UNIVERSITY OF TWENTE

BURSTS IN BRAIN ACTIVITY A MEAN FIELD REDUCTION

Author: Erwin LUESINK Bachelor Committee: Dr. H.G.E. MEIJER Prof. Dr. S.A. VAN GILS Dr. R.M.J. VAN DAMME

JULY 2015

1 ABSTRACT

The goal of this bachelor assignment is to mathematically reduce the neuronal dynamics of a microscopic model of several hundreds of Izhikevich neurons so that it may be used to model several thousands of neurons. That requires a mean field reduction and transforms the microscopic model into a macroscopic model. The reduction is done analytically, by means of separation of variables of the differential equations describing the system. By means of this reduction, it is possible to draw conclusions on neuronal behaviour on macroscopic scale. It is shown that the reduction presented works for one type of neuron and that it has to be adapted to work for the other types. An idea is presented on how to go around this problem. A reduced model for a single population of excitatory neurons is derived and shown and a model that also includes inhibitory neurons is built.

2 TABLE OF CONTENTS

1	Abst	ract		2	
2	Table	e of Con	ntents	3	
3	Introduction			4	
4	Theo	ory		5	
	4.1	Coupli	ng	6	
	4.2	Neuror	nal behaviour	7	
		4.2.1	Unstimulated Neurons	8	
		4.2.2	Stimulated Neurons	11	
	4.3	Micros	scopic Model	16	
5	Meth	nods		25	
	5.1	Qualita	ative approach	26	
	5.2	Mean-l	Field Reduction - LIF Neurons	26	
		5.2.1	Population Density Approach	26	
		5.2.2	The Diffusion Approximation	27	
	5.3	Analyti	ic Reduction - Izhikevich Neurons	30	
		5.3.1	CH Neurons	32	
		5.3.2	RS, FS and LTS Neurons	34	
		5.3.3	Coupling	35	
6	Resu	lts		37	
7	Discussion				
8	Conclusions			44	
9	References			45	
10) Appendices				
	10.1	Append	dix A	46	
	10.2	Append	dix B	46	

3 INTRODUCTION

The processes that occur in the brain are governed by billions of cells called neurons. These neurons exhibit different kinds of behaviour depending on their characteristics and their parameters. A specific kind of neuronal behaviour is spiking; when the membrane threshold potential of a spiking neuron is exceeded, it will fire a spike or action potential. Spikes also come in different forms and shapes, but our focus lies with bursts. Bursting neurons fire a number of spikes in close proximity (± 0.025 s). Particularly interesting are bursts that are followed by long pauses consisting of quiescence. This pattern, called a burst-suppression pattern (BSP), resembles behaviour that is also seen in epilepsy, thereby making investigations of these patterns very interesting.

As a result of the knowledge that is available on neuronal behaviour, many models exist for neuronal analysis. Thereby man can make accurate predictions about processes that occur in the brain without having to perform the experiments every single time. These many models have been developed to model either single cells in very high detail, or model specific areas of the brain. By using the microscopic model, [2], it is possible to generate accurate information on a small number of neurons, for large numbers, the model is too computationally expensive.

The goal of this thesis is to reduce a detailed microscopic model by means of mean-field theory, but maintain the important characteristics that the initial model had. Thus a model is desired that can simulate the excitatory and inhibitory population without losing the bursts and some other important characteristics of bursts. When such a model has been developed, it may be compared to the original model and to experimental data, thereby confirm or disprove the hypothesis that bursts are stopped by inhibitory activation and synaptic depression.

Mean-field theory is a means to get from a high dimensional model towards a smaller, comprehensible, low dimensional model. There a many different methods, such as the diffusion approach [3] or the diffusion map approach [1]. The method that is used here is of an analytical nature, as shown in [7]. By using phase plane analysis, the effects of different parameters on the behaviour of the population can be analyzed. Inside the total population, one must distinguish between the inhibitory and the excitatory subpopulation. These subpopulations contain different types of neurons. These neurons have individual sets of equations to model their respective dynamics, but in general, the dynamics do not vary too much from neuron to neuron. This makes it possible to make several assumptions. These allow the neglecting of different features of the microscopic model in order to make the reduced model simpler but valid.

4 THEORY

To be able to do a good reduction, the dynamics of the different neurons must first be understood. The microscopic model is based on Izhikevich neurons [4]. Apart from different forms of inhibitory and excitatory neuron dynamics as described in [5], the model also contains synaptic dynamics (Tsodyks-Markram [6]), delays, spike time dependent plasticity, synaptic potency and synaptic depression. The majority of the variables is initialized randomly upon starting the a simulation with the model, thus different simulations provide different results. The variables and parameters used will be explained upon first usage, but for review, here are all symbols in one table.

Symbol	Quantity	SI Unit
t	time	S
v(t)	membrane potential	V
u(t)	recovery variable	V
I(t)	membrane current	A
$I_{post}(t)$	post synaptic current	A
Iext	average external current	A
R	membrane resistance	Ω
a	Izhikevich recovery strength	
b	Izhikevich sensitivity recovery variable	
С	Izhikevich reset potential	
d	Izhikevich recovery potential elevation	
J	synaptic efficacy	As^{-1}
N	number of neurons	
τ	time constant	S
δ	action potential spike	
•1	index for inhibitory	
$\cdot E$	index for excitatory	
$H_{\omega}(\cdot)$	Smooth approximation to <i>H</i>	
r	mean population firing rate	s ⁻¹
p(v, t)	probability density	
F(v, t)	probability flux	
μ_{a}	drift	V
σ^2	diffusion	$(V)^2$
$\phi(\mu,\sigma)$	population transfer function	s ⁻¹
V_L	leak/resting potential	V
Vreset	reset potential	V
heta	firing threshold	
w(t)	white noise process	
$H(\cdot)$	Heaviside step function	
\overline{g}	maximum conductance	mho
q	impulse response	
(S)s	(total) synaptic activation	

Since our entire model is based on the Izhikevich neuron [4], the theory of the dynamics of the Izhikevich neuron is essential. The model consists of two equations and a reset; a nonlinear first order differential equation that describes the membrane potential and a linear first order differential equation in the recovery variable. The reset function sets the membrane potential back to its reset value after the neuron has fired. In mathematical notation that is

$$\frac{\mathrm{d}v}{\mathrm{d}t} = 0.04v(t)^2 + 5v(t) + 140 - u(t) + RI(t),$$

$$\frac{\mathrm{d}u}{\mathrm{d}t} = a(bv(t) - u(t))$$

and the auxiliary after-spike reset, given by

if
$$v \le 30 \, mV$$
, then
$$\begin{cases} v \leftarrow c \\ u \leftarrow u + d \end{cases}$$

By means of varying the constants a, b, c, d and the dendritic current input I, it is possible to show all kinds of spiking neuron behaviour [4]. These are the dynamics of a single neuron. Upon coupling neurons over the dendritic current input, the number of dimensions rises by two per additional neuron, since each individual neuron is described by two differential equations and its membrane potential must be monitored in order for this reset to work. This is not a continuous process and it is impossible to make population dynamics when this reset is still there. The next step therefore is to do a mean-field reduction that removes this reset. Since all spiking neurons have a similar output, it is possible to reduce the number of dimensions of the population dynamics by predicting the behaviour. The focus lies on bursts, thus these must remain. First, a burst has to be defined. There exist different types of bursting. Tonic bursting, which occurs e.g. in chattering neurons, is a neuronal activity identified by periodic bursts of spikes when stimulated by constant current. There is also phasic bursting, which happens when a neuron upon activation fires a single burst. A neuron may also fire when stimulated by inhibitory pulses. The corresponding behaviour falls out into two similar sorts of bursting that occurs in the excitatory stimulation, which are called rebound bursting and inhibition-induced bursting, similar to tonic and phasic, respectively. There are many models of neuronal activity, but not all of them model bursts. In [5], a number of models is tested for their simulation of twenty different neuro-computational properties. The models by Hodgkin and Huxley, Wilson and Hindmarsh-Rose are potentially interesting since they do not abolish bursting neurons, yet they are difficult to work with due to their complexity. That motivates the choice for the Izhikevich model in the microscopic model.

4.1 COUPLING

The Izhikevich neuron has to be coupled to other neurons in order to model a population. The dendritic current in reality is a very complex, almost noisy input because of all the synaptic connections from other neurons. For simplicity, the output signal of other neurons is nothing more than a spike, so that the *RI* term in the first equation of the model will have the

following definition:

$$RI_i = \tau \sum_{j=1}^N J_{ij} \sum_k \delta(t - t_j^{(k)}).$$

This equation shows the total synaptic current flowing from cell j into cell i. This is merely a summation of N presynaptic neuronal spikes, modeled as δ -spikes. The J_{ij} term is a weight factor, the synaptic efficacy, measuring the effect of the δ -spike from neuron j to neuron i. The occurrence of N indicates that there are now 2N dimensions, because for each neuron in the population, the membrane potential and the recovery variable must be calculated in order to identify the effect it has on the neurons with which it has synaptic connections, which is very cumbersome. Thus the next step is to do a mean-field reduction such to get the model to be low dimensional. The basis of the microscopic model now looks as follows:

$$\begin{split} \frac{\mathrm{d}v_i}{\mathrm{d}t} &= 0.04v_i^2 + 5v_i + 140 - u_i + \tau \sum_{j=1}^N J_{ij} \sum_k \delta(t - t_j^{(k)}),\\ \frac{\mathrm{d}u_i}{\mathrm{d}t} &= a_i (b_i v_i - u_i), \end{split}$$

with the reset

if
$$v_i \leq 30 mV$$
, then
$$\begin{cases} v_i \leftarrow c_i \\ u_i \leftarrow u_i + d_i \end{cases}$$

4.2 NEURONAL BEHAVIOUR

Now that the basis of the microscopic model is there, one may opt for the reduction. To do a good mean field reduction, the dynamics of the neurons must be understood well. Therefore each type of neuron will be extensively studied by means of phase plane analysis. The Izhikevich model is two dimensional, thus phase plane analysis will give all the information that is required. Each type of neuron has a unique set of a, b, c, d to model its behaviour. In the original Izhikevich model, there are about 20 types of different neurons. Not all types are used in the microscopic model, but the types that are used are given here, accompanied by the parameter values used to model them:

Excitatory	a	b	С	d
Regular spiking (RS)	0.02	0.2	-65	8
Chattering (CH)	0.02	0.2	-50	2
Inhibitory	а	b	С	d
Inhibitory Fast spiking (FS)	a 0.1	b 0.2	c -65	d 2

Important is to notice that the values do not vary much. That means that their respective phase planes are quite similar, which is shown in the phase planes below.

4.2.1 UNSTIMULATED NEURONS

Slight differences in the phase plane can cause great deviation in behaviour; a regular spiking neuron is very different from a chattering neuron even though their phase planes do not seem to vary much initially. The following figure contains all of the phase planes of the respective neuron types. There is no stimulation current, so I = 0. The red circle represents the start of an orbit, the black square shows where the orbit ends.

• RS Neuron



Figure 4.1: This phase plane belongs to the regular spiking neuron, this is the benchmark for the other neurons.

• CH Neuron



Figure 4.2: This phase plane belongs to the chattering neuron. The reset voltage is higher, which means that there is more time for the neuron to fire action potentials.

• FS Neuron



Figure 4.3: This phase plane belongs to the fast spiking neuron. It is similar to the regular spiking neuron, but more active. That explains the low value for d. Also a is higher, that indicates that the field strength in the vertical direction is stronger.

• LTS Neuron



Figure 4.4: This phase plane belongs to the low-threshold spiking neuron. This neuron looks very similar to the regular spiking neuron, but the higher value for *b* causes the *u*-nullcline to tilt, lowering the firing threshold. By very little stimulation, this neuron will fire.

The phase planes look all very similar. The inhibitory neurons are more active than the excitatory, which can be seen in the phase planes. For the FS neuron, the high value for *a* causes the strength of the vector field in the vertical direction to be higher. As a result, the neuron is much quicker at its equilibrium state. The LTS neuron has a low threshold, thus by little stimulation it may already fire, thus it fires more often than the excitatory neurons. The most important difference is between the neurons is the reset value. The RS, FS and LTS neurons all have the same *c*, only the CH neurons have a different value. This will make a large difference upon stimulation.

4.2.2 STIMULATED NEURONS

The unstimulated neurons all have a stable equilibrium point, thus they remain dormant. Upon stimulation with a constant current I = 10mA, the behaviour drastically changes. The starting point of the orbit remains the same. A black circle denotes a reset.

• RS Neuron



Figure 4.5: This phase plane belongs to the regular spiking neuron. It resets once about 8mV above the initial point, resets again and then it has found a periodic spiking rate, which can also be seen in the next figure.



Figure 4.6: The regular spiking behaviour of the stimulated RS neuron.

• CH Neuron



Figure 4.7: This phase plane belongs to the chattering neuron. Here, the bursting behaviour is evident. Since the reset is set at -50mV, the neuron has a lot of time before it is back inside the *v*-nullcline. That in combination with a low value for *d* causes these rapid spikes.



Figure 4.8: The stimulated CH neuron produces a lot of spikes in close proximity after which a new burst starts.

• FS Neuron



Figure 4.9: This phase plane belongs to the fast spiking neuron. It is more active than the regular spiking neuron in the sense that its d value is much lower, removing the part of the orbit that would follow the v-nullcline in case of the RS neuron.



Figure 4.10: It produces similar periodic spike trains as the RS neuron, but much faster.

• LTS Neuron



Figure 4.11: This phase plane belongs to the low-threshold spiking neuron. This behaviour resembles the fast spiking neuron, since we are way above the threshold potential, the difference is that the fast spiking neuron has a higher vertical field strength, causing a steeper decline.



Figure 4.12: The spike trains that the LTS neuron produces is similar to the RS and the FS neuron, but it differs in the speed of spike train production.

As expected, the high reset value in the chattering neurons cause the behaviour of this particular type to deviate a lot from the rest. Whereas the other neurons are spiking periodically, the chattering neurons show bursts.

4.3 MICROSCOPIC MODEL



Figure 4.13: The microscopic model in graphic form

Now that the dynamics of the different neurons is known, the simulations of the microscopic model can now be understood. It is important to realize that the microscopic model is more complicated than just a coupled network of 4 types of neurons, it also contains spike-timing dependent plasticity (STDP), a delay in signal transfer and synaptic depression and potency. Spike-timing dependent plasticity influences strength of the synaptic connections. If an input spike to a neuron occurs immediately before the output spike of that particular neuron, then that input signal is stronger. The opposite of this process, where the input signal is just after the output action potential, the input signal is made weaker. This is spike-timing dependent plasticity. The process continues until some of the initial connections remain, whereas the influence of all others has become negligible. The other effects, synaptic depression and its counterpart, synaptic potency, are long term effects that also have influence on the strength of the synaptic connections. This process works with neurotransmitters that balance the neuronal activity. If neurons would only receive positive feedback, they would eventually reach a state of inactivity or too much activity; this is countered by teamwork of synaptic potency and depression. The networks consists of the four types of neurons described above.

The following simulations are done with the microscopic model [2]. The data is generated through a C++ program and the data is then analyzed with MATLAB. All simulations are done with a half-to-half synaptic connectivity, normal distributed neurons (meaning that their characteristic *a*, *b*, *c*, *d* values are drawn from a normal distribution with a small variance) and a delay of 3ms. The upper 20% of the neuron population is inhibitory and the bottom 80% is excitatory. The first simulations resemble an entire day, which is necessary to find the distribution of the inter burst times. This feature is used later to draw conclusions on how well the reduced model works.

• Default Simulation - 24 hours with 100 neurons



Figure 4.14: This is a 24 hour (86400 seconds) simulation of 100 neurons. The left figure shows the entire simulation, the right figure is a subset of the left.



Figure 4.15: Having zoomed in even further, the left figure shows what a single burst looks like. The right shows that the inter burst timings are exponentially distributed.



• Default Simulation - 24 hours with 200 neurons

Figure 4.16: This is a 24 hour simulation of 200 neurons. On the left side, the simulation over the full 86400 seconds. The right figure shows a subset of the left.



Figure 4.17: The left figure shows such a burst for 200 neurons. The burst is significantly larger since the number of neurons affecting each other is now larger. The right figure shows that the distribution is exponential.

• Default Simulation - 300 seconds



Figure 4.18: The left figure is the model with all its default parameters. Although the right figure does not show an exponential distribution, this is classified as statistically insignificant because the simulation time is short.



Figure 4.19: The bursts are not affected by simulation time, this burst has the exact same behaviour as the burst in the 24 hour simulation.

• No Synaptic Connection



Figure 4.20: In the left figure it can be seen that, as expected in the situation of no synaptic connection, there are no population bursts, since the network now consists of 200 individual neurons. The right figure, the histogram, confirms this.



Figure 4.21: There are no bursts, the excitatory population is very inactive, whereas the inhibitory population contains 5 fast spiking neurons, which are much more active, but not bursting.

• No Long-Term Effects



Figure 4.22: No long term effects do not cause a significant difference compared to the default simulation. This is expected since the simulation is only 300 seconds long and the long term effects take hours to become active.



Figure 4.23: The burst has the same appearance as all the others. The inhibitory population starts bursting a fraction earlier, but that does not change the overall behaviour.

• No Synaptic Depression



Figure 4.24: No synaptic depression shows interesting behaviour. In the left figure, the excitatory population shows a non bursting regime twice (the two dense pillars), where the activity is much higher. The right figure is a subset of the left.



Figure 4.25: In the left figure, there is zoomed in on the simulation deeply. The excitatory population displays no bursts whereas the inhibitory population is bursting with a very low interburst time, as can be seen in the right figure.

• Only Chattering Neurons



Figure 4.26: The left figure shows a population with only chattering neurons. This is a good basis for further comparison with the reduced model later. The right figures shows the exponential distribution again.



Figure 4.27: Only chattering neurons that are bursting.



• Only Chattering Neurons without Synaptic Depression

Figure 4.28: The figure on the left shows that the population is much more active than with synaptic depression. The right figure does however, show that there is no strange behaviour among bursts.



Figure 4.29: A single burst does not look very different either, apart from its length, it is a little shorter than with synaptic depression.

Both 24 hour simulations were done using the default values of the C++ program [2]. Figures 4.14 up to and including figure 4.17 show the exponential distribution of the inter burst times and the normal appearance of a burst. The short default simulation shows a similar pattern as the long simulations. However, the inter burst times are quite odd in this particular case, but that is due to the length of the simulation. In the long run, these oddities fade under the statistical dominance of the exponential distribution. Hence, the right figure in figure 4.18 is considered statistically insignificant for the conclusion on the type of distribution. In the case of no synaptic connection, which is achieved by setting all parameters that determine the synaptic connection to zero (a = 0), it is expected that there are no population bursts. That is because the input of any neuron does not reach any other neuron. As a result, the neurons in this simulation will only fire upon exceeding their thresholds. No long term effects, achieved by setting a_m and a_p to zero, do not have much influence either, but that is also because the simulation times are short. Upon removing the synaptic depression, $a_m = 0$, the simulation shows very different behaviour. The excitatory population shows the activity pattern in a non-epileptic case (without bursts and quiescence), but the inhibitory population is bursting with a very small inter burst time. Upon adapting the code such that the program simulates only chattering neurons, it is found that the bursts are still finite, but they are longer than normal. This is because the inhibitory population that normally would deactivate the excitatory population has been completely removed. The bursts are still finite due to the way the chattering neurons are modeled. In the phase plane in figure 4.7, the orbit shows a number of quick action potentials, but with an increasing u variable. That means that the *u*-nullcline is further away for each consecutive spike. As a result, before crossing the nullcline, the orbit descends and after crossing, ascends. That means that the reset after the last spike will always be inside the *v*-nullcline again, drawing the burst to a halt. Upon removing the synaptic depression, the population of only chattering neurons becomes a lot more active, but does not show any non-epileptic activity; it only bursts a lot more often. This gives an indication that the synaptic depression has a large influence on the activity of a population with both inhibitory and excitatory neurons, but mainly on the inhibitory population. It is even so that the large amount of inhibitory bursts damps out the excitatory bursts, which explains the pattern seen in figure 4.24 and 4.25.

5 Methods

The microscopic model is now understood. The mean-field reduction may be done. To understand what the important ideas and assumptions in such a reduction are, two types of mean-field reductions are shown. The analytic reduction is the one that is used in order to reduce the dynamics of the Izhikevich neurons. The population density - diffusion approximation is the theory behind any reduction in which the firing rate is the macroscopic variable to be determined. Apart from doing such a reduction, there is also the possibility to build a macroscopic model from scratch. This is presented as a qualitative approach.

5.1 QUALITATIVE APPROACH

The desired neuronal behaviour is bursting. Therefore one may also look at what exactly makes a neuron burst and more importantly, what makes a neuron stop bursting. A burst is a number of spikes in close proximity. A spike is the output signal of a spiking neuron when the membrane potential is larger than the threshold. Thus bursting means that the membrane potential shortly after firing a spike is again above the threshold, causing the neuron fire another spike. This happens a number of times before the membrane potential is below the threshold and quiescence follows. A model can be made from scratch based on biophysically sensible descriptions of neurons, but also mathematically by investigation of the behaviour and simply imitating that with mathematics. Building up a model by means of the qualitative approach is not within the scope of this work, but it is important to know that there are multiple ways to get to a good model. An example of the qualitative approach on microscopic dynamics is the famous Hodgkin-Huxley model, this is a 4-D model with gating variables, which are modeled as voltage dependent variables and act based on earlier voltages, causing highly nonlinear behaviour. A simplification of this particular model is the Izhikevich model, [5] presents this qualitative approach. By giving the mathematical form of the different spikes that a spiking neuron produces, the Izhikevich model is able to show all forms of neuronal behaviour and is 2-D, allowing for phase plane analysis, as shown in section theory. Also direct population models have been made. A famous example of this is the Wilson and Cowan model.

5.2 MEAN-FIELD REDUCTION - LIF NEURONS

A mean-field reduction has to be done to reduce the number of dimensions drastically and thereby making computations significantly less cumbersome. There are a number of methods available for these types of reductions, which require a number of assumptions.

5.2.1 POPULATION DENSITY APPROACH

There is a method to find macroscopic variables for LIF (leaky integrate and fire) neurons. The assumptions that need to be made:

- The nonstationary temporal evolution of the spiking dynamics can be captured by simple models of neurons.
- · The dynamics of afferent neurons is neglected.
- The history of each neuron input/output is uncorrelated.
- · Every neuron has the same behaviour averaged over time as averaged over space.
- The minimal kick step *J* is very small and the overall firing rate is very large. In this case, all high order terms become neglegible compared to the low order terms.

By using the simulations of the detailed model, the population activity can be extracted directly from the simulations, since that is what is being modeled. By looking at intervals Δt_i across the simulation time, the number of action potentials in that window can simply be counted. It is important to think about what is behind the activity, whether that is because all neurons have approximately the same membrane potential or half of the neurons is above that level and the other half is below. The population density is left to chance, the Fokker-Planck equation for the population density can be derived [3]. In general, neurons with the same state at a certain time have had a different state beforehand compared to each other. That means that the state of all the of the neurons that where initially the same, may have a completely changed at a certain time further. This randomness is caused by fluctuations in the currents. A key assumption to make this model work is to assume that the afferent input currents are in no way correlated with each other. The resulting Kramers-Moyal expansion of the Chapman-Kolmogorov equation is

$$\frac{\partial p(v,t)}{\partial t} = \sum_{k=1}^{\infty} \frac{(-1)^k}{k!} \frac{\partial^k}{\partial v^k} \Big[p(v,t) \lim_{\mathrm{d}t \to 0} \frac{1}{\mathrm{d}t} \langle \epsilon^k \rangle_v \Big].$$

This equation is based on the moments $\langle e^k \rangle_v$. We sum over these moments up to infinity. An important question to ask is whether that is necessary. The first two moments of the equation above are the interesting components, called drift (μ) and diffusion (σ^2), respectively.

5.2.2 THE DIFFUSION APPROXIMATION

• The sums of the synaptic gating variables can be replaced by a fluctuating term and a DC component.

After doing this particular mean-field reduction, it is found that the original model, consisting of numerous equation per leaky integrate and fire (LIF) neuron have become a small number of population equations. Although a LIF neuron is very different from the Izhikevich neuron, the idea that is behind the theory of reduction has a similar character. The population equations are presumably nonlinear and self-consistent. The equation that we found for p(v, t) requires the moments $\langle \epsilon^k \rangle_v$. The first two moments of the are calculated by simply evaluating the limit

$$M^{(k)} = \lim_{dt \to 0} \langle \epsilon^k \rangle_v = \langle J^k \rangle Nr(t)$$

for k = 1, 2. In this equation, $\langle J \rangle$ is the average weight efficacy between the neurons. This term can be derived from the single cell dynamics. In the coupling of the neurons, the synaptic efficacy or weight efficacy J_{ij} denoted the effect of a presynaptic signal on a postsynaptic neuron. Upon transition from single cell dynamics to population dynamics, we calculate the average effect of presynaptic signals to postsynaptic neurons by means of $\langle J \rangle$. The *r* represents the mean population firing rate. To determine the mpf-rate, the number of spikes in tiny time windows $\{dt_i\}$ for the entire duration is counted and divided by the number of neurons *N* in the population. We have abolished moments with k > 2, this is called the diffusion approximation. It is assumed that the history of each neuron input/output current is uncorrelated and it also assumed that all of the neurons have the same behaviour averaged over time as averaged over the space of all the system's states. By mean-field theory, the transition from single neuron dynamics to population dynamics is possible, by expressing the infinitesimal change in the membrane potential of the population as [3]

$$dV_E(t) = \langle J \rangle N_E r_E(t) dt - \frac{V_E(t) - V_L}{\tau_E} dt,$$

$$dV_I(t) = \langle J \rangle N_I r_I(t) dt - \frac{V_I(t) - V_L}{\tau_I} dt,$$

The $\langle J \rangle Nr$ term thus denotes the effect of presynaptic output on postsynaptic neurons. We do not yet have an expression for r, but assuming that we can find one, we continue. Now that we have the population dynamics of both types of neurons, we must still realize that these equations do not model any synaptic behaviour, nor the effect of the excitatory neurons on the inhibitory and vice versa. In principle, the mpf-rate could be calculated from an experiment, but we want the mpf-rate to be known beforehand. Namely, determining the rate function after simulation means that we end up with an expression that would render every simulation with the same rate function, identical to the first one. Also, no information on bursting can be contained in the rate function by determining it simply from simulations, because the population had shown a more constant activity, we can find the same mpf-rate as for the population that bursts. To account for these temporal effects, it is necessary to construct a peristimulus time histogram (PSTH). This does not change the way in which r is calculated, but it does grant more insight in what the underlying population is doing. The PSTH is constructed by calculating the number of spikes in a tiny bin k_i and creating a bar based on the number of spikes in that bin k_i .

$$A_E(t)\Delta t = \frac{1}{N_E} \int_t^{t+\Delta t} \sum_{j \in N_E} \sum_f \delta(t - t_j^{(f)}) dt,$$
$$A_I(t)\Delta t = \frac{1}{N_I} \int_t^{t+\Delta t} \sum_{j \in N_I} \sum_f \delta(t - t_j^{(f)}) dt.$$

Returning to the Kramers-Moyal expansion, the infinite sum is now approximated by the drift and diffusion approximation. The resulting equation describing the population density is called the Fokker-Planck equation, given by

$$\frac{\partial p(v,t)}{\partial t} = \frac{1}{2\tau} \sigma^2(t) \frac{\partial^2 p(v,t)}{\partial v^2} + \frac{\partial}{\partial v} \left[\left(\frac{v - V_L - \mu(t)}{\tau} \right) p(v,t) \right].$$

If the drift is linear and the diffusion is constant, the equation describes an Ornstein-Uhlenbeck process. By definition, the Ornstein-Uhlenbeck process describes the velocity of a massive Brownian particle (a particle doing a random walk), under the effects of friction. In this case the Ornstein-Uhlenbeck process describes the membrane potential evolution under the effects of depolarization. We introduce the flux of probability, defined by

$$F(v,t) = -\frac{v - V_L - \mu}{\tau} p(v,t) - \frac{\sigma^2}{2\tau} \frac{\partial p(v,t)}{\partial v}$$

so that the Fokker-Planck equation can be written into a continuity equation

$$\frac{\partial p(v,t)}{\partial t} = -\frac{\partial F(v,t)}{\partial v}.$$

28

However, our input current for an individual neuron is still deterministic and given by the presynaptic current of that neuron and external input, the equation for RI_i described in 4.2.1. We can rewrite that equation in terms of population variables, the drift and the diffusion, and we add noise to accommodate for random firing of presynaptic neurons. RI is now given by

$$RI(t) = \mu(t) + \sigma \sqrt{\tau} w(t).$$

Here w(t) is a white noise process. The stationary solution of the continuity equation has to agree to the following boundary conditions:

$$p(\theta, t) = 0,$$
$$\frac{\partial p(\theta, t)}{\partial v} = -\frac{2r\tau}{\sigma^2}$$

which say that the probability density at the threshold is zero and that the derivative of probability density with respect to the membrane voltage at the threshold gives the average firing rate r of the population, respectively. It does this by self-consistent arguments. This means that r is expressed as r = f(r). The reset function sets the part of the population that is at the threshold back to the reset potential. This can be added to the continuity equation in the following way:

$$\frac{\partial p(v,t)}{\partial t} = -\frac{\partial}{\partial v} \Big[F(v,t) + r(t-t_{ref})H(v-v_{reset}) \Big]$$

H represents the Heaviside step function, which is defined as $H(x) = \int_{-\infty}^{x} \delta(s) ds$. The solution to this equation, satisfying the boundary conditions that we set, is:

$$p_{s}(v) = \frac{2r\tau}{\sigma} \exp\left(-\frac{v-V_{L}-\mu}{\sigma^{2}}\right) \cdot \int_{\frac{v-V_{L}-\mu}{\sigma}}^{\frac{\theta-V_{L}-\mu}{\sigma}} H\left(x-\frac{V_{reset}-V_{L}-\mu}{\sigma}\right) e^{x^{2}} dx.$$

0 17

Neurons are generally not instantaneous in any kind of behaviour that they show, so the reset does not immediately set the neuron back to its starting value, but it takes some time for this to happen. This is called the refractory period and we denote it by t_{ref} . That means that there is a fraction of the neurons in the population in the refractory period, denoted by $r \cdot t_{ref}$. If we take this into account, we get the following equation, describing the probability of the entire sample space, which is the total population. This must equal 1 by the laws of probability.

$$\int_{-\infty}^{\theta} p_s(v) \,\mathrm{d}v + r \cdot t_{ref} = 1.$$

Using the definition of p_s and solving for r, the population transfer function ϕ is obtained

$$r = \phi(\mu, \sigma) = \left[t_{ref} + \tau \sqrt{\pi} \int_{\frac{\nu - V_L - \mu}{\sigma}}^{\frac{\theta - V_L - \mu}{\sigma}} e^{x^2} (1 + \operatorname{erf}(x)) \, \mathrm{d}x \right]^{-1}.$$

This equation is found by setting the boundary conditions for the stationary solution. Thus the equation in r that was found describes the stationary dynamics of the population(s),

because this can be generalized for the excitatory and inhibitory populations. The set of stationary, self-reproducing rates r_i with i = E, I can be found by solving the coupled self-consistency equations

$$r_i = \phi(\mu_i, \sigma_i).$$

To solve the equations that were derived a moment ago for both populations, the differential equations describing the approximate dynamics of the system must be integrated, which has, as fixed-point solutions, the exact equation that was just found. These differential equations each have their own respective time scale τ_i with i = E, I. Writing out the index *i* for each equation,

$$\tau_E \frac{\mathrm{d}r_E}{\mathrm{d}t} = -r_E + \phi(\mu_E, \sigma_E),$$

$$\tau_I \frac{\mathrm{d}r_I}{\mathrm{d}t} = -r_I + \phi(\mu_I, \sigma_I).$$

These equations show that the population firing rate depends on the input current (firstpassage time formula ϕ), which in turn depends on the firing rate. Thus the *r* must be determined self-consistently, which is computationally cumbersome, as it requires realistic synaptic dynamics and higher order corrections. [8] proposes a simplified approach in solving the self-consistent equations.

This shows the theory of behind the one of the most general mean field reductions. But this reduction is for neurons that are described by a single differential equation. It is therefore not suitable for the Izhikevich neuron, but it is important to understand the background of the mean field theory. The analytic approach that will be done next, will seem very different at first glance, but as it will turn out, also a firing rate is found.

5.3 ANALYTIC REDUCTION - IZHIKEVICH NEURONS

Since the Izhikevich neuron model contains two equations, we cannot simply use the diffusion approach. A reduction for the Izhikevich neuron consists of phase plane adaption as shown in [7], which will be reproduced here. In the theory of the Izhikevich neuron, the phase planes of each type of neuron were shown. By adding another branch to the v-nullcline, the reset can be removed. This is necessary because the reset requires continuous monitoring of the v-variable, for every single neuron. It is thus impossible to use the system as it is now to model population behaviour. It requires a change in the dynamics, which seems a violation to the initial model. However, orbits that are close to this additional branch corresponds to a neuron that is bursting, which is a process that is inherent to the type of neuron. That means that the bursting condition is a binary process and as a result, the exact shape and position of this branch is hardly important.

From the phase planes, it can be deduced that variation of the recovery variable u is much slower than the variation of membrane potential v. This allows us to treat u as a constant parameter with respect to the differential equation describing v. By replacing -u + RI by Λ ,

the set of two interconnected differential equations reduces to a single individual equation, given by

$$\frac{\mathrm{d}v}{\mathrm{d}t} = 0.04 v^2 + 5v + 140 + \Lambda.$$

This differential equation is nonlinear, but by means of separation of variables, we can find an analytic solution.

$$\int \frac{\mathrm{d}v}{0.04v^2 + 5v + 140 + \Lambda} = \int \mathrm{d}t,$$
$$\frac{10}{\sqrt{4\Lambda - 65}} \arctan\left(\frac{2v + 125}{5\sqrt{4\Lambda - 65}}\right) = t(\Lambda; v).$$

This solution can be used to find the time it takes for $v|_{v=c}$ to go to $v|_{v=30}$ with caution, since the arctan function is symmetric, which means that there are two solutions t_{spike} satisfying

$$t_{spike}(\Lambda; c) = t(\Lambda; 30) - t(\Lambda; c)$$

a positive one and a negative one. The restriction necessary to find only the positive solution is $0.04c^2 + 5c + 140 + \Lambda > 0$. This is important because the right hand side of the differential equation describing the reduced system has to be greater than zero in order to diverge towards $v|_{v=30}$. Inside a burst, the instantaneous firing rate is now determined as the reciprocal of the inter spike times, since every spike follows directly after the other. The bursting neuron (CH neuron) is achieved when there is no equilibrium point. To make sure that the equilibrium point is absent, the *u*-nullcline has to be cut along $v|_{v=c}$ into two parts, of which the right part has to be raised. This raise is achieved by introducing f_{min} , the minimum firing rate for a neuron at which it can still be called a bursting neuron. This also has a physiological meaning, since large cells have lower firing rates that small ones. The minimum firing rate is given by

$$f_b(\Lambda; c) = \begin{cases} \max\left(\frac{1}{T_s(\Lambda; c)}, f_{\min}\right) & 0.04c^2 + 5c + 140 + \Lambda > 0, \\ f_{\min} & \text{otherwise.} \end{cases}$$

Yet, not every neuron is always bursting, distinction must be made between bursting and non-bursting. The actual firing rate becomes

$$f(\nu,\Lambda;c) = H_{\omega}(\nu-c)f_b(\Lambda;c).$$

Here, H_{ω} is the smooth approximation to the Heaviside step function, with steepness parameter ω . This function is centered round the reset to distinguish between bursting and non-bursting. The function H_{ω} is defined as

$$H_{\omega}(v-c) = \frac{1}{1+e^{-\omega(v-c)}}.$$

The reset $v \leftarrow c$ is now taken care of, but the reset has an additional term $u \leftarrow u + d$ which is not yet in the reduced model. We can introduce this by adding the firing rate function to the dynamics of u. Since every spike causes u to be raised with d, the reduced recovery variable u_r depends on df, the time averaged increase rate

$$\frac{\mathrm{d}u_r}{\mathrm{d}t} = a(bv_r - u_r) + d \cdot f(v_r, \Lambda; c).$$

5.3.1 CH NEURONS

The branch is still not added to the phase plane. So far, the u variable has been adapted and the firing rate f was determined. The shape and exact position of the branch does not matter, except for its maximum, which must be at the same height as the intersection of the vnullcline with c. The branch can be added by incorporating an additional term in the system of DEs. The new system of DEs becomes

$$\frac{\mathrm{d}v_r}{\mathrm{d}t} = 0.04v_r^2 + 5v_r + 140 - u_r + I - \xi e^{\eta(v_r - c)}$$
$$\frac{\mathrm{d}u_r}{\mathrm{d}t} = a(bv_r - u_r) + df(v_r, u_r, I; c).$$

There has to be a difference between neuron behaviour and since the chattering neurons are the ones that produce bursts, the new branch is determined for this type first. Let n_v denote the *v*-nullcline and n_{v_r} denote the v_r -nullcline, which contains the new branch. n'_{v_r} is the derivative of the v_r -nullcline with respect to the potential. Then the following equations must hold.

$$n_{v}(v) = 0.04v^{2} + 5v + 140 + I_{s}$$

$$n_{v_{r}}(v) = n_{v}(v) - \xi e^{\eta(v-c)},$$

$$n_{v_{r}}(c+\kappa) = n_{v}(c,$$

$$n_{v_{r}}'(c+\kappa) = 0.$$

The horizontal separation is given by κ . Upon solving these equations, we find:

$$\eta = \frac{n'_{\nu}(c+\kappa)}{n_{\nu}(c+\kappa) - n_{\nu}(c)},$$
$$\xi = \frac{n_{\nu}(c+\kappa) - n_{\nu}(c)}{e^{\eta\kappa}},$$

with n'_{ν} being the derivative of n_{ν} with respect to the potential. The value for κ must not be too small, since the branch will become too steep. Too large values for κ lead to a too gradual branch. Both will affect the timing and the subthreshold behaviour of the neuron. Typically κ has a value in the range of [0.5,2.5]. In [7], the value for κ is chosen to be 0.8. The phase



plane of the chattering neuron can now be generated and a comparison can be made with v - t graph in order to compare the accuracy of the reduction.

Figure 5.1: This phase plane belongs to the reduced chattering neuron. The reset is gone, thus also the spikes, it is now a smooth approximation to the dynamics with the reset.



Figure 5.2: The approximation is not perfect, but the time between bursts is very accurate.

5.3.2 RS, FS AND LTS NEURONS

To avoid the reset for the periodically spiking neurons, it is necessary to do a similar reduction. However, the reset *c* is now on the left-hand side of the minimum of the *v*-nullcline. That means that the branch cannot simply be added in the same way as before, since the neuron will fire only after going past that minimum. To leave the subthreshold behaviour intact, a slightly different approach is necessary. The additional branch must be shifted to the right further than before. That is because the constraints that have been set require a separation distance κ to hold. This $\kappa > 5$, because

- The intersection of the *v*-nullcline and the reset value *c* is at -65mV and the minimum of the *v*-nullcline is at -62.5mV, thus the distance between them is 2.5.
- The *v*-nullcline is a parabola, thus symmetric around its minimum.
- The distance between the intersection just described and its mirror image is thus 5.
- For the constraints to be valid, $\kappa > 5$.

If κ is chosen smaller, η and ξ will become negative and turn the branch 180 degrees around turning point v - c. That will completely demolish the dynamics. This problem is solved in [7] by setting the reset value c at -55mV which is to the right of the v-nullcline, thus any $\kappa \in [0.5, 2.5]$ suffices. The constraints as they were set in the paragraph on chattering neurons can be left intact in both cases. The coupled population model that is presented in at the end of the paragraph Results will use c = -55mV for the neurons that are not the chattering neurons as well, since the κ approach requires a significant amount of numerical computing and testing.

The right value for κ is found when it provides a good fit for the firing rate function. Since the non reduced single cell dynamics provide periodic fire rates for values of *I*, an f - I diagram will allow comparison between the non reduced and the reduced single cell dynamics for the remaining types of neurons. In the following figure the f - I diagram is shown for the unreduced single cell dynamics of the RS neuron. For different values of κ this diagram may be made for the reduced single cell dynamics of the RS neuron. The one that gives the best fit is the best κ .



Figure 5.3: The firing rate for the unreduced single cell dynamics of the RS neuron.

By adapting the κ value such that the reduction shows the same f - I diagram, a good value is found. This is not done here because of the time it takes to find such a good value. Also, for the inhibitory neurons, this approach is slightly different, because the *u*-nullcline is in at an other position. This altogether makes up for a very time expensive process.

5.3.3 COUPLING

The single cell dynamics with a reset function have now been transformed into reduced single cell dynamics. Populations dynamics are desired, thus the global activity is taken into consideration. A network of *N* neurons can be randomly connected by letting the output of a neuron by the synaptic input of the post-synaptic neuron. It is assumed that the output, a spike, produces a spike in the synapse as well. The response of the synapse is $q(t - \hat{t})$, such that the linear operator *Q* makes $Qq = \delta$, which is the response that is desired. In [7] $Q = \frac{d}{dt} + \alpha$. The spike \hat{t} is simply the time at which a spike arrives at the synapse. The post-synaptic current becomes

$$I_{post} = \overline{g}q(t-\hat{t})(v_{post} - v_{rev}).$$

Here, \overline{g} is the maximal conductance, V_{rev} is the associated reversal potential and V_{post} is the membrane potential of the post-synaptic neuron. For any neuron *i* a duration

$$T_i(t) = \{ \hat{t}_i, j \in \mathbb{N} \mid 0 < \hat{t}_1 < \dots < \hat{t}_n \le t \}$$

collects all (or none, the set may be empty) spikes of the neuron in that duration. Define the synaptic activation s_i of the post-synaptic neuron as the convolution sum of the spike times T_i with the response of the synapse $q(t - \hat{t})$. Thus

$$s_i(t) = \sum_{\hat{t} \in T_i(t)} q(t - \hat{t}).$$

$$Qs_i(t) = \sum_{\hat{t} \in T_i(t)} \delta(t - \hat{t}).$$

Not all neurons are connected to each other and they are also not connected with uniform synaptic weight. Let J_{ij} represent the synaptic efficacy as before. Then $J_{ij} = 0$ means that neuron *i* is not connected to neuron *j* and $J_{ij} = 1$ means that the post-synaptic signal of neuron *j* is felt by *i* in the same amplitude that the signal when it left neuron *j*. The post-synaptic current departing from neuron *j* towards neuron *i* is given by

$$I_{syn,i}(t) = \overline{g} \sum_{j=1}^{N} J_{ij} s_j(t) (v_i(t) - v_{rev}).$$

Now that the individual neurons can be coupled by means of $I_{syn,i}$, there is still nothing said about population dynamics. By means of three assumptions, it is possible to find lumped network activity.

• The exact time that a spike arrives at a post-synaptic neuron is not necessary. The individual spike trains can be averaged by representing them with the firing rate. This comes down to replacing the single cell dynamics of an Izhikevich neuron by the reduced system. The post-synaptic signal is then described by

$$Qs_i = f(v_i, u_i, I_{ext} - I_{syn,i}).$$

*I*_{ext} is the average external input to the neurons.

• The neurons are connected randomly, but there is a lot of knowledge about how many connection a single neuron has in specific regions of the brain. Let W be the random variable describing the synaptic weights, such that the synaptic weights J_{ij} are distributed independently in the same way that W is. Define

$$\langle J_{ij} \rangle = \mathbb{E}W,$$

 $S(t) = \sum_{i=1}^{N} s_i(t)$

• Now the most important assumption. Neurons that receive a similar input react also similarly, so they remain close to each other in phase space. It is therefore sufficient use the following averages to approximate the membrane potential and the recovery variable.

$$v(t) = \frac{1}{N} \sum_{i=1}^{N} v_i(t),$$
$$u(t) = \frac{1}{N} \sum_{i=1}^{N} u_i(t).$$

36

This makes the dynamics of the population

$$\frac{\mathrm{d}v}{\mathrm{d}t} = \frac{1}{N} \sum_{i=1}^{N} 0.04 v_i^2 + 5v_i + 140 - u_i + I_{ext} - I_{syn,i} - \xi e^{\eta(v_i - c)} \qquad \approx g(v, u, I_{ext} - I_{syn}),$$

$$\frac{\mathrm{d}u}{\mathrm{d}t} = \frac{1}{N} \sum_{i=1}^{N} a(bv_i - u_i) + df(v_i, u_i, I_{ext} - I_{syn,i}; c) \qquad \approx h(v, u, I_{ext} - I_{syn}),$$

$$\begin{split} g(v, u, I_{ext} - I_{syn}) &= 0.04v^2 + 5v + 140 - u + I_{ext} - I_{syn} - \xi e^{\eta(v-c)}, \\ h(v, u, I_{ext} - I_{syn}) &= a(bv-u) + df(v, u, I_{ext} - I_{syn}; c). \end{split}$$

 $I_{syn}(t) = \overline{g} \langle J_{ij} \rangle S(t) (v(t) - v_{rev}).$

The post-synaptic signal depends on the firing rate and on the number of neurons. The final equation for the reduced model becomes

$$QS = Nf(v, u, I_{ext} - I_{syn}).$$

6 **Results**

The dynamics of the population are now described by three differential equations. The external current I_{ext} is a noise term, thus the DE describing v is stochastic in nature. This means that using MATLAB's standard ODE solvers are not useful, because they solve only deterministic systems of equations. Although MATLAB itself does have some stochastic differential equation solvers, a simple adapted Euler forward approach will suffice here. Therefore, the reduced model is constructed using the Euler-Maruyama scheme. In its formal definition, the Euler-Maruyama scheme is as follows. Consider a stochastic differential equation in a general form

$$\mathrm{d}X = f(X)\,\mathrm{d}t + g(X)\,\mathrm{d}W,$$

where *W* is a Wiener process. Upon solving this SDE on some time interval [0, T], the Euler-Maruyama approximation to the true solution *X* is a Markov chain *Y*. By making a partition of the interval [0, T] in pieces of dt > 0, with dt = T/N, with *N* the number of subintervals, the SDE can be rewritten into

$$Y[n+1] = Y[n] + f(Y[n]) dt + g(Y[n]) dW,$$

$$dW = W[n+1] - W[n].$$

The latter expression can be rewritten into a simpler term, since W is a collection of simply a normal distributed random variables that describe a white noise process. The SDE for the membrane potential does not contain such a function g(X), the noise term is simple. The final formal definition of the Euler-Maruyama scheme becomes:

$$Y[n+1] = Y[n] + f(Y[n]) dt + \sigma \sqrt{dtB}.$$

Here, *B* is a random number drawn from a normal distribution N(0, 1) and σ is the variance of the noise. Now the equations that were found in the previous paragraph can be discretized. The system in this scheme looks as follows:

$$\begin{split} v[n+1] &= v[n] + \left(0.04v[n]^2 + 5v[n] + 140 - u[n] - \xi \exp^{\eta(v-c)} - I_{syn} \right) dt + \sigma \sqrt{dt}B, \\ u[n+1] &= u[n] + \left(a(bv[n] - u[n]) + df(v[n], u[n], I_{ext} - I_{syn}; c \right) dt, \\ S[n+1] &= S[n] + \left(-\alpha S[n] + Nf(v[n], u[n], I_{ext} - I_{syn}; c \right) dt, \end{split}$$

with *n* = 0, 1, 2, ...

The square brackets here denote that the functions v, u and S are now discrete. This can as it is, be inserted into MATLAB with the right values for the constants and deliver a nice model for a single population of identical neurons. For a small simulation (30 seconds), the algorithm is fast and reasonably reliable. It is not great as it may in some cases explode. By doing longer simulations, the inter burst period may be analyzed to verify the quality of the reduction. If all is well, the inter burst period is exponentially distributed.

The following simulations are done with *a*, *b*, *c*, *d* the values corresponding to chattering neurons. I_{ext} is constant at 6mA with $\sigma = 2$, this is the same amount of stimulation as used in the simulations of the microscopic model. *B* is drawn from N(0, 1). The connections in the network are made by setting $\overline{g} = 0.002$, $\langle J_{ij} \rangle = 0.03$, $\alpha = 0.1$ and $v_{rev} = 0$. The population consists of 5000 neurons. The value for ω is set at 120 and $\kappa = 0.8$.



Figure 6.1: A 3000s simulation. The top left figure shows the average membrane potential. The top right figure shows the phase plane, which has exactly the same shape as the reduced single cell phase plane. The inter burst times are approximately exponentially distributed as shown in the bottom left figure. The bottom right figure shows a subset of the top left.



Figure 6.2: A 300s simulation. The top left figure shows the average membrane potential. The top right figure shows the phase plane, which has exactly the same shape as the reduced single cell phase plane. The inter burst times are approximately exponentially distributed as shown in the bottom left figure. The bottom right figure shows a subset of the top left.

The simulations both show the exponential distribution that is desired. The reduction therefore is good. Since the reduced model simulations show a population of only chattering neurons, any time the membrane voltage is above -50mV, the population is bursting. The time between those peaks can be found by using the find function in MATLAB. A histogram of these times is presented in the bottom left figure. The horizontal axis represents the time between those peaks in milliseconds. Compare figures 6.1 and 6.2 to figures 4.26 and 4.28 and it is evident that the timescale in the histogram is also very similar. The top right figure, the phase plane, is used to show that the simulation is indeed a simulation of chattering neurons, because upon comparison with figure 5.1, it is found that the phase planes match up very well. This leaves to conclude that for chattering neurons the reduction is good.

For a simulation with multiple populations, it must be decided how much influence they

have on each other, thus determining the average synaptic weight. This can be modeled by using the scheme above and adapt it for the number of populations. First, it is verified that the dynamics are the same as in the previous simulations. By means of a short simulation (30s) and looking at the phase plane of the populations, it can be seen that the dynamics are fine.



Figure 6.3: The left figure shows the phase plane with the two excitatory subpopulations and one inhibitory. Since they have the same shape as in figure 6.1 and 6.2, the dynamics are correct. The right figure shows the average membrane potential of the three individual subpopulations.

The I_{syn} variable contains the information of the surrounding populations. These coupling equations have been copied from [7].

$$\begin{split} I_{syn}^{inh} &= G_{inh}^{exc2} \cdot S_{exc2}[n-1] \Big(E_{exc} - v_{inh}[n-1] \Big) \\ I_{syn}^{exc1} &= G_{exc1}^{inh} \cdot S_{inh}[n-1] \Big(E_{inh} - v_{exc1}[n-1] \Big) \\ I_{syn}^{exc2} &= \Big(G_{exc2}^{exc1} \cdot S_{exc1}[n-1] + G_{exc2}^{exc2} \Big) \Big(E_{exc} - v_{exc2}[n-1] \Big) \end{split}$$

Here, G_j^i determines the conductance from population *j* to population *i* and is depending on the number of cells in network *j*. Its definition is

$$G_{exc1}^{inh} = N_{inh} \cdot p_{exc1}^{inh} \cdot g_{exc}^{inh}$$

$$G_{exc2}^{exc1} = N_{exc1} \cdot p_{exc2}^{exc1} \cdot g_{exc2}^{exc1}$$

$$G_{exc2}^{exc2} = N_{exc2} \cdot p_{exc2}^{exc2} \cdot g_{exc2}^{exc2}$$

$$G_{exc2}^{exc2} = N_{exc2} \cdot p_{exc2}^{exc2} \cdot g_{exc2}^{exc2}$$

 $E_{population}$ determines the degeneration of the population. A coupled model with lumped Izhikevich neurons has been created. By setting the parameters in the model to the following values:

Excitatory 1		Excitatory 2		Inhibitory	
Parameter	Value	Parameter	Value	Parameter	Value
a	0.01	a	0.03	a	0.02
b	0.2	b	0.3	b	0.2
С	-50	С	-55	с	-55
d	2	d	2	d	2
I _{ext}	3	I _{ext}	3	I _{ext}	2
Eexc	0			E _{inh}	0

The connectivity parameters are set at:

Parameter	Value	Parameter	Value
p_{exc1}^{inh}	0.3	g_{exc1}^{inh}	0.02
p_{exc2}^{exc1}	0.1	g_{exc2}^{exc1}	0.02
p_{exc2}^{exc2}	0.1	g_{exc2}^{exc2}	0.005
p_{inh}^{exc2}	0.1	g_{inh}^{exc2}	0.02

A simulation with this setup containing 100 inhibitory neurons and 600 excitatory neurons (300 of each sort) with $\sigma = 1$ gives



Figure 6.4: From the phase plane in the left figure it can be seen that there is something wrong in the coupling. The right figure shows the three individual populations, from which it can be seen that the exc2-population is malfunctioning.

The coupling as it is done here is not correct. The *u*-variable as can be seen in figure 6.4, reaches a value that is unrealistic. That causes the dynamics to be invalid. Using the exact same stimulation values as in the model used in [7], where $(I_{ext}^{exc1}, I_{ext}^{exc2}, I_{ext}^{inh}) = (-3, 6, 0)$, the simulation shows



Figure 6.5: From the phase plane in the left figure it can be seen that the populations are inactive. The right figure shows that three individual populations are all at rest.

This last simulation in figure 6.5 shows no spikes or bursts, the populations are at rest. That indicates once more that the coupling is incorrect, since it does not give the same results as in [7]. Upon redefining the coupling correctly, the simulations of coupled populations must turn out fine as well.

7 DISCUSSION

The microscopic model contains apart from the four types of neurons and their dynamics, also some other effects. These are not in the reduced model. One may improve the reduced model by incorporating these effects. The long term effects and the spike timing dependent plasticity can be added to the S equation as another term. The delay can be added by transforming the set of differential equations into a set of delay differential equations. There may also be chosen for a different numerical approximation. The Euler-Maruyama scheme that is used is a very efficient method to model stochastic differential equations, but there are more accurate options (such as the extended Verlet algorithm). This particular scheme is chosen because it is quick and accurate enough. The reduction for the periodic spiking neurons can also be improved. Apart from the numerical search for the right value for κ , it should also be possible to do this analytically, since there is an analytic solution available. Such a solution is better than one found using heuristics, as it is possible to find a good κ heuristically, but that is not necessarily the optimal solution. When using an analytic solution, it can be reasoned that the solution is optimal. This has not been done, which means that the reduced model shows a neat reduction of the chattering neurons, but does not include any regular spiking neuron. Namely, by setting the reset value to -55mV, the type of neuron is changed, the dynamics are very different, but the firing rate of this new type of neuron can be made to match the RS, FS or LTS neuron. That makes the comparison between the microscopic and the macroscopic model difficult since they do not model the same neurons. Also, as it turned out, the coupling is not done correctly. That means that is impossible to compare on coupled population level, which is unfortunate. On single population level, the simulations of the macroscopic model are in accordance with the microscopic model.

Experiments may be done to verify the macroscopic model. Apart from verification, it would also be interesting to see the influence of synaptic depression on the inhibitory population and the excitatory population. From the numerical simulations of a coupled population and an isolated excitatory population, it appeared that the synaptic depression had a significant influence on only the inhibitory population, as a short term effect. If the synaptic depression causes so much activation in the inhibitory population, the excitatory population will not burst.

8 CONCLUSIONS

The reduction is very good for the chattering neurons, as it was in [7]. For periodic spiking neurons, it is must be changed. The excitatory population can be simulated by means of the reduced model and can be verified by experiments. In such an experiment, the inhibitory population must be set to inactive and the synaptic potency and depression may be left they way they are. Then, with an approximately constant synapse strength, the right connectedness and noisy input with the same amplitude as used in the simulations, the experiment should show the same result. For future work, it is important to notice that higher dimensional systems can be reduced while leaving the subthreshold behaviour intact. For 1-D systems there are many very good mean-field reductions, for instance the LIF neuron approximation using the theory of Fokker-Planck equations. In higher dimensional models there must be sought for the difference between fast dynamics and slow dynamics in order to temporarily reduce it to a one dimensional model. From that point onwards, 1-D mean field reductions may be applied.

9 References

- [1] T.A. Frewen C.R. Laing and I.G. Kevrekidis. Reduced models for binocular rivalry. *Journal of Computational Neuroscience*, 28:459–476, 2010.
- [2] J. Dijkstra. Adaptation to low frequent stimuli in computational and cultured neuronal networks. *University of Twente*, 2014.
- [3] P.A. Robinson M.Breakspear G. Deco, V.K. Jirsa and K. Friston. The dynamic brain: From spiking neurons to neural masses and cortical fields. *PLoS Computational Biology*, 4, 2008.
- [4] E.M. Izhikevich. Simple model of spiking neurons. *IEEE Transactions on Neural Networks*, 14, 2003.
- [5] E.M. Izhikevich. Which model to use for cortical spiking neurons. *IEEE Transactions on Neural Networks*, 15:1063–1070, 2004.
- [6] H. Markram M. Tsodyks, K. Pawelzik. Neural networks with dynamic synapses. *Neural Computation*, 10:821–835, 1998.
- [7] S. Visser and S.A. Van Gils. Lumping izhikevich neurons. *EPJ Nonlinear Biomedical Physics*, 6, 2014.
- [8] K.F. Wong and X.J. Wang. A recurrent network mechanism of time integration in perceptual decisions. *Journal of Neuroscience*, 4:1314–1328, 2006.

10 Appendices

10.1 APPENDIX A

The C++ program [2] is executed on a windows 8 platform. The compiler used is of a g++ nature, Netbeans 8 namely. This compiler will not work on windows without an UNIX environment and a backup program. These are Cygwin and MinGW respectively. Apart from the standard Netbeans libraries, also the boost library will need to be downloaded. When this is all set up correctly, the program may be run. The values that were used in the 24 hour simulations are the default values. It is important to realize that this program is computationally expensive in the sense that simulations with more than 250 neurons take longer in real time than its eigentime. This means that if one wishes to simulate 300 neurons over 500 seconds (called the eigentime), the real time simulation may take over 1000 seconds.

10.2 APPENDIX B

The MATLAB programs that were made in order to generate the phase planes, the population simulations and the analysis of the population simulations may be requested at e.luesink@ student.utwente.nl, because presenting it here would require a significant amount of space.