Introduction to Biological Signals & Systems

Simulation Exercise

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Part I

1 HH Model (Assuming $I = 0$)

1.1

There is a single equilibrium point of the system when $V_K < V < V_{Na}$, which is:

$$\begin{gathered} V_0 = -74.4\,[mV] \\ n_0 = 0.31 \\ m_0 = 0.052 \\ h_0 = 0.596 \end{gathered}$$

1.2

The eigenvalues of the Jacobian in the single equilibrium point we found are:

$$\lambda = \begin{pmatrix} -4.726 \\ -0.178 + 0.432i \\ -0.178 - 0.432i \\ -0.12 \end{pmatrix}$$

We notice that the Real part of all the eigenvalues is negative, so this is a stable equilibrium point. This makes sense as it is the Resting Potential.

1.3

Simulation of the system presenting the transient effects:

- At time T_0=0.5697 [ms] the potential is decreasing and isn't developing to an Action Potential.
- At Time T_1=0.5707 [ms] the potential is increasing and developing to an Action Potential.

In the figure [1], we can how the state variables change in time, in response to different-length current pulses.

2 2D HH Model (Assuming $I = 0$)

2.1

The equilibrium point of the 2D HH model, when $n_0 = h_0 = 0.35 + \frac{9}{90}$, is:

$$\begin{gathered} V_0 = -62.8\,[mV] \\ n_0 = h_0 = 0.45 \\ m_0 = 0.18 \end{gathered}$$

The eigenvalues of the Jacobian in the single equilibrium point we found are:

$$\lambda = \begin{pmatrix} 3.0325 \\ -7.7229 \end{pmatrix}$$

We can notice that both eigenvalues are Real, and since one eigenvalue is positive and the other is negative, we can conclude that this equilibrium point is a saddle point.

In the figure [2], we can see the flow lines near the equilibrium point ($V_0 = -62.8\,[mV]$, $m_0 = 0.18$) in the state-space.

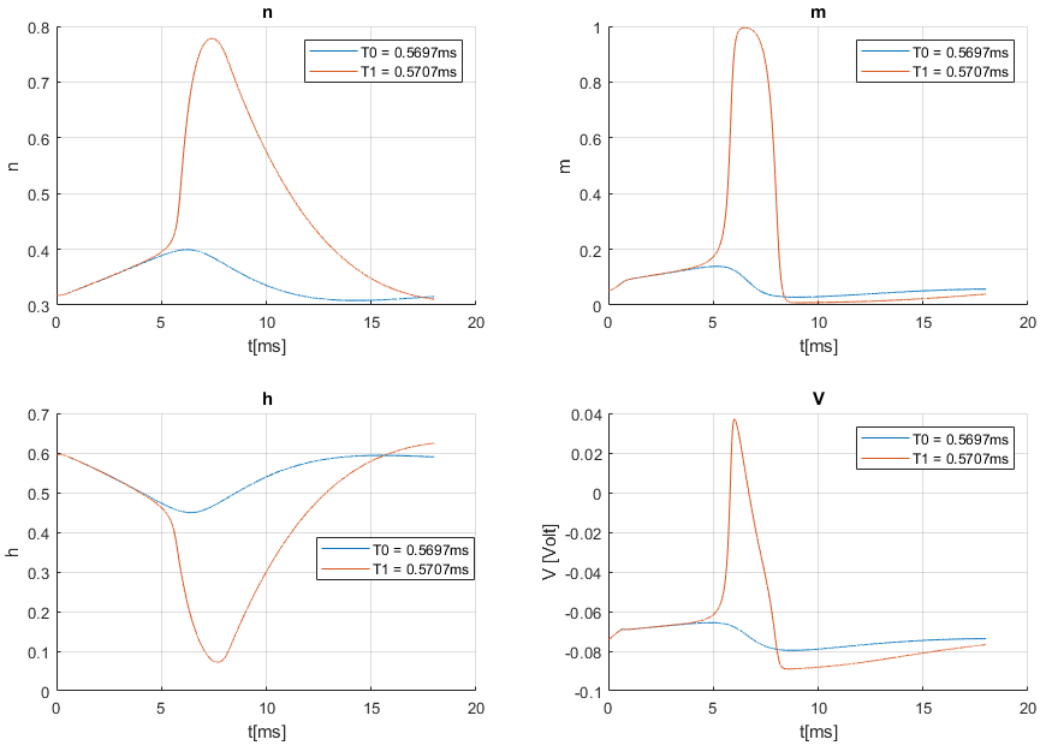

Figure 1: n, m, h, V changing in time for different T's

2.2

When using the 2D HH model, there is no threshold voltage that defines whether the membrane potential will develop to an Action Potential or not. This is due to that fact that this model is based on 2 variables – V and m, and they both dictate the terms for an Action Potential to develop (terms = threshold curve).

As such, near the saddle point, we can define the threshold curve geometrically by the eigenvectors leading directly to the saddle point (including the saddle point itself). Away from the saddle point, we can define the threshold curve geometrically by the trajectories leading directly to the saddle point.

The threshold curve split the phase space in half – any trajectory starting from the upper-right half would enable an Action Potential to develop, while trajectories starting from the bottom-left half would get the membrane potential to decrease.

Using the same graph from the previous section, we can present the threshold curve as the red line (notice that there is no "threshold voltage" because the line is not vertical). Seen in figure [3].

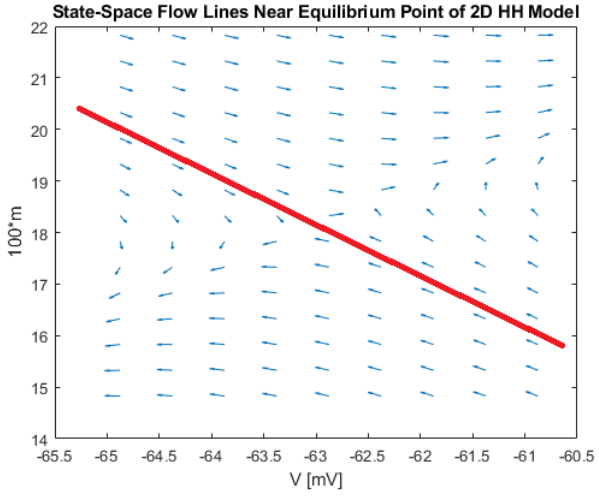

Figure 3: Flow lines near the equilibrium point with the threshold curve

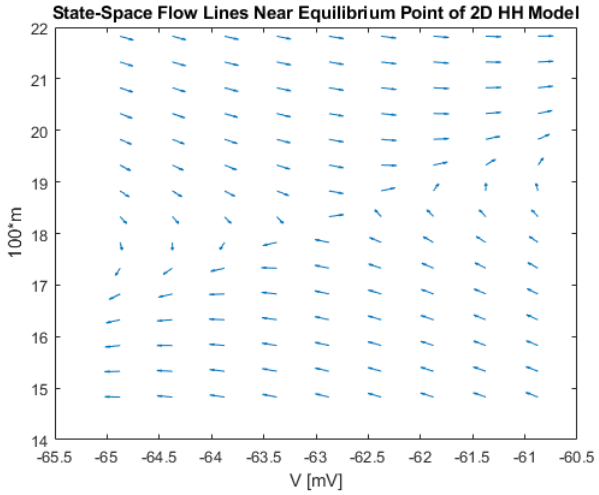

Figure 2: Flow lines near the equilibrium point

3 Comparison between full HH Model to 2D HH Model (Assuming $I = 0$)

3.1

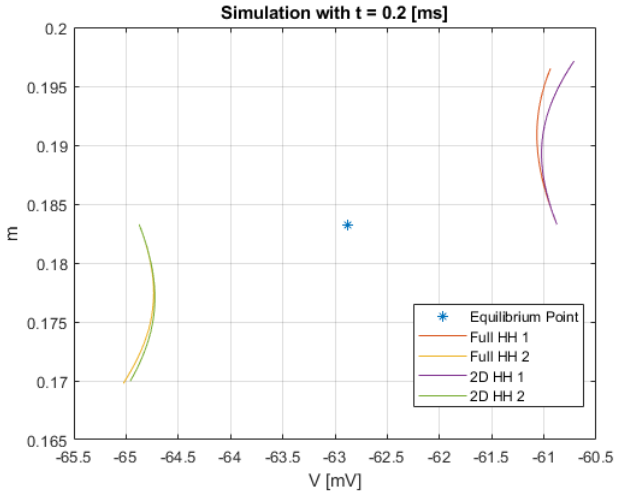

Figure 4: Simulation of $t = 0.2\,[ms]$, comparing the full HH model to the 2D HH mode

In the graph in figure [4], we can see how each model "develops" through time, while both start from the same exact starting points:

1. Point 1 ($V_0 + 2\,[mV]$) right of the equilibrium point – should lead to an increasing membrane potential and to an Action Potential.
2. Point 2 ($V_0 - 2\,[mV]$) left of the equilibrium point – should lead to a decreasing membrane potential.

We can see that for each starting point, both models behave similar and provide close results. It can be explained by the fact that the 2D HH model refers to the parameters n and h as constants, so their effect on the model is negligible. When examining the full HH model, these parameters are not constant, but since this simulation is very short in time – we can say that the parameters n and h almost do not change, and that is why we get very similar results between the two models (the 2D HH approximation is good for short periods of time).

3.2

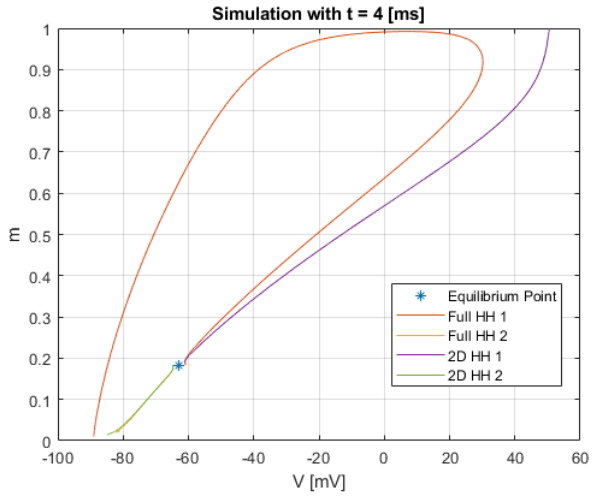

Figure 5: Simulation of $t = 4\,[ms]$, comparing the full HH model to the 2D HH mode

In the graph we can see how each model "develops" through time, while both start from the same exact starting points:

1. Point 1 ($V_0 + 2\,[mV]$) right of the equilibrium point – should lead to an increasing membrane potential and to an Action Potential.

2. Point 2 ($V_0 - 2\,[mV]$) left of the equilibrium point – should lead to a decreasing membrane potential.

We can see that both models behave similarly when starting from Point 2 (left of equilibrium) – the values of V and m decrease and get away from the equilibrium point.

When starting from Point 1 (right of equilibrium) the two models behave entirely different:

1. 2D HH model (purple line) – the values of V and m increase, causing an Action Potential, and keep on rising away from the equilibrium point until reaching another equilibrium.

2. Full HH model (orange line) – the values of V and m increase, causing an Action Potential, and then the parameters n and h take their place in restraining the membrane potential, so the values of V and m fall back to the other side (left of equilibrium point).

This simulation demonstrates the differences between the models in longer time periods, in which the parameters n and h can no longer be referred to as constants, and they do change and affect the entire model through time (in contrary to the 2D HH approximation).

Part II

4 HH Model (Assuming $I = a \cdot u\,(t)$)

4.1

Running a simulation of HH for $I = 1.778u\,(t)\,[\mu A]$, we got:

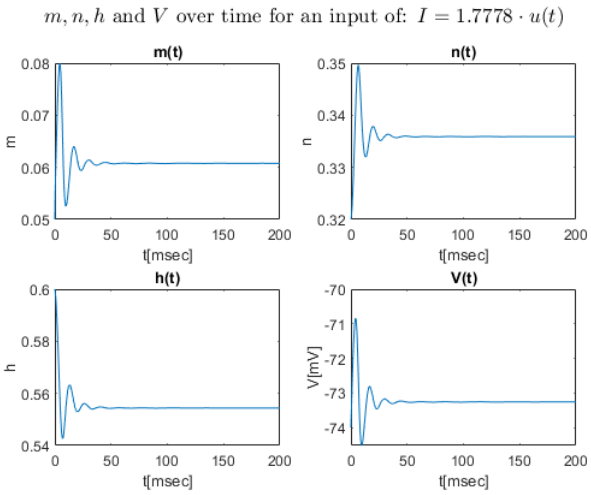

Figure 6: Simulation for the full HH for an input of $I = 1.778u\,(t)$

We can see that there is no potential achieved, since all the values of m, n, h, V go quickly back to one. The voltage doesn't even begin to pass zero.

Since the current is small, it is safe to assume that there is no change to the types of nodes we found in section [1.2] in part I. Therefore, there is still a stable point somewhere in the vicinity of:

$$V_0 = -74.4\,[mV]$$
$$n_0 = 0.31$$
$$m_0 = 0.052$$
$$h_0 = 0.596$$

Which is what the state stabilizes at.

4.2

Now for an input current of $I = 5u\,(t)\,[\mu A]$:

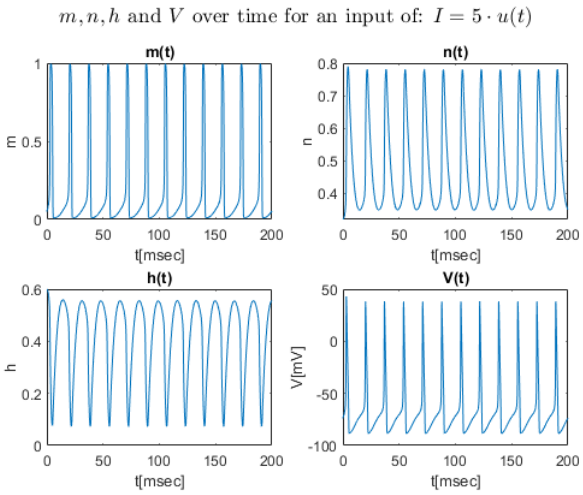

Figure 7: Simulation for the full HH for an input of $I = 5u\,(t)$

As we can see, there is a continuous Action potential.

4.3

Looking at the pulses in figure [7], we can see that the maximum potential of the pulse goes down with time, which means that we have an adaptation behavior.

4.4

One more current:

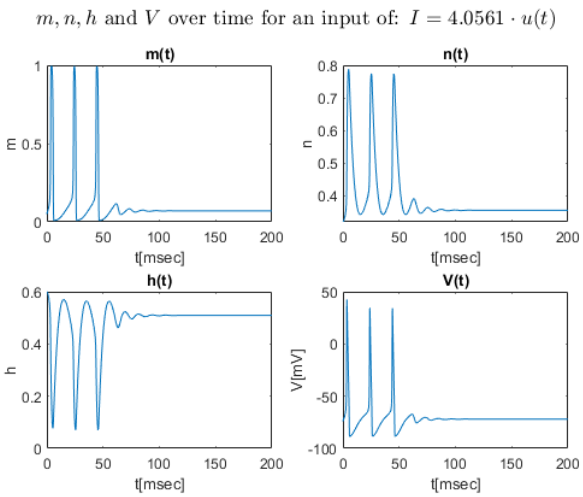

Figure 8: Simulation for the full HH for an input of $I = 4.056u\,(t)$

We can see here that although we do get a few pulses, it doesn't continue ad infinitum.

Looking for the greatest current for which there is no Action potential, and the lowest current for which it is continual, we got the two following plots:

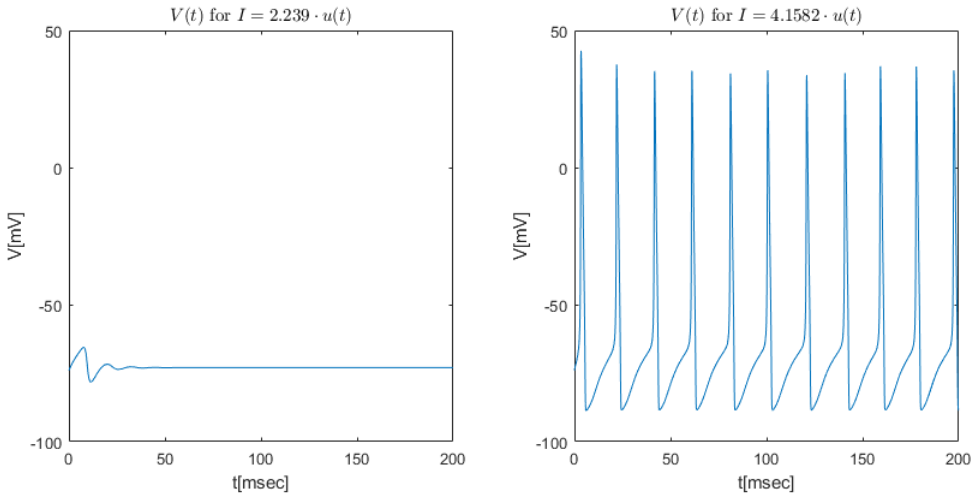

Figure 9: Voltages for an input of $I = u(t)$ and $I = u(t)$

By iterating over possible values of $a \in (1.78, 5)$, and searching for when there is a Action potential and when there are many, we reached the values:

$$a_{max\ with\ no\ PP} = 2.24\,[\mu A]$$
$$a_{min\ with\ infinite\ PPs} = 4.16\,[\mu A]$$

5 2D HH Model (Assuming $I = 0$) - nullclines

5.1

We'll find the nullcline for $\dot{n} = 0$:

$$\dot{n} = \alpha_n(V)(1-n) - \beta_n(V)\,n = 0$$
$$\Rightarrow n = \frac{\alpha_n(V)}{\alpha_n(V) - \beta_n(V)}$$

We'll plug in the voltages and get the $\dot{n}$-nullcline. We'll get the $\dot{V}$-nullcline numerically.

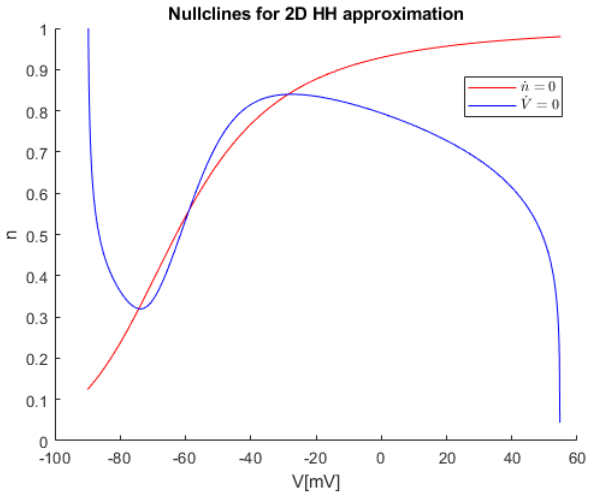

Figure 10: $\dot{n}$ and $\dot{V}$ nullclines for $I = 0\,[\mu A]$

5.2

For each sector, the sign of $\dot{n}$ and $\dot{V}$ remains the same. This is because the derivatives are continuous, and therefore, between a change of sign, there resides a nullcline. We can see this clearly in the following figure, where each color corresponds to a gradient direction.

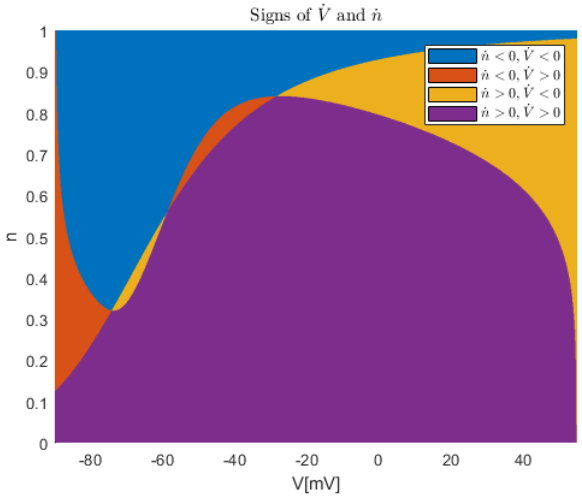

Figure 11: Signs of $\dot{V}$ and $\dot{n}$

5.3

The equilibrium points are equilibrium points, because for them the gradient is nil. Meaning if we arrive there, then:

$$\left(\dot{n}\left(V_0, n_0\right), \dot{V}\left(n_0, V_0\right)\right) = (0, 0)$$

and therefore won't move from the state.

We found the points and the corresponding eigenvalues of the Jacobians:

V	n	Eigenvalues	Type
-73.8811	0.3197	$-0.1038 + 0.4673i$ $-0.1038 - 0.4673i$	Stable focus
-59.2367	0.5510	21.2981 -0.0812	Saddle-point
-28.4833	0.8398	$1.1682 + 4.9443i$ $1.1682 - 4.9443i$	Unstable focus

Table 1: Equilibrium points, their eigenvalues and their types

The type of equilibrium point can be derived directly from the real of the eigenvalues - $\Re\left(\lambda_i\right)$. If its positive, then the point is unstable in that direction, if it is negative, the point is stable.

5.4

We took the two beginning points: $(-69, 0.35)$ and $(-68, 0.35)$ The outcome:

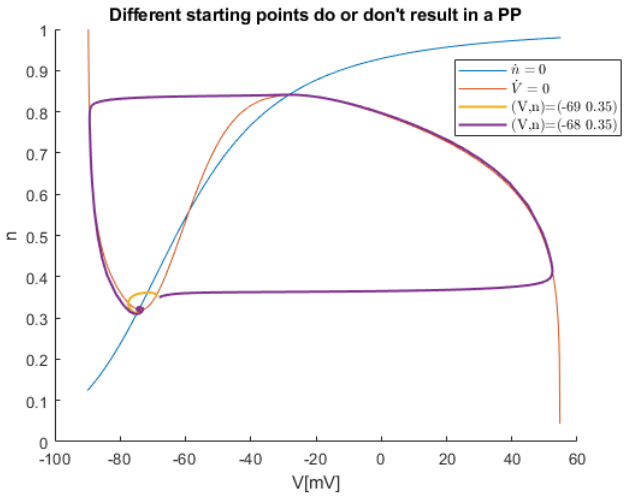

Figure 12: Two paths in the state space of the 2D HH equation

5.5

The nullclines are lines for which either $\dot{n} = 0$ or $\dot{V} = 0$. Since n and V are the axes of the state space, therefore the path of the state must cross the nullcline perpendicular to the axes of the nullcline (north-south for $\dot{V}$ and east-west for $\dot{n}$).

Because of this, whenever we near a nullcline, depending on the sign of the derivatives, we will approach a perpendicular angle. But looking at the graphs, the functions are never perpendicular to the axes they describe ($\dot{n}$ to n and $\dot{V}$ to V). In addition, looking at the colors fig [11], we can see that for each color, we must cross a certain nullcline - purple must be followed by a cross of $\dot{V} = 0$, Yellow must be followed by a cross of the $\dot{n} = 0$ nullcline (because for yellow, $\dot{n} > 0$), blue must be followed by a cross of the $\dot{V} = 0$ nullcline, this time downwards, and orange by crossing $\dot{n} = 0$ from left to right. Even in the small areas in the middle this holds.

5.6

The border between the two options is somewhere around the $\dot{V} = 0$ nullcline. Since in the purple zone we have $\dot{n} > 0$, the trajectory can cross into the small yellow area that is close to the stable point, and then it quickly converges to the stable point without an Action potential. On the other hand, there is some value V_0 for which the trajectory can't enter the small yellow zone, and is therefore pushed towards the larger yellow zone (remember it must cross the $\dot{V} = 0$ nullcline), and this causes the action potential.

It can be thought of as that the current (of Sodium) needs enough of a voltage to cause it to surge, and thus create the Action potential. If the voltage is too close to the normal one, then there will only be a slight change in n and this won't cause the surge.

5.7

The beginning point depends on n as well as V, and therefore there is no threshold V which decides whether there will be an Action potential or not.

6 2D HH Model (Assuming $I > 0$) - bifurctions and cyclic behavior

6.1

The nullclines look much the same, as can be seen in fig[13].

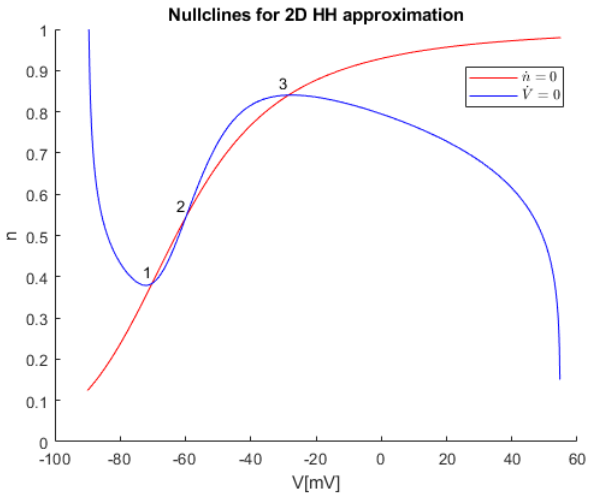

Figure 13: $\dot{n}$ and $\dot{V}$ nullclines for $I = 6.5\,[\mu A]$

The equilibrium points and their eigenvalues are:

V	n	Eigenvalues	Type
-70.2530	0.3836	$0.3113 + 0.5160i$ $0.3113 - 0.5160i$	Unstable focus
-59.8040	0.5457	18.8544 -0.0712	Saddle-point
-28.4569	0.8404	$1.0739 + 4.9719i$ $1.0739 - 4.9719i$	Unstable focus

Table 2: Equilibrium points, their eigenvalues and their types

6.2

The values of the equilibrium points changed a little, but are almost the same, the eigenvalues of the first point switched sign, and therefore the point is now unstable. What was without a current a stable point, is now an unstable one. This basically means that unless the beginning state is exactly one of the equilibrium points, the system will be in a perpetual change of state thanks to the input current.

6.3

Using a form of binary search (we know that there is only one bifurcation, and therefore for currents above it, the real of the eigenvalues is positive and on the other side, the real is negative), we found that the value is approximately:

$$\boxed{I_0 = 2.9\,[\mu A]}$$

6.4

6.4.1

We will number each equilibrium point as given in figure [13]

According to the Poincaré index theorem:

$$N = S + 1$$

(N are the number of focus points, and S are the number of saddle points). Therefore there can be cyclic loops around:

1. Point 1.
2. Point 3.
3. Points 1,2 and 3.

6.4.2

Using the rectangular route in fig [14], we can see that along it, all routes are inwards - according to the gradients divided by colors. This gives us an outer ring, and we are given an inner ring for $I \geq I^*$for which all paths lead outwards. This gives us a closed area, without equilibrium points, and for which no route leaves the area. And therefore according to the Poincaré-Bendixon theorem, there is a closed circuit within this area, and all other paths within this area lead to it.

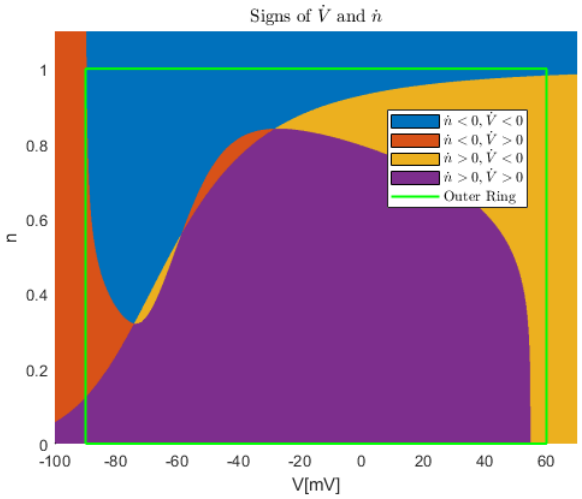

Figure 14: Outer ring for which all trajectories are inwards

6.5

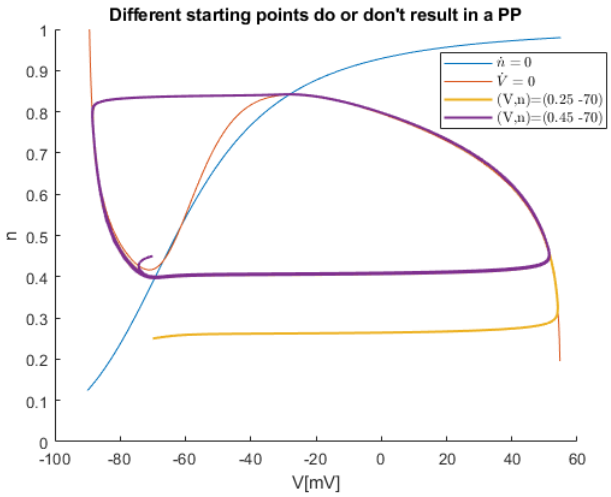

Figure 15: Routes for starting points $(-70, 0.25)$ and $(-70, -.45)$

These two simulations show how the routes for the two starting points converge to one single route, which is a circuit. This proves (in a graphical manner) that indeed we do have a closed circuit route around all three equilibrium points.