1 Neuronal Network

The network is composed of two populations of leaky integrate and fire neurons: 3200 excitatory neurons and 800 inhibitory ones, the network connectivity is sparse and random such that the recurrent connection is strongly inhibitory. Both populations receive the same excitatory external input taken to represent the activity from afferents.

The mechanism underpinning the communication of two neurons is the release of neurotransmitters at the synaptic level. When the presynaptic neuron receives a spike a cert amount of neurotransmitters is released into the synaptic cleft, neurotransmitters diffuse in the cleft and bind with postsynaptic receptors which then open, inducing a postsynaptic current. I use the Short Term Plasticity model (STP) to describe the dynamics of neurotransmitter resources at the presynaptic terminal.

The goal is to investigate how the network oscillations (if present) are modulated by constant external input. I consider the network without any kind of synaptic plasticity and then compare it with the case in presence of STP.

The network activity is quantified by individual spikes times of each neuron, the instantaneous population firing rate, and the Local Field Potential (LFP), computed as the sum of the absolute values of excitatory and inhibitory current only from the excitatory population.

I start by examining the network response to 2 seconds long constant signal with two different input rates, 47.7 and 58.8 Hz. Raster plots in Figure (2) show that the neuronal firing seem to be random and, an increasing of external input, lead to an increase of populations activity in terms of both LFP and population firing rates.
The presence of oscillatory states is investigated using spectral analysis (Figure (1)). The power spectrum density suggests, in both cases, that two major oscillations occur: the LFP is characterized by 16.0 and 20.0 Hz frequency oscillations in the first case, while it is characterized by 27.0 and 42.0 Hz frequencies in the second one. The power spectra of population firing rate suggest another interesting feature: oscillations in the gamma range (60-100 Hz) arise with stronger external input. According to common sense, these results underline strong external inputs lead to higher frequency oscillations.

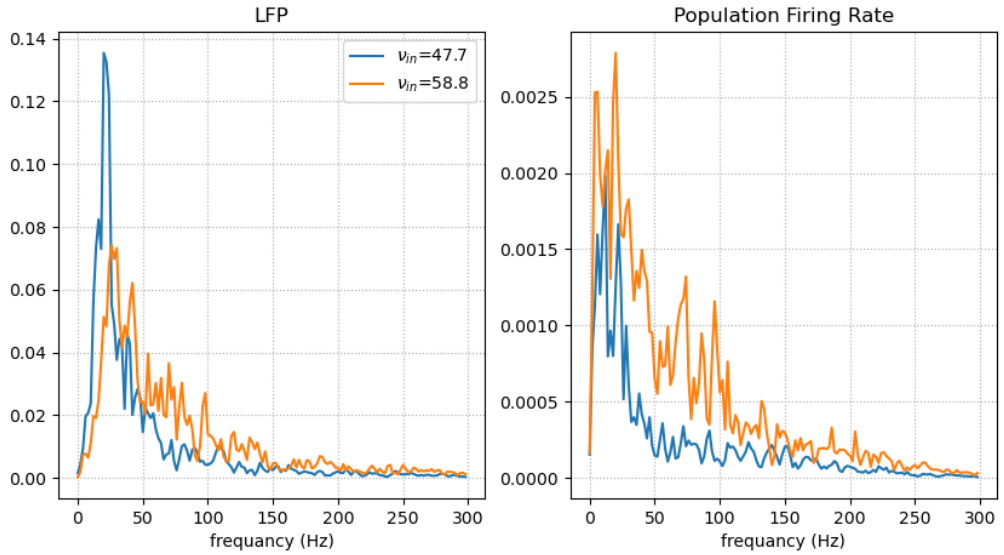

Figure 1: **LFP and excitatory firing rate power spectrum.** Spectral analysis of network without STP with two different input rates: 47.7 Hz (blue) and 58.8 Hz (orange). Welch time window is set to 500 ms such that the frequency resolution is about 2.0 Hz.

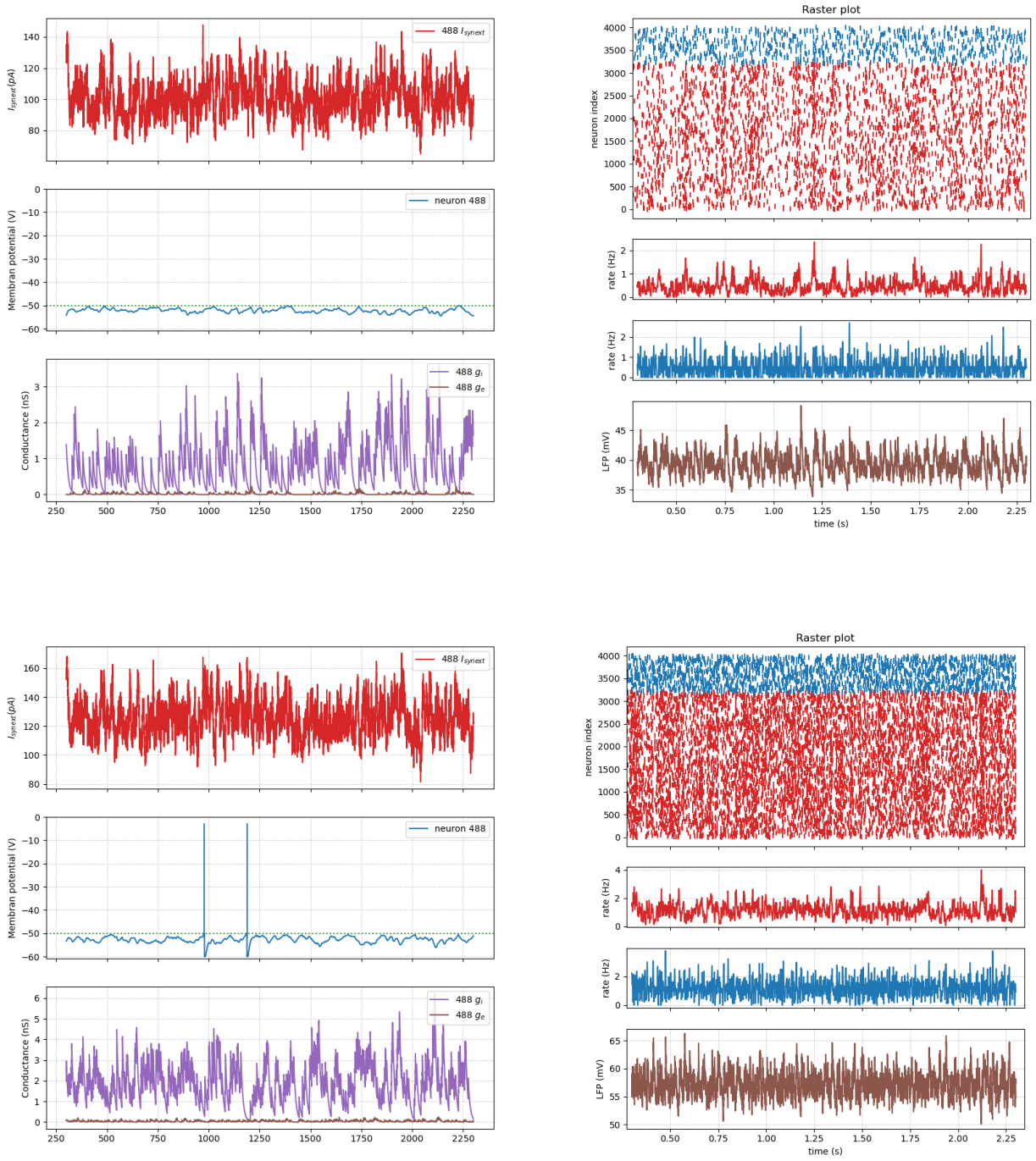

Figure 2: **Dynamics of the network without STP receiving a constant signal, with two different rates.** (Top row) Neuron variable dynamics (left) and network dynamics (right) with a constant signal of 47.7 Hz. (Bottom row) Neuron variable dynamics (left) and network dynamics (right) with a constant signal of 58.8 Hz.
Each simulation runs for 2.3 second with transient time of 300 ms.

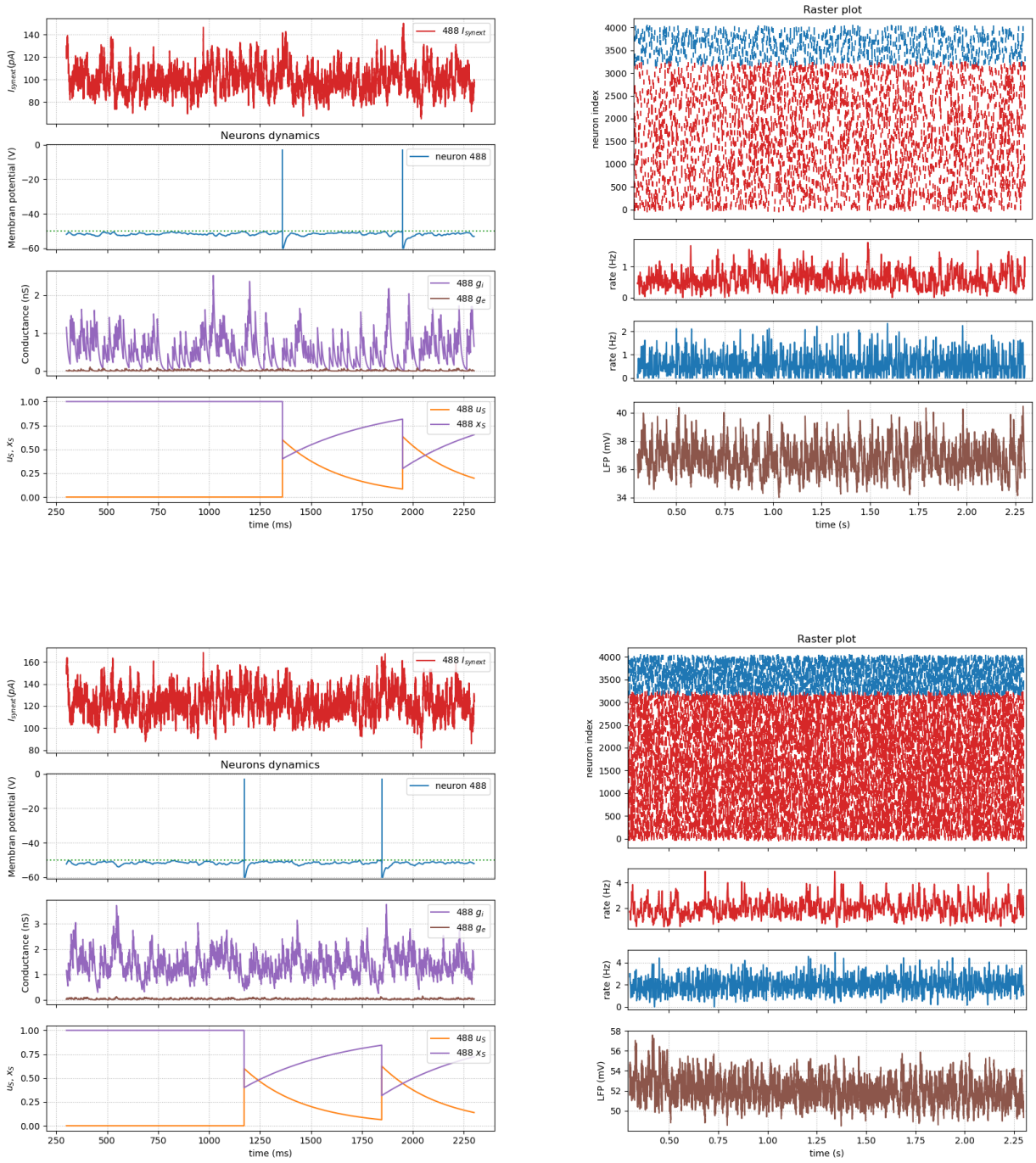

Figure 3: **Dynamics of the network with STP receiving a constant signal, with two different rates.** (Top row) Neuron variable dynamics (left) and network dynamics (right) with a constant signal of 47.7 Hz. (Bottom row) Neuron variable dynamics (left) and network dynamics (right) with a constant signal of 58.8 Hz.
Each simulation runs for 2.3 second with transient time of 300 ms.

The same type of approach has been used to analyze network behavior where synaptic plasticity is modeled by STP.
The dynamics of neuronal variables is profoundly affected taking into account synaptic plasticity. The quantity of neurotransmitters released at each spikes is no longer constant, but changes over the entire simulation time, this phenomenon modulates the dynamics of the postsynaptic conductances decreasing

their average value. Thus the dynamics of the membrane potential, due to the weaker recurrent inputs, show less extensive fluctuations than the previous scenario. (see left panels in Figure (2) and in Figure (3)).
The most remarkable consequence is the networks show an increase in their frequencies response, as you can see in raster plots in Figure (3) and in the spectral densities in Figure (4).
Now LFP oscillates in a range of 10-30 Hz with low external input while a dominant frequency of 40 Hz is present with the higher input rate (left panel Figure (4)). It is interesting to note how the gamma oscillations, present in the population firing rate in Figure (1), are not longer visible in right panel of Figure (4).

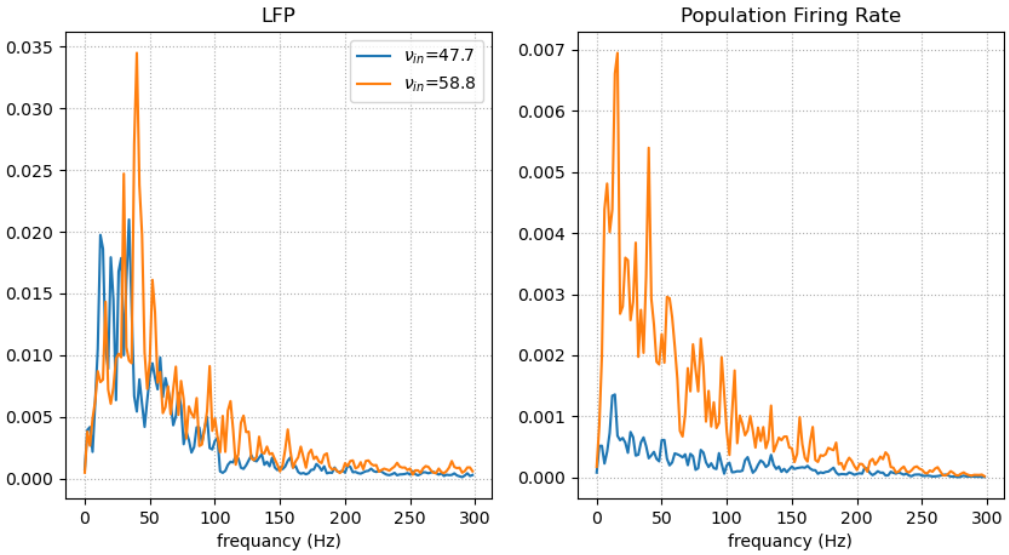

Figure 4: **LFP and excitatory firing rate power spectrum (STP).** Spectral analysis of network with STP with two different input rates: 47.7 Hz (blue) and 58.8 Hz (orange). Welch time window is set to 500 ms such that the frequency resolution is about 2.0 Hz.

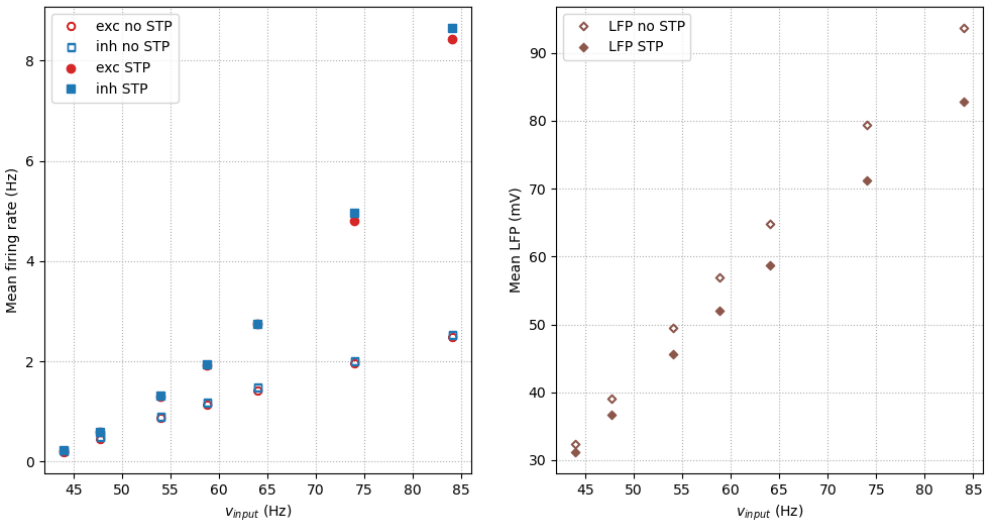

Figure 5: **Averange Population Activities with respect to different inputs.** (Left panel) Average excitatory firing rate (red) and Average inhibitory firing rate (blue). (Right panel) Average LFP (brown). All the values are computed in the presence (fully colored symbols) and in absence (edge colored symbols) of STP.

Different external inputs are presented to the network to better understand its dynamical behavior. According to the previous results, the higher average population activity occurs in presence of strong external input. An inspection of the firing rate from the excitatory and inhibitory network (left panel Figure (5)) shows that the increase in external input leads to an increase in the average range in the network; moreover, the network with synaptic plasticity shows a significantly lower firing rate. The situation changes if we look at LFP, where the presence of plasticity leads to the decrease of its average value (right panel Figure (5)).

Finally I compare the results about network responses concerning the presence of synaptic plasticity (Figure (6)). The only noticeable difference is the absence of gamma oscillations in LFPs with high external inputs, Figure 6B, indeed, suggests that synaptic plasticity kill this type of network response.

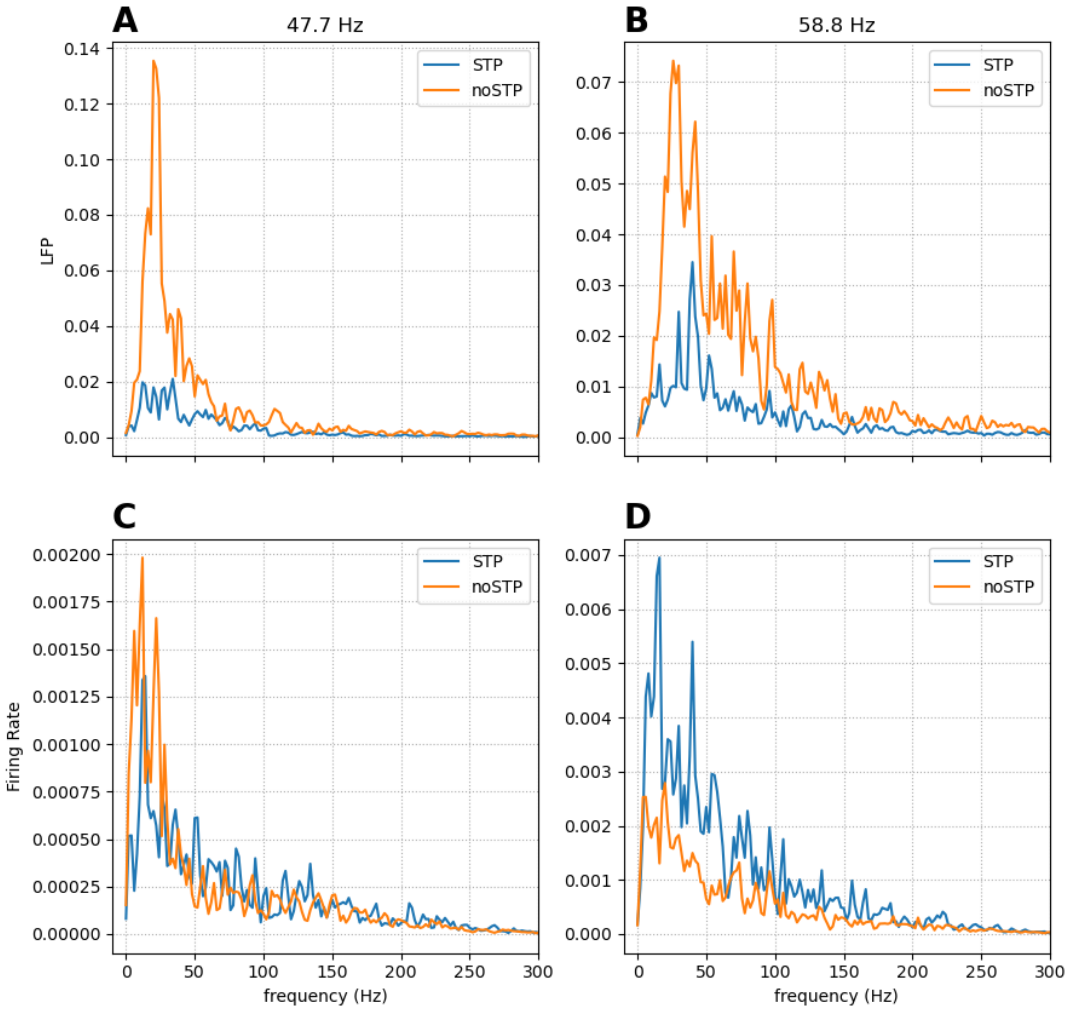

Figure 6: **LFP and firing rate power spectra concerning synaptic plasticity.** (A-C) input rate equal to 47.7 Hz. (B-D) input rate of 58.8 Hz.

Excitatory Inhibitory Balance

Previous studies concern the responses of an unbalanced network with a strong inhibitory recurrent connections. What happens if the balance between excitatory and inhibitory connections is restored? Do os-

cillatory states still arise?
The excitatory/inhibitory balance implies the total excitatory synaptic strength ingoing each neuron is equal to the inhibitory ones:

$$w_e N_e p_e = w_i N_i p_i \tag{1}$$

where $N_x p_x$ is the average number of ingoing synapses from population x ($x = e, i$) and w_x is the synaptic strength. Substituting networks parameters (see Appendix) into equation (1), provide the relation that the probability connection variables must satisfy to have a balanced network:

$$p_e = 5 p_i \tag{2}$$

I have chosen $p_e = 0.05$ and $p_i = 0.01$ and, following the same procedure of previous studies, I have investigated the network response to different constant signals.

It is clear, even if the input rates are different, both neuron dynamics and network response is deeply changes with respect to unbalanced case. Most remarkable differences are present in populations firing rate and in the LFP (right panels of Figure (8) and Figure (2)) where, at least by eyes, the responses seem to show more synchronously time evolution.
I have tried to quantifies this differences looking at the power spectra. From the results in Figure (7) emerge the a slight increase of input rate leads to an important increase of power spectrum in the range of β oscillations (10-30 Hz).

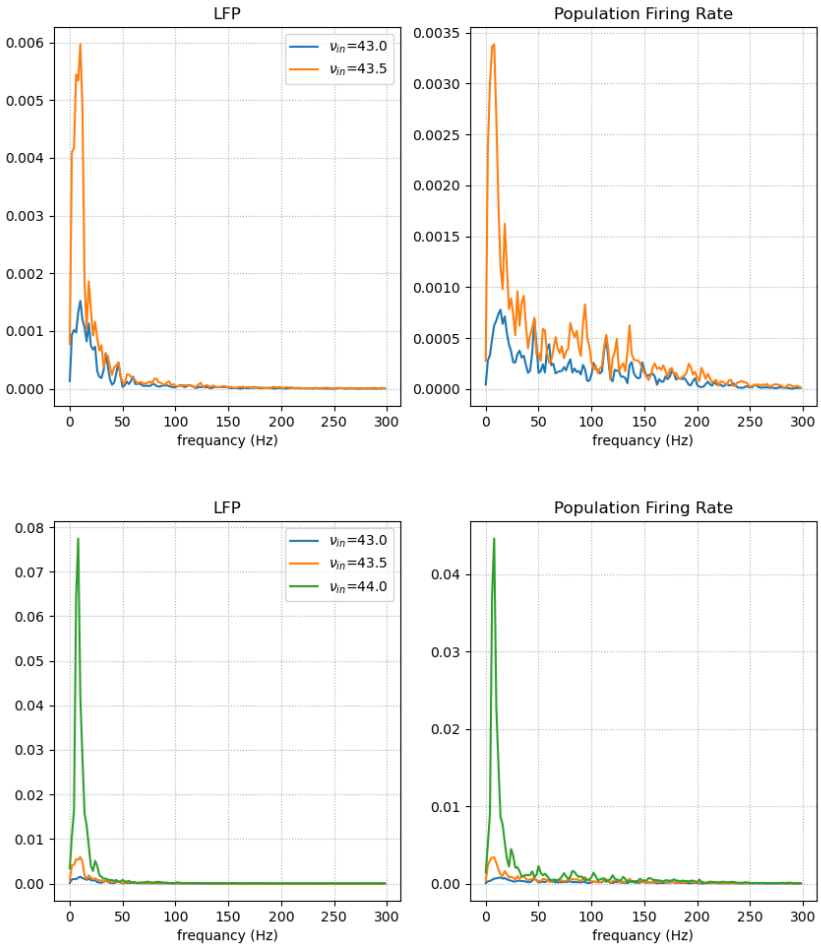

Figure 7: **LFP and firing rate power spectra of balanced network.** Spectral analysis with respect three different input rates, 43.0 Hz and 43.5 Hz (top row) and 44.0 Hz (bottom row). Starting from the lower input: LFP oscillations arise at 10 Hz (blue), 10 and 18 Hz (orange), 8 and 24 Hz (green), Firing rate oscillations arise at 14 Hz (blue), 6 and 16 Hz (orange), 8 and 24 Hz (green).

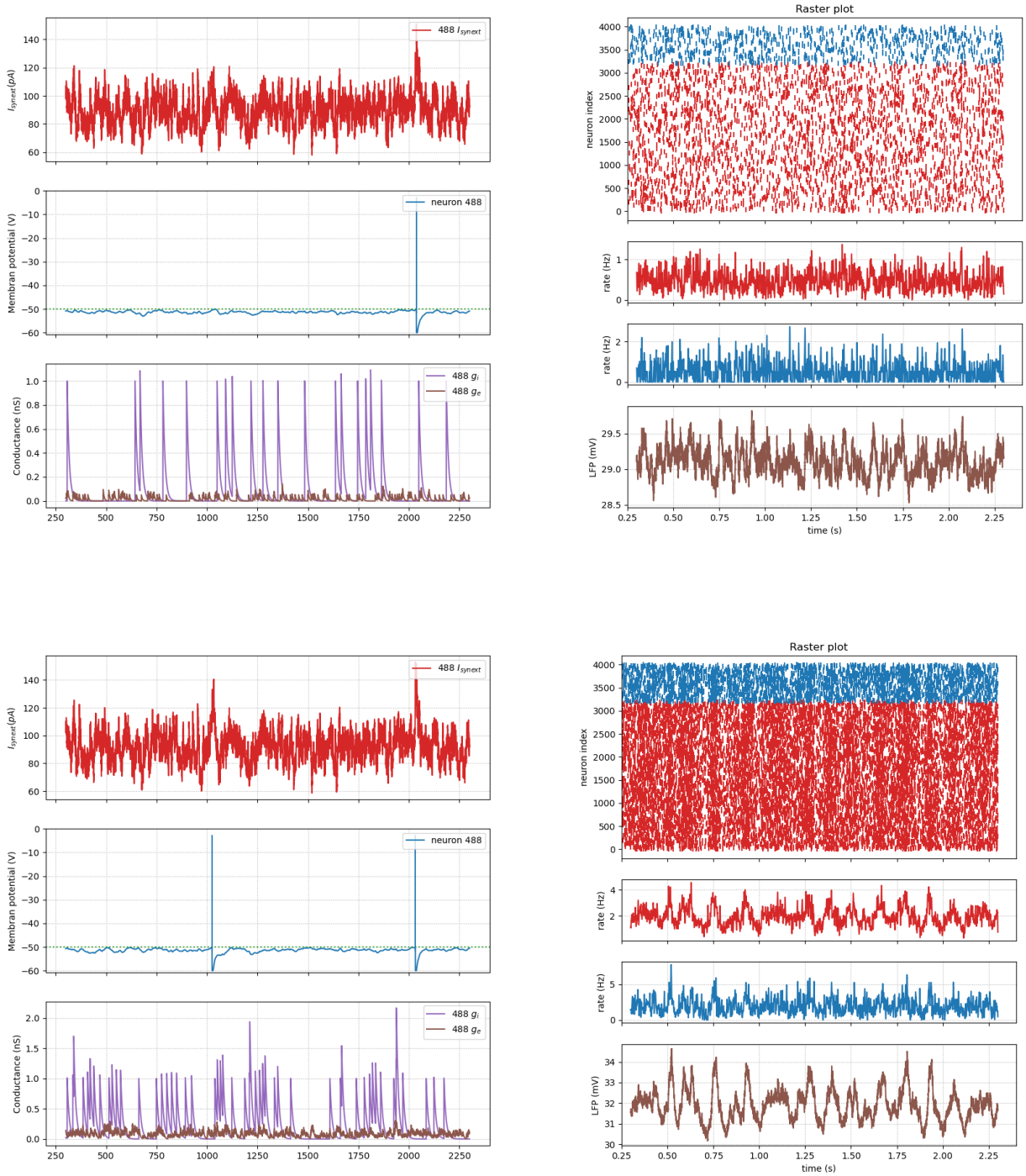

Figure 8: **Dynamics of the balanced network receiving a constant signal, with two different rates.** (Top row) Neuron variable dynamics (left) and network dynamics (right) with a constant signal of 43.0 Hz. (Bottom row) Neuron variable dynamics (left) and network dynamics (right) with a constant signal of 44.0 Hz.
Each simulation runs for 2.3 second with transient time of 300 ms.

The differences between balance and unbalance network are highlighted in Figure (9).

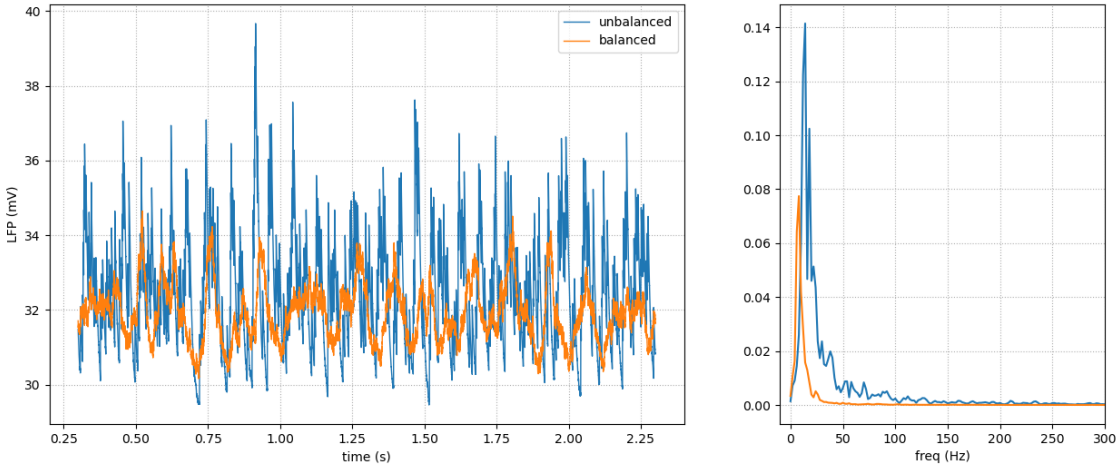

Figure 9: **Compare balance and unbalance network responses.** (left panel) LFP time evolution of unbalanced (blue) and balanced (orange) network. (right panel) Power spectrum densities. input rate 44.0 Hz

Inhibitory and Excitatory firing rate

Previous studies concern network where all neurons receive the same external input (see Methods-External Input), in this scenario average populations firing rate are very similar (Figure (5)). In literature some cortical neuronal network presents heterogeneous connections about external signal: both populations receive excitatory external input with inhibitory neurons receiving stronger inputs than excitatory ones.[2] [3]

According to this evidence, I want analyse the ratio between average populations activity with respect to the sinaptic strength of external input. Thus, external inputs is assumed to arise from 160 external synapses with conductance w_e on excitatory and $\alpha\, w_e$ on inhibitory neurons, where α is the parameter that measures how much the external input on inhibitory population is stronger then on excitatory ones. A new variable g is introduced to quantify the excitatory and inhibitory recurrent balance:

$$g = \frac{p_e}{p_i} \tag{3}$$

Keep fixed the network parameters w_x and N_x ($x = e, i$), the value $g = 5$ satisfies the balance condition (1), if $g < 5$ the network presents strong inhibitory recurrent connections, complementary $g > 5$ represents the case where the recurrent excitation prevails.

The hypothesis is the average populations activity are related with α: $\alpha = 1$ stands for homogeneous case whereby the two populations respond with the same firing rate, with $\alpha > 1$ external inputs on inhibitory are stronger, providing an higher inhibitory activity, $\alpha < 1$ represents the complementary scenario.

Average populations firing rates are investigating setting $\alpha = 1.3$ and $g = 5$. The inhibitory activity is higher than excitary one for all input rates, in particular the difference between the two firing rates keeps almost constant over the input signal (18.4 ± 4.8 Hz) while the ratio seems to follow an exponential decay (from 49 to 2) (Figure(10)).
Finally, it is interesting to analyse the firing rate behavior changing the parameters α and g. Keeping fixed $\alpha = 1.3$, the inhibitory firing rate is always higher than excitatory one regardless of the degrees of balance, furthermore, decreasing g, i.e. increasing recurrent network inhibition, provides a decreasing of network activity over all input rates (left panel Figure (11)). Instead, with $\alpha = 1.0$ both populations roughly show the same level of activity (right panel Figure (11)).

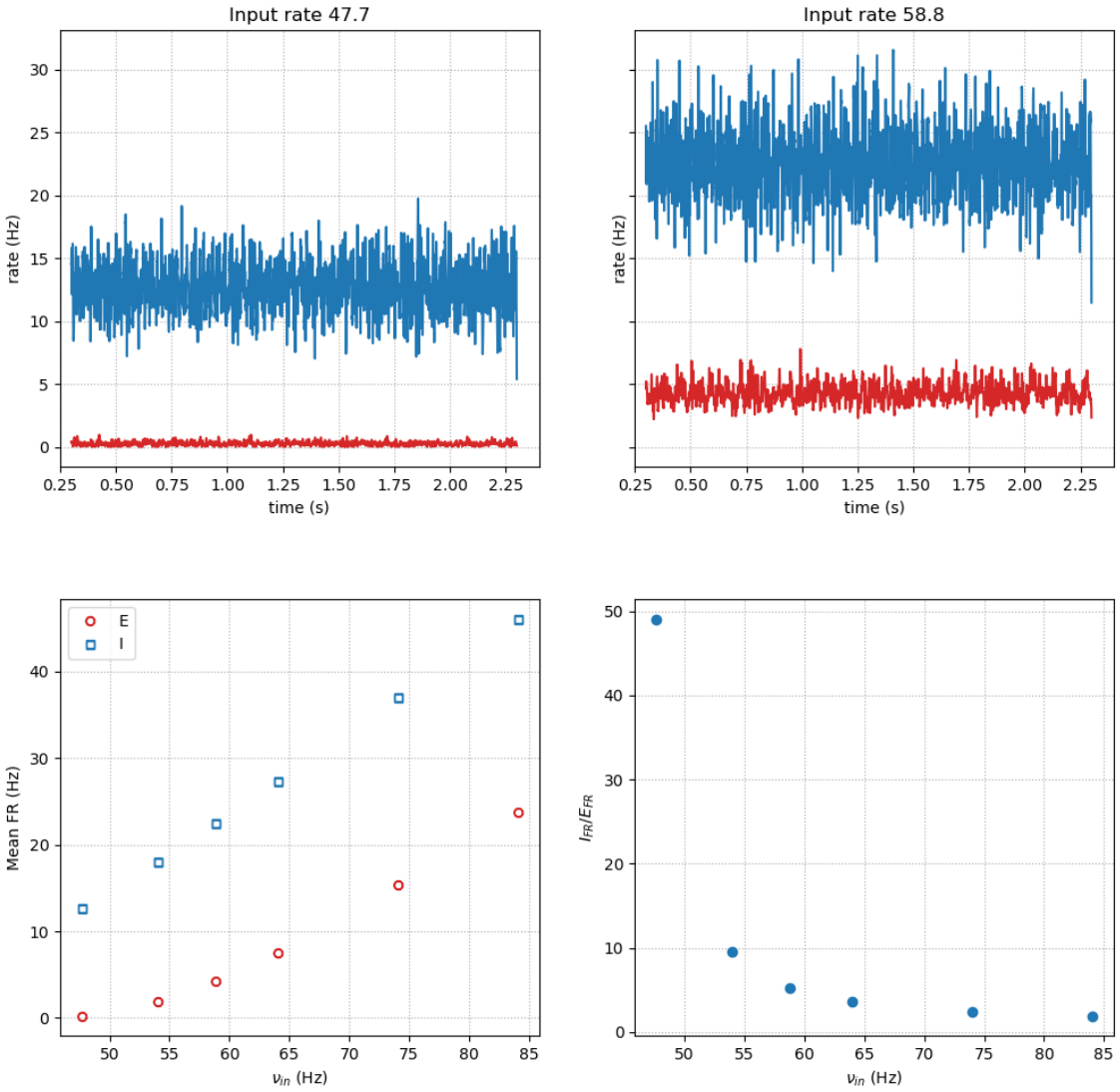

Figure 10: **Excitatory and Inhibitory firing rates.** (Top row) Excitatory (red) and Inhibitory (blue) firing rates with respect to two different input signal. Parameters: $\alpha = 1.3$ provides excitatory external synaptic strength equal to 50pS (65pS) on excitatory (inhibitory) neurons, $g = 5$.(Bottom row) Average firing rate (left) and I/E ratio (right) versus input frequency ν_{in}.

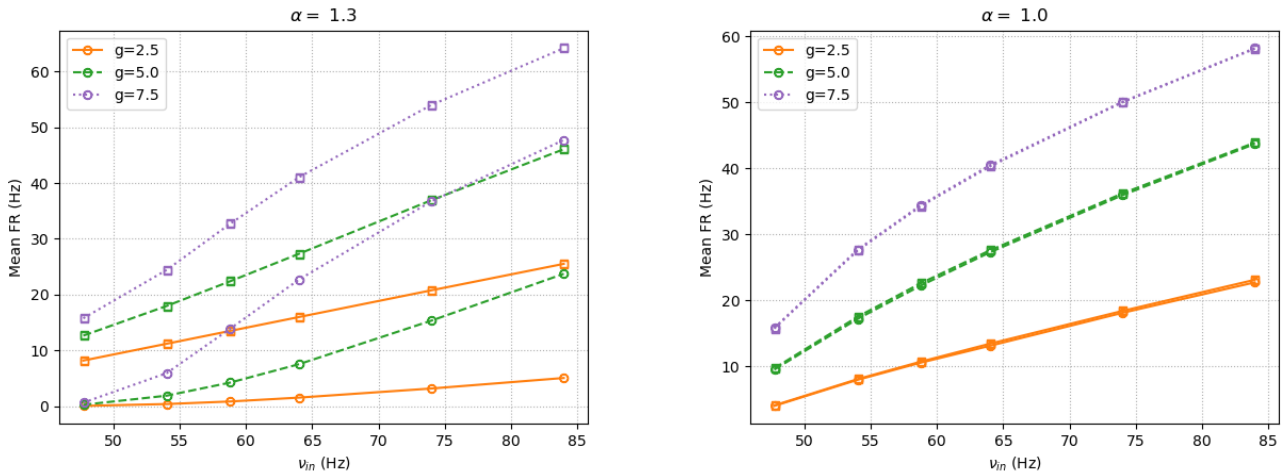

Figure 11: **Excitatory and Inhibitory firing rates against α and g.** Excitatory (circle marker) and Inhibitory (square marker) firing rate with respect to $\alpha = 1.3$ (left panel) and $\alpha = 1.0$ (right panel).

Methods

Model

The simulated network is composed of $N_e = 3200$ excitatory neurons and $N_i = 800$ inhibitory ones. The network is randomly connected: the connecting probability with an excitatory neuron is 0.05 while it is 0.2 with an inhibitory one, such that each cell receives, on average, the same amount of recurrent input. Because the inhibitory synaptic strength is 20 times greater than excitatory one (see parameters values in Appendix), the entire network has a strong inhibitory recurrent connection.
All neurons are described by conductance-based leaky integrate and fire (LIF) dynamics; each of them is described by its membrane potential V that evolve according to:

$$\begin{aligned} \frac{dV}{dt} &= \frac{g_l(E_l - V) + g_e(E_e - v) + g_i(E_i - V) + I_{ex}}{C_m} \\ \frac{dg_e}{dt} &= -\frac{g_e}{\tau_e} \\ \frac{dg_i}{dt} &= -\frac{g_i}{\tau_i} \end{aligned} \tag{4}$$

where C_m is the membrane capacitance, g_e and g_i are respectively the excitatory and inhibitory synaptic conductance with a simple exponential dynamics characterized by τ_e and tau_i time constants, and I_{ex} is a constant input current. When the membrane potential crosses the threshold V_{th}, the neuron fires causing the following consequences: the neuron potential is reset at a value V_r, the neuron cannot fire against for a refractory time τ_r and the postsynaptic conductance increased by w_e (excitatory) or w_i (inhibitory).
All initial state chose in a random fashion: membrane potentials are uniformly distributed between -60 mV (reverse potential) and -50 mV (firing threshold), the conductance values are uniformly distributed between 0 and w_x ($x = e, i$).

Synaptic plasticity

In most models of neuronal systems, neurons are connected by chemical synapses that are activated by action potentials fired by presynaptic neurons. In the following, we use the phenomenological description of neocortical synapses exhibiting short- term plasticity originally introduced by Tsodyks and Markram (Tsodyks et al. 1998; Tsodyks 2005). According to this description, synaptic release is modeled by the product of two variables u_S and x_S, where u_S loosely relates to the neurotransmitter resources "docked" for release by the Ca^{2+} sensor for synaptic exocytosis of neurotransmitter, and x_S represents the fraction of total neurotransmitter available for release (Fuhrmann et al. 2002; Tsodyks 2005). Between action potentials, u_S decays to 0 at rate Ω_f while x_S recovers to 1 at rate Ω_d , i.e.

$$\begin{aligned} \frac{du_S}{dt} &= -\Omega_f u_S \\ \frac{dx_S}{dt} &= \Omega_d(1 - x_S) \end{aligned} \tag{5}$$

The arrival of an action potential triggers calcium influx at the presynaptic terminal, which moves a fraction U_0 of the neurotransmitter resources not scheduled for release $(1-u_S)$ to the readily releasable "docked" state (u_S). Subsequently, a fraction u_S of the available neurotransmitter resources is released as r_S while x_S is reduced by the same amount; that is,

$$\begin{aligned} u_S &\to u_S + U_0(1 - u_S) \\ r_S &\to u_S x_S \\ x_S &\to x_S - r_S \end{aligned} \tag{6}$$

In addiction, excitatory (inhibitory) synapses will increase the excitatory (inhibitory) conductance in the postsynaptic neurons whenever a presynaptic action potential arrives, i.e.

$$\begin{aligned} g_e &\to g_e + w_e r_S \\ g_i &\to g_i + w_i r_S \end{aligned} \tag{7}$$

External Input

External inputs were assumed to arise from 160 external excitatory synapses with conductance 0.05 nS (w_e) without any kind of plasticity. The synapses are activated by random Poisson spike trains, with a given rate. The set of equations 4 on page 10 became:

$$\begin{aligned} \frac{dV}{dt} &= \frac{g_l(E_l - V) + g_e(E_e - v) + g_i(E_i - V) + g_{ext}(E_e - v)}{C_m} \\ \frac{dg_e}{dt} &= -\frac{g_e}{\tau_e} \\ \frac{dg_i}{dt} &= -\frac{g_i}{\tau_i} \\ \frac{dg_{ext}}{dt} &= -\frac{g_{ext}}{\tau_e} \end{aligned} \tag{8}$$

In this case, the external current is not a constant but fluctuates around its mean value. The rate of Poisson spikes trains is selected such that the firing rate of equation (4) is equal to the firing rate of equation(8).

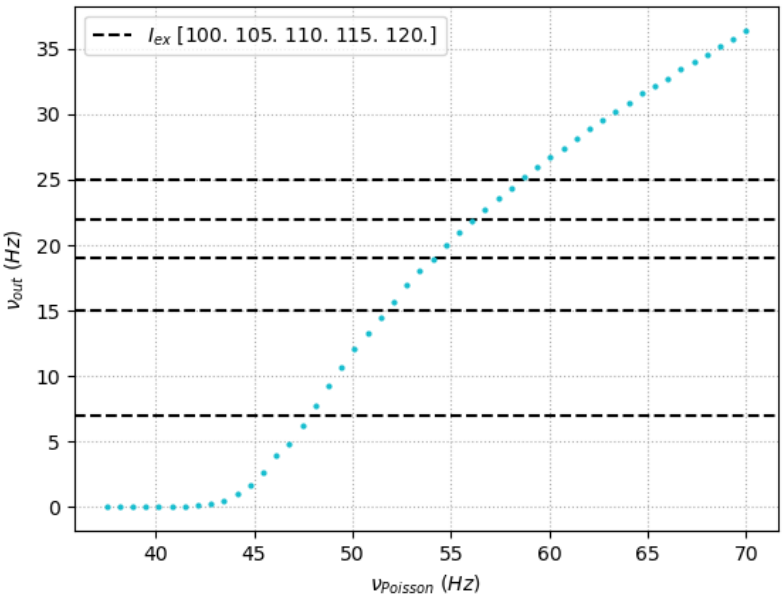

Figure 12: **Characteristic curve of Poisson Inputs.** The neuron firing rate ν_{out} is estimated over 300 independent simulations.

Appendix

Symbol	Name in code	Value	Units	Description
			Neuron parameters	
C_m	`C_m`	198	pF	Membrane capacitance
E_i	`E_i`	-60	mV	Leak reversal potential
g_l	`g_l`	9.99	nS	Leak conductance
V_r	`V_r`	-60	mV	Reset potential
V_θ	`V_th`	-50	mV	Firing threshold
τ_r	`tau_r`	5	ms	Refractory period
			Synapses parameters	
Ω_d	`Omega_d`	2	s^{-1}	Synaptic depression rate
Ω_f	`Omega_f`	3.33	s^{-1}	Synaptic facilitation rate
U_0	`U_0`	0.6	-	Resting synaptic release probability
w_e	`w_e`	50	pS	Excitatory synaptic conductance
w_i	`w_i`	1	nS	Inhibitory synaptic conductance
τ_e	`tau_e`	5	ms	Excitatory synaptic time constant
τ_i	`tau_i`	10	ms	Inhibitory synaptic time constant
E_e	`E_e`	0	mV	Excitatory synaptic reversal potential
E_i	`E_i`	-80	mV	Inhibitory synaptic reversal potential

References

[1] Stimberg M., Goodman D.F.M., Brette R., Pittà M.D. (2019) Modeling Neuron–Glia Interactions with the Brian 2 Simulator. In: De Pittà M., Berry H. (eds) Computational Glioscience. Springer Series in Computational Neuroscience. Springer, Cham.

[2] Mazzoni A, Panzeri S, Logothetis NK, Brunel N (2008) Encoding of Naturalistic Stimuli by Local Field Potential Spectra in Networks of Excitatory and Inhibitory Neurons. PLOS Computational Biology 4(12): e1000239. https://doi.org/10.1371/journal.pcbi.1000239

[3] Brunel N, Wang XJ. What determines the frequency of fast network oscillations with irregular neural discharges? I. Synaptic dynamics and excitation-inhibition balance. J Neurophysiol. 2003 Jul;90(1):415-30. doi: 10.1152/jn.01095.2002. Epub 2003 Feb 26. PMID: 12611969.