Multimodal integration through inhibition mediated phaselocking

(Bachelorproject)

Matthijs Dorst, s1380982, m.c.dorst@ai.rug.nl,
R.A.J. van Elburg *

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Abstract

We hypothesize that multimodal integration can occur through inhibition mediated double phaselocking on a population of cortical pyramidal neurons. Using the NEURON modelling environment two network structures are created: a simple network is used to simulate double phaselocking on multiple oscillatory input streams by a pyramidal cell in a noisy stimulus condition, demonstrating that a more coherent stimulus can induce an increase in connection strength through a spike timing dependent plasticity model for an AMPA synapse. A more complex network is then used to demonstrate how single pyramidal cells can be recruited to entrain for multiple inputs while populations of inhibitory interneurons stabilize the network and mediate selecting only specific pyramidal cells.

1 Introduction

It has been observed that two non-harmonic oscillations can occur within the same cortical column [1]. There are strong indications that these oscillations play an important role in (temporarily) binding neuron assemblies [2] and can facilitate learning [3]. Specifically, inhibition mediated phaselocking in pyramidal cells could result in increased network plasticity explaining pyramidal cell entrainment [4][5].

Enhanced gamma band oscillations are known to be correlated with stimulus selection [6]. It has been shown [7] that more coherent excitatory stimuli are more likely to elicit a postsynaptic event than less coherent stimuli. When the target includes inhibitory interneurons this effect has been shown to increase significantly [8] which might be related to selective attention [3].

Combining findings from prior research could possibly explain phenomena on a larger scale. It has already been suggested that focused attention can promote more coherent stimuli [9] [8]. More coherent stimuli receive a competition bias [3] facilitating synaptic spike-timing dependent plasticity [2]. Models exist in the NEURON [10] simulation environment which demonstrate these effects [11] and experiments on rats and humans appear to confirm these theoretical findings [1] or at least indicate phaselocking to multiple frequencies is possible in L5 pyramidal cells.

What remains yet to be demonstrated is how these findings can be combined to create a network model capable of using synchronized input to drive inhibitory and excitatory neuron assemblies, causing specific pyramidal cells to phaselock on multiple input frequencies thereby increasing their plasticity and 'learning' to encode for multiple concepts. If this can be demonstrated using plausible neuron models, the next step is to show how this can be used in a network to create sparse representations of multimodal stimuli.

The purpose of this research is thus to determine if inhibition mediated double phaselocking to two distinct oscillatory input streams is capable of recruiting a sparse subset of a neural population into a sparse population code for a multimodal concept.

2 Methods

2.1 General Approach

The main focus of this research is best described using the research question defined previously:

Can inhibition mediated double phase locking to two oscillatory input streams recruit a sparse subset of a pyramidal-cell population into a population code for a multimodal concept?

This yields three distinct subquestions to answer:

1. Are pyramidal cells capable of phase locking to two oscillatory input streams?
2. Is spike-time dependent plasticity a viable method to recruit a sparse subset of a neuronal population?
3. Can recruited pyramidal cells then be demonstrated to encode for both modalities?

Using a NEURON simulation [10] it is possible to obtain theoretical answers to each of these questions. A simplified network consisting of a single pyramidal cell is linked to two partially modulated populations of simulated AMPA synapses to determine whether the modeled pyramidal cells are capable of phase locking on two oscillatory input streams. The pyramidal cell is based on Destexhe's models [12][13][14], adapted for network simulation by Van Elburg, while basic AMPA synapses are updated with a spike-timing dependent plasticity model.

A more complex network is required to determine whether STDP is a viable method to recruit a sparse subset of a neuronal population. Using a larger pyramidal cell population as well as a small population of inhibitory interneurons it should be possible to induce pyramidal cell phase locking to simulated input streams, connected to both the population of pyramidal cells as well as the interneuron population [15].

To answer the final question, the complex network is augmented with a switch to replace the rate modulated input synapses with unmodulated input. If connection strengths are significantly increased after a learning period on modulated input, recruited pyramidal cells (by then phase locked on the oscillatory input streams) should maintain increased connection strength for the duration of the testing period. The recruited cells can then be said to encode for the multimodal concept.

2.2 Simulation details

2.2.1 Input stimulus

Spikes are generated by a poisson process, interspike intervals are negatively exponentially distributed. The input stimulus frequencies are locked to:

$$f_{s_1} = 30 \tag{2.1}$$

$$f_{s_2} = 30 \cdot e^{\frac{1}{2}} \approx 49.5 \tag{2.2}$$

These stimuli are then used as input for simulated synapses on the soma of the target cells. For the simple network model each population of input stimuli consists of 150 rate modulated cells and 150 unmodulated cells. The complex network uses 400 rate modulated cells in each stimulus population. Firing delay times are generated through a Guassian delay generator, where spike thresholds are set uniformly to 0V.

See figure 1 for an example of spike times for 400 cells rate modulated to 30Hz, taken over a period of 1000ms.

Once the network has recruited a sparse subset of the pyramidal cell population, the rate modulated input is replaced by random noise on synapses with identical connection strengths to model activation from the same origin without attention. An example of unmodulated input for a population of 8 pyramidal cells is shown in figure 2.

Note that total stimulus input remains constant between both populations, since no rate modulation occurs for the unmodulated input source.

2.2.2 Synapse details

The inhibitory synapses between interneurons and pyramidal cells are based on first order GABA

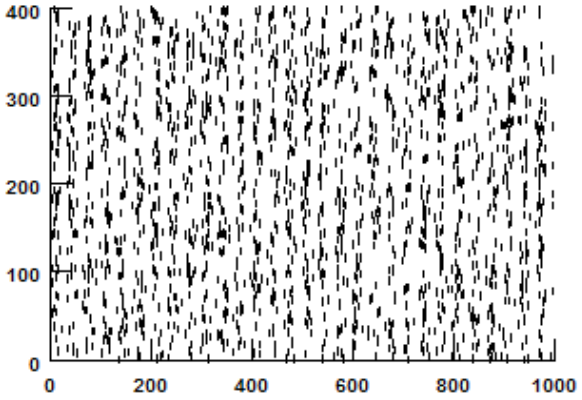

Figure 1: Spike times for 400 input cells rate modulated to 30Hz

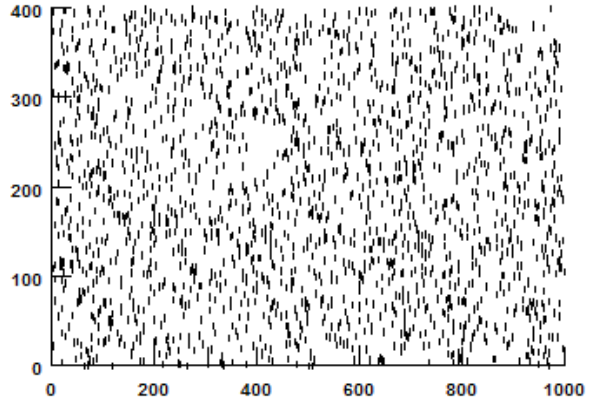

Figure 2: Spike times for 400 input cells, unmodulated

models [16] updated by Van Elburg for use in the NEURON simulation environment.

For the excitatory connections between input stimuli and pyramidal cells, inputs and interneurons and interneurons and pyramidal cells a standard AMPA model is augmented with a spike time dependent plasticity (STDP) model [4][17][18]. The following plasticity rules are implemented for long term potentiation (LTP) and long term depression (LTD) respectively:

$$\delta w = w_{pre} - w_{min} \quad (2.3)$$

$$w_{post} = w_{min} + \delta w \cdot (1 + p \cdot e^{\frac{t_{pre} - t_{post}}{p_\tau}}) \quad (2.4)$$

$$w_{post} = w_{min} + \delta w \cdot (1 - d \cdot e^{\frac{t_{post} - t_{pre}}{d_\tau}}) \quad (2.5)$$

Using $p = 0.15$ as potentiation factor, $d = 0.10$ as depression factor and $w_{min} = 0.001uS$ as lower limit for the synaptic weight. Asymetric weight change effectiveness time constants are used to promote stable Hebbian learning [18]: $p_\tau = 17ms$ and $d_\tau = 34ms$.

2.2.3 Simple network model layout

Phase locking of pyramidal cells to single spike trains has been well studied in general [15][19]. However, phase locking to multiple input streams is less frequently encountered [5][1]. Network topology and input stimuli for the simple network are chosen to facilitate double phase locking by the pyramidal cell.

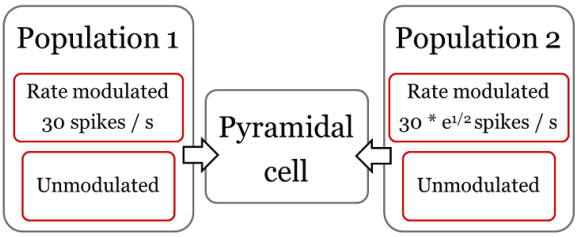

Figure 3: Model layout, simple network

Figure 3 shows the network topology of the simple network used to demonstrate the ability of pyramidal cells to phase lock to multiple oscillatory input streams. Each input population consists of 150 rate modulated cells and 150 unmodulated cells. Both populations are fed to the pyramidal cell simultaneously. After an initial training period the spike timings are then recorded in a phase space diagram. Grouping of spikes with significant correlation indicates that double phase locking has occurred during the testing period; see also section 3.

2.2.4 Complex network model layout

In a more complex setting fast spiking inhibitory interneurons are added to the network to facilitate recruiting a sparse subset of a population of pyramidal cells [5][12][15][19]. To this end two populations of 3 interneurons each are connected to the pyramidal cell population. A rate modulated population of 400 input stimuli is connected to both

the interneuron populations as well as the pyramidal cell population, as in figure 4. After the initial training phase, the rate modulated input stimuli are set to produce unmodulated input of equal net input, see figure 2.

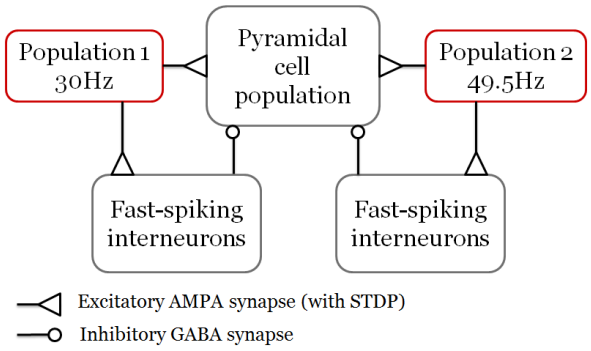

Figure 4: Model layout, complex network

In addition, to all neurons an excitatory unmodulated noisy stimulus is offered through which the initial pyramidal cell recruiting selection is made.

3 Results

3.1 Double phase locking on a single pyramidal cell

Spike timings have been recorded for a single pyramidal cell in the simple network scenario. After an initial training period of 6500 ms, the spike timings are offset to the phase of both oscillatory input streams. The result is shown as phase diagram in figure 5.

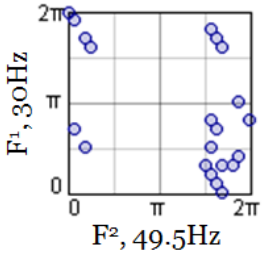

Figure 5: Phase lock on single pyramidal cell

As can clearly be seen a large portion of spikes occur during the start of the phase for s_1 and near the end of the phase for s_2. Performing a bivariate Kuiper test for a uniform distribution [20] confirms with asymptotic significance of $p < 0.001$ that the spikes are indeed not distributed uniformly but phase locked on both frequencies.

Performing a univariate Kuiper test in addition for each phase leads to an interesting result: for Pyramidal cell 6 the univariate phaselock on f_{s_2} is significant ($p = 0.003$) while the phase lock on f_{s_1} appears not to be ($p = 0.085$). Interpreting these values as indication of how well the cell performs phase locking on a specific input modality yields the conclusion that the cell demonstrates a preference for phase locking to one input over the other. This is an important result and is seen again in table 1 where synaptic strengths to both input sources are not equal. As will be discussed, this might be an indication that double phaselocking (in this model) is not stable for extended durations. However, since focused attention duration is usually much shorter [21] than the used training period this might not be an issue.

To illustrate the effect of rate modulation the synaptic connection weights over time during the initial training phase are shown in figure 6:

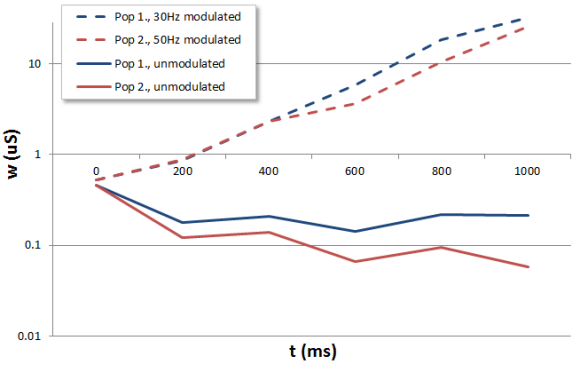

Figure 6: Synaptic weight change over time

As can be seen synaptic weight for the unmodulated cells in the input populations remain mostly constant while connection strengths continuously increase for rate modulated input. The increase is in fact exponential once stable phase locking has occurred and yields unrealistic synaptic strengths for longer durations.

3.2 Recruiting a spare subset of a neuronal population

By measuring the amount of phase locking to occur for each pyramidal cell in the population it should be possible to observe individual cells being recruited. After an initial training period the phase diagram for each pyramidal cell can be analyzed, see figure 7. For this scenario, the network as depicted in figure 4 was trained for 12.000ms and tested for 1.000ms.

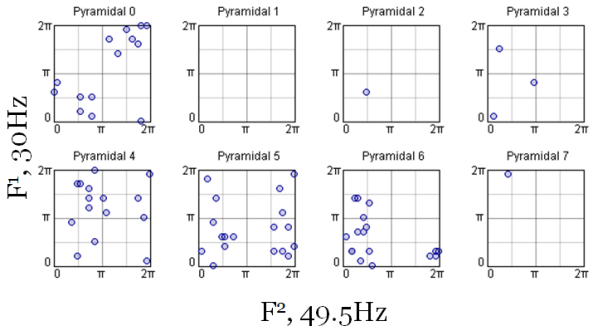

Figure 7: Dual phase locking on pyramidal cell population

In this case dual phase locking has occurred to within statistical significance for pyramidal cells 5 and 6, and near significant amounts for cell 0 (using a bivariate Kuiper-statistics test with $p < 0.05$).

3.2.1 Multimodal concept encoding

Following an initial training period where network input stimuli are rate modulated to the given frequencies it is possible to provide unmodulated input from the same stimuli to test whether the cells for which double phase locking occurred fire more often. If this is the case it suggests that double phase locking is a means to train specific cells in a population to encode for a multimodal concept. In table 1 synaptic connection weights to all pyramidal cells in the pyramidal cell population are listed for both stimuli, both after the initial training period (s_1 and s_2) as well as after a 1000ms testing period (t_1 and t_2). In addition the number of spikes during this testing period is listed.

As should be clear the phase locked cell, Pyramidal 6, shows greatest combined connection strengths both at the start and end of the training period (where the connection weights after the training period refer to the connections from the unmodulated stimulus to the pyramidal cell). Remarkable here is that the unmodulated input still prefers and enforces the synapses to previously recruited cells, contrary to the weight change for unmodulated input in the simple network scenario. It is furthermore clear that the recruited cells fire more for this input than unrecruited cells: grouping cells 0, 5 and 6 and performing an independent samples T-Test for equality of means on spike counts confirms inequality with $p = 0.005$, indicating that recruited cells fire significantly more often than unrecruited cells when presented with unmodulated input after an initial training period.

Cell	w_{s1}	w_{s2}	$w_{t1}^{t=1000}$	$w_{t2}^{t=1000}$	Spikes
0	1.169	9.044	1.055	16.655	5
1	0.962	1.168	0.962	1.168	0
2	0.905	1.175	0.905	1.175	0
3	1.524	1.152	1.973	1.134	2
4	8.539	1.420	14.002	1.464	4
5	40.946	1.151	100.677	1.140	8
6	111.795	1.068	221.856	1.040	7
7	0.972	1.276	0.972	1.276	0

Table 1: Connection weights during training (w_s) and testing (w_t), and number of spikes during the testing phase. All weights listed in uS.

4 Discussion

4.1 General results & validity

When examining the obtained results they appear to match previous research in this area: the modeled pyramidal cells are capable of phase locking as expected [1][5] and modulated input is clearly capable of increasing connection weights relative to unmodulated input [8][3].

In a more complex setting modulated input still appears to be capable of recruiting selected pyramidal cells in a neuronal population through inhibitory interneuron mediated double phase locking [15]. Recruited cells can be read out during a testing period where their connection strengths to the selected input are significantly increased.

However, network stability does not appear to be guaranteed, unlike previous models based on similar principles [18]. As a result the testing and training durations must be chosen carefully to preserve the stimulus connection diversity required for double phase locking: training for too long often results in a cell phase locking only to a single input. While this matter was not subject of this research, it should be noted that the network does not appear to be stable. Likewise, the employed training duration of 12.000ms is unrealistic in real world focused attention tasks, where values around 1000ms are more commonly encountered. However shorter training durations do not yield enough spikes to determine whether double phase locking has occurred in a given pyramidal cell.

The most likely cause for the instability is an unstable spike-timing dependent plasticity model. Even though effective time constants are chosen to favor long term depression, connection weights tend to increase strongly after initial recruitment. In figure 7 and table 1 this is already hinted at by the difference in significance of phase locking for both input frequencies and weight difference for a single cell to both inputs. The double phase lock might not in fact be stable, even though dynamic stability should be possible in similar settings [16]. It is speculated that an initial minor imbalance in connection strengths between both input modalities is increased over time. This effect is countered by introducing noise and inhibition causing spike times to deviate from optimal learning values, thus partially negating the otherwise recursive connection strength increase mechanism. However, since both oscillatory inputs do not produce the same amount of spikes (due to the differences in their frequencies) the double phase lock will inevitable degrade to a single phase lock unless learning for the most frequently encountered input modality stabilizes, which requires the proposed changes to either the synaptic model or the network itself.

4.2 Further research

While the models provided build forth on previous research in the field and even incorporate existing, validated models for neurons and synapses, there is still the obvious question of external validity: can these theoretical findings be duplicated in *in vitro* experiments? Will biologists be able to confirm that spike timing dependent plasticity is capable of recruiting a sparse subset of a neuronal population, or are these theoretical findings as elusive to duplicate as other more complex models of intelligence and learning? Advances in measuring equipment might allow us to measure connection weights [9][18] yet finding a network of the specified topology and measuring the required synaptic strengths might proof more difficult.

There is relatively little research available on spike timing dependent plasticity models (in NEURON for example [22]). Incorporating a lower level model of synaptic mechanisms combined with a greater focus on network stability should increase viability and usability of these results. While it is useful to show that the mechanisms as proposed are indeed capable of simulating multi modal concept encoding, these results are insignificant if they can only be obtained in ideal-world situations. Combining research into stable learning and more complex oscillatory network dynamics should be capable of furthering this particular area of research.

It is therefore recommended that other network topologies are studied and the effects of fast spiking inhibitory interneurons on pyramidal double phase-locking be examined in more detail. Increasing the size of the pyramidal cell population might result in more significant double phaselocking occurring after shorter, more realistic training periods. Adding excitatory connections from the pyramidal cell population to the fast spiking interneuron populations might further mediate individual pyramidal cell recruitment during a realistic training period.

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