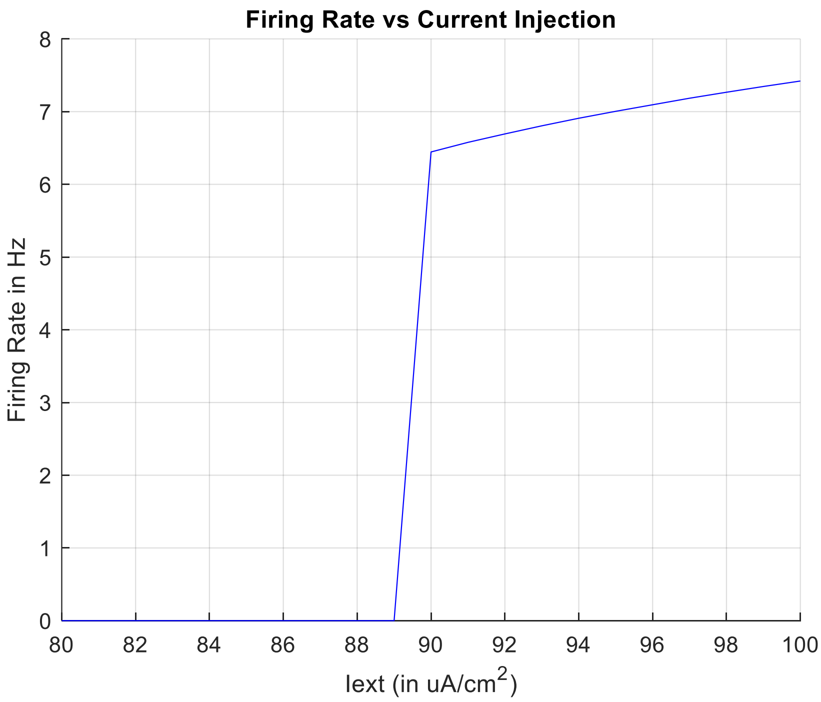
------------------------- Part 9 -> Iext = 90 uA/cm^2-------------------------

The equilibrium point is located at (-2.659687e+01,1.293793e-01)

The eigen values are 0.001753+0.057170i , 0.001753-0.057170i

Unstable spiral ending on a limit cycle





10. Saddle point

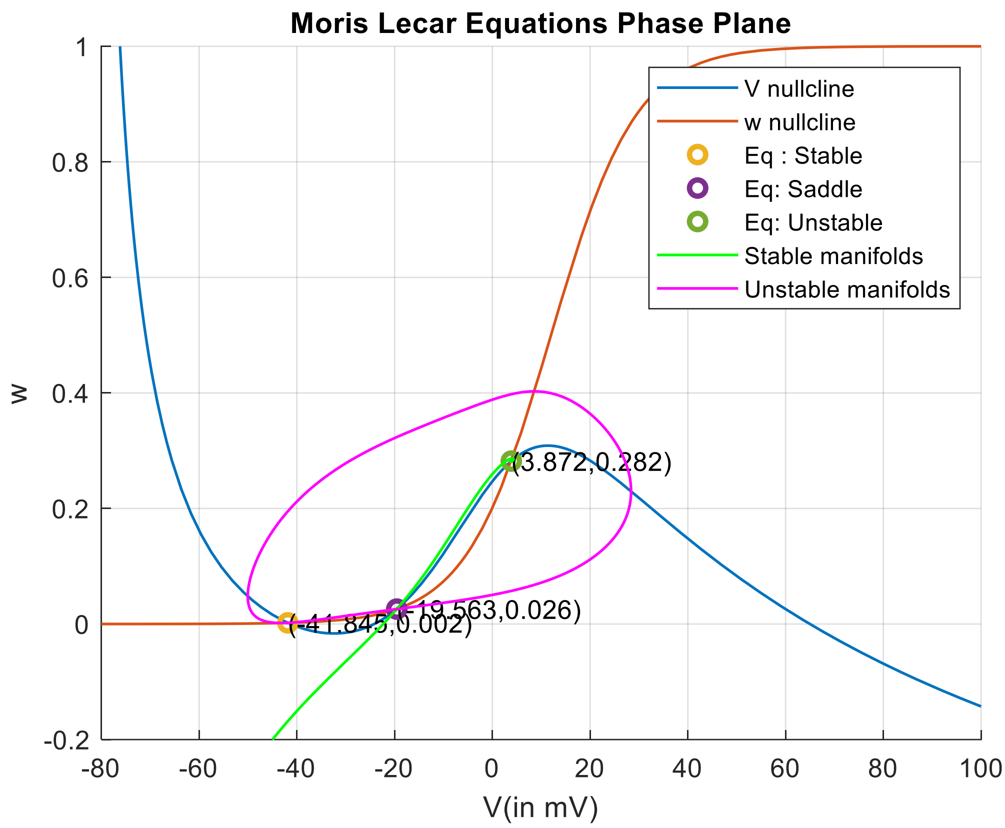
Equilibrium points are :

1. (-41.845162, 0.002047) : stable
2. (-19.563243, 0.025883) : saddle
3. (3.871510, 0.282051) : unstable spiral

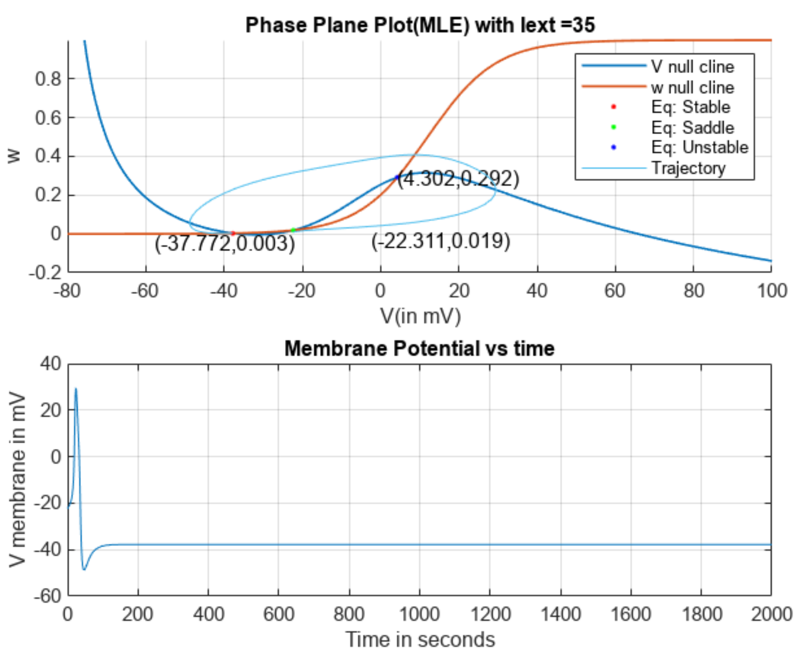
Equilibrium point 1 : The eigen values are -0.071544+0.000000i , -0.156766+0.000000i

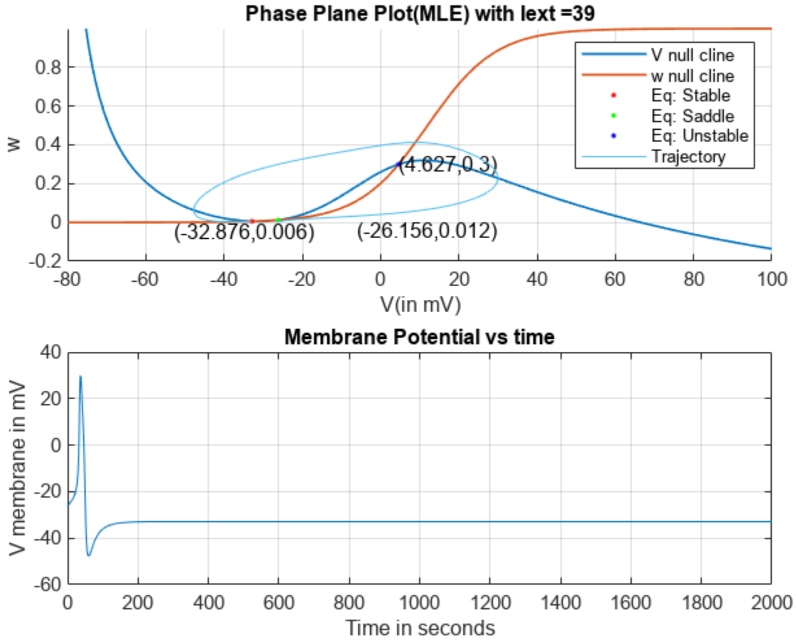
Equilibrium point 2 : The eigen values are 0.153619+0.000000i , -0.067328+0.000000i

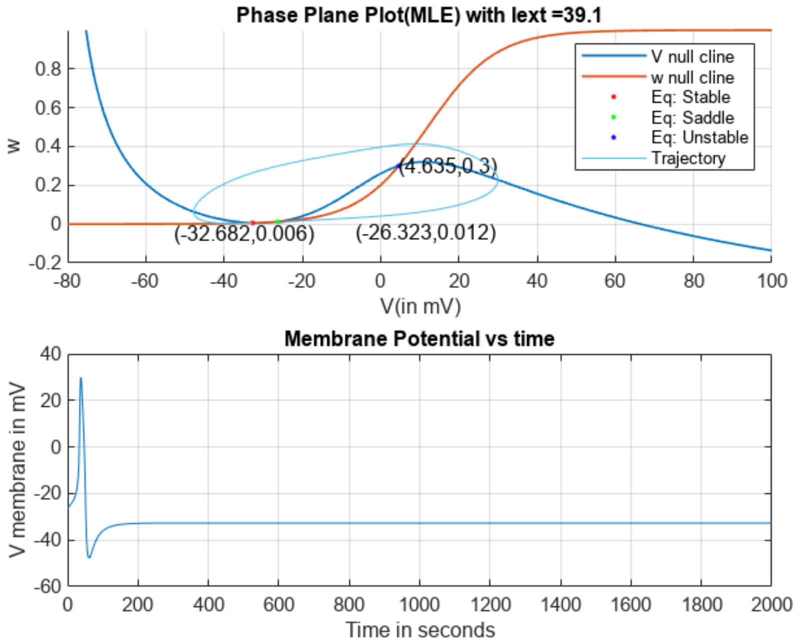
Equilibrium point 3 : The eigen values are 0.093868+0.172310i , 0.093868-0.172310i

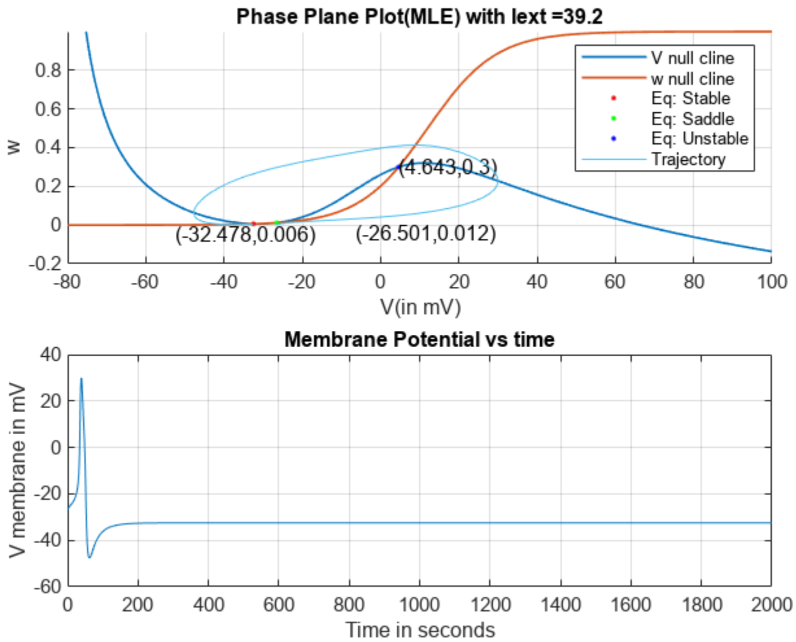


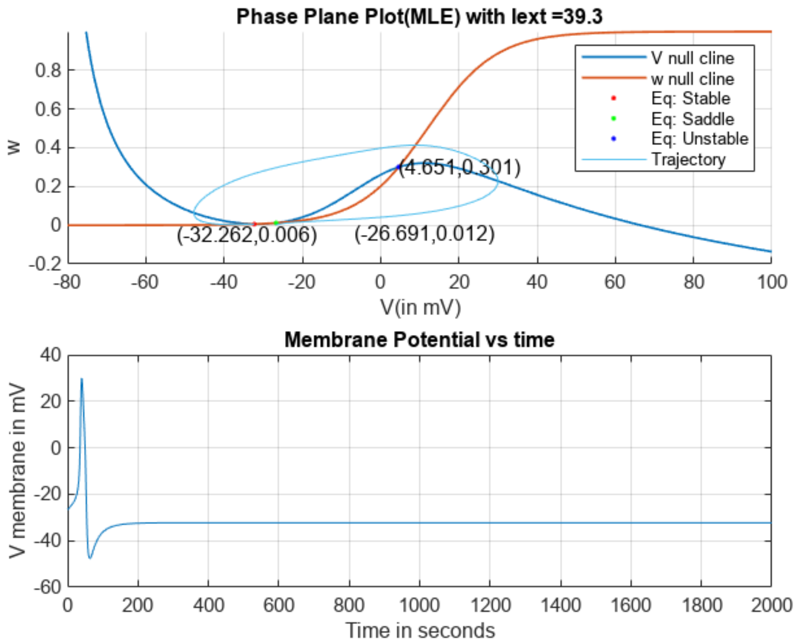
11. Phase plane trajectories and membrane potential waveform

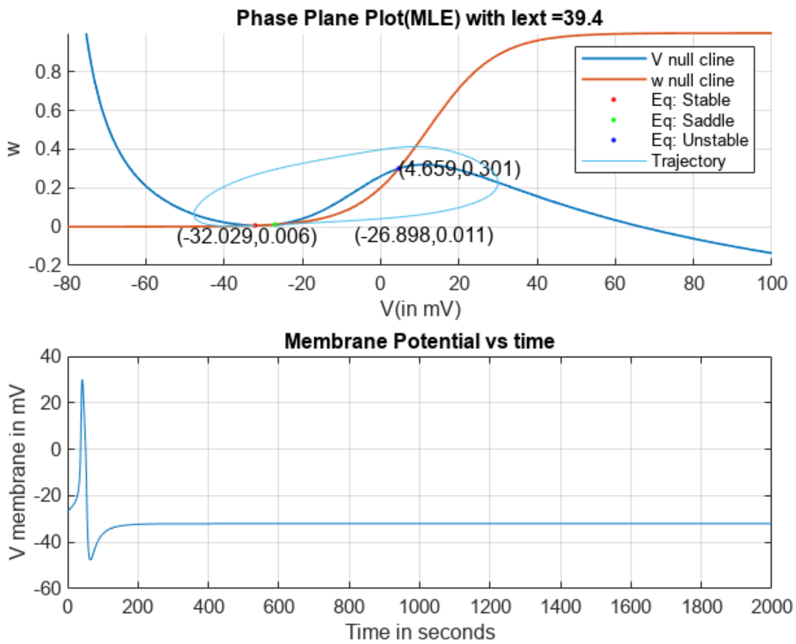


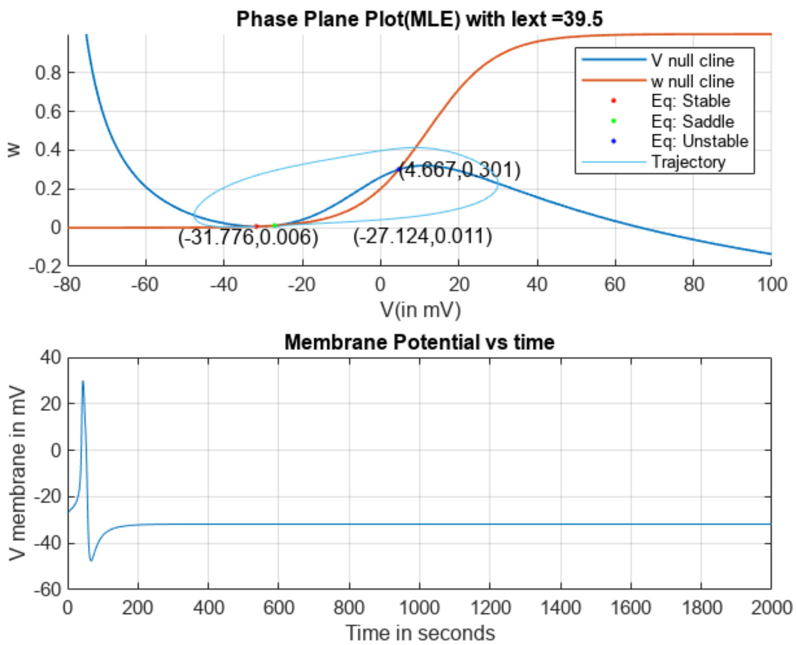

Phase Plane Plot(MLE) with Iext =39
V null cline
w null cline
Eq: Stable
Eq: Saddle
Eq: Unstable
Trajectory
(4.627,0.3)
(-32.876,0.006)
(-26.156,0.012)
w
V(in mV)
Membrane Potential vs time
V membrane in mV
Time in seconds

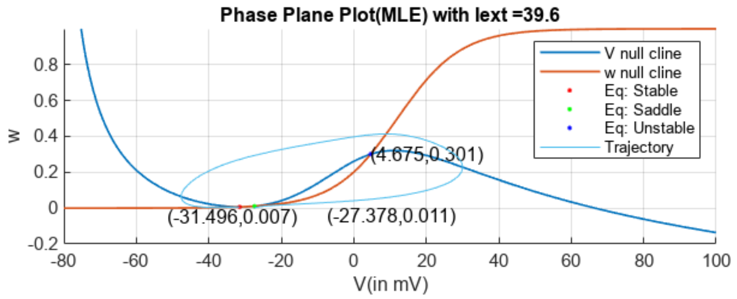

Phase Plane Plot(MLE) with Iext =39.1
V null cline
w null cline
Eq: Stable
Eq: Saddle
Eq: Unstable
Trajectory
(4.635,0.3)
(-32.682,0.006)
(-26.323,0.012)
w
V(in mV)
Membrane Potential vs time
V membrane in mV
Time in seconds

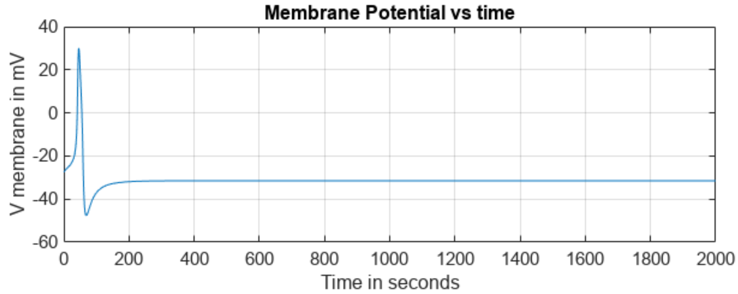

Phase Plane Plot(MLE) with Iext =39.2
V null cline
w null cline
Eq: Stable
Eq: Saddle
Eq: Unstable
Trajectory
(4.643,0.3)
(-32.478,0.006)
(-26.501,0.012)
w
V(in mV)
Membrane Potential vs time
V membrane in mV
Time in seconds

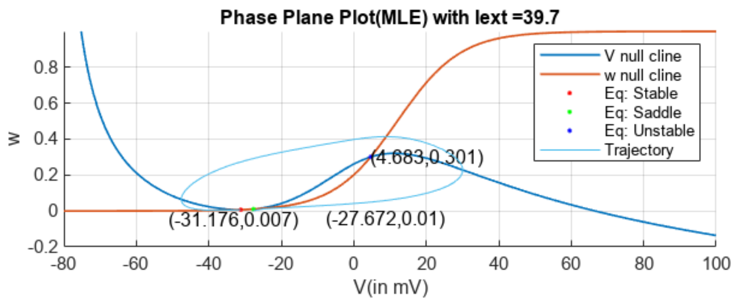

Phase Plane Plot(MLE) with Iext =39.3
V null cline
w null cline
Eq: Stable
Eq: Saddle
Eq: Unstable
Trajectory
(4.651,0.301)
(-32.262,0.006)
(-26.691,0.012)
w
V(in mV)
Membrane Potential vs time
V membrane in mV
Time in seconds

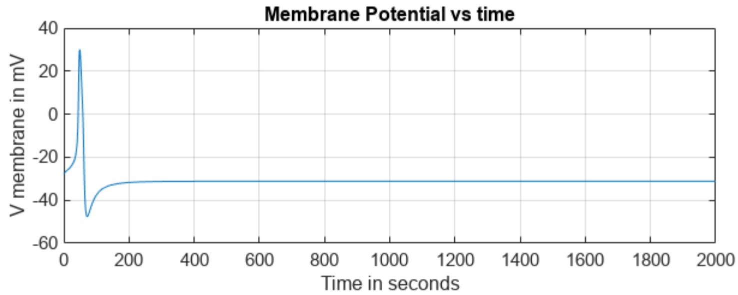

Phase Plane Plot(MLE) with Iext =39.4
V null cline
w null cline
Eq: Stable
Eq: Saddle
Eq: Unstable
Trajectory
(4.659,0.301)
(-32.029,0.006)
(-26.898,0.011)
w
V(in mV)
Membrane Potential vs time
V membrane in mV
Time in seconds

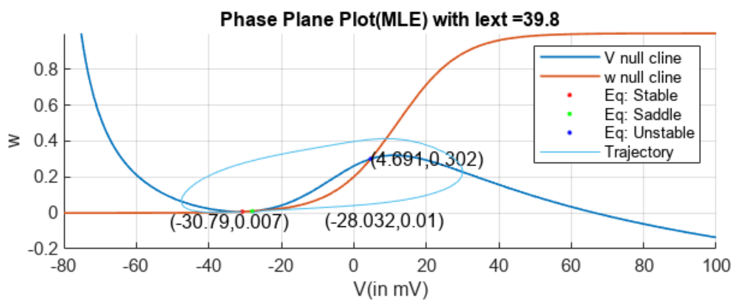

Phase Plane Plot(MLE) with Iext =39.5
V null cline
w null cline
Eq: Stable
Eq: Saddle
Eq: Unstable
Trajectory
(4.667,0.301)
(-31.776,0.006)
(-27.124,0.011)
w
V(in mV)
Membrane Potential vs time
V membrane in mV
Time in seconds

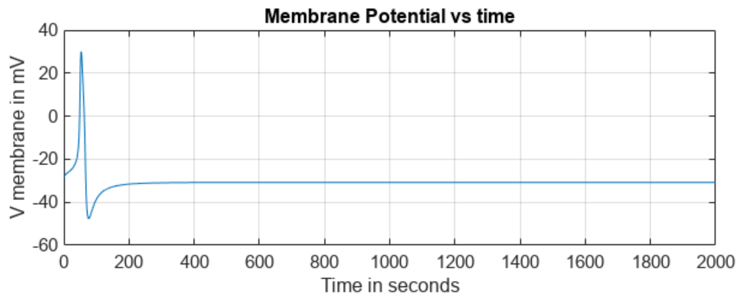

Phase Plane Plot(MLE) with Iext =39.6
V null cline
w null cline
Eq: Stable
Eq: Saddle
Eq: Unstable
Trajectory
(4.675,0.301)
(-31.496,0.007)
(-27.378,0.011)
w
V(in mV)

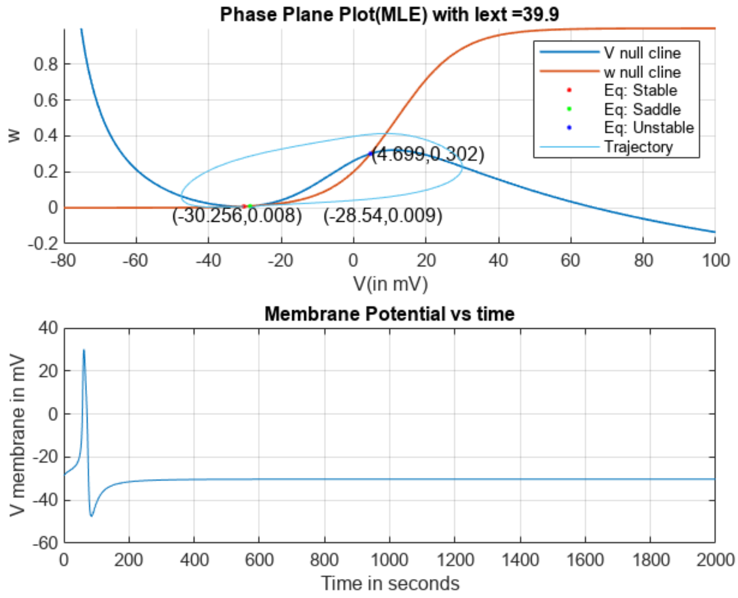

Membrane Potential vs time
V membrane in mV
Time in seconds

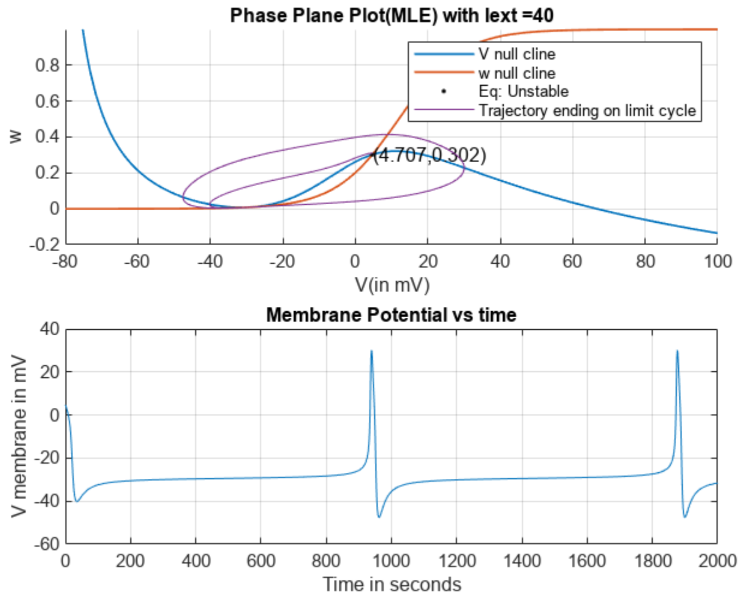

Phase Plane Plot(MLE) with Iext =39.7
V null cline
w null cline
Eq: Stable
Eq: Saddle
Eq: Unstable
Trajectory
(4.683,0.301)
(-31.176,0.007)
(-27.672,0.01)
w
V(in mV)

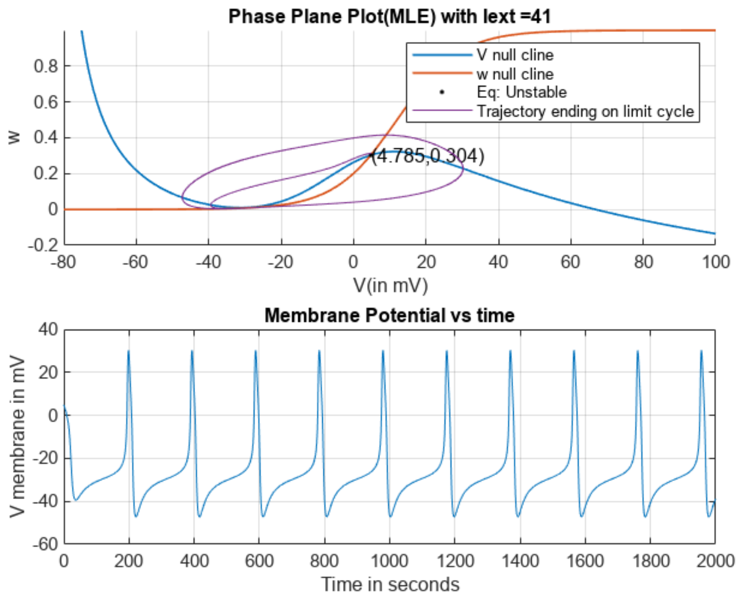

Membrane Potential vs time
V membrane in mV
Time in seconds

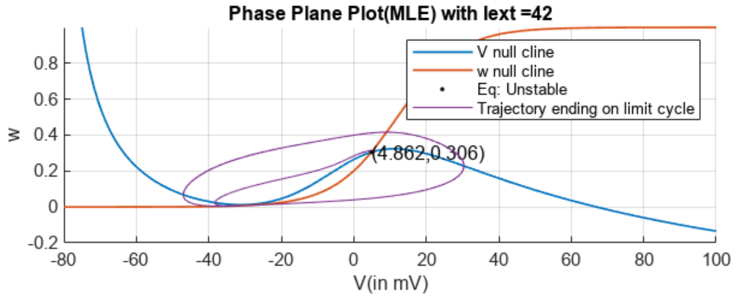

Phase Plane Plot(MLE) with Iext =39.8
V null cline
w null cline
Eq: Stable
Eq: Saddle
Eq: Unstable
Trajectory
(4.691,0.302)
(-30.79,0.007)
(-28.032,0.01)
w
V(in mV)

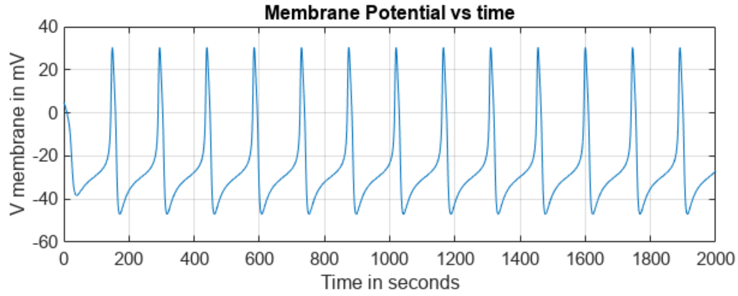

Membrane Potential vs time
V membrane in mV
Time in seconds

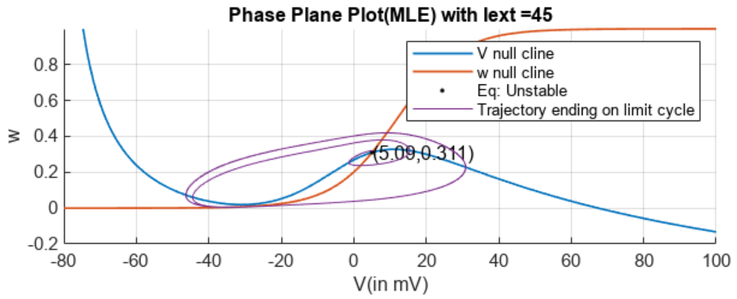

Phase Plane Plot(MLE) with Iext =39.9
V null cline
w null cline
Eq: Stable
Eq: Saddle
Eq: Unstable
Trajectory
(4.699,0.302)
(-30.256,0.008)
(-28.54,0.009)
w
V(in mV)
Membrane Potential vs time
V membrane in mV
Time in seconds

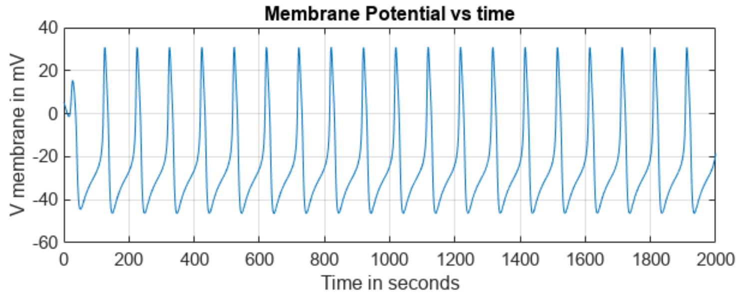

Phase Plane Plot(MLE) with Iext =40
V null cline
w null cline
Eq: Unstable
Trajectory ending on limit cycle
(4.707,0.302)
w
V(in mV)
Membrane Potential vs time
V membrane in mV
Time in seconds

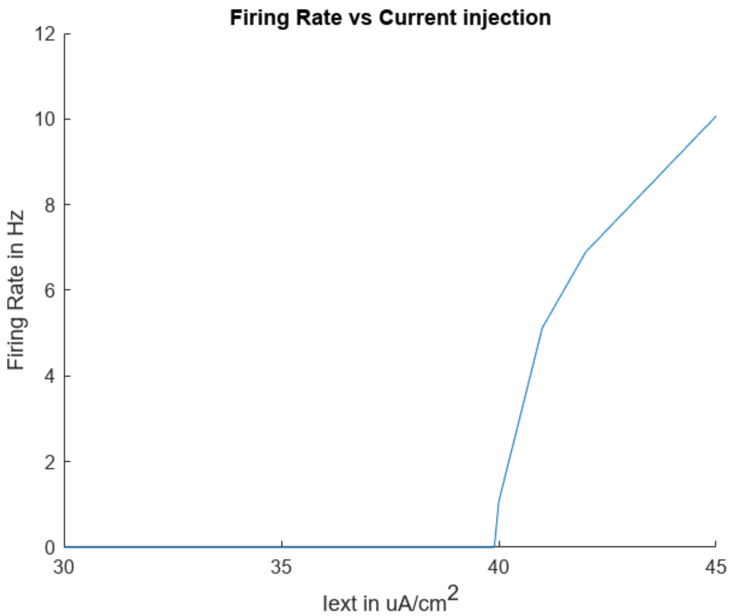

Phase Plane Plot(MLE) with Iext =41
V null cline
w null cline
Eq: Unstable
Trajectory ending on limit cycle
(4.785,0.304)
w
V(in mV)
Membrane Potential vs time
V membrane in mV
Time in seconds











For I_ext < 40uA/cm^2 there are 3 equilibrium points. As I_ext increases the V null cline moves upwards and two equilibrium points (with V_m < 0) move towards each other. After this only the unstable equilibrium point at positive membrane potential is remaining which moves further towards higher V_m as I_ext increases. Firing rate increases at a decreasing rate as current injection is increased beyond the threshold.

12.

Hodgkin Huxley equations

$$\frac{C\,dV}{dt} = I_{ext} - \bar{G}_{Na}\, m^3 h\,(V - E_{Na}) - \bar{G}_K\, n^4\,(V - E_K) - G_L\,(V - E_L)$$

$$\frac{dx}{dt} = \alpha_x(1-x) - \beta_x x$$

$$= \alpha_x - (\alpha_x + \beta_x)\,x$$

$$= \frac{\left(\frac{\alpha_x}{\alpha_x+\beta_x}\right) - x}{\frac{1}{\alpha_x+\beta_x}}$$

$$\frac{dx}{dt} = \frac{x_\infty(V) - x}{T_x(V)}$$

$\bar{G}_K = 36\,mS/cm^2$ $\qquad \alpha_n = \dfrac{-0.01\,(V+50)}{\exp\left[-\frac{(V+50)}{10}\right]-1}$

$E_K = -72\,mV$

$\phi = 1$ $\qquad \beta_n = 0.125\exp\left[-\dfrac{(V+60)}{80}\right]$

$\bar{G}_{Na} = 120\,mS/cm^2$ $\qquad \alpha_m = \dfrac{-0.1\,(V+35)}{\exp\left[-\frac{(V+35)}{10}\right]-1}$

$E_{Na} = 55\,mV$

$\beta_m = 4\exp\left[-\dfrac{(V+60)}{18}\right]$

$\alpha_h = 0.07\exp\left[-\dfrac{(V+60)}{20}\right]$

$\beta_h = \dfrac{1}{\exp\left[\frac{-(V+30)}{10}\right]+1}$

$G_L = 0.3\,mS/cm^2$ $\qquad \phi = \theta^{(T-6.3)/10}, \; \theta = 3$

$E_L =$ to be determined $\quad T = 6.3 \Rightarrow \phi = 1 \quad C = 1\,\mu F/cm^2$

$V_r = -60mV$

$m = m_\infty(V_r)$

$h = h_\infty(V_r)$

$n = n_\infty(V_r)$

$I_{ext} = 0$

$$0 = I_{ext} - \bar{G}_{Na} m^3 h (V_r - E_{Na}) - \bar{G}_K n^4 (V_r - E_K) - G_L (V_r - E_L)$$

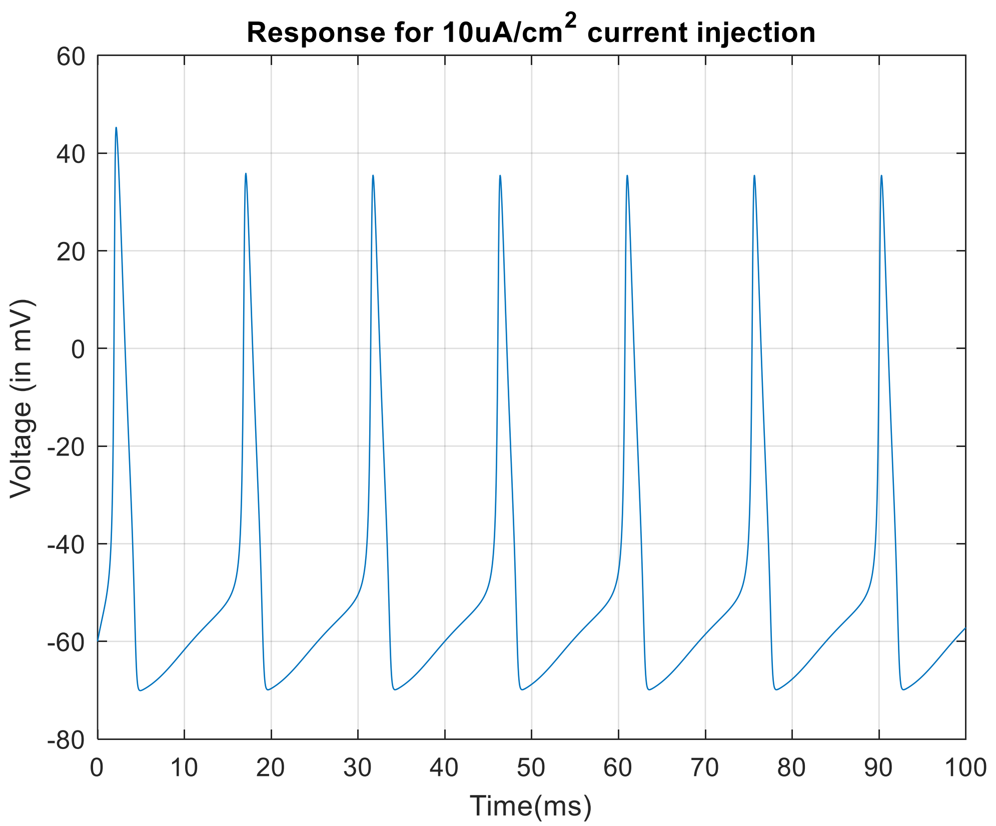
$$\Rightarrow E_L = -\frac{1}{G_L}\left(I_{ext} - \bar{G}_{Na} m^3 h (V_r - E_{Na}) - \bar{G}_K n^4 (V_r - E_K) - G_L V_r \right)$$

$$E_L = V_r - \frac{1}{G_L}\left(I_{ext} - \bar{G}_{Na} m^3 h (V_r - E_{Na}) - \bar{G}_K n^4 (V_r - E_K) \right)$$

To avoid $\frac{0}{0}$ form, we add a small value $\varepsilon = 10^{-9}$ to the exponential terms in α_x and β_x.

Units are consistent.

13. E_Leak = -49.40 mV

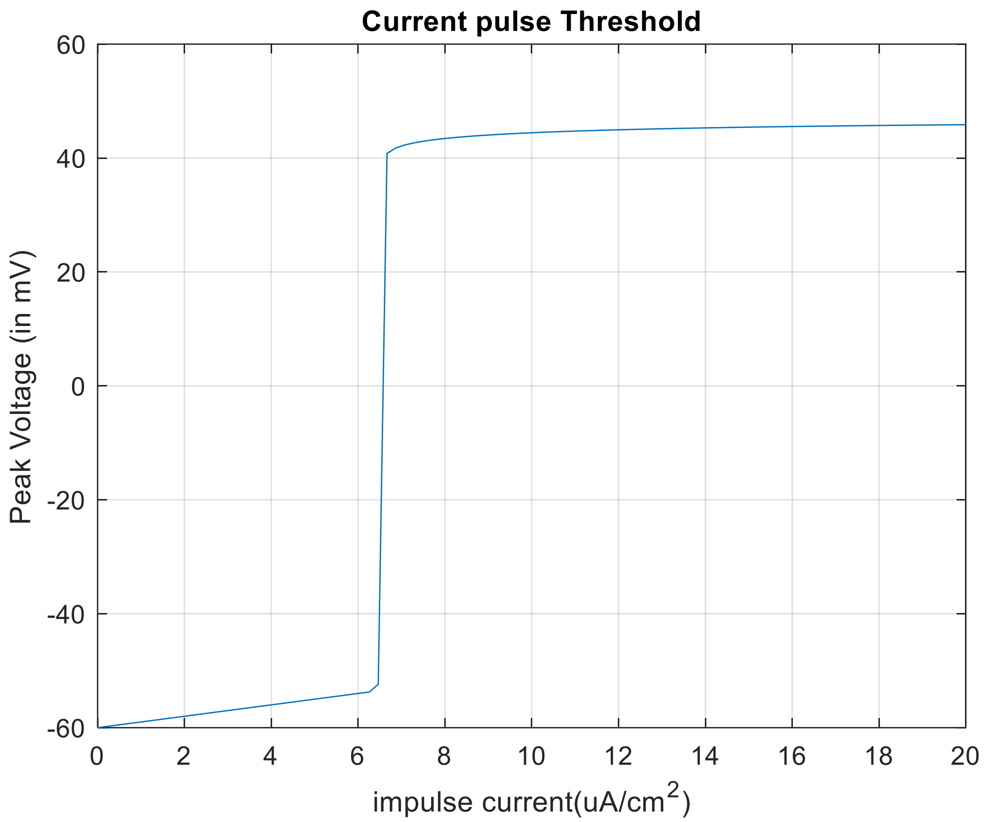


14. Equilibrium Point : V=-60.000000 n=0.317677 m=0.052932 h=0.596121

The eigen values are -4.675345+0.000000i , -0.202718+0.383061i , -0.202718-0.383061i , -0.120659+0.000000i

Stable

Threshold: 6.565657 uA/cm^2



15.

Iext = 8

Equilibrium Point 1 : V=-55.355128 n=0.390607 m=0.090048 h=0.430515

The eigen values are -4.690140+0.000000i , -0.034549+0.566792i , -0.034549-0.566792i , -0.135013+0.000000i

Stable

Iext = 9

Equilibrium Point 1 : V=-54.952404 n=0.397027 m=0.094133 h=0.416502

The eigen values are -4.730588+0.000000i , -0.014865+0.578298i , -0.014865-0.578298i , -0.136960+0.000000i

Stable

Iext = 10

Equilibrium Point 1 : V=-54.572150 n=0.403092 m=0.098131 h=0.403419

The eigen values are -4.774093+0.000000i , 0.004122+0.588328i , 0.004122-0.588328i , -0.138902+0.000000i

Unstable

Iext = 11

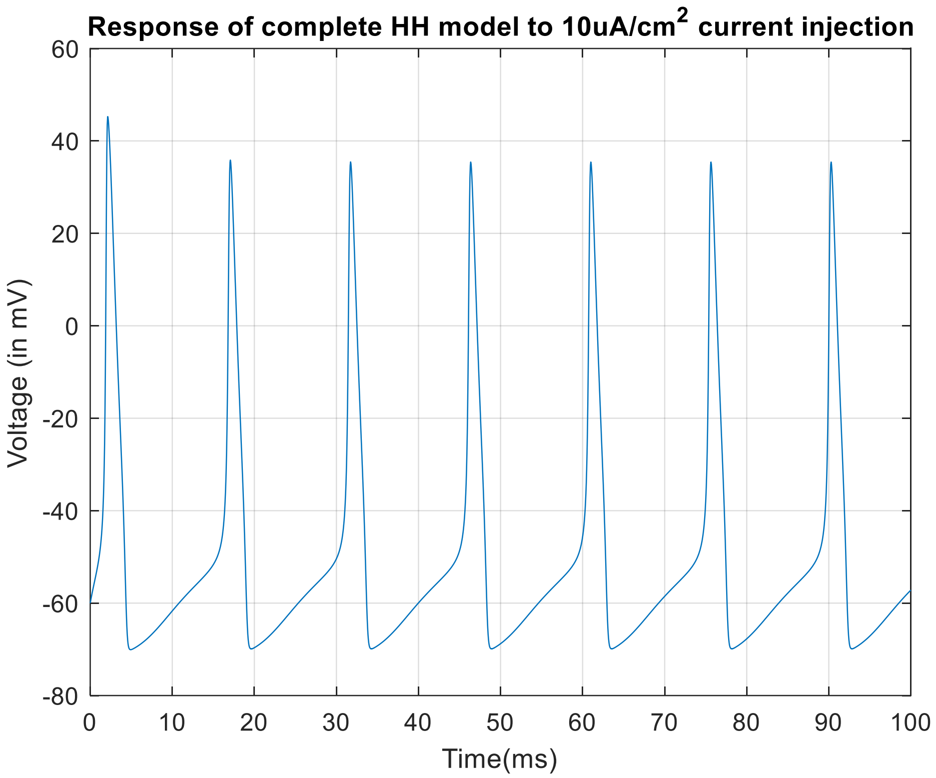
Equilibrium Point 1 : V=-54.211777 n=0.408841 m=0.102052 h=0.391169

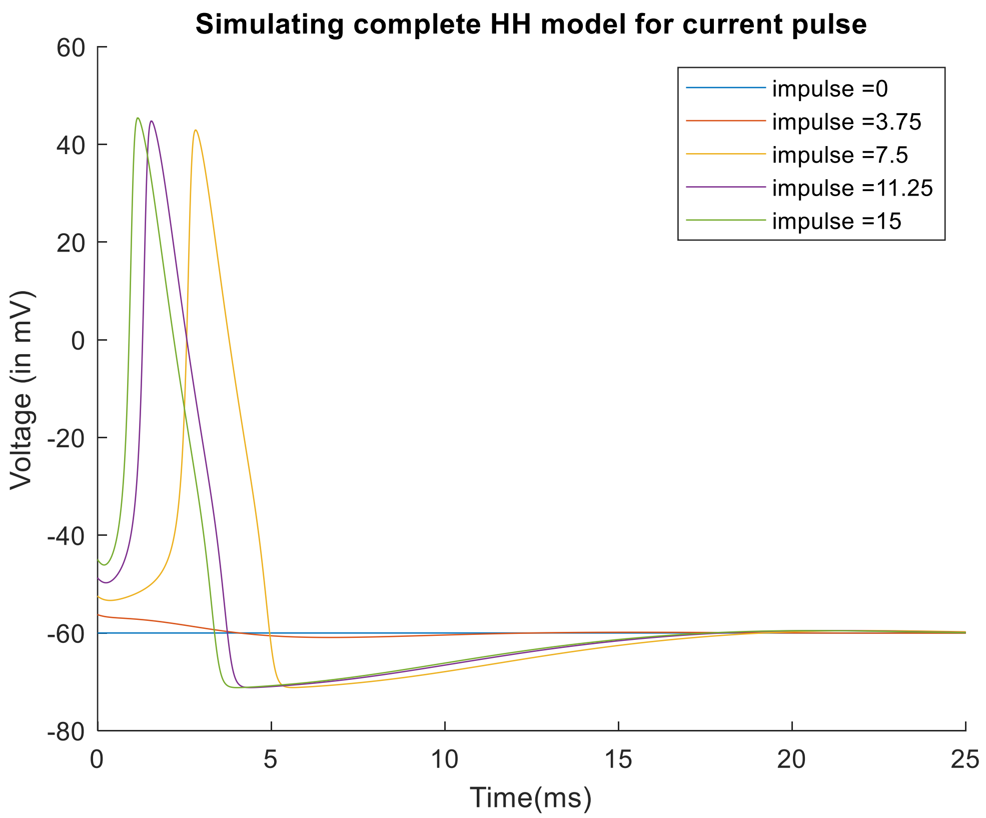
The eigen values are -4.819956+0.000000i , 0.022390+0.597090i , 0.022390-0.597090i , -0.140836+0.000000i

Unstable

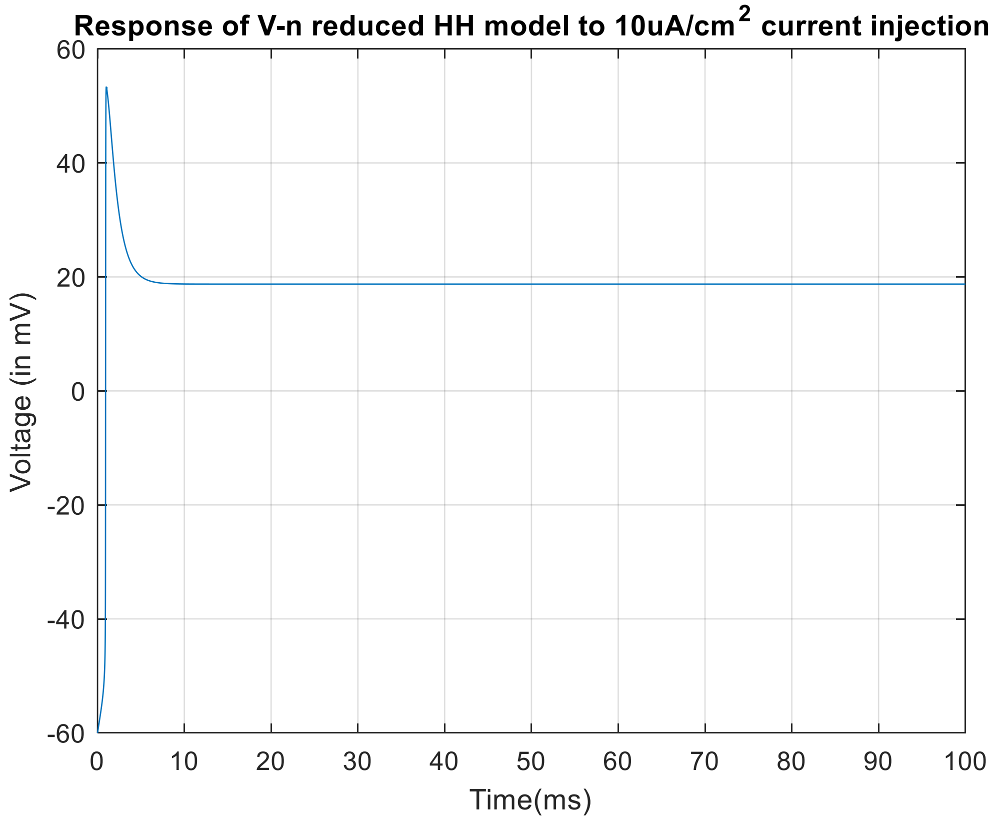
Iext = 12
Equilibrium Point 1 : V=-53.869127 n=0.414306 m=0.105899 h=0.379667
The eigen values are -4.867630+0.000000i , 0.039926+0.604761i , 0.039926-0.604761i , -0.142760+0.000000i
Unstable

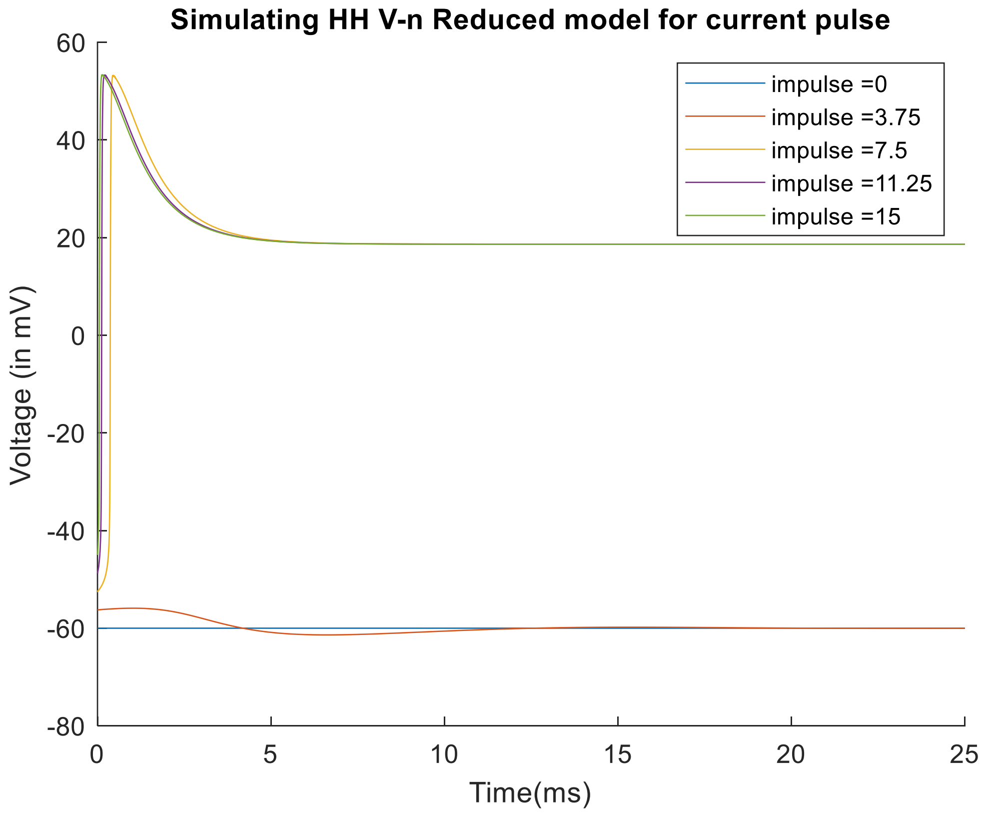
16. Comparison of complete and V-n reduced Hodgin Huxley system
Complete System:





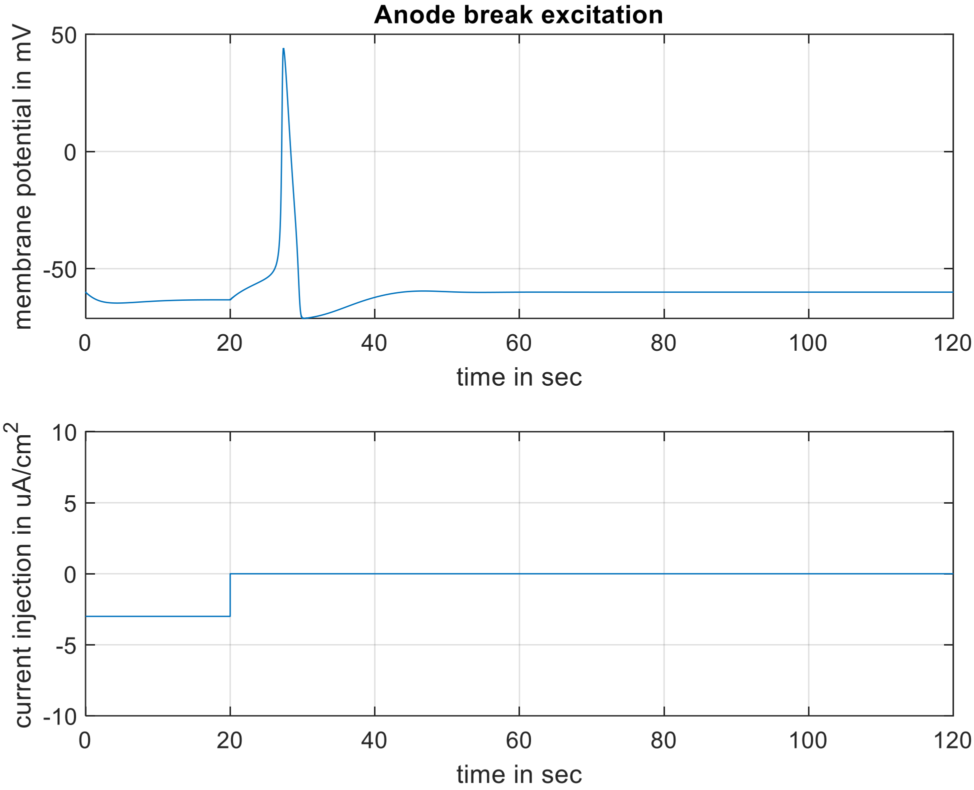
V-n reduced HH system





The complete and the V-n reduced HH system both show the same threshold but the V-n reduced system only generates one action potential since the h gates are not allowed to close since they are fixed at h_inf(Vr) (Vr is the resting membrane potential). So increase in V_m results in increase in m, which in turn increases V_m. But after reaching +20mV the h gates are still open so the potential doesn't fall. The spikes are very sharp in the reduced system because m is assumed to reach m_inf(V) instantly and also the opposing effect of h gates has been removed.

17. Anode Break Excitation



When current injection is negative, the membrane potential decreases. m, n are activation gates and h is an inactivation gate. So as V_m falls, m and n both decrease and h increases. When current injection is stopped, V_m quickly reaches V_r (resting membrane potential). Time constant of m<<n<h. So m quickly reaches m_inf(V_r). Since h is the slowest varying, it is at a higher value while n is low. So the inflow of Na+ ions is much higher than what it is at V_r normally. n is low so K+ ions are unable to leave the cell soma. Na+ current causes membrane potential to rise and start the positive feedback between V and m that generates an action potential. If m,n,h all were to have the same time constant, ABE would be impossible.

18.

Stability analysis for Iext = -3 uA/cm^2

Equilibrium point 1 : The eigen values are -0.610135+0.000000i , -5.823581+0.000000i

------------stable---------------

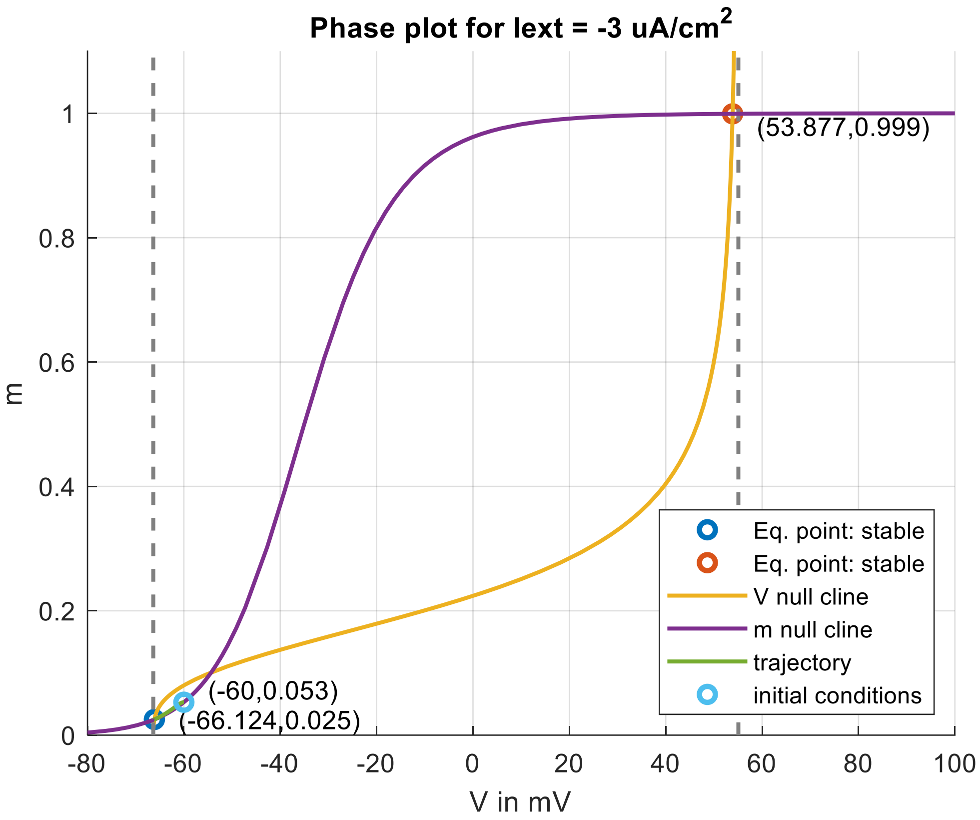
Equilibrium point 2 : The eigen values are -72.030536+0.000000i , -8.894267+0.000000i

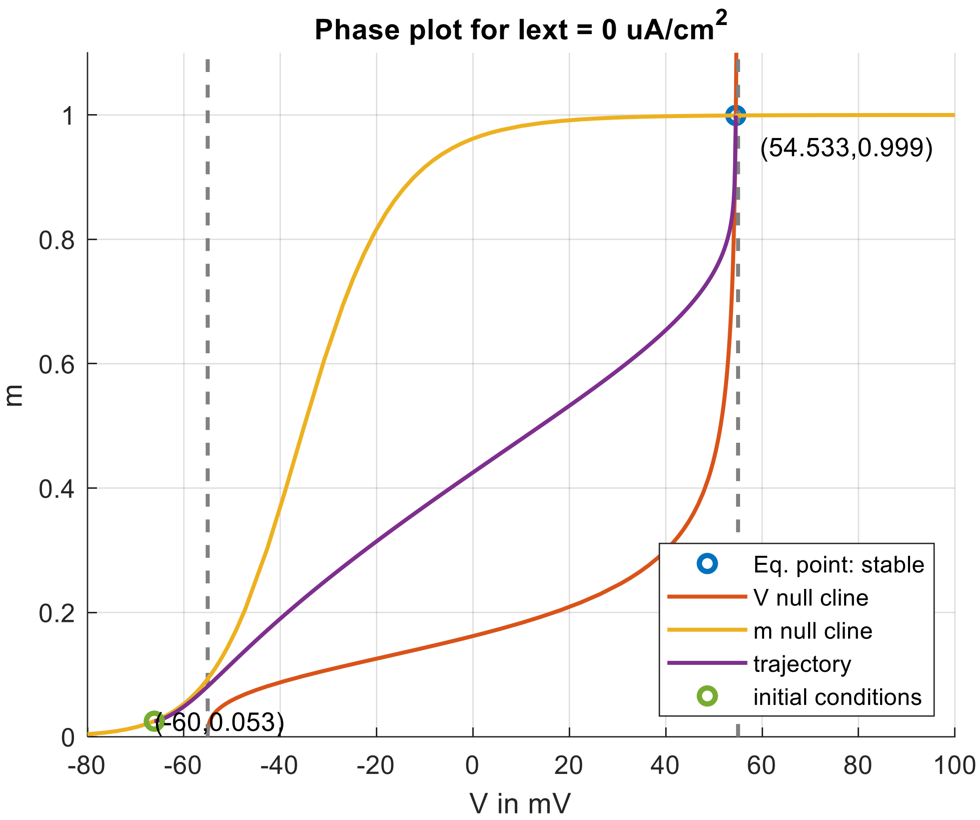
------------stable---------------

Stability analysis for Iext = 0 uA/cm^2

Equilibrium point 1 : The eigen values are -94.198758+0.000000i , -8.960666+0.000000i

------------stable---------------





For I_ext = -3 uA/cm^2 there is a stable equilibrium point near the resting membrane potential. When current injection is removed i.e I_ext is changed to 0 uA/cm^2, in the new system there is no equilibrium point near V_r. There is still one stable equilibrium point at ~ +40mV. This is where the trajectory ends and in moving from near V_r to +40mV we observe an action potential.

Sohini Gupta (20EE38032)