Theoretical Neuroscience I
Teacher: Prof. Jochen Braun
Assistant Teacher: Ehsan Kakaei
Name: Lee Po Shing & Fahmida Aktar
Date: 16th November, 2017

Exercise 3: Leaky Integrate & Fire Neuron

Introduction

Although single-compartment model (SCM) is useful in understanding the electrochemical properties of cell membrane at resting state, it does not fully capture all features in the cell membrane. As in the previous exercise, it was assumed that the reversal potential of a membrane is a 0*mV*. It is, however, not the real case, as it is determined by the extra- and intra-cellular concentration ratios plus the relative conductance ratio of different ions, i.e. around -70*mV*. Therefore, as in Fig.1, the current of passing through the resistor is determined by the difference between membrane voltage (as V_{mem}) and the reversal potential E_{rev}. In addition, the response of membrane voltage does not resemble the situation during an action potential, as the conductances of different ions are set as constant in SCM.

Based on SCM, extra components were added in the leaky integrate & fire model (LIF model), notably including a spiking mechanism. Despite being artificial and neglecting the biophysics of action potential, LIF model is a useful tool to approximate the activity of a neuron. Once it increases to a certain threshold this model, the V_{mem} will be reset to a lower value. This provides a mechanism not only to mimic the sharp of an action potential, but also to illustrate the firing of action potential under a certain current input.

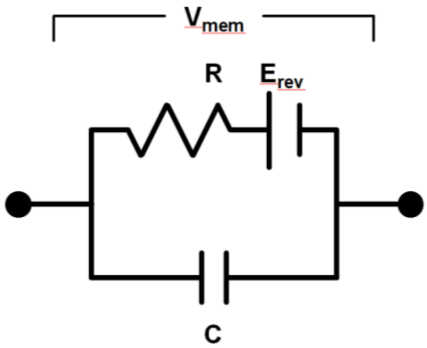

Fig. 1 Modified electrical circuit in single-compartment model The lipid bilayer of a neuron is representated as a capacitor (annotated as C), whereas the channels on the membrane are symbolized by a resistor (as R). The two components are connected in parallel. The battery in serial with the resistor annotated the reversal potential of a membrane (E_{rev}), for which the actual driving force passing through the resistor is the difference between membrane voltage V_{mem} and E_{rev}.

In this exercise, based on the LIF model with a spiking mechanism, the change of membrane voltage (V_{mem}) across the time was computed under different current injected into the cell (I_e) using Matlab. In addition, the time when a spike occurs (t_{spike}) and the inter-spike intervals (t_{isi}) were also recorded in order to investigate the relationship between spiking frequency ($1/t_{isi}$) and the current input.

Method

In this exercise, different vectors were generated for illustrating LIF. Since the focus is to observe the changes of current and voltage across the time, a time vector (*t* in the code) from 0 to 500*ms* with step-size (*dt* in the code) of 0.1*ms* was generated. Next, vectors for I_e (*Ie1*, *Ie2 and Ie3* in the code) were generated for three different situations: a constant current, a sinusoidal oscillating current with low frequency (4*Hz*) and a ramping current. The amplitude of the current (I_0, *I0* in the code) was set at 12nA/mm^2. The formula for the sinusoidal current was as followed:

$$I_e(t) = I_0 \cdot sin(2\pi f t)\,, \;\; f = frequency$$

And for the ramping current, the formula was as followed:

$$I_e(t) = I_0 \cdot t/150$$

For the voltage, the initial voltage (V_0) was set as -65mV. Based on the following equation:

$$\frac{dV_{mem}(t)}{dt} = \frac{1}{\tau_m}[r_m \cdot I_e(t) + E_L - V_{mem}(t)]$$

The three vectors for V_{mem} (*Vm1*, *Vm2* and *Vm3* in the code) were generated using for-loop function in Matlab by:

$$V_{mem}(t + \Delta t) = V_{mem}(t) \cdot e^{\frac{-dt}{\tau_m}} + [I_e(t) \cdot r_m + E_L]\left(1 - e^{\frac{-dt}{\tau_m}}\right)$$

In addition, an if-statement was added after calculation of $V_{mem}(i+1)$ in the for-loop for the spiking mechanism. If the calculated value was larger than a threshold of -50mV (*V_th* in the code), the value would be reset at the initial voltage of -65mV, i.e.

$$V_{mem}(t + \Delta t) = V_{mem}(1) \quad\; if\; V_{mem}(i + 1) \geq -50mV$$

Correspondingly, the time $t(t+\Delta t)$, i.e. t_{spike}, will be accumulated in a vector *reset_steps* in the code. This will be used to calculate t_{isi} (*tisi* in the code) at the end of each session.

In the above, the resistance (r_m, *Rm* in the code) and capacitance (c_m, *Cm* in the code) of the membrane were defined as 1.5$M\Omega mm^2$ and 20nF/mm^2. The time-constant of membrane (τ_m, *Taum* in the code) was therefore 30*ms* based on the following relationship:

$$\tau_m = r_m \cdot c_m$$

Results & Discussion

Steady current input triggers periodically spiking mechanism

Under a constant current supply of 12*nA/mm*^{2}, the membrane voltage showed a regular pattern of a steady rise followed by a sudden fall (Fig. 2). Specifically, the steady rise resembled the early pattern observed in previous SCM model, namely a rise with a gradual decrease in slope. After the rise reached -50*mV*, a sudden drop to -65*mV* was noticed. This showed that the spiking mechanism was successfully triggered as required. In addition, the spiking mechanism was triggered regularly periodically with an inter-spike interval of 53.8*ms*, i.e. 18.6*Hz*. The relationship between current input and spiking frequency will be discussed in later session.

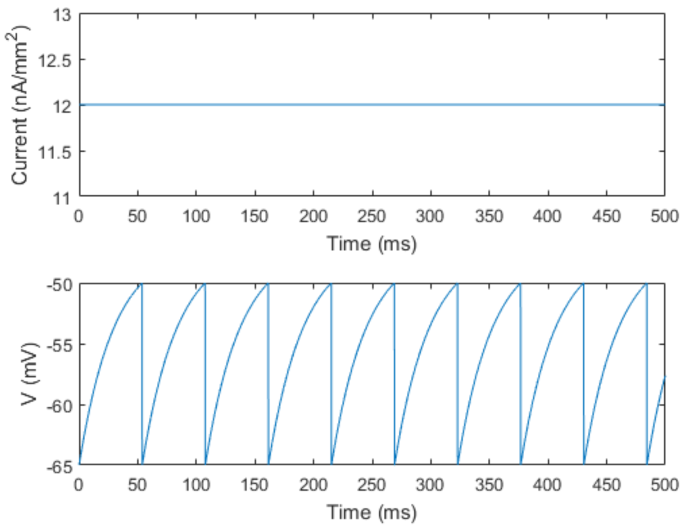

Fig. 2 Constant current input and the corresponding voltage across time In the lower panel, under a constant current supply of 12*nA/mm*^{2}, the induced change in membrane voltage showed a periodic pattern. In particular, sudden drops of voltage, when was the spiking mechanism being triggered, were observed in every 53.8*ms*.

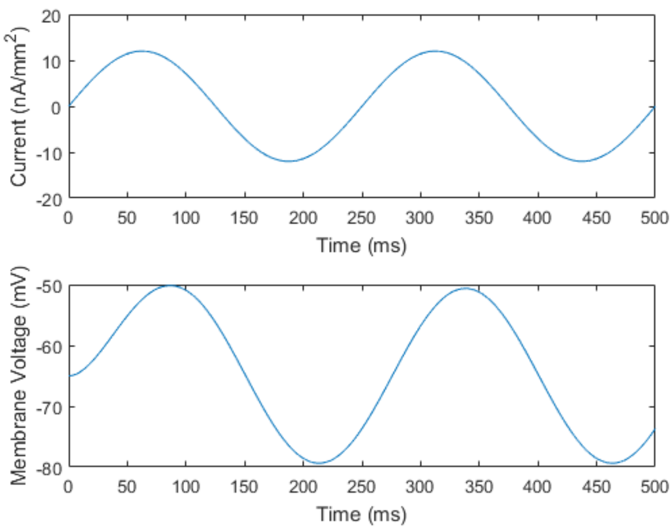

Fig. 3 Sinusoidal current input of 4Hz and the corresponding membrane voltage across the time No spike was recorded.

4Hz-sinusodial current does not trigger spiking mechanism

With a sinusoidal current of 4*Hz*, the membrane voltage showed a sinusoidal oscillation between -50 and -65*mV* (Fig. 3). As in the previous exercise, the oscillation of the membrane voltage showed a phase delay than the current input. Nevertheless, no sudden drop of voltage was observed. This was because the peak of membrane voltage never reached above -50*mV*, as the oscillation frequency was too fast to allow enough current passing through the resistor. The spiking mechanism could be triggered, if the frequency of oscillation was even slower (Data not shown).

Ramping current increases the rate of spiking

With an increasing current across the time, the frequency of spikes increases (Fig. 4). As in the situation with constant current, the membrane voltage showed patterns consisting of a steady increasing phase and a sudden drop. The difference was that, in this situation, the patterns repeated in an increasing rate. This is as expected, as the rate of increase in membrane voltage increases when the current input increases, and therefore the time required reaching the threshold is also shorter. Interestingly, when the reciprocals of t_{isi} were plotted against the currents at the time when the spikes occurred, a linear relationship was observed (Fig. 5). This is as predicted based on formula provided.

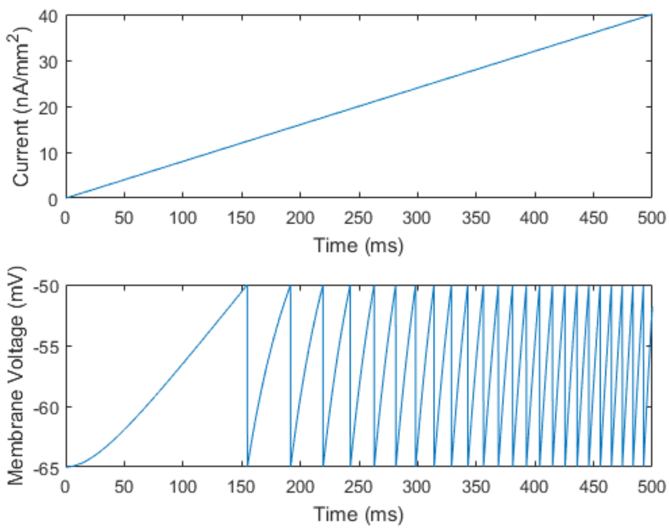

Fig. 4 Ramping voltage from 0 to 40nA/mm^2 and the corresponding membrane voltage Under a ramping voltage, the frequency of spiking increased when the current increased.

Numerical analysis of the dynamical equation

Assuming $V_{mem}(t) = A \cdot e^{B(t)} + C$,

$$\frac{dV_{mem}(t)}{dt} = \frac{1}{\tau_m}[r_m \cdot I_e(t) + E_L - V_{mem}(t)]$$

$$A \cdot e^{B(t)} \cdot \frac{dB(t)}{dt} = \frac{1}{\tau_m}[r_m \cdot I_e(t) + E_L - V_{mem}(t)]$$

$$\left(A \cdot e^{B(t)} + C\right) \cdot \frac{dB(t)}{dt} - C \cdot \frac{dB(t)}{dt} = \frac{1}{\tau_m}[r_m \cdot I_e(t) + E_L - V_{mem}(t)]$$

$$(C - V_{mem}(t)) \cdot \frac{dB(t)}{dt} = -\frac{1}{\tau_m}[r_m \cdot I_e(t) + E_L - V_{mem}(t)]$$

$$\begin{cases} C = r_m \cdot I_e(t) + E_L, assuming\ I_e(t)\ is\ a\ constant \\ \dfrac{dB(t)}{dt} = -\dfrac{1}{\tau_m} \end{cases}$$

$$\therefore B(t) = -\frac{t}{\tau_m}$$

When t=0,

$$A \cdot e^{-\frac{0}{\tau_m}} \cdot \frac{-1}{\tau_m} = \frac{1}{\tau_m}[r_m \cdot I_e(0) + E_L - V_{mem}(0)]$$

$$A = V_{mem}(0) - r_m \cdot I_e(0) - E_L$$

$$\therefore V_{mem}(t) = (V_{mem}(0) - r_m \cdot I_e(0) - E_L) \cdot e^{-\frac{t}{\tau_m}} + r_m \cdot I_e(t) + E_L$$

Therefore,

$$V_{mem}(t+\Delta t) = (V_{mem}(0) - r_m \cdot I_e(0) - E_L) \cdot e^{-\frac{t+\Delta t}{\tau_m}} + r_m \cdot I_e(t+\Delta t) + E_L$$

Assuming $I_e(t+\Delta t) = I_e(t)$,

$$V_{mem}(t+\Delta t) = V_{mem}(t) \cdot e^{-\frac{\Delta t}{\tau_m}} - [r_m \cdot I_e(t) + E_L] \cdot e^{-\frac{\Delta t}{\tau_m}} + r_m \cdot I_e(t) + E_L$$

$$V_{mem}(t+\Delta t) = V_{mem}(t) \cdot e^{-\frac{\Delta t}{\tau_m}} + [r_m \cdot I_e(t) + E_L] \cdot (1 - e^{-\frac{\Delta t}{\tau_m}})$$

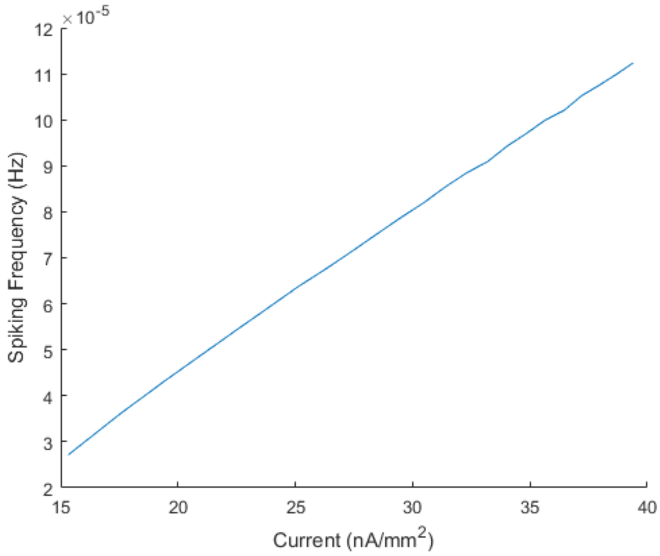

Fig. 5 Relationship between current input and spiking frequency in ramping current Linear relationship was observed between the current at the time when a spike occurred and the reciprocal of t_{isi}