1 Introduction

Gliotransmission modulates neurotransmitter release at synaptic level and the effects strongly depend on the presynaptic firing rate. Our interest is focus on how gliotrasmission modulation on glutamatergic synaptic release drives network dynamics. With this regards it is crucial understand the consequences on network dynamics due to short-term plasticity and the role of recurrent input on firing rate and LFP oscillation .

Neuronal network presents heterogeneous connections about external signal: both populations receive excitatory external input with inhibitory neurons receiving stronger inputs than excitatory ones. The external inputs is assumed to arise from 160 external synapses with conductance w_e on excitatory and $s\,w_e$ on inhibitory neurons, where s is the parameter that measures how much the external input on inhibitory population is stronger then on excitatory ones in the particular, for $s = 1$ the homogeneous connections is restored.
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. Fixed the number of neurons and the synaptic strength, the "degrees of balance" is defined as follow:

$$g = \frac{p_e}{p_i} = \frac{w_i\, N_i}{w_e\, N_e} \tag{2}$$

The values of g and w_e characterize the recurrent dynamics while s regulates the external driving force on network. In Figure (1) is shown the mean value of population firing rates and LFP for parameters in [1].

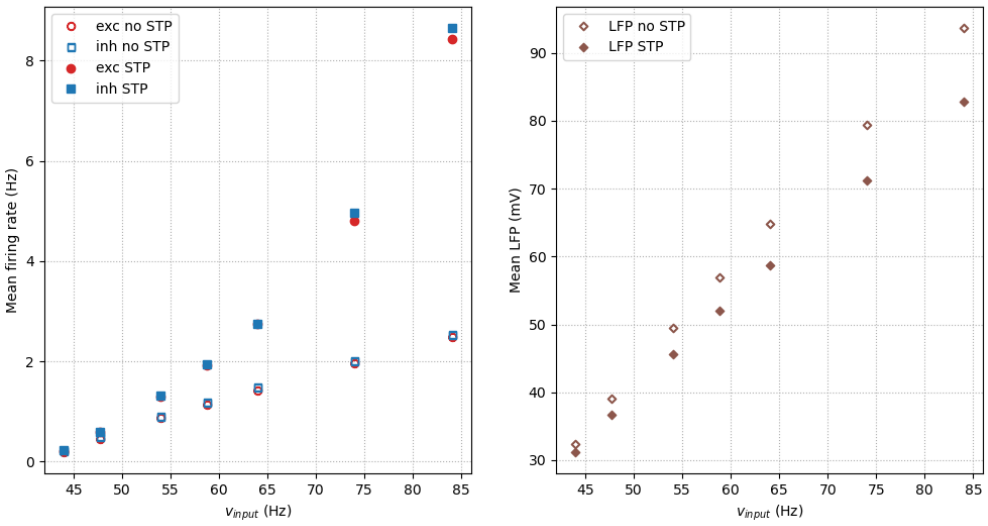

Figure 1: **Averange Population Activities with respect to different inputs.** (Left panel) Average excitatory firing rate (red) and Average inhibitory firing rate (blue). (Right panel) Average LFP (brown). All the values are computed in the presence (fully colored symbols) and in absence (edge colored symbols) of STP. Parameters: $s = 1$, $g = 0.25$, $w_e = 0.05$ nS

The filtering characteristic curve of gliotransmission modulation for homosynaptic scenario (closed-loop circuit) gives some insight about the "windows" where the gliotransmission effects are visible. With presynaptic firing rate between 0 and 3 Hz, the combination of release-descresing effect and astrocytic-induced facilitation provides the bell-shaped curve while, for higher value, the neurotransmitter release is indifferent to astrocytic modulation (Figure (2)).

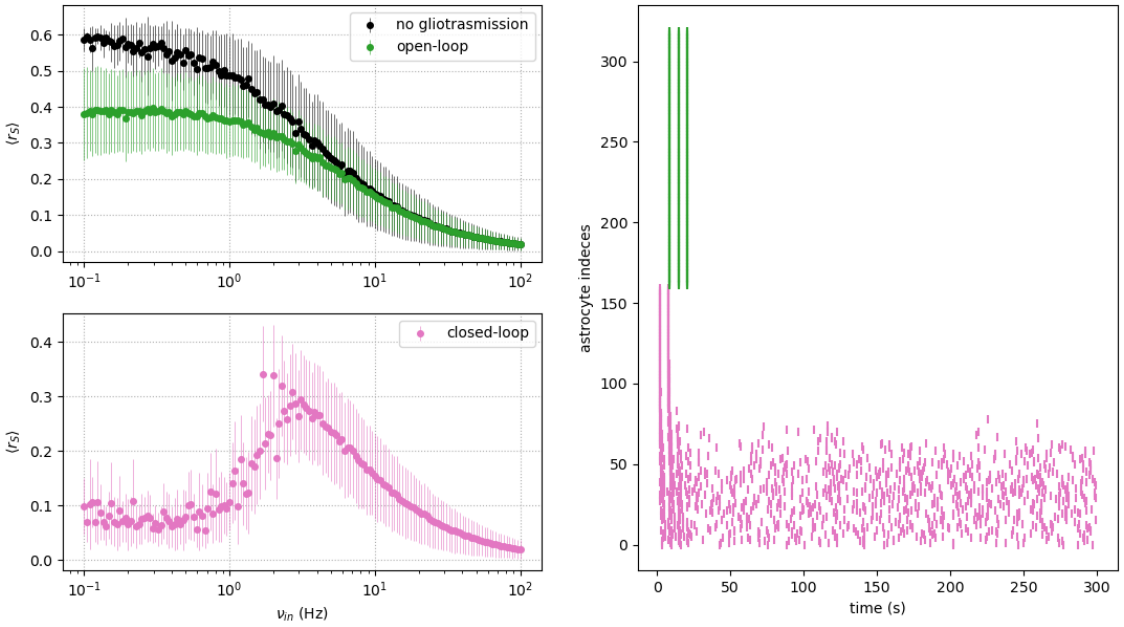

Figure 2: **Average release probability for different incoming action potential**. Average of r_S of 160 independent synapses for the three different situation, time simulation covers 300 second for each synapse but only the data after 50 seconds are taken to evaluate mean and standard deviation, integration steps is 1 ms. (top left) No gliotrasmission and open-loop situation, there are no differences of filtering behavior. (bottom left) The lwo-pass filter becomes a band-pass filter in closed-loop circuit due to the combination of release-decreasing and facilitation effects. (right panel) GREs raster plot about open (green) and closed (pink) situation.

The analysis about gliotransmission modulation tells that, after astrocytic activation, release-decreasing effect and facilitation respectively tends to reduce and increase recurrent current. Thus, to visualize this combination of effects, the recurrent excitatory current must be comparable to inhibitory recurrent currents such that network dynamics is not only driven by inhibitions. Simultaneously, the mean firing rate of modulated population - in principle astrocytes could modulate both excitatory or inhibitory population - has to be less then ∼3.0 Hz.

Dynamics in astrocytic steady state

Figure (2) provides important cues about the networks behaviour in astrocytic steady state. Indeed, from filtering characteristic curves of simple (black trace) and tripartite synapses in homosynaptic connection (pink trace), three different regions emerges depends on presynaptic firing rate ν_{syn}:

- **zone 1 -** $\nu_{syn} < 1$ Hz. Astrocytic steady state is close enough to threshold value C_θ such that gliorelease firing rate does not allow the facilitation effect. The mean value of neurotransmitter release probability is deeply modulated and the synaptic dynamics is very different to simple scenario.
- **zone 2 -** $1 < \nu_{syn} < 3$ Hz. Astrocytic state state increases with presynaptic firing rate and the gliorelease firing rate allows the facilitation effects. As a consequence, the mean value of neurotransmitter concentration increase with presynaptic firing rate until the limit value imposed by the upper bound of simple synapse.
- **zone 3 -** $\nu_{syn} > 3$ Hz. Presynaptic firing rate cannot sustain further gliotransmission release and the characteristic curves in simple and tripartite synapses coincide.

The main dynamical changes induced by gliotransmission happen for presynaptic firing rate below 3 Hz, whereby the neurotransmitter release probability is strongly modulated. Furthermore it is possible to investigate both qualitatively and quantitatively the dynamical features induces by glia in zone 1 and in

zone 2. For low presynaptic firing rate, indeed, the decrease-release effect dominate the system leads to a low values of $\langle r_S \rangle$, in other words there are not dynamical changes in astrocytic steady state. Otherwise, for higher presynaptic firing rate, the facilitation effects induced by gliotrasmission provides dynamical changes for long time observation.

The average value of neurotransmitter concentration in ECS is computed for long time simulation (240 seconds) to elucidate the dynamical features induced by gliomodulation in astrocytic steady state (after 40 seconds). According to above qualitatively description, for presynaptic firing in zone 1, the release-decreasing effect dominates the dynamics thus neurotransmitter concentration is statistically lower than simple synapses and does not emerge any kind of dynamical feature (Figure (3)). For presynaptic firing rate in zone 2, otherwise, it is clearly visible a sort of saturation dynamical behavior driving the system at its limit value, however this values is lower than simple synapses due to thevalue of neurotransmitter release probability (Figure (4)).

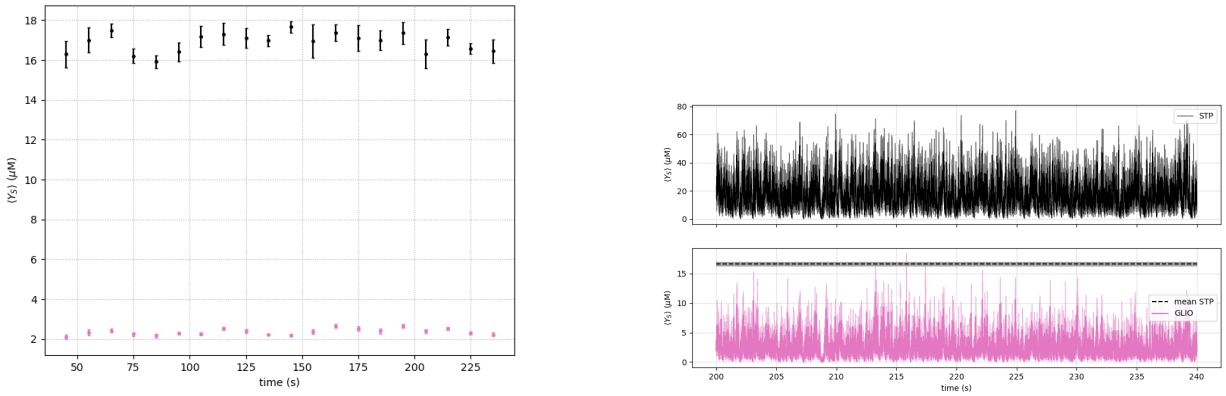

Figure 3: **Neurotransmitter concentration dynamics in astrocytic steady state, zone 1**. Average neurotransmitter concentration dynamics for presynapitc firing rate of 0.5 Hz, in both panels simple synapse is represented in black while tripartite in pink. (left panel) Dynamical representation over total time simulation in steady state, i.e. from 40 to 240 seconds. Each datum is the mean of Y_S over 10 seconds, the error is computed through blocking technique. (right panel) Average neurotransmitter concentration dynamics across 160 independent measurements from 200 seconds to 240 seconds.

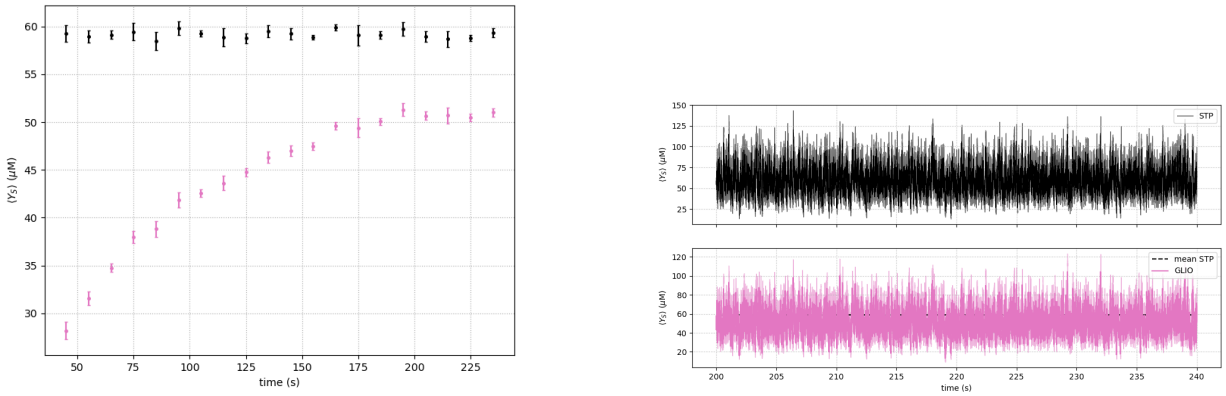

Figure 4: **Neurotransmitter concentration dynamics in astrocytic steady state, zone 1**. Average neurotransmitter concentration dynamics for presynapitc firing rate of 2.6 Hz, in both panels simple synapse is represented in black while tripartite in pink. (left panel) Dynamical representation over total time simulation in steady state, i.e. from 40 to 240 seconds. Each datum is the mean of Y_S over 10 seconds, the error is computed through blocking technique. (right panel) Average neurotransmitter concentration dynamics across 160 independent measurements from 200 seconds to 240 seconds.

The Report is organized as follow. At the beginning the baseline condition is investigated to better understand the role of STP on network dynamics with respect to the nature of external connection and re-

current balance; then astrocytes are added and the effects of gliotrasmission modulation are monitored by population firing rate and LFP.

Neural network and the role of STP

Neuronal connections are provided by STP synapses both for excitatory and inhibitory recurrent input. What is the role of plasticity in network dynamics and what is the nature of oscillations in such type of network?
Two different external input are presented to a balanced network with heterogeneous external input ($g = 5.0$ and $s = 1.15$) and to network with homogeneous external connection driven by strong inhibitory recurrent current ($g = 0.25$ and $s = 1.00$). Network activity is quantified by monitoring the individual spike time of each neurons and the equivalent firing rates distribution, the instantaneous population firing rate, the average synaptic current and the LFP. In both scenario the synaptic plasticity introduces a degrees of freedom acting on neurons connections such that, according to STP depletion, the synaptic strength decreases with presynaptic firing rate. This evidence generates different dynamical behaviors depends on the intensity of external input and the nature of external connection.

Heterogeneous external connection - $g = 5.0$ and $s = 1.15$

Heterogeneous external connections provide inhibitory population's firing rate higher than excitatory one (Figure (5)), while the balance leads to an equivalent value for the two type of recurrent currents.

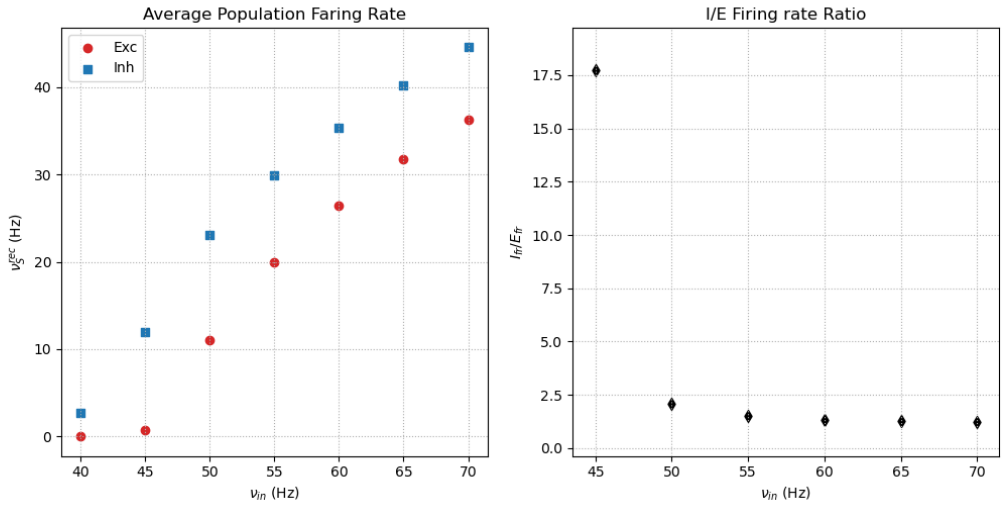

Figure 5: **Average population firing rates in heterogeneous scenario.** (left panel) Average excitatory (red balls) and inhibitory (blue square) firing rate.(right panel) Ratio between inhibitory and excitatory recurrent currents, the ratio I_{fr}/E_{fr} lies into the range 10-2 between input frequencies 47 - 55 Hz. Parameters: $g = 5.0$, $s = 1.15$ and $w_e = 0.05$ nS, time simulation 2.3 second with of step 0.05 ms, only data after 300 ms are tacking into account to compute the mean values.

For the lower input of 7.63 kHz the network with (Figure (7)) and without (Figure (6)) plasticity show different neurons' firing rate distributions and power spectral spectra . In particular, low frequencies of population firing rate emerge in presence of STP. The nature of this oscillation could be explained by the lower synaptic connection and the different values of excitatory and inhibitory recurrent current. Looking at a completely independent pool of neurons with same external connection and same parameters of previous networks, the low frequencies does not emerge (Figure (8). However, in the three scenario, LFP's power spectra show noisy behavior, except for a weak pronounced oscillation at 9 Hz in the precence of STP that coincides with the weighted average of neurons' firing rate. From this evidence it could be possible that this networks dynamics is not a "emerging feature" due to the synaptic connection but it is a simple mirror of single neurons dynamics.

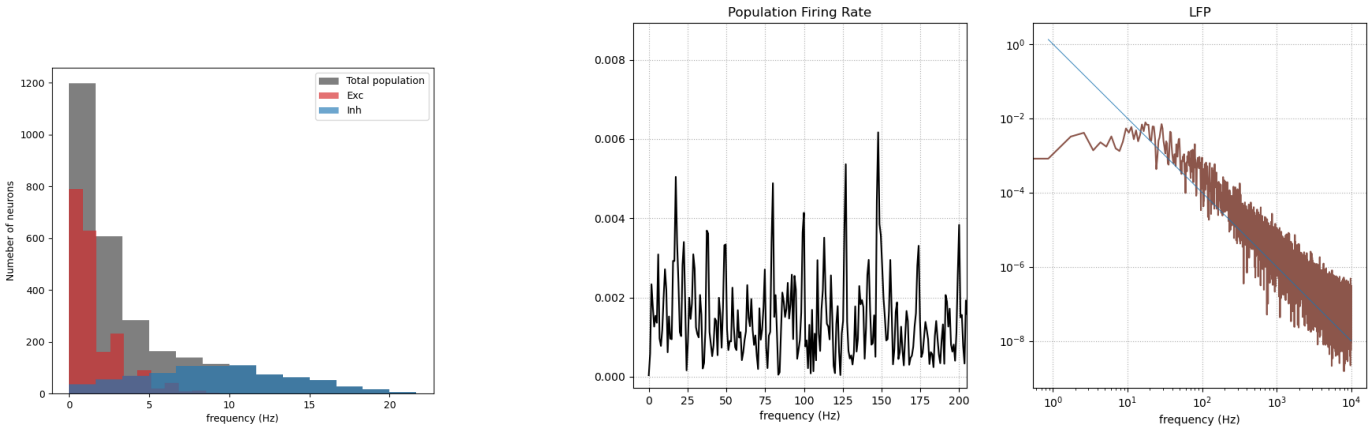

Figure 6: **Firing rate and spectral analysis of network without plasticity, 7.63 kHz**.

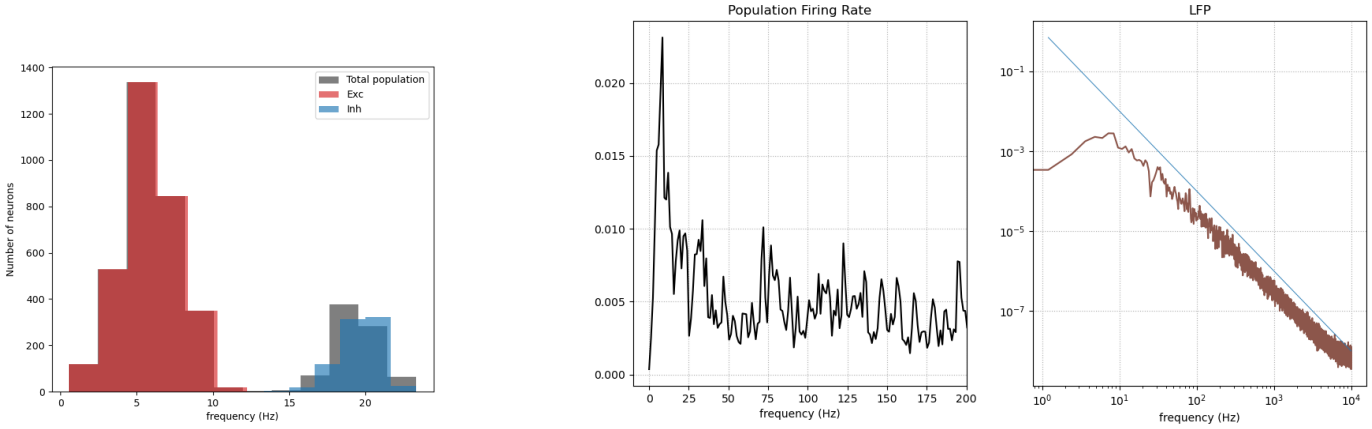

Figure 7: **Firing rate and spectral analysis of network with STP, 7.63 kHz**.(left panel) Single neurons firing rate distribution, two different distribution are clearly visible fro E (mean 5.8 Hz) and I population (mean 19.4 Hz). (Right panel) Power spectrum of population firing rate and LFP, power spectra are averaged from 5 trials 3 seconds with different realization of Poisson input, only data after 500 ms are taken to compute the analysis. There is a pronounced oscillation at 9 Hz.

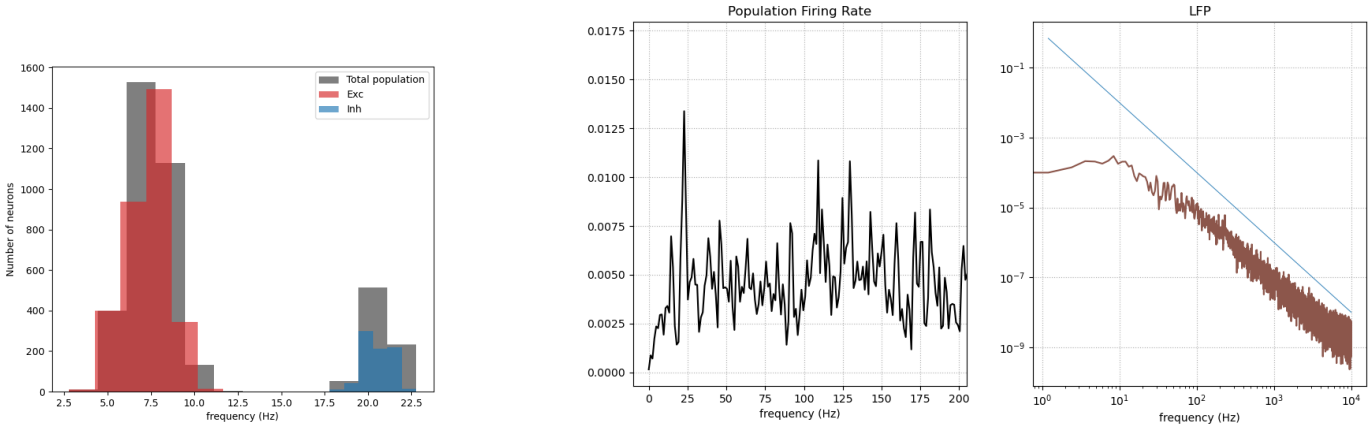

Figure 8: **Firing rate and spectral analysis of network without synaptic connections, 7.63 kHz**.

Cross correlation function between neurons with higher firing rate and mean values of Coefficient of Varia-

tion (CV) across all neurons are computed.
CV POPULATION - STP
exc : 0.04362
inh : 0.06143
CV POPULATION - no connection
exc : 0.04821
inh : 0.06204

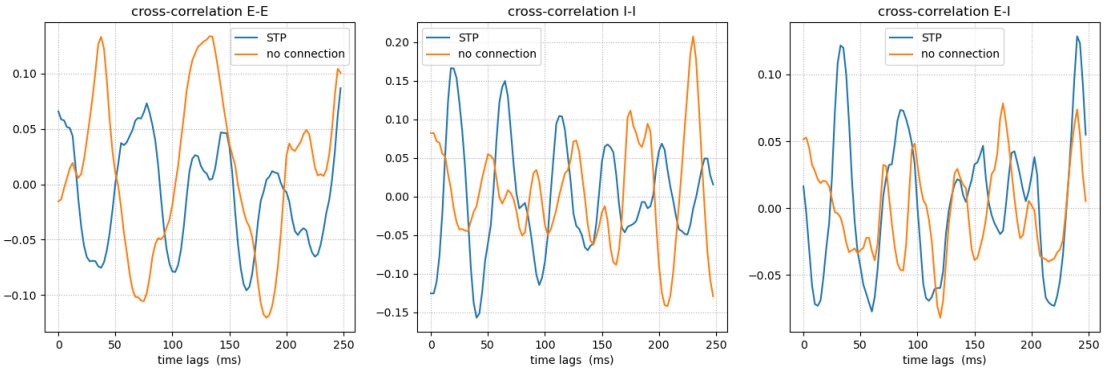

Figure 9: **Cross correlation function inter- and intra-population, $g = 5.0$ - 7.63 kHz**

Alarming results follow from the analysis for the higher input of 11.20 kHz. As illustrates in Figure (11), network dynamics with STP show two different frequencies -36 and 44 Hz - in population firing rate emerging from noise signal. Looking at single neurons' firing rate distribution, however, this oscillations coincide with the mean values of neurons firing rate. Moreover, a pool of non-connected neurons with same parameters shows a similar behavior, the only difference is the noise's intensity (Figure (12). For high external input I have expected a desynchronization due to STP but, at same time, this results suggests that the oscillation are not "emerging feature" caused by connection, conversely derives from single neuron dynamics, this is underlined also in absence of plasticity (Figure (10)) where network oscillations lie into the range of single neurons oscillations. A plausible conclusion is that the network oscillations, for this set of parameters, do not underline any kind of emerging dynamics but are the mirror of single neurons behavior.

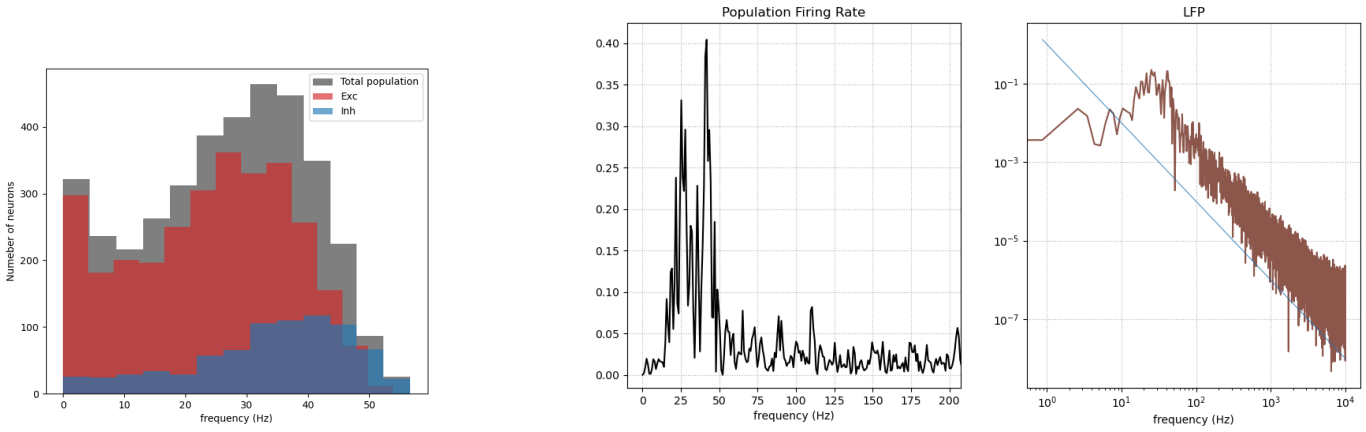

Figure 10: **Firing rate and spectral analysis of network without plasticity, 11.20 kHz**.

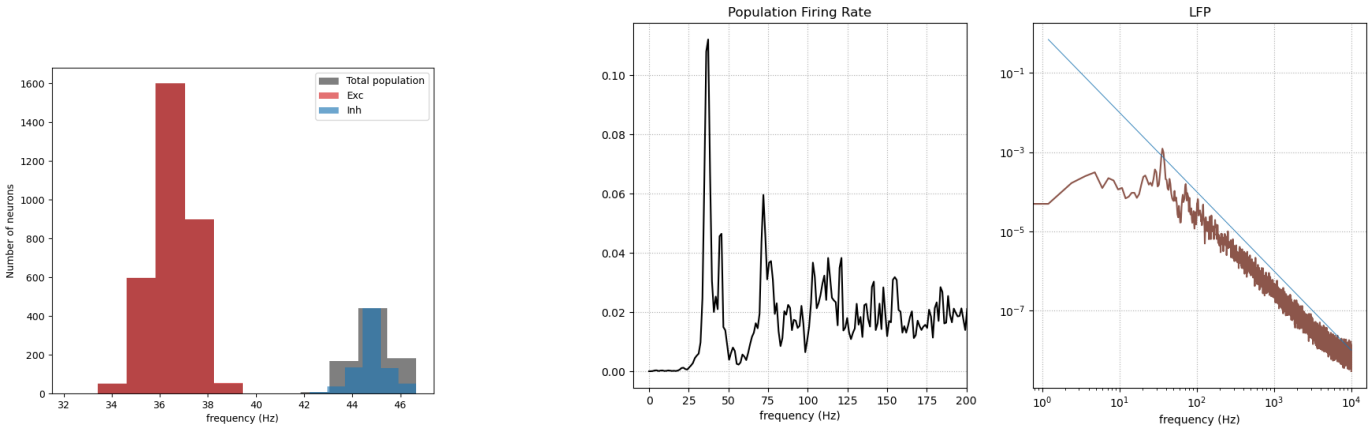

Figure 11: **Firing rate and spectral analysis of network with STP, 11.20 kHz**.(left panel) Single neurons firing rate distribution, two different distribution are clearly visible for E (mean 36 Hz) and I population (mean 44 Hz). (Right panel) Power spectrum of population firing rate and LFP, power spectra are averaged from 5 trials 3 seconds with different realization of Poisson input, only data after 500 ms are taken to compute the analysis. There are a pronounced oscillations at 36 Hz and 44 Hz

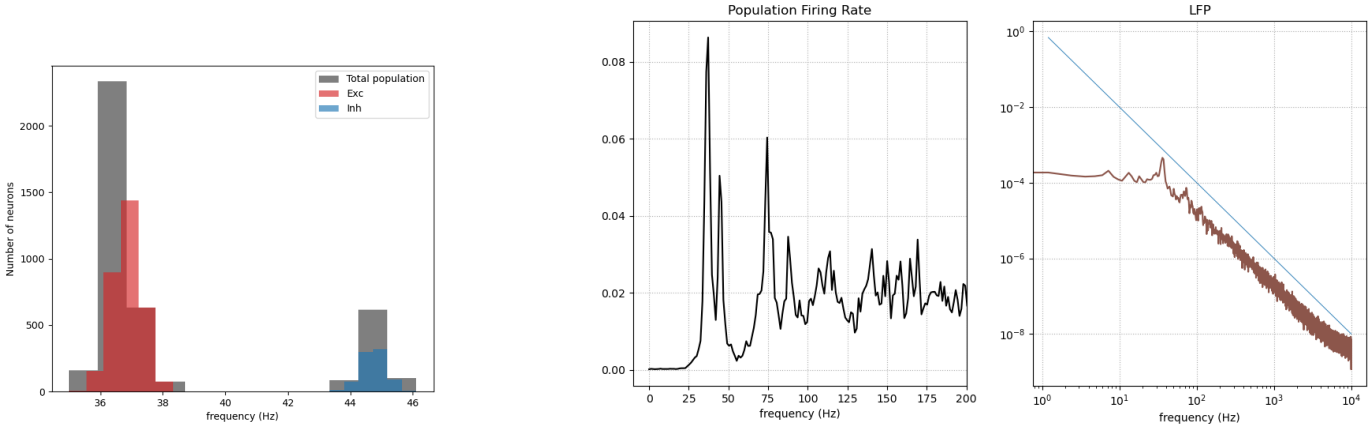

Figure 12: **Firing rate and spectral analysis of network without synaptic connections, 11.20 kHz**. Power spectrum is averaged over 4 different trial.

CV POPULATION - STP
exc : 0.06378
inh : 0.06383
CV POPULATION - no connection
exc : 0.06367
inh : 0.06372

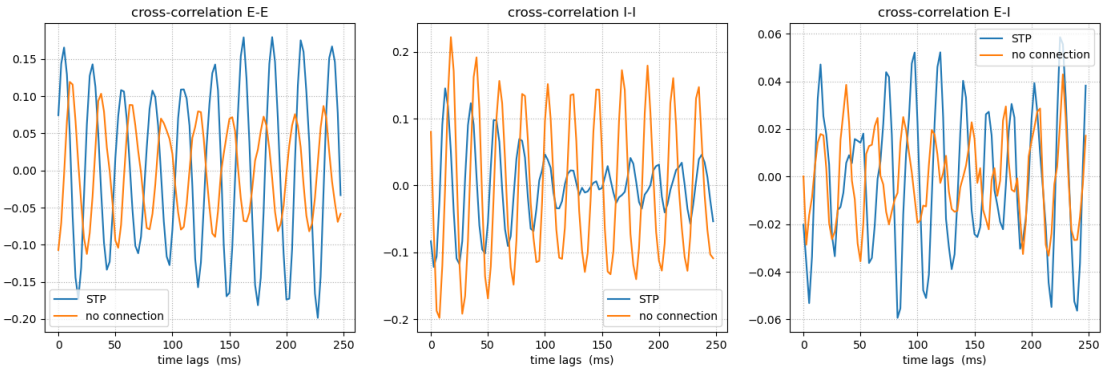

Figure 13: **Cross correlation function iter- and intra-population,** $g = 5.0$ **- 11.20 kHz**

Homogeneous external connection and unbalanced network - $g = 0.25$ and $s = 1.00$

Homogeneous external input implies a similar firing rate for inhibitory and excitatory population (see Figure (1)). Network analysis follows the same procedure of previous scenario and the result are (luckily) deeply encouraging.

When an input of 7.63 kHz is presented, neurons in both type of networks show irregular activity in terms of emitted spikes, but oscillations of 10-20 Hz emerge looking at population firing rate and LFP power spectral. Thus this type of oscillations emerge due to neurons connection (data not shown). This considerations are more visible for higher external input, 11.20 kHz. The pool of non-interacting neurons have the same feature of heterogeneous situation, i.e. network shows oscillation at same neuron firing rate Figure(16). However, with STP and also without plasticity, all single element fires at low frequencies in irregular fashion (see distribution in Figure (15) and (14)) but simultaneously networks oscillate at 36 Hz in LFP and population firing rate.

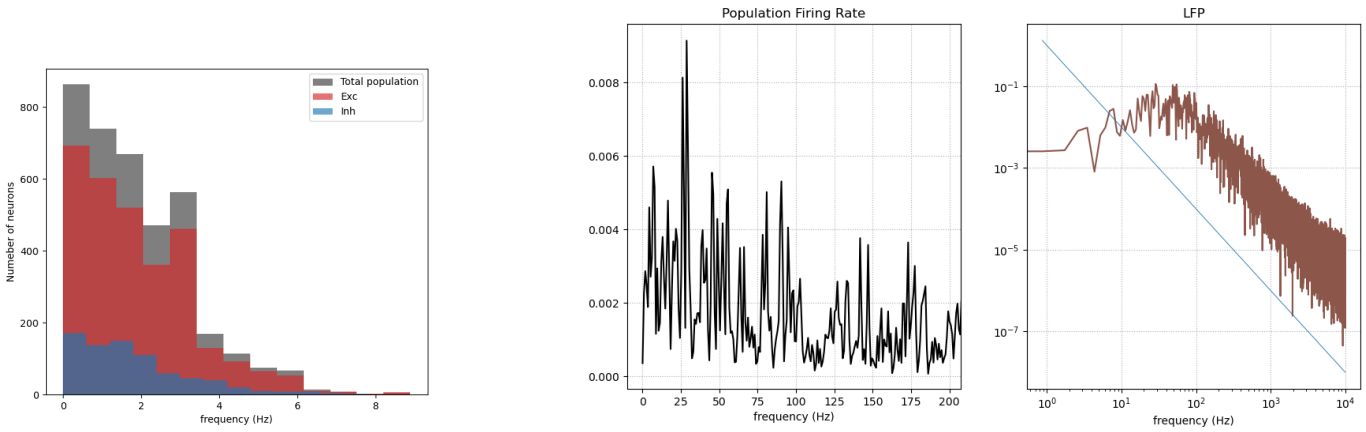

Figure 14: **Firing rate and spectral analysis of network without plasticity, 11.20 kHz**.

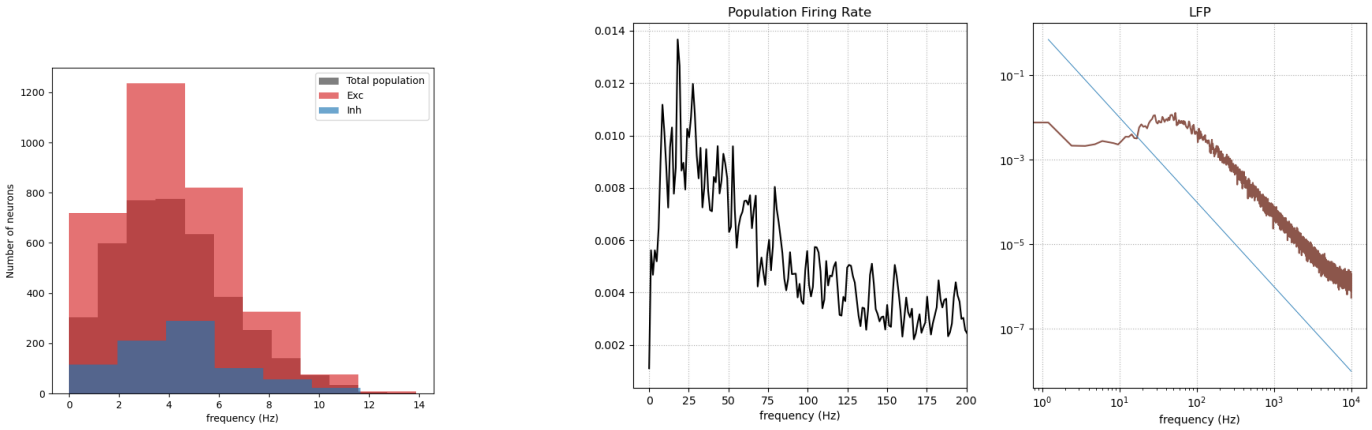

Figure 15: **Firing rate and spectral analysis of network with STP, 11.20 kHz**. (left panel) Single neurons firing rate distribution, two different distribution are clearly visible for E (mean 4.32 Hz) and I population (mean 4.38 Hz). (Right panel) Power spectrum of population firing rate and LFP, power spectra are averaged from 5 trials for 3 seconds with different realization of Poisson input, only data after 500 ms are taken to compute the analysis. There is a pronounced oscillation at 18 Hz

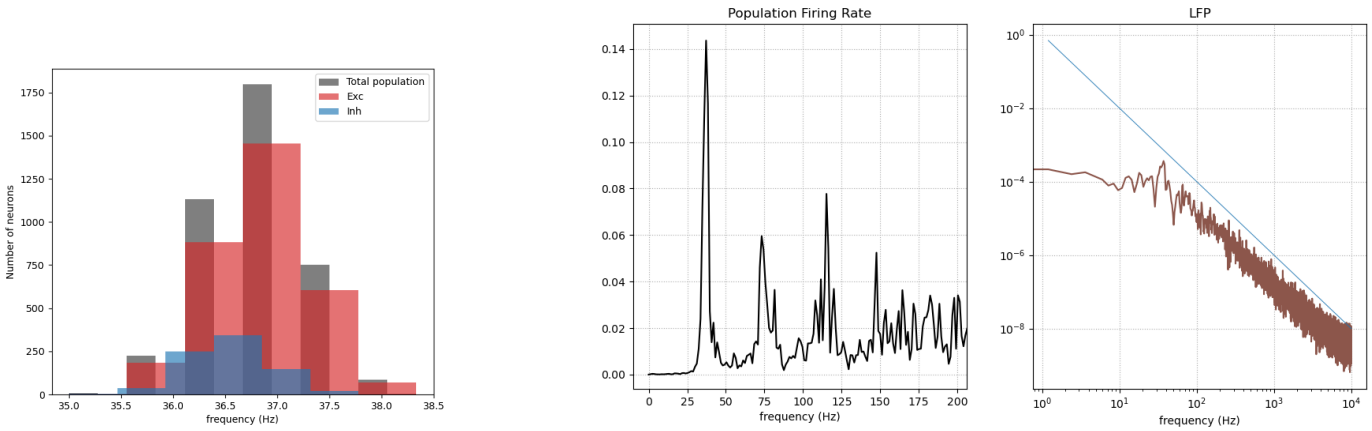

Figure 16: **Firing rate and spectral analysis of network without synaptic connections, 11.20 kHz**.

CV POPULATION - STP
exc : 0.03485
inh : 0.03493
CV POPULATION - no connection
exc : 0.06367
inh : 0.06367

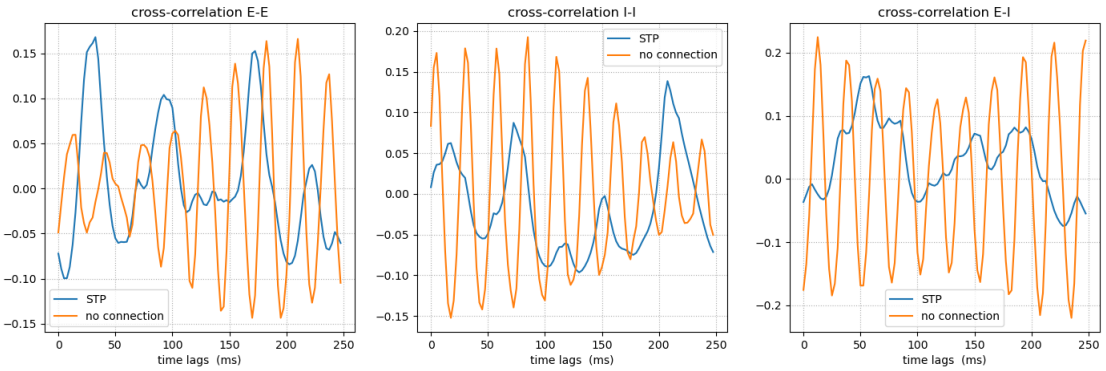

Figure 17: **Cross correlation function iter- and intra-population,** $g = 0.25$ **- 11.20 kHz**

One possible conclusion is this model does shows a proper scaling feature with respect to the ratio about recurrent currents, thus only for strong inhibitory parameters the dynamical behavior is compatible with fisiological data. Anyway, to illustrate the action of gliomodulation, the following network are selected:

- $g = 5.0$ $s = 1.15$: provides fast spiking inhibitory neurons and recurrent balance with the problem underline in previous paragraph. The effect of gliotrasmission is clearly visible
- $g = 0.25$ $s = 1.00$: does not provide fast spiking and, as illustrate below, the astrocytic modulation is not easy visible at network level.
- $g = 1.5$ $s = 1.05$: middle ground between two previous model.

The problem arise in the fist one depends on the high increasing of recurrent excitation with respect the same amount of recurrent inhibition. One possible way to increase the recurrent exitatory input keeping fix the original ([1]) E/I ratio is changing the synaptic strength according to:

$$\begin{aligned} g = \frac{p_e}{p_i} = \frac{w_i\, N_i}{w_e\, N_e} \\ \tilde{w_x}\tilde{p_x}N_x = w_x p_x N_x \end{aligned} \tag{3}$$

The fist equation sets the recurrent balance and, in particular, $g > 0.25$ leads to increase the excitation. The second one allows to change new synaptic strength (tilde variables) for both type of neurons ($x = e, i$) keeping fix the original E/I ratio (right side of equation).

2 Neuron-Glia Network

Neuron-Glia network is composed by two population of LIF neurons: N_e excitatory and N_i inhibitory, the network connectivity is sparse and random and is provided by short-term plasticity synapses, only the glutamatergic synapses are modulated by N_a astrocytes in homosynaptic fashion.
Neuro-Glia network dynamics is studied looking at release-decreasing effects for short time simulation - 12 seconds - and the goal is to analysed what kind of differences introduce the gliamodulation on "baseline" networks dynamics (before astrocytic activation). Each networks is stimulated by constant external stimulus at 7.63 kHz and both the mean values and the power spectra are computed over a time windows of 2.5 seconds as in baseline condition. In each simulation the astrocytes' firing divides the time window in three different regions: the first one is the baseline condition where the gliotrasmission is not activated yet, in the second (after GRE1 - 2.85 seconds) and in the third (after GRE2 - 9.10 seconds) the modulation is present.

Heterogeneous external connection - $g = 5.0$ and $s = 1.15$

The data about fast spiking activity of inhibitory neurons lead to introduce the heterogeneous external connection. For this situation inhibitory neurons receive stronger external input than exitatory ones. The main consequence is the populations firing rates are not longer equals, in particular the inhibitory firing rate is higher than excitatory one (Figure (5).

The external excitatory input activats both populations in different way: the current on excitatory is 98.36 ± 0.06 pA and on inhibitory is 117.23 ± 0.07 pA. After the gliotrasmission, recurrent excitatory current decreases and the original degrees changes Figure (18).

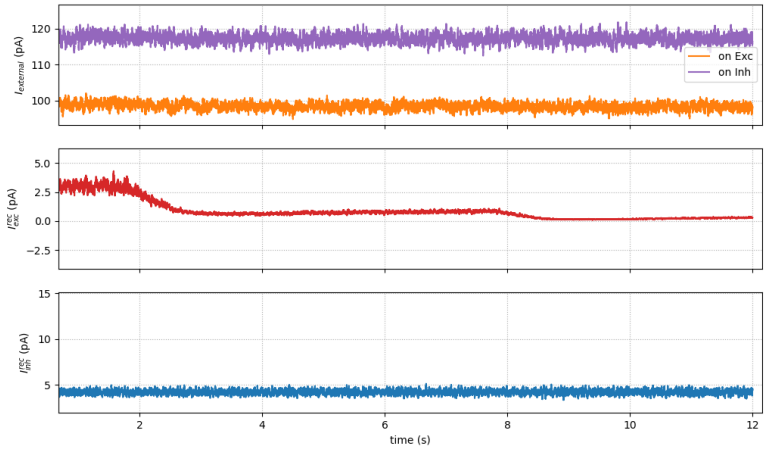

Figure 18: **Network $g = 5.0$ - $s = 1.15$, external and recurrent current, 7.63 kHz.** (Top panel) External excitatory input on inhibitory (purple) and exitatory (orange) population. (middle panel) Recurrent excitatory current. baseline: 3.02 ± 0.02 pA; GRE1: 0.72 ± 0.01 pA; GRE2: 0.19 ± 0.08 pA. (bottom panel) Recurrent inibitory current. 3.7± 1.9 pA. Mean and standard deviation are computed on a sample of 200 excitatory and inhibitory neurons. The error is estimated by blocking techniques.

The release-decreasing effects are clearly visible looking at the mean values of firing rate in Table (1), astrocytes secretions leads to decrease the firing rate but, the main effect of the gliotrasmission is the to annihilation of the network oscillation in baseline condition shown in left panel of Figure(7), the power spectra both in GRE1 an in GRE2 shows the typical noise behavior.

Baseline	after GRE 1	after GRE 2
8.60 ± 0.03 Hz	6.67 ± 0.03 Hz	6.24 ±0.02 Hz
exc: mean=5.85 Hz	exc: mean=3.85	mean=3.41 Hz
inh: mean=19.59 Hz	inh: mean=17.90	inh: mean=17.55 Hz

Table 1: Population firing rate at baseline condition, after GRE1 (4 - 6.5 s) and after GRE2 (9 - 11.5 second). Mean and standard error are compute over the convolution of original signal by Gaussian filter of 5 ms width. The error is estimate by blocking technique.

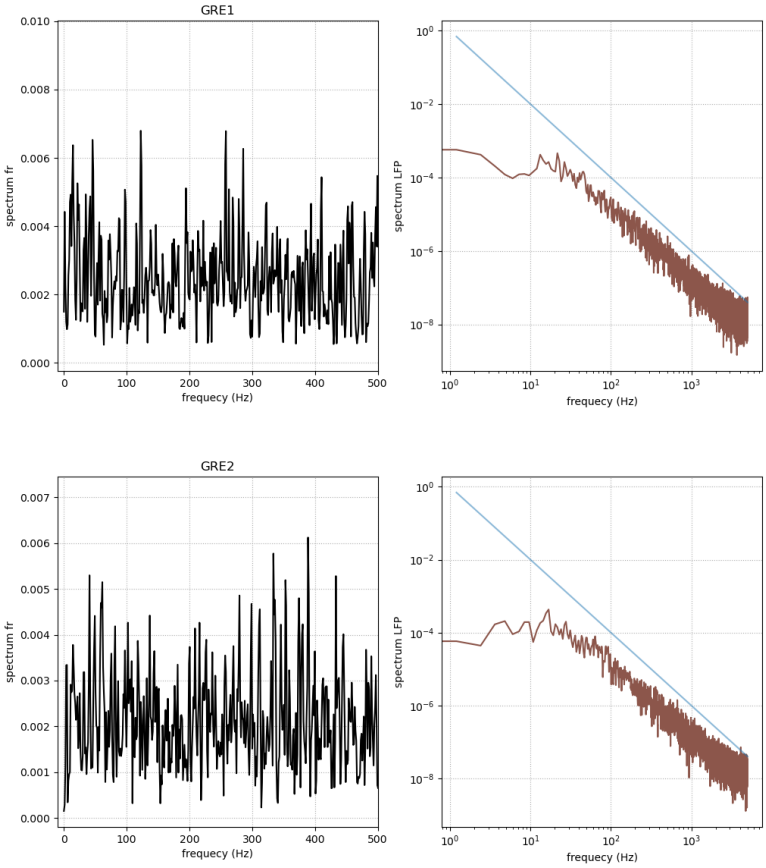

Figure 19: **Network $g = 5.0$ - $s = 1.15$, spectral analysis after astrocytic activation, 7.63 kHz**. (Top row) after GRE1. (bottom row) after GRE2

In conclusion the modulation of glutamatergic synapses leads to decrease excitatory input, therefore changing the recurrent balance. The network oscillation generates in baseline condition for original recurrent ratio is compromise after astrocityc modulation and, for this reason disappears. Due to excitatory neurons' firing rate distribution (Figure (20)) it could be possible by facilitation effects that, in steady states, the original balance is - at least partially - restore and the networks oscillation arise again.

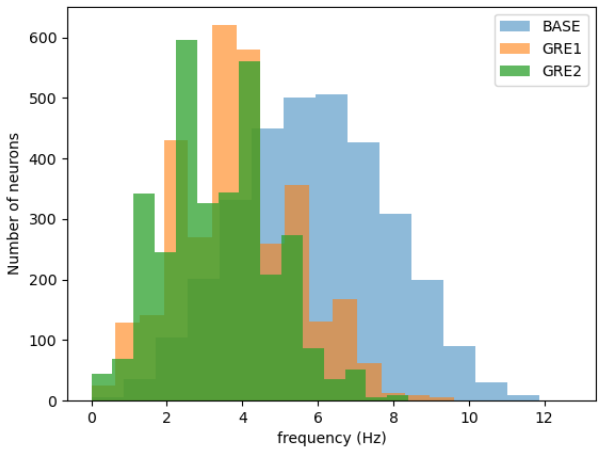

Figure 20: **Excitatory firing rate distribuction, $g = 5.0$ - $s = 1.15$, 7.63 Hz** How firing rate distrubution changes with two consecutive astrocytic activation.

Homogeneous external connection - $g = 0.25$ and $s = 1.00$

In this section I want to analysis the network dynamics defined by the same parameters in [1] but the external input comes from synaptic contacts. With this set of parameters the external input activates in the same way both type of neurons, and the networks dynamics is driven by strong recurrent inhibition. In this situation the release-decreasing effect modulates the excitatory recurrent current (Figure (21)) but, despite the previous situation, the changes of population firing rate are not such stronger (see value in table (2)), for istance there is not statistical differences between baseline and GRE1 values.

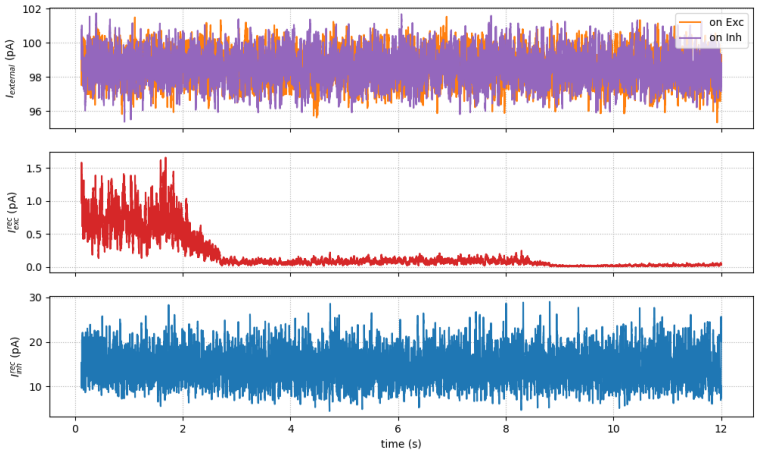

Figure 21: **Network $g = 0.25$ - $s = 1.00$, external and recurrent current, 7.63 kHz.** (Top panel) External excitatory input on inhibitory (purple) and exitatory (orange) population: 98.55 ± 0.04 pA. (middle panel) Recurrent excitatory current. baseline: 0.68 ± 0.03 pA; GRE1: 0.081 ± 0.002 pA; GRE2: 0.019 ± 0.001 pA. (bottom panel) Recurrent inibitory current. 14.5 ± 0.2 pA. Mean and standard deviation are computed on a sample of 200 excitatory and inhibitory neurons. The error is estimated by blocking techniques.

Baseline	after GRE 1	after GRE 2
0.61 ± 0.01 Hz	0.60 ± 0.01 Hz	0.574 ± 0.009 Hz
exc: mean=0.6102 Hz	exc: mean=0.6066	mean=0.5723 Hz
inh: mean=0.5977 Hz	inh: mean=0.5810	inh: mean=0.5818 Hz

Table 2: Population firing rate at baseline condition, after GRE1 (4 - 6.5 s) and after GRE2 (9 - 11.5 second). Mean and standard error are compute over the convolution of original signal by Gaussian filter of 5 ms width. The error is estimate by blocking technique.

Even if the changes are not such stronger, the gliotrasmissions leads to effects on network oscillations in terms of power spectrum. The power spectrum in baseline condition shows oscillations into the range of 10 Hz arising from noise (top panel in Figure (22)), after the first astrocytic activation the intensity of noise seem to be less stronger. In other words the network oscillation might be more synchronized. A plausible explanation might be found into the ratio between recurrent inputs. In baseline condition network dynamics is driven by a ratio $I_{exc}/I_{inh} = 0.05$ while after GRE1 this ratio becomes 0.005 and, in both situation, networks oscillation arise in the same frequencies. This consideration drives me to the conclusion that network dynamics is completely inflenced by recurrent inhibition and, in this way, the recurrent excitatory inputs only acts as a nuisance. After GRE1 this nuisance is attenuate, therefore the network oscillations have been freed from the high noise's intensity, and it can be found this feature also after GRE2 (data not schown). Inserisci la parte del rapport fr/noise per validare quanto detto, se vuoi anche la sincronizzazione.

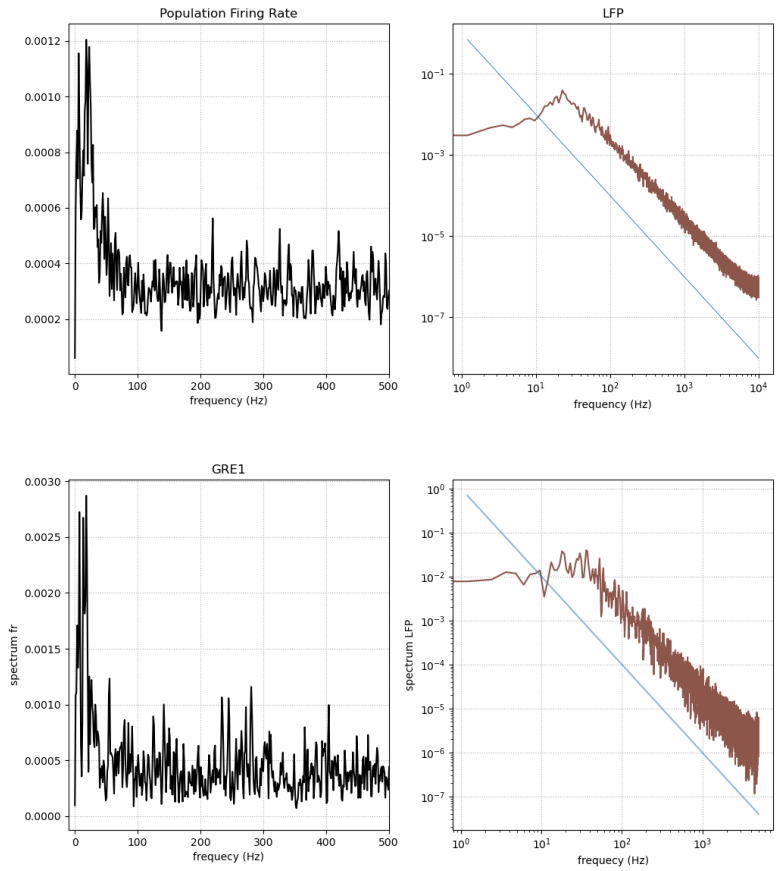

Figure 22: **Network $g = 0.25$ - $s = 1.00$, spectral analysis before and after astrocytic activation, 7.63 kHz**. (Top row) baseline condition - mean over 5 trial. (bottom row) after GRE1 single trial

The last consideration concern the firing rate distribution. In this situation, ideed, the bulk of excitatory neurons fire at rate low than 1 Hz (Figure (23)), thus in the steady state the release-decreasing effects continues to dominate the facilitation and, as a consequence, the values of recurrent excitation should not reach it's original value.

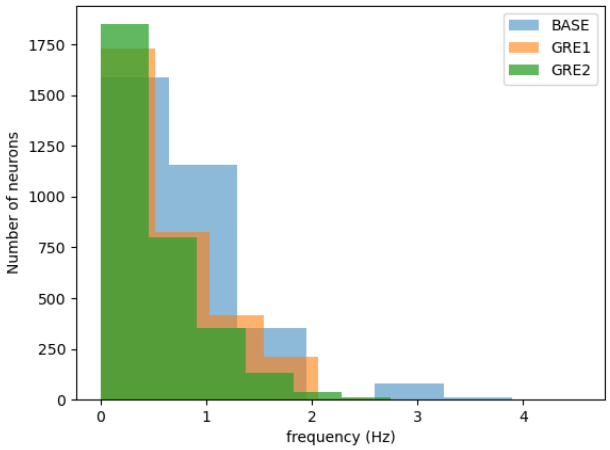

Figure 23: **Excitatory firing rate distribuction, $g = 0.25$ - $s = 1.00$, 7.63 Hz** How firing rate distrubution changes with two consecutive astrocytic activation.

Middle ground - $g = 1.5$ **and** $s = 1.05$

From the analysis of previous network, it is possible deduce two different limitations: the former does not shows emerging feature on networks dynamics, the latter does not describe fast spiking feature of inhibitory population. For this reason I have gone for a set of parameters in the middle ground: $g = 1.5$ and $s = 1.05$.

According to heterogeneous external connections the inhibitory population fires with a mean firing rate higher than excitatory one, in particular into the range 44 - 55 Hz, the ratio goes from 10 to 2.5 (Figure (24)).

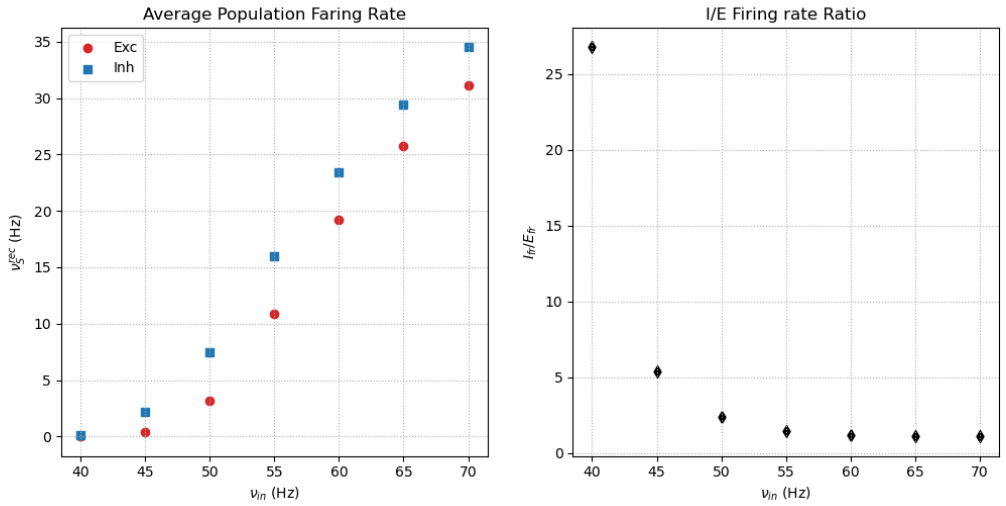

Figure 24: **Average population firing rates in heterogeneous scenario -** $g = 1.5$ **and** $s = 1.05$**.** (left panel) Average excitatory (red balls) and inhibitory (blue square) firing rate.(right panel) Ratio between inhibitory and excitatory recurrent currents, the ratio I_{fr}/E_{fr} lies into the range 10-2.5 between input frequencies 47 - 55 Hz. Parameters: $g = 1.5$, $s = 1.05$ and $w_e = 0.05$ nS, time simulation 3.5 second with of step 0.05 ms, only data after 500 ms are tacking into account to compute the mean values.

Without any king of astrocytic modulation, i.e. baseline condition, and for an input frequency of 7.63 kHz, the neurons fire in irregular fashion at frequency lower than 10 Hz while network oscillation at 15 Hz emerges from population firing rate power spectrum (Figure (25)).

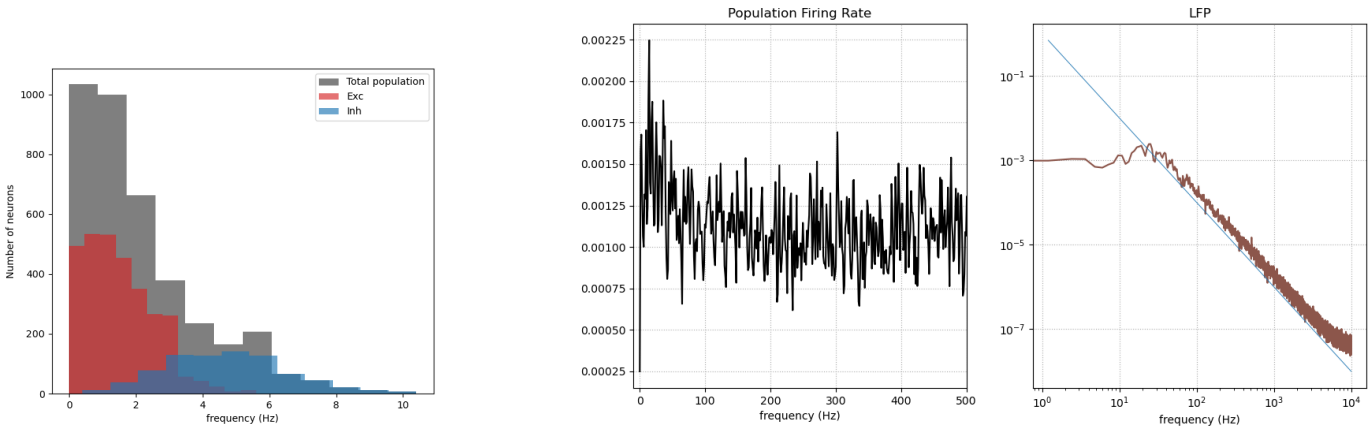

Figure 25: **Firing rate and spectral analysis of network** $g = 1.5$ **and** $s = 1.05$**, 7.63 kHz**.(left panel) Single neurons firing rate distribution, all neurons fire at rate lower than 10 Hz. (Right panel) Power spectrum of population firing rate and LFP, power spectra are averaged from 6 trials for 3 seconds with different realization of Poisson input, only data after 500 ms are taken to compute the analysis. There is a pronounced oscillation at 15 Hz.

As in the previous discussion, a decreasing of firing rate is appreciable as well as power spectra in Figure (26), in particular it is visible a modulation of lower than 1 Hz according to the filtering characteristic induced by short time simulation. and the gliomodulation tends to press the neurons firing rate to lower value moving the mean of distribution on left Figure(27).

Baseline	after GRE 1	after GRE 2
2.05 ± 0.05 Hz	1.85 ± 0.01 Hz	1.814 ± 0.008 Hz
exc: mean=1.4153 Hz	exc: mean=1.2372	mean=1.2080 Hz
inh: mean=4.6170 Hz	inh: mean=4.3080	inh: mean=4.2400 Hz

Table 3: Population firing rate at baseline condition, after GRE1 (4 - 6.5 s) and after GRE2 (9 - 11.5 second). Mean and standard error are compute over the convolution of original signal by Gaussian filter of 5 ms width. The error is estimated by blocking technique.

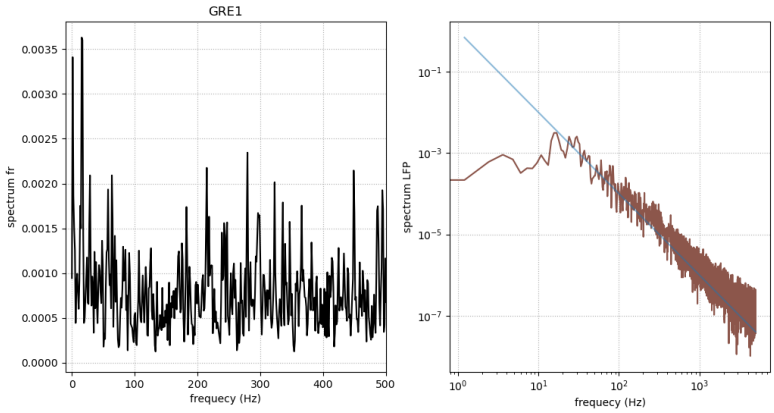

Figure 26: **Network** $g = 0.25$ **-** $s = 1.00$**, spectral analysis after astrocytic activation, 7.63 kHz**.

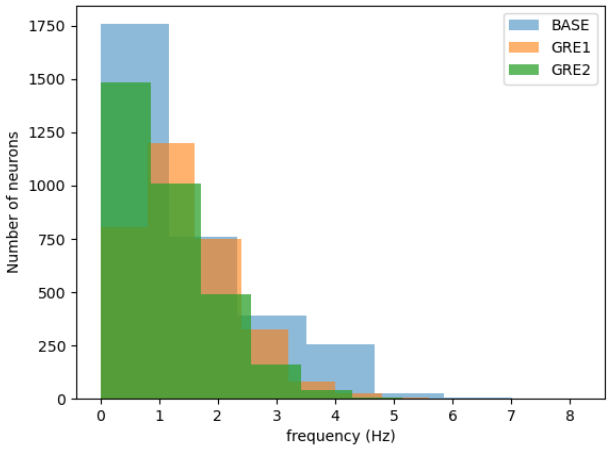

Figure 27: **Excitatory firing rate distribuction,** $g = 1.5$ **-** $s = 1.05$**, 7.63 Hz** How firing rate distrubution changes with two consecutive astrocytic activation.

3 Summary and considerations

In conclusion the gliotrasmission modulation in this study-cases point out different feature with respect to network parameters: for a recurrent balance (first scenario) network destroy oscillations coming from the

low level of synaptic connection induced by STP, for strong inhibitory network (second scenario) the glia basically act as a denoising filter. However, this type of behaviors can be interpreted as a consequence of release-decreasing effect that decrease recurrent excitatory currents. All the dynamical and spectra consideration above strongly depends on original excitatory/inhibitory balance.
The interesting considerations emerge in the astrocytic steady state - after 20-30 seconds - thereby release-decreasing effect is flanked by facilitation. Accordingly, depends on the neurons' firing rate distribution and the original E/I ratio, it could be possible visualize dynamical feature as the growing of network oscillation that became 'fixed' at saturation time. In this sense in it should be possible analyse what happens if, for same circumstance (for instance a neuro-disease that kills astrocytes), the gliotrasmission modulation is not further presents: in this case, what is the sort of network oscillation emerging by tripartite synapses?

Appendix A Astrocytic connection distribution

Only excitatory synapses can activate astrocytes and be modulated by them, restricting in this way our focus on the experimentally well-characterized pathway of closed-loop glutamatergic gliotransmission. Both neurons and astrocytes are arranged on square lattices with distance of 59 μm (Figure (28)), in particular the astrocyte is responsible for which excitatory synapse is specified on the basis of the spatial position of postsynaptic neurons with respect to N_a astrocytes, in this way only one astrocyte surrounds postsynaptic neuron and is connected with its impinging excitatory synapses. Therefore, the number of connected neurons with astrocytes distribution is constant (Figure (29)).
To avoid the problem about the anomalus distribution presents in [1], also inhibitory neurons have a spatial position into the grid and I set the number of astrocytes N_a equals to the whole neuronal population ($N_e + N_i = 4000$)

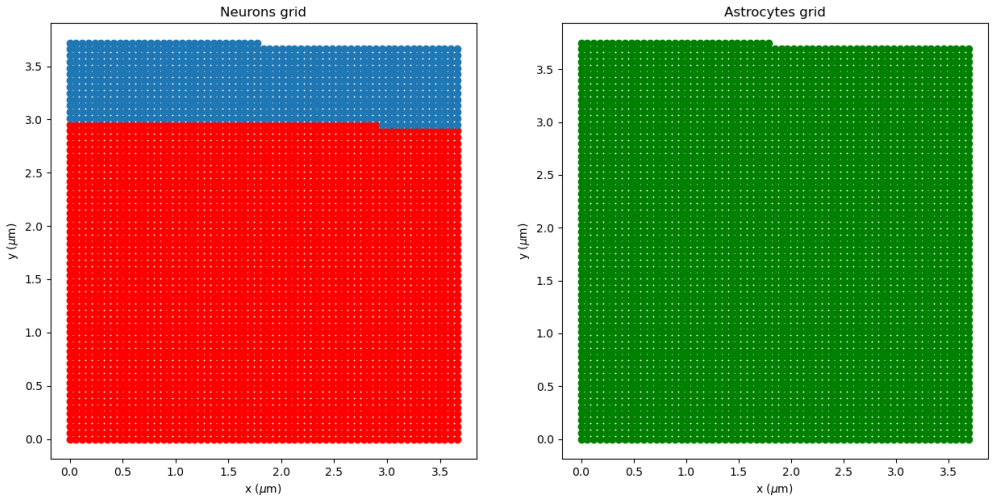

Figure 28: **Neurons and astrocytes spatial arrangement.** (left panel) Excitatory (red) and inhibitory (blue) arrangement. (right panel) Astrocytic arrangement.

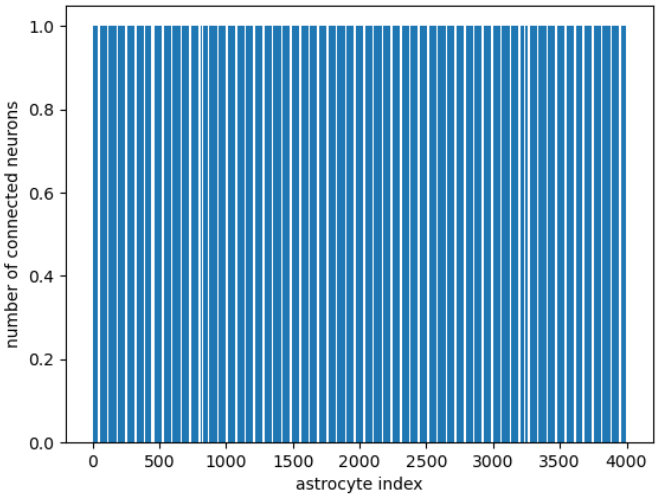

Figure 29: **Connected neurons distribution.**

Appendix B Homogeneous external connection and high excitatory recurrent current, $g = 5.0$ - $s = 1.0$

Previous results drives me to assume that the gliorelease modulation and in particular the release-decreasing effect is stronger for high recurrent excitatory input: The first step is to consider the same network with different degrees of balance g.

Keep fixed the number of neurons, synaptic strength and the probability connection, balance between recurrent inputs is provided by $g = 5$. Mean population firing rate are noticeably higher with respect to the previous case, due to the strong excitatory input, but the ratio I_{fr}/E_{fr} is still equals to 1.

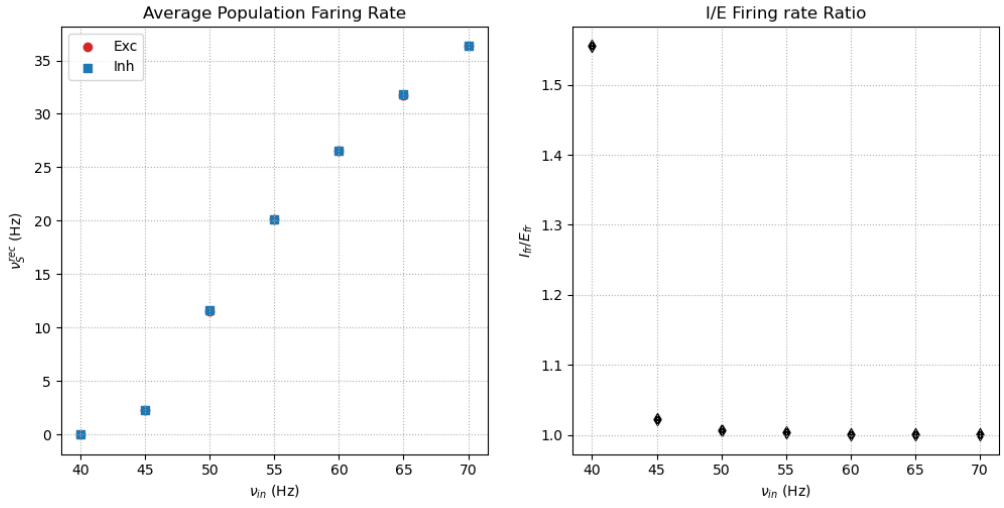

Figure 30: **Average populations firing rate, balanced network:** $g = 5.0$**,** $s = 1.0$ **and** $w_e = 0.05$ **nS**. (left panel) Average excitatory (red balls) and inhibitory (blue square) firing rate.(right panel) Ratio between inhibitory and excitatory recurrent currents. Interesting range to study gliorelease modulation is 42-50 Hz. Parameters: $g = 0.25$, $s = 1.0$ and $w_e = 0.05$ nS, time simulation 2.3 second with of step 0.05 ms, only data after 300 ms are tacking into account to compute the mean values.

To complete this preliminary study the network for $\nu_{in} = 7.63$ kHz is analysed for 20 seconds long time simulation. As expected, calcium oscillation shows 3 self oscillation and, for each of then, recurrent excitatory current is modulated, interesting at 20.0 seconds, both firing rate and excitatory input reach the values just after the first GRE. For this set of parameters both excitatory and inhibitory firing rates show visible modification due to astrocytic connection and, tough the systems does not reach its steady states, the facilitation effects is already appreciable.

It is possible deduce same important question: How the ratio $\mathrm{I}_{exc}/\mathrm{I}_{inh}$ drives network oscillations in presence of STP? The gliotransmission modulation modulates this quantity during time evolution, how this effect drives the whole dynamical systems? Is it possible to derive a mean filed description of network dynamics?

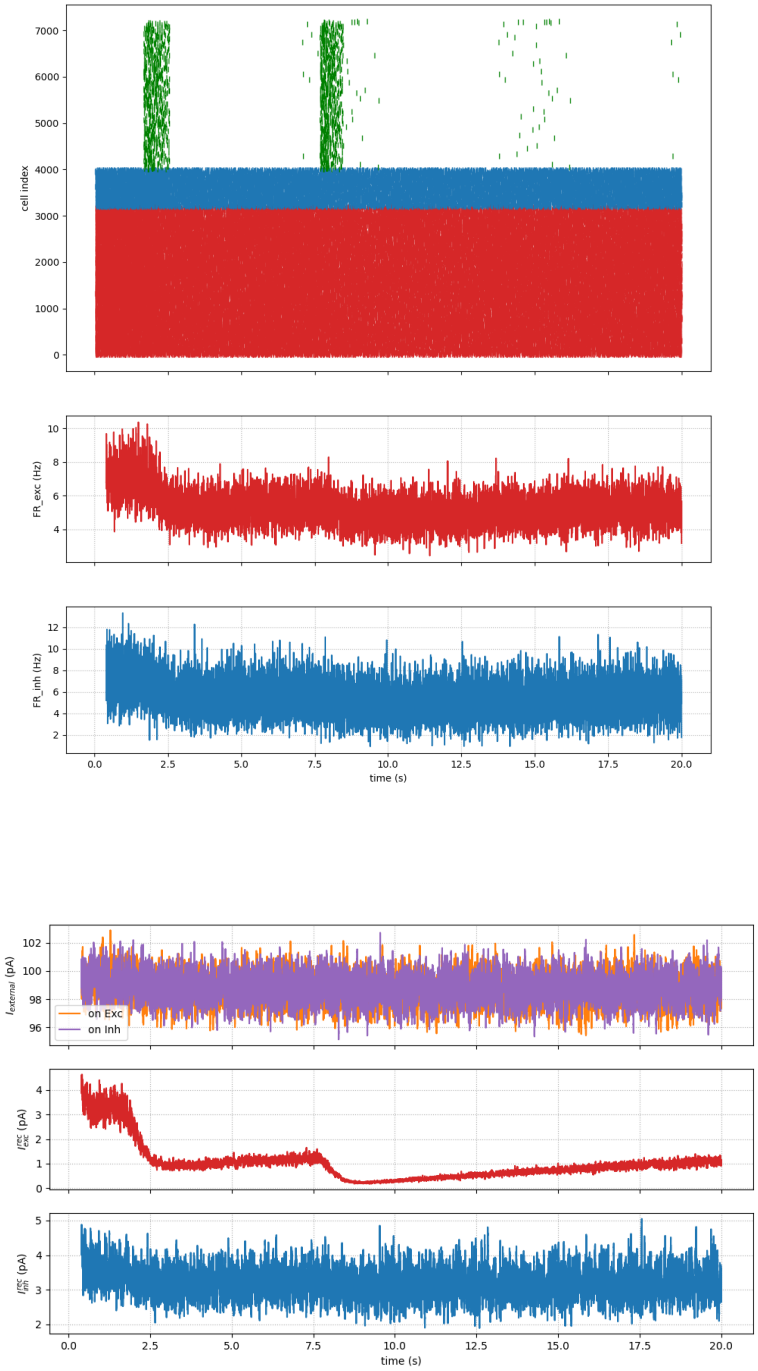

Figure 31: **Dynamics of the network for homogeneous connection, 20 seconds long simulation**. (Top row) Raster plot and population firing rates. Firing rates are smoothed thought gaussian filtering with windows of 1 ms. Notably the astrocytic activation deeply affected the recurrent currents balance: I_{exc}/I_{inh} passes from 0.95 to 0.14. (Bottom row) Mean values over 200 excitatory and inhibitory neurons of recurrent and external input. Parameters: $\nu_{in} = 47.7 * 160 = 7.63$ kHz, $g = 5.0$, $s = 1.0$ and $w_e = 0.05$ nS, time simulation 20 second with of step 0.1 ms, transient time 0.4 seconds

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.