EC60007 Project-2

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Part-1: Morris Lecar Equations (MLE)

1. Proof that the given units are a consistent set of units:

Given units:

$t \rightarrow ms$ (time)

$I \rightarrow \mu A/cm^2$ (current / (flux))

$V \rightarrow mV$ (Voltage)

$C \rightarrow \mu F/cm^2$ (capacitance)

$G \rightarrow mS/cm^2$ (conductance)

① Ohms law

$$V = \frac{I}{G}$$

$$\Rightarrow \text{Volt}(V) = \frac{\text{Ampere}(A)}{\text{Seimens}(S)}$$

$$\Rightarrow V = \left(\frac{10^{-6} \times A/cm^2}{10^{-3}\ S/cm^2}\right) \times 10^3$$

$$\Rightarrow 10^{-3} \times V = \frac{10^{-6}\ A/cm^2}{10^{-3}\ S/cm^2}$$

$$\Rightarrow mV = \frac{\mu A/cm^2}{mS/cm^2}$$

$\Rightarrow$ Ohms law verified for these set of units

② $q = CV$

$$\Rightarrow i = C\frac{dV}{dt}$$

$$\underbrace{A}_{\text{Ampere}} = \underbrace{F}_{\text{Farad}}\ \frac{\overbrace{(V)}^{\text{volt}}}{\underbrace{(S)}_{\text{second}}}$$

$$\Rightarrow \frac{10^{-6} \times A}{cm^2} = \frac{10^{-6} \times F}{cm^2} \times \frac{(10^{-3} \times V)}{(10^{-3} \times s)}$$

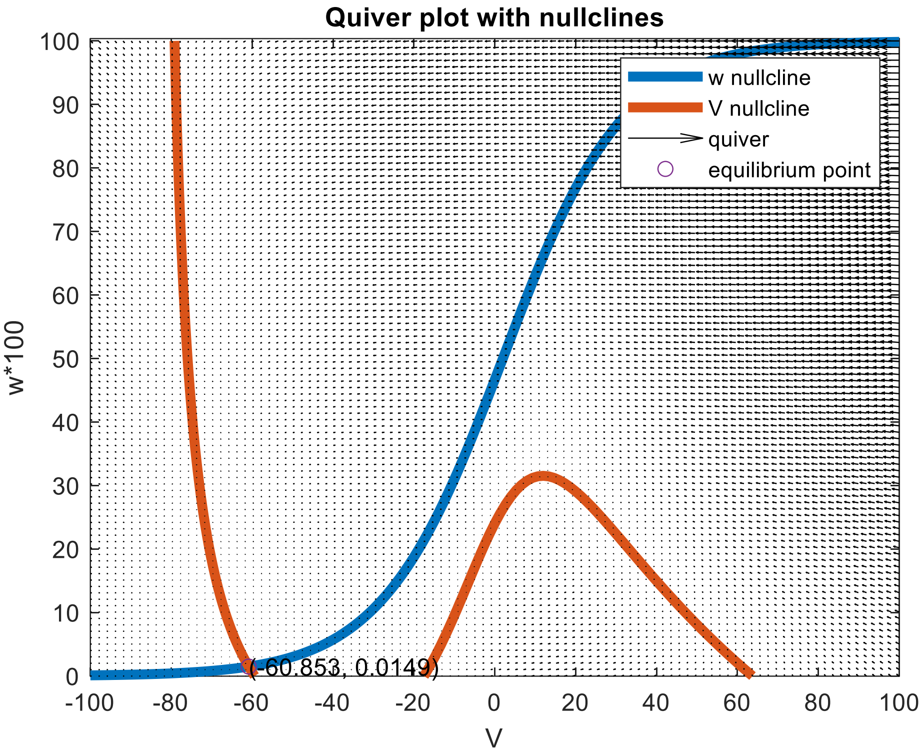
$$\Rightarrow \mu A/cm^2 = (\mu F/cm^2)\frac{(mV)}{(ms)}$$

$\Rightarrow$ Formula ② verified for the given set of units

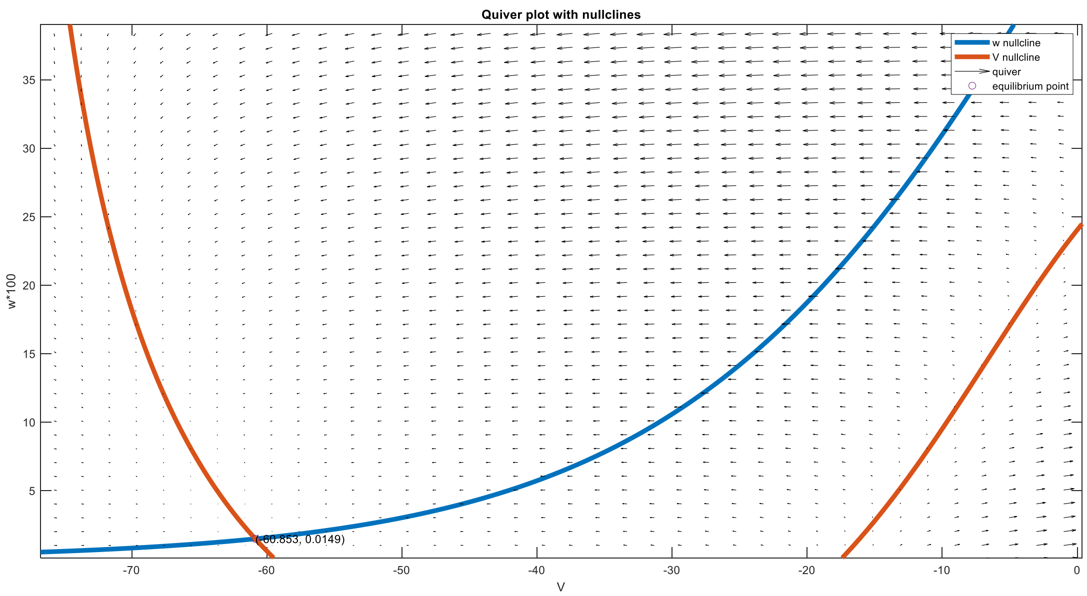
If unit of conductance is µS/cm^2, the unit of current must also be changed to µA/cm^2, to be consistent for Ohm's law, as shown above.

No, the solution is not unique, as the units of capacitance, voltage etc. can be changed to make the system of units consistent.

2. The two different methods to calculate the equilibrium point with Iext = 0 are:
    - Finding the intersection point of the two nullclines.
    - Finding the value of Veq by solving V nullcline = 0 and then substituting the value of Veq to find weq.



Zoomed in quiver plot near the equilibrium point (-60.853, 0.0149) shows the arrows converging into the equilibrium point, indicating that it is a stable equilibrium point.



3. Computing the Jacobian and deducing stability

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3. computing jacobian to find eigenvalue of eqm point and deduce stability
The jacobian is:
[    -0.10042615477026999446346998799143,  -9.2578471070762035291461890021775]
[0.000080808599610082574108150914545472, -0.082499470338981838302896218370 35]

The eigen values are:
- 0.091462812554625916383183103180889 + 0.025841287824958238650010236584772i
- 0.091462812554625916383183103180889 - 0.025841287824958238650010236584772i

Therefore the stability = Equilibrium point is stable and spiral
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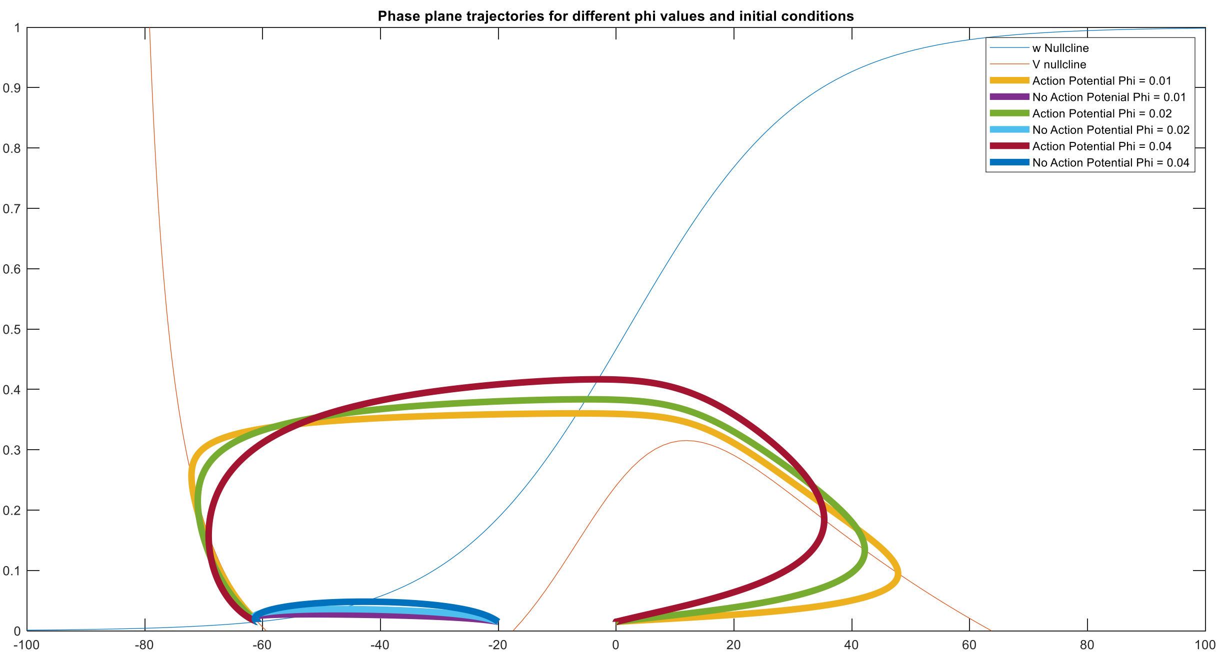
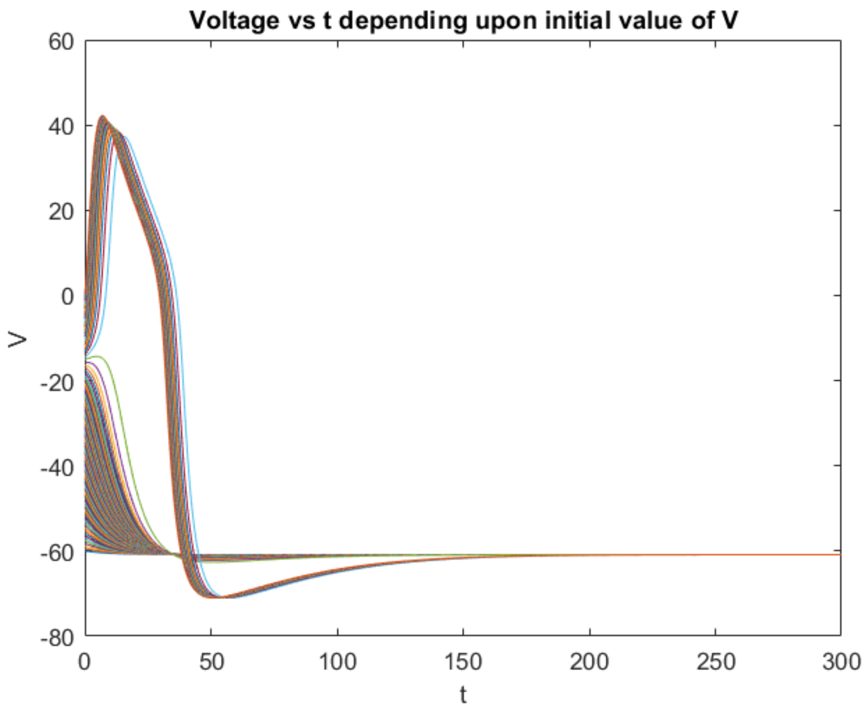
4. The default numerical tolerance values built into Matlab (AbsTol = 10^{-6} and RelTol = 10^{-3}) are reasonable for MLE because the parameters of MLE with the given set of units are accurate up to the 3rd decimal, and hence an absolute tolerance of the order 10^-6 is sufficient. If the unit of voltage variable is changed to kV from mV, the Veq value will be approximately -0.000060853, which is accurate till the 9th decimal place, hence AbsTol = 10^{-6} is not sufficient, it should be changed to at least AbsTol = 10^{-12}.

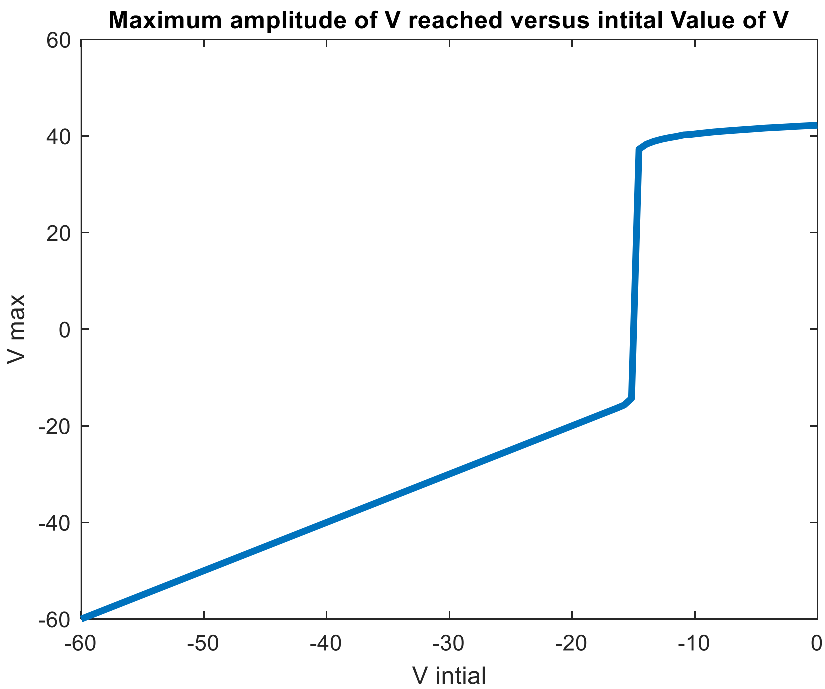
5.



For an initial condition that can generate an action potential, it is observed from the above graphs that as phi is increased the maximum positive voltage reached decreases, but the onset of the action potential happens faster. Since phi is known as the ‘temperature’ factor and is used to control the time constants, the above observation is valid.

6.





Yes, the MLE with the given set of parameters does show threshold depolarization as it rapidly increases after a particular initial voltage. However, it is not a 'true threshold'. This is because after it reaches the condition of suprathreshold, the maximum amplitude does not remain constant, but gradually increases. Hence, the action potential is not showing 'all or none' behaviour.

7. Investigation the effect of Iext on nullclines, equilibrium points and trajectories

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7. Investigating effect of Iext on nullclines, equilibrium point and trajectories with different initial conditions
For Iext = 86, stability = Equilibrium point is stable and spiral
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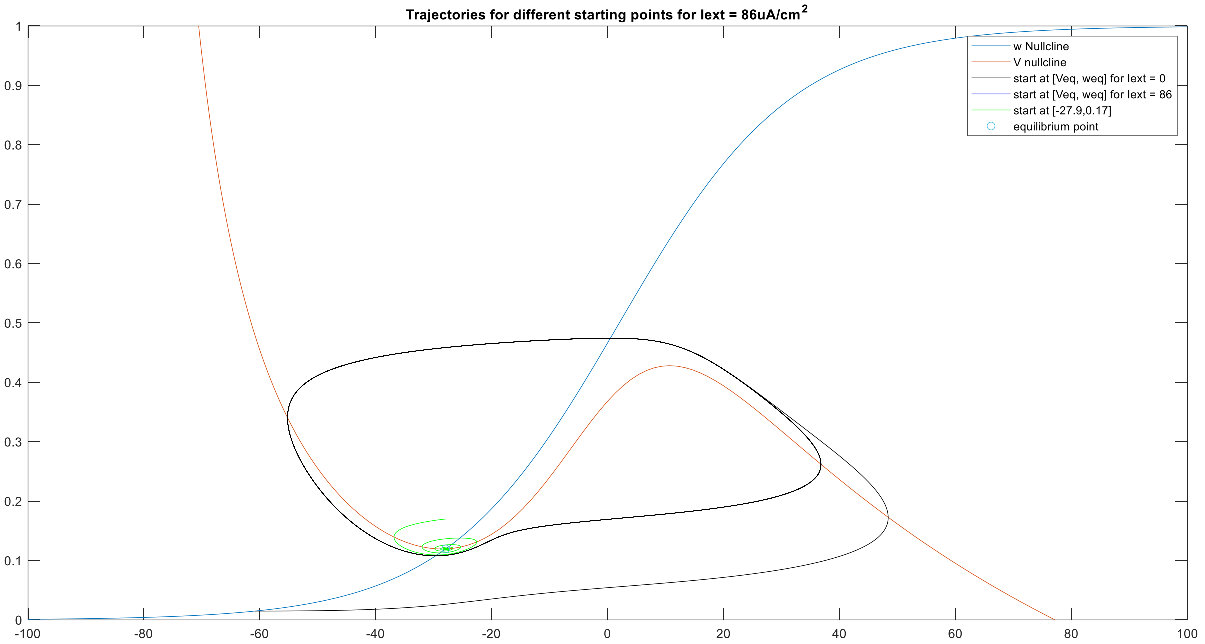


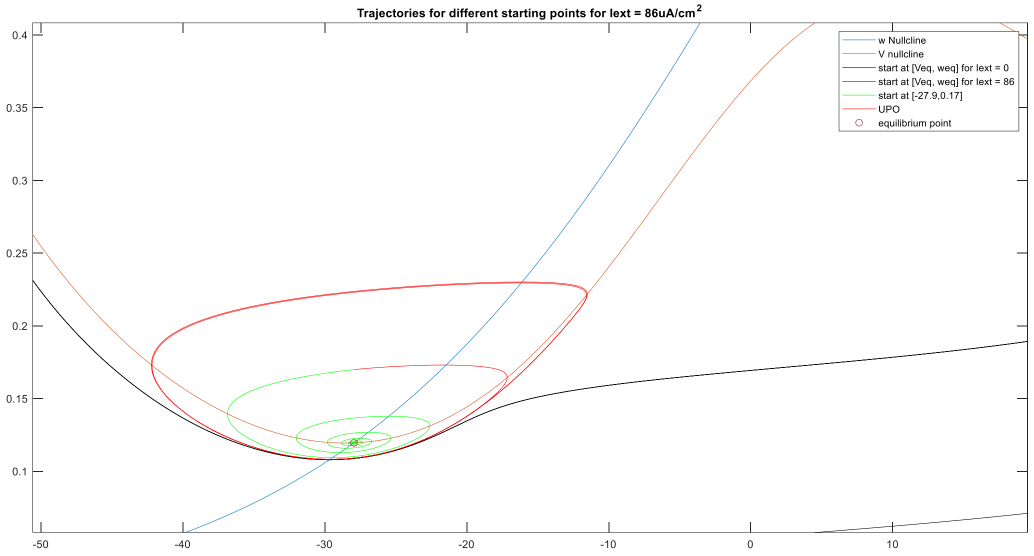
Case-1: When initial conditions are set to the equilibrium point for Iext = 0, the trajectory forces into a limit cycle.

Case-2: When initial conditions are set to the equilibrium point for Iext = 86, there is no emerging trajectory, and, as expected, the point remains at the equilibrium point.

Case-3: When initial conditions are set close to the equilibrium point for Iext=86, the trajectory spirals into the equilibrium point.

In Case-1, action potentials are generated once the limit cycle begins. This method can be used to observe the rate of firing in an experiment. The observation in case-2 can be used in an experiment to determine stability of equilibrium point.

8. Plot showing unstable periodic orbit



The dark red line shows the unstable periodic orbit (UPO). Any point that lies outside the UPO ends up on the limit cycle and any point that lies inside the UPO ends up on the stable spiral point. In this way, the UPO acts as true threshold.

9. Checking the equilibrium point for different values of Iext

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9. Checking the equilibrium pointd for various Iext
Iext = 80, Equilibrium point [V,n] = [-29.97,0.11], Stability = Equilibrium point is stable and spiral
Iext = 86, Equilibrium point [V,n] = [-27.95,0.12], Stability = Equilibrium point is stable and spiral
Iext = 90, Equilibrium point [V,n] = [-26.60,0.13], Stability = Equilibrium point is stable and spiral
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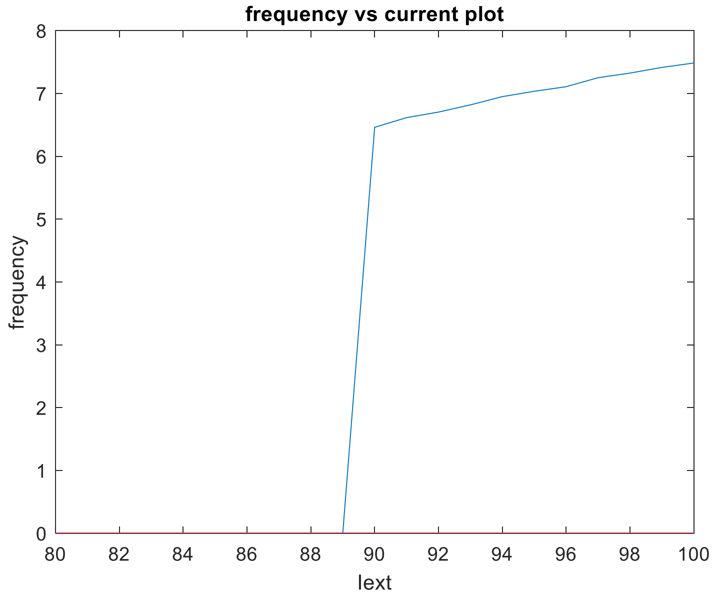
Plot of rate of firing vs current



10. Analysis of MLE for parameter set 2

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10. MLE for parameter set-2
Equilibrium point 1, [Veq, weq] = [-41.85, 0.00], Stability = Equilibrium point is stable
Equilibrium point 2, [Veq, weq] = [-19.56, 0.03], Stability = Equilibrium point is saddle point
Equilibrium point 3, [Veq, weq] = [3.87, 0.28], Stability = Equilibrium point is unstable and spiral
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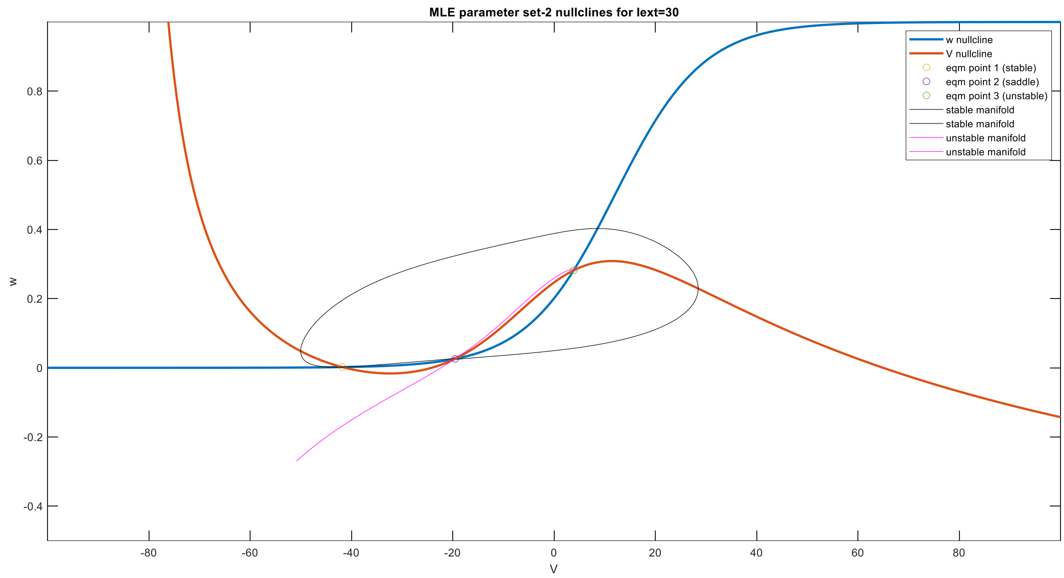
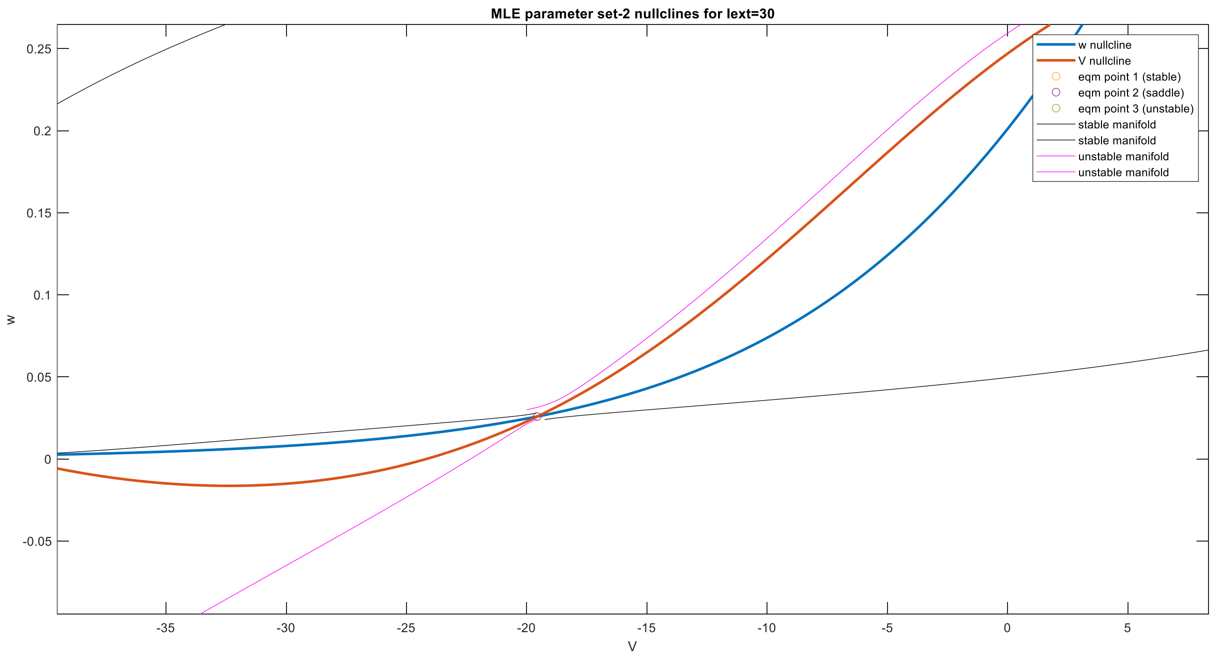
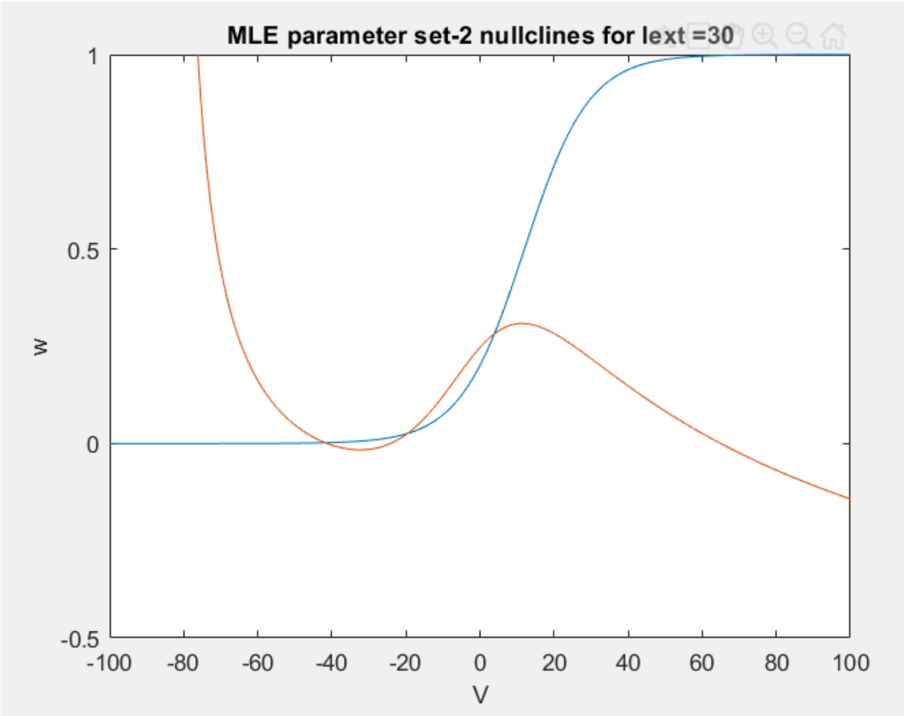
Plot of nullclines, equilibrium points and manifolds for MLE parameter set-2

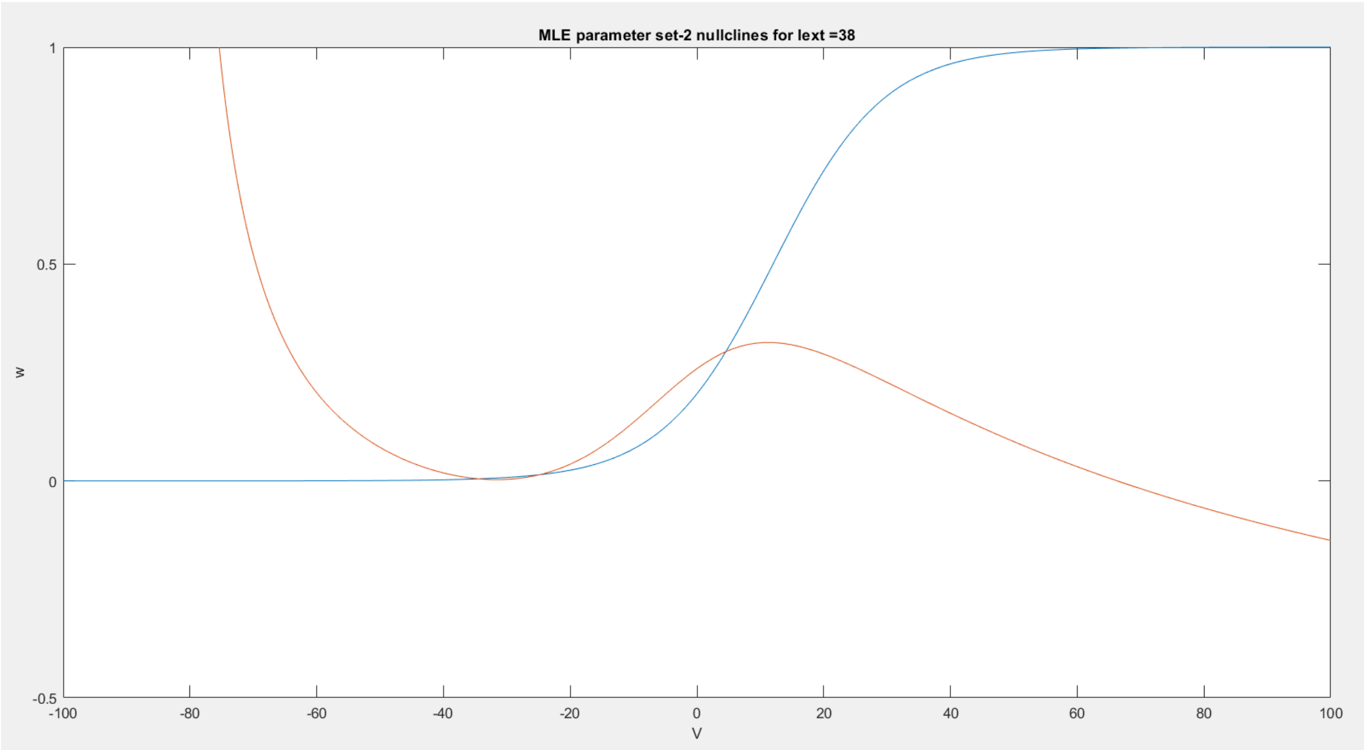


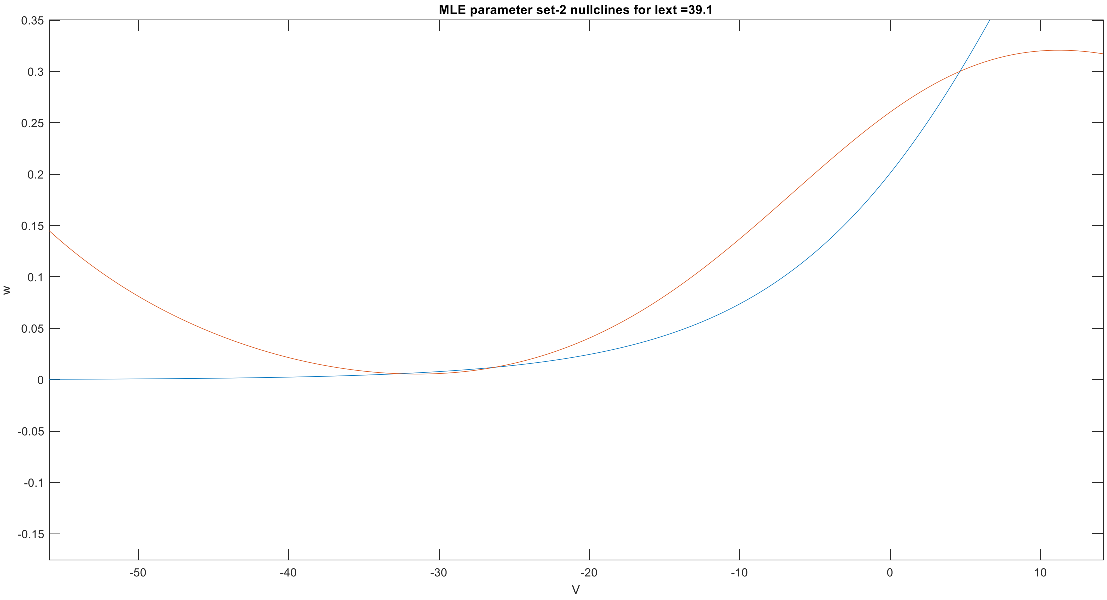
Zoomed in near the stable equilibrium point

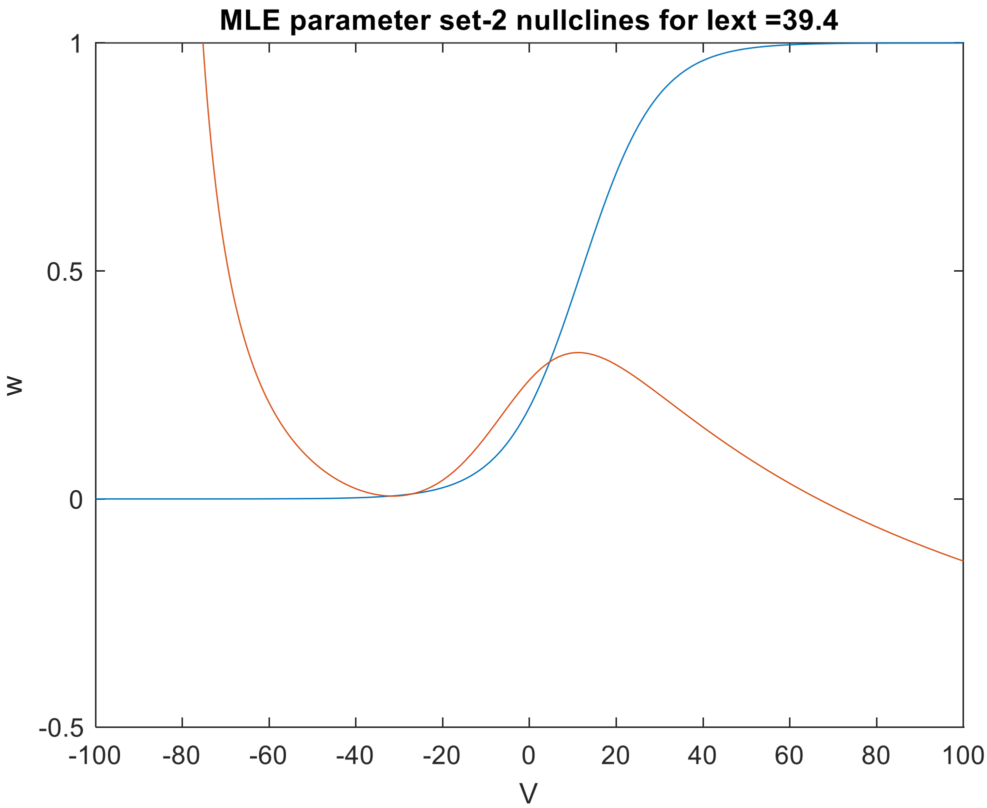


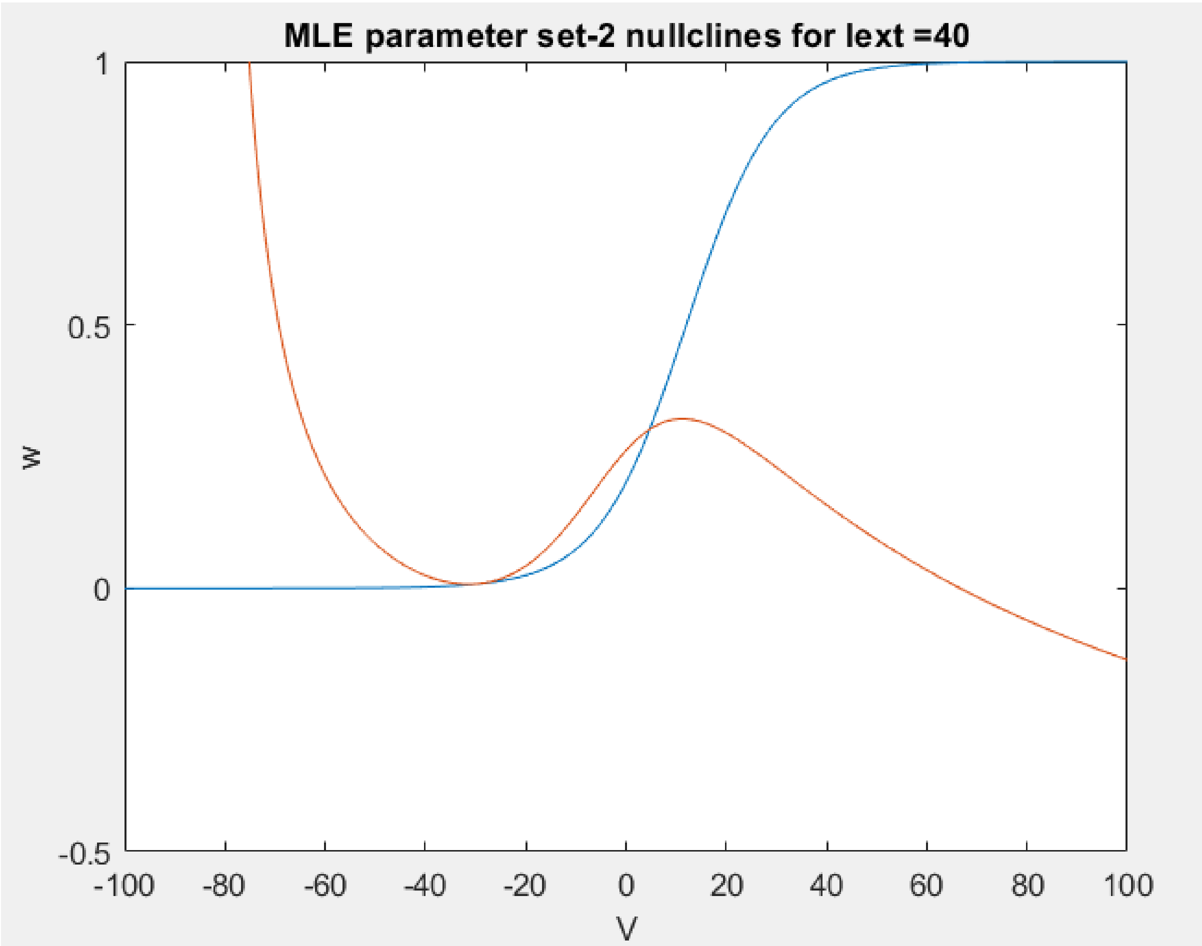
11. Phase plane plots of MLE parameter set 2 for different values of Iext

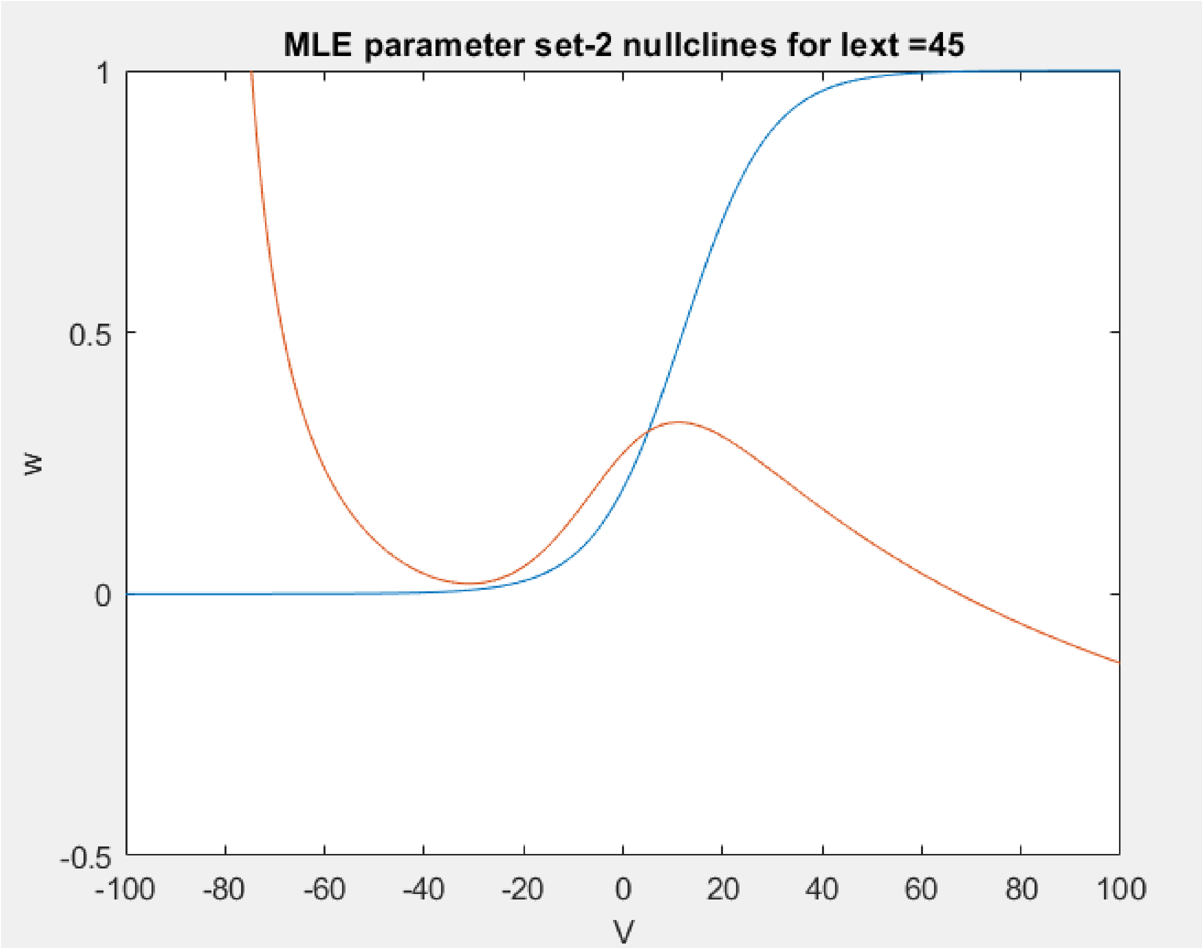


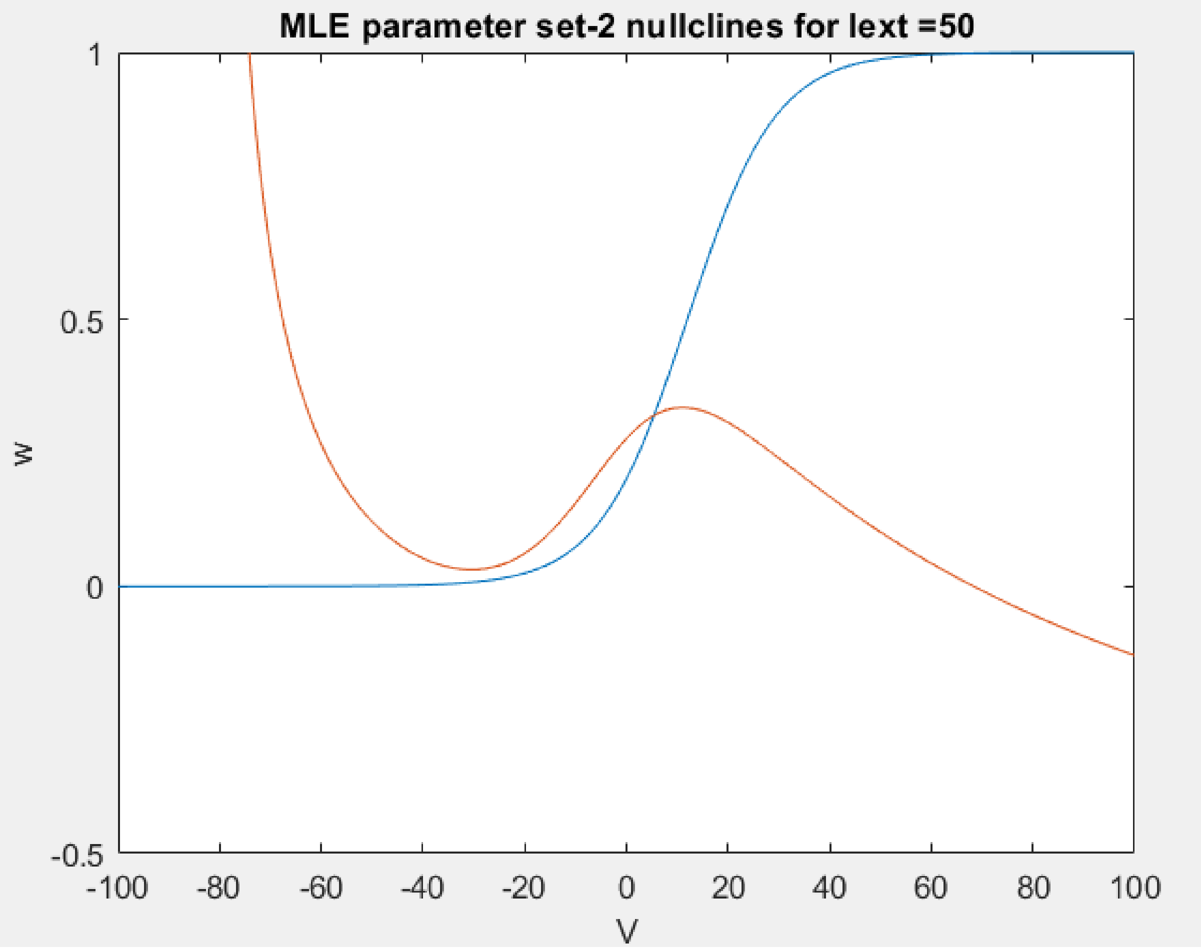


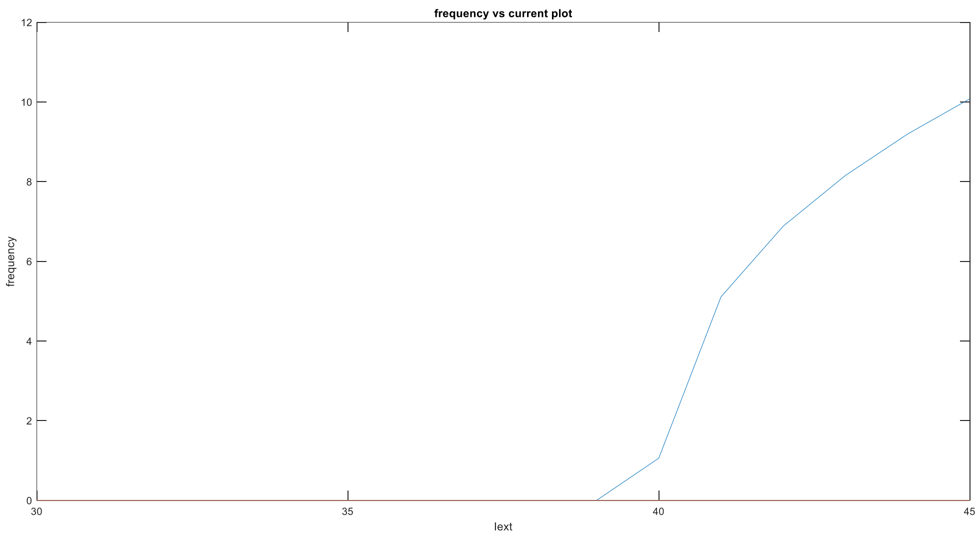

MLE parameter set-2 nullclines for Iext =39.1
w
V
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
-0.05
-0.1
-0.15
-50
-40
-30
-20
-10
0
10


MLE parameter set-2 nullclines for Iext =39.4
w
V
1
0.5
0
-0.5
-100
-80
-60
-40
-20
0
20
40
60
80
100


MLE parameter set-2 nullclines for Iext =40
1
0.5
0
-0.5
-100
-80
-60
-40
-20
0
20
40
60
80
100
w
V


MLE parameter set-2 nullclines for Iext =45
w
V
1
0.5
0
-0.5
-100
-80
-60
-40
-20
0
20
40
60
80
100





As shown above, from Iext = 30 to 39, there are 3 equilibrium points, somewhere between 39 and 40; the saddle and stable points annihilate each other.

Also, from Iext = 40 to 50 there is only 1 equilibrium point. The frequency vs current plot indicates that firing occurs after Iext = 39, and steadily increases subsequently.

Part-2: Hodgkin and Huxley model

12. To take care of an and am whose denominators and numerators both might become equal to 0 for certain values of V, a small term, (1e-12) is added to the denominator so that a 0/0 condition is not reached.

13. To find Eleak so that Vrest = -60 mV

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13. To find Eleak so that Vrest = -60mV
Eleak = -49.40
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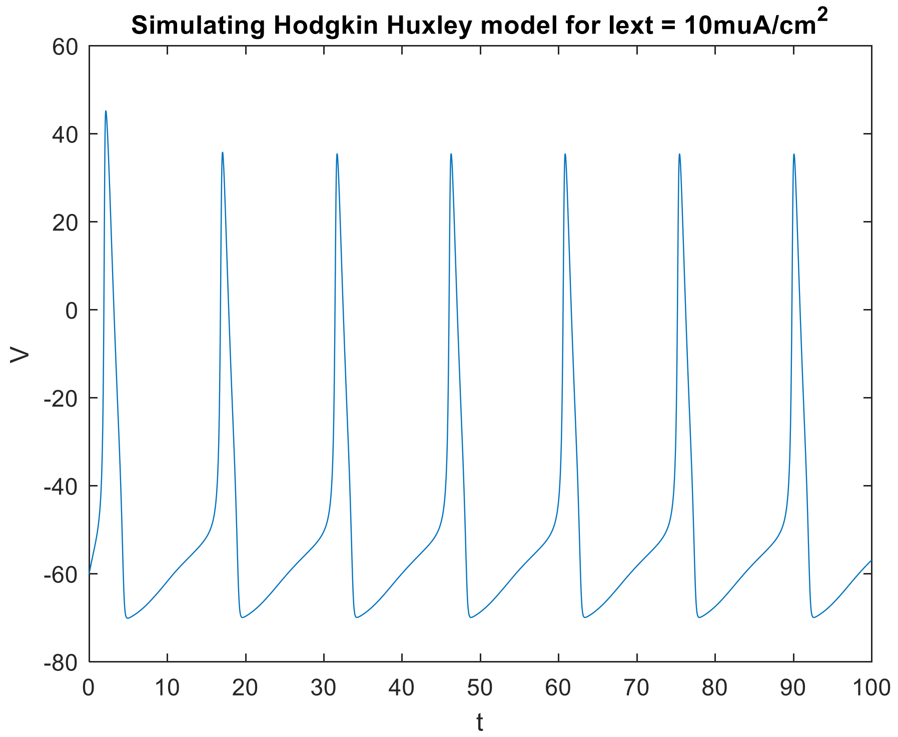

14. Results

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14. To check stability of model at rest with Iext = 0 and to find threshold voltage
Iext = 0, stability = Equilibrium point is stable
Impulse current threshold = 6.46 Therefore, Voltage threshold = -53.54
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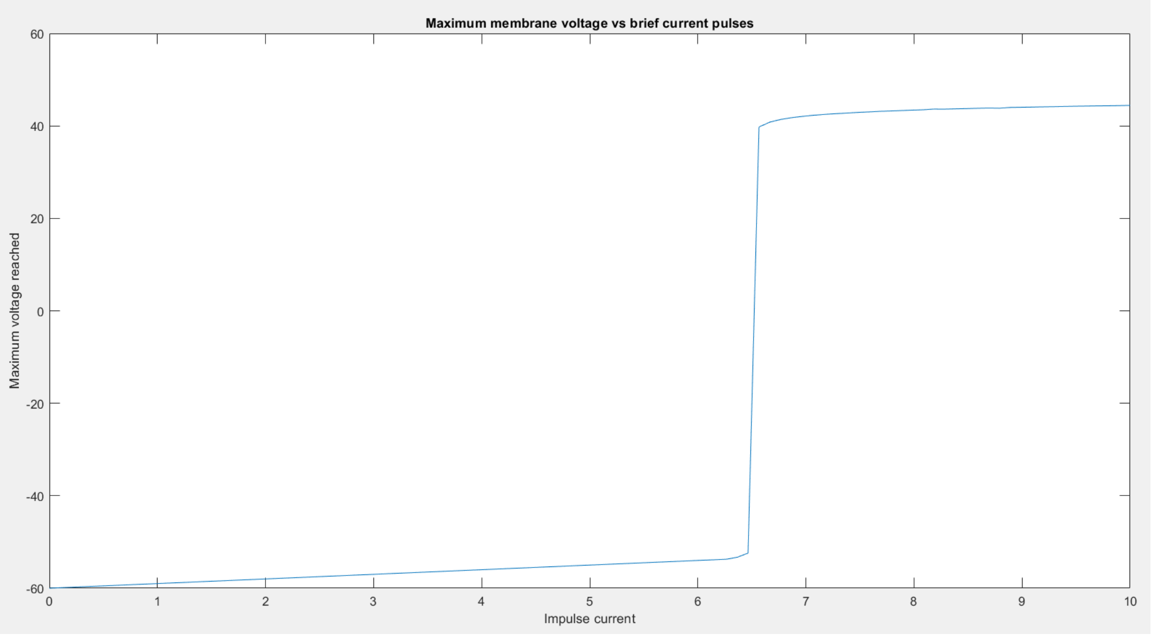
Plot of Maximum membrane voltage vs impulse current



15. Stability analysis result

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15. To check stability of equilibrium point for various Iext
Iext = 8, stability = Equilibrium point is stable
Iext = 9, stability = Equilibrium point is stable
Iext = 10, stability = Cant say
Iext = 11, stability = Cant say
Iext = 12, stability = Cant say
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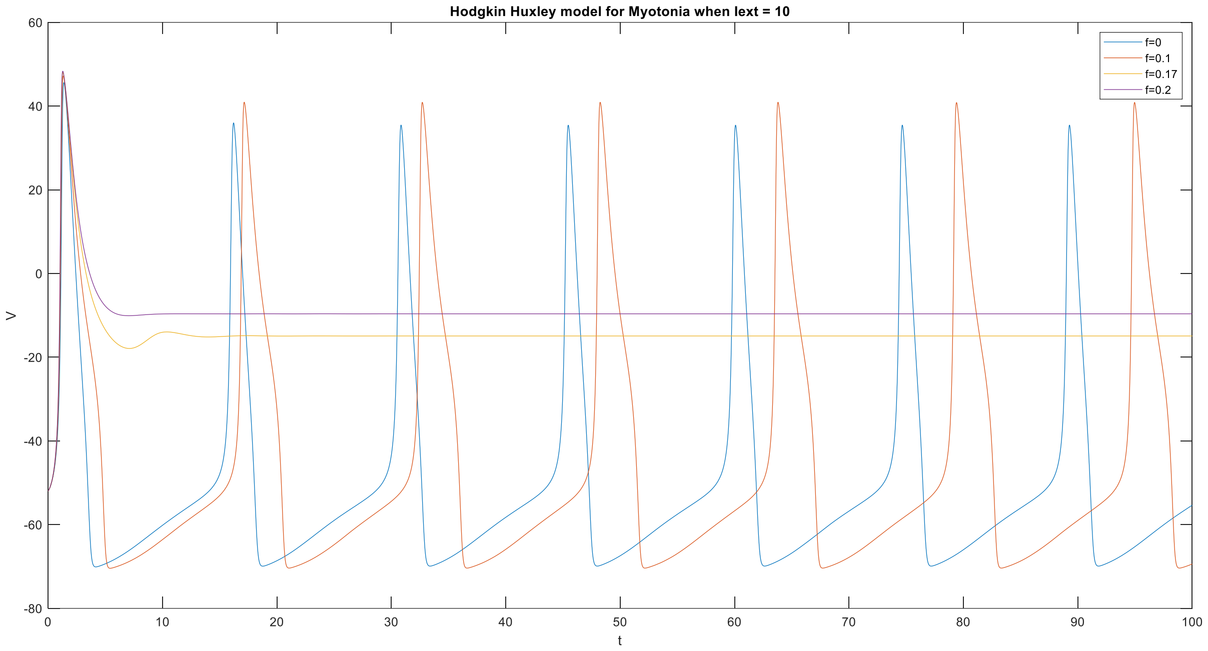
16. Plot of membrane potential V vs. time for modified HH model for Mytonia

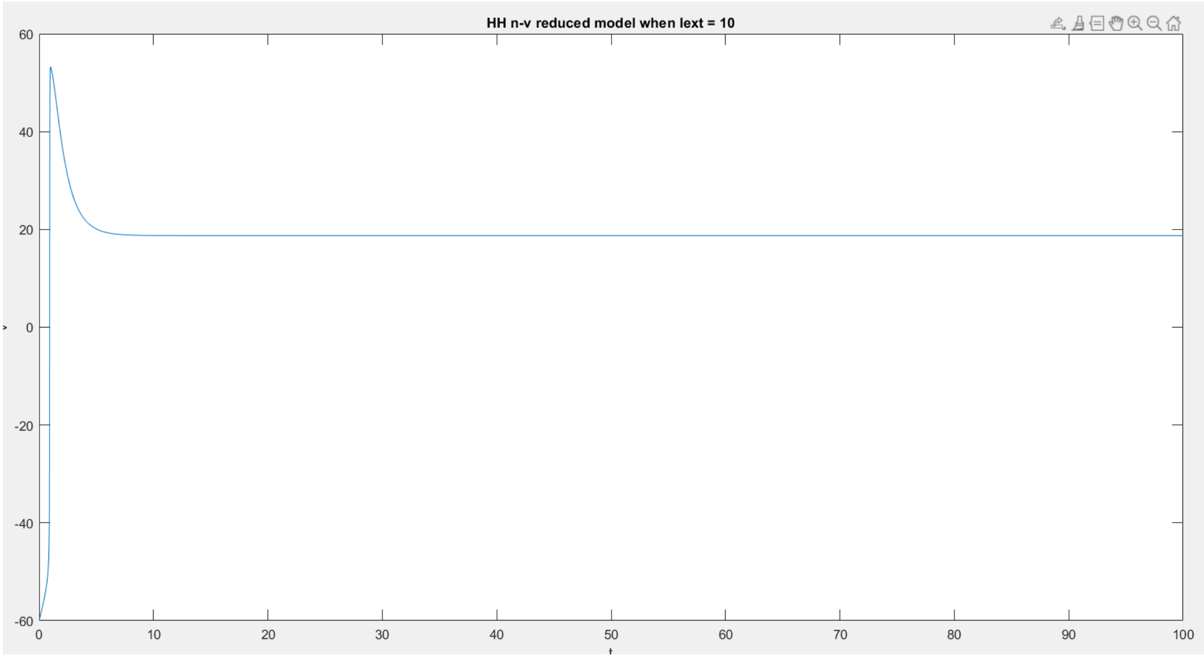


Here, f denotes the fraction of Na+ channels that do not inactivate, so that the sodium current in the modified HH model is given by

$I_{Na} = g_{Na}\,(1\text{-}f)m^3h(V\text{-}E_{Na}) + g_{Na}m^3(V\text{-}E_{Na})$

For f = 0 and f = 0., action potential is produced but for f = 0.17 and f = 0.2, no action potential is produced. Although action potential is produced for f = 0.1, the shape is different, it takes more time to return back to Vrest since the number of inactivation gates are reduced.

17. Plot of HH n-v reduced model started at Vrest with Iext = 10



A rise in membrane voltage is observed, that finally saturates to reach a steady potential. The general behaviour is similar to the full model, but there are a few differences. The refractory period is not visible in this plot, and it does not return to Vrest, but rather reaches a steady potential higher than that of Vrest.

Plot of maximum membrane voltage reached vs impulse current

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17. V-n reduced model of HH
Impulse current threshold = 4.14 µA/cm^2, Therefore, V threshold = -55.86 mV
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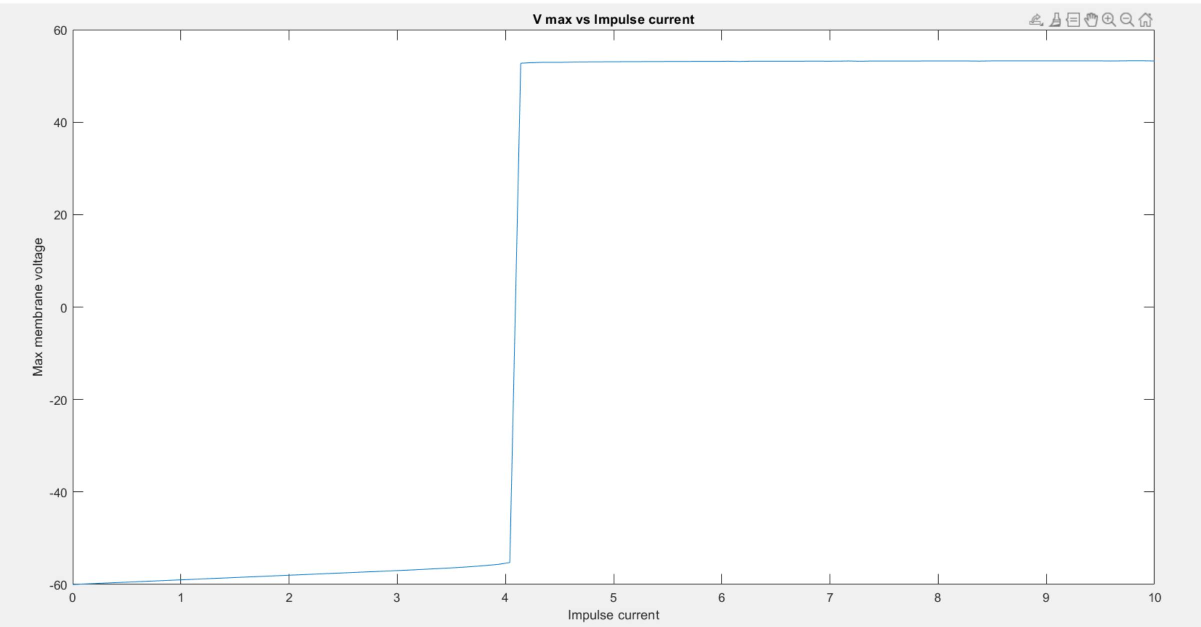
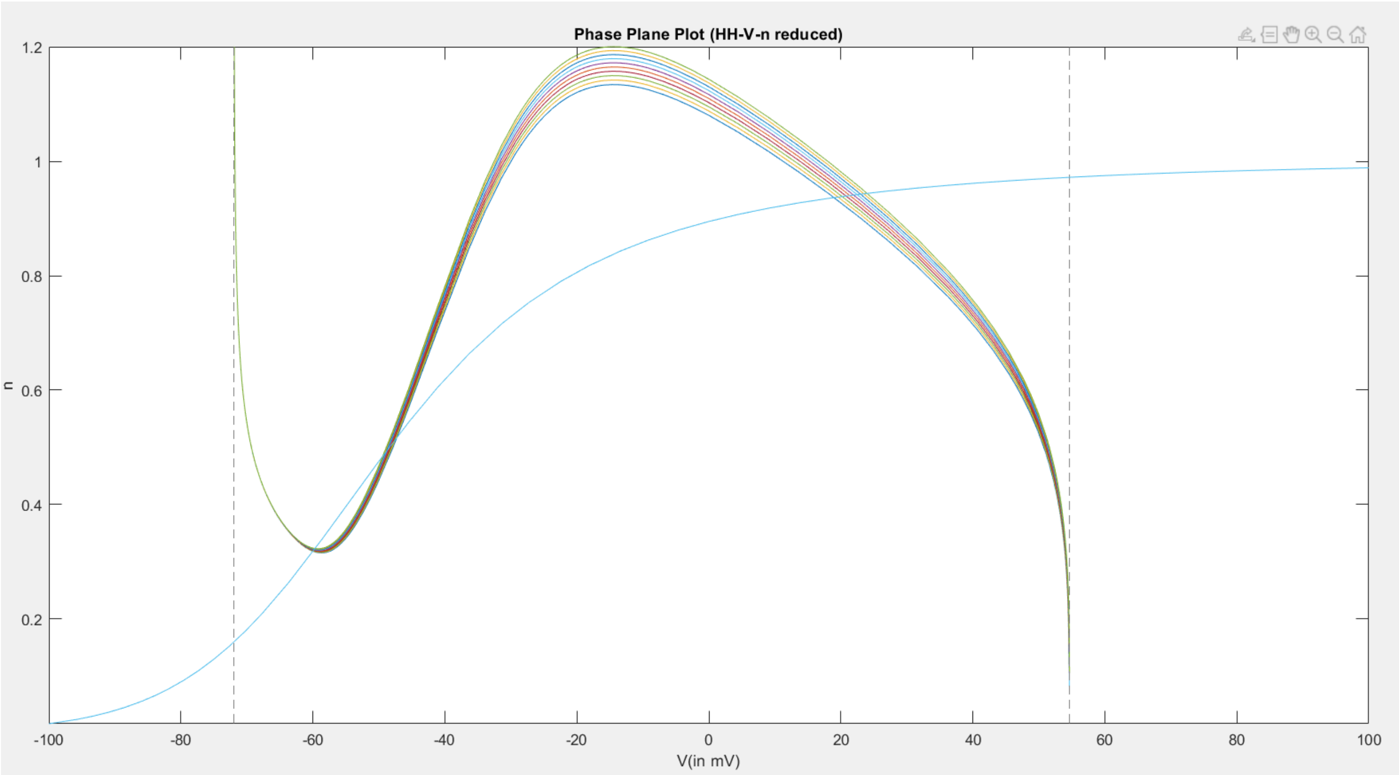
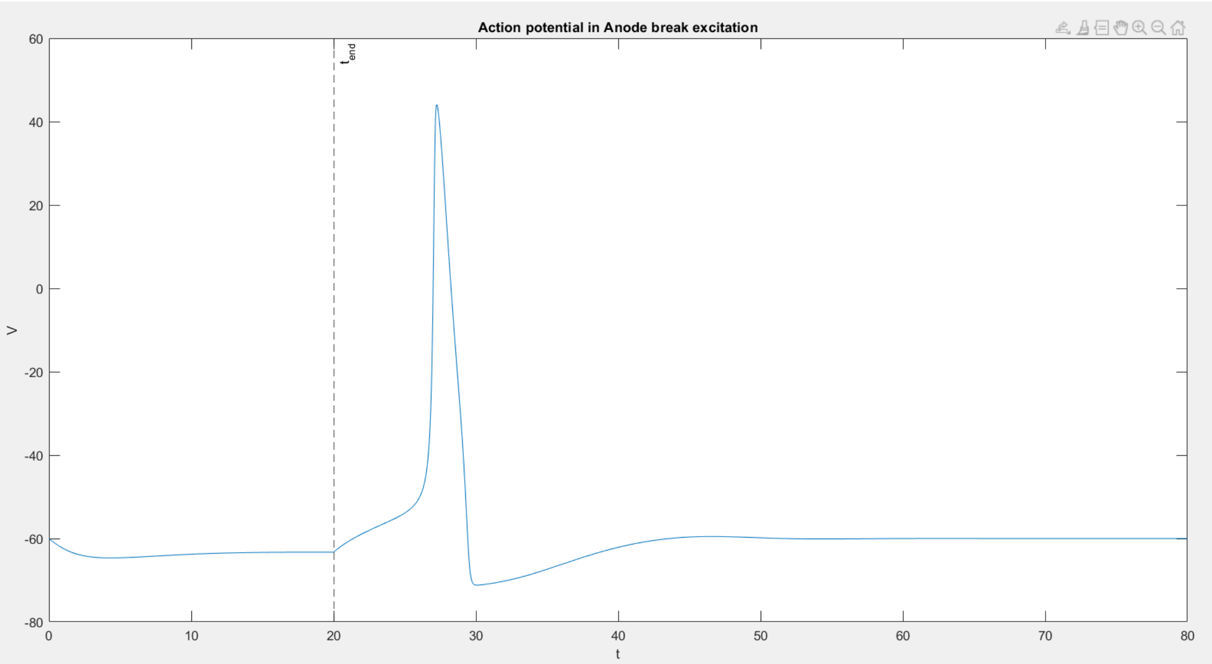


18. Plot of phase plane for HH V-n reduced system for different values of f

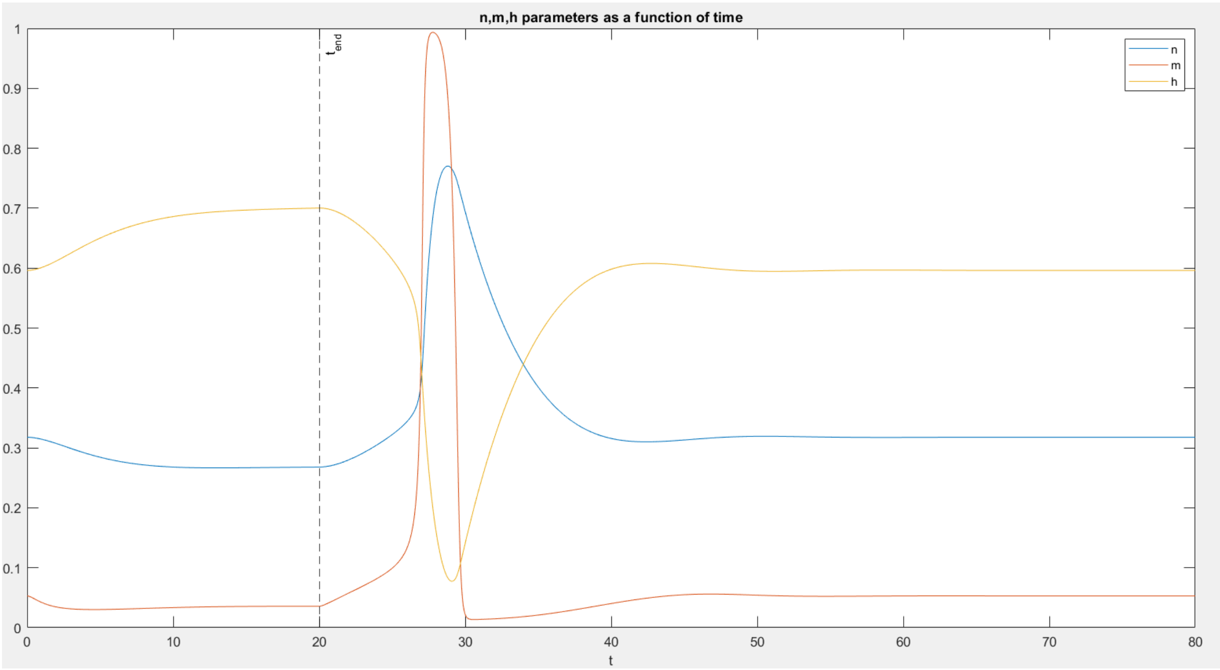


Change in f has no effect on n-nullcline, however as f increases the right part of the V nullcline tends to go down. There are 3 equilibrium points which are stable spiral, saddle and unstable.

19. Plot of action potential in anode break excitation

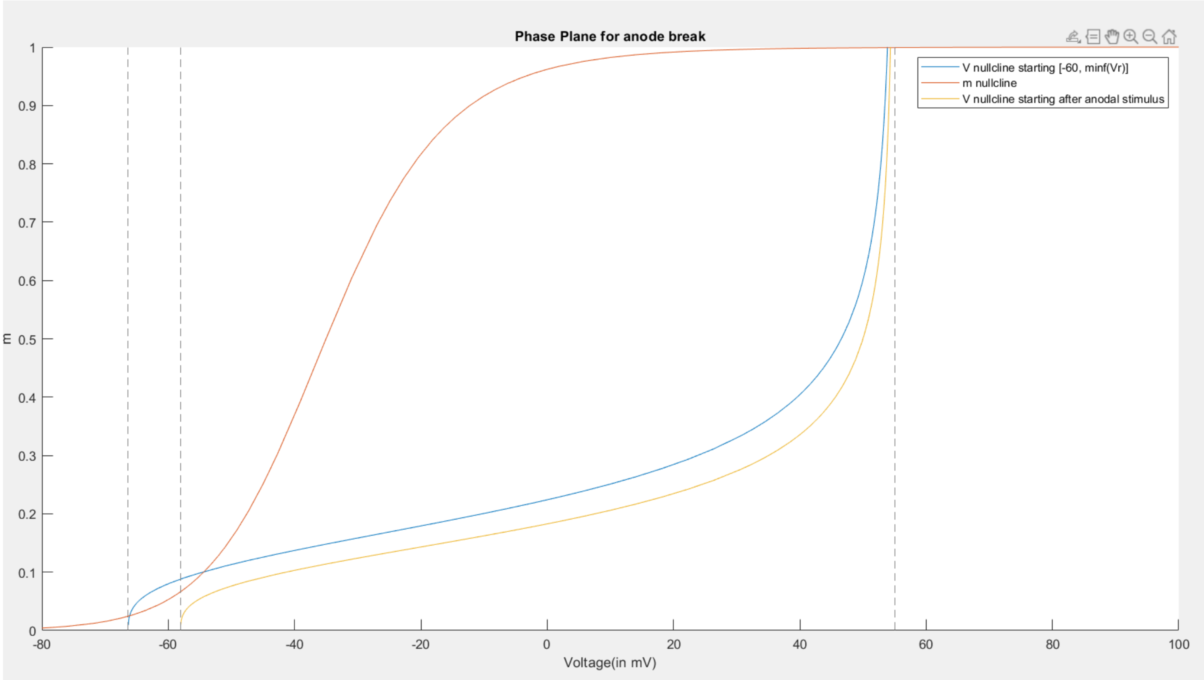


Plot of variation in n, m, h before and after the end time (t_{end}) of anodal stimulus



As shown above, after t_{end}, h is greater than h inf at Vrest and n is less than n inf at Vrest whereas m remains almost the same. This scenario is identical to that of a net positive current injection into the system. As observed before, this results in an action potential. This phenomenon is known as action potential due to anode-break excitation.

20. Plot of V-m phase plane for demonstrating anode break excitation:



Characterisation of equilibrium points for:

Part-1: Starting from the value where membrane potential is at rest, -60mV

Part-2: Starting from the value at the end of the anodal stimulus to produce the anode break excitation

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20. Anode break excitation in V-m reduced HH (in phase plane)
For part1
Equilibrium point 1 = -66.12, 0.03   Stability = Equilibrium point is stable
Equilibrium point 2 = -54.33, 0.10   Stability = Equilibrium point is saddle point
Equilibrium point 3 = 53.88, 1.00    Stability = Equilibrium point is stable

For part-2
Equilibrium point 1 = 54.35, 1.00    Stability = Equilibrium point is stable
```

As observed in part-1, the phase plane contains an equilibrium point close to Vrest, that is the equilibrium point 2 shown above. However, in part-2 no such equilibrium point exists near Vrest. This is because the stable and saddle points in part-1 annihilated each other just at the end of the hyperpolarisation caused by the anodal stimulus. This observation can also be used to explain the anode-break action potential, as the point close to Vrest is no longer a stable equilibrium point. The only stable equilibrium point is near 54.35 mV, that causes the system to undergo depolarization, and that in turn leads to an action potential.