Mathematical Neuroscience - Assignment 1

Hindmarsch and Rose single-neuron model

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In this assignment we analytically and numerically investigate the Hindmarsh and Rose neuron model (HRM), characterized by the following system:

$$\frac{dv}{dt} = -v^3 + 3v^2 - r + I$$
$$\frac{dr}{dt} = 5v^2 - 1 - r$$

Where t represents time, v represents membrane voltage, r represents a recovery variable and I represents external current applied to stimulate the neuron.

1 Analytical investigation of HRM

For this section we investigate the neuron in an environment without external applied current, $I = 0$. We also define and use functions f and g that depend only on the voltage of the membrane, $f(v) = -v^3 + 3v^2$ and $g(v) = 5v^2 - 1$.

Question 1: The steady state of the HRM depends only on voltage

To show that the steady state $E = (v*_, r_*)$ of the HRM can be written as $E = (v_*, f(v_*))$ where v_* satisfies $f(v_*) - g(v_*) = 0$, we note the following.

The steady state (equilibrium) of the system is defined as the situation in which neither dynamical variable changes, that is, $\frac{dv}{dt} = 0$ and $\frac{dr}{dt} = 0$. After substituting the voltage-dependent functions f and g into the system, assuming no applied current, and setting $\frac{dv}{dt} = \frac{dr}{dt} = 0$ we obtain the following:

$$\frac{dv}{dt} = f(v) - r = 0$$
$$\frac{dr}{dt} = g(v) - r = 0$$

From which it is clear, that at the system's equilibria, $r = f(v) = g(v)$, holds. Thus, at the equlibrium voltages where v_* satisfies $f(v_*) - g(v_*) = 0$, we can say that $r = f(v_*) = g(v_*)$ and we can therefore express the equilibria or steady states as $E = (v_*, f(v_*)) = (v_*, g(v_*))$.

Question 2: Equilibria of HRM

In Question 1, we saw that at equilibrium, $f(v) - r = g(v) - r$, and as such, the membrane voltages v_* at which this relationship holds can be found by solving $f(v) - g(v) = -v^3 - 2v^2 + 1 = 0$, which corresponds to finding the roots of the cubic function $f(v) - g(v)$. We used Wolfram Alpha and found the following roots: $v_{*1} = \frac{-1-\sqrt{5}}{2}$,$v_{*2} = -1$, $v_{*3} = \frac{-1+\sqrt{5}}{2}$.

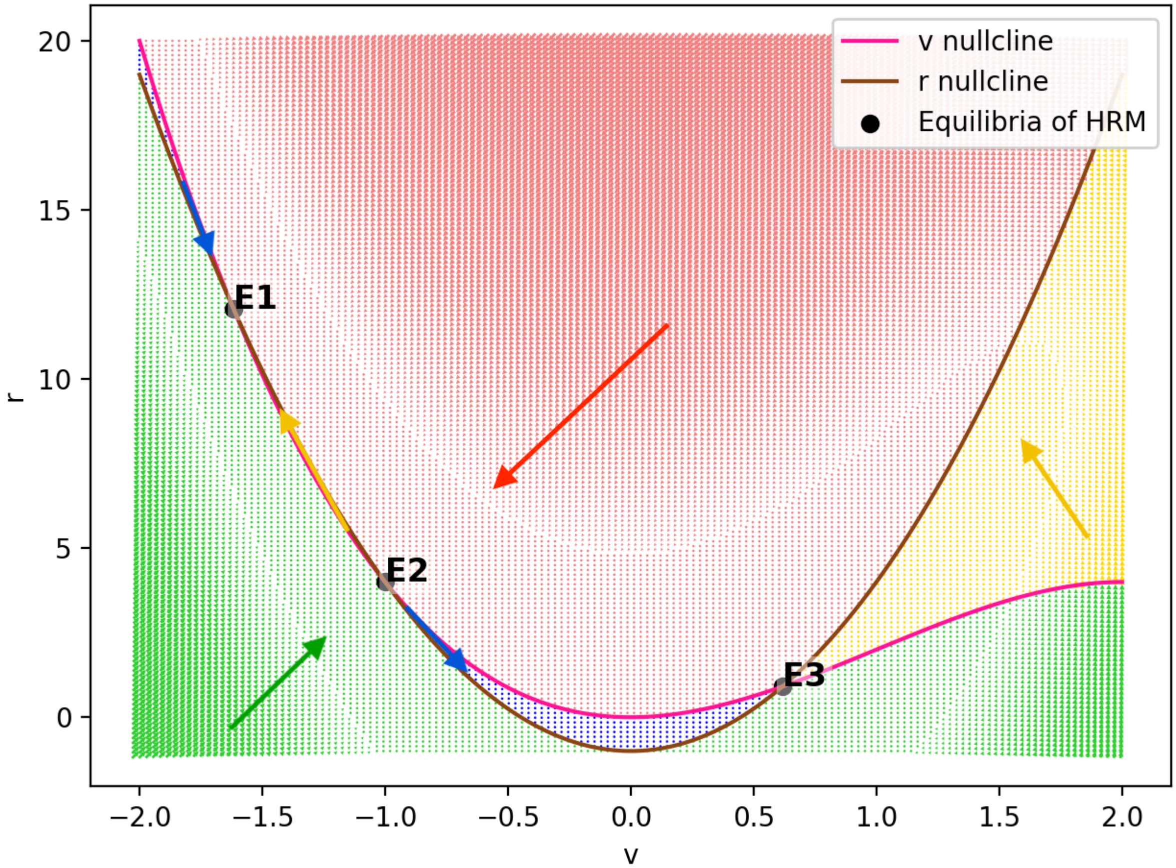


Figure 1: HRM model phase portrait. Big arrows (hand-drawn) indicate the general direction of all small arrows in the given part of the phase plane, corresponding to the same color. The phase portrait contains 10,000 small arrows indicating the $\frac{dv}{dt}, \frac{dr}{dt}$ at that state of the system.

Using $r = f(v_*) = g(v*)$ from Question 1 and the found equilibrium voltages $v_{*1/2/3}$, the 3 equilibria of the HRM system occur at the following v_* and r_*:

$$E_1 = (v_{*1}, r_{*1}) = (v_{*1}, g(v_{*1})) = (\frac{-1-\sqrt{5}}{2}, \frac{13+5\sqrt{5}}{2})$$
$$E_2 = (v_{*2}, r_{*2}) = (v_{*2}, g(v_{*2})) = (-1, 4)$$
$$E_3 = (v_{*3}, r_{*3}) = (v_{*3}, g(v_{*3})) = (\frac{-1+\sqrt{5}}{2}, \frac{13-5\sqrt{5}}{2})$$

Question 3: Phase portrait and nullclines of HRM

Here we present a relevant region of the phase plane around the equilibria obtained using a custom-written Python script, highlighting the equilibria, nullclines and direction of derivatives at 10,000 parameter combinations in regions surrounding the equilibria.

This phase portrait already reveals a lot about the system and, in fact, we can already determine the stability of the equilibria (Question 5) just based on this phase portrait. We note that the nullclines partition the phase space into 6 regions, corresponding to the 6 large arrows in Figure 1. The derivatives in these

6 regions falls into four categories signified by the colors of the large arrows and the underlying points in the vector field in Figure 1 blue: $\frac{dv}{dt} > 0, \frac{dr}{dt} < 0$, green: $\frac{dv}{dt} > 0, \frac{dr}{dt} > 0$, yellow: $\frac{dv}{dt} < 0, \frac{dr}{dt} > 0$, red: $\frac{dv}{dt} < 0, \frac{dr}{dt} < 0$.

As a bonus, below I provide a qualitative analysis of the equilibria based on the phase portrait here, which will be solidified by analyses in Questions 4 and 5. First, E1 seems to be a stable, attracting equilibrium, as vectors in all four regions of the phase plane are drawn towards it. Exactly what kind of stable equilibrium E1 is will be shown (also as a bonus) in Question 5. Second, E2 is a saddle, since it divides 2 opposing attracting regions and 2 opposing repelling regions of the phase plane. Based on this, we could already infer that the determinant of the Jacobian at this equilibrium will be negative, as we show in Question 5. Lastly, E3 appears to be an unstable, repelling equilibrium, as vectors in all of the regions surrounding it seem to follow orbits around it without necessarily being attracted to it. Exactly what kind of unstable equilibrium E3 is will be shown (also as a bonus) in Question 5.

Question 4: Jacobian of HRM

To show that the trace and determinant of $J(E)$ depend on v_* but not r_*, we simply compute the Jacobian of the HRM. For notation purposes, we refer to $\frac{dv}{dt} = x(v,r)$ and $\frac{dr}{dt} = y(v,r)$. The Jacobian of HRM is then:

$$J(E)_{(v*,r*)} = \begin{bmatrix} a & b \\ c & d \end{bmatrix} = \begin{bmatrix} \frac{\partial x}{\partial v} & \frac{\partial x}{\partial r} \\ \frac{\partial y}{\partial v} & \frac{\partial y}{\partial r} \end{bmatrix}_{(v*,r*)} = \begin{bmatrix} -3v^2 + 6v & -1 \\ 10v & -1 \end{bmatrix}_{(v*,r*)}$$

From the above, it is clear that any property of the Jacobian of HRM (including trace and determinant) only depends on v and not r, since v is the only variable that appears in the Jacobian. More explicitly:

$$\begin{aligned} \text{trace}J(E) &= a + d = -3v^2 + 6v - 1 = \tau(v*) \\ detJ(E) &= ad - bc = 3v^2 + 4v = \Delta(v*) \end{aligned}$$

To prove the statements in S2, it suffices to identify $1 - \sqrt{2/3}$ and $1 + \sqrt{2/3}$ as the quadratic roots of $\tau(v)$, and given that $\tau(v)$ is an inverted concave parabola because its quadratic term is negative, at voltages between the roots of $\tau(v)$, $\tau(v) > 0$ and at all other voltages $\tau(v) < 0$. We can use the same exact argument in reverse for $\Delta(v)$, which is a convex parabola because of the positive quadratic term, with roots at $-4/3$ and 0. Therefore, at voltages between the roots of $\Delta(v)$, $\Delta(v) < 0$ and at all other voltages $\Delta(v) > 0$. We can visualize the above observations by plotting $\tau(v)$ and $\Delta(v)$ with their roots in Figure 2.

Question 5: Nature of HRM Equilibria

To determine the stability of equilibria of HRM, we construct a Trace-Determinant diagram (Figure 3) and place the equilibria found in Question 2 on the diagram, to determine their nature. We see that E_1 has $\tau(v) < 0$ and $\Delta > 0$ which means that E_1 is a stable, attracting equilibrium, and by realizing that $0 < \Delta(v) < \frac{\tau(v)^2}{4}$, we can classify E_1 as a sink. With E_2 we see that $\Delta(v) < 0$ and thus we can classify E_2 as a saddle. Lastly, for E_3 $\tau(v) > 0$ and $\Delta > 0$, which makes it an unstable, repelling equilibrium. Observing that $\Delta(v) > \frac{\tau(v)^2}{4}$, we can classify E_3 as a spiral source.

We could have determined the stability, but not the exact nature of all the equilibria, explicitly using S2 from Question 4, as follows. Noticing that $v_{*1} < -4/3$, we could classify E_1 as a stable equilibrium ($\tau(v) < 0$ and $\Delta > 0$). Identifying $-4/3 < v_{*2} < 0$, we could identify E_2 as a saddle, just because $\Delta < 0$. Lastly, because $1 - \sqrt{2/3} < v_{*3} < 1 + \sqrt{2/3}$, $\tau(v) > 0$ and $\Delta > 0$, making it an unstable equilibrium.

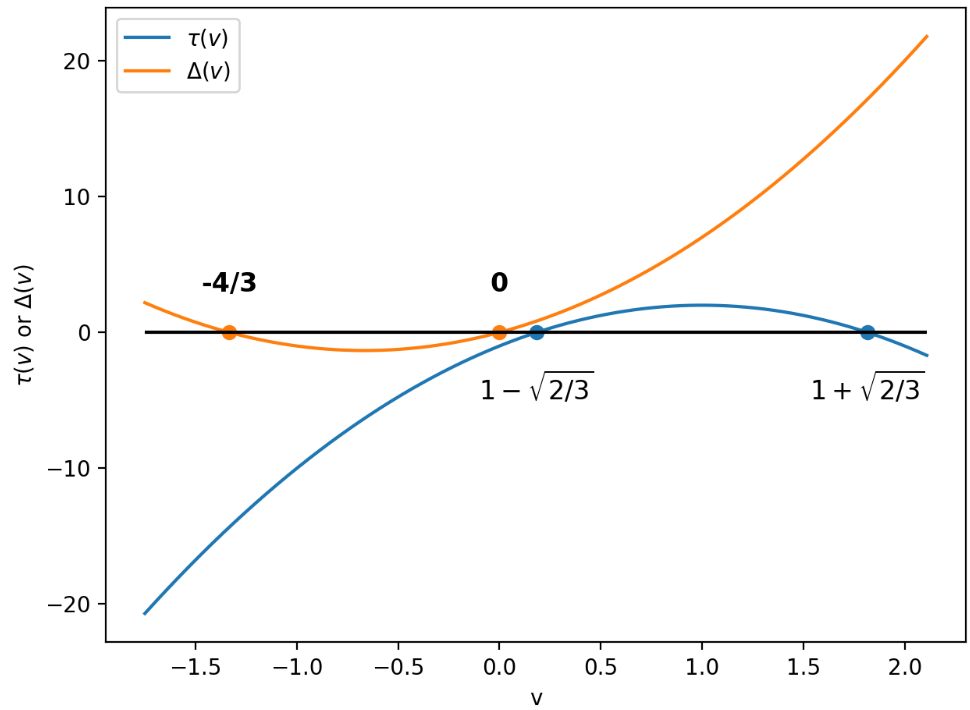


Figure 2: $\tau(v*)$ and $\Delta(v*)$

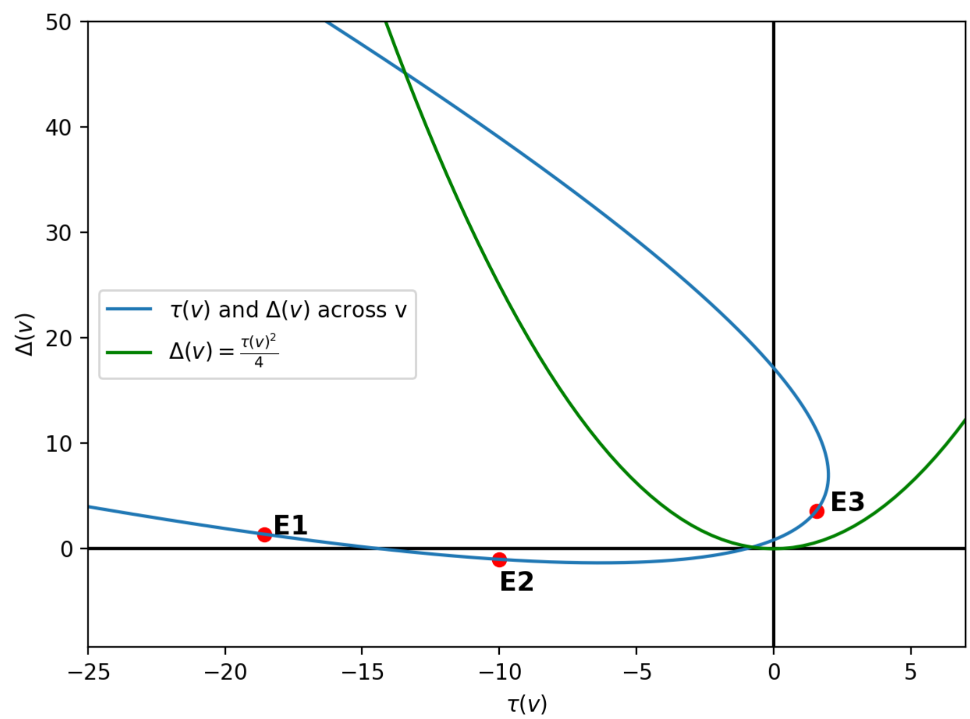
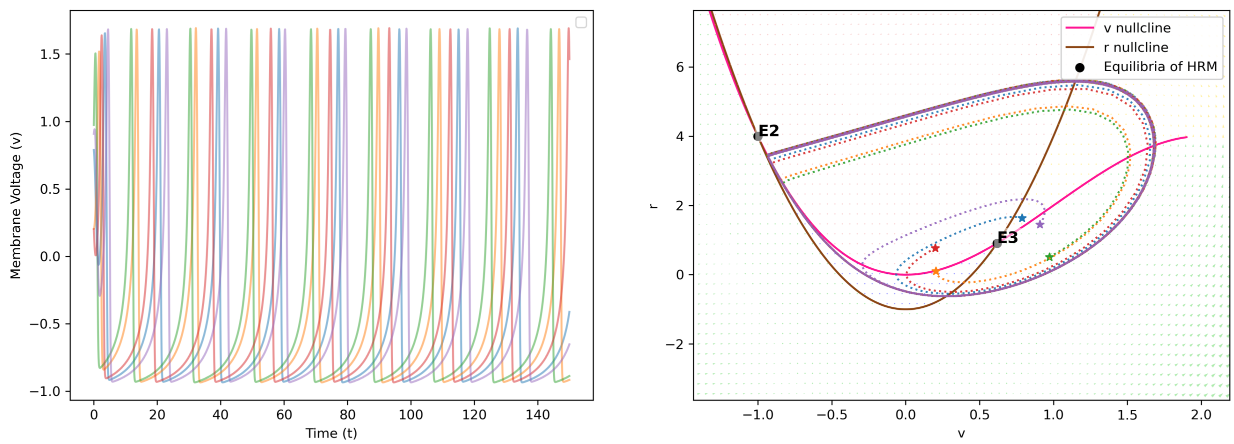


Figure 3: Trace-Determinant diagram with equilibria of HRM model

2 Numerical investigation of HRM

2.1 Question 6: HRM can produce repeating self-sustaining spikes in absence of external current

To show that HRM can produce repeating spikes without external current, we note that this can only be the case if we start the system at a high enough voltage, which makes sense both biologically and mathematically, based on the nature of the equilibria. Therefore, we started the system in region around E_3 and saw that the unstable E_3 repelled the system onto a limit cycle surrounding E_3, where the system stayed and continued to spike (Fig 4).



(a) Voltage trace of HRM showing periodic spiking in absence of external current

(b) System trajectories during periodic spiking in absence of external current

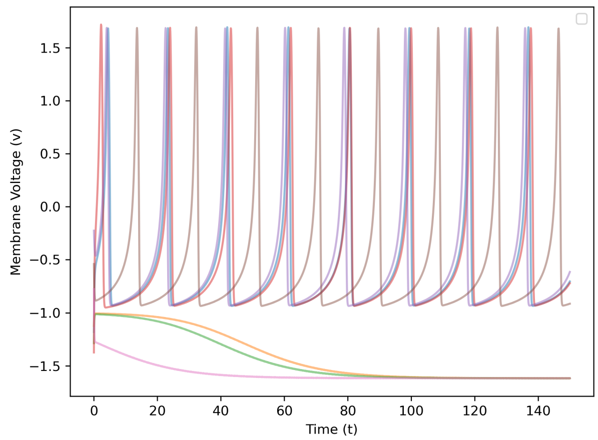
Figure 4: Self-sustained spiking of HRM in absence of external current

2.2 Question 7: HRM bistability

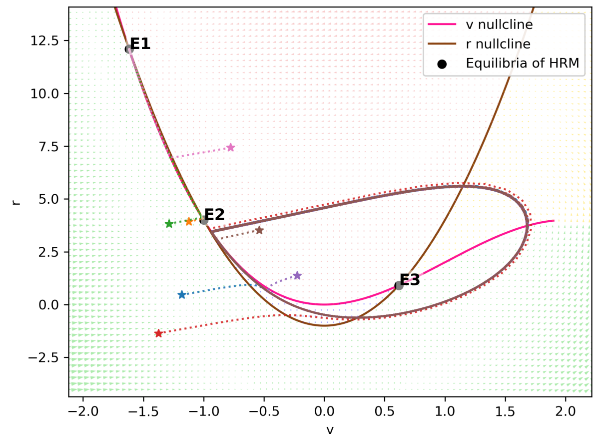
To investigate bistability, we noted the crucial role of the saddle equilibrium E_2 and started the system in regions that would be repelled along the unstable directions from E_2. Starting the system between E_1 and E_2 led to a quick fall in voltage, to the "resting state", and this could be observed in the phase plane by the convergence of trajectories into the E_1 sink (Fig 5). Conversely, starting the system between E_2 and E_3, led to spiking and attraction to a limit cycle surrounding E_3 (Fig 5), as already observed in Question 6.

2.3 Question 8: Suppressing periodic spikes with external current

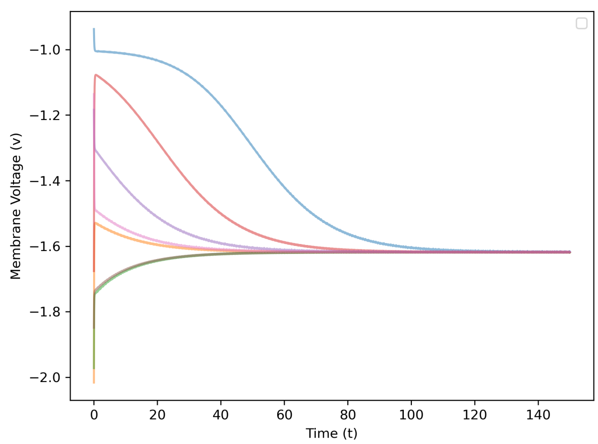
Assuming an HRM neuron is spiking periodically (for this question, we used initial conditions $v = -0.99, r = 2$, which result in periodic spiking, see $I_{applied} = 0$ in Fig. 6), as shown in Questions 6 and 7, there are two ways to suppress periodic spikes with external current. The intuitive way is to apply a negative current that will decrease the voltage. Once the voltage is low enough, the system will be attracted to the resting state E_1 and stop spiking (Fig. 6). The more interesting approach is to suppress spikes by applying a high positive current and "overloading" the system, to the point where it will also be attracted to the resting state E_1 but from "above" (Fig. 6). We can see that the latter can occur after injection of current resulting in a quick 'burst' of activity before returning to resting state. Providing an exact estimate of the current at which oscillations are suppressed is slightly complicated because it might depend on how long the current is applied and at which point of the spike the current is applied. However, when comparing various levels of applied current, it seems that at least from our initial conditions, $I_{applied} \leq -2.5$ leads to return to resting



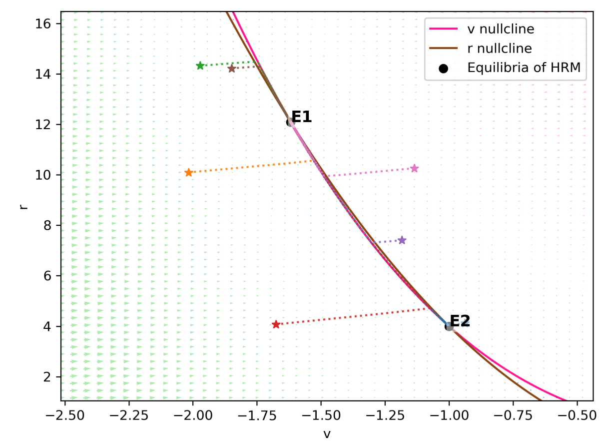
(a) Voltage trace of HRM showing bi-stability between resting state (E_1 sink) and spiking (E_3 limit cycle).



(b) System trajectories showing bi-stability between resting state (E_1 sink) and spiking (E_3 limit cycle).



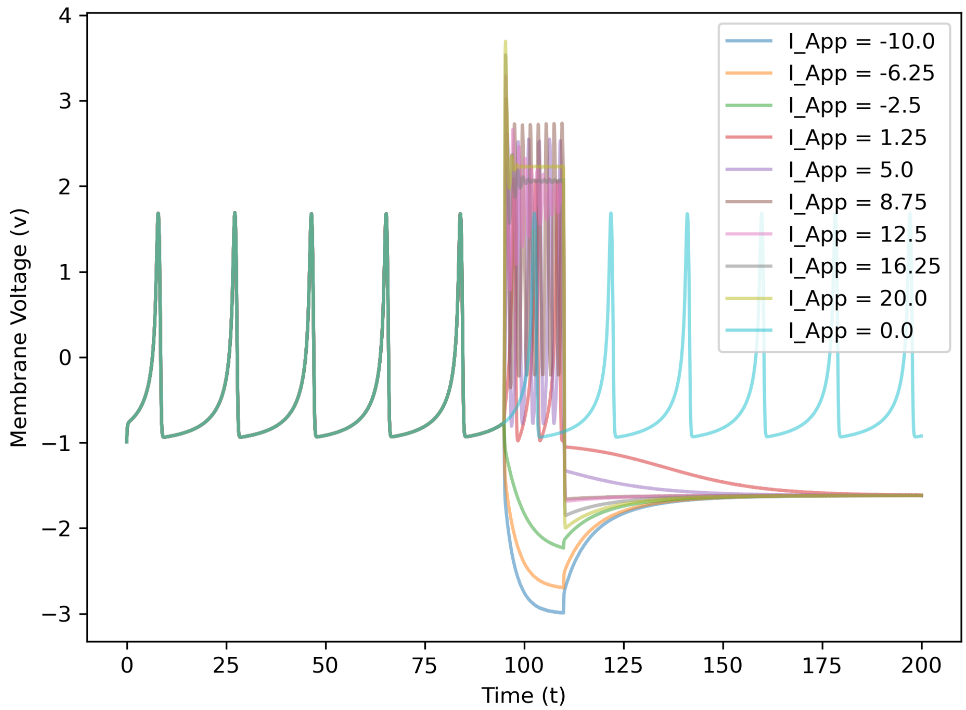
(c) Voltage trace of HRM showing attraction to resting state when starting at low voltage.



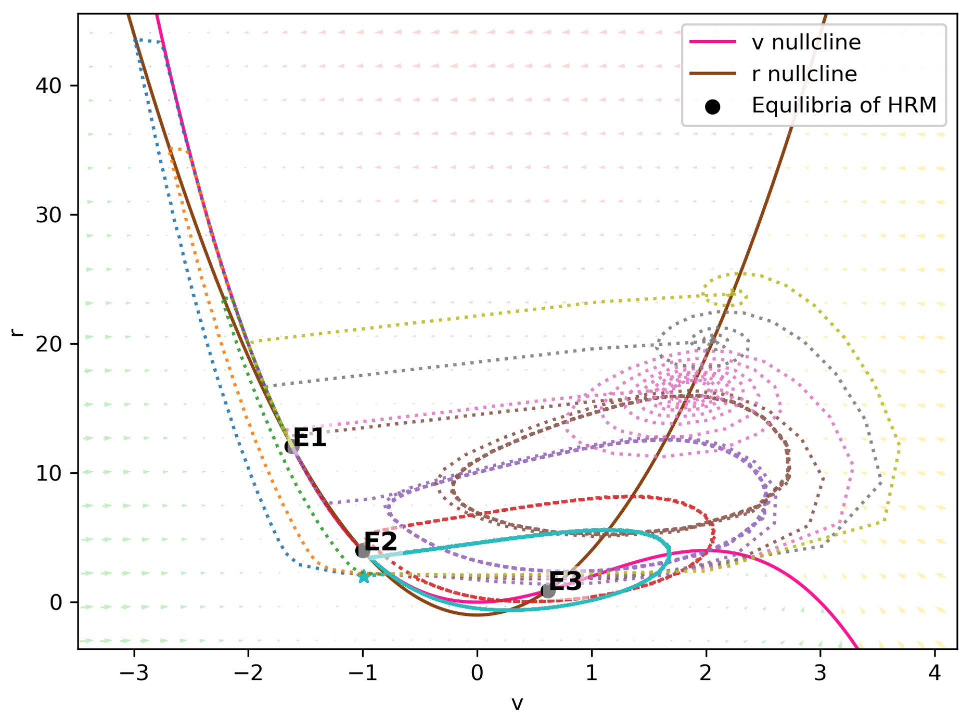
(d) System trajectories around showing attraction to resting state at low voltage.

Figure 5: Bistability of HRM: Resting state equilibrium E_1 and Spiking limit cycle surrounding E_3

state via direct attraction to E_1 from the left side of the phase plane, while $1.25 \leq I_{applied} \leq 8.75$ leads to a temporary burst of high-frequency spiking during current application, followed by return to resting state E_1 from the right side of the phase plane. Lastly $I_{applied} \geq 12.5$ represents perhaps supraphysiological levels of stimulation and results in strange voltage traces that show a slight fluctuation, followed by constant elevated voltage, followed by a steep drop, and return to resting state once applied current is alleviated. In qualitative terms, it seems that, when the system is pushed out of the limit cycle surrounding E_3, the system will stop spiking an return to resting state.



(a) Voltage traces of HRM showing suppression of periodic spiking with varying levels of external current



(b) System trajectories when suppressing periodic spikes with varying levels of external current

Figure 6: Suppression of periodic spiking with application of external current