NEURAL COMPUTATION ASSIGNMENT

Study of an Integrate-and-Fire Neuron with Short-Term Depression

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Module

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30 - 04 - 2020

Introduction

The purpose of this assignment is to study the properties and behaviour of a Leaky Integrate-and-Fire (LIF) neuron with synaptic depression. The starting point is a LIF model with the following dynamics:

$$\tau_m \frac{dV}{dt} = -(V - V_{rest}) + R_m I_{ext} \tag{1}$$

where τ_m is the membrane time constant, V_{rest} is the resting potential, R_m is the membrane resistance and I_{ext} is an external current. In this context, a *firing* event is registered when V reaches a value V_{thres}, which is followed by the voltage of the neuron being reset to V_{rest}. Results corresponding to this model are included in question 1.

The model can be extended by considering that the external input actually corresponds to a synaptic current I_{syn}, which follows a discrete jump and a subsequent exponential decay every time a hypothetical *pre* neuron fires.

$$\frac{dI_{syn}}{dt} = -\frac{I_{syn}}{\tau_{syn}} + I_0 \sum_k \delta(t - t_k) \tag{2}$$

where τ_{syn} is the time constant for the synaptic input decay and I_0 is the amount of current added to I_{syn} at *pre* firing times ($t = t_k$). For simplicity, the time interval between *pre* firings is kept constant $T_{syn} = t_{k+1} - t_k = const$. This can be understood as a constant firing rate at input, which will be denoted $\nu_{syn} = T_{syn}^{-1}$. This extension of the model is studied in question 2.

Finally, short-time synaptic depression can be modeled by multiplying the synaptic current by a factor p, that can be understood as a *vesicle release probability.* Initially, p has value 1, which is decremented ($p(t_k + dt) = fp(t_k)$; $0 < f < 1$) when a presynaptic firing occurs, and (in the absence of synaptic events) has an exponential trajectory towards 1:

$$\frac{dp}{dt} = -\frac{p-1}{\tau_{stp}} - (1-f)p \sum_k \delta(t - t_k) \tag{3}$$

with τ_p the time constant of p and t_k the same as in (2). By adding this equation to (1) and (2), one completes the model of a LIF neuron with synaptic depression, that corresponds to questions 3, 4, 5 and 6:

$$\tau_m \frac{dV}{dt} = -(V - V_{rest}) + R_m I_{syn} \tag{4}$$

$$\frac{dI_{syn}}{dt} = -\frac{I_{syn}}{\tau_{syn}} + pI_0 \sum_k \delta(t - t_k) \tag{5}$$

$$\frac{dp}{dt} = -\frac{p-1}{\tau_{stp}} - (1-f)p \sum_k \delta(t - t_k) \tag{6}$$

The different parameters of the model are included in table 1.

Table 1: LIF model parameters

v_{rest}	v_{thres}	R_m	τ_m	τ_{syn}	I_0	τ_{stp}	f
$0mV$	$10mV$	$1M\Omega$	$10ms$	$2ms$	$50nA$	$100ms$	0.95

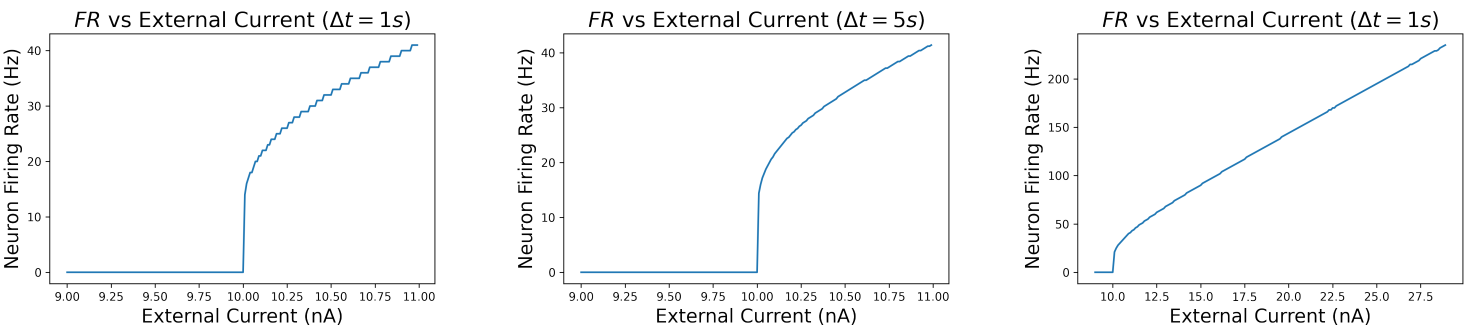
Questions

1: Before we use the synapse, we stimulate the neuron with an external current. Simulate the integrate-and-fire neuron for about a second. Plot the relation between the firing rate in Hz and the external input current.

What is being asked to plot is the F-I curve of the neuron. Because it is a LIF model, there is a current I_{min} below which the neuron is silent (it does not fire). If one imposes that the voltage is driven to the threshold voltage, then:

$$R_m I_{ext} = V_{thres} \Longrightarrow I_{min} = \frac{V_{thres}}{R_m} = 10nA \tag{7}$$

One would expect firing to happen only for $I_{ext} > I_{min}$. This behaviour is indeed observed in figure 1.



(a) (b) (c)

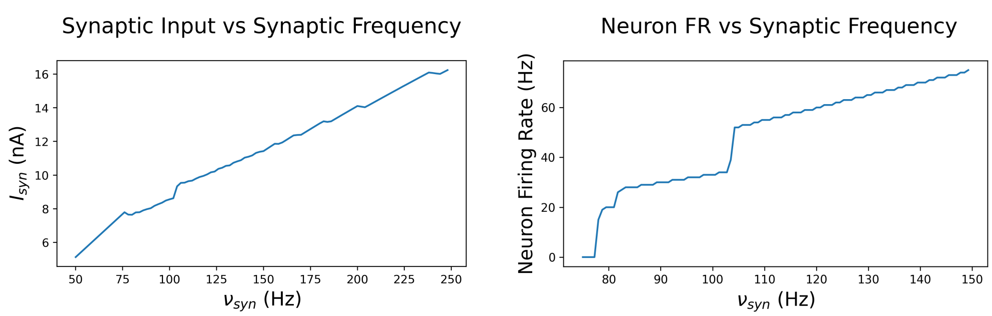
Figure 1: Figures (a) and (b): firing rate as a function of the applied external current, computed over a total simulation time of 1000 and 5000 ms (respectively). Figure (c): same for a wider external current range.

The reason why one can observe *jumps* in figure 1(a) is because firing rate (FR) is computed over $1000ms$ ($1s$). The FR thus corresponds to the number of firings (which is discrete). If one lets more time go by (for example 5 seconds) the curve becomes smoother (figure 1(b)). In figure 1(c) the transition to a the linear behaviour characteristic of high drives can be observed.

2: Next, we drive the neuron instead by a synapse. Activation of the synapse leads to a current $I(t) = I_0 \exp(-t/\tau_{syn})$, where $I_0 = 50\mu A$ and $\tau_{syn} = 2ms$. (Short-term synaptic depression is not implemented yet at this stage). Implement code to periodically stimulate the synapse. For practical reasons, reset the synaptic current to zero with every post-synaptic spike. Plot the relation between the firing rate of the neuron and the stimulation rate of the synapse. (You should require a few hundred Hz to make it fire).

To study the relation of the neuron FR with ν_{syn}, we start by selecting a reasonable range of ν_{syn} and plotting the mean value of I_{syn} (figure 2(a)). Next, in figure 2(b), we select a range of synaptic frequencies that result in a similar average synaptic current to that studied in question 1; we select the range $(75-150)$ Hz, which results in an average I_{syn} of $(8-11)$ nA. Given the small time constant of synaptic currents, these will have a shape similar to that of a Dirac delta (they will be short and sharp), which is different from the constant current injected in results shown in figure 1. For this reason, while the average synaptic current can be an indicative of how the total amount of charge compares to that in the previous simulation, one would expect differences in results.

The first difference one observes is that the neuron starts to fire before reaching an average synaptic current of 10nA (the minimum input required in question 1). This can be seen by comparing the ν_{syn} value at which firing starts in figure 2(b) ($\nu_{syn} \approx 75$Hz) with its corresponding synaptic current average in figure 2(a) ($I_{syn} \approx 8$nA). Because now the current is not distributed uniformly across time, it is possible for some time intervals to have a higher (than average) integrated synaptic current, which results in a firing event. It should be noted that when firing events start taking place, the average synaptic current drops slightly; this is due to the imposed condition that, upon the neuron firing, the synaptic current must be reset to 0.



(a)

(b)

Figure 2: Figure (a): average synaptic current (over 1 second) for a given synaptic rate ν_{syn}. Figure (b): neuron firing rate, also as a function of synaptic firing frequency.

In figure 2(b), one can see how, apart from the expected jump at the initiation of firings, there are two more discrete events (at around 80 and 105 Hz). To get more insight on this, we plot the voltage as a function of time for a ν_{syn} right before and right after these points; the results are included in figure 3. As expected, in figures 3(a)-(b), one can see how the cell goes from oscillating in a regime that is close but never reaches the 10 mV (no firing) to a state in which there are periodic firings. In the pairs of figures 3(c)-(d) and 3(e)-(f) there is a discrete change: the number of synaptic events that take place within the period of the neuron firings. In the first pair the number of synaptic events per neuron firing goes from 4 to 3, and in the second it transitions from 3 to 2. To understand the effect of this, one must note the two processes that are taking place simultaneously: one is the shrinking of the period corresponding to the synaptic oscillations, and the other is the increase of the amplitudes of these oscillations. While

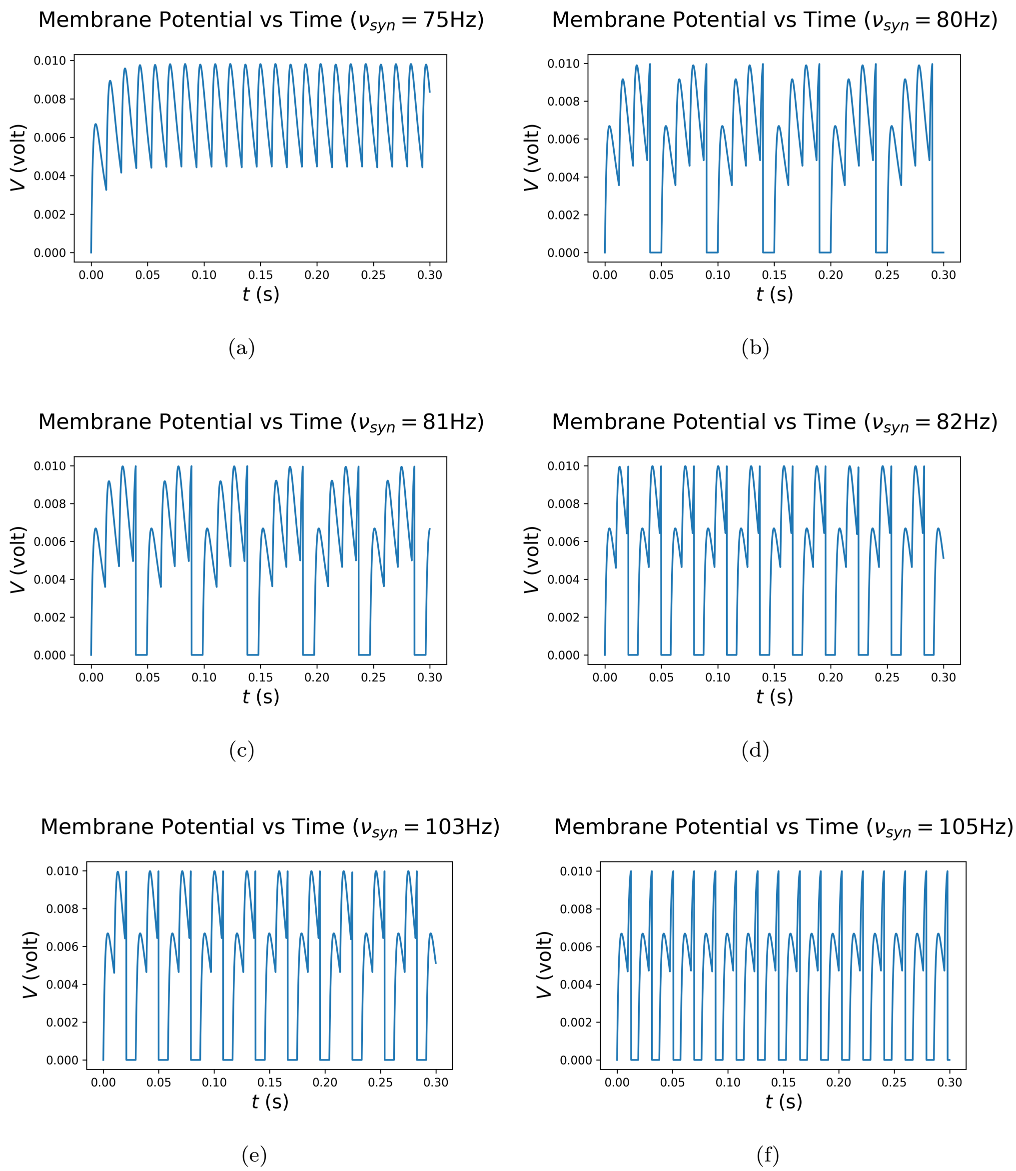


Figure 3: All figures: membrane potential over 300 ms for different synaptic frequencies (see titles). The values are chosen to match the points around which there are discrete events in figure 2(b).

the first has a direct effect on the FR, the second can only be observed in the FR plot when the penultimate maximum is able to reach the 10 mV threshold, thus reducing the firing period by one synaptic period unit. To confirm this, one can compute the neuron firing period jump (ΔT_{FR}) as follows:

$$\Delta T_{FR} = \frac{1}{FR'} - \frac{1}{FR} \tag{8}$$

and it must hold that

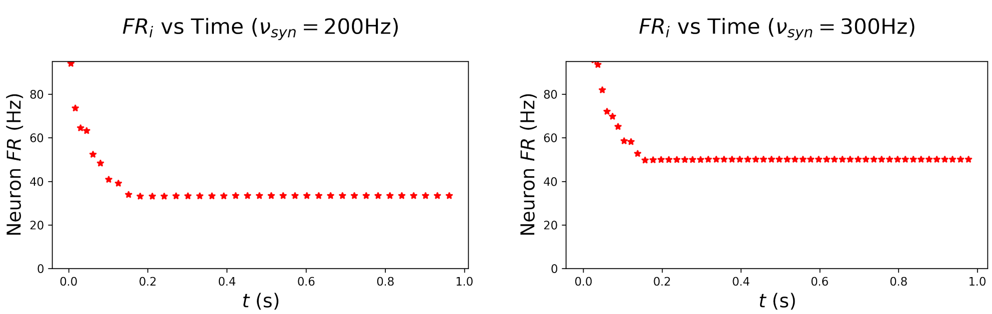
$$\frac{1}{\Delta T_{FR}} \approx \frac{1}{-T_{syn}} = -\nu_{syn} \tag{9}$$

The results of this can be seen in table 2. It can be noted how the predicted values fall with reasonable accuracy within the interval of confidence[1]

Table 2: Results for discrete FR increments

transition	$\frac{-1}{\Delta T_{FR}}$(Hz)	ν_{syn}(Hz)	FR (Hz)	FR'(Hz)
$(4 \rightarrow 3)$	87 ± 20	81.5	20 ± 1	26 ± 1
$(3 \rightarrow 2)$	98.2 ± 7.8	104	34 ± 1	52 ± 1

3: Next, we implement a synaptic depression model. The release probability $p(t)$ is multiplied with a factor f on every synaptic event, where $f = 0.95$. The release probability recovers with a time-constant $\tau_{stp} = 100ms$ to a value of $p_{rest} = 1$. (This model is different from the lecture notes). We don't implement stochastic release, but only consider its average effect. Thus assume that $p(t)$ multiplies the synaptic current, so that the current amplitude from a single synaptic activation at time t_s, becomes $p(t_s)I_0$ instead of I_0. To see the effect of synaptic depression on the firing, plot the instantaneous firing rate in response to a stimulus that at time 0 steps from 0 to a given constant rate. That is, plot at time t_i, the value of $1/(t_i - t_{i-1})$, where t_i is the time of spike i.



(a)

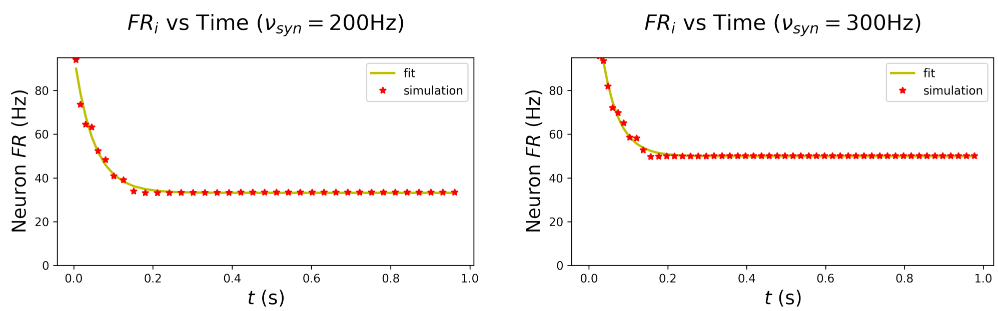
(b)

Figure 4: Figures (a) and (b): Instantaneous firing rate as a function of time at synaptic frequencies of 200 and 300Hz (respectively) after implementing short-term depression.

Results (figure 4) show how the implemented synaptic depression has an inhibitory effect on the neuron. As the time of the simulation goes by, the probability of vesicles release (which p models) decreases and, subsequently, the synaptic input and the firing rate.

[1] As mentioned before, the error of the firing rate values is assumed to be 1. From there, the error is propagated as $\delta(\frac{1}{\Delta T_{FR}}) = \sqrt{(\frac{\partial f}{\partial FR'})^2 + (\frac{\partial f}{\partial FR})^2}$, with $f = \frac{FR'FR}{FR'-FR}$

4: Fit the time course of the instantaneous firing rate to an exponential curve $f = a\exp(-t/b) + c$. How should one interpret the meaning of a, b and c? Plot the time constant from the fit versus the stimulation rate. Interpret the result.



(a) (b)

Figure 5: Figure (a): same as figure 4(a), including fit to equation (10) (in yellow). Figure (b): same for figure 4(b).

Figure 5 adds to the plots in figure 4 the corresponding fit to the a function of the form:

$$FR = a\exp(-t/b) + c \tag{10}$$

It is clear that $(a+c)$ corresponds to the initial firing rate and c to the asymptotic value of FR, while b corresponds to the time constant of the exponential decay observed in figure 5. To gain some insight into these results, let's try to find an expression of this type for the firing rate. To do this, we will describe exponential dynamics of p to infer also exponential dynamics for FR, provided that the conditions for a linear relationship between them are met.
For a very high synaptic frequency, the sum of the Dirac deltas can be expressed as ν_{syn}:

$$\frac{dI_{syn}}{dt} = -\frac{I_{syn}}{\tau_{syn}} + pI_0\nu_{syn} \tag{11}$$

$$\frac{dp}{dt} = -\frac{p-1}{\tau_{stp}} - (1-f)p\nu_{syn} \tag{12}$$

Now, equation (12) can be rearranged as:

$$\frac{dp}{dt} = -\left(\frac{1}{\tau_{stp}} + (1-f)\nu_{syn}\right)\left[p - \frac{1}{1+(1-f)\nu_{syn}\tau_{stp}}\right] \tag{13}$$

This expression is notably informative: it shows that, at long timescales, p follows an exponential decay towards the subtracting term in the squared brackets with a time constant inverse the expression inside the round brackets. One can thus define

$$\tau_{eff} \equiv \left(\frac{1}{\tau_{stp}} + (1-f)\nu_{syn}\right)^{-1} \tag{14}$$

$$p_\infty \equiv \frac{1}{1+(1-f)\nu_{syn}\tau_{stp}} \tag{15}$$

and then:

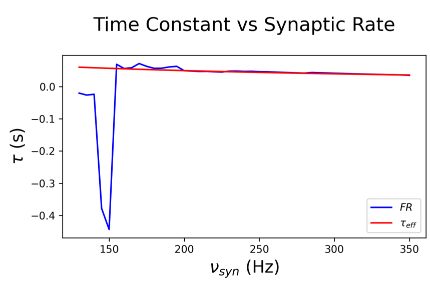
$$p(t) = 1 + (p_\infty - 1)e^{-t/\tau_{eff}} \tag{16}$$

For this exponential behaviour to propagate to the FR, (i) the synaptic input must be high enough (so that there is a linear dependence on I_{syn}) and also (ii) the dynamics of I_{syn} need to be much faster than those of the voltage (i.e. $\tau_{syn} \ll \tau_m$, so that the synaptic input is in turn linear in p). In an ideal scenario, where the dependence on p is linear, the dynamics of the firing rate follow those of p:

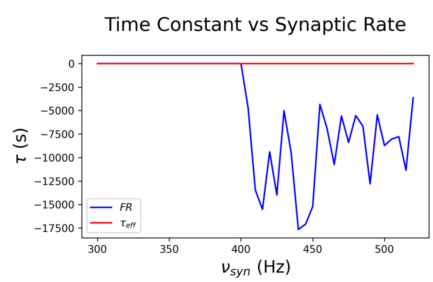
$$FR(t) = FR_0 + (FR_\infty - FR_0)e^{-t/\tau_{eff}} \tag{17}$$

with $FR_0 = FR(p=1)$, $FR_\infty = FR(p=p_\infty)$.

Nevertheless, one can observe how condition (ii) is true only to certain extent ($\tau_{syn} = 2$ ms, $\tau_m = 10$ ms), and the strength of condition (i) does indeed change during the course of the simulation (as p gets smaller so does the synaptic input).



(a)



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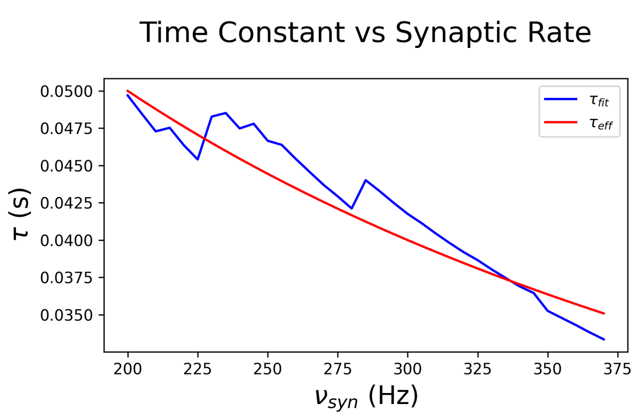

(c)

Figure 6: In all figures: time constant of the FR decay (parameter b in equation 10, in blue) as a function of ν_{syn}. In red, effective time constant, computed with equation (14). First two plots (a), (b) were used to find the regime for which FR has exponential decay and the third one to both see what is the behaviour of the τ_{fit} and test the robustness of the approximations done to get equation (13)

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In figures 6(a), (b), one can observe how the fit constant is continuous in the interval 200-400 Hz. The extreme values observed out if this regime correspond to the shape of the function not being exponential (hence the meaning of the calculated time constant is none). After checking the valid interval, one can plot the the results obtained in the time constant calculation (figure 6(c)). Results show a reasonable match between τ_{fit}, and the theoretical value of the effective time constant, τ_{eff}, calculated with equation (14). At the big-picture level, the decrease of τ (both theoretical and in simulations) is expected, given that the synaptic rate is increased and p reaches its oscillatory stable regime faster.

5: What is the eventual behaviour of $p(t)$ during prolonged constant periodic stimulation? Derive the equation and compare your calculations to your simulations.

By inspecting the dynamics of p, one can see that the value p_k (corresponding to the value of p right before the presynaptic neuron fires for k^{th} time) and the value p_{k+1} (same scenario with presynaptic firing $k+1$) are related as follows:

$$p_{k+1} = 1 - (1 - fp_k)\exp\Big(-\frac{T_{syn}}{\tau_{stp}}\Big) \tag{18}$$

One can set $p_{k+1} = p_k \equiv p^*$ and solve equation (18):

$$p^* = \frac{1 - \exp\Big(-\frac{T_{syn}}{\tau_{stp}}\Big)}{1 - f\exp\Big(-\frac{T_{syn}}{\tau_{stp}}\Big)} \tag{19}$$

It should be noted how p^* is the value for which p remains unchanged after one synaptic period, but the value of p can indeed change during the corresponding time interval. In the case where these oscillations are very small, it can be considered an approximation of a fixed point. Some quick tests one can do on this result are:

- $f \to 1 \implies p^* \to 1$: this limit corresponds to the absence of dynamics in p, which would be constant and equal to 1
- $f \to 0 \implies p^* \to 1 - \exp\Big(-\frac{T_{syn}}{\tau_{stp}}\Big)$: at the first presynaptic event p is immediately driven to 0, follows an exponential trajectory towards 1 and, at the next presynaptic event - at point $1 - \exp\Big(-\frac{T_{syn}}{\tau_{stp}}\Big)$ - repeats this process indefinitely.
- $T_{syn} \gg \tau_{stp} \implies p^* \to 1$: this limit corresponds to synaptic events happening at a very slow timescale compared to the time constant of p. The value of p should be able to recover (to one) from one presynaptic event to another.
- $T_{syn} \ll \tau_{stp} \implies p^* \to 0$: this limit corresponds to synaptic events happening at a very fast timescale compared to the time constant of p. In this context, p is decreased faster than it is driven to 1. The fixed point thus corresponds to the minimum value p can reach, 0 (both conceptually, given that it is a probability, and numerically, because it is decreased by multiplication with $f \in (0,1)$). In the regime where the coefficient is small but greater than 0, a Taylor expansion can be done and equation (15) is recovered:

$$p^* \approx \frac{1 - (1 - \frac{T_{syn}}{\tau_{stp}})}{1 - f(1 - \frac{T_{syn}}{\tau_{stp}})} = \frac{1}{1 + (1-f)\nu_{syn}\tau_{stp}} \tag{20}$$

this is the regime where most of our simulations take place and for which an exponential decay of the FR and p exists.

Simulations confirm that the predicted $p*$ value guides the horizontal asymptote for all the different presynaptic frequencies. It should be noted how, for higher frequencies, the recovery time (T_{syn}) is smaller and p looks more continuous, while for small frequencies the drive to 1 (in the contrary direction to suppression kicks) can act freely for longer time, thus resulting in the observed oscillations.

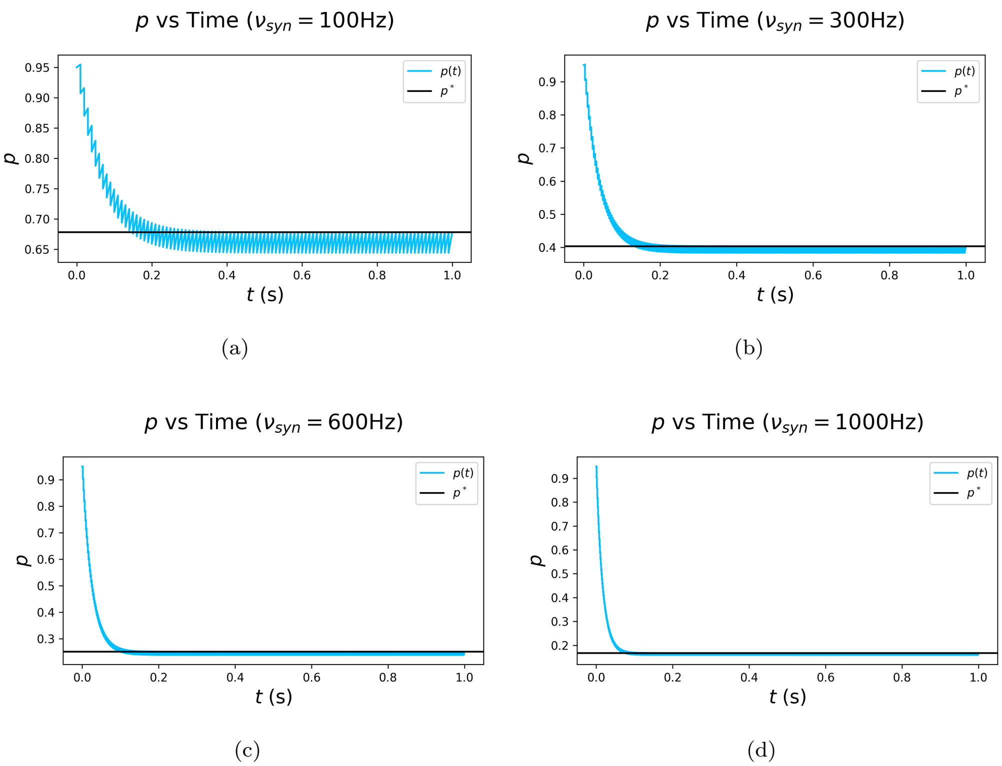


Figure 7: All figures: p as a function of time for different synaptic frequencies (see titles).

6: In a typical situation we expect many synapses to provide input to the model rather than the single one used here. How should parameters in the model be changed to lead to the same firing pattern as in question 3, but with N identical synapses, each firing at an N times lower rate?

The question presents two different scenarios:

single-input (original) dynamics

$$\tau_m \frac{dV}{dt} = -(V - V_{rest}) + R_m I_{syn} \tag{21}$$

$$\frac{dI_{syn}}{dt} = -\frac{I_{syn}}{\tau_{syn}} + pI_0 \sum_k \delta(t - t_k) \tag{22}$$

$$\frac{dp}{dt} = -\frac{p-1}{\tau_{stp}} - (1-f)p\sum_k \delta(t-t_k) \tag{23}$$

multi-input dynamics

$$\tau_m \frac{dV}{dt} = -(V - V_{rest}) + R_m \sum_{i=1}^{N} I_{syn}^{(i)} \tag{24}$$

$$\frac{dI_{syn}^{(i)}}{dt} = -\frac{I_{syn}^{(i)}}{\tau'_{syn}} + I'_0 \sum_k \delta(t - t_k^{(i)}) \tag{25}$$

$$\frac{dp^{(i)}}{dt} = -\frac{p^{(i)}-1}{\tau'_{stp}} - (1-f')p^{(i)}\sum_k \delta(t-t_k^{(i)}) \tag{26}$$

and asks what should the new parameters (indicated with primes) be in order to obtain a similar behaviour.

Our final goal is to obtain the same voltage dynamics, which implies

$$I_{syn} = \sum_{i=1}^{N} I_{syn}^{(i)} \tag{27}$$

Because the time constant of synaptic current is small compared to the synaptic period (T_{syn}), one can consider that the sum of N currents will follow the same dynamics as the current resulting from N synaptic events. This becomes a worse and worse approximation with an increase in the synaptic frequency (for $\nu_{syn} = 500$ Hz, the period is already 2ms, which is equal to τ_{syn})). To model this, we consider N presynaptic neurons, each with a constant input current such that the period is NT_{syn}. The initial voltage is chosen such that they fire one after the other with an interval of T_{syn} between them. This behaviour is indeed confirmed in figure 8.

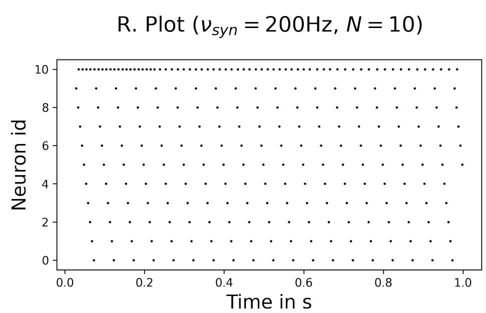
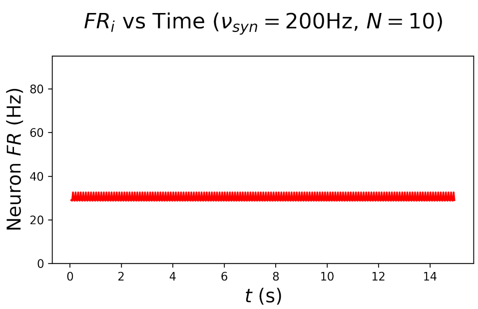


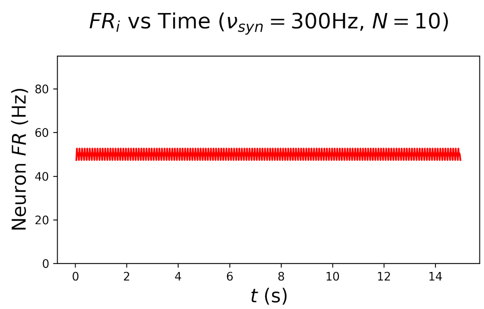
Figure 8: Raster plot of a multi-input model. Neuron id's 0-9 correspond to presynaptic neurons and number 10 is the postsynaptic neuron (under the dynamics proposed in the second solution approach, explained below).

By letting τ'_{syn} and I'_0 be τ_{syn} and I_0, thus, the problem is now reduced to having each synaptic current increased in a similar manner to single-input dynamics, which is in turn translated into each of the $p^{(i)}$ follow similar dynamics to those of equation (23). Two solutions are proposed:

1. Fix all p values to be p^* (equation (19)) : we lose the first hundreds of milliseconds dynamics (exponential decay of firing rate), but our model behaves as in the stable regime of single-input. To model this, one eliminates p dynamics (the synaptic kick is constant). Results can be observed in figure 9, where, as one would expect, there exponential decay disappears (there are no p dynamics). The value of FR_i matches the stable regime for these values (see figure 5).



(a)



(b)

Figure 9: Figures (a) and (b): instantaneous firing rate of a neuron with a constant p value for a (global) synaptic frequency of 200 and 300 Hz (respectively). Both neurons have 10 presynpatic neurons.

2. Increase the time constant to avoid p recover from one presynaptic event to the other (which now are very sparse). Because we want to have the same fixed point, by inspecting equation (19) that, given a $T'_{syn} = NT_{syn}$, the value of p^* is conserved if $\tau'_{stp} = N\tau_{stp}$. This will inevitably also slow the dynamics of the FR decay.
   In figure 10, theoretical predictions are confirmed in simulations. The final stable value of both FR and p is the same as in single-input dynamics. As mentioned above, the main difference is the timescale at which the exponential decay takes place, which now is N times higher (note the total simulation time of each figure).

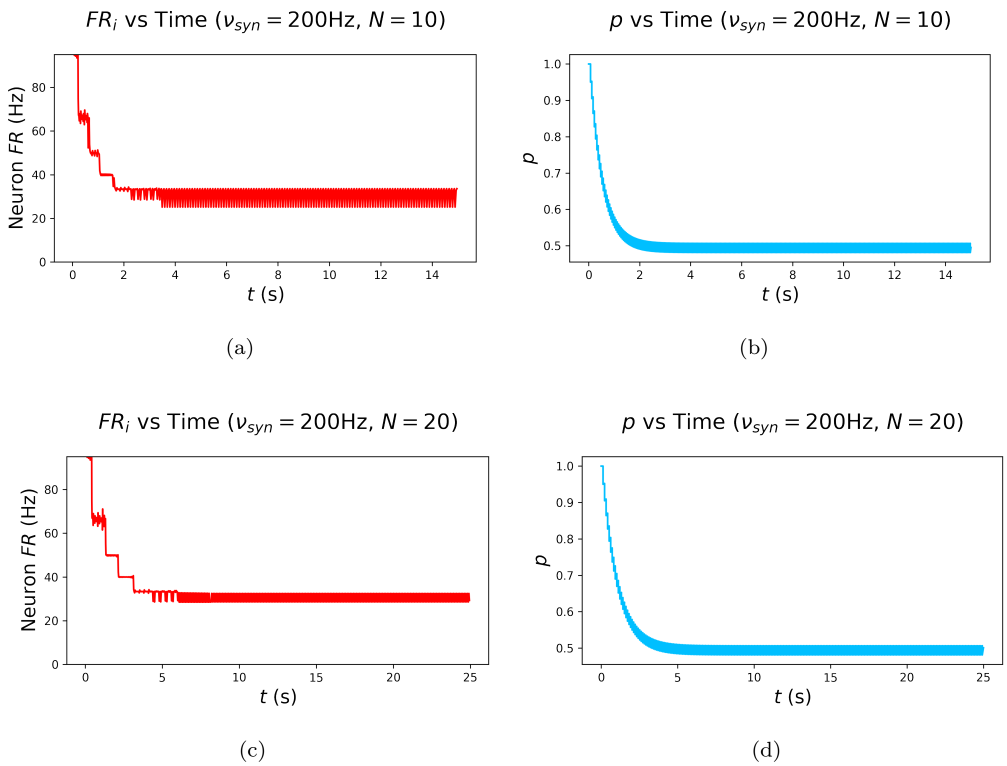


Figure 10: Figures (a) and (b): instantaneous firing rate and p (respectively) as a function of time, for a synaptic (global) frequency of 200Hz and 10 presynaptic neurons. Showed p corresponds to presynaptic neuron with id 0. Figures (c) and (d): same for 20 presynaptic neurons.