Probabilistic Approaches for describing Neural Population Density

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Πιθανοθεωρητικές Προσεγγίσεις για την Περιγραφή της Πυκνότητας Νευρωνικών Πληθυσμών

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Περίληψη

Οι πληροφορίες στον εγκέφαλο μεταδίδονται μέσα απο τους νευρώνες. Αυτό γίνεται μέσω αλλαγών στο δυναμικό ηρεμίας της μεμβράνης, δηλαδή το δυναμικό όταν ο νευρώνας δεν δέχεται σήμα. Ο νευρώνας δέχεται σήματα απο άλλους νευρώνες στις συνάψεις και τα σήματα αυτά αλλάζουν το δυναμικό ηρεμίας του. Οι αλλαγές αυτές προκύπτουν απο την ροή ιόντων μέσα και έξω απο το κύτταρο, η οποία είναι δυνατή λόγω ειδικών διόδων που υπάρχουν στην μεμβράνη. Μια δίοδος μπορεί να είναι είτε ανοιχτή είτε κλειστή και αυτό εξαρτάται από το δυναμικό της μεμβράνης και απο κάποιες ουσίες, τους νευροδιαβιβαστές, οι οποίες απελευθερώνονται απο άλλους νευρώνες και μπορούν είτε να διεγείρουν ή να αναστείλουν το κύτταρο. Όταν το δυναμικό φτάσει κάποιο κατώφλι, τότε δημιουργείται νευρικός παλμός. Η μετάδοση της πληροφορίας στον εγκέφαλο μοντελοποιείται μέσω του ρυθμού παραγωγής παλμών ή μέσω των στιγμών που είχαμε παλμό. Σε αυτή την εργασία, θα χωρίσουμε τους νευρώνες σε πληθυσμούς απο 'όμοιους' νευρώνες και θα φτιάξουμε μια συνάρτηση πυκνότητας για κάθε πληθυσμό. Στην συνέχεια, ανάλογα με τις υποθέσεις που θα έχουμε κάθε φορά, θα βρούμε την εξίσωση που θα περιγράφει την εξέληξη αυτης της συνάρτησης.
Το πρώτο κεφάλαιο αναφέρεται σε κάποια βασικά βιολογικά χαρακτηριστικά των νευρώνων, τα οποία είναι απαραίτητα για να καταλάβουμε τα μοντέλα που περιγράφονται στα επόμενα κεφάλαια. Στο κεφάλαιο αυτό, επίσης, περιγράφεται ο νευρώνας ως ενα κύκλωμα *RC*.
Στο δεύτερο κεφάλαιο δείχνουμε οτι η διαδικασία *Ornstein − Uhlenbeck* είναι κατάλληλη να περιγράψει την εξέληξη του δυναμικού, δεδομένου οτι ο νευρώνας δέχεται σήματα με κάποιο ρυθμό *Poisson*.
Στο τελευταίο κεφάλαιο προσθέτουμε κι άλλες υποθέσεις, οι οποίες αφορούν τις αγωγιμότητες, τις συνάψεις αλλα και τον τρόπο που συνδέονται διαφορετικοί πληθυσμοί νευρώνων μεταξύ τους και φτιάχνουμε τις αντίστοιχες εξισώσεις.

Κλείνοντας, θα ήθελα να ευχαριστήσω τους καθηγητές του τμήματος Μαθηματικών, κ. Ιωάννη Στρατή και κ. Δημήτριο Χελιώτη, για την βοήθεια και την καθοδήγηση τους και στην εργασία αυτή αλλά και κατά τη διάρκεια των μεταπτυχιακών μου σπουδών. Ιδιαιτέρως ευχαριστώ τον κ. Δημήτριο Πινότση, καθώς χωρίς την δική του βοήθεια δεν θα ήταν εφικτή η συγκεκριμένη διπλωματική εργασία.

Εξεταστική Επιτροπή:

- Ι.Στρατής, Καθηγητής, Ε.Κ.Π.Α. (Επιβλέπων)
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Abstract

Probabilistic approaches model neural population density directly and bypass direct simulations of individual neurons. In this Dissertation, we will review Fokker-Planck equations that describe population density dynamics and summarize the flow and dispersion of states.
These can be derived by grouping together single units into statistically similar populations. A statistical description of each population is given by a probability density function that expresses the distribution of neuronal states (i.e., membrane potential) over the population. In general, neurons with the same state V(t) at a given time t have a different history because of random fluctuations in the input current I(t). Starting from a spiking model that describe the activity of individual cells, we first derive the time evolution of the population density. Depending on our assumptions, we derive a different equation.
In chapter 2, where we have made the assumption that the arrival times of synaptic inputs are Poisson distributed, we derive the Fokker-Planck equation. In chapter 3 , we introduce more assupmtions and derive different equations. We then use this equation to introduce mean field models that describe ensemble responses and discuss their application in describing neuronal interactions at the mesoscopic scale.

Advisors:

- D. Pinotsis (Department of Brain and Cognitive Sciences,M.I.T.)
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Chapter 1

Basic Biology

In order to understand the equations describing the population density approach, we first need to know what a neuron is. In this chapter we will briefly describe the structure of a neuron and its electrical properties.

1.1 Neurons

Neurons are the basic signaling units of the nervous system. Neurons communicate with each other at synapses. There are approximately 10^{11} neurons in the human brain and 10^{15} synapses.

The structure of a neuron can be divided into three parts :

1. **The dendrites** : The dendrites form the “input lines” of the cell. Neurons usually have several dendrites and they often branch out in a tree-like fashion, that can be very large. In many cases, the majority of the surface area of the cell is taken up by the dendrites. Neurons usually have some sort of general orientation. Dendrites that lie at the top of the neuron are called apical dendrites and those that lie at the base are called basal dendrites.

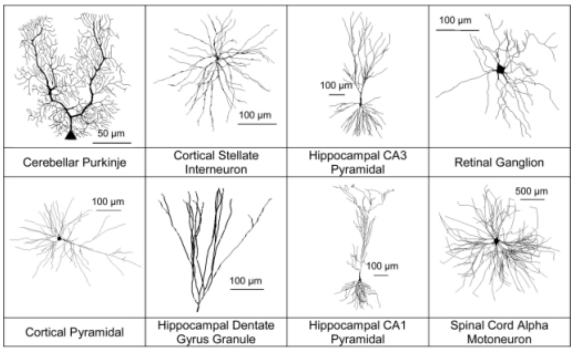

Figure 1.1: Different types of dendrites. Figure from wikimedia.org.

2. **The soma** : The soma plays the role of integrating all of the inputs of the cell to produce some output.

3. **The axon** : The axon forms the "output line". It typically leaves the soma as a single thin process but then branches out in order to connect to other cells.

The axon is the major conducting unit of the neuron. It can convey information great distances by propagating a transient electrical signal, the action potential. Large axons are surrounded by a fatty insulating sheath called myelin. This is essential for high-speed conduction of action potentials. The sheath is interrupted at regular intervals by nodes of Ranvier. The action potential represents a change in the neuron's membrane potential. Neurons maintain a potential difference of about 65mV across their external membrane and this resting potential can be altered and can, therefore, serve as a signaling mechanism.

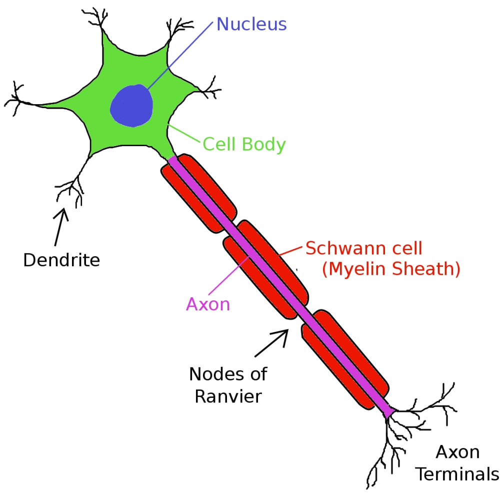

Figure 1.2: Typical structure of a neuron. Figure from wikimedia.org.

The action potential corresponds to a change in resting potential that propagates along the axon and is initiated when the membrane potential reaches some threshold. Once this threshold is reached, the signal propagates in an all-or-none fashion, i.e. the amplidute and the duration of the signal is always the same, no matter how it is generated. After each action potential, there is a period during which a second impulse cannot be initiated, the refractory period.

The synapse: Neurons communicate with each other at synapses. The cell sending the signal is called the presynaptic cell and the cell receiving it is called the postsynaptic cell. Synapses can be either electrical or chemical.

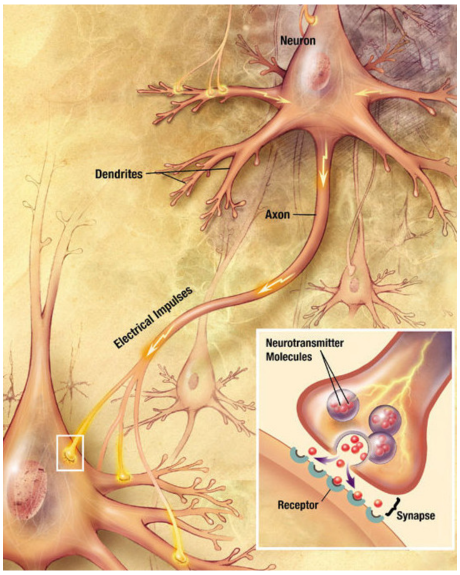

Figure 1.3: A chemical synapse. Figure from wikimedia.org.

In chemical synapses there is a space, called the synaptic cleft, separating the presynaptic from the postsynaptic cell. Most presynaptic neurons terminate near the dendrites of the postsynaptic cell , where they release chemicals, called neurotransmitters. Neurotransmitters diffuse across the synaptic cleft causing changes in the membrane potential , which may either increase or decrease relative to its resting potential. Depending on the nature of the neurotransmitter and the type of receptor it binds to, the membrane potential may become less negative (depolarization) and the synapse is called excitatory, or more negative (hyperpolarization) in which case the synapse is called inhibitory. For example, a positively charged ion, such as Na^+, entering the cell will raise the membrane potential, which means that it will bring it closer to zero, and the cell is depolarized, while a positively charged ion, such as K^+, leaving the cell or a negatively charged ion, such as Cl^-, entering the cell will hyperpolarize it.

1.2 Electrical properties of neurons

The cell membrane is a lipid bilayer 3 to 4nm thick that is impermeable to most charged molecules. This makes the cell membrane act as a *capacitor* by separating the charges lying along its interior and exterior surfaces.

Numerous ion-conducting *channels* embedded in the cell membrane lower the membrane resistance for ion flow. The resulting membrane conductance depends on the density and types of ion channels, many of which are highly selective, allowing only a single type of ion to pass through. The channels capacity for conducting ions across the membrane can be modified by many factors, such as the membrane potential, the internal concentration of various intracellular messengers or the extracellular concentration of neurotransmitters.

In addition to ion channels, the membrane also contains selective *pumps* that expend energy to maintain differences in the concentration of ions inside and outside the cell. For example, Na^+ is much more concentrated outside a neuron than inside it, and K^+ concentation is higher inside than outside. When a neuron is inactive it has a resting potential, as we mentioned before and this potential is an equilibrium point at which the flow of ions into the cell matches that out of the cell. The potential can change if the balance of ion flow is changed by the opening or closing of ion channels.

The fact that there is typically an excess negative charge on the inside surface of the cell membrane and a balancing positive charge on its outside surface, makes the cell membrane to create a *capacitance*, C_m , so the voltage across the membrane , V, and the amount of this excess charge, Q, are related by the equation for capacitor :

$$Q = C_m V. \tag{1.1}$$

The membrane capacitance is proportional to the surface area of the cell, A, and this constant of proportionality, called the specific membrane capacitance, is the capacitance per unit area of the membrane ($C_m = c_m A$).

The capacitance of a neuron determines how much current is required to make the membrane potential change at a given rate. To hold the membrane potential steady at a level different from its resting value also requires current, but this current is determined by the membrane resistance. For example, if we inject a small constant current, I_e, into a neuron through an electrode, the membrane capacitance shifts from its resting value by an amount ΔV given by Ohm's law :

$$\Delta V = I_e R_m, \tag{1.2}$$

where R_m is the *membrane resistance*. Since Ohm's law assumes that R_m is constant over the range ΔV, we have to restrict to small currents and small ΔV.

The membrane resistance is the inverse of the *membrane conductance*, which is proportional to the cell's surface area. The constant of proportionality is the membrane conductance per unit area, which we write as $\frac{1}{r_m}$, where r_m is the specific membrane resistance, ($R_m = \frac{r_m}{A}$).

The product of the membrane capacitance and the membrane resistance is called *membrane time constant*, $\tau_m = R_m C_m = r_m c_m$, and sets the basic time scale for changes in the membrane potential.

Ions pass through channel pores due to electrical forces and diffusion. Voltage differences between the exterior and the interior of the cell produce forces on ions. Negative membrane potentials attract positive ions into the cell and repel negative ions. In addition, ions diffuse through channels due to concentration differences inside and outside the neuron. These differences are maintained by the ion pumps within the cell membrane.

It is convenient to characterize the current flow due to diffusion in terms of an *equilibrium potential*, which is defined as the membrane potential at which current flow due to electric forces cancels the diffusive flow. The potential differences across the membrane biases the flow of ions into or out of a neuron.
A conductance with equilibrium (or reversal) potential E tends to move the membrane potential of the neuron toward the value E. When $V > E$ this means that positive current will flow outward, and when $V < E$ positive current will flow inward.

The total current flowing across the membrane through all of its channels is called the *membrane current* of the neuron. The total current is determined by summing currents due to all of the different types of channels within the cell membrane, including voltage-dependent and synaptic currents. In order to compare neurons of different sizes, it is convenient to use the membrane current per unit area of cell membrane, i_m, and then the total membrane current is obtained by $I_m = i_m A$

We label the different types of channels in a cell membrane with an index i. The current carried by a set of channels of type i with reversal potential E_i, vanishes when $V = E_i$. For many types of channels, the current increases or decreases approximately linearly when the membrane potential deviates from this value. The difference $V - E_i$ is called the driving force, and the membrane current per unit area due to the type i channels is $g_i(V - E_i)$, where g_i is the conductance per unit area due to these channels.

Summing over the different types of channels, we obtain the total membrane current :

$$i_m = \sum_i g_i(V - E_i). \tag{1.3}$$

The currents carried by ion pumps that maintain the concentration gradients that make equilibrium potentials non zero are called *leakage current*. These pumps are assumed to work at steady rates, so the currents they generate can be included in a time-independent leakage conductance.
All of the time-independent contributions to the membrane current can be expressed in a single leakage term : $\bar{g_L}(V - E_L)$.

1.3 Integrate-and-Fire Models

In the integrate-and-fire model the state of the neuron is characterized by its membrane potential. This model is a point neuron (single compartment) model in which the spatial structure of the neuron associated with the dendrites is neglected.

The general model of an integrate and fire neuron is :

$$\tau \frac{dV}{dt} + (V - E_r) + G_e(t)(V - E_e) + G_i(t)(V - E_i) = 0. \tag{1.4}$$

where $\tau = C/g_r$ is the membrane time constant, C is the membrane capacitance, $g_{e/i}(t)$ is the time varying excitatory/inhibitory conductance, g_r is a fixed resting conductance and $G_{e/i}(t) = g_{e/i}(t)/g_r$.
When the conductances are non-zero, they draw the voltage toward their respective equilibrium potentials.

The voltage is $V(t) < v_{th}$ and the threshold (which is fixed) is between : $E_r < v_{th} < E_e$.

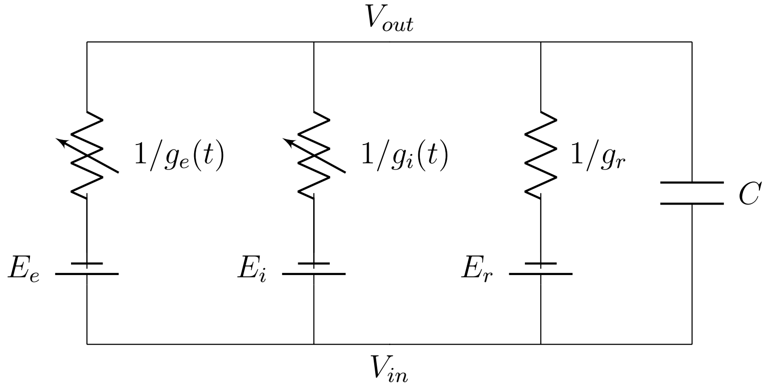

Figure 1.4: Equivalent circuit of an integrate and fire neuron

The neuron fires a spike, when the voltage reaches v_{th}. After each spike, the voltage is reset to v_{reset}. The output of a neuron is the set of times at which the neuron spikes. The inputs to a neuron are the times of excitatory and inhibitory synaptic inputs, which determine the synaptic conductances, $g_e(t)$ and $g_i(t)$.

When the neuron is at rest, the synaptic conductances are zero, while when it receives synaptic inputs the synaptic conductance increases.
An excitatory or inhibitory synaptic input at time $T^k_{e/i}$ will produce a conductance change similar to a delta function of magnitude :

$$A^k_{e/i} = \int \widehat{G}^k_{e/i}(t)dt, \tag{1.5}$$

where $\widehat{G}^k_{e/i}(t)$ is the change in $G_{e/i}(t)$ due to the synaptic input at time $T^k_{e/i}$. Under this approximation, the voltage jumps when a neuron receives an input. If we solve equation (3.7) for the time interval from immediately preceding to immediately following the synaptic input $(T^{k-}_{e/i}, T^{k+}_{e/i})$, we get :

$$\Delta v = \Big(1 - e^{-\Gamma^k_{e/i}}\Big)\Big[E_{e/i} - V(T^{k-}_{e/i})\Big], \tag{1.6}$$

where $\Delta v = V(T^{k+}_{e/i}) - V(T^{k-}_{e/i})$ is the jump size and $\Gamma^k_{e/i} = A^k_{e/i}/\tau$.

Indeed, suppose there is an excitatory synaptic input in the time interval (T^-, T^+) and we want to solve equation (3.7) in this interval :

$$\tau\frac{dV}{dt} + G_e(t)(V - E_e) = 0 \Rightarrow \frac{dV}{dt} + \frac{G_e(t)}{\tau}V = \frac{G_e(t)E_e}{\tau} \Rightarrow$$

$$\Big(V(t)\exp\big(\int_0^t \frac{G_e(s)}{\tau}ds\big)\Big)' = \frac{G_e(t)}{\tau}E_e\exp\big(\int_0^t \frac{G_e(s)}{\tau}ds\big) \Rightarrow$$

$$V(T^+)\exp\big(\int_0^{T^+} \frac{G_e(s)}{\tau}ds\big) - V(T^-)\exp\big(\int_0^{T^-} \frac{G_e(s)}{\tau}ds\big) =$$

$$= \int_{T^-}^{T^+} \frac{G_e(t)}{\tau}E_e\exp\big(\int_0^t \frac{G_e(s)}{\tau}ds\big)dt \Rightarrow$$

$$V(T^+)\exp\big(\int_0^{T^+} \frac{G_e(s)}{\tau}ds\big) - V(T^-)\exp\big(\int_0^{T^-} \frac{G_e(s)}{\tau}ds\big) =$$

$$= E_e\int_{T-}^{T+}\Big(\exp\big(\int_0^t \frac{G_e(s)}{\tau}ds\big)\Big)'dt \Rightarrow$$

$$V(T+) = V(T^-)\exp\big(-\int_{T^-}^{T^+} \frac{G_e(s)}{\tau}ds\big) +$$
$$+ E_e\exp\big(-\int_0^{T^+} \frac{G_e(s)}{\tau}ds\big)\Big[\exp\big(\int_0^{T^+} \frac{G_e(s)}{\tau}ds\big) - \exp\big(\int_0^{T^-} \frac{G_e(s)}{\tau}ds\big)\Big] \Rightarrow$$

$$V(T+) = V(T^-)\exp\big(-\int_{T^-}^{T^+} \frac{G_e(s)}{\tau}ds\big) + E_e\Big[1 - \exp\big(-\int_{T^-}^{T^+} \frac{G_e(s)}{\tau}ds\big)\Big] \Rightarrow$$

$$\Delta v = V(T^+) - V(T^-) = V(T^-)\exp(-\Gamma) - V(T^-) + E_e\big(1 - \exp(-\Gamma)\big) \Rightarrow$$

$$\Delta v = \big[1 - \exp(-\Gamma)\big]\big[E_e - V(T^-)\big].$$

We see that the size of the voltage jump is proportional to

$$\Gamma^{*k}_{e/i} = 1 - e^{-\Gamma^k_{e/i}}, \tag{1.7}$$

which depends on the size of the conductance change.
We also see that for very large synaptic conductance change we have $\Gamma^k_{e/i} \to \infty$ and $\Gamma^{*k}_{e/i} \to 1$, so $V(T^{k+}_{e/i}) \to E_{e/i}$.

In our model we have two sources of randomness : the arrival times of synaptic inputs and the size of synaptic conductance changes. The synaptic input rates, $\nu_e(t)$ and $\nu_i(t)$ are specified (in general, they are determined by the firing rates of presynaptic neurons).
The arrival times of the synaptic inputs, $T^k_{e/i}$, are assumed to be given by a Poisson process with mean rate $\nu_{e/i}(t)$. The size of the synaptic conductance changes , $\Gamma^k_{e/i}$, are assumed to be random numbers with some given distribution. This means that the $\Gamma^{*k}_{e/i}$ are also random numbers with a distribution determined by that of $\Gamma^k_{e/i}$.
We define :

$$\tilde{F}_{\Gamma^*_{e/i}}(x) = P\big(\Gamma^*_{e/i} > x\big), \tag{1.8}$$

which is the complementary cumulative distribution for $\Gamma^*_{e/i}$.

In the next chapter, we will only use the assumption that the arrival times of the synaptic inputs are Poisson distributed and we will show that the Ornstein-Uhlenbeck process can be used to describe the time course of the membrane potential. Then, is the last chapter, we will see how we can model the neuron if we add more assupmtions.

Deterministic Input: For a fixed threshold and constant injected current I, ignoring the synaptic current, equation (1.4) becomes :

$$\tau \frac{dV(t)}{dt} = E_L - V + RI. \tag{1.9}$$

We see that for $I = 0$ the membrane potential decays exponentially to $V = E_L$, with time constant τ. Thus, E_L is the resting potential of the cell.

Now, the solution of equation (1.9) is :

$$V(t) = E_L + RI + (V(0) - E_L - RI)\exp(-\frac{t}{\tau}). \tag{1.10}$$

Suppose that at time $t = 0$, the neuron has just fired a spike and is thus at the reset potential, so that $V(0) = V_{reset}$.
The next action potential will occur when the membrane potential reaches the threshold, say at time $t = t_{isi}$, when :

$$V(t_{isi}) = V_{th} = E_L + RI + (V_{reset} - E_L - RI)\exp(-\frac{t_{isi}}{\tau}). \tag{1.11}$$

If we solve this for t_{isi}, we can determine the interspike interval for constant current I, or equivalently its inverse,called the interspike interval firing rate of the neuron :

$$r_{isi} = \frac{1}{t_{isi}} = \Big[\tau \ln\Big(\frac{RI + E_L - V_{reset}}{RI_{+}E_L - V_{th}}\Big)\Big]^{-1}. \tag{1.12}$$

For sufficiently large values of I, we can use the linear approximation of the logarithm, ($\ln(1+z) \simeq z$, for small z):

$$r_{isi} \simeq \Big[\frac{E_L - V_{th} + RI}{\tau(V_{th} - V_{reset})}\Big],$$

which shows that the firing rate grows linearly with I for large I.

Chapter 2

Ornstein-Uhlenbeck Process

2.1 Fokker-Planck Equation

In this section we will begin with the Langevin equation :

$$\frac{dX}{dt} = -\theta^{-1}X + \Lambda(t), \tag{2.1}$$

where $\theta > 0$ and $\Lambda(t)$ a Langevin force,
and we will prove that the transition probability function of $X(t)$:

$$f(x,t|x_0) = \frac{\partial}{\partial x}P\{X(t) \leq x|X(0) = x_0\}, \tag{2.2}$$

is the solution of the Fokker-Planck equation :

$$\frac{\partial f}{\partial t} = \frac{\partial}{\partial x}(\theta^{-1}xf) + \frac{\sigma^2}{2}\frac{\partial^2 f}{\partial x^2}, \tag{2.3}$$

that satisfies the initial condition :

$$\lim_{t \to 0} f(x,t|x_0) = \delta(x - x_0). \tag{2.4}$$

After doing so, we will show that the Ornstein-Uhlenbeck process, i.e. the process described by eq.(2.1), can be used to describe the time course of the neuron's membrane potential, under the assumption that the arrival times of the synaptic inputs are Poisson distributed.

2.1.1 Differential form of the Chapman-Kolmogorov equation

Suppose we have a Markov process with a continuum of state values in continuous time.Then we have the Chapman-Kolmogorov equation:

$$f(x,t+\Delta t|x_0,t_0)=\int f(x,t+\Delta t|y,t)f(y,t|x_0,t_0)dy, \tag{2.5}$$

with $X(t+\Delta t)=x,\;\; X(t)=y,\;\; X(t_0)=x_0.$

If we substract from both sides $f(x,t|x_0,t_0)$ we get:

$$f(x,t+\Delta t|x_0,t_0)-f(x,t|x_0,t_0)=\int f(x,t+\Delta t|y,t)f(y,t|x_0,t_0)dy-f(x,t|x_0,t_0). \tag{2.6}$$

Let $g(x)$ be a smooth function with compact support.
We multiply both sides of (2.6) with $\frac{g(x)}{\Delta t}$ and integrate over the state space to get :

$$\begin{aligned}&\int g(x)\frac{f(x,t+\Delta t|x_0,t_0)-f(x,t|x_0,t_0)}{\Delta t}dx=\\&=\frac{1}{\Delta t}\int g(x)\int f(x,t+\Delta t|y,t)f(y,t|x_0,t_0)dydx-\frac{1}{\Delta t}\int g(x)f(x,t|x_0,t_0)dx.\end{aligned} \tag{2.7}$$

If we substitute in the first integral of the right hand side of eq.(2.7) the Taylor expansion around y for $g(x)$:

$$g(x)=g(y)+\sum_{n=1}^{\infty}\frac{d^n g(y)}{dy^n}\frac{(x-y)^n}{n!}, \tag{2.8}$$

and we take the limit as $\Delta t\to 0$ we obtain:

$$\begin{aligned}\int g(x)\frac{\partial f}{\partial t}dx=&\lim_{\Delta t\to 0}\frac{1}{\Delta t}\int g(y)f(y,t|x_0,t_0)dy\int f(x,t+\Delta t|y,t)dx\\&+\sum_{n=1}^{\infty}\frac{1}{n!}\int\left\{\frac{d^n g(y)}{dy^n}f(y,t|x_0,t_0)\lim_{\Delta t\to 0}\frac{1}{\Delta t}\int(x-y)^n f(x,t+\Delta t|y,t)dx\right\}dy\\&-\lim_{\Delta t\to 0}\frac{1}{\Delta t}\int g(x)f(x,t|x_0,t_0)dx.\end{aligned} \tag{2.9}$$

Now, after using the condition :

$$\int f(x,t+\Delta t|y,t)dx=1, \tag{2.10}$$

and setting :

$$A_n(x,t)=\lim_{\Delta t\to 0}\frac{1}{\Delta t}\int(y-x)^n f(y,t+\Delta t|x,t)dy \tag{2.11}$$

we get:

$$\int g(x)\frac{\partial f}{\partial t}dx = \sum_{n=1}^{\infty}\frac{1}{n!}\int \frac{d^n g(x)}{dx^n} f(x,t|x_0,t_0)A_n(x,t)dx. \tag{2.12}$$

An integration by parts gives us :

$$\int \frac{d^n g(x)}{dx^n} f(x,t|x_0,t_0)A_n(x,t)dx = (-1)^n \int g(x)\frac{\partial^n}{\partial x^n}\Big[A_n(x,t)f(x,t|x_0,t_0)\Big], \tag{2.13}$$

where we have used the fact that $g(x)$ and its derivatives vanish at the ends of the integration interval.

So, equation (2.12) finally becomes :

$$\int g(x)\Big\{\frac{\partial f}{\partial t} - \sum_{n=1}^{\infty}\frac{(-1)^n}{n!}\frac{\partial^n}{\partial x^n}\Big[A_n(x,t)f(x,t|x_0,t_0)\Big]\Big\}dx = 0. \tag{2.14}$$

Since $g(x)$ was arbitrary we get :

$$\frac{\partial f}{\partial t} = \sum_{n=1}^{\infty}\frac{(-1)^n}{n!}\frac{\partial^n}{\partial x^n}\Big[A_n(x,t)f(x,t|x_0,t_0)\Big]dx, \tag{2.15}$$

which is the differential form of equation (2.5).

The functions $A_n(x,t)$ are called infinitesimal moments of the process.
If the process is stationary, then the transition probability density function depends only on the difference between the present time and the initial value:

$$f(y,t+\Delta t|x,t) = f(y,\Delta t|x,0). \tag{2.16}$$

This means that the infinitesimal moments do not depend on time.

If we set $y - x = X(t+\Delta t) - X(t) = \Delta x$ we get:

$$A_n(x,t) = \lim_{\Delta t\to 0}\frac{\langle(\Delta x)^n)|X(t)=x\rangle}{\Delta t}. \tag{2.17}$$

Next, we will see that for the Ornstein-Uhlenbeck process, A_n vanish for $n \geq 3$, and then (2.15) will give as the Fokker-Planck equation.

2.1.2 The Langevin Equation for one variable

The general Langevin equation for one variable is :

$$\frac{dy}{dt} = A(y,t) + B(y,t)\Lambda(t), \tag{2.18}$$

where $\Lambda(t)$ is a Langevin force, i.e. is a Gaussian process with statistical properties:

$$\langle \Lambda(t) \rangle = 0 \quad and \quad \langle \Lambda(t_1)\Lambda(t_2) \rangle = 2D\delta(t_1 - t_2). \tag{2.19}$$

The terms $A(y,t), B(y,t)$ are called drift and diffusion terms, respectively. Equation (2.18) is a first order differential equation, so each sample function of $\Lambda(t)$ determines $y(t)$ uniquely when $y(t_0)$ is given. Due to the delta-correlated nature of $\Lambda(t)$, the values of $\Lambda(t)$ at previous times, say $t' < t_0$, cannot influence the conditional probabilities at times $t > t_0$. This makes the solution of the Langevin equation a Markovian process. Because of the presence of $\Lambda(t)$, equation (2.18) is a stochastic differential equation and solving it means determining the statistical properties of $y(t)$.
The higher-order moments of $\Lambda(t)$ are obtained from the second ones, by assuming relations like those of the multivariate Gaussian case, i.e. (from Wick's formula) all odd moments vanish and :

$$\begin{aligned}\langle \Lambda(t_1)\Lambda(t_2)\Lambda(t_3)\Lambda(t_4) \rangle = (2D)^2[&\langle \Lambda(t_1)\Lambda(t_2) \rangle \langle \Lambda(t_3)\Lambda(t_4) \rangle \\ &+ \langle \Lambda(t_1)\Lambda(t_3) \rangle \langle \Lambda(t_2)\Lambda(t_4) \rangle + \\ &+ \langle \Lambda(t_1)\Lambda(t_4) \rangle \langle \Lambda(t_2)\Lambda(t_3) \rangle.\end{aligned} \tag{2.20}$$

Now, the integral form of (2.18) is :

$$y(t+\Delta t) - y = \int_t^{t+\Delta t} A[y(t_1), t_1]dt_1 + \int_t^{t+\Delta t} B[y(t_1), t_1]\Lambda(t_1)dt_1, \tag{2.21}$$

where y stands for the initial value $y(t)$.

Expanding $A(y,t), B(y,t)$ around y:

$$\begin{aligned}A[y(t_1), t_1] &= A(y, t_1) + A'(y, t_1)[y(t_1) - y] + \dots, \\ B[y(t_1), t_1] &= B(y, t_1) + B'(y, t_1)[y(t_1) - y] + \dots,\end{aligned} \tag{2.22}$$

where the prime denotes the partial derivative with respect to y at the initial value, we get:

$$\begin{aligned}y(t+\Delta t) - y = &\int_t^{t+\Delta t} A(y, t_1)dt_1 + \int_t^{t+\Delta t} A'(y, t_1)[y(t_1) - y]dt_1 + \dots \\ &+ \int_t^{t+\Delta t} B(y, t_1)\Lambda(t_1)dt_1 + \int_t^{t+\Delta t} B'(y, t_1)[y(t_1) - y]\Lambda(t_1)dt_1 + \dots\end{aligned} \tag{2.23}$$

If we write $y(t_1) - y$ in the form (2.21) we get:

$$y(t+\Delta t) - y = \int_t^{t+\Delta t} A(y,t_1)dt_1 + \int_t^{t+\Delta t} A'(y,t_1) \int_t^{t_1} A(y,t_2)dt_2dt_1 +$$

$$+ \int_t^{t+\Delta t} A'(y,t_1) \int_t^{t_1} B(y,t_2)\Lambda(t_2)dt_2dt_1 \dots$$

$$+ \int_t^{t+\Delta t} B(y,t_1)\Lambda(t_1)dt_1 + \int_t^{t+\Delta t} B'(y,t_1)\Lambda(t_1) \int_t^{t_1} A(y,t_2)dt_2dt_1 +$$

$$+ \int_t^{t+\Delta t} B'(y,t_1)\Lambda(t_1) \int_t^{t_1} B(y,t_2)\Lambda(t_2)dt_2dt_1 \dots \tag{2.24}$$

We repeat this until only Langevin forces and the functions $A(y,t), B(y,t)$ and their derivatives appear on the right side of (2.24).

Taking the average of this equation for a fixed $y = y(t)$ and using (2.19) we get:

$$\langle y(t+\Delta t) - y \rangle = \int_t^{t+\Delta t} A(y,t_1)dt_1 + \int_t^{t+\Delta t} A'(y,t_1) \int_t^{t_1} A(y,t_2)dt_2dt_1 +$$

$$+ 2D \int_t^{t+\Delta t} B'(y,t_1) \int_t^{t_1} B(y,t_2)\delta(t_2 - t_1)dt_2dt_1 \dots, \tag{2.25}$$

and using the fact that :

$$\int_{t_0}^{t_1} f(t)\delta(t - t_0)dt = \frac{1}{2}f(t_0),$$

we get:

$$\int_t^{t_1} B(y,t_1)\delta(t_2 - t_1)dt_2 = \frac{1}{2}B(y,t_1).$$

Now we can find :

$$A_1(y,t) = \lim_{\Delta t \to 0} \frac{1}{\Delta t} \langle y(t+\Delta t) - y \rangle$$

$$= A(y,t) + DB(y,t)\frac{\partial B(y,t)}{\partial y}. \tag{2.26}$$

The integrals not written down do not contribute in the limit $\Delta t \to 0$:
Each Langevin term is accompanied by an integral, the lowest-order terms are written down in (2.25) while the higher-order terms are of two types:

- Integrals of the form:

  $$\langle \int_t^{t+\Delta t} \dots \Lambda(t_1)dt_1 \int_t^{t+t_1} \dots \Lambda(t_2)dt_2 \int_t^{t+t_2} \dots \Lambda(t_3)dt_3 \int_t^{t+t_3} \dots \Lambda(t_4)dt_4 \rangle$$

  which, due to (2.20), will only give a contribution proportional to $(\Delta t)^2$

- Integrals with no Langevin force, which are proportional to $(\Delta t)^n$, with n being the number of simple integrals

Both types will vanish when we devide by Δt and take the limit $\Delta t \to 0$.
Using the same arguments, we find :

$$\begin{aligned} A_2(y,t) &= \lim_{\Delta t \to 0} \frac{1}{\Delta t} \langle (y(t+\Delta t) - y)^2 \rangle \\ &= \lim_{\Delta t \to 0} \frac{1}{\Delta t} \int_t^{t+\Delta t} B(y,t_1) \int_t^{t+\Delta t} B(y,t_2) 2D\delta(t_1 - t_2)dt_2 dt_1 \\ &= 2DB^2(y,t), \end{aligned} \tag{2.27}$$

and $A_m(y,t) = 0$, for $m \geq 3$.

We finally get, from (2.15) :

$$\frac{\partial f}{\partial t} = -\frac{\partial}{\partial y}\Big\{[A(y,t) + DB(y,t)\frac{\partial B(y,t)}{\partial y}]f\Big\} + D\frac{\partial^2}{\partial y^2}[B^2(y,t)f], \tag{2.28}$$

which is the Fokker-Planck equation for the Ornstein-Uhlenbeck process defined by (2.18)

2.2 The Ornstein-Uhlenbeck process for a model neuron

In this section, we will see that the Ornstein-Uhlenbeck process can be used to describe the time course of the neuron's membrane potential.

Consider a neuron with $p+q$ dendrites, a firing threshond S and zero resting potential. We assume that each dendrite carries point like excitatory or inhibitory signals that are Poisson distributed in time.
Let $a_k \;\; (k=1,2,\dots,p)$, $b_\ell \;\; (\ell=1,2,\dots,q)$ be the rates at which excitatory and inhibitory inputs travel along the synaptic pathways and let $e_k>0$ $(k=1,2,\dots,p)$, $i_\ell<0$ $(\ell=1,2,\dots,q)$ be the excitatory and inhibitory postsynaptic potentials.

Now, if at a certain time we have a membrane potential x, then the arrival at that time of an excitatory input through the k-th pathway will change the membrane potential through :

$$x \to x + e_k, \tag{2.29}$$

And the arrival of an inhibitory input at the l-th pathway will change it as :

$$x \to x + i_\ell. \tag{2.30}$$

We also assume that in the absence of inputs, the membrane potential decays exponentially toward its resting value, with a time constant θ. This means that $X(t)$ has a continuum of states and it's also a Markov process. So its transition probability density function satisfies the Chapman-Kolmogorov equation :

$$f(x,t+\Delta t|x_0) = \int_{-\infty}^{\infty} f(x,\Delta t|z) f(z,t|x_0)dz. \tag{2.31}$$

We want to find an expression for $f(x,\Delta t|z)$. From equations (2.29), (2.30) and the Poisson assumption we have:

$$\begin{aligned} f(x,\Delta t|z) = \Big\{1 - \Delta t\Big[\sum_{k=1}^{p} a_k + \sum_{k=1}^{q} b_k\Big]\Big\}\delta(x-(z-z\frac{\Delta t}{\theta})) \\ + \Delta t \sum_{k=1}^{p} a_k \delta[x-(z-z\frac{\Delta t}{\theta}+e_k)] \\ + \Delta t \sum_{k=1}^{q} b_k \delta[x-(z-z\frac{\Delta t}{\theta}+i_k)]. \end{aligned} \tag{2.32}$$

If we put equation (2.32) in (2.31) we have :

$$
\begin{aligned}
f(x,t+\Delta t|x_0) = \int_{-\infty}^{\infty} \Big\{ &\{1-\Delta t[\sum_{k=1}^{p} a_k + \sum_{k=1}^{q} b_k]\}\delta(x-(z-z\frac{\Delta t}{\theta}))+ \\
&+\Delta t \sum_{k=1}^{p} a_k \delta[x-(z-z\frac{\Delta t}{\theta}+e_k)]+ \\
&+\Delta t \sum_{k=1}^{q} b_k \delta[x-(z-z\frac{\Delta t}{\theta}+i_k)]\Big\} f(x,\Delta t|z) f(z,t|x_0)dz \\
&= (1+\frac{\Delta t}{\theta})[1-\Delta t(\sum_{k=1}^{p} a_k + \sum_{k=1}^{q} b_k)] f(x+\frac{\Delta t}{\theta}x, t|x_0)+ \\
&+\Delta t(1+\frac{\Delta t}{\theta}) \sum_{k=1}^{p} a_k f((x-e_k)(1+\frac{\Delta t}{\theta}), t|x_0)+ \\
&+\Delta t(1+\frac{\Delta t}{\theta}) \sum_{k=1}^{q} b_k f((x-i_k)(1+\frac{\Delta t}{\theta}), t|x_0) \\
&= (1+\frac{\Delta t}{\theta})\Big[f(x+\frac{\Delta t}{\theta}x, t|x_0)+ \\
&+\Delta t \sum_{k=1}^{p} a_k (f((x-e_k)(1+\frac{\Delta t}{\theta}), t|x_0) - f(x+\frac{\Delta t}{\theta}x, t|x_0)) \\
&+\Delta t \sum_{k=1}^{q} b_k (f((x-i_k)(1+\frac{\Delta t}{\theta}), t|x_0) - f(x+\frac{\Delta t}{\theta}x, t|x_0))\Big]. \qquad (2.33)
\end{aligned}
$$

In the calculations we have used :

- $\delta[\phi(y)] = \frac{\delta(y-\bar{y})}{|\phi'(\bar{y})|}$, where ϕ is monotonic and $\phi(\bar{y}) = 0$.

- $(1-\frac{\Delta t}{\theta})^{-1} \simeq 1+\frac{\Delta t}{\theta}$.

From equation (2.33) we have :

$$
\begin{aligned}
\frac{\partial f}{\partial t} &= \lim_{\Delta t\to 0}\frac{f(x,t+\Delta t|x_0)-f(x,t|x_0)}{\Delta t} = \\
&= \lim_{\Delta t\to 0}\Big[\frac{(1+\frac{\Delta t}{\theta})f(x+\frac{\Delta t}{\theta}x,t|x_0)-f(x,t|x_o)}{\Delta t}+ \\
&+(1+\frac{\Delta t}{\theta})[\sum_{k=1}^{p}a_k(f((x-e_k)(1+\frac{\Delta t}{\theta}),t|x_0)-f(x+\frac{\Delta t}{\theta}x,t|x_0))+ \\
&+\sum_{k=1}^{q}b_k(f((x-i_k)(1+\frac{\Delta t}{\theta}),t|x_0)-f(x+\frac{\Delta t}{\theta}x,t|x_0))]\Big] = \\
&= \lim_{\Delta t\to 0}\Big[\frac{(1+\frac{\Delta t}{\theta})f(x+\frac{\Delta t}{\theta}x,t|x_0)-f(x,t|x_o)}{\Delta t}\Big]+ \\
&+\sum_{k=1}^{p}a_k(f(x-e_k,t|x_0)-f(x,t|x_0))+ \\
&+\sum_{k=1}^{q}b_k(f(x-i_k,t|x_0)-f(x,t|x_0))] = \\
&= \lim_{\Delta t\to 0}\Big[\frac{(f(x+\frac{\Delta t}{\theta}x,t|x_0)-f(x,t|x_o)}{\Delta t}+\frac{1}{\theta}(f(x+\frac{\Delta t}{\theta}x,t|x_0)\Big]+ \\
&+\sum_{k=1}^{p}a_k(f(x-e_k,t|x_0)-f(x,t|x_0))+ \\
&+\sum_{k=1}^{q}b_k(f(x-i_k,t|x_0)-f(x,t|x_0))] = \\
&= \lim_{h\to 0}\Big[\frac{x}{\theta}\frac{(f(x+h,t|x_0)-f(x,t|x_o)}{\Delta t}\Big]+\frac{1}{\theta}f(x,t|x_0)+ \\
&+\sum_{k=1}^{p}a_k(f(x-e_k,t|x_0)-f(x+\ t|x_0))+ \\
&+\sum_{k=1}^{q}b_k(f(x-i_k,t|x_0)-f(x,t|x_0))] = \\
&= \frac{x}{\theta}\frac{\partial f(x,t|x_0)}{\partial x}+\frac{1}{\theta}f(x,t|x_0)+ \\
&+\sum_{k=1}^{p}a_k(f(x-e_k,t|x_0)-f(x,t|x_0))+ \\
&+\sum_{k=1}^{q}b_k(f(x-i_k,t|x_0)-f(x,t|x_0))] = \\
&= \frac{\partial(\theta^{-1}xf)}{\partial x}+\sum_{k=1}^{p}a_k(f(x-e_k,t|x_0)-f(x,t|x_0))+ \\
&+\sum_{k=1}^{q}b_k(f(x-i_k,t|x_0)-f(x,t|x_0))].
\end{aligned}
\tag{2.34}
$$

Now, expanding the functions $f(x-e_k,t|x_0),\ f(x-i_k,t|x_0)$ as Taylor series about x we get :

$$f(x-e_k,t|x_0)-f(x,t|x_0)=\sum_{n=1}^{\infty}\frac{(-1)^n}{n!}e_k^n\frac{\vartheta^n}{\vartheta x^n}f, \tag{2.35}$$

and :

$$f(x-i_k,t|x_0)-f(x,t|x_0)=\sum_{n=1}^{\infty}\frac{(-1)^n}{n!}i_k^n\frac{\vartheta^n}{\vartheta x^n}f, \tag{2.36}$$

so equation (2.34) becomes :

$$\frac{\partial f}{\partial t}=\frac{\partial(\theta^{-1}xf)}{\partial x}+\sum_{n=1}^{\infty}\frac{(-1)^n}{n!}\frac{\partial^n}{\partial x^n}\Big[(\sum_{k=1}^{p}a_k e_k^n+\sum_{k=1}^{q}b_k i_k^n)f\Big], \tag{2.37}$$

and by setting:

$$A_1=-\frac{x}{\theta}+\eta_1, \tag{2.38}$$

$$A_r=\eta_r\ \ (r==2,3...), \tag{2.39}$$

$$\eta_n=\sum_{k=1}^{p}a_k e_k^n+\sum_{k=1}^{q}b_k i_k^n\ \ (n=1,2\dots), \tag{2.40}$$

we get :

$$\frac{\partial f}{\partial t}=\sum_{n=1}^{\infty}\frac{(-1)^n}{n!}\frac{\partial^n}{\partial x^n}(A_n f). \tag{2.41}$$

Next we perform a diffusion approximation such that :

$$\eta_r=0\quad (r=3,4\dots),$$

while $|\eta_1|<\infty$ and $0<\eta_2<\infty$.
This can be done by letting all a_k's and b_k's diverge, while making all postsynaptic potentials infinitely small. To do so we suppose that $p>q$ and set:

$$a_k=\alpha_k\delta^{-2},\quad b_k=\beta_k\delta^{-2},\quad i_k=d_k\delta,\quad e_k=c_k\delta,\quad k=1,\dots,q,$$

$$a_r=\alpha_r\delta^{-1},\quad e_r=c_r\delta,\quad r=q+1,\dots,p,$$

where $d_k<0,\ \alpha_k,\beta_k>0,\ c_k=-\frac{\beta_k d_k}{\alpha_k},\ \ k=1,\dots,q,$
and $c>0,\ \ r=q+1,\dots,p.$

With this approximation we get, for $\delta \to 0$:

$$\eta_1 = \sum_{r=q+1}^{p} \alpha_r c_r,$$

$$\eta_2 = \sum_{k=1}^{q} \beta_k d_k^2 (1 + \frac{\beta_k}{\alpha_k}),$$

$$\eta_r = 0 \qquad r = 3, 4 \ldots$$

This way equation (2.41) becomes :

$$\frac{\partial f}{\partial t} = -\frac{\partial}{\partial x}\Big[\big(- \frac{x}{\theta} + \eta\Big) f\Big] + \frac{\sigma^2}{2}\frac{\partial^2 f}{\partial x^2}, \tag{2.42}$$

where $\eta = \eta_1$ and $\sigma^2 = \eta_2$.

Now, letting $x - \eta\theta \to x$ and $x_0 - \eta\theta \to x_0$ we get the Fokker-Planck equation :

$$\frac{\partial f}{\partial t} = \frac{\partial}{\partial x}\big(\frac{x}{\theta} f\big) + \frac{\sigma^2}{2}\frac{\partial^2 f}{\partial x^2},$$

with the initial condition:

$$\lim_{t \to 0} f(x, t|x_0) = \delta(x - x_0).$$

2.2.1 First Passage Time

Let $S > x_0$ and :

$$T \equiv T(S, x_0) = \inf\{t : X(t) > S | X(0) = x_0\}. \tag{2.43}$$

be the first passage time of $X(t)$ through S with probability density function :

$$g(S, t|x_0) \equiv g(t) = \frac{\partial}{\partial t} P\{T \leq t\}. \tag{2.44}$$

In this section we will calculate the statistics of T.
Let :

$$t_n(S|x_0) = \int_0^\infty t^n g(S, t|x_0) dt \qquad (n = 1, 2, \dots) \tag{2.45}$$

be the n-th order moment of T and :

$$g_\lambda \equiv g_\lambda(S|x_0) = \int_0^\infty e^{-\lambda t} g(S, t|x_0) dt \tag{2.46}$$

be the Laplace transform of g.

If g_λ is known, we can express the moments as :

$$t_n(S|x_0) = (-1)^n \Big(\frac{d^n g_\lambda}{d\lambda^n}\Big)_{\lambda=0}. \tag{2.47}$$

Indeed :

$$\begin{aligned} \frac{d^n g_\lambda}{d\lambda^n} &= \frac{d^n}{d\lambda^n} \int_0^\infty e^{-\lambda t} g(S, t|x_0) dt = \\ &= \int_0^\infty \frac{d^n}{d\lambda^n} \big(e^{-\lambda t}\big) g(S, t|x_0) dt = \\ &= (-1)^n \int_0^\infty t^n e^{-\lambda t} g(S, t|x_0) dt, \end{aligned} \tag{2.48}$$

and for $\lambda = 0$ we get (2.47).
From equation (2.47) we get the mean M and variance V of the first passage time :

- $M(S|x_0) = -\Big(\frac{dg_\lambda}{d\lambda}\Big)_{\lambda=0}$.
- $V(S|x_0) = \Big(\frac{d^2 g_\lambda}{d\lambda^2}\Big)_{\lambda=0} - \Big[\Big(\frac{dg_\lambda}{d\lambda}\Big)^2_{\lambda=0}\Big]$.

So, in order to determine mean and variance we need the Laplace transform of the first passage time probability density function.

We know that $(Siegert, 1951)$ g_λ is the solution of:

$$(L_0 - \lambda)g_\lambda = 0, \tag{2.49}$$

with boundary conditions :

i)

$$\lim_{x_0 \to S} g_\lambda(S|x_0) = 1, \tag{2.50}$$

and

ii)

$$\lim_{x_0 \to -\infty} g_\lambda(S|x_0) = 0, \tag{2.51}$$

where :

$$L_0 = A_1(x_0)\frac{d}{dx_0} + \frac{1}{2}A_2\frac{d^2}{dx_0^2}, \tag{2.52}$$

and A_1, A_2 are given by equation (2.38) and (2.39) So , g_λ is the solution of :

$$\frac{\sigma^2}{2}\frac{d^2 g_\lambda}{dx_0} - \frac{x_0}{\theta}\frac{dg_\lambda}{dx_0} - \lambda g_\lambda = 0, \tag{2.53}$$

satisfying the conditions (2.50) and (2.51).
Now, if we set $x_0 = -\big(\sigma^2\theta y\big)^{1/2}$ we get :

$$\frac{dg_\lambda}{dx_0} = \frac{dg_\lambda}{dy}\frac{dy}{dx_0} = -\frac{2y^{1/2}}{\sqrt{\sigma^2\theta}}\frac{dg_\lambda}{dy}, \tag{2.54}$$

and:

$$\frac{d^2 g_\lambda}{dx_0^2} = \frac{d}{dy}\Big(- \frac{2y^{1/2}}{\sqrt{\sigma^2\theta}}\frac{dg_\lambda}{dy}\Big)\frac{dy}{dx_0} = \frac{2}{\sigma^2\theta}\frac{dg_\lambda}{dy} + \frac{4y}{\sigma^2\theta}\frac{d^2 g_\lambda}{dy^2}, \tag{2.55}$$

so equation (2.53) becomes :

$$\frac{\sigma^2}{2}\frac{d^2 g_\lambda}{dx_0} - \frac{x_0}{\theta}\frac{dg_\lambda}{dx_0} - \lambda g_\lambda = 0 \Rightarrow$$

$$\frac{\sigma^2}{2}\Big[\frac{2}{\sigma^2\theta}\frac{dg_\lambda}{dy} + \frac{4y}{\sigma^2\theta}\frac{d^2 g_\lambda}{dy^2}\Big] + \frac{\sqrt{\sigma^2\theta}y^{1/2}}{\theta}\Big(- \frac{2y^{1/2}}{\sqrt{\sigma^2\theta}}\frac{dg_\lambda}{dy}\Big) - \lambda g_\lambda = 0 \Rightarrow$$

$$\frac{1}{\theta}\frac{dg_\lambda}{dy} + \frac{2y}{\theta}\frac{d^2 g_\lambda}{dy^2} - \frac{2y}{\theta}\frac{dg_\lambda}{dy} - \lambda g_\lambda = 0 \Rightarrow$$

$$y\frac{d^2 g_\lambda}{dy^2} + \frac{dg_\lambda}{dy}\Big(\frac{1}{2} - y\Big) - \frac{\lambda\theta}{2}g_\lambda = 0. \tag{2.56}$$

Now, setting $g_\lambda(y) = e^{y/2}u_\lambda(y)$, we have :

$$\frac{dg_\lambda}{dy} = \frac{d}{dy}\Big(e^{y/2}u_\lambda(y)\Big) = \frac{e^{y/2}}{2}u_\lambda + e^{y/2}\frac{du_\lambda}{dy}, \tag{2.57}$$

and :

$$\frac{d^2g_\lambda}{dy^2} = \frac{d}{dy}\Big(\frac{e^{y/2}}{2}u_\lambda + e^{y/2}\frac{du_\lambda}{dy}\Big) = e^{y/2}\frac{d^2u_\lambda}{dy^2} + e^{y/2}\frac{du_\lambda}{dy} + \frac{e^{y/2}}{4}u_\lambda, \tag{2.58}$$

and equation (2.56) becomes :

$$y\Big[e^{y/2}\frac{d^2u_\lambda}{dy^2} + e^{y/2}\frac{du_\lambda}{dy} + \frac{e^{y/2}}{4}u_\lambda\Big] + \Big(\frac{e^{y/2}}{2}u_\lambda + e^{y/2}\frac{du_\lambda}{dy}\Big)\Big(\frac{1}{2} - y\Big) - \frac{\lambda\theta}{2}e^{y/2}u_\lambda = 0 \Rightarrow$$

$$y\frac{d^2u_\lambda}{dy^2} + y\frac{du_\lambda}{dy} + \frac{y}{4}u_\lambda + \frac{1}{4}u_\lambda - \frac{y}{2}u_\lambda + \frac{1}{2}\frac{du_\lambda}{dy} - y\frac{du_\lambda}{dy} - \frac{\lambda\theta}{2}u_\lambda = 0 \Rightarrow$$

$$y\frac{d^2u_\lambda}{dy^2} + \frac{1}{2}\frac{du_\lambda}{dy} + u_\lambda\Big(\frac{1}{4} - \frac{y}{4} - \frac{\lambda\theta}{2}\Big) = 0. \tag{2.59}$$

Finally, setting $y = \frac{z^2}{2}$ we get :

$$\frac{du_\lambda}{dy} = \frac{du_\lambda}{dz}\frac{dz}{dy} = \frac{1}{z}\frac{du_\lambda}{dz}, \tag{2.60}$$

and :

$$\frac{d^2u_\lambda}{dy^2} = -\frac{1}{z^3}\frac{du_\lambda}{dz} + \frac{1}{z^2}\frac{d^2u_\lambda}{dz^2}, \tag{2.61}$$

and equation (2.59) becomes :

$$\frac{z^2}{2}\Big(- \frac{1}{z^3}\frac{du_\lambda}{dz} + \frac{1}{z^2}\frac{d^2u_\lambda}{dz^2}\Big) + \frac{1}{2z}\frac{du_\lambda}{dz} + u_\lambda\Big(\frac{1}{4} - \frac{z^2}{8} - \frac{\lambda\theta}{2}\Big) = 0 \Rightarrow$$

$$\frac{d^2u_\lambda}{dz^2} + u_\lambda\Big(- \lambda\theta + \frac{1}{2} - \frac{z^2}{4}\Big) = 0. \tag{2.62}$$

Equation (2.62) is known as the Weber equation and its general solution is a linear combination of the two independent solutions $D_{-\lambda\theta}(z)$ and $D_{-\lambda\theta}(-z)$, where $D_\nu(z)$ is the Parabolic Cylinder Function, :

$$u_\lambda(z) = AD_{-\lambda\theta}(z) + BD_{-\lambda\theta}(-z),$$

where A, B are arbitrary constants.

Applying backward the transformations we get :

$$g_\lambda(x_0) = \exp\Big[\frac{x_0^2}{2\sigma^2\theta}\Big]\Big[AD_{-\lambda\theta}\Big(-\frac{\sqrt{2}x_0}{\sqrt{\sigma^2\theta}}\Big) + BD_{-\lambda\theta}\Big(\frac{\sqrt{2}x_0}{\sqrt{\sigma^2\theta}}\Big)\Big].$$

Now, we can find A, B from the boundary conditions (2.50), (2.51), but for the condition (2.51) we will first write :

$$\lim_{x_0\to -b} g_\lambda(S|x_0) = 0,$$

and then we will let $b \to \infty$. We get :

$$A = \frac{\exp\Big[\frac{-S^2}{2\sigma^2\theta}\Big]}{D_{-\lambda\theta}\Big(-\frac{\sqrt{2}S}{\sqrt{\sigma^2\theta}}\Big) - \frac{D_{-\lambda\theta}\Big(\frac{\sqrt{2}b}{\sqrt{\sigma^2\theta}}\Big)}{D_{-\lambda\theta}\Big(-\frac{\sqrt{2}b}{\sqrt{\sigma^2\theta}}\Big)} D_{-\lambda\theta}\Big(\frac{\sqrt{2}S}{\sqrt{\sigma^2\theta}}\Big)},$$

and :

$$B = \frac{\exp\Big[\frac{-S^2}{2\sigma^2\theta}\Big]}{D_{-\lambda\theta}\Big(\frac{\sqrt{2}S}{\sqrt{\sigma^2\theta}}\Big) - \frac{D_{-\lambda\theta}\Big(-\frac{\sqrt{2}b}{\sqrt{\sigma^2\theta}}\Big)}{D_{-\lambda\theta}\Big(\frac{\sqrt{2}b}{\sqrt{\sigma^2\theta}}\Big)} D_{-\lambda\theta}\Big(-\frac{\sqrt{2}S}{\sqrt{\sigma^2\theta}}\Big)}.$$

Now, by using the asymptotic expansions of the Parabolic Cylinder Function :

$$D_{-\lambda\theta}(x) = \exp\big(-\frac{x^2}{4}\big)x^{-\lambda\theta}\Big[1 + O\big(\frac{1}{x^2}\big)\Big],$$

and :

$$D_{-\lambda\theta}(-x) = \frac{\sqrt{2\pi}}{\Gamma(\lambda\theta)}\exp\big(-\frac{x^2}{4}\big)x^{\lambda\theta-1}\Big[1 + O\big(\frac{1}{x^2}\big)\Big],$$

and taking the limit $b \to \infty$ we get :

$$A = \frac{\exp\Big[\frac{-S^2}{2\sigma^2\theta}\Big]}{D_{-\lambda\theta}\Big(-\frac{\sqrt{2}S}{\sqrt{\sigma^2\theta}}\Big)},$$

and $B = 0$.
So the solution is :

$$g_\lambda(S|x_0) = \exp\Big[\frac{(x_0-\eta\theta)^2 - (S-\eta\theta)^2}{2\sigma^2\theta}\Big]\frac{D_{-\lambda\theta}\Big(\frac{\sqrt{2}(\eta\theta - x_0)}{\sqrt{\sigma^2\theta}}\Big)}{D_{-\lambda\theta}\Big(\frac{\sqrt{2}(\eta\theta - S)}{\sqrt{\sigma^2\theta}}\Big)},$$

where we have set $x_0 = x_0 - \eta\theta$ and $S = S - \eta\theta$.

Now, using :

$$D_\nu(z) = 2^{\frac{\nu}{2}}\Big[\frac{\Gamma(1/2)}{\Gamma(\frac{1}{2}-\frac{\nu}{2})}\Phi\Big(-\frac{\nu}{2};\frac{1}{2};\frac{z^2}{2}\Big) + \frac{z}{\sqrt{2}}\frac{\Gamma(-1/2)}{\Gamma(-\frac{\nu}{2})}\Phi\Big(\frac{1}{2}-\frac{\nu}{2};\frac{3}{2};\frac{z^2}{2}\Big)\Big],$$

we finally get :

$$g_\lambda(S|x_0) = \frac{\Phi\Big(\frac{\lambda\theta}{2};\frac{1}{2};\frac{(\eta\theta-x_0)^2}{\sigma^2\theta}\Big)}{\Phi\Big(\frac{\lambda\theta}{2};\frac{1}{2};\frac{(\eta\theta-S)^2}{\sigma^2\theta}\Big) - \frac{2(\eta\theta-S)}{\sqrt{\sigma^2\theta}}\frac{\Gamma\Big(\frac{\lambda\theta+1}{2}\Big)}{\Gamma\Big(\frac{\lambda\theta}{2}\Big)}\Phi\Big(\frac{\lambda\theta+1}{2};\frac{3}{2};\frac{(\eta\theta-S)^2}{\sigma^2\theta}\Big)}$$

$$+\frac{\frac{(\eta\theta-x_o)}{\sqrt{\sigma^2\theta}}\Phi\Big(\frac{\lambda\theta+1}{2};\frac{3}{2};\frac{(\eta\theta-x_0)^2}{\sigma^2\theta}\Big)}{\frac{\eta\theta-S}{\sqrt{\sigma^2\theta}}\Phi\Big(\frac{\lambda\theta+1}{2};\frac{3}{2};\frac{(\eta\theta-S)^2}{\sigma^2\theta}\Big) - \frac{1}{2}\frac{\Gamma\Big(\frac{\lambda\theta}{2}\Big)}{\Gamma\Big(\frac{\lambda\theta+1}{2}\Big)}\Phi\Big(\frac{\lambda\theta}{2};\frac{1}{2};\frac{(\eta\theta-S)^2}{\sigma^2\theta}\Big)},$$

and now from (2.47) we can find the mean and variance of the first passage time.

Chapter 3

Populations of Neurons

We already described the time course of a neuron's membrane potential under the assumption that the arrival times of the synaptic inputs are Poisson distributed and now we want to model populations of neurons if we add more assupmtions. In the general case we have that the state of a neuron v is described by:

$$\frac{dv}{dt} = F(v) + S(v, g(t)). \tag{3.1}$$

For example, in the leaky integrate and fire model, we have :

$$C\frac{dV}{dt} = S(t) - \frac{1}{R}(V - V_r), \tag{3.2}$$

where C is the capacitance, R the resistance and $S(t)$ the current associated with the neuron's membrane.

In this chapter, we will assume that the arrival times of the synaptic inputs are given by a Poisson process with mean rate $\nu_{e/i}(t)$ and also that the size of the synaptic conductance changes , $\Gamma^k_{e/i}$, are random numbers with some given distribution. After deriving the evolution equation for the probability density function for a single population, we will connect populations of neurons to derive the equations for a network of neurons.

3.1 The population density approach

We want to model the evolution of the probability density :

$$p(v,t)dv = P\big(V(t) \in (v, v+dv)\big), \qquad E_i \leq v \leq v_{th}. \tag{3.3}$$

which for a population of many similar neurons can be interpreted as a population density. So for a fixed time, the population density describes the distribution of neurons over all possible states.

In order to do so we need to make some assumptions. First, we assume that there are a large number of similar neurons in each population. By "similar" we mean that they have the same biophysical properties, such as the capacitance, the resting conductance and distribution of synaptic conductances. We also assume that each neuron in the population receives excitatory and inhibitory synaptic input with the same average rate ($\nu_e(t)$ and $\nu_i(t)$). Finally, we assume that the arrival times of synaptic events are random variables given by a Poisson process.

Now, we want to derive the evolution equation for the probability density function for a single population when the synaptic input rates are given functions of time. This is based on conservation of probability.

We have the probability contained in (a, b):

$$P\{V(t) \in (a,b)\} = \int_a^b p(v',t)dv'.$$

This probability can change only through the flux of probability across the endpoints of the interval. By positive/negative flux at a point v we mean the probability per unit time of crossing v from below/above. Letting $J(v,t)$ = flux of probability across v at time t, we have :

$$\begin{aligned} J(a,t) - J(b,t) &= \frac{\partial}{\partial t} P\{V(t) \in (a,b)\} \\ &= \frac{\partial}{\partial t} \int_a^b p(v',t)dv'. \end{aligned} \tag{3.4}$$

If we let $b = v$ and we differentiate by v we get :

$$\frac{\partial\Big(J(a,t)-J(v,t)\Big)}{\partial v}=\frac{\partial}{\partial v}\Big(\frac{\partial}{\partial t}\int_a^v p(v',t)dv'\Big)\Rightarrow$$

$$-\frac{\partial J}{\partial v}(v,t)=\frac{\partial p}{\partial t}(v,t), \quad E_i<v<v_{th}. \tag{3.5}$$

When an integrate and fire neuron crosses v_{th}, it fires a spike. Also, movement of a neuron across a voltage corresponds to probability flux across that voltage. So, the population firing rate is the flux across threshold :

$$r(t)=J(v_{th},t).$$

After the spike the voltage is reset to v_{reset}. This produces a source of probability at v_{reset}. Now, equation (3.5) becomes :

$$\frac{\partial p}{\partial t}(v,t)=-\frac{\partial J}{\partial v}(v,t)+\delta(v-v_{reset})J(v_{th},t) \qquad E_i<v<v_{th}. \tag{3.6}$$

We now want to calculate an expression for the flux $J(v,t)$. In order to do so, we will use equation (1.4) and we will also break the flux into three components :

$$J(v,t)=J_\ell(v,t)+J_e(v,t)+J_i(v,t), \tag{3.7}$$

where J_ℓ is the leakage flux toward E_r due to the resting conductance, J_e is the excitation flux toward E_e due to the excitatory conductance and J_i is the inhibition flux toward E_i due to the inhibitory conductance.

1. **Leakage flux**

   The voltage evolution due to leakage is obtain from equation (1.4) with $G_{e/i}=0$:

   $$\frac{dV}{dt}=-\frac{1}{\tau}(V-E_r). \tag{3.8}$$

   This means that the voltage decays exponentially toward the resting potential, E_r. This movement of the voltage corresponds to a leakage flux. If $V(t)\in(E_i,E_r)$, then $V(t)$ increases, creating a positive leakage flux across all $v\in(E_i.E_r)$. If $V(t)\in(E_r,v_{th})$, then the voltage decreases creating a negative flux.

   Suppose that $v\in(E_i,E_r)$, then the only movement of neurons across v is upward and the leakage flux at v is the probability per unit time that a neuron

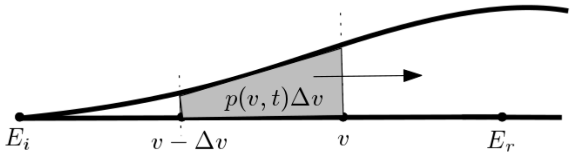

Figure 3.1: Neurons cross a fixed voltage v from below

crosses v from below. We first look at the probability of a neuron crossing v in some short time Δt. The voltage will cross v in the time interval $(t, t+\Delta t)$ if $V(t) \in (v-\Delta v, v)$, where :

$$\Delta v = \frac{dV}{dt}\Delta t + O(\Delta t^2). \tag{3.9}$$

Indeed, if we expand $V(t+\Delta t)$ as a Taylor series around t and keep only a few terms, we have:

$$V(t+\Delta t) = V(t) + \Delta t\frac{dV}{dt} + O(\Delta t^2).$$

Now, by the moment $t+\Delta t$ the voltage will have already crossed v, so:

$$\begin{aligned}
&V(t+\Delta t) > v \Rightarrow \\
&V(t) + \Delta t\frac{dV}{dt} + O(\Delta t^2) > v \Rightarrow \\
&V(t) > v - \Delta t\frac{dV}{dt} - O(\Delta t^2).
\end{aligned}$$

Now, the probability of a neuron being in that interval is :

$$p(v,t)\Delta v = p(v,t)\frac{dV}{dt}\Delta v + O(\Delta t^2). \tag{3.10}$$

So the leakage flux, which is the probability per unit time that a neuron crosses v, is :

$$\begin{aligned}
J_\ell(v,t) &= \frac{p(v,t)\Delta v}{\Delta t} + O(\Delta t) \\
&= p(v,t)\frac{dV}{dt} + O(\Delta t).
\end{aligned} \tag{3.11}$$

Letting $\Delta t \to 0$ and using equation (3.8) we get :

$$J_\ell(v,t) = -\frac{1}{\tau}(v-E_r)p(v,t). \tag{3.12}$$

2. **Excitation flux**

When a neuron receives an excitatory input, the voltage will jump upward because we modeled the conductance change as a delta function. This will create a positive flux across the jumped voltages, the excitation flux.

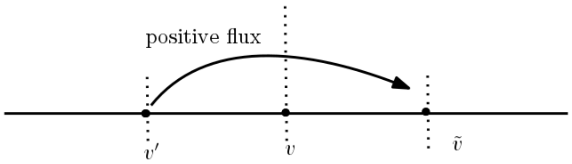

Figure 3.2: Positive flux of probability across v, due to an excitatory input

To calculate the excitation flux across a voltage v, we first calculate the probability that a neuron with voltage $V(t) = v',\ \ v' < v$, will cross v , given that it received an excitatory synaptic input.

After receiving an excitatory input, the neuron that had initial voltage $V(t) = v'$ will jump to the voltage $\tilde{v}$, where (from equation (1.6)) :

$$\tilde{v} = v' + \Gamma_e^*(E_e - v'). \tag{3.13}$$

Now, if $\tilde{v} > v$, then the excitatory input will cause the neuron to cross the voltage v, creating positive flux at v. This condition is equivalent to :

$$\Gamma_e^* > \frac{v - v'}{E_e - v}. \tag{3.14}$$

Γ_e^* is a random variable, so the probability of meating this condition is :

$$\tilde{F}_{\Gamma_e^*}\Big(\frac{v - v'}{E_e - v}\Big). \tag{3.15}$$

So, expression (3.15) is the probability that a neuron with voltage $V(t) = v',\ \ v' < v$, will cross v, given that it received an excitatory synaptic input. The excitatory synaptic input rate , $\nu_e(t)$, is the probability per unit time that a neuron will receive excitatory input. Since the random input times are given by a Poisson process and are independent of Γ_e^*, the probability per unit time that a neuron with voltage v' will cross v is :

$$\nu_e(t)\tilde{F}_{\Gamma_e^*}\Big(\frac{v - v'}{E_e - v}\Big). \tag{3.16}$$

In order for a neuron to cross v from v', the neuron must start with $V(t) = v'$ and the probability of $V(t) \in (v', v' + dv')$ is $p(v', t)dv'$. So the total flux of probability from $V(t) \in (v', v' + dv')$ across v is :

$$\nu_e(t)\tilde{F}_{\Gamma_e^*}\Big(\frac{v - v'}{E_e - v}\Big)p(v', t)dv'. \tag{3.17}$$

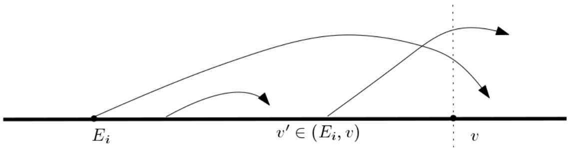

Figure 3.3: A neuron could cross v from any voltage $v' \in (E_i, v)$

Any neuron with voltage in the interval (E_i, v) could contribute to the flux, if it received enough excitatory input. So the total excitation flux at v is :

$$J_e(v, t) = \nu_e(t) \int_{E_i}^{v} \tilde{F}_{\Gamma_e^*}\Big(\frac{v - v'}{E_e - v}\Big)p(v', t)dv'. \tag{3.18}$$

3. **Inhibition flux**

For the calculation of the inhibiton flux, there are two differences. First, a neuron can cross v only if its voltage is in the interval (v, v_{th}). Second, the flux is negative, since neurons cross v by moving to lower voltages. So, the total inhibition flux is:

$$J_i(v, t) = -\nu_i(t) \int_{v}^{v_{th}} \tilde{F}_{\Gamma_i^*}\Big(\frac{v - v'}{E_i - v}\Big)p(v', t)dv'. \tag{3.19}$$

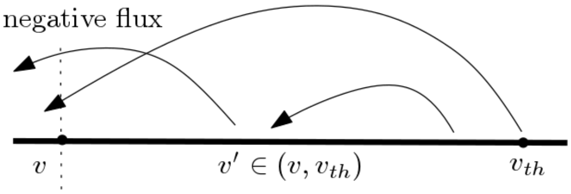

Figure 3.4: Negative flux of probability across v, inhibition flux.

3.2 Network equations

In this section we will model networks of neurons. In order to do this, we only need two more steps. First, we will group neurons into many populations and create a population density for each group. Then, we will connect these populations via their firing rates to form networks of population densities.

In order to group neurons into populations, we must choose groups that satisfy the assumptions of the previous section. We must have similar neurons, so that they can be described by one population density, and the populations must be large enough.

Now, we form a population density for each group of neurons: $p^k(v,t), \quad k = 1, 2, \ldots, N$, where N is the number of populations. Each population has a firing rate, $r^k(t)$, and each population evolves according to the population density model equations.

The difference between network equations and the single population equations is that the synaptic input rates for each population in the network are not given function. They are determined by the firing rates of the presynaptic populations as well as any external input rate. To calculate these input rates we thus need the connectivity of the network, $W_{jk}, \quad j, k = 1, 2, \ldots, N$.
W_{jk} is the number of presynaptic neurons from population j that project to each postsynaptic neuron in population k.

Each population is either excitatory or inhibitory. We denote by $\Lambda_{E/I}$ the set of excitatory/inhibitory indices, i.e. $\{p^k(v,t) | k \in \Lambda_{E/I}\}$ is the set of excitatory/inhibitory populations.
If the excitatory/inhibitory external input rates to population k are $\nu^k_{e/i,o}(t)$, then the total input rates to population k are :

$$\nu^k_{e/i}(t) = \nu^k_{e/i,o}(t) + \sum_{j \in \Lambda_{E/I}} W_{jk} \int_0^\infty \alpha_{jk}(t') r^j(t-t') dt', \tag{3.20}$$

where $\alpha_{jk}(t')$ is the distribution of latencies of synapses from population j to population k.

So, the equations of the population density approach with populations $k = 1, 2, \dots, N$ are :

$$\frac{\partial p^k}{\partial t}(v,t) = -\frac{\partial J^k}{\partial v}(v,t) + \delta(v - v_{reset})J^k(v_{th}, t), \tag{3.21}$$

$$J^k(v,t) = J^k_\ell(v,t) + J^k_e(v,t) + J^k_i(v,t), \tag{3.22}$$

$$J^k_\ell(v,t) = -\frac{1}{\tau}(v - E_r)p^k(v,t), \tag{3.23}$$

$$J^k_e(v,t) = \nu^k_e(t)\int_{E_i}^{v} \tilde{F}_{\Gamma^*_e}\Big(\frac{v - v'}{E_e - v}\Big)p^k(v',t)dv', \tag{3.24}$$

$$J^k_i(v,t) = -\nu^k_i(t)\int_{v}^{v_{th}} \tilde{F}_{\Gamma^*_i}\Big(\frac{v - v'}{E_i - v}\Big)p^k(v',t)dv', \tag{3.25}$$

$$r^k(t) = J^k(v_{th}, t), \tag{3.26}$$

$$\nu^k_{e/i}(t) = \nu^k_{e/i,o}(t) + \sum_{j \in \Lambda_{E/I}} W_{jk} \int_0^\infty \alpha_{jk}(t')r^j(t - t')dt'. \tag{3.27}$$

3.3 Diffusion Approximation

We can make a diffusion approximation to the previous equations, that will give us a diffusion equation that can be solved more quickly. In order to do so, we make the assumption that the synaptic inputs are small, which means that the voltage jumps due to synaptic inputs are also small.

We assume that p is sufficiently smooth, so that we can approximate the value of $p(v', t)$ with the first two terms of a Taylor series centered around v:

$$p(v', t) = p(v, t) + (v' - v)\frac{\partial p}{\partial v}(v, t) + \frac{(v' - v)^2}{2}\frac{\partial^2 p}{\partial v^2}(\xi, t), \tag{3.28}$$

where ξ is between v' and v. If we neglect the third term we make an error that is less than :

$$M(v' - v)^2,$$

where :

$$M = \frac{1}{2}\max_{v,t}\left|\frac{\partial^2 p}{\partial v^2}(v, t)\right|.$$

Now, substituting the first two terms of equation (3.28) into equation (3.24) we get the diffusion approximation for the excitation flux :

$$\begin{aligned}
J_e(v, t) &= \nu_e(t)\int_{E_i}^{v} \tilde{F}_{\Gamma_e^*}\Big(\frac{v - v'}{E_e - v}\Big)p(v', t)dv' \\
&= \nu_e(t)\int_{E_i}^{v} \tilde{F}_{\Gamma_e^*}\Big(\frac{v - v'}{E_e - v}\Big)\Big(p(v, t) + (v' - v)\frac{\partial p}{\partial v}(v, t)\Big)dv' \\
&= \nu_e(t)\big[C_{1e}(v)p(v, t) - C_{2e}(v)\frac{\partial p}{\partial v}(v, t)\big],
\end{aligned} \tag{3.29}$$

where:

$$C_{1e}(v) = \int_{Ei}^{v} \tilde{F}_{\Gamma_e^*}\Big(\frac{v - v'}{E_e - v'}\Big)dv', \tag{3.30}$$

$$C_{2e}(v) = \int_{Ei}^{v} \tilde{F}_{\Gamma_e^*}\Big(\frac{v - v'}{E_e - v'}\Big)(v - v')dv', \tag{3.31}$$

while for the inhibition flux we get :

$$J_i(v,t) = -\nu_i(t)\big[C_{1i}(v)p(v,t) - C_{2i}(v)\frac{\partial p}{\partial v}(v,t)\big], \tag{3.32}$$

where:

$$C_{1i}(v) = \int_v^{v_{th}} \tilde{F}_{\Gamma_i^*}\Big(\frac{v-v'}{E_i-v'}\Big)dv', \tag{3.33}$$

$$C_{2i}(v) = \int_v^{v_{th}} \tilde{F}_{\Gamma_i^*}\Big(\frac{v-v'}{E_i-v'}\Big)(v-v')dv'. \tag{3.34}$$

Under this approximation, we get the following diffusion equation:

$$\begin{aligned}
\frac{\partial p}{\partial t} &= -\frac{\partial}{\partial v}\Big(J_\ell + J_e + J_i\Big) = \\
&= -\frac{\partial}{\partial v}\Big(-\frac{v-E_r}{\tau}p + \nu_e(t)\big[C_{1e}(v)p(v,t) - C_{2e}(v)\frac{\partial p}{\partial v}(v,t)\big] - \\
&\quad - \nu_i(t)\big[C_{1i}(v)p(v,t) - C_{2i}(v)\frac{\partial p}{\partial v}(v,t)\big]\Big) = \\
&= \frac{\partial}{\partial v}\Big[\Big(\frac{v-E_r}{\tau} - \nu_e(t)C_{1e}(v) + \nu_i(t)C_{1i}(v)\Big)p\Big] + \\
&\quad + \frac{\partial}{\partial v}\Big[\Big(\nu_e(t)C_{2e}(v) + \nu_i(t)C_{2i}(v)\Big)\frac{\partial p}{\partial v}\Big],
\end{aligned} \tag{3.35}$$

with firing rate :

$$r(t) = -\nu_e(t)C_{2e}(v_{th})\frac{\partial p}{\partial v}(v_{th},t), \tag{3.36}$$

where we used the fact that $p(v_{th},t) = 0$ and $C_{2i}(v_{th}) = 0$.

Now, the error in the approximation for the excitation flux is less than:

$$\nu_e(t)M\int_{E_i}^{v} \tilde{F}_{\Gamma_e^*}\Big(\frac{v-v'}{E_e-v'}\Big)(v'-v)^2dv', \tag{3.37}$$

and changing the variables to $\gamma = \frac{v-v'}{E_e-v'}$, we get :

$$\nu_e(t)M(E_e-v)^3\int_0^{\frac{v-v'}{E_e-v'}}\tilde{F}_{\Gamma_e^*}(\gamma)\frac{\gamma^2}{(1-\gamma)^4}d\gamma <$$

$$< \nu_e(t)M(E_e-E_i)^3\int_0^1\tilde{F}_{\Gamma_e^*}(\gamma)\frac{\gamma^2}{(1-\gamma)^4}d\gamma, \tag{3.38}$$

since $E_i < v < E_e$.

We denote the integral by I, and we will simplify it through integration by parts:

$$\begin{aligned} I &= \int_0^1\tilde{F}_{\Gamma_e^*}(\gamma)\frac{\gamma^2}{(1-\gamma)^4}d\gamma \\ &= \int_0^1\tilde{F}_{\Gamma_e^*}(\gamma)\Big(\frac{(1-\gamma)^3+\gamma^3}{3(1-\gamma)^3}\Big)'d\gamma \\ &= \Big[\tilde{F}_{\Gamma_e^*}(\gamma)\Big(\frac{(1-\gamma)^3+\gamma^3}{3(1-\gamma)^3}\Big)\Big]_0^1 - \int_0^1\frac{\partial}{\partial\gamma}\tilde{F}_{\Gamma_e^*}(\gamma)\frac{(1-\gamma)^3+\gamma^3}{3(1-\gamma)^3}d\gamma \\ &= -\frac{1}{3}+\int_0^1 f_{\Gamma_e^*}(\gamma)\frac{(1-\gamma)^3+\gamma^3}{3(1-\gamma)^3}d\gamma \\ &= \int_0^1 f_{\Gamma_e^*}(\gamma)\Big[\frac{(1-\gamma)^3+\gamma^3}{3(1-\gamma)^3}-\frac{1}{3}\Big]d\gamma \\ &= \int_0^1 f_{\Gamma_e^*}(\gamma)\frac{\gamma^3}{3(1-\gamma)^3}d\gamma, \end{aligned} \tag{3.39}$$

where :

$$f_{\Gamma_e^*}(\gamma) = -\frac{\partial}{\partial\gamma}\tilde{F}_{\Gamma_e^*}(\gamma). \tag{3.40}$$

In the calculation of the boundary term we used the fact that :

$$\tilde{F}_{\Gamma_e^*}(0) = 1,$$

and the assumption :

$$\lim_{\gamma\to 1^-}\frac{\tilde{F}_{\Gamma_e^*}(\gamma)}{(1-\gamma)^3} = 0.$$

Note that, from (3.40), we have :

$$\int_0^1 f_{\Gamma_e^*}(\gamma)d\gamma = 1,$$

since $0 < \Gamma_e^* < 1$.

So, we finally have that the error is less than :

$$\nu_e(t)\frac{M}{3}(E_e - E_i)^3 \int_0^1 f_{\Gamma_e^*}(\gamma)\frac{\gamma^3}{(1-\gamma)^3}d\gamma. \tag{3.41}$$

If the excitatory synaptic conductances are small, then $f_{\Gamma_e^*}(\gamma)$ is almost zero except for small γ, so the integral in (3.41) is the third moment of Γ_e^* to smallest order in γ.
So the error is proportional to the third moment of Γ_e^*, which is small when the synaptic conductances are small.

In the same way, we can find that the error for the inhibition flux is less than:

$$\nu_i(t)\frac{M}{3}(v_{th} - E_i)^3 \int_0^1 f_{\Gamma_i^*}(\gamma)\frac{\gamma^3}{(1-\gamma)^3}d\gamma$$

with $f_{\Gamma_i^*}(\gamma)$ being the probability density function for Γ_i^*.

Appendix A

Probabilities

Let X be a random variable with a probability distribution $f(x)$. The probability distribution is a non-negative function, $f(x) \geq 0$, with $f(x)dx$ being the probability that $x \in (x, x+dx)$, and it is normalised in the sense $\int f(x)dx = 1$, where the integral extends over the whole range of X.

- **Averages and Moments**

  The average of a function $g(X)$ is defined as :

  $$\langle g(X) \rangle = \int g(x) f(x) dx,$$

  and the moments of X correspond to the special case $g(x) = x^m$:

  $$\mu_m = \langle X^m \rangle = \int x^m f(x) dx, \quad m = 1, 2, \ldots$$

- **Characteristic function**

  The characteristic function is defined as :

  $$G(k) = \langle e^{ikX} \rangle = \int e^{ikx} f(x) dx.$$

  By expanding the exponential and interchanging the order of the series and the integral, we get :

  $$G(k) = \sum_{m=0}^{\infty} \frac{(ik)^m}{m!} \int x^m f(x) dx = \sum_{m=0}^{\infty} \frac{(ik)^m}{m!} \mu_m.$$

  From this we can see that :

  $$\mu_m = (-i)^m \frac{\partial^m}{\partial k^m} G(k) \Big|_{k=o},$$

  which is why $G(k)$ is the moment generating function.

- **Cumulants**

  The cumulants, k_m, are defined as :

  $$\ln G(k) = \sum_{m=1}^{\infty} \frac{(ik)^m}{m!} k_m.$$

  From this we get that the first n cumulants can be expressed by the first n moments.For the first four cumulants we have:

  - $k_1 = \mu_1$
  - $k_2 = \mu_2 - \mu_1^2$
  - $k_3 = \mu_3 - 3\mu_2\mu_1 + 2\mu_1^3$
  - $k_4 = \mu_4 - 4\mu_3\mu_1 - 3\mu_2^2 + 12\mu_2\mu_1^2 - 6\mu_1^4$

  We see that the first cumulant is equal to the first moment, and the second cumulant is equal to the variance.

- **The Gaussian Distribution**

  The Gaussian distribution is defined as :

  $$f(x) = \frac{1}{\sqrt{2\pi\sigma^2}} \exp\Big[- \frac{(x-\mu)^2}{2\sigma^2} \Big],$$

  and with characteristic function :

  $$G(k) = \exp(i\mu k - \frac{1}{2}\sigma^2 k^2).$$

  The logarithm of this function has terms up to quadratic in k only, so all the cumulants after the second one vanish, which is a characteristic property of the Gaussian distribution.

Once we define a stochastic variable X, we can define quantities Y as functions of X by :

$$Y(t) = h(X,t),$$

which are called stochastic processes. A stochastic process is called:

- **stationary** when the moments are not affected by a shift in time, i.e.:

  $$\langle Y(t_1 + \tau), \ldots, Y(t_n + \tau) \rangle = \langle Y(t_1), \ldots, Y(t_n) \rangle.$$

- **Gaussian** if, for all $t_1 < \cdots < t_n$ the n-vector $(Y(t_1), \ldots, Y(t_n))$ is multivariate normally distributed

- **Markovian** if, for all $t_1 < \cdots < t_n$:

  $$P(y_n, t_n | y_1, t_1, \ldots, y_{n-1}, t_{n-1}) = P(y_n, t_n | y_{n-1}, t_{n-1}).$$

For every Markov process we have the Chapman-Kolmogorov equation :

$$f(x,t|x_0,t_0) = \int f(x,t|y,\tau)f(y,\tau|x_0,t_0).$$

Novikov Theorem and Wick formula: For a multivariate Gaussian distribution with zero mean :

$$P(x) = \sqrt{\frac{\det \hat{A}}{(2\pi)^n}} \exp\Big(-\frac{1}{2} x\hat{A}x \Big),$$

the Novikov theorem says that the averages of the type $\langle x_i f(x) \rangle$ can be obtained as :

$$\langle x_i f(x) \rangle = \sum_m \langle x_i x_m \rangle \Big\langle \frac{\partial f}{\partial x_m} \Big\rangle.$$

If we set $f(x) = x_j x_k x_l$ and use the fact that $\dfrac{\partial x_i}{\partial x_m} = \delta_{im}$ we get :

$$\begin{aligned} \langle x_i x_j x_k x_l \rangle &= \sum_m \langle x_i x_m \rangle \langle \delta_{jm} x_k x_l + x_j \delta_{km} x_l + x_j x_k \delta_{lm} \rangle \\ &= \langle x_i x_j \rangle \langle x_k x_l \rangle + \langle x_i x_k \rangle \langle x_j x_l \rangle + \langle x_i x_l \rangle \langle x_j x_k \rangle, \end{aligned}$$

which is Wick's formula.

The Poisson Process

Definition 1. *A random process $\{N(t), t \in [0,\infty)\}$ is said to be a counting process if $N(t)$ is the number of events that occured from time 0 up to time t. For a counting process, we assume:*

1. $N(0) = 0$,
2. $N(t) \in \{0,1,2,\dots\}$, *for all* $t \in [0,\infty)$,
3. *for* $0 \le s < t$, $N(t) - N(s)$ *shows the number of events that occur in the interval* $(s,t]$.

Definition 2. *Let $\{X(t), t \in [0,\infty)\}$ be a continuous-time random process. We say that $X(t)$ has independent increments if, for all $0 \le t_1 < t_2 < t_3 < \cdots < t_n$, the random variables $X(t_2)-X(t_1), X(t_3)-X(t_2), \dots, X(t_n)-X(t_{n-1})$ are independent.*

Definition 3. *A discrete random variable X is said to be a Poisson random variable with parameter μ, $X \sim Poisson(\mu)$, if its range is $R_X = \{0,1,2,3,\dots\}$ and:*

$$P_X(k) = \begin{cases} \frac{e^{-\mu}\mu^k}{k!}, & \text{if} \quad k \in R_X, \\ \\ 0, & \text{otherwise.} \end{cases}$$

For a Poisson variable we also know that :

1. If $X \sim Poisson(\mu)$ then $E(X) = \mu$ and $Var(X) = \mu$.
2. If $X_i \sim Poisson(\mu_i)$, for $i = 1, 2, \ldots, n$ and the X_i's are independent, then
$$X_1 + X_2 + \ldots, X_n \sim \text{Poisson}(\mu_1 + \mu_2 + \cdots + \mu_n).$$
3. The Poisson distrinution can be viewed as the limit of binomial distribution.

Definition 4. *Let $\lambda > 0$ be fixed. The counting process $\{N(t), t \in [0, \infty)\}$ is called a Poisson process with rate λ if :*

1. *$N(0) = 0$.*
2. *$N(t)$ has independent increments.*
3. *The number of arrivals in any interval of length $\tau > 0$ has $Poisson(\lambda\tau)$ distribution.*

A second definition for a Poisson process is :

Definition 5. *Let $\lambda > 0$ be fixed. The counting process $\{N(t), t \in [0, \infty)\}$ is called a Poisson process with rate λ if :*

1. *$N(0) = 0$.*
2. *$N(t)$ has independent and stationary increments.*
3. *We have that :*
$$\begin{aligned} P\big(N(\Delta) = 0\big) &= 1 - \lambda\Delta + o(\Delta), \\ P\big(N(\Delta) = 1\big) &= \lambda\Delta + o(\Delta), \\ P\big(N(\Delta) \geq 2\big) &= o(\Delta). \end{aligned}$$

Appendix B

Weber Equation

The Weber equation is defined as :

$$u''(z) + (\nu + \frac{1}{2} - \frac{z^2}{4})u(z) = 0. \tag{B.1}$$

The solutions of equation (1) are called parabolic cylinder functions, $D_\nu(z)$. The two independent solutions are given by $u_1 = D_\nu(z)$ and $u_2 = D_{\nu-1}(iz)$, where :

$$\begin{aligned} D_\nu(z) &= 2^{\frac{\nu}{2}+\frac{1}{4}} z^{-\frac{1}{2}} W_{\frac{\nu}{2}+\frac{1}{4},-\frac{1}{4}}(\frac{z^2}{2}) \\ &= \frac{2^{\frac{\nu}{2}} e^{-\frac{z^2}{4}} (-iz)^{\frac{1}{4}} (iz)^{\frac{1}{4}}}{\sqrt{z}} U(-\frac{\nu}{2}, \frac{1}{2}, \frac{z^2}{2}), \end{aligned} \tag{B.2}$$

where $W_{k,m}(z)$ is the Whittaker Function and $U(a, b, z)$ is a confluent Function of the first kind.

For ν a nonnegative integer, the solution D_ν reduces to :

$$\begin{aligned} D_\nu(x) &= 2^{-\frac{\nu}{2}} e^{-\frac{x^2}{4}} H_\nu(\frac{x}{\sqrt{2}}) \\ &= e^{-\frac{x^2}{4}} H_{e_\nu}(x), \end{aligned} \tag{B.3}$$

where $H_\nu(x)$ is a Hermite polynomial and H_{e_ν} is a modified Hermite polynomial.

The parabolic cylinder functions D_ν satisfy the recurrence relations :

$$D_{\nu+1}(z) - zD_\nu(z) + \nu D_{\nu-1}(z) = 0. \tag{B.4}$$

$$D'_\nu(z) + \frac{z}{2} D_\nu(z) - \nu D_{\nu-1}(z) = 0. \tag{B.5}$$

For ν real we have :

$$\int_0^\infty \big[D_\nu(t)\big]^2 dt = \pi^{\frac{1}{2}} 2^{-\frac{3}{2}} \frac{\Phi_0(\frac{1}{2} - \frac{\nu}{2}) - \Phi_0(-\frac{\nu}{2})}{\Gamma(-\nu)}, \tag{B.6}$$

where $\Gamma(z)$ is the Gamma function and ϕ_0 is the polygamma function of order 0.

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