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22CH30028
PROJECT II WRITEUP

1. **Verifying the consistency of chosen units:**
Milliseconds (ms), microamps/cm^2 (μA/cm^2), millivolts (mV), microfarads/cm^2 (μF/cm^2), millisiemens/cm^2 (mS/cm^2)

Ohm's law: I = g x V
I = μA/cm^2; g = mS/cm^2; V = mV
⇨ I = 1 μA/cm^2 = 10^{-6} A/cm^2
⇨ g x V = 1 (mS/cm^2) * mV
⇨ g x V = 10^{-3} x (S/cm^2) * 10^{-3} (V)
⇨ g x V = 10^{-6} A/cm^2

Capacitance formula:
⇨ I = C $\frac{dV}{dt}$
⇨ Current = Capacitance x $\frac{\text{Voltage}}{\text{Time}}$
⇨ 1 μA/cm² = 1 μF/cm² x $\frac{1\text{ mV}}{1\text{ ms}}$
⇨ 10^{-6} A/cm² = 10^{-6} F/cm² x $\frac{10\text{^}(-3)\text{ V}}{10\text{^}(-3)\text{ s}}$
⇨ 10^{-6} A/cm² = 10^{-6} A/cm²
All the units are consistent

Choice of units:
Conductance density – μS/cm^2
Other units:
Current density = nA
Capacitance = nF
Voltage = mV
Time = ms

However, this is not an "unique" solution. As long as the units are consistent with the other formulae used in the solutions, then that choice is permitted. For instance, keeping conductance unit constant, "voltage" units could be anything as long as it is of the same order as time (as it is a ratio). Consequently, current unit would have to be adjusted accordingly so that Ohm's law holds.

2. **Modelling of Moris Lecur equations**:

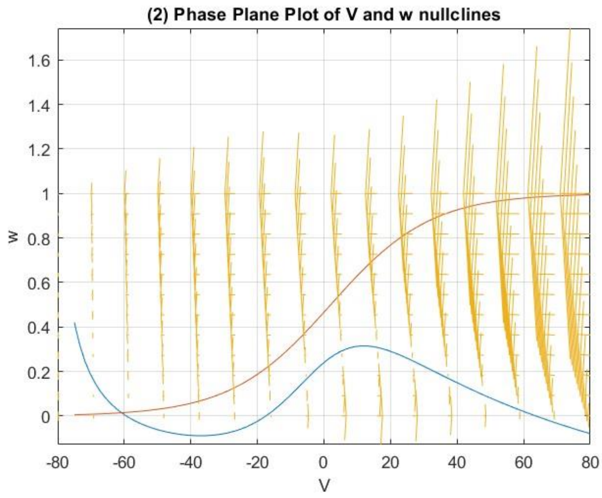
Finding equilibrium points of MLE model, eigenvalues and nature of those equilibrium points:

Method I: *vpasolve* (Uses symbolic computation along with numerical methods)

$$x_{k+1} = x_k - J^{-1}(x_k)\cdot F(x_k)$$
$$J(x_k) = \text{Jacobian matrix } J_{ij} = \frac{\partial F_i}{\partial x_j}$$

Results:
V_equi = - 60.8554
w_equi = 0.0149

Method II: *fzero* (uses Iterative convergence method)
Results:
V_equi = - 60.8554
w_equi = 0.014915



▲ Quiver plot & phase plane plot for MLE

3. **Analysis of equilibrium points:**
For I_{ext} = 0:
Equilibrium points: [V, w] = [-60.8554, 0.0149]

Jacobian @ [V = -60.8554, w = 0.0149]:
$$\begin{bmatrix} -0.1004 & -9.2578 \\ 0.0000 & -0.0320 \end{bmatrix}$$
Eigenvalues:
λ_1 = - 0.0959
λ_2 = - 0.0366

The type of equilibrium is: *Stable Equilibrium*

4. **Numerical tolerance values:**
Relative tolerance = 10^{-3} units
Absolute tolerance = 10^{-6} units

Range of V that is relevant to the simulation = -60 **mV** to 0 **mV**
Range of *w* = 0 to 1
Order of time ~ **ms**
Hence, 10^{-3} units of tolerance is sufficient to accommodate any small changes in the values of V, w and other parameters while performing simulations. It also makes sure that ODE solvers and root finding algorithms are not affected by round off errors.

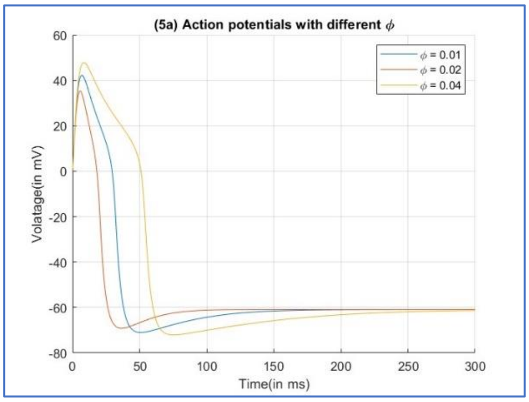
If voltage was measured in kV . . . then the values of *AbsTol* and *RelTol* would change accordingly:

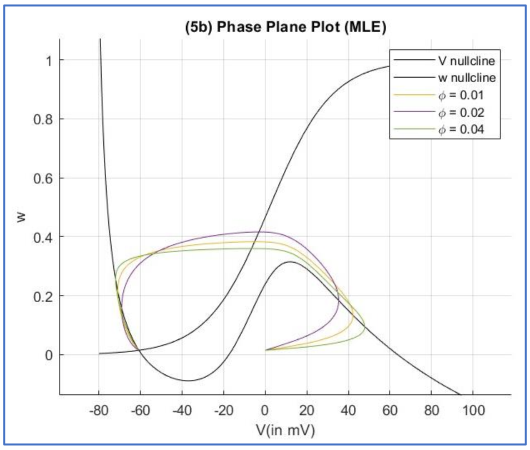
1 mV → 10^{-6} units of tolerance
1 V → 10^{-3} units of tolerance
1 kV → 1 unit of tolerance

RelTol is a ratio of $\frac{change\ in\ value}{initial\ value}$ and does not depend on units
Therefore, relative tolerance remains the same.

AbsTol = 1 unit
RelTol = 10^{-3} units

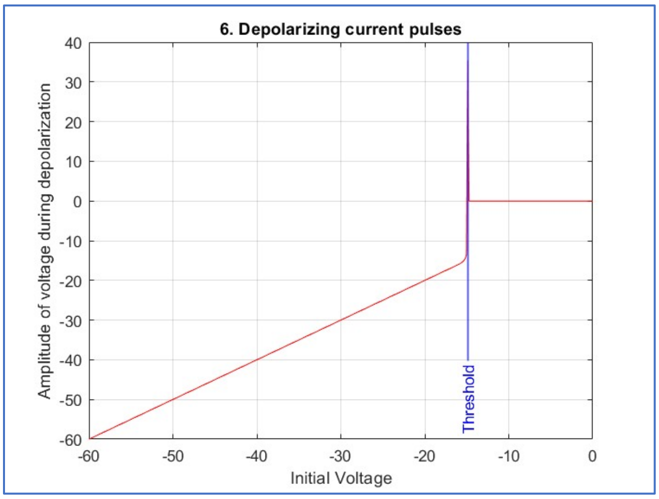
5. **Generate an action potential using MLE and plot phase plane diagram:**





- With increasing values of φ, the limit cycle becomes larger, resulting in more sustained oscillations.

6. **Depolarizing current pulses & Threshold behavior:**



Threshold voltage under depolarizing current = **- 14.89 mV**

Threshold potential refers to the membrane potential beyond which the neuron can generate an action potential. If the neuron is excited to a potential lower than the threshold, then the neuron simply returns back to its resting potential without an action potential.

7. **Run the model with I_{ext} = 86 µA/cm²:**

[1] *Initial conditions @ equilibrium point for $I_{ext} = 0$*

Equilibrium points ~ [V, w] = [-60.8554, 0.0149]

$$\text{Jacobian} = \begin{bmatrix} -0.1004 & -9.2578 \\ 0.0000 & -0.0320 \end{bmatrix}$$

Eigenvalues: λ_1 = - 0.0959 and λ_2 = - 0.0366

Trajectory → **Limit Cycle**

[2] *Initial conditions @ equilibrium point for I_{ext} = 86 µA/cm²*

Equilibrium points: (V, w) = (-27.9524, 0.1195)

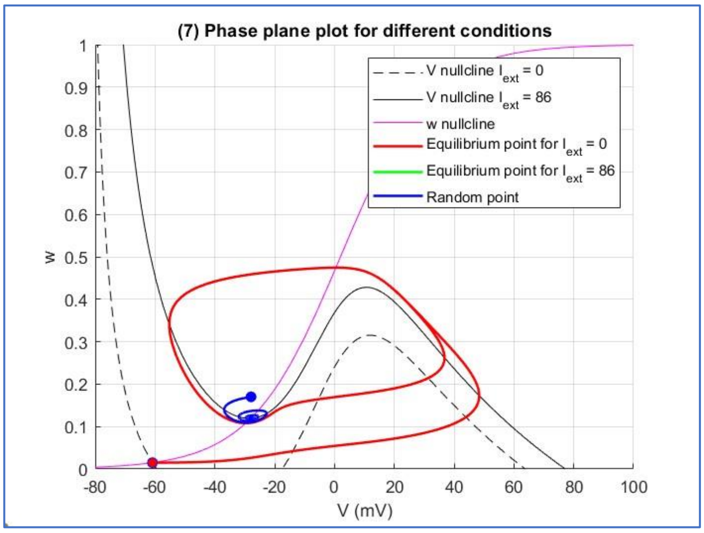
Jacobian =
[0.0090 - 22.419]
[0.0002 - 0.0225]

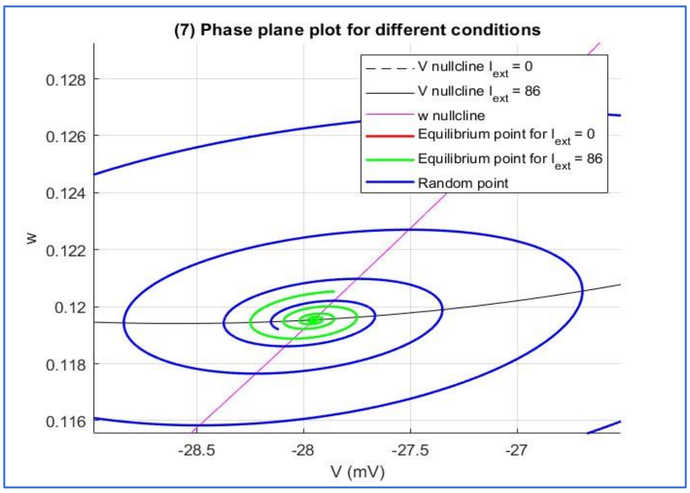
Eigenvalues:
λ_1 = - 0.0068 + 0.0574i
λ_2 = - 0.0068 - 0.0574i

Nature of equilibrium – **Stable Spiral**
Trajectory → Stable spiral (back to the equilibrium point)

[3] *Random point* [- 27.9, 0.17]

Trajectory → Stable spiral (back to the equilibrium point)

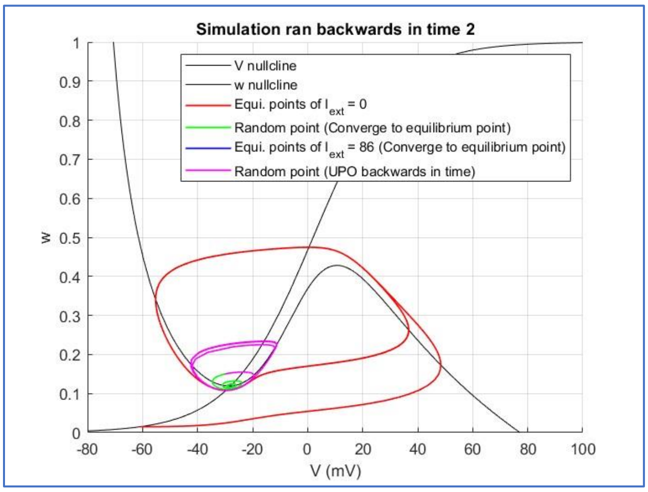


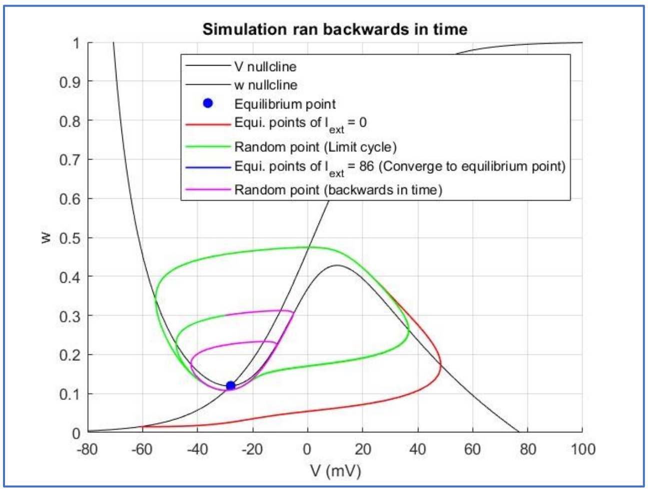


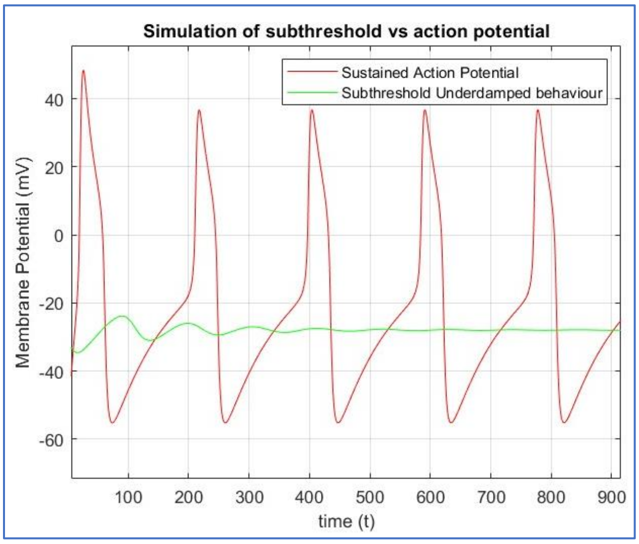
Applying external current shifts the equilibrium point of the system to a new value and [1] leads to a limit cycle while [2] leads to a stable spiral into the new equilibrium point.

[1] indicates an experiment where the neuron exhibits sustained oscillations while in experiment [2] the neuron fires off an action potential and returns to its resting potential.

8. **Two stable states of I_{ext} = 86 μA/cm^2 – converging to equilibrium point and converging to limit cycle:**

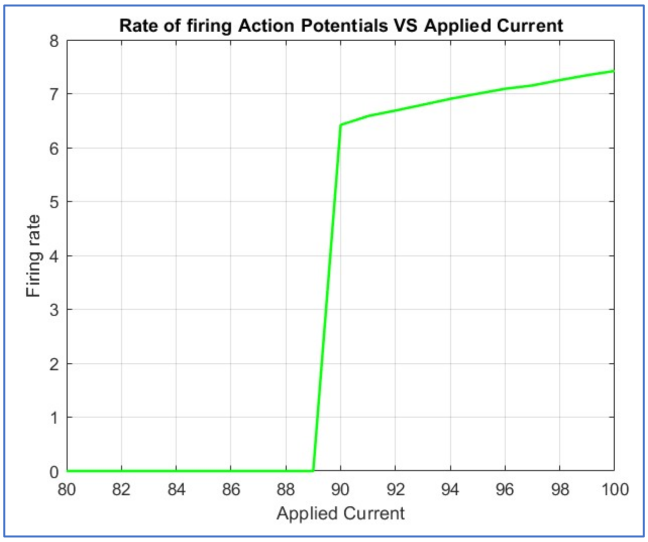


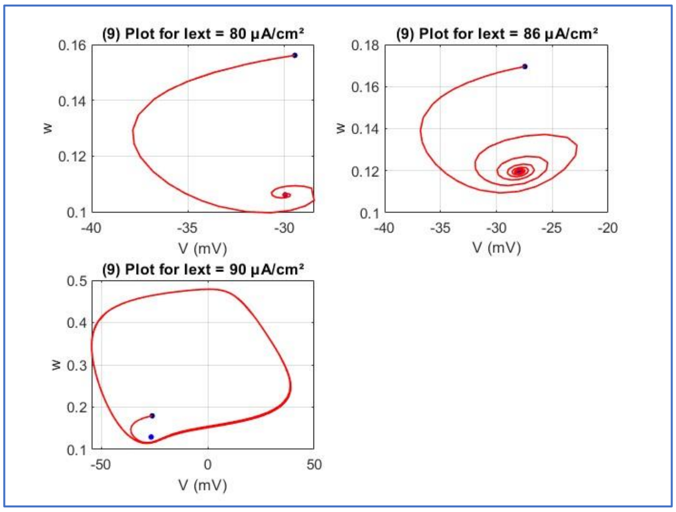




9. **Analyze equilibrium points for different external currents**

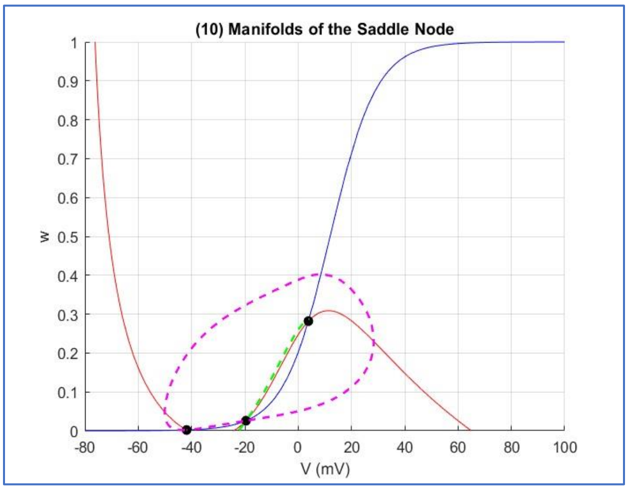
I_{ext} μA/cm^2	Equilibrium point	Jacobian	Eigenvalues	Nature of Equi.
80	V = - 29.97 W = 0.11	$\begin{matrix} -0.0127 & -21.6135 \\ 0.0001 & -0.0229 \end{matrix}$	- 0.0178 + 0.0557i - 0.0178 - 0.0557i	Stable Spiral
86	V = - 27.95 W = 0.12	$\begin{matrix} 0.0090 & -22.4190 \\ 0.0002 & -0.0225 \end{matrix}$	- 0.0068 + 0.0574i - 0.0068 - 0.0574i	Stable spiral
90	V = - 26.60 W = 0.13	$\begin{matrix} -0.0127 & 21.6135 \\ 0.0001 & -0.0229 \end{matrix}$	0.0018 + 0.0572i 0.0018 - 0.0572i	Unstable Spiral

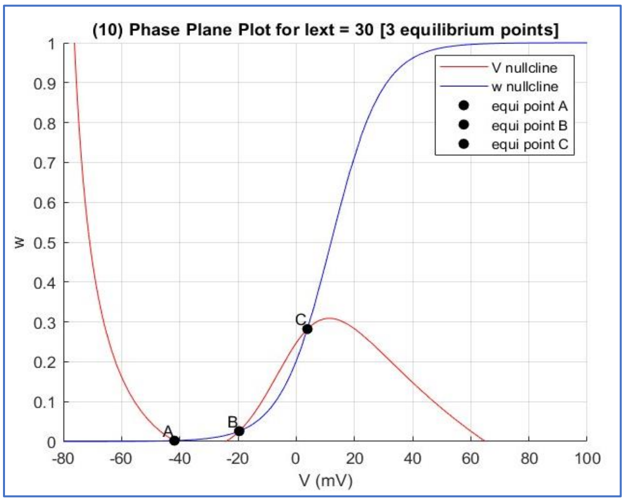




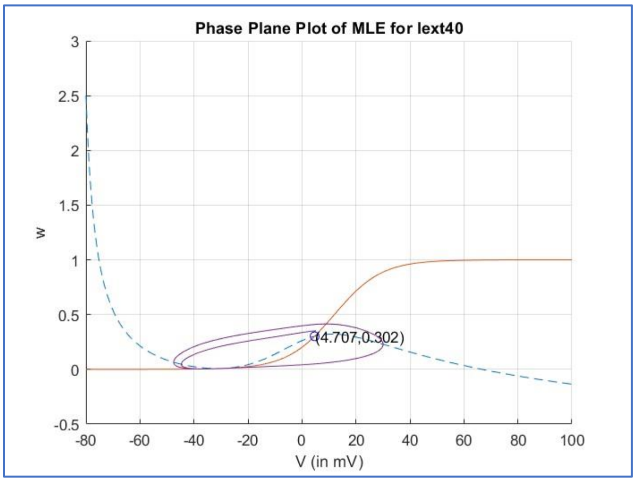
10. **Characterize equilibrium points for I_{ext} = 30 μA/cm^2**

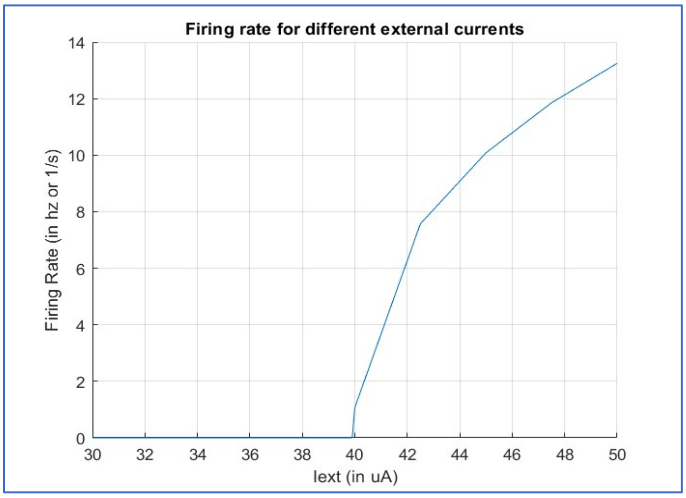
Equilibrium Points	Jacobian	Eigenvalues	Nature of Equilibrium
V = - 41.845 w = 0.002	$\begin{matrix} -0.0645 & -16.8619 \\ 0.0000 & -0.1638 \end{matrix}$	- 0.0715 - 0.1568	Stable equilibrium
V = - 19.563 w = 0.026	$\begin{matrix} 0.1824 & -25.7747 \\ 0.0003 & -0.0961 \end{matrix}$	0.1536 - 0.0673	Saddle point
V = 3.8715 w = 0.2821	$\begin{matrix} 0.2563 & -35.1486 \\ 0.0016 & -0.0685 \end{matrix}$	0.0939 + 0.1723i 0.0939 - 0.1723i	Unstable Spiral





11. **Characteristics of equilibrium points from I_{ext} = 30 – 50**





I_{ext}	No. of equilibrium points
30	3
35	3
39	3
39.1	3
39.2	3
39.3	3
39.4	3
39.5	3
39.6	3
39.7	3
39.8	3
39.9	3
40	1
42.5	1
45	1
47.5	1
50	1

12. **Modelling of HODGKIN HUXLEY Equations**

$$C\frac{dV}{dt} = I_{ext} - G_K(V-E_K) - G_{Na}(V-E_{Na}) - G_L(V-E_L)$$

$$G_K = \bar{G}_K n^4(V,t) \qquad G_{Na} = \bar{G}_{Na} m^3(V,t)\, h(V,t) \qquad G_L = \bar{G}_L$$

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

For the delayed-rectifier potassium channel:

$\bar{G}_K = 36$ mS/cm² $\quad E_K = -72$ mV $\quad \alpha_n = \dfrac{-0.01\,\phi\,(V+50)}{\exp[-(V+50)/10] - 1} \quad \beta_n = 0.125\,\phi\,\exp[-(V+60)/80]$

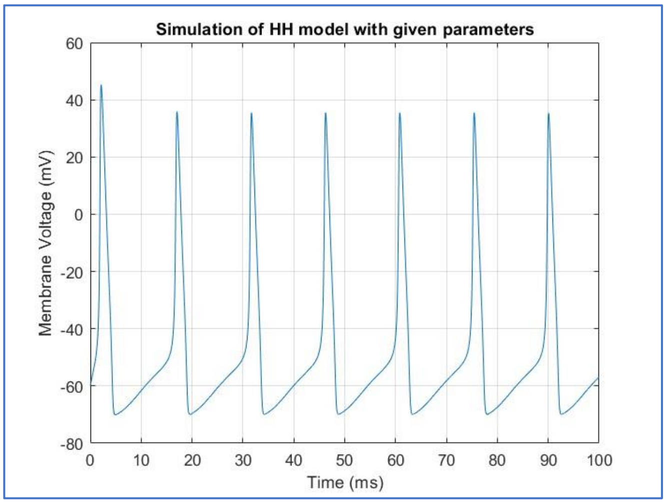
For the sodium channel:

$\bar{G}_{Na} = 120$ mS/cm² $\quad E_{Na} = 55$ mV $\quad \alpha_m = \dfrac{-0.1\,\phi\,(V+35)}{\exp[-(V+35)/10] - 1} \quad \beta_m = 4\,\phi\,\exp[-(V+60)/18]$

$\alpha_h = 0.07\,\phi\,\exp[-(V+60)/20] \quad \beta_h = \dfrac{\phi}{\exp[-(V+30)/10] + 1}$

13. **Determination of E_L for resting potential @ -60 mV & Generation of action with I_{ext} = 10 μA/cm²**

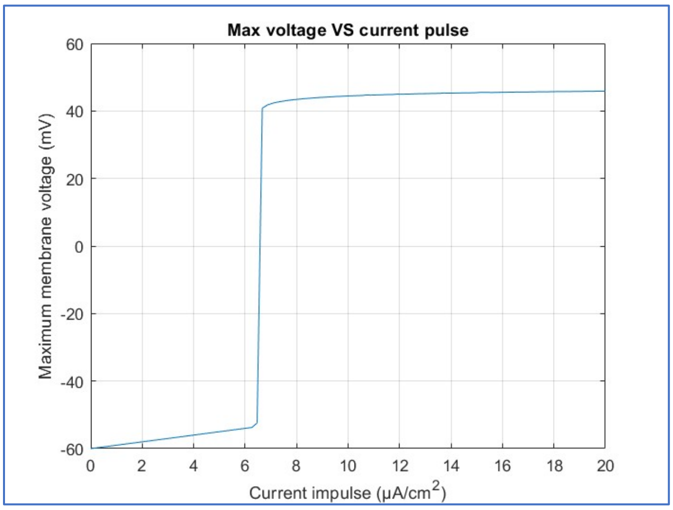
E_L = - 49.401 mV



14. **Stability of model @ I_{ext} = 0 and Threshold voltage**

Equilibrium points for I_{ext} = 0
V = - 60.00 mV
n = 0.32
m = 0.05
h = 0.60

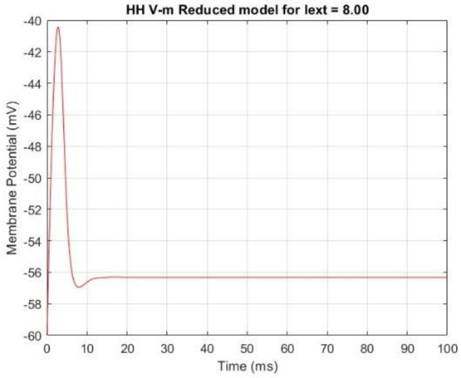
Threshold Current = 6.67 μA/cm²

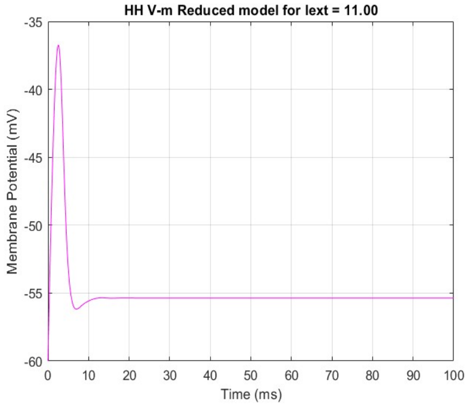


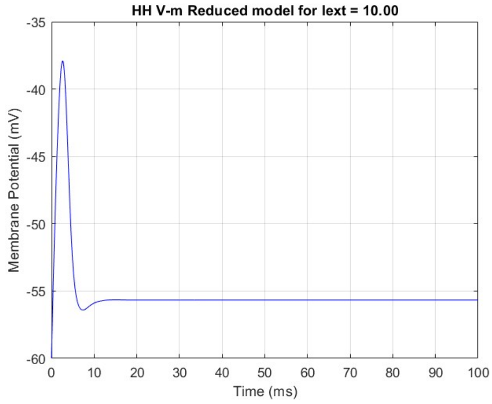
15. **Characterization of equilibrium points for steady state current injections**

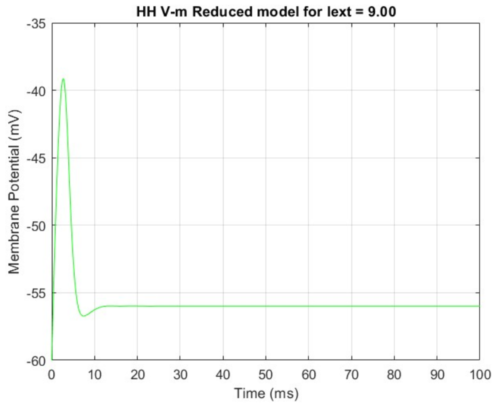
I_{ext}	Equilibrium point	Eigenvalues	Nature of Equilibrium
8.0	V = - 55.36 n = 0.39 m = 0.09 h = 0.43	- 4.6901 - 0.0345 + 0.5668i - 0.0345 - 0.5668i - 0.1350	Stable Equilibrium
8.5	V = - 55.15 n = 0.39 m = 0.09 h = 0.42	- 4.7099 - 0.0246 + 0.5727i - 0.0246 - 0.5727i - 0.1360	Stable Equilibrium
9.0	V = - 54.95 n = 0.40 m = 0.09 h = 0.42	- 4.7306 - 0.0149 + 0.5783i - 0.0149 - 0.5783i - 0.1370	Stable Equilibrium
9.5	V = - 54.76 n = 0.40 m = 0.10 h = 0.41	- 4.7520 - 0.0053 + 0.5835i - 0.0053 - 0.5835i - 0.1379	Stable Equilibrium
10.0	V = - 54.57 n = 0.40 m = 0.10 h = 0.40	- 4.7741 0.0041 +0.5883i 0.0041 -0.5883i - 0.1389	Saddle point
10.5	V = - 54.39 n = 0.41 m = 0.10 h = 0.40	- 4.7968 0.0133 +0.5929i 0.0133 -0.5929i - 0.1399	Saddle point
11.0	V = - 54.21 n = 0.41 m = 0.10 h = 0.39	- 4.8200 0.0224 +0.5971i 0.0224 -0.5971i - 0.1408	Saddle point
11.5	V = - 54.04 n = 0.41 m = 0.10 h = 0.39	- 4.8436 0.0312 +0.6011i 0.0312 -0.6011i - 0.1418	Saddle point
12.0	V = - 53.87 n = 0.41 m = 0.11 h = 0.38	- 4.8676 0.0399 +0.6048i 0.0399 -0.6048i - 0.1428	Saddle point

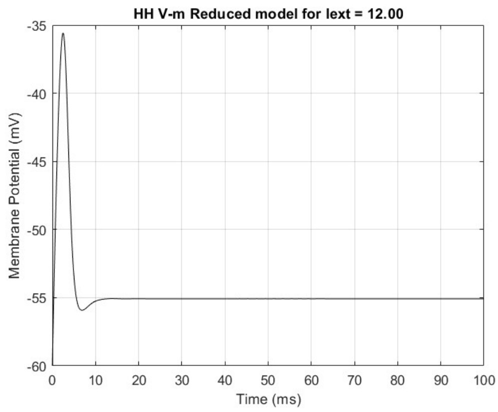
16. **HODGKIN HUXLEY V-m REDUCED MODEL**







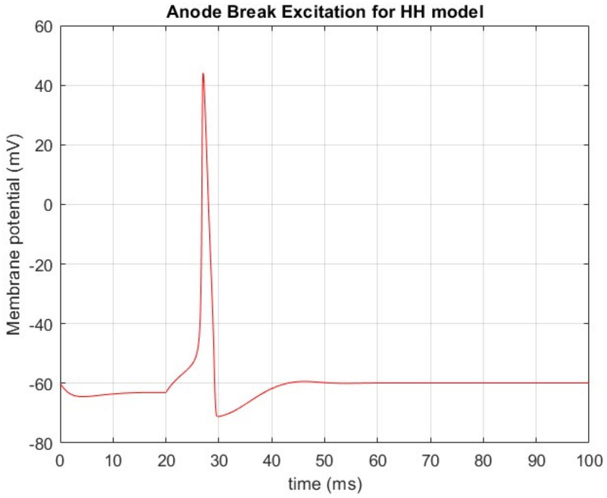




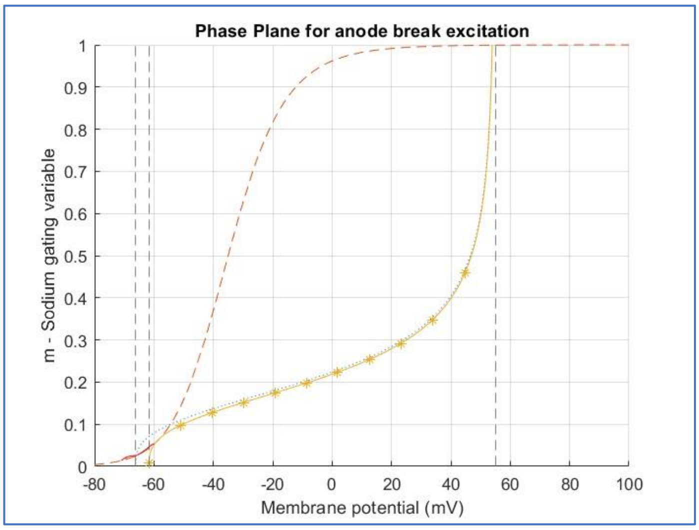
17. **<u>ANODE BREAK EXCITATION for HH Model</u>**

Hyperpolarising current = - 3 μA/cm^2

- Due to the hyperpolarising current, the amount of Na^+ channels available increases more than those available at resting potential.
- When the current is taken off, due to the new amount of available Na^+ channels, the threshold voltage decreases substantially
- The neuron is easily able to generate action potential.
- A real neuron generates repeated action potentials after a hyperpolarising current, but HH model can explain the generation of only one spike.



Hyperpolarising current applied from 0 to 20 ms



18. **<u>Characterization of equilibrium points of HH model at different conditions</u>**

(i) Equilibrium Point for n and h @ Resting potential

V = -54.394575
m = 0.100047

Jacobian =
[- 0.7383 234.986]
[0.0354 - 3.2553]

Eigenvalues: 1.1501, - 5.1437

Type of equilibrium: **Saddle Point**

(ii) Equilibrium Point for n and h @ final values of anodal stimulus

V = 54.334898
m = 0.999220

Jacobian =
[- 83.7260 166.2055]
[0.0005 - 8.9416]

Eigenvalues: - 83.7271, - 8.9406

Type of equilibrium: **Stable Equilibrium**