Neuroscience Homework 1

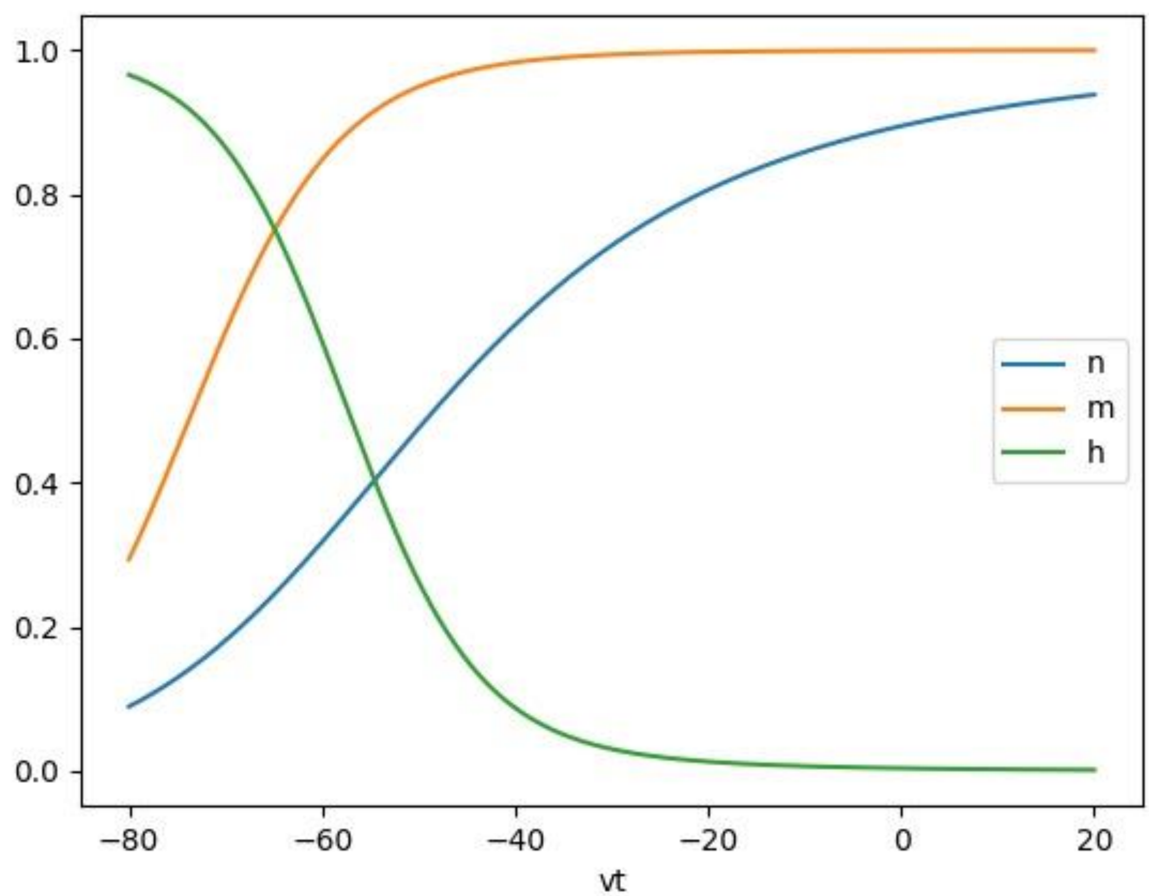
Nima Alizadeh – 98100504

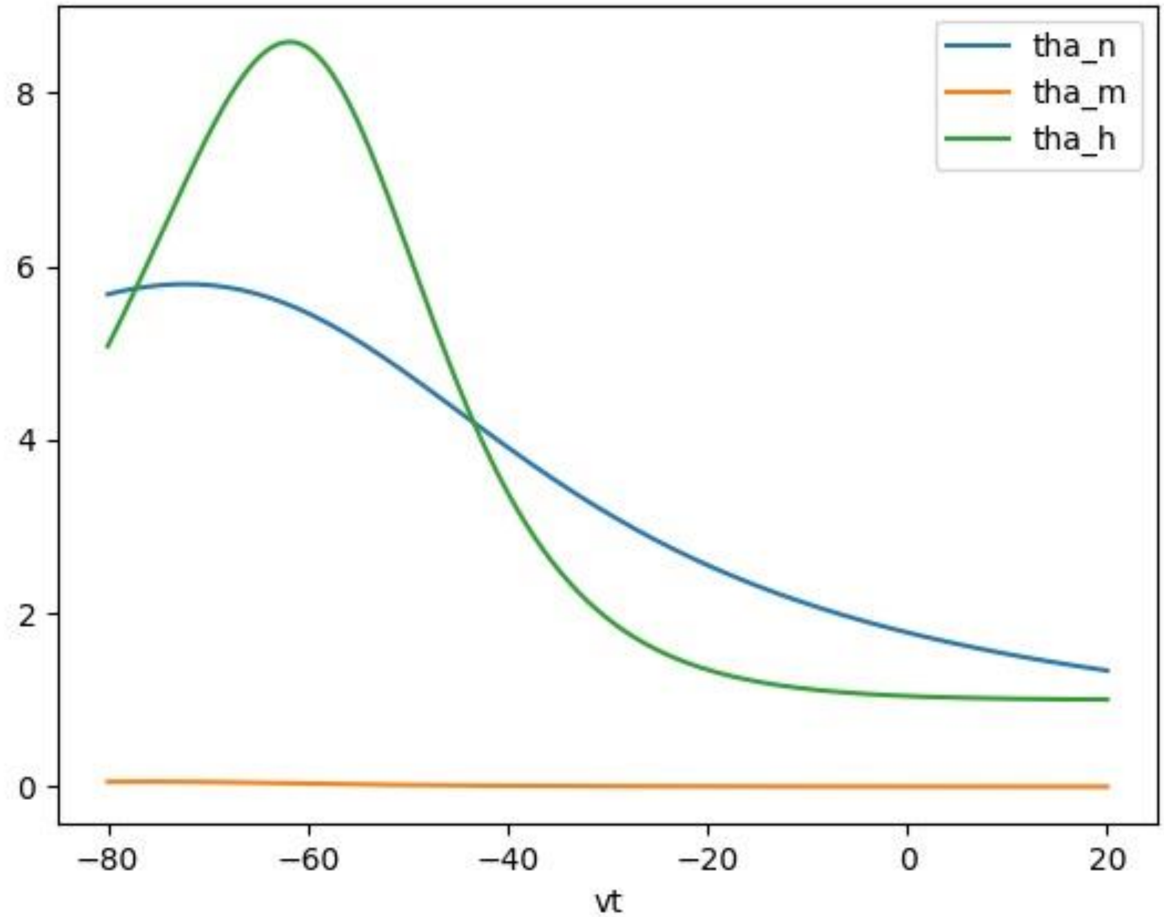
April 2022

Problem 1 : Hodgkin-Huxley model

In this problem we are going to implement the dynamic of a neuron which acts according to Hodgkin-Huxley model.

1- Plot time constants and steady state of m,n,h with respect to voltage. Based on the outputs, explain how sodium and potassium channels work.

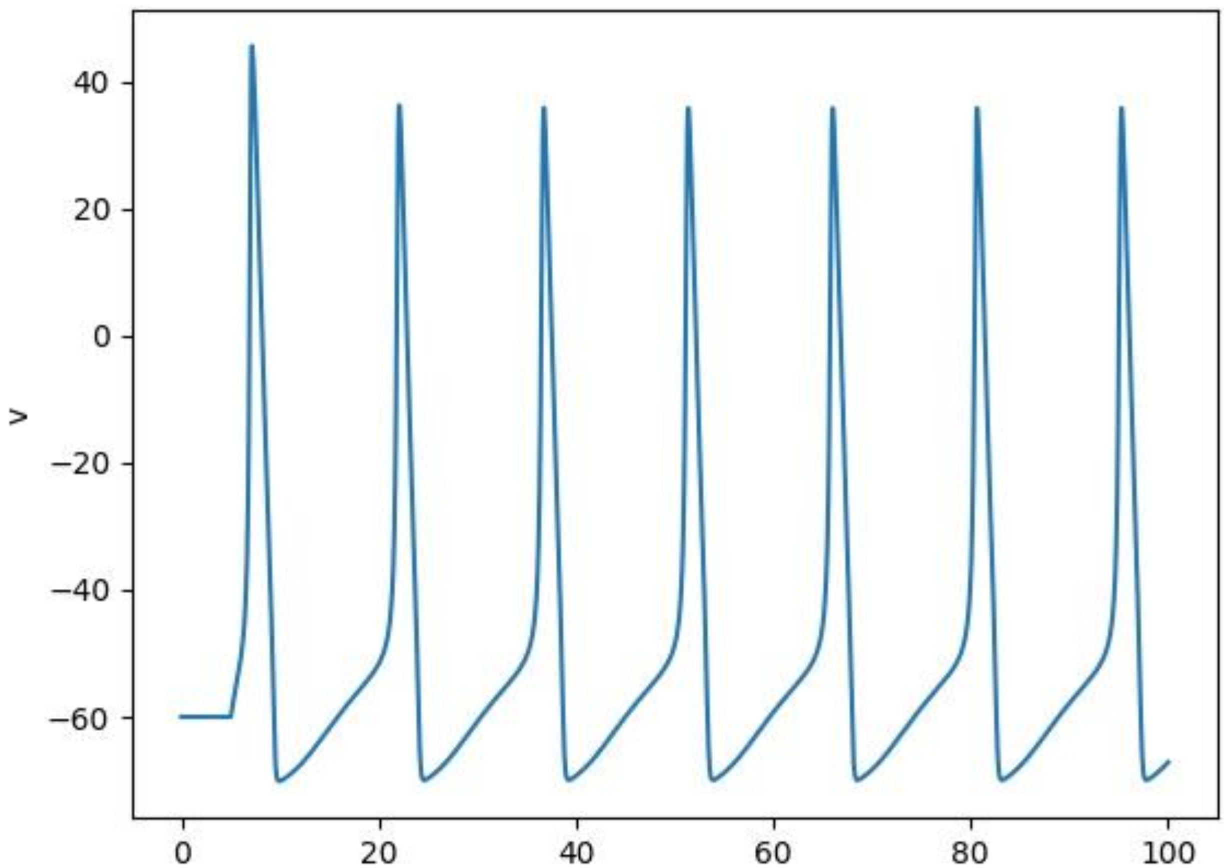




According to time constants plot, since sodium channel has a small time constant for opening (τ_m is small) its opening probability (m) increases rapidly as the voltage is increased and hence, the channel gets open. Then after a while (since τ_h is large) the probability of the inactivation gate being open (h) will decrease and tend to zero, therefor, the total probability of sodium channel being open (m^3h) tends to zero and so the channel will get closed.

Since $\tau_n > \tau_m$ it will take more time for the potassium channel to get open compared to the sodium channel and so it will open in larger voltage, and also it will have more chance of being open in large voltage, because n_∞ is large and close to one.

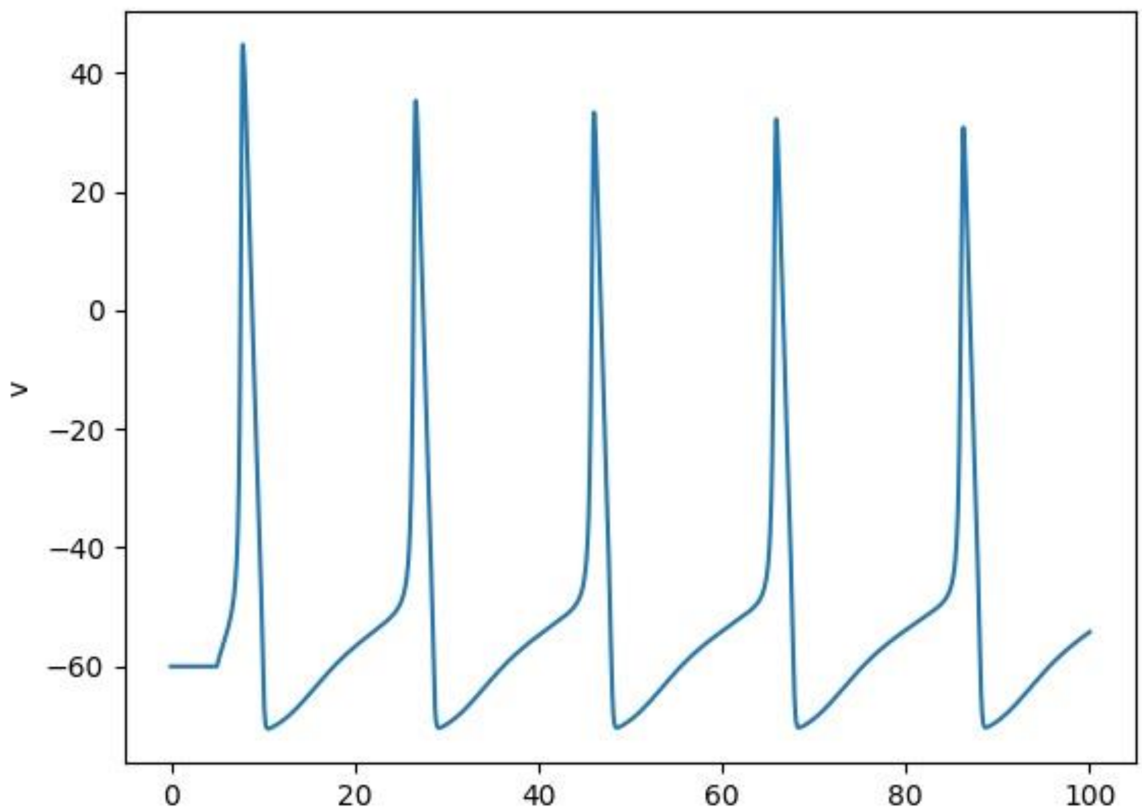
2- Plot voltage per time for a neuron, with a proper external current which causes spiking of the neuron.



Plot of voltage for an external current of 20 mA during 100 ms.

3- Find the smallest value for external current that causes spiking. Plot voltage curve for this external current.

Minimum value of external current which makes neuron spike is 6.21 mA.



4- Find the smallest amount of time an external current has to be applied to make the neuron spike. Set the value of the current to be the minimum found in the previous problem

An external current of 6.21 mA needs to be applied for roughly 20.2 ms to make the neuron spike.

5- Compute the domain and frequency of the spiking of a neuron for different values of external current.

Following table contains the domain and frequency of the spiking of a neuron for different values of external current. Changes in voltage with a domain larger than 60 mV are considered as spike (although in reality, a spike domain should be about 100 mV).

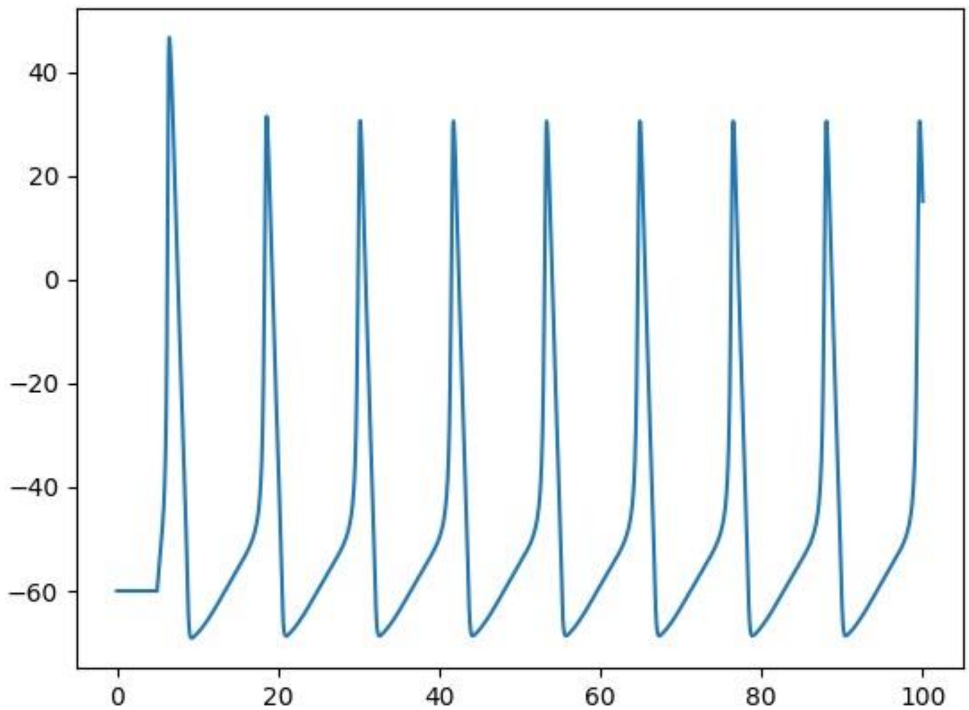
Current (mA)	Frequency (1/ms)	Domain (mV)
8	0.062	113
10	0.066	110
15	0.076	103
20	0.090	100
30	0.100	92
40	0.111	85
50	0.116	80
60	0.120	72
70	0.125	65
80	0.133	60

6- Based on the results of problems 3 and 5, describe the behavior of spiking of a neuron for different values of external current.
We know that for large external current, model won't spike. Find the upper bound of external current and plot the voltage of neuron for it.

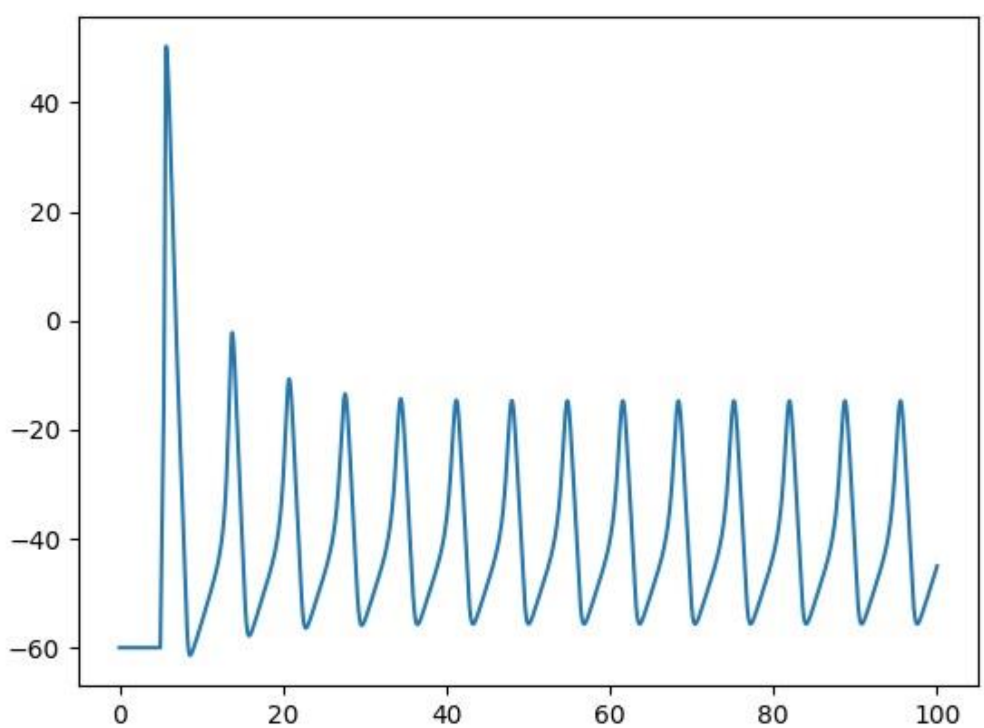
as it can be seen from the previous results, for too small values of the external current, neuron won't spike. As the external current increases (and passes the lower bound of spiking) the frequency of spikes increase and their domain decreases. When external current gets too large, the domain of the oscilations in voltage becomes small and model stops spiking.

it is a bit hard to talk about an exact upper bound for the external current. For I=20 mV or higher, the domain becomes smaller than 100 mV, which we can say that we don't have spikes anymore. For larger values external current, domain continues to decrease, as for inputs of the order 180 mA, we don't have any oscillations.

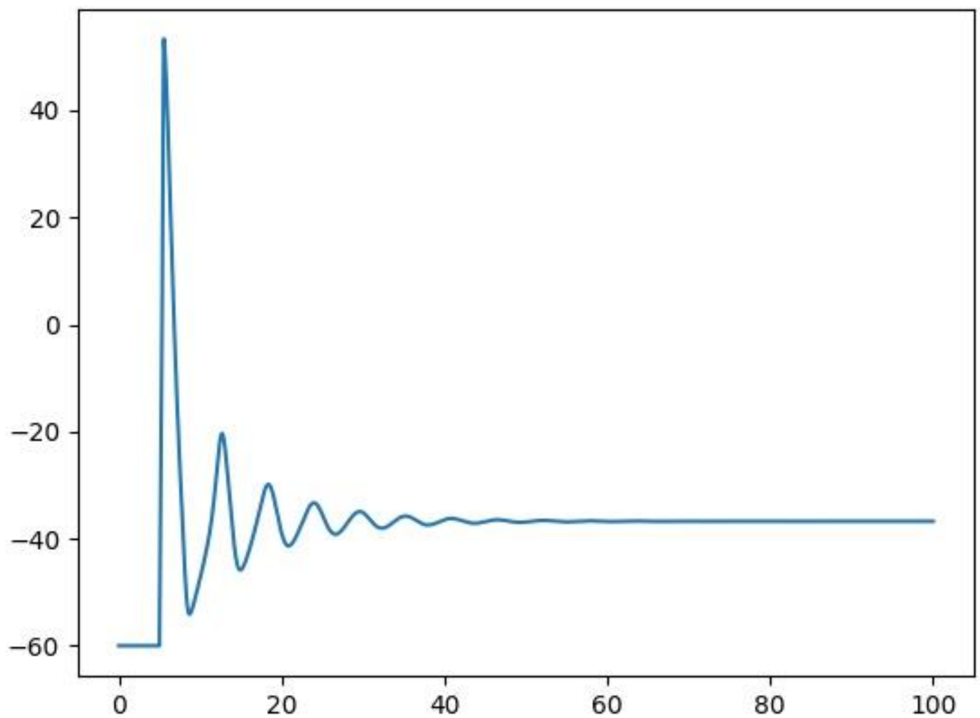
Plot for I_{ext}=20 mA:



Plot for I_{ext}=100 mA:

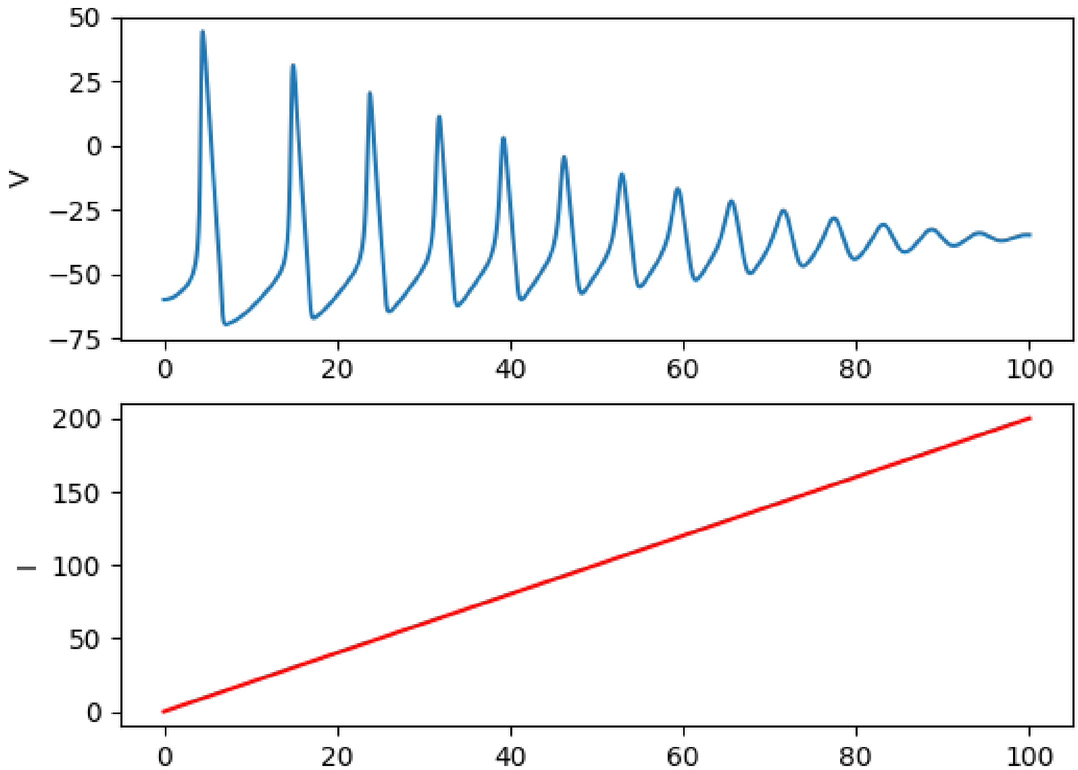


Plot for I_{ext}=180 mA:



7- Consider a small current I_1 , which doesn't make the neuron spike, and also a large current I_2 , which again doesn't cause spiking. Now, take an external current which varies linearly from I_1 to I_2 and plot the voltage of neuron for it. Explain the result.

We take $I_1=0$ and $I_2=200$. Plot of voltage would be

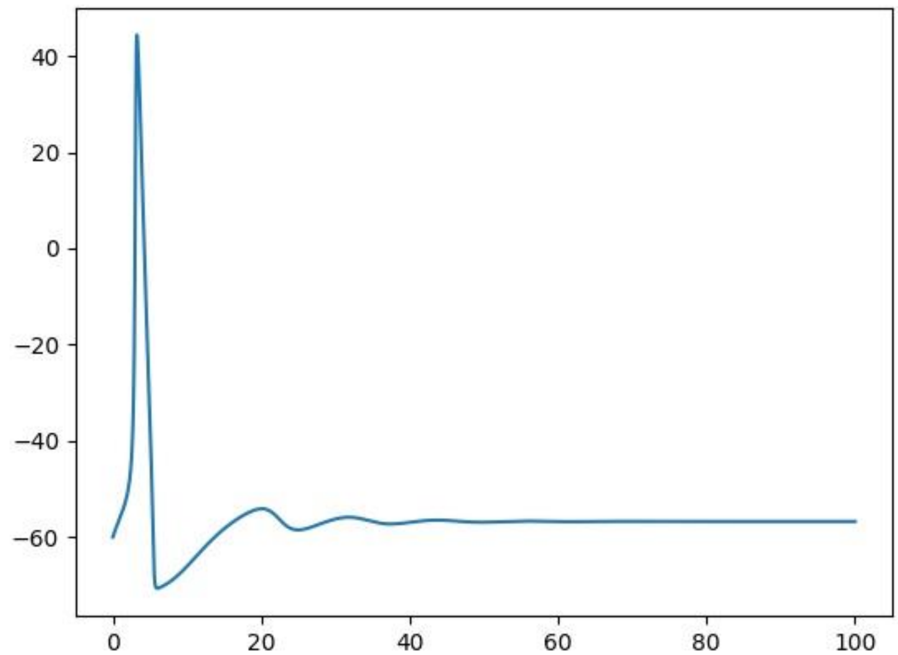


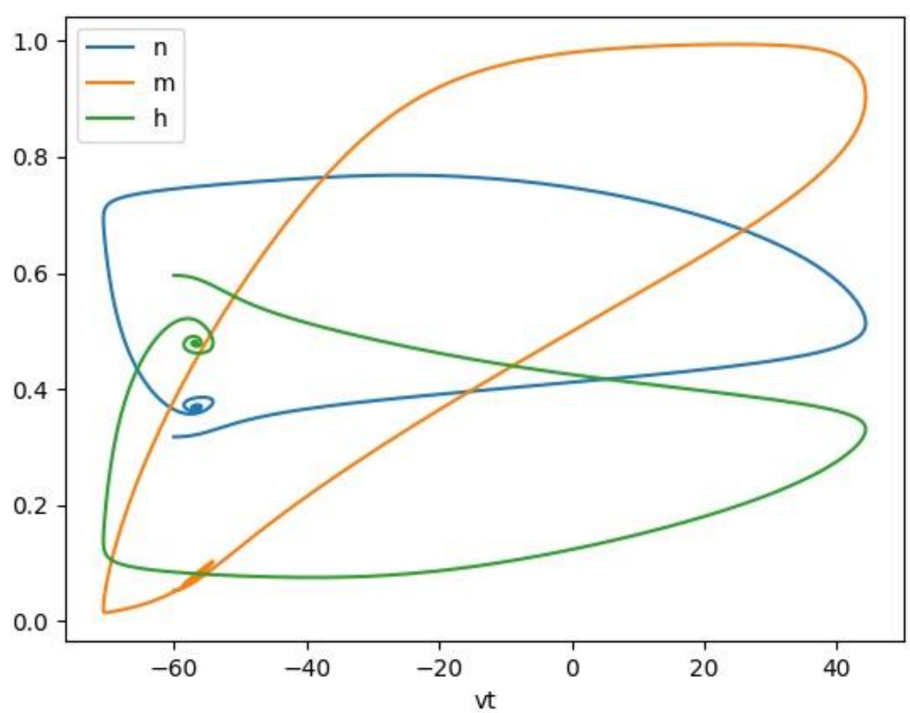
As it can be seen from the plot, at first, for small currents (bigger than lower bound) the neuron will start spiking with large domain and small frequency. As the current increases, domain of the spike starts to decrease and the frequency increases (we also see this in the previous problem)

For large enough currents (larger than upper bound) deviation of voltage becomes small and is not considered as spike.

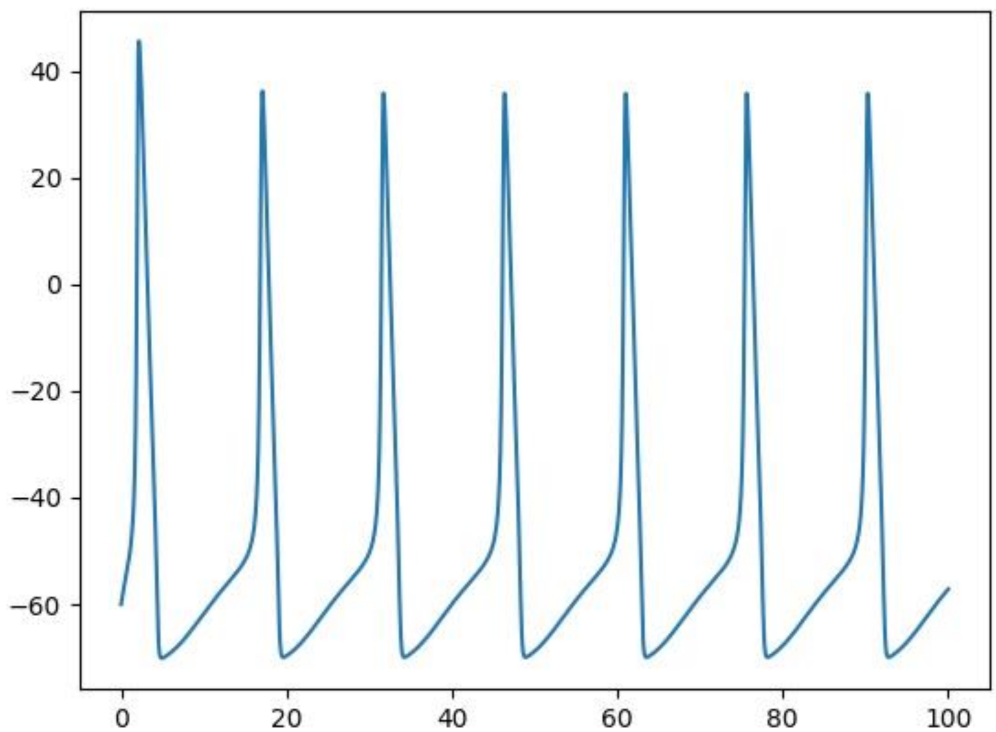
8- Consider three different values of the external current: a small value that doesn't cause spiking, another with proper value that makes the neuron spike periodically, and last one with large value that again doesn't cause spiking. Plot m, n, h as voltage for these external currents and explain the result.

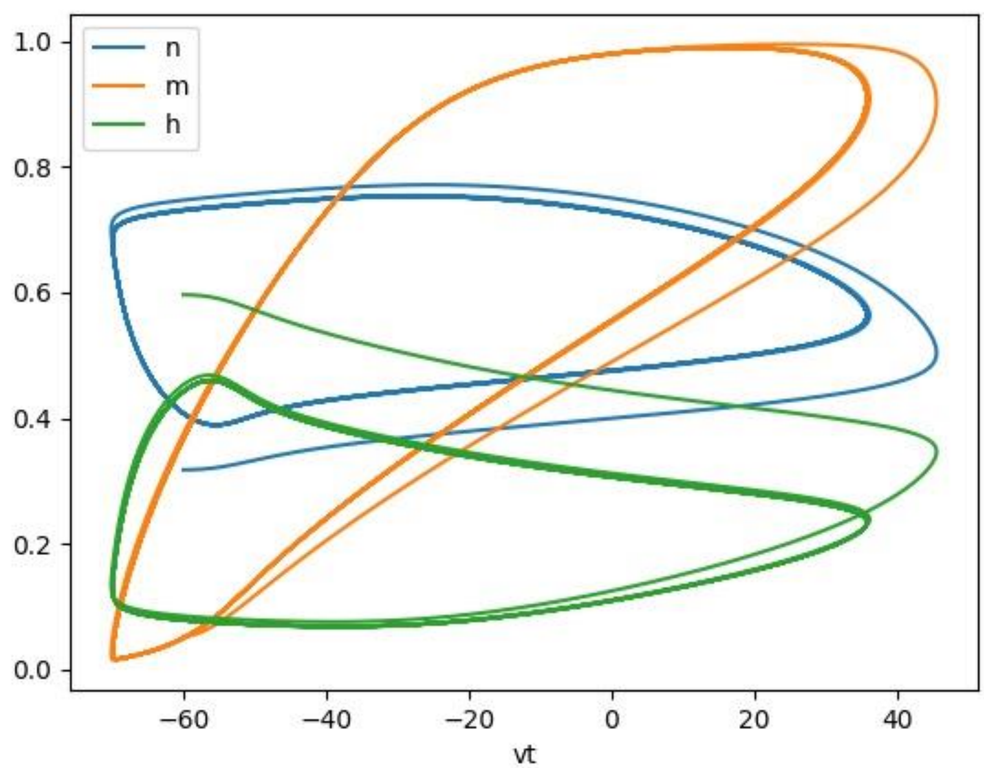
For small current (I_{ext} = 5 mA) plots would be



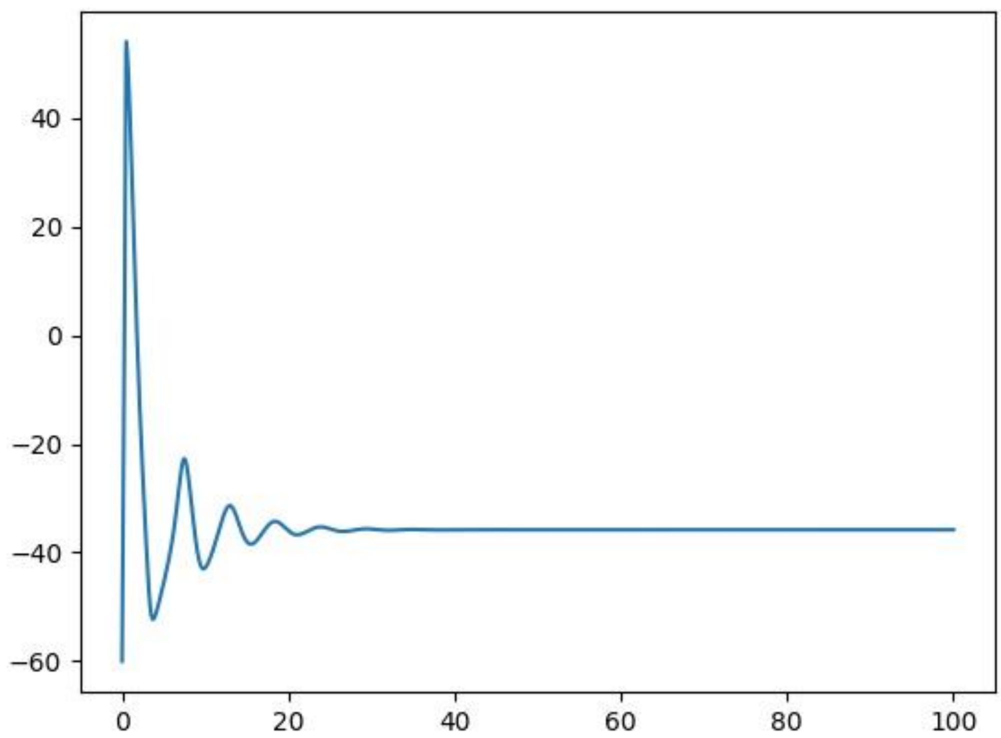


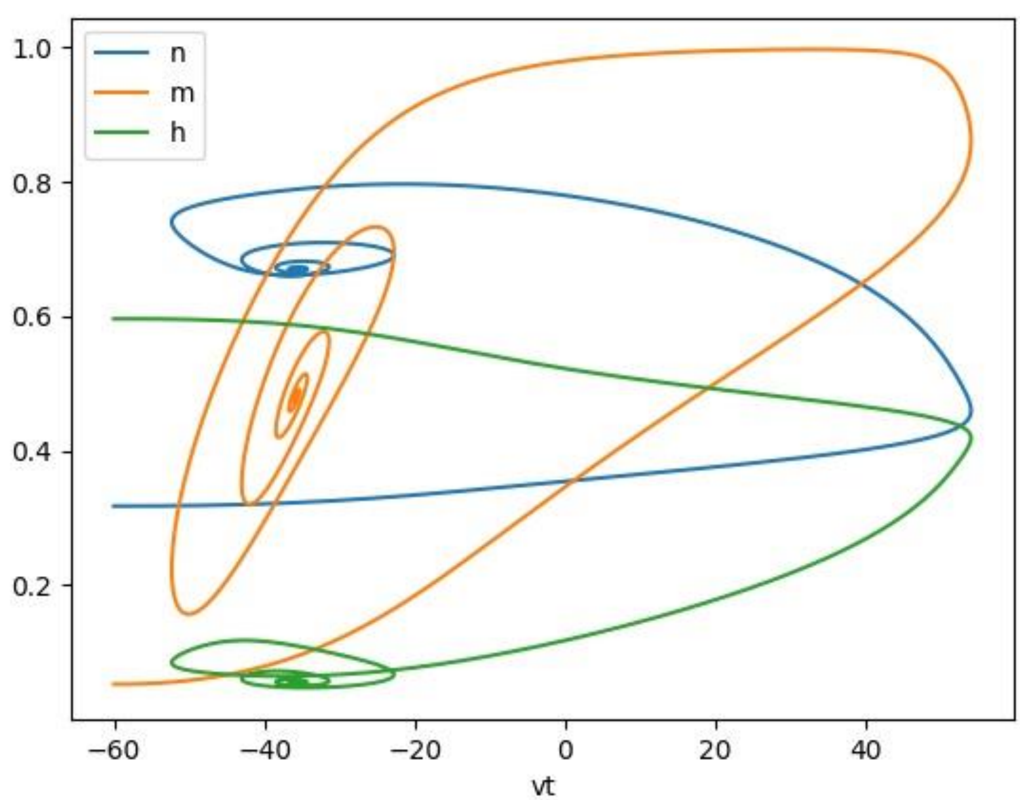
For proper value of current (I_{ext}=10 mA) plots would be





For large value of current (I_{ext}=200 mA), plots would be





Small current:

When the external current is small, model won't spike (except a single voltage increase in the beginning, which is not considered as spike) hence, values of n, m, h would be roughly constant since the neuron is in resting state (again, except for an initial change because of the increase in voltage in the beginning)

In this resting state, both sodium and potassium channels are more likely to be closed, so values of n, m would be small and h would larger (as it can be seen in the figure)

Proper current:

When the external current is proper, model would start spiking periodically. During each of these periods, we first have gradual increase of voltage from roughly -70 mV to -55 mV. At the end of this interval, it is more likely to sodium channels to get open, and it can be seen from the plot that the value of m increases and h roughly remains constant, verifying the claim.

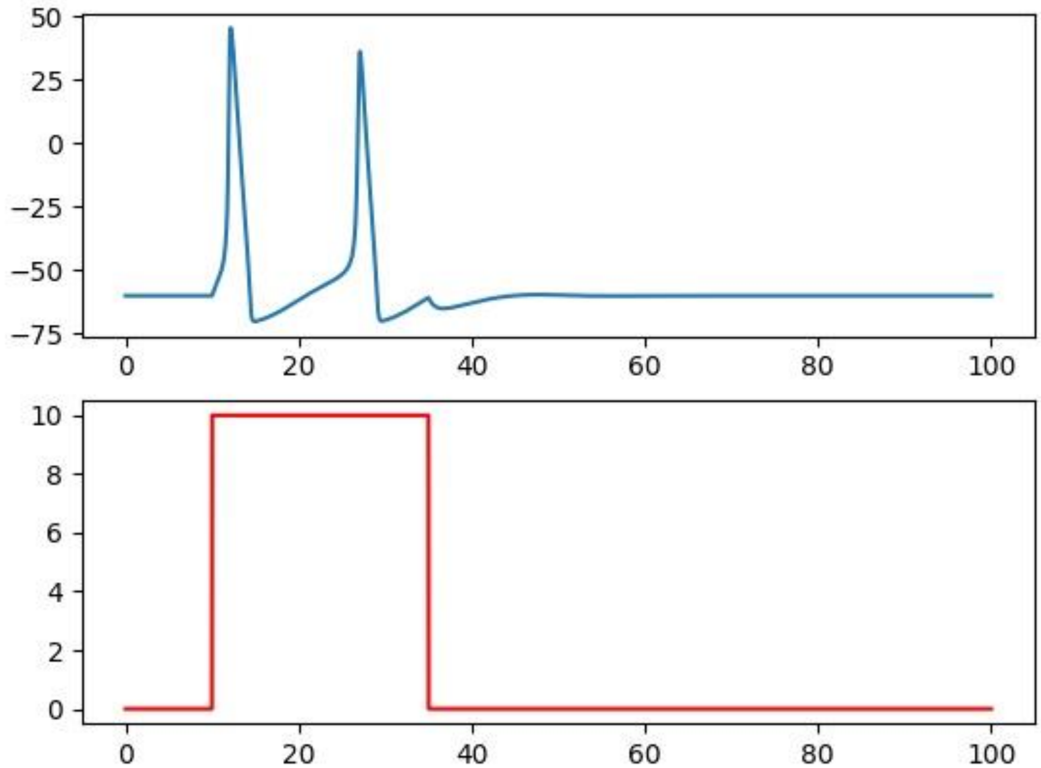
After the voltage passes -55 mV, sodium channels start to open intensively, and we can see that the value of m continues to increase and h still has a rather small value. When voltage reaches to large positive values (about 30 or 40 mV) sodium channels start to close, and so m starts to decrease and h increases. On the other hand, since potassium channels would start to open in this state, value of n starts to increase. As the voltage continues to decrease, potassium channels would start to get close, and so the value of n would decrease as the voltage decreases.

Large current:

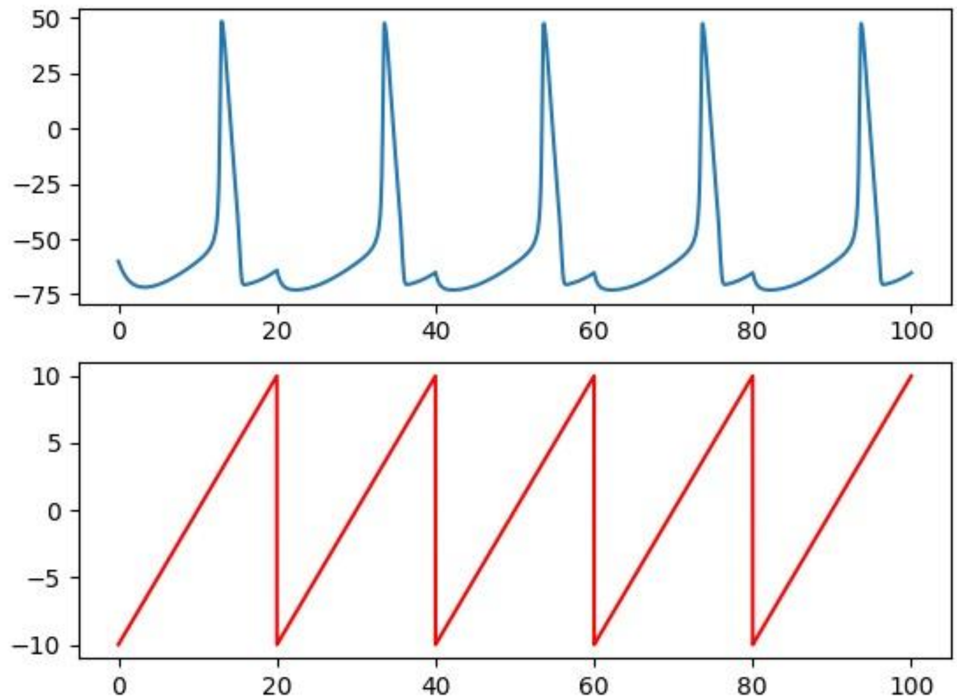
When the external current is too large, model won't spike (except a single voltage increase in the beginning and some small fluctuations, which are not considered as spike) hence, values of n, m, h would be roughly constant since the neuron is in resting state (again, except for an initial change because of the increase in voltage in the beginning)

9- Plot the voltage of the neuron when external current has the form of sinus, triangular, pulse and chirp wave. Describe the changes in voltage for sinus wave.

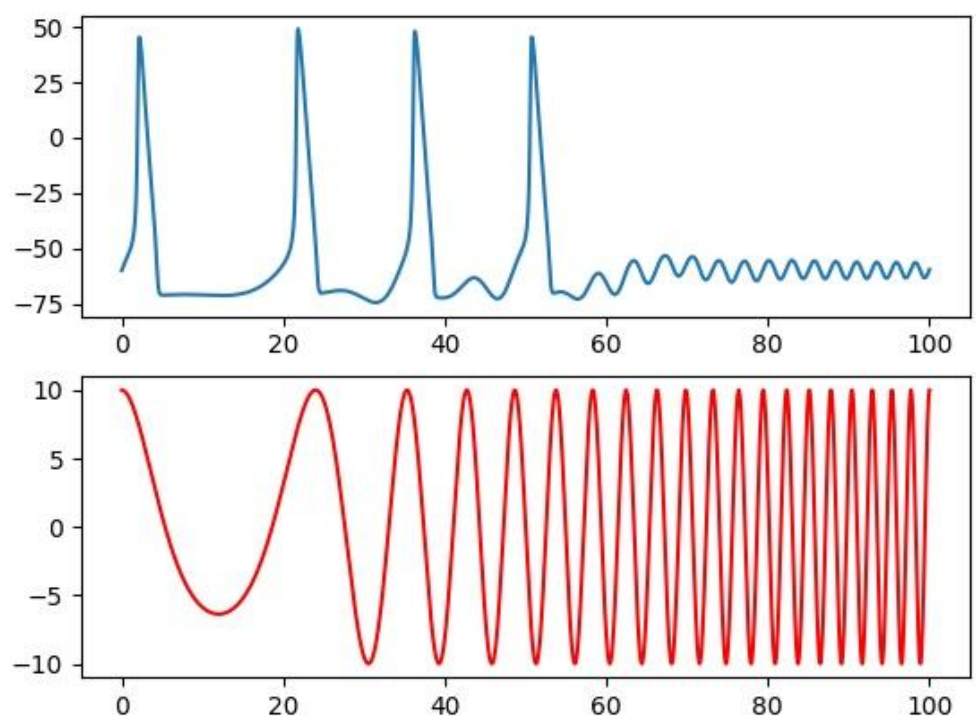
Pulse wave:



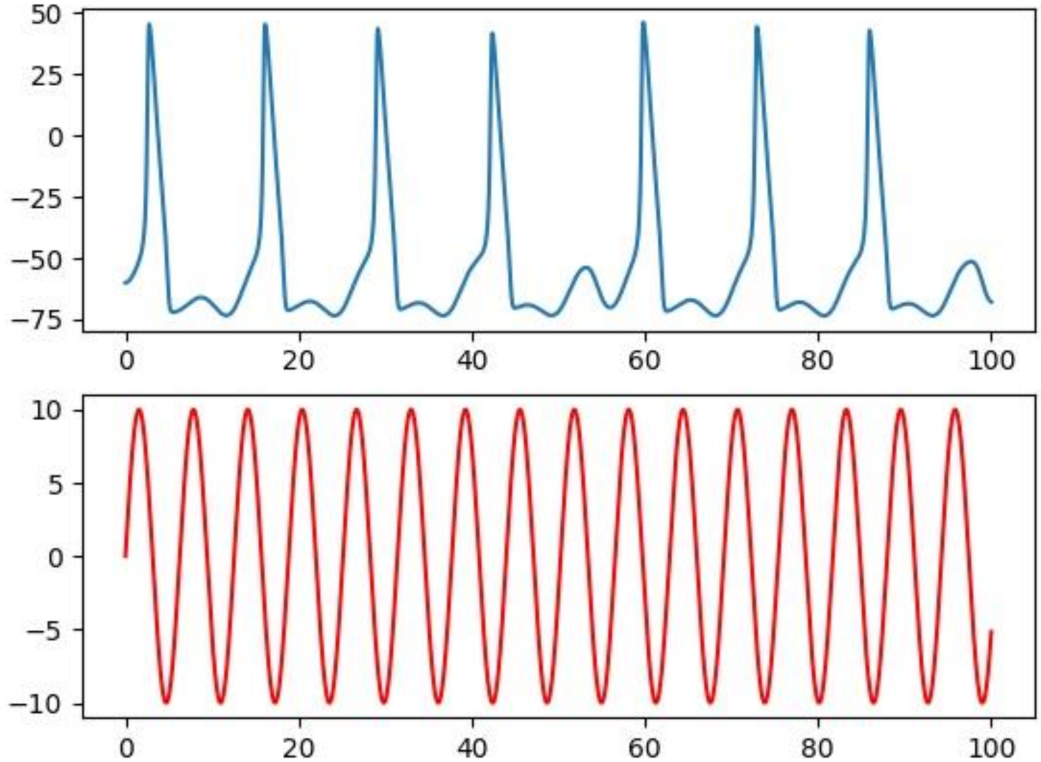
Triangular (sawtooth) wave:



Chirp wave:

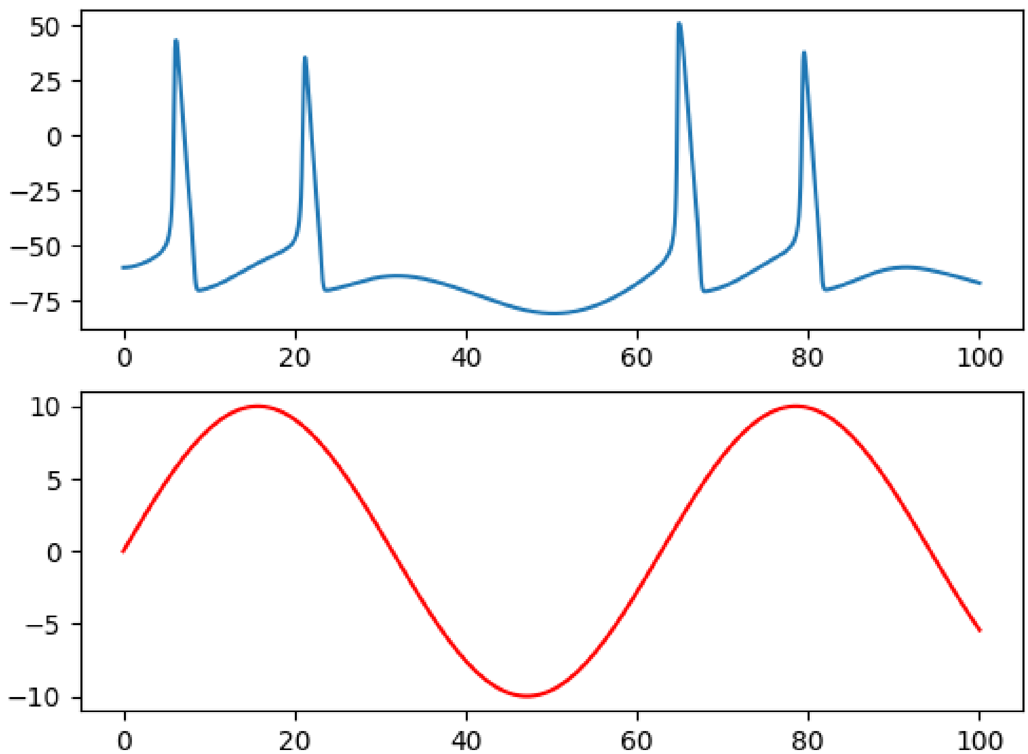


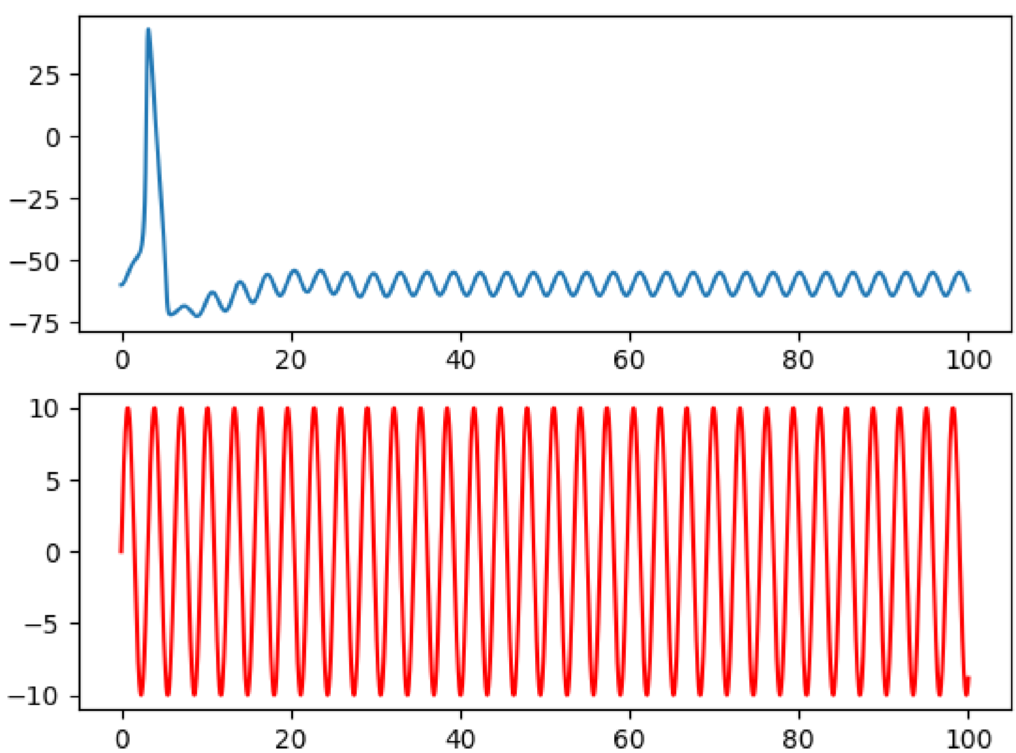
Sine wave:



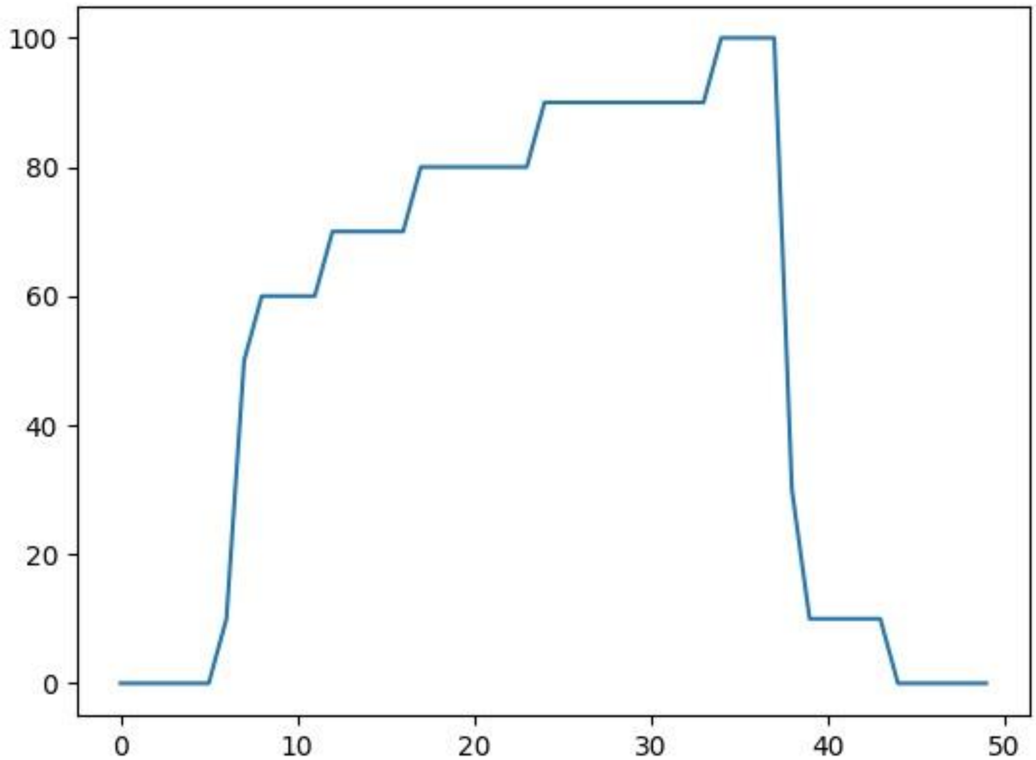
For the sine wave, we can see that the period of the wave is 2π, the model spikes periodically with a period roughly twice of the period of the sine wave. This also happens for larger periods, and the spiking happens with a higher rate when the sine wave approaches its maximum.

For too small periods (or large frequencies of sine wave) neuron does not spike.


50
25
0
−25
−50
−75
0
20
40
60
80
100
10
5
0
−5
−10
0
20
40
60
80
100


25
0
−25
−50
−75
0
20
40
60
80
100
10
5
0
−5
−10
0
20
40
60
80
100

10-Plot Firing rate-I_{ext} for H-H model. Explain the result



It can be seen from the plot that firing rate increases as the external current varies from 0 to roughly 40. This is because of the increase in the frequency of spikes, which is demonstrated before. When current gets larger than 40, firing rate falls to zero, because as we have seen before, domain and the maximum voltage reached by the neuron will decrease as the current increases, and so for large values on current, voltage won't pass the threshold and so we won't have any spike, causing firing rate to become zero.

Problem 2 : Izhikevich's model

In this problem we are going to implement the dynamic of a neuron which acts according to Izhikevich's model.

1- Explain the role of the second variable u in these equations.

Variable u is a recovery variable used for negative feedback to v (membrane voltage) and it is responsible for inactivation.

If we look at the equations, v is coupled with u through a positive function (abv) which means that as v increases, u will also increase. On the other hand, v is also coupled with u through a negative function (-u), meaning that when u is increased, it will cause v to decrease.

If we try to represent the model in reality, u accounts for the activation of potassium ionic channels and inactivation of sodium ionic channels, which both cause v to decrease [1].

2- Explain the role of parameters a, b, c, d in these equations.

a: determines the time scale of recovery variable u. when a gets large, recovery would be quicker. Its dimension is reciprocal of time (1/ms)

b: describes the sensitivity of the recovery variable u to the sub-threshold fluctuations of v. larger values of b results strong coupling of u and v, causing low-threshold spiking. b is dimensionless.

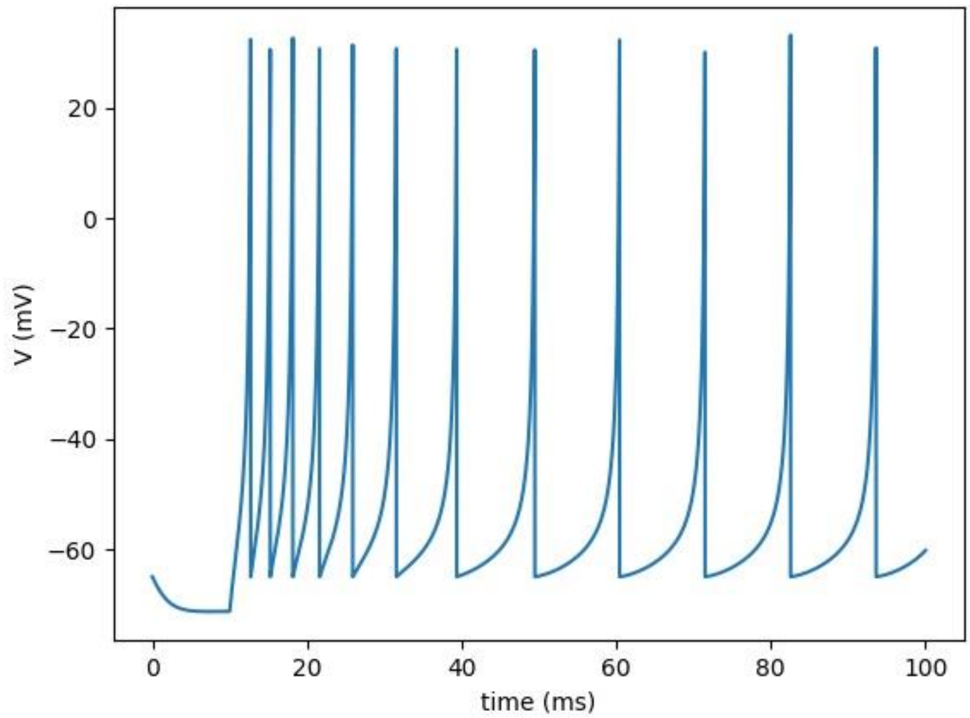
c: reset value of the membrane potential after spiking. we manually set v=c when model spikes. Dimension of c is Volt (or mV).

d: update value of recovery variable after spike. Dimension of d is Volt (or mV).

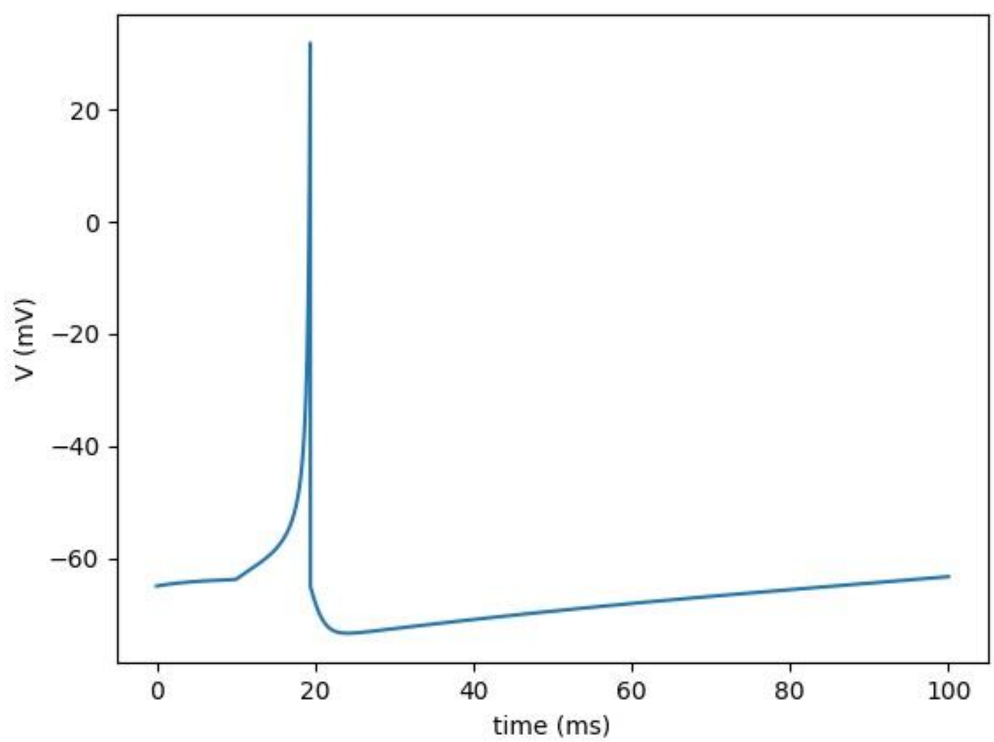
[1]

3- Let's examine five different types of spiking using this model, by setting certain values for constants a, b, c, d. Plot the voltage of neuron in each type for 100 ms.

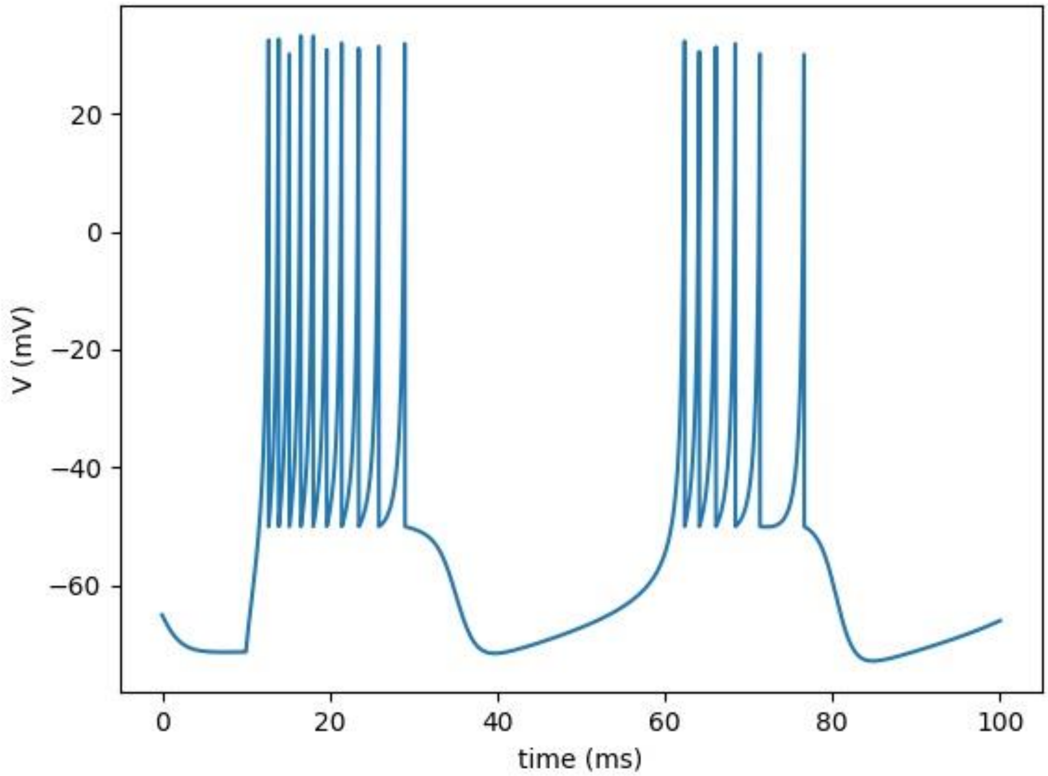
Tonic Spiking: a=0.02, b=0.2, c=-65, d=2, h=15



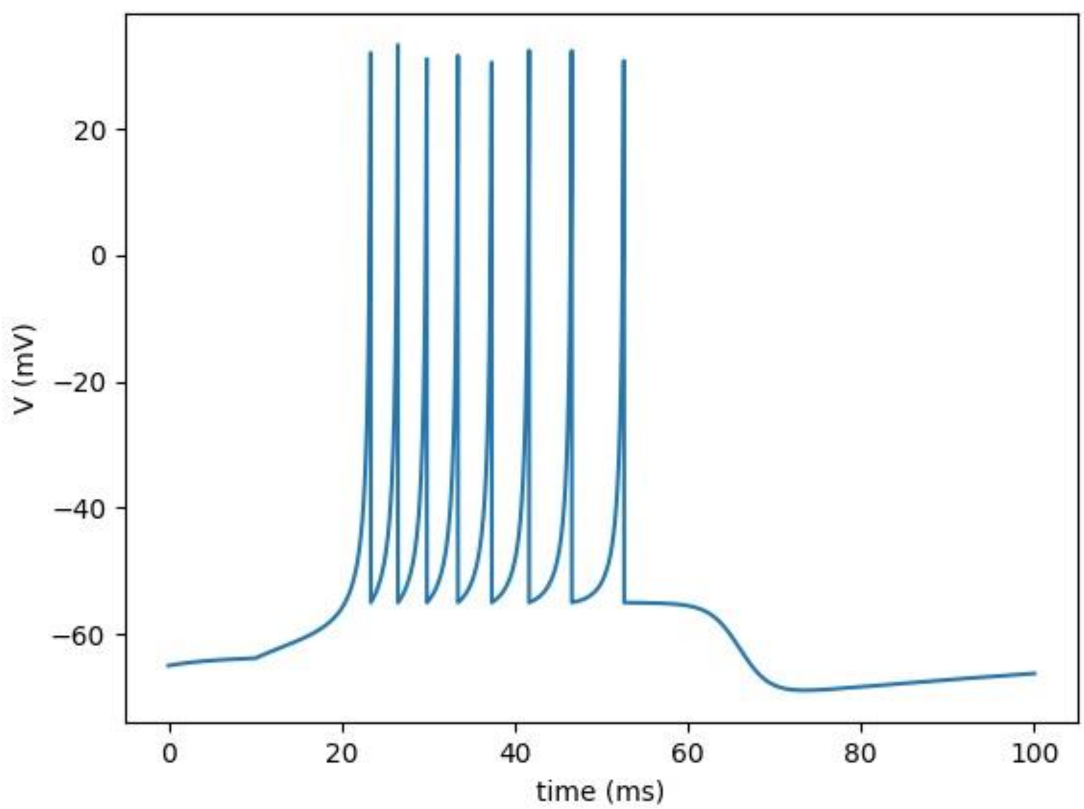
Phasic Spiking: a=0.02, b=0.25, c=-65, d=6, h=1



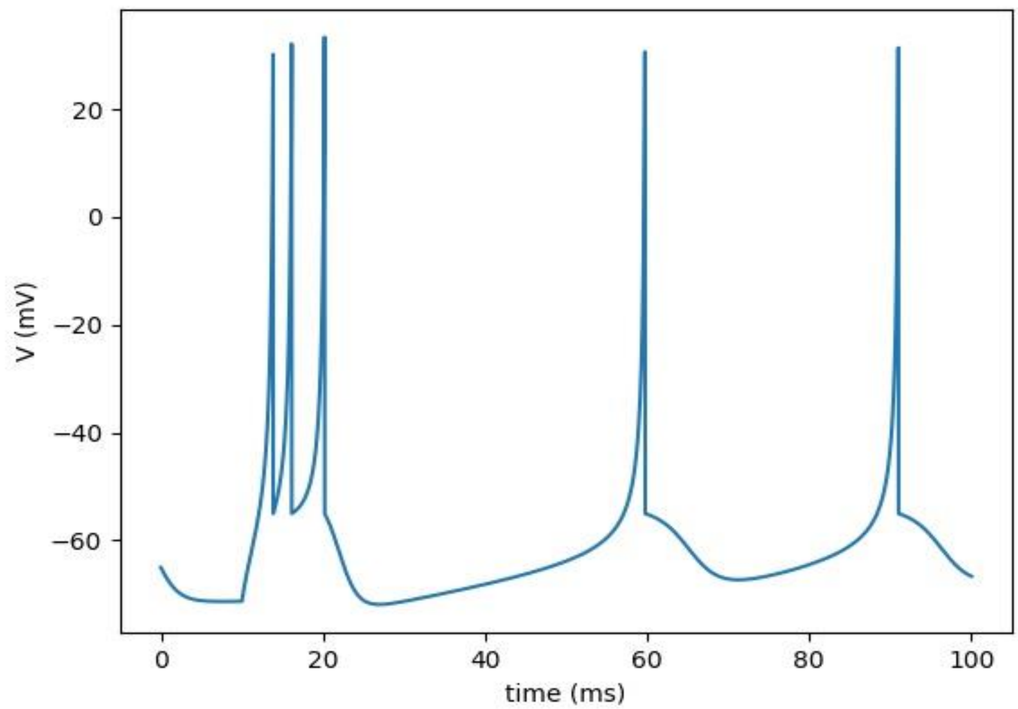
Tonic Bursting: a=0.02, b=0.2, c=-50, d=2, h=15



Phasic Bursting: a=0.02, b=0.25, c=-55, d=0.05, h=0.6

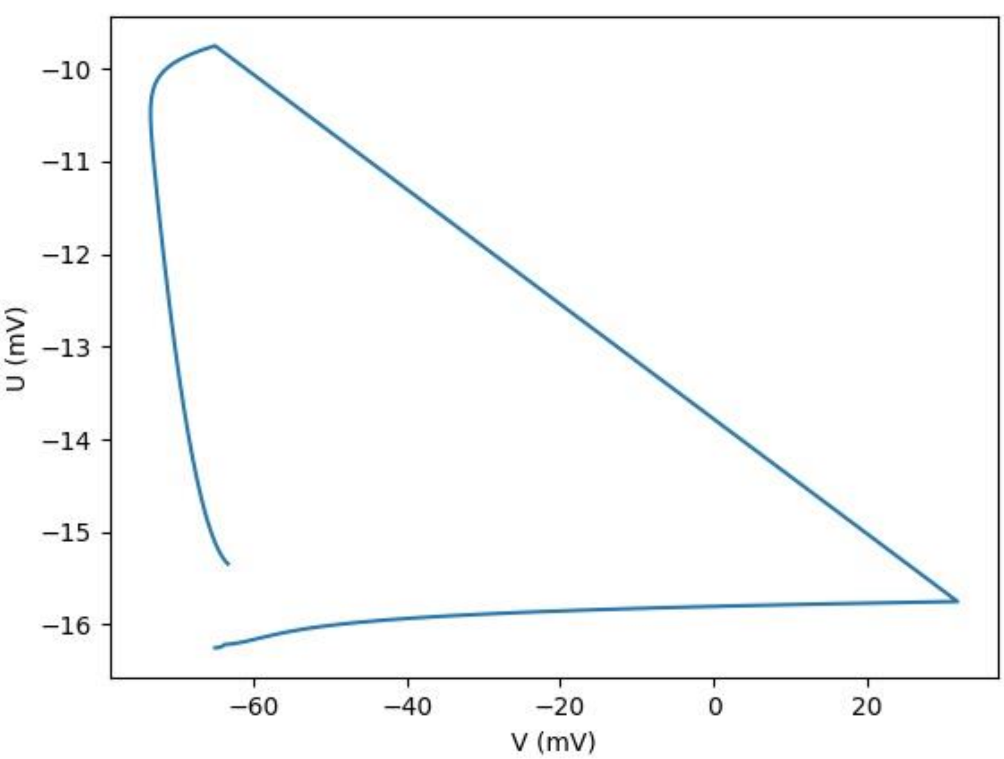


Mixed Model: a=0.02, b=0.2, c=-55, d=4, h=10



It is easy to see that these plots verify the functionality of each type of spiking (see [2])

4- Plot v-u of phasic spiking pattern and describe the result



This plot is verified by Izhikevich's equations for this type of spiking. as we can see, at first there is an increase in voltage from -65 mV to 30 mV (threshold) with small increase in u. then the voltage is manually set to c=-65 mV and u is set to u+d=u+6. Then we have a decrease in u, which again makes sense due to the phase plane of u and v (and also, the differential equation for u, noticing that v is small).

Problem 3: Noisy Output Model

In this problem, we will demonstrate Noisy output Model, which is a LIF model in which the threshold of spiking is assumed to be random with a sigmoid distribution around a certain threshold V_{th} with following CDF:

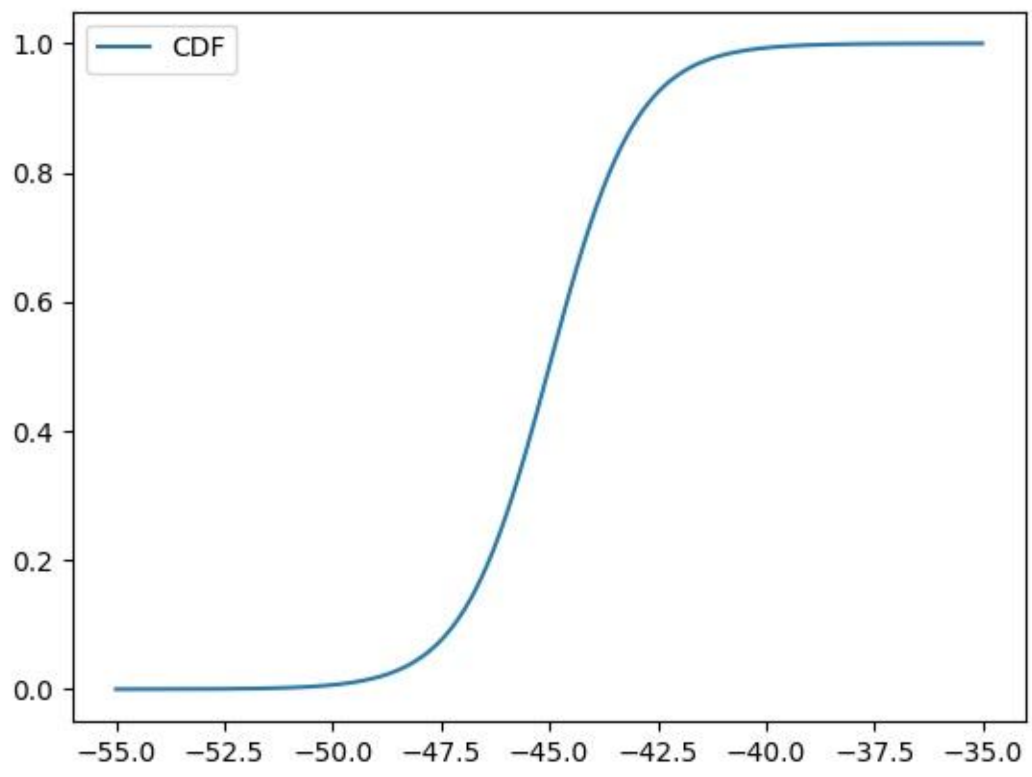
$$\rho(t) = \beta(1 + tanh(\gamma(V_t - V_{th})))$$

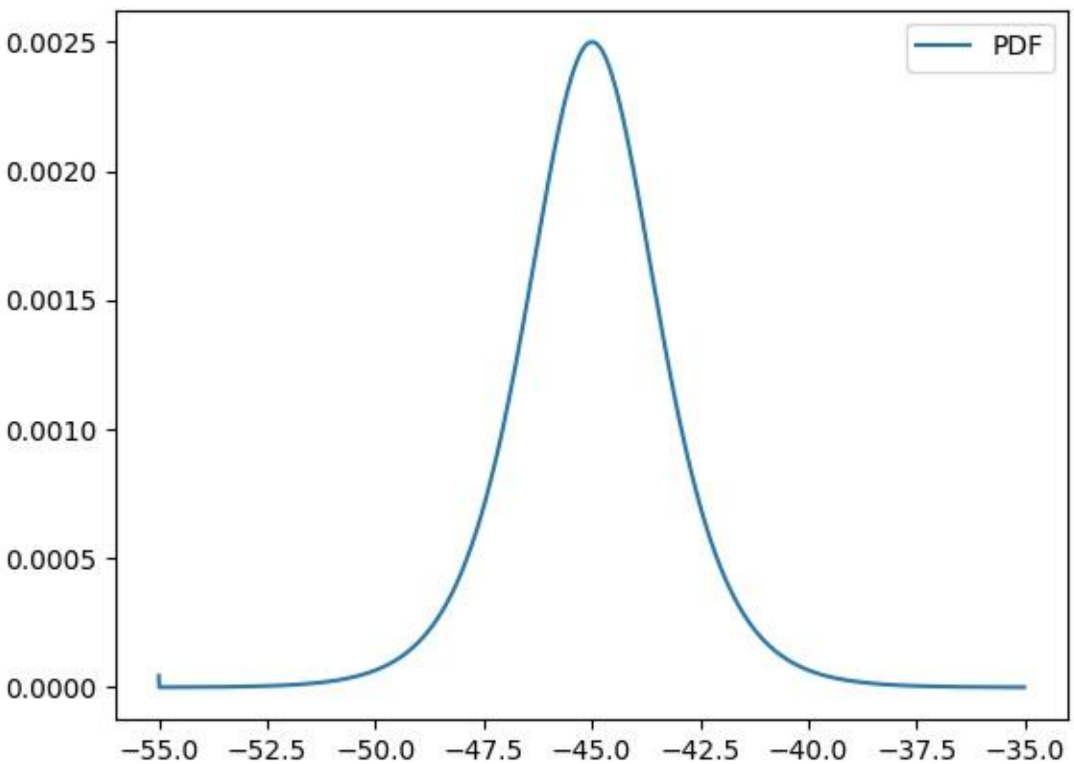
Voltage is calculated in the same way as LIF:

$$\frac{dv}{dt} = -v(t) + RI(t)$$

1- Plot CDF and PDF of this distribution. Explain why this distribution can properly model the threshold of a neuron.

Plot of CDF and PDF for γ=0.5:





If we use this model to predict the threshold for spiking, we will have a probabilistic threshold which gets value based on a distribution around a fixed constant threshold. Having non deterministic threshold can help removing noises and also describes the behavior of neurons in reality much better, as in real world, threshold of spiking for a neuron is not fixed and may vary.

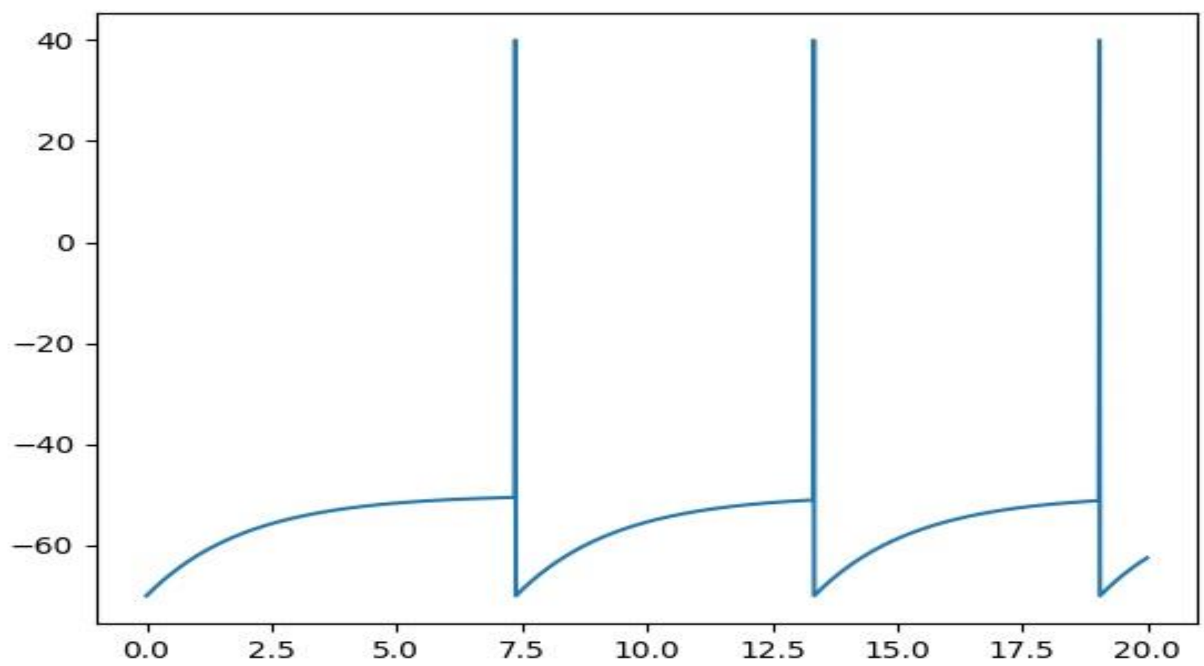
Effect of γ: value of γ determines how deterministic the model is. For large γ, model would be close to constant and less probabilistic. We set γ=0.5 to have non-zero probabilities in the interval [-50,-40], in order to achieve proper randomness.

2- For the following constants, simulate model for 20 ms and plot neuron voltage.

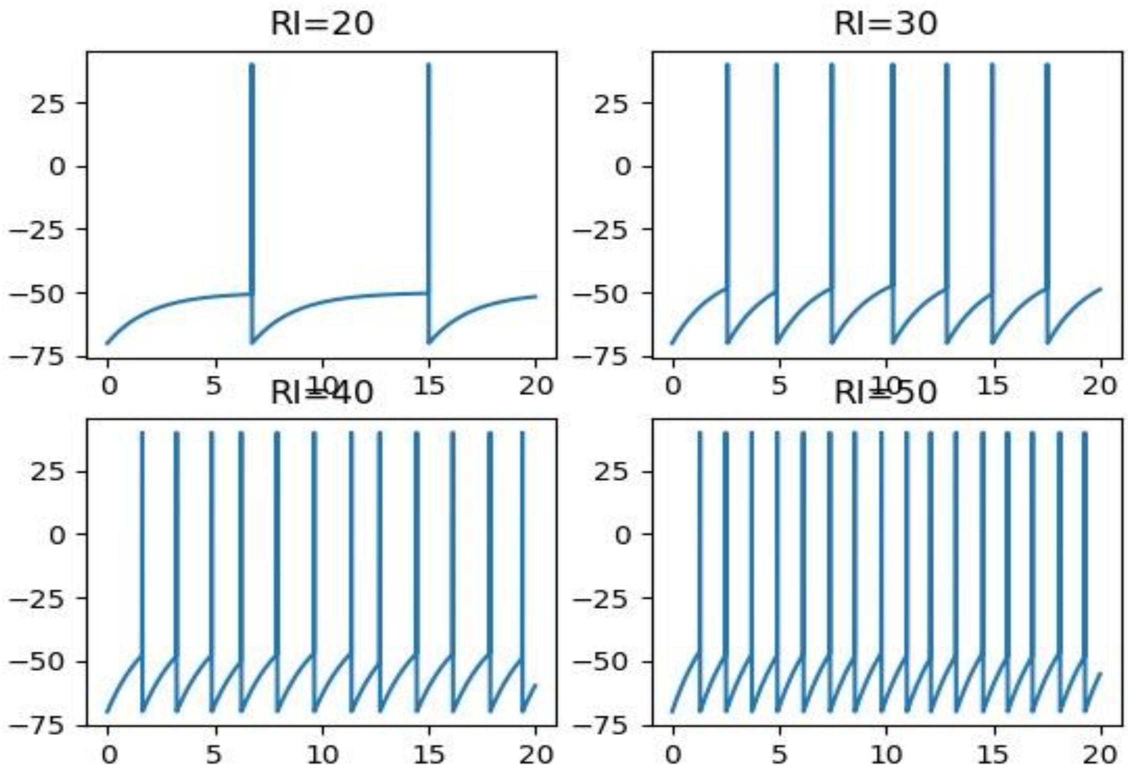
$$RI = 20mV, V_{th} = -45mV, V_{rest} = -70mV, \tau_m = \text{arbitrary}$$

Explain the effect of RI on the output of the model.

Plot of voltage:



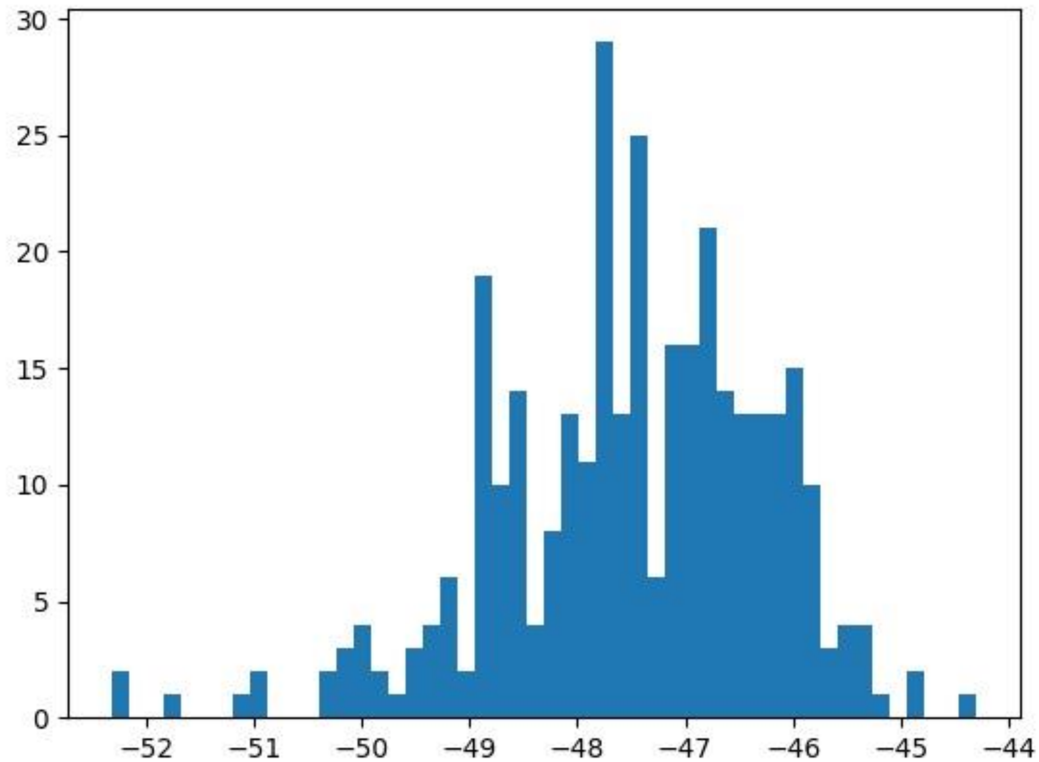
To see the effect of RI better, let us plot the voltage of the neuron for different values of RI:



It can be seen that by increasing RI, frequency of the spiking of the model increases. This makes sense to reality, as RI actually represents the external current applied to the neuron, and the neuron is expected to spike more intensively (with higher frequency) as RI increases.

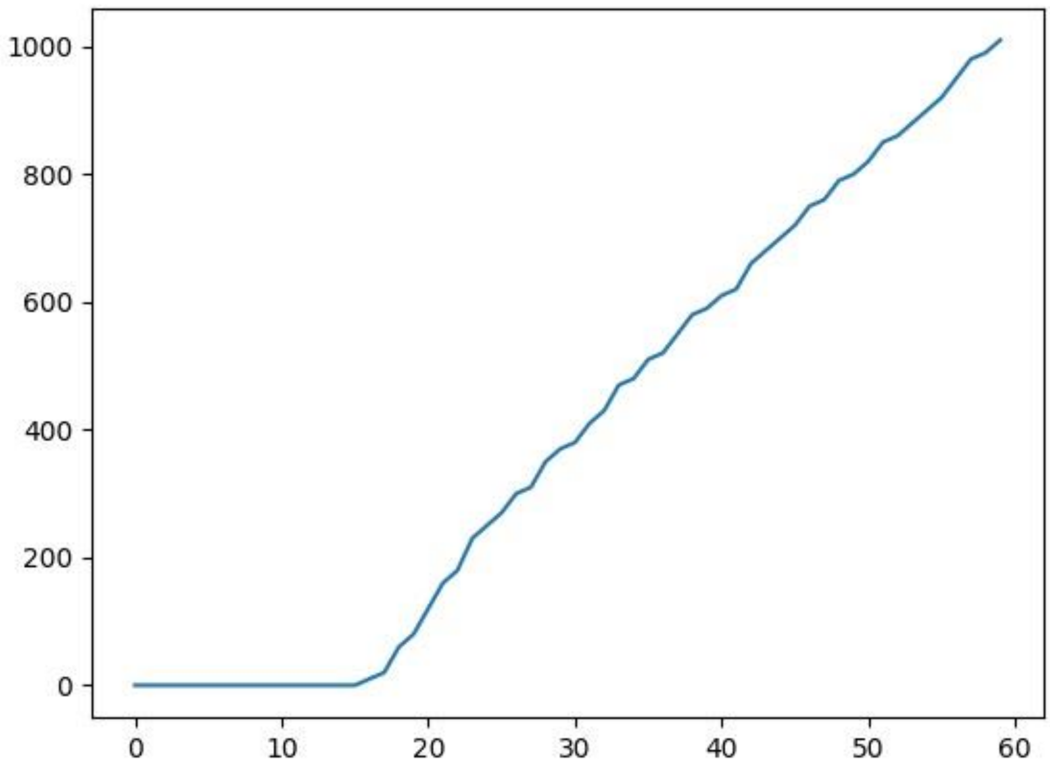
3- Plot the histogram of the voltages in which model has spiked.

We set RI=50 mV and increase the duration to 400 ms in order to have more samples for the histogram:



4- Plot firing rate with respect to external current. Set R=1mΩ and change I. explain the behavior of the output.

We set duration to be 100 ms and vary I from 0 to 60:



It can be seen from the plot that as external current increases, firing rate is also increased and the model spikes more rapidly and intensively. This makes sense, as we have seen in second problem that larger external current increases the frequency of spikes.

Problem 4: Integrate and Fire Models

Do a research about Perfect Integrate and Fire model and Leaky Integrate and Fire model. Write down your results and compare these two models.

Perfect Integrate and Fire model:

This is one of the earliest neural models, first introduced by Louis Lapicque in 1907. In this model, the input current (I(t)) is assumed to be proportional to the changes in membrane voltage ($\frac{dv}{dt}$) by the following equation:

$$I(t) = C\frac{dv}{dt}$$

If an input current is given, the membrane potential will increase until it reaches a threshold V_{th}. At this time, voltage is reset to a resting potential and spike would happen.

Although this model is rather simple, it doesn't describe adaptation and leakage. Also, if a low input current is applied to the neuron that doesn't cause the voltage to reach its firing threshold, then voltage will remain on that stage until a new current is applied, and this behavior does not make sense with neurons in reality.[3]

Leaky Integrate and Fire model:

This model is also traced back to Louis Lapicque, and considers the current cause by the diffusion in the membrane of the neuron. In the equation of this model, we have a term representing this current:

$$C_m\frac{dv}{dt} = I(t) - \frac{V}{R}$$

Where V is the potential of the membrane and R is the membrane resistance. By multiplying both sides of the equation in R we get

$$\tau_m\frac{dv}{dt} = RI(t) - V(t)$$

Just like PIF, in LIF we have a threshold potential V_{th}, which a spike happens when membrane voltage passes this threshold, and then it would be reset.

It can be seen from the equation that for constant I(t), if $I = \frac{V_{th}}{R}$ or higher, then neuron will spike. Also, this model can be used for inhibitory neurons as well. One of the disadvantages of the LIF is that it does not contain neuronal adaptation so that it cannot describe an experimentally measured spike train in response to constant input current. Also, this model is highly simplified and neglects many aspects of neuronal dynamics. In particular, input, which may arise from presynaptic neurons or from current injection, is integrated linearly, independently of the state of the postsynaptic neuron.

Unlike PIF, in LIF we have a term for the membrane leak, which makes this model more exact compared to PIL. In PIF, we have basically set R=infinity.[3][4]

Problem 5: Bifurcation

1- Plot the bifurcation diagram for the system $\dot{x} = x^2 + a$.

First let us check the fixed points of the system by setting $\dot{x}$=0. So

$$x^2 + a = 0 \;\Rightarrow x = \pm\sqrt{-a}$$

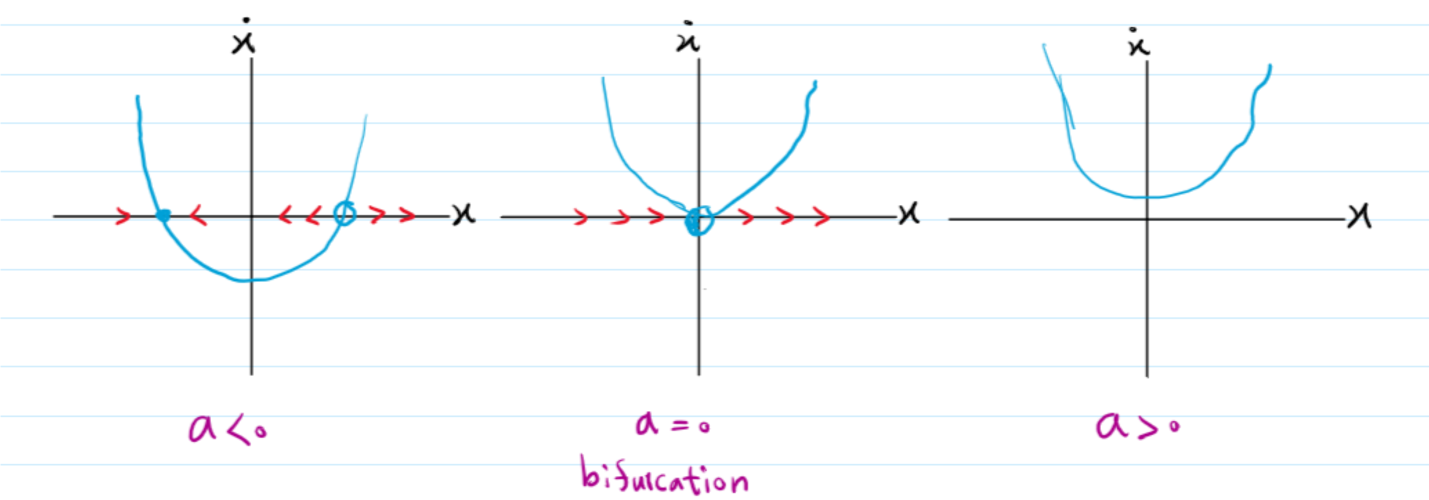
For positive a, fixed points would be imaginary. For a=0, we have bifurcation and when a<0, there are two fixed points, one stable and other unstable.

To determine the stability in the third case, we need to take derivatives from

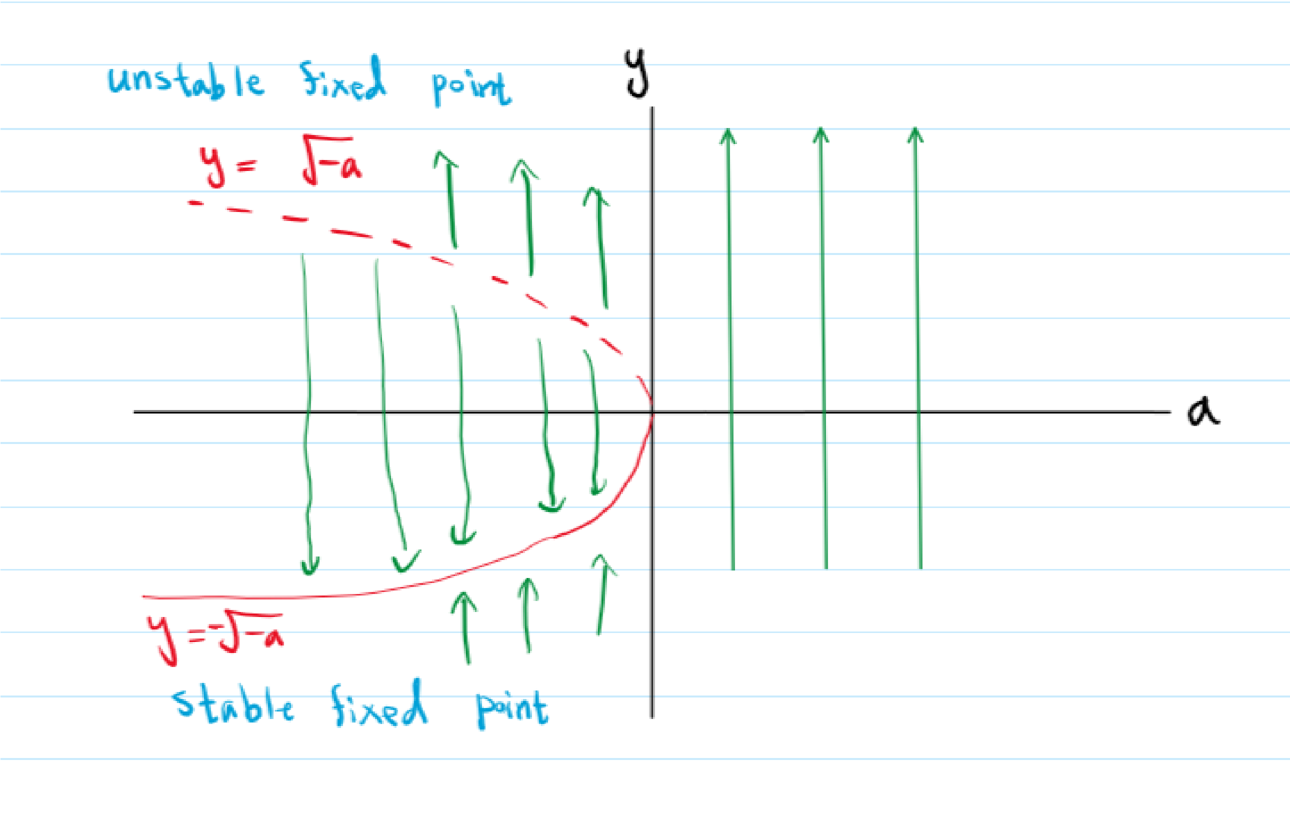
F(x)=x^2+a and plug x=y (y is the fixed point) if the result is negative, fixed point is stable and vice versa.

$$f'(x) = 2x, y = \pm\sqrt{-a} \Rightarrow f'(y) = 2y = \pm 2\sqrt{-a}$$

So for $y = \sqrt{-a}$ fixed point is unstable and for $y = -\sqrt{-a}$, the fixed point is stable.



Now we can plot bifurcation diagram from these informations:



2- Consider the first degree system $\dot{x} = f(x)$. Show that saddle node bifurcation for this system occurs when $f'(x) = 0$

Notice that the stability of the fixed points is based on the sign of f'(x), as we mentioned in the previous part. When f'(x)=0, we have a change in the stability, meaning that one side of the point is stable and the other side is not, causing bifurcation (we can see this in the previous part as well, when for r=0, point x=0 which causes f'(x)=0 is bifurcation).

Problem 6: Phase Plane

Consider the following model:

$$\begin{cases} \frac{V_E}{dt} = (-V_E + [M_{EE}V_E + M_{EI}V_I - \gamma_E]_+)/\tau_E \\ \frac{V_I}{dt} = (-V_E + [M_{IE}V_E + M_{II}V_I - \gamma_I]_+)/\tau_I \end{cases}$$

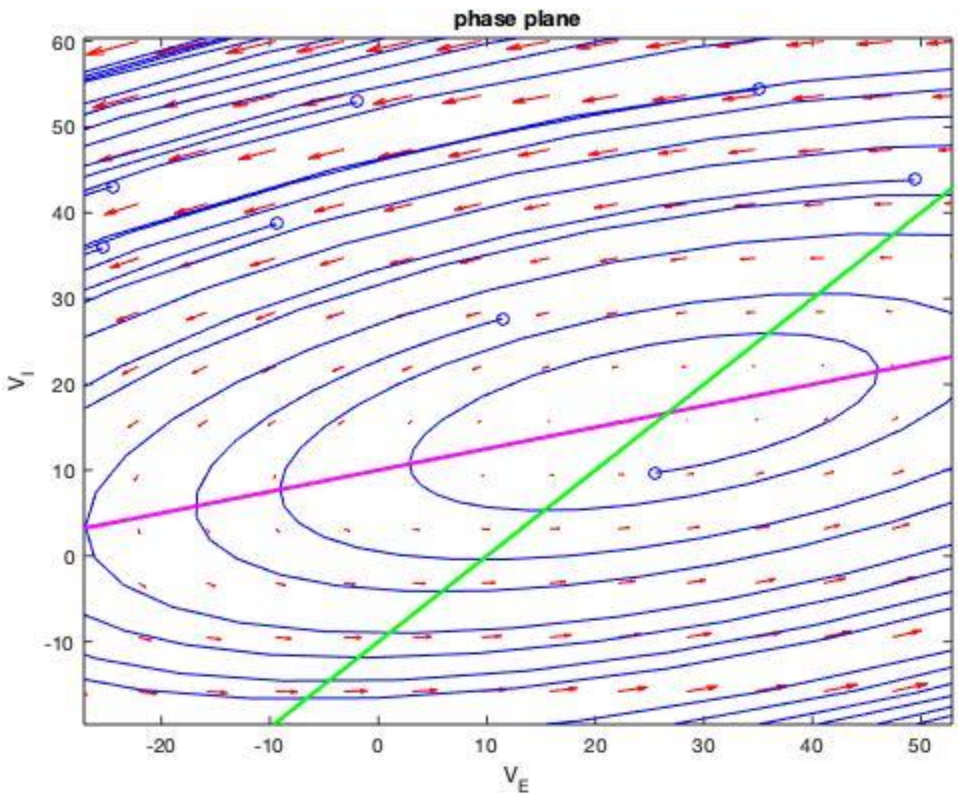
This model describes the behavior of a network of two excitatory and inhibitory neurons. Following code plots the phase plane of this equation:

```
clc
clear
figure
% initial parameters
noip = 10;
interval = 60;
Mee = 1.25;
Mei = -1;
Mie = 1;
Mii = 0;
Ye = -10;
Yi = 10;
Te = 0.01;
Ti = 0.05;
f = @(t,Y) [(-Y(1)+Mee*Y(1)+Mei*Y(2)-Ye)/Te;(-Y(2)+Mie*Y(1)+Mii*Y(2)-Yi)/Ti];
y1 = linspace(-interval,interval,20);
y2 = linspace(-interval,interval,20);
% creates two matrices one for all the x-values on the grid, and one for
% all the y-values on the grid. Note that x and y are matrices of the same
% size and shape, in this case 20 rows and 20 columns
[x,y] = meshgrid(y1,y2);
u = zeros(size(x));
v = zeros(size(x));
```

```
% we can use a single loop over each element to compute the derivatives at
% each point (y1, y2)
t=0; % we want the derivatives at each point at t=0, i.e. the starting time
for i = 1:numel(x)
Yprime = f(t,[x(i); y(i)]);
u(i) = Yprime(1);
v(i) = Yprime(2);
end
quiver(x,y,u,v,'r');
xlabel('V_E')
ylabel('V_I')
% axis tight equal;
hold on
for i = 1:noip
[ts,ys] = ode45(f,[0,50],[rand()*interval*((-1)^floor(rand()*interval)); ...
rand()*interval*((-1)^floor(rand()*interval))]);
plot(ys(:,1),ys(:,2),'b')
plot(ys(1,1),ys(1,2),'bo') % starting point
plot(ys(end,1),ys(end,2),'ks') % ending point
xlim([-interval interval]);
ylim([-interval interval]);
end
syms t
fplot((t+Ye-Mee*t)/Mei,'m','LineWidth',2);
fplot((Yi-Mie*t)/(Mii-1),'g','LineWidth',2);
title("phase plane")
hold('off')
```

1- Run the code for nois=15. Argue about the fixed point and its stability.

Figure of the phase plane :

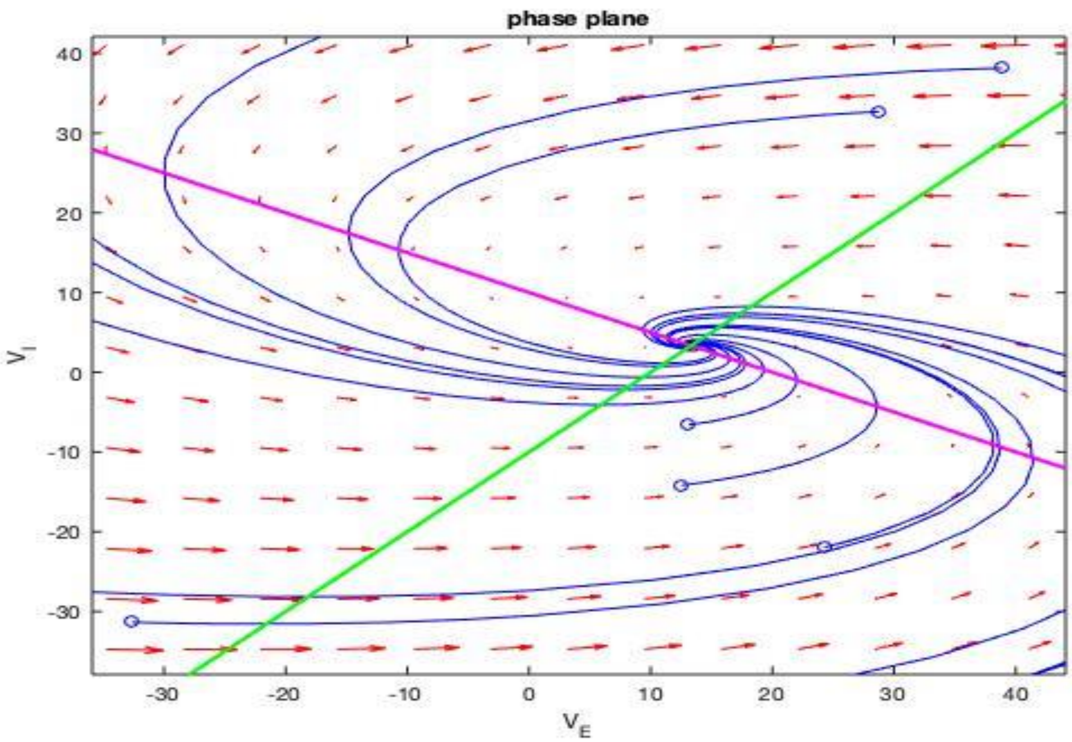


As it can be seen in the figure, fixed point is focus (trajectories are turning around the fixed point) and unstable (because if we start from a point near it, we will be pushed away from it). This happens when both eigenvalues are imaginary and their real part is positive.

2- Fix all parameter and change the value of M_{EE} and report the changes on the phase plane.

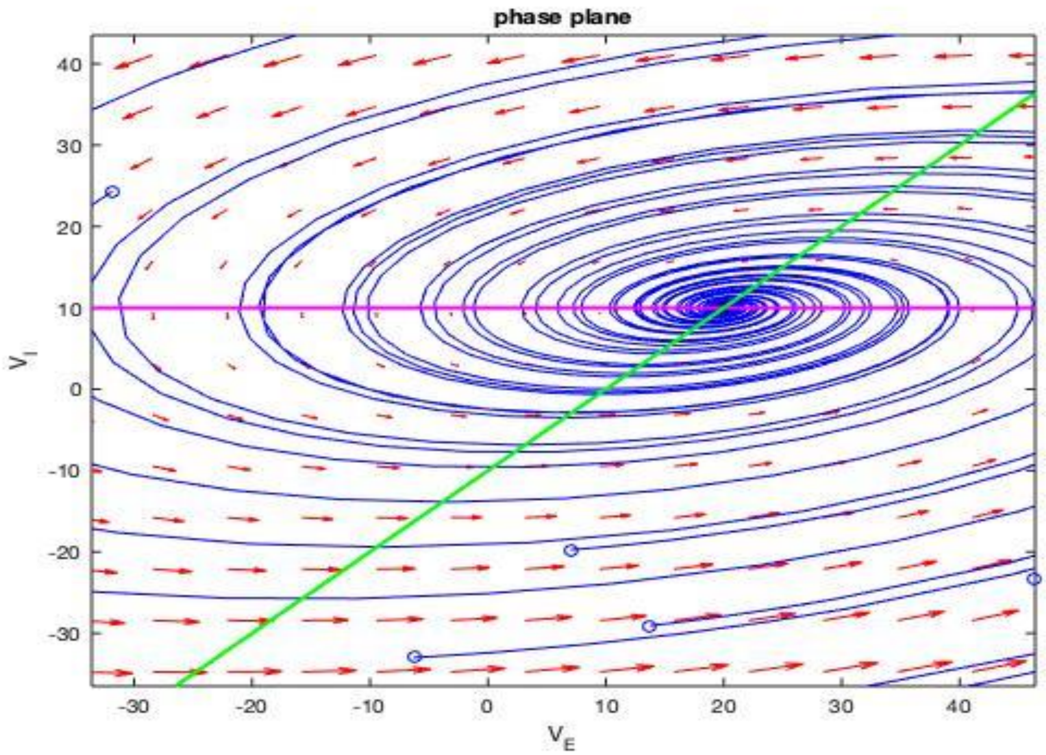
We have already seen the phase plane for M_{EE}=1.25. let us test some smaller values:

M_{EE}=0.5:



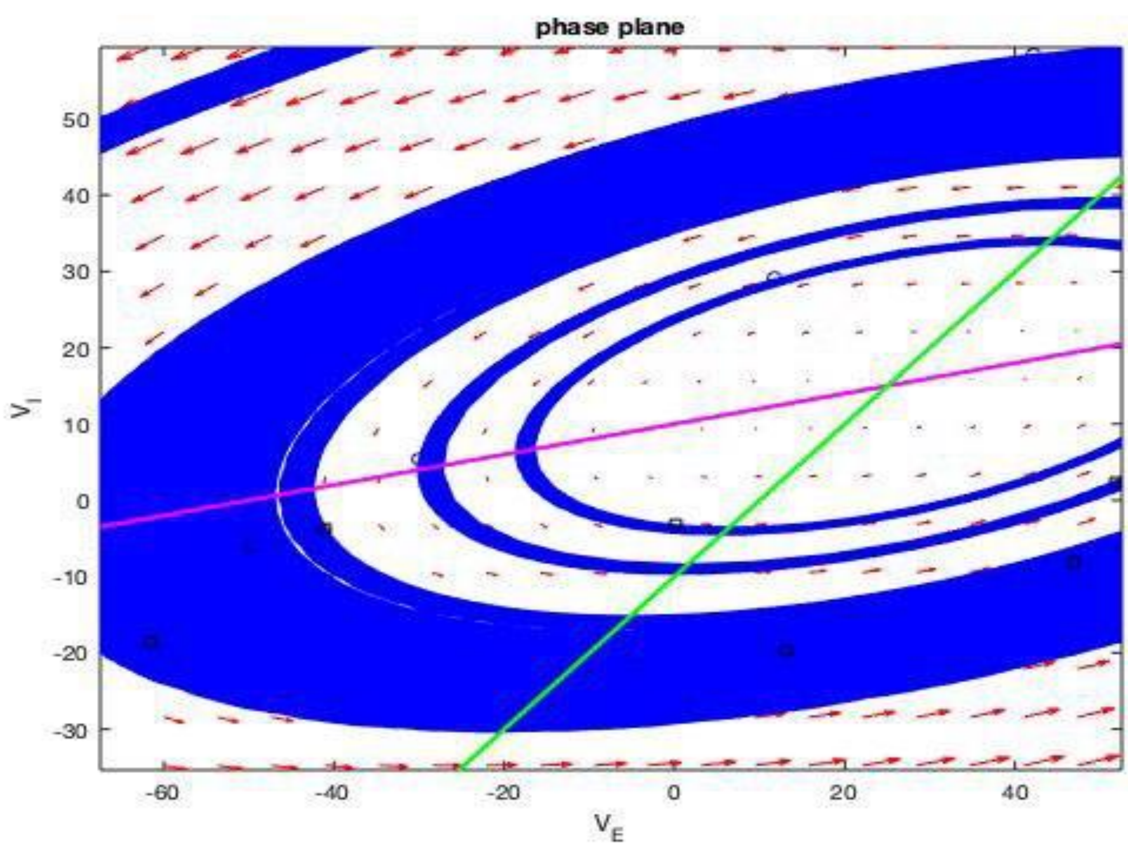
Fixed point is still focus but it is now stable, because trajectories approach to it for nearby starting points.

$M_{EE}=1$



Again, the fix point is same as the previous one.

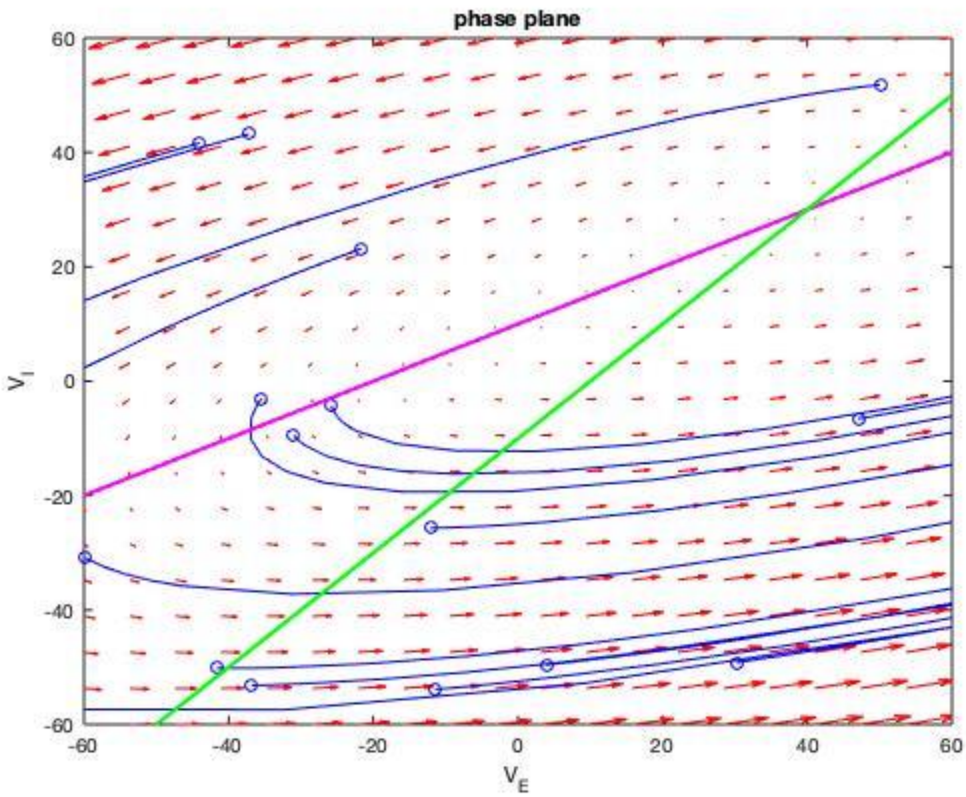
$M_{EE}=1.2$



Fix point is bifurcation in this case.

Now we test it for larger values of M_{EE}

M_{EE}=1.5

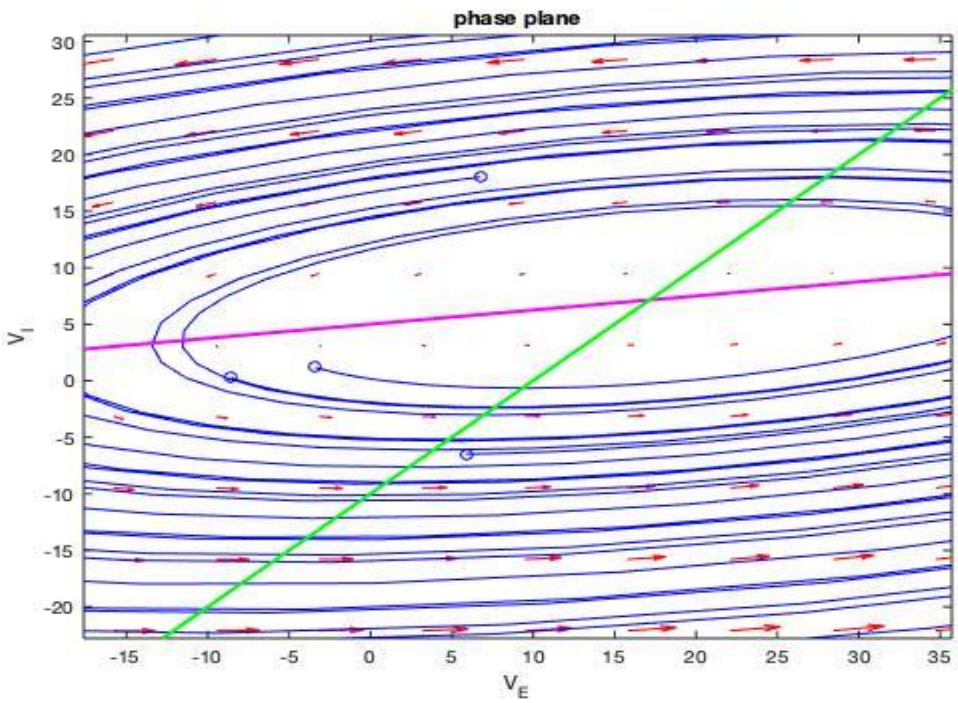


Fixed-point becomes unstable-focus, which is expected, since we have passed the value that made the point bifurcation.

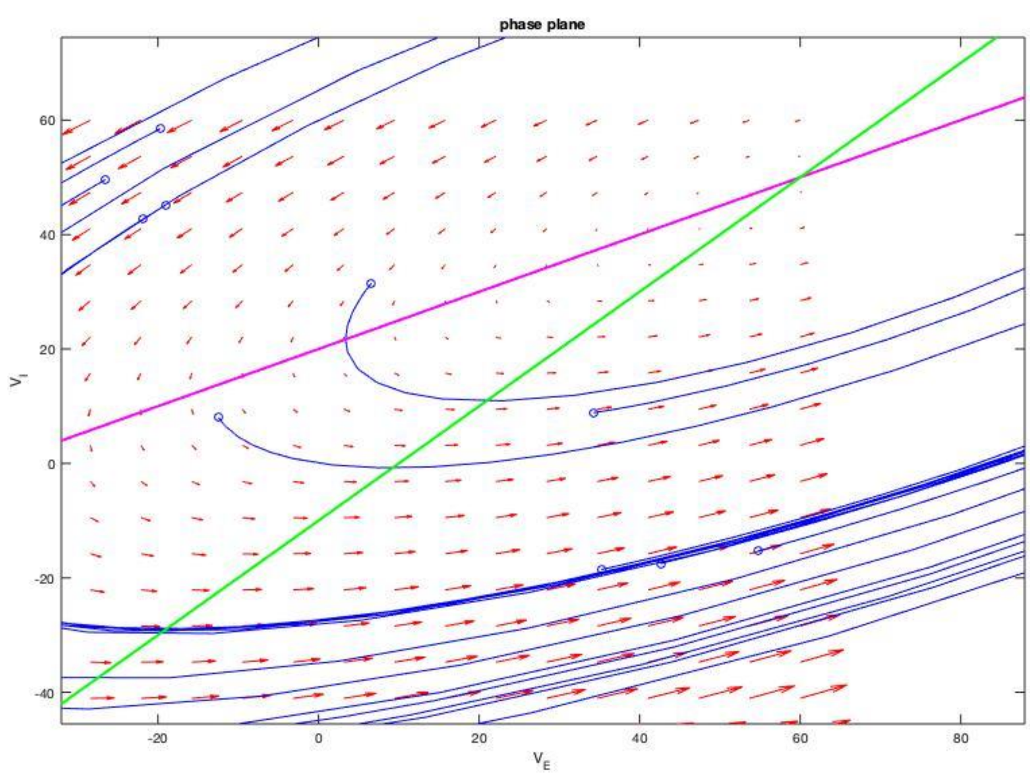
3- Do previous problem for M_{Ei}, M_{iE}, M_{ii}.

For M_{Ei}, we test three values -2,-0.5,0.5 (-1 is already tested)

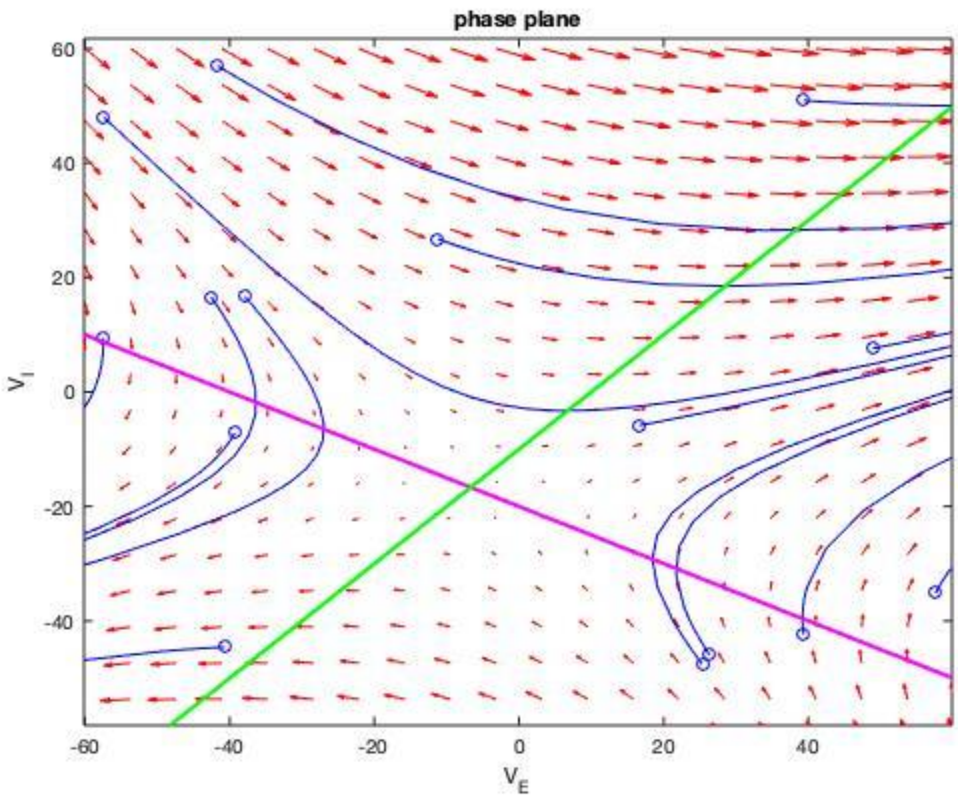
M_{Ei}=-2: fixed point is focus and unstable



M_{Ei}=-0.5: again, fixed point is focus and unstable

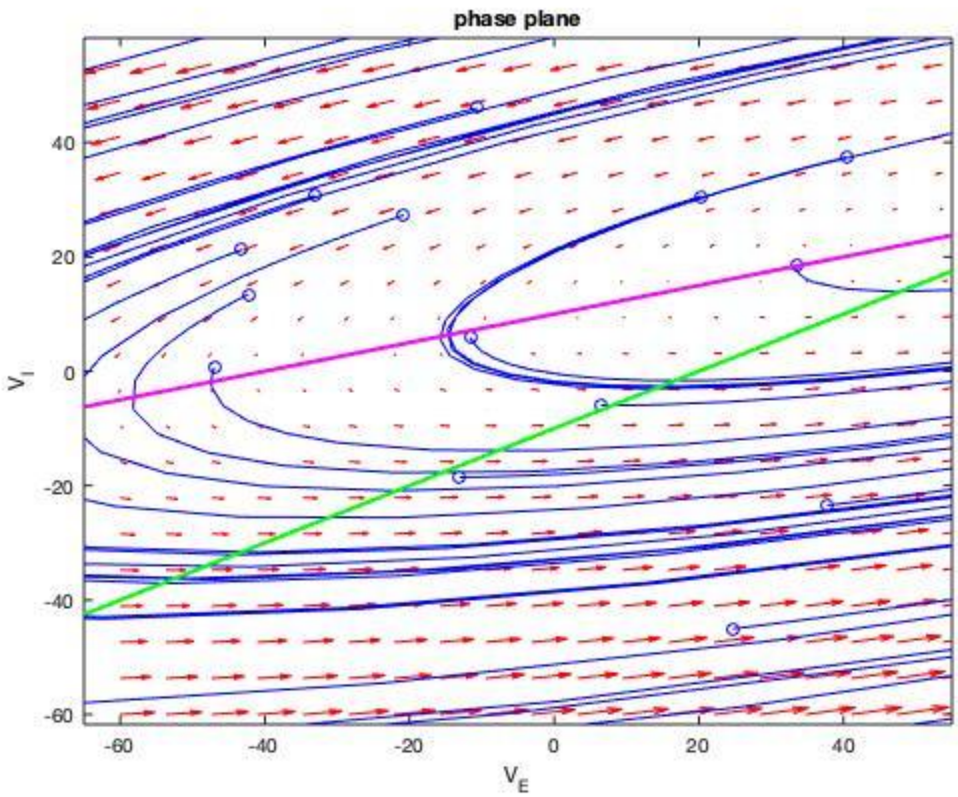


M_{Ei}=0.5: fixed point is sadle and unstable

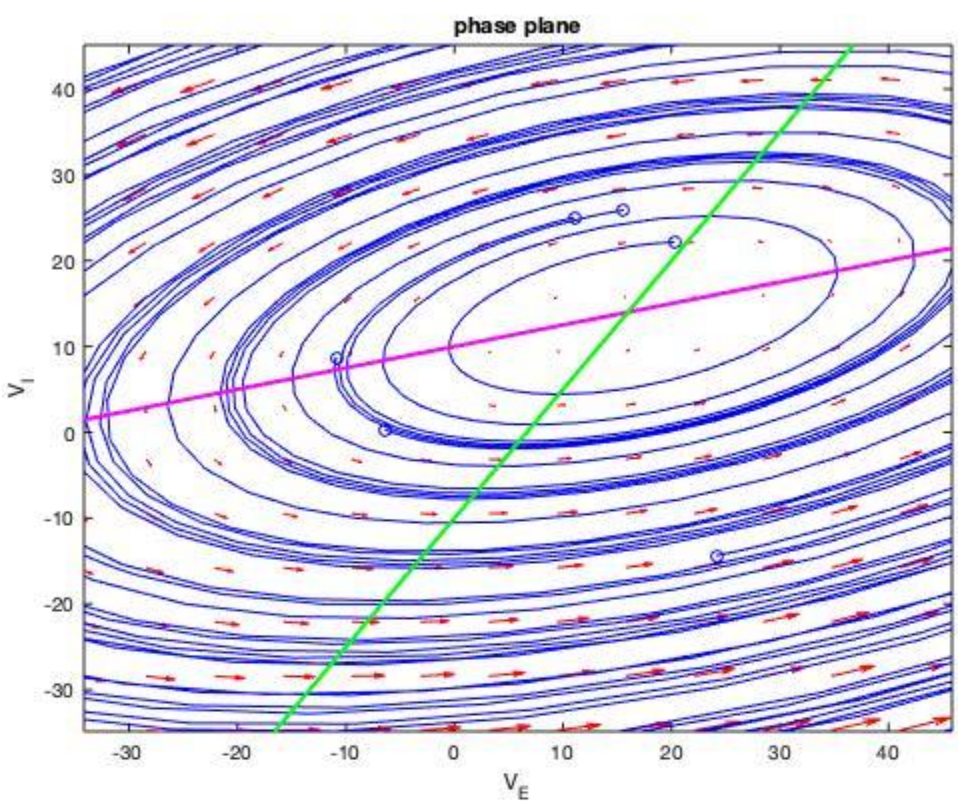


For M_{IE}, we test three values 0.5,1.5,2,7 (1 is already tested)

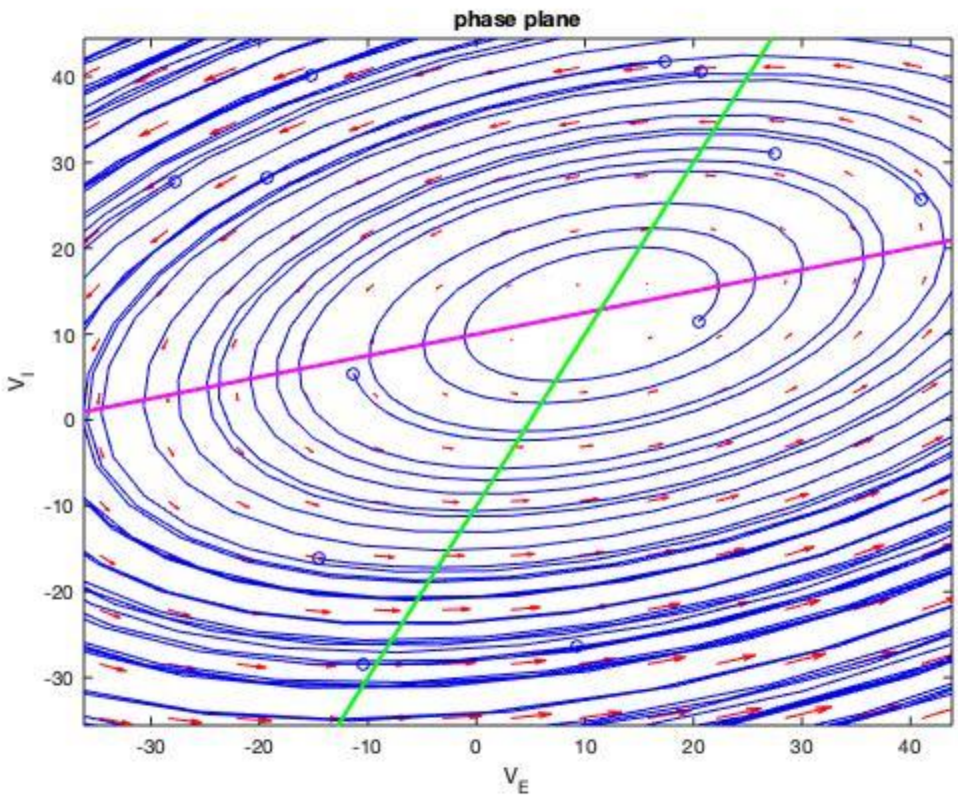
M_{IE}=0.5 : fixed point is focus and unstable.



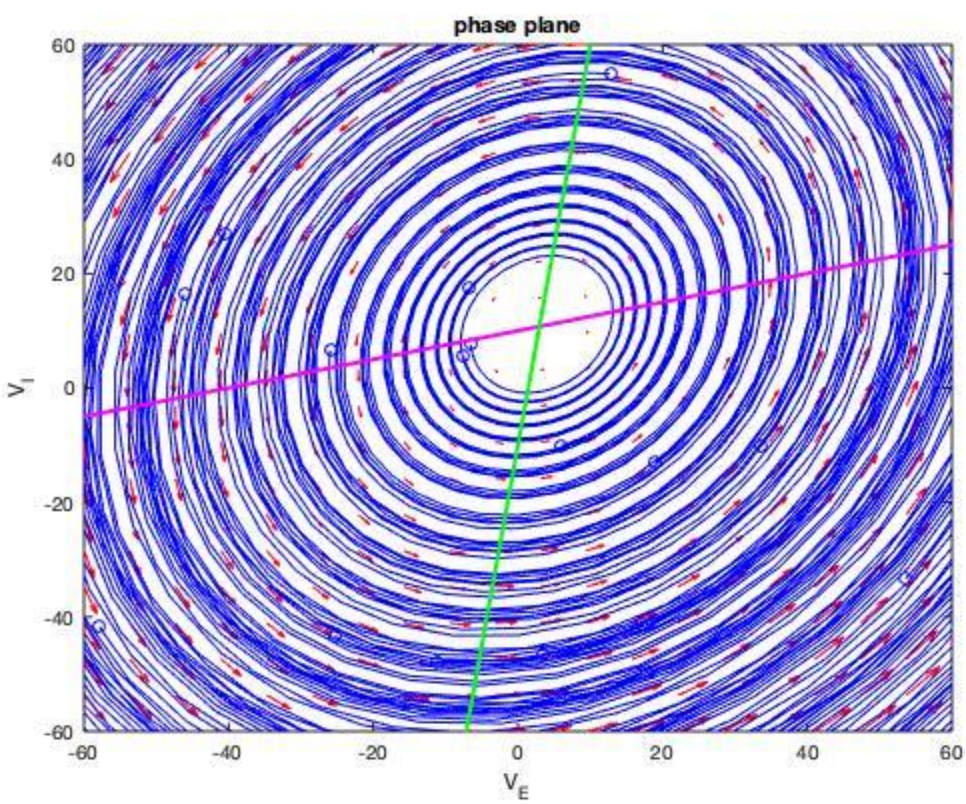
M_{IE}=1.5: again, fixed point is focus and unstable.



M_{IE}=2 : fixed point is focus and unstable.



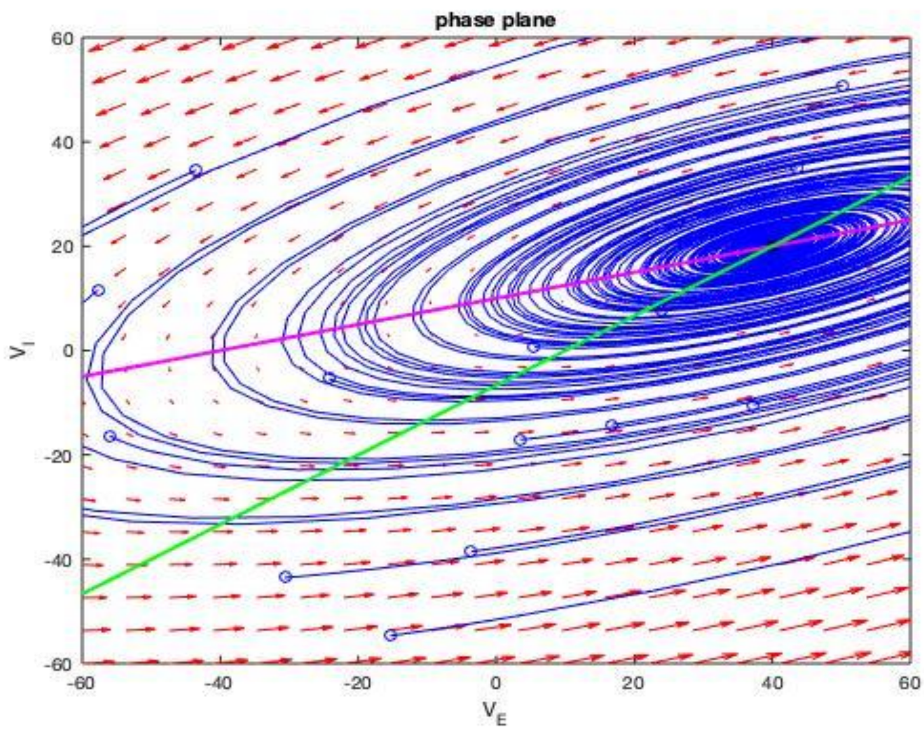
M_{IE}=7: fixed point is focus and unstable.



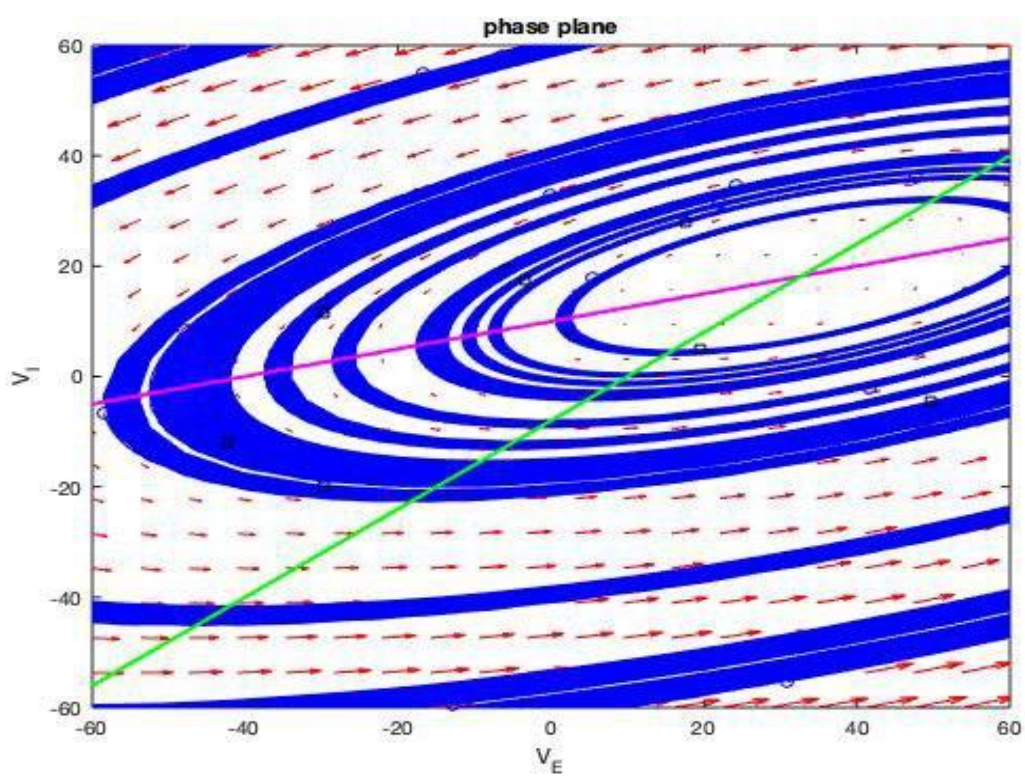
Even for large values of M_{Ie}, fixed point remains focus and unstable.

For M_{II}, we test three values -0.5,-0.25,0.5,1.1 (0 is already tested)

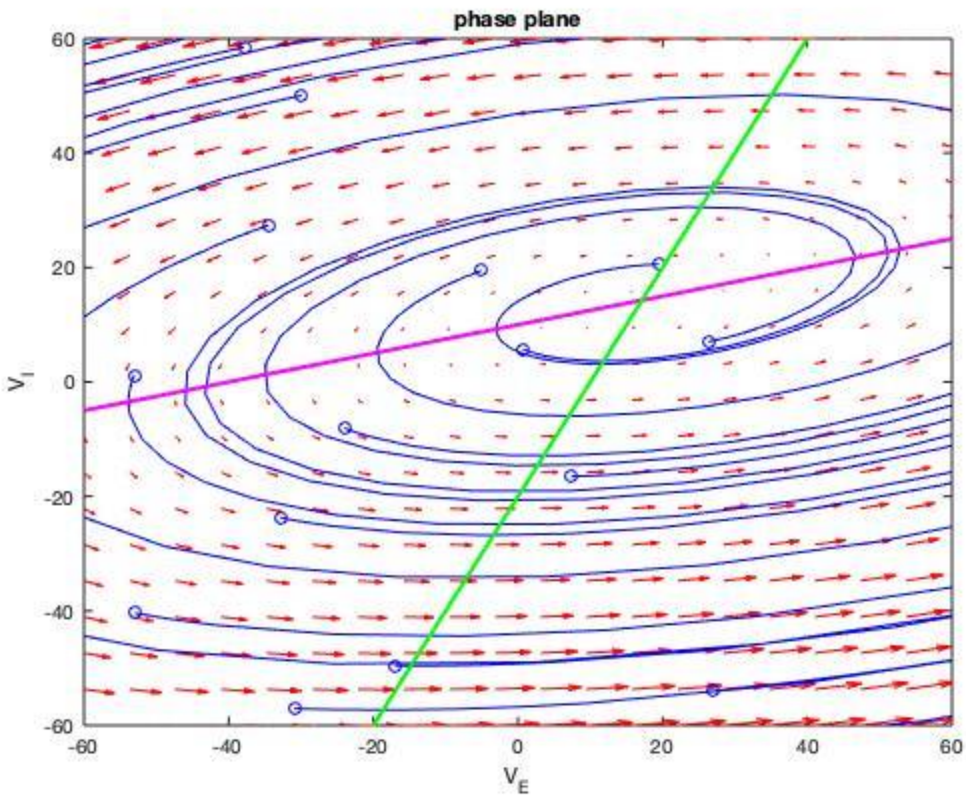
M_{II}= -0.5: fixed point is focus and stable.



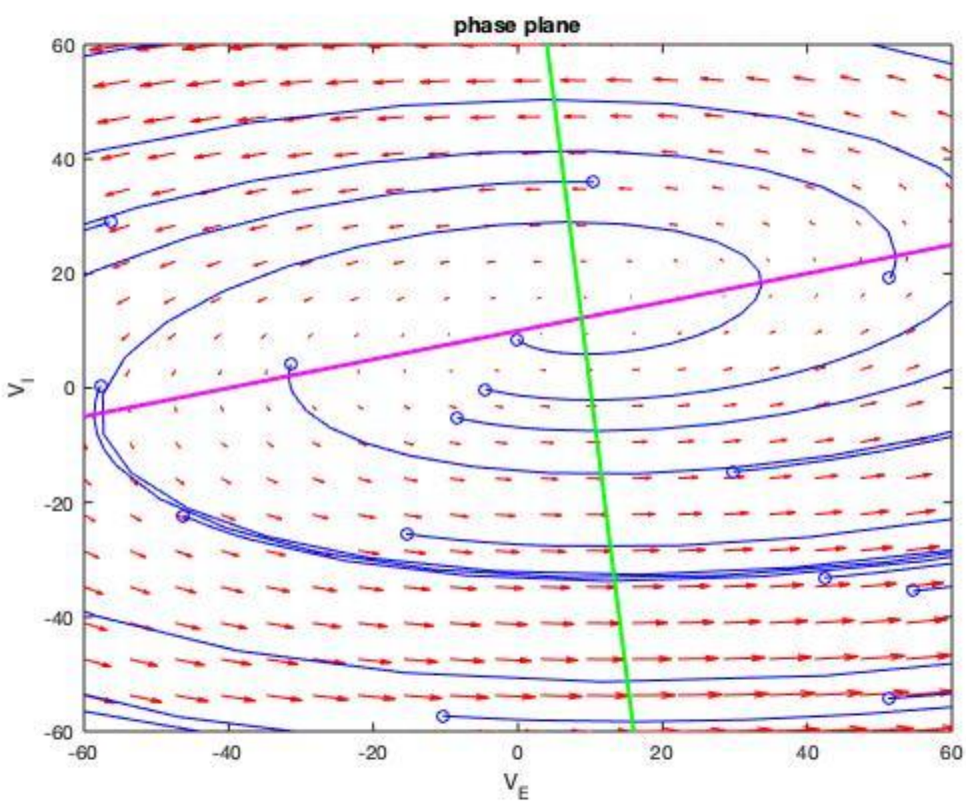
M_{II}= -0.25: fixed point is bifurcation.



M_{II}= 0.5: fixed point is focus and unstable.



M_{II}= 1.1: fixed point is focus and unstable.



We can see that as we change the value from -0.5 to 1.1, fixed point becomes unstable.

4- The noip variable in the code defines the number of starting points. Is it possible that we have a starting point which doesn't pass any limit cycle?

Yes, it is possible if the initial point is on the intersection of the nullclines (fixed point of the phase plane). Reason for this is that for the fixed point we have:

$$\frac{dv_E}{dt} = 0, \frac{dv_I}{dt} = 0$$

So if we start from fixed point, there will be no change in V_E or V_I, and hence, the point won't move or pass any limit cycle.

Problem 7

One of most important concepts and tools used in research is statistical tests. Write down anything you can about t-test and p-value. Information about other tests worth extra points

t-test (student's t-test):

In statistics, hypothesis testing is one of the most powerful tools for predicting or verifying the properties of a population. In this method we have a null hypothesis H_0, and we use different statistical tests to verify or reject this hypothesis.

Student's t-test, in statistics, a method of testing hypotheses about the mean of a small sample drawn from a normally distributed population when the population standard deviation is unknown.

t-tests is usually used for the following situations:

- A **one-sample** location test of whether the mean of a population has a value specified in a null hypothesis.
- A **two-sample** location test of the null hypothesis such that the means of two populations are equal.

As an example to see how this test works, assume that we have a normal population and we are trying to estimate its mean (standard deviation is unknown) and we have taken n samples with mean $\bar{X}$. If m is the actual mean of the population, then the random variable

$$t = \frac{\bar{X} - m}{\frac{s}{\sqrt{n}}}$$

(where s is sample standard deviation) has t-distribution, which is a known distribution. Now, using the properties of t-distribution, we can find a 95% confidence interval for m and finally, check whether the mean given by the null hypothesis fall inside this interval. If not, we can reject null hypothesis with 5% confidence level. A similar approach can be done for two different populations (which are assumed to have equal variance) to check whether their mean is equal. For this case, assume that sample mean and variance of the populations are mean1, mean2, var1, var2, respectively with sample sizes n1 and n2. Then the value

$$t = \frac{mean1 - mean2}{\frac{(n1-1)var1^2 + (n2-1)var2^2}{n1 + n2 - 2}\sqrt{\frac{1}{n1} + \frac{1}{n2}}}$$

Has t-distribution with n1+n2-2 degree of freedom (this value is called t-value) and all we need to do is to check whether zero falls inside the 95% confidence interval or not.[5][6][7]

p-value:

In hypothesis testing (which is explained in the previous part) the p-value is the probability of obtaining test results at least as extreme as the results actually observed, under the assumption that the null hypothesis is correct. Basically, p-value is a number describing how likely it is that your samples would have occurred by random chance, assuming that null hypothesis is true.

A very small p-value means that such an extreme observed outcome would be very unlikely under the null hypothesis, and can be enough to reject the null hypotheses. Reporting p-values of statistical tests is common practice in academic publications of many quantitative fields. [7][8][9]

Z-test:

Z-test is very similar to t-test, except in the case that the populations should be normal and their variance should be known. In this case, the random variable

$$z = \frac{\bar{X} - m}{\frac{\sigma}{\sqrt{n}}}$$

would have normal distribution (σ is the standard deviation of the population) and we can do everything we used to do in t-test, here as well.

Z-test is rarely used in practice, compared to t-test, because it is usually hard to determine the variance of a population. [7][10]

Shapiro-Wilk Test:

Shapiro-Wilk Test is a test used to check whether our population has normal distribution (null hypothesis is that the samples are normal) the test statistic for this test (which is used to compute p-value) is given by the following formula :

$$W = \frac{(\sum a_i x_i)^2}{\sum (x_i - \bar{x})^2}$$

Where x_i are samples and a_i are constants generated from the covariances, variances and means of the sample (size n) from a normally distributed sample.[11][12]

References

[1] Eugene M. Izhikevich , "Simple Model of Spiking Neurons" , IEEE TRANSACTIONS ON NEURAL NETWORKS, VOL. 14, NO. 6, NOVEMBER 2003

https://courses.cs.washington.edu/courses/cse528/07sp/izhi1.pdf

[2] Naureen Ghani, "Izhikevich Model of Cortical Spiking Neurons"

http://www.columbia.edu/cu/appliedneuroshp/Spring2018/Spring18SHPAppliedNeuroLec5.pdf

[3] Wikipedia

https://en.wikipedia.org/wiki/Biological_neuron_model#:~:text=Perfect%20Integrate%2Dand%2Dfire,-One%20of%20the&text=When%20an%20input%20current%20is,the%20model%20continues%20to%20run.

[4] Wulfram Gerstner W, Kistler WM, Naud R, Paninski L (24 July 2014). *Neuronal dynamics : from single neurons to networks and models of cognition*. Cambridge, United Kingdom. ISBN 978-1-107-06083-8. OCLC 861774542

[5] https://www.britannica.com/science/Students-t-test

[6] https://en.wikipedia.org/wiki/Student%27s_t-test

[7] Thomas H. Wonnacott, "introductory statistics"

[8] https://en.wikipedia.org/wiki/P-value

[9] https://www.simplypsychology.org/p-value.html

[10] https://en.wikipedia.org/wiki/Z-test

[11] https://www.statisticshowto.com/shapiro-wilk-test/

[12] https://en.wikipedia.org/wiki/Shapiro%E2%80%93Wilk_test