5. Simplified Neuron Models

In chapter 3, we have introduced the HH model which is the earliest model of action potential (AP) generation in an axon. It shows how voltage-sensitive dynamics of sodium and potassium channels results in generation of APs. But real neurons have a much large variety of ion channels. There are dozens of voltage- and Ca2+-gated channels known today. Combinations of these channels can give rise to an astronomically large number of neuron models. Even the HH model, the simplest model of AP generation that we encountered so far, has 4 differential equations, three of them being nonlinear. More realistic neuron models with larger number of ion channels can easily become mathematically untractable. It would be desirable to construct simplified models, with fewer variables, and milder nonlinearities, in such a way that the reduced model preserves the essential dynamics of their more complex versions. One of the first reduced model of that kind is the Fitzhugh-Nagumo neuron model.

5.1 FitzHugh-Nagumo model

FitzHugh-Nagumo model is a two-variable neuron model, constructed by reducing the 4-variable HH model, by applying suitable assumptions.

Hodgkin- Huxley model:

$$C\frac{dv}{dt}+\bar{g}_{Na}\,m^3h\left(v-E_{Na}\right)+\bar{g}_k\,n^4\left(v-E_k\right)+g_L\left(v-E_L\right)=I_{at}$$

$$\frac{dm}{dt}=\alpha_m(V_m)(1-m)-\beta_m(V_m)m$$

$$\frac{dh}{dt}=\alpha_h(V_m)(1-h)-\beta_h(V_m)h$$

$$\frac{dn}{dt}=\alpha_n(V_m)(1-n)-\beta_n(V_m)n$$

Assumptions:-

The time scales for m, h and n variables are not all of the same order. These disparities provide a basis for eliminating some of the gating variables.

1) Since the time scale for m is much smaller than that of the other two, we assume that m relaxes faster than the other two gating variables. Therefore, we let,

$\frac{dm}{dt}=0$ i.e.,

$$\frac{dm}{dt} = \alpha_m(v)(1-m) - \beta_m(v)(m)$$

$$0 = \alpha_m(v) - (\alpha_m(v) + \beta_m(v))(m)$$

$$m = \frac{\alpha_m(v)}{\alpha_m(v) + \beta_m(v)} \qquad (5.1.1)$$

2) h varies too slowly. Therefore, we let h to be a constant, $h = h_0$

The resulting system has only two variables (v, n). After transformation to dimensionless variables, and some approximations, the resulting FN model may be defined as,

$$\frac{dv}{dt} = f(v) - w + I_m \qquad (5.1.2)$$

where $$f(v) = v(a-v)(v-1) \qquad (5.1.3)$$

$$\frac{dw}{dt} = bv - rw \qquad (5.1.4)$$

In the above system, v is analogous to the membrane voltage, and w represents all the three gating variables.

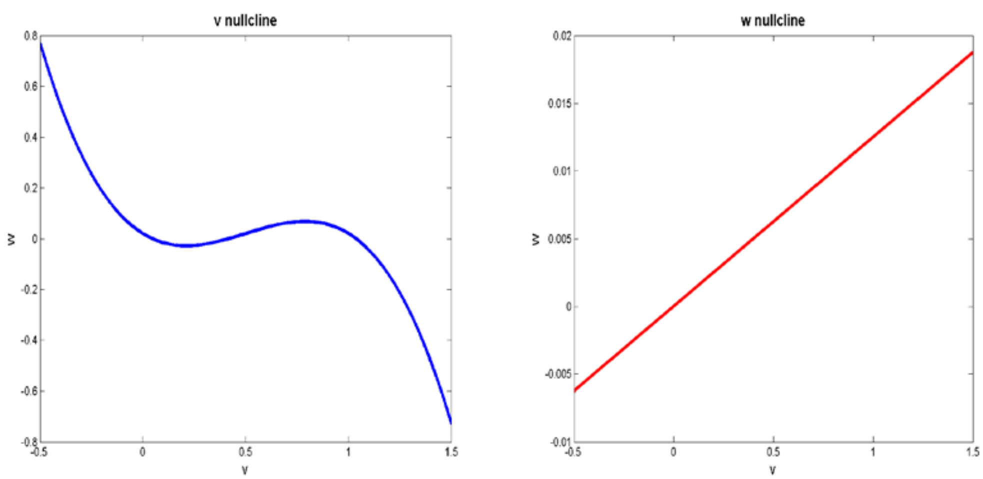

Figure 5.1.1: The nullclines V and w

The two nullclines of the above system are,

$$F(v,w) \equiv f(v) - w + I_a = 0 \qquad \text{(F-nullcline)}$$

$$g(v,w) \equiv bv - rw = 0 \qquad \text{(g-nullcline)}$$

To examine the stability of a stationary point, we calculate the Jacobian, A, of the system at that point.

$$A = \begin{bmatrix} \dfrac{\partial F}{\partial v} & \dfrac{\partial F}{\partial \omega} \\ \dfrac{\partial g}{\partial v} & \dfrac{\partial g}{\partial \omega} \end{bmatrix} = \begin{bmatrix} f'(v) & -1 \\ b & -r \end{bmatrix}$$

$$\tau = f'(v) - r \tag{5.1.5}$$

$$\Delta = f'(v)(-r) \tag{5.1.6}$$

The type of the stationary point can be expressed in terms of determinant, Δ, and trace, τ,of the Jacobian, using the following rules:

- if$\Delta < 0$, the stationary point is a saddle irrespective of the value of τ .
- if $\Delta > 0$, $\tau < 0$, stable point
- if$\Delta > 0$, $\tau > 0$, unstable point.

$$\Delta > 0$$

$$f'(v)(-r) > -b$$

$$f'(v) r < b$$

$$f'(v) < \frac{b}{r} \tag{5.1.7}$$

That is, $\Delta > 0$, when the slope of the F-nullcline is lesser than slope of w-nullcline.

$$\tau > 0, \Rightarrow f'(v) - r > 0$$

$$\Rightarrow f'(v) > 0 \quad (approx) \tag{5.1.8}$$

Now let us consider the behavior of FN model as external current I_a is gradually increased.

5.1.1) I_a=0, Excitability

The phase-plane shown below depicts the situation when I_a=0. There is only one stationary point at the origin.

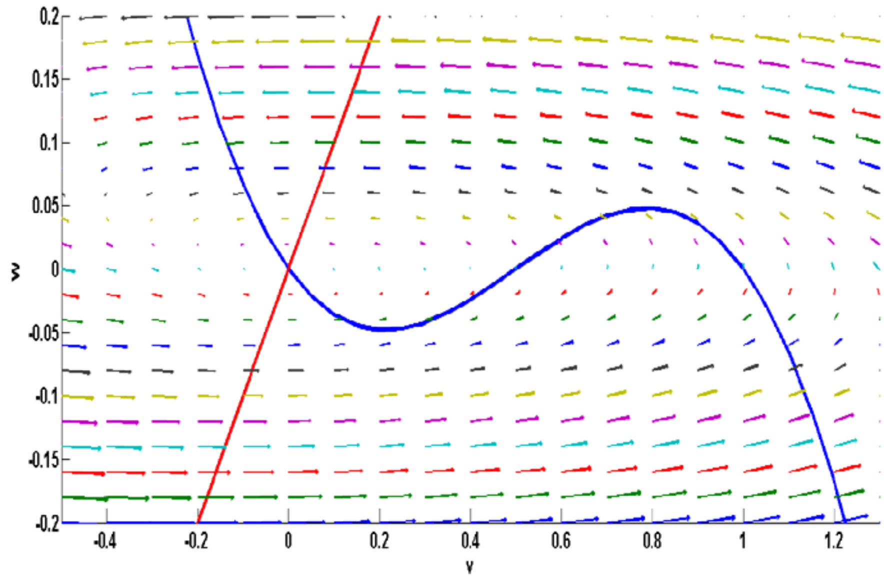

Figure 5.1.1.1: Phase plane analysis: Excitability at a=0.5; b=0.1; r=0.1; I_a=0

Stability of origin:

a) Slope of F-nullcline> slope of w-nullcline $\Delta > 0$

b) $f'(v) < 0, \Rightarrow \tau < 0$

$\therefore$ Origin is stable.

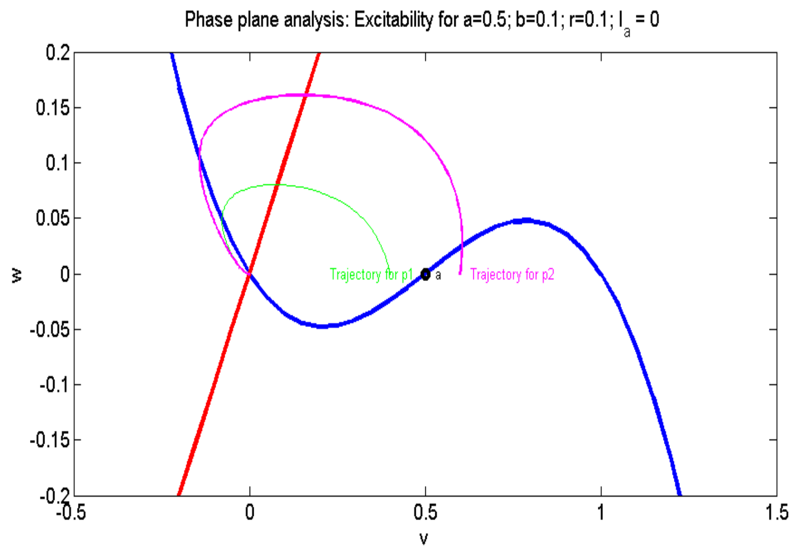

Figure 5.1.1.2: The points a,p1,p2 and their trajectories

Consider the evolution of the variable v (membrane voltage) when the initial condition is at points p1 or p2 (fig. 5.1.1.2).

This behavior will first be anticipated using loose arguments, and then confirmed using simulations.
The F- and w-nullclines in fig. (5.1.1.1,5.1.1.2) above intersect only at one point (the origin) and therefore divide the plane into four regions, numbered from 1 to 4 (fig. 5.1.1.1). The flow patterns in the four regions can be seen to be as follows:

Region 1: $\dot{v} < 0,\ \dot{w} > 0$
Region 2: $\dot{v} < 0,\ \dot{w} < 0$
Region 3: $\dot{v} > 0,\ \dot{w} < 0$
Region 4: $\dot{v} > 0,\ \dot{w} < 0$

We have just talked about the signs of $\dot{v},\ \dot{w}$, but it must be noted that, far from the null-clines, the magnitude of $\dot{w}$ is much smaller than that of $\dot{v}$, since b,r<<1.
We divide the F-null-cline into three segments: Segment 1 (to the left of point M), Segment 2 (between points M and N) and Segment 3 (to the right of point N). We will refer to these segments in the following discussion.

Let us now consider the two initial conditions:

Initial condition at p_1: This point is inside region 1. Therefore the flow is leftwards, with a small upward component. The system state approaches the origin and settles there, confirming our earlier result that the origin is the only stable point.

Initial condition at p_2: This point is inside region 4, where the flow is rightwards with a small upward component. Therefore the system state moves rightwards until it hits the F-nullcline inside Segment 3. Since the flow has no horizontal component on the F-nullcline, the small upward component pushes the state upwards. In Segment 3 of F-nullcine there is a tendency for the state stay on the F-nullcline, since the flow is leftwards on its right, and rightwards on its left. Therefore, the state creeps along the F-nullcline in the upward direction until it reaches the topmost point, N, on the F-nullcline. Beyond this point the flow is still upwards and leftwards while the F-nullcline bends downwards. Therefore, the state leaves the F-nullcline and drifts leftwards until it reaches Segment 1. The situation now similar to what we encountered on Segment 3, but with a downward flow component. Therefore the state creeps downward along Segment 3 until reaches the origin where it finally settles down.

Therefore, when p2 is the initial condition, the system exhibits this large excursion by which the membrane voltage reaches a maximum before it returns to the origin. Such an excursion of membrane voltage resembles an action potentials.

Therefore the FitzHugh-Nagumo neuron model exhibits excitability. For the initial membrane less than a threshold value (=a), the voltage quickly returns to zero (fig. 5.1.1.3). When the initial voltage exceeds the threshold (=a), the voltage exhibits an action potential (fig. 5.1.1.3).

$p_1, p_2 \Rightarrow$ Initial voltages $\quad v(0)$

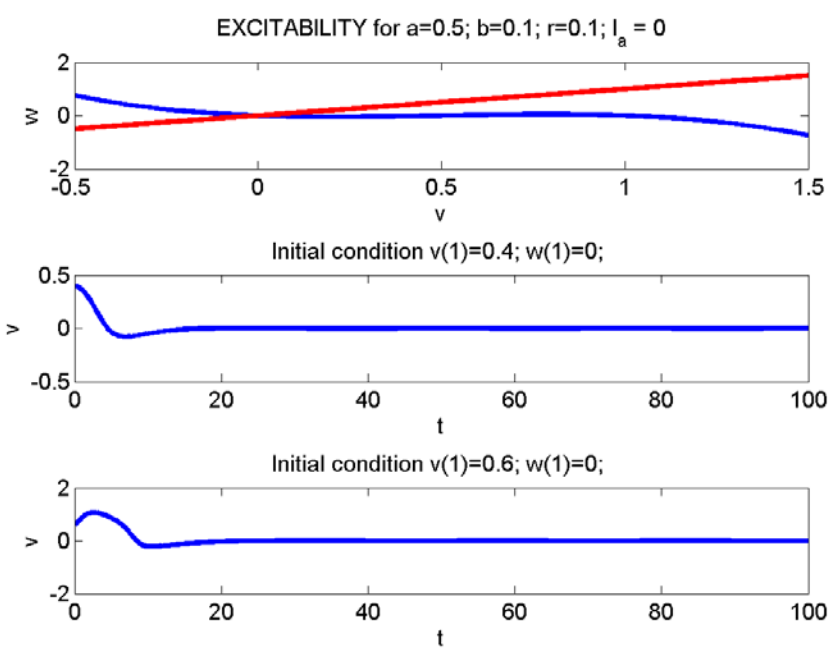

Figure 5.1.1.3: a) The nullclines vand w, and 'v' simulation from b) p1 and c) p2

5.1.2) Limit Cycles (Ia> 0):

As I_a increases, for a range of values of I_a, the w-nullcline intersections the F-nullcline in the "middle branch" where the F-nullcline has a positive slope. In this case too there only a single intersection.

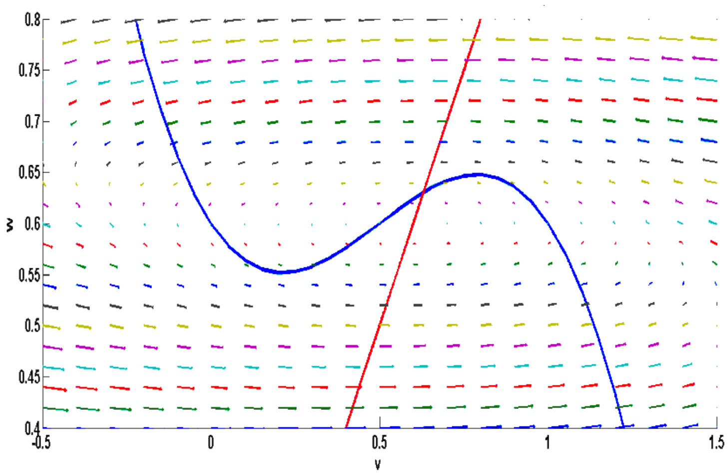

Figure 5.1.2.1: Phase plane analysis: Oscillations at a=0.5; b=0.1; r=0.1; I_a=0.6

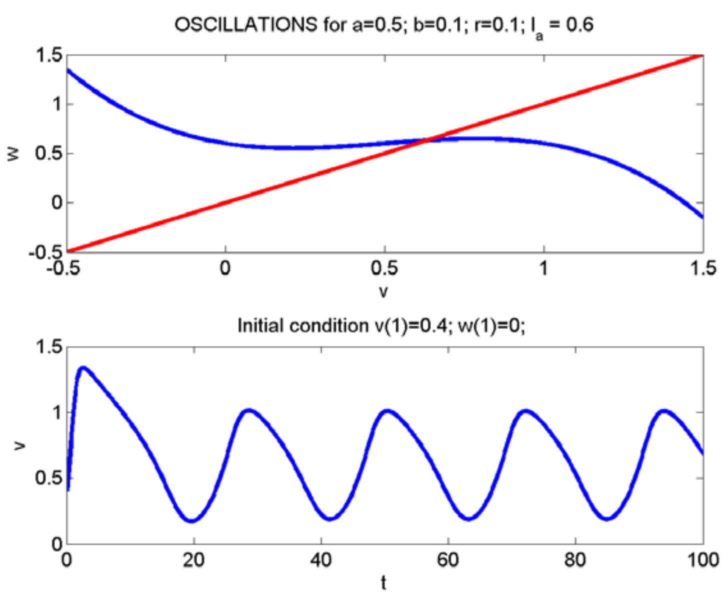

Figure 5.1.2.2: a) The nullclines v and w and 'v' simulation with initial b) v(1)=0.4

$\tau = f'(v) > 0$ Therefore, the stationary point is unstable.

The rough ‘arrowplot’ in fig.(5.1.2.1) above shows that there is a ‘circulating field’ around the stationary point, which is unstable. Thus it can be expected that there is a limit cycle enclosing the stationary point, which is actually true. Fig. 5.1.2.2 shows the oscillations in membrane voltage (v) produced by a MATLAB program.

5.1.3) Depolarization (higher I_a):

As I_a increases further, the two nullclines intersect in the “right branch” of the F-nullcline where the slope of F-nullcline is negative.

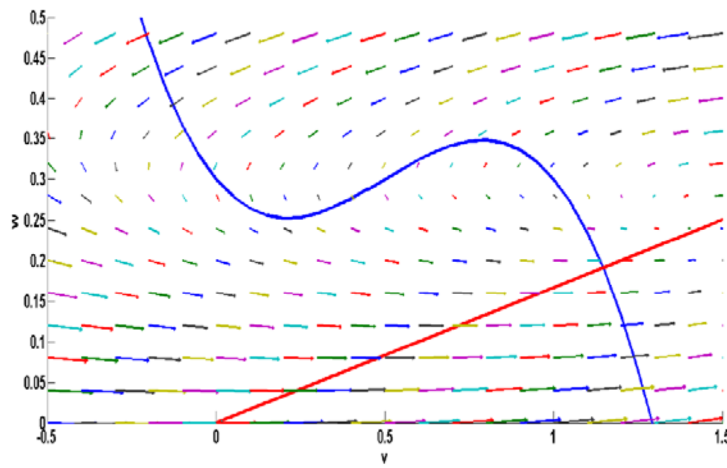

Figure 5.1.3.1: Phase plane analysis: Depolarisation at a=0.5; b=0.1; r=0.6; I_a=0 .3

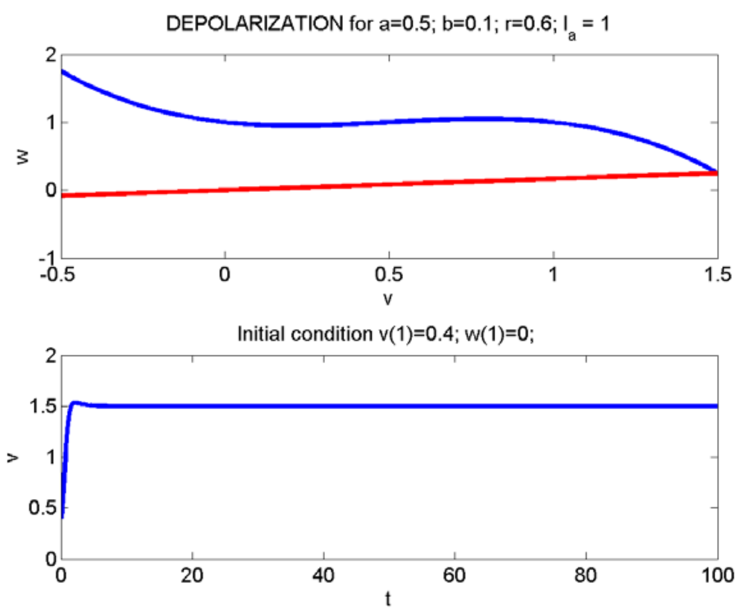

Figure 5.1.3.2: a) The nullclines v and w and 'v' simulation with initial b) v(1)=0.4

Since,

$$f'(v) < \frac{b}{r}, \Delta > 0$$

$$\tau = f'(v) > 0$$

We know that the stationary point is stable.In this case, the membrane voltage remains stable at a high value. This corresponds to regime 4 (in fig 5.1.3.2) in the HH model where for a sufficiently high current, the neuron does not fire but remains tonically depolarized.

5.1.4) Bistability

Some real neurons exhibit bistable behavior – their membrane voltage can remain at tonically high ("UP" state) or tonically low ("DOWN" state) values. These UP/DOWN neurons are found in for example in medium spiny neurons of Basal ganglia striatum.

The FN model exhibits bistability for a certain range of model parameters.

Fig. 5.1.4.1 below shows a configuration in which the null-clines intersect at three points (p1, p2 and p3). It can easily be shown that p1 and p3 are stable, and p2 is a saddle.

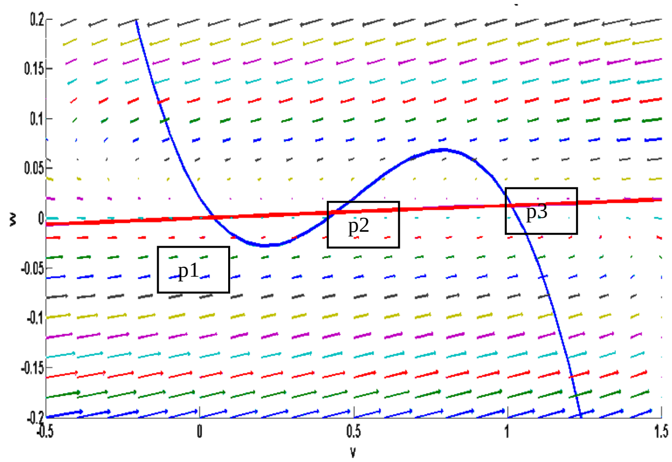

Figure 5.1.4.1: Phase plane analysis: Neuronal on-off bi-stable behavior at a=0.5; b=0.01; r=0.8; I_a=0.02

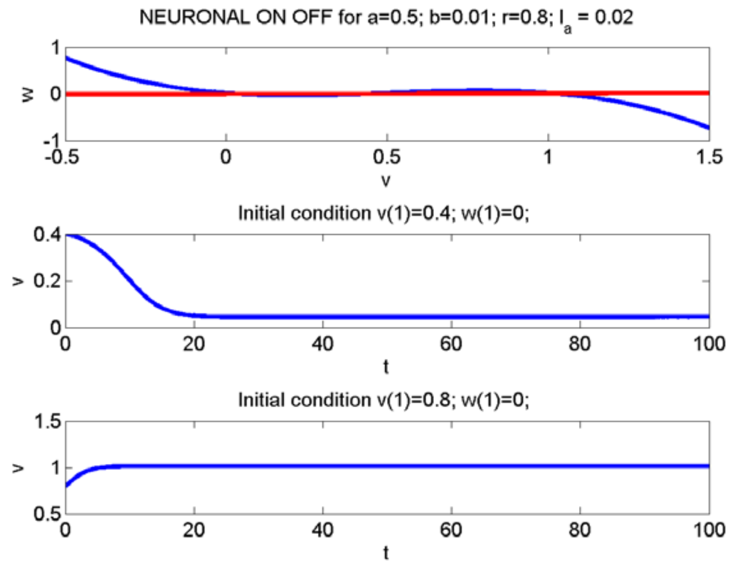

Figure 5.1.4.2: a) The nullclines v and w, and 'v' simulation with initial b) p1: v(1)=0.4 c) p3: v(1) = 0.8

@ p1: (V(1) = 0.4)

$$f'(v) < 0 < \frac{b}{r},\ \Delta\ > 0$$
$$\tau = f'(v) < 0,\ stable$$

@p2: (V(1) = 0.5)

$$f'(v) > \frac{b}{r},\ \Delta < 0$$
$$\tau = f'(v) > 0,\quad saddle\ node$$

@p3: (V(1) = 0.8)

$$f'(v) < 0 < \frac{b}{r},\ \Delta\ > 0$$
$$\tau = f'(v) < 0,\ stable$$

FN model in this case, can remain stable at either p1(low v value, DOWN state) or at p3 (high v value, UP state).