Activity Report 2013

Project-Team SISYPHE

Signals and SYStems in PHysiology & Engineering
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Creation of the Project-Team: 2007 July 01.

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2. Overall Objectives

2.1. Overall Objectives

SISYPHE (SIGnals and Systems in PHysiology and Engineering) is studying questions about some complex
dynamical systems issued from Physiology and Engineering: modeling; identification and observation from
signals; real-time health monitoring or control; questions of system theory arising from the emerging domain
of “quantum engineering”. The research topics are the following:

Neuroscience & Neuroendocrinology: Regulation of the Gonadotrope axis. Controlled conservation laws
for structured cell populations; Dynamical systems and neuroendocrinology; Innovative computational and
theoretical tools for slow-fast dynamics

Quantum engineering: controlled quantum systems. Measurement based feedback; Dissipation engineering.

Classical engineering: Monitoring and control of complex systems. Modeling, signal analysis and control
with medical applications; Modeling, signal analysis and control for general engineering.

2.2. Highlights of the Year

Results in control of quantum systems obtained by Mazyar Mirrahimi and his former PhD student Zaki Leghtas
in close collaboration with the teams of Michel Devoret and Robert Schoelkopf (Department of Applied
Physics of Yale University) have been published in Nature ([49], [57]); Science ([47], [60]); Physical Review
Letters ([46], [53]).

3. Research Program

3.1. Towards two new project-teams MYCENAE and QUANTIC

Based on promising results obtained in Cell Biology and Neurosciences and Quantum physics, the research
program anticipates the evolution of Sisyphe into two project-teams in Applied Mathematics:
- MYCENAE (Multiscale dYnamiCs in neuroENdocrine AxEs), a project-team led by Frédérique Clément,
created in Jan. 2014.
- QUANTIC (QUANTum Information Circuits), led by Mazyar Mirrahimi (the team has been created in Sept
2013 ; the project proposal is still under review).

3.2. Neuroscience & Neuroendocrinology: Regulation of the Gonadotrope axis

Participants: Benjamin Aymard, Frédérique Clément, Mathieu Desroches, Soledad Fernández Garcia, Albert
Granados Corsellas, Elif Kóksal, Maciej Krupa, Lucile Megret, Sixtine Passot, Marie Postel, Jonathan
Touboul, Alexandre Vidal.

This work was mostly undertaken in the framework of the REGATE (REgulation of the GonAdoTropE axis)
Inria Large Scale Initiative Action, that focuses on mathematical neuroendocrinology issues applied to the
hypothalamo-pituitary-gonadal (HPG) axis.
3.2.1. Controlled conservation laws for structured cell populations

We have studied the theoretical and numerical questions raised by our multiscale model of follicle selection. This is needed to fully exploit the model potential in terms of biological interpretation and to enable us to forecast the ovulation rate according to the different physiological and endocrine scenarios that we have elaborated [40]. To describe the terminal stages of follicular development on a cell kinetics basis and account for the selection process operated amongst follicles, we have previously developed a multiscale model describing the cell density in each follicle, that can be roughly considered as a \((N \times 2D)\) system of weakly coupled transport equations with controlled velocities and source term [10], [11]. Even if, in some sense, this model belongs to the class of renewal equations for structured populations, it owns a number of specificities that render its theoretical and numerical analysis particularly challenging: weak nonlinearity due to the moment-based formulation of velocities and source term, discontinuities in the (cell-phase dependent) velocities and densities (due to the mitosis event), 2D effects (e.g. shear or waterproof interface). On the theoretical ground, we have obtained rigorous results on the existence and uniqueness of weak solutions with bounded initial data [56], so that the well-posedness of the model in its most generic formulation is now well established. In the framework of hybrid optimal control, we have proved that there exists an optimal bang-bang control with only one switching time for the optimal ovulatory trajectory, in the case when the density is approximated by Dirac masses [38], which in some sense generalizes former results obtained in a low-dimensional ODE case [89]. We can also conjecture that every optimal control is a bang-bang control with only one switching time for our PDE case, but the formal proof of it remains to be stated. From the rigorous reduction (exponential convergence in one of the structuring variable) and averaging of the renewal (mitosis) term, we have obtained a simpler system of coupled nonlinear ODEs (corresponding to the zero and first-order moments of the initial PDEs), from which the dynamics of one given follicle can be studied with respect to the pressure exerted collectively by all other growing follicles, in a dynamical game-like framework. On the numerical ground, we have conceived a new method to deal with the discontinuous coefficients [35] and designed a finite-volume scheme implemented on a parallel architecture [84] to overcome some computational difficulties and perform intensive simulation campaigns.

We have also investigated the physiological balance (as well as pathological or genetically-encoded unbalance) between the oocyte growth and proliferation of follicular cells in the earliest stages of follicular morphodynamics, when the very low number of follicular cells excludes the use of a deterministic formalism. To remain in a dynamical framework consistent (in the limit) with PDE renewal equations, we have adapted a stochastic and discrete formalism initially developed in the framework of ecological modeling (e.g. [88]) to design a stochastic model of early follicular development with its own specificities [39]: 2D population structuring according both to a space variable (distance from the surface of the oocyte) and an age variable (progression along the division cycle), non-zero sized individuals with possible local overcrowding, multiscale formulation (with three interacting scales intricately merged on the dynamical ground).

3.2.2. Dynamical systems and neuroendocrinology

We have previously proposed in [5], and further analyzed in [4], a mathematical model accounting for the alternating pulse and surge pattern of GnRH secretion. The model is based on the coupling between two dynamical systems running on different time scales. The faster system corresponds to the average activity of GnRH secreting neurons, which is forced by the slower system that corresponds to the average activity of regulatory neurons. The analysis of the slow-fast dynamics exhibited within and between both systems allows one to explain the different patterns (slow oscillations, fast oscillations and periodic surge) of GnRH secretion both qualitatively and quantitatively.

In an endocrinology-oriented study, we have explained how the dynamics-based constraints imposed on the model parameters amount to embedding time- and dose-dependent steroid control within the model [23]. We then investigated the plasticity of the model and performed in silico experiments inspired from available experimental protocols: luteal deficiency affecting the surge amplitude, surge blockade induced by administration of luteal levels of progesterone during the follicular phase, short-term effects of either progesterone or estradiol bolus administration on the pulse properties.
On the dynamical ground, further exploration of the model has revealed other possible secretion regimes. In particular, during the transition from a surge back to the subsequent pulsatile phase, a pause consisting of small oscillations superimposed on a long-duration pulse may occur. A detailed examination of the pause has revealed that it is shaped by mixed-mode oscillations (MMO); the small oscillations are related to the passage of the slow nullcline of the secreting system through a fold point of its fast nullcline. We have computed families of orbit segment undergoing very brutal transitions upon parameter variation in the vicinity of the fold, by applying pseudo-arclength continuation algorithms (as implemented in AUTO) to one-parameter families of well-posed two-point boundary value problems. We have derived a variety of reductions that allowed us to obtain results both on the local dynamics near the fold (rigorous characterization of small canards and sectors of rotation) and the global dynamics (existence of an attracting unique limit cycle, which is underlain by a return map) [16].

We have also started to investigate the question of GnRH neuron synchronization on a mesoscopic scale. We have studied how synchronized events in calcium dynamics can arise from the average electric activity of individual neurons, from seminal experiments of calcium imaging performed on embryonic GnRH neurons [116]. Our model reproduces the occurrence of synchronized calcium peaks, superimposed on asynchronous, yet oscillatory individual background dynamics, as well as additional experimental observations (partial recruitment, doublets of synchronization) [50]. Using phase-plane analysis, we have constrained the model behavior so that it meets not only qualitative but also quantitative specifications derived from the experiments, including the precise control of the frequency of the synchronization episodes.

On a data-oriented ground, we have designed an algorithm (DynPeak) for the monitoring of LH (luteinizing hormone) pulse frequency (that mirrors GnRH pulse frequency in many -but not all- cases), basing ourselves both on the available endocrinological knowledge (pulse shape and duration with respect to the frequency regime) and synthetic LH data generated by a simple model [25] (Joint work with Claire Médigue (hormonal data analysis) and Serge Steer (software development)). We have performed the algorithm on different sets of both synthetic and experimental LH time series. We have further diagnosed possible sources of outliers in the series of IPIs which is the main output of the algorithm.

### 3.2.3. Innovative computational and theoretical tools for slow-fast dynamics

We have extended the study of the recently discovered torus canard phenomenon [98], that underlies the transition between the spiking and bursting regimes in neuronal models, and can be roughly considered as the combination of a canard phenomenon with a fast rotating dynamics. We have generalized the previous results to a larger class of bursters (such as the classical Hindmarsh-Rose and Wilson-Cowan models), whose bursting regime ends by a slow passage through a fold bifurcation of limit cycles and we have analyzed the underlying bifurcation structure by means of continuation tools [87], [92].

We have developed new approaches to compute one-parameter families of isolas, which are isolated bifurcation branches encountered in multiple timescale dynamics, especially in a neuroscience context (e.g. isolas of spiking, bursting or MMO solutions). The main difficulty consists in computing at once an entire isola and continuing it as a single object in the parameter space, despite its inherent instability. We have proposed a new strategy, implemented as a series of Matlab routines [83], that enables one to perform multiple parallel continuation runs, subject to specific constraints between the different solution branches. Starting from a known (typically stable) solution obtained by direct simulation, our continuation approach combines the discretization of isolas into (possibly numerous) nodes with the use of periodic boundary conditions and a “phase-like” condition generalizing that implemented for the continuation of limit cycles. In addition, the stability of nodes is checked and possible bifurcations undergone by the nodes or isolas are detected in the course of the continuation.

We have investigated the slow-fast behavior of families of limit cycles in piecewise-linear systems approximations of multiple timescale systems, which are known to reproduce the rich dynamical repertoire of smooth systems while being amenable to more direct analysis. We have revisited previous work from the 1990s in order to complete the definition of a “canard cycle” in this context. We have shown that, even in the partial extension (where the fast nullcline is formed by 3 pieces instead of 4 for the entire extension), key features of canard cycles, such as the explosive behavior in parameter space and the shape with respect to the fast nullcline, are preserved [43].
We have extended our previous work [93] on *epsilon-free methods*, whose main advantage lies in not assuming the presence of a small parameter. In the case of planar slow-fast systems, the main idea is to associate strong changes of curvature with loci of inflection points of the flow in the phase plane projection, in order to detect transitions from fast to slow epochs and vice-versa and to estimate the timescale ratio when it is hidden. We have shown that inflection lines, that can be easily computed, provide a good approximation to the excitability threshold [7]. We have also studied the possible topological configurations of inflection lines, both in the singular limit and away from it, both in the “canard regime” (where the canard point corresponds to a tangency between two connected components of the inflection set) and in the “relaxation regime”.

3.3. Quantum engineering: controlled quantum systems  
**Participants:** Joachim Cohen, Loïc Herviou, Mazyar Mirrahimi, Pierre Rouchon, Pierre Six.

These research activities are done in collaboration with the permanent researchers of the future QUANTIC project-team, members of Laboratoire Pierre Aigrain, Benjamin Huard (CNRS), François Mallet (UPMC). They have benefited from important scientific exchanges and collaborations with the teams of Serge Haroche, Jean-Michel Raimond and Michel Brune at Laboratoire Kastler Brossel (LKB) and Collège de France and those of Michel Devoret and Robert Schoelkopf at the Department of Applied Physics of Yale University. The collaborations with the team of LKB have led to the first experimental realization of a real-time quantum feedback protocol allowing us to stabilize a highly non-classical state of quantum field trapped inside a microwave cavity [21]. This major breakthrough has been particularly highlighted in the 2012 physics Nobel prize attributed to Serge Haroche.

By focusing on two different but similar types of experimental setups, consisting of cavity quantum electrodynamical systems and quantum Josephson circuits, we aim to prepare highly non-classical states of a microwave field and protect these states against decoherence. Two different approaches are considered: 1- real-time measurement, quantum filtering and feedback; 2- dissipation engineering also called reservoir engineering. Through the first methodology, we try to propose new experimental feedback protocols based on a fast real-time processing of measurement signal, followed by a state estimation applying the filtered signal and finally designing simple feedback laws based on the estimated state. The second methodology consists in designing new quantum circuit schemes that allow to orient the system’s coupling to its environment in such a way that evacuates the undesired entropy induced by un-controlled noise sources.

3.3.1. Measurement based feedback  
In the framework of the PhD thesis of Hadis Amini [81], we have developed the mathematical methods [1], [82], [34] underlying a recent quantum feedback experiment stabilizing photon-number states [21]. We consider a controlled system whose quantum state, a finite dimensional density operator, is governed by a discrete-time nonlinear Markov process. In open-loop, the measurements are assumed to be quantum non-demolition (QND) measurements. This Markov process admits a set of stationary pure states associated to an orthonormal basis. These stationary states provide martingales crucial to prove the open-loop stability: under simple assumptions, almost all trajectories converge to one of these stationary states; the probability to converge to a stationary state is given by its overlap with the initial quantum state. From these open-loop martingales, we construct a supermartingale whose parameters are given by inverting a Metzler matrix characterizing the impact of the control input on the Kraus operators defining the Markov process. This supermartingale measures the “distance” between the current quantum state and the goal state chosen from one of the open-loop stationary pure states. At each step, the control input minimizes the conditional expectation of this distance. It is proven that the resulting feedback scheme stabilizes almost surely towards the goal state whatever the initial quantum state. This state feedback takes into account a known constant delay of arbitrary length in the control loop. This control strategy is proved to remain also convergent when the state is replaced by its estimate based on a quantum filter. It relies on measurements that can be corrupted by random errors with conditional probabilities described by a known left stochastic matrix. Closed-loop simulations corroborated by experimental data illustrate the interest of such nonlinear feedback scheme for the photon box.
In the framework of the postdoctoral stay of Ram Abhinav Somaraju within our group, we generalized these methods to infinite dimensional quantum stochastic systems [59]. Through this work, we studied the approximate state feedback stabilization of an infinite dimensional quantum stochastic system towards a target state. We can choose an (unbounded) strict Lyapunov function that is minimized at each time-step in order to prove (weak-∗) convergence of probability measures to a final state that is concentrated on the target state with (a pre-specified) probability that may be made arbitrarily close to 1. The feedback parameters and the Lyapunov function are chosen so that the stochastic flow that describes the Markov process may be shown to be tight (concentrated on a compact set with probability arbitrarily close to 1). We then use Prohorov’s theorem and properties of the Lyapunov function to prove the desired convergence result.

We have also investigated the stabilization of the dynamical state of a superconducting qubit [47], [37], [107]. In a series of papers, A. Korotkov and his co-workers suggested that continuous weak measurement of the state of a qubit and applying an appropriate feedback on the amplitude of a Rabi drive, should maintain the coherence of the Rabi oscillations for arbitrary time. Here, in the aim of addressing a metrological application of these persistent Rabi oscillations, we explore a new variant of such strategies. This variant is based on performing strong measurements in a discrete manner and using the measurement record to correct the phase of the Rabi oscillations. Noting that such persistent Rabi oscillations can be viewed as an amplitude-to-frequency convertor (converting the amplitude of the Rabi microwave drive to a precise frequency), we propose another feedback layer consisting of a simple analog phase locked loop to compensate the low frequency deviations in the amplitude of the Rabi drive.

3.3.2. Dissipation engineering

In the framework of the PhD thesis of Zaki Leghtas [104], we have introduced a new quantum gate that transfers an arbitrary state of a qubit into a superposition of two quasi-orthogonal coherent states of a cavity mode, with opposite phases [111]. This qcMAP gate is based on conditional qubit and cavity operations exploiting the energy level dispersive shifts, in the regime where they are much stronger than the cavity and qubit linewidths. The generation of multi-component superpositions of quasi-orthogonal coherent states [49], non-local entangled states of two resonators and multi-qubit GHZ states can be efficiently achieved by this gate. We also propose a new method, based on the application of this gate, to autonomously correct for errors of a logical qubit induced by energy relaxation. This scheme encodes the logical qubit as a multi-component superposition of coherent states in a harmonic oscillator. The error correction is performed by transferring the entropy to an ancila qubit and resetting the qubit. We layout in detail how to implement these operations in a practical system. We directly addresses the task of building a hardware-efficient and technically realizable quantum memory.

We have also studied the application of dissipation engineering techniques to perform a high-performance and fast qubit reset [46]. Qubit rest is crucial at the start of and during quantum information algorithms. Our protocol, nicknamed DDROP (Double Drive Reset of Population) is experimentally tested on a superconducting transmon qubit and achieves a ground state preparation of at least 99.5% in times less than 3µs; faster and higher fidelity are predicted upon parameter optimization.

3.4. Classical engineering: Monitoring and control of complex systems

We consider questions of modeling, identification, signal analysis and control with medical or general engineering applications in the continuation of some of the themes presented Section 4.3.

- **Glycemic control in ICUs.** Besides the medical questions, the applied mathematics approach is used for contributing to the development of reliable medical devices in cooperation with industry.

- **Reduced order cardiac modeling and applications.** We consider modeling questions related to Heart Failure with preserved Ejection Fraction (HFpEF): origin of this diastolic dysfunction and compensatory mechanisms. This is relying on previous results on excitation-contraction modeling on the cell scale.

- **Identification of transmission line characteristics.** We consider inverse scattering techniques and adapted solutions for the weak-loss estimation problem.
4. Application Domains

4.1. Mathematical neuroendocrinology

Mathematical neuroendocrinology is a new field that uses mathematical modeling and analysis to help interpret neuroendocrine knowledge and design new functional assumptions or experiments. Neuroendocrinology itself is a biological scientific field at the interface between Neurosciences, Endocrinology and Physiology (and even Developmental Biology in the case of the HPG axis); it studies neural networks in the brain that regulate, and that form, neuroendocrine systems. Neuroendocrinology necessarily includes the understanding and study of peripheral physiological systems that are regulated by neuroendocrine mechanisms. Hence, in addition to our studies dedicated to the hypothalamic and pituitary levels, we do embed the target peripheral system (the gonads) in our approach of the HPG axis, with a special interest in the cell dynamics processes involved in the morphogenesis of ovarian follicles.

On the central level, we are specifically interested in the following crucial questions arising from basic and clinical neuroendocrinology: (i) How does the network-level superslow secretion rhythm of the hypothalamic hormone GnRH emerge as pulses from the fast individual dynamics of neurons? (ii) How is GnRH pulsatility switched either on or off along the different steps of the reproductive life? (iii) How is the frequency of GnRH pulses encoded and decoded by its target pituitary cells? On the peripheral level, we address the following crucial questions arising from basic and clinical reproductive and developmental biology: (i) What are the multiscale bases of the selection process operated amongst ovarian follicles that guarantees the species-specific ovulation rate in mammals? (ii) Which configurations of the HPG axis allow for selection escape and poly-ovulating strategies, as observed naturally in prolific species or in strain-specific genetic mutations? (iii) How does the interaction between the oocyte and its surrounding follicular cells shape the morphology of the follicle in the early stages?

4.2. Quantum engineering

A new field of quantum systems engineering has emerged during the last few decades. This field englobes a wide range of applications including nano-electro-mechanical devices, nuclear magnetic resonance applications, quantum chemical synthesis, high resolution measurement devices and finally quantum information processing devices for implementing quantum computation and quantum communication. Recent theoretical and experimental achievements have shown that the quantum dynamics can be studied within the framework of estimation and control theory, but give rise to new models that have not been fully explored yet.

The QUANTIC team’s activities are defined at the theoretical and experimental border of this emerging field with an emphasis on the applications in quantum information, computation and communication. The main objective of this interdisciplinary team formed by applied mathematicians (Mazyar Mirrahimi and Pierre Rouchon) and experimental physicists (Benjamin Huard and François Mallet) is to develop quantum devices ensuring a robust processing of quantum information.

On the theory side, this is done by following a system theory approach: we develop estimation and control tools adapted to particular features of quantum systems. The most important features, requiring the development of new engineering methods, are related to the concept of measurement and feedback for composite quantum systems. The destructive and partial nature of measurements for quantum systems lead to major difficulties in extending classical control theory tools. Indeed, design of appropriate measurement protocols and, in the sequel, the corresponding quantum filters estimating the state of the system from the partial measurement record, are themselves bricks of the quantum system theory to be developed.

On the experimental side, we develop new quantum information processing devices based on quantum superconducting circuits. Indeed, by combining superconducting circuits in low temperatures and using techniques from micro-wave measurements, the macroscopic and collective degrees of freedom such as the voltage and the current are forced to behave according to the laws of quantum mechanics. Our quantum devices are aimed to protect and process the quantum information through these integrated circuits.
4.3. Monitoring and control of complex systems

Questions of modeling, identification, signal analysis and control are important in many medical or general engineering applications. We consider some very prospective questions as well as engineering questions raised by challenging industrial projects. The topics considered are the following:

Modeling, signal analysis and control with medical applications:

- 3D cardiac modeling for personalized medicine. Our main contribution to Inria collective effort in this field (project-teams Asclepios, MACS, REO, Sisyph) is the so-called “Bestel-Clément-Sorine” model of contraction of cardiac muscle [86], at the origin of the 3D electromechanical direct and inverse modeling of the heart at Inria. This model is based on ideas originating from the kinetic equation theory, used to model, on the molecular scale, the controlled collective behavior of actin-myosin nanomotors at the root of muscle contraction. The classical Huxley’s model was recovered on the sarcomere scale by using moment equations and a controlled constitutive law on the tissue scale was obtained using the same type of scaling techniques. The model, now embedded in heart simulators is used in various studies [55], [3], [112], [110].

- Semiclassical analysis of cardiovascular signals. This work began with the article [91] and the PhD of M. Laleg-Kirati [100], [99], [102]. The theory and a validation of a new method of blood pressure analysis are now published [51], [101].

The main idea is to consider a signal \( x \rightarrow y(x) \) to analyze as the multiplication operator \( \phi \rightarrow y\phi \) on some function space, and to analyze it as a potential. The signal is represented by the spectrum of an associated Schrödinger operator, combined with a semi-classical quantification: 
\[
-h^2 \frac{d^2}{dx^2} - y(x) \quad \text{with} \quad h > 0 \quad \text{small}.
\]
For signals looking as “superpositions of bumps” (e.g. the systolic pulse, the dichrotic notch for the arterial pulse pressure), this leads to some kind of nonlinear Fourier analysis [51]. The spectral parameters associated with the arterial pressure can be useful cardiovascular indices, e.g. for noninvasive blood flow estimation [101]. In the arterial pressure case, this is equivalent to approximate the traveling pressure pulse by a N-soliton solution of a Korteweg-de Vries (KdV) equation [91] and using ideas similar to the Lax pair representation of \( N \)-solitons and proof technique for the weak dispersion limit of KdV. A striking result is that an \( N \)-soliton is a very good representation of the arterial pressure waveform for values of \( N \) as small as \( N = 3 \). The representation of pulse-shaped signals is parcimonious, having only \( 2N \) parameters [113].

- Multiscale signal analysis of cardiovascular signals: collaboration with Julien Barral (former member of Sisyph) and partners of the ANR project DMASC. The starting point was the common idea that "A Healthy Heart Is a Fractal Heart". We have developed a method to test the existence of scale laws in signals and applied it to RR signals: the heart rate is not always fractal or even multifractal in an Healthy Heart [19].

- Modeling and control of CARMAT Total Artificial Heart. This TAH has been implanted for the first time in a patient in Dec 2013. We have contributed to this industrial project since 2008 on modeling and control questions during the post-doc of Karima Djabella (now at CARMAT), Frédéric Vallais and the two-year contract for supervising Julien Bernard (CARMAT control engineer). It was an opportunity for valorizing some results on the baroreflex control [94] or heart rate variability during exercise [90].

- Glycemic control in Intensive Care Units (ICUs): Blood glucose is a key biological parameter in ICU since the study of van den Berghe et al [123] who demonstrated decreased mortality in surgical intensive care patients in association with tight glycemic control (TGC), based on intensive insulin therapy. But there was only one ICU and the protocol was not formalized. Trying to decrease mortality in standard ICUs by using computer aided glycemic control is still a challenge. Previous studies have failed because of high rates of severe hypoglycaemia. The last one was NICE-SUGAR [117] with a 2% increase in mortality (death ratio from any cause within 90 days after randomization compared between control and TGC patients). In cooperation with Pierre Kalfon (Intensive Care, Hospital of Chartres) and in the framework of a CIFRE contract with a small medtech company LK2 (Tours, France), we have studied the origins of these failures and proposed more robust control algorithms tuned using a database of representative “virtual patients” [95], [96] and the PhD of A. Guerrini. [31]. A first version of the controller has been tested in a large clinical study CGAO-REA [70], [48].
- Cardiorespiratory signal processing in ICUs: cooperation with François Cottin (INSERM 902, Génopôle, Evry), Andry Van de Louw (Service de Réanimation Polyvalente, Centre Hospitalier Sud-Francilien, Evry) on the analysis of the effect of mechanical ventilation [118], [120], [119].

Modeling, signal analysis and control for general engineering:

Identification of nonlinear systems: from algorithms to a popular matlab toolbox:
- Identification of nonlinear systems: with Jiandong Wang (Associate Professor, Beijing University, China) [122], [121]: Block-oriented nonlinear system identification.
- Development of the Matlab System Identification ToolBox (SITB). See Section 5.1.

Identification of transmission line characteristics: from algorithms to electronic experiments. Collaboration with CEA LIST (Lab of applied research on software-intensive technologies) and LGEP (Laboratoire de génie électrique de Paris) with Florent Loete [106] (ANR projects SEEDS, 0-DEFECT, INSCAN, SODDA).

We have extended to some networks the seminal work of Jaulent [97] for the real line: all the information contained in a measured reflection coefficient can be obtained by solving an inverse scattering problem for a system of Schrödinger or Zakharov-Shabat equations on the graph of the network, which allows one to recover the geometry of the network and some electrical characteristics for nonuniform lossless electrical star-shaped networks [26]. An efficient method to solve the associated Guelfand-Levitan-Marchenko equations has been studied and is used in the software ISTL (see Section 5.2) [61], [114], [115]. An engineering methodology based on this approach has been described [29] and some first experimental results obtained [106].

Monitoring and control of automotive depollution systems: with RENAULT (Karim Bencherif, Damiano Di Penta and PhD students): [75], [20], [85].

Oscillatory systems in Control: reduced modeling, analysis, identification and synthesis: this is the topic of a cooperation with ITA (São José dos Campos, Brazil) [33].

5. Software and Platforms

5.1. SITB: The Matlab System Identification ToolBox

Participant: Qinghua Zhang.

This development is made in collaboration with Lennart Ljung (Linköping University, Sweden), Anatoli Juditsky (Joseph Fourier University, France) and Peter Lindskog (NIRA Dynamics, Sweden).

The System Identification ToolBox (SITB) is one of the main Matlab toolboxes commercialized by The Mathworks. Inria participates in the development of its extension to the identification of nonlinear systems which is released since 2007. It includes algorithms for both black box and grey box identification of nonlinear dynamic systems. Inria is mainly responsible for the development of black box identification, with nonlinear autoregressive (NLARX) models and block-oriented (Hammerstein-Wiener) models.

5.2. ISTL: Inverse Scattering for Transmission Lines

Participants: Michel Sorine, Qinghua Zhang.

ISTL is a software for numerical computation of the inverse scattering transform for electrical transmission lines. In addition to the inverse scattering transform, it includes a numerical simulator generating the reflection coefficients of user-specified transmission lines. With the aid of a graphical interface, the user can interactively define the distributed characteristics of a transmission line. It is registered at Agence pour la Protection des Programmes (APP) under the number IDDN.FR.001.120003.000.S.P.2010.000.30705.

5.3. CGAO: Contrôle Glycémique Assisté par Ordinateur

Participants: Alexandre Guerrini, Michel Sorine.
The software CGAO developed with LK2 and P. Kalfon (Hospital Louis Pasteur, Chartres) provides efficient monitoring and control tools that will help physicians and nursing staff to avoid hyperglycaemia and hypoglycaemia episodes in Intensive Care Units. The controller determines the insulin infusion rate, glucose bolus and scheduling of blood glucose measurement on the basis of the standard available glycaemia measurements. A first version, CGAO_v1, has been used in a large clinical study CGAO-REA (see Section 6.3.1). An improved version, CGAO_v2 registered at APP under the number IDDN.FR.001.360019.002.S.P.2009.000.31230 is now used by the company Fresenius Kabi (see Section 7.1).

5.4.  DYNPEAK: a Scilab toolbox and a Web service for the analysis of LH (Luteinizing Hormone) secretion rhythms

Participants:  Frédérique Clément, Claire Médigue, Serge Steer, Mouhamadoul Bachir Syll, Alexandre Vidal, Qinghua Zhang.

DYNPEAK is a software dedicated to the analysis of the pulsatile rhythm of secretion of the pituitary hormone LH, that aims at providing the final users (experimentalists and clinicians) with a simple-to-use version of the algorithm developed in [25]. It has been implemented as a Scilab atom toolbox (http://atoms.scilab.org/toolboxes/Dynpeak) and registered in APP under the reference DynPeak V1.0, IDDN.FR.001.360015.000.S.P.2013.000.10000. The web service version of DynPeak (https://dynpeak.inria.fr), still in test, has also been updated and a new release is planned for a next future.

5.5. The Cardiovascular toolbox for Scilab

Participants:  Claire Médigue, Michel Sorine, Serge Steer.

This Cardiovascular toolbox is an “atom” of Scilab developed by Serge Steer to distribute the cardiovascular signal processing tools designed and intensively used internally in the team for several years by Claire Médigue, Alessandro Monti and Michel Sorine. It includes baroreflex analysis using a multi channel non stationary signal analysis method; the cardiovascular signal spectral analysis using time-frequency decomposition and signal demodulations methods, e.g. for respiratory sinus arrhythmia analysis. It replaces LARY_CR, the former software package dedicated to the study of cardiovascular and respiratory rhythms [108].

5.6. K-Assessor: assessment of controllers

Participants:  Habib Jreige, Michel Sorine.

This development is made in collaboration with the small business enterprise SciWorks Technologies (Jim Pioche). We have defined a method to assess SISO (Single Input / Single Output) controllers based on square or cubic tables of metadata easily manipulated on a computer and easily interpretable by control experts and field experts (emergency doctors in our case) who can use them to jointly tune a risk estimator. The agreement between experts is obtained using a ROC-analysis approach. The software K-Assessor implements this methodology. It is registered at APP under the number IDDN.FR.001.390011.000.S.P.2013.000.10000.

6. New Results

6.1. Neuroscience & Neuroendocrinology: Regulation of the Gonadotrope axis

6.1.1. A numerical method for transport equations with discontinuous flux functions: application to mathematical modeling of cell dynamics

Participants:  Benjamin Aymard, Frédérique Clément, Frédéric Coquel, Marie Postel.
We have proposed a numerical method to handle discontinuous fluxes arising in transport-like equations [35]. More precisely, we have studied hyperbolic PDEs with flux transmission conditions at interfaces between subdomains where coefficients are discontinuous. A dedicated finite volume scheme with a limited high order enhancement has been adapted to treat the discontinuities arising at interfaces. The validation of the method has been done on one- and two-dimensional toy problems for which exact solutions are available, allowing us to do a thorough convergence study. We have then applied the method to a biological model focusing on complex cell dynamics [40] that initially motivated this study and illustrates the full potentialities of the scheme.

6.1.2. Adaptive mesh refinement strategy for a nonconservative transport problem

Participants: Benjamin Aymard, Frédérique Clément, Marie Postel.

In the framework of transport equations it is usual to need long time simulations, and therefore large physical domains to cover a phenomenon. On the other hand it can happen that only a small time varying portion of the domain is interesting. This motivates the use of adaptivity for the spatial discretization. Biological models involving cell development are often nonconservative to account for cell division. In that case the threshold controlling the spatial adaptivity may have to be time-dependent in order to keep up with the progression of the solution. We have tackled the difficulties arising when applying a multiresolution method to a transport equation with discontinuous fluxes modeling localized mitosis [76]. The analysis of the numerical method is performed on a simplified model and numerical scheme. An original threshold strategy is proposed and validated thanks to extensive numerical tests. It is then applied to a biological model in both cases of distributed and localized mitosis.

6.1.3. Coupled Somatic Cell Kinetics and Germ Cell Growth: Multiscale Model-Based Insight on Ovarian Follicular Development

Participants: Frédérique Clément, Philippe Michel, Danielle Monniaux, Thomas Stiehl.

We have designed a stochastic individual-based model describing the first stages of follicular development, where the cell population is structured with respect to age (progression within the cell cycle) and space (radial distance from the oocyte) [39]. The model accounts for the molecular dialogue existing between the oocyte and granulosa cells. Three dynamically interacting scales are considered in the model: (i) a microscopic, local scale corresponding to an individual cell embedded in its immediate environment, (ii) a mesoscopic, semi-local scale corresponding to anatomical or functional areas of follicles and (iii) a macroscopic, global scale corresponding to the morphology of the follicle. Numerical simulations were performed to reproduce the 3D morphogenesis of follicles and follow simultaneously the detailed spatial distribution of individual granulosa cells, their organization as concentric layers or functional cell clones and the increase in the follicle size. Detailed quantitative simulation results have been provided in the ovine species, in which well characterized genetic mutations lead to a variety of phenotypic follicle morphogenesis. The model can help to explain pathological situations of imbalance between oocyte growth and follicular cell proliferation.

6.1.4. Innovative computational and theoretical tools for slow-fast dynamics

Participants: Mathieu Desroches, Maciej Krupa.

Mixed-Mode Bursting Oscillations: Dynamics created by a slow passage through spike-adding canard explosion in a square-wave burster [44]. This work concerns the phenomenon of Mixed-Mode Bursting Oscillations (MMBOs). These are solutions of fast-slow systems of ordinary differential equations that exhibit both small-amplitude oscillations (SAOs) and bursts consisting of one or multiple large-amplitude oscillations (LAOs). The name MMBO is given in analogy to Mixed-Mode Oscillations, which consist of alternating SAOs and LAOs, without the LAOs being organized into burst events. In this article, we show how MMBOs are created naturally in systems that have a spike-adding bifurcation or spike-adding mechanism, and in which the dynamics of one (or more) of the slow variables causes the system to pass slowly through that bifurcation. Canards are central to the dynamics of MMBOs, and their role in shaping the MMBOs is two-fold: saddle-type canards are involved in the spike-adding mechanism of the underlying burster and permit one to understand the number of LAOs in each burst event, and folded-node canards arise due to the slow passage effect and control the number of SAOs. The analysis is carried out for a prototypical fourth-order system of this type, which consists
of the third-order Hindmarsh-Rose system, known to have the spike-adding mechanism, and in which one of the key bifurcation parameters also varies slowly. We also include a discussion of the MMBO phenomenon for the Morris-Lecar-Terman system. Finally, we discuss the role of the MMBOs to a biological modeling of secreting neurons.

Canards in piecewise-linear systems: explosions and super-explosions [43]. We show that a planar slow-fast piecewise-linear (PWL) system with three zones admits limit cycles that share a lot of similarity with van der Pol canards, in particular an explosive growth. Using phase-space compactification, we show that these quasi-canard cycles are strongly related to a bifurcation at infinity. Furthermore, we investigate a limiting case in which we show the existence of a continuum of canard homoclinic connections that coexist for a single-parameter value and with amplitude ranging from an order of $\varepsilon$ to an order of 1, a phenomenon truly associated with the non-smooth character of this system and which we call super-explosion.

Some results have been obtained concerning numerical continuation techniques for planar slow-fast systems [42] and short-term synaptic plasticity in the deterministic Tsodyks-Markram model that leads to unpredictable network dynamics [41].

6.2. Quantum engineering: controlled quantum systems
Participants: Joachim Cohen, Loïc Herviou, Mazyar Mirrahimi, Pierre Rouchon, Pierre Six.

6.2.1. Schrödinger cat states and hardware efficient quantum error correction
We introduce a new gate that transfers an arbitrary state of a qubit into a superposition of two quasi-orthogonal coherent states of a cavity mode, with opposite phases [52]. Such a highly non-classical state is often called a Schrödinger cat state. This qcMAP gate is based on conditional qubit and cavity operations exploiting the energy level dispersive shifts, in the regime where they are much stronger than the cavity and qubit linewidths. The generation of multi-component superpositions of quasi-orthogonal coherent states, non-local entangled states of two resonators and multi-qubit GHz states can be efficiently achieved by this gate.

In a second contribution [53], we propose to use an encoding of a quantum bit of information in a four-component Schrödinger cat state to ensure its protection against the photon loss, being the major source of decoherence for such a quantum harmonic oscillator. This protection is ensured by an efficient quantum error correction scheme employing the nonlinearity provided by a single physical qubit coupled to the cavity. We describe in detail how to implement these operations in a circuit quantum electrodynamics system. This directly addresses the task of building a hardware-efficient quantum memory and can lead to important shortcuts in quantum computing architectures.

As an important step towards the realization of such a protected quantum memory, in a collaboration with the team of Robert J. Schoelkopf at Yale university, we have successfully realized the encoding protocol of [52] using a 3D transmon qubit coupled to a waveguide cavity resonator with a highly ideal off-resonant coupling [60]. This dispersive interaction is much greater than decoherence rates and higher-order nonlinearities to allow simultaneous manipulation of hundreds of photons. We created cat states as large as 111 photons and created superpositions of up to four coherent states. This control creates a powerful interface between discrete and continuous variable quantum computation and could enable applications in metrology and quantum information processing. This important achievement was published in Science and was also highlighted in Science Perspectives [103].

6.2.2. Quantum reservoir (dissipation) engineering
We have studied the application of dissipation engineering techniques to perform a high-performance and fast qubit reset [64]. Qubit reset is crucial at the start of and during quantum information algorithms. In a collaboration with the team of Michel H. Devoret at Yale university, our protocol, nicknamed DDROP (Double Drive Reset of Population) was experimentally tested on a superconducting transmon qubit and achieves a ground state preparation of at least 99.5% in times less than $3\mu$s; faster and higher fidelity are predicted upon parameter optimization [46].
Next, we proposed a dissipation engineering scheme that prepares and protects a maximally entangled state of a pair of superconducting qubits [54]. This is done by off-resonantly coupling the two qubits to a low-Q cavity mode playing the role of a dissipative reservoir. We engineer this coupling by applying six continuous-wave microwave drives with appropriate frequencies. The two qubits need not be identical. We show that our approach does not require any fine-tuning of the parameters and requires only that certain ratios between them be large. This protocol was experimentally realized in a collaboration with the team of M. H. Devoret at Yale university [57]. Unlike conventional, measurement-based schemes, this autonomous approach uses engineered dissipation to counteract decoherence, obviating the need for a complicated external feedback loop to correct errors. Instead, the feedback loop is built into the Hamiltonian such that the steady state of the system in the presence of drives and dissipation is a Bell state, an essential building block for quantum information processing. Such autonomous schemes, which are broadly applicable to a variety of physical systems, will be an essential tool for the implementation of quantum error correction. This important result appeared in Nature back-to-back to another paper by the group of D.J. Wineland (2012 Nobel prize winner) at NIST implementing similar ideas on another physical system consisting of trapped ion qubits [105].

6.2.3. Quantum measurement and measurement-based feedback

Measuring a quantum system can randomly perturb its state. The strength and nature of this back-action depend on the quantity that is measured. In a partial measurement performed by an ideal apparatus, quantum physics predicts that the system remains in a pure state whose evolution can be tracked perfectly from the measurement record. This property was proved in a collaboration with the group of Michel H. Devoret (Yale university) using a superconducting qubit dispersively coupled to a cavity traversed by a microwave signal [47]. The back-action on the qubit state of a single measurement of both signal quadratures was observed and shown to produce a stochastic operation whose action is determined by the measurement result. This accurate monitoring of a qubit state is an essential prerequisite for measurement-based feedback control of quantum systems. Indeed, in another experiment performed by our collaborators at ENS (team of Benjamin Huard and François Mallet), we demonstrated stabilization of an arbitrary trajectory of a superconducting qubit by such a measurement-based feedback [37]. The protocol benefits from the long coherence time ($T_2 > 10\mu s$) of the 3D transmon qubit, the high efficiency (82%) of the phase preserving Josephson amplifier, and fast electronics ensuring less than 500 ns delay. At discrete time intervals, the state of the qubit is measured and corrected in case an error is detected. For Rabi oscillations, where the discrete measurements occur when the qubit is supposed to be in the measurement pointer states, we demonstrate an average fidelity of 85% to the targeted trajectory. Incidentally, we demonstrate a fast reset protocol allowing to cool a 3D transmon qubit down to 0.6% in the excited state.

6.3. Classical engineering: Monitoring and control of complex systems

6.3.1. Modeling, signal analysis and control with medical applications

**Participants:** Alexandre Guerrini, Lisa Guigue, Claire Médigue, Michel Sorine, Serge Steer.

*Reduced order cardiac modeling and applications.* See Section 4.3 for complements. We consider two topics:
- Personalized medicine: a first validation on clinical data of our model of controlled contraction of cardiac muscle has been obtained [55].
- Heart Failure with preserved Ejection Fraction (HFpEF): this work is done in collaboration with Bijan Gahleh (INSERM U955). Our objective is to define markers of HFpEF identifiable from noninvasive measurements. After having assembled a high precision ECG acquisition and post-processing system, we have measured multi-lead ECG on pigs treated to induce HFpEF, cf. B. Gahleh et al [109]. The analysis of the diastolic electric interval (e.g. P-wave, PR interval etc.) is ongoing.

*Semiclassical analysis of cardiovascular signals.* A summary of the theory is now published [51].

**CGAO-REA:** *Computerized Glucose Control in Critically Ill Patients.* The version CGAO_v1 of our controller (see Sections 4.3), has been used in a large multi-center study, CGAO-REA (35 active ICUs, more than 3500 included patients). Mortality has not been changed [70], [48] but the protocol is now formalized and tunable. CGAO-REA has proved that our controller is robust in the real life context and comparable to human control with its present tuning. Improving the tuning (in particular the glycemic target) seems possible.
6.3.2. Diagnosis of inhomogeneous insulation degradation in electric cables by distributed shunt conductance estimation

Participant: Qinghua Zhang.

For the diagnosis of inhomogeneous insulation degradation in electric cables, the estimation of distributed shunt conductance is studied in this work. Gradual growth of the shunt conductance is a consequence of degradation of the dielectric properties of the insulator. The proposed estimation method is based on voltage and current measurements at a single end of the cable. After the linearization of the bilinear term of the telegrapher's equations through a perturbation approach, the Kalman filter is applied to transform the problem of dynamic system parameter estimation to a simple linear regression problem. Numerical simulations are made to demonstrate the feasibility of the proposed method. In particular, it is shown that the weak sensitivity of the available measurements to the shunt conductance can be compensated by long time data samples. See [61] for more details.

6.3.3. Feasibility of reflectometry techniques for non destructive evaluation of external post-tensioned cables

Participants: Michel Sorine, Qinghua Zhang.

Nowadays a considerable number of bridges is reaching an age when renovating operations become necessary. For some bridges, external post-tension is realized with cables protected in ducts, with the residual internal space imperfectly filled with a fluid cement grout. Detecting the problems of injection in the ducts is visually impossible from the outside. In collaboration with IFSTTAR (Institut Français des Sciences et Technologies des Transports, de l’Aménagement et des Réseaux) through the I4S team common to Inria and IFSTTAR, the feasibility of reflectometry techniques for cable health monitoring is investigated via numerical simulations and laboratory experiments. The main idea consists in adding electrically conductive tapes along a duct so that the duct and the added tapes can be treated as an electrical transmission line. It is then possible to apply advanced reflectometry methods developed by the SISYPHE project-team, initially for true electric cables.

6.3.4. Nonlinear system identification

Participants: Boyi Ni, Michel Sorine, Qinghua Zhang.

In the framework of the joint Franco-Chinese ANR-NSFC EBONSI project (see Section 8.1.1), the topics studied this year on nonlinear system identification are mainly on the detection of asymmetric control valve stiction from oscillatory data based on a method for extended Hammerstein system identification, and on the identification of Wiener systems.

The study on control valve stiction is motivated by the detection of control valves with asymmetric stiction resulting in oscillations in feedback control loops. The joint characterization of the control valve and the controlled process is formulated as the identification of a class of extended Hammerstein systems. The input nonlinearity is described by a point-slope-based hysteretic model with two possibly asymmetric ascent and descent paths. An iterative identification method is proposed, based on the idea of separating the ascent and descent paths subject to the oscillatory input and output. The structure of the formulated extended Hammerstein system is shown to be identifiable, and the oscillatory signals in feedback control loops are proved to be informative by exploiting the cyclo-stationarity of these oscillatory signals. Numerical, experimental and industrial examples confirm the effectiveness of the proposed identification method.

Wiener system identification has been investigated this year by focusing on the estimation of the finite impulse response (FIR) of the linear subsystem. Under the assumption of Gaussian input distribution, this work mainly aims at addressing a deficiency of the well-known correlation-based method for Wiener system identification: it fails when the nonlinearity of the Wiener system is an even function. This method is, in the considered Gaussian input case, equivalent to the best linear approximation (BLA), which exhibits the same deficiency. A new method is developed this year, based on a weighted principal component analysis (wPCA). Its consistency is proved for Wiener systems with either even or non even nonlinearities. Its computational cost is almost the same as that of a standard PCA. Numerical simulations are made to compare the new wPCA-based method to the correlation-based method for different Wiener systems with nonlinearities more or less close to an even function.
6.3.5. Model-based fault diagnosis for descriptor systems

Participants: Abdouramane Moussa Ali, Qinghua Zhang.

This work is about fault diagnosis for linear time varying descriptor systems, the discrete time counterpart of dynamic systems described by differential-algebraic equations. The Kalman filter for descriptor systems is first revisited by completing existing results about its properties that are essential for the purpose of fault diagnosis. Based on the analysis of the effects of the considered actuator and sensor faults on the innovation of the Kalman filter, it is shown that the considered fault diagnosis problem in linear time varying descriptor systems can be transformed to a classical linear regression problem formulated by appropriately filtering the input-output data. Following this result, algorithms for fault diagnosis through maximum likelihood estimation are then developed.

In the framework of the ITEA2 MODRIO project (see Section 8.2.1), this work is in preparation for studying hybrid system monitoring, aiming at extending existing results from state-space systems to descriptor systems in the modes of a hybrid system.

6.3.6. Analysis of the Behavior of Networks of Dynamical Systems

Participant: Pierre-Alexandre Bliman.

We have established convergence results for some continuous-time dynamics which are analogs to ant colony optimization algorithms that solve shortest path problems. Global asymptotic stability has been shown, and the speed of convergence has been calculated explicitly and shown to be proportional to the difference between the reciprocals of the second shortest and the shortest paths. Such precise results are missing in the context of ant colony optimization algorithms (which are discrete-time dynamical systems). The systems studied are special instances of networks of dynamical systems which represent the evolution of some state variable on each path, coupled in a competitive way through global macroscopic quantity. Such models are related to simple forms of models studied in mathematical epidemiology, which will be the subject of further work. This work is done in cooperation with Amit Bhaya from COPPE, Universidade Federal de Rio de Janeiro. Papers have been submitted [77].

7. Bilateral Contracts and Grants with Industry

7.1. CGAO_v2 contract: glycemic control system

Participants: Alexandre Guerrini, Michel Sorine.

Our work on glycaemic control done in the framework of the CIFRE contract of A. Guerrini [31] with LK2 (Tours, France), has led to develop an improved controller, CGAO_v2 (see Sections 4.3 and 5.3). This year, our rights on CGAO_v2 have been sold to LK2 which has packaged it with a user interface in a system used by Fresenius-Kabi in their control software master GC.

7.2. SciWorks Technologies contract: development of K-Assessor

Participants: Habib Jreige, Michel Sorine.

The development and a first application of K-Assessor (see Section 5.6) has been done with SciWorks Technologies: risk analysis for master GC, a software of Fresenius-Kabi dedicated to glycemic control assistance based on the control algorithm CGAO_v2 (see Section 5.3).

8. Partnerships and Cooperations

8.1. National Initiatives

8.1.1. ANR project EBONSI: Extended Block-Oriented Nonlinear System Identification

Participants: Boyi Ni, Michel Sorine, Qinghua Zhang.
The main idea of block-oriented nonlinear system identification is to model complex systems with interconnected simple blocks. Such models cover many industrial applications and are simple enough for theoretic studies. In EBONSI we extend classical block-oriented nonlinear models to new model structures motivated by applications, and relax some traditional restrictions on experimental conditions. This international project is jointly funded by the French ANR and the Chinese National Natural Science Foundation (NSFC) from 2011 to 2014. The partners are SISYPHE (project leader), the Centre de Recherche en Automatique de Nancy (CRAN), and the Laboratory of Industrial Process Monitoring and Optimization of Peking University.

8.1.2. ANR project 0DEFECT: On-board fault diagnosis for wired networks

Participants: Mohamed Oumri, Michel Sorine, Qinghua Zhang.

Due to the increasing number of electric and electronic equipments in automotive vehicles, the reliability of electric connections is becoming more and more important. The project 0DEFECT aims at developing tools for on-board diagnosis of failures in electric wire connections in automotive systems. The project is funded by Agence Nationale de la Recherche (ANR) from 2009 to Jan 2013. The partners are CEA LIST (project leader), Renault Trucks, Freescale, PSA, Delphi, Supelec LGEP and Inria.

8.1.3. ANR project SODDA: Soft Defects Diagnosis in wired networks

Participants: Michel Sorine, Qinghua Zhang.

The need for detection, localization and characterization of defects in a cable network has led to the ANR projects SEEDS followed by 0-DEFECT in the automotive domain, INSCAN for cables along railways. These projects provide the foundations of diagnosis methods for cables – with a proof of feasibility in the case of hard defects (short-circuit, open circuit) - and some theoretical results on the associated inverse problems in the case of soft faults. They also made it possible to identify their limits. One of the principal limits of these methods, based on the principles of reflectometry, is the difficulty of detecting soft defects. If it was possible to detect and locate precisely these defects, that would help for preventive maintenance or prognosis. The objective of SODDA is to study the signatures of the soft defects, by combining theory and experiment, and to design and test innovative methods adapted to these signatures which are very difficult to detect. The project is run by an academic consortium, in close connection with an industrial board, responsible for keeping the work in realistic and relevant use cases. The Inria teams involved are POEMS and Sisyphe.

8.1.4. ANR project EPOQ2: Estimation PrOblems for Quantum & Quantumlike systems

Participants: Mazyar Mirrahimi, Pierre Rouchon, Michel Sorine.

The project EPOQ2 is an ANR “Young researcher” project led by Mazyar Mirrahimi (Sisyphe). Its goal is to address a class of inverse problems arising from either the emerging application domain of “quantum engineering” or from some classical applications where a natural quantization lead to quantum-like systems, as it is the case in particular for inverse scattering for transmission lines. This research is in collaboration with the Pierre Aigrain laboratory at ENS Paris, Michel Devoret and Rob Schoelkopf at Yale University and Pierre Rouchon from Ecole Nationale Supérieure des Mines de Paris.

8.1.5. Inria Large Scale Initiative Action REGATE

REGATE (REgulation of the GonAdoTropE axis) has been a 4-year Large Scale Initiative Action funded by Inria in May 2009 dedicated to the modeling, simulation and control of the gonadotrope axis. The action is coordinated by Frédérique Clément. The Inria participants to this action are researchers of 2 Inria research teams, Contrainites and Sisyphe. There are also participants from INRA, Université Libre de Bruxelles (Unité de Chronobiologie théorique), Université Paris 6 (Laboratoire Jacques-Louis Lions) and the Florida State University.

The closing meeting of REGATE has hold this year on April 9th. Beyond its academic achievements (see more details on the publication page of the website), REGATE has played a significant role on the national level, in the constitution of the transversal research group “Integrative and translational approaches of human and animal reproduction” (GdR REPRO), that was initiated by ITMO (Multi OrganizationThematic Institute)) BCDE (Cell Biology, Development and Evolution).
8.2. European Initiatives

8.2.1. Collaborations in European Programs, except FP7

**MODRIO: Model Driven Physical Systems Operation.** This ITEA 2 (Information Technology for European Advancement) project is joined by partners from Austria, Belgium, Finland, France, Germany, Italy and Sweden. See the complete list on the MODRIO page of the ITEA 2 call 6 website. The involved Inria project-teams are PARKAS, S4 and SISYPHE. It is coordinated by EDF, France.

To meet the evermore stringent safety and environmental regulations for power plants and transportation vehicles, system operators need new techniques to improve system diagnosis and operation. Open standards are necessary for different teams to cooperate by sharing compatible information and data. The objective of the MODRIO project is to extend modeling and simulation tools based on open standards from system design to system diagnosis and operation.

**ERNSI: European Research Network System Identification.** The SISYPHE project-team is involved in the activities of the European Research Network on System Identification (ERNSI) federating major European research teams on system identification. See the website of ERNSI. Funded as a SCIENCE project (1992 - 1995), HCM Project (1993-1996), TMR Project (1998 - 2003), this network, currently coordinated by Bo Wahlberg, Automatic Control, KTH, Stockholm, is still very active.

Partners: KTH (Sweden), Inria (France), TUD (Technische Universität Darmstadt), TUW (Vienna University of Technology), UCAM-DENG (University of Cambridge), ELEC (Vrije Universiteit Brussel), ULIN (Sweden), UNIPD (Italy).

8.3. International Initiatives

8.3.1. Inria International Partners

8.3.1.1. Declared Inria International Partners

Collaborations in Neuroscience & Neuroendocrinology:
- Boston University: joint publications [87], [92] (with John Burke, Tasso Kaper and Mark Kramer).
- University of Sevilla (Spain): joint publications [43] (with Emilio Freire and Enrique Poncè), participation in PhD examination boards (Mathieu Desroches).
- Joint publications with individual collaborators: Thomas Stiehl (IWR Heidelberg) [39] ; David Avitabile (School of Mathematical Sciences, University of Nottingham) [83] and Serafim Rodrigues (Centre for Robotics and Neural Systems, Plymouth University) [83], [7].
- Florida State University: joint work on GnRH decoding, with Richard Bertram and Joël Tabak, in the framework of the doctoral committee of Patrick Fletcher.

Collaborations in Quantum engineering:
The collaborations with the teams of Michel Devoret and Robert Schoelkopf, enforced through a two-year sabbatical visit of Maryam Mirrahimi at Yale university, have led to a set of contributions ranging from the theoretical analysis and performance optimization of ongoing experiments on weak quantum measurements [47] and preparation of non-classical field states through single photon Kerr effect [49] to the design of new experiments on single qubit cooling by reservoir engineering techniques [46] and development of new quantum gates allowing the transfer of quantum information from a superconducting qubit to a cavity mode [111].

Collaborations in Classical engineering:
Long-term collaboration of Qinghua Zhang with Lennart Ljung (Linköping University, Sweden) and Peter Lindskog (NIRA Dynamics, Sweden) that led to the development of the System Identification ToolBox (SITB) is one of the main Matlab toolboxes commercialized by The Mathworks and several papers.
8.4. International Research Visitors

8.4.1. Visits of International Scientists

Koen TIELS, Vrije Universiteit Brussel, Department of Fundamental Electricity and Instrumentation, from the group of Johan SCHOUKENS, has visited us during October 2013.

8.4.2. Visits to International Teams

Mazyar Mirrahimi spent four months in the Quantronics Laboratory of Michel Devoret and in the Rob Schoelkopf Lab at Yale University.

9. Dissemination

9.1. Scientific Animation

P.-A. Bliman:
- Chargé de mission at Direction Générale de la Recherche et de l’Innovation, Ministère de l’Enseignement Supérieur et de la Recherche (since 2012, part-time, 60%) ; Scientist in charge of latin America at Direction des Affaires Internationales, Inria (since 2009, part-time, 20%) ; Member of the Scientific Committees of the regional collaboration program MATH AmSud and STIC AmSud (since 2009).
- Associate Editor of Systems & Control Letters (since 2008) ; Reviewer for IEEE Transactions on Automatic Control, Automatica... ; Expert for Fonds National de la Recherche Scientifique (FNRS), Belgium ; Member of the Conference Editorial Board of European Control Association (EUCA), actuating for 13th European Control Conference, Strasbourg, June 2014.


Appointed member of the scientific board of the BCDE (Cell Biology, Development and Evolution) ITMO (Multi OrganizationThematic Institute) of the French National Alliance for Life and Health Sciences http://www.aviesan.fr/en.

M. Mirrahimi: Associate Editor of Systems & Control Letters ; Member of IFAC Technical Committee on Distributed Parameter Systems.

M. Sorine: Member of IFAC Technical Committee on the Biological and Medical Systems (IFAC TC 8.2) ; Member of the scientific board of the ITMO Circulation, Metabolism and Nutrition (Multi Organization Thematic Institute of the French National Alliance for Life and Health Sciences).

Q. Zhang is Member of two IFAC Technical Committees on 1/ Fault Detection, Supervision and Safety of Technical Processes ; 2/ Modelling, Identification and Signal Processing.

9.2. Teaching - Supervision - Juries

9.2.1. Teaching

Master: P.-A. Bliman, “Advanced tools for system analysis and design by Linear Matrix Inequalities (LMI) techniques”, Instituto Tecnológico de Aeronáutica, São José dos Campos (SP), Brazil (3h).


Master: S. Steer, “Traitement numérique du signal et application aux signaux physiologiques”, 32 heures, M2, Université d’Evry, France.
9.2.2. Supervision


9.3. Popularization

The high profile publications in *Nature* and *Science* are popularizing the new field of quantum engineering.

10. Bibliography

Major publications by the team in recent years


Publications of the year

Doctoral Dissertations and Habilitation Theses
[31] A. Guerrini. , Évaluation des performances de systèmes d’assistance au contrôle pour la réanimation : Application au contrôle de la glycémie, Université Paris-Sud Orsay, June, 21 2013


[33] T. Pereira Das Chagas. , Stabilisation d’orbits périodiques pour des systèmes en temps discret et en temps continu, Université Paris Sud - Paris XI and Instituto Tecnológico de Aeronáutica, June 2013, Thèse en co-tutelle avec l’ Instituto Tecnológico de Aeronáutica - São José dos Campos - SP - Brésil, http://hal.inria.fr/tel-00852424

**Articles in International Peer-Reviewed Journals**


[59] R. A. Somaraju, M. Mirrahimi, P. Rouchon. Approximate stabilization of an infinite dimensional quantum stochastic system, in "Reviews in Mathematical Physics", February 2013, vol. 25, n° 1 [DOI : 10.1142/S0129055X13500013], http://hal.inria.fr/hal-00829864


Invited Conferences


International Conferences with Proceedings
[63] F. LEI, J. WANG, Q. ZHANG. Identification of extended Hammerstein systems for modeling sticky control valves under general types of input signals, in "CCC 2013 - 32nd Chinese Control Conference", Xi’an, China, July 2013, http://hal.inria.fr/hal-00854683


[65] A. MOUSSA ALI, Q. ZHANG. Adaptive observer based fault diagnosis applied to differential-algebraic systems, in "5th IFAC Symposium on System Structure and Control", Grenoble, France, February 2013, http://hal.inria.fr/hal-00776818


National Conferences with Proceedings


Conferences without Proceedings


[72] M. DESROCHES. Inflection lines near canards in 2D and 3D systems, in "Workshop on Slow-Fast Dynamics: Theory, Numerics and Application to Earth and Life Sciences", Barcelona, Spain, June 2013, http://hal.inria.fr/hal-00854374

Research Reports

[74] M. BRØNS, M. DESROCHES, M. KRUPA., Epsilon-free curvature methods for slow-fast dynamical systems, 2013, http://hal.inria.fr/hal-00832547

Patents and standards


Other Publications

[76] B. AYMARD, F. CLÉMENT, M. POSTEL., Adaptive mesh refinement strategy for a nonconservative transport problem, 2013, http://hal.inria.fr/hal-00865429

[77] P.-A. BLIMAN, A. BHAYA, E. KASZKUREWICZ, J. JAYADEVA., Convergence results for continuous-time dynamics arising in ant colony optimization, 2013, Submitted, http://hal.inria.fr/hal-00923900

[78] A. GRANADOS, M. KRUPA, F. CLÉMENT., Border collision bifurcations of stroboscopic maps in periodically driven spiking models, 2013, http://hal.inria.fr/hal-00910277

[79] A. GRANADOS, M. KRUPA, F. CLÉMENT., Frequency decoding subject to dose conservation: firing rate response of periodically driven spiking models, 2013, http://hal.inria.fr/hal-00870383

[80] M. KRUPA, B. AMBROSIO, M. A. AZIZ-ALAOUI., Weakly coupled two slow- two fast systems, folded node and mixed mode oscillations, 2013, http://hal.inria.fr/hal-00786195

References in notes


