

# Influence of external input and inhibitory synapses on the balance of a sparsely connected network of Leaky Integrate-and-Fire neurons.

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Bachelor thesis psychobiology

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ABSTRACT TO BE DONE

# Influence of external input and inhibitory synapses on the balance of a sparsely connected network of Leaky Integrate-and-Fire neurons.

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## Introduction

Understanding the computations underlying the activity we see in the human brain remains a big topic for research. Especially the irregular firing of neurons in the human cortical brain has been a topic for debate. One explanation is that the timing of the input is synchronized enough to evoke action potentials, as there is summation of input signals (Softky & Koch, 1993). A contradictory explanation says that synchronization is not necessary as long as there is a strong balance between excitation and inhibition. The average input is subthreshold and because of the stochastic input neurons react on minor deviations of the average, which lead to irregular firing (Shadlen & Newsome, 1998).

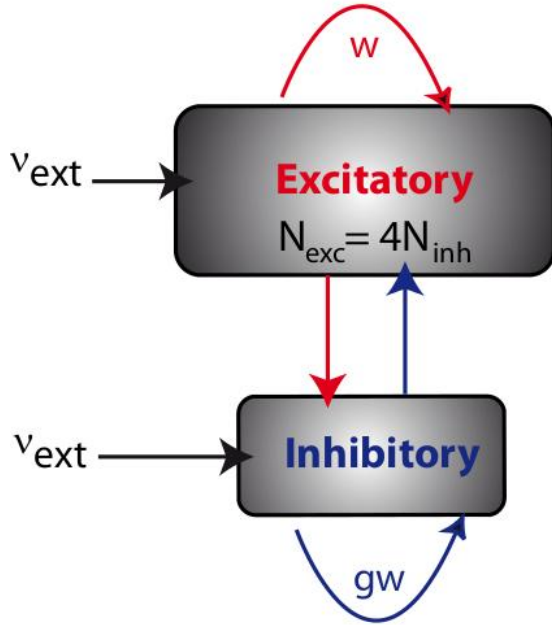
In order to examine the hypotheses it is very useful to perform simulations on computational models of the human cortex. In computational neuroscience there are numerous neuron and network models, all of them having advantages and disadvantages. Mostly the consideration is based on the computational performance versus biological plausibility (Izhikevich, 2004). Usually, one chooses the simplest model which still contains the minimal features to be able to answer the research question.

When examining the network dynamics of the cortex, simple neuron models are preferred, as the focus is more on the behavior of the network than on that of the single neurons. Moreover with simple neuron models there remains computational power left for large

network simulations. For the examination of cortical networks the connections should be recurrent as in the human brain. Thus a commonly used network is the sparsely connected Balanced random network (Brunel, 2000; Remme & Wadman, 2012; Yger & Harris, 2013).

The balanced random network, also called balanced network, is a large scale network of sparsely connected Leaky Integrate-and-Fire (LIF) neurons. It is called balanced as the network, when initialized, neither fades out nor becomes hyperactive. LIF neurons only take a few parameters in account which cause a linear approximation of the subthreshold membrane potential. A spike itself is not modeled. The behavior of a balanced network of the simplest LIF neurons is extensively examined, both analytically and computationally (Brunel, 2000).

This study showed that the balanced network could settle in four different states, based on synchrony and regularity. The network could reach the synchronous regular state, where single neuron fire regularly with a time constant similar to the refractory period and there is a lot of network synchrony. If neurons fire regularly but the different neurons asynchronously, it is called the asynchronous regular state. If single neurons fire irregularly, the network could reach the synchronous irregular and the asynchronous irregular states. The key parameters in the differentiation between these four states are the amount of external input (each neuron receives stochastic background input) and the



**Figure 1. Visualization of a balanced network.** A balanced network with a population of excitatory and inhibitory connection, both connected with itself and each other. Each neuron receives 4 times more excitatory input than inhibitory. Moreover each neuron receives external input.  $w$  is the conductance and  $g$  is the weight of the inhibitory conductance. (From <http://www.yger.net/the-balanced-network/>)

ratio between the conductance of excitatory versus inhibitory synapses (see Figure 1).

Other studies showed that network models with more biological plausible LIF neurons, in which the synapse is described in more detail, can reach balanced states as well (Yger & Harris, 2013). However, it is still unknown if these networks can reach the different states of synchrony and regularity, and whether the transitions between these states are similar to those of the simpler neuron model. **It is therefore examined whether a network model with more biological plausible LIF neurons can reach balanced states which differentiate between synchrony and regularity.** It is hypothesized that a balanced state will be reached, and that it is possible to differentiate between the different states, although the transitions will differ from simpler models.

This is examined by implementing a balanced network of LIF neurons and systematically

quantifying the regularity and synchrony of different combinations of the external input and relative strength of inhibitory synapses, which were the key parameters in *Brunel 2000*. It is expected that it is possible to differentiate between the four states bases on the quantification. Whether these transitions will be nominal or continuously is unknown, as the involved parameters are not linearly correlated to one another.

## Materials and Methods

### Simulations

Simulations of the spiking neurons were performed using the BRIAN 2 simulator (Goodman & Brette, 2009) with a fixed time step  $dt = 0.1 ms$  and a membrane time constant of  $\tau_m = 20 ms$ . All simulations were performed on a Packard bell EasyNote TK with 4GB RAM and 2,3 GHz AMD Athlon II P360 processor.

### Simple neuron model

For the simple LIF neuron model (adapted from *Brunel, 2000*) the following equation is used:

$$\tau_m V_i(t) = -V_i(t) + RI_i(t),$$

where  $RI_i(t)$  is the input each neuron receives, both from external input and from other neurons in the network. The external input is described by the equation:

$$RI_i(t) = \mu(t) + \sigma\sqrt{\tau}\eta_i(t),$$

where  $\mu(t)$  is the constant external input described by :

$$\mu(t) = v_{ext}\theta,$$

where  $v_{ext}$  is the frequency of external input and  $\theta$  is the threshold.  $\sigma\sqrt{\tau}\eta_i(t)$  represents the fluctuating input.  $\sigma$  is described by

$$\sigma = J\sqrt{C_E v_{ext} \tau},$$

where  $J$  represents the PSP amplitude,  $C_E$  represents the number of connections of excitatory neurons and  $\eta_i(t)$  represents Gaussian white noise with mean = 0 and SD = 1. Input from other neurons in the network is described by:

$$V_{post} = V_{pre} + (-g)J,$$

where  $V_{post}$  is the membrane potential after a spike,  $V_{pre}$  is the membrane potential before a spike and  $g$  is the relative strength of a inhibitory synapse ( $g = -1$  for excitatory synapses). The fixed parameter values are  $\theta = 20 \text{ mV}$ ,  $J = 0.1 \text{ mV}$ , the transmission delay  $D = 1.5 \text{ ms}$ , the refractory period  $\tau_{rp} = 2 \text{ ms}$  and the reset value after a spike  $V_r = 10 \text{ mV}$ . The remaining parameter space is thus the relative strength of the inhibitory synapses  $g$  and the external firing rate  $v_{ext}$ .

The number of excitatory ( $N_E$ ) versus inhibitory ( $N_I$ ) neurons are, resembling the ratio of anatomical estimates for neocortex, respectively 1600 and 400. The sparseness of the network ( $\epsilon$ ), which is the fraction of the number of total neurons which are connected with each neuron, was originally 0.1 (with a total number of neurons of 12500). However, to keep the simulations feasible, the number of neurons is scaled down, so the sparseness has to be scaled as well in order to retain balance (Golomb & Hansel, 2000). This new sparseness ( $\epsilon_{nieuw}$ ) value is described by:

$$\frac{1}{\epsilon_{nieuw}} - \frac{1}{N_{nieuw}} = \frac{1}{\epsilon_{oud}} - \frac{1}{N_{oud}}$$

where  $N_{nieuw} = 2000$ ,  $\epsilon_{oud} = 0.1$  and  $N_{oud} = 12500$ . After application of this scaling, the sparseness of the network  $\epsilon_{nieuw} = 0.4098$ . This means that every neuron has 0.4098 chance it receives a connection from any other neuron.

### More complex neuron model

The more complex neuron (adapted from Yger & Harris, 2013) is quite similar to the simple neuron model. However, in the more complex model, the conductance of excitatory and inhibitory neurons decays according to a linear equation after a spike instead of just an event at the spike time. Moreover, when a spike is fired, the conductance changes which leads indirectly to a change in membrane potential. In contrast, the simple model directly changes the membrane potential after a spike, without influence of the conductance.

In this model the equation of a neuron is:

$$C_m \frac{dV(t)}{dt} = g_{leak}(V_{leak} - V(t)) + g_{exc}(t)(E_{exc} - V(t)) + g_{inh}(t)(E_{inh} - V(t))$$

where  $C_m$  is the membrane conductance, here defined as  $\tau_m g_{leak}$ . The leak conductance  $g_{leak} = 10 \text{ nS}$ , the resting membrane potential  $V_{leak} = -75 \text{ mV}$ , the threshold  $V_{thresh} = -50 \text{ mV}$ , the reset potential  $V_{reset} = -55 \text{ mV}$  and the refractory period  $\tau_{refrac} = 5 \text{ ms}$ .

The synapses are modeled as instant changes of conductance when a spike is triggered, followed by an exponential decay, described by:

$$\tau_{exc} \frac{dg_{exc}(t)}{dt} = -g_{exc}$$

$$\tau_{inh} \frac{dg_{inh}(t)}{dt} = -g_{inh}$$

where the excitatory and inhibitory synaptic time constant are respectively  $\tau_{exc} = 5 \text{ ms}$  and  $\tau_{inh} = 10 \text{ ms}$  and reversal potentials are  $E_{exc} = 0 \text{ mV}$  and  $E_{inh} = -80 \text{ mV}$ .

To keep the simulations feasible, 800 excitatory and 200 inhibitory neurons are used. The sparseness  $\epsilon = .1915$ , scaled from .05 with 4500 neurons, as described

previously. Synaptic delays are randomly chosen from a uniform distribution between 0.1 and 5 *ms*. Initial synaptic conductances were randomly chosen from Gaussian distribution with means  $g_{exc} = 1 \text{ nS}$  and  $g_{inh}$  with  $SD = \frac{mean}{3}$ . Finally, each neuron receives input from an independent Poisson spike train at 300 *Hz*, through an excitatory synapse with conductance of  $g_{ext}$ . So the remaining parameter space in this model consists of the mean value of  $g_{inh}$  and the value for  $g_{ext}$ . The parameter values are varied in the simulations.

### Quantification of regularity and synchrony of the more complex model

For the parameters  $g_{inh}$  and  $g_{ext}$  exploratory simulations, based on previous studies, were performed in order to determine the range of values for the simulations. The range for  $g_{inh}$  is between 1 and 10 *nS*, for  $g_{ext}$  between 2 and 11 *nS*, as values  $< 2 \text{ nS}$  result in a network with too little activity. For these different values the network activity is quantified for regularity and synchrony. The regularity of a network is quantified by the coefficient of variation (CV), which is described by:

$$CV_{net} = \frac{1}{N} \sum_{i=1}^n \frac{SD_{ISI_n}}{mean_{ISI_n}}$$

where  $CV_{net}$  is the average CV value of a network,  $N$  the number of neurons in the network and  $ISI$  the distribution of the inter-spike-intervals.

The synchrony is quantified by a synchrony measure (SM), which is described by:

$$SM_{net} = \frac{1}{\sum_{i=1}^t freq_t} \frac{1}{T} \sum_{j=1}^t freq_t$$

where  $SM_{net}$  is the measure for synchrony of a network,  $freq$  is the frequency on a time step  $t$  and  $T$  the number of time steps. The

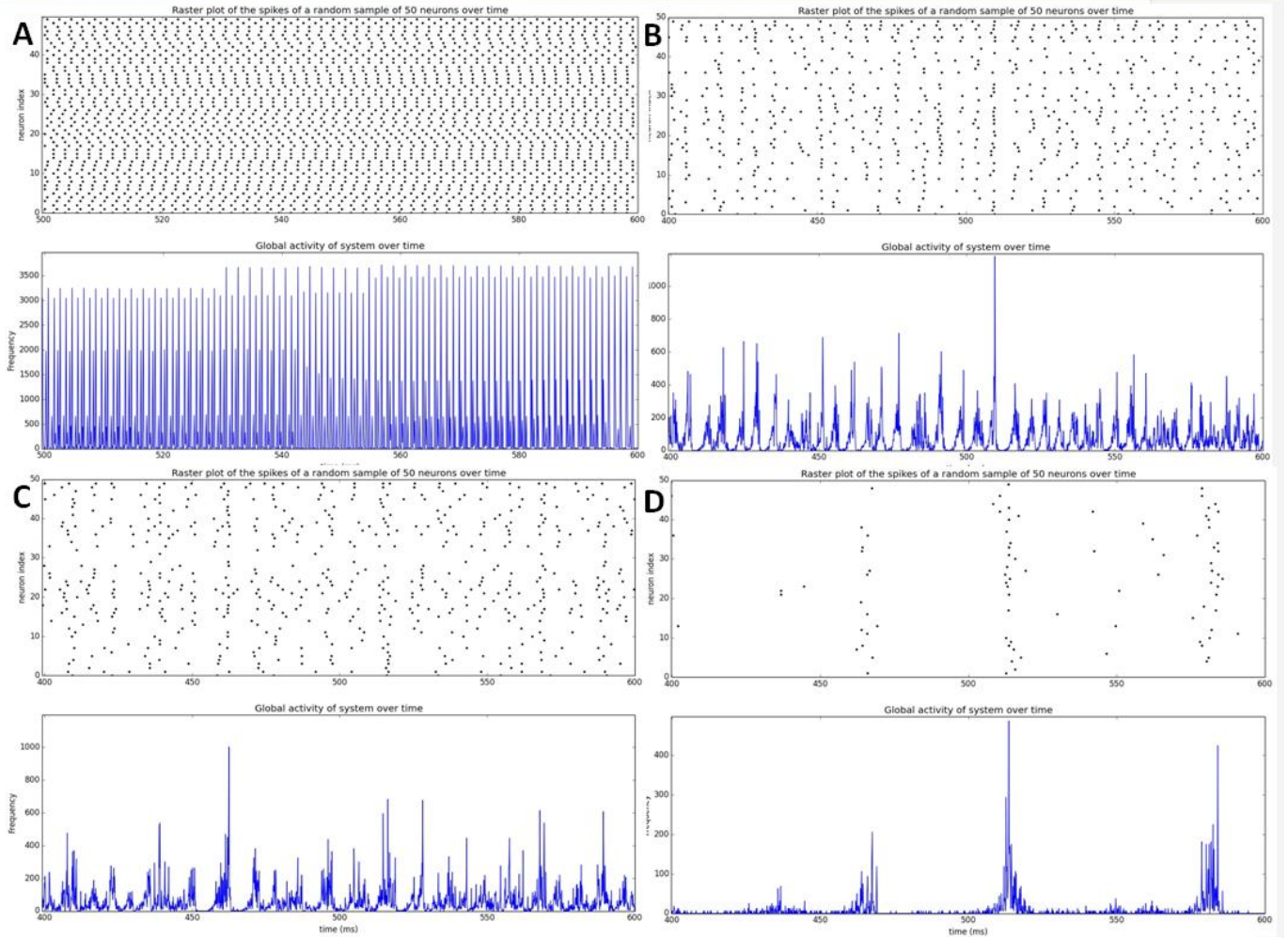
average frequency is corrected for the total activity of a network, so the SM is not biased by the total activity of a network, but merely by the level of synchrony.

### Statistics

After the quantification of both regularity and synchrony is completed, k means analysis were performed in order to objectively cluster the different parameter sets in different states. For the determination of the clusters the Elbow method is used (Ketchen Jr. & Shook, 1996). With this method the number of clusters is plotted against the total distance of the points of a cluster to the centre of that cluster. This distance usually decreases as the number of clusters increases. Initially the decrease is high and there usually is a flipping point after which the decrease is much lower. This is called the elbow point, and the value of the number of clusters of that point is used for the k means analysis. For the k means analysis the quantification data is scaled so both variables have the same weight in the determination of clusters. For the scaling each data point is divided by the total of the variable, so a fraction is used for the analysis.

### Results

The first step was to examine whether the same balanced states as *Brunel, 2000* could be reached with the simple neuron model. The Synchronous Regular (SR) state was reached with  $g = 3$  &  $v_{ext} = 2$ . The Synchronous Irregular (SI) state was reached with  $g = 6$  &  $v_{ext} = 4$ . The Asynchronous Regular (AR) state was reached with  $g = 5$  &  $v_{ext} = 2$ . The Asynchronous Irregular (AI) state, was reached with  $g = 4.5$  &  $v_{ext} = 0.9$  (see figure 2). Given that these balanced states could be reached with the simple neuron model, the model was extended to the more complex neuron model in order to see whether that model could reach different states as well.

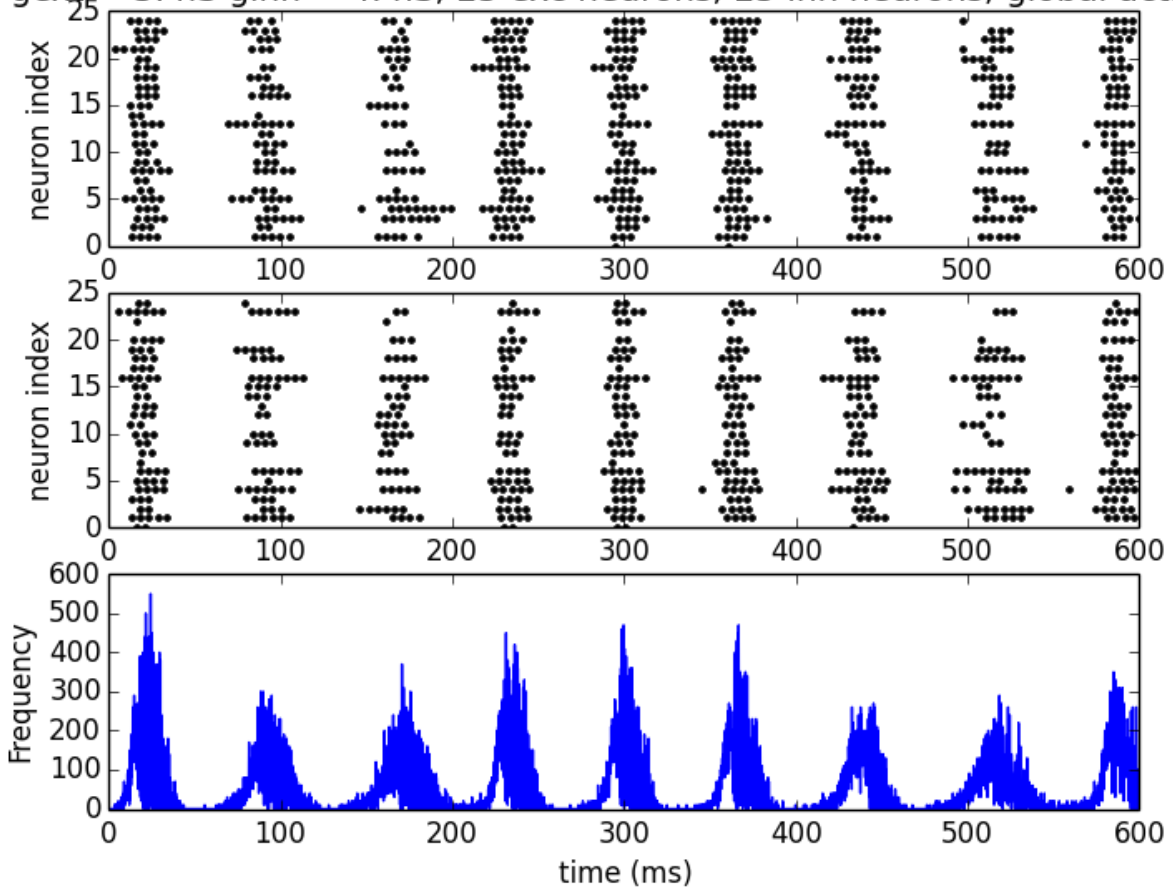


**Figure 2. Classification of different states of a balanced network of the simple neuron model.** Simulation of a network of 1600 excitatory and 400 inhibitory neurons with a sparseness of 0.4098. For all four situations the spiking behavior of 50 randomly chosen neurons of the population is shown in the upper plot, and the global activity of the network in the lower plot. **A.** The Synchronous Regular (SR) state, where neurons are synchronized and neurons spike regular (only the during refractory period the neurons are silent;  $g = 3$  &  $v_{ext} = 2$ ). **B.** The Synchronous Irregular (SI) state, where there is still synchrony in the global activity, but single neurons fire irregular ( $g = 6$  &  $v_{ext} = 4$ ). **C.** The Asynchronous Regular (AR) state, where is much less synchrony, but single neurons do tend to fire regular ( $g = 5$  &  $v_{ext} = 2$ ). **D.** The Asynchronous Irregular (AI) state, where the frequency is too low to speak of synchrony, and single neurons spike irregular ( $g = 4.5$  &  $v_{ext} = 0.9$ ).

To examine this, initial parameter values of *Yger & Harris, 2013* ( $g_{inh} = 8 \text{ nS}$ ,  $g_{ext} = 1 \text{ nS}$ ) were taken as starting point. With these values there was no balance, so the external input was increased to  $g_{ext} = 4 \text{ nS}$  in order to reach a balanced state. From this point an explorative simulation was conducted to find the ranges of interest to find different balanced states. Simulations were conducted with  $g_{inh}$  between 1 and 10  $\text{nS}$  and  $g_{ext}$  between 1 and 10  $\text{nS}$ . This resulted in different states of balanced networks.

When external input was too low ( $g_{ext} < 2 \text{ nS}$ ) there was too little activity to speak of a balanced network. When external input is increased and inhibition is kept low, the network reaches the SR state. When inhibition increases, roughly between 3 and 5  $\text{nS}$ , there appears a state not described in the simple neuron model: a Bursting Synchronous state (BS; see Figure 3). When inhibition is increased more, there arises a sort of AI state. Without quantification it is hard to determine whether there are SI and AR states. Therefore

$g_{ext} = 3$ .  $nS$   $g_{inh} = 4$ .  $nS$ ; 25 exc neurons; 25 inh neurons; global activity



**Figure 3. Network activity of a network in the Bursting State (BS).** Simulation of a more complex neuron network of 800 excitatory and 200 inhibitory neurons with a sparseness  $\varepsilon = 0.1915$ . The spiking behavior of 50 randomly chosen neurons of the population is shown in the upper plot, and the global activity of the network in the lower plot. Parameters used are  $g_{inh} = 4$   $nS$ ,  $g_{ext} = 3$   $nS$  and the network shows bursting behavior.

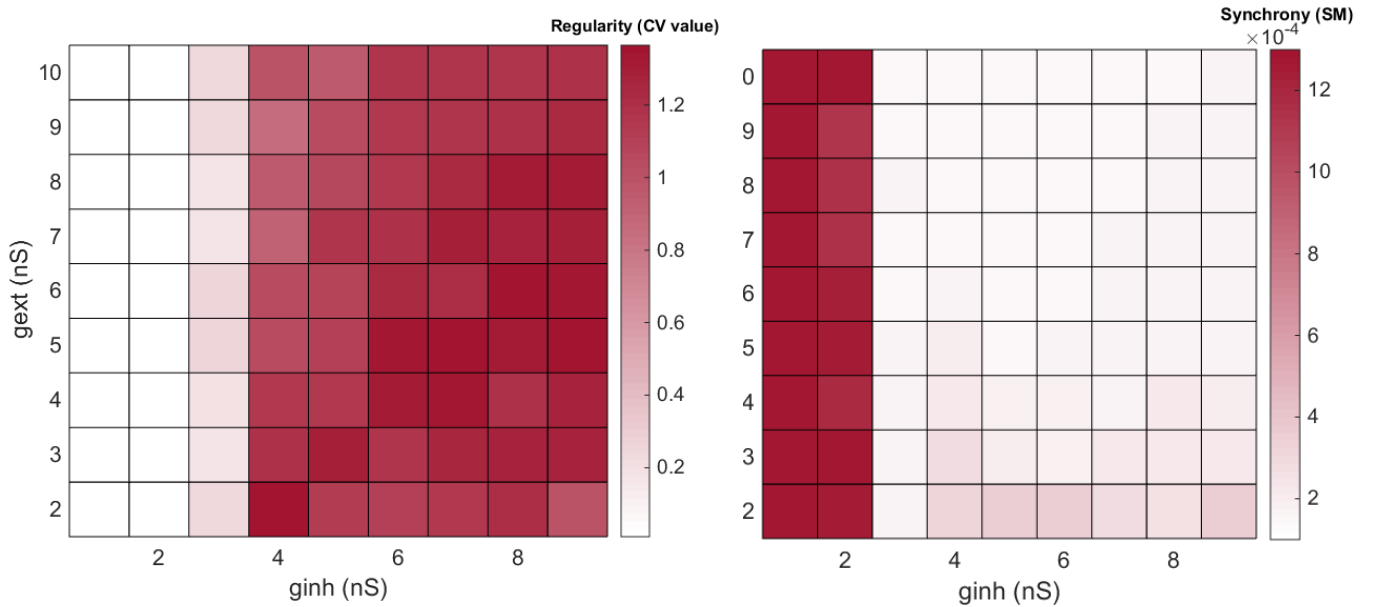
simulations were performed again to calculate the objective measure for regularity and synchrony.

To be able to differentiate different states objectively, the Coefficient of Variation (CV) and the Synchrony Measure (SM) were calculated for respectively regularity and synchrony. A low CV value means regular behavior, CV values around 1 are similar to a Poisson process, and therefore highly irregular. The different values of the CV are plotted in Figure 4. The figure shows that values of  $g_{inh} < 3$ , independent of the value of  $g_{ext}$ , all cause very regular spiking behavior.  $g_{inh} = 3$  is a transition value, as all

values of  $g_{inh} > 3$  cause very irregular behavior.

For synchrony a similar approach is used. However, a high SM value means synchronous behavior in contrast to the CV values. The SM values are plotted in figure 4. Values of  $g_{inh} < 3$  show very synchronous behavior. Moreover, for low values of  $g_{ext}$  the network shows more synchronous behavior than higher values of  $g_{ext}$ . When the measures for regularity and synchrony are combined, the SR state, for  $g_{inh} < 3$ , is easily visible. But to classify other states, objective quantification is needed.





**Figure 4. Plots of the degree of regularity (left) and synchrony (right) of balanced networks with more complex neurons with different parameter sets.** On the left the regularity of the network is plotted for the parameters  $g_{inh} = 1 - 10 \text{ nS}$  and  $g_{ext} = 2 - 11 \text{ nS}$ . On the right the same ranges are used, but now the degree of synchrony is plotted.

K means analysis is used as objective classification method. The elbow method is used to determine the number of clusters. As shown in Figure 5, the flipping point is at 3 clusters, so k means will be performed with 3 clusters. The analysis reveals 3 clearly separated clusters (figure 5): The SR state (green), a transition state where some neurons are still in the SR state whereas other are more silent (yellow) and a AI state, where irregular neurons fire asynchronously (blue).

## Discussion

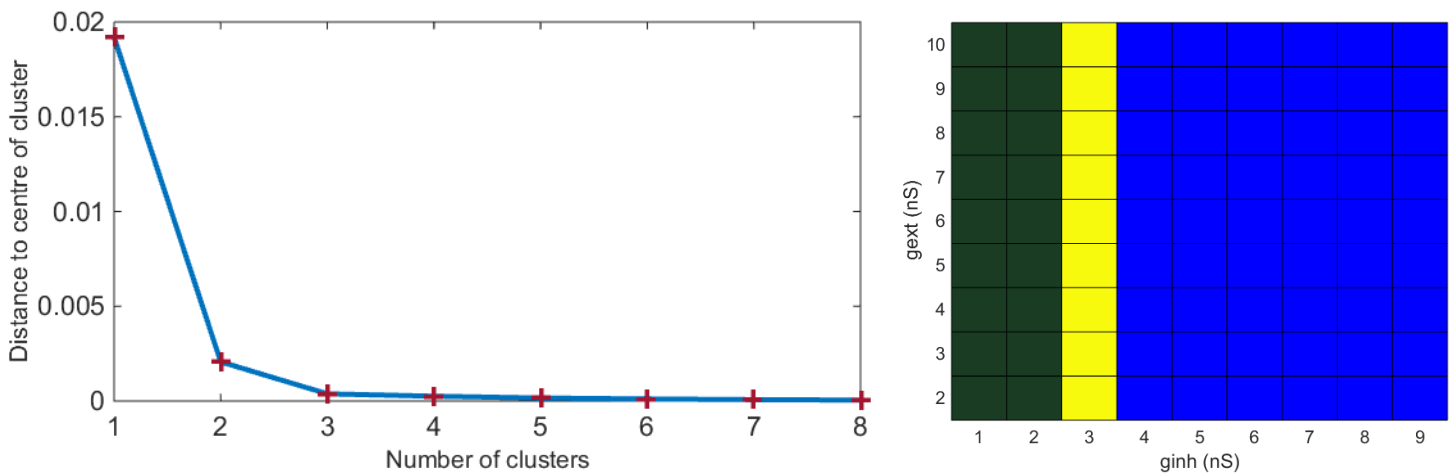
After four different balanced states of the simple neuron model were found, it was examined whether a more complex neuron model could settle in four different states, based on regularity and synchrony, as well. Cluster analysis showed that there were merely three different states, where the difference was solely based on both parameters together. So there is a synchronous regular state, a transition state and a asynchronous irregular state. This is probably because the networks show a different global activity: bursting behaviour. So The more complex model could reach

balanced states, but the behavior differs a lot from the simple neuron model, as the more complex model shows strong bursting behavior.

This difference in behavior could have several causes. Firstly, the extra feature, which makes the network more complex, could explain the difference. This extra feature, the exponential decay of the conductance which was raised after a spike, causes that when a spike is fired, the postsynaptic neuron remains more sensitive for another spike. Therefore a neuron fires regularly in a burst. However, the time constant of the inhibitory synapse is higher, which means the inhibitory neurons remain longer sensitive so eventually the burst is inhibited and there is some time no spiking. After some time the external input is strong enough to get the neuron in a burst again.

Besides this explanation, which could be a plausible one, there is one other difference between the networks which could have a major influence. The more complex neuron models has initial conductance weights drawn from a Gaussian distribution, whereas the simple model has fixed values. In the network





**Figure 5. K means analysis of the more complex neuron model to cluster based on regularity and synchrony.** On the left the elbow method is shown. The flipping point is at 3 cluster, which means that 3 clusters are used for the k means analysis. On the right the output of the k means analysis is shown. Three clusters are grouped based on regularity and synchrony. The green cluster is the SR state, the yellow cluster the transition state and the blue cluster the AI state.

behavior this is represented in the transition states, which is more present in the more complex model. This could be due this neuron characteristic, as there are neurons with low conductance and neurons with high conductance. This means that when  $g_{inh}$  increases some neurons with a high initial conductance still receive enough external input to fire regularly, whereas the neurons with a lower conductance receive too little external input en start firing less. This causes less regularity and synchrony, but enough to prevent the bursting state.

Moreover there is a whole range of other parameter set used for the more complex neuron model compared to the simple model. Two different models are used so it is impossible to explain the influence of every parameter. It is probable that the two parameters previously discussed have the biggest share in the different behavior, especially because this could be theoretically explained. However, it should be kept in mind that these two parameters are not the only candidates.

The simple neuron model, thoroughly examined by *Brunel, 2000*, was used to

examine irregular behavior of a network in order to say something about what causes the irregular behavior in the human brain. In this study, an adaptation of the model of *Yger & Harris, 2013* is quantified for regularity and synchrony as well, and appears to behave as an asynchronous irregular network as well. As this is a more biological plausible network, it could be used to examine the influence of different parameters on the activity, and predictions for human cortical activity can be made.

Future studies can show what the influence of other parameters is on the activity of a balanced network, especially the irregular asynchronous state. Furthermore, more realistic components of neurons or synapses can be added and their influence examined. With the continuing growth of the computational power, more detailed models of neurons can be connected in a large scale network and simulations can still be run in a reasonable time. This could give more insight in how these networks behave and how they are influenced, and hopefully this will lead to a better understanding of the computations made in the human brain.

Examined is whether a more complex neuron model can reach balanced states similar to a simpler neuron model which can do. It is shown that this more complex neuron model is able to do that, but that the behavior is different, due to extra biological plausible characteristics. This model and extensions of it can be used to examine influence of different parameters of a neuron on the network activity. This network activity resembles the cortical activity in the human brain. Future research can help to understand the underlying mechanisms of this activity and therefore get more insight in the computations of the human cortical brain.

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