Optimal control of deterministic and stochastic neuron models, in finite and infinite dimension. Application to the control of neuronal dynamics via Optogenetics

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Contrôle optimal de modèles de neurones déterministes et stochastiques, en dimension finie et infinie. Application au contrôle de la dynamique neuronale par l'Optogénétique.

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Résumé

Let but de cette thèse est de proposer différents modèles mathématiques de neurones pour l'Optogénétique et d'étudier leur contrôle optimal. L'Optogénétique permet de modifier génétiquement des neurones choisis pour leur conférer une sensibilité à la lumière. L'exposition à une longueur d'onde spécifique permet alors de produire des potentiels d'action, sans stimulation électrique extérieure. Il existe de nombreuses façons de modéliser la dynamique du potentiel de membrane d'un neurone. Les premiers modèles déterministes ont rapidement cohabité avec des modèles stochastiques, justifiés par la nature profondément stochastique des mécanismes d'ouverture et de fermeture des canaux ioniques. Suivant la prise en compte ou non de la propagation du potentiel d'action le long de l'axone, les modèles résultants sont de dimension infinie ou finie. Nous souhaitons prendre en compte ces différentes facettes de la modélisation de l'activité neuronale pour proposer des versions contrôlées de différents modèles et étudier leur contrôle optimal.

Dans une première partie, nous définissons une version contrôlée des modèles déterministes de dimension finie, dits à conductances, dont font partie les modèles d'Hodgkin-Huxley et de Morris-Lecar. Cette version contrôlée se présente sous deux déclinaisons suivant le modèle de Channelrhodopsin-2 (ChR2, le canal ionique sensible à la lumière, implanté génétiquement dans les neurones). Pour ces modèles à conductances, nous étudions un problème de temps minimal pour obtenir un potentiel d'action en partant d'un état d'équilibre du système. Le problème de contrôle optimal résultant est un problème de temps minimal pour un système affine mono-entrée dont nous étudions les singulières. Nous appliquons une méthode numérique directe pour observer les trajectoires et contrôles optimaux. Cela nous permet de comparer les deux modèles de ChR2 envisagés, ainsi que les modèles à conductances entre eux, à travers leur comportement face au contrôle optogénétique. Le contrôle optogénétique apparaît alors comme une nouvelle façon de juger de la capacité des modèles à conductances de reproduire les caractéristiques de la dynamique du potentiel de membrane, observées expérimentalement.

Dans une deuxième partie, nous définissons un modèle stochastique en dimension infinie pour prendre en compte le caractère aléatoire des mécanismes des canaux ioniques et la propagation des potentiels d'action le long de l'axone. Le modèle prend la forme d'un processus de Markov déterministe par morceaux (PDMP) contrôlé, à valeurs dans un espace de Hilbert. Nous établissons un cadre théorique pour définir une large classe de PDMPs contrôlés en dimension infinie, dans laquelle le contrôle intervient dans les trois caractéristiques locales du PDMP, et dont fait partie le modèle d'Optogénétique. Nous prouvons le caractère fortement Markovien des processus ainsi définis et donnons leur générateur infinitésimal. Nous traitons un problème de contrôle optimal à horizon de temps fini. Nous introduisons des contrôles relâchés, étudions le processus de décision Markovien

(MDP) inclus dans le PDMP et montrons l'équivalence des deux problèmes. L'application du principe de programmation dynamique sur le MDP permet de donner des conditions suffisantes pour que le MDP soit contractant, assurant ainsi l'existence de contrôles optimaux relâchés pour le MDP, et donc aussi pour le PDMP initial. Nous donnons ensuite des hypothèses de convexités suffisantes à l'existence de contrôles optimaux ordinaires. Le cadre assez large du modèle théorique nous permet de discuter de nombreuses variantes pour le modèle d'Optogénétique stochastique en dimension infinie. Enfin, nous étudions l'extension du modèle à un espace de Banach réflexif, puis, dans un cas particulier, à un espace de Banach non réflexif.

Mots-clés

Processus de Markov déterministes par morceaux, contrôle optimal, équations aux dérivées partielles, contrôles relâchés, processus de Markov décisionnels, programmation dynamique, systèmes de contrôles déterministes affines, problème de temps minimal, méthodes directes, modèles de neurones, Optogénétique.

Optimal control of deterministic and stochastic neuron models, in finite and infinite dimension. Application to the control of neuronal dynamics via Optogenetics.

Abstract

The aim of this thesis is to propose different mathematical neuron models that take into account Optogenetics, and study their optimal control. Optogenetics allows to genetically modify targeted neurons to give them light sensitivity. Exposure to a specific wavelength then triggers action potentials, without any external electrical stimulation. There are several ways to model the dynamics of a neuron membrane potential. The first deterministic models soon coexisted with stochastic models, introduced to reflect the stochastic nature of the opening and closing mechanisms of ion channels. When the action potential propagation along the axon is considered, the finite-dimensional models become infinite-dimensional. We want to take into account those different aspects of the modeling of neuronal activity to propose controlled versions of several models and to study their optimal control.

In a first part, we define a controlled version of finite-dimensional, deterministic, conductance based neuron models, among which are the Hodgkin-Huxley model and the Morris-Lecar model. This controlled version comprises in fact two models, depending on two Channelrhodopsin-2 models (ChR2, the light-sensitive ion channel, genetically implanted in neurons). For these controlled conductance-based models, we study the optimal control problem that consists in steering the system from equilibrium to an action potential, in minimal time. The control system is a single-input affine system and we study its singular extremals. We implement a direct method to observe the optimal trajectories and controls. It allows us to compare the two ChR2 models considered, and also the conductance-based models. The optogenetic control appears as a new way to assess the capability of conductance-based models to reproduce the characteristics of the membrane potential dynamics experimentally observed.

In a second part, we define an infinite-dimensional stochastic model to take into account the stochastic nature of the ion channel mechanisms and the action potential propagation along the axon. The model is a controlled piecewise deterministic Markov process (PDMP), taking values in an Hilbert space. We design a theoretical framework to define a large class of infinite-dimensional controlled PDMPs, in which the control acts on the three local characteristics of the PDMP, and in which belongs the optogenetic model. We prove that the resulting process is strongly Markovian and we give its infinitesimal generator. We address a finite time optimal control problem. We define relaxed controls for this class of processes and we study the Markov decision process (MDP) embedded in the PDMP. We show the equivalence of the two control problems. We apply dynamic programming on the MDP and give sufficient conditions under which it is contracting. Those conditions ensure the existence of a relaxed optimal control for the MDP, and thus, for the initial PDMP as well. We also give sufficient convexity assumptions to obtain ordinary optimal controls. The theoretical framework is large enough to consider several modifications of the infinite-dimensional stochastic optogenetic model. Finally, we study the extension of the model to a reflexive Banach space, and then, on a particular case, to a nonreflexive Banach space.

Keywords

Piecewise deterministic Markov processes, optimal control, partial differential equations, relaxed controls, Markov decision processes, dynamic programming, deterministic affine control systems, minimal time problems, direct methods, neuron models, Optogenetics.

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Introduction

The aim of this thesis is to introduce, study and control some deterministic and stochastic mathematical models that take into account the effect of Optogenetics on the dynamics of the membrane potential of excitable cells, and especially neurons. Said very roughly, Optogenetics allows to control excitable cells via light stimulation. Via the optimal control of the mathematical models we introduce, we address the two main following questions.

> *Starting from equilibrium, how fast can we make a neuron spike by light stimulation ?*
>
> *Are we capable to design a light stimulation input to obtain any given membrane potential output ?*

We have worked in two directions. On the one hand, we studied the time optimal control of finite-dimensional deterministic models of neurons with genetically modified channels. In this part we investigated existence of singular controls, both theoretically and numerically. On the other hand, we considered infinite-dimensional controlled piecewise deterministic Markov processes models of neurons with a finite number of channels, some of them genetically modified. In this theoretical study, we proved existence of optimal controls for a finite time optimal control problem.

In this introduction, we recall the basic functioning of excitable cells and how they are usually mathematically modeled. We then present the field of Optogenetics and we stress out the main characteristics that need to be considered when modeling its effect on the membrane potential. This allows us to include an Optogenetics part to neuron models. In the second part of the Introduction, we present the mathematical tools used in our study and the main results of this Thesis.

0.1 Neuron models and Optogenetics

0.1.1 Neuronal dynamics and conductance-based models

Excitable cells, such as neurons, cardiac cells or muscle fibers, are capable of receiving and transmitting information via small electrical currents. This information is encoded in the difference of potential across the membrane of the cell, a lipid bilayer crossed by proteins called ion channels. This lipid bilayer serves as an insulator between the intracellular and the extracellular media and the membrane potential is due to the difference in the concentration of ions inside and outside the cell. The ion channels allow specific ions to float through the membrane and constitute thereby gates across the membrane. On the one hand, the opening of ion channels leads to a change in the concentration of ions inside and outside the cell and thus to a change of the membrane potential. On the other hand, the mechanisms governing the opening and the closing of the ion channels depend on the membrane potential around the channel and we call the ion channels voltage-gated for that reason. Selective channels are called by the name of the ions they let enter in the cell. We represent, on Figure 1 below, two types of selective voltage-gated ion channels.

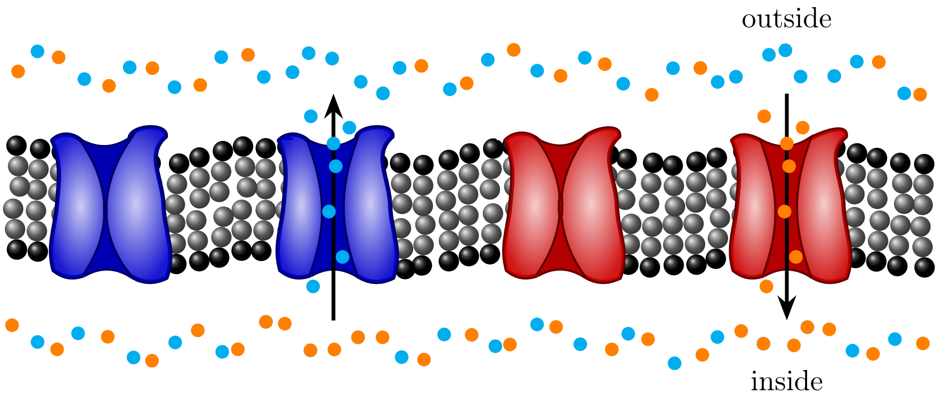


Figure 1 – Two types of selective ion channels across the lipid bilayer membrane of an excitable cell

Excitable cells have the particularity to possess a membrane potential threshold beyond which a fast and important increase of the membrane potential can take place, called an action potential, or a spike. Action potentials are generated by input signals in the soma and then propagate along the axon to trigger output signals at the synapses that become inputs for the connected neurons. On Figure 2 below is represented the basic morphology of a neuron.

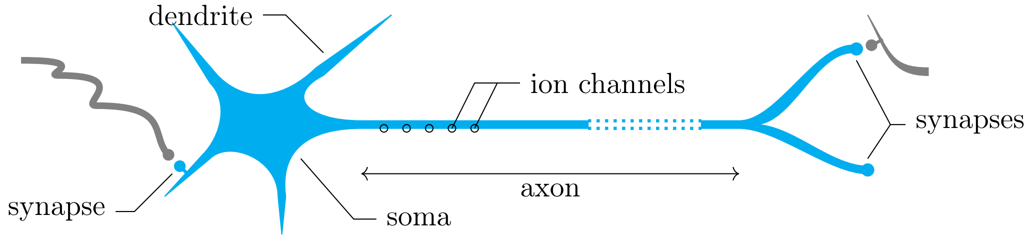


Figure 2 – Basic morphology of a neuron

Excitable cells can be stimulated by the application of an external electrical current, opening the way to the control of neural dynamics. This control plays a crucial part in understanding the role of a specific type of excitable cells inside a large population of different other types of cells, and thus also in fixing pathological behaviors. We can for instance mention pacemakers or brain electrical stimulation as methods based on electrical stimulation to cure pathological behaviors of the heart or the brain.

Because the understanding and control of neural dynamics is such a powerful tool in the investigation of the role of excitable cells, the modeling of those dynamics has received an increasing attention. Based on experimental data from the frog nerve electrical stimulation, Lapicque first introduced a simple electrical circuit representing the evolution of the membrane potential during stimulation [Lap07]. This principle of an equivalent electrical circuit has then been used by the Nobel prize recipients Hodgkin and Huxley to describe mathematically the dynamics of the membrane potential of the giant squid axon [HH52]. Many other models then followed to form the class of conductance-based models. Nevertheless, these first deterministic models fail to explain a fundamental experimental observation. When submitted to a repeated given input, the response of a single neuron is never exactly the same. This observation suggests that there exists a deep stochastic component in the biological mechanisms that generate and propagate action potentials. The widely adopted explanation for that randomness is the fact that the opening and closing of ion channels are subject to thermal noise, and are thus stochastic mechanisms ([CW96], [WKAK98]). The role of noise in neural dynamics has been deeply investigated in [Wai10]. We will recall later how the deterministic models can be viewed as limits of the stochastic models. The principle of the equivalent electrical circuit is the cornerstone to all the models, both deterministic and stochastic, finite and infinite-dimensional, that are studied hereafter. For this reason, let us now describe it in some detail in the case of the Hodgkin-Huxley model so that the incorporation of light-gated channels will be easily understood later. We will then be able to qualitatively and briefly describe what we consider to be the four main ways to model neural dynamics, that is deterministic and stochastic models, either finite-dimensional or infinite-dimensional, and the relations between them.

The lipid membrane of the giant squid axon is described by a capacitance $C > 0$. The voltage-gated ion channels in the Hodgkin-Huxley model can be of potassium (K^+) type or sodium (Na^+) type. They are represented by conductances $g_K > 0$ and $g_{Na} > 0$. The ion flows are driven by electrochemical gradients represented by batteries whose voltages $E_x \in \mathbb{R}$ equal the membrane potential corresponding to the absence of ion flow of type x. They are called equilibrium potentials in the sense that they correspond to the membrane potential for which the distribution of ions is uniform inside and outside the cell. The sign of the difference between the membrane potential and E_x gives the direction of the driving force.

The ion flow across the membrane generates the electrical current in the circuit, the possible movements of ions inside the cell being neglected. To each type x of ion channel is associated a macroscopic ion current I_x. The total membrane current is the sum of the capacitive current and all the ion currents considered. They include a leakage current that accounts for the passive flow of some other ions across the membrane. This current is associated to a fixed conductance g_L and will always be noted I_L. The macroscopic ion current I_K (resp. I_{Na}) is the result of the ion flow through all the ion channels of type K^+ (resp. Na^+). From these considerations, we can represent the equivalent electrical circuit on Figure 3 below.

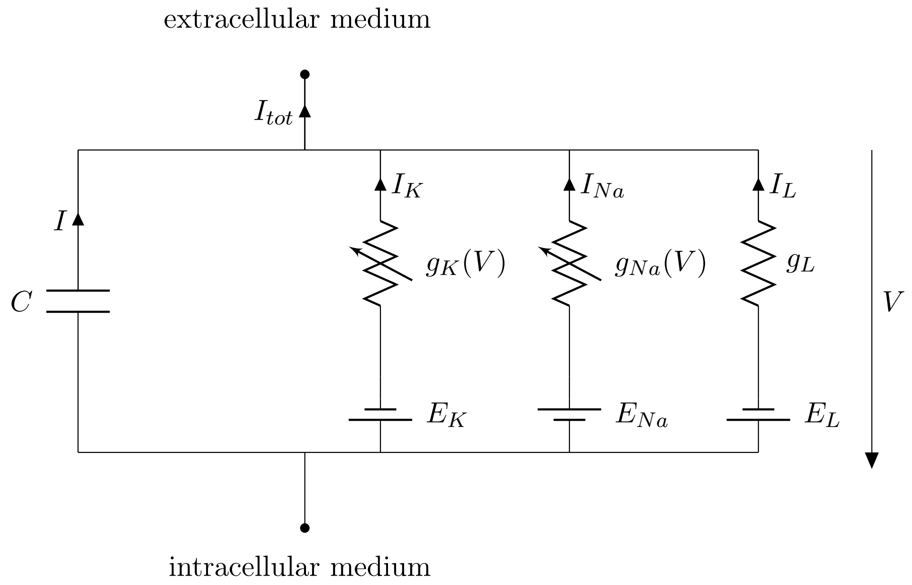


Figure 3 – Equivalent circuit for the Hodgkin-Huxley model

The total current I_{tot} is given by

$$I_{tot} = I + I_K + I_{Na} + I_L,$$

with $I = C\frac{\mathrm{d}V}{\mathrm{d}t}$.

Now, from this equivalent electrical circuit, the deterministic and stochastic models we are interested in essentially diverge in the way the conductances are modeled. To get a brief understanding of the situation, in stochastic models, the number of ion channels in the neuron is considered small enough for the thermal noise to have an impact on the evolution of the membrane potential. Ion channels are thus represented by finite-state pure jump processes with transitions depending on the membrane potential. Between jumps of these processes, the membrane potential follows the same deterministic dynamics as in deterministic models. For this reason, *Piecewise Deterministic Markov Processes* ([Dav84], [Dav93], [Jac06]), abbreviated PDMPs, appear to be the right class of stochastic processes to adopt. They are presented in detail in the mathematical part of this Introduction. In the case of deterministic models, the number of ion channels is considered large enough so that the opening probability of certain type of channel, rather than the opening probability of a single channel, becomes the relevant variable to account and the evolution of this opening probability is deterministic. In the case of the infinite-dimensional Hodgkin-Huxley model, it has been proved in [Aus08] that the deterministic model can be obtained by taking the limit of a stochastic model when the number of ion channels goes to infinity. Finite-dimensional models are obtained when the neuron is viewed as an isopotential compartment and the propagation along the axon is not considered. Infinite-dimensional models are derived from finite-dimensional ones by adding a diffusive term to the equation of evolution of the membrane potential, and ion channels are scattered along the axon.

0.1.2 Light-gated ion channels and Optogenetics mathematical modeling

We now present the field of Optogenetics, focusing on how light stimulation can be mathematically incorporated as a control in the models of excitable cells. Optogenetics is a recent but already thriving technique that allows to provoke or prevent electrical shocks in living tissues, by means of a suitable light stimulation ([Dei11],[Boy15],[Dei15]). A reliable control in a living tissue was successfully obtained for the first time in [BZB+05]. Since then, the number of publications on the subject, in the field of Biology, has literally blown up. Optogenetics has for principle the genetic modification of excitable cells for them to express various *rhodopsins*. Rhodopsins constitute a class of ion channels whose opening and closing are triggered by light stimulation. Optogenetics does not only come down to the mere photoexcitation or photoinhibition of targeted cells, it has to provide a gain or a loss of function for precise events. Hence, a millisecond-timescale temporal precision is required since it is the natural timescale of events such as action potentials or synaptic currents. Invasive electrical stimulation and the monitoring of induced activity in neurons was possible in intact brain tissues before Optogenetics. Nevertheless, some specific neurons are often buried deep into the tissue, making it almost impossible to assign a precise role to each class of neurons. That is what Optogenetics promises, as a non-invasive technique with high temporal resolution.

Being at the border of several disciplines, Optogenetics requires

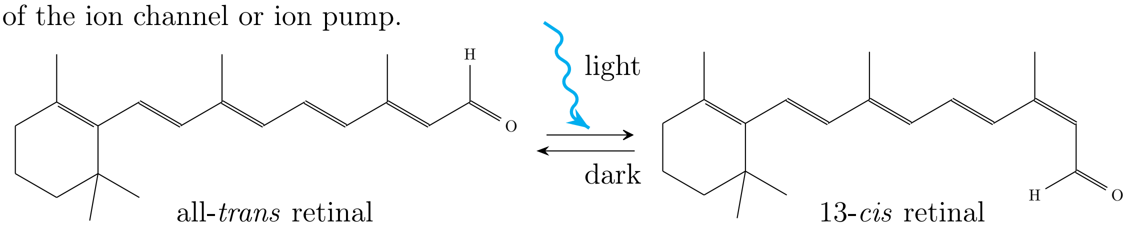
— control tools (rhodopsins) that can be administrated to specific cells,

— technologies to route the light (lasers, optic fibers),

— methods to follow the evolution of the implanted tools (fluorescent indicators, recordings of electrical activity).

We now enter in more detail into the biological description of the first point, the behavior of rhodopsins, so that the mathematical models adopted hereafter appear natural to the reader. Furthermore, we want to emphasize the main characteristics of this tools that are subject to changes in the future in order to provide robust models with respect to these characteristics.

A rhodopsin is the association of an opsin, a light-sensitive protein, and retinal, one of the three forms of vitamine A. It is the main brick of the mechanisms of vision. Some few words can be written here to apprehend the role of retinal in the opening mechanism of rhodopsins. Upon absorption of a photon, the all-*trans* retinal undergoes a conformational change to 13-*cis* retinal that modifies its spatial occupation. This modification, called isomerization and represented on Figure 0.1.2 below almost directly leads to the opening of the ion channel or ion pump.



Opsins are found throughout the whole living world and are involved in most photosensitive processes. Microbial opsins are different from their mammalian counterparts mainly because they constitute a single-component system, photosensitivity and ionic conductivity mechanisms are carried out by the same protein. The first microbial opsin identified, and the most studied one, is the proton pump called *Bacteriorhodopsin* (BR) [OS71], found in some single-celled mircroorgarnisms called *Archaea*. BR pumps protons from the cytoplasm to the extracellular medium and is thought to play various roles in cellular physiology. *Halorhodopsin* (HR) is a Chloride pump activated by yellow light stimulation, found in an *archaebacteria* [MYM77]. It distinguishes itself from BR by pumping Chloride ions from the extracellular medium into the cell. Finally, *Channelrhodopsin* (ChR1 and ChR2) is a third class of microbial opsins, identified in the green algae *Chlamydomonas reinhardtii*. If its structure is very close to the one of BR, its conductive activity is entirely decoupled from its photocycle. Each rhodopsin is sensitive to a specific wavelength and the exposition to a different wavelength produces no effect at all. This very important feature of light stimulation, compared to electrical stimulation, gives it an additional degree of freedom that can be exploited to carry out several stimulations at the same time, with different results.

If Optogenetics dates back to 1971, scientists did not believe in the use of microbial opsins for more than three decades, considering that these foreign proteins would be toxic for cells, that the photocurrents generated would be too weak and too slow to be useful and that the need to bind with retinal for the photon absorption would be a huge handicap. Since [BZB+05], it has been proved that BR, HR and ChR2 could all three trigger or inhibit relevant photocurrents in response to different light wavelengths. Besides, vertebrate tissues naturally contain retinal so that the optogenetic control is possible even in intact mammalian brains and in moving animals. Finally, viruses can be designed to administer the opsin to a specific population of neurons, leaving the others unmodified. This gives an extra advantage to Optogenetics over electrical stimulation in the investigation of neural functions since it can probe the role of a specific population of neurons whereas electrical stimulation has an effect on a whole tissue volume, regardless of the types of neurons it comprises.

Let us now add some words on the two specific rhodopsins that are the chloride pump NpHR and the cation channel ChR2, that respectively provide inhibition and excitation of excitable cells (see Figure 4).

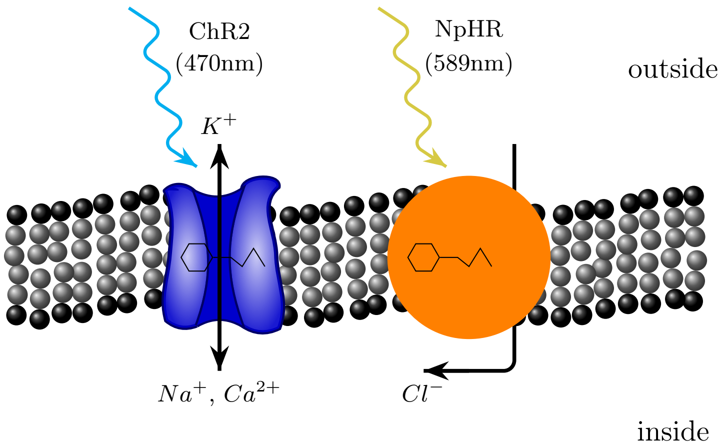


Figure 4 – Two types of selective ion channels across the lipid bilayer membrane of an excitable cell

ChR2 was independently identified by three research groups in 2002-2003 ([N$^+$02]-[N$^+$03], [SJS02], [S$^+$03]). When the all-*trans* retinal absorbs a photon, its isomerization induces the opening of the channel of at least 6 Å. In a few milliseconds, the retinal retakes its all-*trans* conformation and the channel closes. ChR2 is a non-selective cation channel that is permeable to Na^+, H^+, Ca^{2+}, and K^+ ions. Once this cation channel opens with the retinal isomerization, the ion flow becomes independent of this isomerization and rather depends on the closing kinetics of the channel. This will be a very important property for the mathematical modeling of a control. In this thesis, we will focus on the mathematical modeling of ChR2 which is nowadays the most used and studied photosensitive ion channel.

NpHR is an opsin from *Natronomonas pharaonis*, analogous to HR, that triggers hyperpolarizing currents with a pic of absorption at 590nm (yellow light). Since ChR2 has a pic of absorption at 470nm (blue light), the two complementary tools NpHR and ChR2 are entirely independent in neurons that would express both of them. An important difference between them is that, being a pump, NpHR requires a constant exposition to light to go through its photocycle, whereas Chr2 does not.

Scientists work on developing mutants of natural rhodopsins to improve five main characteristics:

1. The channel/pump conductance to get larger photocurrents. For example, the wild-type ChR2 conductance is estimated to be of 1pS, a value lower than the average conductance of usual ion channels.
2. The opening and closing kinetics of the channel/pump, in competition with the photosensitivity.
3. The photosensitivity of the channel/pump, in competition with kinetics.
4. The spectral response of the channel/pump, that is, the possibility to speed up the recovery from the desensitized phase by a second stimulation with a different wavelength.
5. The membrane expression of the channel/pump with a goal of a uniform distribution with adequate expression.

The stochastic models of Section 2 will be completely robust with regards to this characteristics in the sense that the mathematical results will not change upon a modification of the model to incorporate a change of any one of this characteristics.

Study of the photocycles to design a mathematical model

Because Optogenetics is a young science, there is almost no mathematical study up to now. We can nevertheless mention [WAK12] where a deterministic mathematical model of ChR2 is used in a dynamical model of cardiac cell for simulation purposes (finite elements method). We are deeply convinced that the mathematical modeling of Optogenetics, with optimal control goals, would be a great help for neuroscientists to go further in the understanding and thus the exploiting of Optogenetics tools. Furthermore, and it is probably one of the most important arguments in favor of a mathematical modeling, since electrical recordings are not altered by light stimulation, contrarily to what happens with electrical stimulation, inverse engineering of the photocurrent produced by Optogenetics could lead to closed-loop feedback controls opening great perspective in medecine. Psychiatrics deseases could for instance benefit a lot of a switch from invasive electrical stimulation to light stimulation, see for instance [AZA$^+$07] for narcolepsy or [LNC12] for depression.

The first step towards a mathematical modeling of Optogenetics is the design of a model for the mechanisms of the individual rhodopsins since they constitute an elementary brick in conductance-based models. This modeling has been quickly addressed by neuroscientists ([HSG05], [BPGH10]). It is based on the study of the rhodopsin photocycles, the different steps of the reaction induced by the absorption of a photon. In few words, voltage-clamp experiments, in which the membrane potential of the studied cell is held constant, allow to record the evolution of the rhodopsin conductance while exposed to light. This recording is based on the acceptance of Ohm's law (for the rhodopsin) so that the recording of the photocurrents produced gives a direct access to the conductance of the rhodopsin. Upon these quantitative experimental observations can be proposed reaction schemes that describe the photocurrent kinetics. As a classical ion channel, during a photocycle, the rhodopsin goes through several states that can be either open or close. Any model that can account for the experimental observations can then be used to propose a mathematical model. In the case of the ChR2, the onset of light is quickly followed by a peak conductance and then a smaller steady-state conductance. Upon a second stimulation, the peak is smaller. In [NGG+09] were introduced two models for ChR2, represented on Figures 5 and 6.

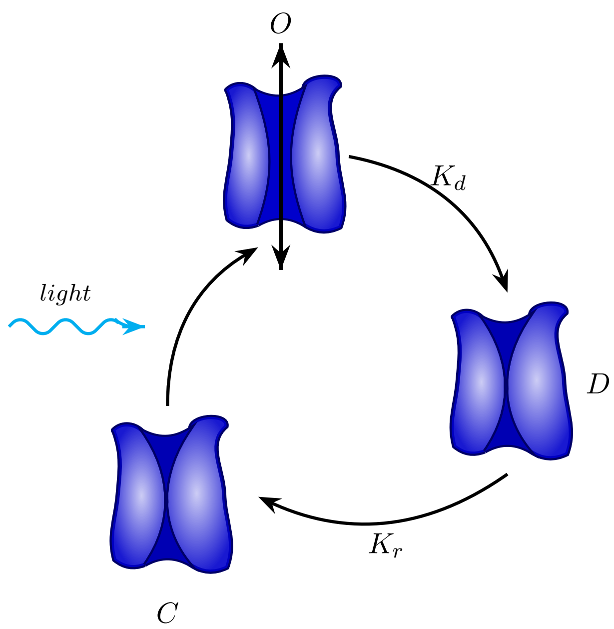


Figure 5 – Reaction scheme for a three-state model of Channelrhodopsin-2 with an open state O and two closed states D and C.

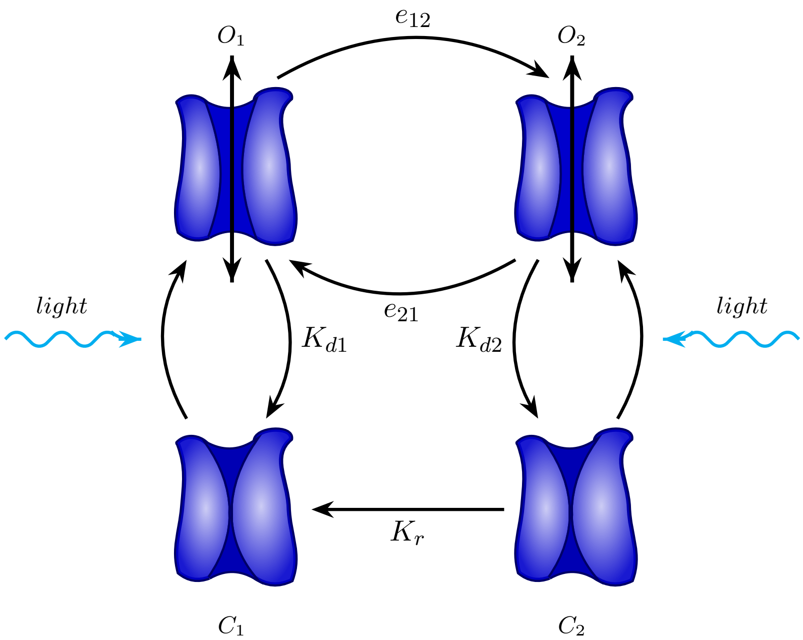


Figure 6 – Reaction scheme for a four-state model of Channelrhodopsin-2 with two open states O_1 and O_2, and two closed states C_1 and C_2.

We want to end our introduction on Optogenetics by expressing some concerns and thoughts. There is no doubt that Optogenetics is already a great tool to go deeper in the understanding of a number of poorly understood and treated diseases, from Alzheimer's disease to Parkinson's disease and epilepsy, among many others. If the medical perspectives are vast, the economical ones are of course even vaster. For these reasons, scientists are literally jumping on applications of Optogenetics. Nevertheless, we regret a bit that it might be at the expense of a deeper understanding of the tool itself. Many mutants are created but hardly studied and the modeling of the associated photocurrents forsaken. The mathematical study of neuron dynamical models has been an undeniable help in the understanding of neural dynamics and we are deeply convinced that the mathematical optimal control study of optogenetic models could be of much help as well and this study needs a preliminary fine modeling of photocurrents. Finally, since Optogenetics opens the way to the control of the brain, ethical preoccupations should always be of great concern when considering applications of Optogenetics. For instance, back to the example of narcolepsy and depression mentioned above, if Optogenetics could eventually cure these problems, how far fetched would it be to imagine optogenetic tools that would make an entire group of people sleep, or angry instead of not depressed ? If this type of question may seem a bit extravagant now, we think that it should be addressed by people dealing with Optogenetics.

0.2 Mathematical tools

In this section, we present some results in various fields of mathematics that we need in our thesis. We begin with a brief but important presentation of optimal control theory. Namely, we introduce results in the case of deterministic finite-dimensional optimal control that will be used in Section 1. Then, we present the framework of infinite-dimensional PDMPs. Since the optimal control problem that we will formulate on a class of infinite-dimensional PDMPs in Chapter 2 will involve dynamic programming on a discrete-time *Markov Decision Process* (MDP), we also write a few results on that subject here.

0.2.1 Finite-dimensional deterministic optimal control

Here we define the optimal control problem on a deterministic finite-dimensional system and introduce all notations and vocabulary used latter in the Thesis. We give some general first-order necessary conditions in the form of the *Pontryagin Maximum Principle* and some sufficient convexity conditions to obtain existence of optimal controls. When these convexity conditions are not fulfilled, it may happen that an optimal control does not exist. To tackle this problem, we then introduce the class of relaxed controls on an elementary example. This class will be needed in Chapter 2. We also discuss the case of affine control systems, which will be the framework of Chapter 1 and we introduce the role of singular trajectories. Finally, we present the *Goh* transformation that will also be used in Chapter 1.

The optimal control problem and the Pontryagin maximum principle

Let $T \in \mathbb{R}_+^*$, $x_0 \in \mathbb{R}^n$, and a metric space U be given. We consider the *control system* in $\mathbb{R}^n$

$$\begin{cases} \dot{x}(t) = b(t, x(t), u(t)), & \text{a.e. } t \in [0,T], \\ x(0) = x_0, \end{cases} \tag{1}$$

where $b : [0,T] \times \mathbb{R}^n \times U \to \mathbb{R}^n$ is a given map. A measurable map $u(\cdot) : [0,T] \to U$ is called a *control*, x_0 is called the *initial state*, and $x(\cdot)$, a solution of (1), is called a *state trajectory* corresponding to $u(\cdot)$. In all applications, to any $x_0 \in \mathbb{R}^n$ and any control $u(\cdot)$ will correspond a unique solution $x(\cdot)$ to (1). We hence refer to (1) as a *input-output relation* with *input* $u(\cdot)$ and *output* $x(\cdot) \equiv x(\cdot; u(\cdot))$. Let M be a subset of $\mathbb{R}^n$ that will represent the target set of the state trajectory. Constraints on the state variable and the control could be added but we will not consider this case since it will not appear in the following applications. We introduce the space of *feasible* controls

$$\mathcal{U}([0,T]) := L^\infty(0,T;U) = \{u : [0,T] \to U \mid u(\cdot) \text{ is bounded}\}.$$

Furthermore, we are given a *cost functional* that measures the performance of a control

$$J(t,u)=\int_0^t f(s,x(s),u(s))\mathrm{d}s+h(x(t)) \tag{2}$$

where $f:[0,T]\times\mathbb{R}^n\times U\to\mathbb{R}^n$ and $h:\mathbb{R}^n\to\mathbb{R}$ are given maps, the first and second terms on the right-hand side of (2) being called, respectively, the *running cost* and the *terminal cost*. The cost functional is well defined on the space of feasible controls.

Definition 0.2.1. *A control $u(\cdot)$ is called an admissible control, and $(x(\cdot),u(\cdot))$ an admissible pair, if*

(i) $u(\cdot)\in\mathcal{U}([0,T])$*;*

(ii) $x(\cdot)$ *is the unique solution of (1) under* $u(\cdot)$ *and* $x(T)\in M$*;*

The set of all admissible controls is denoted by $\mathcal{U}_{ad}([0,T])$. We now state the optimal control problem for this finite-dimensional deterministic control system.

Problem (D). Minimize $J(T,u)$ over $\mathcal{U}_{ad}([0,T])$.

Problem (D) is said to be *finite* if (2) has a finite lower bound, and is said to be *(uniquely) solvable* if there is a (unique) $\bar{u}(\cdot)\in\mathcal{U}_{ad}([0,T])$ such that

$$J(T,\bar{u})=\inf_{u(\cdot)\in\mathcal{U}_{ad}([0,T])}J(T,u). \tag{3}$$

Any $\bar{u}(\cdot)\in\mathcal{U}_{ad}([0,T])$ satisfying (3) is called an *optimal control* and the corresponding state trajectory $\bar{x}(\cdot)\equiv x(\cdot;\bar{u}(\cdot))$ and $(\bar{x}(\cdot),\bar{u}(\cdot))$ are respectively called an *optimal state trajectory* and an *optimal pair*.

To state the Pontryagin maximum principle, we will assume the following

(D1) (U,d) is a separable metric space.

(D2) The maps $b:[0,T]\times\mathbb{R}^n\times U\to\mathbb{R}^n$, $f:[0,T]\times\mathbb{R}^n\times U\to\mathbb{R}$ and $h:\mathbb{R}^n\to\mathbb{R}$ are measurable, and there exist a constant $l>0$ and a modulus of continuity $\bar{\omega}:[0,\infty)\to[0,\infty)$ such that for $\varphi(t,x,u)=b(t,x,u),f(t,x,u),h(x)$, we have

$$\begin{cases}|\varphi(t,x,u)-\varphi(t,\hat{x},\hat{u})|\le l|x-\hat{x}|+\bar{\omega}(d(u,\hat{u})),\\ \qquad\qquad\qquad\qquad \forall t\in[0,T],\quad x,\hat{x}\in\mathbb{R}^n,\quad u,\hat{u}\in U,\\ |\varphi(t,0,u)|\le l, \qquad\qquad \forall(t,u)\in[0,T]\times U.\end{cases} \tag{4}$$

(D3) The maps b, f and h are C^1 in x, and there exists a modulus of continuity $\bar{\omega}:[0,\infty)\to[0,\infty)$ such that for $\varphi(t,x,u)=b(t,x,u),f(t,x,u),h(x)$, we have

$$\begin{aligned}&|\varphi_x(t,x,u)-\varphi_x(t,\hat{x},\hat{u})|\le\bar{\omega}(|x-\hat{x}|+d(u,\hat{u})),\\ &\qquad\qquad\qquad\qquad \forall t\in[0,T],\quad x,\hat{x}\in\mathbb{R}^n,\quad u,\hat{u}\in U,\end{aligned} \tag{5}$$

with φ_x the partial derivative of x with respect to the state variable.

Under (D1)-(D2), (1) admits a unique solution and $\mathcal{U}_{ad}([0,T]) = \mathcal{U}([0,T])$.

Theorem 0.2.1. *(see [PBGM74], [Tré08, Theorem 7.2.1]) Let (D1)-(D3) hold. Let $(\bar{x}(\cdot), \bar{u}(\cdot))$ be an optimal pair of Problem (D). Then there exist an absolutely continuous map $p(\cdot) : [0,T] \to \mathbb{R}^n$, called adjoint vector, and a real number $p^0 \leq 0$, such that the pair $(p(\cdot), p^0)$ is nontrivial, and such that, for almost all $t \in [0,T]$,*

$$\begin{aligned} \dot{\bar{x}}(t) &= \frac{\partial H}{\partial p}(t, \bar{x}(t), p(t), p^0, u(t)), \\ \dot{p}(t) &= -\frac{\partial H}{\partial x}(t, \bar{x}(t), p(t), p^0, u(t)), \end{aligned} \tag{6}$$

where

$$H(t, x, p, p^0, u) = \langle p, b(t, x, u) \rangle + p^0 f(t, x, u)$$

is the system's Hamiltonian and we have the maximum condition almost everywhere in $[0,T]$

$$H(t, \bar{x}(t), p(t), p^0, \bar{u}(t)) = \max_{v \in U} H(t, \bar{x}(t), p(t), p^0, v). \tag{7}$$

If moreover, the final time to reach the target set M is not fixed, we have the condition, called tranversality condition on the Hamiltonian, at the final time T

$$\max_{v \in U} H(T, \bar{x}(T), p(T), p^0, v) = 0. \tag{8}$$

If moreover, the control system is autonomous, i.e. if b and f does not depend on t, then H do not depend on t, and we have

$$\forall t \in [0,T], \qquad \max_{v \in U} H(\bar{x}(t), p(t), p^0, v) = Cst,$$

so that if the final time is not fixed, (8) becomes

$$\forall t \in [0,T], \qquad \max_{v \in U} H(\bar{x}(t), p(t), p^0, v) = 0.$$

If moreover, M is a manifold of $\mathbb{R}^n$ with tangent space $T_{\bar{x}(T)}M$ at $\bar{x}(T) \in M$, then the adjoint vector can be constructed so as to satisfy the tranversality condition

$$p(T) \perp T_{\bar{x}(T)}M, \tag{9}$$

called transversality condition on the adjoint vector.

Remark 0.2.1. *If the manifold takes the form*

$$M = \{x \in \mathbb{R}^n \mid F_1(x) = \cdots = F_k(x) = 0\},$$

where the functions F_i are of class C^1 on $\mathbb{R}^n$, then condition (9) takes the form

$$\exists\, \kappa_1, \ldots, \kappa_k \in \mathbb{R},\, p(T) = \sum_{i=1}^{k} \kappa_i \nabla F_i(\bar{x}(T)).$$

An infinite-dimensional version of Theorem 0.2.1 can be found in [LY95] for *Partial Differential Equations* (PDEs), a stochastic version in [YZ99] for *Stochastic Differential Equations* (SDEs) and an infinite-dimensional stochastic version in [LZ14] for *Stochastic Partial Differential Equations* (SPDEs).

Definition 0.2.2. *An extremal of the optimal control problem is the quadruple $(x(\cdot), p(\cdot), p^0, u(\cdot))$ solution to equations (6) and (7). If $p^0 = 0$, the extremal is called abnormal, and if $p^0 \neq 0$ the extremal is called normal.*

Remark 0.2.2. *If $M = \mathbb{R}^n$, i.e. there is no target set, an extremal of the optimal control problem is necessarily normal, because of the transversality condition (9) and the nontriviality of $(p(\cdot, p^0))$, and we can set $p^0 = -1$. When the target set does not cover the whole state space, abnormal optimal extremal may exist, for instance if there is only one state trajectory joining the initial state and the target set, see also [LS12, Section 2.6.4] for the study of the harmonic oscillator which present strictly abnormal extremals.*

Convexity assumptions and existence of optimal controls

We now give some convexity conditions that ensure existence of optimal controls. When these conditions are not fulfilled, optimal controls may not exist and we present an elementary example of such a situation. The solution to overcome that problem is then presented in the form of relaxed controls.

(DE1) U is a compact subset of $\mathbb{R}^k$, $k \in \mathbb{N}^*$, and $M = \mathbb{R}^n$ (*i.e.* there is no target set).

(DE2) For every $(t, x) \in [0, T] \times \mathbb{R}^n$, the epigraph of extended velocities

$$(b, f)(t, x, U) := \{(b_i(t, x, u), f(t, x, u) + \gamma) \mid u \in U, \quad i = 1, 2, \ldots, n, \quad \gamma \geq 0\}$$

is a convex set of $\mathbb{R}^{n+1}$.

Theorem 0.2.2. *(see [Tré08, Theorem 6.2.1], [YZ99, Theorem 5.1 p66]) Under (DE1), (D2) and (DE2), if Problem (D) is finite, then it admits an optimal control.*

Non-convex problems and relaxed controls.

We now give an example where assumption (DE2) is not fulfilled and there is no optimal control. Consider the control system on $\mathbb{R}$ defined by

$$y'(t) = u(t), \qquad y(0) = 0, \tag{10}$$

with control space $U := \{-1\} \cup \{1\}$, time horizon $T := 1$, and cost function

$$y_0(t,u) = \int_0^t y(s)^2 \mathrm{d}s. \tag{11}$$

For this control system, there exist minimizing sequences, for instance

$$u^n(t) := \begin{cases} 1 & t \in [2k/n, (2k+1)/n), \\ -1 & t \in [(2k+1)/n, (2k+2)/n), \end{cases}$$

in the sense that

$$u^n \in \mathcal{U}([0,T]) \quad \forall n \in \mathbb{N}^*, \text{ and } \lim_{n\to\infty} y_0(1,u^n) = 0.$$

Nevertheless, assumption (DE2) is not fulfilled and it is easy to see that there does not exist an optimal control for this problem since the minimizing control $u \equiv 0$ does not belong to $\mathcal{U}([0,T])$. To solve this problem, instead of looking at controls as functions taking values in the control set U, we consider controls μ whose values are probability measures in U. This process consists indeed in convexifying the control set U so that convexity assumptions are fulfilled with this new control set. Since $U = \{-1\} \cup \{1\}$, these measures are $\mu(t) = a(t)\delta_1 + (1 - a(t))\delta_{-1}$, $0 \leq a(t) \leq 1$. With the new control space, the dynamics becomes

$$y'(t) = \int_U u\mu(t, \mathrm{d}u), \qquad y(0) = 0. \tag{12}$$

The cost function does not change since it does not depend directly on the control. The enlarged control space contains the original one and an original control $u(\cdot) \in \mathcal{U}_{ad}([0,T])$ can be obtained from a relaxed one by setting $a(t) = 1$ when $u(t) = 1$ and $a(t) = 0$ when $u(t) = 0$. In the enlarged control space, an optimal control exists and takes the form

$$\mu(t) = \frac{1}{2}\delta_1 + \frac{1}{2}\delta_{-1}.$$

When enlarging a control space, special care has to be taken so that every relaxed control can be approached by original ones. To do so, a topology has to be put on the relaxed control space. In finite dimension, the right topology to consider is called the Young topology and we recall now its construction. Relaxed controls have been introduced by Warga ([War62b], [War62a]) and Gamkrelidze ([Gam87]) as an extension to control problems of Young measures ([You69]) from the calculus of variations.

Let $X = L_1([0,T]; C(U))$ be the set of functions $f(t,u)$, measurable in t, continuous in u, such that

$$||f||_X := \int_0^T \sup_{u\in U} |f(t,u)| dt < \infty.$$

$(X, ||\cdot||_X)$ is a Banach space. Its dual space is $X^* = L_\infty([0,T], C^*(U))$ with norm

$$||v||_* = \operatorname*{ess\,sup}_{t\in[0,T]} ||v_t||_{C^*} < \infty.$$

The topology to consider on X^* is the *weak* topology* under which a sequence (v^n) of elements of X^* converges to $v \in X^*$ if and only if $(v^n, f) \to (v, f)$ for all $f \in X$, with duality pairing defined by

$$(v, f) = \int_0^T \int_U f(t,u) v_t(du) dt.$$

For the *weak* topology* the unit ball $B_1 = \{v \in X^* : ||v||_* \leq 1\}$ is compact by Alaoglu's Theorem.

We denote by $\mathcal{R}([0,T])$ the set of relaxed controls defined by:

$$\mathcal{R}([0,T]) := \{\mu : [0,T] \to \mathcal{P}(U) \text{ measurable}\},$$

where $\mathcal{P}(U)$ is the set of all probabilities on U. It can be shown that $\mathcal{R}([0,T])$ is a closed subset of B_1 and thus is compact. Actually we even have $||v||_* = 1$ for all $v \in \mathcal{R}([0,T])$. The Young topology $\mathcal{Y}$ is then defined as the relative weak* topology of $\mathcal{R}([0,T])$ considered as a subset of B_1. Thus $(\mathcal{R}([0,T]), \mathcal{Y})$ is a compact space. It can be shown that the set $\mathcal{U}([0,T])$ of ordinary controls is dense in $\mathcal{R}([0,T])$ with respect to this topology ([Gam87, Theorem 3.2]). Moreover, the solution of the relaxed control system

$$\begin{cases} \dot{x}(t) = \displaystyle\int_U b(t, x(t), u)\mu(t, \mathrm{d}u), & \text{a.e. } t \in [0,T], \\ x(0) = x_0, \end{cases} \tag{13}$$

is continuous in the control as stated by the following Theorem.

Theorem 0.2.3. *(see Warga [War72]) Assume that b is bounded and Lipschitz continuous on $\mathbb{R}^n$, uniformly in $[0,T] \times U$. Take $\mu \in \mathcal{R}([0,T])$, and let ϕ be the unique solution of the relaxed control system*

$$\phi'(t) = \int_U b(t, \phi(t), u)\mu(t, \mathrm{d}u), \quad \phi(0) = x \in \mathbb{R}^n.$$

Then the map $(x, \mu) \to \phi$ is continuous from $\mathbb{R}^n \times \mathcal{R}([0,T]) \to C([0,T]; \mathbb{R}^n)$ for any $T \in \mathbb{R}_+$, with $C([0,T]; \mathbb{R}^n)$ the space of continuous function on $[0,T]$, with values in $\mathbb{R}^n$, endowed with the uniform norm.

The infinite-dimensional analogue of Theorem 0.2.3 will be a key result in Chapter 2.

Affine control systems, singular extremals and the Goh transformation

Affine control systems are special cases where the function $b : [0,T] \times \mathbb{R}^n \times U \to \mathbb{R}^n$ takes the form

$$b(t,x,u) = b_0(t,x) + ub_1(t,x), \qquad (t,x,u) \in [0,T] \times \mathbb{R}^n \times U, \tag{14}$$

with $b_0, b_1 : [0,T] \times \mathbb{R}^n \to \mathbb{R}^n$. Let us consider the optimal control problem with free time horizon t_f of the affine control system defined by (1) and (14) and the cost functional $J(t,u) = t$ defined by (2) with $f \equiv 1$ and $h \equiv 0$. Suppose furthermore that the control space U is a segment of $\mathbb{R}$ for this particular example, $U = [u_{min}, u_{max}]$ with $u_{min} < u_{max}$. For this problem, the Hamiltonian of the system writes

$$H(t,x,p,p^0,u) = \langle p, b_0(t,x)\rangle + u\langle p, b_1(t,x)\rangle + p^0,$$

so that the maximum condition (7) leads to the optimal control

$$\bar{u}(t) = u_{min}\mathbf{1}_{\varphi(t)<0} + u_{max}\mathbf{1}_{\varphi(t)\geq 0} \tag{15}$$

whenever the function $\varphi(t) := \langle p(t), b_1(t,\bar{x}(t))\rangle$, called *switching function*, does not vanish on any subinterval of $[0,t_f]$, $\mathbf{1}_B$ being the indicator function of a subset B of $\mathbb{R}_+$. Such a control is called *bang-bang*, it alternates between minimum and maximum values of U, with switching times given by the sign changes of the switching function φ. An extremal of the system such that the switching function vanishes on a subinterval I of $[0,t_f]$ is called singular. If the associated control is optimal, it is called a singular optimal control. Singular optimal controls exist and their investigation is of critical importance when dealing with time optimal affine control problems. The term singular can be understood if we replace the case of affine control system in the general theory of optimal control. Indeed, the switching function φ can be expressed as the first order derivative of the Hamiltonian with respect to the control variable

$$\varphi(t) = \frac{\partial H}{\partial u}(t,\bar{x}(t),p(t),p^0,\bar{u}(t))$$

and the condition $\varphi(t) = 0$ corresponds to the first-order necessary condition for the Hamiltonian to have a maximum in the interior of the control set U. Now, for a general optimal control problem, an extremal is called singular over an open interval I if the first-order necessary condition

$$\frac{\partial H}{\partial u}(t,\bar{x}(t),p(t),p^0,\bar{u}(t)) = 0$$

is satisfied for $t \in I$, and if the matrix of the second-order partial derivatives,

$$\frac{\partial^2 H}{\partial u^2}(t, \bar{x}(t), p(t), p^0, \bar{u}(t))$$

is singular. This matrix is a real number for single-input control system and a real matrix for *multi-input* control systems, that is when the control set U is a subset of $\mathbb{R}^k$ with $k \geq 2$. In the case of minimal time single-input control problems, the second-order partial derivative is always 0 so that any optimal control that takes values in the interior of the control set is singular. Finally, singular controls are also, and equivalently defined via the *end-point mapping* E_T defined on $\mathcal{U}([0,T])$ by

$$E_T(u) := x(T),$$

with $x(\cdot)$ the solution of (1) with $u \in \mathcal{U}([0,T])$. A control $u \in \mathcal{U}([0,T])$ is said to be singular if u is a critical point of the end-point mapping E_T, i.e. its differential at u, $DE_T(u)$, is not surjective.

We now develop an elementary example of a singular optimal control and then introduce the Goh transformation as a tool to simplify the investigation of the existence of singular extremals. Consider the control system

$$\begin{cases} \dot{x}_1(t) = 1 - x_2^2(t) \\ \dot{x}_2(t) = u(t), \end{cases}$$

with the control $u(\cdot)$ taking values in $[-1,1]$ and consider the minimal time control problem that consists in steering the system from the origin to $(1,0)$ in minimal time. It is easy to see that the optimal control is here constant and equals 0 with a minimal time of 1. Indeed, if the control is not 0 then x_2^2 becomes strictly positive, which slows down x_1. This optimal control is singular and corresponds to the vanishing of the switching function as we see now. The Hamiltonian of the system writes

$$H(x, p, p^0, u) = p_1(1 - x_2^2) + p_2 u + p^0,$$

and the adjoint system is

$$\begin{cases} \dot{p}_1(t) = 0 \\ \dot{p}_2(t) = 2p_1(t)x_2(t), \end{cases}$$

The switching function is $\varphi(t) = p_2(t)$. The optimal trajectory corresponds to $x_2 \equiv 0$ so that $\dot{p}_2 \equiv 0$. Since the target set is reduced to a single point, tranversality conditions on the adjoint variable at the final time are void and we can take $p_2(1) = 0$ and $p_1(1) \neq 0$ to respect the Pontryagin maximum principle, so that φ vanishes along the optimal trajectory.

The Goh transformation allows to reduce the dimension of the control system to simplify the study of singular extremals as we explain now.

Assume that there is no constraint whatsoever on the control space U and that the control $u(\cdot)$ can be taken as regular as needed. Then, every control system in $\mathbb{R}^n$ can be viewed as an affine control system in $\mathbb{R}^{n+1}$ with respect to a new control v if we set $\dot{u} = v$. If the original control system is defined by (1), then the associated affine control system is

$$\begin{cases} \dot{y}(t) = \tilde{b}_0(t, y(t)) + v(t)\tilde{b}_1(t, x), & \text{a.e. } t \in [0, T], \\ y(0) = y_0 \in \mathbb{R}^n, \end{cases} \tag{16}$$

with $y(\cdot) = (x(\cdot), u(\cdot))$, $\tilde{b}_0(\cdot) = (b(\cdot), 0)$ and $\tilde{b}_1(\cdot) \equiv (0, \ldots, 0, 1) \in \mathbb{R}^{n+1}$. The converse transformation is called the Goh transformation and will play a crucial role in the investigation of singular trajectories in Chapter 1. The next definition formalizes this transformation.

Definition 0.2.3. *Consider the autonomous affine single-input control system of $\mathbb{R}^n$, $\dot{x} = b_0(x) + ub_1(x)$, and assume that $n \geq 2$. Let $x_0 \in \mathbb{R}^n$ such that $b_1(x_0) \neq 0$. There exists an open set E containing x_0 such that $b_{1|E} = (0, \ldots, 0, 1)$, $(x^1, \ldots, x^n)$ are coordinates of $\mathbb{R}^n$, and the restriction of the control system to E can be written as*

$$\dot{x}' = b'(x', x^n), \qquad \dot{x}^n = b^n(x) + u,$$

where $x' = (x^1, \ldots, x^{n-1})$, and $b' : \mathbb{R}^n \to \mathbb{R}^{n-1}$, $b^n : \mathbb{R}^n \to \mathbb{R}$ are such that $b_0 = (b', b^n)$. The system $\dot{x}' = b'(x', x^n)$, where x^n is the control variable and which is defined on an open set E' of $\mathbb{R}^{n-1}$, is called the reduced control system associated with the original one. If $H = \langle p, b_0(x) + ub_1(x)\rangle$ is the Hamiltonian of the original control system, we set $H'(x', p', x^n) = \langle p', b'(x', x^n)$, where $p' = (p_1, \ldots, p_{n-1})$ is the adjoint vector of x'.

The singular extremals of the control system and the reduced control system are linked by the following Lemma (see [BdM98]).

Lemma 0.2.1. *The pair (x, p) is the projection of a solution (x, p, u) of*

$$\dot{x} = \frac{\partial H}{\partial p}, \quad \dot{p} = -\frac{\partial H}{\partial x}, \quad \langle p, b_1(x)\rangle = 0,$$

if and only if (x', p', x^n) is a solution of

$$\dot{x}' = \frac{\partial H'}{\partial p'}, \quad \dot{p'} = -\frac{\partial H'}{\partial x'}, \quad \frac{\partial H'}{\partial x^n} = 0.$$

Moreover the following relations are satisfied

(i)

$$\left(\frac{\mathrm{d}}{\mathrm{d}t}\langle p(t), b_1(x(t))\rangle\right)_{|(x,p,u)} = \langle p(t), [b_0, b_1](x(t))\rangle = -\frac{\partial H'}{\partial x^n}_{|(x',p',x^n)}.$$

(ii)
$$\left(\frac{\partial}{\partial u}\frac{\mathrm{d}^2}{\mathrm{d}t^2}\langle p(t), b_1(x(t))\rangle\right)_{|(x,p,u)} = -\langle p(t), \mathrm{ad}^2_{b_1} b_0(x(t))\rangle = -\frac{\partial^2 H'}{\partial x^{n^2}}_{|(x',p',x^n)},$$

where $[b_0, b_1] = \mathrm{ad}_{b_0} b_1$ *is the Lie bracket of the vector fields* b_0 *and* b_1*, so that* $\mathrm{ad}^2_{b_1} b_0 = [b_1, [b_1, b_0]]$.

Lie brackets will be properly defined in Chapter 1.

0.2.2 A class of infinite-dimensional Piecewise Deterministic Markov Processes

PDMPs where introduced by Davis [Dav84] in the finite-dimensional case and then extended to infinite dimension in [BR11a]. This class of processes is well suited to describe any stochastic nondiffusive phenomenon and we will give a general bibliography on the subject in the introduction of Chapter 2. Here, we present a special class of Hilbert valued PDMPs that falls into the framework built in [BR11a]. In particular, we give conditions that lead to existence and uniqueness of the solutions of the PDEs considered. It is not the most general class that can be defined following the finite-dimensional work of Davis. In particular, boundary conditions will not be needed in our models so that deterministic forced jumps will not be considered. Furthermore, the space of continuous component of the process will not depend on the jumping component. These extensions could be quite straightforwardly conducted if they appeared relevant for some models in the future. In Chapter 2, we will incorporate a control to this class and extend Theorem 0.2.4 below.

We consider a Gelfand triple ($V \subset H \subset V^*$) such that H is a separable Hilbert space and V a separable, reflexive Banach space continuously and densely embedded in H. The pivot space H is identified with its dual H^*, V^* is the topological dual of V. H is then continuously and densely embedded in V^*. We will denote by $||\cdot||_V$, $||\cdot||_H$, and $||\cdot||_{V^*}$ the norms on V, H, and V^*, by $(\cdot,\cdot)$ the inner product in H and by $\langle\cdot,\cdot\rangle$ the duality pairing of (V, V^*). Note that for $v \in V$ and $h \in H$, $\langle h, v\rangle = (h, v)$. Let D be a finite set, the state space of the discrete variable and let $T > 0$ be the finite time horizon. The process we are going to define has two components that take values in $H \times D$. The Hilbert valued component is continuous and the discrete one has jumps that make it *càdlàg* (right continuous with left limits). The dynamics of these two components are entirely coupled and we proceed now to their descriptions.

For every $d \in D$, we consider the autonomous PDE

$$\begin{cases} \dot{v}(t) = -Lv(t) + f_d(v(t)), \\ v(0) = v_0, \quad v_0 \in V, \end{cases} \tag{17}$$

with $-L : V \to V^*$ such that

1. $-L$ is linear, monotone;
2. $||Lx||_{V^*} \leq c + c_1||x||_V$ with $c > 0$ and $c_1 \geq 0$;
3. $\langle Lx, x\rangle \geq c_2||x||_V^2, \quad c_2 > 0$;
4. $-L$ generates a strongly continuous semigroup $(S(t))_{t\geq 0}$ on H such that $S(t) : H \to H$ is compact for every $t > 0$ (immediately compact),

and $f_d : H \to H$ a Lipschitz continuous function. For $(d, v_0) \in D \times H$, we will denote by $\phi_\cdot^d(v_0) : \mathbb{R}_+ \to H$ the flow of PDE (17). Under these assumptions, (17) is well-posed, it admits a unique solution in $C([0, T]; H)$ whose expression is given by the mild formulation

$$\phi_t^d(v_0) = S(t)v_0 + \int_0^t S(t-s)f_d(\phi_s^d(v_0))\mathrm{d}s. \tag{18}$$

We will make an extensive use of this formulation in Chapter 2. The necessity of an autonomous equation is justified by the flow property it implies, which will provide the resulting process with the strong Markov property. For $(d, v_0) \in D \times H$, the flow property reads

$$\phi_{t+s}^d(v_0) = \phi_t^d(\phi_s^d(v_0)), \qquad (t, s) \in \mathbb{R}_+^2. \tag{19}$$

PDE (17) describes the dynamics of the continuous component of the piecewise deterministic process between two consecutive jumps of the discrete variable.

The jump mechanisms are described by a jump rate function $\lambda : H \times D \to \mathbb{R}_+$ and a transition measure $\mathcal{Q} : H \times D \to \mathcal{P}(D)$, where $\mathcal{P}(D)$ denotes the set of probability measures on D and we make the following assumptions

1. For every $d \in D$, $\lambda(d, \cdot) : H \to \mathbb{R}_+$ is locally Lipschitz continuous, that is, for every compact set $K \subset H$, there exists $l_\lambda(K) > 0$, independent of d since D is finite, such that
$$|\lambda(d, x) - \lambda(d, y)| \leq l_\lambda(K)||x - y||_H \qquad \forall (x, y) \in K^2.$$
Furthermore, there exist $M_\lambda, \delta > 0$ such that
$$\delta \leq \lambda(d, x) \leq M_\lambda, \forall x \in H.$$
2. The function $\mathcal{Q} : H \times D \times \mathcal{B}(D) \to [0, 1]$ is a transition probability such that $x \to \mathcal{Q}(\{p\}|x, d)$ is continuous for all $(d, p) \in D^2$ (weak continuity) and $\mathcal{Q}(\{d\}|v, d) = 0$ for all $v \in H$.

The assumptions on λ ensure in particular that the resulting process does not blow up. The principles of the construction of the PDMP $(v(t), d(t))_{t\geq 0}$ are the following.

- Starting from the initial deterministic condition $(v(0), d(0)) = (v_0, d_0) \in H \times D$, the PDMP is given on $[0, T_1)$ by

$$v(t) = \phi_t^{d_0}(v_0), \qquad d(t) = d_0 \qquad \forall t \in [0, T_1),$$

where T_1 denotes the time of the first jump of the discrete component.

- The distribution of T_1 is defined by the jump rate function λ through the survival function

$$\begin{aligned}\chi_t(d_0, v_0) &= \mathbb{P}(T_1 > t \mid v(0) = v_0, d(0) = d_0) \\ &= \exp\left(-\int_0^t \lambda(d_0, \phi_s^{d_0}(v_0))\mathrm{d}s\right).\end{aligned}$$

The probability $\mathbb{P}$ will be defined below.

- When a jump occurs at time T_1, the conditional distribution of the target state d_1 is given by the transition measure $\mathcal{Q}$

$$\mathbb{P}(d(T_1) = d_1 \mid T_1) = \mathcal{Q}(\{d_1\} \mid \phi_{T_1}^{d_0}(v_0), d_0),$$

and the continuous component does not jump.

- This procedure is then repeated with the new starting point $(v(T_1), d(T_1)) = (\phi_{T_1}^{d}(v_0), d_1)$.

We now recall the mathematical construction of the process, following [Dav93] for the finite-dimensional case. This construction will be used in Chapter 2 where we extend it to infinite-dimensional controlled PDMPs.

Let $(\Omega, \mathcal{F}, \mathbb{P})$ be the probability space of sequences of independent uniformly distributed random variables on [0,1]. The process $(X_t = (v_t, d_t))_{t\geq 0}$ taking values in $H \times D$ is then constructed as follows. Let $(v_0, d_0) \in H \times D$ and $\omega = (\omega_n, n \geq 1) \in \Omega$.

1. The initial condition is deterministic and is given by

$$(v_0(\omega), d_0(\omega)) = (v_0, d_0).$$

2. The continuous component $v(\omega)$ is given by (18) with $d = d_0$ as long as the discrete component $d(\omega)$ remains equal to d_0. The first jump time of $d(\omega)$ is defined by

$$T_1(\omega) = \inf\{t \geq 0 \mid \chi_t(d_0, v_0) \leq \omega_1\}.$$

3. At time $T_1(\omega)$, v does not jump and the discrete component is updated according to $\mathcal{Q}(\cdot \mid \phi_{T_1}^{d_0}(v_0), d_0)$. There exists a measurable function $f_1 : [0,1] \to D$ such that

$$d_{T_1(\omega)}(\omega) = f_1(\omega_1)$$

4. The algorithm is then repeated and for $n \in \mathbb{N}^*$

$$T_{n+1}(\omega) = T_n(\omega) + \inf\{t \geq 0 \mid \chi_t(v_{T_n(\omega)}(\omega), d_{T_n(\omega)}(\omega)) \leq \omega_n\},$$

and there exists a measurable function $f_n : [0,1] \to D$ such that

$$d_{T_n(\omega)}(\omega) = f_n(\omega_n),$$

so that for $t \in [T_n(\omega), T_{n+1}(\omega))$

$$\begin{cases} v_t(\omega) = \phi_{t-T_n(\omega)}^{d_{T_n(\omega)}}(v_{T_n(\omega)}(\omega)), \\ d_t(\omega) = d_{T_n(\omega)}(\omega). \end{cases}$$

Theorem 0.2.4. *(see [BR11a, Theorem 4]) The stochastic process $(X_t = (v_t, d_t))_{t\geq 0}$ is a homogeneous strong Markov càdlàg piecewise deterministic process. The domain $\mathcal{D}(\mathcal{G})$ of its extended generator $\mathcal{G}$ is the set of bounded measurable functions $f : H \times D \to \mathbb{R}$ such that the map $t \to f(\phi_t^d(v), d)$ is absolutely continuous for almost every $t \in \mathbb{R}_+$ for any $(v, d) \in H \times D$. Furthermore, for $f \in \mathcal{D}(\mathcal{G})$, the extended generator is given by*

$$\begin{aligned} \mathcal{G}f(v(t), d(t)) = {} & \frac{\mathrm{d}f}{\mathrm{d}t}(v(t), d(t)) \\ & + \lambda(v(t), d(t)) \sum_{\tilde{d} \in D} (f(v(t), \tilde{d}) - f(v(t), d(t)))\mathcal{Q}(\{\tilde{d}\} \mid v(t), d(t)). \end{aligned}$$

PMDPs for the modeling of membrane potential dynamics

Here we illustrate, on the Morris-Lecar model [LM81], how PMDPs are well suited to take into account the stochastic mechanisms of the opening and closing of ion channels. The infinite-dimensional deterministic Morris-Lecar model is a system of two coupled partial differential equations describing the evolution of the membrane potential at a given point of the axon and the proportion of open channels. The axon is modeled by a one-dimensional cable represented by the segment I. The equations for the infinite-dimensional deterministic Morris-Lecar model are

$$\begin{cases} \partial_t \nu = \dfrac{1}{C}\partial_{xx}\nu + \dfrac{1}{C}\Big(g_K\omega(V_K - \nu) + g_{Ca}m_\infty(\nu)(V_{Ca} - \nu) \\ \qquad\qquad + g_L(V_L - \nu)\Big), \\ \partial_t \omega = \alpha(\nu)(1 - \omega) - \beta(\nu)\omega, \end{cases} \tag{20}$$

with $\nu_t(x)$ the membrane potential at position $x \in I$ on the axon at time $t \in I$ and $\omega_t(x)$ the proportion of open sodium channels. The opening and closing mechanisms of the sodium channels can be interpreted with Figure 7.

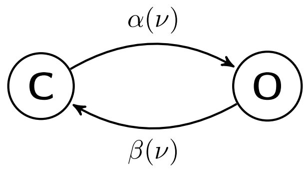


Figure 7 – Representation of the opening and closing of sodium channels.

At a given point along the axon, when the membrane potential equals ν, the sodium channels open at rate $\alpha(\nu)$ and close at rate $\beta(\nu)$. We can take into account the stochasticity of these mechanisms by affecting a probability to the opening and the closing. From what is done in [Aus08] for the Hodgkin-Huxley model, we can assimilate the axon to the segment $I = [0, 1]$. For a given scale $N \in \mathbb{N}^*$, the axon is populated with $N-1$ channels at position $z_i = \frac{i}{N}$ for $i \in \{1, \dots, N-1\}$. For the Morris-Lecar model, each sodium channel at position z_i can be either open or closed. The configuration of all the sodium channels at time t is thus represented by a vector d_t with values in the finite set $D := \{o, c\}^N$ and we write $d_t(i)$ the sate of the sodium channel at time t and at position z_i, for $i \in \{1, \dots, N-1\}$. Now, if the membrane potential at position z_i was held fixed, the process $(d_t(i), t \geq 0)$ would be a continuous time Markov chain. However, since the membrane potential evolves through time and the jump rates of opening and closing are voltage-dependent, the evolution of $d_t(i)$ is given by

$$\begin{cases} \mathbb{P}(d_{t+h}(i) = o \mid d_t(i) = c) = \alpha(\nu_t(z_i))h + \mathrm{o}(h), \\ \mathbb{P}(d_{t+h}(i) = c \mid d_t(i) = o) = \beta(\nu_t(z_i))h + \mathrm{o}(h). \end{cases} \tag{21}$$

Between jumps of the discrete component d_t, the evolution of the membrane potential is given by the following partial differential equation

$$\begin{aligned} C\partial_t \nu_t = \partial_{xx}\nu_t + \frac{1}{N}\sum_{i=1}^{N-1} g_{d_t(i)}(V_K - \nu_t(z_i))\delta_{z_i} \\ + g_{Ca} m_\infty(\nu_t)(V_{Ca} - \nu_t) + g_L(V_L - \nu), \quad \nu_0 = v \in H_0^1(I), \end{aligned} \tag{22}$$

with $g_{d_t(i)}$ the conductance of the sodium channel when in state $d_t(i)$ ($g_o = g_K$ and $g_c = 0$) and $\nu_t \in H_0^1(I)$. The process $(\nu_t, d_t)_{t\geq 0}$ is a PDMP with values in $H_0^1(I) \times D$.

For the generalized Hodgkin-Huxley model, where the ion channels can be in more that two states, it was proved in [Aus08] that the PDMP defined by (21) and (22) converges in probability, in an appropriate space, towards the deterministic version given by (20). Generalization of this convergence result was obtained in [RTW12] where a law of large numbers in proved for a general class of models, called compartmental models, which links the stochastic and deterministic systems. A martingale central limit theorem is also proved, it connects the stochastic fluctuations around the deterministic limiting process to diffusion processes.

This type of infinite-dimensional PDMPs conductance-based models of neurons were extensively studied in [Gen13] where, among other results, averaging theorems are derived for processes displaying several time scales.

0.2.3 Markov Decision Processes

Inside every PDMP defined above is embedded a discrete-time Markov chain with values in $[0,T] \times H \times D$ constituted of the jump times and the jump locations of the process. Moreover, there exists a one-to-one correspondence between the PDMP and a pure jump process that we describe now. Consider the PDMP $(X_t = (v_t, d_t))_{t\geq 0}$ of Theorem 0.2.4. The jump times T_k of X can be retrieved by the formula

$$\{T_k, k = 1, \ldots, n\} = \{s \in (0,T] | d_s \neq d_{s^-}\},$$

all jumps being detected since the discrete component has to change when a jump occurs ($\mathcal{Q}(\{d\}|v,d) = 0$ for all $v \in H$). We can associate to X a pure jump process $(Z_t)_{t\geq 0}$ taking values in $[0,T] \times H \times D$ in a one-to-one correspondence as follows,

$$Z_t := (T_k, v_{T_k}, d_{T_k}), \qquad T_k \leq t < T_{k+1}.$$

Conversely, given the sample path of Z on $[0,T]$ starting from $Z_0 = (T_0^Z, v_0^Z, d_0^Z)$, we can recover the path of X on $[0,T]$. Denote Z_t as (T_t^Z, v_t^Z, d_t^Z) and define $T_0 := T_0^Z$ and $T_k := \inf\{t > T_{k-1} | T_t^Z \neq T_{t^-}^Z\}$. Then

$$\begin{cases} X_t = (\phi_t^{d_0^Z}(v_0^Z), d_0^Z), & t < T_1, \\ X_t = (\phi_{t-T_k}^{d_{T_k}^Z}(v_{T_k}^Z), d_{T_k}^Z), & T_k \leq t < T_{k+1}. \end{cases}$$

The embedded discrete-time Markov chain $(Z'_n)_{n\geq 0}$ is defined from $(Z_t, t \geq 0)$ by adding a cemetery state Δ_∞ to $[0,T] \times H \times D$. Then, $(Z'_n)_{n\geq 0}$ is defined by the stochastic kernel $\mathcal{Q}'$ given, for Borel sets $B \subset [0,T]$, $E \subset H$, $C \subset D$ sets, and $(t,v,d) \in [0,T] \times H \times D$, by

$$\mathcal{Q}'(B \times C \mid t,v,d) = \int_0^{T-t} \lambda(d, \phi_s^d(v))\chi_s(d,v)\mathbf{1}_B(t)\mathbf{1}_E(\phi_t^d(v))Q(C \mid \phi_t^d(v), d),$$

and $\mathcal{Q}'(\{\Delta_\infty\} \mid t,v,d) = \chi_{T-t}^d(v)$, and $\mathcal{Q}'(\{\Delta_\infty\} \mid \Delta_\infty) = 1$. Note that $Z'_n = Z_n$ as long as $T_n \leq T$.

For the controlled PDMPs defined in Chapter 2, the local characteristics $(\phi, \lambda, \mathcal{Q})$ depend on the control variable. Thus, the kernel $\mathcal{Q}'$ of the embedded Markov chain depends also on the control and it is called a Markov decision process. We define here a special class of infinite-horizon discrete-time MDPs and we present dynamic programming on these processes. We only briefly sketch the issues that arise and the mathematical objects we are interested in. In particular, we do not discuss here the finiteness of the integrals we manipulate. All the material needed for this introduction and Chapter 2 can be found in [BS78].

Let E be a Borel space and U a Borel set of a Polish space. To define a controlled discrete-time Markov chain, we first need to define the controls, called *decision rules*. A *policy* is a sequence $(u_n, n \in N)$ of controls with values in U that tells the observer the action to take at any stage n. A policy is said to be *Markovian* if it only depends on the current state of the chain. Otherwise, it is said to be *history-dependent*, in which case it may depend on the entire history of states and controls. We will recall in Chapter 2 that for our problem, history-dependent policies will not be better than Markovian ones and we thus focus on Markovian policies now. Policies can be *randomized* if necessary, as discrete counterparts of the relaxed controls defined above. A *randomized decision rule* is a probability measure γ on U. We denote by $\mathcal{U} := \mathcal{P}(U)$ the set of all randomized decision rules on U (i.e. the set of all probability measures on U). A *randomized policy* is thus a sequence $(\gamma_n, n \in \mathbb{N}) \in \mathcal{U}^{\mathbb{N}}$ of probability measures on U. We use the notations $\mu : E \to \mathcal{U}$ for Markovian randomized decision rule, and $\tilde{\pi} = (\mu_n, n \in \mathbb{N})$ for Markovian randomized policies. Randomized policies, or relaxed policies, will be of great use in Chapter 2. Let $\pi = (u_n, n \in N)$ be an ordinary Markovian policy, that is, a sequence of measurable maps, $u_n : E \to U$, $n \in \mathbb{N}$. Let $(Z_n^\pi, n \geq 0)$ be the associated controlled discrete-time Markov chain defined by a stationary transition kernel $\mathcal{Q}' : E \times U \to \mathcal{P}(E)$ such that for all borel subset B of E and $n \in \mathbb{N}$

$$\mathbb{P}^\pi(Z_{n+1}^\pi \in B | Z_n^\pi) = \mathcal{Q}'(B | Z_n^\pi, u_n(Z_n^\pi)).$$

We consider a cost function $g : E \times U \to \mathbb{R}_+$ and an expected cost functional at horizon $N \in \mathbb{N}^*$ defined by

$$J_{N\pi}(Z_0) := \mathbb{E}^\pi \left[\sum_{k=0}^{N-1} g(Z_k^\pi, u_k(Z_k^\pi)) \right], \tag{23}$$

for a Markov chain starting at $Z_0 \in E$. The finite-horizon problem consists in finding a finite Markovian policy $\pi^* = (u_0, \cdots, u_{N-1})$ that minimizes the cost (23) over N stages, that is

$$J_N^*(Z_0) := \inf_\pi J_{N\pi}(Z_0) = J_{N\pi^*}(Z_0)$$

The infinite-horizon problem consists in finding a Markovian policy $\pi = (u_n, n \in \mathbb{N})$ that minimizes

$$J_\pi(Z_0) := \mathbb{E}^\pi \left[\sum_{k=0}^{\infty} g(Z_k^\pi, u_k(Z_k^\pi)) \right] = \lim_{N\to\infty} J_{N\pi}(Z_0), \tag{24}$$

and we write $J^*(Z_0) := \inf_\pi J_\pi(Z_0)$. More precisely, we are interested in finding optimal *stationary policies*, i.e. policies $\pi = (u, u, \cdots)$ constituted of a unique decision rule $u : E \to U$ infinitely repeated. When there are no convexity assumptions on the stochastic kernel $\mathcal{Q}'$ and the cost function g, we work with relaxed policies. For $\gamma \in \mathcal{U}$ and $z \in E$, we thus extend the definitions of $\mathcal{Q}'$ and g to $\mathcal{U}$ by

$$\begin{cases} \mathcal{Q}'(\cdot \mid z, \gamma) := \int_U \mathcal{Q}'(\cdot \mid z, u)\gamma(\mathrm{d}u), \\ g(z, \gamma) := \int_U g(z, u)\gamma(\mathrm{d}u). \end{cases}$$

The finite-horizon problem, respectively infinite-horizon problem, is then to find a finite relaxed Markovian policy $\bar{\pi}^* = (\mu_0, \dots, \mu_N)$, respectively a relaxed Markovian policy $\bar{\pi}^* = (\mu_n, n \in \mathbb{N})$, that minimizes $J_{N\bar{\pi}}(Z_0)$, respectively $J_{\bar{\pi}}(Z_0)$, over all the finite relaxed Markovian policies, respectively relaxed Markovian policies. As for the nonrelaxed case, the final goal is to find an optimal stationary relaxed Markovian policy $\bar{\pi}^* = (\mu, \mu, \dots)$.

We can now describe the *Dynamic Programming* algorithm for this problem, starting with the finite-horizon problem. Consider the mapping R, defined for any real-valued function f on E by

$$Rf(z, \gamma) = g(z, \gamma) + (\mathcal{Q}' f)(z, \gamma), \qquad (z, \gamma) \in E \times \mathcal{U},$$

with $(\mathcal{Q}'f)(z, \gamma) := \int_E f(x)\mathcal{Q}'(\mathrm{d}x|z, \gamma) = \int_E \int_U f(x)\mathcal{Q}'(\mathrm{d}x|z, u)\gamma(\mathrm{d}u)$. Consider also for any relaxed decision rule $\mu : E \to \mathcal{U}$, the operator T_μ defined by

$$\begin{aligned} T_\mu f(z) &= Rf(z, \mu(z)) \\ &= \int_U g(z, u)\mu(\mathrm{d}u|z) + \int_E \int_U f(x)\mathcal{Q}'(\mathrm{d}x|z, u)\mu(\mathrm{d}u|z). \end{aligned}$$

This operator generates a time-shift of one stage on the problem and we can briefly show, by induction, that for $Z_0 \in E$ and a relaxed policy $\pi = (\mu_n, n \in N)$, we have

$$J_{N\bar{\pi}}(Z_0) = (T_{\mu_0} \cdots T_{\mu_{N-1}})(J_0)(Z_0),$$

where J_0 is the zero function (*i.e.* $J_0(z) = 0$, $\forall z \in E$). Indeed, for $Z_0 \in E$ and a relaxed policy $\bar{\pi} = (\mu_n, n \in N)$,

$$J_{1\bar{\pi}}(Z_0) = \int_U g(Z_0, u)\mu_0(\mathrm{d}u|Z_0) = T_{\mu_0}(J_0)(z),$$

with the notation $\mu_0(\cdot|Z_0) := \mu_0(Z_0) \in \mathcal{U}$, and for $k \in \mathbb{N}$,

$$\begin{aligned}\mathbb{E}[g(Z_{k+1}, \mu_{k+1}(Z_{k+1}))|Z_k] &= \mathbb{E}[\int_U g(Z_{k+1}, u_{k+1})\mu_{k+1}(\mathrm{d}u_{k+1}|Z_{k+1})|Z_k] \\ &= \int_U \int_E \int_U g(x, u_{k+1})\mu_{k+1}(\mathrm{d}u_{k+1}|x)\mathcal{Q}'(\mathrm{d}x|Z_k, u_k)\mu_k(\mathrm{d}u_k|Z_k).\end{aligned}$$

It follows that

$$\begin{aligned}\mathbb{E}[g(Z_{k+1}, \mu_{k+1}(Z_{k+1}))] = \int_U \Big(&\int_E \int_U \cdots \int_E \int_U g(x_{k+1}, u_{k+1}) \\ &\times \mu_{k+1}(\mathrm{d}u_{k+1}|x_{k+1})\mathcal{Q}'(\mathrm{d}x_{k+1}|x_k, u_k)\cdots \\ &\times \mu_1(\mathrm{d}u_1|x_1)\mathcal{Q}'(\mathrm{d}x_1|Z_0, u_0)\Big)\mu_0(\mathrm{d}u_0|Z_0),\end{aligned}$$

Now let $\bar{\pi}_s = (\mu_{n+1}, n \in \mathbb{N})$ the shifted policy obtained from $\bar{\pi}$. From the previous equality we get

$$\begin{aligned}J_{(N+1)\bar{\pi}}(Z_0) &= \int_U g(Z_0, u)\mu_0(\mathrm{d}u|Z_0) + \int_U \int_E J_{N,\bar{\pi}_s}(x_1)\mathcal{Q}'(\mathrm{d}x_1|Z_0, u_0)\mu_0(\mathrm{d}u_0|Z_0) \\ &= T_{\mu_0} J_{N\bar{\pi}_s}(Z_0),\end{aligned}$$

and by the induction hypothesis we obtain

$$J_{(N+1)\pi}(Z_0) = T_{\mu_0}(T_{\mu_1}\cdots T_{\mu_N}(J_0))(Z_0) = (T_{\mu_0}T_{\mu_1}\cdots T_{\mu_N})(J_0)(Z_0).$$

Now, going back to the infinite-horizon problem, the goal is to show that a stationary optimal policy can be found and to compare J^* and $J^*_\infty := \lim_{N\to\infty} J^*_N$. To do so, consider the operator T defined for $f : E \to \mathbb{R}$ by

$$Tf(z) = \inf_{u\in U} \left\{g(z, u) + \mathcal{Q}'f(z, u)\right\}. \tag{25}$$

In Chapter 2, the assumptions on the local characteristics $(\phi, \lambda, \mathcal{Q})$ and the cost function g we will allow us to show that $J^*_N = T^N$. Moreover, we will prove that J^* is the unique fixed point of the operator T, in a space of continuous functions. The equation $TJ^* = J^*$ is the *Bellman equation* of dynamic programming.

0.3 Results of the Thesis

We give here a brief review of the main results of the Thesis, chapter by chapter. Since each chapter has its own introduction, we want this review to be a guide for the reading for the thesis and we do not present in much detail the mathematical object that we use. In particular, the extended bibliography is not given here, it can be found in the corresponding chapter. Chapter 1 and 2 constitute each one a preprint of an article soon to be submitted.

0.3.1 Chapter 1

In this chapter, we define and study, in terms of optimal control, finite-dimensional, deterministic neuron models controlled by Optogenetic. To the best of our knowledge, the optimal control of Optogenetic models has never been addressed before and we build a general mathematical framework to incorporate an Optogenetic effect in conductance-based neuron models. This allows us to study the optimal control of various widely studied models such as the Hodgkin-Huxley model or the Morris-Lecar model. For this presentation to be more explicit, we will present the results on the Morris-Lecar model throughout this section. The corresponding results for the FitzHugh-Nagumo model, the reduced Hodgkin-Huxley model and the complete Hodgkin-Huxley model can be found in Chapter 1. The dynamical system for the Morris-Lecar model is

$$(ML)\begin{cases}\dot{\nu}(t) = \dfrac{1}{C}\Big(g_K\omega(t)(V_K-\nu(t)) + g_{Ca}m_\infty(\nu(t))(V_{Ca}-\nu(t)) \\ \qquad\qquad + g_L(V_L-\nu(t))\Big), \\ \dot{\omega}(t) = \alpha(\nu(t))(1-\omega(t)) - \beta(\nu(t))\omega(t),\end{cases}$$

with $\nu(\cdot)$ the membrane potential and $\omega(\cdot)$ the gating variable for the sodium channels. We use the two models of ChR2 presented in Section 0.1.2 (Figures 5 and 6). The dynamical systems associated to this models are, respectively

$$(ChR2-3States)\begin{cases}\dot{o}(t) = u(t)(1-o(t)-d(t)) - K_d o(t), \\ \dot{d}(t) = K_d o(t) - K_r d(t),\end{cases}$$

and

$$(ChR2–4States)\begin{cases}\dot{o}_1(t) = \varepsilon_1 u(t)(1-o_1(t)-o_2(t)-c_2(t)) - (K_{d1}+e_{12})o_1(t) + e_{21}o_2(t), \\ \dot{o}_2(t) = \varepsilon_2 u(t)c_2(t) + e_{12}o_1(t) - (K_{d2}+e_{21})o_2(t), \\ \dot{c}_2(t) = K_{d2}o_2(t) - (\varepsilon_2 u(t) + K_r)c_2(t),\end{cases}$$

with $u(\cdot)$ the control. The control system is obtained by combining the conductance-based model and either one or the other ChR2 models. For the ChR2-3-states model we get

$$(ML-ChR2-3States)\begin{cases}\dot{\nu}(t)=\dfrac{1}{C}\Big(g_K\omega(t)(V_K-\nu(t))+g_{Ca}m_\infty(\nu(t))(V_{Ca}-\nu(t))\\ \qquad\qquad+g_{ChR2}o(t)(V_{ChR2}-\nu(t)))+g_L(V_L-\nu(t))\Big),\\ \dot{\omega}(t)=\alpha(\nu(t))(1-\omega(t))-\beta(\nu(t))\omega(t),\\ \dot{o}(t)=u(t)(1-o(t)-d(t))-K_d o(t),\\ \dot{d}(t)=K_d o(t)-K_r d(t).\end{cases}$$

The optimal control problem we address is the spiking of a single neuron, starting from its resting state, in minimal time. Mathematically, it consists in steering the (ML-ChR2-3States) system, from an equilibrium to a membrane potential threshold corresponding to an action potential. The main objectives are to investigate this problem theoretically and numerically to probe the relevance of the different neuron models through their behavior with regard to Optogenetic. Indeed, the introduction of a perturbation in the system, in form of a control, gives a new way to test the models as good representation of the dynamical evolution of a neuron membrane potential.

Regarding the theoretical part of the study, the problem appears as a single-input affine system and we investigate the existence of singular extremals.

The ChR2-3-states model

We are able to drastically simplify the investigation of singular extremals by a Goh-type transformation. The following theorem is written for the Morris-Lecar model and it is valid for any conductance-based model.

Theorem 0.3.1. *The existence of optimal singular extremals in the minimal time spiking problem for the control system (ML-ChR2-3States) is equivalent to the existence of optimal singular extremals in the same problem but for the reduced system on* $\mathbb{R}^2$

$$(ML)\begin{cases}\dot{\nu}(t)=\dfrac{1}{C}\Big(g_K\omega(t)(V_K-\nu(t))+g_{Ca}m_\infty(\nu(t))(V_{Ca}-\nu(t))\\ \qquad\qquad+g_{ChR2}o(t)(V_{ChR2}-\nu(t)))+g_L(V_L-\nu(t))\Big),\\ \dot{\omega}(t)=\alpha(\nu(t))(1-\omega(t))-\beta(\nu(t))\omega(t),\end{cases}$$

where o is the new control variable.

Theorem 0.3.1 thus allows to reduce the dimension of the control system to the dimension of the original uncontrolled conductance-based model. For 2-dimensional neuron models such the FitzHugh-Nagumo model, the Morris-Lecar model or the reduced Hodgkin-Huxley model, we are able to prove the absence of optimal singular extremals. The optimal controls are thus bang-bang and we prove that they necessarily begin with a maximal arc. For the complete Hogdkin-Huxley model, the resulting 4-dimensional system is too complicated to theoretically certify the absence of optimal singular extremals. Banb-bang optimal controls are observed numerically.

The ChR2-4-states model

We cannot perform the same reduction for the ChR2-4-states model. We give the structure of the Lie brackets and the expression of a possible singular control, if it exists. Numerically, we never observe singular controls.

Numerical results

Physiologically, we already mentioned in section 0.1.2 that the ChR2 has a depolarizing effect on the neuron membrane. We thus expect physiologically to observe a spike when the control is maximal, and the more light we put into the system, the faster the spike. This is the base for the discussion and the interpretation of the numerical results.

We implement a direct method with the `ampl` language and using the `ipopt` nonlinear solver. For each conductance-based neuron model, we compare the performances of the ChR2-3-states and the ChR2-4-states models. We repeat the procedure for several values of the maximal control. Indeed, since we did not exclude theoretically optimal singular controls for the ChR2-4-states, they can appear above some threshold of the control and thus we scan a reasonable range of values for the maximal control. The first value correspond to a physiological value computed from data found in the literature. From this set of experiment, we can distinguish two main classes of neurons that we call the physiological and nonphysiological classes.

The physiological class. The first class comprises the Fitzhugh-Nagumo model, the reduced Hodgkin-Huxley model and the complete Hodgkin-Huxley. These three models behave as physiologically expected. The optimal control has at most one switching time from a maximal control to a minimal control and the more light (i.e. the higher the maximal value of the control) we put in the system, the faster the spike. For the Fitzhugh-Nagumo model, the ChR2-4-states version sensibly outperforms the ChR2-3-states model. Indeed, it spikes faster and require less light (Figure 8).

The Hodgkin-Huxley models are very interesting for several reasons. Taken separately, both models give the same qualitative and quantitative results for the two versions of ChR2. Indeed, except for low values of the maximal control for which the ChR2-4-state version slightly outperforms the ChR2-3-states, the optimal trajectory of the membrane potential and the optimal control strikingly coincide. Besides, the response of the system

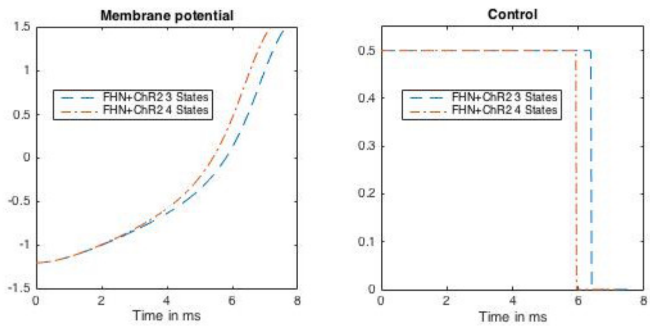
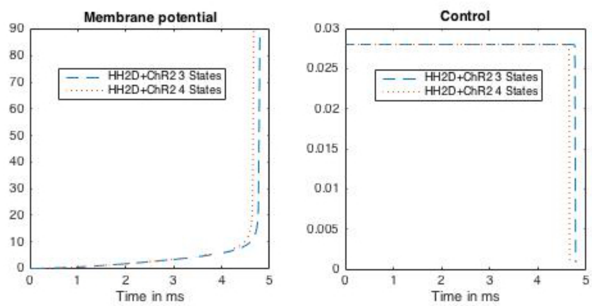
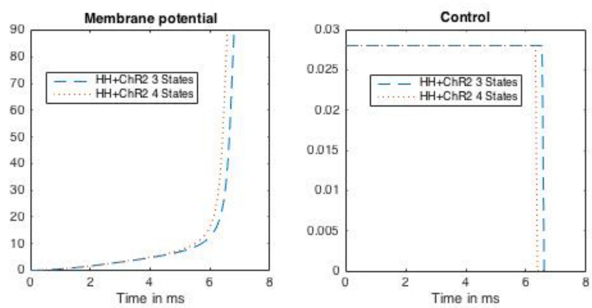


Figure 8 – Optimal trajectory and bang-bang optimal control for the FHN-ChR2-3-states and FHN-ChR2-4-states models with $u_{max} = 0.5$.

does not qualitatively change when we change the numerical values for the ChR2 model. We thus qualify these models as robust with respect to the ChR2 modeling. Furthermore, if the relevance of the reduced Hodgkin-Huxley model has not a satisfying mathematical foundation (see Section 1.3.3), optogenetic control provides a new argument in favor of this reduction to be a good approximation of the complete model. Indeed, the reduced Hodgkin-Huxley model and the complete model behave exactly the same with respect to the control (Figure 9).



a)



b)

Figure 9 – Optimal trajectory and bang-bang optimal control for a) the reduced and b) the complete Hodgkin-Huxley models with $u_{max} = 0.028$.

The nonphysiological class. The second class comprises the Morris-Lecar model alone. This model provides a nonintuitive response to optogenetic stimulation. For the first set of numerical values that we use, we observed an optimal control with three switching times, for both the ChR2-3-states and ChR2-4-states versions. For this set of numerical values, the performances of the ChR2-3-states and ChR2-4-states versions are also nonintuitive since we can note the existence of a threshold for the maximal value of the control below which the ChR2-3-states version outperforms the ChR2-4-states (Figure 10).

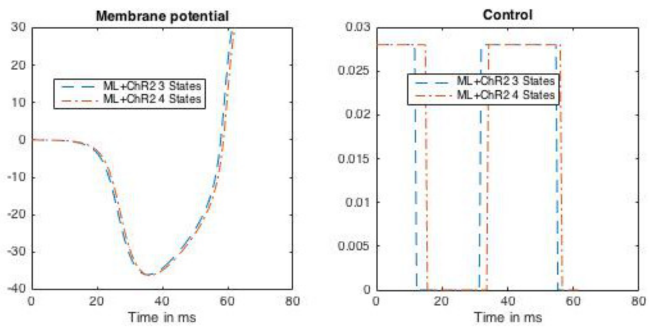


Figure 10 – Optimal trajectory and bang-bang optimal control for the ML-ChR2-3-states and ML-ChR2-4-states models with $u_{max} = 0.028$.

This means that the neuron spikes faster if the light is switched on and off several times instead of being kept on. For this particular set of numerical values, the gain with respect to constant stimulation is very small. Nevertheless, with another set of numerical values, still taken from the literature, the constant stimulation fails to trigger a spike while the optimal control obtained succeeds. To decide whether the number of switching times is an intrinsic characteristic of the model, we change the numerical value of the equilibrium potential of ChR2 (V_{ChR2}) and we observe an optimal control with only two switching times. The Morris-Lecar model is thus not robust with respect to the ChR2 modeling, contrarily to the Hodgkin-Huxley models. Its number of switching times depends on the numerical values chosen for the ChR2 model and the optimal control is not intuitive. The results for the Morris-Lecar model also emphasize the benefits of the optimal control study since it provides a control that triggers a spike in a system that would otherwise not spike under constant stimulation.

0.3.2 Chapter 2

In this chapter we first define an infinite-dimensional controlled PDMP, where the control acts on the three local characteristics $(\phi, \lambda, \mathcal{Q})$ of the process. If the study of infinite-dimensional PDMPs and the optimal control of finite-dimensional PDMPs have been separately considered, the optimal control of infinite-dimensional PDMPs is a fairly untreated subject. The difficulty in defining controlled PDMPs arises from the fact that the state space has to be enlarged in order to obtain strongly Markovian processes. Furthermore, since we work with Markovian processes, we want to obtain Markovian optimal controls in the optimal control problems we address. This is another reason why the state space has to be again enlarged. Before enlargement, the infinite-dimensional controlled PDMP can be defined similarly to the uncontrolled PDMP of Section 0.2.2. Consider the same state space $H \times D$, a closed subset U of a compact polish space Z as the control space, and for $d \in D$ the controlled PDE

$$\begin{cases} \dot{v}_t = -Lv_t + f_d(v_t, a(t)), \\ v_0 = v, \quad v \in V. \end{cases} \tag{26}$$

with $a \in A := \{a : (0,T) \to U \text{ measurable}\}$. We write $\phi^a_\cdot(v,d)$ the flow of (26) and give assumptions under which (26) admits a unique solution. The jump rate function $\lambda : H \times D \times U \to \mathbb{R}_+$ and the transition measure $\mathcal{Q} : H \times D \times U \to \mathcal{P}(D)$ depend now both on the control variable. It is immediate to note that, defined as it is, the flow of (26) does not enjoy the flow property, that reads here $\phi^a_{t+s}(v,d) = \phi^a_t(\phi^a_s(v,d),d)$.

The enlarged process is defined on the space $\Xi := H \times D \times [0,T] \times [0,T] \times H$ by adding to the original components $(v_t, d_t)_{t \geq 0}$, the time elapsed since the last jump, denoted τ_t, the time of the last jump denoted h_t and the location of the continuous component v at the time of the last jump, denoted ν_t. Components τ_t and ν_t make the resulting process strongly Markovian. The time of the last jump makes Markovian the optimal control obtained later. Define also the space $\Upsilon := H \times D \times [0,T]$ in which the embedded MDP will take values. The space of admissible control strategies $\mathcal{A}$ for the enlarged PDMP is then defined by

$$\mathcal{A} := \{\alpha : \Upsilon \to \mathcal{U}_{ad}([0,T];U) \text{ measurable}\},$$

with $\mathcal{U}_{ad}((0,T),U) := \{a \in L^1((0,T),Z) | a(t) \in U \text{ a.e.}\}$.

We prove in Theorem 2.1.2 that there exists a filtered probability space satisfying the usual conditions such that to each admissible control strategy $\alpha \in \mathcal{A}$ is uniquely associated a strongly Markovian infinite-dimensional PDMP $(X^\alpha_t)_{t \geq 0}$ with values in Ξ. Moreover, the continuous component of this PDMP is locally bounded (in H), uniformly in $t \in [0,T]$.

The embedded MDP is then defined by its stochastic kernel $\mathcal{Q}' : \Upsilon \cup \{\Delta_\infty\} \times \mathcal{U}_{ad}((0,T),U) \to \Upsilon \cup \{\Delta_\infty\}$ given by

$$\mathcal{Q}'(\Sigma|z,a) = \int_0^{T-h} \rho_t \mathrm{d}t,$$

for any $z := (v,d,h) \in \Upsilon$, Borel set $\Sigma := B \times C \times E \in \mathcal{B}(\Upsilon)$ and $a \in \mathcal{U}_{ad}([0,T],U)$, where

$$\rho_t := \lambda_d(\phi_t^a(z), a(t))\chi_t^a(z)\mathbf{1}_E(h+t)\mathbf{1}_B(\phi_t^a(z))\mathcal{Q}(C|\phi_t^a(z), d, a(t)),$$

with $\phi_t^a(z)$ the flow of the PDE for the enlarged process, and $\mathcal{Q}'(\{\Delta_\infty\}|z,a) = \chi_{T-h}^a(z)$, and $\mathcal{Q}'(\{\Delta_\infty\}|\Delta_\infty, a) = 1$.

We then define the space relaxed control strategies $\mathcal{A}^{\mathcal{R}}$ by

$$\mathcal{A}^{\mathcal{R}} := \{\mu : \Upsilon \to \mathcal{R}([0,T];U) \text{ measurable}\},$$

with $\mathcal{R}([0,T],U) := \{\mu \in \mathcal{R}([0,T],Z) | \mu(t)(U) = 1 \text{ a.e. in } [0,T]\}$ and $\mathcal{R}([0,T],Z)$ the set of all transition probability measures from $([0,T],\mathcal{B}([0,T]),Leb)$ into $(Z,\mathcal{B}(Z))$. We extend the definition of the local characteristics of the PDMP and the stochastic kernel of the embedded MDP to the space of relaxed controls. For $(v,d) \in H \times D$ and $\gamma \in M_+^1(Z)$,

$$\begin{cases} f_d(v,\gamma) := \int_Z f_d(v,u)\gamma(\mathrm{d}u), \\ \lambda_d(v,\gamma) := \int_Z \lambda_d(v,u)\gamma(\mathrm{d}u), \\ \mathcal{Q}(C|v,d,\gamma) := (\lambda_d(v,\gamma))^{-1} \int_Z \lambda_d(v,u)\mathcal{Q}(C|v,d,u)\gamma(\mathrm{d}u), \end{cases}$$

and for $z := (v,d,h) \in \Upsilon$ and $\gamma \in \mathcal{R}([0,T],U)$,

$$\mathcal{Q}'(B \times C \times E|z,\gamma) := \int_0^{T-h} \tilde{\rho}_t \mathrm{d}t, \tag{27}$$

for Borel sets $B \subset H$, $C \subset D$, $E \subset [0,T]$, where

$$\begin{aligned} \tilde{\rho}_t &:= \chi_t^\gamma(z)\mathbf{1}_E(h+t)\mathbf{1}_B(\phi_t^\gamma(z)) \int_Z \lambda_d\Big(\phi_t^\mu(z), u\Big)\mathcal{Q}\Big(C|\phi_t^\mu(z), d, u\Big)\gamma(t)(\mathrm{d}u), \\ &= \chi_t^\gamma(z)\mathbf{1}_E(h+t)\mathbf{1}_B(\phi_t^\gamma(z))\lambda_d\Big(\phi_t^\gamma(z), \gamma(t)\Big)\mathcal{Q}\Big(C|\phi_t^\gamma(z), d, \gamma(t)\Big) \end{aligned}$$

and $\mathcal{Q}'(\{\Delta_\infty\}|z,\gamma) = \chi_{T-h}^\gamma(z)$, and $\mathcal{Q}'(\{\Delta_\infty\}|\Delta_\infty,\gamma) = 1$.

Once the PDMP and the associated MDP have been properly defined for relaxed control strategies, we consider an optimal control problem with finite time horizon and quadratic cost for the PDMP. The resulting optimal control for the MDP is an infinite-horizon problem as defined in Section 0.2.3. We show that the two problems are equivalent and that the operator T defined by (25) is contracting from a space of continuous function into itself. Thus it admits a unique fixed point and we show that this fixed point is the value function of the optimal control problem. More precisely, we state and show an existence theorem for a general contracting MDP (Theorem 2.3.3) and then we show that the assumptions made on the PDMP that the conditions for Theorem 2.3.3 to be valid are satisfied. The main difficulty of this part is to design a framework in which the complicated cost function and stochastic kernel associated to relaxed controls are continuous. One crucial point is the continuity of the mapping

$$\phi : (z, \gamma) \in \Upsilon \times \mathcal{R}([0,T], U) \to \phi^{\gamma}_{\cdot}(z) = S(0)v + \int_0^{\cdot} \int_Z S(\cdot - s) f_d(\phi^{\gamma}_s(z), u)\gamma(s)(\mathrm{d}u)\mathrm{d}s,$$

from $\Upsilon \times \mathcal{R}$ in $C([0,T]; H)$, where $(S(t)_{t\geq 0})$ is the strongly continuous semigroup generated by L.

The motivation for this work is again Optogenetics and we want to take into account the randomness of ion channels and the propagation of action potentials along the axon. The general framework described above allows us to define an infinite-dimensional controlled Hodgkin-Huxley model and to state an existence theorem of optimal ordinary control strategies. The neuron axon is represented by the segment $I := [0,1]$. For a scale $N \in \mathbb{N}^*$ we define $I_N := \mathbb{Z} \cap N\mathring{I}$. We consider the Gelfand triple (V, H, V^*) with $V := H^1_0(I)$ and $H := L^2(I)$ and a finite set D representing all the possible ion channel states.

Definition 0.3.1. ***Stochastic controlled infinite-dimensional Hodgkin-Huxley-ChR2 model****.* *Let $N \in \mathbb{N}^*$. We call N^{th} stochastic controlled infinite-dimensional Hodgkin-Huxley-ChR2 model the controlled PDMP $(v(t), d(t)) \in V \times D_N$ defined by the following characteristics:*

— *A state space $V \times D_N$ with $D_N = D^{I_N}$.*

— *A control space $U = [0, u_{max}]$, $u_{max} > 0$.*

— *A set of uncontrolled PDEs: For every $d \in D_N$,*

$$\begin{cases} v'(t) = \dfrac{1}{C_m}\Delta v(t) + f_d(v(t)), \\ v(0) = v_0 \in V, \quad v_0(x) \in [V_-, V_+] \quad \forall x \in I, \\ v(t,0) = v(t,1) = 0, \quad \forall t > 0, \end{cases} \tag{28}$$

with

$$\mathcal{D}(\Delta) = V,$$

$$f_d(v) := \frac{1}{N}\sum_{i\in I_N}\Big(g_K \mathbf{1}_{\{d_i=n_4\}}(V_K - v(\frac{i}{N})) + g_{Na}\mathbf{1}_{\{d_i=m_3h_1\}}(V_{Na} - v(\frac{i}{N})) \qquad (29)$$

$$+ g_{ChR2}(\mathbf{1}_{\{d_i=O_1\}} + \rho\mathbf{1}_{\{d_i=O_2\}})(V_{ChR2} - v(\frac{i}{N})) + g_L(V_L - v(\frac{i}{N}))\Big)\delta_{\frac{i}{N}},$$

with $\delta_z \in V^*$ the Dirac mass at $z \in I$.

— *A jump rate function $\lambda : V \times D_N \times U \to \mathbb{R}_+$ defined for all $(v, d, u) \in H \times D_N \times U$ by*

$$\lambda_d(v,u) = \sum_{i\in I_N}\sum_{x\in D}\sum_{\substack{y\in D,\\ y\neq x}} \sigma_{x,y}(v(\frac{i}{N}),u)\mathbf{1}_{\{d_i=x\}}, \qquad (30)$$

with $\sigma_{x,y} : \mathbb{R}\times U \to \mathbb{R}_+^*$ smooth functions for all $(x,y)\in D^2$.

— *A discrete transition measure $\mathcal{Q} : V \times D_N \times U \to \mathcal{P}(D_N)$ defined for all $(v, d, u) \in E \times D_N \times U$ and $y \in D$ by*

$$\mathcal{Q}(\{d^{i:y}\}|v,d) = \frac{\sigma_{d_i,y}(v(\frac{i}{N}),u)\mathbf{1}_{\{d_i\neq y\}}}{\lambda_d(v,u)}, \qquad (31)$$

where $d^{i:y}$ is obtained from d by putting its i^{th} component equal to y.

The optimal control problem we address is defined as follows. Suppose we are given a *reference signal $V_{ref} \in V$*. The control problem is then to find $\alpha \in \mathcal{A}$ that minimizes the following expected cost

$$J_z(\alpha) = \mathbb{E}_z^\alpha\left[\int_0^T \big(\kappa||X_t^\alpha(\phi) - V_{ref}||_V^2 + \alpha(X_t^\alpha)\big)\,\mathrm{d}t\right], \quad z \in \Upsilon, \qquad (32)$$

where $\mathcal{A}$ is the space of control strategies, Υ is defined as before, $X_\cdot^\alpha$ is the controlled PDMP and $X_\cdot^\alpha(\phi)$ its continuous component (the membrane potential).

Theorem 0.3.2. *Under a set of assumptions on the local characteristics of the PDMP $(L, f_d, \lambda, \mathcal{Q})$ that can be found in Section 2.1.1, there exists an optimal control strategy $\alpha^* \in \mathcal{A}$ such that for all $z \in \Upsilon$,*

$$J_z(\alpha^*) = \inf_{\alpha\in\mathcal{A}} \mathbb{E}_z^\alpha\left[\int_0^T \big(\kappa||X_t^\alpha(\phi) - V_{ref}||_V^2 + \alpha(X_t^\alpha)\big)\,\mathrm{d}t\right],$$

and the value function $z \to \inf_{\alpha\in\mathcal{A}} J_z(\alpha)$ is continuous on Υ.

Finally, the large possibilities that cover our theoretical framework allow us to discuss several modifications of the model, such as the places where the control appears, the models of ChR2 that can be considered, or the control space that can be taken infinite-dimensional.

0.3.3 Chapter 3

This chapter gathers additional results on the infinite-dimensional controlled PDMP defined in Chapter 2. First, we prove that, provided a supplementary assumption on the semigroup that drives the deterministic motion, the continuous component of a sequence of relaxed trajectories of the PDMP (the membrane potential in our applications), associated to a sequence of relaxed control strategies, is tight in $C([0,T],H)$. This constitute a first step towards a relaxation result for the relaxed infinite-dimensional controlled PDMP. Relaxation theorems ensure that relaxed control systems can be approximately replicated by ordinary ones so that relaxed control systems stay closely related to the original ones. To prove such results, one way is to show that the ordinary control space is densely embedded in the relaxed one and then, show that if a sequence of relaxed controls converges, then the associated sequence of relaxed processes converges to the process associated with the limiting relaxed control. For the infinite-dimensional controlled PDMP, the next step would be to prove the tightness of the entire process and then to identify a unique limit, for instance by studying the sequence of generators, that uniquely characterize the processes. We report the discussion on why the tightness of the continuous component of the PDMP is easy and why the tightness of the whole process and the identification of a limiting process are much harder because we need too much mathematical material with respect to the goal of this section.

The second part of the chapter has for main objective to extend the definition of infinite dimensional controlled PDMPs to Banach spaces, possibly nonreflexive. We first define the process for a separable and reflexive Banach space and we prove that the part of Chapter 2 that changes can be adapted for the main results to remain valid. Namely, we prove that the theorem of existence of optimal controls is still true in this new framework. We then treat the case when the Banach space is not reflexive. In this case, the dual semigroup is not necessarily strongly continuous, a crucial point in the proof of the previous results. We illustrate this problem on an elementary example. The solution is to consider the Phillips dual, also called sometimes sun dual, that consists in the part of the dual space in which the dual semigroup is strongly continuous. Let E be Banach space and $(A, D(A))$ the infinitesimal generator of a strongly continuous semigroup $(S(t))_{t\geq 0}$ in E.

Definition 0.3.2. *The Phillips dual $E^{\odot}$ of E with respect to $(A, D(A))$ is defined by*

$$E^{\odot} := \{y^* \in E^* | \lim_{t\downarrow 0} ||S^*(t)y^* - y^*||_{E^*} = 0\}$$

and we call the semigroup given by the restricted operators

$$S(t)^{\odot} := S(t)^{*}_{|E^{\odot}}, \quad (t \geq 0),$$

the Phillips semigroup. We will denote by $A^{\odot}$ its infinitesimal generator

We then show that $E^{\odot}$ corresponds to the closure of the domain of the dual infinitesimal generator A^* in E^*, $E^{\odot} = \overline{D(A^*)}$ and that the Phillips dual semigroup $(S^{\odot}(t))_{t\geq 0}$ is strongly continuous in $E^{\odot}$. We then consider the Phillips dual $E^{\odot\odot}$ of $E^{\odot}$ with respect to $(A^{\odot}, D(A^{\odot}))$ and prove that E is linearly and continuously embedded in $E^{\odot\odot}$. All the previous results are know, but since the use of nonreflexive Banach spaces is not that recurrent, we rewrite the proofs in the most elementary way. The case we are interested in is when E and $E^{\odot\odot}$, the Banach space E being then called $\odot$-reflexive. Then, we advantageously replace the space E^* by $E^{\odot}$ and the dual semigroup $(S(t)^*)_{t\geq 0}$ by the Phillips dual semigroup $(S^{\odot}(t))_{t\geq 0}$ in the proof for the reflexive case and obtain the same results.

In our applications, we may want to consider $C([0,1])$ instead of $L^2(0,1)$ for the membrane potential if we argue that it should be continuous along the axon. We thus develop the case of the Laplacian, denoted by Δ_c, in $C([0,1])$ and we prove the following theorem.

Theorem 0.3.3. *The operator $(\Delta_c, D(\Delta_c))$ with domain defined by*

$$D(\Delta_c) := \left\{ y \in C^2([0,1]) \mid y'(0) = y'(1) = 0 \right\},$$

generates an immediately compact analytic semigroup of contractions $(S(t))_{t\geq 0}$ in $C([0,1])$, defined for $y \in C([0,1])$

$$(S(t)y)(s) = \int_0^1 k_t(s,r)y(r)\mathrm{d}r, \quad (t > 0, s \in [0,1])$$

with

$$k_t(s,r) := 1 + 2\sum_{n=1}^{\infty} e^{-\pi^2 n^2 t}\cos(n\pi s)\cos(n\pi r).$$

The kernel $k_t(\cdot,\cdot)$ is continuous and positive on $[0,1]^2$.
The space $C([0,1])$ is $\odot$-reflexive with respect to $(\Delta_c, D(\Delta_c))$ and we have

$$C([0,1])^{\odot} = L^1(0,1),$$

and

$$\Delta_c^{\odot} = \Delta_1, \qquad S^{\odot}(t) = S_1(t) \quad (t \geq 0),$$

with Δ_1 *the infinitesimal generator of an immediately compact analytic semigroup* $(S_1(t))_{t\geq 0}$ *defined on the domain* $D(\Delta_1)$ *consisting of elements* $y \in L^1([0,1])$ *such that there exists* $z(=\Delta_1 y)$ *in* $L^1([0,1])$ *with*

$$\int_0^1 y(x)v''(x)\mathrm{d}x = \int_0^1 z(x)v(x)\mathrm{d}x \tag{33}$$

for every $v \in C^2([0,1])$ *with* $v'(0) = v'(1) = 0$.
Finally, for $y \in L^1(0,1)$,

$$S(t)^{\odot}y(s) = \int_0^1 k_t(s,r)y(r)\mathrm{d}r, \quad (t \geq 0).$$

0.3.4 Perspectives

Since the study of mathematical optogenetic models is at its beginnings, the perspectives in this area and the possible directions to go towards are tremendously vast. We present here some directions linked to our work.

On deterministic conductance-based models

It would be interesting to continue the numerical study of the controlled Morris-Lecar model and try to identify bifurcation points for the number of switching times.

Other types of optimal control problems would also be very interesting. For instance, we know that more than the shape of the spikes, the time elapsed between consecutive spikes conveys a lot of information. We could propose a close problem to the one we study as follows. Consider a controlled conductance-based and the optimal control problem that consists in steering the system from a point corresponding to a state right after a spike, to the next spike in minimal time. The formulation of this control problem is the exact same one as the problem we study and for two-dimensional neuron models with the ChR2-3-states model, we know that the optimal control is bang-bang. The difficulty would lie in the determination of the right value for the starting point. If we want this problem to accurately correspond to the minimization of the inter-spike arrival time, we need to determine the values of the control system that correspond to a time right after a spike. This is quite easy for the variables of the conductance-based model but much more delicate for the variables of the ChR2 model. Indeed, they are many controls that lead to the firing of the neuron and the choice is crucial. Since the relevant goal of this problem is to minimize the time between several consecutive spikes (and not just between two spikes), that is the minimization of the inter-spike arrival of a spike train, we must chose a point of the ChR2 model that also minimizes the time between the two previous spikes. One way to chose a relevant starting point could be to use the previous problem to initialize this one.

Finally, another interesting problem could be the tracking of a reference signal, as in Chapter 2, while minimizing the intensity of the light used (i.e. the control). Again, this problem is closely linked to the one we studied in terms singular extremals. Furthermore, the numerical methods we used could be as well implemented.

Numerical methods for the infinite-dimensional controlled PDMP

In chapter 2 we prove the existence of optimal controls for a wide class of infinite-dimensional PDMPs. It would be nice, for theses processes, to implement numerical methods in order to compute the optimal controls, or at least approximations of these optimal controls. One efficient way to address numerical optimal control problems for PDMPs is to use quantization methods that consist in replacing the state and control spaces by discrete spaces and work with approximations of the processes on these discrete spaces ([GN98], [PPP04], [dSDZ15]).

Population of neurons

Our study is entirely based on single neuron models. The next reasonable step would be to consider networks of neurons. Optimal control of populations of neurons have been addressed outside the optogenetic framework ([LDR13], [TTS$^+$15]). Optogenetics would probably provide new insights on optimal control of populations of neurons since this technique is able to target specific neuron types. It would then be very interesting to consider populations of neurons of several types, some types expressing ChR2, and thus responsive to light stimulation, and some types insensitive to light stimulation. It would allow to try and investigate the role of a specific type of neurons on the rest of the population.

A link between the stochastic and the deterministic models

The uncontrolled version of the infinite-dimensional stochastic Hodgkin-Huxley model of Definition 0.3.1 converges to the infinite-dimensional deterministic Hodgkin-Huxley model when the scale N goes to infinity ([Aus08], [RTW12]). It would be great to study the link between the controlled models. For example, does the optimal control that provides Theorem 0.3.2 converge to an optimal control of the limiting deterministic model ? This is a fair question, nevertheless, they are many questions hidden inside it. First, before considering optimal control problems, is the deterministic controlled Hodgkin-Huxley model a limit for the stochastic version when the scale N goes to infinity ? This question is in fact linked to the relaxation question addressed in Chapter 3 and thus not trivial. Moreover, the appropriate notion of convergence to study sequences of optimal control problems is Γ-convergence ([BM82], [Mas93]). If we write $(X_t^{\alpha,N})_{t\geq 0}$ the N^{th} stochastic controlled infinite-dimensional Hodgkin-Huxley-ChR2 process of Definition 0.3.1 to emphasize the dependence on the scale N, then the study of Γ-convergence for the sequence of control problems associated with the sequence of processes $((X_t^{\alpha,N})_{t\geq 0})_{N\in\mathbb{N}^*}$ and the cost defined by (32) would imply to show that for a converging sequence $(\alpha_N)_{N\geq\infty}$ of control strategies, possibly relaxed, the sequence of processes $(((X_t^{\alpha_N,N})_{t\geq 0})_{N\in\mathbb{N}^*})$ converges to the solution of the deterministic controlled Hodgkin-Huxley system associated to the limiting control. Besides, this limiting control would have to be properly defined since controls for the deterministic model and the stochastic model are not the same mathematical objects.

Chapter 1

Minimal time spiking in various ChR2-controlled neuron models

Introduction

In this chapter we investigate, theoretically and numerically, the minimal time control, via Optogenetics, of some widely used finite-dimensional deterministic neuron models such as the Hodgkin-Huxley model ([HH52]), the Morris-Lecar model ([LM81]) and the FitzHugh-Nagumo model ([Fit61]). Control of neuron models has been addressed in the literature in different ways. One popular way to investigate this problem is to look at phase reductions of non-linear evolution systems, consisting in reducing the system of equations to a single first-order differential equation, with for essential goal numerical computations of the dynamic programming formulation of the problem ([BMH04], [NM11]). Integrate-and-fire models, which are also a simplification of nonlinear sytems to single first-order linear differential equations, receiving stochastic inputs, have been studied in [FT03] in order to minimize the variance of the membrane potential, arguably linked to the variance of the final time, while reaching a given membrane potential threshold in fixed time. Theses simplifications allow the authors to obtain a nice analytic expression for the optimal control. A stochastic integrate-and-fire model has also been used in [LDL14] to find an optimal electrical stimulation to spike in a desired time, a problem close to ours, with numerical computation purposes.

All these studies were exclusively based on control via electrical stimulation. Optogenetics allows a control of excitable cells of a different nature. This recent and thriving technique is based on light stimulation ([Dei11],[Boy15],[Dei15]). It has for cornerstone the genetical modification of excitable cells for them to express new ion channels whose opening and closing are triggered by the absorption of photons. In particular, it is able to target specific populations of neurons. Indeed, by designing viruses that will aim at these populations only, the light stimulation will have no effect on the other populations that do not express the new ion channels. This makes Optogenetics a noninvasive technique, in contrast to electrical stimulation that reaches a whole volume of tissue, regardless of the types of neurons that populate this volume. Furthermore, optical devices such as optic fibers and lasers allow to reach deeply embedded populations of neurons. It then provides Optogenetics with a tremendous advantage over electrical stimulation in the exploration of neural tissues and neural functions. The risk of tissue damage is also decreased with this technique. The perspectives of applications in medicine are thus colossal with, among others, the promise to help understand and treat Alzheimer's disease ([RRP+15]), Parkinson's disease ([CXZ15]), epilepsy ([PH15]), vision loss ([GMBH+15]), narcolepsy ([AZA+07]) and even depression ([LNC12]).

Our work is based on one of these light-gated ion channels called *Channelrhodopsin* (ChR2). It is a depolarizing non-selective cation channel that opens upon a stimulation with blue light. One of the neural events that contains a lot of information is the latency time between two consecutive *action potentials* or *spikes* (a large depolarization of the membrane potential when it goes beyond some threshold). Here we want to specifically address the time optimal control of the first spike in various neuron models, for two different mathematical models of ChR2 introduced in [NGG+09]. Indeed, the mathematical formulation of this problem is really close to the one of the optimal control of the latency time between two spikes. In particular, the investigation of singular trajectories is the same. To the best of our knowledge, this optimal control problem has never been studied before, neither in terms of electrical stimulation, nor in terms of light stimulation.

In Section 1.1 we set the mathematical framework of conductance-based neuron models and we recall some results of minimal time control problems for affine control systems, and the role of singular controls. We then present in Section 1.2 the mathematical model of ChR2 and how the resulting models can be incorportated in conductance-based models. We apply our results to various neuron models in Section 1.3. For the ChR2-3-state model, we prove that there are no singular optimal controls for two-dimensional models (FitzHugh-Nagumo, Morris-Lecar, reduced Hodgkin-Huxley models) and we give the expression of the *bang-bang* optimal control. We illustrate these results with numerical computations of the optimal controls by means of a direct method. For the ChR2- 4-states model, we numerically observe optimal bang-bang controls. Along the review of the different models, we insist on how optimal control appears as a great tool to discuss and compare neuron models. In particular, it emphasizes a peculiar behavior of the Morris-Lecar model, compared to the other ones, and gives a new argument in favor of the reduced Hodgkin-Huxley model.

Although we focus in this paper on neuron models, our treatment of conductance-based model can be applied to any excitable cells such as cardiac cells for example (see [WAK12] for a work on application of Optogenetics in cardiac cells for simulation purposes).

1.1 Preliminaries

1.1.1 Conductance based models

Conductance based models form a popular class of simple biophysical models used to represent the activity of an excitable cell, such as a neuron or a cardiac cell. The principle is to give an equivalent circuit representation of the cell by assigning an electrical component to each meaningful biological component of the cell. Finite-dimensional conductance-based models represent the cell as a single isopotential electrical compartment. The lipid bilayer membrane of the cell is represented by a capacitance $C > 0$. Across the membrane are disposed voltage-gated ion channels, represented by conductances $g_x > 0$ whose values depend on the type x of the channel. An ion channel is a protein that constitutes a gate across the membrane. It has the ability to let ions flow across the membrane or to prevent them from doing so. Ion channels are said selective in the sense that they act as a filter of certain types of ions. The main types of ion channels are potassium (K^+) channels, sodium (Na^+) channels and calcium (Ca^{2+}) channels. The ion flows are driven by electrochemical gradients represented by batteries whose voltages $E_x \in \mathbb{R}$ equal the membrane potential corresponding to the absence of ion flow of type x. For that matter, they are called equilibrium potentials. The sign of the difference between the membrane potential and E_x gives the direction of the driving force. The channels are all called voltage-gated because their opening and closing depend on the potential difference across the membrane. This means that the conductances g_x are variable conductances, depending on the membrane potential.

The ion flow across the membrane generates an electrical current in the circuit, the possible movements of ions inside the cell being neglected. To each type x of ion channels is associated a macroscopic ion current I_x. The total membrane current is the sum of the capacitive current and all of ionic currents considered. In all models we consider in this paper, the ionic currents include a leakage current that accounts for the passive flow of some other ions across the membrane. This current is associated to a fixed conductance g_L and is always denoted by I_L.

Every macroscopic ion current I_x is the result of the ion flow through all the ion channels of type x. Since the number of ion channels in an excitable cell is very large, the macroscopic conductance g_x is a function of the probability $n_x \in [0,1]$ that a channel of type x opens. In fact, the channels of type x are constituted by several subpopulations of gates that have different dynamics. For that matter, let $k_x \in \mathbb{N}^*$ be the number of subpopulations of the channels of type x and write $(n_{x_1}, \dots, n_{x_{k_x}}) \in [0,1]^{k_x}$ the probabilities that each gate of the subpopulation opens, that is, n_{x_i} represents the probability that a gate of type x_i opens. The time evolution of these probabilities in each subpopulation depends on the membrane potential and is of first order. For $i \in \{1, \dots, k_x\}$, it is represented on Figure 1.1 and the dynamical system governing n_{x_i} is the following

$$\dot{n}_{x_i}(t) = \alpha_{x_i}(V)(1 - n_{x_i}) - \beta_{x_i}(V)n_{x_i}, \tag{1.1}$$

where α_{x_i} and β_{x_i} are smooth functions of the membrane potential V.

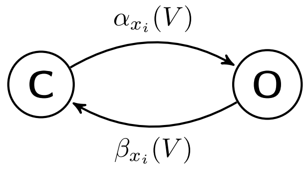


Figure 1.1 – Ion channel of type x_i

This dynamics can be easily interpreted as follows : when the potential across the membrane is equal to V, ion channels in the subpopulation of type x_i open at rate $\alpha_{x_i}(V)$ and close at rate $\beta_{x_i}(V)$.

The macroscopic conductance g_x is then given by

$$g_x(n_x) = \bar{g}_x f_x(n_{x_1}, \ldots, n_{x_{k_x}}),$$

where $\bar{g}_x$ is the maximum conductance of the channel (i.e., the conductance when all the channels of type x are open) and f_x is a smooth function depending on the type of the channel.

The macroscopic current I_x of type x is given by Ohm's law. Taking into account the equilibrium potential E_x, we get

$$\begin{aligned} I_x &= g_x(V - E_x) \\ &= \bar{g}_x f_x(n_{x_1}, \ldots, n_{x_{k_x}})(V - E_x). \end{aligned}$$

In Figure 1.2 below we give the example of a conductance-based model with two types of channels with conductances g_1 and g_2.

The total current I_{tot} is given by

$$I_{tot} = I + I_1 + I_2 + I_L,$$

where $I = C\frac{\mathrm{d}V}{\mathrm{d}t}$, $I_{1,2} = g_{1,2}(V)(V - E_{1,2})$ and $I_L = g_L(V - E_L)$.

The first conductance-based model dates back to the seminal work of Hogkin and Huxley ([HH52]) on the squid giant axon. In voltage-clamp experiments (i.e., experiments in which the membrane potential was held fixed), they showed how the ionic currents could be interpreted in terms of changes in Na^+ and K^+ conductances. From the experimental data, they inferred the dependencies, on the membrane potential and the time, of these

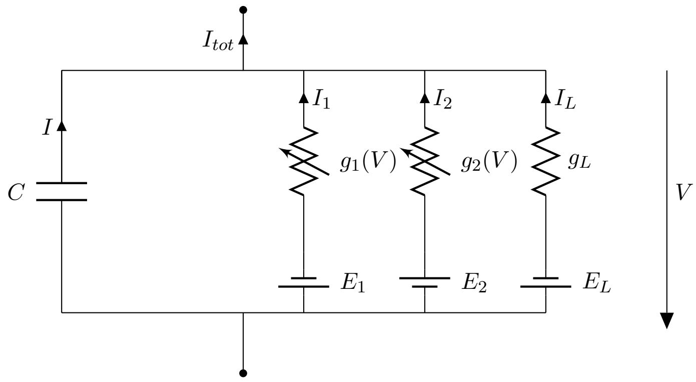


Figure 1.2 – Equivalent circuit for a conductance-based model with two types of channels

conductances. The resulting mathematical model became very popular because it was able to reproduce all key biophysical properties of an action potential. The K^+ channels are composed of a single population. Let us denote by n the probability that a channel of type K^+ opens. The K^+ conductance is given by

$$g_K = \bar{g}_K n^4.$$

The population of Na^+ is composed of two subpopulations and we write m and h the corresponding probabilities that a certain type of gate opens. The Na^+ conductance is given by

$$g_{Na} = \bar{g}_{Na} m^3 h.$$

The total membrane current I_{tot} is then given by

$$I_{tot} = C\frac{\mathrm{d}V}{\mathrm{d}t} + \bar{g}_K n^4(V - E_K) + \bar{g}_{Na} m^3 h(V - E_{Na}) + g_L(V - E_L),$$

with V the membrane potential. If an external current I_{ext} is applied to the cell, we can write the dynamic system (HH) for the evolution of the membrane potential

$$(HH)\begin{cases} C\dot{V}(t) = \bar{g}_K n^4(t)(E_K - V(t)) + \bar{g}_{Na} m^3(t)h(t)(E_{Na} - V(t)) \\ \qquad\qquad + g_L(E_L - V(t)) + I_{ext}(t), \\ \dot{n}(t) = \alpha_n(V(t))(1 - n(t)) - \beta_n(V(t))n(t), \\ \dot{m}(t) = \alpha_m(V(t))(1 - m(t)) - \beta_m(V(t))m(t), \\ \dot{h}(t) = \alpha_h(V(t))(1 - h(t)) - \beta_h(V(t))h(t). \end{cases}$$

The expression of the functions α_x and β_x and the numerical values of the constants can be found in Appendix 1.B.

To end this section, we give a formal mathematical definition of what we will refer to as a conductance-based model in the sequel.

Definition 1.1.1. *Conductance based model.*
Let $n \in \mathbb{N}^*$. Let also $k \in \mathbb{N}^*$ and for all $i \in \{1, \ldots, k\}$, let $j_i \in \mathbb{N}^*$ such that $\sum_{i=1}^{k} j_i = n-1$. We call n-dimensional conductance-based model the following dynamical system in $\mathbb{R}^n$

$$\dot{x}_1(t) = \frac{1}{C}\Big(\sum_{i=1}^{k} \bar{g}_i f_i(x_{j_1+\cdots+j_{i-1}+1}(t), \ldots, x_{j_1+\cdots+j_{i-1}+j_i}(t))\big(E_i - x_1(t)\big)\Big),$$

with the convention that $j_1 + \cdots + j_{i-1} + 1 = 2$ and $j_1 + \cdots + j_{i-1} + j_i = j_1$ for $i = 1$, and for $i \in \{2, \ldots, n\}$,

$$\dot{x}_i(t) = \alpha_i(x_1(t))(1 - x_i(t)) - \beta_i(x_1(t))x_i(t),$$

where $C > 0$ and for all $i \in \{1, \ldots, k\}$ and $l \in \{2, \ldots, n\}$

— $\bar{g}_i > 0$, $f_i : \mathbb{R}^{j_i} \to \mathbb{R}_+$ *is a smooth function,*

— $\alpha_l, \beta_l : \mathbb{R} \to \mathbb{R}$ *are smooth functions such that for all* $v \in \mathbb{R}, \alpha_l(v) + \beta_l(v) \neq 0$.

We finally require that the previous dynamical system exhibits an equilibrium point $x^\infty \in \mathbb{R}^n$, that we call resting state, defined by the following equations

$$x_i^\infty = \frac{\alpha_i(x_1^\infty)}{\alpha_i(x_1^\infty) + \beta_i(x_1^\infty)}, \quad \forall i \in \{2, \ldots, n\},$$

and

$$0 = \sum_{i=1}^{k} \bar{g}_i f_i(x^\infty_{j_1+\cdots+j_{i-1}+1}, \ldots, x^\infty_{j_1+\cdots+j_{i-1}+j_i})\big(E_i - x_1^\infty\big)$$

Conductance based models are uniquely defined on $\mathbb{R}_+$. The initial conditions $y \in \mathbb{R}^n$ that we consider are physiological conditions with y_1 in a physiological range for the membrane potential of the cell considered, basically $y_1 \in [V_{min}, V_{max}]$ with $-\infty < V_{min} < V_{max} < +\infty$, and $y_i \in [0, 1]$ for all $i \in \{2, \ldots, n\}$.

1.1.2 The Pontryagin Maximum Principle for minimal time single-input affine problems

In this section we recall the necessary optimality conditions of the Pontryagin Maximum Principle applied to the specific affine problem that we investigate in the sequel.
Consider the minimum time problem for a smooth single-input affine system:

$$\dot{x}(t) = F_0(x(t)) + u(t)F_1(x(t)), \quad x(0) = x_{eq} \in \mathbb{R}^n, \tag{1.2}$$

where $x(t) \in \mathbb{R}^n$ and x_{eq} solution of $F_0(x) = 0$ (i.e., an equilibrium point for the uncontrolled system). The control domain $U := [0, u_{max}]$ is a segment of $\mathbb{R}_+$, with $u_{max} > 0$. The state variable must satisfy the final condition $x(t_f) \in M_f$ where

$$M_f := \{x \in \mathbb{R}^n | x_1 = V_f\},$$

with $V_f > 0$ a given constant that will later correspond to the potential of a spike. The set of admissible controls, denoted $\mathcal{U}_{ad}$, is the subset of the measurable applications from $\mathbb{R}_+$ to U, denoted by $\mathcal{L}(\mathbb{R}_+, U)$, such that (1.2) has a unique solution on $\mathbb{R}_+$.

We introduce the Hamiltonian $\mathcal{H} : \mathbb{R}^n \times \mathbb{R}^n \times \mathbb{R}_- \times U \to \mathbb{R}$ defined for $(x, p, p^0, u) \in \mathbb{R}^n \times \mathbb{R}^n \times \mathbb{R}_- \times U$ by

$$\mathcal{H}(x, p, p^0, u) := \langle p, F_0(x)\rangle + u\langle p, F_1(x)\rangle + p^0, \tag{1.3}$$

where $\langle \cdot, \cdot \rangle$ is the scalar product on $\mathbb{R}^n$, $p \in \mathbb{R}^n$ is the adjoint vector and $p^0 \leq 0$ a non-positive number. The Pontryagin Maximum Principle (see [PBGM74], [Tré08, Theorem 7.2.1]) states that if the trajectory $t \to x^u(t)$, $t \in [0, t_f]$ associated with the admissible control $u \in \mathcal{U}_{ad}$ is optimal on $[0, t_f]$, then there exists $p : [0, t_f] \to \mathbb{R}^n$ absolutely continuous and $p^0 \in \mathbb{R}_-$ such that (p, p^0) is non zero and such that p satisfy the following equations, almost everywhere in $[0, t_f]$:

$$\begin{aligned}
\dot{x}^u(t) &= \frac{\partial \mathcal{H}}{\partial p}(x^u(t), p(t), p^0, u(t)), \\
\dot{p}(t) &= -\frac{\partial \mathcal{H}}{\partial x}(x^u(t), p(t), p^0, u(t)).
\end{aligned}$$

Moreover, the following maximum condition must be satisfied on $[0, t_f]$:

$$\mathcal{H}(x^u(t), p(t), p^0, u(t)) = \max_{v \in U} \mathcal{H}(x^u(t), p(t), p^0, v). \tag{1.4}$$

In view of the initial and final conditions on the state variable, the transversality condition on $p(0)$ is empty and the one on $p(t_f)$ gives

$$\begin{aligned}
p_1(t_f) &= \lambda_1 \in \mathbb{R}, \\
p_i(t_f) &= 0, \quad \forall i \in \{2, \dots, n\}.
\end{aligned}$$

In our particular setting, the augmented system does not depend on the time variable. This implies that the right hand side of (1.4) is constant on $[0, t_f]$. Now since there is no final cost and because the final time is not fixed, we also have

$$\max_{v\in U} \mathcal{H}(x^u(t_f), p(t_f), p^0, v) = 0.$$

The two latter remarks imply that for all $t \in [0, t_f]$

$$\mathcal{H}(x^u(t), p(t), p^0, u(t)) = 0 = \max_{v\in U} \mathcal{H}(x^u(t), p(t), p^0, v), \tag{1.5}$$

which can be written, in view of (1.3):

$$\langle p(t), F_0(x^u(t))\rangle + u(t)\langle p(t), F_1(x^u(t))\rangle + p^0 = 0 \tag{1.6}$$

$$= \langle p(t), F_0(x^u(t))\rangle + \max_{v\in U} v\langle p(t), F_1(x^u(t))\rangle + p^0. \tag{1.7}$$

In the case of single-input affine systems, the maximum condition (1.7) gives the expression of the optimal control:

$$u(t) := \begin{cases} u_{max}, & \text{if } \langle p(t), F_1(x^u(t))\rangle > 0, \\ 0, & \text{if } \langle p(t), F_1(x^u(t))\rangle < 0, \\ \text{undetermined}, & \text{if } \langle p(t), F_1(x^u(t))\rangle = 0. \end{cases}$$

The function $\varphi(t) := \langle p(t), F_1(x^u(t))\rangle$, whose sign gives the expression of the optimal control is called the switching function. If it does not vanish on any subinterval I of $[0, t_f]$, the optimal control is a succession of constant controls called bang-bang control. The switching times between the two constant modes are given by the change of sign of the switching function φ. This conclusion fails if there exists a subinterval I of $[0, t_f]$ along which the switching function vanishes. The control on I is then called singular and this situation has to be further investigated.

Finally, the non-triviality of (p, p^0) reduces in fact to the one of p because if $p(t) = 0$ for a given $t \in [0, t_f]$ then $p^0 = 0$ because of (1.6).

The investigation of the existence of singular trajectories will be done later for our different models but for now let us state that if there exists a subinterval I on which the switching function vanishes, with u the corresponding control, then from the Pontryagin Maximum Principle, (x^u, p, u) is the solution, on I, of the following equations:

$$\dot{x}^u(t) = \frac{\partial \mathcal{H}}{\partial p}(x^u(t), p(t), p^0, u(t)), \quad \dot{p}(t) = -\frac{\partial \mathcal{H}}{\partial x}(x^u(t), p(t), p^0, u(t)), \quad \langle p(t), F_1(x^u(t))\rangle = 0. \tag{1.8}$$

1.2 Control of conductance-based models via Optogenetics

In this section we consider a general conductance-based model in $\mathbb{R}^n$, with $n \in \mathbb{N}^*$, of the form

$$\dot{x}(t) = f_0(x(t)), \quad t \in \mathbb{R}_+, \quad x(0) = x_0 \in \mathcal{D} \subset \mathbb{R}^n, \tag{1.9}$$

with f_0 a smooth vector field in $\mathbb{R}^n$ and $\mathcal{D}$ physiological domain.

Optogenetics is a recent and innovative technique which allows to induce or prevent electric shocks in living tissue, by means of light stimulation. Succesfully demonstrated in mammalian neurons in 2005 ([BZB+05]), the technique relies on the genetic modification of cells in order for them to express particular ionic channels, called rhodopsins, whose opening and closing are directly triggered by light stimulation. One of these rhodopsins comes from an unicellular flagellate algae, *Chlamydomonas reinhardtii*, and has been baptized Channelrhodopsin-2 (ChR2). It is a cation channel that opens when illuminated with blue light.

Since the field is very young, the mathematical modeling of the phenomenon is quite scarce. Some models have been proposed, based on the study of the photocycles that the channel go through when it absorbs a photon (see [NGG+09] for a 3-states model and [HEG05] for a 4-states model). In [NGG+09], the authors study two models for the ChR2 that are able to reproduce the photocurrents generated by the light stimulation of the channel. Those models are constituted by several states that can be either conductive (the channel is open) or non-conductive (the channel is closed). Transitions between those states are spontaneous, depend on the membrane potential or are triggered by the absorption of a photon. This kind of models has already been used to simulate photocurrents in cardiac cells. In [WAK12], the authors include ChR2 photocurrents into an infinite dimensional model and use finite differences and elements to simulate the system. The optimal control of such a system is not investigated in this paper. Here we are interested in both 3-states and 4-states models of Nikolic and al. [NGG+09]. The 3-states model has one open state o and two closed states c and d while the 4-states model has two open states o_1 and o_2, and two closed states c_1 and c_2. Their transitions are represented on Figures 1.3 and 1.4.

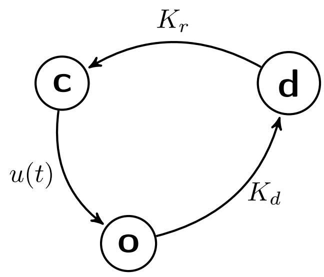


Figure 1.3 – ChR2 three states model

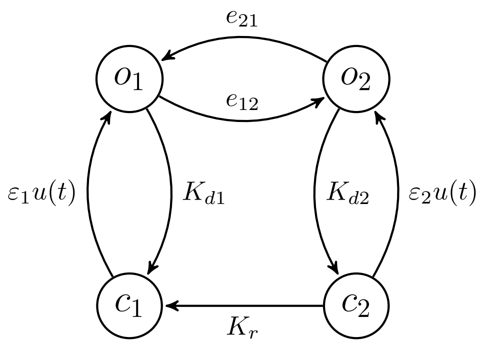


Figure 1.4 – ChR2 four states model.

In the 3-states model, the transition from the dark adapted close state c and the open state o is controlled by a function $u(t)$, proportional to the intensity of the light applied to the neuron. In our model, the intensity is then the control variable. The transition from the open state to the light adapted close state d is spontaneous and has a time constant very small in front of the one of the transition from d to c (i.e. $1/K_d << 1/K_r$). This last transition represents the fact that the protein has to regenerate before being able to go through a new cycle. The 4-states model can be similarly interpreted. The transitions from closed states to open states are triggered by light stimulation and all the other transitions are independent of the intensity of the light applied to the neuron. Hence, ε_1, ε_2, e_{12}, e_{21}, K_{d1}, K_{d2} and K_r are all positive constants. This constitutes our general assumption on the models we study. Indeed, we assume that the transitions from closed states to open states depend linearly on the light and that all the others are independent of the light. This assumption is not too heavy since it leads to models that still reproduces the shape of the photocurrents produced by the channel, and experimentally measured. Furthermore, it makes our control system affine. The dynamical system based on Figures 1.3 and 1.4 is given by

$$\begin{cases} \dot{o}(t) = u(t)(1 - o(t) - d(t)) - K_d o(t) \\ \dot{d}(t) = K_d o(t) - K_r d(t), \end{cases} \tag{1.10}$$

and

$$\begin{cases} \dot{o}_1(t) = \varepsilon_1 u(t)(1 - o_1(t) - o_2(t) - c_2(t)) - (K_{d1} + e_{12})o_1(t) + e_{21}o_2(t), \\ \dot{o}_2(t) = \varepsilon_2 u(t)c_2(t) + e_{12}o_1(t) - (K_{d2} + e_{21})o_2(t), \\ \dot{c}_2(t) = K_{d2}o_2(t) - (\varepsilon_2 u(t) + K_r)c_2(t). \end{cases} \tag{1.11}$$

In the 3-states model, the conductance of the ChR2 channel is assumed to be proportional to the probability $o(t)$ that the channel opens, so that the ion current associated to ChR2 channels is given by

$$I_{ChR2}(t) = g_{ChR2}o(t)(V_{ChR2} - v(t)),$$

with v the membrane potential of the channel, g_{ChR2} the maximal conductance of the channel and V_{ChR2} the equilibrium potential of the channel. See Appendix 1.C for the numerical computation of these constants. In the 4-states model, the open states are assumed to be of different conductivity so that

$$I_{ChR2}(t) = g_{ChR2}(o_1(t) + \rho o_2(t))(V_{ChR2} - v(t)),$$

with $\rho \in (0, 1)$. We can now include these two models of ChR2 in a conductance-based model defined in the previous section.

Definition 1.2.1. *i) We call ChR2-3-states controlled conductance-based model, the system given by*

$$\begin{cases} \dot{x}(t) = f_0(x(t)) + \dfrac{1}{C} g_{ChR2}o(t)(V_{ChR2} - x_1(t))\mathbf{e}_1 \\ \dot{o}(t) = u(t)(1 - o(t) - d(t)) - K_d o(t) \\ \dot{d}(t) = K_d o(t) - K_r d(t), \end{cases} \tag{1.12}$$

with $\mathbf{e}_1 = (1, 0, \ldots, 0) \in \mathbb{R}^n$. *We rewrite this system in* $\mathbb{R}^{n+2}$ *in the affine form*

$$\dot{y}(t) = \tilde{f}_0(y(t)) + u(t)f_1(y(t)), \quad t \in \mathbb{R}_+, \tag{1.13}$$

with $y(\cdot) = (x(\cdot), o(\cdot), d(\cdot))$, $\tilde{f}_0(y) = (f_0(x)+\frac{1}{C}g_{ChR2}o(t)(V_{ChR2}-x_1(t))\mathbf{e}_1, -K_d o, K_d o - K_r d)$ *and* $f_1(y) = (1-o-d)\partial_o$, *where* ∂_o *is the derivative with respect to the variable* o.

ii) We call ChR2-4-states controlled conductance-based model, the system given by

$$\begin{cases} \dot{x}(t) = f_0(x(t)) + \dfrac{1}{C} g_{ChR2}(o_1(t) + \rho o_2(t))(V_{ChR2} - x_1(t))\mathbf{e}_1 \\ \dot{o}_1(t) = \varepsilon_1 u(t)(1 - o_1(t) - o_2(t) - c_2(t)) - (K_{d1} + e_{12})o_1(t) + e_{21}o_2(t), \\ \dot{o}_2(t) = \varepsilon_2 u(t)c_2(t) + e_{12}o_1(t) - (K_{d2} + e_{21})o_2(t), \\ \dot{c}_2(t) = K_{d2}o_2(t) - (\varepsilon_2 u(t) + K_r)c_2(t). \end{cases} \tag{1.14}$$

We also rewrite the system in $\mathbb{R}^{n+3}$,

$$\dot{z}(t) = \hat{f}_0(z(t)) + u(t)f_2(z(t)), \quad t \in \mathbb{R}_+, \tag{1.15}$$

with $z(\cdot) = (x(\cdot), o_1(\cdot), o_2(\cdot), c_2(\cdot))$,

$$\hat{f}_0(z) = (f_0(x) + \frac{1}{C} g_{ChR2}(o_1(t) + \rho o_2(t))(V_{ChR2} - x_1(t))\mathbf{e}_1,$$
$$- (K_{d1} + e_{12})o_1 + e_{21}o_2, e_{12}o_1 - (K_{d2} + e_{21})o_2, K_{d2}o_2 - K_r c_2),$$

and

$$f_2(z) = \varepsilon_1(1 - o_1 - o_2 - c_2)\partial_{o_1} + \varepsilon_2 c_2 \partial_{o_2} - \varepsilon_2 c_2 \partial_{c_2}.$$

Notation. *Let $k \in \mathbb{N}^*$. We use two ways to write a vector field $F : \mathbb{R}^k \to \mathbb{R}^k$. For $x \in \mathbb{R}^k$, we write either*

— $F(x) = (F_1(x), \dots, F_k(x))$, *or*

— $F(x) = F_1(x)\partial_1 + \cdots + F_k(x)\partial_k$,

where $F_i : \mathbb{R}^k \to \mathbb{R}$ is the i^{th} coordinate of F and ∂_i is the partial derivative along the i^{th} direction, for $i \in \{1, \dots, k\}$.

We already used this mixed notation in Definition 1.2.1 above. The second notation will be useful for the computation of Lie brackets later in this paper.

Note that for a bounded measurable function $u : \mathbb{R}_+ \to \mathbb{R}$ and a starting point $((o_0, d_0), (o_1, o_2, c_2)) \in \mathbb{R}^2 \times \mathbb{R}^3$, the systems (1.10) and (1.11) admit a unique solution, absolutely continuous on $\mathbb{R}_+$. Thus, for all bounded measurable function $u : \mathbb{R}_+ \to \mathbb{R}$ and all initial conditions $y_0 \in \mathcal{D} \times \mathbb{R}^2$ and $z_0 \in \mathcal{D} \times \mathbb{R}^3$, the systems (1.12) and (1.14) have a unique solution, defined on $\mathbb{R}_+$ and such that $x(\cdot)$ is of class C^1 and $(o(\cdot), d(\cdot))$ and $(o_1(\cdot), o_2(\cdot), c_2(\cdot))$ are absolutely continuous on $\mathbb{R}_+$.

1.2.1 The minimal time spiking problem

The control problem we are interested in here can be formulated for both ChR2 models. Consider a conductance-based neuron model in its resting state. If no light is applied to the neuron (i.e. $u \equiv 0$) then the system stays in this resting state. We want to find the optimal control that triggers a spike in minimum time when starting from the resting state. To do so, let $V_s > 0$ be the membrane potential that we decide to be corresponding to a spike. Since the control is proportional to the intensity of the light applied to the neuron, the control space U will be a segment $[0, u_{max}]$, with $u_{max} > 0$. Let $x_{eq} \in \mathbb{R}^n$ a resting state of the conductance-based model. In the next two sections, we formulate the mathematical problem for both ChR2 models.

The ChR2 3-states model

Let $y_0 = (x_{eq}, 0, 0) \in \mathbb{R}^{n+2}$ be our starting point. The state $(0, 0)$ for the system (1.10) corresponds to a neuron being in the dark for quite a long period of time (i.e. all the ChR2 channels are in the dark adapted close state c). From y_0, we then want to reach in minimal time (denoted t_f) the manifold

$$M_s := \{y \in \mathbb{R}^{n+2} | y_1 = V_s\}.$$

As in Section 1.1.2 we define $\mathcal{H} : \mathbb{R}^{n+2} \times \mathbb{R}^{n+2} \times \mathbb{R}_- \times U \to \mathbb{R}$ the Hamiltonian of the system for $(y, p, p^0, u) \in \mathbb{R}^{n+2} \times \mathbb{R}^{n+2} \times \mathbb{R}_- \times U$ by

$$\mathcal{H}(y, p, p^0, u) := \langle p, \tilde{f}_0(y)\rangle + u\langle p, f_1(y)\rangle + p^0. \tag{1.16}$$

This control problem falls into the framework of Section 1.1.2. If there is no singular extremal, the optimal control is bang-bang and is given by the sign of the switching function. Let $p = (p_x, p_o, p_d) : \mathbb{R}_+ \to \mathbb{R}^{n+2}$ be the adjoint vector of the Pontryagin Maximum Principle. The switching function reads, for $t \in [0, t_f]$,

$$\varphi(t) := (1 - o(t) - d(t))p_o(t) \text{ or also } (1 - y_{n+1}(t) - y_{n+2}(t))p_{n+1}(t).$$

In the absence of singular extremals, if we write $u^* : [0, t_f] \to U$ the optimal control, then

$$u^*(t) = u_{max}\mathbf{1}_{\varphi(t)>0}, \quad \forall t \in [0, t_f].$$

The ChR2 4-states model

We define here the same quantities for the 4-states model. Let $z_0 = (x_{eq}, 0, 0, 0) \in \mathbb{R}^{n+3}$ be our starting point. From z_0, we then want to reach in minimal time (denoted t_f) the manifold

$$M_s := \{z \in \mathbb{R}^{n+3} | y_1 = V_s\}.$$

The Hamiltonian $\mathcal{H} : \mathbb{R}^{n+3} \times \mathbb{R}^{n+3} \times \mathbb{R}_- \times U \to \mathbb{R}$ is defined for $(z, q, q^0, u) \in \mathbb{R}^{n+3} \times \mathbb{R}^{n+3} \times \mathbb{R}_- \times U$ by

$$\mathcal{H}(y, q, q^0, u) := \langle q, \hat{f}_0(z)\rangle + u\langle q, f_2(z)\rangle + q^0. \tag{1.17}$$

Let $q : \mathbb{R}_+ \to \mathbb{R}^{n+2}$ be the adjoint vector of the Pontryagin Maximum Principle. The switching function writes, for $t \in [0, t_f]$,

$$\psi(t) := \varepsilon_1(1 - o_1(t) - o_2(t) - c_2(t))q_{o_1}(t) + \varepsilon_2 c_2(t)q_{o_2}(t) - \varepsilon_2 c_2(t)q_{c_2}(t).$$

Singular extremals correspond to vanishing switching functions. We will treat the two ChR2 models in a different way. Indeed, the 3-states model is theoretically tractable and is the object of the following section. The 4-states will be investigated numerically.

1.2.2 The Goh transformation for the ChR2 3-states model

We state and prove here our main reduction result regarding the existence of optimal singular controls for the ChR2-3-states control problem.

Theorem 1.2.1. *The existence of optimal singular extremals in the spiking problem in minimal time for the control system (1.12) is equivalent to the existence of optimal singular extremals in the same problem but for the reduced system on* $\mathbb{R}^n$

$$\dot{x} = f_0(x) + o\tilde{f}_1(x), \tag{1.18}$$

where o is the control variable and $\tilde{f}_1(x) = \frac{1}{C} g_{ChR2}(V_{ChR2} - x_1)\mathbf{e}_1$.

This notion of equivalence is to be understood in the sense of the necessary conditions (1.8) of the Pontryagin maximum principle, for the existence of singular extremals. It means that the necessary conditions (1.8) for the original control system (1.12) are satisfied if and only if the necessary conditions for the reduced control system (1.18) are also satisfied. The proof of Theorem 1.2.1 is based on Lemma 1.2.1 below and is given further in this section.

Every nonlinear control system of the form $\dot{x} = f(x, u)$ can be interpreted as an affine one by making the transformation $\dot{u} = v$ and considering the variable v as the new control and the variable (x, u) as the new state variable. The inverse transformation, called the Goh transformation, is a great tool for the investigation of singular extremals and will reveal itself fundamental here to show the absence of optimal singular trajectories in the models we will consider later.

Notations. *To every couple of points $y := (x, o, d) \in \mathbb{R}^{n+2}$ and $p := (p_x, p_o, p_d) \in \mathbb{R}^{n+2}$ we associate a couple of points of $\mathbb{R}^{n+1}$ defined by $\tilde{y} := (x, d)$ and $\tilde{p} := (p_x, p_d)$. Moreover, we write the corresponding reduced Hamiltonian $\tilde{\mathcal{H}}$ defined for $(\tilde{y}, \tilde{p}, p^0) \in \mathbb{R}^{n+1} \times \mathbb{R}^{n+1} \times \mathbb{R}_-$ and $o \in \mathbb{R}$ by $\tilde{\mathcal{H}}(\tilde{y}, \tilde{p}, p^0, o) := \langle \tilde{p}, \bar{f}_0(\tilde{y})\rangle + o\langle \tilde{p}, \tilde{f}_1(\tilde{y})\rangle + p^0$, where the vector fields $\bar{f}_0$ and $\tilde{f}_1$ are defined, for all $\tilde{y} = (x, d) \in \mathbb{R}^{n+1}$, by $\bar{f}_0(\tilde{y}) = (f_0(x), -K_r d)$ and $\tilde{f}_1(\tilde{y}) := g_{ChR2}(V_{ChR2} - \tilde{y}_1)\partial_1 + K_d\partial_{n+1}$.*

The following lemma is the first step to reduce the dimension of the system that has to be considered to investigate the existence of singular extremals.

Lemma 1.2.1. *(y, p) is the projection, on the space of continuous functions from $\mathbb{R}_+$ to $\mathbb{R}^{n+2} \times \mathbb{R}^{n+2}$, of a solution (y, p, u) of*

$$\dot{y}(t) = \frac{\partial \mathcal{H}}{\partial p}(y(t), p(t), p^0, u(t)), \quad \dot{p}(t) = -\frac{\partial \mathcal{H}}{\partial y}(y(t), p(t), p^0, u(t)), \quad \langle p(t), f_1(y(t))\rangle = 0. \tag{1.19}$$

if and only if $p_o \equiv 0$, $\dot{o} = (1-o-d)u - K_d o$ *and* $(\tilde{y}, \tilde{p})$ *is a solution of*

$$\dot{\tilde{y}}(t) = \frac{\partial \tilde{\mathcal{H}}}{\partial \tilde{p}}(\tilde{y}(t), \tilde{p}(t), p^0, o(t)), \quad \dot{\tilde{p}}(t) = -\frac{\partial \tilde{\mathcal{H}}}{\partial \tilde{y}}(\tilde{y}(t), \tilde{p}(t), p^0, o(t)), \quad \langle \tilde{p}(t), \tilde{f}_1(\tilde{y}(t)) \rangle = 0. \tag{1.20}$$

This lemma shows that singular extremals of (1.12) are directly related to singular extremals of the following, and still affine control system:

$$\begin{cases} \dot{x}(t) = f_0(x(t)) + g_{ChR2}o(t)(V_{ChR2} - x_1(t))\mathbf{e}_1, \\ \dot{d}(t) = K_d o(t) - K_r d(t), \end{cases} \tag{1.21}$$

where the control is now the variable o.

In the models that we are going to study in the sequel, we will see that this transformation allows to conclude to the absence of optimal singular extremals.

Proof. of Lemma 1.2.1. The proof comes from the general result of Section 1.9.4 of [BK93] and the shape of our particular model. If we keep on writing $y = (x, o, d)$, system (1.19) gives on an interval I of $[0, t_f]$:

$$\begin{cases} \dot{x} = f_0(x) + g_{ChR2}o(V_{ChR2} - x_1)\mathbf{e}_1, \\ \dot{d} = K_d o - K_r d, \\ \dot{o} = (1-o-d)u - K_d o, \\ \dot{p}_x = -J_{f0}^t p_x + g_{ChR2} o p_{x_1} \mathbf{e}_1, \\ \dot{p}_d = u p_o + K_r p_d, \\ \dot{p}_o = -g_{ChR2}(V_{ChR2} - x_1)p_{x_1} - K_d p_d + (u + K_d)p_o, \\ 0 = (1-o-d)p_o, \end{cases} \tag{1.22}$$

where J_{f0}^t is the transpose of the Jacobian matrix of $\tilde{f}_0$. For continuity reasons, we get that either $p_o \equiv 0$ or $(1-o-d) \equiv 0$ on I. If $(1-o-d) \equiv 0$ then $-K_r d = \dot{o} + \dot{d} \equiv 0$ so that $d \equiv 0$ and $o \equiv 1$. But $d \equiv 0 \Rightarrow \dot{d} \equiv 0$ so that $\dot{o} \equiv 0$ which is incompatible with $o \equiv 1$, since $\dot{o} = -K_d o$. We conclude that, necessarily, $p_o \equiv 0$ on I. This equality implies that $\dot{p}_o \equiv 0$ and from the penultimate equation of (1.22) we get $-g_{ChR2}(V_{ChR2} - x_1)p_{x_1} - K_d p_d \equiv 0$ which also writes $\langle \tilde{p}, \tilde{f}_1(\tilde{y}) \rangle \equiv 0$. Now the first two equations of (1.22) correspond to

$$\dot{\tilde{y}}(t) = \frac{\partial \tilde{\mathcal{H}}}{\partial \tilde{p}}(\tilde{y}(t), \tilde{p}(t), p^0, o(t)),$$

and the 4^{th} and 5^{th} equations correspond to

$$\dot{\tilde{p}}(t) = -\frac{\partial \tilde{\mathcal{H}}}{\partial \tilde{y}}(\tilde{y}(t), \tilde{p}(t), p^0, o(t)).$$

We just showed that (1.19) $\Rightarrow$ ($p_o \equiv 0$ and (1.20)).

Suppose now that $p_o \equiv 0$ on I and that (1.20) is satisfied and let us show that (1.19) is satisfied. The first two equations of (1.20) give the 1^{st}, 2^{nd}, 4^{th} and 5^{th} equations of (1.19). Moreover, $p_o \equiv 0$ implies that the last equation of (1.19) is satisfied and that $\dot{p}_o \equiv 0$. Taking into account that $0 \equiv \langle \tilde{p}, \tilde{f}_1(\tilde{y}) \rangle = -g_{ChR2}(V_{ChR2} - x_1)p_{x_1} - K_d p_d$, we obtain the 6^{th} equation of (1.19). Finally, the 3^{rd} equation of (1.19) is satisfied as a hypothesis, which ends the proof.

□

Proof of Theorem 1.2.1. The result of Lemma 1.2.1 is the first step of the proof. To finish up with it, consider the spiking problem in minimum time for the reduced system (1.21) :

$$\begin{cases} \dot{x}(t) = f_0(x(t)) + g_{ChR2} o(t)(V_{ChR2} - x_1(t))\mathbf{e}_1, \\ \dot{d}(t) = K_d o(t) - K_r d(t), \end{cases}$$

Remark that the dynamics of the variables x and d are completely decoupled. Furthermore, the targeted manifold is only defined by the location of variable x_1. These two remarks imply that an optimal control for system (1.21) has to be optimal for the even more reduced control system :

$$\dot{x}(t) = f_0(x(t)) + g_{ChR2} o(t)(V_{ChR2} - x_1(t))\mathbf{e}_1.$$

□

1.2.3 Lie bracket configurations for the ChR2 4-states model

In the case of the ChR2 4-states model, we will observe numerically that the optimal control is bang-bang for various values of the maximum intensity u_{max}. Here we give the expression of the first Lie brackets, that we first define. Lie brackets are the appropriate tool to investigate singular extremals. We give two equivalent definitions, depending on the notation used for the vector fields.

Let $k \in \mathbb{N}^*$ and $g, h : \mathbb{R}^k \to \mathbb{R}^k$ two vector fields of class C^1. Let $(g_1, \ldots, g_k)$ and $(h_1, \ldots, h_k)$ their coordinate mappings. The Lie bracket $[g, h] : \mathbb{R}^k \to \mathbb{R}^k$ of g and h is the vector field defined for $x \in \mathbb{R}^k$ by

$$[g, h](x) = J_h(x)g(x) - J_g(x)h(x),$$

or equivalently by

$$[g, h](x) = \sum_{i=1}^{k} \sum_{j=1}^{k} \big(g_j(x)\partial_j h_i(x) - h_j(x)\partial_j g_i(x)\big)\partial_i,$$

where J_h and J_g are the Jacobian matrices of h and g. The expression $J_h(x)g(x)$ has to be understood as the product of the $k \times k$-matrix by the k-vector. Further in this paper we will use the convenient notation

$$\mathrm{ad}_h g := [h, g]$$

that allows to reduce expressions of multiple Lie brackets. Finally, one important relation for the computation of singular controls is the following. Let (x^u, p) be an extremal pair of the Pontryagin maximum principle associated to a control u. Then for any smooth vector field $h : \mathbb{R}^k \to \mathbb{R}^k$ and all $t \in [0, t_f]$,

$$\frac{\mathrm{d}}{\mathrm{d}t}\langle p(t), h(x^u(t))\rangle = \langle p(t), [F_0, h](x^u(t))\rangle + u(t)\langle p(t), [F_1, h](x^u(t))\rangle. \tag{1.23}$$

In most cases, a singular optimal control $\bar{u}$ would have the expression

$$\bar{u}(t) = \frac{\langle q(t), \mathrm{ad}^2_{\hat{f}_0} f_2(z(t))\rangle}{\langle q(t), \mathrm{ad}^2_{f_2} \hat{f}_0(z(t))\rangle}.$$

Indeed, if I is an interval of $[0, t_f]$ on with the switching function ψ vanishes, then for $t \in I$,

$$\begin{aligned}
&\psi(t) = 0,\\
&\dot{\psi}(t) = \langle q(t), [\hat{f}_0, f_2](z(t))\rangle = 0,\\
&\ddot{\psi}(t) = \langle q(t), \mathrm{ad}^2_{\hat{f}_0} f_2(z(t))\rangle - \bar{u}(t)\langle q(t), \mathrm{ad}^2_{f_2}\hat{f}_0(z(t))\rangle = 0,
\end{aligned}$$

The expressions of $[\hat{f}_0, f_2]$ and $\mathrm{ad}^2_{f_2}\hat{f}_0$ are not too much complicated since theses brackets have non zero components only on the directions z_1, z_{n+1}, z_{n+2} and z_{n+3} (independently of $n \in \mathbb{N}^*$), which we also write v, o_1, o_2 and c_2. We will not give the expression of $\mathrm{ad}^2_{\hat{f}_0} f_2$ because it is too long and of small interest since we will treat the problem numerically. Let us just mention that it has non zero components on all the directions of the state space $\mathbb{R}^{n+3}$.

$$\begin{aligned}
[\hat{f}_0, f_2](z) = &-\Big(\varepsilon_1(1 - o_1 - o_2 - c_2) + \varepsilon_2 \rho c_2\Big)\frac{1}{C} g_{ChR2}(V_{ChR2} - v)\partial_v\\
&+ \Big(\varepsilon_1(1 - o_1 - o_2 - c_2)(e_{12} + K_{d1}) + \varepsilon_1 K_{d1} o_1 + (\varepsilon_1 K_r - \varepsilon_2 e_{21})c_2\Big)\partial_{o_1}\\
&+ \Big(- \varepsilon_1(1 - o_1 - o_2 - c_2)e_{12} + \varepsilon_2 K_{d2} o_2 + \varepsilon_2(e_{21} + K_{d2} - K_r)c_2\Big)\partial_{o_2}\\
&- \varepsilon_2 K_{d2}(o_2 + c_2)\partial_{c_2},
\end{aligned}$$

and

$$
\begin{aligned}
\mathrm{ad}^2_{f_2}\hat{f}_0(z) = &-\Big((\varepsilon_1)^2(1-o_1-o_2-c_2)+(\varepsilon_2)^2\rho c_2\Big)\frac{1}{C}g_{ChR2}(V_{ChR2}-v)\partial_v \\
&-\varepsilon_1\Big(\varepsilon_1(1-o_1-o_2-c_2)(e_{12}+K_{d1})+\varepsilon_1 K_{d1}o_1-(\varepsilon_1 K_r-\varepsilon_2 e_{21})c_2\Big)\partial_{o_1} \\
&-\Big((\varepsilon_1)^2(1-o_1-o_2-c_2)e_{12}+(\varepsilon_2)^2K_{d2}o_2+(\varepsilon_2)^2(-e_{21}+K_{d2}-K_r)c_2\Big)\partial_{o_2} \\
&+(\varepsilon_2)^2K_{d2}(o_2+c_2)\partial_{c_2}.
\end{aligned}
$$

1.3 Application to some neuron models with numerical results

In this section, we apply the reduction results of Section 1.2.2 to some widely used models and support our theoretical results with numerical results. These theoretical results regard the ChR2-3-states model and we also investigate numerically the associated ChR2-4-states models. The numerical results are obtained by direct methods based on the `ipopt` routine [WB06] to solve nonlinear optimization problems, and implemented with the `ampl` language [FGK02]. For a survey on numerical methods in optimal control, see [Tré12]. The numerical values used for the ChR2-3-states and 4-states models are those of Appendices 1.C.1 and 1.C.2. For each neuron model that we study, namely the FitzHugh-Nagumo model, the Morris-Lecar model and the reduced and complete Hodgkin-Huxley models, we implement the direct method for the ChR2-3-states and 4-states models and compare them. We repeat the computation for several values of the the maximum control value in order to try and detect possible singular optimal controls. Indeed, it would be possible that a singular optimal control only appears above some threshold of the maximal control value. Nevertheless, no model numerically displays such controls. We then compare the neuron models between them in terms of their behavior with respect to optogenetic control. Physiologically, Channelrhdopsin has a depolarizing effect on a neuron membrane so that it is physiologically intuitive to expect that we need to switch on the light to obtain a spike, and the more light we put in the system, the faster the spike will occur. We propose to distinguish between two classes of models. The first class comprises neuron models that display the intuitive physiological response to optogenetic stimulation and the second class comprises neuron models that display an unexpected response.

1.3.1 The FitzHugh-Nagumo model

The FitzHugh-Nagumo model is not exactly a conductance-based model but a two-dimensional simplification of the Hodgkin-Huxley model. This model takes his name from the initial work of FitzHugh [Fit61] who suggested the system and Nagumo [NAY62] who gave the equivalent circuit. The idea was to find a simpler model that still featured the mathematical properties of excitation and propagation.

The ChR2-3-states model

The $ChR2$-3-states controlled FitzHugh-Nagumo model is

$$(FHN)\begin{cases}\dot{v}(t)=v(t)-\frac{1}{3}v^3(t)-w(t)+\frac{1}{C}g_{ChR2}o(t)(V_{ChR2}-v(t)),\\ \dot{w}(t)=c(v(t)+a-bw(t)),\\ \dot{o}(t)=u(t)(1-o(t)-d(t))-K_do(t),\\ \dot{d}(t)=K_do(t)-K_rd(t),\end{cases}$$

where v is the membrane potential and w a conductance-like variable that provides a negative feedback, and a, b and c are constants. In the original model, the numerical values of these constants were $a=0.7$, $b=0.8$ and $c=0.08$. The adjoint equations write

$$(FHN_{adj})\begin{cases}\dot{p}_v(t)=-p_v(t)(1-v^2(t)-\frac{1}{C}g_{ChR2}o(t))-cp_w(t),\\ \dot{p}_w(t)=p_v(t)+bcp_w(t),\\ \dot{p}_o(t)=-\frac{1}{C}g_{ChR2}(V_{ChR2}-v(t))p_v(t)+(u(t)+K_d)p_o(t)-K_dp_d(t),\\ \dot{p}_d(t)=u(t)p_o(t)+K_rp_d(t),\end{cases}$$

and the switching function is $\varphi(t)=(1-o(t)-d(t))p_o(t)$. The following lemma gives the optimal control for the minimal time control of the ChR2-controlled FitzHugh-Nagumo model.

Proposition 1.3.1. *The optimal control $u^*:\mathbb{R}_+\to U$ for the minimal time control of the FitzHugh-Nagumo model is bang-bang and given by*

$$u^*(t)=u_{max}\mathbf{1}_{p_o(t)>0},\quad \forall t\in[0,t_f].$$

Furthermore, the optimal control begins with a bang arc of maximal value, i.e.

$$\exists t_1\in[0,t_f],u^*(t)=u_{max},\forall t\in[0,t_1].$$

Proof. Let us show that there is no optimal singular extremals. The results for conductance-based models given in section 1.2.2 are straightforwardly applicable to the FitzHugh-Nagumo model and the reduced control system is the following

$$
(FHN')\begin{cases} \dot{v}(t) = v(t) - \frac{1}{3}v^3(t) - w(t) + \frac{1}{C}g_{ChR2}u(t)(V_{ChR2} - v(t)) \\ \dot{w}(t) = c(v(t) + a - bw(t)) \end{cases}
$$

The adjoint equations for this system are

$$
(FHN'_{adj})\begin{cases} \dot{p}_v(t) = -p_v(t)(1 - v^2(t) - \frac{1}{C}g_{ChR2}u(t)) - cp_w(t) \\ \dot{p}_w(t) = p_v(t) + bcp_w(t) \end{cases}
$$

The vector fields defining the affine system (FHN') are

$$
\begin{aligned} f_0(v,w) &= (v - \frac{1}{3}v^3 - w)\partial_v + c(v + a - bw)\partial_w \\ f_1(v,w) &= \frac{1}{C}g_{ChR2}(V_{ChR2} - v)\partial_v \end{aligned}
$$

For the reduced system, the switching function is given by

$$
\phi(t) = \langle p(t), f_1(v(t), w(t))\rangle = \frac{1}{C}g_{ChR2}(V_{ChR2} - v(t))p_v(t).
$$

Investigation of singular trajectories

Assume that there exists an open interval I along which the switching function vanishes. Then for all $t \in I$,

$$
\langle p(t), f_1(v(t), w(t))\rangle = 0.
$$

By continuity, this means that either v is constant and equals V_{ChR2} on I or p_v vanishes on I. The constant case is not possible since it implies from the dynamical system (FHN) that w would also be constant on I, but (V_{ChR2}, w) is not an equilibrium point of the uncontrolled system, for any $w \in \mathbb{R}$. Then, necessarily, p_v vanishes on I. This implies that $\dot{p}_v$ also vanishes and from (FHN_{adj}), p_w vanishes on I. This is incompatible from the Pontryagin maximum principle.

We showed that the reduced system does not present any singular extremals and from Theorem 1.2.1, the original system (FHN) neither. The optimal control is then bang-bang and is given by the sign of the switching function of the original system. Taking into account that for all $t \in [0, t_f]$, $1 - o(t) - d(t) > 0$ we get

$$
u^*(t) = u_{max}\mathbf{1}_{p_o(t)>0}, \quad \forall t \in [0, t_f].
$$

Finally, to show that the first arc correspond to a maximal control, suppose that $u^*(0) = 0$. Then system (FHN) stays in its resting state, contradicting time optimality.

□

We implement the direct method for this problem with a targeted action potential $V_s := 1.5mV$ and a control evolving in $[0, 0.1]$. The numerical values of the constants (a, b, c) are set to the usual values $(0.7, 0.8, 0.08)$. Since this model is not physiological, we chose the values for the constants C, g_{ChR2}, V_ChR2 and u_{max} quite arbitrarily, with the constraint that the behavior of the control system should not stray away from the uncontrolled system. When the control is off, the system stays at rest, as seen on Figure 1.5.

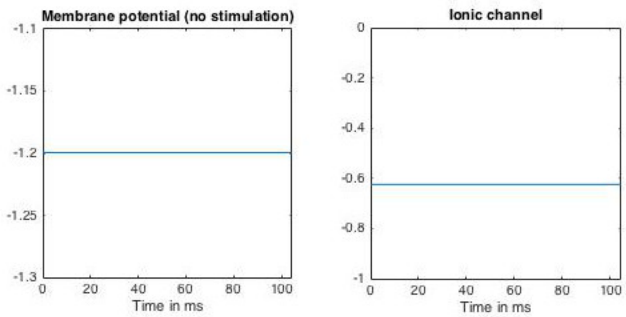


Figure 1.5 – In the absence of stimulation, the neuron stays in its resting state.

We represent on Figure 1.6 the evolution of the optimal trajectory of the membrane potential and the optimal control. As predicted, the optimal control is bang-bang and starts with a maximal arc. It has a unique switching time which means that there is no need to keep the light on all the way to the spike, an interesting fact for the controller. This optimal control can be qualified as physiological, the light must stay on until a point where the system is "launched" toward the spike and no further illumination is required.

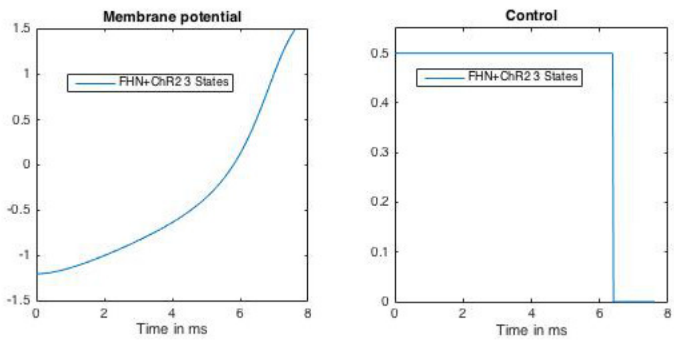


Figure 1.6 – Optimal trajectory and control for the FHN-ChR2-3-states model with $u_{max} = 0.5$.

The ChR2-4-states model

The ChR2-4-states model gives the same shape of optimal trajectory and control. We can compare the two ChR2 models and observe the results for different values of u_{max} on Figure 1.7. The ChR2-4-states model outperforms the ChR2-3-states on two scales. It leads to a faster spike while requiring less time in the light to fire. This phenomenon seems to be independent of the maximal value of the control. The gain is of around 6% in the four cases.

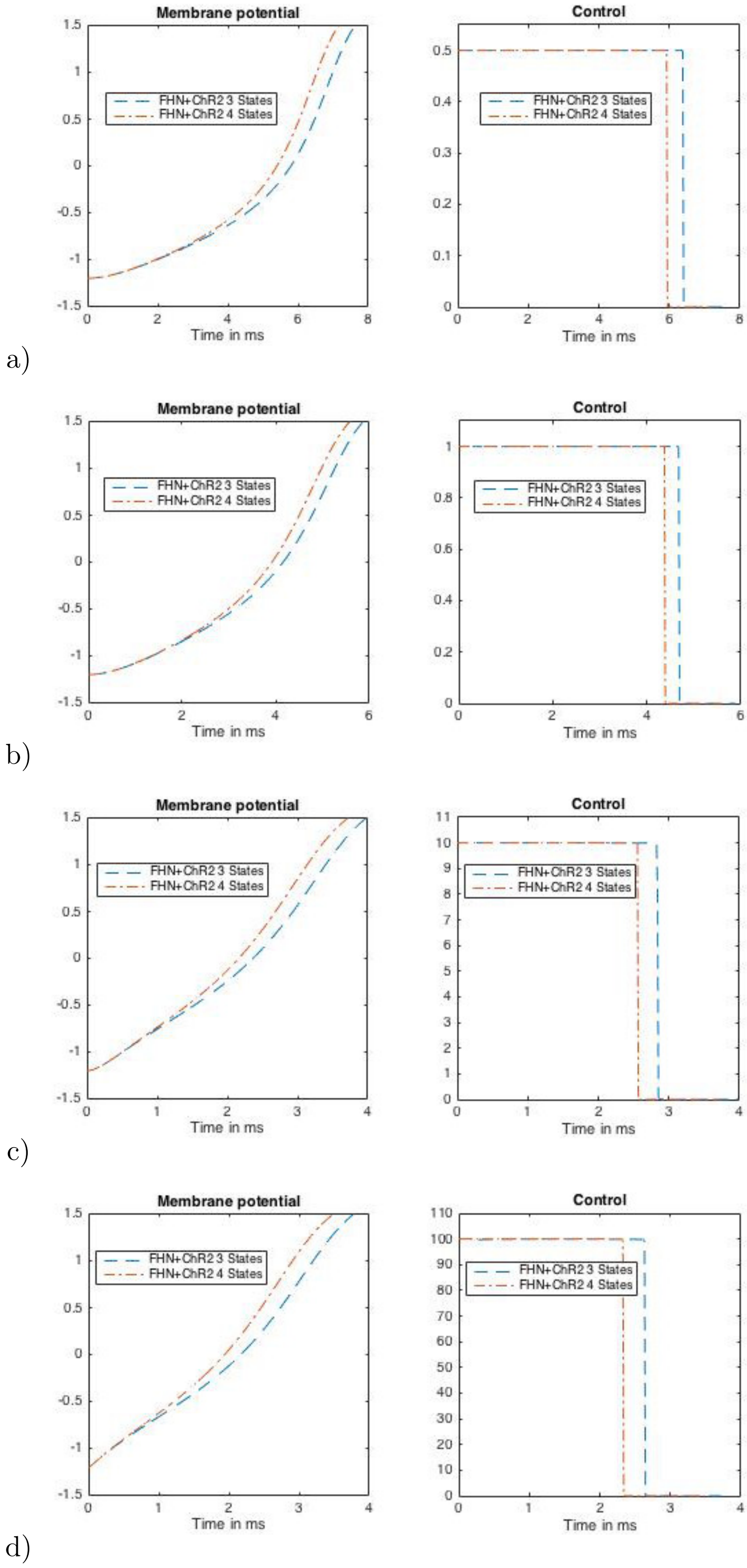


Figure 1.7 – Optimal trajectory and bang-bang optimal control for the FHN-ChR2-3-states and FHN-ChR2-4-states models with u_{max} = a) 0.5, b) 1, c) 10, d) 100.

1.3.2 The Morris-Lecar model

The Morris-Lecar model is a reduced conductance-based model taking into account a Ca^{2+} current for excitation and a K^+ current for recovery ([LM81]). It comes from the experimental study of the oscillatory behavior of the membrane potential in the barnacle muscle. The original model is of dimension 3, but it is conveniently and commonly reduced to a two-dimensional model by invoking the fast dynamics of the Ca^{2+} conductance in front of the other variables. This conductance is then replaced by its steady-state.

The ChR2-3-states model

The ChR2-3-states controlled Morris-Lecar model is given by

$$(ML)\begin{cases} \dot{\nu}(t) = \dfrac{1}{C}\Big(g_K\omega(t)(V_K-\nu(t)) + g_{Ca}m_\infty(\nu(t))(V_{Ca}-\nu(t)) \\ \qquad\qquad + g_{ChR2}o(t)(V_{ChR2}-\nu(t)) + g_L(V_L-\nu(t))\Big), \\ \dot{\omega}(t) = \alpha(\nu(t))(1-\omega(t)) - \beta(\nu(t))\omega(t), \\ \dot{o}(t) = u(t)(1-o(t)-d(t)) - K_d o(t), \\ \dot{d}(t) = K_d o(t) - K_r d(t), \end{cases}$$

with

$$\begin{aligned} m_\infty(\nu) &= \frac{1}{2}\left(1+\tanh\left(\frac{\nu-V_1}{V_2}\right)\right), \\ \alpha(\nu) &= \frac{1}{2}\phi\cosh\left(\frac{\nu-V_3}{2V_4}\right)\left(1+\tanh\left(\frac{\nu-V_3}{V_4}\right)\right), \\ \beta(\nu) &= \frac{1}{2}\phi\cosh\left(\frac{\nu-V_3}{2V_4}\right)\left(1-\tanh\left(\frac{\nu-V_3}{V_4}\right)\right), \end{aligned}$$

where ν is the membrane potential, ω is the probability of opening of a K^+ channel and $m_\infty(\nu)$ represent the steady state of the probability of opening of a Ca^{2+} channel. The numerical constants of the model are given in Appendix 1.A. The adjoint equations read

$$(ML_{adj})\begin{cases} \dot{p}_\nu(t) = \dfrac{1}{C}p_\nu(t)\Big(g_K\omega(t) + g_{Ca}m_\infty(\nu(t)) + g_{ChR2}o(t) + g_L - g_{Ca}m'_\infty(\nu(t))(V_{Ca}-\nu(t))\Big) \\ \qquad\qquad - p_\omega(t)\Big(\alpha'(\nu(t))(1-\omega(t)) - \beta'(\nu(t))\omega(t)\Big), \\ \dot{p}_\omega(t) = -\dfrac{1}{C}g_K(V_K-\nu(t))p_\nu(t) + \Big(\alpha(\nu(t)) + \beta(\nu(t))\Big)p_\omega(t), \\ \dot{p}_o(t) = -\dfrac{1}{C}g_{ChR2}(V_{ChR2}-\nu(t))p_\nu(t) + (u(t)+K_d)p_o(t) - K_d p_d(t), \\ \dot{p}_d(t) = u(t)p_o(t) + K_r p_d(t), \end{cases}$$

and the switching function is again $\varphi(t) = (1 - o(t) - d(t))p_o(t)$. Proposition 1.3.2 gives the same conclusion as Proposition 1.3.1 for the ChR2-controlled Morris-Lecar model.

Proposition 1.3.2. *The optimal control $u^* : \mathbb{R}_+ \to U$ for the minimal time control of the Morris-Lecar model is bang-bang and given by*

$$u^*(t) = u_{max}\mathbf{1}_{p_o(t)>0}, \quad \forall t \in [0, t_f].$$

Furthermore, the optimal control begins with a bang arc of maximal value

$$\exists t_1 \in [0, t_f], u^*(t) = u_{max}, \forall t \in [0, t_1].$$

Proof. We apply the result of Theorem 1.2.1 and study the existence of singular extremals for the following reduced system

$$(ML') \begin{cases} \dot{\nu}(t) = \dfrac{1}{C}\Big(g_K\omega(t)(V_K - \nu(t)) + g_{Ca}m_\infty(\nu(t))(V_{Ca} - \nu(t)) \\ \qquad\qquad + g_{ChR2}u(t)(V_{ChR2} - \nu(t)) + g_L(V_L - \nu(t))\Big), \\ \dot{\omega}(t) = \alpha(\nu(t))(1 - \omega(t)) - \beta(\nu(t))\omega(t), \end{cases}$$

The adjoint equations for this system are

$$(ML'_{adj}) \begin{cases} \dot{p}_\nu(t) = \dfrac{1}{C}p_\nu(t)\Big(g_K\omega(t) + g_{Ca}m_\infty(\nu(t)) + g_{ChR2}u(t) + g_L - g_{Ca}m'_\infty(\nu(t))(V_{Ca} - \nu(t))\Big) \\ \qquad\qquad - p_\omega(t)\Big(\alpha'(\nu(t))(1 - \omega(t)) - \beta'(\nu(t))\omega(t)\Big), \\ \dot{p}_\omega(t) = -\dfrac{1}{C}g_K(V_K - \nu(t))p_\nu(t) + (\alpha(\nu(t)) + \beta(\nu(t)))p_\omega(t), \end{cases}$$

The vector fields defining the affine system (ML') are

$$\begin{aligned} f_0(\nu, \omega) &= \frac{1}{C}\Big(g_K\omega(V_K - \nu) + g_{Ca}m_\infty(\nu)(V_{Ca} - \nu) + g_L(V_L - \nu)\Big)\partial_\nu \\ &\quad + \Big(\alpha(\nu)(1 - \omega) - \beta(\nu)\omega\Big)\partial_\omega \\ f_1(\nu, \omega) &= \frac{1}{C}g_{ChR2}(V_{ChR2} - v)\partial_\nu \end{aligned}$$

For the reduced system, the switching function is given by

$$\phi(t) = \langle p(t), f_1(\nu(t), \omega(t))\rangle = \frac{1}{C}g_{ChR2}(V_{ChR2} - \nu(t))p_\nu(t).$$

Investigation of singular trajectories

Assume that there exists an open interval I along which the switching function vanishes. Then for all $t \in I$,

$$\langle p(t), f_1(v(t), w(t)) \rangle = 0.$$

As for the FitzHugh-Nagumo model, there is no $\omega \in [0,1]$ such that (V_{ChR2}, ω) is an equilibrium point of the uncontrolled Morris-Lecar model, so that necessarily p_ω vanishes on I. From (ML') we deduce that for all $t \in I$,

$$p_\omega(t)\Big(\alpha'(\nu(t))(1-\omega(t)) - \beta'(\nu(t))\omega(t)\Big) = 0,$$

and since p cannot vanish on I then

$$\alpha'(\nu(t))(1-\omega(t)) - \beta'(\nu(t))\omega(t) = 0.$$

This means that the singular extremal is localized in the domain A of $\mathbb{R}^2$ given by

$$A := \{(\nu, \omega) \in \mathbb{R}^2 | \alpha'(\nu)(1-\omega) - \beta'(\nu)\omega = 0\}.$$

We can rewrite it in a more convenient way

$$A = \left\{(\nu, \omega) \in \mathbb{R}^2 | \omega = \frac{\alpha'(\nu)}{\alpha'(\nu) + \beta'(\nu)} \text{ and } \nu \neq V_3 \right\},$$

where V_3 is the numerical constant appearing in the definition of the functions α and β. Domain A is represented on Figure 1.8 below and it is easy to see that any trajectory of the dynamical system (ML') has an empty intersection with A because for all $(\nu, \omega) \in A$, $\omega \in]-\infty, 0[\cup]1, +\infty[$, whereas the second component of the trajectory always stays in $[0,1]$.

The end of the proof is similar to the proof of Proposition 1.3.1.

□

Remark 1.3.1. *Let us briefly show how the investigation of singular trajectories for the complete system before reduction is much more difficult. To do so, consider the controlled Morris-Lecar model (ML) with its system of adjoint equations (ML_{adj}) and the vector fields defined for $x = (\nu, \omega, o, d) \in \mathbb{R}^4$ by*

$$F_0(x) := \frac{1}{C}\Big(g_K\omega(V_K - \nu) + g_{Ca}m_\infty(\nu)(V_{Ca} - \nu) + og_{ChR2}(V_{ChR2} - \nu) + g_L(V_L - \nu)\Big)\partial_\nu$$
$$\Big(\alpha(\nu)(1-\omega) - \beta(\nu)\omega\Big)\partial_\omega - K_d o\partial_o + (K_d o - K_r d)\partial_d,$$

and

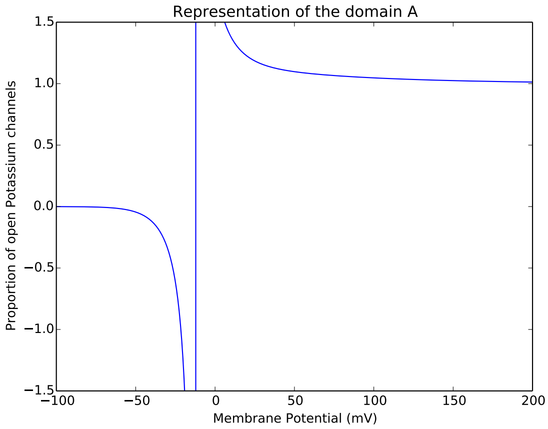


Figure 1.8 – Representation of the manifold in which a singular trajectory must evolve.

$$F_1(x) = (1 - o - d)\partial_o.$$

Proposition 1.3.3. *Let (x, p, u) be a singular extremal of $(ML) - (ML_{adj})$ on an open interval I of $[0, t_f]$. Then, without any further assumption,*

$$\langle p(t), \mathrm{ad}^k_{F_0} F_1(x(t))\rangle \equiv 0, \quad \langle p(t), \mathrm{ad}^k_{F_1} F_0(x(t))\rangle \equiv 0, \quad \langle p(t), [F_1, \mathrm{ad}^2_{F_0} F_1](x(t))\rangle \equiv 0,$$

on I for all $k \in \{1, 2, 3\}$.

Keeping in mind that we already proved that there is no optimal singular control, if we consider the system before reduction, Proposition 1.3.3 means that we need to consider the following system of equations to rule out optimal singular extremals

$$\begin{aligned} \langle p, [F_0, \mathrm{ad}^3_{F_1} F_0]\rangle + u\langle p, \mathrm{ad}^4_{F_1} F_0\rangle \equiv 0, \\ \langle p, [F_0, [F_1, \mathrm{ad}^2_{F_0} F_1]]\rangle + u\langle p, \mathrm{ad}^2_{F_1}(\mathrm{ad}^2_{F_0} F_1)\rangle \equiv 0, \\ \langle p, \mathrm{ad}^4_{F_0} F_1\rangle + u\langle p, [F_1, \mathrm{ad}^3_{F_0} F_1]\rangle \equiv 0, \end{aligned}$$

on I.

Proof of Proposition 1.3.3. Let $t \in I$. From the equalities $\langle p(t), F_1(x(t))\rangle = 0$ and $\langle p(t), [F_0, F_1](x(t))\rangle = 0$ we infer that

$$\begin{cases} p_o(t) = 0, \\ \dfrac{1}{C} g_{ChR2}(V_{ChR2} - \nu(t))p_v(t) + K_d p_d(t) = 0. \end{cases} \tag{1.24}$$

It can also be proved that $\mathrm{ad}^3_{F_1} F_0 = -[F_0, F_1]$. The rest of the equalities are all given by (1.24).

□

For this model, we implemented the direct method with the numerical values of Appendices 1.A and 1.C.1. The targeted action potential has been fixed to 30mV. Direct methods consist in transforming the control problem into a nonlinear optimization problem of the form

$$\min F(z)$$

under the algebraic constraints

$$\begin{aligned} G(z) &= 0, \\ H(z) &= 0, \end{aligned}$$

where F is the cost functional of the control problem (here the final time), the equality constraints come from the discretization of the dynamical system, the inequality constraints are used to specify the domain of the variables, and z is the vector of the discretized variables.

The optimal control for the ChR2-3-states model is bang-bang and begins with a maximal arc. For the numerical values of Appendices 1.A and 1.C.1, it displays three switching times. We represent on Figure 1.9 the optimal trajectory of the membrane potential and the optimal control, for the physiological value of the maximal value control, computed in Appendix 1.C.1, and also the trajectory obtained under constant maximal stimulation, just to observe that the optimal control obtained is indeed better than the constant maximal stimulation. The difference is very small, of the order of a millisecond, nevertheless, the counter-intuitive stimulation still outperforms the constant maximal stimulation. In order to show that the difference between the counter-intuitive optimal stimulation and the constant maximal stimulation can be huge, we implement the direct method on a system with different numerical values for the constants of the Morris-Lecar model (the Type I neuron of [SHL04, Table 1], see Table 1.A.2, in Appendix 1.C.1), and values for the ChR2-3-states model remaining unchanged, except for $V_{ChR2} = 0.1$mV. The result is striking, the constant stimulation even fails to trigger a spike while the stimulation with three switching times makes the neuron fire (see Figure 1.10). It is important to note that the presence of three switching times is not an intrinsic characteristic of the Morris-Lecar model itself. Indeed, we can find optimal controls with only two switches if we change the value for the equilibrium potential of the ChR2, keeping all the other constants of the model unchanged (Figure 1.11).

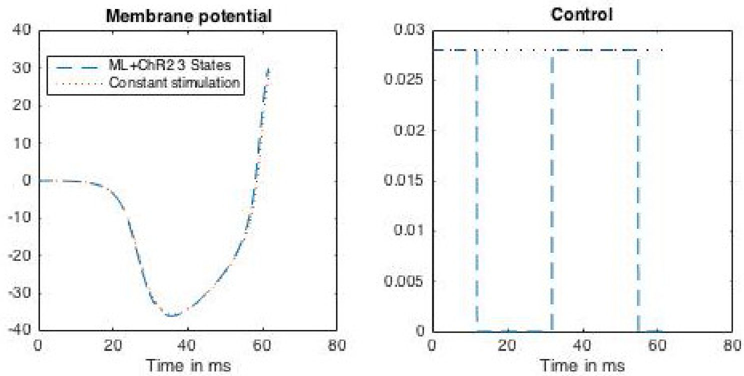


Figure 1.9 – Optimal trajectory and bang-bang optimal control for the ML-ChR2-3-states model.

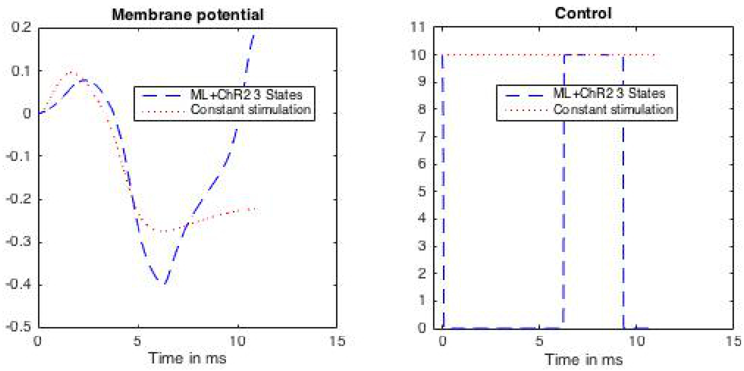


Figure 1.10 – Optimal trajectory and bang-bang optimal control for the ML-ChR2-3-states model with numerical values of [SHL04, Table 1]. The constant stimulation fails to trigger a spike.

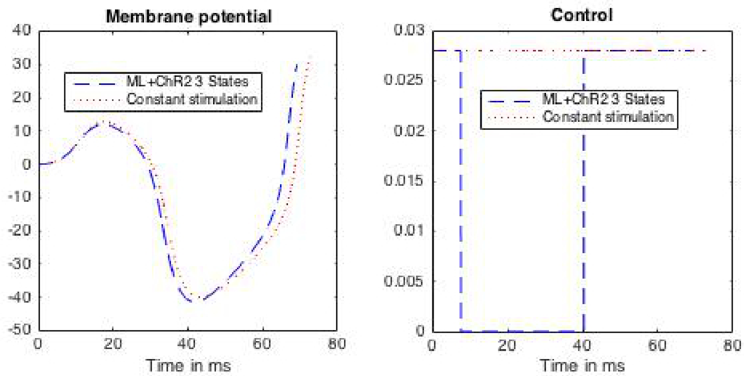
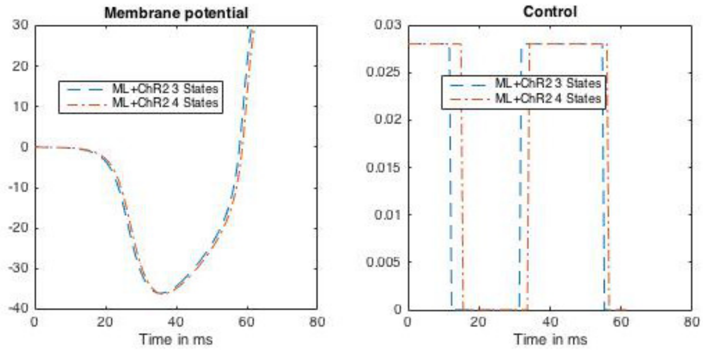


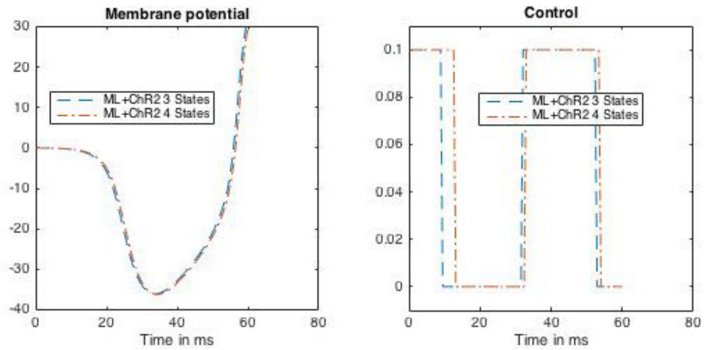
Figure 1.11 – Optimal trajectory and bang-bang optimal control for the ML-ChR2-3-states model with numerical values of Appendix 1.A and $VChR2 = 20$mV. The optimal control has only two switches.

The ChR2-4-states model

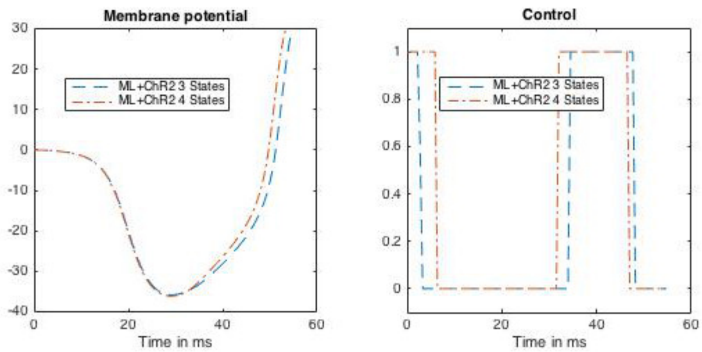
The shape of the optimal trajectory and control of the ChR2-4-states model correspond to the one of the ChR2-3-states model. Nevertheless, for small values of u_{max}, including the physiological value computed in Appendix 1.C.1, the ChR2-3-states model outperforms the ChR2-4-states model whereas for larger values of u_{max}, the opposite happens (Figure 1.12). The threshold where this phenomenon happens is around the value $u_{max} = 0.1$. Furthermore, the difference grows larger when u_{max} increases. This is an unusual behavior that suggests that the Morris-Lecar is less robust than the FitzHugh-Nagumo model, or the Hodgkin-Huxely models, as we are going to see.



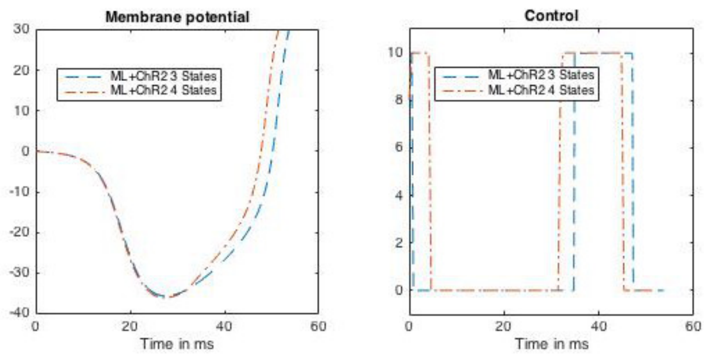
a)



b)



c)



d)

Figure 1.12 – Optimal trajectory and bang-bang optimal control for the ML-ChR2-3-states and ML-ChR2-4-states models with u_{max} = a) 0.028, b) 0.1, c) 1, d) 10.

1.3.3 The reduced Hodgkin-Huxley model

Similarly to the reduction of the initial Morris-Lecar model, there exists a popular reduction of the Hodgkin-Huxley model to a 2-dimensional conductance-based model. This reduction is based on the observation that, on the one hand, the variable m is much faster than the other two gating variables n and h, and on the other hand, the variable h is almost a linear function of the variable n ($h \simeq a + bn$). These observations lead to a new system of equations derived from (HH) by setting the variable m in its stationary state $m(t) = m_\infty(t)$ and taking the variable h as above.

$$(HH_{2D}) \begin{cases} C\dfrac{\mathrm{d}V}{\mathrm{d}t} = g_K n^4(t)(V_K - V(t)) + g_{Na} m_\infty^3(V)(a + bn(t))(V_{Na} - V(t)) \\ \qquad\qquad + g_L(V_L - V(t)), \\ \dfrac{\mathrm{d}n}{\mathrm{d}t} = \alpha_n(V(t))(1 - n(t)) - \beta_n(V(t))n(t), \end{cases}$$

with $m_\infty(v) = \frac{\alpha_m(v)}{\alpha_m(v)+\beta_m(v)}$. It is important to note that, although the time constants of the ion channels have been mathematically investigated (see for example [RW08]), the approximation of the variable h is purely based on observation, and not on a rigorous mathematical reduction. Nevertheless, if the linear approximation seems questionable when the membrane potential is held fixed (Figure 1.13), it becomes quite remarkable when the whole system (HH) is considered as in Figure 1.14 for a periodic behavior and Figure 1.15 for a transitory behavior, with different initial membrane potentials V_0. The different behaviors are obtained by tuning the external current I_{ext} that is applied.

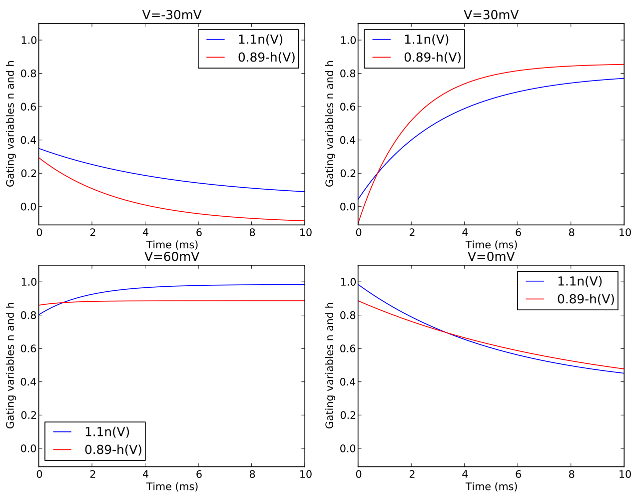


Figure 1.13 – Linear approximation of the variable h when the membrane potential is held fixed at -30, 0, 30 and 60mV.

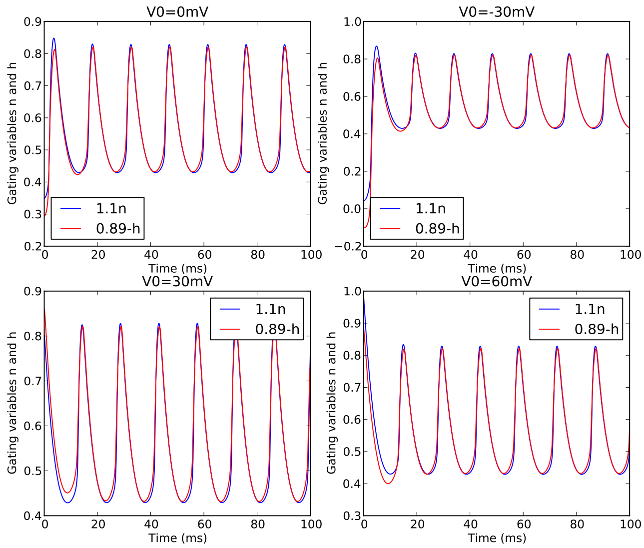


Figure 1.14 – Linear approximation of the variable h for a periodic behavior of system (HH) and initial membrane potential of -30, 0, 30 and 60mV.

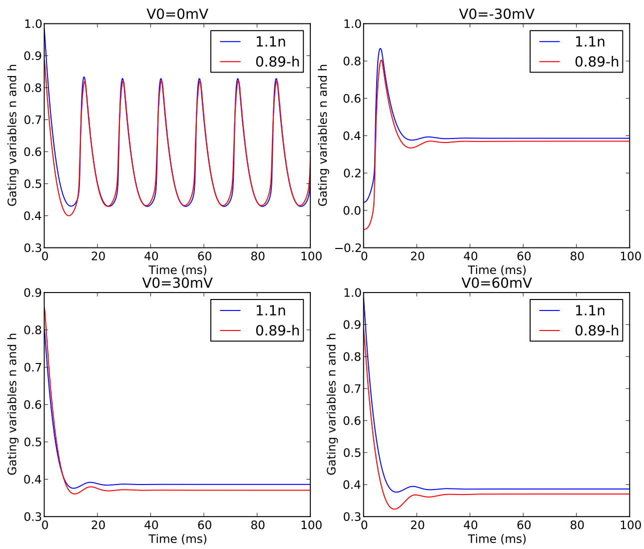


Figure 1.15 – Linear approximation of the variable h for a transitory behavior of system (HH) and initial membrane potential of -30, 0, 30 and 60mV.

The ChR2-3-states model

In terms of singular controls, this model behaves similarly to the Morris-Lecar model. There is no singular extremal for the same reasons, and the optimal control is bang-bang with the same expression (the proof is exactly the same). The direct method is implemented with the numerical values of Appendices 1.B and 1.C.1, the targeted action potential has been fixed to 90mV. The optimal control is physiological here and has in fact no switching time, the light has to be on all the way to the spike (see Figure 1.16).

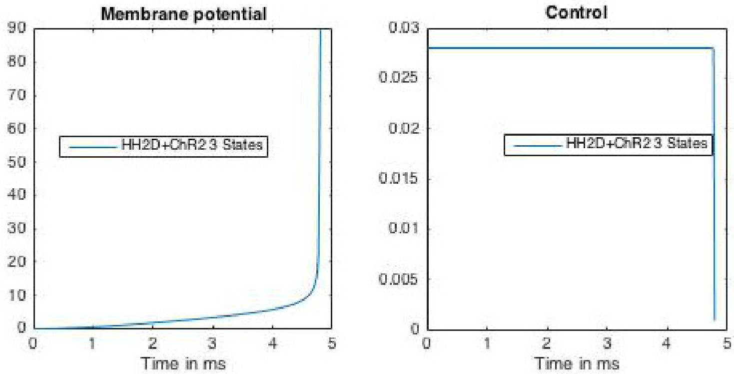


Figure 1.16 – Optimal trajectory and bang-bang optimal control for the HH2D-ChR2-3-states model.

The ChR2-4-states model

The ChR2-4-states model is interesting because it shows that the Hodgkin-Huxley behaves in the opposite way of the Morris-Lecar model. Indeed, the ChR2-4-states model slightly outperforms the ChR2-3-states model, and requires less light, for small values of u_{max}, including the physiological value of $u_{max} = 0.028$. Furthermore, when u_{max} increases, the 3-states and 4-states models exactly match, both in terms of optimal trajectory and optimal control (Figure 1.17). This means that the ChR2-3-states model is a good approximation of the ChR2-4-states model, in terms of optimal control, for the reduced Hodgkin-Huxley. This is a nice property since the ChR2-3-states is theoretically tractable in terms of singular controls.

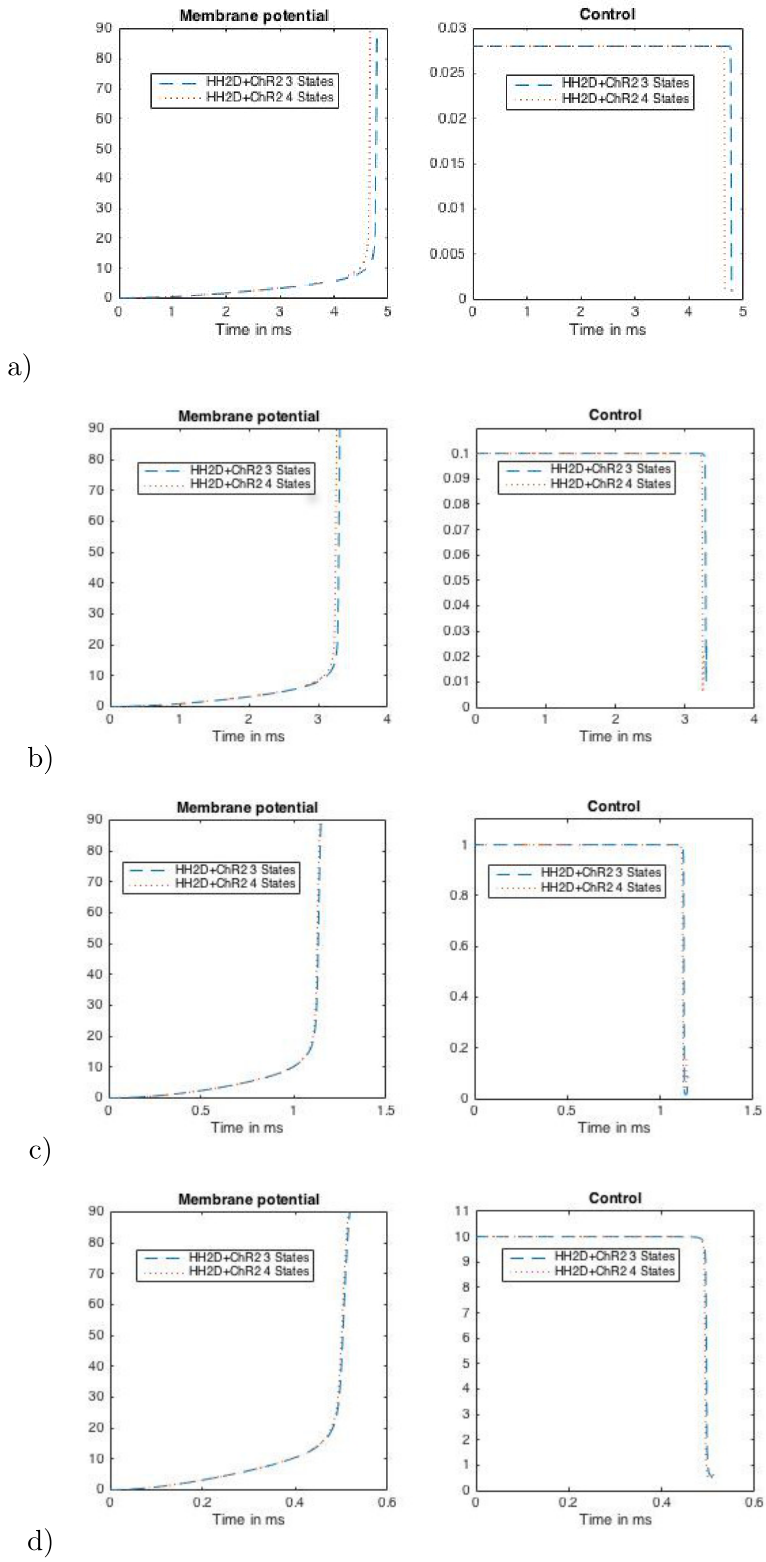


Figure 1.17 – Optimal trajectory and bang-bang optimal control for the HH2D-ChR2-3-states and HH2D-ChR2-4-states models with u_{max} = a) 0.028, b) 0.1, c) 1, d) 10.

1.3.4 The complete Hodgkin-Huxley model

The ChR2-3-states model

The complete Hodgkin-Huxley model is more difficult to analyze mathematically, and optimal singular controls cannot be excluded a priori as for the previous models. Nevertheless, singular controls do not appear in our numerical simulations. Figure 1.18 shows the optimal trajectory and control for numerical values taken in Appendices 1.B and 1.C.1.

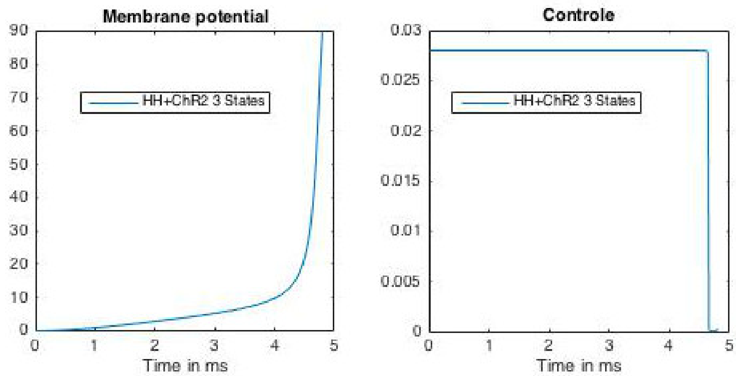


Figure 1.18 – Optimal trajectory and bang-bang optimal control for the HH-ChR2-3-states model.

The ChR2-4-states model

We observe the same phenomenon than for the reduced Hodgkin-Huxley model, that is, for small values of u_{max}, the ChR2-4-states model slightly outperforms the ChR2-3-states model and when u_{max} increases, both models match (Figure 1.19). This constitutes a new argument in favor of the reduced Hodgkin-Huxley model since it captures the features of the complete model in terms of optimal control. Finally, the fact that both Hodgkin-Huxley models have almost the same behavior for the two ChR2 models means that they can be qualified as robust with regards to the mathematical modeling of ChR2.

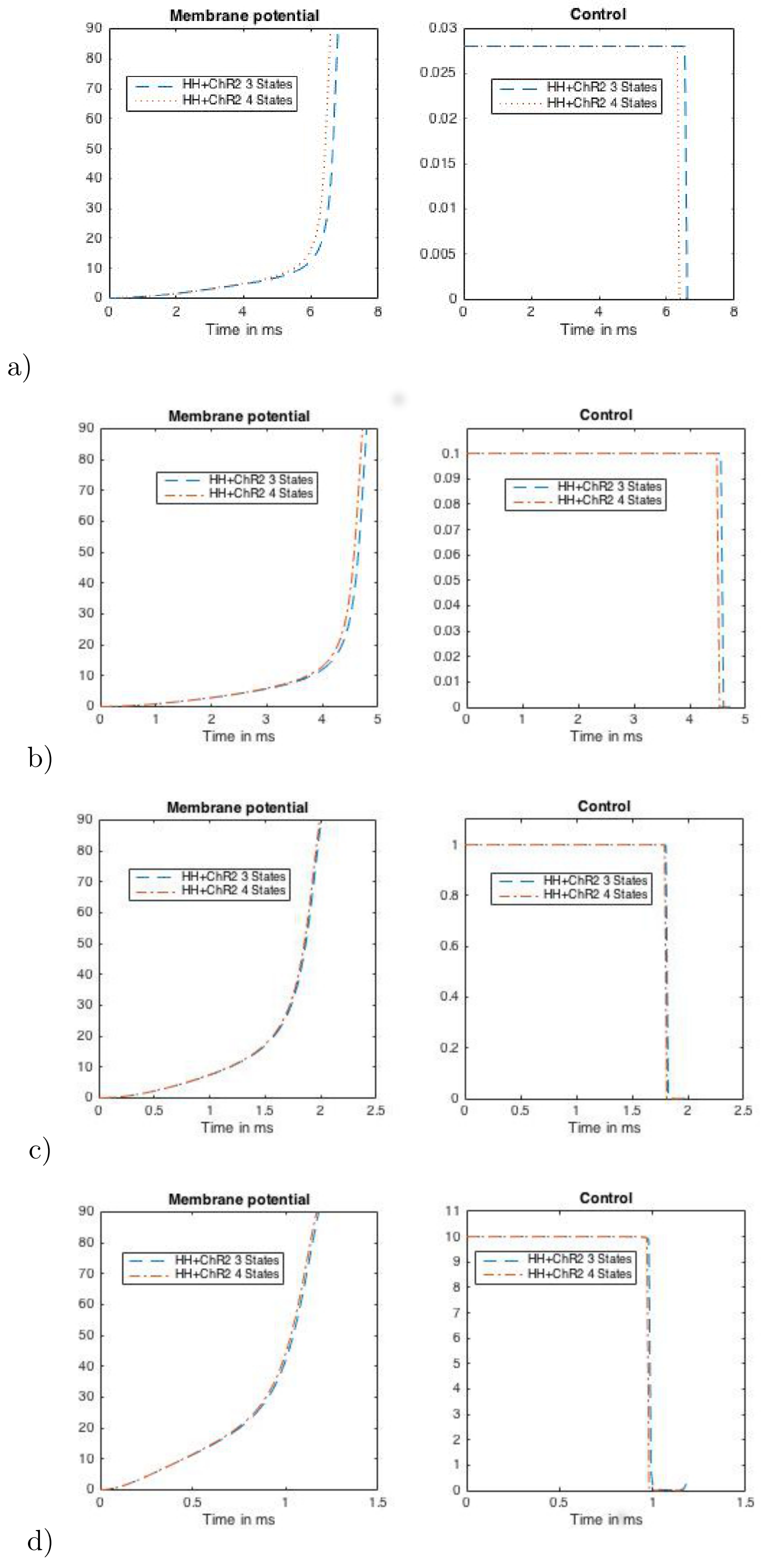


Figure 1.19 – Optimal trajectory and bang-bang optimal control for the HH-ChR2-3-states and HH-ChR2-4-states models with u_{max} = a) 0.028, b) 0.1, c) 1, d) 10.

1.3.5 Conclusions on the numerical results

We begin with comments on the two versions of the ChR2 models for each neuron model. For every neuron model that we numerically treat, the ChR2-3-states and the ChR2-4-states versions behave qualitatively the same. We observe no optimal singular controls and the shapes of optimal controls and optimal trajectories are similar. Nevertheless, we can note some distinctions between the neuron models. For the FitzHugh-Nagumo model, the ChR2-4-states version always outperforms the ChR2-3-states version. This is also the case for the two Hodgkin-Huxley models with the important difference that, when the control maximal value increases, the optimal trajectory and optimal control quantitatively match. The Hodgkin-Huxley models are thus very robust with respect to the ChR2 modeling. The Morris-Lecar model displays an unusual behavior when we compare the ChR2-3-states and the ChR2-4-states versions. Indeed, for low values of the control maximal value, including the physiological value computed in Appendix 1.C.1, the ChR2-3-states version outperforms the ChR2-4-states version and the opposite happens when the control maximal value increases.

As announced at the beginning of Section 1.3, the numerical results invite to distinguish between two main behavior of neuron models with respect to optogenetic control. Most of the models, that is all the models except the Morris-Lecar, behave as physiologically expected. The optimal control is bang-bang, begins with a maximal arc, and has at most one switch. The Morris-Lecar model has more than one switch. This means that it is more efficient to switch on and off the light several times than just keep the light on almost all the way up to the spike. That is why we qualify this model as nonphysiological. Moreover, by only changing the value of the ChR2 equilibrium potential (V_{ChR2}) we can observe a change of the number of switches. Finally, the behavior of the Morris-Lecar model emphasizes the critical importance of optimal control since it allows to find a control that triggers a spike when the expected physiological stimulation (with at most one switch) fails to trigger a spike.

Appendix

Appendix 1.A Numerical constants for the Morris-Lecar model

The numerical values of the several constants and their physiological meaning are taken from [DG13] and gathered in Table 1.A.1.

Table 1.A.1 – Meaning and numerical values of the constants appearing in the Morris-Lecar model

$V_1 =$	-1.2 mV	Fitting parameter
$V_2 =$	18 mV	Fitting parameter
$V_3 =$	2 mV	Fitting parameter
$V_4 =$	30 mV	Fitting parameter
$g_{Ca} =$	4.4 μS/cm^2	Maximal conductance of Ca^{2+} channels
$g_K =$	8 μS/cm^2	Maximal conductance of K^+ channels
$g_L =$	2 μS/cm^2	Conductance associated with the leakage current
$V_{Ca} =$	120 mV	Equilibrium potential of Ca^{2+} ions
$V_K =$	-84 mV	Equilibrium potential of K^+ ions
$V_L =$	-60 mV	Equilibrium potential for the leak current
$C =$	20 μF/cm^2	Membrane capacitance
$\phi =$	0.04 ms^{-1}	Fitting parameter

Table 1.A.2 gathers the numerical values for Figure 1.10.

Table 1.A.2 – Meaning and numerical values of the constants, taking from [SHL04], appearing in the Morris-Lecar model

$V_1 =$	-0.01 mV	Fitting parameter
$V_2 =$	0.15 mV	Fitting parameter
$V_3 =$	0.1 mV	Fitting parameter
$V_4 =$	0.145 mV	Fitting parameter
$g_{Ca} =$	1.0 μS/cm^2	Maximal conductance of Ca^{2+} channels
$g_K =$	2.0 μS/cm^2	Maximal conductance of K^+ channels
$g_L =$	0.5 μS/cm^2	Conductance associated with the leakage current
$V_{Ca} =$	1.0 mV	Equilibrium potential of Ca^{2+} ions
$V_K =$	-0.7 mV	Equilibrium potential of K^+ ions
$V_L =$	-0.5 mV	Equilibrium potential for the leak current
$C =$	1.0 μF/cm^2	Membrane capacitance
$\phi =$	0.333 ms^{-1}	Fitting parameter

Appendix 1.B Numerical constants for the Hodgkin-Huxley model

$$\alpha_n(V) = \frac{0.1 - 0.01V}{e^{1-0.1V} - 1}, \qquad \beta_n(V) = 0.125e^{-\frac{V}{80}},$$
$$\alpha_m(V) = \frac{2.5 - 0.1V}{e^{2.5-0.1V} - 1}, \qquad \beta_m(V) = 4e^{-\frac{V}{18}},$$
$$\alpha_h(V) = 0.07e^{-\frac{V}{20}}, \qquad \beta_h(V) = \frac{1}{e^{3-0.1V} + 1}.$$

The following table gathers the numerical values of the Hodgkin-Huxley model, as given in the original paper [HH52].

Table 1.B.1 – Meaning and numerical values of the constants appearing in the Hodgkin-Huxley model

$\bar{g}_K =$	36 μS/cm^2	Maximal conductance of K^+ channels
$\bar{g}_{Na} =$	120 μS/cm^2	Maximal conductance of Na^{2+} channels
$g_L =$	0.3 μS/cm^2	Conductance associated with the leakage current
$E_{Na} =$	115 mV	Equilibrium potential of Na^{2+} ions
$E_K =$	-12 mV	Equilibrium potential of K^+ ions
$E_L =$	-10.6 mV	Equilibrium potential for the leak current
$C =$	0.9 μF/cm^2	Membrane capacitance

The equilibrium potential E_L of the leakage current is usually set so that the equilibrium value of the (HH) system is such that $V = 0$.

Appendix 1.C Numerical constants for the ChR2 models

1.C.1 The 3-states model

The constants of the model are the rates K_d and K_r of the transitions between the open state and the light adapted closed state and between the two closed states, the maximal conductance g_{ChR2} and the equilibrium potential V_{ChR2}. As specified in Section 1.2, we assume that these rates are constants during the evolution in order to obtain an affine control system. For the numerical computations, we took the values given in Table 1 of [NGG+09]:

$$K_d = 0.2 \text{ ms}^{-1}, \qquad K_r = 0.021 \text{ ms}^{-1}.$$

The maximal conductance is given by the formula $g_{ChR2} = \rho_{ChR2} g^*_{ChR2}$, with ρ_{ChR2} the density of channels and g^*_{ChR2} the conductance of a single channel. These values are taken from [FAM12] to obtain

$$g_{ChR2} = 0.65 \text{ mS} \cdot \text{cm}^{-2}.$$

As mentioned right after in Appendix 1.B, the physiological equilibrium membrane potential is mathematically shifted to equal 0. The equilibrium potential of the $ChR2$ that is usually measured around 0 ([FAM12]) and very often taken as 0 ([FAM12],[NGG+09]). The exact value 0 would raise a mathematical problem because since we shifted the value of E_L so that $V = 0$ corresponds to the equilibrium point of the uncontrolled system we start from. Indeed, $V = 0$ would also correspond to an equilibrium point of the controlled system, regardless of the value of the control. For this reason, we shifted the value of V_{ChR2} and took it equal to 60mV. This value corresponds to the shift of the membrane resting potential for the Morris-Lecar and Hodgkin-Huxley models.

Finally we can give an estimation of the physiological maximal value u_{max} of the control. Indeed, upon illumination, the transition rate between the dark adapted closed state and the open state in [NGG+09] is εF where $\varepsilon = 0.5$ is the quantum efficiency and F is given by the formula

$$F = \frac{\sigma_{ret}\phi}{w_{loss}},$$

where $\sigma_{ret} \simeq 10^{-8}\mu\text{m}^2$ is the retinal cross section (cross section of the photon receptor on the $ChR2$), $\phi = 6.2 \times 10^9 \text{ ph} \cdot \mu\text{m}^{-2} \cdot \text{s}^{-1}$ is the original flux of photons and $w_{loss} = 1.1$ is a loss factor. As for the numerical value of K_d and K_r we took the one of Table 1 in [NGG+09] for the value of ϕ. With these values we get

$$u_{max} = 0.028 \text{ ms}^{-1}.$$

1.C.2 The 4-states model

The numerical values for the ChR2-4-states model are taken from [FAM12] and gathered in Table 1.C.1 below

Table 1.C.1 – Numerical values of the constants appearing in the ChR2-4-States model

$K_{d1} =$	0.13 ms^{-1}	Decay rate
$K_{d2} =$	0.025 ms^{-1}	Decay rate
$e_{12} =$	0.053 ms^{-1}	Transition rate
$e_{21} =$	0.023 ms^{-1}	Transition rate
$K_r =$	0.004 ms^{-1}	Recovery rate
$\varepsilon 1 =$	0.5	Quantum efficency for o_1
$\varepsilon 2 =$	0.1	Quantum efficency for o_2
$g_1 =$	50 fS	o_1 state conductance
$\rho =$	0.05	Relative conductance of the open states
$\rho^*_{ChR2} =$	130 μm^{-2}	ChR2 density
$g_{ChR2} =$	0.65 mS $\cdot$ cm^{-2}	$ChR2$ maximal conductance

Chapter 2

Optimal control of infinite-dimensional piecewise deterministic Markov processes and application to the control of neuronal dynamics via Optogenetics

Introduction

Optogenetics is a recent and innovative technique which allows to induce or prevent electric shocks in living tissues, by means of light stimulation. Successfully demonstrated in mammalian neurons in 2005 ([BZB$^+$05]), the technique relies on the genetic modification of cells to make them express particular ionic channels, called rhodopsins, whose opening and closing are directly triggered by light stimulation. One of these rhodopsins comes from an unicellular flagellate algae, *Chlamydomonas reinhardtii*, and has been baptized Channelrodhopsins-2 (ChR2). It is a cation channel that opens when illuminated with blue light.

Since the field of Optogenetics is young, the mathematical modeling of the phenomenon is quite scarce. Some models have been proposed, based on the study of the photocycles initiated by the absorption of a photon. In 2009, Nikolic and al. [NGG$^+$09] proposed two models for the ChR2 that are able to reproduce the photocurrents generated by the light stimulation of the channel. Those models are constituted of several states that can be either conductive (the channel is open) or non-conductive (the channel is closed). Transitions between those states are spontaneous, depend on the membrane potential or are triggered by the absorption of a photon. For example, the four-states model of Nikolic and al.

[NGG+09] has two open states (o_1 and o_2) and two closed states (c_1 and c_2). Its transitions are represented on Figure 2.1

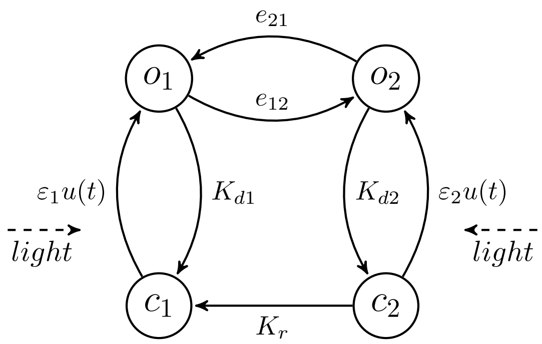


Figure 2.1 – Simplified four states ChR2 channel : ε_1, ε_2, e_{12}, e_{21}, K_{d1}, K_{d2} and K_r are positive constants.

The purpose of this chapter is to extend to infinite dimension the optimal control of *Piecewise Deterministic Markov Processes* (PDMPs) and to define an infinite-dimensional controlled Hodgkin-Huxley model, containing ChR2 channels, as an infinite-dimensional controlled PDMP and prove existence of optimal ordinary controls. We now give the definition of the model.

We consider an axon, described as a 1-dimensional cable and we set $I = [0, 1]$ (the more physical case $I = [-l, l]$ with $2l > 0$ the length of the axon is included here by a scaling argument). Let $D_{ChR2} := \{o_1, o_2, c_1, c_2\}$. Individually, a ChR2 features a stochastic evolution which can be properly described by a Markov Chain on the finite space constituted of the different states that the ChR2 can occupy. In the four-states model above, two of the transitions are triggered by light stimulation, in the form of a parameter u that can evolve in time. Here $u(t)$ is physically proportional to the intensity of the light with which the protein is illuminated. For now, we will consider that when the control is on (*i.e.*, when the light is on), the entire axon is uniformly illuminated. Hence for all $t \geq 0$, $u(t)$ features no spatial dependency.

The deterministic Hodgkin-Huxley model was introduced in [HH52]. A stochastic infinite-dimensional model was studied in [Aus08], [BR11a], [GT12] and [RTW12]. The Sodium (Na^+) channels and Potassium (K^+) channels are described by two pure jump processes with state spaces $D_1 := \{n_0, n_1, n_2, n_3, n_4\}$ and
$D_2 := \{m_0h_1, m_1h_1, m_2h_1, m_3h_1, m_0h_0, m_1h_0, m_2h_0, m_3h_0\}$.

For a given scale $N \in \mathbb{N}^*$, we consider that the axon is populated by $N_{hh} = N - 1$ channels of type Na^+, K^+ or $ChR2$, at positions $\frac{1}{N}(\mathbb{Z} \cap N\mathring{I})$. In the sequel we will use the notation $I_N := \mathbb{Z} \cap N\mathring{I}$. We consider the Gelfand triple (V, H, V^*) with $V := H_0^1(I)$ and $H := L^2(I)$. The process we study is defined as a controlled infinite-dimensional *Piecewise Deterministic Markov Process* (PDMP). All constants and auxiliary functions in the next definition will be defined further in the paper.

Definition 2.0.1. ***Stochastic controlled infinite-dimensional Hodgkin-Huxley-ChR2 model.*** *Let $N \in \mathbb{N}^*$. We call N^{th} stochastic controlled infinite-dimensional Hodgkin-Huxley-ChR2 model the controlled PDMP $(v(t), d(t)) \in V \times D_N$ defined by the following characteristics:*

- *A state space $V \times D_N$ with $D_N = D^{I_N}$ and $D = D_1 \cup D_2 \cup D_{ChR2}$.*
- *A control space $U = [0, u_{max}]$, $u_{max} > 0$.*
- *A set of uncontrolled PDEs: For every $d \in D_N$,*

$$\begin{cases} v'(t) = \dfrac{1}{C_m}\Delta v(t) + f_d(v(t)), \\ v(0) = v_0 \in V, \quad v_0(x) \in [V_-, V_+] \quad \forall x \in I, \\ v(t,0) = v(t,1) = 0, \quad \forall t > 0, \end{cases} \tag{2.1}$$

with

$$\begin{aligned} &\mathcal{D}(\Delta) = V, \\ &f_d(v) := \frac{1}{N}\sum_{i \in I_N} \Big(g_K \mathbf{1}_{\{d_i = n_4\}}(V_K - v(\frac{i}{N})) + g_{Na}\mathbf{1}_{\{d_i = m_3h_1\}}(V_{Na} - v(\frac{i}{N})) \\ &\qquad + g_{ChR2}(\mathbf{1}_{\{d_i=o_1\}} + \rho\mathbf{1}_{\{d_i=o_2\}})(V_{ChR2} - v(\frac{i}{N})) + g_L(V_L - v(\frac{i}{N}))\Big)\delta_{\frac{i}{N}}, \end{aligned} \tag{2.2}$$

with $\delta_z \in V^*$ the Dirac mass at $z \in I$.

- *A controlled jump rate function $\lambda : V \times D_N \times U \to \mathbb{R}_+$ defined for all $(v, d, u) \in H \times D_N \times U$ by*

$$\lambda_d(v, u) = \sum_{i \in I_N} \sum_{x \in D} \sum_{\substack{y \in D, \\ y \neq x}} \sigma_{x,y}(v(\frac{i}{N}), u)\mathbf{1}_{\{d_i = x\}}, \tag{2.3}$$

with $\sigma_{x,y} : \mathbb{R} \times U \to \mathbb{R}_+^*$ smooth functions for all $(x, y) \in D^2$. See Table 2.1 in Section 2.4.1 for the expression of those functions.

- *A controlled discrete transition measure $\mathcal{Q} : V \times D_N \times U \to \mathcal{P}(D_N)$ defined for all $(v, d, u) \in E \times D_N \times U$ and $y \in D$ by*

$$\mathcal{Q}(\{d^{i:y}\}|v, d) = \frac{\sigma_{d_i,y}(v(\frac{i}{N}), u)\mathbf{1}_{\{d_i \neq y\}}}{\lambda_d(v, u)}, \tag{2.4}$$

where $d^{i:y}$ is obtained from d by putting its i^{th} component equal to y.

From a biological point of view, the optimal control problem consists in mimicking an output signal that encodes a given biological behavior, while minimizing the intensity of the light applied to the neuron. For example, it can be a time-constant signal and in this case, we want to change the resting potential of the neuron to study its role on its general behavior. We can also think of pathological behaviors that would be fixed in this way. The minimization of light intensity is crucial because the range of intensity experimentally reachable is quite small and is always a matter of preoccupation for experimenters. These considerations lead us to formulate the following mathematical optimal control problem.

Suppose we are given a *reference signal* $V_{ref} \in V$. The control problem is then to find $\alpha \in \mathcal{A}$ that minimizes the following expected cost

$$J_z(\alpha) = \mathbb{E}_z^\alpha \left[\int_0^T \left(\kappa ||X_t^\alpha(\phi) - V_{ref}||_V^2 + \alpha(X_t^\alpha) \right) \mathrm{d}t \right], \quad z \in \Upsilon, \tag{2.5}$$

where $\mathcal{A}$ is the space of control strategies, Υ an auxiliary state space that comprises $V \times D_N$, $X_\cdot^\alpha$ is the controlled PDMP and $X_\cdot^\alpha(\phi)$ its continuous component.

We will prove the following result.

Theorem 2.0.1. *Under the assumptions of Section 2.1.1, there exists an optimal control strategy $\alpha^* \in \mathcal{A}$ such that for all $z \in \Upsilon$,*

$$J_z(\alpha^*) = \inf_{\alpha \in \mathcal{A}} \mathbb{E}_z^\alpha \left[\int_0^T \left(\kappa ||X_t^\alpha(\phi) - V_{ref}||_V^2 + \alpha(X_t^\alpha) \right) \mathrm{d}t \right],$$

and the value function $z \to \inf_{\alpha \in \mathcal{A}} J_z(\alpha)$ is continuous on Υ.

Piecewise Deterministic Markov Processes constitute a large class of Markov processes suited to describe a tremendous variety of phenomena such as the behavior of excitable cells ([Aus08],[BR11a],[PTW12]), the evolution of stocks in financial markets ([BR09]) or the congestion of communication networks ([DGR02]), among many others. PDMPs can basically describe any non diffusive Markovian system. The general theory of PDMPs, and the tools to study them, were introduced by Davis ([Dav84]) in 1984, at a time when the theory of diffusion was already amply developed. Since then, they have been widely investigated in terms of asymptotic behavior, control, limit theorems and CLT, numerical methods, among others (see for instance [BdSD12], [CD08], [CD11], [CDMR12] and references therein). PDMPs are jump processes coupled with a deterministic evolution between the jumps. They are fully described by three local characteristics: the deterministic flow ϕ, the jump rate λ, and the transition measure $\mathcal{Q}$. In [Dav84], the temporal evolution of a PDMP between jumps (i.e. the flow ϕ) is governed by an Ordinary Differential Equation (ODE). For that matter, this kind of PDMPs will be referred to as finite-dimensional in the sequel.

Optimal control of such processes have been introduced by Vermes ([Ver85]) in finite dimension. In [Ver85], the class of *piecewise open-loop* controls is introduced as the proper class to consider to obtain strongly Markovian processes. A Hamilton-Jabobi-Bellman equation is formulated and necessary and sufficient conditions are given for the existence of optimal controls. The standard broader class of so-called *relaxed* controls is considered and it plays a crucial role in getting the existence of optimal controls when no convexity assumption is imposed. This class of controls has been studied, in the finite-dimensional case, by Gamkrelidze ([Gam87]), Warga ([War62b] and [War62a]) and Young ([You69]). Relaxed controls provide a compact class that is adequate for studying optimization problems. Still in finite dimension, many control problems have been formulated and studied such as optimal control ([FSS04]), optimal stopping ([cRDG00]) or controllability ([GM15]). In infinite dimension, relaxed controls were introduced by Ahmed ([Ahm83], [AT78], [AX93]). They were also studied by Papageorgiou in [Pap89] where the author shows the strong continuity of relaxed trajectories with respect to the relaxed control. This continuity result will be of great interest in this paper.

A formal infinite-dimensional PDMP was defined in [BR11a] for the first time, the set of ODEs being replaced by a special set of Partial Differential Equations (PDE). The extended generator and its domain are provided and the model is used to define a stochastic spatial Hodgkin-Huxley model of neuron dynamics. The optimal control problem we have in mind here regards those Hodgkin-Huxley type models. Seminal work on an uncontrolled infinite-dimensional Hodgkin-Huxley model was conducted in [Aus08] where the trajectory of the infinite-dimensional stochastic system is shown to converge to the deterministic one, in probability. This type of model has then been studied in [RTW12] in terms of limit theorems and in [GT12] in terms of averaging. The extension to infinite dimension heavily relies on the fact that semilinear parabolic equations can be interpreted as ODEs in Hilbert spaces.

To give a sense to Definition 2.0.1 and to Theorem 2.0.1, we will define a controlled infinite-dimensional PDMP for which the control acts on the three local characteristics. We consider controlled semilinear parabolic PDEs, jump rates λ and transition measures $\mathcal{Q}$ depending on the control. This kind of PDE takes the form

$$\dot{x}(t) = Lx(t) + f(x(t), u(t)),$$

where L is the infinitesimal generator of a strongly continuous semigroup and f is some function (possibly nonlinear). The optimal control problem we address is the finite-time minimization of an unbounded expected cost functional along the trajectory of the form

$$\min_u \mathbb{E} \int_0^T c(x(t), u(t)) \mathrm{d}t,$$

where $x(\cdot)$ is the continuous component of the PDMP, $u(\cdot)$ the control and $T > 0$ the finite time horizon, the cost function $c(\cdot, \cdot)$ being potentially unbounded.

To address this optimal control problem, we use the fairly widespread approach that consists in studying the imbedded discrete-time Markov chain composed of the times and the locations of the jumps. Since the evolution between jumps is deterministic, there exists a one-to-one correspondence between the PDMP and a pure jump process that enable to define the imbedded Markov chain. The discrete-time Markov chain belongs to the class of *Markov Decision Processes* (MDPs). This kind of approach has been used in [FSS04] and [BR10] (see also the book [HY08] for a self-contained presentation of MDPs). In these articles, the authors apply dynamic programming to the MDP derived from a PDMP, to prove the existence of optimal relaxed strategies. Some sufficient conditions are also given to get non-relaxed, also called ordinary, optimal strategies. However, in both articles, the PDMP is finite dimensional. To the best of our knowledge, the optimal control of infinite-dimensional PDMPs has not yet been treated and this is one of our main objectives here, along with its motivation, derived from the Optogenetics, to formulate and study infinite-dimensional controlled neuron models.

The paper is structured as follows. In Section 2.1 we adapt the definition of a standard infinite-dimensional PDMP given in [BR11a] in order to address control problems of such processes. To obtain a strongly Markovian process, we enlarge the state space and we prove an extension to controlled PDMPs of [BR11a, Theorem 4]. We also define in this section the MDP associated to our controlled PDMP and that we study later on. In Section 2.2 we use the results of [Pap89] to define relaxed controlled PDMPs and relaxed MDPs in infinite dimension. Section 2.3 gathers the main results of the paper. We show that the optimal control problems of PDMPs and of MDPs are equivalent. We build up a general framework in which the MDP is contracting. The value function is then shown to be continuous and existence of optimal relaxed control strategies is proved. We finally give in this section, some convexity assumptions under which an ordinary optimal control strategy can be retrieved.

The final Section 2.4 is devoted to showing that the previous theoretical results apply to the model of Optogenetics previously introduced. Several variants of the model are discussed, the scope of the theoretical results being much larger than the model of Definition 2.0.1.

2.1 Theoretical framework for the control of infinite-dimensional PDMPs

2.1.1 The enlarged process and assumptions

In the present section we define the infinite-dimensional controlled PDMPs that we consider in this paper in a way that enables us to formulate control problems in which the three characteristics of the PDMP depend on an additional variable that we call the control parameter. In particular we introduce the *enlarged process* which enable us to address optimization problems in the subsequent sections.

Let $(\Omega, \mathcal{F}, (\mathcal{F}_t)_{t\geq 0}, \mathbb{P})$ be a filtered probability space satisfying the usual conditions.

We consider a Gelfand triple ($V \subset H \subset V^*$) such that H is a separable Hilbert space and V a separable, reflexive Banach space continuously and densely embedded in H. The pivot space H is identified with its dual H^*, V^* is the topological dual of V. H is then continuously and densely embedded in V^*. We will denote by $||\cdot||_V$, $||\cdot||_H$, and $||\cdot||_{V^*}$ the norms on V, H, and V^*, by $(\cdot,\cdot)$ the inner product in H and by $\langle\cdot,\cdot\rangle$ the duality pairing of (V, V^*). Note that for $v \in V$ and $h \in H$, $\langle h, v\rangle = (h, v)$.

Let D be a finite set, the state space of the discrete variable and Z a compact Polish space, the control space. Let $T > 0$ be the finite time horizon. Intuitively a controlled PDMP $(v_t, d_t)_{t\in[0,T]}$ should be constructed on $H \times D$ from the space of *ordinary control rules* defined as

$$A := \{a : (0, T) \to U \text{ measurable}\},$$

where U, the *action space*, is a closed subset of Z. Elements of A are defined up to a set in $[0, T]$ of Lebesgue measure 0. The control rules introduced above are called *ordinary* in contrast with the *relaxed* ones that we will introduce and use in order to prove existence of optimal strategies. When endowed with the coarsest σ-algebra such that

$$a \to \int_0^T e^{-t} w(t, a(t))dt$$

is measurable for all bounded and measurable functions $w : \mathbb{R}_+ \times U \to \mathbb{R}$, the set of control rules A becomes a Borel space (see [Yus80, Lemma 1]). This will be crucial for the discrete-time control problem that we consider later. Conditionally to the continuous component v_t and the control $a(t)$, the discrete component d_t is a continuous-time Markov chain given by a jump rate function $\lambda : H \times D \times U \to \mathbb{R}_+$ and a transition measure $\mathcal{Q} : H \times D \times U \to \mathcal{P}(D)$.

Between two consecutive jumps of the discrete component, the continuous component v_t solves a controlled semilinear parabolic PDE

$$\begin{cases} \dot{v}_t = -Lv_t + f_d(v_t, a(t)), \\ v_0 = v, \quad v \in V. \end{cases} \tag{2.6}$$

For $(v, d, a) \in H \times D \times A$ we will denote by $\phi^a(v, d)$ the flow of (2.6). Let $T_n, n \in \mathbb{N}$ be the jump times of the PDMP. Their distribution is then given by

$$\mathbb{P}[T_{n+1} - T_n | T_n, v_{T_n}, d_{T_n}] = \exp\left(-\int_0^{\Delta t} \lambda\Big(\phi^a_{t+s-T_n}(v_{T_n}, d_{T_n}), d_t, a(t + s - T_n)\Big)\mathrm{d}s\right), \tag{2.7}$$

for $t \in [T_n; T_{n+1})$. When a jump occurs, the distribution of the post jump state is given by

$$\mathbb{P}[d_t = d | d_{t^-} \neq d_t] = \mathcal{Q}(\{d\} | d_t, v_t, a(t)). \tag{2.8}$$

The triple $(\lambda, \mathcal{Q}, \phi)$ fully describes the process and is referred to as the local characteristics of the PDMP.

We will make the following assumptions on the local characteristics of the PDMP.

(H(λ)) For every $d \in D$, $\lambda_d : H \times Z \to \mathbb{R}_+$ is a function such that:

1. There exists $M_\lambda, \delta > 0$ such that:

$$\delta \leq \lambda_d(x, z) \leq M_\lambda, \quad \forall (x, z) \in H \times Z.$$

2. $z \to \lambda_d(x, z)$ is continuous on Z, for all $x \in H$.
3. $x \to \lambda_d(x, z)$ is locally Lipschitz continuous, uniformly in Z, that is, for every compact set $K \subset H$, there exists $l_\lambda(K) > 0$ such that

$$|\lambda_d(x, z) - \lambda_d(y, z)| \leq l_\lambda(K) ||x - y||_H \quad \forall (x, y, z) \in K^2 \times Z.$$

(H($\mathcal{Q}$)) The function $\mathcal{Q} : H \times D \times Z \times \mathcal{B}(D) \to [0, 1]$ is a transition probability such that: $(x, z) \to \mathcal{Q}(\{p\} | x, d, z)$ is continuous for all $(d, p) \in D^2$ (weak continuity) and $\mathcal{Q}(\{d\} | x, d, z) = 0$ for all $(x, z) \in H \times Z$.

(H(L)) $L : V \to V^*$ is such that:

1. L is linear, monotone;
2. $||Lx||_{V^*} \leq c + c_1 ||x||_V$ with $c > 0$ and $c_1 \geq 0$;
3. $\langle Lx, x \rangle \geq c_2 ||x||_V^2, \quad c_2 > 0$;
4. $-L$ generates a strongly continuous semigroup $(S(t))_{t \geq 0}$ on H such that $S(t) : H \to H$ is compact for every $t > 0$. We will denote by M_S a bound, for the operator norm, of the semigroup on $[0, T]$.

(H(f)) For every $d \in D$, $f_d : H \times Z \to H$ is a function such that:

1. $x \to f_d(x, z)$ is Lipschitz continuous, uniformly in Z, that is,

$$||f_d(x, z) - f_d(y, z)||_H \leq l_f ||x - y||_H \quad \forall (x, z) \in H \times Z, \quad l_f > 0.$$

2. $(x, z) \to f_d(x, z)$ is continuous from $H \times Z$ to H_w, where H_w denotes the space H endowed with the topology of weak convergence.

Let us make some comments on the assumptions above. Assumption (H(λ))1. will ensure that the process is *regular*, i.e. the number of jumps of d_t is almost surely finite in every finite time interval. Assumption (H(λ))2. will enable us to construct relaxed trajectories. Assumptions (H(λ))3. and (H($\mathcal{Q}$)) will be necessary to obtain the existence of optimal relaxed controls for the associated MDP. Assumptions (H(L))1.2.3. (H(f)) will ensure the existence and uniqueness of the solution of (2.6). Note that all the results of this paper are unchanged if assumption (H(f))1 is replaced by

(H(f))' For every $d \in D$, $f_d : H \times Z \to H$ is a function such that:

1. $x \to -f_d(x, z)$ is continuous monotone, for all $z \in Z$.
2. $||f_d(x, z)||_H \leq b_1 + b_2||x||_H, \quad b_1 \geq 0, b_2 > 0$, for all $z \in Z$.

In particular, assumption (H(f)) implies (H(f))'2. and we will use the constants b_1 and b_2 further in this paper. Note that they can be chosen uniformly in D since it is a finite set. To see this, note that $z \to f_d(0, z)$ is a weakly continuous on the compact space Z and thus weakly bounded. It is then strongly bounded by the Uniform Boundedness Principle.

Finally, assumptions (H(f))3. and (H(L))4. will respectively ensure the existence of solutions for the relaxed counterpart of (2.6) and the strong continuity of theses solutions with regards to the relaxed control. For that last matter, the compactness of Z is also required. The following theorem is a reminder that the assumption on the semigroup does not make the problem trivial since it implies that L is unbounded when H is infinite-dimensional.

Theorem 2.1.1. *(see [EN00, Theorem 4.29])*

1. *For a strongly continuous semigroup $(T(t))_{t\geq 0}$ the following properties are equivalent*
   (a) *$(T(t))_{t\geq 0}$ is immediately compact.*
   (b) *$(T(t))_{t\geq 0}$ is immediately norm continuous, and its generator has compact resolvent.*
2. *Let X be a Banach space. A bounded operator $A \in \mathcal{L}(X)$ has compact resolvent if and only if X is finite-dimensional.*

We define $\mathcal{U}_{ad}((0, T), U) := \{a \in L^1((0, T), Z) | a(t) \in U \text{ a.e.}\} \subset A$ the space of *admissible rules.* Because of (H(L)) and (H(f)), for all $a \in \mathcal{U}_{ad}((0, T), U)$, (2.6) has a unique solution belonging to $L^2((0, T), V) \cap H^1((0, T), V^*)$ and moreover, the solution belongs to $C([0, T], H)$ (see [Pap89] for the construction of such a solution). We will make an extensive use of the mild formulation of the solution of (2.6), given by

$$\phi^a_t(v, d) = S(t)v + \int_0^t S(t-s) f_d(\phi^a_s(v, d), a(s)) \mathrm{d}s, \tag{2.9}$$

with $\phi^a_0(v, d) = v$. One of the keys in the construction of a controlled PDMP in finite or infinite dimension is to ensure that ϕ^a enjoys the flow property $\phi^a_{t+s}(v, d) = \phi^a_s(\phi^a_t(v, d), d)$ for all $(v, d, a) \in H \times D \times \mathcal{U}_{ad}((0, T), U)$ and $(t, s) \in \mathbb{R}_+$. It is the flow property that guarantees the Markov property for the process. Under the formulation (2.9), it is easy to see that the solution ϕ^a cannot feature the flow property for any reasonable set of admissible rules. In particular, the jump process $(d_t, t \geq 0)$ given by (2.7) and (2.8) is not Markovian. Moreover in control problems, and especially in Markovian control problems, we are generally looking for feedback controls which depend only on the current state variable so that at any time, the controller needs only to observe the current state to be able to take an action. Feedback controls would ensure the flow property. However they impose a huge restriction on the class of admissible controls. Indeed, feedback controls would be functions $u : H \times D \to U$ and for the solution of (2.6) to be uniquely determined, the function $x \to f_d(x, u(x,d))$ needs to be Lipschitz continuous. It would automatically exclude discontinuous controls and therefore would not be adapted to control problems. To avoid this issue, Vermes introduced piecewise open-loop controls (see [Ver85]): after a jump of the discrete component, the controller observes the location of the jump, say $(v, d) \in H \times D$ and chooses a control rule $a \in \mathcal{U}_{ad}((0,T), U)$ to be applied until the next jump. The time elapsed since the last jump must then be added to the state variable in order to see a control rule as a feedback control. While Vermes [Ver85] and Davis [Dav93] only add the last post jump location we also want to keep track of the time of the last jump in order to define proper controls for the Markov Decision Processes that we introduce in the next section, and to eventually obtain optimal feedback policies. According to these remarks, we now enlarge the state space and define control strategies for the enlarged process. We introduce first several sets that will be useful later on.

Definition 2.1.1. *Let us define the following sets* $\Theta(T, 2) := \{(t, s) \in [0, T]^2 \mid t + s \leq T\}$, $\Xi := H \times D \times \Theta(T, 2) \times H$ *and* $\Upsilon := H \times D \times [0, T]$.

Definition 2.1.2. *Control strategies. Enlarged controlled PDMP. Survival function.*
a) The set $\mathcal{A}$ *of admissible control strategies is defined by*

$$\mathcal{A} := \{\alpha : \Upsilon \to \mathcal{U}_{ad}([0, T]; U) \text{ measurable}\}.$$

b) On Ξ *we define the enlarged controlled PDMP* $(X_t^\alpha)_{t\geq 0} = (v_t, d_t, \tau_t, h_t, \nu_t)_{t\geq 0}$ *with strategy* $\alpha \in \mathcal{A}$ *as follows:*

— $(v_t, d_t)_{t\geq 0}$ *is the original PDMP,*

— τ_t *is the time elapsed since the last jump at time* t*,*

— h_t *is the time of the last jump before time* t*,*

— ν_t *is the post jump location right after the jump at time* h_t.

c) Let $z := (v, d, h) \in \Upsilon$. *For* $a \in \mathcal{U}_{ad}([0, T]; U)$ *we will denote by* $\chi_\cdot^a(z)$ *the solution of*

$$\frac{\mathrm{d}}{\mathrm{d}t}\chi_t^a(z) = -\chi_t^a(z)\lambda_d(\phi_t^a(z), a(t)), \qquad \chi_0^a(z) = 1,$$

and its immediate extension $\chi_\cdot^\alpha(z)$ *to* $\mathcal{A}$ *such that the process* $(X_t^\alpha)_{t\geq 0}$ *starting at*

$(v, d, 0, h, v) \in \Xi$, *admits* $\chi^{\alpha}_{\cdot}$ *as survival function:*

$$\mathbb{P}[T_1 > t] = \chi^{\alpha}_t(z).$$

The notation $\phi^a_t(z)$ *means here*

$$\phi^a_t(z) := S(t)v + \int_0^t S(t-s) f_d(\phi^a_s(z), a(s))\mathrm{d}s.$$

and $\phi^{\alpha}_t(z)$ *means*

$$\phi^{\alpha}_t(z) := S(t)v + \int_0^t S(t-s) f_d(\phi^{\alpha}_s(z), \alpha(z)(s))\mathrm{d}s.$$

Remark 2.1.1. *i)Thanks to [Yus80, Lemma 3], the set of admissible control strategies can be seen as a set of measurable feedback controls acting on* Ξ *and with values in* U*. The formulation of Definition 2.1.2 is adequate to address the associated discrete-time control problem in Section 2.1.3.*
ii) In view of Definition 2.1.2, given $\alpha \in \mathcal{A}$*, the deterministic dynamics of the process* $(X^{\alpha}_t)_{t\geq 0} = (v_t, d_t, \tau_t, , h_t, \nu_t)_{t\geq 0}$ *between two consecutive jumps obeys the initial value problem*

$$\begin{cases} \dot{v}_t = -Lv_t + f_d(v_t, \alpha(v, d, s)(\tau_t)), & v_s = v \in E, \\ \dot{d}_t = 0, \qquad d_s = d \in D, \\ \dot{\tau}_t = 1, \qquad \tau_s = 0, \\ \dot{h}_t = 0, \qquad h_s = s \in [0, T], \\ \dot{\nu}_t = 0, \qquad \nu_s = v_s = v, \end{cases} \tag{2.10}$$

with s *the last time of jump. The jump rate function and transition measure of the enlarged PDMP are straightforwardly given by the ones of the original process and will be denoted the same (see Appendix 2.A for their expression).*
iii) If the relation $t = h_t + \tau_t$ *indicates that the variable* h_t *might be redundant, recall that we keep track of it on purpose. Indeed, the optimal control will appear as a function of the jump times so that keeping them as a variable will make the control feedback.*
iv) Because of the special definition of the enlarged process, for every control strategy in $\mathcal{A}$*, the initial point of the process* $(X^{\alpha}_t)_{t\geq 0}$ *cannot be any point of the enlarged state space* Ξ*. More precisely we introduce in Definition 2.1.3 below the space of coherent initial points.*

Definition 2.1.3. *Space of coherent initial points.*
Take $\alpha \in \mathcal{A}$ *and* $x := (v_0, d_0, 0, h_0, v_0) \in \Xi$ *and extend the notation* $\phi^{\alpha}_t(x)$ *of Definition 2.1.2 to* Ξ *by*

$$\phi^{\alpha}_t(x) := S(t)v_0 + \int_0^t S(t-s) f_{d_0}(\phi^{\alpha}_s(x), \alpha(v_0, d_0, h_0)(s))\mathrm{d}s$$

The set $\Xi^\alpha \subset \Xi$ of coherent initial points is defined as follows

$$\Xi^\alpha := \{(v,d,\tau,h,\nu) \in \Xi \mid v = \phi^\alpha_\tau(\nu,d,0,h,\nu)\}. \tag{2.11}$$

Then we have again, for all $x := (v_0,d_0,\tau_0,h_0,\nu_0) \in \Xi^\alpha$,

$$\phi^\alpha_t(x) := S(t)v_0 + \int_0^t S(t-s)f_{d_0}(\phi^\alpha_s(x), \alpha(\nu_0,d_0,h_0)(s))\mathrm{d}s$$

Note that (X^α_t) can be constructed like any PDMP by a classical iteration that we recall in Appendix 2.A for the sake of completeness.

Proposition 2.1.1. *The flow property.*
Take $\alpha \in \mathcal{A}$ and $x := (v_0,d_0,\tau_0,h_0,\nu_0) \in \Xi^\alpha$. Then $\phi^\alpha_{t+s}(x) = \phi^\alpha_t(\phi^\alpha_s(x), d_s, \tau_{s+h_0}, h_s, \nu_s)$ for all $(t,s) \in \mathbb{R}^2_+$ with $s \geq \tau_0$.

Notation. *Let $\alpha \in \mathcal{A}$. For $z \in \Upsilon$, we will use the notation $\alpha_s(z) := \alpha(z)(s)$. Furthermore, we will sometimes denote by $\mathcal{Q}_\alpha(\cdot|v,d)$ instead of $\mathcal{Q}(\cdot|v,d,\alpha_\tau(\nu,d,h))$ for all $(v,d,\tau,h,\nu) \in \mathcal{A} \times \Xi^\alpha$.*

2.1.2 A probability space common to all strategies

Up to now thanks to Definition 2.1.2 we can formally associate the PDMP $(X^\alpha_t)_{t\in\mathbb{R}_+}$ to a given strategy $\alpha \in \mathcal{A}$. However, we need to show that there exists a filtered probabily space satisfying the usual conditions under which, for every control strategy $\alpha \in \mathcal{A}$, the controlled PDMP $(X^\alpha_t)_{t\geq 0}$ is a homogeneous strong Markov process. This is what we do in the next theorem which provides an extension of [BR11a, Theorem 4] to controlled infinite-dimensional PDMPs and some estimates on the continuous component of the PDMP.

Theorem 2.1.2. *Suppose that assumptions (H(λ)), (H($\mathcal{Q}$)), (H(L)) and (H(f)) (or (H(f))') are satisfied.*
a) There exists a filtered probability space satisfying the usual conditions such that for every control strategy $\alpha \in \mathcal{A}$ the process $(X^\alpha_t)_{t\geq 0}$ introduced in Definition 2.1.2 is a homogeneous strong Markov process on Ξ with extended generator $\mathcal{G}^\alpha$ given in Appendix 2.B.
b) For every compact set $K \subset H$, there exists a deterministic constant $c_K > 0$ such that for all control strategy $\alpha \in \mathcal{A}$ and initial point $x := (v,d,\tau,h,\nu) \in \Xi^\alpha$, with $v \in K$, the first component v^α_t of the control PDMP $(X^\alpha_t)_{t\geq 0}$ starting at x is such that

$$\sup_{t\in[0,T]} ||v^\alpha_t||_H \leq c_K.$$

The proof of Theorem 2.1.2 is given in Appendix 2.B. In the next section, we introduce the MDP that will allow us to prove the existence of optimal strategies.

2.1.3 A Markov Decision Process (MDP)

Because of the particular definition of the state space Ξ, the state of the PDMP just after a jump is in fact fully determined by a point in Υ. In Appendix 2.B we recall the one-to-one correspondence between the PDMP on Ξ and the included pure jump process $(Z_n)_{n\in\mathbb{N}}$ with values in Υ. This pure jump process allows to define a Markov Decision Process $(Z'_n)_{n\in\mathbb{N}}$ with values in $\Upsilon \cup \{\Delta_\infty\}$, where Δ_∞ is a cemetery state added to Υ to define a proper MDP. In order to lighten the notations, the dependence on a control strategy $\alpha \in \mathcal{A}$ of both jump processes is implicit. The stochastic kernel $\mathcal{Q}'$ of the MDP satisfies

$$\mathcal{Q}'(B \times C \times E|z, a) = \int_0^{T-h} \rho_t \mathrm{d}t, \tag{2.12}$$

for any $z := (v, d, h) \in \Upsilon$, Borel sets $B \subset H$, $C \subset D$, $E \subset [0, T]$, and $a \in \mathcal{U}_{ad}([0, T], U)$, where

$$\rho_t := \lambda_d(\phi_t^a(z), a(t))\chi_t^a(z)\mathbf{1}_E(h + t)\mathbf{1}_B(\phi_t^a(z))\mathcal{Q}(C|\phi_t^a(z), d, a(t)),$$

with $\phi_t^a(z)$ given by (2.9) and $\mathcal{Q}'(\{\Delta_\infty\}|z, a) = \chi_{T-h}^a(z)$, and $\mathcal{Q}'(\{\Delta_\infty\}|\Delta_\infty, a) = 1$. The conditional jumps of the MDP $(Z'_n)_{n\in\mathbb{N}}$ are then given by the kernel $\mathcal{Q}'(\cdot|z, \alpha(z))$ for $(z, \alpha) \in \Upsilon \times \mathcal{A}$. Note that $Z'_n = Z_n$ as long as $T_n \leq T$, where T_n is the last component of Z_n. Since we work with Borel state and control spaces, we will be able to apply techniques of [BS78] for discrete-time stochastic control problems, without being concerned by measurability matters. See [BS78, Section 1.2] for an illuminating discussion on these measurability questions.

2.2 Relaxed controls

Relaxed controls are constructed by enlarging the set of ordinary ones, in order to convexify the original system, and in such a way that it is possible to approximate relaxed strategies by ordinary ones. The difficulty in doing so is twofold. First, the set of relaxed trajectories should not be much larger than the original one. Second, the topology considered on the set of relaxed controls should make it a compact set and, at the same time, make the flow of the associated PDE continuous. Compactness and continuity are two notions in conflict so being able to achieve such a construction is crucial. Intuitively a relaxed control strategy on the action space U corresponds to randomizing the control action: at time t, instead of taking a predetermined action, the controller will take an action with some probability, making the control a transition probability. This has to be formalized mathematically.

Notation and reminder. Z is a compact Polish space, $C(Z)$ denotes the set of all real-valued continuous, necessarily bounded, functions on Z, endowed with the supremum norm. Because Z is compact, by the Riesz Representation Theorem, the dual space $[C(Z)]^*$

of $C(Z)$ is identified with the space $M(Z)$ of Radon measures on $\mathcal{B}(Z)$, the Borel σ-field of Z. We will denote by $M_+^1(Z)$ the space of probability measures on Z. The action space U is a closed subset of Z. We will use the notations $L^1(C(Z)) := L^1((0,T), C(Z))$ and $L^\infty(M(Z)) := L^\infty((0,T), M(Z))$.

2.2.1 Relaxed controls for a PDE

Let $\mathcal{B}([0,T])$ denote the Borel σ-field of $[0,T]$ and *Leb* the Lebesgue measure. A transition probability from $([0,T], \mathcal{B}([0,T]), Leb)$ into $(Z, \mathcal{B}(Z))$ is a function $\gamma : [0,T] \times \mathcal{B}(Z) \to [0,1]$ such that

$$\begin{cases} t \to \gamma(t, C) \text{ is measurable for all } C \in \mathcal{B}(Z), \\ \gamma(t, \cdot) \in M_+^1(Z) \text{ for all } t \in [0,T]. \end{cases}$$

We will denote by $\mathcal{R}([0,T], Z)$ the set of all transition probability measures from $([0,T], \mathcal{B}([0,T]), Leb)$ into $(Z, \mathcal{B}(Z))$.
Recall that we consider the PDE (2.6):

$$\dot{v}_t = Lv_t + f_d(v_t, a(t)), \quad v_0 = v, \quad v \in V, \quad a \in \mathcal{U}_{ad}([0,T], U). \tag{2.13}$$

The relaxed PDE is then of the form

$$\dot{v}_t = Lv_t + \int_Z f_d(v_t, u)\gamma(t)(\mathrm{d}u), \quad v_0 = v, \quad v \in V, \quad \gamma \in \mathcal{R}([0,T], U), \tag{2.14}$$

where $\mathcal{R}([0,T], U) := \{\gamma \in \mathcal{R}([0,T], Z) | \gamma(t)(U) = 1 \text{ a.e. in } [0,T]\}$ is the set of transition probabilities from $([0,T], \mathcal{B}([0,T]), Leb)$ into $(Z, \mathcal{B}(Z))$ with support in U. The integral part of (2.14) is to be understood in the sense of Bochner-Lebesgue as we show now. The topology we consider on $\mathcal{R}([0,T], U)$ follows from [Bal84] and because Z is a compact metric space, it coincides with the usual topology of relaxed control theory of [War72]. It is the coarsest topology that makes continuous all mappings

$$\gamma \to \int_0^T \int_Z f(t,z)\gamma(t)(\mathrm{d}z)\mathrm{d}t \in \mathbb{R},$$

for every Carathéodory integrand $f : [0,T] \times Z \to \mathbb{R}$, a Carathéodory integrand being such that

$$\begin{cases} t \to f(t,z) \text{ is measurable for all } z \in Z, \\ z \to f(t,z) \text{ is continuous a.e.,} \\ |f(t,z)| \leq b(t) \text{ a.e., with } b \in L^1((0,T), \mathbb{R}). \end{cases}$$

This topology is called the weak topology on $\mathcal{R}([0,T], Z)$ but we show now that it is in fact metrizable. Indeed, Carathéodory integrands f on $[0,T]\times Z$ can be identified with the Lebesgue-Bochner space $L^1(C(Z))$ via the application $t\to f(t,\cdot)\in L^1(C(Z))$. Now, since $M(Z)$ is a separable (Z is compact), dual space (dual of $C(Z)$), it enjoys the Radon-Nikodym property. Using [DU77, Theorem 1 p. 98], it follows that $[L^1(C(Z))]^*=L^\infty(M(Z))$. Hence, the weak topology on $\mathcal{R}([0,T],Z)$ can be identified with the w^*-topology in $(L^\infty(M(Z)),L^1(C(Z)))$, the latter being metrizable since $L^1(C(Z))$ is a separable space (see [DS88, Theorem 1 p. 426]). This crucial property allows to work with sequences when dealing with continuity matters with regards to relaxed controls.

Finally, by Alaoglu's Theorem, $\mathcal{R}([0,T],U)$ is w^*-compact in $L^\infty(M(Z))$, and the set of original admissible controls $\mathcal{U}_{ad}([0,T],U)$ is dense in $\mathcal{R}([0,T],U)$ (see [Bal84, Corollary 3 p. 469]).

For the same reasons why (2.13) admits a unique solution, by setting $\bar{f}_d(v,\gamma):=\int_Z f_d(v,u)\gamma(\mathrm{d}u)$, it is straightforward to see that (2.14) admits a unique solution. The following theorem gathers the results of [Pap89, Theorems 3.2 and 4.1] and will be of paramount importance in the sequel.

Theorem 2.2.1. *If assumptions (H(L)) and (H(f)) (or (H(f))') hold, then*
a) the space of relaxed trajectories (i.e. solutions of 2.14) is a convex, compact set of $C([0,T],H)$. It is the closure in $C([0,T],H)$ of the space of original trajectories (i.e. solutions of 2.13).
b) The mapping that maps a relaxed control to the solution of (2.14) is continuous from $\mathcal{R}([0,T],U)$ into $C([0,T],H)$.

2.2.2 Relaxed controls for infinite-dimensional PDMPs

First of all, note that since the control acts on all three characteristics of the PDMP, convexity assumptions on the fields $f_d(v,U)$ would not necessarily ensure existence of optimal controls as it does for partial differential equations. Such assumptions should also be imposed on the rate function and the transition measure of the PDMP. For this reason, relaxed controls are even more important to prove existence of optimal controls for PDMP. For what has been done for PDE above, we are now able to define relaxed PDMPs. The next definition is the relaxed analogue of Definition 2.1.2.

Definition 2.2.1. *Relaxed control strategies, relaxed local characteristics.*
a) The set $\mathcal{A}^{\mathcal{R}}$ of relaxed admissible control strategies for the PDMP is defined by

$$\mathcal{A}^{\mathcal{R}}:=\{\mu:\Upsilon\to\mathcal{R}([0,T];U)\ \textit{measurable}\}.$$

Given a relaxed control strategy $\mu\in\mathcal{A}^{\mathcal{R}}$ and $z\in\Upsilon$, we will denote by $\mu^z:=\mu(z)\in\mathcal{R}([0,T];U)$ and $\mu^z_t:=\mu^z(t,\cdot)$ the corresponding probability measure on $(Z,\mathcal{B}(Z))$.
b) For $\gamma\in M^1_+(Z)$, $(v,d)\in H\times D$ and $C\in\mathcal{B}(D)$, we extend the jump rate function and transition measure as follows

$$\begin{cases} \lambda_d(v,\gamma) := \displaystyle\int_Z \lambda_d(v,u)\gamma(\mathrm{d}u), \\ \mathcal{Q}(C|v,d,\gamma) := (\lambda_d(v,\gamma))^{-1} \displaystyle\int_Z \lambda_d(v,u)\mathcal{Q}(C|v,d,u)\gamma(\mathrm{d}u), \end{cases} \tag{2.15}$$

the expression for the enlarged process being straightforward. This allows us to give the relaxed survival function of the PDMP and the relaxed mild formulation of the solution of (2.14)

$$\begin{cases} \dfrac{\mathrm{d}}{\mathrm{d}t}\chi_t^{\mu}(z) = -\chi_t^{\mu}(z)\lambda_d(\phi_t^{\mu}(z),\mu_t^z), \qquad \chi_0^{\mu}(z) = 1, \\ \phi_t^{\mu}(z) = S(t)v + \displaystyle\int_0^t \int_Z S(t-s)f_d(\phi_s^{\mu}(z),u)\mu_s^z(\mathrm{d}u)\mathrm{d}s, \end{cases} \tag{2.16}$$

for $\mu \in \mathcal{A}^{\mathcal{R}}$ and $z := (v,d,h) \in \Upsilon$. For $\gamma \in \mathcal{R}([0,T],U)$, we will also use the following notation

$$\begin{cases} \chi_t^{\gamma}(z) = \exp\left(-\displaystyle\int_0^t \lambda_d(\phi_s^{\gamma}(z),\gamma(s))\mathrm{d}s\right), \\ \phi_t^{\gamma}(z) = S(t)v + \displaystyle\int_0^t \int_Z S(t-s)f_d(\phi_s^{\gamma}(z),u)\gamma(s)(\mathrm{d}u)\mathrm{d}s, \end{cases}$$

The following proposition is a direct consequence of Theorem 2.1.2b).

Proposition 2.2.1. *For every compact set $K \subset H$, there exists a deterministic constant $c_K > 0$ such that for all control strategy $\mu \in \mathcal{A}^{\mathcal{R}}$ and initial point $x := (v,d,\tau,h,\nu) \in \Xi^{\alpha}$, with $v \in K$, the first component v_t^{μ} of the control PDMP $(X_t^{\mu})_{t\geq 0}$ starting at x is such that*

$$\sup_{t\in[0,T]} ||v_t^{\mu}||_H \leq c_K.$$

The relaxed transition measure is given in the next section through the relaxed stochastic kernel of the MDP associated to our relaxed PDMP.

2.2.3 Relaxed associated MDP

Let $z := (v,d,h) \in \Upsilon$ and $\gamma \in \mathcal{R}([0,T],U)$. The relaxed stochastic kernel of the relaxed MDP satisfies

$$\mathcal{Q}'(B \times C \times E|z,\gamma) = \int_0^{T-h} \tilde{\rho}_t \mathrm{d}t, \tag{2.17}$$

for Borel sets $B \subset H$, $C \subset D$, $E \subset [0,T]$, where

$$\begin{aligned} \tilde{\rho}_t &:= \chi_t^{\gamma}(z)\mathbf{1}_E(h+t)\mathbf{1}_B(\phi_t^{\gamma}(z)) \int_Z \lambda_d\Big(\phi_t^{\gamma}(z),u\Big)\mathcal{Q}\Big(C|\phi_t^{\gamma}(z),d,u\Big)\gamma(t)(\mathrm{d}u), \\ &= \chi_t^{\gamma}(z)\mathbf{1}_E(h+t)\mathbf{1}_B(\phi_t^{\gamma}(z))\lambda_d\Big(\phi_t^{\gamma}(z),\gamma(t)\Big)\mathcal{Q}\Big(C|\phi_t^{\gamma}(z),d,\gamma(t)\Big) \end{aligned}$$

and $\mathcal{Q}'(\{\Delta_\infty\}|z,\gamma) = \chi^\gamma_{T-h}(z)$, and $\mathcal{Q}'(\{\Delta_\infty\}|\Delta_\infty,\gamma) = 1$, with, as before, the conditional jumps of the MDP $(Z'_n)_{n\in\mathbb{N}}$ given by the kernel $\mathcal{Q}'(\cdot|z,\mu(z))$ for $(z,\mu) \in \Upsilon \times \mathcal{A}^{\mathcal{R}}$.

2.3 Main results

Here, we are interested in finding optimal controls for optimization problems involving infinite-dimensional PDMPs. For instance, we may want to track a targeted "signal" (as a solution of a given PDE, see Section 2.4). To do so, we are going to study the optimal control problem of the imbedded MDP defined in Section 2.1.3. This strategy has been for example used in [BR10] in the particular setting of a decoupled finite-dimensional PDMP, the rate function being constant.

2.3.1 The optimal control problem

Thanks to the preceding sections we can consider ordinary or relaxed costs for the PDMP X^α or the MDP and their corresponding value functions. For $z := (v,d,h) \in \Upsilon$ and $\alpha \in \mathcal{A}$ we denote by $\mathbb{E}^\alpha_z$ the conditional expectation given that $X^\alpha_h = (v,d,0,h,v)$ and by $X^\alpha_s(\phi)$ the first component of X^α_s. Furthermore, we denote by $X^\alpha_s := (v_s, d_s, \tau_s, h_s, \nu_s)$, then the shortened notation $\alpha(X^\alpha_s)$ will refer to $\alpha_{\tau_s}(\nu_s, d_s, h_s)$. Theses notations are straightforwardly extended to $\mathcal{A}^{\mathcal{R}}$. We introduce a running cost $c : H \times Z \to \mathbb{R}_+$ and a terminal cost $g : H \to \mathbb{R}_+$ satisfying

(H(c)) $(v,z) \to c(v,z)$ and $v \to g(v)$ are nonnegative quadratic functions, that is there exists $(a,b,c,d,e,f,g,h,i,j) \in \mathbb{R}^9$ such that for $v, z \in H \times Z$,

$$c(v,u) = a||v||^2_H + b\bar{d}(0,u)^2 + c||v||_H\bar{d}(0,u) + d||v||_H + e\bar{d}(0,u) + f,$$
$$g(v) = h||v||^2_H + i||v||_H + j,$$

with $\bar{d}(\cdot,\cdot)$ the distance on Z.

Remark 2.3.1. *This assumption might seem a bit restrictive, but it falls within the framework of all the applications we have in mind. More importantly, it can be widely loosened if we slightly change the assumptions of Theorem 2.3.1. In particular, all the following results, up to Lemma 2.3.7, are true and proved for continuous functions $c : H \times Z \to \mathbb{R}_+$ and $g : H \to \mathbb{R}_+$. See Remark 2.3.4 below.*

Definition 2.3.1. *Ordinary value function for the PDMP X^α.*
For $\alpha \in \mathcal{A}$, we define the ordinary expected total cost function $V_\alpha : \Upsilon \to \mathbb{R}$ and the corresponding value function V as follows:

$$V_\alpha(z) := \mathbb{E}^\alpha_z\left[\int_h^T c(X^\alpha_s(\phi), \alpha(X^\alpha_s))\mathrm{d}s + g(X^\alpha_T(\phi))\right], \quad z := (v,d,h) \in \Upsilon, \tag{2.18}$$

$$V(z) = \inf_{\alpha \in \mathcal{A}} V_\alpha(z), \quad z \in \Upsilon. \tag{2.19}$$

Assumption (H(c)) ensures that V_α and V are properly defined.

Definition 2.3.2. *Relaxed value function for the PDMP X^μ.*
For $\mu \in \mathcal{A}^{\mathcal{R}}$ we define the relaxed expected cost function $V_\mu : \Upsilon \to \mathbb{R}$ and the corresponding relaxed value function $\tilde{V}$ as follows:

$$V_\mu(z) := \mathbb{E}_z^\mu \left[\int_h^T \int_Z c(X_s^\mu(\phi), u)\mu(X_s^\mu)(\mathrm{d}u)\mathrm{d}s + g(X_T^\mu(\phi)) \right], \quad z := (v, d, h) \in \Upsilon, \tag{2.20}$$

$$\tilde{V}(z) = \inf_{\mu \in \mathcal{A}^{\mathcal{R}}} V_\mu(z), \quad z \in \Upsilon. \tag{2.21}$$

We can now state the main result of this section.

Theorem 2.3.1. *Under assumptions (H(λ)), (H($\mathcal{Q}$)), (H(L)), (H(f)) and (H(c)), the value function $\tilde{V}$ of the relaxed optimal control problem on the PDMP is continuous on Υ and there exists an optimal relaxed control strategy $\mu^* \in \mathcal{A}^{\mathcal{R}}$ such that*

$$\tilde{V}(z) = V_{\mu^*}(z), \qquad \forall z \in \Upsilon.$$

Remark 2.3.2. *All the subsequent results that lead to Theorem 2.3.1 would be easily transposable to the case of a lower semicontinuous cost function. We would then obtain a lower semicontinuous value function.*

The next section is dedicated to proving Theorem 2.3.1 via the optimal control of the MDP introduced before. Let us briefly sum up what we are going to do. We first show that the optimal control problem of the PDMP is equivalent to the optimal control problem of the MDP and that an optimal control for the latter gives an optimal control strategy for the original PDMP. We will then build up a framework, based on so called bounding functions (see [BR10]), in which the value function of the MDP is the fixed point of a contracting operator. Finally, we show that under the assumptions of Theorem 2.3.1, the relaxed PDMP X^μ belongs to this framework.

2.3.2 Optimal control of the MDP

Let us define the ordinary cost c' on $\Upsilon \cup \{\Delta_\infty\} \times \mathcal{U}_{ad}([0,T];U)$ for the MDP defined in Section 2.1.3. For $z := (v, d, h) \in \Upsilon$ and $a \in \mathcal{U}_{ad}([0,T];U)$,

$$c'(z, a) := \int_0^{T-h} \chi_s^a(z)\, c(\phi_s^a(z), a(s))\mathrm{d}s + \chi_{T-h}^a(z) g(\phi_{T-h}^a(z)), \tag{2.22}$$

and $c'(\Delta_\infty, a) := 0$.
Assumption (H(c)) allows c' to be properly extended to $\mathcal{R}([0,T],U)$ by the formula

$$c'(z,\gamma) = \int_0^{T-h} \chi_s^\gamma(z) \int_Z c(\phi_s^\gamma(z), u)\gamma(s)(\mathrm{d}u)\mathrm{d}s + \chi_{T-h}^\gamma(z) g(\phi_{T-h}^\gamma(z)), \tag{2.23}$$

and $c'(\Delta_\infty, \gamma) = 0$ for $(z,\gamma) \in \Upsilon \times \mathcal{R}([0,T],U)$. Remark that the function c' is nonnegative (because c and g are nonnegative). We can now define the expected cost function and value function for the MDP.

Definition 2.3.3. *Cost and value functions for the MDP (Z'_n).*
For $\alpha \in \mathcal{A}$ (resp. $\mu \in \mathcal{A}^{\mathcal{R}}$), we define the total expected cost J_α (resp. J_μ) and the value function J (resp. J')

$$J_\alpha(z) = \mathbb{E}_z^\alpha \left[\sum_{n=0}^{\infty} c'(Z'_n, \alpha(Z'_n)) \right], \qquad J_\mu(z) = \mathbb{E}_z^\mu \left[\sum_{n=0}^{\infty} c'(Z'_n, \mu(Z'_n)) \right],$$
$$J(z) = \inf_{\alpha \in \mathcal{A}} J^\alpha(z), \qquad J'(z) = \inf_{\mu \in \mathcal{A}^{\mathcal{R}}} J_\mu(z),$$

for $z \in \Upsilon$ and with $\alpha(Z'_n)$ (resp. $\mu(Z'_n)$) being elements of $\mathcal{U}_{ad}([0,T],U)$ (resp. $\mathcal{R}([0,T],U)$).

The finiteness of theses sums will by justified later by Lemma 2.3.2.

The equivalence Theorem

In the following theorem we prove that the relaxed expected cost function of the PDMP equals the one of the associated MDP. Thus, the value functions also coincide. For the finite-dimensional case we refer the reader to [Dav93] or [BR10] where the discrete component of the PDMP is a Poisson process and therefore the PDMP is entirely decoupled. The PDMPs that we consider are fully coupled.

Theorem 2.3.2. *The relaxed expected costs for the PDMP and the MDP coincide: $V_\mu(z) = J_\mu(z)$ for all $z \in \Upsilon$ and relaxed control $\mu \in \mathcal{A}^{\mathcal{R}}$. Thus, the value functions $\tilde{V}$ and J' coincide on Υ.*

Remark 2.3.3. *Since we have $\mathcal{A} \subset \mathcal{A}^{\mathcal{R}}$, the value functions $V_\alpha(z)$ and $J_\alpha(z)$ also coincide for all $z \in \Upsilon$ and ordinary control strategy $\alpha \in \mathcal{A}$*

Proof. Let $\mu \in \mathcal{A}^{\mathcal{R}}$ and $z = (v,d,h) \in \Upsilon$ and consider the PDMP X^μ starting at $(v,d,0,h,v) \in \Xi^\mu$. We drop the dependence in the control in the notation and denote by $(T_n)_{n\in\mathbb{N}}$ the jump times, and $Z_n := (v_{T_n}, d_{T_n}, T_n) \in \Upsilon$ the point in Υ corresponding to $X^\mu_{T_n}$. Let $H_n = (Z_0, \dots, Z_n)$, $T_n \le T$. For a purpose of concision we will rewrite

$\mu^n := \mu(Z_n) \in \mathcal{R}([0,T],U)$ for all $n \in \mathbb{N}$.

$$V_\mu(z) = \mathbb{E}_z^\mu\left[\sum_{n=0}^{\infty}\int_{T\wedge T_n}^{T\wedge T_{n+1}}\int_Z c(X_s^\mu(\phi),u)\mu_{s-T_n}^n(\mathrm{d}u)\mathrm{d}s + \mathbf{1}_{\{T_n\le T<T_{n+1}\}}g(X_T^\mu(\phi))\right]$$
$$= \sum_{n=0}^{\infty}\mathbb{E}_z^\mu\left[\mathbb{E}_z^\mu\left[\int_{T\wedge T_n}^{T\wedge T_{n+1}}\int_Z c(X_s^\mu(\phi),u)\mu_{s-T_n}^n(\mathrm{d}u)\mathrm{d}s + \mathbf{1}_{\{T_n\le T<T_{n+1}\}}g(X_T^\mu(\phi))|H_n\right]\right],$$

all quantities being non-negative. We want now to examine the two terms that we call $\mathcal{I}_1$ and $\mathcal{I}_2$ separately. For $n \in \mathbb{N}$, we start with

$$\mathcal{I}_1 := \mathbb{E}_z^\mu\left[\int_{T\wedge T_n}^{T\wedge T_{n+1}}\int_Z c(X_s^\mu(\phi),u)\mu_{s-T_n}^n(\mathrm{d}u)\mathrm{d}s|H_n\right]$$

that we split according to $T_n \le T < T_n + 1$ or $T_{n+1} \le T$ (if $T \le T_n$, the corresponding term vanishes). Then

$$\mathcal{I}_1 = \mathbf{1}_{\{T_n\le T\}}\mathbb{E}_z^\mu\left[\int_{T_n}^{T}\int_Z c(X_s^\mu(\phi),u)\mu_{s-T_n}^n(\mathrm{d}u)\mathbf{1}_{\{T_{n+1}>T\}}\mathrm{d}s|H_n\right]$$
$$+ \mathbb{E}_z^\mu\left[\mathbf{1}_{\{T_{n+1}\le T\}}\int_{T_n}^{T_{n+1}}\int_Z c(X_s^\mu(\phi),u)\mu_{s-T_n}^n(\mathrm{d}u)\mathrm{d}s|H_n\right].$$

By the strong Markov property and the flow property, the first term on the RHS is equal to

$$\mathbf{1}_{\{T_n\le T\}}\mathbb{E}_z^\mu\left[\int_0^{T-T_n}\int_Z c(X_{T_n+s}^\mu(\phi),u)\mu_s^n(\mathrm{d}u)\mathbf{1}_{\{T_{n+1}-T_n>T-T_n\}}\mathrm{d}s|H_n\right]$$
$$= \mathbf{1}_{\{T_n\le T\}}\chi_{T-T_n}^\mu(Z_n)\int_0^{T-T_n}\int_Z c(\phi_s^\mu(Z_n),u)\mu_s^n(\mathrm{d}u)\mathrm{d}s.$$

Using the same arguments, the second term on the RHS of $\mathcal{I}_1$ can be written as

$$\mathbf{1}_{\{T_n\le T\}}\int_0^{T-T_n}\int_Z \lambda_{d_n}(\phi_t^\mu(Z_n),u)\mu_t^n(\mathrm{d}u)\chi_t^\mu(Z_n)\int_0^t\int_Z c(\phi_s^\mu(Z_n),u)\mu_t^n(\mathrm{d}u)\mathrm{d}s\mathrm{d}t,$$

An integration by parts yields

$$\mathcal{I}_1 = \mathbf{1}_{\{T_n\le T\}}\int_0^{T-T_n}\chi_t^\mu(Z_n)\int_Z c(\phi_t^\alpha(Z_n),u)\mu_t^n(\mathrm{d}u)\mathrm{d}t.$$

Moreover

$$\mathcal{I}_2 := \mathbb{E}_z^\mu\left[\mathbf{1}_{\{T_n\le T<T_{n+1}\}}g(X_T^\mu)|H_n\right] = \mathbf{1}_{\{T_n\le T\}}\chi_{T-T_n}^\mu(Z_n)g(\phi_{T-T_n}^\mu(Z_n))$$

By definition of the Markov chain $(Z_n')_{n\in\mathbb{N}}$ and the function c', we then obtain for the total expected cost of the PDMP,

$$\begin{aligned} V_\mu(z) &= \sum_{n=0}^{\infty} \mathbb{E}_z^\mu \Bigg[\mathbf{1}_{\{T_n \le T\}} \int_0^{T-T_n} \chi_t^\mu(Z_n) \int_Z c(\phi_t^\alpha(Z_n), u) \mu_t^n(\mathrm{d}u) \mathrm{d}t \\ &\qquad + \mathbf{1}_{\{T_n \le T\}}\, \chi_{T-T_n}^\mu(Z_n) g(\phi_{T-T_n}^\mu(Z_n)) \Bigg] \\ &= \mathbb{E}_z^\mu \left[\sum_{n=0}^{\infty} c'(Z_n', \mu(Z_n')) \right] = J_\mu(z). \end{aligned}$$

□

Existence of optimal controls for the MDP

We now show existence of optimal relaxed controls under a contraction assumption. We use the notation $\mathcal{R} := \mathcal{R}([0,T];U)$ in the sequel. Let us also recall some notations regarding the different control sets we consider.

— u is an element of the control set U.

— $a : [0,T] \to U$ is an element of the space of admissible control rules $\mathcal{U}_{ad}([0,T],U)$

— $\alpha : \Upsilon \to \mathcal{U}_{ad}([0,T],U)$ is an element of the space of admissible strategies for the original PDMP.

— $\gamma : [0,T] \to M_+^1(Z)$ is an element of the space of relaxed admissible control rules $\mathcal{R}$.

— $\mu : \Upsilon \to \mathcal{R}$ is an element of the space of relaxed admissible strategies for the relaxed PDMP.

The classical way to address the discrete-time stochastic control problem that we introduced in Definition 2.3.3 is to consider an additional control space that we will call the space of Markovian policies and denote by Π. Formally $\Pi := \left(\mathcal{A}^{\mathcal{R}}\right)^{\mathbb{N}}$ and a Markovian control policy for the MDP is a sequence of relaxed admissible strategies to be applied at each stage. The optimal control problem is to find $\pi := (\mu_n)_{n\in\mathbb{N}} \in \Pi$ that minimizes

$$J_\pi(z) := \mathbb{E}_z^\pi \left[\sum_{n=0}^{\infty} c'(Z_n', \mu_n(Z_n')) \right].$$

Now denote by $J^*(z)$ this infimum. We will in fact prove the existence of a stationary optimal control policy that will validate the equality

$$J^*(z) = J'(z).$$

Let us now define some operators that will be useful for our study and state the first theorem of this section. Let $w : \Upsilon \to \mathbb{R}$ a continuous function, $(z, \gamma, \mu) \in \Upsilon \times \mathcal{R} \times \mathcal{A}^{\mathcal{R}}$ and define

$$
\begin{aligned}
Rw(z,\gamma) &:= c'(z,\gamma) + (\mathcal{Q}'w)(z,\gamma),\\
\mathcal{T}_\mu w(z) &:= c'(z,\mu(z)) + (\mathcal{Q}'w)(z,\mu(z)) = Rw(z,\mu(z)),\\
(\mathcal{T}w)(z) &:= \inf_{\gamma\in\mathcal{R}} \left\{c'(z,\gamma) + (\mathcal{Q}'w)(z,\gamma)\right\} = \inf_{\gamma\in\mathcal{R}} Rw(z,\gamma),
\end{aligned}
$$

where $(\mathcal{Q}'w)(z,\gamma) := \int_\Upsilon w(x)\mathcal{Q}'(\mathrm{d}x|z,\gamma)$ which admits also the expression

$$
\int_0^{T-h} \chi_t^\gamma(z) \int_Z \lambda_d\Big(\phi_t^\gamma(z),u\Big) \int_D w\Big(\phi_t^\gamma(z),r,h+t\Big)\mathcal{Q}\Big(\mathrm{d}r|\phi_t^\gamma(z),d,u\Big)\gamma(t)(\mathrm{d}u)\mathrm{d}t.
$$

Theorem 2.3.3. *Assume that there exists a subspace $\mathbb{C}$ of the space of continuous bounded functions from Υ to $\mathbb{R}$ such that the operator $\mathcal{T}:\mathbb{C}\to\mathbb{C}$ is contracting and the zero function belongs to $\mathbb{C}$. Assume furthermore that $\mathbb{C}$ is a Banach space. Then J' is the unique fixed point of $\mathcal{T}$ and there exists an optimal control $\mu^*\in\mathcal{A}^{\mathcal{R}}$ such that*

$$
J'(z) = J_{\mu^*}(z), \qquad \forall z\in\Upsilon.
$$

All the results needed to prove this Theorem can be found in [BS78]. We break down the proof into the two following elementary propositions, suited to our specific problem. Before that, recall that from [BS78, Proposition 9.1 p.216], Π is the adequate control space to consider since history-dependent policies do not improve the value function.

Let us now consider the n-stages expected cost function and value function defined by

$$
J_{n\pi}(z) := \mathbb{E}_z^\pi\left[\sum_{i=0}^{n-1} c'\Big(Z_i',\mu_i(Z_i')\Big)\right] \qquad J_n(z) := \inf_{\pi\in\Pi}\mathbb{E}_z^\pi\left[\sum_{i=0}^{n-1} c'\Big(Z_i',\mu_i(Z_i')\Big)\right]
$$

for $n\in\mathbb{N}$ and $\pi := (\mu_n)_{n\in\mathbb{N}}\in\Pi$. We also set $J_\infty := \lim_{n\to\infty} J_n$.

Proposition 2.3.1. *Let assumptions of Theorem 2.3.1 hold. Let $v,w:\Upsilon\to\mathbb{R}$ such that $v\le w$ on Υ, and let $\mu\in\mathcal{A}^{\mathcal{R}}$. Then $\mathcal{T}_\mu v\le\mathcal{T}_\mu w$. Moreover*

$$
J_n(z) = \inf_{\pi\in\Pi}(\mathcal{T}_{\mu_0}\mathcal{T}_{\mu_1}\dots\mathcal{T}_{\mu_{n-1}}0)(z) = (\mathcal{T}^n 0)(z),
$$

with $\pi := (\mu_n)_{n\in\mathbb{N}}$ and J_∞ is the unique fixed point of $\mathcal{T}$ in $\mathbb{C}$.

Proof. The first relation is straightforward since all quantities defining $\mathcal{Q}'$ are nonnegative. The equality $J_n = \inf_{\pi\in\Pi}\mathcal{T}_{\mu_0}\mathcal{T}_{\mu_1}\dots\mathcal{T}_{\mu_{n-1}}0$ is also immediate since $\mathcal{T}_\mu$ just shifts the process of one stage (see also [BS78, Lemma 8.1, p194]).

Let $I\in\mathbb{C}$, $\varepsilon>0$ and $n\in\mathbb{N}$. For every $k\in\{1..n-1\}$, $\mathcal{T}^k I\in\mathbb{C}$ and so there exist $\mu_0,\mu_1,\dots,\mu_{n-1}\in\left(\mathcal{A}^{\mathcal{R}}\right)^n$ such that

$$\mathcal{T}_{\mu_{n-1}} I \leq \mathcal{T} I + \varepsilon, \quad \mathcal{T}_{\mu_{n-2}} \mathcal{T} I \leq \mathcal{T}\mathcal{T} I + \varepsilon, \quad \ldots \quad , \mathcal{T}_{\mu_0} \mathcal{T}^{n-1} I \leq \mathcal{T}\mathcal{T}^{n-1} I + \varepsilon.$$

We then get

$$\begin{aligned}\mathcal{T}^n I &\geq \mathcal{T}_{\mu_0} \mathcal{T}^{n-1} I - \varepsilon \geq \mathcal{T}_{\mu_0} \mathcal{T}_{\mu_1} \mathcal{T}^{n-2} I - 2\varepsilon \geq \quad \cdots \quad \geq \mathcal{T}_{\mu_0} \mathcal{T}_{\mu_1} \ldots \mathcal{T}_{\mu_{n-1}} I - n\varepsilon \\ &\geq \inf_{\pi \in \Pi} \mathcal{T}_{\mu_0} \mathcal{T}_{\mu_1} \ldots \mathcal{T}_{\mu_{n-1}} I - n\varepsilon.\end{aligned}$$

Since this last inequality is true for any $\varepsilon > 0$ we get

$$\mathcal{T}^n I \geq \inf_{\pi \in \Pi} \mathcal{T}_{\mu_0} \mathcal{T}_{\mu_1} \ldots \mathcal{T}_{\mu_{n-1}} I,$$

and by definition of $\mathcal{T}$, $\mathcal{T} I \leq \mathcal{T}_{\mu_{n-1}} I$. Using the first relation of the proposition we get

$$\mathcal{T}^n I \leq \mathcal{T}_{\mu_0} \mathcal{T}_{\mu_1} \ldots \mathcal{T}_{\mu_{n-1}} I.$$

Finally, $\mathcal{T}^n I = \inf_{\pi \in \Pi} \mathcal{T}_{\mu_0} \mathcal{T}_{\mu_1} \ldots \mathcal{T}_{\mu_{n-1}} I$ for all $I \in \mathbb{C}$ and $n \in \mathbb{N}$. We deduce from the Banach fixed point theorem that $J_\infty = \lim_{n \to \infty} \mathcal{T}^n 0$ belongs to $\mathbb{C}$ and is the only fixed point of $\mathcal{T}$.

□

Proposition 2.3.2. *There exists $\mu^* \in \mathcal{A}^{\mathcal{R}}$ such that $J_\infty = J_{\mu^*} = J'$.*

Proof. By definition, for every $\pi \in \Pi$, $J_n \leq J_{n\pi}$, so that $J_\infty \leq J^*$. Now from the previous proposition, $J_\infty = \inf_{\gamma \in \mathcal{R}} RJ_\infty(\cdot, \gamma)$, $\mathcal{R}$ is a compact space and RJ_∞ is a continuous function. We can thus find a measurable mapping $\mu^* : \Upsilon \to \mathcal{R}$ such that $J_\infty = \mathcal{T}_{\mu*} J_\infty$. $J_\infty \geq 0$ so from the first relation of the previous proposition, for all $n \in \mathbb{N}$, $J_\infty = \mathcal{T}^n_{\mu*} J_\infty \geq \mathcal{T}^n_{\mu*} 0$ and by taking the limit $J_\infty \geq J_{\mu^*}$. Since $J_{\mu^*} \geq J^*$ we get $J_\infty = J_{\mu^*} = J^*$. We conclude the proof by remarking that $J^* \leq J' \leq J_{\mu^*}$. □

The next section is devoted to proving that the assumptions of Theorem 2.3.3 are satisfied for the MDP.

Bounding functions and contracting MDP

The concept of bounding function that we define below will ensure that the operator $\mathcal{T}$ is a contraction. The existence of the space $\mathbb{C}$ of Theorem 2.3.3 will mostly result from Theorem 2.2.1 and again from the concept of bounding function.

Definition 2.3.4. *Bounding functions for a PDMP.*

Let c (resp. g) be a running (resp. terminal) cost as in Section 2.3.1. A measurable function $b : H \to \mathbb{R}_+^*$ is called a bounding function for the PDMP if there exist constants $c_c, c_g, c_\phi \in \mathbb{R}_+$ such that
(i) $c(v,u) \le c_c b(v)$ for all $(v,u) \in H \times Z$,
(ii) $g(v) \le c_g b(v)$ for all $v \in H$,
(iii) $b(\phi_t^\gamma(z)) \le c_\phi b(v)$ for all $(t,z,\gamma) \in [0,T] \times \Upsilon \times \mathcal{R}$, $z = (v,d,h)$.

Given a bounding function for the PDMP we can construct one for the MDP with or without relaxed controls, as shown in the next lemma (cf. [BR11b, Definition 7.1.2 p.195]).

Lemma 2.3.1. *Let b is a bounding function for the PDMP. We keep the notations of Definition 2.3.4. Let $\zeta > 0$. The function $B_\zeta : \Upsilon \longmapsto \mathbb{R}_+^*$ defined by $B_\zeta(z) := b(v)e^{\zeta(T-h)}$ for $z = (v,d,h)$ is an upper bounding function for the MDP. The two inequalities below are satisfied for all $(z,\gamma) \in \Upsilon \times \mathcal{R}$,*

$$c'(z,\gamma) \le B_\zeta(z) c_\phi \left(\frac{c_c}{\delta} + c_g\right), \tag{2.24}$$

$$\int_\Upsilon B_\zeta(y)\mathcal{Q}'(\mathrm{d}y|z,\gamma) \le B_\zeta(z)\, c_\phi\, \frac{M_\lambda}{(\zeta+\delta)}\ . \tag{2.25}$$

Proof. Take $(z,\gamma) \in \Upsilon \times \mathcal{R}$, $z = (v,d,h)$. On the one hand from (2.23) and Definition 2.3.4 we obtain

$$\begin{aligned} c'(z,\gamma) &\le \int_0^{T-h} e^{-\delta s} c_c c_\phi b(v)\mathrm{d}s + e^{-\delta(T-h)} c_g c_\phi b(v) \\ &\le B_\zeta(z) e^{-\zeta(T-h)} c_\phi \left(c_c \frac{1-e^{-\delta(T-h)}}{\delta} + e^{-\delta(T-h)} c_g \right), \end{aligned}$$

which immediately implies (2.24). On the other hand

$$\begin{aligned} \int_\Upsilon B_\zeta(y)\mathcal{Q}'(\mathrm{d}y|z,\gamma) &= \int_0^{T-h} \chi_s^\gamma(z) b(\phi_s^\gamma(z)) e^{\zeta(T-h-s)} \int_Z \lambda_d(\phi_s^\gamma(z),u)\mathcal{Q}(D|\phi_s^\gamma(z),u)\gamma_s(\mathrm{d}u)\mathrm{d}s \\ &\le e^{\zeta(T-h)} b(v) c_\phi M_\lambda \int_0^{T-h} e^{-\delta s} e^{-\zeta s}\mathrm{d}s \\ &= B_\zeta(z) c_\phi \frac{M_\lambda}{\zeta+\delta}\left(1 - e^{-(\zeta+\delta)(T-h)}\right) \end{aligned}$$

which implies (2.25).

□

Let b be a bounding function for the PDMP. Consider ζ^* such that $C := c_\phi \frac{M_\lambda}{\zeta^*+\delta} < 1$. Denote by B^* the associated bounding function for the MDP. We introduce the Banach space

$$\mathcal{L}^* := \{v : \Upsilon \to \mathbb{R} \text{ continuous }; \ ||v||_* := \sup_{z\in\Upsilon} \frac{|v(z)|}{|B^*(z)|} < \infty\}. \qquad (2.26)$$

The following two lemmas give an estimate on the expected cost of the MDP that justifies manipulations of infinite sums.

Lemma 2.3.2. *The inequality* $\mathbb{E}_z^\gamma \left[B^*(Z_k')\right] \leq C^k B^*(z)$ *holds for any* $(z, \gamma, k) \in \Upsilon \times \mathcal{R} \times \mathbb{N}$.

Proof. We proceed by induction on k. Let $z \in \Upsilon$. The desired inequality holds for $k = 0$ since $\mathbb{E}_z^\gamma \left[B^*(Z_0')\right] = B^*(z)$. Suppose now that it holds for $k \in \mathbb{N}$. Then

$$\begin{aligned} \mathbb{E}_z^\gamma \left[B^*(Z_{k+1}')\right] &= \mathbb{E}_z^\gamma \left[\mathbb{E}_z^\gamma \left[B^*(Z_{k+1}')|Z_k'\right]\right] \\ &= \mathbb{E}_z^\gamma \left[\int_\Upsilon B^*(y)\mathcal{Q}'(\mathrm{d}y|Z_k', \gamma)\right] \\ &= \mathbb{E}_z^\gamma \left[B^*(Z_k')\frac{\int_\Upsilon B^*(y)\mathcal{Q}'(\mathrm{d}y|Z_k', \gamma)}{B^*(Z_k')}\right]. \end{aligned}$$

Using (2.25) and the definition of C, we conclude that $\mathbb{E}_z^\gamma \left[B^*(Z_{k+1}')\right] \leq C\mathbb{E}_z^\gamma \left[B^*(Z_k')\right]$ and by the assumption on k $\mathbb{E}_z^\gamma \left[B^*(Z_{k+1}')\right] \leq C^{k+1}B^*(z)$. □

Lemma 2.3.3. *There exists* $\kappa > 0$ *such that for any* $(z, \mu) \in \Upsilon \times \mathcal{A}^{\mathcal{R}}$,

$$\mathbb{E}_z^\mu \left[\sum_{k=n}^\infty c'(Z_k', \mu(Z_k'))\right] \leq \kappa \frac{C^n}{1 - C} B^*(z).$$

Proof. The results follows from Lemma 2.3.2 and from the fact that

$$c'(Z_k', \mu(Z_k')) \leq B^*(Z_k)c_\phi \left(\frac{c_c}{\delta} + c_g\right)$$

for any $k \in \mathbb{N}$. □

We now state the result on the operator $\mathcal{T}$.

Lemma 2.3.4. $\mathcal{T}$ *is a contraction on* $\mathcal{L}^*$*: for any* $(v, w) \in \mathcal{L}^* \times \mathcal{L}^*$,

$$||\mathcal{T}v - \mathcal{T}w||_{B^*} \leq C\,||v - w||_{B^*},$$

where $C = c_\phi \frac{M_\lambda}{\zeta^* + \delta}$.

Proof. We prove here the contraction property. The fact $\mathcal{T} : \mathcal{L}^* \to \mathcal{L}^*$ is less straightforward and is addressed in the next section. Let $z := (v, d, h) \in \Upsilon$. Let us recall that for functions $f, g : \mathcal{R} \to \mathbb{R}$

$$\sup_{\gamma\in\mathcal{R}} f(\gamma) - \sup_{\gamma\in\mathcal{R}} g(\gamma) \leq \sup_{\gamma\in\mathcal{R}} \left(f(\gamma) - g(\gamma)\right).$$

Moreover since $\inf_{\gamma\in\mathcal{R}} f(\gamma) - \inf_{\gamma\in\mathcal{R}} g(\gamma) = \sup_{\gamma\in\mathcal{R}}(-g(\gamma)) - \sup_{\gamma\in\mathcal{R}}(-f(\gamma))$, we have

$$\mathcal{T}v\,(z) - \mathcal{T}w\,(z) \leq \sup_{\gamma\in\mathcal{R}} \int_0^{T-h} \chi_s^\gamma(z) \int_Z \lambda_d(\phi_s^\gamma(z), u)\mathcal{I}(u,s)\,\gamma(s)(\mathrm{d}u)\mathrm{d}s,$$

where

$$\mathcal{I}(u,s) := \int_D \Big(v(\phi_s^\gamma(z), r, h+s) - w(\phi_s^\gamma(z), r, h+s)\Big)\mathcal{Q}(\mathrm{d}r|\phi_s^\gamma(z), d, u),$$

so that

$$||\mathcal{T}v - \mathcal{T}w||_{B^*} \leq \sup_{(z,\gamma)\in\Upsilon\times\mathcal{R}} \int_0^{T-h} \chi_s^\gamma(z) \int_Z \lambda_d(\phi_s^\gamma(z), u)\mathcal{J}(s,u)\gamma(s)(\mathrm{d}u)\mathrm{d}s$$

where

$$\mathcal{J}(s,u) := \int_D \frac{B^*(\phi_s^\gamma(z), r, h+s)}{B^*(z)}||v-w||_{B^*}\,\mathcal{Q}(\mathrm{d}r|\phi_s^\gamma(z), d, u)$$

We then conclude that

$$\begin{aligned}
||\mathcal{T}v - \mathcal{T}w||_{B^*} &\leq \sup_{(z,\gamma)\in\Upsilon\times\mathcal{R}} \int_0^{T-h} e^{-\delta s} M_\lambda c_\phi e^{-\zeta^* s}\mathrm{d}s\,||v-w||_{B^*} \\
&\leq M_\lambda c_\phi\,||v-w||_{B^*} \int_0^{T-h} e^{-(\delta+\zeta^*)s}\mathrm{d}s \\
&\leq C||v-w||_{B^*}.
\end{aligned}$$

□

Continuity properties

Here we prove that the trajectories of the relaxed PDMP are continuous w.r.t. the control and that the operator R transforms continuous functions in continuous functions.

Lemma 2.3.5. *Assume that (H(L)) and (H(f)) are satisfied. Then the mapping*

$$\phi : (z,\gamma) \in \Upsilon\times\mathcal{R} \to \phi_\cdot^\gamma(z) = S(0)v + \int_0^\cdot \int_Z S(\cdot - s) f_d(\phi_s^\gamma(z), u)\gamma(s)(\mathrm{d}u)\mathrm{d}s$$

is continuous from $\Upsilon\times\mathcal{R}$ *in* $C([0,T];H)$.

Proof. This proof is based on the result of Theorem 2.2.1. Here we add the joint continuity on $\Upsilon\times\mathcal{R}$ whereas the continuity is just on $\mathcal{R}$ in [Pap89]. Let $t\in[0,T]$ and let $(z,\gamma)\in\Upsilon\times\mathcal{R}$. Assume that $(z_n,\gamma_n)\to(z,\gamma)$. Since D is a finite set, we take the discrete topology on it and if we denote by $z_n = (v_n, d_n, h_n)$ and $z = (v,d,h)$, we have the equality $d_n = d$ for n

large enough. So for n large enough we have

$$\begin{aligned}\phi_t^{\gamma_n}(z_n)-\phi_t^{\gamma}(z) &= S(t)v_n - S(t)v + \int_0^t\int_Z S(t-s)f_d(\phi_t^{\gamma_n}(z_n),u)\gamma_n(s)(\mathrm{d}u)\mathrm{d}s \\ &\quad - \int_0^t\int_Z S(t-s)f_d(\phi_t^{\gamma}(z),u)\gamma(s)(du)\mathrm{d}s \\ &= S(t)v_n - S(t)v \\ &\quad + \int_0^t\int_Z S(t-s)[f_d(\phi_t^{\gamma_n}(z_n),u)\gamma_n(s)(\mathrm{d}u) - f_d(\phi_t^{\gamma}(z),u)\gamma_n(s)(\mathrm{d}u)]\mathrm{d}s \\ &\quad + \int_0^t\int_Z S(t-s)[f_d(\phi_t^{\gamma}(z),u)\gamma_n(s)(\mathrm{d}u) - f_d(\phi_t^{\gamma}(z),u)\gamma(s)(\mathrm{d}u)]\mathrm{d}s.\end{aligned}$$

From(H(f))1. we get

$$||\phi_t^{\gamma_n}(z_n)-\phi_t^{\gamma}(z)||_H \le M_S||v_n-v||_H + M_S l_f\int_0^t ||\phi_s^{\gamma_n}(z_n)-\phi_s^{\gamma}(z)||_H\mathrm{d}s + ||\ell_n(t)||_H$$

where $\ell_n(t) := \int_0^t\int_Z S(t-s)[f_d(\phi_t^{\gamma}(z),u)\gamma_n(s)(\mathrm{d}u) - f_d(\phi_t^{\gamma}(z),u)\gamma(s)(\mathrm{d}u)]\mathrm{d}s$. By the Gronwall lemma we obtain a constant $C>0$ such that

$$||\phi_t^{\gamma_n}(z_n)-\phi_t^{\gamma}(z)||_H \le C(||v_n-v||_H + \sup_{s\in[0,T]}||\ell_n(s)||_H).$$

Since $\lim_{n\to+\infty}||v_n-v||_H = 0$, the proof is complete if we show that the sequence of functions $(||\ell_n||_H)$ uniformly converges to 0 on $[0,T]$.

Let us denote $x_n(t) := \int_0^t\int_Z S(t-s)f_d(\phi_t^{\gamma}(z),u))\gamma_n(s)(\mathrm{d}u)\mathrm{d}s$. Using the same argument as the proof of [Pap89, Theorem 3.1], there is no difficulty in proving that $(x_n)_{n\in\mathbb{N}}$ is compact in $C([0,T],H)$ so that, passing to a subsequence if necessary, we may assume that $x_n\to x$ in $C([0,T],H)$. Now let $h\in H$.

$$\begin{aligned}(h,\ell_n(t))_H &= \int_0^t\int_Z (h, S(t-s)f_d(\phi_t^{\gamma}(z),u)))_H\gamma_n(s)(\mathrm{d}u)\mathrm{d}s \\ &\quad - \int_0^t\int_Z (h, S(t-s)f_d(\phi_t^{\gamma}(z),u)))_H\gamma(s)(\mathrm{d}u)\mathrm{d}s \xrightarrow[n\to\infty]{} 0,\end{aligned}$$

since $(t,u)\to(h,S(t-s)f_d(\phi_t^{\gamma}(z),u)))_H\in L^1(C(Z))$ and $\gamma_n\to\gamma$ weakly* in $L^\infty(M(Z)) = [L^1(C(Z))]^*$. Thus, $x(t) = \int_0^t\int_Z S(t-s)f_d(\phi_t^{\gamma}(z),u)\gamma(s)(\mathrm{d}u)\mathrm{d}s$ $\mathcal{L}eb$-a.s. and by continuity, the equality is valid everywhere so that $\ell_n(t) = x_n(t)-x(t)$ for all $t\in[0,T]$, proving the uniform convergence of $||\ell_n||_H$ on $[0,T]$.

□

The next lemma establishes the continuity property of the operator R.

Lemma 2.3.6. *Suppose that assumptions (H(L)), (H(f)), (H(λ)), (H(Q)), (H(c)) are satisfied. Let b be a continuous bounding function for the PDMP. Let $w : \Upsilon \times U \to \mathbb{R}$ be continuous with $|w(z,u)| \leq c_w B^*(z)$ for some $c_w \geq 0$. Then*

$$(z,\gamma) \to \int_0^{T-h} \chi_s^\gamma(z) \left(\int_Z w(\phi_s^\gamma(z), d, h+s, u)\gamma(s)(\mathrm{d}u) \right) \mathrm{d}s$$

is continuous on $\Upsilon \times \mathcal{R}$, with $z := (v,d,h)$. Quite straightforwardly,

$$(z,\gamma) \to Rw(z,\gamma) = c'(z,\gamma) + Q'w\,(z,\gamma)$$

is continuous on $\Upsilon \times \mathcal{R}$.

Proof. See Appendix 2.C. □

It now remains to show that there exists a bounding function for the PDMP. This is the result of the next lemma.

Lemma 2.3.7. *Suppose assumptions (H(L)), (H(f)) and (H(c)) are satisfied. Now define $\tilde{c}$ and $\tilde{g}$ from c and g by taking the absolute value of the coefficients of these quadratic functions. Let $M_2 > 0$. Define $M_3 := (M_2 + b_1 T)M_S e^{M_S b_2 T}$ and $b : H \to \mathbb{R}_+$ by*

$$b(v) := \begin{cases} b_{M_3} := \max\limits_{||x||_H \leq M_3} \max\limits_{u \in U} \tilde{c}(x,u) + \max\limits_{||x||_H \leq M_3} \tilde{g}(x), & \text{if } ||v||_H \leq M_3, \\ \max\limits_{u \in U} \tilde{c}(v,u) + \tilde{g}(v), & \text{if } ||v||_H > M_3, \end{cases} \tag{2.27}$$

is a continuous bounding function for the PDMP.

Proof. For all $(v,u) \in H \times U$, $c(v,u) \leq b(v)$ and $g(v) \leq b(v)$. Now let $(t,z,\gamma) \in [0,T] \times \Upsilon \times \mathcal{R}$, $z = (v,d,h)$.

— If $||\phi_t^\gamma(z)||_H \leq M_3$, $b(\phi_t^\gamma(z)) = b_{M_3}$. If $||v||_H \leq M_3$ then $b(v) = b_{M_3} = b(\phi_t^\gamma(z))$. Otherwise, $||v||_H > M_3$ and $b(v) > b_{M_3} = b(\phi_t^\gamma(z))$.

— If $||\phi_t^\gamma(z)||_H > M_3$ then $||v||_H > M_2$ and $||\phi_t^\gamma(z)||_H \leq ||v||_H M_3/M_2$ (See 2.40 in Appendix 2.B). So,

$$b(\phi_t^\gamma(z))) = \max_{u \in U} \tilde{c}(\phi_t^\gamma(z),u) + \tilde{g}(\phi_t^\gamma(z)) \leq b\left(\frac{M_3}{M_2} v\right) \leq \frac{M_3^2}{M_2^2} b(v),$$

since $M_3/M_2 > 1$.

□

Remark 2.3.4. *Lemma 2.3.7 ensures the existence of a bounding function for the PDMP. To broaden the class of cost functions considered, we could just assume the existence of a bounding for the PDMP in Theorem 2.3.1 and then, the assumption on c and g should just be the continuity.*

2.3.3 Existence of an optimal ordinary strategy

Ordinary strategies are of crucial importance because they are the ones that the controller can implement in practice. Here we give convexity assumptions that ensure the existence of an ordinary optimal control strategy for the PDMP.

(A) (a) For all $d \in D$, the function $f_d : (y,u) \in H \times U \to E$ is linear in the control variable u.

(b) For all $d \in D$, the functions $\lambda_d : (y,u) \in H \times U \to \mathbb{R}_+$ and $\lambda_d \mathcal{Q} : (y,u) \in H \times U \to \lambda_d(y,u)\mathcal{Q}(\cdot|y,d,u)$ are respectively concave and convexe in the control variable u.

(c) The cost function $c : (y,u) \in E \times U \to \mathbb{R}_+$ is convex in the control variable u.

Theorem 2.3.4. *Suppose that assumptions (H(L)), (H(f)), (H(λ)), (H(Q)), (H(c)) and (A) are satisfied. If we consider* $\mu^* \in \mathcal{A}^{\mathcal{R}}$ *an optimal relaxed strategy for the PDMP, then the ordinary strategy* $\bar{\mu}_t := \int_Z u\mu_t^*(du) \in \mathcal{A}$ *is optimal, i.e.* $V_{\bar{\mu}}(z) = \tilde{V}_{\mu^*}(z) = V(z), \quad \forall z \in \Upsilon$.

Proof. This result is based on the fact that for all $(z,\gamma) \in \Upsilon \times \mathcal{R}$, $(Lw)(z,\gamma) \geq (Lw)(z,\bar{\gamma})$, with $\bar{\gamma} = \int_Z u\gamma(\mathrm{d}u)$. Indeed, the fact that the function f_d is linear in the control variable implies that for all $(t,z,\gamma) \in [0,T] \times \Upsilon \times \mathcal{R}$, $\phi_t^\gamma(z) = \phi_t^{\bar{\gamma}}(z)$. The convexity assumptions (A) give the following inequalities

$$\int_Z \lambda_d(\phi_s^\gamma(z),u)\gamma(s)(\mathrm{d}u) \leq \lambda_d(\phi_s^{\bar{\gamma}}(z),\bar{\gamma}(s)),$$

$$\int_Z \lambda_d(\phi_s^\gamma(z),u)\mathcal{Q}(E|\phi_s^\gamma(z),d,u)\gamma(s)(\mathrm{d}u) \geq \lambda_d(\phi_s^{\bar{\gamma}}(z),\bar{\gamma}(s))\mathcal{Q}(E|\phi_s^{\bar{\gamma}}(z),d,\bar{\gamma}(s)),$$

$$\int_Z c(\phi_s^\gamma(z),u)\gamma_s(\mathrm{d}u) \geq c(\phi_s^{\bar{\gamma}}(z),\bar{\gamma}_s),$$

for all $(s,z,\gamma,E) \in [0,T] \times \Upsilon \times \mathcal{R} \times \mathcal{B}(D)$, so that in particular $\chi_t^\gamma(z) \geq \chi_t^{\bar{\gamma}}(z)$. We can now denote for all $(z,\gamma) \in \Upsilon \times \mathcal{R}$ and $w : \Upsilon \to \mathbb{R}_+$,

$$\begin{aligned}
(Lw)(z,\gamma) = &\int_0^{T-h} \chi_s^\gamma(z) \int_Z c(\phi_s^\gamma(z),u)\gamma(s)(\mathrm{d}u)\mathrm{d}s + \chi_{T-h}^\gamma(z) g(\phi_{T-h}^\gamma(z)) \\
&+ \int_0^{T-h} \chi_s^\gamma(z) \int_Z \lambda_d(\phi_s^\gamma(z),u) \int_D w(\phi_s^\gamma(z),r,h+s)\mathcal{Q}(\mathrm{d}r|\phi_s^\gamma(z),d,u)\gamma(s)(\mathrm{d}u)\mathrm{d}s \\
\geq &\int_0^{T-h} \chi_s^{\bar{\gamma}}(z) c(\phi_s^{\bar{\gamma}}(z),\bar{\gamma}(s))\mathrm{d}s + \chi_{T-h}^{\bar{\gamma}}(z) g(\phi_{T-h}^{\bar{\gamma}}(z)) \\
&+ \int_0^{T-h} \chi_s^{\bar{\gamma}}(z) \int_Z \lambda_d(\phi_s^{\bar{\gamma}}(z),u) \int_D w(\phi_s^{\bar{\gamma}}(z),r,h+s)\mathcal{Q}(\mathrm{d}r|\phi_s^{\bar{\gamma}}(z),d,u)\gamma(s)(\mathrm{d}u)\mathrm{d}s.
\end{aligned}$$

Furthermore,

$$\int_Z \lambda_d(\phi_s^{\bar{\gamma}}(z), u) \int_D w(\phi_s^{\bar{\gamma}}(z), r, h+s)\mathcal{Q}(\mathrm{d}r|\phi_s^{\bar{\gamma}}(z), d, u)\gamma(s)(\mathrm{d}u) \geq \\ \lambda_d(\phi_s^{\bar{\gamma}}(z), \bar{\gamma}(s)) \int_D w(\phi_s^{\bar{\gamma}}(z), r, h+s)\mathcal{Q}(\mathrm{d}r|\phi_s^{\bar{\gamma}}(z), d, \bar{\gamma}(s)),$$

so that

$$\begin{aligned}(Lw)(z,\gamma) \geq &\int_0^{T-h} \chi_s^{\bar{\gamma}}(z) c(\phi_s^{\bar{\gamma}}(z), \bar{\gamma}(s))\mathrm{d}s + \chi_{T-h}^{\bar{\gamma}}(z) g(\phi_{T-h}^{\bar{\gamma}}(z)) \\ &+ \int_0^{T-h} \chi_s^{\bar{\gamma}}(z)\lambda_d(\phi_s^{\bar{\gamma}}(z), \bar{\gamma}(s)) \int_D w(\phi_s^{\bar{\gamma}}(z), r, h+s)\mathcal{Q}(\mathrm{d}r|\phi_s^{\bar{\gamma}}(z), d, \bar{\gamma}(s)) \\ &= (Lw)(z, \bar{\gamma}).\end{aligned}$$

□

2.3.4 An elementary example

Here we treat an elementary example that satisfies the assumptions made in the previous two sections.

Let $V = H_0^1([0,1])$,$H = L^2([0,1])$, $D = \{-1, 1\}$, $U = [-1, 1]$. V is a Hilbert space with inner product

$$(v, w)_V := \int_0^1 v(x)w(x) + v'(x)w'(x)\mathrm{d}x.$$

We consider the following PDE for the deterministic evolution between jumps

$$\frac{\partial}{\partial t} v(t,x) = \Delta v(t,x) + (d+u)v(t,x),$$

with Dirichlet boundary conditions. We define the jump rate function for $(v, u) \in H \times U$ by

$$\lambda_1(v,u) = \frac{1}{e^{-||v||^2}+1} + u^2, \qquad \lambda_{-1}(v,u) = e^{-\frac{1}{||v||^2+1}} + u^2,$$

and the transition measure by $\mathcal{Q}(\{-1\}|v, 1, u) = 1$, and $\mathcal{Q}(\{1\}|v, -1, u) = 1$.

Finally, we consider a quadratic cost function $c(v, u) = K||V_{\mathrm{ref}} - v||^2 + u^2$, where $V_{\mathrm{ref}} \in D(\Delta)$ is a reference signal that we want to approach.

Lemma 2.3.8. *The PDMP defined above admits the continuous bounding function*

$$b(v) := ||V_{\mathrm{ref}}||_H^2 + ||v||_H^2 + 1. \tag{2.28}$$

Furthermore, the value function of the optimal control problem is continuous and there exists an optimal ordinary control strategy.

Proof. The proof consists in verifying that all assumptions of Theorem 2.3.4 are satisfied. Assumptions (H($\mathcal{Q}$)), (H(c)) and (A) are straightforward. For $(v,u) \in H \times U$, $1/2 \leq \lambda_1(v,u) \leq 2$ and $e^{-1} \leq \lambda_{-1}(v,u) \leq 2$. The continuity in the variable u is straightforward and the locally Lipschitz continuity comes from the fact that the functions $v \to 1/(e^{-||v||^2}+1)$, and $v \to e^{-\beta(v)}$, with $\beta(v) := 1/(||v||^2+1)$, are Fréchet differentiable with derivatives $v \to 2(v,\cdot)_H/(e^{-||v||^2}+1)^2$, and $v \to 2(v,\cdot)_H\beta^2(v)e^{-\beta(v)}$.
$-\Delta v : w \in V \to \int_0^1 v'(x)w'(x)\mathrm{d}x$ so that $-\Delta : V \to V^*$ is linear. Let $(v,w) \in V^2$.

$$\langle -\Delta(v-w), v-w\rangle = \int_0^1 ((v-w)'(x))^2\mathrm{d}x \geq 0.$$

$$|\langle -\Delta v, w\rangle|^2 = |\int_0^1 v'(x)w'(x)\mathrm{d}x|^2 \leq \int_0^1 (v'(x))^2\mathrm{d}x \int_0^1 (w'(x))^2\mathrm{d}x \leq ||v||_V^2||w||_V^2,$$

and so $||-\Delta v||_{V^*} \leq ||v||_V$. $\langle -\Delta v, v\rangle = \int_0^1 (v'(x))^2\mathrm{d}x \geq C'||v||_V^2$, for some constant $C' > 0$, by the Poincaré inequality.

Now, define for $k \in \mathbb{N}^*$, $f_k(\cdot) := \sqrt{2}\sin(k\pi\cdot)$, a Hilbert base of H. On H, $S(t)$ is the diagonal operator

$$S(t)v = \sum_{k\geq 1} e^{-(k\pi)^2t}(v,f_k)_H f_k.$$

For $t > 0$, $S(t)$ is a contracting Hilbert-Schmidt operator.
For $(v,w,u) \in H^2 \times U$, $f_d(v,u) = (d+u)v$ and

$$||f_d(v,u) - f_d(w,u)||_H \leq 2||v-w||_H, \qquad ||f_d(v,u)||_H \leq 2||v||_H.$$

This means that for every $z = (v,d,h) \in \Upsilon$, $\gamma \in \mathcal{R}([0,T],U)$ and $t \in [0,T]$, $||\phi_t^\gamma(z)||_H \leq e^{2T}||v||_H$.

□

2.4 Application to the model in Optogenetics

2.4.1 Proof Theorem 2.0.1

We begin this section by making some comments on Definition 2.0.1. In (2.1), $C_m > 0$ is the membrane capacitance and V_- and V_+ are constants defined by $V_- := \min\{V_{Na}, V_K, V_L, V_{ChR2}\}$ and $V_+ := \max\{V_{Na}, V_K, V_L, V_{ChR2}\}$. They represent the physiological domain of our process. In (2.2), the constants $g_x > 0$ are the normalized conductances of the channels of type x and $V_x \in \mathbb{R}$ are the driving potentials of the channels. The constant $\rho > 0$ is the relative conductance between the open states of the $ChR2$. For a matter of coherence with the theoretical framework presented in the paper, we will prove Theorem 2.0.1 for the mollification of the model that we define now. This model is very close to the one of Definition 2.0.1. It is obtained by replacing the Dirac masses δ_z by their mollifications ξ_z^N that are defined as follows. Let φ be the function defined on $\mathbb{R}$ by

$$\varphi(x) := \begin{cases} Ce^{\frac{1}{x^2-1}}, & \text{if } |x| < 1, \\ 0, & \text{if } |x| \geq 1, \end{cases} \tag{2.29}$$

with $C := \left(\int_{-1}^{1} \exp\left(\frac{1}{x^2-1}\right) \mathrm{d}x\right)^{-1}$ such that $\int_{\mathbb{R}} \varphi(x)\mathrm{d}x = 1$.

Now, let $U_N := \left(\frac{1}{2N}, 1 - \frac{1}{2N}\right)$ and $\varphi_N(x) := 2N\varphi(2Nx)$ for $x \in \mathbb{R}$. For $z \in I_N$, the N^{th} mollified Dirac mass ξ_z^N at z is defined for $x \in [0,1]$ by

$$\xi_z^N(x) := \begin{cases} \varphi_N(x-z), & \text{if } x \in U_N \\ 0, & \text{if } x \in [0,1] \setminus U_N. \end{cases} \tag{2.30}$$

For all $z \in I_N, \xi_z^N \in C^\infty([0,1])$ and $\xi_z^N \to \delta_z$ almost everywhere in $[0,1]$ as $N \to +\infty$, so that $(\xi_z^N, \phi)_H \to \phi(z)$, as $N \to \infty$ for every $\phi \in C(I, \mathbb{R})$. The expressions $v(i/N)$ in Definition 2.0.1 are also replaced by $(\xi_{i/N}^N, v)_H$. The decision to use the mollified Dirac mass over the Dirac mass can be motivated by two main reasons. First of all, as mentioned in [BR11a], the concentration of ions is homogeneous in a spatially extended domain around an open channel so the current is modeled as being present not only at the point of a channel, but in a neighborhood of it. Second, the smooth mollified Dirac mass leads to smooth solutions of the PDE and we need at least continuity of the flow. Nevertheless, the results of Theorem 2.0.1 remain valid with the Dirac masses and we refer the reader to Section 2.4.2.

The following lemma is a direct consequence of [BR11a, Proposition 7] and will be very important for the model to fall within the theoretical framework of the previous sections.

Lemma 2.4.1. *For every $y_0 \in V$ with $y_0(x) \in [V_-, V_+]$ for all $x \in I$, the solution y of (2.1) is such that for $t \in [0,T]$,*

$$V_- \leq y(t,x) \leq V_+, \quad \forall x \in I.$$

Physiologically speaking, we are only interested in the domain $[V_-, V_+]$. Since Lemma 2.4.1 shows that this domain is invariant for the controlled PDMP, we can modify the characteristics of the PDMP outside the domain $[V_-, V_+]$ without changing its dynamics. We will do so for the rate functions $\sigma_{x,y}$ of Table 2.1. From now on, consider a compact set K containing the closed ball of H, centered in zero and with radius $\max(V_-, V_+)$. We will rewrite $\sigma_{x,y}$ the quantities modified outside K such that they all become bounded functions. This modification will enable assumption (H(λ))1. to be verified.

The next lemma shows that the stochastic controlled infinite-dimensional Hodgkin-Huxley-ChR2 model defines a controlled infinite-dimensional PDMP as defined in Definition 2.1.2 and that Theorem 2.1.2 applies.

Lemma 2.4.2. *For $N \in N^*$, the N^{th} stochastic controlled infinite-dimensional Hodgkin-Huxley-ChR2 model satisfies assumptions (H(λ)), (H($\mathcal{Q}$)), (H(L)) and (H(f)). Moreover, for any control strategy $\alpha \in \mathcal{A}$, the membrane potential v^α satisfies*

$$V_- \leq v_t^\alpha(x) \leq V_+, \quad \forall (t,x) \in [0,T] \times I.$$

Proof. The local Lipschitz continuity of λ_d from $H \times Z$ in $\mathbb{R}^+$ comes from the local Lipschitz continuity of all the functions $\sigma_{x,y}$ of Table 2.1.2 and the inequality $|(\xi_z^N, v)_H - (\xi_z^N, w)_H| \leq 2N||v-w||_H$. By Lemma 2.4.1, the modified jump rates are bounded. Since they are positive, they are bounded away from zero, and then, Assumption (H(λ)) is satisfied. Assumption (H($\mathcal{Q}$)) is also easily satisfied. We showed in Section 2.3.4 that (H(L)) is satisfied. As for f_d, the function does not depend on the control variable and is continuous from H to H. For $d \in D$ and $(y_1, y_2) \in H^2$,

$$f_d(y_1) - f_d(y_2) = \frac{1}{N} \sum_{i \in I_N} \Big(g_K \mathbf{1}_{\{d_i = n_4\}} + g_{Na} \mathbf{1}_{\{d_i = m_3 h_1\}} + g_{ChR2}(\mathbf{1}_{\{d_i = O_1\}} + \rho \mathbf{1}_{\{d_i = O_2\}}) + g_L \Big) (\xi^N_{\frac{i}{N}}, y_2 - y_1)_H \xi^N_{\frac{i}{N}}.$$

We then get

$$||f_d(y_1) - f_d(y_2)||_H \leq 4N^2 (g_K + g_{Na} + g_{ChR2}(1+\rho) + g_L) ||(y_2 - y_1)||_H.$$

Finally, since the continuous component v_t^α of the PDMP does not jump, the bounds are a direct consequence of Lemma 2.4.1.

□

Proof of Theorem 2.0.1. In Lemma 2.4.2 we already showed that assumptions (H(λ)), (H($\mathcal{Q}$)), (H(L)) and (H(f)) are satisfied. The cost function c is convex in the control variable and norm quadratic on $H \times Z$. The flow does not depend on the control. The rate function λ is linear in the control. the function $\lambda \mathcal{Q}$ is also linear in the control. We conclude that all the assumptions of Theorem 2.3.1 are satisfied and that an optimal ordinary strategy can be retrieved.

□

We end this section with an important remark that significantly extends the scope of this example. Up to now, we only considered stationary reference signals but nonautonomous ones can be studied as well, as long as they feature some properties. Indeed, it is only a matter of incorporating the signal reference $V_{\text{ref}} \in C([0,T],H)$ in the process by adding a variable to the PDMP. Instead of considering H as the initial state space for the continuous component, we consider $\tilde{H} := H \times H$.

This way, the part on the control problem is not impacted at all and we consider the continuous cost function $\tilde{c}$ defined for $(v,\bar{v},u) \in \tilde{H} \times U$ by

$$\tilde{c}(v,\bar{v},u) = \kappa||v-\bar{v}||_H^2 + u + c_{\min}, \tag{2.31}$$

the result and proof of lemma 2.0.1 remaining unchanged with the continuous bounding function defined for $v \in H$ by

$$b(v) := \begin{cases} \kappa M_3^2 + \kappa \sup\limits_{t\in[0,T]} ||V_{ref}(t)||_H^2 + u_{max}, & \text{if } ||v||_H \leq M_3, \\ \kappa||v||_H^2 + \kappa \sup\limits_{t\in[0,T]} ||V_{ref}(t)||_H^2 + u_{max}, & \text{if } ||v||_H > M_3. \end{cases}$$

In the next section, we present some variants of the model and the corresponding results in terms of optimal control.

Table 2.1 – Expression of the individual jump rate functions.

In $D_1 = \{n_0,n_1,n_2,n_3,n_4\}$:

$\sigma_{n_0,n_1}(v,u) = 4\alpha_n(v)$, $\sigma_{n_1,n_2}(v,u) = 3\alpha_n(v)$, $\sigma_{n_2,n_3}(v,u) = 2\alpha_n(v)$, $\sigma_{n_3,n_4}(v,u) = \alpha_n(v)$
$\sigma_{n_4,n_3}(v,u) = 4\beta_n(v)$, $\sigma_{n_3,n_2}(v,u) = 3\beta_n(v)$, $\sigma_{n_2,n_1}(v,u) = 2\beta_n(v)$, $\sigma_{n_1,n_0}(v,u) = \beta_n(v)$.

In $D_2 = \{m_0h_1,m_1h_1,m_2h_1,m_3h_1,m_0h_0,m_1h_0,m_2h_0,m_3h_0\}$:

$\sigma_{m_0h_1,m_1h_1}(v,u) = \sigma_{m_0h_0,m_1h_0}(v,u) = 3\alpha_m(v)$, $\sigma_{m_1h_1,m_2h_1}(v,u) = \sigma_{m_1h_0,m_2h_0}(v,u) = 2\alpha_m(v)$,
$\sigma_{m_2h_1,m_3h_1}(v,u) = \sigma_{m_2h_0,m_3h_0}(v,u) = \alpha_m(v)$, $\sigma_{m_3h_1,m_2h_1}(v,u) = \sigma_{m_3h_0,m_2h_0}(v,u) = 3\beta_m(v)$,
$\sigma_{m_2h_1,m_1h_1}(v,u) = \sigma_{m_2h_0,m_1h_0}(v,u) = 2\beta_m(v)$, $\sigma_{m_1h_1,m_0h_1}(v,u) = \sigma_{m_1h_0,m_0h_0}(v,u) = \beta_m(v)$.

In $D_{ChR2} = \{o_1,o_2,c_1,c_2\}$:

$\sigma_{c_1,o_1}(v,u) = \varepsilon_1 u$, $\sigma_{o_1,c_1}(v,u) = K_{d1}$, $\sigma_{o_1,o_2}(v,u) = e_{12}$, $\sigma_{o_2,o_1}(v,u) = e_{21}$
$\sigma_{o_2,c_2}(v,u) = K_{d2}$, $\sigma_{c_2,o_2}(v,u) = \varepsilon_2 u$, $\sigma_{c_2,c_1}(v,u) = K_r$.

$\alpha_n(v) = \frac{0.1-0.01v}{e^{1-0.1v}-1}$, $\beta_n(v) = 0.125e^{-\frac{v}{80}}$,

$\alpha_m(v) = \frac{2.5-0.1v}{e^{2.5-0.1v}-1}$, $\beta_m(v) = 4e^{-\frac{v}{18}}$,

$\alpha_h(v) = 0.07e^{-\frac{v}{20}}$, $\beta_h(v) = \frac{1}{e^{3-0.1v}+1}$.

2.4.2 Variants of the model

We begin this section by giving arguments showing that the results of Theorem 2.3.1 remain valid for the model of Definition 2.0.1, which does not exactly fits into our theoretical framework. Then, the variations we present concern the model of ChR2, the addition of other light-sensitive ionic channels, the way the control acts on the three local characteristics and the control space. The optimal control problem itself will remain unchanged. First of all, let us mention that since the model of Definition 2.0.1 satisfies the convexity conditions (A), the theoretical part on relaxed controls is not necessary for this model. Nevertheless, the model of ChR2 presented on Figure 2.1 is only one among several others, some of which do not enjoy a linear, or even concave, rate function λ. For those models, that we present next, assumption (A) fails and the relaxed controls are essential.

We will not present them here, but the previous results for the Hodgkin-Huxley model remain straightforwardly unchanged for other neuron models such as the FitzHugh-Nagumo model or the Morris-Lecar model.

Optimal control for the original model

In the original model, the function f_d is defined from V to V^*. Nevertheless, the semigroup of the Laplacian regularizes Dirac masses (see [Aus08, Lemma 3.1]) and the uniform bound in Theorem 2.1.2 is in fact valid in V, the solution belonging to $C([0,T],V)$. This is all we need since the control does not act on the PDE. This is why the domain of our process is $V \times D_N$ and not just $H \times D_N$, and all computations of the proofs of the previous sections can be done in the Hilbert space V. From this consideration, and using the continuous embedding of $H_0^1(I)$ in $C_0(I)$ we can justify the local Lipschitz continuity of λ_d from $V \times Z$ in $\mathbb{R}^+$. Indeed, it comes from the local Lipschitz continuity of all functions $\sigma_{x,y}$ of Table 2.1 and from the inequality

$$|v(\frac{i}{N}) - w(\frac{i}{N})| \leq \sup_{x\in I} |v(x) - w(x)| \leq C||v - w||_V.$$

Finally, [BR11a, Proposition 5] states that the bounds of Lemma 2.4.2 remain valid with Dirac masses.

Modifications of the ChR2 model

We already mentioned the paper of Nikolic and al. [NGG$^+$09] in which a three states model is presented. It is a somehow simpler model than the four states model of Figure 2.1 but it gives good qualitative results on the photocurrents produced by the ChR2. In first approximation the model can be considered to depend linearly in the control as seen on Figure 2.1.

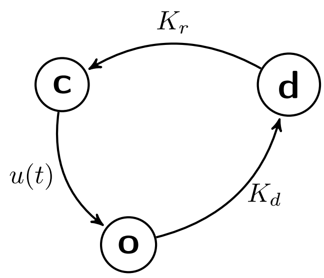


Figure 2.1 – Simplified ChR2 three states model

This model features one open state o and two closed states, one light-adapted d and one dark-adapted c. This model would lead to the same type of model as in the previous Section. In fact, the time constants $1/K_d$ and $1/K_r$ are also light dependent with a dependence in $\log(u)$. The corresponding model is represented on Figure 2.2 below

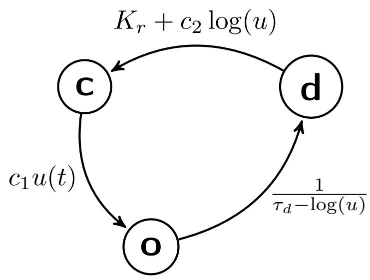


Figure 2.2 – ChR2 three states model

Some mathematical comments are needed here. On Figure 2.2, the control u represents the light intensity and c_1, c_2, K_r and τ_d are positive constants. This model of ChR2 is experimentally accurate for intensities between 10^8 and 10^{10} $\mu\text{m}^2 \cdot \text{s}^{-1}$ approximately. We would then consider $U := [0, u_{max}]$ with $u_{max} \simeq 10^{10}$ $\mu\text{m}^2 \cdot \text{s}^{-1}$. Furthermore,

$$\lim_{u \to 0} K_r + c_2 \log(u) = -\infty, \qquad \lim_{u \to 0} \frac{1}{\tau_d - \log(u)} = 0.$$

The first limit is not physical since rate jumps between states are positive numbers. The second limit is not physical either because it would mean that, in the dark, the proteins are trapped in the open state o, which is not the case. In the dark, when $u = 0$, the jump rates corresponding to the transition $o \to d$ and $d \to c$ are positive constants. For this reason, the functions $\sigma_{o,d}$ and $\sigma_{d,c}$ should be smooth functions such that they are equal to the rates of Figure 2.2 for large intensities, but still with $\tau_d - \log(u) > 0$, and converge to $K_d^{\text{dark}} > 0$ and $K_r^{\text{dark}} > 0$ respectively, when u goes to 0. The resulting rate function λ is not concave and thus does not satisfy assumption (A) anymore. We can only affirm the existence of optimal relaxed strategies.

The four states model of Figure 2.1 is also an approximation of a more accurate model that we represent on Figure 2.3 below. The transition rates can depend on either the

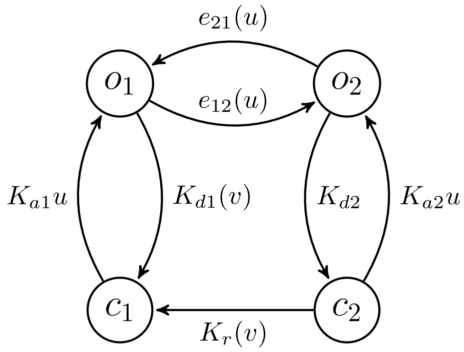


Figure 2.3 – ChR2 channel : K_{a1}, K_{a2}, and K_{d2} are positive constants.

membrane potential v or the irradiance u, which is the control variable. The details of the model and the numerical constants can be found in [WXK+13]. Note that the model of Figure 2.3 is already an approximation of the model in [WXK+13] because the full model in [WXK+13] would not lead to a Markovian behavior for the ChR2 (the transition rates would depend on the time elapsed since the light was switched on).

$$
\begin{aligned}
K_{d1}(v) &= K_{d1}^{(1)} - K_{d1}^{(2)} \tanh((v+20)/20), \\
e_{12}(u) &= e_{12d} + c_1 \ln(1+u/c), \\
e_{21}(u) &= e_{21d} + c_2 \ln(1+u/c), \\
K_r(v) &= K_r^{(1)} \exp(-K_r^{(2)} v),
\end{aligned}
$$

with $K_{d1}^{(1)}$, $K_{d1}^{(2)}$, e_{12d}, e_{21d}, c, c_1 and c_2 positive constants. As for the model of Figure 2.2, the mathematical definition of the function σ_{o_1,c_1} should be such that it is a positive smooth function and equals $K_{d1}(v)$ in some subset of the physiological domain $[V_-, V_+]$. The resulting rate function λ will be concave but the function $\lambda\mathcal{Q}$ will not be convex (it will be concave as well). Hence, Assumption (A) is not satisfied.

Addition of other light-sensitive ion channels

Channelrhodopsin-2 has a promoting role in eliciting action potentials. There also exists a chlorine pump, called Halorhodopsin (NpHR), that has an inhibitory action. NpHR can be used along with ChR2 to obtain a control in both directions. Its modelisation as a multistate model was considered in [NJGS13]. The transition rates between the different states have the same shape that the ones of the ChR2 and the same simplifications are possible. This new light-sensitive channel can be easily incorporated in our stochastic model and we can state existence of optimal relaxed and/or ordinary control strategies depending on the level of complexity of the NpHR model we consider. It is here important to remark that since the two ionic channels do not react to the same wavelength of the light, the resulting control variable would be two-dimensional with values in $[0, u_{max}]^2$. This would not change the qualitative results of the previous sections.

Modification of the way the control acts on the local characteristics

Up to now, the control acts only on the rate function, and also on the measure transition via its special definition from the rate function. Nevertheless, we can present here a modification of the model where the control acts linearly on the PDE. This modification amounts to considering that the control variable is directly the gating variable of the ChR2. Indeed, we showed in Section 1.2.2 that the optimal control of the deterministic counterpart of the stochastic Hodgkin-Huxley-ChR2 model, in finite dimension and with the three states ChR2 model of Figure 2.1, is closely linked to the optimal control of

$$\begin{cases} \dfrac{\mathrm{d}V}{\mathrm{d}t} = g_K n^4(t)(V_K - V(t)) + g_{Na} m^3(t)h(t)(V_{Na} - V(t)) \\ \qquad\qquad + g_{ChR2} u(t)(V_{ChR2} - V(t)) + g_L(V_L - V(t)), \\ \dfrac{\mathrm{d}n}{\mathrm{d}t} = \alpha_n(V(t))(1 - n(t)) - \beta_n(V(t))n(t), \\ \dfrac{\mathrm{d}m}{\mathrm{d}t} = \alpha_m(V(t))(1 - m(t)) - \beta_m(V(t))m(t), \\ \dfrac{\mathrm{d}h}{\mathrm{d}t} = \alpha_h(V(t))(1 - h(t)) - \beta_h(V(t))h(t), \end{cases}$$

where the control variable is the former gating variable o. Now the stochastic counterpart of the last model is such that the function f_d is now linear in the control and the rate function λ and the transition measure function $\mathcal{Q}$ do not depend on the control any more. Finally, by adding NpHR channels to this model, we would obtain a fully controlled infinite-dimensional PDMP in the sense that the control would then act on the three local characteristics of the PDMP. Depending on the model of NpHR chosen, we would obtain relaxed or ordinary optimal control strategy.

Modification of the control space

In all models discussed previously, the control has no spatial dependence. Any light-stimulation device, such as a laser, has a spatial resolution and it is possible that we do not want or cannot stimulate the entire axon. For this reason, spatial dependence of the control should be considered. Now, as long as the control space remains a compact Polish space, spatial dependence of the control could be considered. We propose here a control space defined as a subspace of the Skorohod space $\mathbb{D}$, constituted of the *càdlàg* functions from $[0, 1]$ to $\mathbb{R}$. This control space represents the aggregation of multiple laser beams that can be switch on and off. Suppose that each of theses beams produce on the axon a disc of light of diameter $r > 0$ that we call spatial resolution of the light. For an axon represented by the segment $[0, 1]$, r is exactly the spatial domain illuminated. We consider now two possibilities for the control space. Suppose first that the spatial resolution is fixed and define $p := \lfloor \frac{1}{r} \rfloor$ and

$$\mathcal{U} := \{u : [0,1] \to [0, u_{max}] \mid u \text{ is constant on } [i/p, (i+1)/p), i = 0, .., p-1, u(1) = u((p-1)/p)\}.$$

Lemma 2.4.3. *$\mathcal{U}$ is a compact subset of $\mathbb{D}$.*

Proof. We tackle this proof by remarking that $\mathcal{U}$ is in bijection with the finite dimensional compact space $[0, u_{max}]^p$. □

In this case, the introduction of the space $\mathbb{D}$ was quite artificial since the control space remains finite-dimensional. Nevertheless, the Skorohod space will be very useful for the other control space. Suppose now that the spatial resolution of the laser can evolve in $[r_{min}, r_{max}]$ with $r_{min}, r_{max} > 0$. Let $p \in \mathbb{N}^*$ the number of lasers used and define

$$\begin{aligned}\tilde{\mathcal{U}} := \{u : [0,1] \to [0, u_{max}] \mid \exists \{x_i\}_{0 \le i \le p} & \text{ subdivision of } [0,1], \\ & u \text{ is constant on } [x_i, x_i + 1), i = 0, .., p-1, \\ & u(1) = u(x_{p-1})\}.\end{aligned}$$

Now $\tilde{\mathcal{U}}$ is infinite-dimensional and the Skorohod space allows us to use the characterization of compact subsets of $\mathbb{D}$.

Lemma 2.4.4. *$\tilde{\mathcal{U}}$ is a compact subset of $\mathbb{D}$.*

Proof. For this proof, we need to introduce some notation and a critera of compactness in $\mathbb{D}$. A complete treatment of the space $\mathbb{D}$ can be found in [Bil68].

Let $u \in \mathbb{D}$ and $\{x_i\}_{0 \le i \le n}$ a subdivision of $[0, 1]$, $n \in \mathbb{N}^*$. We define, for $i \in \{0, .., n-1\}$,

$$w_u([x_i, x_{i+1})) := \sup_{x,y \in [x_i, x_{i+1})} |u(x) - u(y)|,$$

and for $\delta > 0$,

$$w'_u(\delta) := \inf_{\{x_i\}} \max_{0 \le i < n} w_u([x_i, x_{i+1})),$$

the infimum being taken on all the subdivisions $\{x_i\}_{0 \le i \le n}$ of $[0, 1]$ such that $x_{i+1} - x_i > \delta$ for all $i \in \{0, .., n-1\}$. Now since $\tilde{\mathcal{U}}$ is obviously bounded in $\mathbb{D}$, from [Bil68, Theorem 14.3], we need to show that

$$\lim_{\delta \to 0} \sup_{u \in \tilde{\mathcal{U}}} w'_u(\delta) = 0.$$

Let $\delta > 0$ with $\delta < r_{min}$ and $u \in \tilde{\mathcal{U}}$. There exists as subdivision $\{x_i\}_{0 \leq i \leq p}$ of $[0, 1]$ such that for every $i \in \{0, .., p-1\}$, u is constant on $[x_i, x_{i+1})$ and $x_{i+1} - x_i > \delta$. Thus $w'_u(\delta) = 0$ which ends the proof.

□

With either $\mathcal{U}$ or $\tilde{\mathcal{U}}$ as the control space, the stochastic controlled infinite-dimensional Hodgkin-Huxley-ChR2 model admits an optimal ordinary control strategy.

Appendix

Appendix 2.A Construction of X^α by iteration

Let $\alpha \in \mathcal{A}$ and let $x := (v, d, \tau, h, \nu) \in \Xi^\alpha$ with $z := (\nu, d, h) \in \Upsilon$. The existence of the probability $\mathbb{P}_x^\alpha$ below is the object of the next section where Theorem 2.1.2 is proved.

— Let T_1 be the time of the first jump of (X_t^α). With the notations of Proposition 2.1.1, the law of T_1 is defined by its survival function given for all $t > 0$ by

$$\mathbb{P}_x^\alpha(T_1 > t) = \exp\left(-\int_0^t \lambda_d\Big(\phi_s^\alpha(x), \alpha(\nu_s, d_s, h_s)(\tau_s)\Big)\mathrm{d}s\right).$$

— For $t < T_1$, X_t^α solves (2.10) starting from x namely $(v_t, d_t, \tau_t, h_t, \nu_t) = (\phi_t^\alpha(x), d, \tau + t, h, \nu)$.

— When a jump occurs at time T_1, conditionally to T_1, $X_{T_1}^\alpha$ is a random variable distributed according to a measure $\hat{\mathcal{Q}}$ on $(\Xi, \mathcal{B}(\Xi))$, itself defined by a measure $\mathcal{Q}$ on $(D, \mathcal{B}(D))$. The target state d_1 of the discrete variable is a random variable distributed according to the measure $\mathcal{Q}(\cdot|\phi_{T_1}^\alpha(x), d_{T_1^-}, \alpha(\nu_{T_1^-}, d_{T_1^-}, h_{T_1^-})(\tau_{T_1^-}))$ such that for all $B \in \mathcal{B}(D)$,

$$\begin{aligned}\hat{\mathcal{Q}}\Big(\{\phi_{T_1}^\alpha(x)\} \times B \times \{0\} \times \{h + \tau_{T_1^-}\} \times \{\phi_{T_1}^\alpha(x)\} | \phi_{T_1}^\alpha(x), d_{T_1^-}, \tau_{T_1^-}, h_{T_1^-}, \nu_{T_1^-}, \alpha(T_1^-)\Big) \\ = \mathcal{Q}\Big(B|\phi_{T_1}^\alpha(s), d, \alpha(\nu, d, h)(\tau + T_1)\Big),\end{aligned}$$

where we use the notation $\alpha(T_1^-) = \alpha(d_{T_1^-}, \tau_{T_1^-}, h_{T_1^-}, \nu_{T_1^-})$. This equality means that the variables v and ν do not jump at time T_1, and the variables τ and h jump in a deterministic way to $\{0\}$ and $\{h + \tau_{T_1^-}\}$ respectively.

— The construction iterates after time T_1 with the new starting point $(v_{T_1}, d_{T_1}, 0, h + T_1, v_{T_1})$.

Formally the expressions of the jump rate and the transition measures on Ξ are

$$\lambda(x,u) := \lambda_d(v,u),$$
$$\hat{\mathcal{Q}}\Big(F\times B\times E\times G\times J|x,u\Big) := \mathbf{1}_{F\times E\times G\times J}(v,0,h+\tau,\nu)\mathcal{Q}\Big(B|v,d,u\Big),$$

with $F\times B\times E\times G\times J\in\mathcal{B}(\Xi)$, $u\in U$ and $x:=(v,d,\tau,h,\nu)\in\Xi$.

Appendix 2.B Proof of Theorem 2.1.2

There are two filtered spaces on which we can define the enlarged process (X^α) of Definition 2.1.2. They are linked by the one-to-one correspondence between the PDMP (X^α) and the included jump process (Z^α) that we define now. We then introduce both spaces since each one of them is relevant to prove useful properties.

Given the sample path $(X^\alpha_s, s\le T)$ such that $X^\alpha_0 := (v,d,\tau,h,\nu)\in\Xi^\alpha$, the jump times T_k of X^α can be retrieved by the formula

$$\{T_k, k=1,\dots,n\} = \{s\in(0,T]|h_s\neq h_{s^-}\}.$$

Moreover we can associate to X^α a pure jump process $(Z^\alpha_t)_{t\ge0}$ taking values in Υ in a one-to-one correspondence as follows,

$$Z^\alpha_t := (\nu_{T_k}, d_{T_k}, T_k), \qquad T_k\le t<T_{k+1}. \tag{2.32}$$

Conversely, given the sample path of Z^α on $[0,T]$ starting from $Z^\alpha_0=(\nu^Z_0,d^Z_0,T^Z_0)$, we can recover the path of X^α on $[0,T]$. Denote Z^α_t as (ν^Z_t,d^Z_t,T^Z_t) and define $T_0:=T^Z_0$ and $T_k:=\inf\{t>T_{k-1}|T^Z_t\neq T^Z_{t^-}\}$. Then

$$\begin{cases} X^\alpha_t = (\phi^\alpha_t(Z^\alpha_0), d^Z_0, t, T^Z_0, \nu^Z_0), & t<T_1,\\ X^\alpha_t = (\phi^\alpha_{t-T_k}(Z^\alpha_{T_k}), d_{T_k}, t-T_k, T^Z_{T_k}, \nu^Z_{T_k}), & T_k\le t<T_{k+1}. \end{cases} \tag{2.33}$$

Let us note that $T^Z_{T_k}=T_k$ for all $k\in\mathbb{N}$, and that by construction of the PDMP all jumps are detected since $\mathbb{P}^\alpha[T_{k+1}=T_k]=0$. When no confusion is possible, we write, for $\alpha\in\mathcal{A}$ and $n\in\mathbb{N}$, $Z_n=Z^\alpha_{T_n}$.

Part 1. The canonical space of jump processes with values in Υ. The following construction is very classical, see for instance Davis [Dav93] Appendix A1. We adapt it here to our peculiar process and to the framework of control. Remember that a jump process is defined by a sequence of inter-arrival times and jump locations

$$\omega = (\gamma_0, s_1, \gamma_1, s_2, \gamma_2, \dots), \tag{2.34}$$

where $\gamma_0 \in \Upsilon$ is the initial position, and for $i \in \mathbb{N}^*$, s_i is the time elapsed between the $(i-1)^{\text{th}}$ and the i^{th} jump while γ_i is the location right after the i^{th} jump. The jump times $(t_i)_{i\in\mathbb{N}}$ are deduced from the sequence $(s_i)_{i\in\mathbb{N}^*}$ by $t_0 = 0$ and $t_i = t_{i-1} + s_i$ for $i \in \mathbb{N}^*$ and the jump process $(J_t)_{t\geq 0}$ is given by $J_t := \gamma_i$ for $t \in [t_i, t_{i+1})$ and $J_t = \Delta$ for $t \geq t_\infty := \lim_{i\to\infty} t_i$, Δ being an extra state, called cemetery.

Accordingly we introduce $Y^\Upsilon := (\mathbb{R}_+ \times \Upsilon) \cup \{(\mathbb{R}_+ \cup \infty, \Delta)\}$. Let $(Y_i^\Upsilon)_{i\in\mathbb{N}^*}$ be a sequence of copies of the space Y^Υ. We define $\Omega^\Upsilon := \Upsilon \times \Pi_{i=1}^\infty Y_i^\Upsilon$ the canonical space of jump processes with values in Υ, endowed with its Borel σ-algebra $\mathcal{F}^\Upsilon$ and the coordinate mappings on Ω^Υ as follows

$$\begin{cases} S_i: & \Omega^\Upsilon \longrightarrow \mathbb{R}_+ \cup \{\infty\}, \\ & \omega \longmapsto S_i(\omega) = s_i, \quad \text{for } i \in \mathbb{N}^*, \\ \Gamma_i: & \Omega^\Upsilon \longrightarrow \Upsilon \cup \{\Delta\}, \\ & \omega \longmapsto \Gamma_i(\omega) = \gamma_i, \quad \text{for } i \in \mathbb{N}. \end{cases} \tag{2.35}$$

We also introduce $\omega_i : \Omega^\Upsilon \to \Omega_i^\Upsilon$ for $i \in \mathbb{N}^*$, defined by

$$\omega_i(\omega) := (\Gamma_0(\omega), S_1(\omega), \Gamma_1(\omega), \dots, S_i(\omega), \Gamma_i(\omega))$$

for $\omega \in \Omega^\Upsilon$. Now for $\omega \in \Omega^\Upsilon$ and $i \in \mathbb{N}^*$, let

$$\begin{aligned} T_0(\omega) &:= 0, \\ T_i(\omega) &:= \begin{cases} \sum_{k=1}^{i} S_k(\omega), & \text{if } S_k(\omega) \neq \infty \text{ and } \Gamma_k(\omega) \neq \Delta, k = 1, \dots, i, \\ \infty & \text{if } S_k(\omega) = \infty \text{ or } \Gamma_k(\omega) = \Delta \text{ for some } k = 1, \dots, i, \end{cases} \\ T_\infty(\omega) &:= \lim_{i\to\infty} T_i(\omega). \end{aligned}$$

and the sample path $(x_t(\omega))_{t\geq 0}$ be defined by

$$x_t(\omega) := \begin{cases} \Gamma_i(\omega) & T_i(\omega) \leq t < T_{i+1}(\omega), \\ \Delta & t \geq T_\infty(\omega). \end{cases} \tag{2.36}$$

A relevant filtration for our problem is the natural filtration of the coordinate process $(x_t)_{t\geq 0}$ on Ω^Υ

$$\mathcal{F}_t^\Upsilon := \sigma\{x_s | s \leq t\},$$

for all $t \in \mathbb{R}_+$. For given starting point $\gamma_0 \in \Upsilon$ and control strategy $\alpha \in \mathcal{A}$, a *controlled probability measure*, denoted $\mathbb{P}_{\gamma_0}^\alpha$, is defined on Ω^Υ by the specification of a family of controlled conditional distribution functions as follows: μ_1 is a controlled probability measure on $(Y^\Upsilon, \mathcal{B}(Y^\Upsilon))$ or equivalently a measurable mapping from $\mathcal{U}_{ad}([0,T];U)$ to the set of probability measures on $(Y^\Upsilon, \mathcal{B}(Y^\Upsilon))$, such that for all $\alpha \in \mathcal{A}$,

$$\mu_1(\alpha(\gamma_0); (\{0\} \times \Upsilon) \cup (\mathbb{R}_+ \times \{\gamma_0\})) = 0.$$

For $i \in \mathbb{N} \setminus \{0,1\}$, $\mu_i : \Omega_i^\Upsilon \times \mathcal{U}_{ad}([0,T];U) \times \mathcal{B}(Y^\Upsilon) \to [0,1]$ are *controlled transition measures* satisfying:

1. $\mu_i(\cdot; \Sigma)$ is measurable for each $\Sigma \in \mathcal{B}(Y^\Upsilon)$,
2. $\mu_i(\omega_{i-1}(\omega), \alpha(\Gamma_{i-1}(\omega)); \cdot)$ is a probability measure for every $\omega \in \Omega^\Upsilon$ and $\alpha \in \mathcal{A}$,
3. $\mu_i(\omega_{i-1}(\omega), \alpha(\Gamma_{i-1}(\omega)); (\{0\} \times \Upsilon) \cup (\mathbb{R}_+ \times \{\Gamma_{i-1}(\omega)\})) = 0$ for every $\omega \in \Omega^\Upsilon$ and $\alpha \in \mathcal{A}$,
4. $\mu_i(\omega_{i-1}(\omega), \alpha(\Gamma_{i-1}(\omega)); \{(\infty, \Delta)\}) = 1$ if $S_k(\omega) = \infty$ or $\Gamma_k(\omega) = \Delta$ for some $k \in \{1, \dots, i-1\}$, for every $\alpha \in \mathcal{A}$.

We need to extend the definition of $\alpha \in \mathcal{A}$ to the state (∞, Δ) by setting $\alpha(\Delta) := u_\Delta$ where u_Δ is itself an isolated cemetery state and α takes in fact values in $\mathcal{U}_{ad}([0,T]; U \cup \{u_\Delta\})$.

Now for a given control strategy $\alpha \in \mathcal{A}$, $\mathbb{P}^\alpha_{\gamma_0}$ is the unique probability measure on $(\Omega^\Upsilon, \mathcal{T}^\Upsilon)$ such that for each $i \in \mathbb{N}^*$ and bounded function f on Ω_i^Υ

$$\begin{aligned}\int_{\Omega^\Upsilon} & f(\omega_i(\omega))\mathbb{P}^\alpha_{\gamma_0}(\mathrm{d}\omega) \\ &= \int_{Y_1^\Upsilon} \cdots \int_{Y_i^\Upsilon} f(y_1, \dots, y_i)\mu_i(y_1, \dots, y_{i-1}, \alpha(y_{i-1}); \mathrm{d}y_i) \\ &\qquad \times \mu_{i-1}(y_1, \dots, y_{i-2}, \alpha(y_{i-2}); \mathrm{d}y_{i-1}) \dots \mu_1(\alpha(\gamma_0); \mathrm{d}y_1),\end{aligned}$$

with α depending only on the variable in Υ when writing "$\alpha(y_{i-1})$" , $y_{i-1} = (s_{i-1}, \gamma_{i-1})$. Let's now denote by $\mathcal{F}^\Upsilon_{\gamma,\alpha}$ and $(\mathcal{F}_t^{\Upsilon,\gamma,\alpha})_{t\geq 0}$ the completed σ-fields of $\mathcal{F}^\Upsilon$ and $(\mathcal{F}_t^\Upsilon)_{t\geq 0}$ with all the $\mathbb{P}^\alpha_\gamma$-null sets of $\mathcal{F}^\Upsilon$. We then rename the intersection of these σ-fields redefine $\mathcal{F}^\Upsilon$ and $(\mathcal{F}_t^\Upsilon)_{t\geq 0}$ so that we have

$$\mathcal{F}^\Upsilon := \bigcap_{\gamma \in \Upsilon \alpha \in \mathcal{A}} \mathcal{F}^\Upsilon_{\gamma,\alpha},$$

$$\mathcal{F}_t^\Upsilon := \bigcap_{\gamma \in \Upsilon \alpha \in \mathcal{A}} \mathcal{F}_t^{\Upsilon,\gamma,\alpha} \text{ for all } t \geq 0.$$

Then $(\Omega^\Upsilon, \mathcal{F}^\Upsilon, (\mathcal{F}_t^\Upsilon)_{t\geq 0})$ is the natural filtered space of controlled jump processes.

Part 2. The canonical space of *càdlàg* functions with values in Ξ. Let Ω_Ξ be the set of right-continuous functions with left limits (*càdlàg* functions), defined on $\mathbb{R}_+$ with values in Ξ. Analogously to what we have done in Part 1, we can construct a filtered space $(\Omega^\Xi, \mathcal{F}^\Xi, (\mathcal{F}^\Xi_t)_{t\geq 0})$ with coordinate process $(x^\Xi_t)_{t\geq 0}$ and a probability $\mathbb{P}^\alpha$ on $(\Omega^\Xi, \mathcal{F}^\Xi)$ for every control strategy $\alpha \in \mathcal{A}$ such that the infinite-dimensional PDMP is a $\mathbb{P}^\alpha$-strong Markov process. For $(t, y) \in \mathbb{R}_+ \times \Omega_\Xi, x^\Xi_t(y) = y(t)$.

We start with the definition of $\mathcal{F}^{\Xi,0}_t := \sigma\{x^\Xi_s | s \leq t\}$ for $t \in \mathbb{R}_+$ and $\mathcal{F}^{\Xi,0} := \vee_{t\geq 0}\mathcal{F}^{\Xi,0}_t$. In Davis [Dav93] p 59, the construction of the PDMP is conducted on the Hilbert cube, the space of sequences of independent and uniformly distributed random variables in $[0, 1]$. In the case of controlled PDMP, the survival function $F(t, x)$ in [Dav93] is replaced by the extension to ξ^α of χ^α defined in Definition 2.1.2 and the construction depends on the chosen control. This extension is defined for $x := (v, d, \tau, h, \nu) \in \Xi^\alpha$ by

$$\chi^\alpha_t(x) := \exp\left(-\int_0^t \lambda_d(\phi^\alpha_s(x), \alpha_{\tau+s}(\nu, d, h))\mathrm{d}s\right),$$

such that for $z := (v, d, h) \in \Upsilon$, $\chi^\alpha_t(z) = \chi^\alpha_t(v, d, 0, h, v)$.

This procedure thus provides for each control $\alpha \in \mathcal{A}$ and starting point $x \in \Xi^\alpha$ a measurable mapping ψ^α_x from the Hilbert cube to Ω_Ξ. Let $\mathbb{P}^\alpha_x := \mathbb{P}\left[(\psi^\alpha_x)^{-1}\right]$ denote the image measure of the Hilbert cube probability $\mathbb{P}$ under ψ^α_x. Now for $x \in \Xi^\alpha$, let $\mathcal{F}^{x,\alpha}_t$ be the completion of $\mathcal{F}^{\Xi,0}_t$ with all $\mathbb{P}^\alpha_x$-null sets of $\mathcal{F}^{\Xi,0}$, and define

$$\mathcal{F}^\Xi_t := \bigcap_{\alpha\in\mathcal{A}, x\in\Xi^\alpha} \mathcal{F}^{x,\alpha}_t. \tag{2.37}$$

The right-continuity of $(\mathcal{F}^\Xi_t)_{t\geq 0}$ follows from the right-continuity of $(\mathcal{F}^\Upsilon_t)_{t\geq 0}$ and the one-to-one correspondence. The right-continuity of $(\mathcal{F}^\Upsilon_t)_{t\geq 0}$ is a classical result on right-constant processes. For theses reasons, we lose the superscripts Ξ and Υ consider the natural filtration $(\mathcal{F}_t)_{t\geq 0}$ in the sequel.

Now that we have a filtered probability space that satisfies the *usual conditions*, let us show that the simple Markov property holds for (X^α_t). Let $\alpha \in \mathcal{A}$ be a control strategy, $s > 0$ and $k \in \mathbb{N}^*$. By construction of the process $(X^\alpha_t)_{t\geq 0}$,

$$\begin{aligned}\mathbb{P}^\alpha[T_{k+1} - T_k > s|\mathcal{F}_{T_k}] &= \exp\left(-\int_0^s \lambda_{d_{T_k}}(\phi^\alpha_t(X^\alpha_{T_k}), \alpha_u(\nu_{T_k}, d_{T_k}, h_{T_k}))\mathrm{d}u\right)\\ &= \chi^\alpha_s(X^\alpha_{T_k}).\end{aligned}$$

Now for $x \in \Xi^\alpha$, $(t, s) \in \mathbb{R}^2_+$ and $k \in \mathbb{N}^*$,

$$\begin{aligned}&\mathbb{P}^\alpha_x[T_{k+1} > t + s|\mathcal{F}_t]\mathbf{1}_{\{T_k\leq t<T_{k+1}\}}\\ &\quad= \mathbb{P}^\alpha_x[T_{k+1} - T_k > t + s - T_k|\mathcal{F}_t]\mathbf{1}_{\{0\leq t-T_k<T_{k+1}-T_k\}}\end{aligned}$$

$$= \exp\left(-\int_{t-T_k}^{t+s-T_k} \lambda_{d_{T_k}}(\phi_u^\alpha(X_{T_k}^\alpha), \alpha_u(\nu_{T_k}, d_{T_k}, h_{T_k}))\mathrm{d}u\right) \mathbf{1}_{\{0\le t-T_k<T_{k+1}-T_k\}} \quad (*)$$
$$= \exp\left(-\int_0^s \lambda_{d_{T_k}}(\phi_{u+t-T_k}^\alpha(X_{T_k}^\alpha), \alpha_{u+t-T_k}(\nu_{T_k} d_{T_k}, h_{T_k}))\mathrm{d}u\right) \mathbf{1}_{\{0\le t-T_k<T_{k+1}-T_k\}}.$$

The equality (*) is the classical formula for jump processes (see Jacod [Jac75]). On the other hand,

$$\begin{aligned}\chi_s^\alpha(X_t^\alpha)\mathbf{1}_{\{T_k\le t<T_{k+1}\}} &= \exp\left(-\int_0^s \lambda_{d_t}\Big(\phi_u^\alpha(X_t^\alpha), \alpha_{u+\tau_t}(\nu_t, d_t, h_t)\Big)\mathrm{d}u\right) \mathbf{1}_{\{T_k\le t<T_{k+1}\}}\\ &= \exp\left(-\int_0^s \lambda_{d_{T_k}}\Big(\phi_u^\alpha(X_t^\alpha), \alpha_{u+t-T_k}(\nu_{T_k}, d_{T_k}, h_{T_k})\Big)\mathrm{d}u\right) \mathbf{1}_{\{T_k\le t<T_{k+1}\}}\\ &= \exp\left(-\int_0^s \lambda_{d_{T_k}}\Big(\phi_{u+t-T_k}^\alpha(X_{T_k}^\alpha), \alpha_{u+t-T_k}(\nu_{T_k} d_{T_k}, h_{T_k})\Big)\mathrm{d}u\right)\\ &\qquad \mathbf{1}_{\{T_k\le t<T_{k+1}\}},\end{aligned}$$

because $X_t^\alpha = \Big(\phi_{t-T_k}^\alpha(X_{T_k}^\alpha), d_{T_k}, t-T_k, h_{T_k}, \nu_{T_k}\Big)$ and by the flow property $\phi_u^\alpha(X_t^\alpha) = \phi_{u+t-T_k}^\alpha(X_{T_k}^\alpha)$ on $\mathbf{1}_{\{T_k\le t<T_{k+1}\}}$.

Thus we showed that for all $x \in \Xi^\alpha$, $(t,s) \in \mathbb{R}_+^2$ and $k \in \mathbb{N}^*$,

$$\mathbb{P}_x^\alpha[T_{k+1} > t+s|\mathcal{F}_t]\mathbf{1}_{\{T_k\le t<T_{k+1}\}} = \chi_s^\alpha(X_t^\alpha)\mathbf{1}_{\{T_k\le t<T_{k+1}\}}.$$

Now if we write $T_t^\alpha := \inf\{s > t : X_s^\alpha \neq X_{s^-}^\alpha\}$ the next jump time of the process after t, we get

$$\mathbb{P}_x^\alpha[T_t^\alpha > t+s|\mathcal{F}_t] = \chi_s^\alpha(X_t^\alpha), \tag{2.38}$$

which means that, conditionally to $\mathcal{F}_t$, the next jump has the same distribution as the first jump of the process started at X_t^α. Since the location of the jump only depends on the position at the jump time, and not before, equality (2.38) is just what we need to prove our process verifies the simple Markov property.

To extend the proof to the strong Markov property, the application of Theorem (25.5) (Davis [Dav93]) on the characterization of jump process stopping times on Borel spaces is straightforward.

From the results of [BR11a], there is no difficulty in finding the expression of the extended generator $\mathcal{G}^\alpha$ and its domain:

— Let $\alpha \in \mathcal{A}$. The domain $D(\mathcal{G}^\alpha)$ of $\mathcal{G}^\alpha$ is the set of all measurable $f : \Xi \to \mathbb{R}$ such that $t \mapsto f(\phi_t^\alpha(x), d, \tau+t, h, \nu)$
(resp. $(v_0, d_0, \tau_0, h_0, \nu_0, t, \omega) \mapsto f(v_0, d_0, \tau_0, h_0, \nu_0) - f(v(t^-,\omega), d(t^-,\omega), \tau(t^-,\omega),$ $h(t^-,\omega), \nu(t^-,\omega)))$ is absolutely continuous on $\mathbb{R}_+$ for all $x = (v, d, \tau, h, \nu) \in \Xi^\alpha$ (resp. a valid integrand for the associated random jump measure).

— Let f be continuously differentiable w.r.t. $v \in V$ and $\tau \in \mathbb{R}_+$. Define h_v as the unique element of V^* such that

$$\frac{\mathrm{d}f}{\mathrm{d}v}[v,d,\tau,h,\nu](y) = \langle h_v(v,d,\tau,h,\nu), y\rangle_{V^*,V} \qquad \forall y \in V,$$

where $\frac{\mathrm{d}f}{\mathrm{d}v}[v,d,\tau,h,\nu]$ denotes the Fréchet-derivative of f w.r.t $v \in E$ evaluated at (v,d,τ,h,ν). If $h_v(v,d,\tau,h,\nu) \in V^*$ whenever $v \in V$ and is bounded in V for bounded arguments then for almost every $t \in [0,T]$,

$$\begin{aligned}\mathcal{G}^\alpha f(v,d,\tau,h,\nu) = \frac{\partial}{\partial \tau} f(v,d,\tau,h,\nu) + \langle h_v(v,d,\tau,h,\nu), Lv + f_d(v,\alpha_\tau(\nu,d,h))\rangle_{V^*,V} \\ + \lambda_d(v,\alpha_\tau(\nu,d,h)) \int_D [f(v,p,0,h+\tau,v) - f(v,d,\tau,h,\nu)]\mathcal{Q}_\alpha(\mathrm{d}p|v,d).\end{aligned} \tag{2.39}$$

The bound on the continuous component of the PDMP comes from the following estimation. Let $\alpha \in \mathcal{A}$ and $x := (v,d,\tau,h,\nu) \in \Xi^\alpha$ and denote by v^α the first component of X^α. Then for $t \in [0,T]$,

$$\begin{aligned}||v_t^\alpha||_H &\le ||S(t)v||_H + \int_0^t ||S(t-s)f_{d_s}(v_s^\alpha, \alpha_{\tau_s}(\nu_s,d_s,h_s))||_H \mathrm{d}s \\ &\le M_S||v||_H + \int_0^t M_S(b_1 + b_2||v_s^\alpha||_H)\mathrm{d}s \\ &\le M_S(||v||_H + b_1 T)e^{M_S b_2 T},\end{aligned} \tag{2.40}$$

by Gronwall's inequality.

Appendix 2.C Proof of Lemma 2.3.6

Part 1. Let's first look at the case when w is bounded by a constant w_∞ and define for $(z,\gamma) \in \Upsilon \times \mathcal{R}$

$$W(z,\gamma) = \int_0^{T-h} \chi_s^\gamma(z) \left(\int_Z w(\phi_s^\gamma(z), d, h+s, u)\gamma(s)(\mathrm{d}u) \right) \mathrm{d}s$$

Now take $(z,\gamma) \in \Upsilon \times \mathcal{R}$ and suppose $(z_n,\gamma_n) \to (z,\gamma)$. Let's write $z = (v,d,h)$ and $z_n = (v_n,d_n,h_n)$ for $n \in \mathbb{N}$. For $s \in [0,T]$, let $w_n(s,u) := w(\phi_s^{\gamma_n}(z_n), d_n, h_n + s, u)$ and $w(s,u) := w(\phi_s^\gamma(z), d, h+s, u)$. Let also $a_n = \min(T-h, T-h_n)$ and $b_n = \max(T-h, T-h_n)$.

Then

$$
\begin{aligned}
|W(z_n,\gamma_n)-W(z,\mu)| \leq & \left|\int_{a_n}^{b_n} \chi_s^{\gamma_n}(z_n)\int_Z w_n(s,u)\gamma_n(s)(\mathrm{d}u)\mathrm{d}s\right| \\
& + \int_0^{T-h} \chi_s^{\gamma_n}(z_n)\int_Z |w_n(s,u)-w(s,u)|\gamma_n(s)(\mathrm{d}u)\mathrm{d}s \\
& + \Big|\int_0^{T-h} \chi_s^{\gamma_n}(z_n)\int_Z w(s,u)\gamma_n(s)(\mathrm{d}u)\mathrm{d}s \\
& \qquad - \int_0^{T-h} \chi_s^{\gamma}(z)\int_Z w(s,u)\gamma_n(s)(\mathrm{d}u)\mathrm{d}s\Big| \\
& + \Big|\int_0^{T-h} \chi_s^{\gamma}(z)\int_Z w(s,u)\gamma_n(s)(\mathrm{d}u)\mathrm{d}s \\
& \qquad - \int_0^{T-h} \chi_s^{\gamma}(z)\int_Z w(s,u)\gamma(s)(\mathrm{d}u)\mathrm{d}s\Big|
\end{aligned}
$$

The first term on the right-hand side converges to zero for $n \to \infty$ since the integrand is bounded.

$$
\begin{aligned}
\int_0^{T-h} \chi_s^{\gamma_n}(z_n)\int_Z |w_n(s,u)-w(s,u)|\gamma_n(s)(\mathrm{d}u)\mathrm{d}s \leq & \int_0^{T-h} e^{-\delta s}\sup_{u\in U}|w_n(s,u)-w(s,u)|\mathrm{d}s \\
& \xrightarrow[n\to\infty]{} 0
\end{aligned}
$$

by dominated convergence and the continuity of w and of ϕ proved in Lemma 2.3.5.

$$
\begin{aligned}
\left|\int_0^{T-h} (\chi_s^{\gamma_n}(z_n)-\chi_s^{\gamma}(z))\int_Z w(s,u)\mu_s^n(\mathrm{d}u)\mathrm{d}s\right| \leq & \, w_\infty \int_0^{T-h} |\chi_s^{\gamma_n}(z_n)-\chi_s^{\gamma}(z)|\,\mathrm{d}s \\
& \xrightarrow[n\to\infty]{} 0
\end{aligned}
$$

again by dominated convergence, provided that for $s \in [0,T]$, the convergence $\chi_s^{\gamma_n}(z_n) \xrightarrow[n\to\infty]{} \chi_s^{\gamma}(z)$ holds. For this convergence to hold it is enough that for $t \in [0,T]$,

$$
\int_0^t \int_Z \lambda_{d_n}(\phi_s^{\gamma_n}(z_n),u)\gamma_n(s)(\mathrm{d}u)\mathrm{d}s \xrightarrow[n\to\infty]{} \int_0^t \int_Z \lambda_d(\phi_s^{\gamma}(z),u)\gamma(s)(\mathrm{d}u)\mathrm{d}s.
$$

It is enough to take n large enough so that $d_n = d$ and to write

$$
\begin{aligned}
& \int_0^t \left(\int_Z \lambda_d(\phi_s^{\gamma_n}(z_n),u)\gamma_n(s)(\mathrm{d}u) - \int_Z \lambda_d(\phi_s^{\gamma}(z),u)\gamma(s)(\mathrm{d}u)\right)\mathrm{d}s = \\
& \qquad \int_0^t \int_Z \left(\lambda_d(\phi_s^{\gamma_n}(z_n),u)-\lambda_d(\phi_s^{\gamma}(z),u)\right)\gamma_n(s)(\mathrm{d}u)\mathrm{d}s
\end{aligned}
$$

$$+\int_0^t \Big(\int_Z \lambda_d(\phi_s^\gamma(z),u)\gamma_n(s)(\mathrm{d}u) - \int_Z \lambda_d(\phi_s^\gamma(z),u)\gamma(s)(\mathrm{d}u)\Big)\,\mathrm{d}s$$

By the local Lipschitz property of λ_d,

$$\left|\int_0^t \int_Z \left(\lambda_d(\phi_s^{\gamma_n}(z_n),u) - \lambda_d(\phi_s^\gamma(z),u)\right)\gamma_n(s)(\mathrm{d}u)\mathrm{d}s\right| \leq l_\lambda \int_0^t ||\phi_s^{\gamma_n}(z_n) - \phi_s^\gamma(z)||_H \mathrm{d}s$$

and $\int_0^t ||\phi_s^{\gamma_n}(z_n) - \phi_s^\gamma(z)||_E \mathrm{d}s \leq t\sup_{s\in[0,T]} ||\phi_s^{\gamma_n}(z_n) - \phi_s^\gamma(z)||_H \xrightarrow[n\to\infty]{} 0$ by Lemma 2.3.5. The second term converges to zero by the definition of the weakly* convergence in $L^\infty(M(Z))$.

Part 2. In the general case where $|w| \leq w_c B^*$, let $w^B(z,u) = w(z,u) - c_w B^*(z) \leq 0$ for $(z,u) \in \Upsilon \times U$. w^B is a continuous function and there exists a nonincreasing sequence (w_n^B) of bounded continuous functions such that $w_n^B \xrightarrow[n\to\infty]{} w^B$. By the first part of the proof we know that

$$W_n(z,\gamma) = \int_0^{T-h} \chi_s^\gamma(z) \int_Z w_n^B(\phi_s^\gamma(z), d, h+s, u)\mu_s(\mathrm{d}u)\mathrm{d}s$$

is bounded, continuous, decreasing and converges to

$$W(z,\gamma) - c_w \int_0^{T-h} \chi_s^\gamma(z) b(\phi_s^\gamma(z)) e^{\zeta^*(T-h-s)}\mathrm{d}s$$

which is thus upper semicontinuous. Since b is a continuous bounding function it is easy to show that

$$(z,\gamma) \to \int_0^{T-h} \chi_s^\gamma(z) b(\phi_s^\gamma(z)) e^{\zeta^*(T-h-s)}\mathrm{d}s$$

is continuous so that in fact W is upper semicontinuous. Now considering the function $w_B(z,u) = -w(z,u) - c_w B^*(z) \leq 0$ we easily show that W is also lower semicontinuous so that finally W is continuous.

Now the continuity of the applications $(z,\gamma) \to c'(z,\gamma)$ and $(z,\gamma) \to (\mathcal{Q}'w)(z,\gamma)$ comes from the previous result applied to the continuous functions defined for $(z,u) \in \Upsilon \times U$ by $w_1(z,u) := c(v,u)$ and $w_2(z,u) := \lambda_d(v,u)\int_D w(v,r,h)\mathcal{Q}(\mathrm{d}r|v,d,u)$ with $z = (v,d,h)$. Here the different assumptions of continuity (H(λ))2.3., (H(c))1. and (H($\mathcal{Q}$)) are needed.

Chapter 3

Additional results

This chapter gathers some additional results on the infinite-dimensional controlled PDMP defined in Chapter 2. The first section is dedicated to showing the tightness of the continuous component of a sequence of controlled infinite-dimensional PDMP associated to a sequence of relaxed control strategies. This constitutes a first step towards the tightness of the whole process in order to prove convergence results called relaxation results. Relaxation results ensure that relaxed trajectories are not far from original trajectories so that the relaxed control system remains closely related to the original one. For our control infinite-dimensional PDMP, it can be formulated as follows.

For every relaxed control strategy $\mu \in \mathcal{A}^{\mathcal{R}}$ and every $\varepsilon > 0$, there exists a control strategy $\alpha \in \mathcal{A}$ such that

$$\sup_{t\in[0,T]} d_\Xi(X_t^\mu, X_t^\alpha) \leq \varepsilon,$$

where $d_\Xi(\cdot,\cdot)$ is a distance on Ξ. For example, we can define this distance for $x_1 = (v_1, d_1, \tau_1, h_1, \nu_1), x_2 = (v_2, d_2, \tau_2, h_2, \nu_2) \in \Xi^2$, by

$$d_\Xi(x_1, x_2) = \max\{||v_1 - v_2||_H, d_D(d_1, d_2), |\tau_1 - \tau_2|, |h_1 - h_2|, ||\nu_1 - \nu_2||_H\},$$

where $d_D(\cdot,\cdot)$ is the discrete distance on D, meaning that we must have $d_t^\mu = d_t^\alpha$ for all $t \in [0, T]$.

The second section extends the scope of the definition of controlled infinite-dimensional PDMPs, and the results of Chapter 2. We first show that the continuous component of the PDMP can take values in separable, reflexive Banach spaces. We then show that the space can also be taken nonreflexive. The difficulty to overcome is that in nonreflexive Banach spaces, the dual of a C^0 semigroup is not necessarily a C^0 semigroup. This, in particular, covers the cases of spaces of continuous functions and spaces of integrable functions. We develop in detail the case of the Laplacian on $C([0,1])$, the space of continuous functions on $[0,1]$.

3.1 Tightness of a sequence of infinite-dimensional controlled PDMPs

Here we prove a tightness result provided an additional assumption on the semigroup. Suppose that we are given a metrizable topology on $\mathcal{A}^{\mathcal{R}}$. The next Theorem is independent of any particular topology.

Theorem 3.1.1. *Let $(e_k, k \geq 1)$ be an orthonormal basis of H and suppose that following assumption is satisfied:*

(H(S)) *There exists $h \in L^1_{loc}(\mathbb{R})$ such that for every $t \in (0,T]$,*

$$\sum_{k=1}^{\infty} ||S(t)e_k||_H^2 \leq h(t).$$

Let $(\mu^n, n \in \mathbb{N})$ denote a sequence of relaxed control strategies that converges to a relaxed control strategy $\mu \in \mathcal{A}^{\mathcal{R}}$. For $n \in \mathbb{N}$, we denote by $(X_t^n, t \geq 0)$ the controlled PDMP associated to μ^n and $(v_t^n, t \geq 0)$ its first component. Then $(v^n, n \in \mathbb{N})$ is tight in $C([0,T], H)$.

Remark 3.1.1. *i) (H(S)) is satisfied for analytic semigroups. It implies in particular that S is an Hilbert-Schmidt semigroup. Hence (H(S)) implies (H(L))4.*

ii) If a semigroup $(S(t))_{t\geq 0}$ satisfies (H(S)) then the dual semigroup $(S^*(t))_{t\geq 0}$ also satisfies (H(S)).

Proof. This proof is largely inspired by the proof of [GT12, Theorem 2]. We use a critera of tightness in Hilbert spaces that we recall after this proof. We beging by showing that $(v^n, n \in \mathbb{N})$ satisfies the Aldous condition. Recall that $M_S > 0$ s a bound of $(S(t))$ on $[0,T]$, i.e. $\sup_{t\in[0,T]} |||S(t)||| \leq M_S$ with $|||\cdot|||$ the operator norm on H. Recall also that for $(v,d,\mu) \in H \times D \times M^1_+(Z)$ we denote by $\bar{f}_d(v,\mu) := \int_Z f_d(v,u)\mu(\mathrm{d}u)$. Because of (H($f$)), $||\bar{f}_d(v,\mu)||_H \leq b_1 + b_2||v||_H, b_1 \geq 0, b_2 > 0$.

Let $(v_0, d_0, T_0) \in \Upsilon$ and K any compact susbset of H containing v_0. For $(t,n) \in [0,T]\times\mathbb{N}$, we denote by $X_t^n =: (v_t^n, d_t^n, \tau_t^n, T_t^n, \nu_t^n)$ the PDMP associated to μ^n and starting at $(v_0, d_0, 0, T_0, v_0)$. Let $\theta > 0$ and τ be a $(\mathcal{F}_t)$-stopping time such that $\tau \leq T - \theta$.

$$
\begin{aligned}
||v^n_{\tau+\theta} - v^n_\tau||_H \leq\ & ||S(\tau+\theta)v_0 - S(\tau)v_0||_H \\
& + \int_0^\tau ||(S(\tau+\theta-s) - S(\tau-s))\bar{f}_{d^n_s}(v^n_s, \mu^n_{\tau^n_s}(\nu^n_s, d^n_s, T^n_s))||_H \mathrm{d}s \\
& + \int_\tau^{\tau+\theta} ||S(\tau+\theta-s)\bar{f}_{d^n_s}(v^n_s, \mu^n_{\tau^n_s}(\nu^n_s, d^n_s, T^n_s))||_H \mathrm{d}s \\
\leq\ & M_S||S(\theta)v_0 - v_0||_H + \int_0^\tau |||S(\tau+\theta-s) - S(\tau-s)|||(b_1 + b_2||v^n_s||_H)\mathrm{d}s \\
& + \int_\tau^{\tau+\theta} M_S(b_1 + b_2||v^n_s||_H)\mathrm{d}s.
\end{aligned}
$$

Because of the strong continuity of $(S(t))$, $||S(\theta)v_0 - v_0||_H \to 0$ when $\theta \to 0$. Furthermore,

$$
\int_\tau^{\tau+\theta} M_S(b_1 + b_2||v^n_s||_H)\mathrm{d}s \leq \theta(b_1 + b_2 c_K) \to 0.
$$

Since $(S(t))_{t\geq 0}$ is immediately compact, it is uniformly continuous on every interval $[\kappa, T]$ with $\kappa > 0$. Let $\kappa > 0$,

$$
\begin{aligned}
\int_0^{\tau-\kappa} |||S(\tau+\theta-s) - S(\tau-s)|||(b_1 + b_2||v^n_s||_H)\mathrm{d}s &\leq C_K \int_0^{\tau-\kappa} |||S(\tau+\theta-s) - S(\tau-s)|||\mathrm{d}s \\
&\leq C_K T \sup_{t\in[\kappa,T]} |||S(t+\theta) - S(t)||| \\
&\xrightarrow[\theta\to 0]{} 0,
\end{aligned}
$$

with $C_K = (b_1 + b_2 c_k)$ and

$$
\int_\tau^{\tau-\kappa} |||S(\tau+\theta-s) - S(\tau-s)|||(b_1 + b_2||v^n_s||_H)\mathrm{d}s \leq 2M_S(b_1 + b_2 c_K)\kappa.
$$

Now let $\delta, M > 0$. We can find $n_0 \in \mathbb{N}$ and $\eta \in (0, T]$ such that for $\theta \in (0, \eta)$

$$
\begin{aligned}
\frac{1}{M}||S(\theta)v_0 - v_0||_H &\leq \frac{\delta}{4}, \\
\frac{1}{M}\eta(b_1 + b_2 c_K) &\leq \frac{\delta}{4}, \\
\frac{1}{M}(b_1 + b_2 c_K)T \sup_{t\in[\frac{1}{n_0},T]} |||S(t+\theta) - S(t)||| &\leq \frac{\delta}{4}, \\
\frac{1}{M}2M_S(b_1 + b_2 c_K)\frac{1}{n_0} &\leq \frac{\delta}{4}.
\end{aligned}
$$

Then, applying Markov inequality, for all $n \geq n_0$ and $\theta \in (0, \eta)$,

$$\mathbb{P}^n(||v^n_{\tau+\theta} - v^n_\tau||_H \geq M) \leq \frac{1}{M}\mathbb{E}^n(||v^n_{\tau+\theta} - v^n_\tau||_H) \leq \delta,$$

so that,

$$\sup_{n\geq n_0} \sup_{\theta\in(0,\rho)} \mathbb{P}^n(||v^n_{\tau+\theta} - v^n_\tau||_H \geq M) \leq \delta.$$

Let us now apply Theorem 3.1.2 to show that for every $t \in [0, T]$, $(v^n_t, n \in \mathbb{N})$ is tight in H. Then, by invoking Theorem 3.1.3, $(v^n, n \in \mathbb{N})$ will be tight in $\mathbb{D}([0, T], H)$ and in $C([0, T], H)$ as well because $v^n \in C([0, T], H)$ for every $n \in \mathbb{N}$.

Let $t \in [0, T]$. Because v^n is bounded in $C([0, T], H)$, the Markov inequality gives that for any $\delta > 0$ there exists $\rho > 0$ large enough such that.

$$\sup_{n\geq 0} \mathbb{P}(||v^n_t||_H > \rho) \leq \frac{c_K}{\rho} \leq \delta.$$

To end the proof, we need to show that for any $\delta, \eta > 0$ we can find $n_0 \in \mathbb{N}$ and a space $L_{\delta,\eta}$ such that

$$\sup_{n\geq n_0} \mathbb{P}(\inf_{v\in L_{\delta,\eta}} ||v^n_t - v||_H > \eta) \leq \delta.$$

For every $h \in H$, $S(t)h = \sum_{k=1}^{\infty} (S(t)h, e_k)_H e_k$. Let $p \in \mathbb{N}^*$ and define for $h \in H$,

$$S_p(t)h := \sum_{k=1}^{p} (S(t)h, e_k)_H e_k,$$

and $v^n_{t,p} := S_p(t)v_0 + \int_0^t S_p(t-s)\bar{f}_{d^n_s}(v^n_s, \mu^n_{\tau^n_s}(v^n_s, d^n_s, T^n_s))\mathrm{d}s$.

Now,

$$\begin{aligned} v_t^n - v_{t,p}^n &= \sum_{k=p+1}^{\infty} (S(t)v_0, e_k)_H e_k + \int_0^t \sum_{k=p+1}^{\infty} (S(t-s)\bar{f}_{d_s^n}(v_s^n, \mu^n_{\tau_s^n}(v_s^n, d_s^n, T_s^n)), e_k)_H e_k \mathrm{d}s \\ &= \sum_{k=p+1}^{\infty} (v_0, S^*(t)e_k)_H e_k + \int_0^t \sum_{k=p+1}^{\infty} (\bar{f}_{d_s^n}(v_s^n, \mu^n_{\tau_s^n}(v_s^n, d_s^n, T_s^n)), S^*(t-s)e_k)_H e_k \mathrm{d}s \end{aligned}$$

with $S^*(t)$ the adjoint operator of $S(t)$.

$$\begin{aligned} ||v_t^n - v_{t,p}^n||_H^2 \leq & \sum_{k=p+1}^{\infty} |(v_0, S^*(t)e_k)_H|^2 \\ & + \int_0^t \sum_{k=p+1}^{\infty} |(\bar{f}_{d_s^n}(v_s^n, \mu^n_{\tau_s^n}(v_s^n, d_s^n, T_s^n)), S^*(t-s)e_k)_H|^2 \mathrm{d}s \\ & \leq ||v_0||_H^2 \sum_{k=p+1}^{\infty} ||S^*(t)e_k||_H^2 \\ & + \int_0^t \sum_{k=p+1}^{\infty} ||\bar{f}_{d_s^n}(v_s^n, \mu^n_{\tau_s^n}(v_s^n, d_s^n, T_s^n))||_H^2 ||S^*(t-s)e_k||_H^2 \mathrm{d}s \\ & \leq ||v_0||_H^2 \sum_{k=p+1}^{\infty} ||S^*(t)e_k||_H^2 + (b_1 + b_2 c_K)^2 \sum_{k=p+1}^{\infty} \int_0^t ||S^*(t-s)e_k||_H^2 \mathrm{d}s. \\ & \xrightarrow[p\to\infty]{} 0, \end{aligned}$$

uniformly in $n \in \mathbb{N}$. Now fix $\delta, \eta > 0$ and let $p \in \mathbb{N}^*$ such that $||v_t^n - v_{t,p}^n||_H \leq \eta\delta$ for every $n \in \mathbb{N}$ and define $L_{\delta,\eta} := \mathrm{span}\{e_i, \quad 1 \leq i \leq p\}$. Since $v_{t,p}^n \in L_{\delta,\eta}$, we get

$$\mathbb{E}(\inf_{v \in L_{\delta,\eta}} ||v_t^n - v||_H) \leq \mathbb{E}(||v_t^n - v_{t,p}^n||_H) \leq \eta\delta,$$

and Markov's inequality gives

$$\mathbb{P}(\inf_{v \in L_{\delta,\eta}} ||v_t^n - v||_H > \eta) \leq \delta,$$

uniformly in $n \in \mathbb{N}$. □

Tightness in Hilbert spaces

Let $\mathbb{D}([0,T],H)$ be the space of càdlàg functions on $[0,T]$ with values in the separable Hilbert space H.

Theorem 3.1.2 (respectively 3.1.3) below give a criterion of tightness in H (respectively in $\mathbb{D}([0,T],H)$). Their proofs can be found in [Mé84].

Theorem 3.1.2. *Let $(e_k, k \geq 1)$ be a basis of H and define, for $k \geq 1$,*

$$L_k = span\{e_i, 1 \leq i \leq k\}.$$

Then $(v^n, n \in \mathbb{N})$ is tight in H if and only if, for any $\delta, \eta > 0$ there exist $\rho > 0, n_0 \in \mathbb{N}$ and $L_{\delta,\eta} \subset \{L_k, k \geq 1\}$ such that

$$\begin{aligned} &\sup_{n \geq n_0} \mathbb{P}(||v^n||_H > \rho) \leq \delta, \\ &\sup_{n \geq n_0} \mathbb{P}(\inf_{v \in L_{\delta,\eta}} ||v^n - v||_H > \eta) \leq \delta. \end{aligned}$$

Theorem 3.1.3. *Assume that $(v^n, n \in \mathbb{N}) \in \mathbb{D}([0,T],H)^{\mathbb{N}}$ satisfy Aldous's condition, namely, for any $\delta, M > 0$, there exist $\rho > 0, n_0 \in \mathbb{N}$ such that, for all stopping times τ such that $\tau + \rho < T$,*

$$\sup_{n \geq n_0} \sup_{\theta \in (0,\rho)} \mathbb{P}(||v^n_{\tau+\theta} - v^n_\tau||_H \geq M) \geq \delta.$$

Assume moreover that for each $t \in [0,T]$, the sequence $(v^n_t, n \in \mathbb{N})$ is tight in H. Then $(v^n, n \in \mathbb{N})$ is tight in $\mathbb{D}([0,T],H)$.

As mentioned in Section 0.3.3, Theorem 3.1.1 is a first step towards a relaxation result for relaxed infinite-dimensional controlled PDMPs. It is striking to note that this theorem is independent of the topology considered on the space of relaxed control strategies. In fact, it is almost a deterministic result since it relies only on the assumptions made on the PDEs that drive the deterministic motion between jumps of the discrete component. Now, because of the strong coupling between the continuous and the discrete components, and because we had to add many variables to the process to define a coherent theoretical Markovian framework, the whole process $(X^n_t = (v^n_t, d^n_t, \tau^n_t, T^n_t, \nu^n_t), t \in [0,T])_{n \in \mathbb{N}}$ is much more complicated and we did not manage to prove a tightness result yet.

Even if we suppose the tightness of the whole process, in order to prove a relaxation theorem, we still need to identify a unique limiting process. To do so, we need to consider a topology on $\mathcal{A}^{\mathcal{R}}$. One topology that we could consider is the topology of uniform convergence from Υ in $\mathcal{R}([0,T],U)$, i.e. we will say that $\mu^n \to \mu$ in $\mathcal{A}^{\mathcal{R}}$ if

$$\sup_{z \in \Upsilon} \left| \int_0^T \int_Z f(t,u) \mu^n_t(z)(\mathrm{d}u)\mathrm{d}t - \int_0^T \int_Z f(t,u) \mu_t(z)(\mathrm{d}u)\mathrm{d}t \right| \to 0.$$

for every Carathéodory integrand $f : [0,T] \times H \to \mathbb{R}$, when $n \to \infty$. As in [CDMR12], we could try to study the sequence of infinitesimal generators

$$\begin{aligned}\mathcal{G}^{\mu^n} f(v,d,\tau,h,\nu) =& \frac{\partial}{\partial \tau} f(v,d,\tau,h,\nu) + \langle h_v(v,d,\tau,h,\nu), Lv + f_d(v,\alpha_\tau(\nu,d,h))\rangle_{V^*,V} \\ &+ \int_U \lambda_d(v,u) \int_D [f(v,p,0,h+\tau,v) \\ &\qquad - f(v,d,\tau,h,\nu)]\mathcal{Q}(\mathrm{d}p|v,d,u)\mu^n_\tau(\nu,d,h)(\mathrm{d}u).\end{aligned}$$

We can note that to prove a convergence result for $\mathcal{G}^{\mu^n}$ we would probably have to assume a pointwise convergence of μ^n in the variable τ (there is no integral on τ in the expression of the generator) and this is excluded in our framework. Pointwise convergence of relaxed controls is not a satisfactory topology to consider relaxed controlled PDEs.

3.2 A new framework for the definition of infinite-dimensional PDMPs

In this section we present an alternative framework, based on the work of Fattorini for PDEs ([Fat94a], [Fat94b], [Fat99]), for the definition of infinite-dimensional controlled PDMPs for which the continuous component takes values in a Banach space, possibly nonreflexive. This framework includes the case where the continuous component of the PDMP takes values in a space of continuous functions. If not otherwise specified, the notations will be those of Chapter 2. In our applications, we may want to consider the space $C^0([0,1])$ for the membrane potential if we argue that the membrane potential should be a continuous spatial function along the axon. We will in particular show that the results of Chapter 2 are valid in this framework.

This framework has the additional feature that it allows to consider noncompact control spaces. For clarity purposes we will still consider the control space Z to be a compact Polish space and focus on the difficulty that constitutes nonreflexive Banach spaces. Furthermore, since in our applications the control is a physical quantity, it is bound to take values in a compact space. We refer the reader to [Fat99, Section 12.5] for a discussion on the different control spaces that can be considered.

We begin with the case of a separable reflexive Banach space. It is important to note that we only need to properly define relaxed trajectories of the PDMP and prove an analogue of Lemma 2.3.5 in order to extend the results of Chapter 2. Indeed, the rest of the results can be directly rewriten for a Banach space. We then present the case of nonreflexive spaces and we develop in detail the case of the Laplacian in $C^0([0,1])$.

Let E be a separable reflexive Banach space with $\langle \cdot, \cdot \rangle_{(E^*,E)}$ its duality pairing. The infinite-dimensional controlled PDMP is constructed on $E \times D$ in the same way as in

Chapter 2 except for the Assumptions (H(L)) and (H(f)) that become

(H(L)b) L is the infinitesimal generator of a strongly continuous semigroup $(S(t))_{t\in\mathbb{R}_+}$ in E, immediately compact, that is, compact for every $t>0$. We denote by M_S a bound of the semigroup on $[0,T]$ for the operator norm.

(H(f)b) For every $d\in D$, $f_d : E\times Z\to E$ is a function such that:

1. For every $y\in E$, the function $z\to f_d(y,z)$ is continuous, hence bounded, in Z.
2. There exists $l_f>0$ such that

$$||f_d(y,z)-f_d(y',z)||_E\leq l_f||y-y'||_E \qquad (y,y'\in E, z\in Z).$$

We still assume (H(λ)) and (H($\mathcal{Q}$)) where the space H is replaced by E. Assumption (H(f)b) allows to give a sense to the relaxed PDE on E

$$\dot{y}(s)=Ly(s)+\int_U f_d(y(s),u)\gamma(s)(\mathrm{d}u),\quad y(0)=y_0\in E, \tag{3.1}$$

with $\gamma(\cdot)\in\mathcal{R}([0,T],U)$. Indeed, this assumption implies that for $d\in D$, $y^*\in E^*$, and $(y(\cdot),\gamma(\cdot))\in C([0,T],E)\times\mathcal{R}([0,T],U)$,

$$||\langle y^*,f_d(y(t),\cdot)\rangle_{(E^*,E)}||_{C(Z)}\leq ||y^*||_{E^*}(l\max_{t\in[0,T]}||y(t)||_E+\max_{u\in U}||f_d(0,u)||_E),$$

and thus

$$t\to\int_U\langle y^*,f_d(y(t),u)\rangle_{(E^*,E)}\gamma(t)(\mathrm{d}u)$$

belongs to $L^1([0,T])$. Since E is reflexive, we can define the function $\mathbf{f}_d : E\times M^1_+(Z)\to E$ such that $\mathbf{f}_d(y)\gamma$ is the unique element of E satisfying

$$\langle y^*,\mathbf{f}_d(y)\gamma\rangle_{(E^*,E)}=\int_U\langle y^*,f_d(y,u)\rangle_{(E^*,E)}\gamma(\mathrm{d}u)$$

for all $y^*\in E^*$. The function $t\to\mathbf{f}_d(y(t))\gamma(t)$ is thus E^*-*weakly* measurable for all $(y(\cdot),\gamma(\cdot))\in C([0,T],E)\times\mathcal{R}([0,T],U)$ and since E is separable, it is strongly measurable. We can now rewrite (3.1) in the integral form that we use in the sequel

$$y(t)=S(t)y_0+\int_0^t S(t-s)\mathbf{f}_d(y(s))\gamma(s)\mathrm{d}s,\quad t\in[0,T],\quad y_0\in E, \tag{3.2}$$

the integral being understood as the Lebesgue-Bochner integral. We now prove the analogue of Lemma 2.3.5 in the case of a Banach space.

Lemma 3.2.1. *Assume that (H(L)b) and (H(f)b) are satisfied. Then the mapping*

$$\phi:(z,\gamma)\in\Upsilon\times\mathcal{R}([0,T],U)\to\phi^\gamma_\cdot(z)=S(t)v+\int_0^\cdot S(\cdot-s)\mathbf{f}_d(\phi^\gamma_s(z))\gamma(s)\mathrm{d}s,$$

with $z = (v, d, h)$, is continuous from $\Upsilon \times \mathcal{R}([0,T], U)$ in $C([0,T]; E)$.

Proof. The proof is in the same spirit that the proof of Theorem 2.3.5 and adapted to the case of a Banach space instead of the Hilbert space H by using the arguments of the proof of [Fat94a, Lemma 5.1] for controlled deterministic PDEs. Recall that contrarily to the more general framework of [Fat94a], the space of relaxed controls is here metrizable and we thus work with sequences. Let $t \in [0,T]$ and let $(z,\gamma) \in \Upsilon \times \mathcal{R}([0,T]; U)$. Suppose $(z^n, \gamma^n) \to (z, \gamma)$. Since D is a finite set, we take the discrete topology on it and if we write $z^n = (v^n, d^n, h^n)$ and $z = (v, d, h)$, we have the equality $d^n = d$ for n large enough. So for n large enough we have

$$\begin{aligned}\phi_t^{\gamma_n}(z_n) - \phi_t^{\gamma}(z) &= S(t)v_n - S(t)v + \int_0^t S(t-s)\mathbf{f}_d(\phi_s^{\gamma_n}(z_n))\gamma_n(s)\mathrm{d}s \\ &\quad - \int_0^t S(t-s)\mathbf{f}_d(\phi_s^{\gamma}(z))\gamma(s)\mathrm{d}s \\ &= S(t)v_n - S(t)v + \int_0^t S(t-s)[\mathbf{f}_d(\phi_s^{\gamma_n}(z_n))\gamma_n(s) - \mathbf{f}_d(\phi_s^{\gamma}(z))\gamma_n(s)]\mathrm{d}s \\ &\quad + \int_0^t S(t-s)[\mathbf{f}_d(\phi_s^{\gamma}(z))\gamma_n(s) - \mathbf{f}_d(\phi_s^{\gamma}(z))\gamma(s)]\mathrm{d}s.\end{aligned}$$

From the Lipschitz property of the function f_d we obtain

$$||\phi_t^{\gamma_n}(z_n) - \phi_t^{\gamma}(z)||_E \leq M_S||v_n - v||_E + l_f M_S \int_0^t ||\phi_s^{\gamma_n}(z_n) - \phi_s^{\gamma}(z)||_E \mathrm{d}s + ||\ell_n(t)||_E$$

where $\ell_n(t) := \int_0^t S(t-s)[\mathbf{f}_d(\phi_s^{\gamma}(z))\gamma_n(s) - \mathbf{f}_d(\phi_s^{\gamma}(z))\gamma(s)]\mathrm{d}s$. By the Gronwall lemma there exists a constant $C > 0$ such that

$$||\phi_t^{\gamma_n}(z_n) - \phi_t^{\gamma}(z)||_E \leq C(M_S||v_n - v||_E + \sup_{s\in[0,T]} ||\ell_n(s)||_E).$$

Since $\lim_{n\to+\infty} ||v_n - v||_E = 0$, the proof is complete if we show that the sequence of functions $(||\ell_n||_E)_{n\in\mathbb{N}}$ uniformly converges to 0 on $[0,T]$.

Let us suppose that $(||\ell_n||_E)_{n\in\mathbb{N}}$ does not converge uniformly to 0 and show that this contradicts $\gamma_n \to \gamma$. According to this assumption there exists $\varepsilon > 0$ such that for every $n \in \mathbb{N}$, there exists an integer $p \geq n$ and $t_p \in [0,T]$ satisfying $||\ell_p(t_p)||_E \geq 2\varepsilon$. Since E is reflexive, $||\ell_p(t_p)||_E = ||\ell_p(t_p)||_{E^{**}} = \sup_{y^*\in E^*, ||y^*||_{E^*}=1} \mid \langle y^*, \ell_p(t_p)\rangle_{(E^*,E)} \mid$ so that there exists a sequence (y_p^*) of elements of E^* with $||y_p^*||_{E^*} = 1$ and $\mid \langle y_p^*, \ell_p(t_p)\rangle_{(E^*,E)} \mid \geq \varepsilon$ which can be rewritten as

$$\left| \int_0^T \int_U \langle \mathbf{1}_{s\in[0,t_p]} S^*(t_p - s) y_p^*, f_d(\phi_s^{\gamma}(z), u)\rangle_{(E^*,E)} (\gamma_p - \gamma)(s)(\mathrm{d}u)\mathrm{d}s \right| \geq \varepsilon. \tag{3.3}$$

We will prove the existence of two subsequences, still denoted by (y_p^*) and (t_p), converging respectively to $y^* \in E^*$ and $t \in [0,T]$ and such that

$$\langle \mathbf{1}_{[0,t_p]}(\cdot)S^*(t_p-\cdot)y_p^*, f_d(\phi_\cdot^\gamma(z),\cdot)\rangle_{(E^*,E)} \xrightarrow[p\to\infty]{} \langle \mathbf{1}_{[0,t]}(\cdot)S^*(t-\cdot)y^*, f_d(\phi_\cdot^\gamma(z),\cdot)\rangle_{(E^*,E)} \quad (3.4)$$

in $L^1([0,T];C(Z))$. This, together with (3.3), contradicts the convergence $\gamma_n \to \gamma$ in $\mathcal{R}([0,T],U)$. By the Alaoglu theorem, we can extract a subsequence, still written (y_p^*), E-weakly convergent to some $y^* \in E^*$. Without changing notations, we assume that we have extracted a subsequence of (t_p) which convergences to some $t \in [0,T]$. Then, using the compactness of $(S(t))_{t\geq 0}$ and hence the one of $(S^*(t))_{t\geq 0}$, we obtain the strong convergence of $S^*(\delta)y_p^*$ to $S^*(\delta)y^*$ for every $\delta > 0$. Now for $\delta > 0$ and $r \leq t_p - \delta$,

$$S^*(t_p - r)y_p^* = S^*(t_p - r - \delta)S^*(\delta)y_p^* \xrightarrow[p\to\infty]{} S^*(t - r - \delta)S^*(\delta)y^* = S^*(t-r)y^*$$

strongly in E^*. Taking $\delta \to 0$ we obtain for all $r \in [0,t)$,

$$S^*(t_p - r)y_p^* \xrightarrow[p\to\infty]{} S^*(t-r)y^*. \quad (3.5)$$

Now let $f^* \in C([0,T];E^*)$. Approximating f^* by piecewise constant functions, we deduce that $\Phi_{f^*} : s \mapsto \langle f^*(s), f_d(\phi_s^\mu(z),\cdot)\rangle_{(E^*,E)}$ is a strongly measurable C(Z)-valued function. Moreover, using Assumption (H(f)b)1.,

$$\sup_{u\in Z} |\Phi_{f^*}(s,u)| \leq \beta_c ||f^*(s)||_{E^*}, \qquad s \in [0,T], \quad (3.6)$$

with $c := \sup\{y \in E \mid ||y||_E \leq \max_{s\in[0,T]} ||\phi_s^\mu(z)||_E\}$. This implies that $s \mapsto \Phi_{f^*}(s,\cdot)$ is an element of $L^1([0,T];C(Z))$. We can apply this argument to the following functions

$$\bar{f}_p^*(s) := \mathbf{1}_{s\in[0,t_p]}S^*(t_p - s)y_p^*,$$
$$\bar{f}^*(s) := \mathbf{1}_{s\in[0,t]}S^*(t - s)y^*,$$

and obtain $\sup_{t\in[0,T],u\in Z} |\Phi_{\bar{f}_p^*}(t,u)| \leq K\beta_c$ and $\sup_{t\in[0,T],u\in Z} |\Phi_{\bar{f}^*}(t,u)| \leq K\beta_c$, with $K > 0$ independent of p. From (3.5) we get that $\bar{f}_p^*(s) \xrightarrow[p\to\infty]{} \bar{f}^*(s)$, for every $s \in [0,T]$. By the dominated convergence theorem, we deduce that

$$\Phi_{\bar{f}_p^*} \xrightarrow[p\to\infty]{} \Phi_{\bar{f}^*}$$

in $L^1([0,T];C(Z))$ which is (3.4). As we already observed, this contradicts $\gamma_p \to \gamma$ and it ends the proof. □

The problem that pose nonreflexive Banach spaces is that if $(S(t))_{t\geq 0}$ is a strongly continuous semigroup on E, it does not necessarily imply that the dual semigroup $(S^*(t))_{t\geq 0}$

is strongly continuous on the dual space E^*. In this case, the proof of Lemma 3.2.1 cannot be conducted as before. We can see this on the elementary example of the translation semigroup on the nonreflexive Banach space $L^1(\mathbb{R})$. We formalize this in the next Proposition and recall the proof of the main properties.

Proposition 3.2.1. *The translation semigroup $(S(t))_{t\leq 0}$ defined on $L^1(\mathbb{R})$ by*

$$S(t)f(s) = f(s+t), \quad t \geq 0, s \in \mathbb{R} \quad f \in L^1(\mathbb{R}),$$

is a strongly continuous semigroup of contractions with infinitesimal generator

$$Af(x) = f'(x)$$

and domain $D(A)$ consisting of all absolutely continuous functions $f \in L^1(\mathbb{R})$ with $f' \in L^1(\mathbb{R})$. The adjoint semigroup $(S(t)^*)_{t\leq 0}$ on $L^1(\mathbb{R})^* = L^\infty(\mathbb{R})$ is defined by

$$S(t)^*f(s) = f(s-t), \quad t \geq 0, s \in \mathbb{R} \quad f \in L^1(\mathbb{R}).$$

It is not strongly continuous on $L^\infty(\mathbb{R})$ and the domain of its infinitesimal generator is not dense in $L^\infty(\mathbb{R})$.

Proof. The semigroup proprety, the contraction property, the expression of the infinitesimal generator and its domain are immediate. Le us show that $(S(t))_{t\geq 0}$ is strongly continuous and that $(S(t)^*)_{t\leq 0}$ is not. Let f be a continuous function on $\mathbb{R}$ with compact support $K \subset [a,b] \subset \mathbb{R}$.

$$\lim_{t\downarrow 0} ||S(t)f - f||_\infty = \lim_{t\downarrow 0} \sup_{s\in\mathbb{R}} |f(s+t) - f(s)| = 0,$$

because f is uniformly continuous on $\mathbb{R}$. Now we get

$$||S(t)f - f||_1 = \int_{\mathbb{R}} |S(t)f(s) - f(s)|\mathrm{d}s \leq (b-a+t)||S(t)f - f||_\infty,$$

and thus

$$\lim_{t\downarrow 0} ||S(t)f - f||_1 = 0.$$

The strong continuity on $L^1(\mathbb{R})$ follows from the density of continuous functions with compact support in $L^1(\mathbb{R})$.
Regarding the adjoint semigroup, it is immediate to see that

$$||S(t)^*\mathbf{1}_{\mathbb{R}_+} - \mathbf{1}_{\mathbb{R}_+}||_{L^\infty(\mathbb{R})} = \sup_{s\in\mathbb{R}} |\mathbf{1}_{\mathbb{R}_+}(s-t) - \mathbf{1}_{\mathbb{R}_+}(t)| = 1,$$

with $\mathbf{1}_{\mathbb{R}_+} \in L^\infty(\mathbb{R})$ the characteristic function of $[0,\infty)$.

□

To tackle this problem, Phillips introduced the *Phillips dual* of a Banach space E and the *Phillips adjoint* of a semigroup on E ([Phi55]). The following definition, Lemma 3.2.2 and Proposition 3.2.2 can be found in [EN00, Section 2.6 p62].

Definition 3.2.1. *Let $(S(t))_{t\geq 0}$ be a strongly continuous semigroup on E, with infinitesimal generator A. We define the Phillips dual $E^{\odot}$ of E by*

$$E^{\odot} := \{y^* \in E^* | \lim_{t\downarrow 0} ||S(t)^* y^* - y^*||_{E^*} = 0\}$$

and we call the semigroup given by the restricted operators

$$S^{\odot}(t) := S(t)^*_{|E^{\odot}}, \quad (t \geq 0),$$

the Phillips semigroup. We will denote by $A^{\odot}$ its infinitesimal generator

The Phillips semigroup is strongly continuous and $E^{\odot}$ is a closed subspace of E^*. It is important to note that the Phillips dual characterizes the couple (E, A) and note just the Banach space E itself. That is why the Phillips dual is always referred to with respect to A. Furthermore, if E is reflexive, the Phillips dual $E^{\odot}$ and the dual E^* coincide for any strongly continuous semigroup (since then the adjoint semigroup is strongly continuous in E^*). The next lemma shows that the Phillips dual is large, in the sens that it contains the domain of A^*, the adjoint operator of A. The proposition that follows characterizes the relation between $A^{\odot}$ and A^*.

Lemma 3.2.2. $D(A^*) \subset E^{\odot}$

Proof. Let $y^* \in D(A^*)$ and $x \in E$. Then

$$\begin{aligned}
\left|\langle S(t)^* y^* - y^*, x\rangle_{(E^*,E)}\right| &= \left|\langle y^*, S(t)x - x\rangle_{(E^*,E)}\right| \\
&= \left|\langle y^*, A\int_0^t S(s)x\mathrm{d}s\rangle_{(E^*,E)}\right| \\
&= \left|\langle A^* y^*, \int_0^t S(s)x\mathrm{d}s\rangle_{(E^*,E)}\right| \\
&\leq tM_S||x||_E||A^* y^*||_{E^*},
\end{aligned}$$

and thus

$$||S(t)^* y^* - y^*||_{E^*} \leq tM_S||A^* y^*||_{E^*} \underset{t\downarrow 0}{\longrightarrow} 0,$$

so that $y^* \in E^{\odot}$.

□

Proposition 3.2.2. *The infinitesimal generator $A^{\odot}$ of the strongly continuous semigroup $(S^{\odot}(t))_{t\geq 0}$ is the part of A^* in $E^{\odot}$, that is,*

$$A^{\odot}y^* = A^*y^* \text{ for } y^* \in D(A^{\odot}) = \{y^* \in D(A^*) \mid A^*y^* \in E^{\odot}\}.$$

Moreover, $E^{\odot} = \overline{D(A^*)}$.

Proof. Since the weak* topology on E^* is weaker than the norm topology, A^* is an extension of $A^{\odot}$. Furthermore, if $y^* \in D(A^*)$ such that $A^*y^* \in E^{\odot}$, since A^* is weakly* closed, we obtain from [EN00, Lemma 1.3 p50] that

$$S^{\odot}(t)y^* - y^* = A^* \int_0^t S^{\odot}(s)y^* \mathrm{d}s = \int_0^t S^{\odot}(s)A^*y^* \mathrm{d}s, \quad (t > 0).$$

Now, from the norm continuity of $s \to S^{\odot}(s)A^*y^*$, we obtain

$$||\frac{1}{t}(S^{\odot}(t)y^* - y^*) - A^*y^*||_{E^*} \leq \frac{1}{t}\int_0^t ||S^{\odot}(s)A^*y^* - A^*y^*||_{E^*} \mathrm{d}s \underset{t\downarrow 0}{\longrightarrow} 0,$$

and thus $y^* \in D(A^{\odot})$. Finally, since $D(A^{\odot})$ is dense in $E^{\odot}$ (as the infinitesimal generator of a strongly continuous semigroup on $E^{\odot}$), we get

$$E^{\odot} = \overline{D(A^*)}.$$

□

For the translation semigroup, $E^{\odot}$ consists of all uniformly continuous functions $f \in L^{\infty}(\mathbb{R})$ and $D(A^{\odot})$ consists of all continuously differentiable functions $f \in E^{\odot}$ with bounded uniformly continuous derivative f'.

We can define an equivalent norm of $||\cdot||_E$ that involves the Phillips dual $E^{\odot}$. For $y \in (E)$ we define

$$||y||_0 := \sup_{y^* \in E^{\odot}, ||y^*||_{E^*} \leq 1} |\langle y^*, y\rangle|.$$

Then we obtain ([Fat99, Lemma 7.4.6]) $||y||_E \leq ||y||_0 \leq M_S||y||_E$ with M_S defined in (H(L)b). Now, in the case where the semigroup $(S(t)_{t\geq 0})$ is immediately norm continuous (as for instance the Laplacian in C([0,1])), we can show that

$$S(t)^*E^* \subset E^{\odot} \qquad (t \geq 0), \tag{3.7}$$

$$S(s+t)^* = S^{\odot}(s)S(t)^* \qquad (s \geq 0, t > 0). \tag{3.8}$$

Indeed, in this case, the adjoint semigroup $(S(t)^*_{t\geq 0})$ is also immediately norm continuous so that for every $t > 0$ and $y^* \in E^*$, $s \to S(s)^*S(t)^*y^* = S(s+t)^*y^*$ is continuous in

$[0,\infty)$ and thus $S(t)^*y^* \in E^\odot$. Now for $y^* \in E^*$, $s \geq 0$ and $t > 0$, since $S(t)^*y^* \in E^\odot$ and $S^\odot(s)$ is the restriction of $S(s)^*$ to $E^\odot$ we get $S(s+t)^*y^* = S(s)^*S(t)^*y^* = S^\odot(s)S(t)^*y^*$.

Now, since $(S^\odot(t))_{t\geq 0}$ is a strongly continuous semigroup in $E^\odot$ we can apply the Phillips adjoint theory and define the double Phillips adjoint semigroup $(S^{\odot\odot}(t) = (S^\odot)^\odot(t))_{t\geq 0}$ as the restriction of the adjoint semigroup $(S^\odot(t)^*)_{t\geq 0}$ to the closure $E^{\odot\odot} = (E^\odot)^\odot$ of $D((A^\odot)^*)$ in $(E^\odot)^*$. We now recall [Fat99, Lemma 7.7.1] and its proof.

Lemma 3.2.3. *a) Up to a change of equivalent norm, there exists a bicontinuous linear imbedding from E into $E^{\odot\odot}$, that is*

$$E \subset E^{\odot\odot}. \tag{3.9}$$

b) We have

$$A \subset A^{\odot\odot}, \qquad S(t) \subset S^{\odot\odot}(t), \quad (t > 0), \tag{3.10}$$

in the sense that if $(y_1, y_2) \in D(A) \times E$, then $(y_1, y_2) \in D(A^{\odot\odot}) \times E^{\odot\odot}$ and $Ay_1 = A^{\odot\odot}y_1$ and $S(t)y_2 = S^{\odot\odot}y_2$.

Proof. The equivalence of the norms $||\cdot||_E$ and $||\cdot||_0$ proves that $E \subset (E^\odot)^*$. Now, for $(y, y^*) \in D(A) \times D(A^\odot)$, we have $\langle A^\odot y^*, y\rangle = \langle A^*y^*, y\rangle = \langle y^*, Ay\rangle$ so that $y \in D((A^\odot)^*)$ and $(A^\odot)^*y = Ay$. This implies that $D(A) \subset E^{\odot\odot}$ and since $D(A)$ is dense in E we obtain (3.9). If $y \in D(A)$ we have $(A^\odot)^*y = Ay \in E \subset E^{\odot\odot}$ and thus $(A^\odot)^*y = A^{\odot\odot}y$. Finally, for $y \in E$, $y^* \in E^\odot$ and $t \geq 0$ we have $\langle y^*, S(t)y\rangle = \langle S^\odot(t)y^*, y\rangle = \langle y^*, S^{\odot\odot}(t)y\rangle$ since $y \in E^{\odot\odot}$ also. □

The case we are interested in is when the nonreflexive space E is nevertheless $\odot$-reflexive in the sense that (3.9) is in fact an equality $E = E^{\odot\odot}$. In this case, it is immediate to see that $A = A^{\odot\odot}$ and $S(t) = S^{\odot\odot}(t)$ for $t > 0$. In the $\odot$-reflexive case with immediately norm continuous semigroup, noting that $(S^\odot(t))_{t\geq 0}$ is as well immediately norm continuous, we can apply (3.8) and (3.7) to $(S^\odot(t))_{t\geq 0}$ and use the $\odot$-reflexivity to obtain

$$S^\odot(t)^*(E^\odot)^* \subset E, \qquad S^\odot(s+t)^* = S(s)S^\odot(t)^*, \quad (s \geq 0, t > 0). \tag{3.11}$$

Now let Ω be a bounded domain of class C^2 in $\mathbb{R}^m$, with boundary Γ. We look at the special case of elliptic operators, that generate analytic, and thus immediately norm continuous semigroups in the nonreflexive Banach space $C(\Omega)$, and for which $C(\Omega)$ is $\odot$-reflexive. The next results are valid for elliptic operators defined by

$$Ly = \sum_{j=1}^m \sum_{k=1}^m \partial^j(a_{jk}(x)\partial^k y) + \sum_{j=1}^m b_j(x)\partial^j y + c(x)y,$$

with a_{jk} and b_j continuously differentiable in Ω and c continuous in $\overline{\Omega}$ with either Dirichlet boundary condition $y(x) = 0$ $(x \in \Gamma)$ or variational boundary condition $\partial^\nu y(x) = \gamma(x)y(x)$ $x \in \Gamma$, where ∂^ν is the derivative in the direction of the conormal vector $\nu_j(x) = \sum_{k=1}^m a_{jk}(x)\eta_k(x)$ with η the outer normal vector.

As mention in the beginning of this Section, we now focus on the Laplacian in $C([0,1])$ with variational boundary condition $\beta : y'(0) = y'(1) = 0$. The next Theorem is the general result [Fat99, Theorem 7.6.3] written in our particular case.

Theorem 3.2.1. *There exists an operator Δ_c that can be characterized in any of the two equivalent forms:*
Strong form:

$$D(\Delta_c) = \left\{ y \in \bigcap_{p\geq 1} W^{2,p}_\beta(0,1) \mid y'' \in C([0,1]) \right\} \tag{3.12}$$

and $\Delta_c y = y''$ with $W^{2,p}_\beta(0,1)$ constituted of the functions of the Sobolev space $W^{2,p}(0,1)$ that satisfy the variational boundary condition β.
Weak form: *$D(\Delta_c)$ consists of all elements $y \in C([0,1])$ such that there exists $z(= \Delta_c y)$ in $C([0,1])$ with*

$$\int_0^1 y(x)v''(x)\mathrm{d}x = \int_0^1 z(x)v(x)\mathrm{d}x \tag{3.13}$$

for every $v \in C^2([0,1])$ with $v'(0) = v'(1) = 0$.
The operator $(\Delta_c, D(\Delta_c))$ generates an immediately compact analytic semigroup of contractions in $C([0,1])$.

Proof. This particular case of [Fat99, Theorem 7.6.3] admits a nicer expression of the domain $D(\Delta_c)$ and we will be able give the expression of the semigroup generated by Δ_c. Indeed, it easy to realize that

$$D(\Delta_c) = \left\{ y \in C^2([0,1]) \mid y'(0) = y'(1) = 0 \right\}.$$

The proof of [Fat99, Theorem 7.6.3] for the Laplacian becomes an exercice that can be found in [EN00]. Since the entire correction is not given in the book, we now proceed to the proof.

$(\Delta_c, D(\Delta_c))$ generates a strongly continuous semigroup in $C([0,1])$

The domain $D(\Delta_c)$ is a subalgebra of $C([0,1])$ ($(fg)'(x) = f'(x)g(x) + f(x)g'(x) = 0$ for $x = 0,1$). $D(\Delta_c)$ contains constant functions and it separates the points of $[0,1]$ so that by the Stone-Weierstrass theorem, $D(\Delta_c)$ is a dense subspace of $C([0,1])$. There is no difficulty in showing that $D(\Delta_c)$ is complete for the graph norm $||\cdot||_{\Delta_c}$ defined by $||y||_{\Delta_c} = ||y||_\infty + ||y''||_\infty$. This means that $(\Delta_c, D(\Delta_c))$ is a closed, densely defined operator. We can give an explicit expression of the semigroup $(S(t))_{t\geq 0}$ on $C([0,1])$, generated by $(\Delta_c, D(\Delta_c))$. Indeed, consider for each $n \in \mathbb{N}$

$$s \to e_n(s) := \begin{cases} 1 & \text{if } n = 0, \\ \sqrt{2}\cos(\pi n s) & \text{if } n \geq 1. \end{cases}$$

These functions all belong to $D(\Delta_c)$ and satisfy

$$\Delta_c e_n = -\pi^2 n^2 e_n.$$

Now let F be the linear space generated by those functions, $F := \text{vect}\{e_n, n \in \mathbb{N}\}$. Since

$$e_n e_m = \begin{cases} e_m & \text{if } n = 0, \\ e_n & \text{if } m = 0, \\ \frac{\sqrt{2}}{2}(e_{n+m} + e_{n-m}) & \text{if } n, m \geq 1, \end{cases}$$

it is easy to see that the Stone-Weierstraas theorem applies again to F, so that it is a dense subalgebra of $C([0,1])$. Consider now, for $n \in \mathbb{N}$, the operator

$$e_n \otimes e_n : y \to \langle y, e_n \rangle e_n := \left(\int_0^1 y(s) e_n(s) \mathrm{d}s \right) e_n,$$

which satisfies

$$||e_n \otimes e_n|| \leq 2$$

and

$$(e_n \otimes e_n) e_m = \delta_{n,m} e_m \tag{3.14}$$

for all $(n,m) \in \mathbb{N}^2$, with $\delta_{n,m} = 0$ if $n \neq m$ and $\delta_{n,n} = 1$. For $t > 0$ we assert that

$$S(t) = \sum_{n=0}^{\infty} e^{-\pi^2 n^2 t} e_n \otimes e_n. \tag{3.15}$$

Indeed, let $T(t) := \sum_{n=0}^{\infty} e^{-\pi^2 n^2 t} e_n \otimes e_n$ for $t > 0$. Then for $f \in C([0,1])$ and $s \in [0,1]$,

$$\begin{aligned} (T(t)y)(s) &= \int_0^1 y(r)\mathrm{d}r + 2\sum_{n=1}^{\infty} e^{-\pi^2 n^2 t} \cos(n\pi s) \int_0^1 y(r)\cos(n\pi r)\mathrm{d}r \\ &= \int_0^1 k_t(s,r) y(r) \mathrm{d}r, \end{aligned}$$

by the Fubini theorem with

$$\begin{aligned} k_t(s,r) &= 1 + 2\sum_{n=1}^{\infty} e^{-\pi^2 n^2 t}\cos(n\pi s)\cos(n\pi r) \\ &= 1 + \sum_{n=1}^{\infty} e^{-\pi^2 n^2 t}(\cos(n\pi(s+r)) + \cos(n\pi(s-r))) \\ &= w_t(s+r) + w_t(s-r), \end{aligned}$$

if we write $w_t(s) := \frac{1}{2} + \sum_{n=1}^{\infty} e^{-\pi^2 n^2 t}\cos(n\pi s)$. It is easy to prove that $k_t(\cdot,\cdot)$ is continuous on $[0,1]^2$. It is less obvious that this function is also positive on $[0,1]^2$. To prove this we are going to show the nice formula given in [EN00] without a proof

$$\frac{1}{2} + \sum_{n=1}^{\infty} e^{-\pi^2 n^2 t}\cos(n\pi s) = \frac{1}{\sqrt{4\pi t}}\sum_{n\in\mathbb{Z}} e^{-\frac{(s+2n)^2}{4t}}. \tag{3.16}$$

This formula can be derived from the Poisson summation formula

$$\sum_{n\in\mathbb{Z}} f(x+n) = \sum_{n\in\mathbb{Z}} \hat{f}(n)e^{2i\pi nx} \tag{3.17}$$

where the function $f : \mathbb{R} \to \mathbb{R}$ is of class C^1 and such that

$$f(x) = O\left(\frac{1}{x^2}\right) \quad (|x| \to \infty), \qquad f'(x) = O\left(\frac{1}{x^2}\right) \quad (|x| \to \infty),$$

and $\hat{f}$ is the Fourier transform of f, *i.e.* $\hat{f}(n) = \int_{-\infty}^{+\infty} f(t)e^{-2i\pi nt}\mathrm{d}t$. Before proving (3.16), we briefly recall the proof of the Poisson summation formula (3.17). Define $\varphi(x) := \sum_{n=-\infty}^{+\infty} f(x+n)$. The function φ is a 1-periodic function and because of the assumptions on f and f', it is easy to show that φ is of class C^1 on $\mathbb{R}$. The Fourier series of φ thus converges normaly on $\mathbb{R}$ with sum φ

$$\varphi(x) = \sum_{n\in\mathbb{Z}} c_n(\varphi)e^{2i\pi nx}, \quad (x \in \mathbb{R}),$$

with

$$\begin{aligned} c_n(\varphi) = \int_0^1 \varphi(t)e^{-2i\pi nt}\mathrm{d}t &= \int_0^1 \sum_{n=-\infty}^{+\infty} f(t+n)e^{-2i\pi nt}\mathrm{d}t \\ &= \sum_{n=-\infty}^{+\infty} \int_0^1 f(t+n)e^{-2i\pi nt}\mathrm{d}t \end{aligned}$$

$$
\begin{aligned}
&= \sum_{n=-\infty}^{+\infty} \int_n^{n+1} f(t)e^{-2i\pi nt}\mathrm{d}t \\
&= \int_{-\infty}^{+\infty} f(t)e^{-2i\pi nt}\mathrm{d}t \\
&= \hat{f}(n),
\end{aligned}
$$

the inversion of $\sum$ and $\int$ being justified by the Fubini theorem.

We apply this formula to the function $f : x \to e^{-\alpha x^2}$ with $\alpha > 0$. We need to compute the Fourier transform of f, which constitute a classical exercise. Define $I(x) := \int_{-\infty}^{+\infty} e^{-\alpha t^2} e^{-2i\pi tx}\mathrm{d}t$ for $x \in \mathbb{R}$, so that $\hat{f}(n) = I(n)$. The function under the integral is of class C^∞ and its derivative is dominated by the integrable function $t \to 2\pi t e^{-\alpha t^2}$ so that I is of class C^1 and

$$
\begin{aligned}
I'(x) &= \frac{i\pi}{\alpha} \int_{-\infty}^{+\infty} -2\alpha t e^{-\alpha t^2} e^{-2i\pi tx} dt \\
&= \frac{i\pi}{\alpha} \left(e^{-\alpha t^2} e^{-2i\pi tx} \Big|_{-\infty}^{+\infty} + 2i\pi x I(x) \right) \\
&= -\frac{2\pi^2}{\alpha} x I(x).
\end{aligned}
$$

We thus obtain $I(x) = I(0)e^{-\frac{\pi^2 x^2}{\alpha}}$ with $I(0) = \int_{-\infty}^{+\infty} e^{-\alpha t^2}\mathrm{d}t = \sqrt{\pi/\alpha}$. From the Poisson summation formula we get

$$
\begin{aligned}
\sum_{n\in\mathbb{Z}} e^{-\alpha(x+n)^2} &= \sqrt{\frac{\pi}{\alpha}} \sum_{n\in\mathbb{Z}} e^{-\frac{\pi^2 n^2}{\alpha}} e^{2i\pi nx} \\
&= \sqrt{\frac{\pi}{\alpha}} \left(1 + \sum_{n=1}^{\infty} \frac{\pi^2 n^2}{\alpha} \left(e^{2i\pi nx} + e^{-2i\pi nx} \right) \right) \\
&= \sqrt{\frac{\pi}{\alpha}} \left(1 + 2\sum_{n=1}^{\infty} \frac{\pi^2 n^2}{\alpha} \cos(2\pi nx) \right) \\
&= \sqrt{\frac{4\pi}{\alpha}} w_{1/\alpha}(2x).
\end{aligned}
$$

We finally obtain (3.16) by taking $\alpha = 1/t$ and $x = s/2$. Now, the fact that, for every $t > 0$, the function $k_t(\cdot, \cdot)$ is positive makes the computation of the norm of the operator $T(t)$ very easy. Indeed, for $t > 0$ and $y \in C([0, 1])$,

$$
||(T(t)y)||_{C([0,1])} = \sup_{s\in[0,1]} | \int_0^1 k_t(s, r)y(r)\mathrm{d}r| \leq ||y||_{C([0,1])} \sup_{s\in[0,1]} \int_0^1 |k_t(s, r)|\mathrm{d}r.
$$

But $\int_0^1 |k_t(s,r)|\mathrm{d}r = \int_0^1 k_t(s,r)\mathrm{d}r$ for all $s \in [0,1]$ and the bound is reached for $g \in C([0,1])$ defined for $s \in [0,1]$ by $g(s) = 1$. Finally, for all $s \in [0,1]$, $\int_0^1 k_t(s,r)\mathrm{d}r = 1$ and we get

$$|||T(t)||| = 1 \tag{3.18}$$

for all $t > 0$. There is no difficulty in showing that for $(t,s) \in \mathbb{R}_+^2$ and $n \in \mathbb{N}$, $T(t+s)e_n = T(t)T(s)e_n$ so that by continuity of the operators and the density of F in E, the semigroup property is valid on E. The strong continuity of the semigroup on F is easy because :

$$\begin{aligned} T(t)e_0 &= e_0 \text{ for all } t \geq 0 \\ T(t)e_n &= e^{-\pi^2 n^2 t} e_n \text{ for all } t \geq 0, n \in \mathbb{N}^*. \end{aligned}$$

Since the semigroup is bounded, the strong continuity extends to E (see [EN00] Proposition 5.3).

Let B be the infinitesimal generator of $(T(t))_{t\geq 0}$. We now prove that Δ_c and B coincide, thus justifying equality (3.15), and that Δ_c generates a strongly continuous semigroup of contractions. For $n \in \mathbb{N}$, $T(t)e_n = e^{-\pi^2 n^2 t} e_n$ so that $e_n \in D(B)$ and

$$\frac{T(t)e_n - e_n}{t} = \frac{e^{-\pi^2 n^2 t} - 1}{t} e_n \xrightarrow[t \to 0^+]{} -\pi^2 n^2 e_n, \quad \text{in } C([0,1]).$$

The dense subalgebra F is thus contained in $D(B)$, $(T(t))_{t\geq 0}$-invariant, and Δ_c and B coincide on F. This implies that F is a core for B (Definition 3.2.2 below) so that $B = \overline{B_{|F}}$ and since Δ_c and B coincide on F, we get $B = \overline{\Delta_{c|F}}$ (see [EN00, Proposition 1.7 p53]). In particular, B is a restriction of Δ_c.

Definition 3.2.2. *Let X be a Banach space. A subspace D of the domain $D(A)$ of a closed linear operator $A : D(A) \subset X \to X$ is called a core for A if D is dense in $D(A)$ for the graph norm and then $A = \overline{A_{|D}}$.*

We now show that $1 \in \rho(\Delta_c) \cap \rho(B)$ to conclude that $\Delta_c = B$ and thus the semigroups $(S(t))_{t\geq 0}$ and $(T(t))_{t\geq 0}$ coincide ($\rho(\Delta_c)$ is the resolvent set of Δ_c, *i.e.* the set of all $\lambda \in \mathbb{C}$ such that the operator $\lambda - \Delta_c : D(\Delta_c) \to C([0,1])$ is bijective). For $g \in C([0,1])$, the function

$$t \to -\int_0^t \mathrm{sh}(t-s)g(s)\mathrm{d}s + \lambda\,\mathrm{ch}(x),$$

with $\lambda = (\int_0^1 \mathrm{ch}(1-s)g(s)\mathrm{d}s)/\,\mathrm{sh}(1)$ is the unique solution in $D(\Delta_c)$ of $(1-\Delta_c)f = g$ so that $1 - \Delta_c : D(\Delta_c) \to C([0,1])$ is bijective.
Now for $s \in [0,1]$ and $y \in C([0,1])$,

$$\int_0^\infty e^{-t}(T(t)y)(s)\mathrm{d}t = \int_0^\infty e^{-s}\int_0^1 y(r)\mathrm{d}r\mathrm{d}s \\ + 2\int_0^\infty \sum_{n=1}^\infty e^{-(\pi^2 n^2+1)t}\cos(n\pi s)\int_0^1 y(r)\cos(n\pi r)\mathrm{d}r\mathrm{d}t,$$

and there is no difficulty to show that $s \to \int_0^\infty e^{-t}(T(t)y)(s)\mathrm{d}t$ belongs to $C([0,1])$. By [EN00, Theorem 1.10 p55], it implies that $1 \in \rho(B)$.

We now show the immediate compacity of the semigroup, equivalently ([EN00, Theorem 4.29 p119]) the joined immediate norm continuity of the semigroup and the compacity of the resolvent of its generator.
Let $t > 0$, $s > 0$, and $y \in C([0,1])$,

$$((T(t) - T(s))y)(x) = 2\sum_{n=1}^\infty \left(e^{-\pi^2 n^2 t} - e^{-\pi^2 n^2 s}\right)\cos(n\pi x)\int_0^1 y(r)\cos(n\pi r)\mathrm{d}r,$$

so that

$$||(T(t) - T(s))y||_{C([0,1])} \leq 2||y||_{C([0,1])}\sum_{n=1}^\infty \left|e^{-\pi^2 n^2 s} - e^{-\pi^2 n^2 t}\right|.$$

The function $s \to e^{-\pi^2 n^2 s} - e^{-\pi^2 n^2 t}$ is continuous in $(0,+\infty)$ for every $n \in \mathbb{N}$ and $\sup_{s>t} \mid e^{-\pi^2 n^2 s} - e^{-\pi^2 n^2 t} \mid\leq e^{-\pi^2 n^2 t}$ so that

$$|||(T(t) - T(s))||| \underset{s\downarrow t}{\longrightarrow} 0.$$

Furthermore, $\sup_{s\in(t/2,t)} \mid e^{-\pi^2 n^2 s} - e^{-\pi^2 n^2 t} \mid\leq e^{-\pi^2 n^2 t/2}$ and so

$$|||(T(t) - T(s))||| \underset{s\uparrow t}{\longrightarrow} 0$$

as well. We can remark here that the argument fails in the case where $t = 0$. Otherwise it would mean that the semigroup is quite trivial (exponential semigroup with bounded generator).

The semigroup $(S(t))_{t\geq 0}$ is immediately compact

From [EN00, Proposition 4.25 p117], the compacity of the resolvent of Δ_c is equivalent to the compacity of the canonical injection $i : (D(\Delta_c), ||\cdot||_{\Delta_c}) \hookrightarrow E$. To show the compacity of the injection, let D be a bounded subset of $D(\Delta_c)$. There exists $M > 0$ such that $||y||_{C([0,1])} + ||y''||_{C([0,1])} \leq M$ for all $y \in D$. Now for $y \in D$ and $(s,t) \in [0,1]^2$, one has

$$\begin{cases} y'(t) = \int_0^t y''(x)\mathrm{d}x, \\ y(t) - y(s) = \int_s^t y'(x)\mathrm{d}x, \end{cases}$$

so that

$$\begin{cases} |y'(t)| \leq M, \\ |y(t) - y(s)| \leq M(t-s), \end{cases}$$

the last inequality giving the equicontinuity in D. The compacity then follows from the Arzéla-Ascoli theorem.

The semigroup $(S(t))_{t\geq 0}$ is analytic

We finish the proof with the analyticity of $(\Delta_c, D(\Delta_c))$. We recall the proof of [EN00, Theorem 4.5 p389] that asserts that $(\Delta_c, D(\Delta_c))$ generates an analytic semigroup of angle $\pi/2$. We prove that $(\Delta_c, D(\Delta_c))$ is a sectorial operator of angle $\pi/2$, that is, the sector

$$\Sigma_\pi := \{\lambda \in \mathbb{C} \mid |\arg(\lambda)| < \pi\} \setminus \{0\}$$

is contained in the resolvent set $\rho(\Delta_c)$ and for each ε $(0, \pi/2)$, there exists $M_\varepsilon \geq 1$ such that

$$|||(\lambda - \Delta_c)^{-1}||| \leq \frac{M_\varepsilon}{|\lambda|} \quad \text{for all } 0 \neq \lambda \in \overline{\Sigma}_{\pi-\varepsilon}. \tag{3.19}$$

Let $\lambda \in \Sigma_\pi$ and define $\mu \in \mathbb{C}$ such that $\lambda = \mu^2$ with $\mathrm{Re}\mu > 0$. We also write $\lambda = |\lambda|e^{i\theta}$. We are going to show that $\lambda \in \rho(\Delta_c)$, i.e. $\forall f \in C([0,1])$, $\exists!\, v \in D(\Delta_c)$, $\lambda v - v'' = f$. Define for $f \in C([0,1])$

$$\begin{aligned} u(x) &:= \frac{1}{2\mu}\int_0^1 e^{-\mu|x-s|} f(s)\mathrm{d}s, \quad x \in [0,1] \\ &= \frac{1}{2\mu}\left(\int_0^x e^{-\mu(x-s)} f(s)\mathrm{d}s + \int_x^1 e^{-\mu(s-x)} f(s)\mathrm{d}s\right) \end{aligned}$$

The function u is of class C^∞ on $[0,1]$ and we have for $x \in [0,1]$

$$u'(x) = \frac{1}{2}\left(-\int_0^x e^{-\mu(x-s)} f(s)\mathrm{d}s + \int_x^1 e^{-\mu(s-x)} f(s)\mathrm{d}s\right)$$

and

$$u''(x) = -f(x) + \mu^2 u(x).$$

The function u is thus a C^2-solution of the equation $\lambda u - u'' = f$ and moreover, it satisfies

$$||u||_{C([0,1])} \leq \frac{||f||_{C([0,1])}}{|\lambda|\cos(\theta/2)}.$$

The function u does not belong to $D(\Delta_c)$ and we now want to compute the solution v of the same equation that belongs to $D(\Delta_c)$ so that $v = (\lambda - \Delta_c)^{-1}f$. Let us thus write $v(x) := c_1 e^{\mu x} + c_2 e^{-\mu x} + u(x)$ a general solution of the equation. For $x \in [0,1]$

$$v'(x) = \mu(c_1 e^{\mu x} - c_2 e^{\mu x}) + \frac{1}{2}\left(-\int_0^x e^{-\mu(x-s)} f(s)\mathrm{d}s + \int_x^1 e^{-\mu(s-x)} f(s)\mathrm{d}s\right),$$

so that

$$v'(0) = \mu(c_1 - c_2) + \frac{1}{2}\int_0^1 e^{-\mu s} f(s)\mathrm{d}s,$$

and

$$v'(1) = \mu(c_1 e^{\mu} - c_2 e^{-\mu}) - \frac{1}{2}\int_0^1 e^{-\mu(1-s)} f(s)\mathrm{d}s.$$

This yields the system

$$\begin{cases} c_1 - c_2 + \gamma_0 = 0, \\ c_1 e^{\mu} - c_2 e^{-\mu} + \gamma_1 = 0, \end{cases}$$

with $\gamma_0 := \frac{1}{2\mu}\int_0^1 e^{-\mu s} f(s)\mathrm{d}s$ and $\gamma_0 := -\frac{1}{2\mu}\int_0^1 e^{-\mu(1-s)} f(s)\mathrm{d}s$. We thus obtain a unique solution $c_2 = \frac{\gamma_0 e^{\mu} - \gamma_1}{e^{\mu} - e^{-\mu}}$ and $c_1 = c_2 - \gamma_0$ since it is easy to check that $e^{\mu} - e^{-\mu} \neq 0$. We now prove the bound (3.19). Let $\varepsilon > 0$ and $\lambda \in \overline{\Sigma}_{\pi-\varepsilon}$. We write $\lambda = \mu^2 = |\lambda| e^{i\theta}$ as before. An easy estimation yields

$$|\gamma_0|, |\gamma_1| \leq \frac{||f||_{C([0,1])}}{2|\mu|\mathrm{Re}(\mu)}.$$

Since $|\theta| \leq \pi - \varepsilon$ and $\mathrm{Re}(\mu) = |\mu||\cos(\theta/2)|$, we have $\mathrm{Re}(\mu) \geq |\mu|\cos((\pi-\varepsilon)/2)$ and thus

$$|\gamma_0|, |\gamma_1| \leq \frac{||f||_{C([0,1])}}{2|\lambda|\cos((\pi-\varepsilon)/2)}.$$

Let $x \in [0,1]$,

$$v(x) = \frac{e^{-\mu}\gamma_0 - \gamma_1}{e^{\mu} - e^{-\mu}} e^{\mu x} + \frac{e^{\mu}\gamma_0 - \gamma_1}{e^{\mu} - e^{-\mu}} e^{-\mu x} + u(x),$$

and thus

$$||v|| \leq \frac{|\gamma_0| + e^{\mathrm{Re}(\mu)}|\gamma_1|}{|e^{\mu} - e^{-\mu}|} + \frac{|\gamma_0| + |\gamma_1|}{|e^{\mu} - e^{-\mu}|} + \frac{||f||_{C([0,1])}}{|\lambda| \cos((\pi - \varepsilon)/2)}.$$

Finally, since $e^{\mathrm{Re}(\mu)}/(|e^{\mu} - e^{-\mu|}) = 1/|1 - e^{-2\mu}| \xrightarrow[|\mu|\to\infty]{} 1$ and $1/(|e^{\mu} - e^{-\mu|}) \xrightarrow[|\mu|\to\infty]{} 0$, we can find a constant $M_\varepsilon > 0$ such that

$$||v|| \leq \frac{||f||_{C([0,1])} M_\varepsilon}{|\lambda|},$$

for $|\lambda|$ large enough. This ends the proof.

□

We now come back to the Phillips dual of $C([0,1])$ with respect to Δ_c. The next proposition is a summary of [Fat99, Theorem 7.6.2, Theorem 7.6.5, Theorem 7.6.6] in the case of Δ_c.

Proposition 3.2.3. *The space $C([0,1])$ is $\odot$-reflexive with respect to Δ_c and we have*

$$C([0,1])^{\odot} = L^1(0,1),$$

and

$$\Delta_c^{\odot} = \Delta_1, \qquad S^{\odot}(t) = S_1(t) \quad (t \geq 0),$$

with Δ_1 the infinitesimal generator of an immediately compact analytic semigroup $(S_1(t))_{t\geq 0}$ defined on the domain $D(\Delta_1)$ consisting of elements $y \in L^1([0,1])$ such that there exists $z(= \Delta_1 y)$ in $L^1([0,1])$ with

$$\int_0^1 y(x)v''(x)\mathrm{d}x = \int_0^1 z(x)v(x)\mathrm{d}x \tag{3.20}$$

for every $v \in C^2([0,1])$ with $v'(0) = v'(1) = 0$.

Proof. The part of the proof on the definition of the Laplacian in $L^1(0,1)$ and the semigroup it generates can be found [Fat83, Theorem 4.8.3]. Let us just mention that Δ_1 is the closure in $L^1(0,1)$ of Δ_c. The part of the proof regarding the Phillips dual can be found in [Fat83, Theorem 4.8.17] in a more general setting and the analycity in [Fat83, Theorem 4.9.3]. Here we go through the main steps of the proof regarding the Phillips dual, in the case of the Laplacian with Dirichlet boundary condition, which is easier than the variational boundary condition. The proof holds for variational boundary condition by means of a renorming of the space (see [Fat83, Theorem 4.9.3]). We thus have

$$D(\Delta_c) = \left\{ y \in C^2([0,1]) \mid y(0) = y(1) = 0 \right\}.$$

We are going to show that the Phillips dual of $C_0([0,1]) := \{y \in C([0,1]) \mid y(0) = y(1) = 0\}$ with respect to Δ_c is $L_1(0,1)$. The dual of $C_0([0,1])$ is the space of functions of bounded variation, that vanish at 0 and 1, that we denote by $BV([0,1])$.
Now let $\nu \in BV([0,1])$ and define a continuous linear functional Φ in $W^{1,2}(0,1)$ by

$$\Phi(y) = \int_0^1 y(x)\nu(\mathrm{d}x).$$

The Sobolev space $W^{1,2}(0,1)$ is continuously embedded in $C([0,1])$ ([Eva98, Theorem 5 p269]) in the sense that there exists a constant $C > 0$ such that for every $y \in W^{1,2}(0,1)$ there exists a version $\tilde{y} \in C([0,1])$ of y that satisfies

$$||\tilde{y}||_{C([0,1])} \leq C||y||_{W^{1,2}(0,1)},$$

and thus

$$|||\Phi|||_{W^{1,2}} \leq C||\nu||_{TV},$$

where $||\cdot||_{TV}$ denotes the total variation of ν. Since the space $W^{1,2}(0,1)$ is linearly and isometrically embedded in $L^2(0,1) \times L^2(0,1)$ through

$$\begin{aligned} W^{1,2}(0,1) &\to L^2(0,1) \times L^2(0,1) \\ y &\mapsto (y, -y'), \end{aligned}$$

we can extend Φ to $L^2(0,1) \times L^2(0,1)$ with the same norm, thanks to the Hahn-Banach theorem. Because of the Riesz representation theorem, we can find $(f_1, f_2) \in L^2(0,1) \times L^2(0,1)$ such that for all $(u,v) \in L^2(0,1) \times L^2(0,1)$,

$$\Phi(u,v) = \int_0^1 (f_1(x)u(x) + f_2(x)v(x))\,\mathrm{d}x.$$

and

$$|||\Phi|||^2_{L^2(0,1)\times L^2(0,1)} = ||f_1||^2_{L^2} + ||f_2||^2_{L^2} \leq C^2||\nu||^2_{TV}.$$

We thus obtain, for $y \in W^{1,2}(0,1)$

$$\Phi(y) = \int_0^1 \big(f_1(x)y(x) - f_2(x)y'(x)\big)\,\mathrm{d}x.$$

Now let $\lambda > 0$ and $\mu \in D(\Delta_c^*) = D((\lambda - \Delta_c)^*)$ and define $\nu = (\lambda - \Delta_c)\mu \in BV([0,1])$ with for $y \in D(\Delta_c)$

$$\int_0^1 (\lambda - \Delta_c)y(x)\mu(\mathrm{d}x) = \int_0^1 y(x)\nu(\mathrm{d}x).$$

We apply the previous procedure to ν to find $(f_1, f_2) \in L^2(0,1) \times L^2(0,1)$ such that

$$\int_0^1 (\lambda - \Delta_c)y(x)\mu(\mathrm{d}x) = \int_0^1 \big(f_1(x)y(x) - f_2(x)y'(x)\big)\,\mathrm{d}x, \qquad (y \in D(\Delta_c)).$$

From the Lax-Milgram theorem applied in the Hilbert space $H_0^1(0,1) := W_0^{1,2}(0,1)$, there exists a unique solution $\tilde{y} \in W_0^{1,2}(0,1)$ of $(\lambda - \Delta_c)y = f_1 + f_2'$ (with f_2' the derivative in the sens of distributions). It follows from an integration by part that

$$\int_0^1 (\lambda - \Delta_c)y(x)\sigma(\mathrm{d}x), \qquad (y \in D(\Delta_c)),$$

with $\sigma(\mathrm{d}x) = \mu(\mathrm{d}x) - \tilde{y}(x)\mathrm{d}x$. Since $(\lambda - \Delta_c)(D(\Delta_c)) = C_0([0,1])$ (see the proof of Theorem 3.2.1), σ vanishes identically in $(0,1)$ and thus $\mu(\mathrm{d}x) = \tilde{y}(x)\mathrm{d}x$ and $D(\Delta_c^*) \subset W_0^{1,2}(0,1)$, with in particular $D(\Delta_c^*) \subset L^1(0,1)$. Since $D(\Delta_c) \subset D(\Delta_c^*)$ and $D(\Delta_c)$ is dense in $L^1(0,1)$ we obtain

$$C_0([0,1])^{\odot} = L^1(0,1).$$

Let us now show that the Phillips dual of $L^1(0,1)$ with respect to Δ_1 (with Dirichlet boundary condition) is indeed $C_0([0,1])^{\odot}$. The dual of $L^1(0,1)$, is $L^\infty(0,1)$. Since Δ_1 is the closure of Δ_c in $L^1(0,1)$, $L^1(0,1)^{\odot} = \overline{D(\Delta_1^*)} = \overline{D(\Delta_c^*)}$. Now, since $D(\Delta_c) \subset D(\Delta_c^*)$, $D(\Delta_c) \subset L^1(0,1)^{\odot}$. Let $y^* \in D(\Delta_c^*)$, considering Δ_c as a operator in $L^1(0,1)$, there exists $f \in L^\infty(0,1)$ such that

$$\int_0^1 y^*(x)\Delta_c y(x)\mathrm{d}x = \int_0^1 f(x)y(x)\mathrm{d}x, \qquad (y \in D(\Delta_c) \subset L^1(0,1)).$$

If Δ_c is thought as an operator in $L^2(0,1)$ and if we write Δ_2 the closure of Δ_c in $L^2(0,1)$, then $D(\Delta_c^*) = D(\Delta_2^*)$ so that $y^* \in D(\Delta_2^*)$ and $\Delta_c^* y^* \in L^2(0,1)$ so that $f \in L^2(0,1)$. But $\Delta_2^* = \Delta_2$ and $D(\Delta_2) = H^2(0,1) \cap H_0^1(0,1)$ so that in fact from general Sobolev inequalities $y^* \in C^1([0,1])$ and y^* satisfies the Dirichlet boundary condition in the classical sense, that is $y^* \in C_0([0,1])$. We thus obtain $D(\Delta_c^*) \subset C_0([0,1])$. Finally, since the L^∞ and the C norms coincide on $C([0,1])$, we must also have $E^{\odot} \subset C_0([0,1])$ as the closure of $D(\Delta_c^*)$ in $L^\infty([0,1])$.

Now, going back to the Laplacian in $C([0,1])$ with variational boundary condition, it is immediate to see that for $y \in L^1([0,1])$

$$S^{\odot}(t)y(s) = \int_0^1 k_t(s,r)y(r)\mathrm{d}r, \quad (t \geq 0).$$

As a matter of fact, we can also give the expression of the dual semigroup $(S(t)^*)_{t\geq 0}$ in $BV([0,1])$, taking values in $L^1([0,1])$

$$S(t)^*\mu(s) = \int_0^1 k_t(s,r)\mu(\mathrm{d}r), \quad (t \geq 0), \qquad \mu \in BV([0,1]).$$

□

We can now define the relaxed PDE (3.1) for $C([0,1])$ by defining the function $\mathbf{f}_d : E \times M_+^1(Z) \to E$ such that $\mathbf{f}_d(y)\gamma$ is the unique element of $(E^{\odot})^*$ satisfying

$$\langle y^*, \mathbf{f}_d(y)\gamma\rangle_{(E^*,E)} = \int_U \langle y^*, f_d(y,u)\rangle_{(E^*,E)}\gamma(\mathrm{d}u)$$

for all $y^* \in E^{\odot}$. The function $t \to \mathbf{f}_d(y(s))\gamma(s)$ is thus an $E^{\odot}$-weakly measurable $(E^{\odot})^*$-valued function. The corresponding integral equation is

$$y(t) = S(t)y_0 + \int_0^t S^{\odot}(t-s)^*\mathbf{f}_d(y(s))\gamma(s)\mathrm{d}s, \tag{3.21}$$

the integrand taking values in E because of 3.11. This integral equation is interpreted using the following Lemma (see [Fat94a, Lemma 6.1]).

Lemma 3.2.4. *a) Let* $g : [0,T] \to (E^{\odot})^*$*,* $E^{\odot}$*-weakly measurable and bounded. Then*

$$s \to S^{\odot}(t-s)^*g(s)$$

is strongly measurable in $[0,t]$*. b) If, in addition,* $||g||_{(E^{\odot})^*} \in L^1((0,1))$*, the* E*-valued function*

$$y(t) = \int_0^t S^{\odot}(t-s)^*g(s)\mathrm{d}s$$

is continuous in $[0,T]$*.*

Finally, under these considerations, the proof of Lemma 3.2.1 remains valid if we replace S^* by $S^{\odot}$ and E^* by $E^{\odot}$.

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