informatics mathematics

Activity Report 2016

Team MATHNEURO

Mathématiques pour les Neurosciences

Inria teams are typically groups of researchers working on the definition of a common project, and objectives, with the goal to arrive at the creation of a project-team. Such project-teams may include other partners (universities or research institutions).

RESEARCH CENTER
Sophia Antipolis - Méditerranée

THEME
Computational Neuroscience and Medecine

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Team MATHNEURO

Creation of the Team: 2016 January 01

Keywords:

Computer Science and Digital Science:

6.1.1. - Continuous Modeling (PDE, ODE)
6.1.2. - Stochastic Modeling (SPDE, SDE)
6.1.4. - Multiscale modeling
6.2.1. - Numerical analysis of PDE and ODE
6.2.2. - Numerical probability
6.2.3. - Probabilistic methods
6.3.4. - Model reduction

Other Research Topics and Application Domains:

1.3. - Neuroscience and cognitive science
1.3.1. - Understanding and simulation of the brain and the nervous system
1.3.2. - Cognitive science
1.4. - Pathologies

1. Members

Research Scientists

Mathieu Desroches [Team leader, Inria, Researcher, HDR]
Pascal Chossat [CNRS, Senior Researcher, HDR]
Olivier Faugeras [Inria, Senior Researcher, HDR]
Maciej Krupa [Inria, Senior Researcher, Advanced Research Position]
Romain Veltz [Inria, Researcher]

PhD Students

Elif Koksal Ersoz [Inria, relais thèse in Dec 2016]
Alex Dolcemascolo [Univ. Nice]
Pascal Helson [Inria, from Oct 2016]
Jamil Salhi [ENIT, until Mar 2016]

Post-Doctoral Fellows

Tomasz Gorski [Inria, from May 2016 until Aug 2016]
Audric Drogoul [Thales, until Nov 2016]
Alexandre Richard [Ecole Polytechnique, from Sep 2016]

Administrative Assistant

Marie-Cecile Lafont [Inria]

Others

Paul Bressloff [University of Utah, International Chair from 2014 until 2019]
Daniele Avitabile [University of Nottingham, Associate Member, from Nov 2016]
Cantin Baron [Master UNS, Internship, from Feb 2016 until Jul 2016]
Quentin Cormier [ENS Lyon, Internship, until Mar 2016]
Raphael Forquet [Master Polytech, Internship, from Oct 2016]

2. Overall Objectives

2.1. Overall Objectives

MATHNEURO focuses on the applications of multi-scale dynamics to neuroscience. This involves the modelling and analysis of systems with multiple time scales and space scales, as well as stochastic effects. We look both at single-cell models, microcircuits and large networks. In terms of neuroscience, we are mainly interested in questions related to synaptic plasticity and neuronal excitability, in particular in the context of pathological states such as epileptic seizures and neurodegenerative diseases such as Alzheimer.

Our work is quite mathematical but we make heavy use of computers for numerical experiments and simulations. We have close ties with several top groups in biological neuroscience. We are pursuing the idea that the "unreasonable effectiveness of mathematics" can be brought, as it has been in physics, to bear on neuroscience.

Modeling such assemblies of neurons and simulating their behavior involves putting together a mixture of the most recent results in neurophysiology with such advanced mathematical methods as dynamical systems theory, bifurcation theory, probability theory, stochastic calculus, theoretical physics and statistics, as well as the use of simulation tools.

We conduct research in the following main areas:

1. Neural networks dynamics
2. Mean-field approaches
3. Neural fields
4. Slow-fast dynamics in neuronal models
5. Synaptic plasticity
6. Visual neuroscience

3. Research Program

3.1. Neural networks dynamics

The study of neural networks is certainly motivated by the long term goal to understand how brain is working. But, beyond the comprehension of brain or even of simpler neural systems in less evolved animals, there is also the desire to exhibit general mechanisms or principles at work in the nervous system. One possible strategy is to propose mathematical models of neural activity, at different space and time scales, depending on the type of phenomena under consideration. However, beyond the mere proposal of new models, which can rapidly result in a plethora, there is also a need to understand some fundamental keys ruling the behaviour of neural networks, and, from this, to extract new ideas that can be tested in real experiments. Therefore, there is a need to make a thorough analysis of these models. An efficient approach, developed in our team, consists of analysing neural networks as dynamical systems. This allows to address several issues. A first, natural issue is to ask about the (generic) dynamics exhibited by the system when control parameters vary. This naturally leads to analyse the bifurcations [8] [37] occurring in the network and which phenomenological parameters control these bifurcations. Another issue concerns the interplay between neuron dynamics and synaptic network structure.

3.2. Mean-field approaches

Modeling neural activity at scales integrating the effect of thousands of neurons is of central importance for several reasons. First, most imaging techniques are not able to measure individual neuron activity (microscopic scale), but are instead measuring mesoscopic effects resulting from the activity of several hundreds to several hundreds of thousands of neurons. Second, anatomical data recorded in the cortex reveal the existence of structures, such as the cortical columns, with a diameter of about $50\mu m$ to $1mm$, containing of the order of one hundred to one hundred thousand neurons belonging to a few different species. The description of this collective dynamics requires models which are different from individual neurons models. In particular, when the number of neurons is large enough averaging effects appear, and the collective dynamics is well described by an effective mean-field, summarizing the effect of the interactions of a neuron with the other neurons, and depending on a few effective control parameters. This vision, inherited from statistical physics requires that the space scale be large enough to include a large number of microscopic components (here neurons) and small enough so that the region considered is homogeneous.
Our group is developing mathematical and numerical methods allowing on one hand to produce dynamic mean-field equations [1] [36] from the physiological characteristics of neural structure (neurons type, synapse type and anatomical connectivity between neurons populations), and on the other so simulate these equations.

3.3. Neural fields

Neural fields are a phenomenological way of describing the activity of population of neurons by delay integro-differential equations. This continuous approximation turns out to be very useful to model large brain areas such as those involved in visual perception. The mathematical properties of these equations and their solutions are still imperfectly known, in particular in the presence of delays, different time scales and of noise.
Our group is developing mathematical and numerical methods for analysing these equations. These methods are based upon techniques from mathematical functional analysis, bifurcation theory [9], equivariant bifurcation analysis, delay equations, and stochastic partial differential equations. We have been able to characterize the solutions of these neural fields equations and their bifurcations, apply and expand the theory to account for such perceptual phenomena as edge, texture [3], and motion perception. We have also developed a theory of the delayed neural fields equations, in particular in the case of constant delays and propagation delays that must be taken into account when attempting to model large size cortical areas [38]. This theory is based on center manifold and normal forms ideas.

3.4. Slow-Fast Dynamics in Neuronal Models

Neuronal rhythms typically display many different timescales, therefore it is important to incorporate this slow-fast aspect in models. We are interested in this modeling paradigm where slow-fast point models (using Ordinary Differential Equations) are investigated in terms of their bifurcation structure and the patterns of oscillatory solutions that they can produce. To insight into the dynamics of such systems, we use a mix of theoretical techniques — such as geometric desingularisation and centre manifold reduction [35] — and numerical methods such as pseudo-arclength continuation [32]. We are interested in families of complex oscillations generated by both mathematical and biophysical models of neurons. In particular, so-called *mixed-mode oscillations (MMOs) [30], [34])*, which represent an alternation between subthreshold and spiking behaviour, and *bursting oscillations* [31], [33], also corresponding to experimentally observed behaviour [29].

Selected publications on this topic: lien.

3.5. Synaptic Plasticity

Neural networks show amazing abilities to evolve and adapt, and to store and process information. These capabilities are mainly conditioned by plasticity mechanisms, and especially synaptic plasticity, inducing a mutual coupling between network structure and neuron dynamics. Synaptic plasticity occurs at many levels of organization and time scales in the nervous system [28]. It is of course involved in memory and learning mechanisms, but it also alters excitability of brain areas and regulates behavioral states (e.g. transition between

sleep and wakeful activity). Therefore, understanding the effects of synaptic plasticity on neurons dynamics is a crucial challenge.
Our group is developing mathematical and numerical methods to analyse this mutual interaction. On the one hand, we have shown that plasticity mechanisms, Hebbian-like or STDP, have strong effects on neuron dynamics complexity, such as dynamics complexity reduction, and spike statistics

3.6. Visual Neuroscience

Our group focuses on the visual system to understand how information is encoded and processed resulting in visual percepts. To do so, we propose functional models of the visual system using a variety of mathematical formalisms, depending on the scale at which models are built, such as spiking neural networks or neural fields. So far, our efforts have been focused on the study of retinal processing, edge and texture perception, motion integration at the level of V1 and MT cortical areas.

4. New Software and Platforms

4.1. New Software

4.1.1. Julia library LSODA.jl

LSODA.jl is a Julia package that interfaces to the liblsoda library, developed by Simon Frost (University of Cambridge), thereby providing a way to use the LSODA algorithm from Linda Petzold and Alan Hindmarsh from Julia.

4.1.2. Julia library PDMP.jl

PDMP.jl This is a joint work of Romain Veltz and Simon Frost.

PDMP.jl is a Julia package that allows simulation of Piecewise Deterministic Markov Processes (PDMP); this encompasses hybrid systems, comprising of continuous and discrete components, as well as processes with time-varying rates. It is based on an implementation of the True Jump Method for performing stochastic simulations of PDMP, and requires solving stiff ODEs in an efficient manner. Sundials.jl is used, but other solvers could be easily added.

5. New Results

5.1. Neural Networks as dynamical systems

5.1.1. A modular architecture for transparent computation in recurrent neural networks

Participants: Giovanni Carmantini [Plymouth University, UK], Peter Beim Graben [Humbolt University (Berlin), Germany], Mathieu Desroches [Inria MathNeuro], Serafim Rodrigues [Plymouth University, UK].

Computation is classically studied in terms of automata, formal languages and algorithms; yet, the relation between neural dynamics and symbolic representations and operations is still unclear in traditional eliminative connectionism. Therefore, we suggest a unique perspective on this central issue, to which we would like to refer as transparent connectionism, by proposing accounts of how symbolic computation can be implemented in neural substrates. In this study we first introduce a new model of dynamics on a symbolic space, the versatile shift, showing that it supports the real-time simulation of a range of automata. We then show that the Gödelization of versatile shifts defines nonlinear dynamical automata, dynamical systems evolving on a vectorial space. Finally, we present a mapping between nonlinear dynamical automata and recurrent artificial neural networks. The mapping defines an architecture characterized by its granular modularity, where data, symbolic operations and their control are not only distinguishable in activation space, but also spatially localizable in the network itself, while maintaining a distributed encoding of symbolic representations. The resulting networks simulate automata in real-time and are programmed directly, in the absence of network training. To discuss the unique characteristics of the architecture and their consequences, we present two examples: (i) the design of a Central Pattern Generator from a finite-state locomotive controller, and (ii) the creation of a network simulating a system of interactive automata that supports the parsing of garden-path sentences as investigated in psycholinguistics experiments.

This work has been published in Neural Networks and is available as [13].

5.1.2. Latching dynamics in neural networks with synaptic depression

Participants: Pascal Chossat [Inria MathNeuro], Martin Krupa [Inria MathNeuro], Frédéric Lavigne [Université de Nice - BCL].

Priming is the ability of the brain to more quickly activate a target concept in response to a related stimulus (prime). Experiments point to the existence of an overlap between the populations of the neurons coding for different stimuli. Other experiments show that prime-target relations arise in the process of long term memory formation. The classical modelling paradigm is that long term memories correspond to stable steady states of a Hopfield network with Hebbian connectivity. Experiments show that short term synaptic depression plays an important role in the processing of memories. This leads naturally to a computational model of priming, called latching dynamics; a stable state (prime) can become unstable and the system may converge to another transiently stable steady state (target). Hopfield network models of latching dynamics have been studied by means of numerical simulation, however the conditions for the existence of this dynamics have not been elucidated. In this work we use a combination of analytic and numerical approaches to confirm that latching dynamics can exist in the context of Hebbian learning, however lacks robustness and imposes a number of biologically unrealistic restrictions on the model. In particular our work shows that the symmetry of the Hebbian rule is not an obstruction to the existence of latching dynamics, however fine tuning of the parameters of the model is needed.

This work has been submitted for publication and is available as [23].

5.1.3. On the Hamiltonian structure of large deviations in stochastic hybrid systems

Participants: Paul Bressloff [University of Utah, USA], Olivier Faugeras [Inria MathNeuro].

We present a new derivation of the classical action underlying a large deviation principle (LDP) for a stochastic hybrid system, which couples a piecewise deterministic dynamical system in $\mathbb{R}^d$ with a time-homogeneous Markov chain on some discrete space Γ. We assume that the Markov chain on Γ is ergodic, and that the discrete dynamics is much faster than the piecewise deterministic dynamics (separation of timescales). Using the Perron-Frobenius theorem and the calculus-of-variations, we show that the resulting Hamiltonian is given by the Perron eigenvalue of a $|\Gamma|$-dimensional linear equation. The corresponding linear operator depends on the transition rates of the Markov chain and the nonlinear functions of the piecewise deterministic system. We compare the Hamiltonian to one derived using WKB methods, and show that the latter is a reduction of the former. We also indicate how the analysis can be extended to a multi-scale stochastic process, in which the continuous dynamics is described by a piecewise stochastic differential equations (SDE). Finally, we illustrate the theory by considering applications to conductance-based models of membrane voltage fluctuations in the presence of stochastic ion channels.

This work has been submitted for publication and is available as [22].

5.1.4. *Large Deviations of a Spatially-Stationary Network of Interacting Neurons*

Participants: Olivier Faugeras [Inria MathNeuro], James Maclaurin [University of Sydney, USA].

In this work we determine a process-level Large Deviation Principle (LDP) for a model of interacting neurons indexed by a lattice $\mathbb{Z}^d$. The neurons are subject to noise, which is modelled as a correlated martingale. The probability law governing the noise is strictly stationary, and we are therefore able to find a LDP for the probability laws Π^n governing the stationary empirical measure $\widehat{\mu}^n$ generated by the neurons in a cube of length $(2n+1)$. We use this LDP to determine an LDP for the neural network model. The connection weights between the neurons evolve according to a learning rule / neuronal plasticity, and these results are adaptable to a large variety of neural network models. This LDP is of great use in the mathematical modelling of neural networks, because it allows a quantification of the likelihood of the system deviating from its limit, and also a determination of which direction the system is likely to deviate. The work is also of interest because there are nontrivial correlations between the neurons even in the asymptotic limit, thereby presenting itself as a generalisation of traditional mean-field models.

This work has been submitted for publication and is available as [25].

5.1.5. *The Period adding and incrementing bifurcations: from rotation theory to applications*

Participants: Albert Granados [Technical University of Denmark, Denmark], Lluís Alsedà [Autonomous University of Barcelona, Spain], Martin Krupa [Inria MathNeuro].

This survey article is concerned with the study of bifurcations of piecewise-smooth maps. We review the literature in circle maps and quasi-contractions and provide paths through this literature to prove sufficient conditions for the occurrence of two types of bifurcation scenarios involving rich dynamics. The first scenario consists of the appearance of periodic orbits whose symbolic sequences and "rotation" numbers follow a Farey tree structure; the periods of the periodic orbits are given by consecutive addition. This is called the *period adding* bifurcation, and its proof relies on results for maps on the circle. In the second scenario, symbolic sequences are obtained by consecutive attachment of a given symbolic block and the periods of periodic orbits are incremented by a constant term. It is called the *period incrementing* bifurcation, in its proof relies on results for maps on the interval. We also discuss the expanding cases, as some of the partial results found in the literature also hold when these maps lose contractiveness. The higher dimensional case is also discussed by means of *quasi-contractions*. We also provide applied examples in control theory, power electronics and neuroscience where these results can be applied to obtain precise descriptions of their dynamics.

This work has been accepted for publication in SIAM Review and is available as [26].

5.2. Neural Fields Theory

5.2.1. *Standing and travelling waves in a spherical brain model: the Nunez model revisited*

Participants: Sid Visser [University of Nottingham, UK], Rachel Nicks [University of Nottingham, UK], Olivier Faugeras [Inria MathNeuro], Stephen Coombes [University of Nottingham, UK].

The Nunez model for the generation of electroencephalogram (EEG) signals is naturally described as a neural field model on a sphere with space-dependent delays. For simplicity, dynamical realisations of this model either as a damped wave equation or an integro-differential equation, have typically been studied in idealised one dimensional or planar settings. Here we revisit the original Nunez model to specifically address the role of spherical topology on spatio-temporal pattern generation. We do this using a mixture of Turing instability analysis, symmetric bifurcation theory, center manifold reduction and direct simulations with a bespoke numerical scheme. In particular we examine standing and travelling wave solutions using normal form computation of primary and secondary bifurcations from a steady state. Interestingly, we observe spatio-temporal patterns which have counterparts seen in the EEG patterns of both epileptic and schizophrenic brain conditions.

This work has been submitted for publication and is available as [27].

5.3. Slow-Fast Dynamics in Neuroscience

5.3.1. Canards, folded nodes and mixed-mode oscillations in piecewise-linear slow-fast systems

Participants: Mathieu Desroches [Inria MathNeuro], Antoni Guillamon [Polytechnic University of Catalunya, Spain], Enrique Ponce [University of Seville, Spain], Rafel Prohens [University of the Balearic Islands, Spain], Antonio E. Teruel [University of the Balearic Islands, Spain], Serafim Rodrigues [Plymouth University, UK].

Canard-induced phenomena have been extensively studied in the last three decades, from both the mathematical and the application viewpoints. Canards in slow-fast systems with (at least) two slow variables, especially near folded-node singularities, give an essential generating mechanism for mixed-mode oscillations (MMOs) in the framework of smooth multiple timescale systems. There is a wealth of literature on such slow-fast dynamical systems and many models displaying canard-induced MMOs, particularly in neuroscience. In parallel, since the late 1990s several papers have shown that the canard phenomenon can be faithfully reproduced with piecewise-linear (PWL) systems in two dimensions, although very few results are available in the three-dimensional case. The present paper aims to bridge this gap by analyzing canonical PWL systems that display folded singularities, primary and secondary canards, with a similar control of the maximal winding number as in the smooth case. We also show that the singular phase portraits are compatible in both frameworks. Finally, we show using an example how to construct a (linear) global return and obtain robust PWL MMOs.

This work has been published in SIAM Review and is available as [16].

5.3.2. Spike-adding in parabolic bursters: the role of folded-saddle canards

Participants: Mathieu Desroches [Inria MathNeuro], Martin Krupa [Inria MathNeuro], Serafim Rodrigues [Plymouth University, UK].

The present work develops a new approach to studying parabolic bursting, and also proposes a novel four-dimensional canonical and polynomial-based parabolic burster. In addition to this new polynomial system, we also consider the conductance-based model of the Aplysia R15 neuron known as the Plant model, and a reduction of this prototypical biophysical parabolic burster to three variables, including one phase variable, namely the Baer-Rinzel-Carillo (BRC) phase model. Revisiting these models from the perspective of slow-fast dynamics reveals that the number of spikes per burst may vary upon parameter changes, however the spike-adding process occurs in an explosive fashion that involves special solutions called canards. This spike-adding canard explosion phenomenon is analysed by using tools from geometric singular perturbation theory in tandem with numerical bifurcation techniques. We find that the bifurcation structure persists across all considered systems, that is, spikes within the burst are incremented via the crossing of an excitability threshold given by a particular type of canard orbit, namely the true canard of a folded-saddle singularity. However there can be a difference in the spike-adding transitions in parameter space from one case to another, according to whether the process is continuous or discontinuous, which depends upon the geometry of the folded-saddle canard. Using these findings, we construct a new polynomial approximation of the Plant model, which retains all the key elements for parabolic bursting, including the spike-adding transitions mediated by folded-saddle canards. Finally, we briefly investigate the presence of spike-adding via canards in planar phase models of parabolic bursting, namely the theta model by Ermentrout and Kopell.

This work has been published in Physica D and is available as [17].

5.3.3. Slow-fast transitions to seizure states in the Wendling-Chauvel neural mass model

Participants: Mathieu Desroches [Inria MathNeuro], Olivier Faugeras [Inria MathNeuro], Martin Krupa [Inria MathNeuro].

We revisit the Wendling-Chauvel neural mass model by reducing it to eight ODEs and adding a differential equation that accounts for a dynamic evolution of the slow inhibitory synaptic gain. This allows to generate dynamic transitions in the resulting nine-dimensional model. The output of the extended model can be related to EEG patterns observed during epileptic seizure, in particular isolated pre-ictal spikes and low-voltage fast oscillations at seizure onset. We analyse the extended model using basic tools from slow-fast dynamical systems theory and relate the main transitions towards seizure states to torus canards, a type of solutions that has been shown to explain the spiking to bursting transition in many neural models. We find that the original ten-dimensional Wendling-Chauvel model can be reduced to eight dimensions, two variables being scaled versions of two other variables of the model. We then obtain a model with four PSP blocks, which is consistent with the block-diagrams typically presented to describe this model. Instead of varying the slow inhibitory synaptic gain parameter B quasi-statically, or just performing numerical bifurcation analysis in B as the structure of the fast subsystem of an hypothetical extended system, we construct a true slow dynamics for B, depending sensitively on the main PSP output of the model, Y0. Near fold bifurcation of limit cycles of the original model, the solution to the extended model performs fast low-amplitude oscillations close to both attracting and repelling branches of limit cycles, which is the signature of a torus canard phenomenon.

This work has been published in Opera Medica & Physiologica and is available as [14].

5.3.4. *Canards in a minimal piecewise-linear square-wave burster*

Participants: Mathieu Desroches [Inria MathNeuro], Soledad Fernández-García [University of Seville, Spain], Martin Krupa [Inria MathNeuro].

We construct a piecewise-linear (PWL) approximation of the Hindmarsh-Rose (HR) neuron model that is minimal, in the sense that the vector field has the least number of linearity zones, in order to reproduce all the dynamics present in the original HR model with classical parameter values. This includes square-wave bursting and also special trajectories called canards, which possess long repelling segments and organise the transitions between stable bursting patterns with n and n?+?1 spikes, also referred to as spike-adding canard explosions. We propose a first approximation of the smooth HR model, using a continuous PWL system, and show that its fast subsystem cannot possess a homoclinic bifurcation, which is necessary to obtain proper square-wave bursting. We then relax the assumption of continuity of the vector field across all zones, and we show that we can obtain a homoclinic bifurcation in the fast subsystem. We use the recently developed canard theory for PWL systems in order to reproduce the spike-adding canard explosion feature of the HR model as studied, e.g., in Desroches et al., Chaos 23(4), 046106 (2013).

This work has been published in Chaos and is available as [15].

5.3.5. *From Canards of Folded Singularities to Torus Canards in a Forced van der Pol Equation*

Participants: John Burke [Boston University, USA], Mathieu Desroches [Inria MathNeuro], Albert Granados [Technical University of Denmark, Denmark], Tasso J. Kaper [Boston University, USA], Martin Krupa [Inria MathNeuro], Theodore Vo [Boston University, USA].

In this article, we study canard solutions of the forced van der Pol equation in the relaxation limit for low-, intermediate-, and high-frequency periodic forcing. A central numerical observation made herein is that there are two branches of canards in parameter space which extend across all positive forcing frequencies. In the low-frequency forcing regime, we demonstrate the existence of primary maximal canards induced by folded saddle nodes of type I and establish explicit formulas for the parameter values at which the primary maximal canards and their folds exist. Then, we turn to the intermediate- and high-frequency forcing regimes and show that the forced van der Pol possesses torus canards instead. These torus canards consist of long segments near families of attracting and repelling limit cycles of the fast system, in alternation. We also derive explicit formulas for the parameter values at which the maximal torus canards and their folds exist. Primary maximal canards and maximal torus canards correspond geometrically to the situation in which the persistent manifolds near the family of attracting limit cycles coincide to all orders with the persistent manifolds that lie near the family of repelling limit cycles. The formulas derived for the folds of maximal canards in all three frequency regimes turn out to be representations of a single formula in the appropriate parameter regimes, and this unification confirms the central numerical observation that the folds of the maximal canards created in the low-frequency regime continue directly into the folds of the maximal torus canards that exist in the intermediate- and high-frequency regimes. In addition, we study the secondary canards induced by the folded singularities in the low-frequency regime and find that the fold curves of the secondary canards turn around in the intermediate-frequency regime, instead of continuing into the high-frequency regime. Also, we identify the mechanism responsible for this turning. Finally, we show that the forced van der Pol equation is a normal form-type equation for a class of single-frequency periodically driven slow/fast systems with two fast variables and one slow variable which possess a non-degenerate fold of limit cycles. The analytic techniques used herein rely on geometric desingularisation, invariant manifold theory, Melnikov theory, and normal form methods. The numerical methods used herein were developed in Desroches et al. (SIAM J Appl Dyn Syst 7:1131–1162, 2008, Nonlinearity 23:739–765 2010).

This work has been published in Journal of Nonlinear Science and is available as [12].

5.3.6. Mixed-mode oscillations in a piecewise-linear system with multiple time scale coupling

Participants: Soledad Fernández-García [University of Seville, Spain], Martin Krupa [Inria MathNeuro], Frédérique Clément [Inria Mycenae].

In this work, we analyze a four dimensional slow?fast piecewise linear system with three time scales presenting Mixed-Mode Oscillations. The system possesses an attractive limit cycle along which oscillations of three different amplitudes and frequencies can appear, namely, small oscillations, pulses (medium amplitude) and one surge (largest amplitude). In addition to proving the existence and attractiveness of the limit cycle, we focus our attention on the canard phenomena underlying the changes in the number of small oscillations and pulses. We analyze locally the existence of secondary canards leading to the addition or subtraction of one small oscillation and describe how this change is globally compensated for or not with the addition or subtraction of one pulse.

This work has been published in Physica D and is available as [18].

5.4. Plasticity

5.4.1. Time-code neurotransmitter release at excitatory and inhibitory synapses

Participants: Serafim Rodrigues [Plymouth University, UK], Mathieu Desroches [Inria MathNeuro], Martin Krupa [Inria MathNeuro], Jesus M. Cortes [Biocruces Institute, Spain], Terrence J. Sejnowski [Salk Institute, USA], Afia B. Ali [University College London, UK].

Communication between neurons at chemical synapses is regulated by hundreds of different proteins that control the release of neurotransmitter that is packaged in vesicles, transported to an active zone, and released when an input spike occurs. Neurotransmitter can also be released asynchronously, that is, after a delay following the spike, or spontaneously in the absence of a stimulus. The mechanisms underlying asynchronous and spontaneous neurotransmitter release remain elusive. Here, we describe a model of the exocytotic cycle of vesicles at excitatory and inhibitory synapses that accounts for all modes of vesicle release as well as short-term synaptic plasticity (STSP). For asynchronous release, the model predicts a delayed inertial protein unbinding associated with the SNARE complex assembly immediately after vesicle priming. Experiments are proposed to test the model?s molecular predictions for differential exocytosis. The simplicity of the model will also facilitate large-scale simulations of neural circuits.

This work has been published in Proceedings of the National Academy of Sciences of the USA (PNAS) and is available as [20].

5.5. Vision in Neuroscience

5.5.1. The relative contribution of noise and adaptation to competition during tri-stable motion perception

Participants: Andrew Meso [Bournemouth University, UK], James Rankin [Center for Neural Science, NYU, USA], Olivier Faugeras [Inria MathNeuro], Pierre Kornprobst [Inria BioVision], Guillaume Masson [Institut de Neuroscience de la Timone, France].

Animals exploit antagonistic interactions for sensory processing and these can cause oscillations between competing states. Ambiguous sensory inputs yield such perceptual multi-stability. Despite numerous empirical studies using binocular rivalry or plaid pattern motion, the driving mechanisms behind the spontaneous transitions between alternatives remain unclear. In the current work, we used a tri-stable barberpole motion stimulus combining empirical and modelling approaches to elucidate the contributions of noise and adaptation to underlying competition. We first robustly characterised the coupling between perceptual reports of transitions and continuously recorded eye direction, identifying a critical window of 480ms before button presses within which both measures were most strongly correlated. Second, we identified a novel non monotonic relationship between stimulus contrast and average perceptual switching rate with an initially rising rate before a gentle reduction at higher contrasts. A neural fields model of the underlying dynamics introduced in previous theoretical work and incorporating noise and adaptation mechanisms was adapted, extended and empirically validated. Noise and adaptation contributions were confirmed to dominate at the lower, and higher, contrasts respectively. Model simulations with two free parameters, controlling adaptation dynamics and direction thresholds, captured the measured mean transition rates for participants. We verified the shift from noise dominated towards adaptation-driven in both the eye direction distributions and inter-transition duration statistics. This work combines modelling and empirical evidence to demonstrate the signal strength dependent interplay between noise and adaptation during tri- stability. We propose that the findings generalise beyond the barberpole stimulus case to ambiguous perception in continuous feature spaces.

This work has been published in Journal of Vision and is available as [19].

6. Partnerships and Cooperations

6.1. Regional Initiatives

Olivier Faugeras is a member of the scientific committee of the "Axe Interdisciplinaire de Recherche de l'Université de Nice Sophia Antipolis" entitled "Modélisation Théorique et Computationnelle en Neurosciences et Sciences Cognitives".

6.2. National Initiatives

6.2.1. ANR

6.2.1.1. SloFaDyBio

Title: a network for Slow-Fast Dynamics in the Biosciences

Programm: ANR “amorçage”

Duration: January 2015 - January 2017 (extension up to January 2018)

Coordinator: Inria

PI: Mathieu Desroches

Partners:
see the webpage of the project.

The SloFaDyBio project targets to gather European researchers from about 10 cost countries in order to build up a network project on “Multi-Scale Dynamics in Neuroscience” and to submit within two years a large-scale proposal to a European funding agency such as COST. The initial fund provided by the ANR is used to meet regularly over this period and write a complete proposal. We now have an operational team and we are in the process of writing a full proposal which will be submitted at the next COST call, that is, at the end of September 2017.

6.3. European Initiatives

6.3.1. FP7 & H2020 Projects

6.3.1.1. HBP

Title: The Human Brain Project

Programm: FP7

Duration: October 2013 - March 2016 (first part) and then : April 2016 - March 2018 (second part)

Coordinator: EPFL

Partners:
see the webpage of the project.

Inria contact: Olivier Faugeras (first part) and then : Romain Veltz (second part)

Understanding the human brain is one of the greatest challenges facing 21st century science. If we can rise to the challenge, we can gain profound insights into what makes us human, develop new treatments for brain diseases and build revolutionary new computing technologies. Today, for the first time, modern ICT has brought these goals within sight. The goal of the Human Brain Project, part of the FET Flagship Programme, is to translate this vision into reality, using ICT as a catalyst for a global collaborative effort to understand the human brain and its diseases and ultimately to emulate its computational capabilities. The Human Brain Project will last ten years and will consist of a ramp-up phase (from month 1 to month 36) and subsequent operational phases.
This Grant Agreement covers the ramp-up phase. During this phase the strategic goals of the project will be to design, develop and deploy the first versions of six ICT platforms dedicated to Neuroinformatics, Brain Simulation, High Performance Computing, Medical Informatics, Neuromorphic Computing and Neurorobotics, and create a user community of research groups from within and outside the HBP, set up a European Institute for Theoretical Neuroscience, complete a set of pilot projects providing a first demonstration of the scientific value of the platforms and the Institute, develop the scientific and technological capabilities required by future versions of the platforms, implement a policy of Responsible Innovation, and a programme of transdisciplinary education, and develop a framework for collaboration that links the partners under strong scientific leadership and professional project management, providing a coherent European approach and ensuring effective alignment of regional, national and European research and programmes. The project work plan is organized in the form of thirteen subprojects, each dedicated to a specific area of activity.
A significant part of the budget will be used for competitive calls to complement the collective skills of the Consortium with additional expertise.

6.4. International Research Visitors

6.4.1. Visits of International Scientists

Invitation of Martin Wechselberger, University of Sydney (Australia), June 2016

Invitation of Daniele Avitabile, University of Nottingham (UK), June 2016

Invitation of James MacLaurin, University of Sydney (Australia), December 2016

Invitation of Tim O’Leary, University of Cambridge (UK), December 2016

Invitation of Antonio Teruel, University of the Balearic Islands (Spain), December 2016

6.4.1.1. Internships

Cantin Baron (collaboration with H. Marie at IPMC, Feb-June 2016)

Raphaël Fourquet (collaboration with H. Marie at IPMC, Feb-June 2016)

6.4.2. Visits to International Teams

Visit of Mathieu Desroches to Daniele Avitabile (University of Nottingham, UK) in April 2016

Visit of Romain Veltz to Cian O'Donnell (University of Bristol, UK) in April 2016

Visit of Mathieu Desroches to Martin Wechselberger (University of Sydney, Australia) in August 2016

Visit of Mathieu Desroches to Vivien Kirk (University of Auckland, New Zealand) in September 2016

Visit of Mathieu Desroches to Daniele Avitabile (University of Nottingham, UK) in April 2016

Visit of Mathieu Desroches to Serafim Rodrigues (Plymouth University, UK) in October 2016

7. Dissemination

7.1. Promoting Scientific Activities

7.1.1. Scientific Events Organisation

7.1.1.1. General Chair, Scientific Chair

Romain Veltz was the General Chair of the 2nd International Conference on Mathematical Neuroscience, held in Antibe-Juan les Pins, May 30 - June 1 2016.

7.1.1.2. Member of the Organizing Committees

Mathieu Desroches was on the Organizing Committee of the MURPHYS-HSFS 2016 Workshop on Hysteresis and Slow-Fast Dynamics held at the Centre de Recerca Matemàtica (CRM) in Barcelona, June 13-17, 2016.

7.1.2. Scientific Events Selection

7.1.2.1. Member of the Conference Program Committees

Pascal Chossat and Martin Krupa were on the Program Committee of the 2nd International Conference on Mathematical Neuroscience, held in Antibe-Juan les Pins, May 30 - June 1 2016.

7.1.3. Journal

7.1.3.1. Member of the Editorial Boards

Olivier Faugeras is the co-editor in chief of the open access Journal of Mathematical Neuroscience.

7.1.3.2. Reviewer - Reviewing Activities

Mathieu Desroches acts as a reviewer for Physica D, SIAM Journal on Applied Dynamical Systems (SIADS), PLoS Computational Biology, Journal of Nonlinear Science, IMA Journal of Applied Mathematics, Journal of Mathematical Neuroscience.

Olivier Faugeras acts as a reviewer for the Journal of Mathematical Neuroscience, the Journal of Computational Neuroscience, the SIAM Journal on Applied Dynamical Systems (SIADS).

Martin Krupa acts as a reviewer for Nonlinearity, Proceedings of the National Academy of Sciences of the USA (PNAS), the SIAM Journal of Applied Dynamical Systems (SIADS).

Romain Veltz acts as a reviewer for Neural Computation, Elife, SIADS, Journal of the Royal Society Interface.

7.1.4. Invited Talks

R. Veltz, “Some applications of hybrid systems in neurosciences”, University of Bristol, April 2016

M. Desroches, “Simplifying singular perturbation theory in the canard regime with piecewise-linear dynamics; application to neuronal models”, Invited Plenary talk, *10th NoLineal Conference*, University of Seville (Spain), June 2016.

M. Desroches, “Canards, folded singularities and bursting”, Invited talk in the mini-symposium *Slow-fast dynamics in neuroscience* at the *10th ECMTB Conference*, Nottingham (UK), July 2016.

M. Desroches, “Spike-adding in parabolic bursters: the role of folded-saddle canards”, Invited talk in the workshop *Dynamics in Life Science, Neuroscience* at the *Volga Neuroscience meeting 2016*, St-Petersburg/Nizhny-Novgorod (Russia), July 2016.

M. Desroches, “Canards in piecewise-linear slow-fast systems”, Invited seminar talk, *Applied Mathematics Seminar*, University of Sydney (Australia), August 2016.

M. Desroches, “Canards in planar piecewise-linear slow-fast systems”, Invited seminar talk, *Applied Mathematics Seminar*, University of Auckland (New Zealand), September 2016.

M. Desroches, “Understanding synaptic mechanisms: why a multi-disciplinary approach is important”, Invited talk in the Symposia meeting *New Techniques in Electro- and Optophysiology*, SFN conference, San Diego (USA), November 2016.

7.2. Teaching - Supervision - Juries

7.2.1. Teaching

Chalk-learning

Master 2 MVA/UPMC: Romain Veltz, Mathematical Methods for Neurosciences, 20 hours, Paris, France.

Master 1 BIM/UPMC: Mathieu Desroches, Modèles Mathématiques et Computationnels en Neuroscience, 30 hours, Paris, France.

7.2.2. Supervision

PhD in progress: Pascal Helson, "Study of plasticity laws with stochastic processes", started in September 2016, co-supervised by Romain Veltz and Etienne Tanré (Inria TOSCA).

PhD in progress: A. Dolcemascolo, "All optical neuromimetic devices", started in January 2016, co-supervised by Romain Veltz and S. Barland (INLN).

PhD completed: Lucile Mégret, “Explosions de cycles: Analyse qualitative, simulations numériques et modèles”, defended on 25 November 2016, co-supervised by Mathieu Desroches and J.-P. Françoise (UPMC).

PhD completed: Giovanni Carmantini, “Dynamical Systems Theory for Transparent Symbolic Computation in Neuronal Networks”, defended on 28 November 2016, co-supervised by Mathieu Desroches and S. Rodrigues (Plymouth University, UK).

PhD completed: Elif Köksal-Ersöz, “A mathematical study on coupled multiple timescale systems, synchronization of populations of endocrine neurons”, defended on 13 December 2016, co-supervised by Mathieu Desroches, J.-P. Françoise (UPMC) and F. Clément (Inria Paris).

7.2.3. Juries

Mathieu Desroches was a jury member for the PhD defence of Catalina Vich (University of the Balearic Islands, Spain) on 4 July 2016. He was also jury member for the PhD defence of Lucile Mégret (UPMC, France) on 25 November 2016 and that of Elif Köksal-Ersöz (Inria Paris / UPMC, France) on 13 December 2016.

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Major publications by the team in recent years

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Publications of the year

Articles in International Peer-Reviewed Journals

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Other Publications

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