UNIVERSITÄT HAMBURG

UNIVERSITAT AUTÒNOMA DE BARCELONA

UNIVERSITÀ DEGLI STUDI DELL'AQUILA

Erasmus Mundus Consortium "MathMods"

Joint Degree of Master of Science in
Mathematical Modelling in Engineering: Theory, Numerics, Applications

In the framework of the
Consortium Agreement and Award of a Joint/Multiple Degree 2013-2019

Master's thesis

Theoretical description of fully-connected neuronal networks and simulations of partially connected neuronal networks to capture their macroscopic properties

Supervisor

Alex Roxin

Candidate

Thimjo Koça
Matricola: 239004

2015/2016

Laurea Magistrale in Ingegneria Matematica
Dipartimento di Ingegneria e Scienze dell'Informazione e Matematica
Università degli Studi dell'Aquila

Contents

1. Introduction

Achieving macroscopic descriptions of neuronal systems starting from their microscopic dynamical description is one of the leading fields of research in Computational Neuroscience [6], [1].
A model proposed in [9] gives a description of a fully-connected network where a certain variability is introduced in the current component of the neuron. In this work the variability is moved in the synaptic weights. The results for this case in the fully-connected network are verified. Further on 2 models are proposed by which simulations in sparser networks can be run to get some insight in these cases.

2. Neuroscience Background

2.1. Nervous System

In an animal's body, the nervous system is responsible for its actions (voluntary and involuntary ones). A lot of studies on the system were done during the 19^{th} century, but due to technical difficulties (e.g. lack of strong enough microscopes), getting clear results was not trivial.
The first claim about the system was ***Reticular Theory***[7] postulated by Joseph von Gerlach and strongly supported by the Nobel laureate Camillo Golgi. According to it the nervous system (brain included) is a single continuous network.
The theory was opposed some years later when using his own discoveries and also other's work Ramon y Cajal came up with the ***Neuron Doctrine***[7] which in its actual form states:

- The neuron is the fundamental structural and functional unit of the brain
- Neurons are discrete cells
- Information flows from the dendrites to the axon via the cell body (terminology later explained in the "Neuron" section)

Both theories had supporters until technological advances made clear evidence in support of the Neuron Doctrine possible.

2.1.1. Brain's Structure

Concentrating on vertebrate species, their system is divided in the Peripheral Nervous System (PNS), made up of nerves and sensors and the Central Nervous System (CNS) which contains the spinal cord and the brain [7]. Because of its complexity and importance the main focus of Neuroscience is on the brain.
Brain itself consists of several regions, the main ones of which are [7]:

- *Hindbrain* which itself is divided into 3 subregions:
  - Medulla Oblongata is responsible for breath control, muscle toning, blood pressure

  - Pons is involved in sleep and arousal and also connected to Cerebellum
  - Cerebellum deals with coordination and timing of voluntary movements, sense of equilibrium, language, attention, etc.

- *Midbrain* is responsible for eye movements, visual and auditory reflexes
- *Reticular Formation* modulates muscle reflexes, breathing and pain perception and also regulates sleep, wakefulness and arousal
- *Thalamus* is a "relay station" for all sensory information to the cortex except for smell which goes directly to the cortex and also regulates sleep/wakefulness
- *Hypothalamus* regulates our basic needs, commonly referred as 4 F-s (Fighting, Fleeing, Feeding and Mating)
- *Cerebrum* Involved in perception, motor control and also in cognitive functions (emotions, learning and memory)
  Itself consists of:
  - Basal Ganglia
  - Hippocampus
  - Amygdala
  - **Cerebral Cortex** which plays important role in functions that "define" what means to be human (language, memory, attention, perception, awareness, thought, consciousness)

Cerebral Cortex

Cerebral Cortex is definitely the most complex region of the brain. It is a layered sheet of neurons, about 3 mm thick, made of approximately 30 billion neurons with 300 trillion connections in total. It is made up of 6 layers, which according to current evidence [7], [2] are relatively uniform in structure and structured in functionality.
This uniformity between the layers has led to the hypothesis that a common computational principle is operating across cortex [7].

2.2. Neurons

Neurons are the cells from which the nervous system is made of. As stated above they are also the fundamental functional unit of the nervous system, therefore they need some special attention.
In this section some key neuron-related topics are treated, starting with some neuron electrophysiology (talking essentially about what physically transmits electric current in neurons) and how neuron's membrane which is generally isolating it (physically and electrically) uses some of its mechanisms to allow

exchange of current when needed, continuing with some simplified neuronal anatomy, a small discussion of synapses and finishing with a simplified description of action potential, the signal type by which neurons communicate.

2.2.1. Neuronal Electrophysiology

Using a simple analogy, neuron can be thought as a bag full of liquid (the cell's membrane [1] being the bag), itself floating into another liquid. These 2 liquid spaces are rich in ionic species.
In the intracellular medium there is a high concentration of:

- $K^+ \rightarrow$ Potassium cations
- $A^- \rightarrow$ Different organic anions

While in the extracellular medium there is high concentration of:

- $Na^+ \rightarrow$ Sodium cations
- $Cl^- \rightarrow$ Chlorine anions

Membrane Potential

Due to 2 forces, which are:

- ***Electric Potential Gradient*** $\rightarrow$ A^- anions attract more K^+ into the cell and repel more Cl^- out of it, favoring deepening of the asymmetry
- ***Concentration*** $\rightarrow$ The concentration of a given ionic species tends naturally to a balance state, a uniformity of concentration in and out of cell. This uniformity is sought through a process called **active transport** during which ions are pumped in and out of the cell via a mechanism called **ionic pump**. This force favors symmetry

a concentration asymmetry for the anions and cations between the inner and outer part of the cell appears. Because of this difference, an electric potential known as **membrane potential**, exists between the 2 spaces. It is the membrane potential and the way it alters that makes up the electric signals that codes information in the nervous system.
An equilibrium of the 2 above forces,gives rise to a 0 net current going through the neuron's membrane which produces a static potential.
It is found experimentally [6] that the resting potential of a neuron is $u_{rest} \approx -65mV$, so $E_K < u_{rest} < E_{Na}$ [2] which means that Na^+ will continuously flow into the cell and K^+ will continuously flow out of it.

[1] A cell membrane is a lipid layer which surrounds the cell's body and enclose its content
[2] E stands for the Nernst Potential (check A)

2.2.2. Neuronal Anatomy

Anatomically the neuron is complicated, but as of their function in processing transmitting electrical signals, 3 are its main parts:

- ***Dendrites*** → They serve as the input of the cell. Electric signals from other neurons enter the actual cell through its dendrites
- ***The body***
- ***Axon*** → Serves as the output of the cell. Electric signals meant to be transmitted to other neurons exit the current cell through its axon

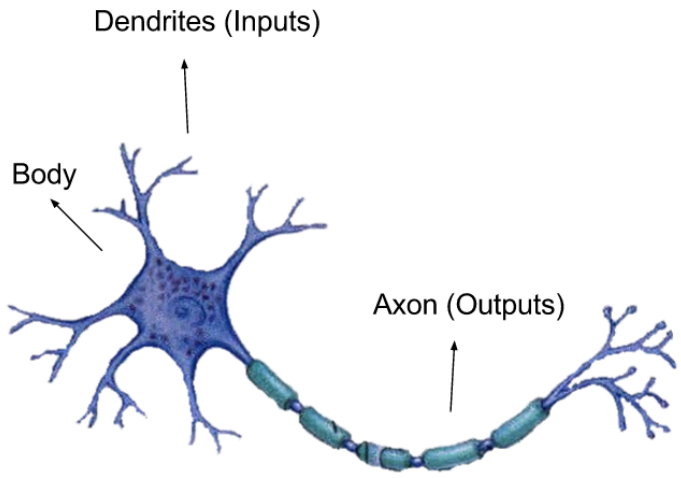


Figure 2.1: Sketch of a Neuron. Its main parts, the axon, the dendrites and the body are shown.

Ionic Channels in the cell's membrane

Ionic channels are some anatomical structures of great importance for the neuron. It is due to them that a neuron can communicate ions (and therefore alter its membrane potential) with other neurons and the outer liquid. These channels are found in the cell's membrane.
The *cell's membrane*, although it generally prevents the inner and outer liquid to mix, it has through its surface some ionic gated-channels [3] which under certain conditions they allow exchange of ions between the 2 media.
Depending on the way their gates are controlled, ionic channels can be classified to:

[3] They are just proteins to which the ions can be attached to travel through the cell's membrane

- Voltage-gated channels → The probability of being open or not depends on the membrane potential
- Chemically-gated channels → The opening of the channels depends on the presence of some specific chemicals
- Mechanically-gated channels → They are sensitive to pressure, stretch, etc.

Their applications will be discussed further in 2.2.3 and 2.2.4.

2.2.3. Synapses

Synapses are structures that allow inter-neuron communication. Essentially they are just the space between the axon of the transmitting neuron and the dendrite of the receiving neuron, which includes also some ionic channels. It is through them that a neuron (in this context called the pre-synaptic neuron) can affect the membrane potential of another neuron (called in this context the post-synaptic neuron).
With respect to the way their transmitting mechanisms work, i.e. the nature of their ionic channels, they can be classified to:

- ***Electric Synapses***
  They have voltage-gated ionic channels. The signal propagation in them is really fast, so they are usually found in cases when neurons synchronization is desired, or when reflexes have to be implemented
- ***Chemical Synapses***
  In this type of synapses the transmitter releases some *neurotransmitters* [4] which can open the chemical-gated channels of the receiver and so signals can pass. They are slower than the electric ones, but they have the ability to customize the amount of current that is transmitted [5] and therefore they are quite useful in implementation of memory for example.

[4] Chemical substances
[5] The control is achieved through alteration of the number of chemical-gated channels that the receiver has [7]

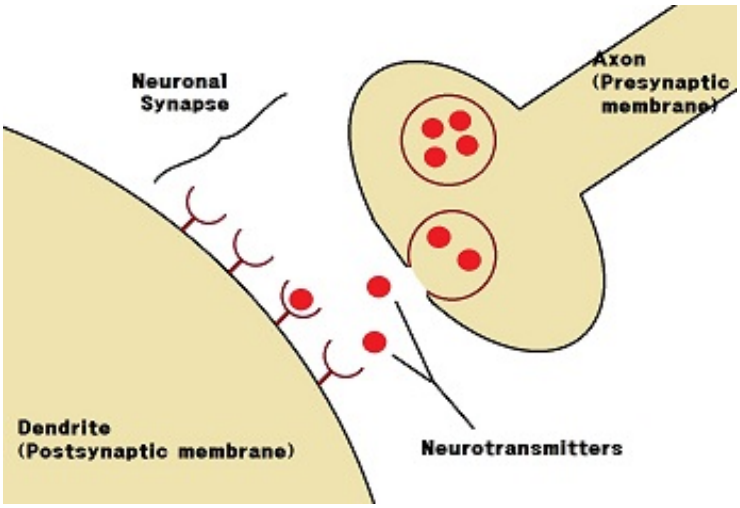


Figure 2.2: Sketch of a Chemical Synapse. The axon of the pre-synaptic cell and the dendrite of the post-synaptic one are shown. Also how the neurotransmitters are released from the pre-synaptic cell and "captured" by the gates of the post-synaptic one

Excitation vs Inhibition

With respect to how a neuron affects another neuron through synapses we can classify them in:

- ***Excitatory Neurons***
  The signals they transmit as pre-synaptic neurons increase the membrane potential of the post-synaptic neuron
- ***Inhibitory Neurons***
  The signals they transmit as pre-synaptic neurons decrease the membrane potential of the post-synaptic neuron

2.2.4. Action Potential

The main type of signal through which neurons communicate with each other is called **action potential** (or **spike**).
Spikes are impulses which are transmitted through the cell's body and cause a synapse to be activated (therefore the post-synaptic neuron's membrane potential to be affected [6]).
Before giving a rough idea of what happens during a spike generation, some terminology should be introduced:

[6] Spikes in inhibitory pre-synaptic cells will lower the post-synaptic cell's membrane potential, while spikes in excitatory post-synaptic cells will raise it

- ***Depolarization*** → The process of raising the membrane potential of a cell
- ***Hyperpolarization*** → The opposite of depolarization, i.e. the process of lowering a cell's membrane potential

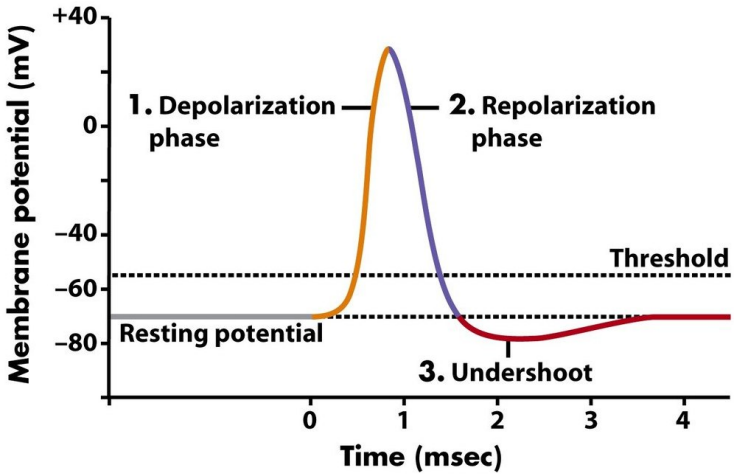


Figure 2.3: Sketch of membrane potential dynamics during a spike. The main fazes are depicted. In gray the neuron is in the resting potential, with yellow the polarization faze, with purple the hyperpolarization (repolarization) faze and with red the "undershoot" (the faze when the neuron is in its refractory period) and reach of resting potential again

A spike in steps:

1. When the membrane potential of the neuron being around its resting potential receives enough input to pass through a *threshold* value, some of its Na^+ ionic channels (the ones that are near the "dendrites-end" of the neuron) open letting Na^+ to enter the cell and strongly depolarizing it
2. In a sequential order more channels through the cell's body and later axon open, too
3. This until a certain level, after which Na^+ channels are again sequentially closed and K^+ channels are sequentially opened letting K^+ ions to go out of the cell causing a hyperpolarization
4. After this, for a short a period, called **refractory period**, membrane potential is lower the resting potential value. During this period the neuron can generally not produce any new spike

Note: Nowadays, there are evidence that a voltage threshold value doesn't really exist [6]. Although, the concepts is used for 2 reasons:

- For its simplicity
- Models that implement it give satisfactory results

2.3. Neuronal Models

After giving the basics about real neurons, naturally the next step would be to talk about neuronal models.
In this section the biologically inspired Hodgkin-Huxley Model is presented first and them some simpler models, adequate for network simulations are introduced.
In general to model neurons the key features are first identified. After this step the neuron is modeled as an electric circuit with its key features being the elements of this circuit. More specifically, an equivalent circuit will contain:

- An ***external*** current modeling the input current of the cell
- A ***capacitor*** modeling the cell's membrane potential
- Some ***conductors*** (or resistors, it's a matter of taste) modeling the conductance ions battle to pass the ionic channels
- Some ***piles*** modeling the Nernst potentials of the ionic species

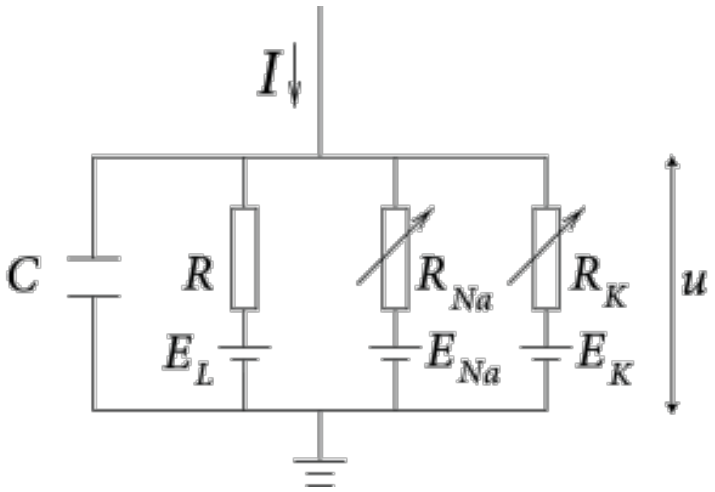


Figure 2.4: Equivalent circuit with Na^+, K^+ and leakage channels proposed in Hogkin-Huxley Model. The capacitor representing the membrane potential, Rs for the ionic channels, E_is for the Nernst Potential of the i^{th} ionic specie and I for the external current.

What differentiates models from each other is:

- The way these parameters evolve in time
- The number of explicit ionic channels modeled

2.3.1. Hodgkin-Huxley Model

Hodgkin-Huxley model is a biologically-inspired model proposed by Sir Alan Lloyd Hodgkin and Sir Andrew Fielding Huxley in 1952 to describe the dynamics of an action potential in the squid's giant axon. For this work they were awarded in 1963 the Nobel Prize in Medicine.
This model could be used to describe the dynamics of neurons in general.
The model for the axon reads:

$$\begin{cases} C\dot{v(t)} = -\sum_k I_k(t) + I(t) \\ \sum_k I_k(t) = g_{Na} m^3(t) h(t)(v(t) - E_{Na}) + g_K n^4(t)(v(t) - E_K) + g_L(v(t) - E_L) \end{cases}$$

where k is indexing the ionic channel, Na stands for sodium, K for potassium, L for the "leakage" current which models the rest of the ionic species combined, g_i is the conductance of the i^{th} specie, E_i is the Nernst potential of the i^{th} specie and m,h and n are some parameters related to the ionic channels' properties
Its complexity makes it a very good option to study single cells dynamics, but at the same time makes it impossible to be applied in neuronal networks.

2.3.2. Integrate-and-Fire Models

In order be able to get some results for populations of neurons through simulations, Hogkin-Huxley model should be simplified so the computational complexity is reduced. The family of Integrate-and-Fire models is class of models widely used in practice for this purpose. Below some its main representatives are introduced.

Classes of Neurons

But before that, a classifications of neurons with respect to their bifurcation will be introduced.
The first study of bifurcations in the neuronal dynamics context was published by Hodgkin [4] in 1948 (even before mathematical studies of bifurcations were done).
In his results Hodgkin identified 3 classes of neurons:

- ***Class 1*** of neurons includes cells in which spike-generation depends on the strength of the applied current and is independent of the current's frequency

- ***Class 2*** of neurons includes cells in which spike-generation occurs in a certain frequency band of the input current and is insensitive to the current's strength
- ***Class 3*** of neurons include cells in which a single spike is generated when an impulse external current is applied and periodic spiking can be generated only for very strong currents

Integrate-and-Fire Models are all models of class 1 neurons.

Linear Integrate-and-Fire

It's the simplest model of the family. Although it is classified here as a simplification of Hodgkin-Huxley, it actually dates earlier then it (1907).
This model interprets a neuron as a circuit containing only a capacitor with a constant capacitance. Therefore the equation describing it is:

$$C\dot{v}(t) = I(t)$$

To improve the accuracy of the model, a refractory period is added after the neuron fires.

Leaky Integrate-and-Fire

To improve further the linear integrate-and-fire model a conductor is added to the circuit to reflect the ionic diffusion that happens when we are away from the Nernst potential.
With this addition we gain the **Leaky Integrate-and-Fire** model which reads:

$$C\dot{v}(t) = I(t) - gv(t)$$

where g stands for the conductance

Quadratic Integrate-and-Fire

Quadratic Integrate-and-Fire (QIF) model is found to be the *canonical* form (or in "dynamical systems jargon" *normal form*) of class 1 neurons [5] and therefore is of particular importance.
In its pure mathematical form, it reads:

$$\tau\dot{v}(t) = av^2(t) + I(t)$$

where a is a constant.
This is the model that is being used in this work.

2.4. Populations of Neurons

Having some simplified models of an acceptable computational complexity for population simulations, the next 2 issues to clarify are:

- How to model synapses
- Which are the macroscopic quantities of importance

2.4.1. Models of Synapses

Modeling synapses will determine how the neurons of a population will interact and therefore affect the dynamics of the model. Below some alternatives are presented.

Variable Synaptic Weights

In a detailed modeled population every synapse would have its own **synaptic weight** by which the current entering the post-synaptic neuron will be multiplied. These weights are variable, they change over time. So given the pre-synaptic variable with index i and the post-synaptic one with index j, the weight will be of the form $w_{ij}(t)$.

Constant Synaptic Weights

Although quite accurate, these kind of models are used only in small networks modeling memory and learning. In networks containing a considerable amount of neurons constant weights, of th eform w_{ij} are preferred.

Synaptic Weights as properties of the neurons

To further simplify the case, synaptic case can be assigned as properties of 1 of the neurons (the pre-synaptic, or the post-synaptic).

a) Property of the pre-synaptic neuron In this case each neuron has a given constant synaptic weight by which the output current after a spike is multiplied. Depending on the nature of the neuron (excitatory or inhibitory) the weight is positive or negative.

b) Synaptic Weights as property of the post-synaptic neuron In a population with only excitatory (or only inhibitory) neurons, each neuron is assigned a constant synaptic weight by which its input current will be multiplied. If the population is made up of both excitatory and inhibitory neurons, then each neuron will be assigned 2 synaptic weights, 1 per each family.

2.4.2. Macroscopic quantities of importance

Neural Coding

An important factor in determining the important macroscopic quantities is clearly the way neurons code information. There are several proposed families of neuronal coding schemes, among which the most important:

- Rate Coding → Information is encoded in the spiking rate of the neurons
- Temporal Coding → Information is encoded in the temporal position of the spikes
- Population Coding → An input is partitioned and encoded in a group of neurons
- Sparse Coding → Different inputs are encoded by strong signals in different, relatively small groups of neurons

Although in different circumstances different schemes seems more plausible, we are interested in rate coding schemes.
Keeping this in mind, the firing rate [7] is the main quantity of study interest and is often coupled with the mean voltage of the population.

[7] A continuous function telling how many spikes will be fired by the network in a given instance of time. Check D for its derivation

3. The Problem

After presented some necessary background, the problem can be introduced.
In [9] a fully connected network of QIF neurons is analytically described by relating its firing rate with its mean voltage.
In doing so each individual neuron is described by:

$$\dot{v_i}(t) = v_i^2(t) + I(t) + \eta_i + Js(t)$$

where v_i is the membrane potential of i^th neuron, I is the external common current (i.e. same for all the neurons), J is the constant synaptic weight (same for every neuron), η_i is a Lorentzian distributed current component of the i^th neuron and s is the mean synaptic activation[1] (i.e. the smoothed average current component containing all the impulses getting generated after a spike).
In that case introducing a variability in the current components the analytic results are obtained.
Using an analogues technique we can obtain similar results by introducing a Lorentzian variability in the synaptic weights instead of the individual current components, i.e.

$$\dot{v_i}(t) = v_i^2(t) + I(t) + J_i s(t)$$

where η_i term is now missing and J_i is Lorentz distributed random variable.
The purpose of this work to first verify numerically the results and furthermore check the behavior of the system in sparser networks.
Two models are presented. The first one uses a single population of neurons, which results in a single distribution of synaptic weights among the neurons of the network.
The second one has 2 separate populations of neurons, one representing an excitatory set of neurons and the other an inhibitory one, which results in every neuron having 2 synaptic weights, one per each population.

[1] Check appendix for details

4. Model A

4.1. Derivation of the macroscopic description from the microscopic one for the case of a single population

4.1.1. Setting up

As a first step starting from the microscopic dynamics of a neuron, we should derive the macroscopic dynamics of the population which will link the spiking rate with mean voltage of the population. The derivation procedure is almost identical to the one in [9].
A QIF neuron's dynamics can be described as follows:

$$\begin{cases} \tau \dot{V} = V^2 + I, if V \leq V_{th} & \text{(4.1a)} \\ V \leftarrow V_r, if V \geq V_{th} & \text{(4.1b)} \end{cases}$$

where $\tau \rightarrow$ is the time constant, $V_{th} \rightarrow$ threshold potential, $V_r \rightarrow$ the reset potential and I $\rightarrow$ a parameter which models the interaction between neurons (model-dependent) and the external input
More specifically I can be expressed as:

$$I = I_{ex} + Js(t)$$

where $I_ex \rightarrow$ common parameter for every neuron,
J $\rightarrow$ the input synaptic weight of a given neuron,
$s(t) \rightarrow$ the mean synaptic activity:

$$s(t) := \frac{1}{N} \sum_{i=1}^{N} \sum_{k \backslash t_j^k < t} \int_{\infty}^{t} a_{\tau_1}(t - t') \delta(t' - t_i^k) dt'$$

where $t_i^k \rightarrow$ the occurrence time of the k^{th} spike of the i^{th} neuron,
$\delta(t) \rightarrow$ the Dirac delta function and
$a_{\tau_1} \rightarrow$ the kernel function which in our model have the following trait:

$$a_{\tau_1} := e^{-t/\tau_1}/\tau_1$$

Considering a continuous population of neurons for which we denote by $\rho(V|I,t)dV$

the fraction of neurons with membrane potential in the interval $[V, V+dV]$ and parameter I at time t, we assume I to be distributed according to a probability distribution g(I).
Considering the conservation of neurons, the continuity equation of our system will read:

$$\partial_t \rho + \partial_V \Big[\frac{V^2 + I}{\tau} \rho \Big] = 0$$

which can be also written as:

$$\tau \partial_t \rho + \partial_V [(V^2 + I)\rho] = 0 \tag{4.2}$$

Next we will have to accept the assumption made in [9], called the **Lorentzian Ansatz (LA)** which claims that no matter what the initial conditions are, the solution of 4.2 will generally have a "Lorentzian" shape:

$$\rho(V|I,t) = \frac{1}{\pi} \frac{x(I,t)}{[V - y(I,t)]^2 + x^2(I,t)} \tag{4.3}$$

(for a mathematical justification of this fact the interested reader can refer to [9])

Mean Synaptic Activity s(t) in a continuous population: Obviously in a continuous population s(t) will have the analogous continuous form:

$$s(t) := \int_{\text{population}} \Big[\sum_{k \backslash z^k < t} \int_{\infty}^{t} a_{\tau_1}(t - t') \delta(t' - z^k) dt' \Big] dz$$

4.1.2. Relating the the half width and center of the Lorentzian to the firing rate and mean voltage

a) r-x relation:
Considering the way QIF neuron's dynamics work, we can see that the firing rate of the population is nothing else then the probability flux at infinity, i.e.:

$$r(I,t) = \rho(V \to \infty | I, t) \dot{V}(V \to \infty | I, t)$$

calculating the above:

$$r(I,t) = \lim_{V \to \infty} \frac{1}{\pi} \frac{x(I,t)}{[V - y(I,t)]^2 + x^2(I,t)} \frac{V^2 + I}{\tau} = \frac{x(I,t)}{\tau \pi}$$

that is:

$$x(I,t) = \tau \pi r(I,t) \tag{4.4}$$

So the r-x relation reads:

$$r(t) = \frac{1}{\tau \pi} \int_{-\infty}^{\infty} x(I,t) g(I) dI \tag{4.5}$$

b) v-y relation:
Considering what the center of a Lorentzian distribution represents:

$$y(I,t) = \text{p.v.} \int_{-\infty}^{\infty} V\rho(I,t)dV$$

where p.v. stands for the ***Cauchy Principal value*** of the integral
We can construct the v-y relation through:

$$v(t) = \int_{-\infty}^{\infty} y(I,t)g(I)dI \tag{4.6}$$

4.1.3. Derivation of the equations

Substituting 4.3 in 4.2 we come up with the following expression:

$$[\tau x(\dot{I},t) - 2x(I,t)y(I,t)]V^2 + 2\{-\tau x(\dot{I},t)y(I,t) + x(I,t)[x^2(I,t) + y^2(I,t)] - xI + \tau x\dot{y}\}V$$
$$+ \{\tau x(\dot{I},t)[x^2(I,t) + y^2(I,t)] + 2x(I,t)y(I,t)I - 2\tau x(I,t)y(I,t)y(\dot{I},t) - 2\tau x^2(I,t)x(\dot{I},t)\} = 0$$

Which can be true in case:

$$\begin{cases} \tau x(\dot{I},t) = 2x(I,t)y(I,t) \\ -\tau x(\dot{I},t)y(I,t) + x(I,t)(x^2(I,t) + y^2(I,t)) - x(I,t)I + \tau x(I,t)y(\dot{I},t) = 0 \\ \tau x(\dot{I},t)[x^2(I,t) + y^2(I,t)] + 2x(I,t)y(I,t)I - 2\tau x(I,t)y(I,t)y(\dot{I},t) - 2\tau x^2(I,t)x(\dot{I},t) = 0 \end{cases}$$

System which is equivalent to:

$$\begin{cases} \tau x(\dot{I},t) = 2x(I,t)y(I,t) & \text{(4.7a)} \\ \tau y(\dot{I},t) = y^2(I,t) + I - x^2(I,t) & \text{(4.7b)} \end{cases}$$

Defining $w(I,t) := x(I,t) + iy(I,t)$ and combining the 2 equations of 4.7 we get:

$$\tau\partial_t w(I,t) = i[I - w^2(I,t)]$$

In our model we want to include the variability in the synaptic weight, specifically we we want each neuron of the population to have a given input synaptic weight. The set of these weights should be distributed as a Lorentzian distribution:

$$g(J) = \frac{1}{\pi}\frac{\Delta J}{(J-\bar{J})^2 + \Delta J^2}$$

So expressing I in it's complete form, we have:

$$\tau\partial_t w(J,t) = i[I_{exp} + Js(t) - w^2(J,t)]$$

To close the above equation we need to somehow related the mean synaptic activity s(t) with w(J, t). The most straightforward way to do so is by making synapses infinitely fast, i.e. in the Kernel function to take $\tau_1 \to 0$.
In this case we will have $s(t) = r(t)$ and therefore:

$$\tau \partial_t w(J,t) = i[I_{exp} + Jr(t) - w^2(J,t)] \tag{4.8}$$

To express the above function only in terms of time, we should make use of 4.5, 4.6, extend the function in the complex domain of J and make use of the residue theorem. More specifically: We make an analytic extension of w(J,t) from the real line to the lower half complex plane.
Our system having finite energy, would be a realistic assumption. In this case, both r(t) and v(t) would have finite values, therefore $x(\eta, t)$ and $y(\eta, t)$ should both have finite values almost everywhere. This fact implies that w(J, t) has also finite values a.e. and therefore its analytic extension i also bounded a.e.
Using the Residue Theorem, we can calculate integrals 4.5 and 4.6 of interest in the lower semi-circle, C with radius R and center at the origin and get:

$$\int_C w(J,t)g(J)dJ = \frac{2\pi i}{\pi} \frac{w(\bar{J} - i\Delta J, t)\Delta J}{-2i\Delta J} = w(\bar{J} - i\Delta J, t) \tag{4.9}$$

We need to prove also that the integral in the arch γ (C excluding the segment

$$-R, R$$

) is 0. To do so, we make use of the fact that w(J, t) is bounded a.e. :

$$\Big| \int_\gamma w(J,t)g(J)dJ \Big| \le \int_\gamma \Big| w(J,t)g(J) \Big| dJ \le M \int_\gamma |g(J)|dJ$$
$$= M\Delta J \int_0^\pi \frac{iRd\theta}{(Re^{i\theta} - \bar{J})^2 + \Delta J^2} \xrightarrow{R\to\infty} 0$$

where $M \ge 0$
So

$$\int_\gamma w(J,t)g(J)dJ \xrightarrow{R\to\infty} 0$$

therefore

$$\pi r(t) + iy(t) = \int_{-\infty}^{\infty} w(J,t)g(J)dJ = w(\bar{J} - i\Delta J, t) \tag{4.10}$$

And so 4.8 needs to be evaluated only for $J = \bar{J} - i\Delta J$.
Substituting the value in 4.8 we gain:

$$\begin{cases} \tau \dot{r} = \dfrac{\Delta J}{\pi} r + 2rv & \text{(4.11a)} \\ \tau \dot{v} = v^2 + I + \tau \bar{J} r - (\tau \pi r)^2 & \text{(4.11b)} \end{cases}$$

4.2. Simulations of the fully-connected network

Simulations run for the fully-connected network agree with the theory, qualitatively and quantitatively.
The following plots are generated from simulations a stable focus of firing rate 30 Hz was expected.
The raster plot (not so clearly) and the histograms of mean firing rates of individual cells as well as the histogram of coefficients of variation of them, give evidence pro the asynchrony of the neurons.

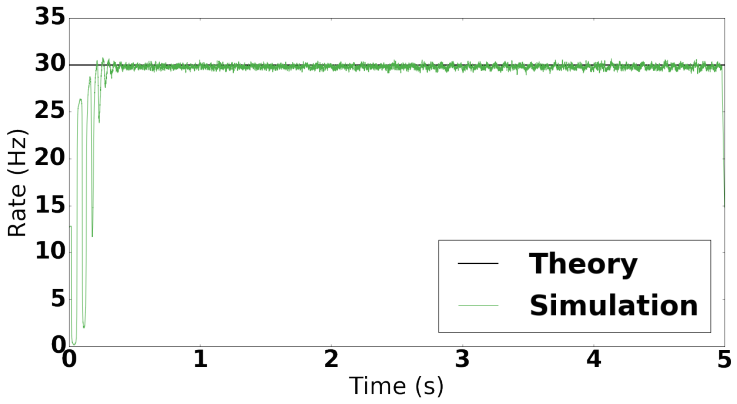
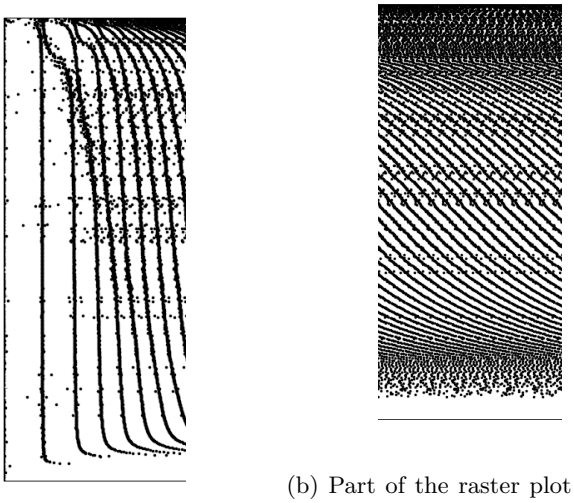


Figure 4.1: Theoretical predction of the firing rate of a fully-connected network with a $\tau = 20ms$, $J = 5$, $\Delta J = 1$ and I tuned so a firing rate of 30 Hz is achieved compared to the simulations results. We can see how the numerical solution oscillates first before reaching the equilibrium value, indicating the existence of a stable focus (as predicted by the theory). The fact that the oscillations initially are not centered around the fixed point can be justified by the initial state of the system where a synchronization between the neurons exist at the beginning of the simulation (evidence of this can be found in the raster plot)



(a) Part of the raster plot from the beginning of simulation. The synchronicity between neurons is clearly evident

(b) Part of the raster plot from a stage when the system has reached the fixed point. Different firing rates can be seen (they are more clearly depicted in the later 2 histograms).

Figure 4.2: Parts of the raster plot at different phases of the simulation. The horizontal line represents time, while the the vertical one the neuron's indices. Dots in the plot represent the occurrence of a spike at that moment in time in that neuron

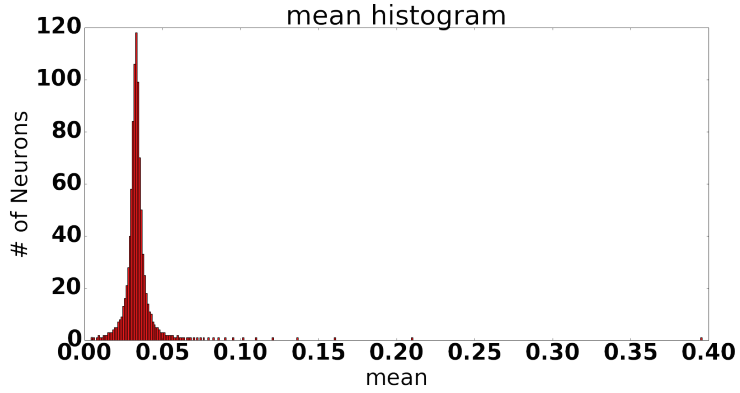


Figure 4.3: Histogram of the Mean Inter-spike time intervals (firing rates) of individual neurons. A wide distribution indicates asynchrony, while a narrow ones speaks for synchronicity

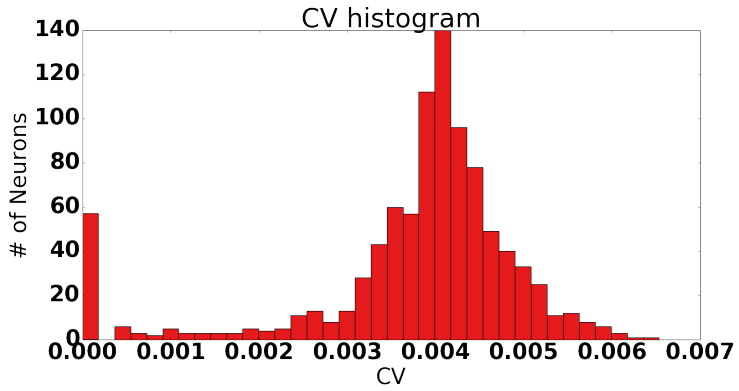


Figure 4.4: Histogram of the coefficients of variation of the inter-spike time intervals of individual neurons

4.3. Results for Sparser Networks

Running simulations with the exact same parameters as before, but for sparser networks[1] produces results as follows:

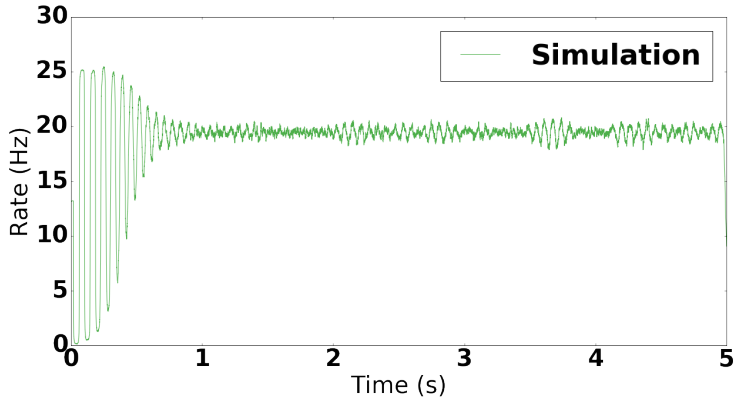


Figure 4.5: Firing Rate for p = 0.5 with the same parameters that produces r = 30 Hz for the fully-connected network. We can see a longer time of convergence is needed, the oscillations are bigger and the fixed point has a lower firing rate value

[1]The way the networks are generated is explained in B

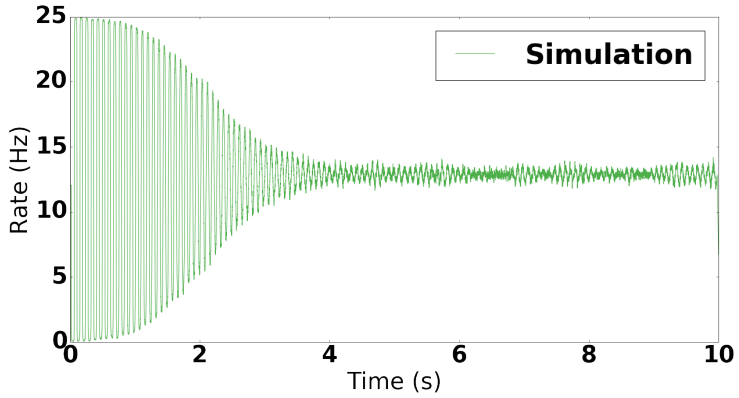


Figure 4.6: Firing Rate for p = 0.1 with the same parameters that produces r = 30 Hz for the fully-connected network. The convergence is even later than the p=0.5 case, the oscillations bigger and the firing rate of the fixed point even lower

In different simulations, for different probability of connection the following facts were noticed:

- As the connectivity decreases, the fixed point which the system approaches stays the same qualitatively (a stable focus), but changes quantitatively (the value of the firing rate decreases)
- The system needs more time to approach the fixed point
- The noise increases as the connectivity decreases

The second point seems reasonable since the dicreased connectivity leads to less recursive current.
The 3rd point can be also justified considering the finite elements effect (in a finite network we're decreasing even more the connected neurons) and the decrease of the recursive current.

4.3.1. Proposed solution

Intuition

Considering the way synapses are modeled and how networks are generated (randomly), we can expect that on average in a network with probability of connection p will loose (1-p) part of recursive current, we can compensate this quantity by the network's external current.
So the proposed macroscopic system is:

$$\begin{cases} \tau\dot{r} = \dfrac{\Delta J}{\pi} r + 2rv & \text{(4.12a)} \\ \tau\dot{v} = v^2 + I + \tau p\bar{J}r - (\tau\pi r)^2 & \text{(4.12b)} \end{cases}$$

where p is the probability of forming a connection between 2 neurons

Results

Indeed simulations produce some really accurate results for the model even for networks with p = 0.01:

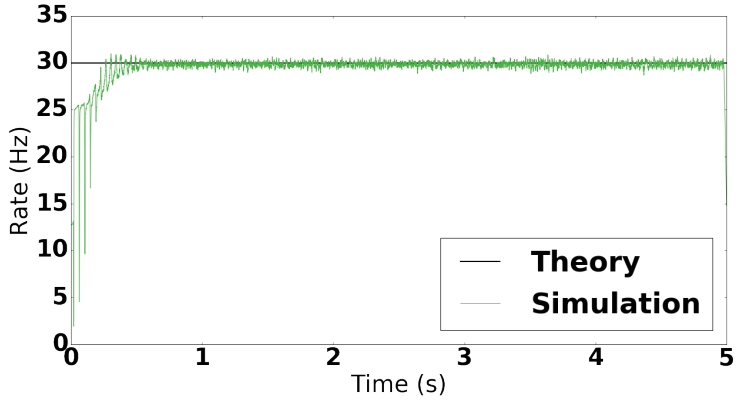


Figure 4.7: Firing Rate for p = 0.5 with parameters decided due to the modified model. Clearly after the correction the firing rate can be predicted quite accurately, initial oscillations last less and the noise around the fixed point is reduced

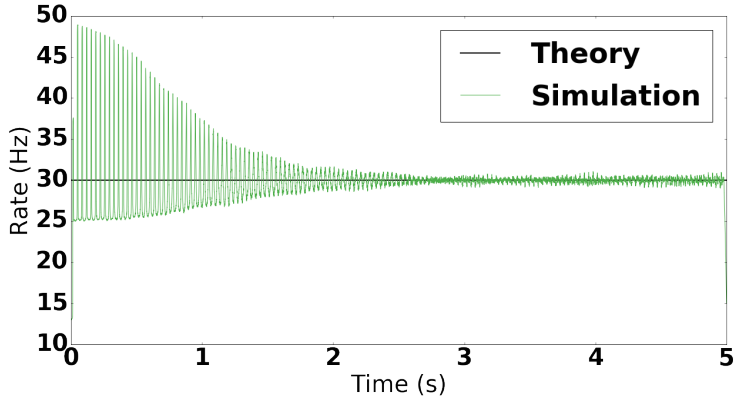


Figure 4.8: Firing Rate for p = 0.1 with parameters decided due to the modified model. Again the results are very good

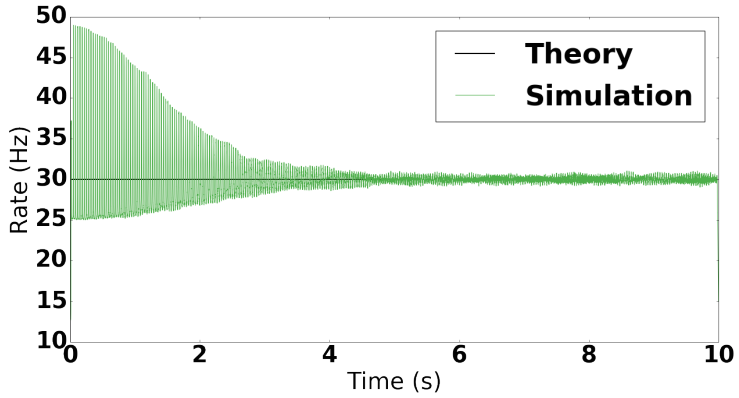


Figure 4.9: Firing Rate for p = 0.05 with parameters decided due to the modified model. Even with this sparseness the convergence is evident

Note

Although results for connected networks are promising there is a problem noticed in the model.
Simulations show that when network gets completely disconnected, the stable focus bifurcates to a stable limit circle which combined with the fact that we are in a 2 dimensional system, gives evidence of a Hopf bifurcation. This behavior is not exhibited by the theoretical model, which in no case predicts such a bifurcation.

5. Model B

5.1. Derivation of the macroscopic description from the microscopic one for the case of 2 populations

In an analogous way, but using 2 population of neurons [1] instead of 1 (one representing the excitatory neurons and the other for the inhibitory ones), we can obtain the following results:

$$\begin{cases} \tau \dot{r_e} = \Delta J/\pi (r_e + r_i) + 2 r_e v_e & \text{(5.1a)} \\ \tau \dot{v_e} = v_e^2 + I_e + \tau (J_e r_e - J_i r_i) - \tau^2 \pi^2 r_e^2 & \text{(5.1b)} \\ \tau \dot{r_i} = \dfrac{\Delta J}{\pi} (r_e + r_i) + 2 r_i v_i & \text{(5.1c)} \\ \tau \dot{v_i} = v_i^2 + I_i + \tau (J_e r_e - J_i r_i) - \tau^2 \pi^2 r_e^2 & \text{(5.1d)} \end{cases}$$

To simplify the case we can consider the case where both populations have same distribution centers ($J_e = J_i = J$) and same external current ($I_e = I_i = I$). In this case, having same initial conditions for both populations, their dynamics will be identical and described by:

$$\begin{cases} \tau \dot{r} = 2r(\Delta J/\pi + v) & \text{(5.2a)} \\ \tau \dot{v} = v^2 + I - (\tau \pi r)^2 & \text{(5.2b)} \end{cases}$$

5.2. Simulation of fully-connected network

Simulations of the fully-connected network again for model B produces some quite accurate results:

[1] having the same width, but different centers

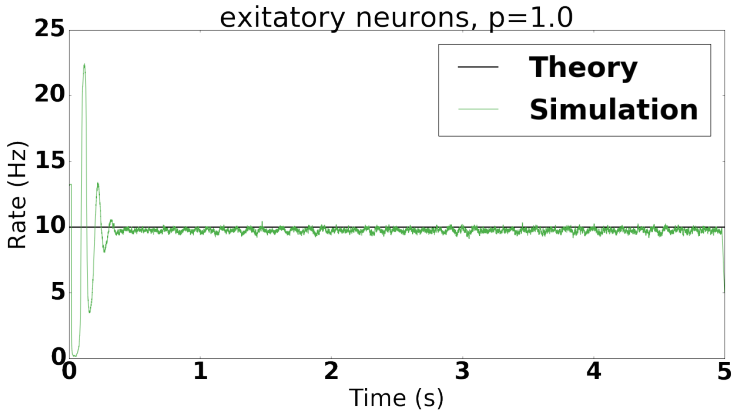


Figure 5.1: Firing Rate for Excitatory Population theoretically and numerically. The simulations are run with $\tau = 20ms$, $\delta J = 1$, $J_e = J_i = 5$ and $I_e = I_i = I$ adapted so a firing rate of 10 Hz is achieved

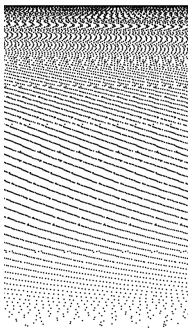


Figure 5.2: Raster Plot of Inhibitory Population. We can see how different neurons fire at different rates (or not fire at all)

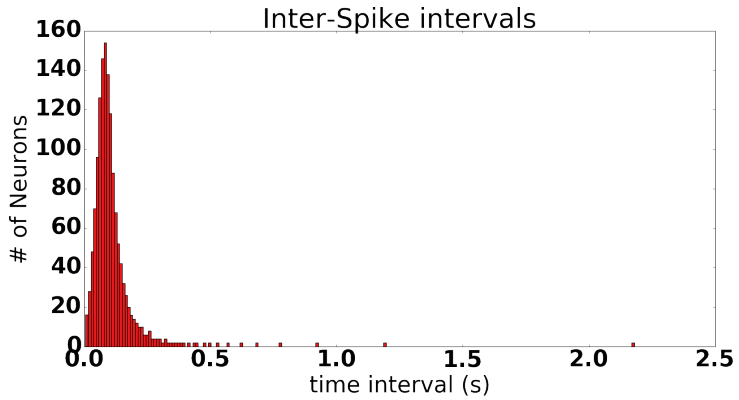


Figure 5.3: Histogram of the Mean Inter-spike Intervals of the Individual Neurons indicating enough asynchrony for the neurons.

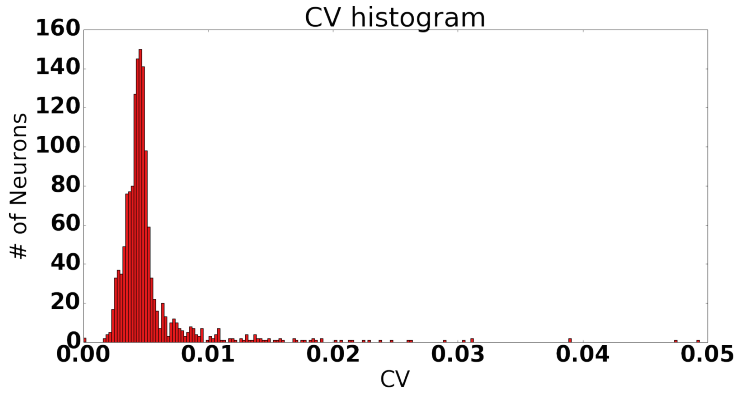


Figure 5.4: Histogram of the Mean Firing Rates of the Individual Neurons

5.3. Results for sparser networks

As for model A, we run simulations with the same parameters that gave the correct results for the fully-connected case. The following results are obtained:

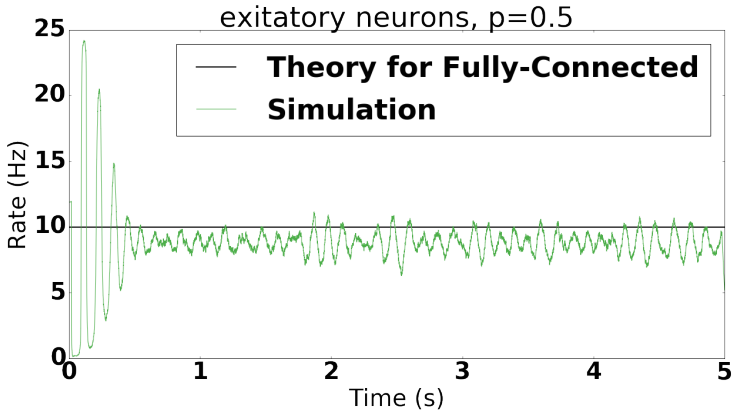


Figure 5.5: Theoretical firing rate of the excitatory population predicted for the fully-connected network is compared to the firing rate obtained by the simulations of a network with p=0.5. The parameters of the simulations being the exact same as the ones that produced the 10 Hz firing rate for the fully-connected network. Clearly the simulations produce a rate lower and more noisy than the fully-connected case, however the drop is not that big compared to the correspondent case in model A

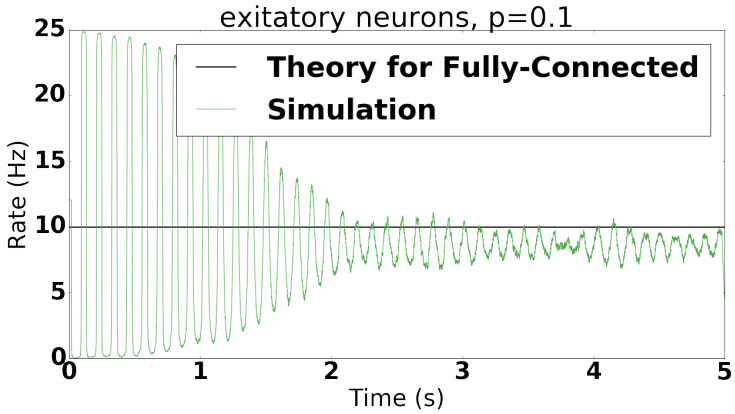


Figure 5.6: Firing rate for excitatory population in a network with p=0.1. Again we see the drop of the firing rate is not that significant compared to the correspondent case in model A

In this model, unlike model A the increase of the sparsity doesn't lower the firing rate of the fixed point significantly.
On the other hand more noise and and latency in the convergence are similar to model A.

5.3.1. Impossibility to introduce the same trick as in Model A

It is clear that the trick used in model A cannot be useful here, since corresponding term is missing here.

5.4. Case of different centers

Below some results where the centers of the inhibitory and excitatory populations differ and where different firing rates for each populations are desired.

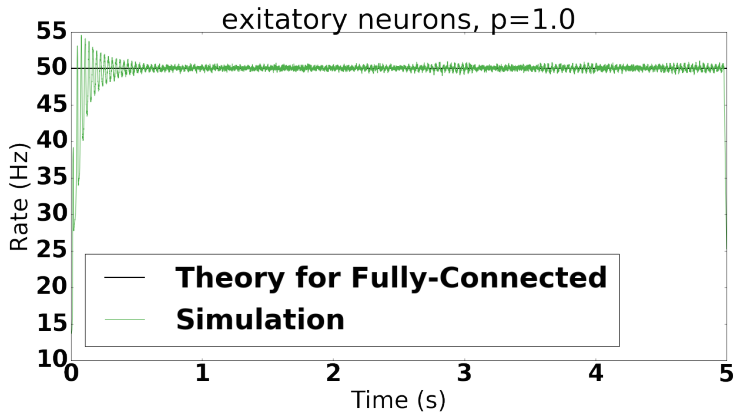


Figure 5.7: Firing Rate for excitatory population theoretically and numerically. The simulations are run with $\tau = 20ms$, $\delta J = 1$, $J_e 8$, $J_i = 5$ and $I_e = I_i = I$ adapted so $r_e = 50Hz$ and $r_i = 30Hz$

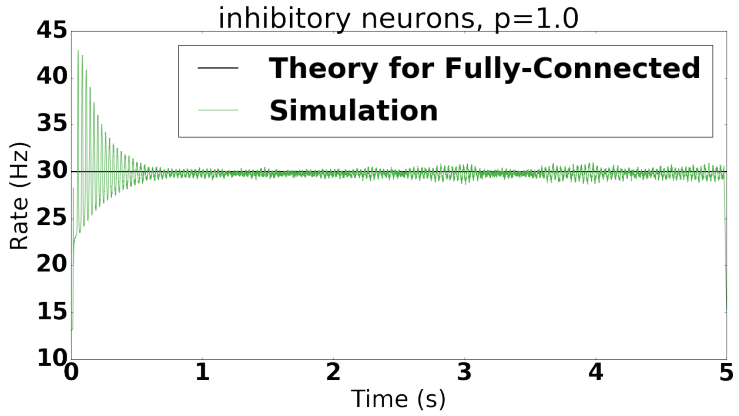


Figure 5.8: Firing Rate for inhibitory population theoretically and numerically. The simulations are run with $\tau = 20ms$, $\delta J = 1$, $J_e 8$, $J_i = 5$ and $I_e = I_i = I$ adapted so $r_e = 50Hz$ and $r_i = 30Hz$

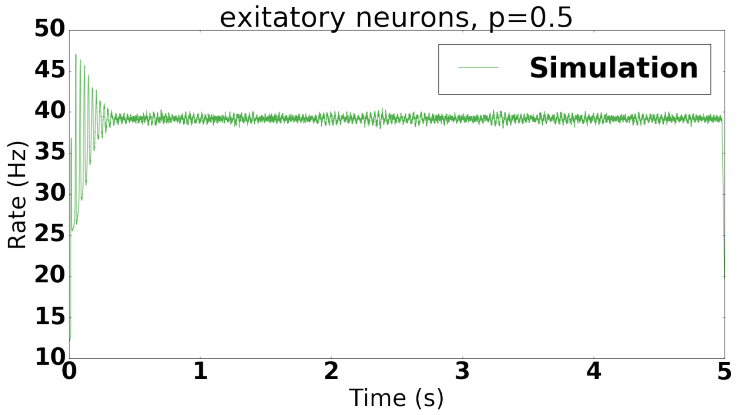


Figure 5.9: Firing Rate for excitatory population with p=0.5. The simulations are run with same parameters that in the fully-connected networked produced $r_e = 50Hz$ and $r_i = 30Hz$

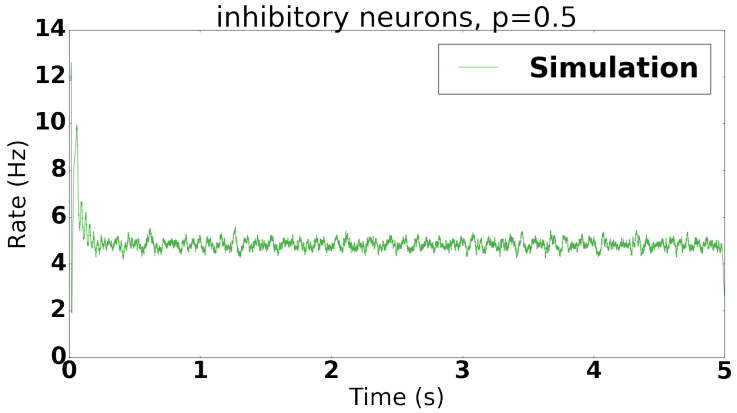


Figure 5.10: Firing Rate for inhibitory population with p=0.5. The simulations are run with same parameters that in the fully-connected networked produced $r_e = 50Hz$ and $r_i = 30Hz$

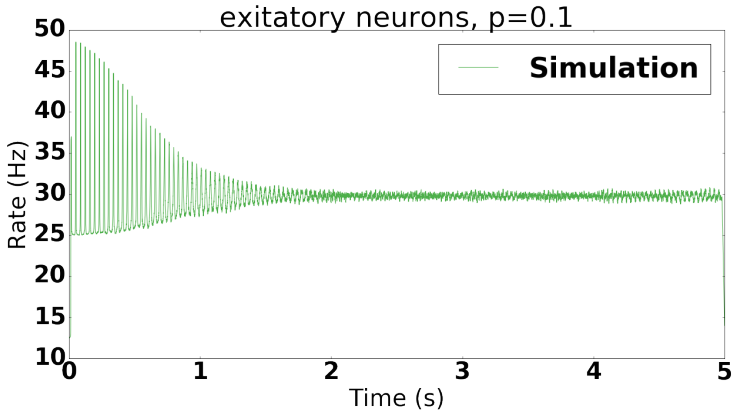


Figure 5.11: Firing Rate for excitatory population with p=0.1. The simulations are run with same parameters that in the fully-connected networked produced $r_e = 50Hz$ and $r_i = 30Hz$

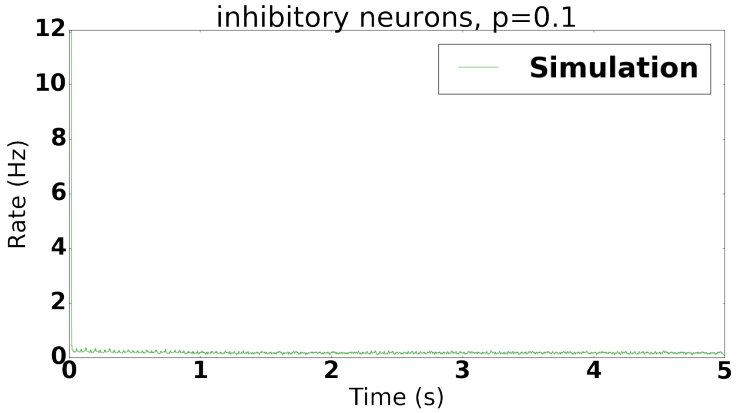


Figure 5.12: Firing Rate for inhibitory population with p=0.1. The simulations are run with same parameters that in the fully-connected networked produced $r_e = 50Hz$ and $r_i = 30Hz$

We notice that in the case where centers are different a very drastic drop of the firing rate value of the fixed point associates the increase of the sparsity in the network. Also, the noise seems to be reduced in this case.

6. Conclusions

After getting the results, the following conclusions seem to arise.

- First of all both model A and model B model accurately the fully-connected cases. All simulations run produces satisfactory results
- Introducing sparsity to the networks doesn't produce any qualitative change of its properties in both models
- The introduced sparsity, as expected affects the synchrony of the neurons. As the system gets sparser, the effect of external current is getting stronger leading to a synchronization between the neurons
- Model A with the introduced modification is able to predict the dynamics of networks, no matter what's the sparsity
- For model B the situation seems more delicate, where for different simulations, quite different quantitative behaviors where observed. More investigation needs to be done to get a clearer picture

An important point is that the system was studied in a regime where the external current was the leading term.
A following work of interest can be to study the sparser networks (with p around 0.1) in a regime where the spikes and not the external current are leading.

Appendices

A. Nernst Potential

Nernst Potential, known also as **Reverse Potential** is the value of the membrane potential at which for a given ionic species the net current through the membrane is 0.

Derivation of Nernst Potential [6]

From thermodynamics, the probability of a molecule being in a given energy state is proportional to the Boltzmann factor:

$$p(E) \propto exp(-E/kT)$$

where k is the Boltzmann constant and T the absolute temperature.
For cations in a static electric field we know that $E(x) = qu(x)$, where x is the ions location, q its charge and u(x) the potential at x.
Using the above fact and interpreting the probability as the normalized density of the ions we can state that:

$$\frac{n(x_1)}{n(x_2)} = exp(-q\frac{u_1(x) - u_2(x)}{kT}$$

where $n(x_i)$ is the density at location x_i
And being in an equilibrium state (i.e. being in a static situation for the potential) we can invert the statement and get:

$$\Delta u = \frac{kT}{q} \ln \frac{n_2}{n_1}$$

which is what is known as *Nernst Potential*

B. Generation of Random Networks

Since in our model we are not interested in particular network architectures, simulation are run on randomly connected networks. A very simple, widely used and efficient way to generate random graphs (networks) is **Erdos-Renyi Model**.
Erdons-Renyi Model comes in 2 flavors, one being [8] introduced in 1959 by Paul Erdos and Alfred Renyi and the other one being [3] introduced independently, but at the same time by Edgar Gilbert.

- Erdons and Renyi's version creates for each vertex the same amount of edges which end to random other vertices
- Edgars' version connects every 2 vertices in the graph (network) by a Bernoulli trial

In our work Edgar's version is used.

C. Parameters of the simulation

Some important facts and parameter values related the simulations done:

- The simulations were all done in Brian2, a simulator build as a Python package
- The integration time step was $100\mu s$
- Populations of 1000 neurons for model A and 1000 excitatory + 1000 inhibitory neurons for model B are used
- The time constant was $\tau = 20ms$
- The refractory period was calculated as proposed in [9]:
  We have $\tau\dot{v} = v^2 + I$ where I in this case includes all the current components (external + internal).
  In a small time interval we can assume constant I and therefore integrate the above equation to get:
  $$\Delta t = arctan(\sqrt{I}/V_t)/\sqrt{I}$$
  where V_t is the threshold potential and Δt is the time that V needs to go from V_t to ∞.
  Now if V_t is high enough, the following approximation still gives very good results:
  $$arctan(\sqrt{I}/V_t)/\sqrt{I} \approx 1/V_t$$
  Considering also the time interval V needs to change from $-\infty$ to V_r, the refractory period reads:
  $$t_{ref} \approx 1/V_r + 1/V_t$$
- A threshold of $V_t = 200V$ produces a satisfactory balance between approximation of the refractory period and numerical time-step and therefore it is used
- For the same reason as above a reset potential $V_r = 200V$ is chosen
- The impulse current that enters a cell after a spike is approximated by an exponential with a very small time constant ($\tau_{sp} = 10dt$ is used, where dt is the integration time-step)
- The window use to produce the firing rate function is 0.04 seconds wide

D. Obtaining a continuous form of the firing rate function

[1] treats a family of methods used to obtain a continuous version of the firing rate. In their essence all of them convolute the spikes train function[1], with a selected function. In its simplest form, a window function is used. Its form is:

$$w(t) := \frac{1}{\Delta t}[u(t + \Delta t/2) - u(t - \Delta t/2)]$$

where u(t) is the Heaviside step function
Denoting the spike train function by s(t), then our firing rate function will read:

$$r(t) := w(t) * s(t)$$

where $*$ is the convolution sign
More refined methods exist, using for example a Gaussian instead of the window function, but since obtained results are satisfactory, we'll stuck with the simple version.

[1] A train of impulses where each impulse represent the occurrence of a spike in the network

Bibliography

[1] Peter Dayan L. F. Abbott. *Theoretical Neuroscience - Computational and Mathematical Modeling of Neural Systems*. The MIT Press, 2005. ISBN: 0-262-04199-5.

[2] Maria Patestas Leslie P. Gartner. *A Textbook of Neuroanatomy*. Blackwell Publishing, 2006. ISBN: 1-4051-0340-X.

[3] Edgar Gilbert. "Random Graphs". In: *Annals of Mathematical Statistics* 30 (1959). DOI: 10.1214/aoms/1177706098.

[4] Alan Lloyd Hodgkin. "The local electric changes associated with repetitive action in a non-medullated axon". In: *Journal of Physiology* 107 (1948).

[5] Eugene M. Izhikevic. *Dynamical Systems in Neuroscience - The Geometry of Excitability and Bursting*. The MIT Press, 2006. ISBN: 978-0-262-09043-8.

[6] Wulfram Gerstner Werner M. Kistler Richard Naud and Liam Paninski. *Neuronal Dynamics: From single neurons to networks and models of cognition*. Cambridge University Press, 2014. ISBN: 9781107635197.

[7] Rajesh Rao. *Computational Neuroscience*. URL: https://www.coursera.org/learn/computational-neuroscience.

[8] Paul Erdos Alfred Renyi. "On random graphs I". In: *Publicationes Mathematicae* 6 (1959).

[9] Ernest Montbrio Diego Pazo Alex Roxin. "Macroscopic Description for Networks of Spiking Neurons." In: *Physical Review X* 5 (2015). DOI: 10.1002/andp.19053221004.