Problem Set #3: Spikes

Hsieh Yu-Guan

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Introduction

Neurons in our brain need to fire signals to communicate with each other. These signals, electrochemical in nature, are refered to as spikes, or action potentials. Here we'll look at several different aspects of this essential element in our nervous system.

1 Spike trains

1.1 Poisson Model

Before discussing how spikes are produced, we'll first work on the statistical description of spike trains (i.e. a seqeunce of spikes and silences from a single neuron). As a first approximation, the generation of a random spike train can be simulated by a Poisson process. We assume that individual spikes are generated mutaually independently with some probability that can be deduced from the instantaneous firing rate.

Since the computer is a discret system, a spike train will just be modeled as an array of 0s and 1s. For example, we create a vector of 1000 elements such that each element of the vector has 25% to be 1.

FIGURE 1: A Bernoulli process of 1000 trials with $p = 0.25$

Next we introduce time units, every 0 or 1 is assocaited with a time bin of lenght Δt ms. Here we choose $\Delta t = 2$ ms and generate a spike train of length 1 sec with the firing rate 25 spikes/sec.

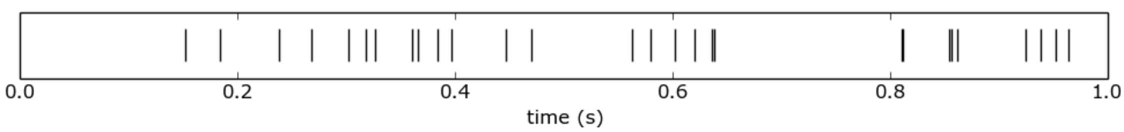

FIGURE 2: A Poisson spike train with an average rate of 25 spikes/sec

In the above figure, there are in effect 28 spikes that are generated. We may be insterested in the distribution of the total number of spikes in each simulation that we refer to as total spike count here. Thus we'll generate 50 spike trains with the same parameters.

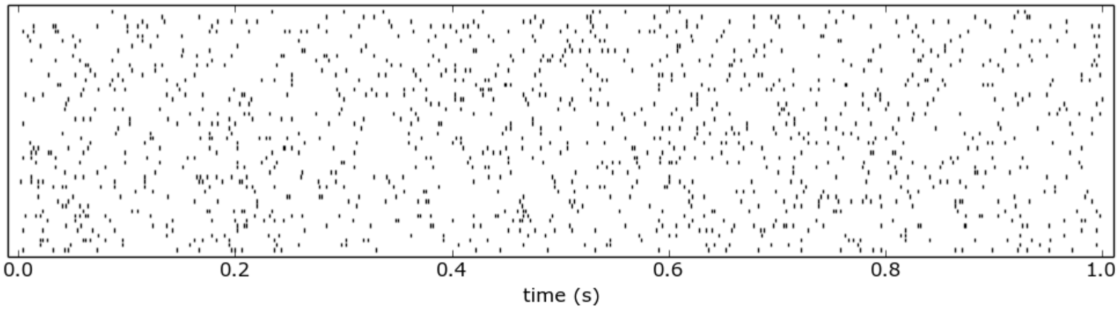

FIGURE 3: 50 Poisson spike trains with firing rate 25 spikes/sec

Then we plot the histogram of total spike counts.

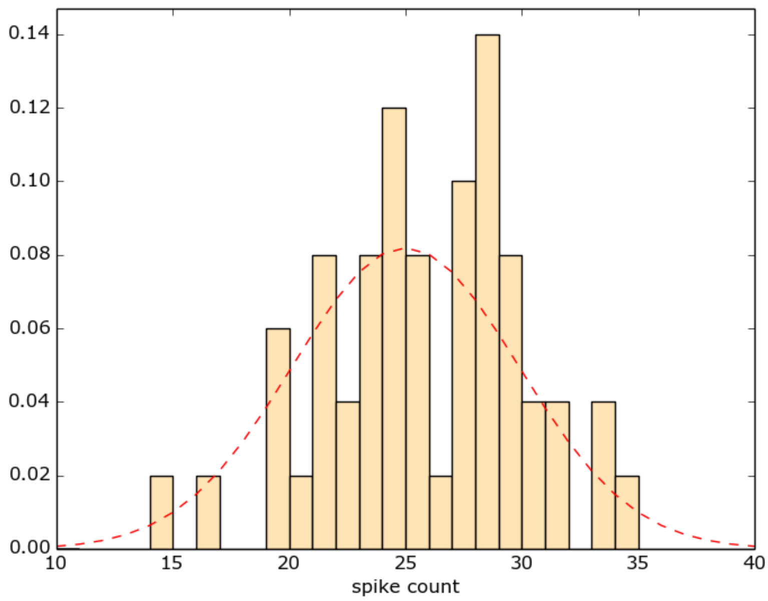

FIGURE 4: Histogram of total spike counts for 50 simulations

According to the central limit theorem, the distribution of spike counts here (which is in fact the binomial distribution $B(500, 0.05)$) can be approximated by the normal distribution $\mathcal{N}(np, np(1-p))$ with $n = 500$ and $p = 0.05$ (the red dashed line in the figure). This can be more or less seen above. However, the theoretical line doesn't fit yet very well the simulation results. It's simply due to the fact that we have too few samples here to describe the distribution, but as we can see later the approximation itself works indeed pretty well.

We also plot the histogram of interspike intervals for the same set of spike trains. This time the histogram follows an exponential distribution, as one might expect (it's a property of the Poisson process).

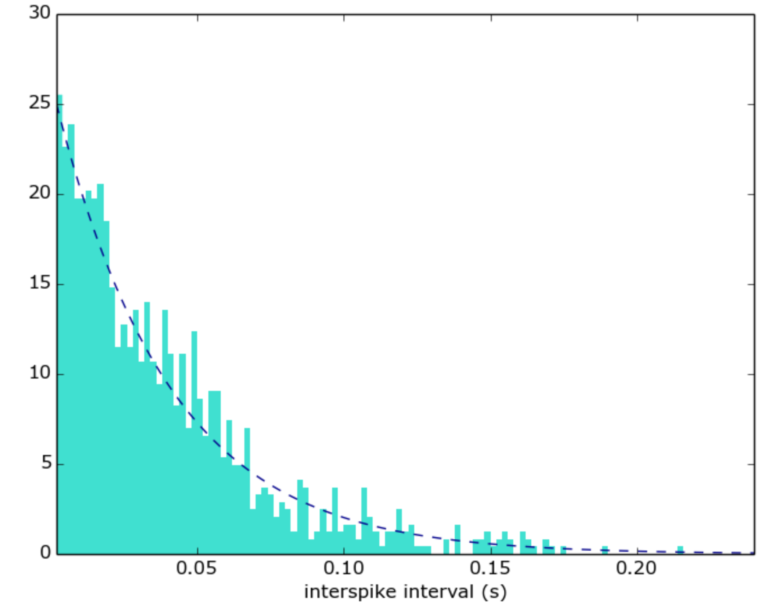

Figure 5: Histogram of interspike intervals counts for 50 simulations

We redo the same plots but with now 500 simulated spike trains.

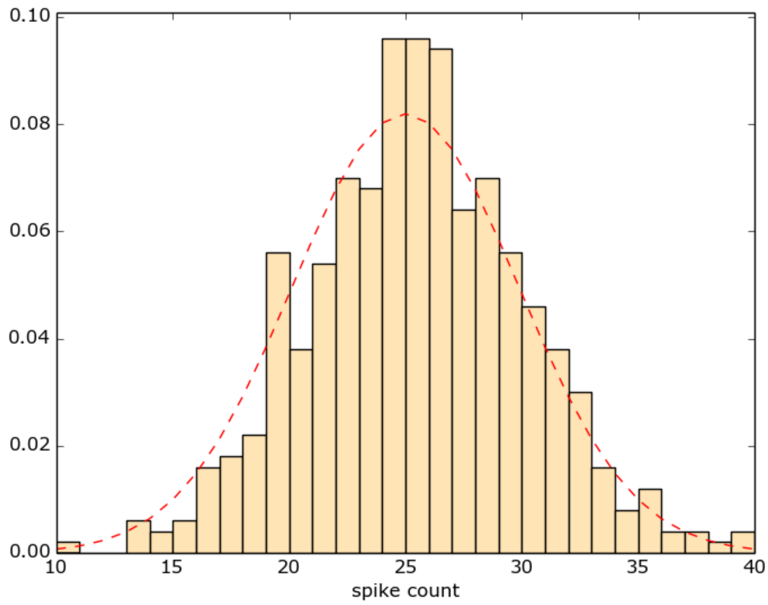

Figure 6: Histogram of total spike counts for 500 simulations

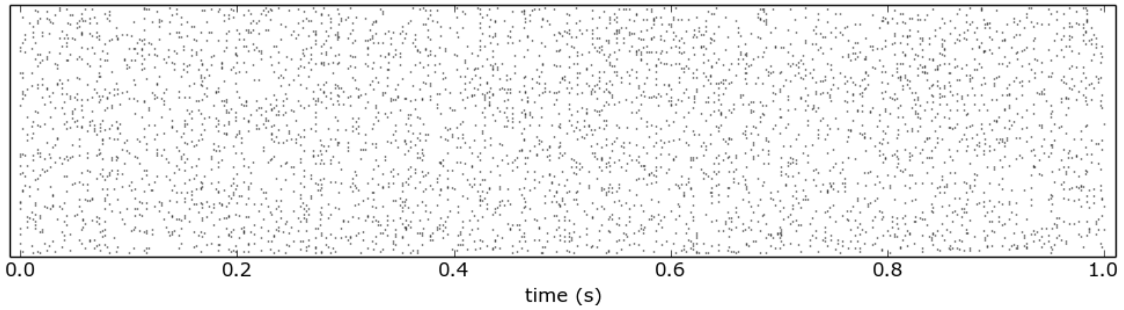

FIGURE 7: 500 Poisson spike trains with firing rate 25 spikes/sec

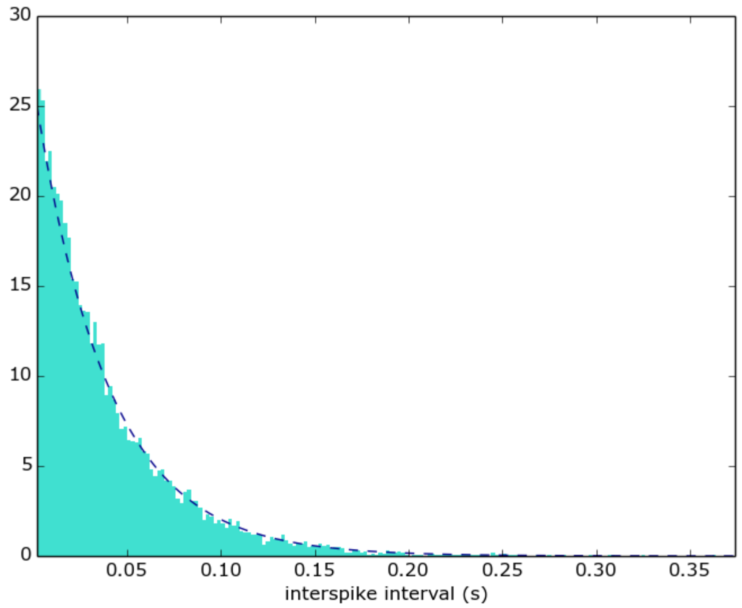

FIGURE 8: Histogram of interspike intervals counts for 500 simulations

We observe that theoretical results fit much better.

1.2 Analysis of spike trains

Besides modeling the spike train generations, we'd also like to do some simple analysis of real spike trains. We use thus the experimental data recorded from a single neuron in the primary somatosensory cortex of a monkey that was experiencing a vibratory stimulus. First we plot the spike trains for the stimulus $f = 8.4$ Hz into the graph below.

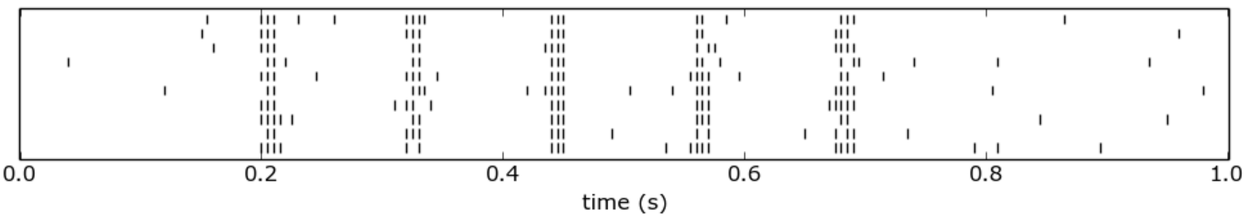

FIGURE 9: Real spike trains recorded from a neuron in the primary somatosensory cortex of a monkey that was experiencing a vibratory stimulus with $f = 8.4$ z

Here we don't observe anymore the poisson process. Instead, we tend to see more spikes at some specific moments that are separated by some fixed length time intervals. We now plot all the recorded spike trains into the same graph. Alternate backgroud colors are meant to indicate different stimuli.

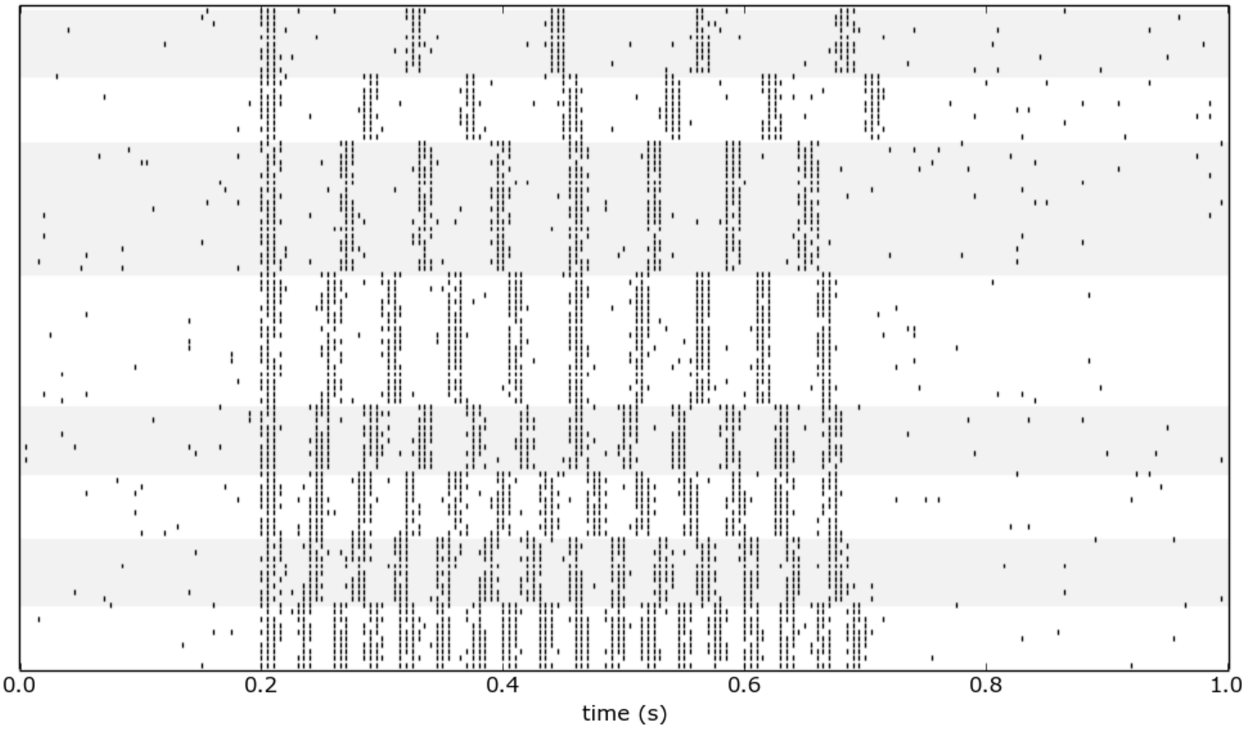

FIGURE 10: Real spike trains recorded from a neuron in the primary somatosensory cortex of a monkey that was experiencing some vibratory stimulus with different frequencies

The corresponding frequency for each dataset is not shown in the graph. In fact from top to bottom the frequency increases and we see that the seperating time intervals also become shorter and the spike count augments. This shall be even clearer if we give the exact numbers. The simulus is only present between $t = 200$ ms and $t = 700$ ms. We compute the average spike count and the standard deviation of spike counts for each stimulus.

TABLE 1: Mean values and standard deviations of spike counts for different stimuli

Frequency (Hz)	8.4	12	15.7	19.6	23.6	25.9	27.7	35
Average spike count m	16.5	19.2	23.6	29.9	35.6	39.5	41.8	52.3
Standard deviation σ	1.80	1.47	1.96	1.58	2.50	5.94	1.89	3.26

Sure when the frequency gets higher, the average spike count increase as well. We plot also the tuing curve of the neuron.

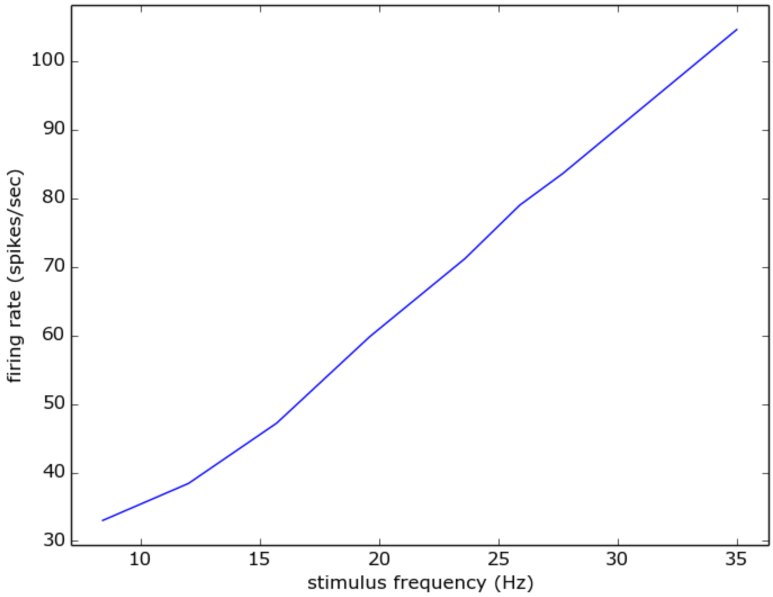

FIGURE 11: Tunning curve of the neuron

The relation between the average firing rate and the stimulus frequency is almost linear. We may also want to show that the mean value and the standad deviation of spike counts are positively correlated and even try to find an explicit relation between these two quantities (for example in the case when the spike count is sampled from some poisson distributions we have $\mu = \sigma^2$). However, with the values given in Table 1, we can not easily draw a conclusion.

2 Leaky Integrate-And-Fire Model

2.1 Model description

Let's look more closely at how spikes are generated in a cell from a biophysical point of view. In a biologically detailed model, we might need to take into account the topology of the neuronal tree and at the same time establish a model for each basic component of the neuron. Finally, the interactions between different components should also be simulated. It can be very complicated and thus, we'll considered a much more simplified model here that however still fits quite well experimental data.

In the leaky integrate-and-fire (LIF) model, the whole neuron is collapsed to a single point. The cell membrane acts like a RC circuit and the relationship between the output voltage $V(t)$ and the input current $I(t)$ is therefore given by

$$C\frac{dV(t)}{dt} = g_L(E_L - V(t)) + I(t) \tag{1}$$

where C is the membrane capacitance, $g_L = 1/R$ is the conductance of the membrane that contributes to the leak term and E_L is the reversal potential. This equation can be solved numerically using the Euler method, that is

$$V(t + \Delta t) = V(t) + \frac{dV(t)}{dt}\Delta t \tag{2}$$

for a small Δt. Otherwise, we can also solve the equation analytically and get

$$V(t) = (V(0) - E_L)\exp(-\frac{t}{\tau_m}) + E_L + \frac{1}{C}\int_0^t \exp(-\frac{s}{\tau_m})I(t-s)ds \quad (3)$$

where $\tau_m = RC$ is the membrane time constant. The analytic solution is useful when the integral has an explicit expression since the result is generally of better precision and the computation gets also faster.

The spiking events are then characterized by a firing time t that is defined by a threshold criterion. In other words, every time when the membrane voltage V reaches a certain threshold V_{th}, the neuron emits an action potential and V is reset to E_L.

2.2 constant stimulation

Let us start by studying a simple example here. Suppose that the integrate-and-fire neuron is stimulated by a constant input current $I(t) = I_0$. We compute first the solution of (1) using the Euler method. For the parameters, we fix $C = 1$nF, $g_L = 0.1\mu$S, $E_L = -70$ mV, $V(0) = E_L$, $I_0 = 1$ nA and $\Delta t = 1$ ms. We run the simulation until $t = 100$ ms.

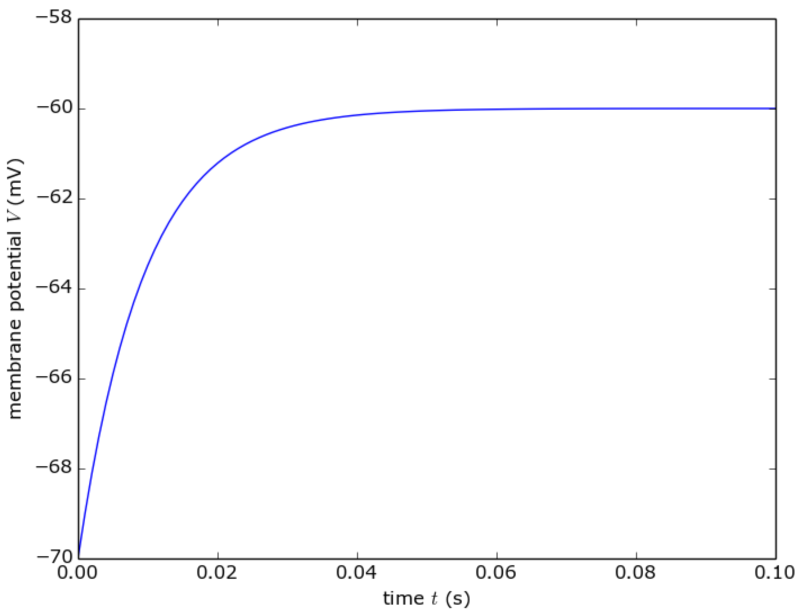

FIGURE 12: LIF model without spiking mechanism with constant input current $I = 1$ nA

We observe an exponential rise to a limit value $V_\infty = E_L + RI_0$. In Figure 13, we compare the results of several different input currents. When I is higher, V climbs faster at the beginning and the final value is as well higher, though, the characteristic time doesn't change.

We may also be interested in the effect of Δt. From a mathematical point of view, the smaller is Δt, the better. In fact, we can see in Figure 14 that when the stepwidth increases, the numerical error with the real value of V gets equally larger (though sure, we can never represent the "real" value in a figure, but say, intuitively). However, more computations are also required when Δt gets smaller, a trade-off needs to be found. It's also shown in the figure that the two curves $\Delta t = 1$ ms and $\Delta t = 0.1$ ms are close, which means that $\Delta t = 1$ ms is already quite a sensible choice that allows us to have a good precision of V.

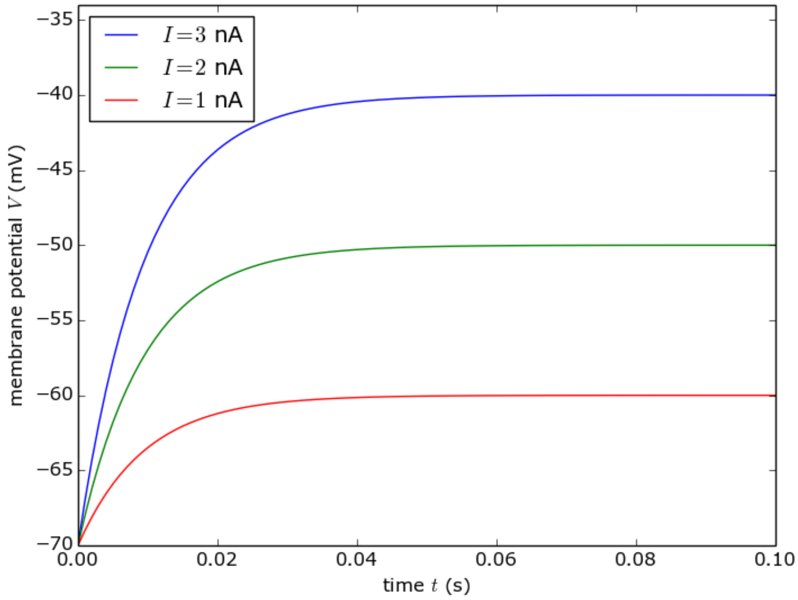

FIGURE 13: Different constant input currents

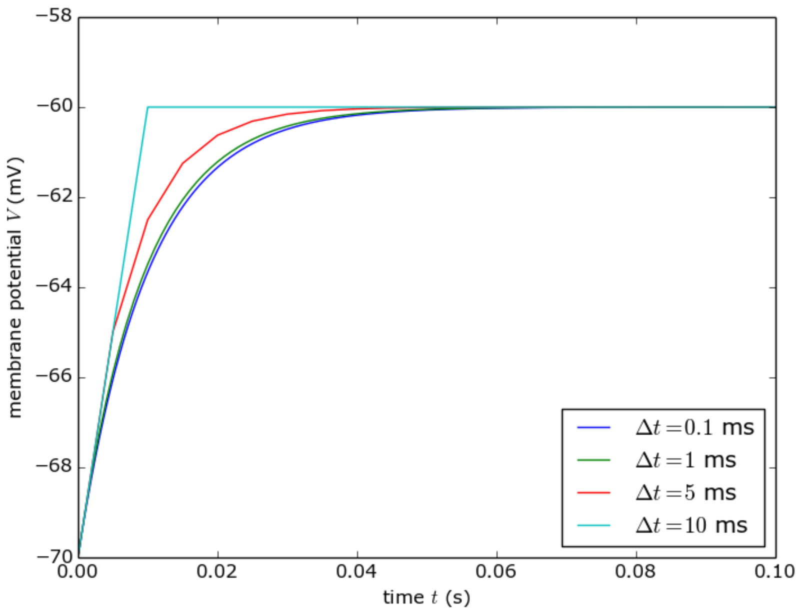

FIGURE 14: Effect of Δt ($I = 1$ nA)

By using the equation (3) we know that in this case the analytic solution is given by

$$V(t) = V_\infty + (V(0) - V_\infty)\exp(-\frac{t}{\tau_m}). \tag{4}$$

The explicit expression allows us to verify the validity of the numerical approach. We compare thereby the plots of the two solutions under the condition $I = 1$ nA. For the numerical part, we use $\Delta t = 1$ ms. As shown in Figure 15, the two curves are similar and with what is mentioned above, if we decrease Δt, we can approach the analytic solution. (This may be confusing, but the plot of the analytic solution in the graph isn't either the true value of V since time is not continue in a computer. In effect, the plot is done by using a time bin of 1 ms.)

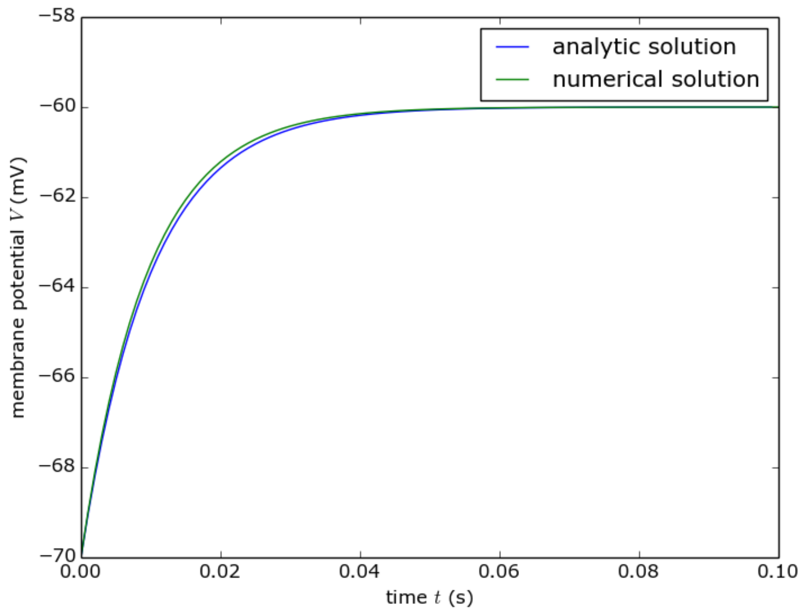

FIGURE 15: Comparison of analytic and numerical solutions ($I = 1$ nA)

We now equip the cell with the simple spiking mechanism as described above. We choose $V_{th} = -63$ mV and vary the value of input current. The results are plotted seperately in oreder to get a better view. Here we use $\Delta t = 0.1$ ms. We can imagine that with a larger stepwidth, we're not able to have a good precision of spike moments.

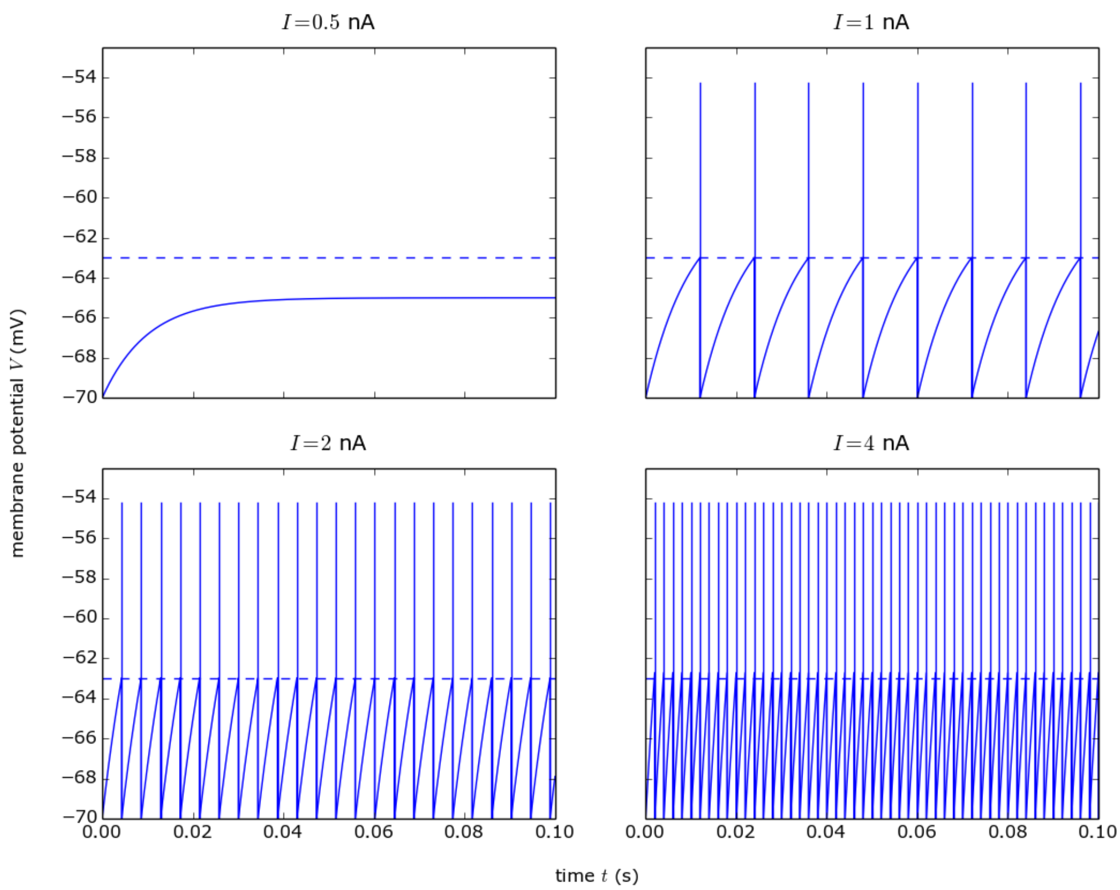

FIGURE 16: LIF model with constant input current

We get more spikes within the first $t = 100$ ms when I augments, which means that the firing rate increases. Nevertheless, smaller Δt is needed to capture a higher firing rate. This can be more or less seen from the case $I = 4$ nA where we have the feeling that spikes are not immediately generated after the threshold is reached. On the other hand, when $I = 0.5$ nA, no spikes are emitted. As a matter of fact, we need to have $V_\infty > V_{th}$ for the neuron to fire. It means that the condition for I is $I > g_L(V_{th} - E_L)$. The exact firing rate can also be computed under this hypothesis, we first compute the time T that it takes for V to reach the threshold V_{th} from E_L, and then we have $f_{firing} = T^{-1}$. The explicit formula is

$$f_{firing} = (\tau_m \log(\frac{E_L - V_\infty}{V_{th} - V_\infty}))^{-1} \tag{5}$$

In the figure below we plot the tunning curve of the neuron, i.e. the number of spikes within 100 ms as a function of the input current I. The two curves are acquired respectivly by using (5) and by simulating directly the integrate-and-fire mechanism.

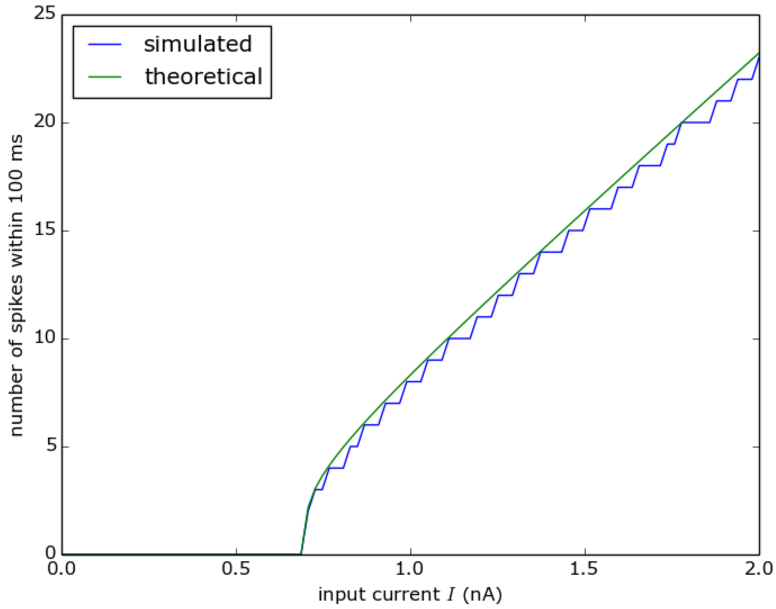

FIGURE 17: Tunning curve of the LIF neuron when I is constant

With the given parameter, $g_L(V_{th} - E_L) = 0.7$ nA. We observe in the graph the neuron starts firing indeed at about $I = 0.7$ nA. The curve obtained by the simulation approximates quite well the theoretical curve. The jadded shape comes from the fact that in the simulation, V is reset for every k time bins for some integer k, so the number of spikes within 100 ms is then $\lfloor 1000/k \rfloor$ (with $\Delta t = 0.1$ ms).

2.3 Refractory period and noise term

For the moment being the stimulus is always a constant current, but we'd like to add some new elements in the model to make it more realistic. The first step is to introduce a refractory period. A simple idea is to fix $V(t) = E_L$ for a small amount of time Δ after each spike, and the differential equation comes into play only after this period. Under this new hypothesis, we plot again the evolution of the membrane voltage V. Here $\Delta = 3$ ms.

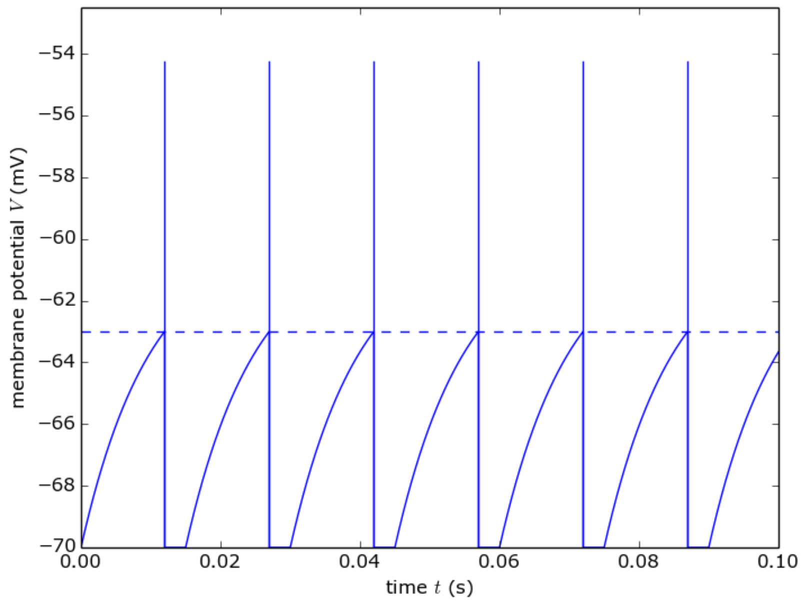

FIGURE 18: LIF neuron with refractory period ($I = 1$ nA)

The new firing rate becomes

$$f_{firing} = (\Delta + \tau_m \log(\frac{E_L - V_\infty}{V_{th} - V_\infty}))^{-1}. \tag{6}$$

It's more realistic since it admits a supremum. We compare the tunning curve of the original model and the model with the refractory period. Due to the reason that is explained before (some innate constraints of the simulated result), we plot the curves using the analytic formulas (5) and (6), which allows us to have a greater variation of I and the difference between two models becomes also clearer.

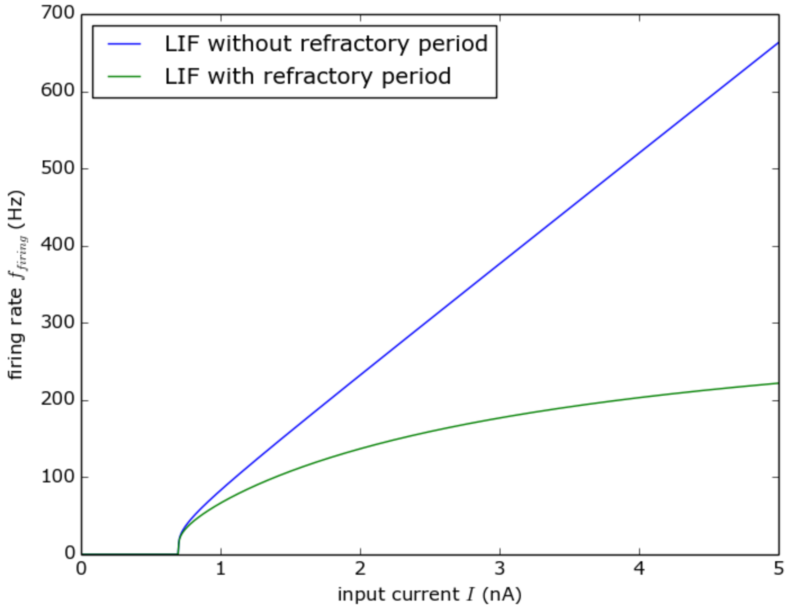

FIGURE 19: Tunning curve of the LIF model with and without refractory period (I constant)

The second step is to add a white noise term $\eta(t)$ in the simulaton, so the differential equation turns into

$$C\frac{dV(t)}{dt} = g_L(E_L - V(t)) + I(t) + \sigma\eta(t) \tag{7}$$

where σ is the magnitude of the noise. To compute the solution, we use the Euler-Maruyama method

$$V(t+\Delta t) = V(t) + \frac{dV(t)}{dt}\Delta t + \sigma\tilde{\eta}(t)\sqrt{\Delta t}. \tag{8}$$

Since we want to add a Gaussian white noise term here, $\tilde{\eta}(t)$ is drawn randomly from a standard Gaussian distribution (sure $\eta(t)$ and $\tilde{\eta}(t)$ are related). To understand where the square root comes from, roughly speaking, when we add a noise term, we want to add a variance but not a mean to the random variable. If we write directly in a discret form, we may have something like (Δt is fixed and we have some discret time moments $t_0, t_1, ..., t_n, t_{n+1}, ...$)

$$X_{n+1} = X_n + a(X_n)\Delta t + b(X_n)\Delta W_n \tag{9}$$

where X is the stochastic process that we are interested in and ΔW_n contributes to the noise term (W is also some stochastic process but we'll not go into detail here). Then what we want to get is in fact

$$\mathrm{E}\left[\Delta X_n \,|\, X_n\right] = a(X_n)\Delta t, \tag{10}$$

$$\mathrm{Var}\left(\Delta X_n \,|\, X_n\right) = b(X_n)^2\Delta t, \tag{11}$$

which means that ΔW_n is of variance Δt, and if we put this back in the equation (8), it corresponds to the term $\tilde{\eta}(t)\sqrt{\Delta t}$. We'll run this model for the choice $\sigma = 1\ \mathrm{mV}\cdot\mathrm{ms}^{-1/2}$.

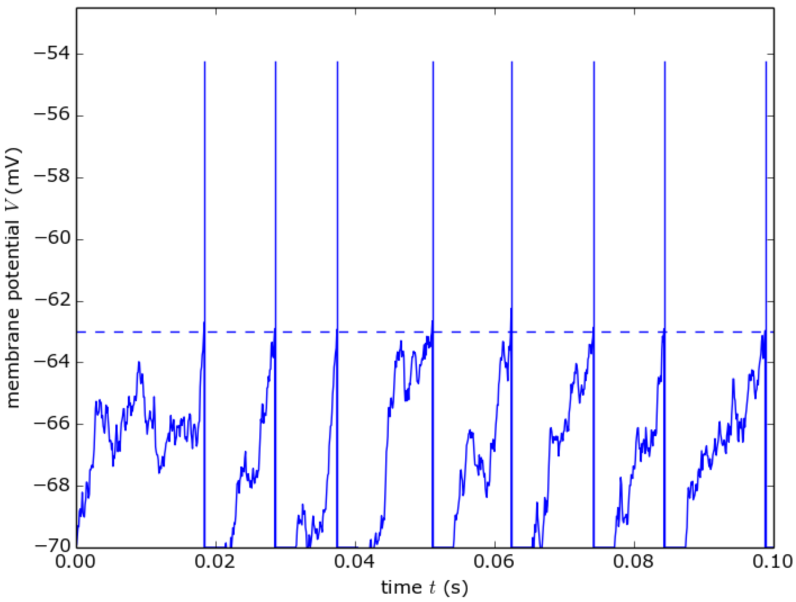

FIGURE 20: LIF neuron with noise and refractory period ($I = 1$ nA)

Now we have introduced refractory period and noise in our model, we plot the generated spike trains with varying noise levels in Figure 21. We notice that when σ is smaller, spike trains are more regular, which is quite sensible, but what is also interesting is to observe that we tend to get more spikes when σ gets larger (V oscillates with greater amplitude).

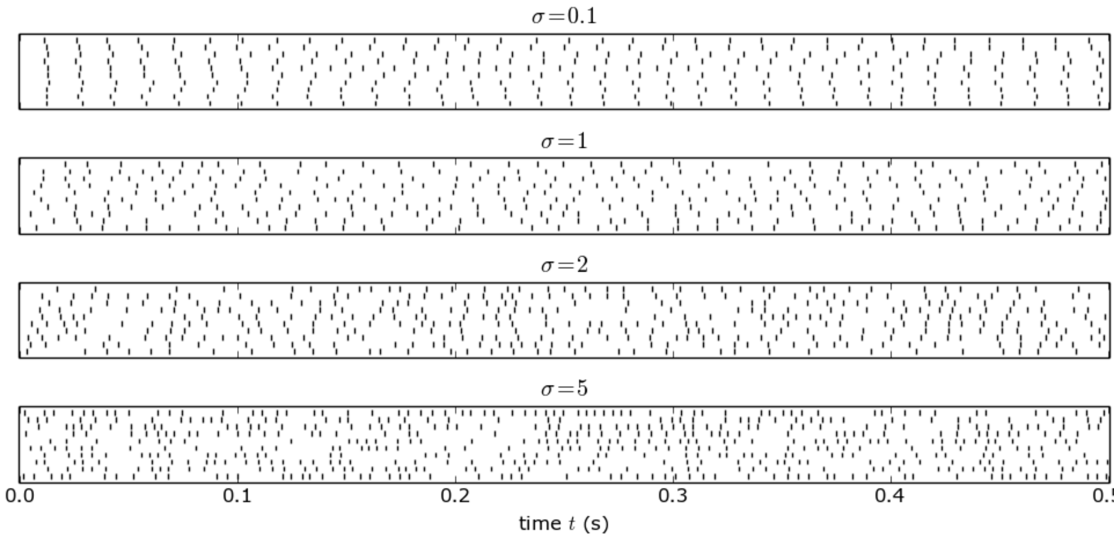

FIGURE 21: Spike trains generated by the above model with cosntant input current $I = 1$ nA and varying σ (in $\mathrm{mV} \cdot \mathrm{ms}^{-1/2}$)

2.4 Compare with experimental data

Our goal is now to generate spike trains that we have seen in 1.2. We first obeserve that we get more spikes at some specific moments while during the rest of the time, spikes are quite sparse and may just come from neuronal noises. Let us say that between some $\tilde{t}$ and $\tilde{t} + \Delta\tilde{t}$ we tend to observe more spikes (in a spike train there are several different $\tilde{t}$). Next, we notice that such a $\tilde{t}$ appears exactly with the frequncy f, while $\Delta\tilde{t}$ seems to be independant of f. From the data, $\Delta\tilde{t} \sim 14$ ms. We can thus assume that I has some constant value during such a period and is zero otherwise, just like what is shown below (with $f = 20$ Hz).

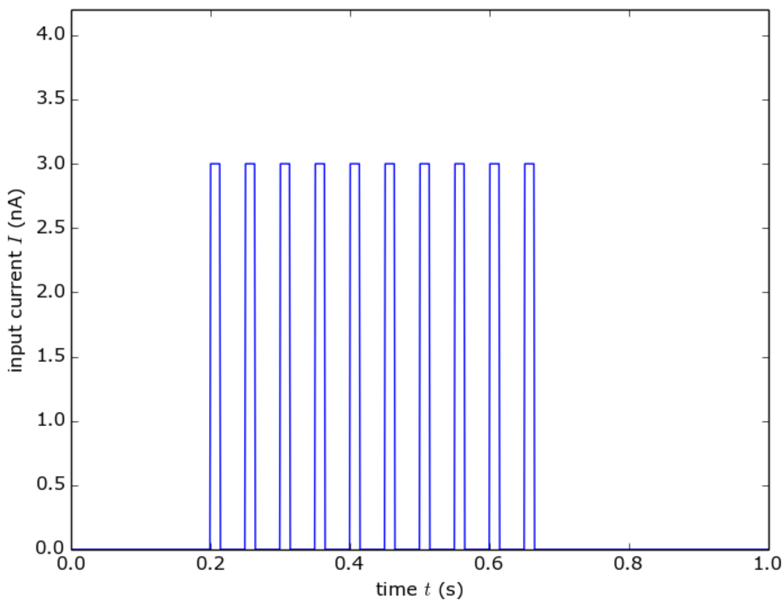

FIGURE 22: An assumption of the input current that can generate spike trains shown in Figure 9

Here the constant value of I is 3 nA. It's a little higher than before. In fact, we observe that spikes are quite dense at these specific moments $\tilde{t}$, which suggests a larger value of I. With these input currents, the spike trains generated by the model are plotted below, as before from top to bottom the frequency increases. The result that we get here is very similar to the experimental data.

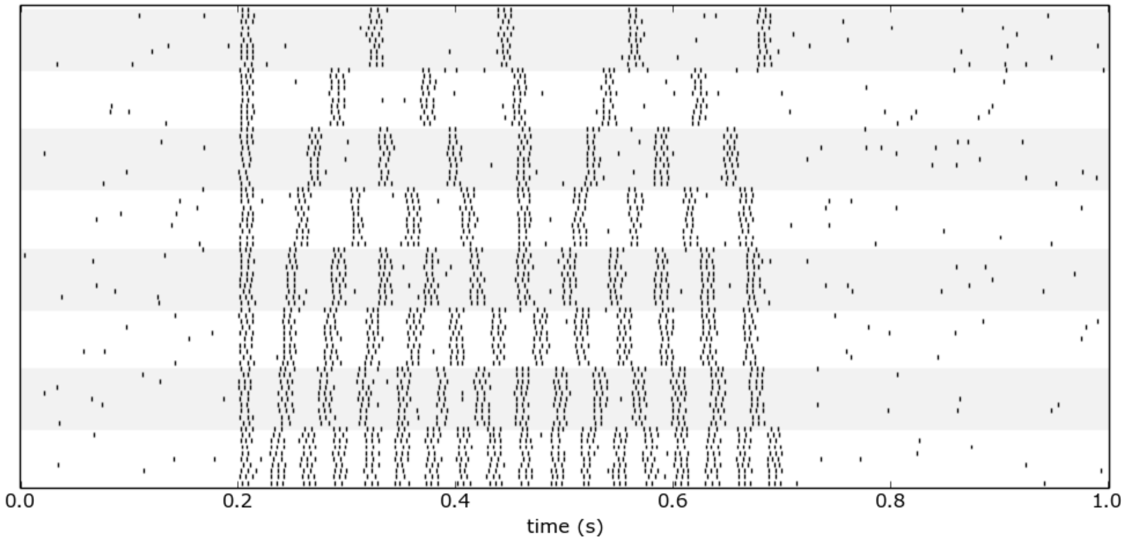

FIGURE 23: Some spike trains generated by the LIF model that are comparable with data in 1.2

2.5 Sinusoidal stimuli

We'll come back to the initial model with neither refractory period nor noise term, but we'll now be interested in time-dependent stimuli. The input current is of the form

$$I(t) = 1 + \sin(2\pi f t) \tag{12}$$

where f is the frequency of the stimulus, expressed in Hz. For the sake of simplicity, we'll ignore all the electrical units (for I, V, etc ...) in this part of simulation and we say that $E_L = 0$ and $V_{th} = 1$. We use a discretization of time in time bins of width 0.1 ms and we'll first plot three different stimuli with frequencies 1 Hz, 5 Hz and 40 Hz for 1 second duration. The result is shown in Figure 24.

A stimulus of frequency f is characterized by a smooth repetive oscillation of amplitude 1 and period $T = f^{-1}$. To see how our neuron responds to this kind of stimuli, we'll first forget the threshold mechanism and solve just the equation (1) using the Euler method. For the membrane parameters, we take $R = 1$ and $\tau_m = 0.1$ s, and we plot the evolution of the membrane potential in response to the current of frequency 1 Hz in Figure 25.

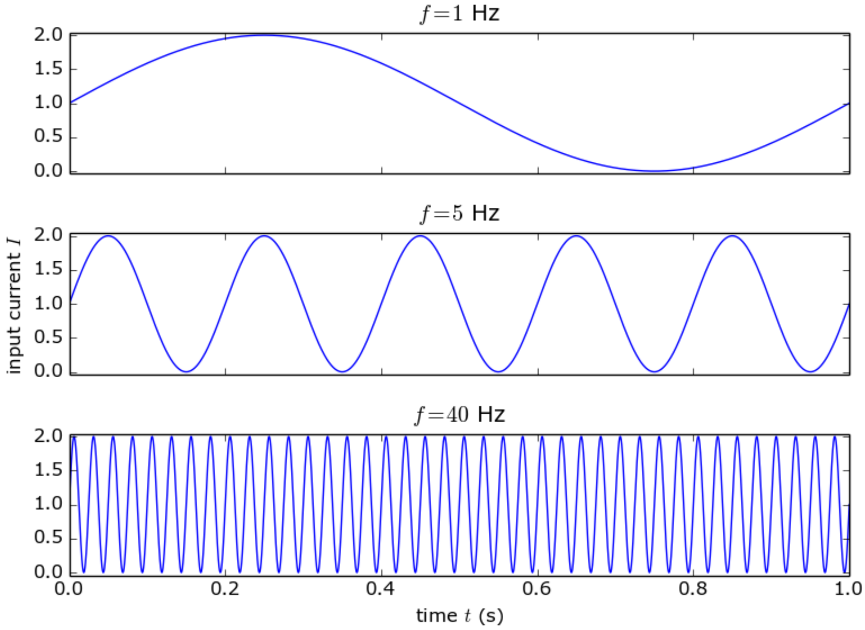

FIGURE 24: Sinusoidal input currents

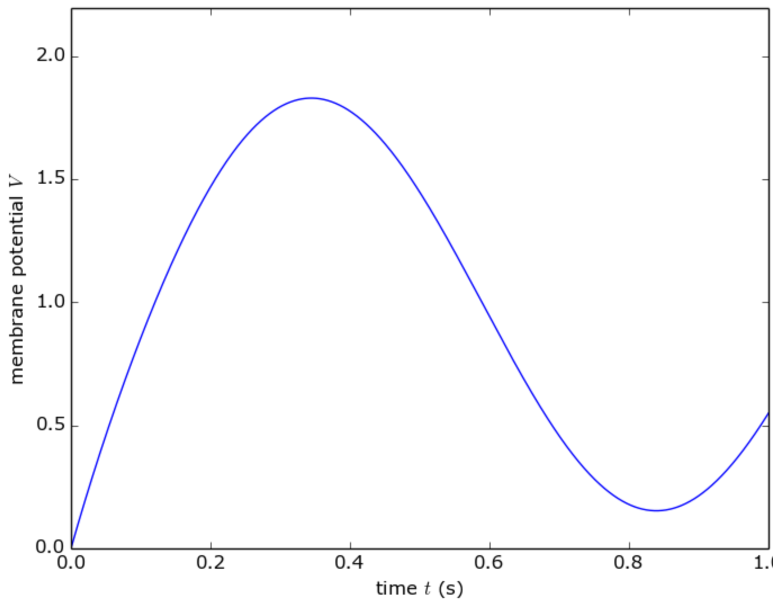

FIGURE 25: LIF neuron without spiking mechanism in response to sinusoidal stimulus of frequency 1 Hz

After comparing the plots of the input current I and the output voltage V, it seems there will be more spikes near the crest of the input current, though there may be a certain delay between V and I. In effect, by using (3), we can deduce the exact solution

$$V(t) = (V(0) - E_L - R + \frac{2\pi f \tau_m R}{4\pi^2 f^2 \tau_m^2 + 1}) \exp(-\frac{t}{\tau_m}) + E_L + R + \frac{R \sin(2\pi f t - \phi)}{\sqrt{4\pi^2 f^2 \tau_m^2 + 1}} \tag{13}$$

where $\phi = \arctan(2\pi f \tau_m)$ is the phase delay of V with respect to I. One may notice that the above equation is not homogeneous. It's simply because the unit of I is neglected here. When t is large enough, the exponentially decreasing term can be ignored (transitional phase), and knowing that $V(0) = E_L = 0$ and $R = 1$, we write

$$V(t) = 1 + \frac{\sin(2\pi f t - \phi)}{\sqrt{4\pi^2 f^2 \tau_m^2 + 1}}. \tag{14}$$

This should justify our intuition about the shape of the V.

We insert again the threshold mechanism and we plot the reponse of the LIF neuron to the three input currents defined above.

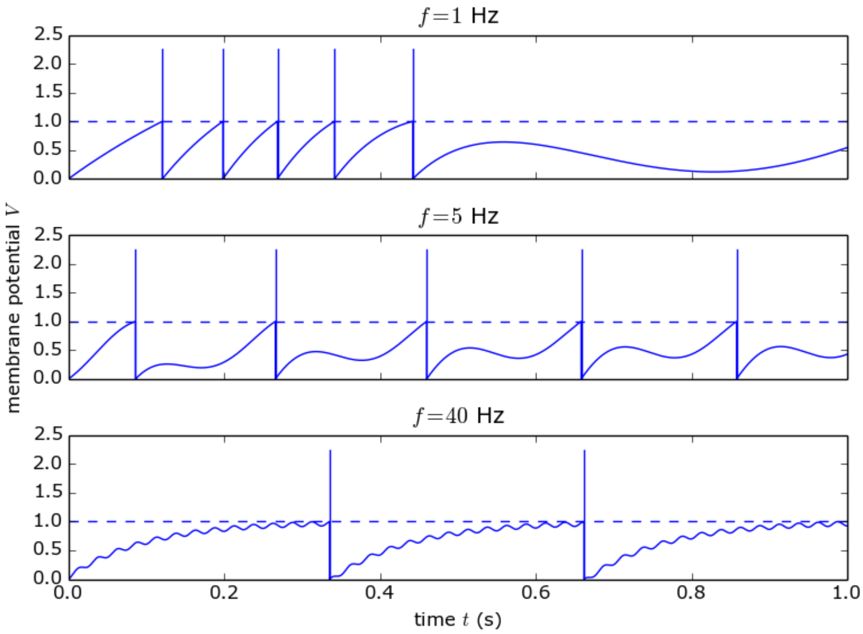

FIGURE 26: LIF neuron in response to sinusoidal stimuli

These curves are quite interesting. For the first input current, as predicted, several spikes are generated near the crest of I, and for the second input current, we get one spike for each period. Finally, in the case where $f = 40$ Hz, the neuron's response seems more exotic: the integral curve is very similar to what we have seen before when the stimulus is constant. By looking at the analytic solution (13), we may have a simple idea of what's happening here. As a matter of fact, when f tends to infinity, the two terms that depend on f decrease to 0 and we find again the equation (4) which is the solution of V for an input current that is constant.

From this analytic solution we also see that the characteristic time plays an important role here. Intuitively, in our case, $\tau_m = 0.1$ ms is too long with respect to a 40 Hz oscillation, thus the neuron is not able to integrate enough voltage to fire a spike in a single period of the stimulus. Nonetheless, the response can be different if we reduce τ_m. For instance, in Figure 27, the characteristic time is reduced to 0.01 s.

We see that the neuron gets sort of more sensitive when τ_m decreases. Let us change τ_m back to 0.1 s and plot the firing rate of the neuron against the frequncy of the input (Figure 28. The firing rate is computed by simulating the model until $t = 25$ s and then devide the number of spikes that we get by 25.

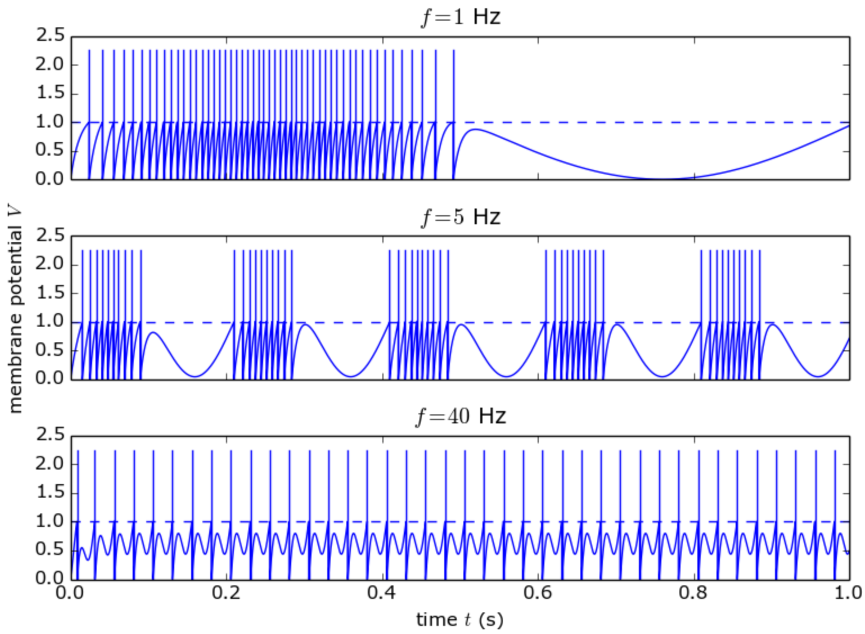

FIGURE 27: LIF neuron in response to sinusoidal stimuli, $\tau_m = 0.01$ s

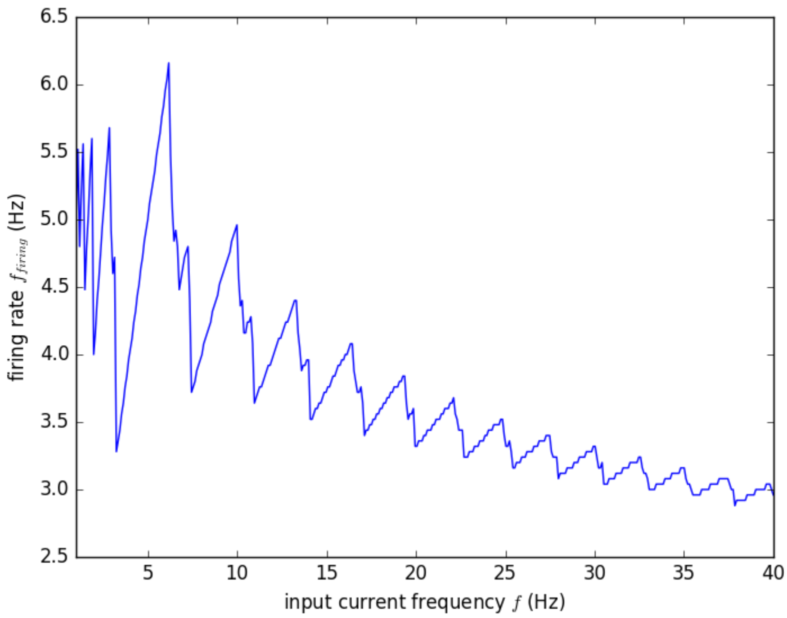

FIGURE 28: Tunning curve of the LIF neuron when I is sinusoidal

It seems that we observe some exponential decay but with oscillations of great amplitude, not very sure. The form of the curve can be explained by studying in more detail the equation (13), mainly by looking at the effect of the sinusoidal term and the exponential term, but here we're rather insterested in the question that if the frequency f of the input current can be coded in this curve. Given some firing rate, we have a range of different possible input frequencies, so the firing rate of this single neuron may not be explicitly coding f, but it can still gives us information about it which can probably be used later to determine f on a larger scale.