Question - 1

To show units of consistent, the factor should be the same on both sides of the equation

$amp/cm^2 = siemens/cm^2 \cdot volts$

$10^{-6}amps/cm^2 = 10^{-3}siemen/cm^2 \cdot 10^{-3}volts$ (10^{-3} factor on both sides)

$amps/cm^2 \cdot seconds = farad \cdot volts$

$10^{-6}amps/cm^2 \cdot 10^{-3}seconds = 10^{-6}farad/cm^2 10^{-3}volts$ ($10^-9 factorsonbothsides$)

If $microsiemens/cm^2$ is used, the set of consistent units can be

$nanoamps/cm^2, microsiemens/cm^2, millivolts, milliseconds, nanofarads, millivolts$

because

$10^{-9}amps/cm^2 = 10^{-6}siemen/cm^2 \cdot 10^{-3}volts$

$10^{-9}amps/cm^2 \cdot 10^{-3}seconds = 10^{-9}farad/cm^2 10^{-3}volts$

It doesn't have to be unique as the factors can be adjusted, another set of consistent units can be

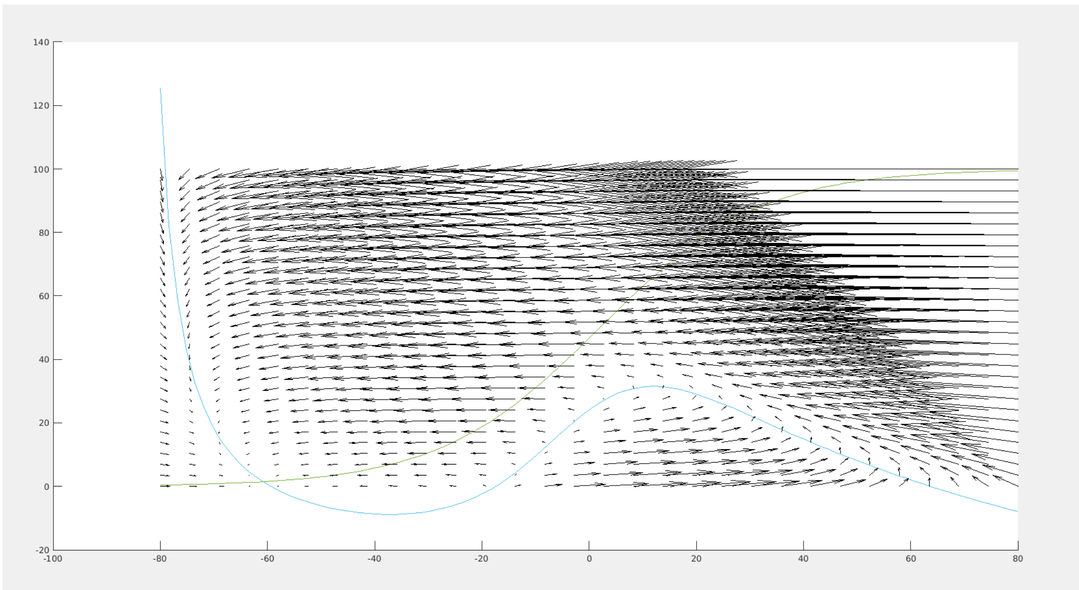
$nanoamps/cm^2, microsiemens/cm^2, millivolts, seconds, microfarads, millivolts$

Question-2

Methods used

1. Newton Raphson method using matlab’s fsolve
2. Iterating through vector arrays and checking if the difference is less than 0.01

Equilibrium point : -60.606 millivolts, 0.012



Question-3

Yes, the equilibrium point is stable, as eigenvalues are negative. Jacobian matrix obtained

```
jacobian matrix of MLE Iext=0
   -0.0992   -9.3576
    0.0000   -0.0319
```

Eigenvalues printed in the console

```
Eigen values of MLE I ext=0, should be stable - both eigen values negative

eigen_values =

   -0.0947
   -0.0365
```

Question-4

The numerical methods in Matlab involve varying timestep sizes. These timestep sizes are adjusted as per the error tolerance mentioned. If we have a larger tolerance, we get larger errors, but the calculation is done quickly. But with less tolerance, we get more accuracy consuming more time.

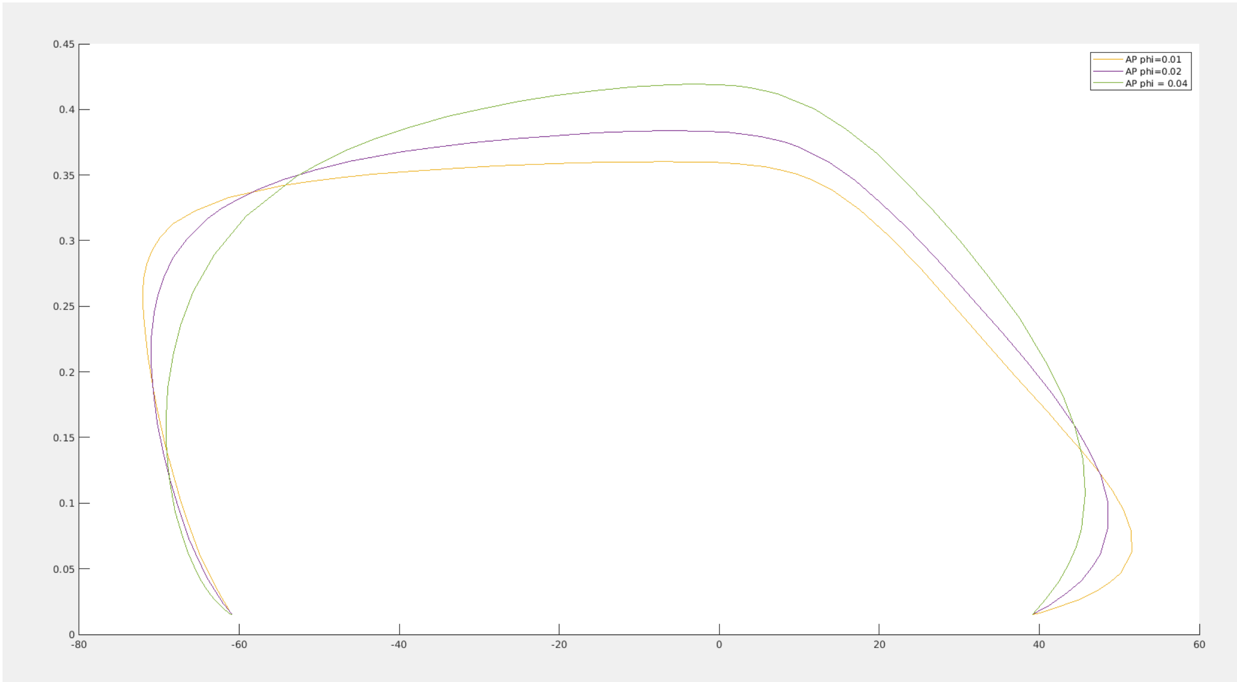
In our case, voltage is of order 10^1, when we use millivolts. If we use kilovolts, then voltages will be of order 10^-3. Hence the tolerances have to be kept lower. Accordingly, AbsTolerance can be 10^-9 and relative tolerance can be 10^-6.

Question-5

With the different values of phi, different trajectories

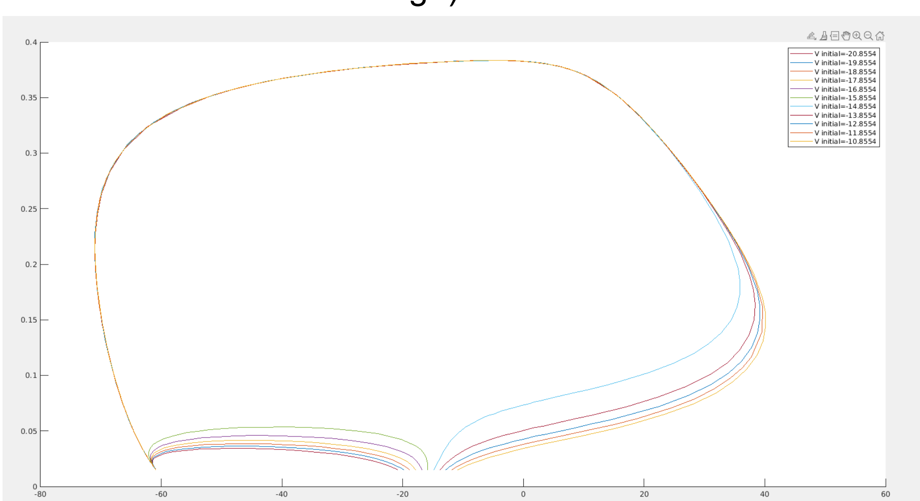
In the case of smaller phi s, we notice that the steeps are horizontal as discussed in R&E.

If ϕ were smaller still, then the phase plane trajectories (except when near the V nullcline) would be nearly horizontal (because dw/dV would be small); the action potential trajectory during the plateau and recovery phases would essentially cling to, and move slowly along, either the right or left branch of the V nullcline. The downstroke would occur at the knee of the V nullcline. The time course would be more like that of a cardiac action potential. Also, in the case of smaller ϕ, the threshold phenomenon would be extremely steep; the middle branch of the V nullcline would act as an approximate separatrix between sub- and superthreshold initial conditions. In contrast, for larger ϕ, the response amplitude is more graded. This theoretical conclusion led Cole, Guttman, and Bezanilla (1970) to demonstrate experimentally that, at higher temperatures, the action potential for squid axon does not behave in an all-or-none manner.

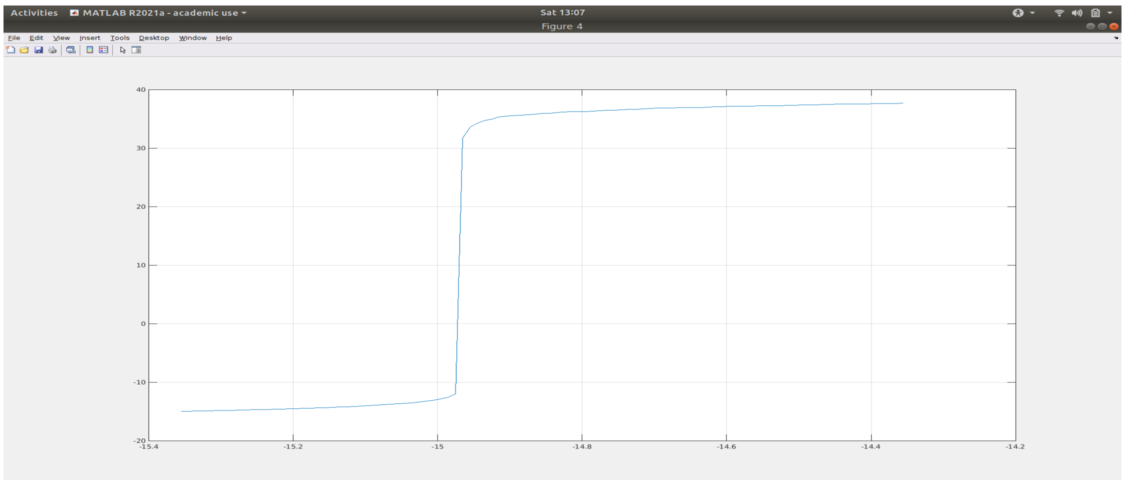


Question-6

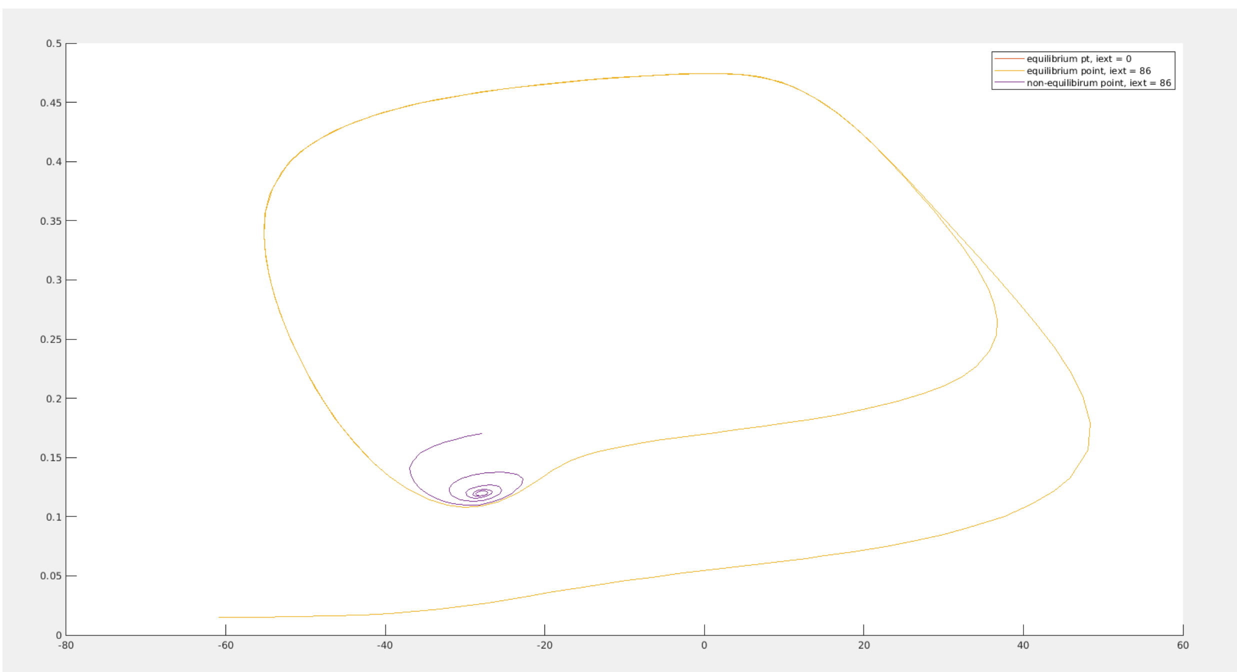
Yes, there is a clear threshold. Till a certain value of the initial value of the voltage, we see subthreshold behaviour- reaching the equilibrium point directly. If the initial voltage is more than a certain value, the equilibrium point is reached after the potential is increased, which is action potential behaviour. (This is not true action potential behaviour. Because true action potential behaviour is all or none, but here Maximum voltage increases with increase in initial voltage)



Maximum Voltage vs initial voltage: We can see that maximum voltage is increased suddenly after a certain initial value of voltage - the threshold voltage. This is threshold-like behaviour. But the difference is that after the threshold the maximum voltage increases, which doesn't happen in real models.



Question-7



1. I external = 0, starting at equilibrium point - Nothing happens, the system stays at rest, hence no trajectory in the above image
2. I external = 86, starting at equilibrium point(old one, when i external = 0): When steady current is given, the equilibrium point has been

shifted to far from the old equilibrium point. Now when we start from the old equilibrium point, we observe a limit cycle.

3. I external - 86, starting at a point near new equilibrium point: Shape of trajectory is an inward spiral. This is because the eigen values of the jacobian are complex with real parts being negative.
   Equilibrium point obtained from Matlab

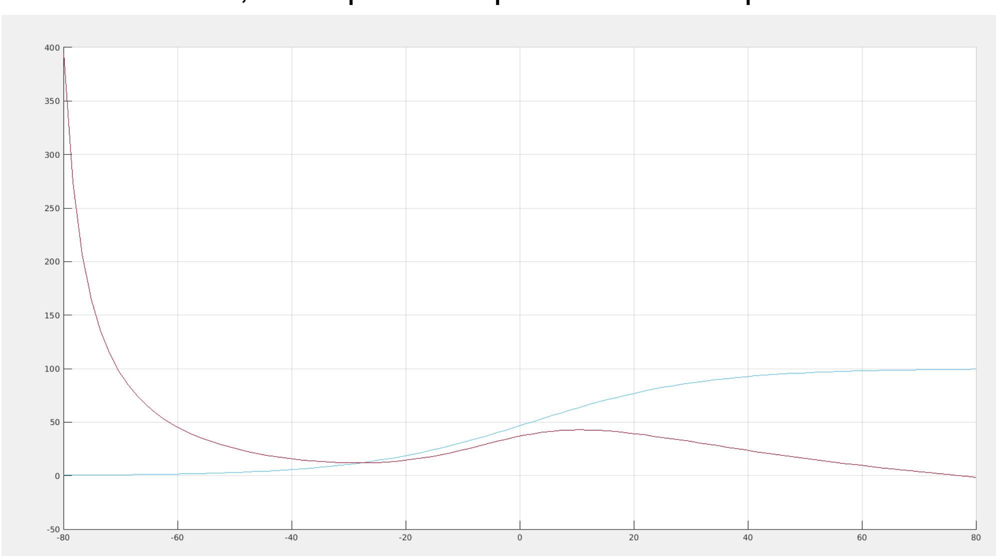
```
Equilibrium pt with iext = 86
  -27.9524
    0.1195
```

   Its eigenvalues - complex, with real part negative justifying inward spiral shape

```
eigen values for i ext = 86

eigen_values3 =

  -0.0068 - 0.0574i
  -0.0068 + 0.0574i
```

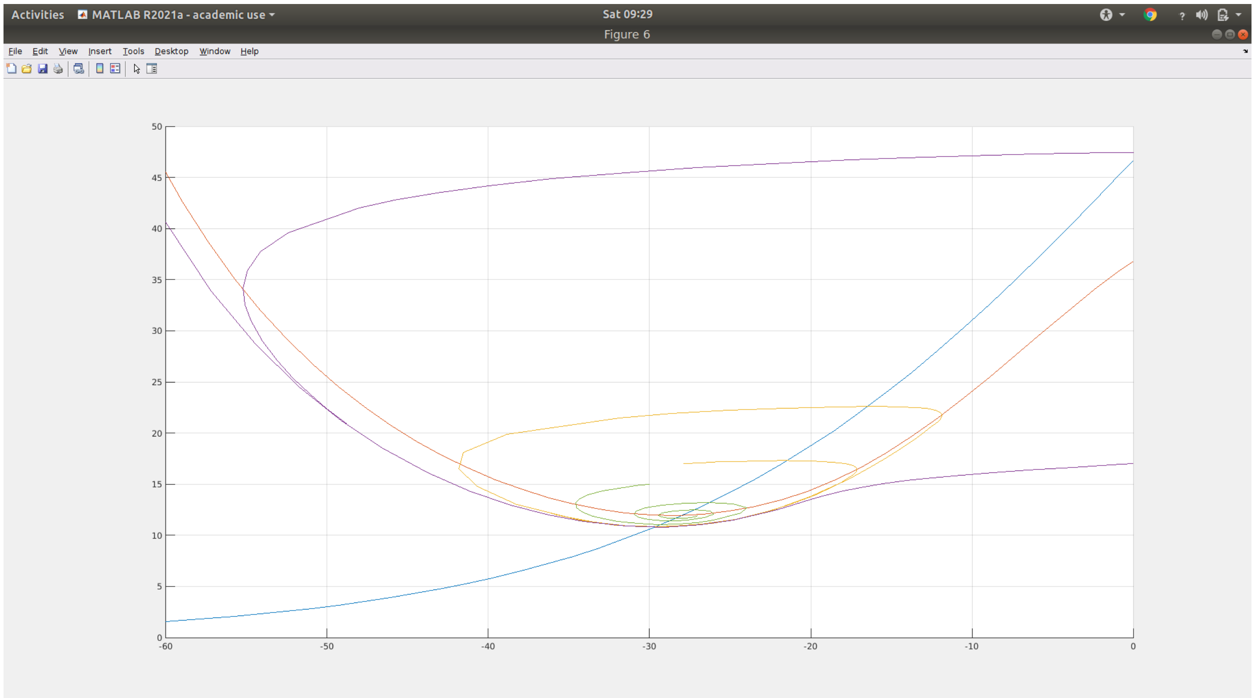
Question-8

When i ext = 86, the equilibrium point is shifted upwards



When run backwards in time, we see that sign of eigenvalues changes. Implying the nature of trajectory when started near to the equilibrium point will be outward spiral.

UPO is obtained by running backwards in time from a nearer point



From the above pic, the green trajectory starts from a point inside the UPO, hence it is stable. But the violet curve starts slightly outside the UPO(at -37.98 12.60), hence ends up in a limit cycle.

Question-9

1. In case of I ext = 80

Equilibrium point

```
x =

   -29.9662
     0.1061
```

Eigenvalues are complex with real values negative => Stable spiral

```
eigen_values3 =

  -0.0178 - 0.0557i
  -0.0178 + 0.0557i
```

2. In case of I ext = 86

```
x =

  -27.9524
    0.1195
```

Eigenvalues are complex with real values negative => Stable spiral

```
eigen_values3 =

  -0.0068 - 0.0574i
  -0.0068 + 0.0574i
```

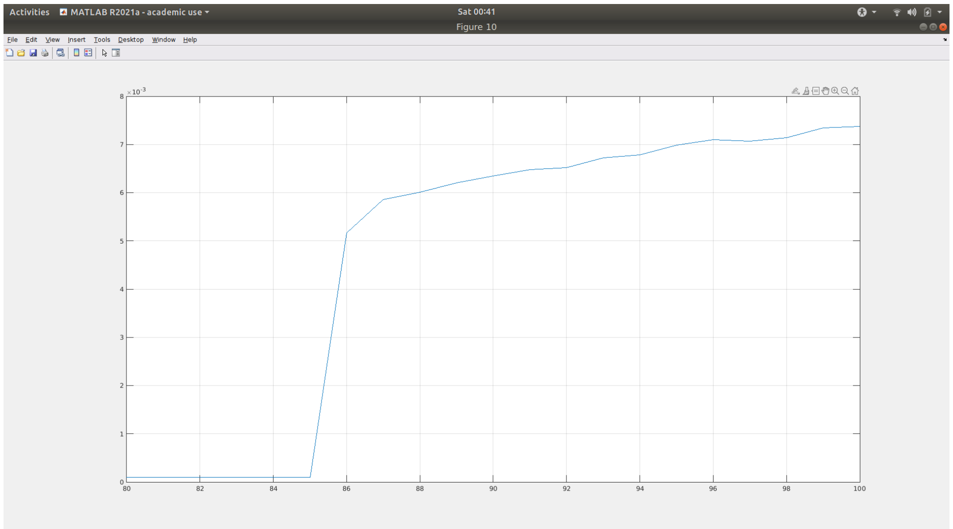
3. In case of I ext = 90

```
x =

  -26.5969
    0.1294
```

Eigenvalues are complex with real values positive => Unstable spiral

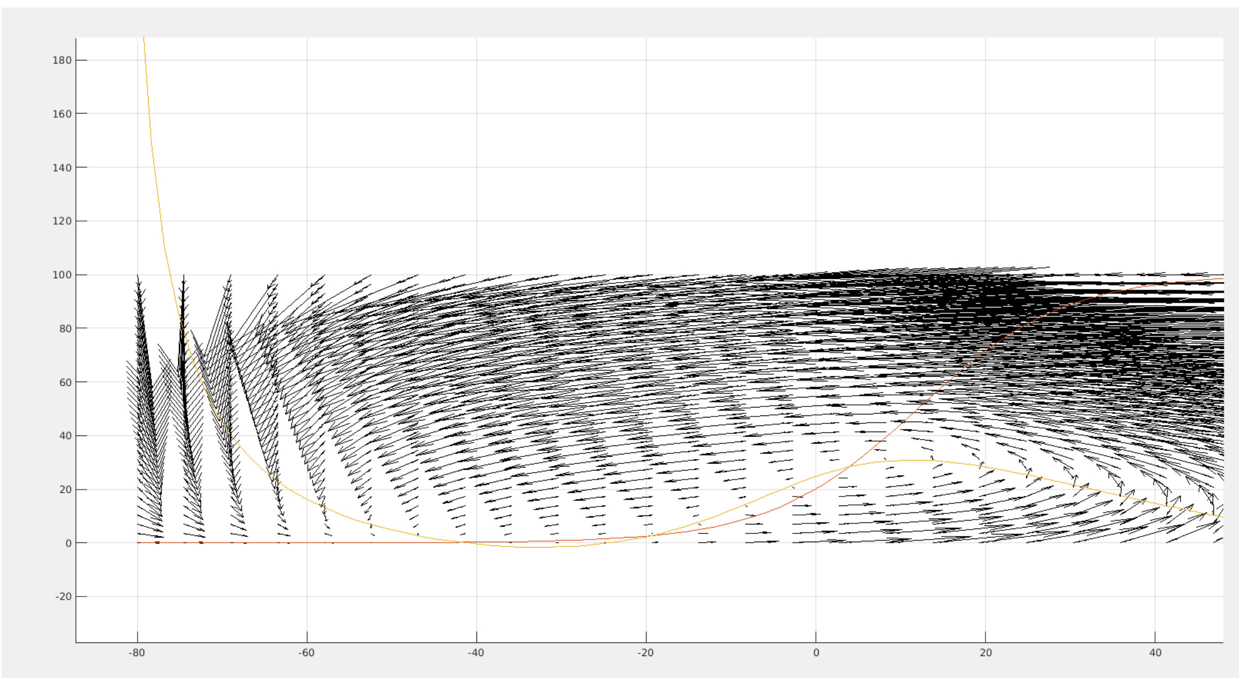
```
eigen_values3 =

   0.0018 - 0.0572i
   0.0018 + 0.0572i
```

For a graph of the frequency of action potential vs applied current, starting from -80 millivolts. We see that applied current increase, the frequency also increases.



Question-10

MLE with 2nd set of variables and i ext = 30



New equilibrium points

```
new equilibrium pts, new set of MLE, iext = 30
  -41.8452  -19.5632    3.8715
    0.0020    0.0259    0.2821
```

For 1st equilibrium point, eigenvalues are negative => stable point

```
eigen_values3 =

   -0.1568
   -0.0715
```

For 2nd equilibrium point, one of them is negative other is positive => saddle node

```
eigen_values3 =

   -0.0673
    0.1536
```

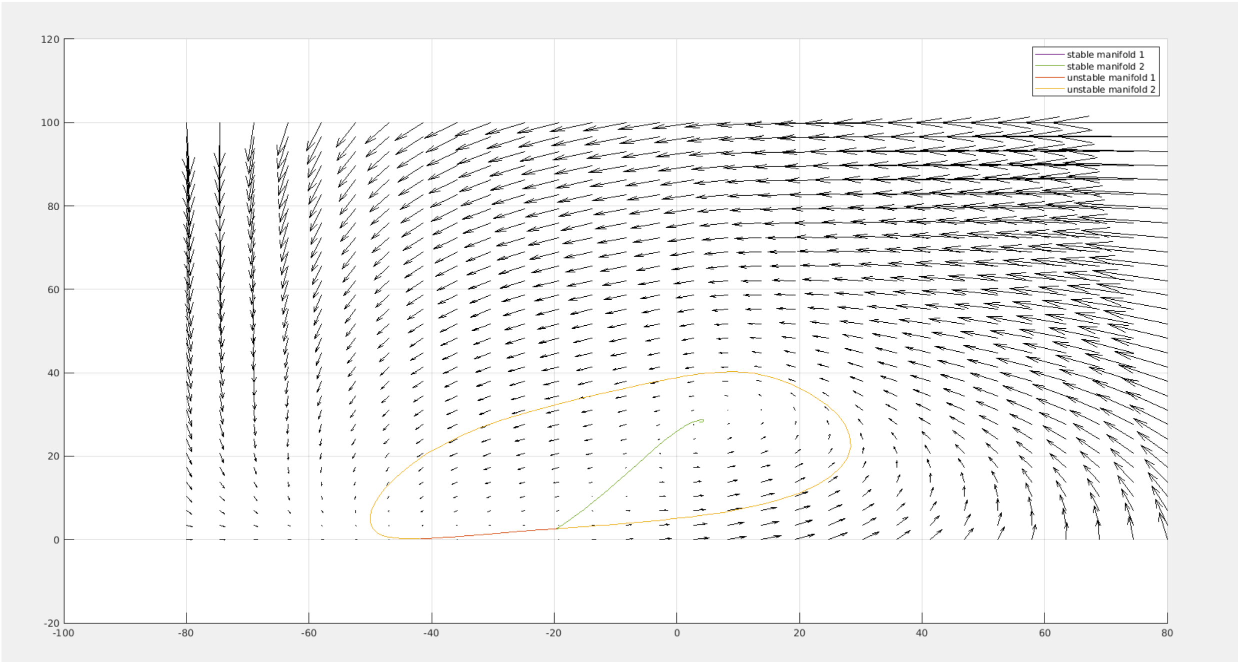
For 3rd equilibrium point, both are complex with real part positive => unstable spiral

```
eigen_values3 =

   0.0939 - 0.1723i
   0.0939 + 0.1723i
```

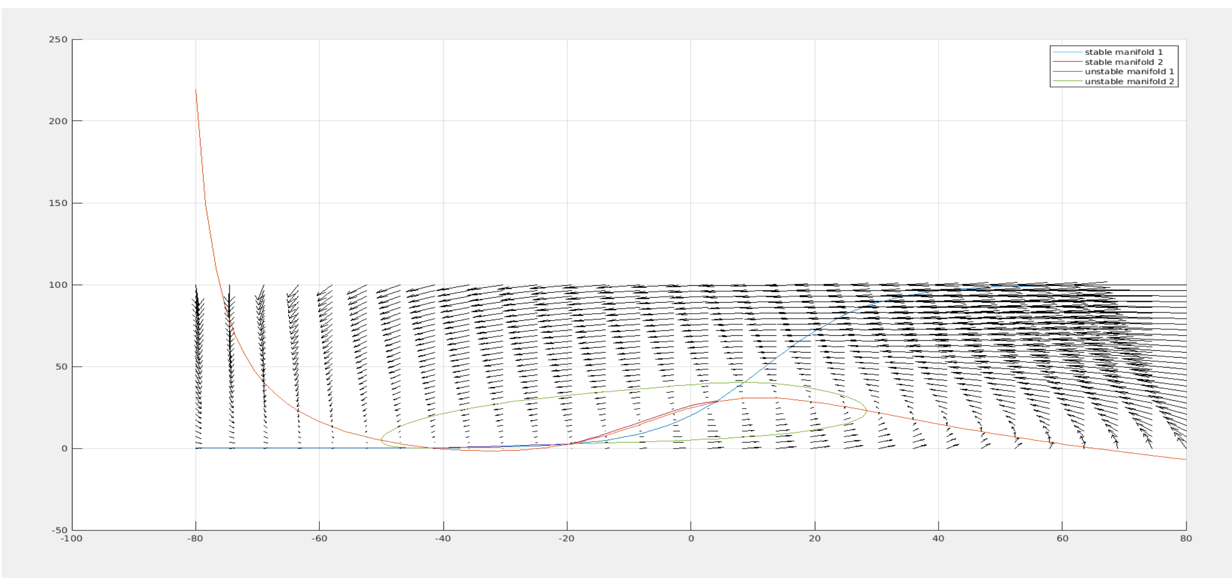
To find manifold find eigen vectors

```
eigen vecs
  103.2328   896.6907
    1.0000     1.0000
```

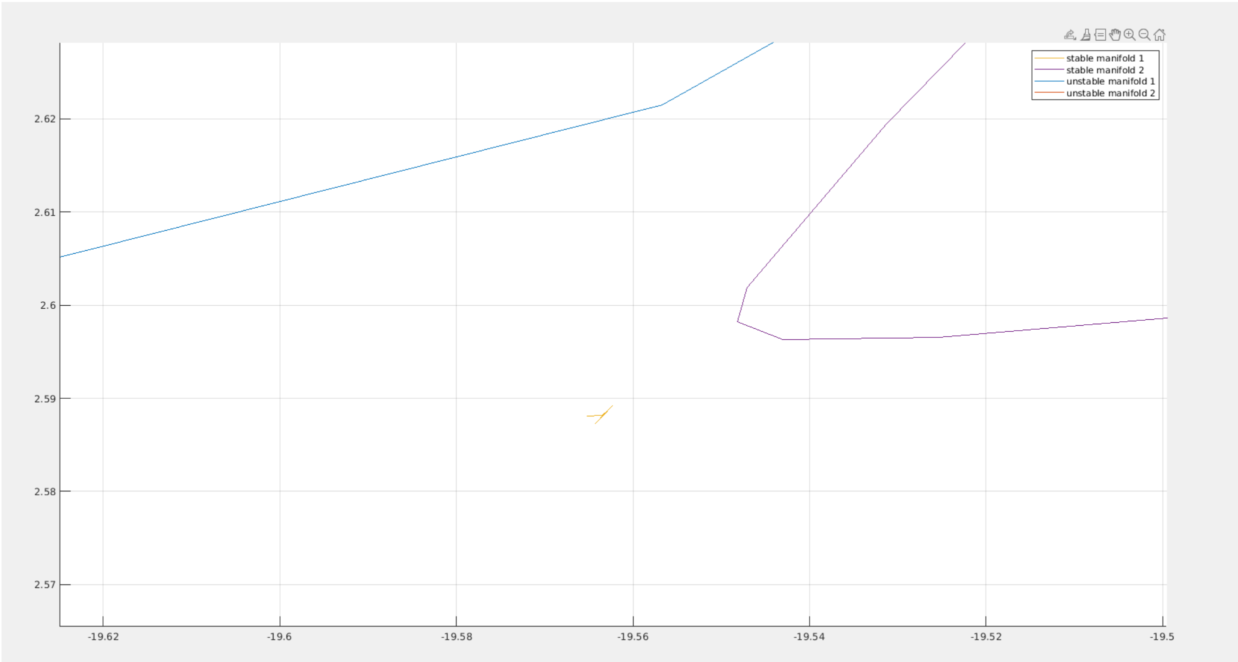
Manifolds with quiver plots



Manifold with nullclines, quiver plots

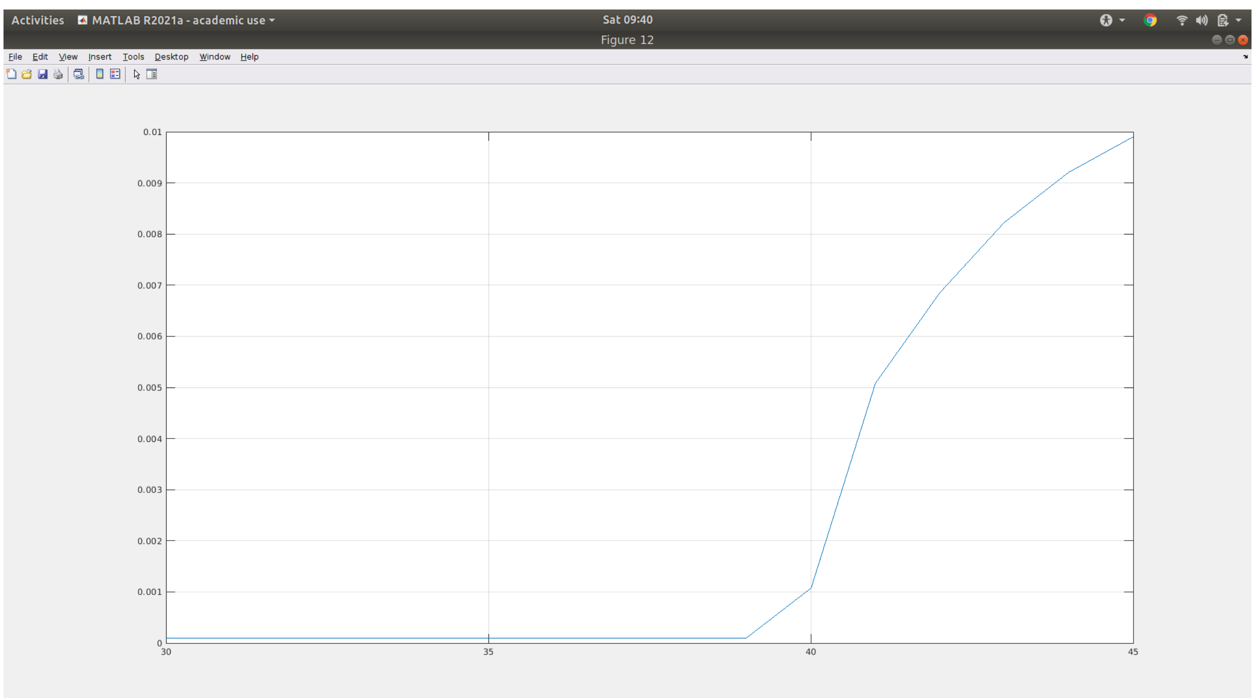


The fourth manifold is small, can be visible on zoom(in orange colour)



Question-11

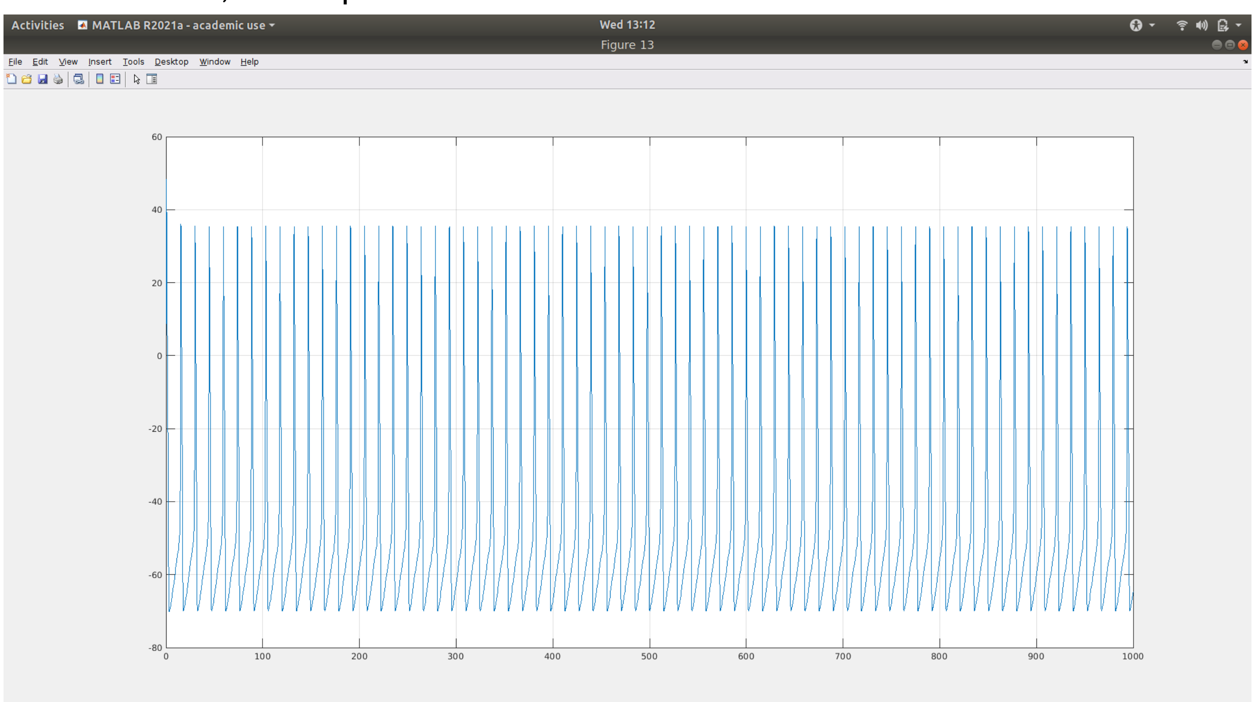
Rate of Action Potential vs applied current - The rate increases with increase in applied current.



From i ext = 30 to 50. We get three equilibrium points in this region and their stability is noted as per the eigenvalues
i=30 to 39, stable, saddle, unstable spiral
From i =40 to 50 there is only 1 equilibrium point. that’s is an unstable spiral

Question-12
Code in the Matlab - A function named “hh”.

Question-13
With i ext = 10, action potential



Value of E leak = -49.401079 millivolts

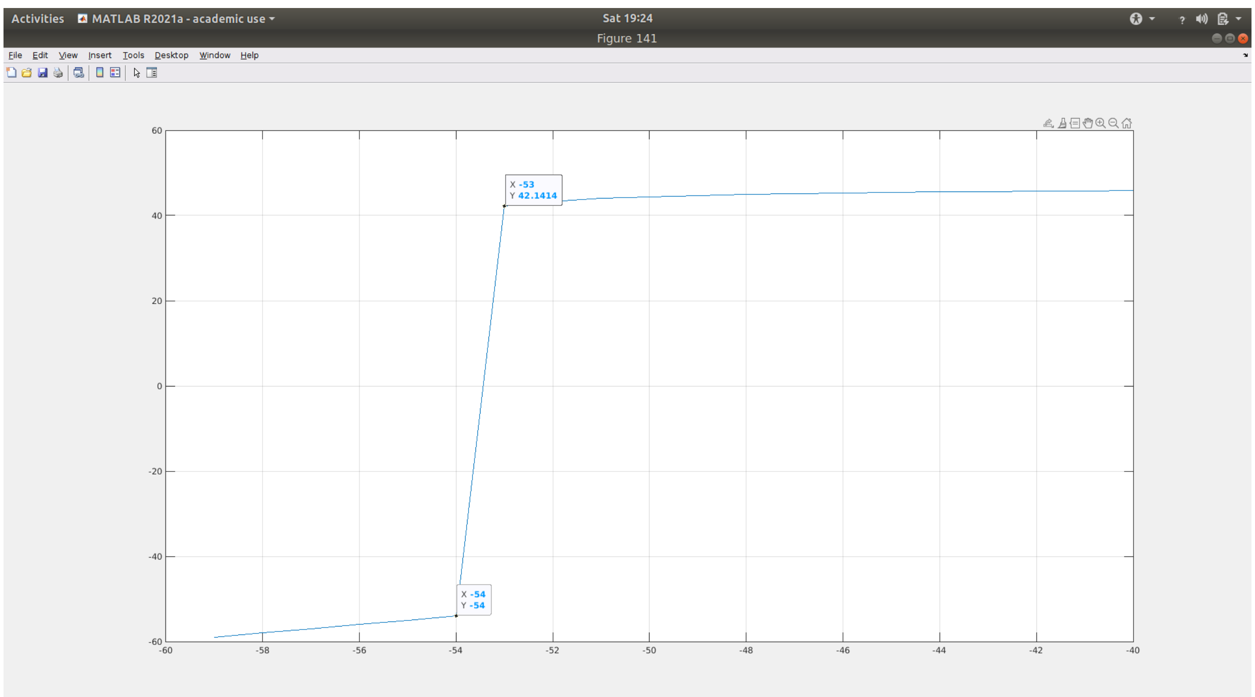
Question-14

```
equilibrium points for hh
v m h n -60.000000 0.052932 0.596121 0.317677
```

The equilibrium points

Eigen values - complex with negative real -> stable spiral

```
eigen values of hh model 4d
  -4.6753 + 0.0000i
  -0.2027 + 0.3831i
  -0.2027 - 0.3831i
  -0.1207 + 0.0000i
```



-53 volts is the threshold of Hodgkin huxley model

Question-15

I ext and eigenvalues

```
I ext is 8.000000
v m h n -55.355128 0.090048 0.430515 0.390607
  -4.6901 + 0.0000i
  -0.0345 + 0.5668i
  -0.0345 - 0.5668i
  -0.1350 + 0.0000i
```

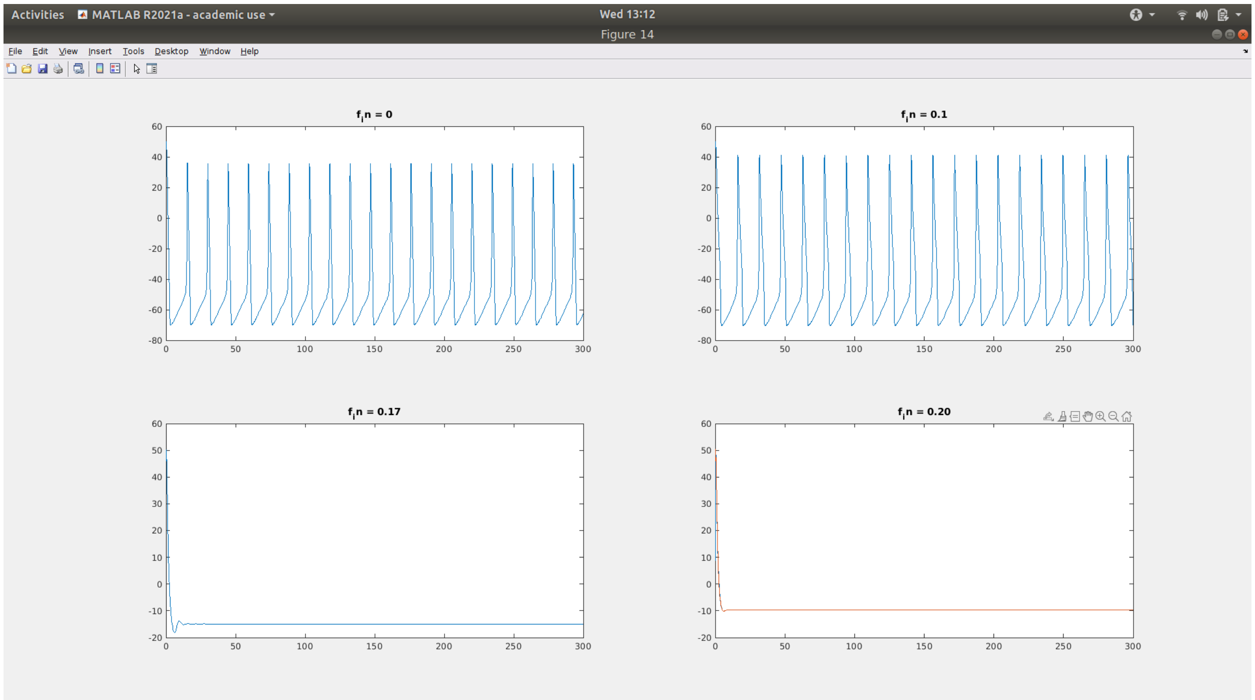
```
I ext is 9.000000
v m h n -54.952404 0.094133 0.416502 0.397027
  -4.7306 + 0.0000i
  -0.0149 + 0.5783i
  -0.0149 - 0.5783i
  -0.1370 + 0.0000i
```

```
I ext is 10.000000
v m h n -54.572150 0.098131 0.403419 0.403092
  -4.7741 + 0.0000i
   0.0041 + 0.5883i
   0.0041 - 0.5883i
  -0.1389 + 0.0000i
```

```
I ext is 11.000000
v m h n -54.211777 0.102052 0.391169 0.408841
  -4.8200 + 0.0000i
   0.0224 + 0.5971i
   0.0224 - 0.5971i
  -0.1408 + 0.0000i

I ext is 12.000000
v m h n -53.869127 0.105899 0.379667 0.414306
  -4.8676 + 0.0000i
   0.0399 + 0.6048i
   0.0399 - 0.6048i
  -0.1428 + 0.0000i
```

For i=8,9 we have a stable point
From i= 10 to 12, we can’t predict the stability of the point

Question -16



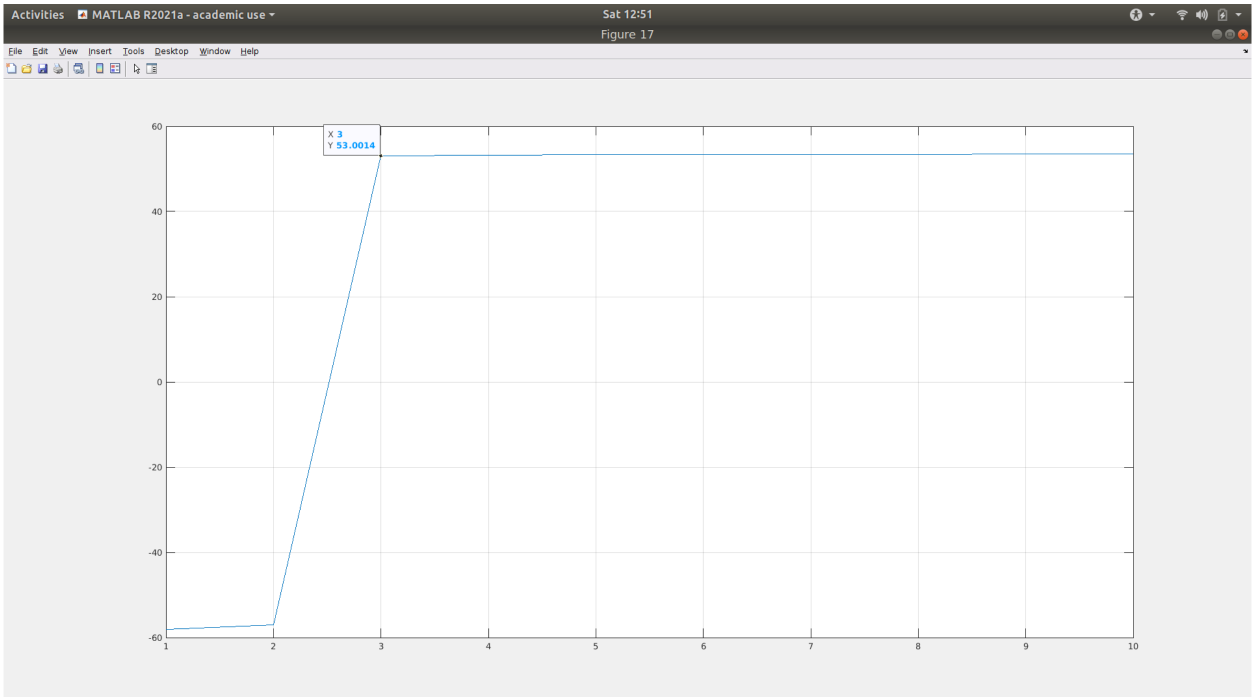
Myotonic Hodgkin Huxley simulations

Qualitative analysis: When f_in is large, it doesn't allow enough sodium ions to pass in. Hence membrane potential won't be able to increase enough for the action potential behaviour.

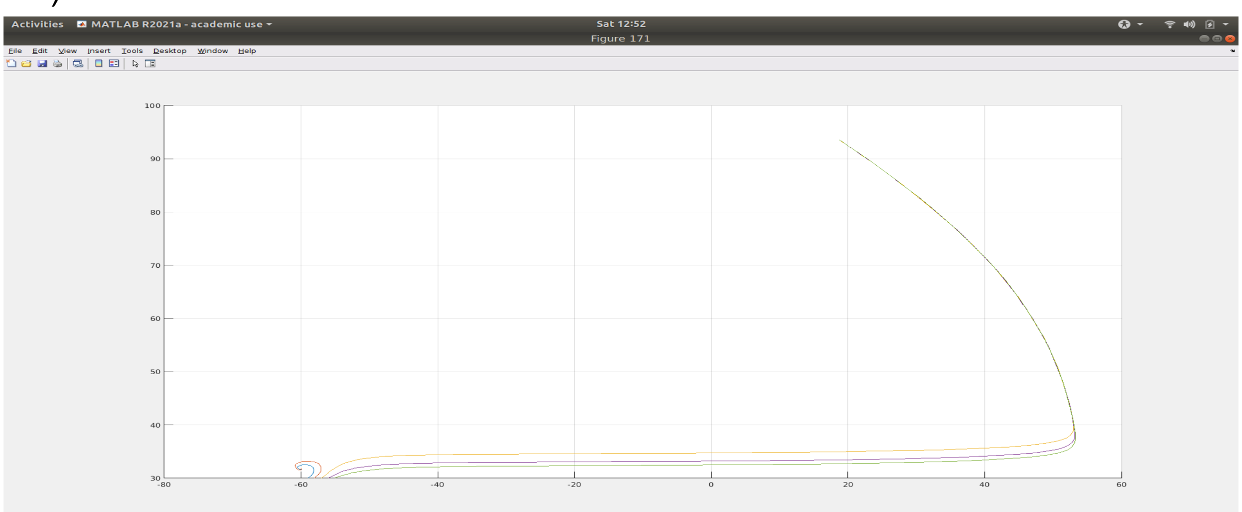
Question-17

Yes, the general behaviour is that V-n reduced model also shows threshold behaviour. The threshold voltage is around 53.0014 millivolts.

m is set of m_infinite(V), and h is set to h at equilibrium



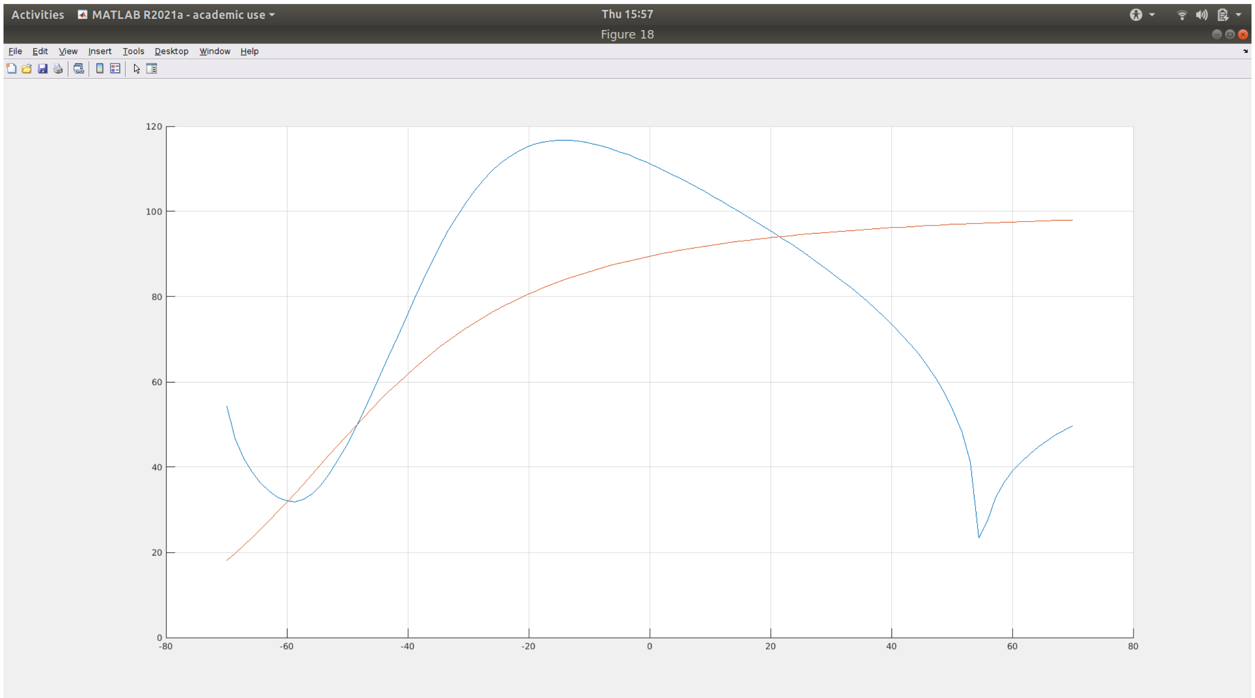
But the key difference from V-n reduced model and the full model is that V-n model is successful only in showing the depolarisation part. As you can see from the below graph,after giving voltages above the threshold, we see a difference in trajectories, but the trajectory does not reach the original equilibrium point(around -60).



Question-18

V vs n

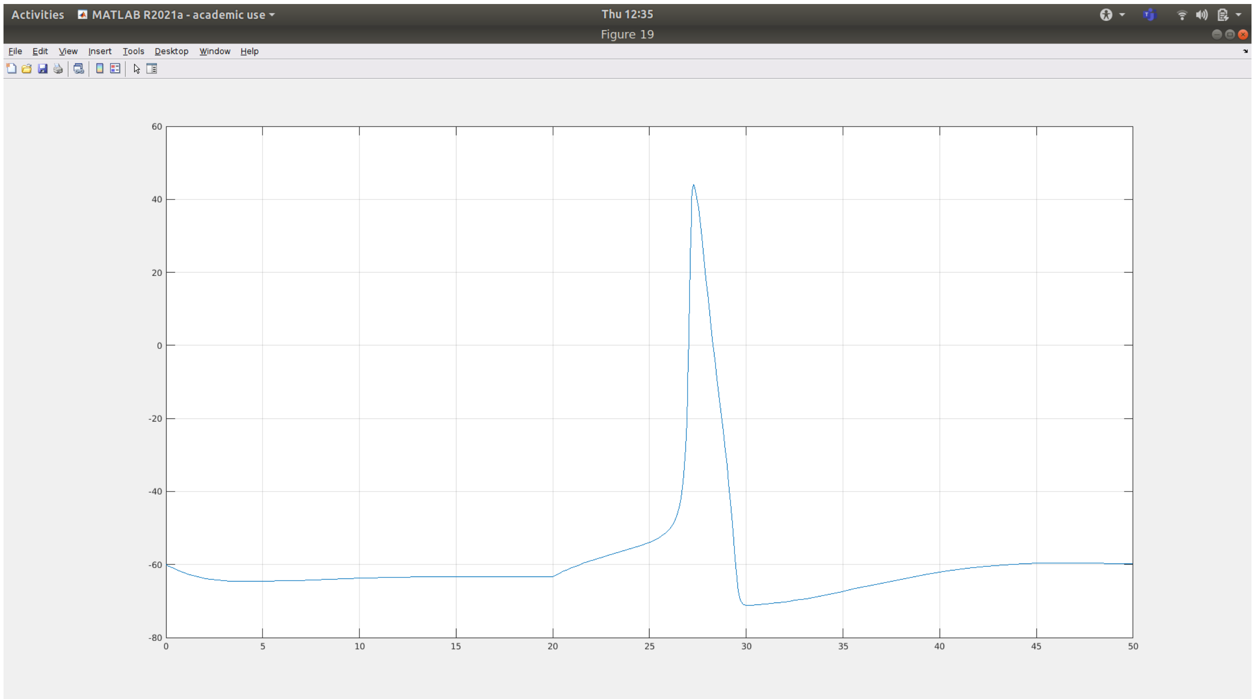
f_ni=0.20: V and n null clines with myotonia 2D HH model



Varying f_ni values with equilibrium points and eigenvalues

```
f_ni is 0.020000    stable spiral   saddle   stable
f_ni is 0.040000    stable spiral   saddle   stable
f_ni is 0.060000    stable spiral   saddle   stable
f_ni is 0.080000    stable spiral   saddle   stable
f_ni is 0.100000    stable spiral   saddle   stable
f_ni is 0.120000    stable spiral   saddle   stable
f_ni is 0.140000    stable spiral   saddle   stable
f_ni is 0.160000    stable spiral   saddle   stable
f_ni is 0.180000    stable spiral   saddle   stable
f_ni is 0.200000    stable spiral   saddle   stable
f_ni is 0.220000    stable spiral   saddle   stable
f_ni is 0.240000    stable spiral   saddle   stable
f_ni is 0.260000    stable spiral   saddle   stable
f_ni is 0.280000    stable spiral   saddle   stable
f_ni is 0.300000    stable spiral   saddle   stable
f_ni is 0.320000    stable spiral   saddle   stable
f_ni is 0.340000    stable spiral   saddle   stable
f_ni is 0.360000    stable spiral   saddle   stable
f_ni is 0.380000    stable spiral   saddle   stable
f_ni is 0.400000    stable spiral   saddle   stable
```

Question-19



When a negative external current is added, the voltage decreases, and the system settles at a voltage(call it V_h) lower than the initial equilibrium potential(call it V_rest). After a short period of time when the external current is removed, the values of m, h, n start changing.

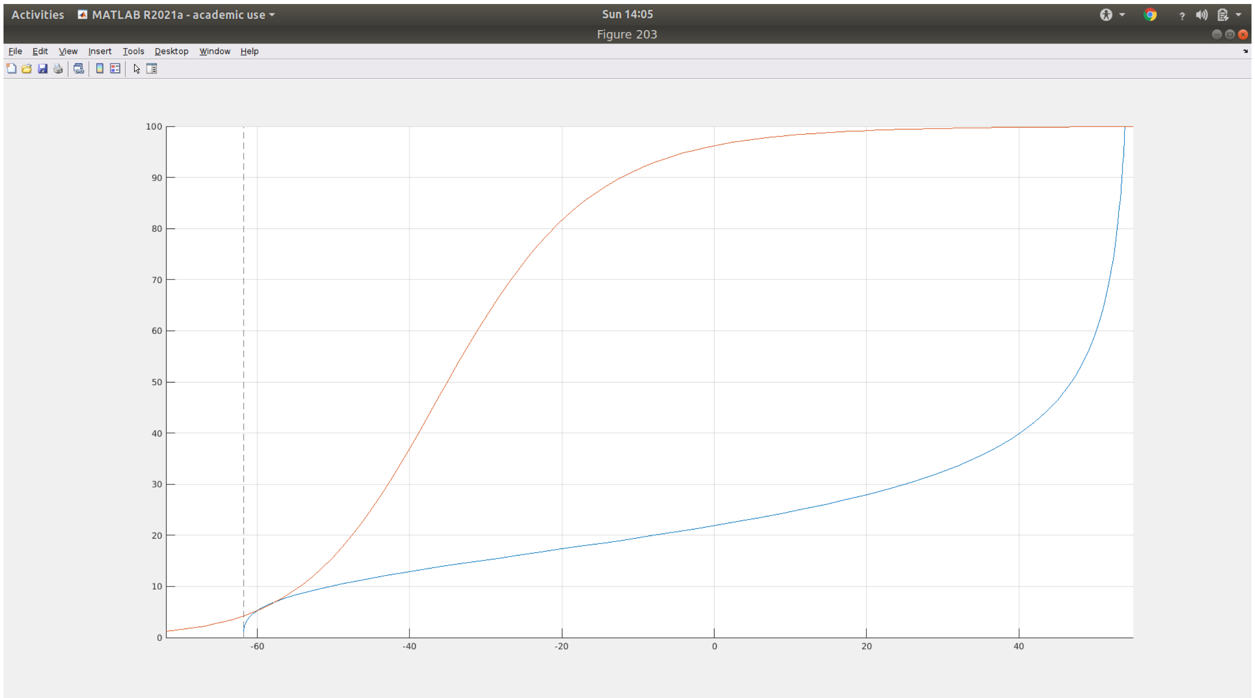
Due to the smaller time constant, the value of m reaches m(V_rest), which is the value of m at V_rest. But due to larger time constants, h is still at h(V_h) and n is still at n(V_n).

And by nature of curves of h and n,
h(V_h) > h(V_rest)
n(V_h) < n(V_rest)

The above implies that the inflow of sodium ions is more than what was at equilibrium(V_rest), also the outflow of potassium ions is less than what was at equilibrium(V_rest). Hence due to the large inflow of sodium current, voltage increases giving rise to action potential behaviour. This is called the Anode break excitation.

Question-20

Case - 1 : n and h are at V rest - There are 3 equilibrium points

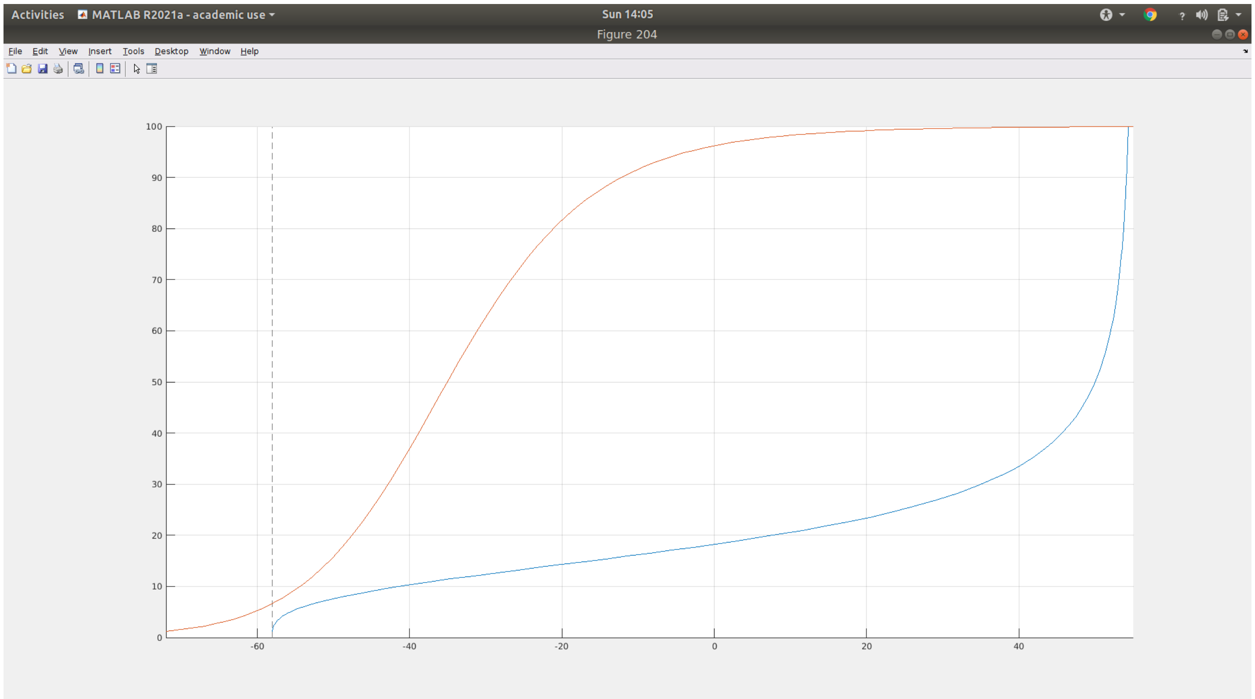


Stability:-

```
eigen values -0.221773 -4.679044 stable

eigen values 0.255926 -4.674764 saddle

eigen values -72.030943 -8.898483 stable
```

Case - 2: n and h are at V_h

There is only 1 equilibrium point - the one at top right. Due to a higher h(higher than h(V rest)) and lower n values(lower than n(V rest)), we see that the v-null cline has shifted so that previously existing 2 equilibrium points have vanished. So in this case, the trajectory will be from the initial point to the only equilibrium point where there is a higher voltage value. This increase of voltage explains action potential behaviour. This phenomenon is known as anode break excitation.



Stability of the single equilibrium point

```
 eigen values -84.917959 -8.942314 stable
>> 
```