

ALMA MATER STUDIORUM · UNIVERSITÀ DI BOLOGNA

SCUOLA DI SCIENZE

Corso di Laurea Magistrale in Matematica

**DYNAMICS OF AN AGE STRUCTURED
NEURON POPULATION WITH THE
ADDITION OF LEARNING PROCESSES**

Tesi di Laurea Magistrale in Analisi Matematica

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Sessione Unica
Anno Accademico 2020-2021

"Dai che ti accompagno"

Estratto

Nel cervello di un mammifero sono presenti più di 10^{10} neuroni strettamente impacchettati e connessi a comporre una fitta rete. Per meglio renderci conto della complessità del problema basta provare a pensare che in ogni piccolo millimetro cubo di tessuto corticale sono contenuti circa 10^5 neuroni, e dunque da esso si dipartono migliaia di impulsi elettrici ogni millisecondo. Il desiderio di indagare la struttura e il funzionamento di un'organizzazione così complessa ha suscitato molte domande affascinanti tra i neuroscienziati: quali sono le informazioni contenute in questo schema di impulsi spazio-temporale? Come possono gli altri neuroni decodificare il segnale? Potrebbe essere possibile per noi leggere questo codice e capire il messaggio in esso contenuto? Il problema comune sottostante a tutte queste domande è quello della codifica neurale, uno dei quesiti fondamentali della neuroscienza. Purtroppo, al momento non sappiamo dare una risposta chiara a queste domande, ma è opinione comune che la maggior parte, se non tutte, le informazioni rilevanti siano contenute nell'indice di fuoco medio di un neurone. Ma il fatto è che non esiste un concetto unico e ben definito di indice medio di fuoco; sperimentalmente possiamo distinguerne almeno tre nozioni che si differenziano per la quantità su cui viene calcolata la media: sul tempo, su più ripetizioni dell'esperimento, o sulla popolazione di neuroni.

Per poter comprendere le ragioni che motivano le ipotesi di lavoro che faremo nella nostra analisi, dobbiamo osservare due evidenze biologiche riguardanti la struttura delle popolazioni di neuroni e la loro attività. In molte aree del cervello i neuroni sono organizzati in gruppi di numerose unità con proprietà simili e che sono connesse per mezzo di forti legami eccitatori. Questi cluster sono denominati *assemblamenti neurali*, ed esempi di rilievo sono le ipercolonne nella corteccia visiva e i fasci di motoneuroni

che si trovano nel sistema nervoso centrale. Abbiamo voluto notare innanzitutto questo fatto perché, a causa della loro forte interconnessione, se anche solo una parte delle cellule che compongono l'assemblamento viene stimolata, l'intero insieme si attiva, e questo legittima la scelta di considerarlo come un'unica unità operativa. Ma questo in realtà significa che stiamo operando una media, perché consideriamo un intero ammasso come una singola cellula, e così facendo possiamo descrivere l'attività dell'intera popolazione neuronale anziché limitarci a quella dei singoli neuroni. In secondo luogo è bene evidenziare una caratteristica chiave nella codifica neurale, e cioè il fatto che la forma degli impulsi emessi dai neuroni varia leggermente durante le scariche. Questo implica che descrivendo la loro attività, la principale fonte di informazioni è costituita dai tempi di scarica o da alcune statistiche su di essi. Questo fatto è così rilevante che molti modelli neuronali trascurano addirittura il meccanismo alla base della generazione degli impulsi, e scelgono di descrivere la dinamica della rete in termini di tempi di scarica.

Una volta delineate le caratteristiche principali di cui è bene essere consapevoli per parlare di neuroni, dobbiamo valutare il ruolo delle connessioni che intercorrono tra essi. Ponendoci al livello di un assemblamento osserviamo che i forti legami di interazione tra le unità determinano una rete omogenea. Per essere più precisi, una tale rete è una situazione in cui tutti i neuroni $1 \leq i \leq N$ sono identici e ricevono lo stesso segnale dall'esterno $I_i^{ext}(t) = I^{ext}(t)$; inoltre, in una popolazione omogenea la forza di interazione tra i neuroni è considerata uniforme, $w_{ij} = \frac{J_0}{N}$, dove J_0 è un parametro di connettività. Per $J_0 = 0$ tutti i neuroni sono indipendenti, mentre un valore $J_0 > 0$ ($J_0 < 0$) implica un legame eccitatorio (inibitorio) tra tutti i neuroni. Ma se facessimo una tale supposizione cambiando la prospettiva e guardando alla rete neuronale nel suo complesso, dove i cluster sono considerati come le unità neuronali, perderemmo molto in termini di realismo. In questo caso è più coerente con l'evidenza biologica considerare la rete come non omogenea, una situazione in cui si presume che gli assemblamenti adattino progressivamente i collegamenti reciproci. Il modo in cui queste interconnessioni variano nel tempo è stato studiato a lungo da diversi scienziati e oggi ci riferiamo al processo di adattamento dei parametri di interazione chiamandolo *apprendimento*, e alla procedura per regolare i pesi w_{ij} come a una *regola di apprendimento*. Esistono numerose regole di apprendimento diverse in letteratura, ma uno degli insiemi più semplici è composto delle

regole di apprendimento di Hebbian, le quali presuppongono che sia la correlazione tra i neuroni pre- e post-sinaptici a determinare i cambiamenti nei canali di comunicazione tra i neuroni.

Fatte queste considerazioni abbiamo gli strumenti per introdurci all'analisi del modello che verrà studiato in questo lavoro di tesi. In particolare, ci concentreremo sul recente lavoro di Torres e Salort [36], nel quale gli autori descrivono la dinamica di una rete di cluster connessi, modellati tramite il tempo trascorso dall'ultima scarica, e che interagiscono reciprocamente tenendo conto di processi di apprendimento. Ovviamente questo studio si inserisce in una già ampia letteratura riguardante l'analisi e la modellazione di reti neurali, che specialmente in tempi recenti ha conosciuto una significativa espansione. Nel caso di reti omogenee, i modelli per l'attività elettrica di un singolo neurone sono la base su cui sono costruiti tutti i modelli di campo medio proposti per comprendere l'attività elettrica di una rete di neuroni interagenti. Questi modelli differiscono l'uno dall'altro nella quantità studiata che, in molti casi, è la densità di neuroni $n(\cdot, t)$, dove \cdot è una quantità che varia nel tempo t e, nel nostro caso, è il tempo s trascorso dall'ultima scarica del neurone. Se tuttavia il primo modello di questo tipo che è stato proposto era stato costruito adattandolo ai dati sperimentali, nelle sue versioni successive il modello di popolazione analizzato utilizzando il tempo trascorso ha via via considerato solo ipotesi minime, mirando a riprodurre i seguenti aspetti del comportamento neuronale: in primo luogo il fatto che molti neuroni generano impulsi in risposta agli stimoli in arrivo; in secondo luogo il fatto che, dopo ogni scarica, il neurone è soggetto a un periodo di refrattarietà prima di recuperare la sua eccitabilità, il che significa che vive una fase in cui è meno sensibile agli stimoli ricevuti.

Inserendosi in una tradizione così ampia, il modello proposto da Torres e Salort si distingue comunque dagli altri per alcune scelte originali volte ad aumentarne la coerenza con l'evidenza biologica. Infatti, la prima novità che si può riscontrare nella loro analisi è la scelta di includere anche la dimensione spaziale come variabile del modello. Ogni posizione corrisponde ad un assembramento che, come detto sopra, è visto come un unico neurone, in cui il recupero post-scarica della membrana è modellato attraverso una indice di fuoco istantaneo che dipende dal tempo trascorso dall'ultima scarica, dagli impulsi ricevuti dai neuroni vicini e la forza delle sue interconnessioni con la rete. Il secondo

contributo significativo che apportano alla tradizione è il fatto di considerare una rete non omogenea in cui i cluster adattano i loro canali di comunicazione attraverso le regole di apprendimento di Hebbian.

Nel corso del presente lavoro di tesi ho condotto un'analisi puntuale di questo modello, curandomi innanzitutto di fornire gli strumenti necessari alla comprensione dell'elaborato, per poi procedere allo studio della buona posizione del modello, alla ricerca dei suoi stati stazionari e alla prova della convergenze esponenziale del modello stesso all'equilibrio. La prefazione, nata in realtà a ricerche ultimate, ha un ruolo prettamente divulgativo. Ho infatti desiderato fornire al lettore un quadro più generale sul ruolo della matematica nella formulazione dei modelli e soprattutto sul valore fisico e fattuale dei risultati provati sul modello nel corso dell'elaborato, mossa dal desiderio di raggiungere e accattivare un più vasto pubblico di lettori.

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Preface

At the end of this work, I found myself thinking about what was the factual, physical meaning of what I had studied. So I have decided to expose the reflections and the investigations raised by this question in this preface that, driven by the desire and the duty of reaching and directly involve the majority of public opinion, I have designed to be understood by anyone, even non-specialist in the mathematical field.

Mathematical theories of populations have affected several form of existence and dynamics of growth. Human population as well as populations of animal, viruses and cells as neurons are just a sample of the various fields in which those theories have been applied. Furthermore, when approaching the study of a population, there are several features we could be interested in. As an example, one might want to investigate the factors determining its age distribution when we are interested in studying the long time behaviour of the population and its sensitivity to changes in birth and death rates. But this is not the only application; as probably everyone had the opportunity to observe in recent times, we can investigate the spread of a contagious phenomenon, and that not only for critical situations like the spread of a virus, but even for the diffusion of a trend, or information. In fact, all these infectious manifestations have in common an indicator that is interesting to deepen, that is the dependence of contagion on parameters, such as contact and quarantine rates. Moreover, the increasingly complex dynamic of ecological systems, economic structures and social apparatus have emphasized the need of encompass in the analysis the interactions that inevitably characterize these systems and shape their developments. In this work, in which we analyse the dynamics of groups of neurons that, as all we know, are linked forming a net, we had to consider this aspect, and we have counted for the interactions evaluating their role through learning rules that

effectively keep track of the contacts and the "feeling" between the assemblies themselves.

But once we have shaped a system of equations that effectively reproduce the dynamics of the neurons, counting for the role of the stimulus received and the total activity at a fixed time, there is a stimulating question to muse with. During this work we have mathematically tackled the problem of determining what the neurons population, modelled through the time elapsed since the last discharge, does after a long time; we have seen that it stabilizes to a steady state. But what does that actually mean? This is a very challenging question. Trying to answer it, I have kept in mind that these thoughts could be extended to a wider range of populations such those we listed before, not only to neurons, and an help in finding a possible answer has come from the volume by Coale about the growth and the structure of human populations, see [6].

There the author has considered a population that neither gains nor loses members by migration, an assumption that is realistically true also for a group of neurons. He claims that at a given moment, the age composition of such a population is determined by the recent sequence of fertility and mortality risk at each age to which the composition has been subject and that, knowing those data, we are able to determine the population overall birth rate, death rate, and rate of increase at each moment. In principle, then, both age composition and vital rates can be determined from the knowledge of the present and past values of fertility and mortality schedules. The real key passage in his argument is determined by the theorem of "weak ergodicity" by Alvaro Lopez. This result states that two arbitrarily chosen age distribution, no matter how different, subject to identical sequences of fertility and mortality, ultimately generate populations with the same age composition. That means that age composition gradually forgets the past and thus that we can effectively reproduce the current age composition of a population even if we don't know its initial age distribution, based only on the recent history of its fertility and mortality. Here comes the point where the steady population plays a crucial role. In his work, through a clever deduction which makes use of Lopez's Theorem, Coale illustrates the interplay between the stability of the age structure and the necessity for the corresponding rates of fertility and mortality to be constant. In fact, we call *stable* a population that is established by a prolonged regime of unchanging fertility and mortality schedule, and from the previous assertion we can say that it is characterized by a fixed

age composition, constant birth and death rates, and constant rate of increase.

That's what a steady population let us to do, and this is true for human as well for neuron population. Moreover, speaking about neurons things are slightly simplified from a certain point of view, because there are less variables to think about. In fact, we don't have to count for the difference of sex in the composition of the population, which means that all the individuals can reproduce, i.e. fire. Another aspect that generalises the previous analysis is that the fertility and the mortality rates for neurons are identical because we make the fundamental assumption that a neuron immediately re-enter its life cycle after firing. This fact bring us to deduce that the neuron population we consider in our analysis remains constant, without effective losses or gains. We know that, realistically, neurons actually dies, but this aspect is not encompassed in the current version of the model; to count for it, we should assume the density of population to be constant with respect to the variable s counting for the time elapsed, but we should abandon the assumption of the mass-conservation with respect to the variable x of the spatial distribution. So, what can we effectively observe in our model when the population achieve a steady state? From the physical point of view, the important and observable part is the activity of neurons from which, at the equilibrium, we can see some patterns as synchronization phenomena in the activity itself. It is indeed complicated to measure the probability of finding a neuron: the density of the population is too abstract. The only observable variables in the model are N and S , which are the activity of the neuron in position x at time t and the amplitude of the stimulus it receives. This means that, for example, the activity of the neurons are synchronizing according to the activity N of the neuron in x , and synchronous regular or irregular activities are ubiquitous in nervous systems, so they are very interesting to be understood. Indeed, they can be at the basis of physiological functions such as respiration, cognitive function or pathological conditions such as, for example, epilepsy. The fact is that these synchronous patterns reflect simultaneous and repetitive discharges of large numbers of neurons in specific assemblies (i.e. positions x) at the level of the brainstem, the cortex, etc, and this could help us in understanding their link with the manifestations just mentioned. Moreover, if we want to go deeper, we can explore how such a coherence, that we can observe in the activity of these neurons, arise from the interplay between the intrinsic neural properties

and the coupling principles underlying the network. But this is a wild field to investigate, so we just stop here and admire so much synergy.

I sincerely hope I have achieved the goal stated at the opening to affect everyone who desires to understand what I have done in this work of thesis. To anyone who wants to continue reading, I hope you find it interesting.

Campagnola Emilia
January, 2021

Introduction

A mammalian brain counts more than 10^{10} densely packed neurons, smartly connected to compose an intricate network. For better understanding the complexity of the problem we can try thinking that in every small cubic millimetre of cortex tissue there are about 10^5 neurons, so thousands of spikes are emitted each millisecond from there. The craving to investigate the structure and the functioning of such an organization has aroused many fascinating questions between neuroscientists: what is the information contained in such a spatio-temporal pattern of pulses? How might other neurons decode the signal? Is it possible for us to read the code and understand the message of the neural activity pattern? These are all questions that refer to the same problem of neural coding, one of the most challenging topic in neuroscience. Actually, at present, there is not a clear answer to these questions, although it is common opinion that most, if not all, of the relevant information is carried by the mean firing rate of the neuron. But the fact is that there is not a unique and well-defined concept of 'mean firing rate'; experimentally we can divide at least three notions of rate that differ in the averaging procedures: either an average over time, or an average over several repetition of the experiment, or an average over a populations of neurons.

To give reason to the working hypothesis that we will do in our analysis, we have to notice two biological evidence concerning the structure of the populations of neurons and their activity. In many areas of the brain, the neurons are organized in groups of numerous units with similar features and strong mutual excitatory connections. These clusters are named *neural assemblies*, and notable examples are hypercolumns in the visual cortex and pools of motor neurons in the central nervous system. This is the first fact that we have to notice because due to this dense connectivity, once a subset of its

cells is stimulated the entire assembly tends to be activated, so that we can consider it as a single operational unit. This actually means that we are operating an averaging procedure, because we consider a whole cluster as a single cell, and thus we are able to describe the main activity of the neuronal population rather than the spiking of individual neurons. The second aspect to outline is actually a key feature in neural coding, namely that the shape of the spikes emitted by the neurons varies a little throughout the discharges. This implies that, describing their activity, the most relevant information is contained in the discharge times or in some statistics over them. This fact is so relevant that many neuronal and networks models even ignore the mechanism at the base of spike generation and choose to describe the neuronal dynamics in terms of discharge times.

Once outlined the main features to be aware of while speaking about neurons, we have to assess the role of the connections within the neurons themselves. Looking at the level of a cell assembly we observe that the strong interaction links between the units determine a sort of all-to-all coupling, which is called *homogeneous network*. To be more precise, a homogeneous network is a situation in which all neurons $1 \leq i \leq N$ are identical and receive the same external input $I_i^{ext}(t) = I^{ext}(t)$; moreover, for an homogeneous population it is assumed that the interaction strength between the neurons is uniform, $w_{ij} = \frac{J_0}{N}$, where J_0 is a connectivity parameter. For $J_0 = 0$ all neurons are independent, while a value $J_0 > 0$ ($J_0 < 0$) implies excitatory (inhibitory) interactions. However, we would lose realism if we made such an assumption generalizing our point of view and looking at the neuronal network as a whole, where the assemblies are considered as the neuronal units. In this case it is more consistent with the biological evidence to consider the network to be *non-homogeneous*, a situation where it is assumed that the assemblies are subjected to an adaptation in their communication links. The way in which these interconnections varies over time have been long investigated by different scientists, and today we refer to the process of "interaction parameter adaptation" as *learning*, and to the procedure for adjusting the weights w_{ij} as a *learning rule*. There are many different learning rules, but one of the simpler set is composed by those known as the Hebbian learning rules, which assume that synaptic adjustments are led by correlated activity of pre- and post-synaptic neurons.

After these considerations we have the tools to enter into the presentation of the

model that will be studied in this thesis. In particular, we will focus on the seminal work by Torres and Salort [36], where the authors describe the dynamic of a network of connected assemblies that are modelled with the time elapsed since last discharge and interacts with each other considering learning processes. Obviously this study fits into an already wide literature about the analysis and modelling of neural networks, that particularly in the past years have known a significant broadening. In the case of homogeneous networks, models for the electrical activity of a single neuron have been the basis for several mean-field models, proposed to understand the electrical activity of a group of interacting neurons. These models differ from each other in the quantity under study that, in most cases, is given by the density of neurons $n(\cdot, t)$, where \cdot is a quantity varying over the time t and, in our case, is the time s elapsed since the last discharge of the neurons. This latter type of model was originally based on stochastic simulations done in Pham et al. [40], and then has been studied by several authors such as Cañizo et al. [2], Chevalier et al. [3], Ly et al. [21], Mischler et al. [26] and Pakdaman et al. [29], [30], [31]. However, while the first model was initially shaped to fit with the experimental data, in its later versions the population model analysed using the elapsed time has encompassed minimal assumptions and reproduces only a minimal set of physiological neuronal properties, which are aimed to reproduce the following aspects of neuronal behaviour: firstly the fact that many neurons generate trains spikes in response to incoming stimulations; secondly, the evidence that, following each discharge, the neuron undergoes a period of refractoriness before recovering its excitability, meaning a phase it is less responsive to inputs [15].

Within such a vast tradition, the model of Torres and Salort still differs from the others for some original choices aimed at increasing the consistency of the model with biological evidence. In fact, the first novelty they propose in their paper is to encompass also the spatial dimension as a parameter in their analysis. Each position corresponds to an assembly that, as said above, is considered as a neuron whom membrane post-discharge recovery is modelled through an instantaneous firing rate that depend on the time elapsed since the last discharge, the inputs by other neighbouring neurons and the strength of interconnections in the network. The second significant contribution they bring to the tradition is the fact of considering a non-homogeneous network where the

assemblies adapt their communications links through Hebbian learning rules.

The puntual analysis of the Neuron Elapsed Time model with spatial dimension introduced by Torres and Salort will be developed in three chapters in this thesis. In Chapter 1 we present some preliminary concepts that it is important to know to have a good understanding of for the further analysis. Firstly, we introduce the elapsed time model structured without the spatial dimension and we show that it is a nonlinear version of the conservative renewal equation, which has been well-studied by many authors [32], [10], [7], [14], [23], [44], [41] in the past as a model for a broad range of biological phenomena like epidemic spread and cell division. Next we proceed with a brief overview of the learning rule adopted in the model and, finally, we introduce the Doeblin's theory that we will use in the final part of this work to study the convergence of the model in the asymptotic limit. In Chapter 2 we focus on the Neuron Elapsed Time model and we prove its well-posedness for the weak interconnection case both for the linear and the non-linear problem. In Chapter 3 we find the stationary states of the problem and, to conclude, we show the convergence to equilibrium following the ideas of Cañizo et al. in [2], by means of Doeblin's theory.

Chapter 1

Preliminary concepts

1.1 Elapsed Time Model and Renewal Equation

In this section we introduce the Conservative Renewal Equation, an usual tool to describe a model of an age structured population, arising in several different contexts. As an example the equation can be used to describe cell proliferation and thus tumour growth. It can be written as a Partial Differential Equation (PDE) on the unknown function $n(t, a) \geq 0$, representing the population density of individuals that at time t are aged a . Historically, this is the first PDE introduced in biology.

To acquire a gradual understanding of the model, we start by presenting it in its linear form. This is usually known after the names of McKendrick and Feller, two pioneers in studying it: the former introduced it for epidemiology, while the latter made an extensive study of it through Markov processes. It is also known as the VonFoerster equation because he was the first one to use it for modelling cell cultures. As a standard model of population dynamics, we present an example of its applications for describing cell division processes. Imagine we are observing a cell line over time and whenever a cell divides, we follow only one of the two daughter cells. Based on this equation we are able to describe the time evolution of the population density $n(t, a)$ of cells of age a at time t , considering n_0 as initial density and the term *age* meaning the time elapsed since

the mitosis of the cell's mother. We obtain

$$\begin{cases} \frac{\partial n}{\partial t}(t, a) + \frac{\partial n}{\partial a}(t, a) + \beta(a)n(t, a) = 0 & t, a > 0 \\ n(t, 0) = \int_0^\infty \beta(a)n(t, a) da & t > 0 \\ n(0, a) = n_0(a) & a \geq 0 \end{cases} \quad (1.1)$$

where the population is structured by an age variable $a \geq 0$ which grows at the same speed as time and is reset to zero according to the rate $\beta(a)$. The boundary condition ensures that the population re-enter the cycle immediately after realizing the activity counted by the variable a .

We can observe that this equation satisfy the conservative property: if integrated with respect to age, we get

$$\begin{aligned} \int_0^\infty \frac{\partial n(t, a)}{\partial t} da + \int_0^\infty \frac{\partial n(t, a)}{\partial a} da + \int_0^\infty \beta(a)n(t, a) da &= 0 \\ \frac{d}{dt} \int_0^\infty n(t, a) da + \lim_{a \rightarrow \infty} n(t, a) - n(t, 0) + n(t, 0) &= 0 \\ \frac{d}{dt} \int_0^\infty n(t, a) da &= 0 \end{aligned}$$

which is just the conservation property, and ensures that, if the density of neurons n_0 is a probability distribution initially, i.e. if $\int_0^\infty n_0(a) da = 1$, then it remains so for subsequent times, i.e. $n(t, \cdot)$ is a probability distribution too, for any time $t \geq 0$. Here, in the computation of the limit of n as a tends to infinity, we can assume that the population density goes to 0 because it is assumed that the distribution vanishes at infinity. In fact, if it is true initially, then it is true for all times, and we assume the initial condition to be compactly supported. Moreover, it is also reasonable biologically since a is supposed to be the age of a cell.

If we want to deepen the reason why that is effectively the equation that models the population density, we can follow this reasoning. Assumed $n(t, a)$ to be the function that specifies the age distribution of the population at time t ; the number of individuals in the age range (a_1, a_2) at time t is given by

$$N \int_{a_1}^{a_2} n(t, a) da,$$

where N is a scaling factor, such as the size of the population at time $t = 0$. At this point it is necessary to make two basic assumptions about the population to prescribe the death and the birth of individuals in the population.

We firstly assume that the change due to the losses that occur in a time interval of length h in a population aged a at time t is proportional to the size of the population and the time interval itself. Thus, the balance of population leads to

$$n(t+h, a+h) - n(t, a) = -d(t, a)n(t, a)h,$$

where $d \geq 0$ is the age-specific death rate of the population. Dividing both sides of this equation by h and passing to the limit for $h \rightarrow 0$, we have

$$\frac{\partial n}{\partial t} + \frac{\partial n}{\partial a} = -d(t, a)n.$$

The second assumption specifies the relation between the birth rate and the age structure of the population. It states that the number of new born into a population in a time interval of length h is given by

$$Nh \int_0^{\infty} b(t, a)n(t, a) da,$$

where $Nhb(t, a)$ is the number of new born by an individual of age a in the time interval $(t, t+h)$ and b is the fertility rate. It follows from this assumption that the density of new born at time t (boundary condition of our system) is given by

$$n(t, 0) = \int_0^{\infty} b(t, a)n(t, a) da,$$

while the initial distribution (initial condition of our system) is assumed to be known

$$n(0, a) = n_0(a).$$

In the specific case of a cell division presented previously, as well as in the one we analyse in this thesis, we have assumed that the death and the birth rates are the same, because a neural cell re-enters a new life cycle immediately after firing.

Switching now to the nonlinear models, the most famous one was proposed by Kermack and McKendrick for epidemiology with continuous state, where the variable a represents the age in the disease [17]. Nowadays these models find an application in a wide

range of domains spanning from epidemiology to ecology, medicine and cell cultures. In 1974, Gurtin and MacCamy [11] proposed the first mathematical study of such nonlinear equations; afterwards it has been vastly studied by several mathematicians using various techniques such as semigroup theory, entropy GRE methods, Laplace transforms or applying the method of characteristics to convert the problem into a system of Volterra integral equations [11], [13], [14], [44]. As an example for the nonlinear system we present the integro-differential equation describing the dynamics of an age-structured interacting neuron population. We can see this system as an initial stage formulation of the problem subsequently analysed in this thesis: this one with the addition of the spatial dimension and learning processes. Consider a population of neurons described by the probability density $n(t, s)$ of finding a neuron in state s at time t , where s represents the time elapsed since the last discharge. The evolution of the neuron population density runs as follows:

$$\begin{cases} \frac{\partial n}{\partial t}(t, s) + \frac{\partial n}{\partial s}(t, s) + p(X(t), s)n(t, s) = 0 & t, s > 0 \\ N(t) := n(t, 0) = \int_0^\infty p(X(t), s)n(t, s) ds & t > 0 \\ n(0, s) = n_0(s) & s \geq 0 \end{cases} \quad (1.2a)$$

where n_0 is supposed to satisfy

$$0 \leq n_0(s) \leq 1, \quad \int_0^\infty n_0(s) ds = 1. \quad (1.2b)$$

The nonlinearity of the system is due to the coefficient $p(X(t), s)$ representing the firing rate of neurons. In fact, it is assumed to depend not only on the state s of the neuron, but also on the environment X , which is the result of the global neural activity and takes into account the interactions between the neurons. When p does not depend on X , we say the network is *disconnected*, and equation (1.2a) reduces to be linear. $N(t)$, then, denotes the density of neurons which are undergoing a discharge at time t . Observing the boundary condition we can deduce that neurons, which randomly fire at a rate p per unit of time, re-enter the cycle from $s = 0$ immediately after they fire. That is also the reason why the variable s can be regarded as the 'age' of neurons, that is the time elapsed since its last discharge.

Here, as for the linear case of the conservative renewal equation, we can observe that solutions to (1.2a) satisfies two remarkable properties: a conservative law that guarantees

$n(t, \cdot)$ to be interpreted as a probability density and an a priori bound reflecting the normalization $p(x, s) \leq 1$; we write

$$\int_0^\infty n(t, s) ds = \int_0^\infty n_0(s) ds = 1 \quad \forall t \geq 0 ,$$

$$0 \leq n(t, s) \leq 1 , \quad 0 \leq N(t) \leq 1 , \quad \forall t \geq 0 , \forall s > 0 .$$

Studying the elapsed-time neural model equation (1.2a) many properties of neural networks have been investigated, but in this thesis we don't want to go further in the analysis of this model since we are interested in a later version encompassing also the spatial dimension.

1.2 Learning Rule

In the elapsed time neuron models discussed so far by neuroscientist, as we said, the networks are assumed to be homogeneous, which means that each synapse is characterized by a single constant parameter w_{ij} that determinates the amplitude of post-synaptic response to an incoming action potential. However, in the model presented by Torres and Salort, the network is supposed to be non homogeneous. This is a further step in shaping a model increasingly consistent with the physical behaviour of the neurons, in fact it reflects some observations made by electrophysiological experiments that reveal that the response amplitude is not fixed, but varies over time due to appropriate stimulation paradigms. These changes may last for hours or days; in case of a persistent changing of the synaptic transmission efficacy, we call this effect *long-term potentiation of synapses* (LTP) if the stimulation paradigm leads to an increase of the synaptic efficacy, conversely, we call it *long-term depression* (LTD) if it leads to a decrease. For our goals, the relevant aspect of this study is that these persistent changes are thought to be the neuronal equivalent of 'learning' and 'memory'.

Formally, in the theory of neural networks, the weight w_{ij} of a connection between neuron i and neuron j is considered as a parameter, and it can be adjusted in order to optimize the performance of a network for a given task. This process of parameter tailor is called *learning*, and it may refer to a wide class of adaptation processes: from the synaptic changes that occur over the development, to the specific changes that are

necessary for us to memorize a visual pattern, even to the process of learning a motor task. We refer to the procedure for adjusting the weights as a *learning rule*: different ones can be proposed, but that of interest in this thesis belongs to the class of learning rules named *Hebbian learning* because they can be motivated by Hebb's principle.

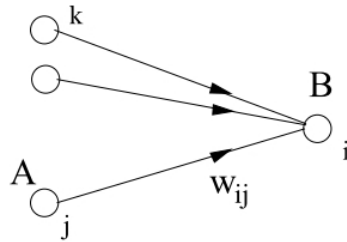


Figure 1.1: The changes at the synapse w_{ij} depend on the state of the presynaptic neuron j , the postsynaptic neuron i and the present efficacy w_{ij} , but not on the state of other neurons k .

In 1949, the psychologist Donald Hebb published his opera *The Organization of Behavior*, aimed to present a theory of behaviour that was based as far as possible on the physiology of the nervous system. In his book he tried to make a sedulous attempt to find some common aspects between the neurological and the psychological conceptions of the behaviour. His discussion takes origin from some clinical facts: he observed the effects of some operations on the human brain, like a clearcut removal of cortex outside a specific area, that in certain cases can have puzzling effects. His goal was to find an anatomical and physiological understanding of what was known psychologically as a concept. The postulate expressed by Hebb describes how the connection from presynaptic neuron A to a postsynaptic neuron B should be modified [Figure 1.1]. For exposing Hebb's principle and formulate a learning rule that follows this criterion we will base on [9].

Hebb's principle When an axon of cell A is near enough to excite cell B or repeatedly or persistently takes part in firing it, some growth process or metabolic changes takes place in one or both cells such that A's efficiency, as one of the cells firing B, is increased.

Today this postulate is rephrased meaning that the correlations in the firing activity of pre- and post-synaptic neurons are responsible of the modifications in the synaptic transmission efficacy. That is the reason why today we refer to correlation-based learning as *Hebbian learning*; he realized that such a mechanism would help to stabilize specific

neuronal activity patterns in the brain. In fact, if we have said that neuronal activity patterns correspond to behaviour, then we can understand that stabilization of specific patterns implies learning of specific types of behaviours.

We now want to focus on how to formulate Hebb's postulate in a mathematical way. We consider a single synapse that transmits signals from a presynaptic neuron j to a postsynaptic neuron i with efficacy w_{ij} . We denote by ν_j the activity of the presynaptic neuron, and by ν_i that of the postsynaptic one. For this purpose, we have to take into account two particularly relevant aspects in Hebb's postulate, that are *locality* and *cooperativity*. It is necessary we deepen these to gain awareness of how synapses interact and for trying to describe their behaviour through equations.

Locality means that the change of the synaptic efficacy can only depend on local variables, that is to say that depends on information that is available at the site of the synapse, but not on the activity of other neurons. Prominent examples are pre- and post- synaptic firing rate or the actual value of synaptic efficacy. Thanks to this property of Hebbian plasticity, we can make a rather general ansatz for the change of synaptic efficacy,

$$\frac{d}{dt}w_{ij} = F(w_{ij}; \nu_i, \nu_j) \quad (1.3)$$

where dw_{ij}/dt is the rate of change of the synaptic coupling strength and F is a so far undetermined function [1], [37], [19]. We can assert that, a part from those considered, there are not others local variables that should be included as additional arguments of F .

As we have highlighted previously, the second aspect of Hebb's postulate we need to explore is cooperativity. It means that for a synaptic weight change to occur, pre- and post- synaptic neuron have to be active simultaneously. This feature allows us to say something more about the function F . If F is sufficiently smooth, we can expand F in a Taylor series about $\nu_i = \nu_j = 0$,

$$\frac{d}{dt}w_{ij} = c_0(w_{ij}) + c_1^{post}(w_{ij})\nu_i + c_1^{pre}(w_{ij})\nu_j + c_2^{post}(w_{ij})\nu_i^2 + c_2^{pre}(w_{ij})\nu_j^2 + c_2^{corr}(w_{ij})\nu_i\nu_j + \mathcal{O}(\nu^3). \quad (1.4)$$

We are particularly interested in the term containing c_2^{corr} in (1.4): it is bilinear in pre- and post- synaptic activity and it implements the condition of simultaneity necessary

for cooperativity in Hebbian learning rules. In fact, if we had a learning rule with only first order terms, we would have a so called *non-Hebbian plasticity*, because a change in the synaptic plasticity would be induced by the pre- or post- synaptic activity alone. Instead, considering the correlation term c_2^{corr} we have cooperativity, and with respect to it we can choose different function F . To set ourselves in the simplest case, we take c_2^{corr} as a fixed positive constant and all the other terms of the Taylor expansion equal to zero. With this choice we obtain the following Hebbian learning

$$\frac{d}{dt}w_{ij} = c_2^{corr} \nu_i \nu_j. \quad (1.5)$$

Observing this equation, we can notice that taking $c_2^{corr} < 0$, if pre- and post- synaptic neuron are active simultaneously, then the learning rule weakens the synaptic transmission efficacy, so it is usually called *anti-Hebbian*.

Another relevant aspect that needs to be highlighted is a consequence of the fact that the synaptic efficacy w_{ij} is bounded; a reasonable assumption, if we look at w_{ij} from a physiological point of view. This evidence implies that F needs to depend on the w_{ij} itself. In fact, if F was independent of w_{ij} , then applying the same stimulus over and over again, F would grow without limit and the same would do the synaptic efficacy w_{ij} because of the meaning of the function F expressed in (1.3), but this is not possible. Observing equation (1.4), one possibility for reaching a saturation of synaptic weights, would be to choose c_2^{corr} as follows:

$$c_2^{corr}(w_{ij}) = \gamma_2(1 - w_{ij}), \quad (1.6)$$

where γ_2 is a positive constant. In this way, while w_{ij} approaches to its maximum value, say $w^{max} = 1$, the parameter c_2^{corr} tends to zero, and so the network loses its correlation.

What is crucial to note is that in Hebb's original proposal it is not encompassed the case of decreasing of the synaptic weights. In these conditions, system's synapses can only be strengthened, and this means that all efficacies will finally saturate at their upper maximum value. However, for any effective learning rule it is essential to require that the weights could eventually decrease, that is what is called a *synaptic depression*. A possible choice to achieve this result can be enforced in equation (1.4) by setting

$$c_0(w_{ij}) = -\gamma_0 w_{ij} \quad (1.7)$$

where γ_0 is a small positive constant representing the rate of decaying to zero of the weight w_{ij} in case of absence of stimulation.

Combining equation (1.6) and (1.7) in (1.4), we obtain a sufficiently general learning rule that reflects the properties discussed so far about the function F encompassing synaptic potentiation and depression:

$$\frac{d}{dt}w_{ij} = \gamma_2(1 - w_{ij})\nu_i\nu_j - \gamma_0w_{ij} . \quad (1.8)$$

The last property of learning rules that need to be highlighted to complete our analysis is *competition*. It could be reasonable to be understood that within a fully connected network, if a neuron strengthens its communication link with a postsynaptic neuron, then the latter has to weaken its communication channels with other neurons it is connected to. Generally speaking, this is a crucial property for any form of self-organization and pattern formation, and in our context can be summarized by saying that synaptic weights can only grow at the expenses of others. From an operative point of view, we can implement competition by normalizing the sum of all weights converging into the same postsynaptic neuron [25]. This operation can be physiologically motivated by a limitation of common synaptic resources; however, it apparently conflicts with the previous analysis, because it violates locality of synaptic plasticity. In fact, normalizing on the connection with neuron i , we not only consider neuron j , but also neuron k connected with i . Nevertheless, this discrepancy can be solved realizing competition of synaptic weight changes using purely local learning rules, see [39], [18], [38], [16].

1.3 The Doeblin's Theory

In this section we briefly present the version of Doeblin's theorem that we use in this thesis, that is the theorem applied to stochastic semi-groups defined in a space of measures or in a L^1 space, i.e. mass- and positivity-preserving semi-groups. We are concerned to illustrate this theory because it allows us, in the last chapter of this thesis, to obtain exponential convergence to equilibrium results for both the linear and the nonlinear formulation of our model. We will firstly study the linear problem; proving that for any initial probability distribution the solution has a positive lower bound after a

fixed time, we will be sure that the associated stochastic semi-group satisfies the Doeblin condition. This latter result ensures us an exponential convergence for the linear problem. After studying the linear case, we prove exponential relaxation to steady state for the nonlinear model by a perturbation argument based on the linear theory, which naturally takes care of the boundary conditions and mass conservation property of our population density function.

There are two main reasons which justify the choice of studying solutions to our problem in the sense of measure. Firstly, the fact that it fits well with the linear theory; secondly, because in this way it is possible to consider the weakly nonlinear case as a perturbation of the linear one. Other two important aspects to note while we are presenting this approach are the fact that, for our problem equation (2.1), the difference between the weakly nonlinear case and the linear one is in the boundary condition, and this is handily rendered through a difference in a measure source term. This is an intuition that we will use to prove the convergence for the nonlinear case in *Theorem 4.0.2.* The last aspect is that with measures solutions we can remember that a Delta function represents an initial population whose age (or structuring variable) is known precisely, as we have in our problem.

We now proceed by exposing the technical definitions and results of this theory which we will use in the convergence to equilibrium results, in the last chapter of this thesis. For doing so we follow [2] and [36].

Definition 1.1 (*Linear Semi-group*). Let X be a measure space and $\mathcal{L}(X)$ the algebra of the linear and continuous operators in X , meaning $P : X \rightarrow X$. We say that a family of operators in $\mathcal{L}(X)$, meaning $\mathcal{F} = \{P_t = P(t) : t \geq 0\}$ is a *semi-group* (or a *semi-group of linear and continuous operators*) if $P_{t+s} = P_t P_s$, $\forall t, s \geq 0$ and $P_0 = I$.

Definition 1.2 (*Stochastic Semi-group*). Let X be a measure space and $P_t : L^1(X) \rightarrow L^1(X)$ be a linear semi-group. We say that P_t is a *stochastic semi-group* if $P_t f \geq 0, \forall f \geq 0$ and $\int_X P_t f = \int_X f, \forall f \in L^1(X)$. In other words, (P_t) preserves the subset of probability densities $\mathcal{P}(X)$.

Definition 1.3 (*Doeblin's Condition*). Let $P_t : L^1(X) \rightarrow L^1(X)$ be a stochastic semi-group. We say that (P_t) *satisfies Doeblin's condition* if there exists $t_0 > 0$, $\alpha \in (0, 1)$

and $\nu \in \mathcal{P}(X)$ such that

$$P_{t_0}f \geq \alpha\nu, \quad \forall f \in \mathcal{P}(X).$$

Once we have introduced these definitions, we can get into the Doeblin's theorem result applied to semi-groups.

Theorem 1.3.1 (Doeblin's Theorem). *Let $P_t : L^1(X) \rightarrow L^1(X)$ be a stochastic semi-group that satisfies Doeblin's condition. Then the semi-group has a unique equilibrium n^* in $\mathcal{P}(X)$. Moreover, for all $n \in \mathcal{P}(X)$ we have*

$$\|P_t(n - n^*)\|_{L^1(X)} \leq \frac{1}{1 - \alpha} e^{-\lambda t} \|n - n^*\|_{L^1(X)} \quad \forall t \geq 0,$$

with $\lambda = -\frac{\log(1-\alpha)}{t_0}$.

After presenting these results, specifically exposed for our future purpose, we could may desire to get a greater awareness of what is lying under this theory and its major result, the Doeblin's theorem. To gain this understanding, we briefly present the meaning of semi-groups in Markov processes following [35]. To simplify the comprehension we assume that the processes that we are dealing with in this analysis take only countably many values and have a discrete time parameter. The fundamental rule underlying this processes is that for proceeding, they have a distribution of their increments that depends on where they are at the time of the increment, but not on where they were in the past. This loose of memory property is said *Markov property*, and the process is called a *Markov chain*. We denote with \mathbb{S} , for *state space*, the set in which the process takes its values. For our previous hypothesis, our processes will have state spaces which are either finite or countably infinite, thus we can suppose, without loss of generality that \mathbb{S} is the set $\{1, \dots, N\}$ if it is finite, or \mathbb{Z}^+ if it is countably infinite.

Before proceeding, we better introduce these concepts presented about Markov chains and loose of memory in a mathematically more precise expression.

Definition 1.4 (*Markov chain*). A Markov chain on a finite or countably infinite state space \mathbb{S} is a family of \mathbb{S} -valued random variables $\{X_n : n \geq 0\}$ with the property that, for all $n \geq 0$ and $(i_0, \dots, i_n, j) \in \mathbb{S}^{n+2}$,

$$\mathbb{P}(X_{n+1} = j | X_0 = i_0, \dots, X_n = i_n) = (P)_{inj},$$

where P is a matrix called *probability transition matrix* whose entries are non-negative and each of whose rows sums to 1. In fact, the (i_n, j) element of the matrix is the probability that X passes from the value at state i_n to that in state j .

We also notice that the use of matrix notation here is clever; in fact, if we call μ the row vector of the initial distribution, naming the vector with i th entry $(\mu)_i = \mathbb{P}(X_0 = i)$, then we have

$$(\mu P^n)_j = \mathbb{P}(X_n = j), \quad n \geq 0, j \in \mathbb{S}$$

where we have adopted the convention that P^0 is the identity matrix and $P^n = PP^{n-1}$, $n \geq 1$.

Usually, speaking about Markov chain we are interested in knowing its distribution after a long time. What we want to do here is to introduce a simple technique which allows us to reach this goal; it is due to Doeblin, and is particularly effective with Markov chains on a finite state space. The emphasis we placed on the finiteness of the space is due to the fact that, at least when the state space is finite, it is reasonable to think that the distribution of the chain will stabilize. To justify this assertion we use a pigeonhole argument: if our chain can go in a single step from a state i to another state j with positive probability, then, since the number of eligible states is finite, a pigeonhole argument shows that this state is going to be visited again and again and that, after a while, the chain's initial distribution is going to get "forgotten". To say it in a mathematical way, we are asserting that for a Markov chain and for sufficiently large n , μP^n will be nearly independent of the initial distribution μ . This reasoning has a fundamental implication: we have that, when m is large, $\mu P^n = (\mu P^{n-m})P^m$ is very nearly equal to μP^m . This allows us to apply Cauchy's convergence criterion to deduce that $\pi = \lim_{n \rightarrow \infty} \mu P^n$ exists. If this were the case, then we would have that $\pi = \lim_{n \rightarrow \infty} \mu P^{n+1} = \lim_{n \rightarrow \infty} (\mu P^n)P = \pi P$. The probability vector π is called a stationary distribution for the semi-group P if $\pi = \pi P$.

Although at the beginning of this discussion we have said to think about finite state spaces, there are situations in which these arguments apply even to those that are infinite. We can say that, if the chain starts somewhere, no matter what the initial state is; then it has a positive probability of visiting some fixed state, and we can assert that it will stabilize. That is the inner meaning of the following

Theorem 1.3.2 (Doebelin's Theorem). *Let P be a transition probability matrix with the property that, for some state $j_0 \in \mathbb{S}$ and $\epsilon > 0$, $(P)_{ij_0} \geq \epsilon$ for all $i \in \mathbb{S}$. Then P has a unique stationary probability vector π , $(\pi)_{j_0} \geq \epsilon$, and, for all initial distribution μ ,*

$$\|\mu P^n - \pi\|_V \leq 2(1 - \epsilon)^n, \quad n \geq 0$$

Chapter 2

The model

2.1 Neuron Elapsed Time model with spatial dimension

We consider a population of neurons distributed in packages that are called the assemblies. For simplicity, we assume that each assembly of neural cells occupies a position $x \in \Omega$, where Ω is a bounded domain of \mathbb{R}^d which models the neural cortex. In this way, we can find an homogeneous network that is considered as a single neuron in each location of the cortex. We can describe the evolution of the assemblies saying that the neurons experience some charging process and, in response to certain stimulus, they undergo a sudden discharge. In response to this happening, other neighboring neurons have their discharge, and this cause-effect process depends on the strength of interconnections in the network since, as we said, it is supposed to be non-homogeneous, so that the interconnections varies along time.

We describe the population of neurons by the probability density $n = n(t, s, x)$ of finding a neuron that at time t , has a time elapsed since its last discharge $s \geq 0$ and occupies the position $x \in \Omega$. Since the network is not considered to be homogeneous, then not all the neurons in it are governed by the same dynamics, and this implies that, after introducing the equation describing the behaviour of the assemblies, we have to include in the system a learning rule that maps and regulates their interactions.

The neural network we consider is modelled through a non-linear renewal system,

where the nonlinearity is given by the rate factor that multiplies the probability density $n(t, s, x)$, since it depends upon the environmental factor S . The laws governing the behaviour of the network are expressed through the following integro-differential equations' system

$$\left\{ \begin{array}{ll} \partial_t n(t, s, x) + \partial_s n(t, s, x) + p(s, S(t, x))n(t, s, x) = 0 & t > 0, s > 0, x \in \Omega \\ N(t, x) := n(t, s = 0, x) = \int_0^\infty p(s, S(t, x))n(t, s, x) ds & t > 0, x \in \Omega \\ n(t = 0, s, x) = n_0(s, x) \geq 0 & s \geq 0, x \in \Omega \\ S(t, x) = \int_\Omega w(t, x, y)N(t, y) dy + I(t, x) & t > 0, x \in \Omega \\ \partial_t w(t, x, y) = -w(t, x, y) + \gamma G(N(t, x), N(t, y)) & t > 0, x, y \in \Omega \\ w(t = 0, x, y) = w_0(x, y) \geq 0 & x, y \in \Omega \end{array} \right. \quad (2.1)$$

In this system, the first three equations, meaning $(2.1)_1$ that describes the evolution of n , its initial data $(2.1)_3$ and the integral boundary condition $(2.1)_2$, correspond to the renewal equation. Here, the function $p : [0, \infty] \times \mathbb{R}$ represents the firing rate of neurons; it depends on the time elapsed s and the function $S(t, x)$, which is the amplitude of stimulation received by the network at time t and position x . Because of the role it covers, we say that the system is *inhibitory* if p is decreasing with respect to S , otherwise if it is increasing the system is said to be *excitatory*. In our analysis we consider two cases for the firing rate p :

$$p_* \leq p \leq p_\infty, \quad \text{for some constants } p_*, p_\infty > 0 \quad (2.2a)$$

$$p_* \mathbf{1}_{s > s_*} \leq p \leq p_\infty, \quad \text{for some constants } p_*, p_\infty, s_* > 0. \quad (2.2b)$$

The hypothesis $(2.2b)$ is a more general case with respect to $(2.2a)$, because it allows p to vanish for values of s within a small interval immediately following a discharge. Indeed, it means that forthwith after a discharge, the neuron undergoes a certain period of refractoriness, during which it does not fire; passed this period, that is, when $s > s_*$, the neuron regains its susceptibility.

Remark 1. It is important to note that $(2.1)_2$ is not required to hold at $t = 0$. Indeed, by $(2.1)_3$ this relation will be satisfied at $t = 0$ if and only if $n_0(s, x)$ satisfies the

compatibility condition

$$N(0, x) = n_0(0, x) = \int_0^\infty p(s, S(0, x))n(0, s, x) ds,$$

which is simply the requirement that the initial data be consistent with the birth process. We do not impose this restriction, because we envisage situations in which the initial age distribution $n_0(s, x)$ is completely arbitrary.

About the function $N(t, x)$, in (2.1)₂, it is the activity of a neuron (i.e. assemblage) at time t and position x . This equation means that this activity corresponds to integrate with respect to s the term with firing rate in the transport equation (2.1)₁, and here we see the fundamental hypothesis we have made that the neurons fire instantaneously. In fact, by defining $N(t, x) := n(t, s = 0, x)$ as the integral boundary condition, we imply that the neuron re-enters the cycle at 'age $s = 0$ ' immediately after firing.

The function $w \in C_b([0, \infty) \times \Omega \times \Omega)$ is the so called *connectivity kernel*, a function that accounts how the system is connected related to where the neurons are located. As we have supposed, the network is not homogeneous, and the equation (2.1)₅ for w reflects exactly this property. Describing the evolution of the kernel, this equation states that w varies following a learning rule that depends on a smooth function $G : \mathbb{R}^2 \rightarrow \mathbb{R}$ and on the activity N at locations x, y . This function is multiplied by a parameter $\gamma > 0$, named *connectivity parameter*. If γ and $\|\frac{\partial p}{\partial S}\|_\infty$ are small, we say that the system (2.1) is under a *weak interconnection regime*; in fact γ has the above meaning, while the infinity norm is to say that the probability of discharging varies little by changing the amplitude of the received stimulus, so the reader can understand the reason why those hypothesis imply a weak interconnection regime. To get an idea of a learning rule inspired from the Hebbian learning we can take $G(N(t, x), N(t, y)) = N(t, x)N(t, y)$. This choice means that if two neurons have simultaneously high activity, their interconnection becomes stronger. The first term of the equation, i.e. $-w$, is an inhibitory term. It means that in absence of the term in G , the kernel can simply decrease to no connectivity. This is the simpler choice for the inhibitory term and it is also biologically reasonable, because it is logical to think that a network could lose as many connections as it has, in a linear relation.

Without loss of generality, we assume for making the further calculation simpler, that the function G satisfies the following estimate:

$$\|G\|_\infty + \|\nabla G\|_\infty \leq 1. \quad (2.3)$$

With these premises we are able to explain the meaning of the equation (2.1)₄ of the system, that describe $S(t, x)$. The integral on y establishes that the amplitude of stimulation received by the neuron in position x is the result of connectivity among all the discharging neurons linked with it. Additionally, the same neuron in x can receive an external input $I \in C_b([0, \infty) \times \Omega)$ that need to be summed to the integral [Figure 2.1].

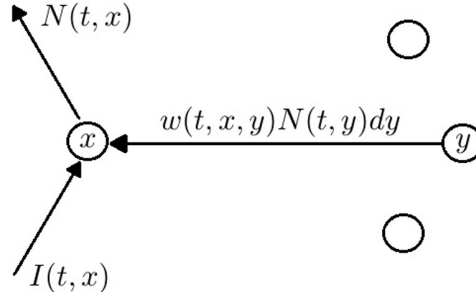


Figure 2.1: A neuron located at position x , at time t discharges and sends $N(t, x)$ to the rest of the network. At the same time this neuron in x receives $I(t, x)$ from the external input and $w(t, x, y)N(t, y)dy$ from a discharging neuron located at y .

To complete the presentation of the system then, we have to say that the couple (n_0, w_0) represents the initial configuration of the system, and the assumptions we make on its components are

$$n_0 \in C_b(\Omega, L_s^1), \quad w_0 \in C_b(\Omega \times \Omega). \quad (2.4)$$

With this hypothesis on the initial data n_0 , we can observe that for each $x \in \Omega$ the L^1 -norm of $n(t, \cdot, x)$ is formally¹ preserved, that is to say that there exists a non-negative

¹Here formally means that we can heuristically prove the mass conservation of n as shown in Chapter 1 referring to the conservative renewal equation. The conservation property confirms that the equation (2.1)₁ provides the evolution of a probability measure; indeed, although it is expected from modelling considerations, it needs to be checked mathematically on the equation for supporting the validity of the model.

function $g \in C_b(\Omega)$ such that

$$\begin{aligned} g(x) &:= \int_0^\infty n_0(s, x) \, ds = \int_0^\infty n(t, s, x) \, ds \geq 0, \quad \forall t > 0, \quad x \in \Omega \\ &\int_\Omega g(x) \, dx = 1. \end{aligned} \tag{2.5}$$

2.2 Well-posedness for the weak interconnection case

Assuming to be under the weak interconnection regime, in this section we prove that system (2.1) is well-posed. We approach the study starting from an auxiliary linear problem, where we make the assumption that the amplitude of stimulation is fixed, and then we proceed to the general non-linear case. In both cases we conduct the demonstrations based on a contraction argument.

Before to start the analysis we need to set the stage with some mathematical concepts [2].

Definition 2.1 (*Mild measure solution*). Assume $p \in W^{1,\infty}((0, +\infty) \times \Omega)$ and is non-negative. A function $n \in C([0, T) \times \Omega, L_s^1)$ defined on an interval $[0, T)$ for some $T \in (0, +\infty]$, is called a *mild measure solution* to (2.1) with initial data $n_0 \in L_s^1$ if it satisfies $n(0, s, x) = n_0(s, x) \geq 0$, and the Duhamel's variation of constants formula

$$n(t, s, x) = T_t n_0(s, x) - \int_0^t T_{t-\tau} (p(s, S(\tau, x)) n(\tau, s, x)) \, d\tau + \int_0^t T_{t-\tau} (N(\tau, x) \delta_0(s)) \, d\tau \tag{2.6}$$

for all $t \in [0, T)$, with

$$N(t, x) := \int_0^\infty p(s, S(t, x)) n(t, s, x) \, ds, \quad t \in [0, T), \tag{2.7}$$

where $T_t n(s) := n(s - t)$ with the understanding that n is zero on $(-\infty, 0)$.

Remark 2. We notice that the second term in (2.6) can be rewritten as

$$\begin{aligned} \int_0^t T_{t-\tau} (N(\tau, x) \delta_0(s)) \, d\tau &= \int_0^t N(\tau, x) \delta_{t-\tau}(s) \, d\tau \\ &= N(t - s) \mathbf{1}_{[0, t]}(s) \\ &= N(t - s) \mathbf{1}_{[0, \infty)}(t - s). \end{aligned}$$

Definition 2.2 (*Weak measure solution*). Assume $p \in W^{1,\infty}([0, +\infty) \times \Omega)$ and is nonnegative. A function $n \in C([0, T) \times \Omega, L^1_s)$ defined on an interval $[0, T)$ for some $T \in (0, +\infty]$, is called a *weak measure solution* to (2.1) with initial data $n_0 \in L^1_s$ if it satisfies $n(0, s, x) = n_0(s, x) \geq 0$, and for each $\varphi \in C_0^\infty$ the function $t \mapsto \int_0^\infty \varphi(s)n(t, s, x) ds$ is absolutely continuous and

$$\begin{aligned} & \frac{d}{dt} \int_0^\infty \varphi(s)n(t, s, x) ds \\ &= \int_0^\infty \partial_s \varphi(s)n(t, s, x) ds - \int_0^\infty p(s, S(t, x))n(t, s, x)\varphi(s) ds + \int_0^\infty N(t, x)\delta_0(s)\varphi(s) ds \end{aligned} \quad (2.8)$$

for almost all $t \in [0, T)$, and

$$N(t, x) = \int_0^\infty p(s, S(t, x))n(t, s, x) ds, \quad \forall t \in [0, T). \quad (2.9)$$

These two definitions are based upon two different mathematical principles, the first is motivated by the Duhamel formula, the latter relies on integration against a test function. Equivalence results between these two definitions are fairly common, but we cite a theorem of Ball (1977) which implies that mild solutions of our equation are equivalent to weak solutions.

Theorem 2.2.1 (Ball). *Assume $p \in W^{1,\infty}([0, +\infty) \times \Omega)$ and is nonnegative. Take $T \in (0, +\infty]$; a function $n \in ([0, T] \times \Omega, L^1_s)$ is a weak measure solution (cf. Definition 2.1) to (2.1) if and only if it is a mild measure solution (cf. Definition 2.2).*

2.2.1 Well-posedness of the linear problem

Set $S \in C_b([0, \infty) \times \Omega)$ be a given function; we proceed in our analysis considering the following linear problem

$$\begin{cases} \partial_t n(t, s, x) + \partial_s n(t, s, x) + p(s, S(t, x))n(t, s, x) = 0 & t > 0, s > 0, x \in \Omega \\ N(t, x) := n(t, s = 0, x) = \int_0^\infty p(s, S(t, x))n(t, s, x) ds & t > 0, x \in \Omega \\ n(t = 0, s, x) = n_0(s, x) \geq 0 & s \geq 0, x \in \Omega \end{cases} \quad (2.10)$$

Our problem is to find a solution that is a *weak solution* and that satisfies $n \in C_b([0, \infty) \times \Omega, L_s^1)$. In doing so, from this request and from the definition, it readily follows that $N \in C_b([0, \infty) \times \Omega)$. Furthermore we notice that, since there is no derivative or integral term involving the position, here the variable x is just a parameter.

Definition 2.3 (*weak measure solution*). Assume $p : [0, \infty) \rightarrow [0, \infty)$ is a bounded measurable function. A function $n \in C([0, T] \times \Omega, L_s^1)$ defined on an interval $[0, T)$ for some $T \in (0, +\infty]$, is called a *weak measure solution* to (2.10) with initial data $n_0 \in L_s^1$ if it satisfies $n(0, s, x) = n_0(s, x) \geq 0$, and

$$n(t, s, x) = T_t n_0(s, x) - \int_0^t T_{t-\tau} (p(s, S(\tau, x))n(\tau, s, x)) \, d\tau + \int_0^t T_{t-\tau} (N(\tau, x)\delta_0(s)) \, d\tau \quad (2.11)$$

for all $t \in [0, T)$, with

$$N(t, x) := \int_0^\infty p(s, S(t, x))n(t, s, x) \, ds, \quad t \in [0, T), \quad (2.12)$$

Now, before proceeding to state and prove the Lemma for the well posedness of the model (2.10), we present the procedure to find the explicit solution of this population model up to time $T > 0$. In order to do that, we use the *Method of characteristics*. We consider the initial data $(t_0, s_0) \in [0, T] \times \mathbb{R}^+$ and we associate to the partial differential equation of our problem the following system of ordinary differential equation

$$\begin{cases} \dot{t}(h) = 1 \\ \dot{s}(h) = 1 \end{cases}$$

The curves who solves this system are the so called *characteristics*, and they are described by

$$\begin{cases} t(h) = h + t_0 \\ s(h) = h + s_0 \end{cases}$$

Now, consider the differential operator working on n , it is such that $Dn = \partial_t n + \partial_s n$, so $Dn(t, s, x) = \lim_{h \rightarrow 0} \frac{n(t+h, s+h, x) - n(t, s, x)}{h}$. In this way our problem turns into

$$Dn(t, s, x) + p(s, S(t, x))n(t, s, x) = 0.$$

Transposing now our problem on the characteristic, so considering

$$\begin{aligned}\bar{n}(h) &= n(t_0 + h, s_0 + h) \\ \bar{p}(h) &= p(s_0 + h, S(t_0 + h, x)),\end{aligned}$$

it becomes

$$\frac{d\bar{n}}{dh} + \bar{p}(h)\bar{n} = 0,$$

which is solved by

$$\begin{aligned}\frac{d\bar{n}}{\bar{n}} + \bar{p}(h) dh &= 0 \\ \log(\bar{n})\Big|_0^h &= - \int_0^h \bar{p}(z) dz \\ \bar{n}(h) &= \bar{n}(0)e^{-\int_0^h \bar{p}(z) dz} \\ n(t_0 + h, s_0 + h, x) &= n(t_0, s_0, x)e^{-\int_0^h \bar{p}(z) dz}\end{aligned}$$

Now, found this solution giving the values of n at all the points on the characteristic through (t_0, s_0) , we made explicit the parameter.

If $h = t$, then substituting in the characteristic equation we find $(t_0, s_0) = (0, s - t)$ so, remembering that the age has to be positive, i.e. it has to be $s > t$, the solution becomes

$$\begin{aligned}n(t, s, x) &= n(0, s - t, x)e^{-\int_0^t p(s-t+\tau, S(\tau, x)) d\tau} \mathbf{1}_{\{s \geq t\}} \\ &= n_0(s - t) \exp\left(-\int_0^t p(s - t + \tau, S(\tau, x)) d\tau\right) \mathbf{1}_{\{s \geq t\}}\end{aligned}$$

If $h = s$, then substituting in the characteristic equation we find $(t_0, s_0) = (t - s, 0)$ so, remembering that the time has to be positive, i.e. it has to be $0 < s < t$, the solution becomes

$$\begin{aligned}n(t, s, x) &= n(t - s, 0, x)e^{-\int_0^s p(\tau, S(t-s+\tau, x)) d\tau} \mathbf{1}_{\{0 < s < t\}} \\ &= N(t, x) \exp\left(-\int_0^s p(\tau, S(t - s + \tau, x)) d\tau\right) \mathbf{1}_{\{0 < s < t\}}.\end{aligned}$$

To conclude, the solution of system (2.10) is given by

$$\begin{aligned}n(t, s, x) &= n_0(s - t) \exp\left(-\int_0^t p(s - t + \tau, S(\tau, x)) d\tau\right) \mathbf{1}_{\{s \geq t\}} + \\ &N(t, x) \exp\left(-\int_0^s p(\tau, S(t - s + \tau, x)) d\tau\right) \mathbf{1}_{\{0 < s < t\}}.\end{aligned}$$

We are now ready to enunciate and prove the following Lemma for the well posedness of the linear model.

Lemma 2.2.2. *Assume that $n_0 \in C_b(\Omega, L_s^1)$ and that $p \in W^{1,\infty}((0, \infty) \times \mathbb{R})$ satisfies (2.2b). Then, for a given $S \in C_b([0, \infty) \times \Omega)$, the equation (2.10) has an unique weak solution $n \in C_b([0, \infty) \times \Omega, L_s^1)$ with $N \in C_b([0, \infty) \times \Omega)$. Moreover n is non-negative and mass conservative, i.e.*

$$\int_0^\infty n_0(s, x) ds = \int_0^\infty n(t, s, x) ds \quad \forall t > 0, x \in \Omega.$$

Proof. We start by noticing that a solution of the linear system (2.10) satisfies the following fixed point equation

$$n(t, s, x) = \Psi[n](t, s, x) := n_0(s - t, x) \exp\left(-\int_0^t p(\tau + s - t, S(\tau, x)) d\tau\right) \mathbf{1}_{\{s > t\}} + N(t - s, x) \exp\left(-\int_0^s p(\tau, S(t - s + \tau, x)) d\tau\right) \mathbf{1}_{\{0 < s < t\}}, \quad (2.13)$$

with $N(t, x) = \int_0^\infty p(u, S(t, x))n(t, u, x) du$, which depends on n .

Now, let $T > 0$ and $X_T := \{n \in C_b([0, T] \times \Omega, L_s^1) : n(0) = n_0\}$; it readily follows that Ψ maps $X_T \rightarrow X_T$, and since L^1 endowed with its norm is a complete space, then also $C_b([0, T] \times \Omega, L_s^1)$ is, and this implies that we can apply the Banach-Caccioppoli fixed point theorem on Ψ defined on X_T .

Step 1. We start by proving that, for $T > 0$ small enough, Ψ has a unique fixed point in X_T , i.e. there exists an unique weak solution of (2.10) defined on $[0, T]$. In order to do so, we use the contraction principle, so consider $n_1, n_2 \in X_T$; we have

$$\begin{aligned} & \int_0^\infty |\Psi[n_1] - \Psi[n_2]|(t, s, x) ds = \\ & = \int_0^\infty |n_0(s - t, x) e^{-\int_0^t p(\tau + s - t, S(\tau, x)) d\tau} \mathbf{1}_{\{s > t\}} + N_1(t - s, x) e^{-\int_0^s p(\tau, S(t - s + \tau, x)) d\tau} \mathbf{1}_{\{0 < s < t\}} - \\ & \quad - n_0(s - t, x) e^{-\int_0^t p(\tau + s - t, S(\tau, x)) d\tau} \mathbf{1}_{\{s > t\}} - N_2(t - s, x) e^{-\int_0^s p(\tau, S(t - s + \tau, x)) d\tau} \mathbf{1}_{\{0 < s < t\}}| ds \\ & = \int_0^t |N_1(t - s, x) - N_2(t - s, x)| \underbrace{\left| \exp\left(-\int_0^s p(\tau, S(t - s + \tau, x)) d\tau\right) \right|}_{< 1} ds \\ & \leq \int_0^t |N_1(t - s, x) - N_2(t - s, x)| ds \\ & \text{substitute } t - s = k \\ & = \int_t^0 |N_1(k, x) - N_2(k, x)| (-1) dk \\ & = \int_0^t |N_1(k, x) - N_2(k, x)| dk \\ & \leq T \sup_{(t, x) \in [0, T] \times \Omega} |N_1 - N_2|(t, x). \end{aligned} \quad (2.14)$$

Estimating the argument of the sup in the former expression and remembering that $S(t, x)$ is fixed, we get

$$\begin{aligned}
|N_1 - N_2|(t, x) &= \left| \int_0^\infty [p(u, S)n_1(t, u, x) - p(u, S)n_2(t, u, x)] du \right| \\
&= \left| \int_0^\infty p(u, S)[n_1(t, u, x) - n_2(t, u, x)] du \right| \\
&\leq p_\infty \int_0^\infty |n_1(t, u, x) - n_2(t, u, x)| du \\
&\leq p_\infty \|n_1(t, x) - n_2(t, x)\|_{L^1_S},
\end{aligned} \tag{2.15}$$

so we can substitute (2.15) in (2.14) obtaining

$$\int_0^\infty |\Psi[n_1] - \Psi[n_2]|(t, s, x) ds \leq Tp_\infty \sup_{(t,x) \in [0,T] \times \Omega} \|n_1(t, x) - n_2(t, x)\|_{L^1_S}, \tag{2.16}$$

thus for $T < \frac{1}{p_\infty}$, we have proved that Ψ is a contraction and therefore there is a unique $n \in X_T$ such that $\Psi[n] = n$. Since the choice of T is independent on n_0 , we can reiterate this argument to get a unique solution of the linear problem (2.10), which is defined for all $t \geq 0$.

Step 2. We now prove the mass conservation property. Since n satisfies the fixed point equation (2.13) and it is a weak solution, it also verifies the following equality

$$\begin{aligned}
n(t, s, x) &= n_0(s - t, x)\mathbf{1}_{\{s > t\}} - \int_0^t p(s - t + \tau, S(\tau, x))n(\tau, s - t + \tau, x) \\
&\quad \mathbf{1}_{\{s > t - \tau\}} d\tau + N(t - s, x)\mathbf{1}_{\{0 < s < t\}},
\end{aligned} \tag{2.17}$$

hence we get the property of mass conservation by integrating with respect to s on $(0, \infty)$ as follows

$$\begin{aligned}
\int_0^\infty n(t, s, x) ds &= \int_0^\infty n_0(s - t, x)\mathbf{1}_{\{s > t\}} ds - \\
&\quad - \int_0^\infty \int_0^t p(s - t + \tau, S(\tau, x))n(\tau, s - t + \tau, x)\mathbf{1}_{\{s > t - \tau\}} d\tau ds + \\
&\quad + \int_0^\infty N(t - s, x)\mathbf{1}_{\{0 < s < t\}} ds \\
&\quad \text{substitute } s - t = y \text{ in the first term and rewrite the second one} \\
&= \int_0^\infty n_0(y, x) dy - \int_0^\infty N(t - s, x)\mathbf{1}_{0 < s < t} ds + \int_0^\infty N(t - s, x)\mathbf{1}_{\{0 < s < t\}} ds \\
&\quad \text{replace } y \text{ with } s \text{ and simplify} \\
&= \int_0^\infty n_0(s, x) ds
\end{aligned} \tag{2.18}$$

Step 3. We now conclude the proof showing that the solution is non-negative. Since n_0 is non-negative, then Ψ preserves positivity, because it sends n_0 to n_0 . By uniqueness of

fixed point then, since $n(t, s, x)$ associated to $n_0 = 0$ in the starting space is a population density and therefore it is non-negative, then also the corresponding solution $n(t, s, x)$ in the arrival space must be non-negative. \square

2.2.2 Well-posedness of the non-linear problem

After presenting the linear problem, we are ready to prove that also the nonlinear system (2.1) is well-posed in the case of weak interconnections².

Theorem 2.2.3 (Well-posedness for weak interconnections). *Assume (2.4)-(2.5) and that $p \in W^{1,\infty}((0, \infty) \times \Omega)$ satisfies (2.2b). Then for*

$$\|g\|_\infty |\Omega| \left\| \frac{\partial p}{\partial S} \right\|_\infty \max \left\{ \|w_0\|_\infty, \gamma \|G|_{[0, p_\infty \|g\|_\infty]^2} \|_\infty \right\} < 1,$$

the system (2.1) has a unique weak solution with $n \in C_b([0, \infty) \times \Omega, L_s^1)$, $N \in C_b([0, \infty) \times \Omega)$, $S \in C_b([0, \infty) \times \Omega)$ and $w \in C_b([0, \infty) \times \Omega \times \Omega)$. Moreover, the system (2.1) is mass-conservative and n is non-negative for all $t > 0$.

Proof. Consider $T > 0$ and a function $S \in C_b([0, \infty) \times \Omega)$ fixed. Based on the previous *Lemma 2.2.2*, we can define the functions $n \in C_b([0, \infty) \times \Omega, L_s^1)$ and $N \in C_b([0, \infty) \times \Omega)$ to get the solution of (2.10). Moreover, we have already proved that the solution of this linear system is mass-conservative and preserves positivity. In order to complete the solution for (2.1), we have then to find a form for w and, hence, for S . The most relevant part of the proof consists in dealing with some estimates to prove a fixed point condition on S , aimed by the same intentions as in *Lemma 2.2.2*.

²Here, as in all the rest of the thesis, we use the notation $\|g\|_1$ although it is supposed to be 1, in order to outline the dependence of g on x . A posteriori the author of the article [36] has noted that this is not relevant for the analysis, and in a subsequent review has abandoned this notation, which we still retain for a greater clarity [T].

Moreover, we keep the notation $\|G\|_\infty$ and $\|\nabla G\|_\infty$, but we observe from estimate (2.21) that we only need the function G to be bounded on the set $[0, p_\infty \|g\|_\infty]^2$. That justifies the choice of normalizing G according to (2.3) and thus to assume those infinity norms less-equal than 1, as the author has done in the last version of his article. Again here and in the rest of the thesis we leave these notations for a greater clarity [T].

Step 1. We complete the solution. We find the solution $w \in C_b([0, \infty) \times \Omega \times \Omega)$ by solving the Cauchy problem formed by the last two equations in system (2.1).

$$\begin{aligned}
\partial_t w(t, x, y) + w(t, x, y) &= \gamma G(N(t, x), N(t, y)) \\
e^t [\partial_t w + w] &= e^t [\gamma G(N(t, x), N(t, y))] \\
\int_0^t (e^\tau \partial_\tau w + e^\tau w) \, d\tau &= \int_0^t e^\tau \gamma G(N(\tau, x), N(\tau, y)) \, d\tau \\
e^t w(t, x, y) - w_0(x, y) &= \int_0^t e^\tau \gamma G(N(\tau, x), N(\tau, y)) \, d\tau \\
w(t, x, y) &= e^{-t} \left[w_0(x, y) + \int_0^t e^\tau \gamma G(N(\tau, x), N(\tau, y)) \, d\tau \right] \\
w(t, x, y) &= e^{-t} w_0(x, y) + \gamma \int_0^t e^{-(t-\tau)} G(N(\tau, x), N(\tau, y)) \, d\tau
\end{aligned} \tag{2.19}$$

It follows that we have a solution of system (2.1) defined on $[0, T]$ if S satisfies the following fixed point condition for all $0 \leq t \leq T$ and $x \in \Omega$

$$S(t, x) = \mathcal{J}[S](t, x) := \int_{\Omega} w(t, x, y) \left(\int_0^\infty p(s, S(t, y)) n(t, s, y) \, ds \right) dy + I(t, x), \tag{2.20}$$

obtained by substituting the equation for $n(t, x)$ in that for $S(t, x)$.

Step 2. Now we want to prove that, for all $T > 0$, \mathcal{J} defines an operator mapping $X_T \rightarrow X_T$ with $X_T := C_b([0, T] \times \Omega)$. In order to do so, we need to prove some estimates that then will occur to achieve this result.

First, we observe the following estimate for the activity $N(t, x)$:

$$\begin{aligned}
|N(t, x)| &\leq \left| \int_0^\infty p_\infty n(t, s, x) \, ds \right| \\
&= p_\infty \left| \int_0^\infty n(t, s, x) \, ds \right| \\
&= p_\infty |g(y)| \\
&\leq p_\infty \|g\|_\infty \quad \forall (t, x) \in [0, T] \times \Omega
\end{aligned} \tag{2.21}$$

and this allows us to restrict the domain of G and its derivatives to the set $[0, p_\infty \|g\|_\infty]^2$.

Next, we can get the following estimates for w from equation (2.19)

$$\begin{aligned}
|w(t, x, y)| &= \left| e^{-t} w_0(x, y) + \gamma \int_0^t e^{-(t-\tau)} G(N(\tau, x), N(\tau, y)) \, d\tau \right| \\
&\leq |e^{-t} w_0(x, y)| + \gamma \left| \int_0^t e^{-(t-\tau)} G(N(\tau, x), N(\tau, y)) \, d\tau \right| \\
&\leq e^{-t} |w_0(x, y)| + \gamma \int_0^t |e^{-(t-\tau)} G(N(\tau, x), N(\tau, y))| \, d\tau \\
&\leq e^{-t} \|w_0\|_\infty + \gamma \int_0^\infty e^{-(t-\tau)} \|G\|_\infty \\
&= e^{-t} \|w_0\|_\infty + \gamma (1 - e^{-t}) \|G\|_\infty \\
&\leq \max \{ \|w_0\|_\infty, \gamma \|G\|_\infty \} \quad \forall (t, x, y) \in [0, T] \times \Omega \times \Omega
\end{aligned} \tag{2.22}$$

With this result it readily follows that for any $S \in X_T$ we have:

$$\begin{aligned}
\|\mathcal{T}[S]\|_\infty &= \sup |\mathcal{T}[S]| = \sup \left| \int_\Omega w(t, x, y) \left(\int_0^\infty p(s, S(t, y)) n(t, s, y) ds \right) dy + I(t, x) \right| \\
&\leq \sup \left| \int_\Omega w(t, x, y) \left(\int_0^\infty p(s, S(t, y)) n(t, s, y) ds \right) dy \right| + \sup |I(t, x)| \\
&\leq \sup \int_\Omega |w(t, x, y) \int_0^\infty p(s, S(t, y)) n(t, s, y) ds| dy + \sup |I(t, x)| \\
&\leq \max \{ \|w_0\|_\infty, \gamma \|G\|_\infty \} p_\infty \sup \int_\Omega \left| \int_0^\infty n(t, s, y) ds \right| dy + \|I(t, x)\|_\infty \\
&\leq \max \{ \|w_0\|_\infty, \gamma \|G\|_\infty \} p_\infty \|g\|_1 + \|I(t, x)\|_\infty
\end{aligned} \tag{2.23}$$

from which we deduce that $\mathcal{T}[S]$ is a continuous and bounded function, which means $\mathcal{T}[S] \in X_T$.

Step 3. Our further goal is proving that, for T small enough, \mathcal{T} is a contraction. Consider $S_1, S_2 \in X_T$; we start by observing that, using (2.19), the difference between w_1 and w_2 fulfils the following inequality:

$$\begin{aligned}
|w_1 - w_2| &= \left| e^{-t} w_0(x, y) + \gamma \int_0^t e^{-(t-\tau)} G(N_1(\tau, x), N_1(\tau, y)) d\tau - \right. \\
&\quad \left. - e^{-t} w_0(x, y) - \gamma \int_0^t e^{-(t-\tau)} G(N_2(\tau, x), N_2(\tau, y)) d\tau \right| \\
&= \left| \gamma \int_0^t e^{-(t-\tau)} [G(N_1(\tau, x), N_1(\tau, y)) - G(N_2(\tau, x), N_2(\tau, y))] d\tau \right| \\
&= \gamma \left| \int_0^t e^{-(t-\tau)} \langle \nabla G, (N_1 - N_2) \rangle d\tau \right| \\
&\leq 2\gamma \|\nabla G\|_\infty \|N_1 - N_2\|_\infty \left| \int_0^t e^{-(t-\tau)} d\tau \right| \\
&\leq 2\gamma \|\nabla G\|_\infty \|N_1 - N_2\|_\infty |1 - e^{-t}| \\
&\leq 2\gamma \|\nabla G\|_\infty \|N_1 - N_2\|_\infty |1 - 1 + t + o(t^2)| \\
&\leq 2\gamma T \|\nabla G\|_\infty \|N_1 - N_2\|_\infty,
\end{aligned} \tag{2.24}$$

and then that the difference between N_1 and N_2 can be estimated by

$$\begin{aligned}
|N_1 - N_2|(t, x) &\leq \int_0^\infty |p(s, S_1(t, x)) n_1(t, s, x) - p(s, S_2(t, x)) n_2(t, s, x)| ds \\
&\quad \text{adding and subtracting } p(s, S_2(t, x)) n_1(t, s, x) \\
&\leq \int_0^\infty |p(s, S_1(t, x)) - p(s, S_2(t, x))| n_1(t, s, x) ds + \int_0^\infty p(s, S_2(t, x)) |n_1 - n_2|(t, s, x) ds \\
&\quad \text{applying the mean value inequality} \\
&\leq \int_0^\infty \left| \frac{\partial p}{\partial S}(S_1 - S_2) \right| n_1(t, s, x) ds + \int_0^\infty p(s, S_2(t, x)) |n_1 - n_2|(t, s, x) ds \\
&\leq \|g\|_\infty \left\| \frac{\partial p}{\partial S} \right\|_\infty \|S_1 - S_2\|_\infty + p_\infty \|n_1 - n_2\|_{L_{t,x}^\infty L_s^1}.
\end{aligned} \tag{2.25}$$

Now, using (2.17) and (2.25) we get the following estimate for the difference between n_1 and n_2

$$\begin{aligned}
& \|n_1 - n_2\|_{L_{t,x}^\infty L_s^1} = \\
& = \sup_{t,x} \left| \int_0^\infty n_0(s-t, x) \mathbf{1}_{\{s>t\}} ds - \int_0^t \int_0^\infty p(s-t+\tau, S_1) n_1(\tau, s-t+\tau, x) \cdot \right. \\
& \quad \cdot \mathbf{1}_{\{s>t-\tau\}} ds d\tau + \int_0^\infty N_1(t-s, x) \cdot \mathbf{1}_{\{0<s<t\}} ds - \int_0^\infty n_0(s-t, x) \mathbf{1}_{\{s>t\}} ds + \\
& \quad + \int_0^t \int_0^\infty p(s-t+\tau, S_2) n_2(\tau, s-t+\tau, x) \mathbf{1}_{\{s>t-\tau\}} ds d\tau + \\
& \quad \left. + \int_0^\infty N_2(t-s, x) \mathbf{1}_{\{0<s<t\}} ds \right| \\
& \leq \sup_{t,x} \left| \int_0^t \int_{t-\tau}^\infty \left[-p(s-t+\tau, S_1) n_1(\tau, s-t+\tau, x) + p(s-t+\tau, S_2) \cdot \right. \right. \\
& \quad \cdot n_1(\tau, s-t+\tau, x) \left. \right] ds d\tau + \int_0^t \int_{t-\tau}^\infty \left[p(s-t+\tau, S_2) n_2(\tau, s-t+\tau, x) - \right. \\
& \quad \left. - p(s-t+\tau, S_2) n_1(\tau, s-t+\tau, x) \right] ds d\tau + \int_0^t (N_2 - N_1)(t-s, x) ds \left| \right. \\
& \leq \sup_{t,x} \left| \int_0^t \int_{t-\tau}^\infty \left[\frac{\partial p}{\partial S}(S_2 - S_1) n_1(\tau, s-t+\tau, x) \right] ds d\tau + \right. \\
& \quad \left. + \int_0^t \int_{t-\tau}^\infty \left[p(s-t+\tau, S_2)(n_2 - n_1)(\tau, s-t+\tau, x) \right] ds d\tau + \right. \\
& \quad \left. + \int_0^t (N_2 - N_1)(t-s, x) ds \right| \\
& \leq \left\| \frac{\partial p}{\partial S} \right\|_\infty \|S_2 - S_1\|_\infty \sup_{t,x} \left| \int_0^t \int_{t-\tau}^\infty n_1(\tau, s-t+\tau, x) ds d\tau \right| + \\
& \quad + p_\infty \|n_2 - n_1\|_{L_{t,x}^\infty L_s^1} \sup_{t,x} \left| \int_0^t d\tau \right| + \sup_{t,x} \left| \int_0^t (N_2 - N_1)(t-s, x) ds \right| \\
& \leq \left\| \frac{\partial p}{\partial S} \right\|_\infty \|S_2 - S_1\|_\infty \|g\|_\infty \sup_{t,x} \left| \int_0^t d\tau \right| + p_\infty \|n_2 - n_1\|_{L_{t,x}^\infty L_s^1} \sup_{t,x} \left| \int_0^t d\tau \right| + \\
& \quad + \left[\|g\|_\infty \left\| \frac{\partial p}{\partial S} \right\|_\infty \|S_2 - S_1\|_\infty + p_\infty \|n_2 - n_1\|_{L_{t,x}^\infty L_s^1} \right] \left(\sup_{t,x} \left| \int_0^t ds \right| \right) \\
& \leq T \left\| \frac{\partial p}{\partial S} \right\|_\infty \|S_2 - S_1\|_\infty \|g\|_\infty + T p_\infty \|n_2 - n_1\|_{L_{t,x}^\infty L_s^1} + \\
& \quad + T \|g\|_\infty \left\| \frac{\partial p}{\partial S} \right\|_\infty \|S_2 - S_1\|_\infty + T p_\infty \|n_2 - n_1\|_{L_{t,x}^\infty L_s^1} \\
& \leq 2T \left\| \frac{\partial p}{\partial S} \right\|_\infty \|S_2 - S_1\|_\infty \|g\|_\infty + 2T p_\infty \|n_2 - n_1\|_{L_{t,x}^\infty L_s^1}
\end{aligned}$$

from which, assuming $T < \frac{1}{2p_\infty}$, it follows that

$$\|n_2 - n_1\|_{L_{t,\infty}^\infty L_s^1} \leq \frac{2T \left\| \frac{\partial p}{\partial S} \right\|_\infty \|g\|_\infty}{1 - 2T p_\infty} \|S_1 - S_2\|_\infty \quad (2.26)$$

Finally, considering all the estimates (2.21)-(2.24), we find that the operator \mathcal{T} fulfils

$$\begin{aligned}
|\mathcal{T}[S_1] - \mathcal{T}[S_2]|(t, x) &= \left| \int_{\Omega} w_1 \left(\int_0^{\infty} p_1 n_1 ds \right) dy + I - \int_{\Omega} w_2 \left(\int_0^{\infty} p_2 n_2 ds \right) dy - I \right| \\
&= \left| \int_{\Omega} w_1 N_1 dy - \int_{\Omega} w_2 N_1 dy + \int_{\Omega} w_2 N_1 dy - \int_{\Omega} w_2 N_2 dy \right| \\
&= \left| \int_{\Omega} N_1 (w_1 - w_2) dy + \int_{\Omega} w_2 (N_1 - N_2) dy \right| \\
&\leq \int_{\Omega} |N_1 (w_1 - w_2)| dy + \int_{\Omega} |w_2 (N_1 - N_2)| dy \\
&\leq \int_{\Omega} |N_1| |w_1 - w_2| dy + \int_{\Omega} |w_2| |N_1 - N_2| dy \\
&\leq \int_{\Omega} |N_1| dy 2\gamma T \|\nabla G\|_{\infty} \|N_1 - N_2\|_{\infty} + \\
&\quad + \max \{ \|w_0\|_{\infty}, \gamma \|G\|_{\infty} \} \|N_1 - N_2\|_{\infty} \int_{\Omega} dy \\
&\leq p_{\infty} \int_{\Omega} |g(y)| dy 2\gamma T \|\nabla G\|_{\infty} \|N_1 - N_2\|_{\infty} + \\
&\quad + \max \{ \|w_0\|_{\infty}, \gamma \|G\|_{\infty} \} \|N_1 - N_2\|_{\infty} \int_{\Omega} dy \\
&\leq p_{\infty} \|g\|_1 2\gamma T \|\nabla G\|_{\infty} \|N_1 - N_2\|_{\infty} + \\
&\quad + \max \{ \|w_0\|_{\infty}, \gamma \|G\|_{\infty} \} \|N_1 - N_2\|_{\infty} |\Omega| \\
&\leq C \|S_1 - S_2\|_{\infty},
\end{aligned} \tag{2.27}$$

where C is a positive constant given by

$$C := \|g\|_{\infty} \left\| \frac{\partial p}{\partial S} \right\|_{\infty} (2\gamma T p_{\infty} \|g\|_1 \|\nabla G\|_{\infty} + |\Omega| \max \{ \|w_0\|_{\infty}, \gamma \|G\|_{\infty} \}) \left(1 + \frac{2T p_{\infty}}{1 - 2T p_{\infty}} \right).$$

Under the conditions $\|g\|_{\infty} |\Omega| \left\| \frac{\partial p}{\partial S} \right\|_{\infty} \max \{ \|w_0\|_{\infty}, \gamma \|G\|_{\infty} \} < 1$ and T small enough, we get $C < 1$, and this proves that \mathcal{T} is a contraction.

Step 4. Now we can prove the uniqueness of the solution. Having proved that \mathcal{T} maps $X_T \rightarrow X_T$ and since X_T is a complete space, from Picard's fixed point argument we get a unique $S \in X_T$ such that $\mathcal{T}[S] = S$. It follows from this argument that there exists a unique solution of (2.1) defined on $[0, T]$. Furthermore, we can iterate this argument to get an unique solution of (2.1) defined for all $t > 0$, because the estimates (2.21) and (2.22) are uniform in T .

Step 5. To conclude, we can assert that the nonlinear system (2.1) is mass-conservative and preserves positivity as the linear one (2.10), because of the construction we have done. \square

Chapter 3

Asymptotic behaviour

In this chapter we are interested in investigating the behaviour of our model in the limit $t \rightarrow \infty$. To this end, we firstly study the stationary states of the model, proving the existence of a steady state and its uniqueness. Subsequently, we concentrate in exposing a result of convergence to equilibrium about system (2.1) after a long time. As we claimed at the beginning of our analysis, we set in the weak interconnection case, i.e. with γ and $\|\frac{\partial p}{\partial S}\|_\infty$ small enough, and we suppose p satisfying (2.2b).

3.1 Stationary states

For proceeding in looking for the stationary states, we assume that the external input function I depends only on position; otherwise, it wouldn't allow for stationary states. We say that (n, N, S, w) is a stationary solution to (2.1) if it satisfies

$$\begin{cases} \partial_s n(s, x) + p(s, S(x))n(s, x) = 0 & s > 0, x \in \Omega \\ N(x) := n(s = 0, x) = \int_0^\infty p(s, S(x))n(s, x) ds & x \in \Omega \\ S(x) = \int_\Omega w(x, y)N(y) dy + I(x) & x \in \Omega \\ w(x, y) = \gamma G(N(x), N(y)) & x, y \in \Omega \end{cases} \quad (3.1)$$

where $n \in L^1_{s,x}$, $N, S \in C_b(\Omega)$ and $w \in C_b(\Omega \times \Omega)$.

If the amplitude S is given, it is possible to calculate n , N and w as follows.

We find the function n by solving the Cauchy problem formed by the first two equations in system (3.1),

$$\begin{aligned}
 \partial_s n(s, x) + p(s, S(x))n(s, x) &= 0 \\
 \frac{\partial n(s, x)}{\partial s} + p(s, S(x))n(s, x) &= 0 \\
 \frac{\partial n(s, x)}{\partial n(s, x)} &= -p(s, S(x)) \\
 \log(n(s, x)) - \log(n(0, x)) &= -\int_0^s p(\sigma, S(x)) \, d\sigma \\
 n(s, x) &= n(0, x) e^{-\int_0^s p(\sigma, S(x)) \, d\sigma} \\
 n(s, x) &= N(x) e^{-\int_0^s p(\sigma, S(x)) \, d\sigma} .
 \end{aligned} \tag{3.2}$$

Furthermore, as condition (2.5) needs to be satisfied, we impose for normalization

$$N(x) = g(x) \left(\int_0^\infty e^{-\int_0^s p(\sigma, S(x)) \, d\sigma} \, ds \right)^{-1}, \tag{3.3}$$

in fact, substituting (3.3) in (3.2) results

$$n(s, x) = \frac{g(x)}{\int_0^\infty e^{-\int_0^s p(\sigma, S(x)) \, d\sigma} \, ds} e^{-\int_0^s p(\sigma, S(x)) \, d\sigma}$$

and it means

$$\begin{aligned}
 \int_\Omega \int_0^\infty n(s, x) \, ds \, dx &= \int_\Omega \int_0^\infty \frac{g(x)}{\int_0^\infty e^{-\int_0^s p(\sigma, S(x)) \, d\sigma} \, ds} e^{-\int_0^s p(\sigma, S(x)) \, d\sigma} \, ds \\
 \int_\Omega \int_0^\infty n(s, x) \, ds \, dx &= \int_\Omega \frac{g(x)}{\int_0^\infty e^{-\int_0^s p(\sigma, S(x)) \, d\sigma} \, ds} \int_0^\infty e^{-\int_0^s p(\sigma, S(x)) \, d\sigma} \, ds \\
 \int_\Omega \int_0^\infty n(s, x) \, ds \, dx &= \int_\Omega g(x) \, dx = 1 .
 \end{aligned}$$

Finally, by defining a function $F : \mathbb{R} \rightarrow \mathbb{R}_+$ such that $F(S) := \left(\int_0^\infty e^{-\int_0^s p(\tau, S) \, d\tau} \, ds \right)^{-1}$, we get

$$\begin{aligned}
 w(x, y) &= \gamma G(N(x), N(y)) \\
 &= \gamma G(g(x)F(S(x)), g(y)F(S(y))) .
 \end{aligned} \tag{3.4}$$

So (3.2), (3.3) and (3.4) form the stationary solution (n, N, S, w) to (3.1) if S satisfies the following fixed point condition

$$S(x) = \mathcal{T}[S](x) := \gamma \int_\Omega G(g(x)F(S(x)), g(y)F(S(y))) \, dy + I(x), \tag{3.5}$$

obtained by substituting (3.3) and (3.4) in the equation for S .

We will proceed now by presenting a result about the function F that is necessary for proving the main result about the stationary states.

Lemma 3.1.1. *Assume that $p \in W^{1,\infty}((0, \infty) \times \Omega)$ satisfies (2.2b). Under these hypothesis, the function $F : \mathbb{R} \rightarrow \mathbb{R}_+$ defined above is bounded and Lipschitz continuous.*

Proof. It is immediate to demonstrate that F is bounded, in fact the following estimate holds:

$$0 < F(S) \leq \left(\int_0^\infty e^{-p_\infty s} ds \right)^{-1} = p_\infty,$$

where the last equality is obtained by solving the integral.

Next, we see that F' is given by the expression

$$\begin{aligned} F'(S) &= - \left(\int_0^\infty e^{-\int_0^s p(\tau, S(x)) d\tau} \right)^{-2} \left[\int_0^\infty e^{-\int_0^s p(\tau, S(x)) d\tau} \left(- \int_0^s \frac{\partial p}{\partial S}(\tau, S) d\tau \right) ds \right] \\ &= F(S)^2 \left[\int_0^\infty e^{-\int_0^s p(\tau, S(x)) d\tau} \left(- \int_0^s \frac{\partial p}{\partial S}(\tau, S) d\tau \right) ds \right], \end{aligned}$$

So, remembering that p satisfies (2.2b), we have the following estimate:

$$\begin{aligned} |F'(S)| &\leq p_\infty^2 \left\| \frac{\partial p}{\partial S} \right\|_\infty \left[\int_0^\infty e^{-\int_0^s p(\tau, S(x)) d\tau} s ds \right] \\ &\leq p_\infty^2 \left\| \frac{\partial p}{\partial S} \right\|_\infty \left[\int_0^\infty e^{-p_*(s-s_*)+s} ds \right] \\ &= p_\infty^2 \left\| \frac{\partial p}{\partial S} \right\|_\infty \left[s \frac{e^{-p_*(s-s_*)+s}}{-p_*} - \int_0^\infty \frac{e^{-p_*(s-s_*)+s}}{-p_*} ds \right]_0^\infty \\ &= p_\infty^2 \left\| \frac{\partial p}{\partial S} \right\|_\infty \frac{e^{-p_*(s-s_*)+s}}{-p_*} \Big|_0^\infty \\ &= p_\infty^2 \left\| \frac{\partial p}{\partial S} \right\|_\infty \frac{e^{p_* s_*}}{p_*} \\ &\text{calculate the exponential with Taylor series expansion} \\ &= p_\infty^2 \left\| \frac{\partial p}{\partial S} \right\|_\infty \frac{1}{p_*} \left[1 + p_* s_* + \frac{p_*^2 s_*^2}{2} + o(p_*^2 s_*^2) \right] \\ &\leq p_\infty^2 \left\| \frac{\partial p}{\partial S} \right\|_\infty \left[\frac{1}{p_*} + \frac{s_*}{p_*} + \frac{s_*^2}{2} \right]. \end{aligned}$$

Hence the function F is Lipschitz. □

Now we are ready to state and prove the theorem that assures us that, in the weak interconnection regime, given $g \in C_b(\Omega)$, there exists a unique steady state for our system (2.1).

Theorem 3.1.2. *Assume that the function $p \in W^{1,\infty}((0, \infty) \times \Omega)$ and satisfies (2.2b), that $g \in C_b(\Omega)$ and $I \in C_b(\Omega)$. For γ small enough, the system (2.1) has a unique stationary state (n^*, N^*, S^*, w^*) , with $n^* \in C_b(\Omega, L_s^1)$ satisfying $\int_0^\infty n^*(s, x) ds = g(x)$ and $N^* \in C_b(\Omega)$, $w^* \in C_b(\Omega \times \Omega)$, which are determined by a unique amplitude of stimulation $S^* \in C_b(\Omega)$ satisfying $\mathcal{T}[S^*] = S^*$.*

Proof. First we notice that the operator $\mathcal{T}[S](x)$ defined in (3.5) maps $C_b(\Omega) \rightarrow C_b(\Omega)$. In fact, $\mathcal{T}[S](x)$ is continuous and bounded because $g \in C_b$ by hypothesis, F is Lipschitz continuous, thus continuous, as proved in *Lemma 3.0.1.* and is bounded as proved at the beginning of the proof of the same Lemma; G is a smooth function, composed by continuous and bounded functions, so $G \in C_b$ itself; then $I \in C_b$ for hypothesis, and from this follows our initial assertion. Furthermore, $(C_b(\Omega), \|\cdot\|_\infty)$ is a complete metric space, so we can apply the contraction theorem on it.

Our goal now is proving that \mathcal{T} is a contraction. Consider $S_1, S_2 \in C_b(\Omega)$; since F is bounded and Lipschitz, it follows that

$$\begin{aligned}
 & |\mathcal{T}[S_1] - \mathcal{T}[S_2]|(x) = \\
 & = \left| \gamma \int_\Omega G(g(x)F(S_1(x)), g(y)F(S_1(y)))g(y)F(S_1(y)) \, dy + I(x) - \right. \\
 & \quad \left. - \gamma \int_\Omega G(g(x)F(S_2(x)), g(y)F(S_2(y)))g(y)F(S_2(y)) \, dy - I(x) \right| \\
 & \leq \left| \gamma \int_\Omega G(g(x)F(S_1(x)), g(y)F(S_1(y)))g(y)F(S_1(y)) \, dy - \right. \\
 & \quad \left. - \gamma \int_\Omega G(g(x)F(S_2(x)), g(y)F(S_2(y)))g(y)F(S_1(y)) \, dy + \right. \\
 & \quad \left. + \gamma \int_\Omega G(g(x)F(S_2(x)), g(y)F(S_2(y)))g(y)F(S_1(y)) \, dy - \right. \\
 & \quad \left. - \gamma \int_\Omega G(g(x)F(S_2(x)), g(y)F(S_2(y)))g(y)F(S_2(y)) \, dy \right| \\
 & \leq \left| \gamma \int_\Omega G(g(x)F(S_1(x)), g(y)F(S_1(y)))g(y)F(S_1(y)) \, dy - \right. \\
 & \quad \left. - \gamma \int_\Omega G(g(x)F(S_2(x)), g(y)F(S_2(y)))g(y)F(S_1(y)) \, dy \right| + \\
 & \quad + \left| \gamma \int_\Omega G(g(x)F(S_2(x)), g(y)F(S_2(y)))g(y)F(S_1(y)) \, dy - \right. \\
 & \quad \left. - \gamma \int_\Omega G(g(x)F(S_2(x)), g(y)F(S_2(y)))g(y)F(S_2(y)) \, dy \right| \\
 & \leq \gamma \int_\Omega \left| [G(g(x)F(S_1(x)), g(y)F(S_1(y))) - G(g(x)F(S_2(x)), g(y)F(S_2(y)))]g(y) \right. \\
 & \quad \left. F(S_1(y)) \right| \, dy + \gamma \int_\Omega |G(g(x)F(S_2(x)), g(y)F(S_2(y)))g(y)[F(S_1(y)) - F(S_2(y))]| \, dy \\
 & \leq \gamma \int_\Omega \left| \langle \nabla G, (g(x)(F(S_1(x)) - F(S_2(x))), g(y)F(S_1(y)) - F(S_2(y))) \rangle > g(y) \right. \\
 & \quad \left. F(S_1(y)) \right| \, dy + \gamma \int_\Omega |G(g(x)F(S_2(x)), g(y)F(S_2(y)))||g(y)||F(S_1(y)) - F(S_2(y))| \, dy \\
 & \text{\textit{F is bounded and Lipschitz}} \\
 & \leq \gamma \int_\Omega \left| \langle \nabla G, (g(x)F'(S)(S_1(x) - S_2(x)), g(y)F'(S)(S_1(y) - S_2(y))) \rangle > ||g(y)|| \right. \\
 & \quad \left. |F(S_1(y))| \, dy + \gamma \int_\Omega |G(g(x)F(S_2(x)), g(y)F(S_2(y)))||g(y)||F'(S)||S_1(y) - S_2(y)| \, dy \right. \\
 & \text{\textit{use Cauchy-Schwarz inequality}} \\
 & \leq 2\gamma \|\nabla G\|_\infty \|g\|_\infty \|F'\|_\infty \|S_2 - S_1\|_\infty \int_\Omega |g(y)| \, dy \|F\|_\infty + \\
 & \quad + \gamma \|G\|_\infty \int_\Omega g(y) \, dy \|F'\|_\infty \|S_2 - S_1\|_\infty \\
 & \leq 2\gamma \|\nabla G\|_\infty \|g\|_\infty \|F'\|_\infty \|S_2 - S_1\|_\infty \|g\|_1 \|F\|_\infty + \gamma \|G\|_\infty \|g\|_1 \|F'\|_\infty \|S_2 - S_1\|_\infty,
 \end{aligned}$$

where $\|G\|_\infty, \|\nabla G\|_\infty$ are considered on the set $[0, p_\infty \|g\|_\infty]^2$.

We have proved that, for γ satisfying $\gamma \|g\|_1 \|F'\|_\infty (2\|g\|_\infty \|F\|_\infty \|\nabla G\|_\infty + \|G\|_\infty) < 1$, the operator \mathcal{T} is a contraction on $C_b(\Omega)$ and so there exists a unique $S^* \in C_b(\Omega)$ such that $\mathcal{T}[S^*] = S^*$.

To conclude, it follows from this result that, using this S^* in the formulas (3.2), (3.3) and (3.4), we get a unique stationary state for system (2.1). \square

3.2 Model convergence in the weak interconnection case

In order to prove model convergence to the stationary state in the weak interconnection case, we make use of the theory of Doeblin applied to stochastic semi-groups. We rely on the concepts we briefly presented in the third section of Chapter 1 and we proceed by steps as we have already done, analysing the linear case first, and then by extending the analysis to the nonlinear one.

3.2.1 Model convergence in the linear case

Given a function $S \in C_b(\Omega)$ we consider the linear problem given by

$$\begin{cases} \partial_t n(t, s, x) + \partial_s n(t, s, x) + p(s, S(x))n(t, s, x) = 0 & t > 0, s > 0, x \in \Omega \\ N(t, x) := n(t, s = 0, x) = \int_0^\infty p(s, S(x))n(t, s, x) ds & t > 0, x \in \Omega \\ n(t = 0, s, x) = n_0(s, x) & s \geq 0, x \in \Omega, \end{cases} \quad (3.6)$$

In Chapter 2 we have proved that this system has an unique solution $n \in C_b([0, \infty) \times \Omega, L_s^1)$, and we have noticed that the variable x is simply a parameter, since there is no derivative or integral term involving the position. This allows us to associate a stochastic semi-group $P_t : L_s^1 \rightarrow L_s^1$ to equation (3.6); for a fixed $x \in \Omega$ it is given by

$$P_t n_0(s, x) = n(t, s, x). \quad (3.7)$$

What we want to prove with the following theorem is a pivotal property on the solution of the system, that is the fact that it exponentially converges to equilibrium.

To complete the proof, which follows the ideas of Cañizo et al. in [2], Torres and Salort apply the Doeblin's Theorem that we have exposed in *Theorem 1.3.1*. We will firstly give a positive lower bound for the solution, that exists after a fixed time and for any initial distribution. This evidence will be the main part of the demonstration, but then it lets us to prove the convergence directly, because it ensures that the associated stochastic semi-group verifies the Doeblin condition.

Theorem 3.2.1. *Consider $n_0 \in C_b(\Omega, L_s^1)$ with its corresponding $g \in C_b(\Omega)$ and suppose that p satisfies (2.2b). Then there exists a unique stationary solution n^* for equation (3.6) satisfying $\int_0^\infty n^*(s, x) ds = g(x)$. Moreover, the solution of (3.6) satisfies*

$$\|n(t, \cdot, x) - n^*(\cdot, x)\|_{L_s^1} \leq \frac{1}{1 - \alpha} e^{-\lambda t} \|n_0(\cdot, x) - n^*(\cdot, x)\|_{L_s^1} \quad \forall t \geq 0, x \in \Omega$$

with $\alpha = p_* s_* e^{-2p_\infty s_*}$ and $\lambda = -\frac{\log(1-\alpha)}{2s_*} > 0$.

Proof. Consider the linear problem (3.6), that we rewrite as follows

$$\begin{cases} \partial_t n(t, s, x) + \partial_s n(t, s, x) + p(s, S(x))n(t, s, x) = N(t, x)\delta_0(s) & t > 0, s \geq 0, x \in \Omega \\ n(t = 0, s, x) = n_0(s, x) & s \geq 0, x \in \Omega. \end{cases} \quad (3.8)$$

Let n be its solution; for fixed $x \in \Omega$, we assert that n fulfils the following inequality

$$n(2s_*, s, x) = P_{2s_*} n_0(s, x) \geq p_* e^{-2p_\infty s_*} \mathbf{1}_{[0, s_*]}(s) g(x) \quad \forall (s, x) \in (0, \infty) \times \Omega, \quad (3.9)$$

and it is the goal of the main part of this proof to demonstrate it.

Step 1. The first step is to find a solution to the linear problem (3.8). To do so we will use Duhamel's formula, so we will firstly find a solution for the homogeneous problem associated to (3.8), and then we will rewrite the solution of the non homogeneous one as a chain of solutions of homogeneous problems as a consequence of the superposition principle.

We set the initial condition data at $t = 0$ and fix $x \in \Omega$; in this way the homogeneous problem becomes

$$\begin{cases} \partial_t n(t, s, x) + \partial_s n(t, s, x) + p(s, S(x))n(t, s, x) = 0 & t > 0, s \geq 0, x \in \Omega \\ n(t = 0, s, x) = n_0(s, x) & s \geq 0, x \in \Omega. \end{cases} \quad (3.10)$$

Considering the semi-group $\tilde{P}_t : L_s^1 \rightarrow L_s^1$ associated with this homogeneous problem, we find that its solution is given by

$$\tilde{n}(t, s, x) = \tilde{P}_t n_0(s, x) = n_0(s - t) \exp \left(- \int_0^t p(s - t + \tau, S(\tau, x)) \, d\tau \right) \mathbf{1}_{\{s > t\}} \quad (3.11)$$

Remark 3. This result readily follows from the equation for the solution of (2.10) that we found in Chapter 2. Since we have assumed that the problem is homogeneous, the condition on N in system (3.10) becomes $N(t, x) = 0$, and this let the second addendum of the equation for the solution to (2.10) to disappear. This fact has also a biological interpretation; since the equation for N is equal to 0, the cells lose their property of re-enter the circle after a discharge, that is to say that the age of the cells s only increases. This means that s is always greater than t , and, as we could expect, this is the only part of the solution of (2.10) that we consider for solving (3.10).

After considering the homogeneous problem for $t = 0$, we solve another problem with initial condition for $t = \tau > 0$, that is to say

$$\begin{cases} \partial_t n(t, s, x) + \partial_s n(t, s, x) + p(s, S(x))n(t, s, x) = 0 & t > 0, s \geq 0, x \in \Omega \\ n(t = \tau, s, x) = N(\tau, x)\delta_0(s) & s \geq 0, x \in \Omega \end{cases} \quad (3.12)$$

The initial condition for (3.12) is the equivalent to say $n(t - \tau = 0, s, x) = N(\tau, x)\delta_0(s)$ so, using the previous result (3.11), we can assert that the solution for (3.12) is given by

$$\tilde{n}(t, s, x) = \tilde{P}_{t-\tau}(N(\tau, x)\delta_0(s)). \quad (3.13)$$

This allows us to conclude that, for Duhamel's formula, the solution to the non homogeneous problem (3.6) is given by

$$n(t, s, x) = P_t n_0(s, x) = \tilde{P}_t n_0(s, x) + \int_0^t \tilde{P}_{t-\tau}(N(\tau, x)\delta_0(s)) \, d\tau. \quad (3.14)$$

Step 2. Now that we have found the solution of (3.6), using (3.11) and (3.14) we can prove the following inequality:

$$\begin{aligned} n(t, s, x) &\geq \tilde{P}_t n_0(s, x) = n_0(s - t) \exp \left(- \int_0^t p(s - t + \tau, S(\tau, x)) \, d\tau \right) \mathbf{1}_{\{s > t\}} \\ &\geq n_0(s - t) e^{-p_\infty t} \mathbf{1}_{\{s > t\}}, \end{aligned} \quad (3.15)$$

and, translating of a value τ , this implies

$$\tilde{P}_{t-\tau}n_0(s, x) \geq n_0(s - t + \tau)e^{-p_\infty(t-\tau)}\mathbf{1}_{\{s>t-\tau\}}. \quad (3.16)$$

Thus, for $t > s_*$ we get

$$\begin{aligned} N(t, x) &= \int_0^\infty p(s, S(x))n(t, s, x) ds \\ &\geq p_* \int_{s_*}^\infty n(t, s, x) ds \\ &\geq p_* \int_t^\infty n(t, s, x) ds \\ &\text{use (3.15)} \\ &\geq p_* e^{-p_\infty t} \int_t^\infty n_0(s - t, x) ds \\ &\geq p_* e^{-p_\infty t} g(x). \end{aligned} \quad (3.17)$$

In this case, using (3.14) we have that, for any $s > 0$ and $t > s + s_*$:

$$\begin{aligned} n(t, s, x) &\geq \int_0^t \tilde{P}_{t-\tau}(N(\tau, x)\delta_0(s)) d\tau \\ &\geq \int_{s_*}^t \tilde{P}_{t-\tau}(p_* e^{-p_\infty \tau} g(x)\delta_0(s)) d\tau \\ &\geq p_* \int_{s_*}^t \delta_0(s - t + \tau) e^{-p_\infty \tau} e^{-p_\infty(t-\tau)} g(x) \mathbf{1}_{\{s-t+\tau>0\}} d\tau \\ &\geq p_* e^{-p_\infty t} \mathbf{1}_{\{0<s<t-s_*\}} g(x) \end{aligned} \quad (3.18)$$

Step 3. Now we have all the elements to conclude the proof, in fact we can get the estimate (3.9) by choosing $t = 2s_*$. This means that the semi-group P_t associated to equation (3.6) satisfies the Doeblin's condition with $t_0 = 2s_*$, $\alpha = p_* s_* e^{-2p_\infty s_*}$ and $\nu = \frac{1}{s_*} \mathbf{1}_{[0, s_*]}(s)$ for functions $n_0(\cdot, x) \in L_s^1$ with $g(x) = 1$. With this result, the exponential convergence to equilibrium readily follows from Doeblin's theorem applied to the semi-group P_t , with $\lambda = -\frac{\log(1-\alpha)}{t_0} > 0$ and with the normalization by $g(x)$. In fact, the Doeblin's theorem we have presented in *Chapter 1* estimates the L^1 norm of the difference $P_t(n - n^*)$; we have taken n_0 for n , so by the linearity of the semi-group P_t and the fact that $P_t(n^*) = n^*$ it follows that $P_t(n_0 - n^*) = P_t(n_0) - P_t(n^*) = n - n^*$, that is exactly the difference that the Theorem for the convergence wants to estimate with the L^1 norm. \square

3.2.2 Model convergence in the non-linear case

The linear theory allows us to determine the asymptotic behaviour of the non-linear system (2.1) as well, always supposing to be in the weak interconnection regime. As for

the previous result, we will make use of the Duhamel's formula and the Doeblin's theory for stochastic semigroups.

Theorem 3.2.2 (Convergence to equilibrium). *Assume (2.4)-(2.5), that $p \in W^{1,\infty}(0, \infty) \times \Omega$ satisfies (2.2b) and that $I \in C_b(\Omega)^1$. For γ and $\|\frac{\partial p}{\partial S}\|_\infty$ small enough, let (n^*, N^*, S^*, w^*) be the corresponding stationary state of (2.1). Then there exist $C, \lambda > 0$ such that the solution n of (2.1) satisfies*

$$\|n(t) - n^*\|_{L_x^\infty L_s^1} + \|w(t) - w^*\|_\infty \leq C e^{-\lambda t} (\|n_0 - n^*\|_{L_x^\infty L_s^1} + \|w_0 - w^*\|_\infty) \quad \forall t \geq 0.$$

Moreover $\|S(t) - S^*\|_\infty$ and $\|N(t) - N^*\|_\infty$ converge exponentially to 0 when $t \rightarrow \infty$.

Proof. We start the demonstration by defining

$$\mathcal{L}_S[n] := -\partial_s n - p(s, S)n + \delta_0(s) \int_0^\infty p(u, S(t, x))n(t, u, x) du,$$

so we can observe that n satisfies the evolution equation

$$\partial_t n = \mathcal{L}_S[n],$$

that can be rewritten as

$$\partial_t n = \mathcal{L}_{S^*}[n] + (\mathcal{L}_S[n] - \mathcal{L}_{S^*}) = \mathcal{L}_{S^*} + h, \quad (3.19)$$

where h is given by

$$\begin{aligned} h(t, s, x) &= (p(s, S^*(x)) - p(s, S(t, x)))n(t, s, x) + \\ &+ \delta_0(s) \int_0^\infty (p(u, S(t, x)) - p(u, S^*(x)))n(t, u, x) du \end{aligned} \quad (3.20)$$

and satisfies the following

$$\begin{aligned} \int_0^\infty h(t, s, x) ds &= \int_0^\infty [p(s, S^*(x)) - p(s, S(t, x))]n(t, s, x) ds + \\ &+ \int_0^\infty \delta_0(s) \int_0^\infty [p(u, S(t, x)) - p(u, S^*(x))]n(t, u, x) du ds \\ &= \int_0^\infty [p(s, S^*(x)) - p(s, S(t, x))]n(t, s, x) ds + \\ &+ \int_0^\infty [p(s, S(t, x)) - p(s, S^*(x))]n(t, s, x) ds \\ &= 0. \end{aligned} \quad (3.21)$$

¹For studying the convergence we assume that I only depends on position in order to have an autonomous system and a semi-group for the linear problem [T].

Formally, the proof is based on the rewriting (3.19) of equation (2.1), because it relies on the result proved for the linear case and we can treat the term h as a perturbation. In order to do this rigorously, we notice that h contains a multiple of δ_0 , so it is necessary to use a solution in a space of measures. This is the reason why we have conducted all our analysis considering weak solution instead of simply mild solution. Mild solutions are more convenient for finding solutions, but weak solutions have a more manageable form. In fact, in *Lemma 2.2.2*. we have actually used the concept of mild solution, but we have taken advantage of the Ball's Theorem to call it weak solution anyway, foreseeing that at this point we would have to make use of this concept.

Now, consider P_t being the linear semi-group associated to operator \mathcal{L}_{S^*} . Since $P_t n^* = n^*$ for all $t \geq 0$, and using Duhamel's formula, we can assert that n fulfils

$$\begin{aligned} n - n^* &= P_t(n_0) + \int_0^\infty P_{t-\tau} h(\tau, s, x) d\tau + P_t(n^*) \\ &= P_t(n_0 - n^*) + \int_0^\infty P_{t-\tau} h(\tau, s, x) d\tau, \end{aligned} \quad (3.22)$$

so what we need to do is to approximate the function h .

Firstly we have to treat the following inequalities:

$$\begin{aligned} \|N(t) - N^*\|_\infty &= \sup_{x \in \Omega} |N(t, x) - N^*(x)| = \\ &= \sup_{x \in \Omega} \left| \int_0^\infty (p(s, S(t, x))n(t, s, x) - p(s, S^*(x))n^*(s, x)) ds \right| \\ &= \sup_{x \in \Omega} \left| \int_0^\infty (p(s, S(t, x))n(t, s, x) - p(s, S^*(x))n^*(s, x) + \right. \\ &\quad \left. + p(s, S^*(x))n(t, s, x) - p(s, S^*(x))n(t, s, x)) ds \right| \\ &\leq \sup_{x \in \Omega} \left| \int_0^\infty (p(s, S(t, x)) - p(s, S^*(x)))n(t, s, x) ds \right| + \\ &\quad + \sup_{x \in \Omega} \left| \int_0^\infty p(s, S^*(x))(n(t, s, x) - n^*(s, x)) ds \right| \\ &\leq \sup_{x \in \Omega} \left| \int_0^\infty \frac{\partial p}{\partial S}(S(t, x) - S^*(x))n(t, s, x) ds \right| + \\ &\quad + \sup_{x \in \Omega} \left| \int_0^\infty p(s, S^*(x))(n(t, s, x) - n^*(s, x)) ds \right| \\ &\leq \|g\|_\infty \left\| \frac{\partial p}{\partial S} \right\|_\infty \|S(t) - S^*\|_\infty + p_\infty \|n(t) - n^*\|_{L_x^\infty L_s^1} \end{aligned}$$

$$\begin{aligned}
\|S(t) - S^*\|_\infty &= \sup_{x \in \Omega} |S(t, x) - S^*(x)| = \\
&= \sup_{x \in \Omega} \left| \int_\Omega (w(t, x, y)N(t, y)) \, dy + I(x) - \int_\Omega (w^*(x, y)N^*(y)) \, dy - I(x) \right| \\
&\leq \sup_{x \in \Omega} \left| \int_\Omega (w(t, x, y)N(t, y)) \, dy - \int_\Omega (w^*(x, y)N^*(y)) \, dy \right| + \\
&\quad + \sup_{x \in \Omega} |I(x) - I(x)| \\
&\leq \sup_{x \in \Omega} \left| \int_\Omega (w(t, x, y)N(t, y) - w^*(x, y)N(t, y) + w^*(x, y)N(t, y) - \right. \\
&\quad \left. - w^*(x, y)N^*(y)) \, dy \right| \\
&\leq \sup_{x \in \Omega} \left| \int_\Omega N(t, y)(w(t, x, y) - w^*(x, y)) \, dy + \int_\Omega w^*(x, y)(N(t, y) - N^*(y)) \, dy \right| \\
&\leq \sup_{x \in \Omega} \left| \int_\Omega N(t, y)(w(t, x, y) - w^*(x, y)) \, dy \right| + \\
&\quad + \sup_{x \in \Omega} \left| \int_\Omega w^*(x, y)(N(t, y) - N^*(y)) \, dy \right| \\
&\leq \sup_{x \in \Omega} \left| \int_\Omega \left(\int_0^\infty p(s, S(t, y))n(t, s, y) \, ds \right) (w(t, x, y) - w^*(x, y)) \, dy \right| + \\
&\quad + \sup_{x \in \Omega} \left| \int_\Omega \gamma G(g(x)F(S(x)), g(y)F(S(y))) (N(t, y) - N^*(y)) \, dy \right| \\
&\leq p_\infty \sup_{x \in \Omega} \int_\Omega \left| \int_0^\infty n(t, s, y) \, ds \right| |w(t, x, y) - w^*(x, y)| \, dy + \\
&\quad + \sup_{x \in \Omega} \left| \int_\Omega \gamma G(g(x)F(S(x)), g(y)F(S(y))) (N(t, y) - N^*(y)) \, dy \right| \\
&\leq p_\infty \|w(t) - w^*\|_\infty \int_\Omega |g(y)| \, dy + \\
&\quad + \gamma \sup_{x \in \Omega} \int_\Omega |G(g(x)F(S(x)), g(y)F(S(y)))| |N(t, y) - N^*(y)| \, dy \\
&\leq p_\infty \|g\|_1 \|w(t) - w^*\|_\infty + \gamma |\Omega| \|G\|_\infty \|N(t) - N^*\|_\infty
\end{aligned}$$

where G is restricted to the set $[0, p_\infty \|g\|_\infty]^2$.

Combining those estimates it follows that

$$\begin{aligned}
\|N(t) - N^*\|_\infty &\leq p_\infty \|n(t) - n^*\|_{L_x^\infty L_s^1} + \\
&\quad \|g\|_\infty \left\| \frac{\partial p}{\partial S} \right\|_\infty [p_\infty \|g\|_1 \|w(t) - w^*\|_\infty + \gamma |\Omega| \|G\|_\infty \|N(t) - N^*\|_\infty] \\
\|N(t) - N^*\|_\infty - \gamma |\Omega| \|G\|_\infty \|g\|_\infty \left\| \frac{\partial p}{\partial S} \right\|_\infty \|N(t) - N^*\|_\infty &\leq p_\infty \|n(t) - n^*\|_{L_x^\infty L_s^1} + \\
&\quad + p_\infty \|g\|_1 \|g\|_\infty \left\| \frac{\partial p}{\partial S} \right\|_\infty \|w(t) - w^*\|_\infty \\
\|N(t) - N^*\|_\infty &\leq \frac{p_\infty \|g\|_1 \|g\|_\infty \left\| \frac{\partial p}{\partial S} \right\|_\infty \|w(t) - w^*\|_\infty + p_\infty \|n(t) - n^*\|_{L_x^\infty L_s^1}}{1 - \gamma |\Omega| \|G\|_\infty \|g\|_\infty \left\| \frac{\partial p}{\partial S} \right\|_\infty}
\end{aligned}$$

and

$$\begin{aligned}
\|S(t) - S^*\|_\infty &\leq p_\infty \|g\|_1 \|w(t) - w^*\|_\infty + \\
&\quad + \gamma |\Omega| \|G\|_\infty \left[\|g\|_\infty \left\| \frac{\partial p}{\partial S} \right\|_\infty \|S(t) - S^*\|_\infty + p_\infty \|n(t) - n^*\|_{L_x^\infty L_s^1} \right] \\
\|S(t) - S^*\|_\infty - \gamma |\Omega| \|G\|_\infty \|g\|_\infty \left\| \frac{\partial p}{\partial S} \right\|_\infty \|S(t) - S^*\|_\infty &\leq p_\infty \|g\|_1 \|w(t) - w^*\|_\infty + \\
&\quad + \gamma |\Omega| \|G\|_\infty p_\infty \|n(t) - n^*\|_{L_x^\infty L_s^1} \\
\|S(t) - S^*\|_\infty &\leq \frac{p_\infty \|g\|_1 \|w(t) - w^*\|_\infty + \gamma |\Omega| \|G\|_\infty p_\infty \|n(t) - n^*\|_{L_x^\infty L_s^1}}{1 - \gamma |\Omega| \|G\|_\infty \|g\|_\infty \left\| \frac{\partial p}{\partial S} \right\|_\infty}
\end{aligned}$$

that, naming $C_1 := \gamma|\Omega|\|G\|_\infty\|g\|_\infty\|\frac{\partial p}{\partial S}\|_\infty < 1$, can be rewritten as

$$\|N(t) - N^*\|_\infty \leq \frac{p_\infty}{1-C_1} (\|g\|_1\|g\|_\infty\|\frac{\partial p}{\partial S}\|_\infty\|w(t) - w^*\|_\infty + \|n(t) - n^*\|_{L_x^\infty L_s^1}) \quad (3.23)$$

$$\|S(t) - S^*\|_\infty \leq \frac{p_\infty}{1-C_1} (\|g\|_1\|w(t) - w^*\|_\infty + \gamma|\Omega|\|G\|_\infty\|n(t) - n^*\|_{L_x^\infty L_s^1}). \quad (3.24)$$

Thus the estimate for h we were looking for is

$$\begin{aligned} \|h(t)\|_{L_x^\infty L_s^1} &= \sup_{x \in \Omega} \left| \int_0^\infty [p(s, S^*(x)) - p(s, S(t, x))] n(t, s, x) ds + \right. \\ &\quad \left. + \int_0^\infty \delta_0(s) \int_0^\infty [p(u, S(t, x)) - p(u, S^*(x))] n(t, u, x) du ds \right| \\ &\leq \sup_{x \in \Omega} \left| \int_0^\infty [p(s, S^*(x)) - p(s, S(t, x))] n(t, s, x) ds \right| + \\ &\quad + \sup_{x \in \Omega} \left| \underbrace{\int_0^\infty \delta_0(s) ds}_{=1} \int_0^\infty [p(s, S(t, x)) - p(s, S^*(x))] n(t, s, x) ds \right| \\ &\leq 2 \sup_{x \in \Omega} \left| \int_0^\infty [p(s, S^*(x)) - p(s, S(t, x))] n(t, s, x) ds \right| \\ &\leq 2 \sup_{x \in \Omega} \int_0^\infty \left| \frac{\partial p}{\partial S} \right| |S^*(x) - S(t, x)| |n(t, s, x)| ds \\ &\leq 2 \|\frac{\partial p}{\partial S}\|_\infty \|S(t) - S^*\|_\infty \|g\|_\infty \\ &\leq \frac{2p_\infty \|g\|_\infty \|\frac{\partial p}{\partial S}\|_\infty}{1-C_1} (\|g\|_1 \|w(t) - w^*\|_\infty + \gamma|\Omega|\|G\|_\infty \|n(t) - n^*\|_{L_x^\infty L_s^1}) \\ &\leq C_2 (\|w(t) - w^*\|_\infty + \|n(t) - n^*\|_{L_x^\infty L_s^1}), \end{aligned} \quad (3.25)$$

where $C_2 = \frac{2p_\infty \|g\|_\infty \|\frac{\partial p}{\partial S}\|_\infty}{1-C_1} \max\{\|g\|_1, \gamma|\Omega|\|G\|_\infty\}$.

On one hand, using *Theorem 4.0.1* about the convergence for the linear case and estimate (3.25), we get from (3.22) the following

$$\begin{aligned} \|n(t) - n^*\|_{L_x^\infty L_s^1} &\leq \|P_t(n_0 - n^*)\|_{L_x^\infty L_s^1} + \int_0^t \|P_{t-\tau} h(\tau)\|_{L_x^\infty L_s^1} d\tau \\ &\leq \frac{e^{-\lambda t}}{1-\alpha} \|n_0 - n^*\|_{L_x^\infty L_s^1} + \frac{1}{1-\alpha} \int_0^t e^{-\lambda(t-\tau)} \|h(\tau)\|_{L_x^\infty L_s^1} d\tau \\ &\leq \frac{e^{-\lambda t}}{1-\alpha} \|n_0 - n^*\|_{L_x^\infty L_s^1} + \frac{C_2}{1-\alpha} \int_0^t e^{-\lambda(t-\tau)} (\|w(\tau) - w^*\|_\infty + \|n(\tau) - n^*\|_{L_x^\infty L_s^1}) d\tau, \end{aligned} \quad (3.26)$$

with $\alpha = p_* \delta_* e^{-2p_\infty s_*}$, $\lambda = -\frac{\log(1-\alpha)}{2s_*} > 0$.

On the other hand, from the equation for w found in (2.19) and that for w^* in (3.4), and by applying (3.23), we deduce

$$\begin{aligned}
& \|w(t) - w^*\|_\infty = \\
& = \sup_{x,y \in \Omega} \left| e^{-t}w_0(x,y) + \gamma \int_0^t e^{-(t-\tau)} G(N(\tau,x), N(\tau,y)) d\tau - w^*(x,y) \right| \\
& = \sup_{x,y \in \Omega} \left| e^{-t}w_0(x,y) + \gamma \int_0^t e^{-(t-\tau)} G(N(\tau,x), N(\tau,y)) d\tau - w^*(x,y) - \right. \\
& \quad \left. - e^{-t}w^*(x,y) + e^{-t}w^*(x,y) \right| \\
& = \sup_{x,y \in \Omega} \left| e^{-t}w_0(x,y) + \gamma \int_0^t e^{-(t-\tau)} G(N(\tau,x), N(\tau,y)) d\tau - e^{-t}w^*(x,y) + \right. \\
& \quad \left. - w^*(x,y)(1 - e^{-t}) \right| \\
& = \sup_{x,y \in \Omega} \left| e^{-t}w_0(x,y) + \gamma \int_0^t e^{-(t-\tau)} G(N(\tau,x), N(\tau,y)) d\tau - e^{-t}w^*(x,y) - \right. \\
& \quad \left. - \gamma G(N^*(x), N^*(y))(1 - e^{-t}) \right| \\
& = \sup_{x,y \in \Omega} \left| e^{-t}w_0(x,y) + \gamma \int_0^t e^{-(t-\tau)} G(N(\tau,x), N(\tau,y)) d\tau - \right. \\
& \quad \left. - e^{-t}w^*(x,y) - \gamma \int_0^t e^{-(t-\tau)} G(N^*(x), N^*(y)) d\tau \right| \\
& \leq \sup_{x,y \in \Omega} \left| e^{-t}w_0(x,y) - e^{-t}w^*(x,y) \right| + \\
& \quad + \sup_{x,y \in \Omega} \left| \gamma \int_0^t e^{-(t-\tau)} G(N(\tau,x), N(\tau,y)) d\tau - \gamma \int_0^t e^{-(t-\tau)} G(N^*(x), N^*(y)) d\tau \right| \\
& \leq e^{-t} \|w_0 - w^*\|_\infty + \\
& \quad + \gamma \sup_{x,y \in \Omega} \left| \int_0^t e^{-(t-\tau)} \langle \nabla G, (N(\tau,x) - N^*(x), N(\tau,y) - N^*(y)) \rangle d\tau \right| \\
& \leq e^{-t} \|w_0 - w^*\|_\infty + \gamma \|\nabla G\|_\infty \int_0^t e^{-(t-\tau)} \|N(\tau) - N^*\|_\infty d\tau \\
& \leq e^{-t} \|w_0 - w^*\|_\infty + C_3 \int_0^t e^{-(t-\tau)} \|w(\tau) - w^*\|_\infty + \|n(\tau) - n^*\|_{L_x^\infty L_s^1} d\tau,
\end{aligned} \tag{3.27}$$

with $C_3 := \frac{2\gamma p_\infty \|G\|_\infty}{1-C_1} \max\{\|g\|_1 \|g\|_\infty \|\frac{\partial p}{\partial S}\|_\infty, 1\}$.

Hence, adding the two norms estimated in (3.26) and (3.27) we get

$$\begin{aligned}
\|n(t) - n^*\|_{L_x^\infty L_s^1} + \|w(t) - w^*\|_\infty & \leq \frac{e^{-\tilde{\lambda}t}}{1-\alpha} (\|n_0 - n^*\|_{L_x^\infty L_s^1} + \|w_0 - w^*\|_\infty) + \\
& + C_4 e^{-\tilde{\lambda}t} \int_0^t e^{\tilde{\lambda}\tau} (\|w(\tau) - w^*\|_\infty + \|n(\tau) - n^*\|_{L_x^\infty L_s^1}) d\tau,
\end{aligned} \tag{3.28}$$

with $\tilde{\lambda} := \min\{\lambda, 1\}$, $C_4 := \max\{\frac{C_2}{1-\alpha}, C_3\}$.

Now, using Gronwall's inequality on (3.28) we get

$$\begin{aligned}
& \|n(t) - n^*\|_{L_x^\infty L_s^1} + \|w(t) - w^*\|_\infty \leq \\
& \leq \frac{e^{-\tilde{\lambda}t}}{1-\alpha} (\|n_0 - n^*\|_{L_x^\infty L_s^1} + \|w_0 - w^*\|_\infty) + C_4 e^{-\tilde{\lambda}t} \int_0^t e^{\tilde{\lambda}\tau} (\|w(\tau) - w^*\|_\infty + \\
& \quad + \|n_0 - n^*\|_{L_x^\infty L_s^1}) d\tau \\
& \leq \frac{e^{-\tilde{\lambda}t}}{1-\alpha} (\|n_0 - n^*\|_{L_x^\infty L_s^1} + \|w_0 - w^*\|_\infty) \exp\left(\int_0^t C_4 e^{-\tilde{\lambda}\tau} e^{\tilde{\lambda}\tau} d\tau\right) \\
& \leq \frac{e^{-\tilde{\lambda}t}}{1-\alpha} (\|n_0 - n^*\|_{L_x^\infty L_s^1} + \|w_0 - w^*\|_\infty) \exp\left(C_4 e^{-\tilde{\lambda}t} \int_0^t e^{\tilde{\lambda}\tau} d\tau\right) \\
& \leq \frac{e^{-\tilde{\lambda}t}}{1-\alpha} (\|n_0 - n^*\|_{L_x^\infty L_s^1} + \|w_0 - w^*\|_\infty) \exp\left(C_4 e^{-\tilde{\lambda}t} \frac{1}{\tilde{\lambda}} (e^{\tilde{\lambda}t} - 1)\right) \\
& \leq \frac{e^{-\tilde{\lambda}t}}{1-\alpha} (\|n_0 - n^*\|_{L_x^\infty L_s^1} + \|w_0 - w^*\|_\infty) \exp\left(C_4 \frac{1}{\tilde{\lambda}} (1 - e^{-\tilde{\lambda}t})\right) \\
& \text{calculate the exponential with Taylor series expansion} \\
& \leq \frac{e^{-\tilde{\lambda}t}}{1-\alpha} (\|n_0 - n^*\|_{L_x^\infty L_s^1} + \|w_0 - w^*\|_\infty) \exp\left(C_4 \frac{1}{\tilde{\lambda}} (1 - 1 + \tilde{\lambda})\right) \\
& \leq \frac{e^{-\tilde{\lambda}t}}{1-\alpha} (\|n_0 - n^*\|_{L_x^\infty L_s^1} + \|w_0 - w^*\|_\infty) e^{C_4 t} \\
& \leq \frac{e^{-\tilde{\lambda}t + C_4 t}}{1-\alpha} (\|n_0 - n^*\|_{L_x^\infty L_s^1} + \|w_0 - w^*\|_\infty) \\
& \leq \frac{e^{-(\tilde{\lambda} - C_4)t}}{1-\alpha} (\|n_0 - n^*\|_{L_x^\infty L_s^1} + \|w_0 - w^*\|_\infty).
\end{aligned}$$

If γ and $\|\frac{\partial p}{\partial S}\|_\infty$ are small enough we obtain the convergence result sought, because it realizes that $C_4 < \tilde{\lambda}$.

Finally, we get the exponential convergence of N and S applying this result to the estimates (3.23) and (3.24) respectively. \square

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Note: All the figures in the paper have been extracted from the above sources.

Ringraziamenti

Giunta al termine del mio corso di studi sono tanti i motivi di gratitudine e altrettanti i volti a cui questi mi rimandano.

Il primo pensiero va alla Prof.ssa Maria Carla Tesi, relatrice di questa tesi di Laurea. Mi rivolgo a lei con profonda gratitudine per avermi sostenuta e accompagnata con le sue conoscenze e carisma ed essere sempre stata presente e disponibile durante tutto il percorso. Ma soprattutto La ringrazio per essersi modulata con professionalità, mescolando serietà, simpatia e schiettezza. Senza i suoi incoraggiamenti probabilmente non avrei osato aprirmi a progetti che temevo troppo grandi per me.

Sono poi convinta che a dare tanto slancio al lavoro abbia contribuito la consapevolezza che questo avrebbe avuto un futuro. Un grazie sincero va quindi a Noemi David per il supporto prezioso sia nelle faccende pratiche, ma soprattutto per avermi incoraggiata condividendomi la sua esperienza.

Ringrazio cordialmente Nicolas Torres, per la grande disponibilità concordata e le conoscenze offerte durante la stesura della tesi e Pierre Gabriel, per il contributo apportato.

Ripensando ora nel suo insieme al percorso che qui si conclude, dico grazie alla mia famiglia. Ringrazio mio padre e mia madre per avermi insegnato a fare fatica per realizzare i miei progetti e per avermi anche sempre permesso di portarli avanti; per avermi sostenuta nei momenti di fragilità assicurandomi la sicurezza che solo un genitore sa infondere. Ringrazio con tanto bene Elisa; in questi anni in cui entrambe abbiamo posto le basi per il nostro domani sono state per me occasioni preziose quelle trascorse

a condividere valori, insicurezze, convinzioni o una pizza margherita sulla scogliera di Lerici al tramonto. Non avrei potuto chiedere una sorella più complementare ma a cui affezionarmi di più di te. Ringrazio amorevolmente Giovanni, che con il suo chiedere con insistenza di essere reso partecipe dei miei studi è stato l'ispiratore della Prefazione a questa tesi. Grazie per tenermi la mano con dolcezza, ri-centrarmi quando mi perdo nel turbinio dei sogni, e operare perché questi si possano realizzare, insieme. Sono felice e grata per la presenza fraterna di Costantino, che ha accompagnato la mia crescita con discrezione, senza far mai mancare il suo appoggio a me e alla mia famiglia.

Esprimo poi la mia gioia per avere accanto amiche straordinarie: presenza preziosa e sicurezza in ogni sfida. Ringrazio Lucia e Valeria per i fiumi di chiacchiere, risate e the fumanti ad ogni stagione; grazie ad Amina, Teresa ed Elena; a Erica e Federica per l'autenticità e dolcezza. Ringrazio le mie coinquiline dello Zoni per avermi fatta sentire a casa nei mesi trascorsi a Bologna; grazie a Matteo e Greta e ai colleghi conosciuti in questo biennio magistrale. Ringrazio Cristina, Tòni, Adrià e Alba per l'allegria che sanno infondere e la vicinanza che mi fanno sempre sentire. Un grande grazie a Megghi che veglia discreta sul mio cammino e a don Daniele Moretto per offrirmi un confronto lucido e costruttivo. In questi anni la presenza di tutti voi è stata preziosa per la mia crescita personale e professionale. Mi sento infine di dire grazie a Silvia che, sebbene probabilmente non ne sia consapevole, mi ha lasciato una solida testimonianza che ha influenzato il mio modo di guardare al futuro come donna e matematica.

Elena Ambroggi
Campagnola Emilia, gennaio 2021