2 Nonlinear integrate-and-fire models

Several Nonlinear models are developed to explore analytically the intrinsic dynamics of large, isolated neuronal networks and to fit to its complex behaviour. They are typically described in the following form i.e

$$\frac{dV}{dt} = F(V) + \frac{1}{C_m} I_{input}(t) \tag{1}$$

where

- V is the membrane potential
- F(V) is a nonlinear function of the membrane potential
- C_m is the membrane potential
- I_{input} is some input current

In order to estimate the non-linear function $F(V)$, Basic electrophysiology provides an equation that relates the capacitive charging current and the summed effect $I_m(V,t)$ of the transmembrane currents to the injected current $I_{in}(t)$

$$C_m \frac{dv}{dt} + I_m(V,t) + I_{noise} = I_{in}(t) \tag{2}$$

$$\rightarrow \qquad \frac{dv}{dt} = -\frac{1}{C_m} I_m(V,t) + I_{noise}(t) + \frac{1}{C_m} I_{in}(t) \tag{3}$$

where

- $I_m(V,t) = I_{in}(t) - C_m \frac{dv}{dt}$, is a time- and voltage-dependent current across the cell membrane.
- $I_{noise}(t)$ is a additional noise which cannot be modelled.

Comparing (3) to (1) we get, we get the noisy estimate of $\hat{F}(\mathrm{V}, t_0)$ given by,

$$\hat{F}(V,t_0) = \left.\frac{dv}{dt}\right|_{t=t_0} - \frac{1}{C_m} I_{input}(t_0) \tag{4}$$

$\left.\frac{dv}{dt}\right|_{t=t_0}$ can be estimated by by finite difference method which is to obtain a difference between consecutive voltage values with a time width of 1mV interval.

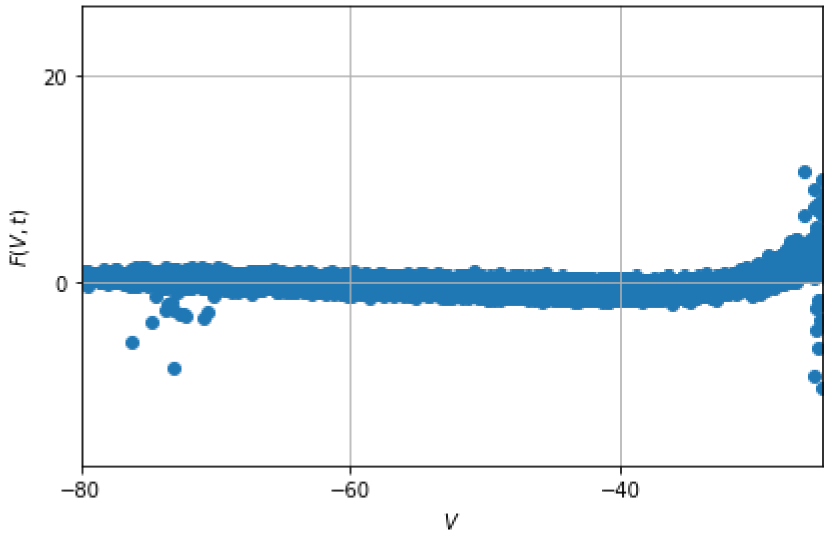
And also, the stochastic current $I_{input}(t_0)$, the ones with the variable amplitudes are being used to inject to the somatosensory pyramidal cells to produce fluctuating voltage traces.

Task 2a

For the sake of gravity these continuous values are being generated and used to observe the spiking behaviour of a nonlinear model.

And also, some modifications are done in the generated vectors as in it is a requirement fit the model to fit with a single differential equation.

Both $\hat{F}(V, t_0)$ and V(t) are parameterized by time, whereas for an I-V curve, a direct relation between the two is required. A scatter plot of V(t) on the x-axis versus found out $\hat{F}(V, t_0)$ on the y-axis is plotted which is as obtained as shown in **Fig(1)**

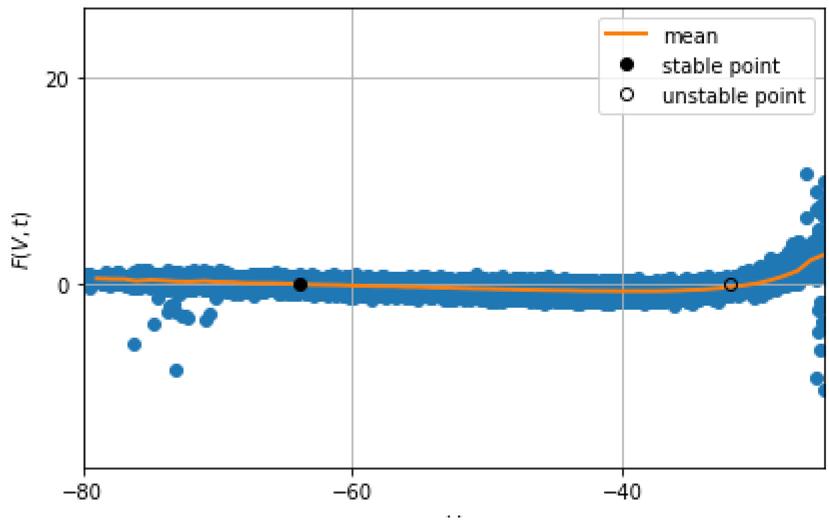


Fig(1)

For a given voltage, a gaussian distribution is seen for the values of the current which could be optimised by taking the average $\hat{F}(V, t_0)$ so that time dependency can be eliminated. And it can be given by,

$$\hat{F}(V) = Mean\left[\hat{F}(V, t)\right] \quad (5)$$

This quantity may be calculated by collecting all the points in the trajectory with a voltage in the range $V \in [-80, -25]$ mV a bin of sufficiently small width say 1mV is chosen. And for all the values falling into this bin there mean value is being calculated to finally get a refined neat path as Fig(2)



Fig(2)

Task 2b

- An equilibrium points can be observed when $\hat{F}(V)$ tends to become '0'. In our model there are two fixed equilibrium points which can be noticed in **Fig(2)**. Especially a point which is located to the **left side** of a plot. Path traversal through this point is an evidence of a linear region of $\hat{F}(V)$ equation where cellular response is passive. As a result the change in voltage is relatively slow. And it is a positive change because $\hat{F}(V) > 0$ which moves towards fixed point. Thus, it is a ***stable*** fixed point. Whereas, a point which is located to the **right side** of a plot is an ***unstable*** fixed point because $\hat{F}(V) < 0$ till the point and also lie in the linear region of the equation. Which gives rise to a steady negative change in voltage, moving away from the fixed point.
- These equilibriums if verified closely they correspond to **spiking behaviour** of a neuron. Where the region around the stable fixed point provides an information about **Resting potential**(as F(V) is becoming '0' implies the change in voltage is becoming '0') and the region around the unstable fixed point provides the information about **Firing threshold** (as F(V) rapidly starts increasing once it passes over the fixed point)

Task 2c

To fit an exponential, integrate-and-fire model to the data using results obtained above. It is given by

$$C_m \frac{dV}{dt} = -g_L(V - E_L) + g_L \Delta_T \exp\left(\frac{V - \vartheta_{rh}}{\Delta_T}\right) + I \qquad (6)$$

with a reset mechanism

$$\text{if} \quad V \geq \vartheta_{reset} \; : \quad V \leftarrow V_{reset} \qquad (7)$$

and an absolute refractory period of Δ_{abs}.

- As per Task2b explanation, the equilibrium points correspond to spiking behaviour of a neuron. Where the region around the stable fixed point provides an information about **Resting potential** and the region around the unstable fixed point provides the information about **Firing threshold.** However, to extract the values of **Resting potential** and **Firing threshold** it is always dependent on the current that is injected i.e
  Case i) If no current is injected then we can clearly come into conclusion that at a stable fixed point lies exactly the value of resting potential so as with the firing or rheobase threshold with the unstable fixed point.
  But if some amount of current is injected to the neuron the change in voltage with respect to time is quite higher as a result F(V) curve shifts slightly towards right resulting a stable fixed point to be a slightly greater than resting potential. And same with the unstable fixed point which is slightly smaller than the threshold.
  From Fig(2) and from the code, the exact values of stable and unstable fixed points correspond to **-32mV** and **-64mV**, respectively.
  Henceforth, as per the above theory **E_L** - Resting potential should be *lesser* than -64mV and $\boldsymbol{\vartheta_{rh}}$ - Firing threshold should be *greater* than -32mV. In our case as per the calibration, **E_L** = -71mV turned out to be a good value to the parameter) .

- From eq.(6) we get

$$C_m \frac{dV}{dt} = -g_L(V - E_L) + g_L \Delta_T \exp\left(\frac{V - \vartheta_{rh}}{\Delta_T}\right) + I$$

$$\rightarrow \quad \frac{dV}{dt} = \frac{1}{C_m}\left[-g_L(V - E_L) + g_L \Delta_T \exp\left(\frac{V - \vartheta_{rh}}{\Delta_T}\right) + I\right] \tag{8}$$

From eq.(1) we get

$$\frac{dV}{dt} = F(V) + \frac{1}{C_m} I_{input}(t)$$

Comparing eq(1) and eq(8) we get

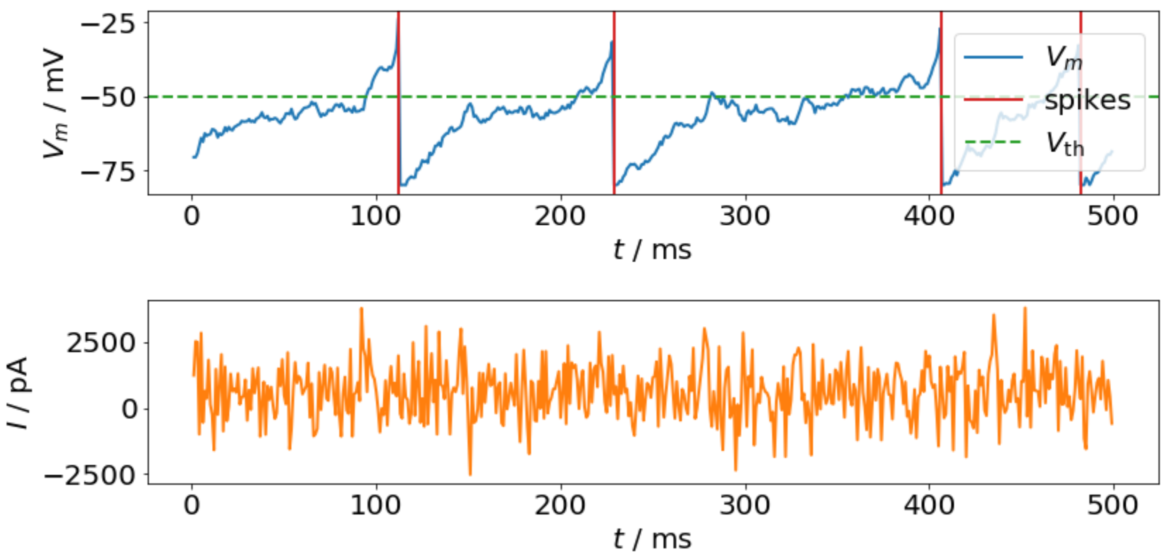
$$F(V) = \frac{1}{C_m}\left[-g_L(V - E_L) + g_L \Delta_T \exp\left(\frac{V - \vartheta_{rh}}{\Delta_T}\right)\right] \tag{9}$$

If we consider only the linear region of the curve by considering only pertaining membrane potential values we can simplify (9) to

$$F(V) = \frac{1}{C_m}\left[-g_L(V - E_L)\right] \tag{10}$$

By plugging in with the all vector fields and constants. Averaging from the vector g_L we come to a best possible value of 32 Siemens.

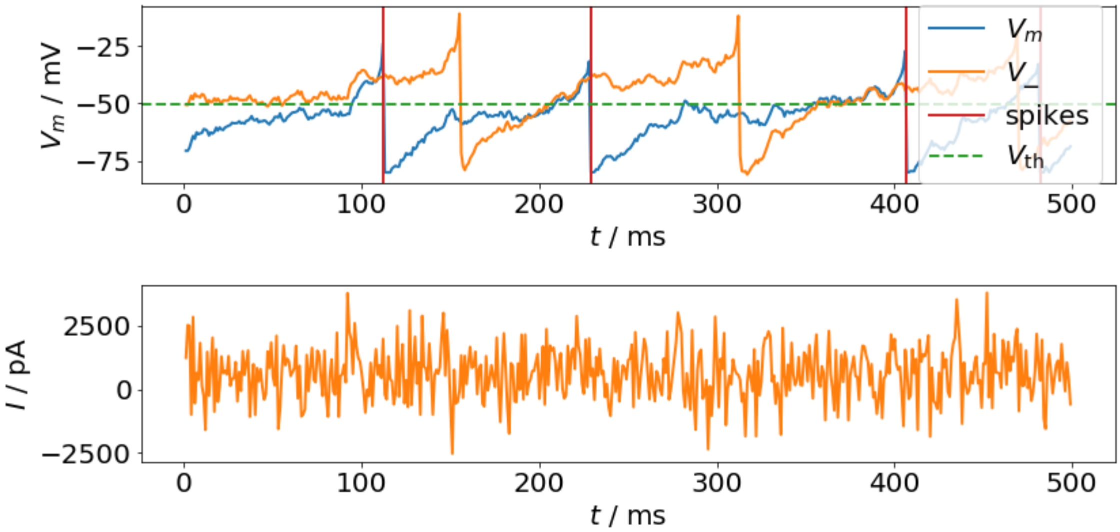
- Below is the spike response of the exponential model with the above found out values plugging in along with the parameters $\Delta_T = 5\,mV$, $\Delta_{abs} = 2\,ms, a = 0, b = 0$ and $V_{reset} = -80\,mV$.



Fig(3)

- Below is the plot of first 500 ms of the recorder membrane potential along with the modelling results.

  It appeared to fit fairly well, might have caused for the deviations because of the choice of resting potential or firing threshold as there is no concrete means to identify the exact value of them. And also could be because of the conductance values.



Fig(4)