Activity Report 2011

Project-Team SISYPHE

SIgnals and SYstems in PHysiology & Engineering

RESEARCH CENTER
Paris - Rocquencourt

THEME
Observation, Modeling, and Control for Life Sciences

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Project-Team SISYPHE

Keywords: Models, Control Theory, Multiscale Models, Integrative Physiology, System Analysis And Control

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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”.

Most studies are motivated, in Physiology, by the cardiovascular and reproductive systems and in Engineering, by some critical engineering systems like electrical networks or by quantum control in some nanosystems.

The research on the reproductive system is done in the framework of REGATE (REgulation of the GonAdoTropE axis), an Inria Large-Scale Initiative Action (LSIA) coordinated by F. Clément.

Research topics:
Signals & Systems

- Dynamical systems modeled by ordinary differential equations: modeling, observation and control.
- Quantum & quantum-like systems: estimation and control.
- Multiscale dynamical systems: analysis of multiscale properties of signals and relations with the underlying dynamical systems.

Applications to Physiology & Engineering

- Model-based observation and control of the cardiovascular system: (multiscale-) model-based signal processing (ECG, pressure, heart-rate). Monitoring and control of cardiac prosthesis.
- Waves propagation in transmission-line networks & Inverse scattering. Application to health monitoring of cabled electrical networks and to the arterial pressure waveform analysis.
- Health monitoring and control of energy conversion systems: glycemic control in critically ill patients ; monitoring of exhaust gas aftertreatment systems.
- Identification and control of some quantum systems: towards “quantum engineering”.
- Multiscale modeling of the controlled follicle selection process & Control of the reproductive axis.

2.2. Highlights

Mazyar Mirrahimi, Adis Hamini and Pierre Rouchon are the co-authors of an article in *Nature*, September 2011 on an application of real-time quantum feedback to the preparation and stabilization of a small number of photons in a cavity [12]. They have proposed the feedback scheme for quantum systems undergoing discrete-in-time non-destructive measurements that is used in this experiment.

3. Scientific Foundations

3.1. System theory for systems modeled by ordinary differential equations

3.1.1. Identification, observation, control and diagnosis of linear and nonlinear systems

Characterizing and inferring properties and behaviors of objects or phenomena from observations using models is common to many research fields. For dynamical systems encountered in the domains of engineering and physiology, this is of practical importance for monitoring, prediction, and control. For such purposes, we consider most frequently, the following model of dynamical systems:

$$\begin{aligned} \frac{dx(t)}{dt} &= f(x(t), u(t), \theta, w(t)) \\ y(t) &= g(x(t), u(t), \theta, v(t)) \end{aligned} \tag{1}$$

where $x(t)$, $u(t)$ and $y(t)$ represent respectively the state, input and output of the system, f and g characterize the state and output equations, parameterized by θ and subject to modeling and measurement uncertainties $w(t)$ and $v(t)$. Modeling is usually based on physical knowledge or on empirical experiences, strongly depending on the nature of the system. Typically only the input $u(t)$ and output $y(t)$ are directly observed by sensors. Inferring the parameters θ from available observations is known as system identification and may be useful for system monitoring [83], whereas algorithms for tracking the state trajectory $x(t)$ are called observers. The members of SISYPHE have gained important experiences in the modeling of some engineering systems and biomedical systems. The identification and observation of such systems often remain challenging because of strong nonlinearities [15]. Concerning control, robustness is an important issue, in particular to ensure various properties to all dynamical systems in some sets defined by uncertainties [62], [63]. The particularities of ensembles of connected dynamical systems raise new challenging problems.

Examples of reduced order models:
- Reduced order modeling of the cardiovascular system for signal & image processing or control applications. See section 3.3.1.
- Excitable neuronal networks & control of the reproductive axis by the GnRH. See section 3.3.2.
- Modeling, Control, Monitoring and Diagnosis of Depollution Systems. See section 6.9.

3.1.2. Observation and control of networks of dynamical systems

Some of the systems we consider can be modeled as Networks of (almost identical) Dynamical Systems (NODS for short). Often, the available sensors provide information only at the macroscopic scale of the network. For example, usually in monitoring systems for electrical transmission line networks, voltage sensors are only available in some nodes. This sensor limitation implies challenging problems for the observation and control of such systems. See e.g. [14]. The control objective may be formulated in terms of some kind of average behavior of the components and of bounds on some deviations from the average. To this end, appropriate modeling techniques must be developed.

The NODS are intensively studied in physics and mathematics (see, e.g. [80] or [64] for a survey). This complex structure gives rise to new dynamical behaviors, ranging from de-correlation to coherent behaviors, such as synchronization or emergence of traveling waves. New control issues are also of particular interest as, here, the problem of control of synchronization. We illustrate this with an example of NODS where each dynamical system i exchanges with the others, $j = 1...N$, in an additive way, a frequent situation in our applications. A example of network based on dynamical systems (1) is [64]:

$$\begin{aligned} \frac{dx_i}{dt} &= f_i(x_i, u_i, \theta_i, w_i) - \Sigma_{j=1}^{N} \mathcal{C}_{i,j} g_j(x_j, u_j, \theta_j, v_j) \\ y &= g(x_1, ...x_N, u_1, ...u_N, \theta_1, ...\theta_N, v_1, ...v_N) \end{aligned} \tag{2}$$

The connectivity matrix $\mathcal{C}$ represents the structure of the network.

NODS and Partial Differential Equations.
Semi-discretization in space of a PDE of evolution or systems of PDE leads to NODS as in the case of electrical transmission line networks, where a system of equations of type (4) is considered (see 3.2.1).

Consider for axample the dynamical population of cells mentioned in section 3.3.2. The coupling between cells is due to the control and the NODS model, with $\mathcal{C} = 0$ and N variable (depending upon the set of trajectories of the cells in the age-maturity plane) corresponds to a particle approximation of a controlled conservation law [9], [8] where, for each follicle f, the cell population is represented in each cellular phase by a density ϕ_f and u_f and U are respectively a local control of follicle f and a global control of all follicles:

$$\frac{\partial \phi_f}{\partial t} + \frac{\partial g_f(u_f)\phi_f}{\partial a} + \frac{\partial h_f(\gamma, u_f)\phi_f}{\partial \gamma} = -\lambda(\gamma, U)\phi_f \tag{3}$$

3.2. System theory for quantum and quantum-like systems

3.2.1. Quantization of waves propagation in transmission-line networks & Inverse scattering

Linear stationary waves. Our main example of classical system that is interesting to see as a quantum-like system is the Telegrapher Equation, a model of transmission lines, possibly connected into a network. This is the standard model for electrical networks, where V and I are the voltage and intensity functions of z and k, the position and frequency and $R(z)$, $L(z)$, $C(z)$, $G(z)$ are the characteristics of the line:

$$\frac{\partial V(z,k)}{\partial z} = -\left(R(z) + jkL(z)\right) I(z,k), \quad \frac{\partial I(z,k)}{\partial z} = -(G(z) + jkC(z))V(z,k) \tag{4}$$

Since the work of Noordergraaf [82], this model is also used for hemodynamic networks with V and I respectively the blood pressure and flow in vessels considered as 1D media, and with $R = \frac{8\pi\eta}{S^2}$, $L = \frac{\rho}{S}$, $C = \frac{3S(r+h)}{E(2r+h)}$ where ρ and η are the density and viscosity of the blood ; r, h and E are the inner radius, thickness and Young modulus of the vessel. $S = \pi r^2$. The conductivity G is a small constant for blood flow. Monitoring such networks is leading us to consider the following inverse problem: *get information on the functions R, L, C, G from the reflection coefficient* $\mathcal{R}(k)$ (ratio of reflected over direct waves) measured in some location by Time or Frequency Domain Reflectometry.

To study this problem it is convenient to use a Liouville transform, setting $x(z) = \int_0^z \sqrt{L(z')C(z')}dz'$, to introduce auxiliary functions $q^{\pm}(x) = \frac{1}{4}\frac{d}{x}\left(\ln \frac{L(x)}{C(x)}\right) \pm \frac{1}{2}\left(\frac{R(x)}{L(x)} - \frac{G(x)}{C(x)}\right)$ and $q_p(x) = \frac{1}{2}\left(\frac{R(x)}{L(x)} + \frac{G(x)}{C(x)}\right)$, so that (4) becomes a Zakharov-Shabat system [68] that reduces to a Schrödinger equation in the lossless case ($R = G = 0$):

$$\frac{\partial v_1}{\partial x} = (q_p - jk)\, v_1 + q^+ v_2, \quad \frac{\partial v_2}{\partial x} = -\left(q_p - jk\right) v_2 + q^- v_1 \tag{5}$$

and $I(x,k) = \frac{1}{\sqrt{2}}\left[\frac{C(x)}{L(x)}\right]^{\frac{1}{4}} (v_1(x,k) + v_2(x,k))$, $V(x,k) = -\frac{1}{\sqrt{2}}\left[\frac{L(x)}{C(x)}\right]^{\frac{1}{4}} (v_1(x,k) - v_2(x,k))$.
Our inverse problem becomes now an inverse scattering problem for a Zakharov-Shabat (or Schrödinger) equation: *find the potentials* $q^{\pm}$ *and* q_p *corresponding to* $\mathcal{R}$. This classical problem of mathematical physics can be solved using e.g. the Gelfand-Levitan-Marchenko method.

Nonlinear traveling waves. In some recent publications [71], [70], we use scattering theory to analyze a measured Arterial Blood Pressure (ABP) signal. Following a suggestion made in [84], a Korteweg-de Vries equation (KdV) is used as a physical model of the arterial flow during the pulse transit time. The signal analysis is based on the use of the Lax formalism: the iso-spectral property of the KdV flow allows to associate a constant spectrum to the non stationary signal. Let the non-dimensionalized KdV equation be

$$\frac{\partial y}{\partial t} - 6y\frac{\partial y}{\partial x} + \frac{\partial^3 y}{\partial x^3} = 0 \tag{6}$$

In the Lax formalism, y is associated to a Lax pair: a Schrödinger operator, $L(y) = -\frac{\partial^2}{\partial x^2} + y$ and an anti-Hermitian operator $M(y) = -4\frac{\partial^3}{\partial x^3} + 3y\frac{\partial}{\partial x} + 3\frac{\partial}{\partial x}y$. The signal y is playing here the role of the potential of $L(y)$ and is given by an operator equation equivalent to (6):

$$\frac{\partial L(y)}{\partial t} = [M(y), L(y)] \tag{7}$$

Scattering and inverse scattering transforms can be used to analyze y in term of the spectrum of $L(y)$ and conversely. The "bound states" of $L(y)$ are of particular interest: if $L(y)$ is solution of (7) and $L(y(t))$ has only bound states (no continuous spectrum), then this property is true at each time and y is a soliton of KdV. For example the arterial pulse pressure is close to a soliton [6].

Inverse scattering as a generalized Fourier transform. For "pulse-shaped" signals y, meaning that $y \in L^1(\mathbb{R}; (1+|x|^2)dx)$, the squared eigenfunctions of $L(y)$ and their space derivatives are a basis in $L^1(\mathbb{R}; dx)$ (see e.g. [79]) and we use this property to analyze signals. Remark that the Fourier transform corresponds to using the basis associated with $L(0)$. The expression of a signal y in its associated basis is of particular interest. For a positive signal (as e.g. the arterial pressure), it is convenient to use $L(-y)$ as $-y$ is like a multi-well potential, and the Inverse scattering transform formula becomes:

$$y(x) = 4 \sum_{n=1}^{n=N} \kappa_n \psi_n^2(x) - \frac{2i}{\pi} \int_{-\infty}^{-\infty} k \mathcal{R}(k) f^2(k,x) dk \tag{8}$$

where ψ_n and $f(k,.)$ are solutions of $L(-y)f = k^2 f$ with $k = i\kappa_n$, $\kappa_n > 0$, for ψ_n (bound states) and $k > 0$ for $f(k,.)$ (Jost solutions). The discrete part of this expression is easy to compute and provides useful informations on y in applications. The case $\mathcal{R} = 0$ ($-y$ is a reflectionless potential) is then of particular interest as $2N$ parameters are sufficient to represent the signal. We investigate in particular approximation of pulse-shaped signals by such potentials corresponding to N-solitons.

3.2.2. Identification & control of quantum systems

Interesting applications for quantum control have motivated seminal studies in such wide-ranging fields as chemistry, metrology, optical networking and computer science. In chemistry, the ability of coherent light to manipulate molecular systems at the quantum scale has been demonstrated both theoretically and experimentally [78]. In computer science, first generations of quantum logical gates (restrictive in fidelity) has been constructed using trapped ions controlled by laser fields (see e.g. the "Quantum Optics and Spectroscopy Group, Univ. Innsbruck"). All these advances and demands for more faithful algorithms for manipulating the quantum particles are driving the theoretical and experimental research towards the development of new control techniques adapted to these particular systems. A very restrictive property, particular to the quantum systems, is due to the destructive behavior of the measurement concept. One can not measure a quantum system without interfering and perturbing the system in a non-negligible manner.

Quantum decoherence (environmentally induced dissipations) is the main obstacle for improving the existing algorithms [67]. Two approaches can be considered for this aim: first, to consider more resistant systems with respect to this quantum decoherence and developing faithful methods to manipulate the system in the time constants where the decoherence can not show up (in particular one can not consider the back-action of the measurement tool on the system); second, to consider dissipative models where the decoherence is also included and to develop control designs that best confronts the dissipative effects.

In the first direction, we consider the Schrödinger equation where $\Psi(t,x)$, $-\frac{1}{2}\Delta$, V, μ and $u(t)$ respectively represent the wavefunction, the kinetic energy operator, the internal potential, the dipole moment and the laser amplitude (control field):

$$i\frac{d}{dt}\Psi(t,x) = (H_0 + u(t)H_1)\Psi(t,x) = (-\frac{1}{2}\Delta + V(x) + u(t)\mu(x))\Psi(t,x), \quad \Psi|_{t=0} = \Psi_0, \tag{9}$$

While the finite dimensional approximations ($\Psi(t) \in \mathbb{C}^N$) have been very well studied (see e.g. the works by H. Rabitz, G. Turinici, ...), the infinite dimensional case ($\Psi(t,.) \in L^2(\mathbb{R}^N;\mathbb{C})$) remains fairly open. Some partial results on the controllability and the control strategies for such kind of systems in particular test cases have already been provided [58], [59], [74]. As a first direction, in collaboration with K. Beauchard (CNRS, ENS Cachan) et J-M Coron (Paris-sud), we aim to extend the existing ideas to more general and interesting cases. We will consider in particular, the extension of the Lyapunov-based techniques developed in [75], [60], [74]. Some technical problems, like the pre-compactness of the trajectories in relevant functional spaces, seem to be the main obstacles in this direction.

In the second direction, one needs to consider dissipative models taking the decoherence phenomena into account. Such models can be presented in the density operator language. In fact, to the Schrödinger equation (9), one can associate an equation in the density operator language where $\rho = \Psi\Psi^*$ represents the projection operator on the wavefunction Ψ ($[A,B] = AB - BA$ is the commutator of the operators A and B):

$$\frac{d}{dt}\rho = -i[H_0 + u(t)H_1, \rho], \tag{10}$$

Whenever, we consider a quantum system in its environment with the quantum jumps induced by the vacuum fluctuations, we need to add the dissipative effect due to these stochastic jumps. Note that at this level, one also can consider a measurement tool as a part of the environment. The outputs being partial and not giving complete information about the state of the system (Heisenberg uncertainty principle), we consider a so-called quantum filtering equation in order to model the conditional evolution of the system. Whenever the measurement tool composes the only (or the only non-negligible) source of decoherence, this filter equation admits the following form:

$$\begin{aligned} d\rho_t = -i[H_0 + u(t)H_1, \rho_t]dt + (L\rho_t L^* - \frac{1}{2}L^*L\rho_t - \frac{1}{2}\rho_t L^*L)dt \\ + \sqrt{\eta}(L\rho_t + \rho_t L^* - \mathrm{Tr}\left[(L+L^*)\rho_t\right]\rho_t)dW_t, \end{aligned} \tag{11}$$

where L is the so-called Lindblad operator associated to the measurement, $0 < \eta \leq 1$ is the detector's efficiency and where the Wiener process W_t corresponds to the system output Y_t via the relation $dW_t = dY_t - \mathrm{Tr}\left[(L+L^*)\rho_t\right]dt$. This filter equation, initially introduced by Belavkin [61], is the quantum analogous of a Kushner-Stratonovic equation. In collaboration with H. Mabuchi and his co-workers (Physics department, Caltech), we would like to investigate the derivation and the stochastic control of such filtering equations for different settings coming from different experiments [76].

Finally, as a dual to the control problem, physicists and chemists are also interested in the parameter identification for these quantum systems. Observing different physical observables for different choices of the input $u(t)$, they hope to derive more precise information about the unknown parameters of the system being parts of the internal Hamiltonian or the dipole moment. In collaboration with C. Le Bris (Ecole des ponts and INRIA), G. Turinici (Paris Dauphine and INRIA), P. Rouchon (Ecole des Mines) and H. Rabitz (Chemistry department, Princeton), we would like to propose new methods coming from the systems theory and well-adapted to this particular context. A first theoretical identifiability result has been proposed [72]. Moreover, a first observer-based identification algorithm is under study.

3.3. Physiological & Clinical research topics

3.3.1. The cardiovascular system: a multiscale controlled system

Understanding the complex mechanisms involved in the cardiac pathological processes requires fundamental researches in molecular and cell biology, together with rigorous clinical evaluation protocols on the whole organ or system scales. Our objective is to contribute to to these researches by developing low-order models of the cardiac mechano-energetics and control mechanisms, for applications in model-based cardiovascular signal or image processing.

We consider intrinsic heart control mechanisms, ranging from the Starling and Treppe effects on the cell scale to the excitability of the cardiac tissue and to the control by the autonomous nervous system. They all contribute to the function of the heart in a coordinated manner that we want to analyze and assess. For this purpose, we study reduced-order models of the electro-mechanical activity of cardiac cells designed to be coupled with measures available on the organ scale (e.g. ECG and pressure signals). We study also the possibility to gain insight on the cell scale by using model-based multiscale signal processing techniques of long records of cardiovascular signals.

Here are some questions of this kind, we are considering:
- Modeling the controlled contraction/relaxation from molecular to tissue and organ scales.
- Direct and inverse modeling the electro-mechanical activity of the heart on the cell scale.
- Nonlinear spectral analysis of arterial blood pressure waveforms and application to clinical indexes.
- Modeling short-term and long-term control dynamics on the cardiovascular-system scale. Application to a Total Artificial Heart.

3.3.2. Reproductive system: follicular development & ovulation control

The ovulatory success is the main limiting factor of the whole reproductive process, so that a better understanding of ovulation control is needed both for clinical and zootechnical applications. It is necessary to improve the treatment of anovulatory infertility in women, as it can be by instance encountered in the PolyCystic Ovarian Syndrome (PCOS), whose prevalence among reproductive-age women has been estimated at up to 10%. In farm domestic species, embryo production following FSH stimulation (and subsequent insemination) enables to amplify the lineage of chosen females (via embryo transfer) and to preserve the genetic diversity (via embryo storage in cryobanks). The large variability in the individual responses to ovarian stimulation treatment hampers both their therapeutic and farming applications. Improving the knowledge upon the mechanisms underlying FSH control will help to improve the success of assisted reproductive technologies, hence to prevent ovarian failure or hyperstimulation syndrome in women and to manage ovulation rate and ovarian cycle chronology in farm species.

To control ovarian cycle and ovulation, we have to deeply understand the selection process of ovulatory follicles, the determinism of the species-specific ovulation rate and of its intra- and between-species variability, as well as the triggering of the ovulatory GnRH surge from hypothalamic neurons.
Beyond the strict scope of Reproductive Physiology, this understanding raises biological questions of general interest, especially in the fields of

Molecular and Cellular Biology. The granulosa cell, which is the primary target of FSH in ovarian follicles, is a remarkable cellular model to study the dynamical control of the transitions between the cellular states of quiescence, proliferation, differentiation, and apoptosis, as well as the adaptability of the response to the same extra-cellular signal according to the maturity level of the target cell. Moreover, the FSH receptor belongs to the seven transmembrane spanning receptor family, which represent the most frequent target (over 50%) amongst the therapeutic agents currently available. The study of FSH receptor-mediated signaling is thus not only susceptible to allow the identification of relaying controls to the control exerted by FSH, but it is also interesting from a more generic pharmacological viewpoint.

Neuroendocrinology and Chronobiology. The mechanisms underlying the GnRH ovulatory surge involve plasticity phenomena of both neuronal cell bodies and synaptic endings comparable to those occurring in cognitive processes. Many time scales are interlinked in ovulation control from the fastest time constants of neuronal activation (millisecond) to the circannual variations in ovarian cyclicity. The influence of daylength on ovarian activity is an interesting instance of a circannual rhythm driven by a circadian rhythm (melatonin secretion from the pineal gland).

Simulation and control of a multiscale conservation law for follicular cells

In the past years, we have designed a multiscale model of the selection process of ovulatory follicles, including the cellular, follicular and ovarian levels [9], [8]. The model results from the double structuration of the granulosa cell population according to the cell age (position within the cell cycle) and to the cell maturity (level of sensitivity towards hormonal control). In each ovarian follicle, the granulosa cell population is described by a density function whose changes are ruled by conservation laws. The multiscale structure arises from the formulation of a hierarchical control operating on the aging and maturation velocities as well on the source terms of the conservation law. The control is expressed from different momentums of the density leading to integro-differential expressions.
Future work will take place in the REGATE project and will consist in:
- predicting the selection outcome (mono-, poly-ovulation or anovulation / ovulation chronology) resulting from given combinations of parameters and corresponding to the subtle interplay between the different organs of the gonadotropic axis (hypothalamus, pituitary gland and ovaries). The systematic exploration of the situations engendered by the model calls for the improvement of the current implementation performances. The work will consist in improving the precision of the numerical scheme, in the framework of the finite volume method and to implement the improved scheme, basing by instance on the current routines designed within the Bearclaw (http://www.amath.unc.edu/Faculty/mitran/bearclaw.html) academic environment,
- solving the control problems associated with the model. Indeed, the physiological conditions for the triggering of ovulation, as well as the counting of ovulatory follicles amongst all follicles, define two nested and coupled reachability control problems. Such particularly awkward problems will first be tackled from a particular approximation of the density, in order to design appropriate control laws operating on the particles and allowing them to reach the target state sets.

Connectivity and dynamics of the FSH signaling network in granulosa cells

The project consists in analyzing the connectivity and dynamics of the FSH signaling network in the granulosa cells of ovarian follicles and embedding the network within the multiscale representation described above, from the molecular up to the organic level. We will examine the relative contributions of the Gα_s and βarrestin-dependent pathways in response to FSH signal, determine how each pathway controls downstream cascades and which mechanisms are involved in the transition between different cellular states (quiescence, proliferation, differentiation and apoptosis). On the experimental ground, we propose to develop an antibody microarray approach in order to simultaneously measure the phosphorylation levels of a large number of signaling intermediates in a single experiment. On the modeling ground, we will use the BIOCHAM (biochemical abstract machine) environment first at the boolean level, to formalize the network of interactions corresponding to the FSH-induced signaling events on the cellular scale. This network will then be enriched with kinetic information coming from experimental data, which will allow the use of the ordinary differential equation level of BIOCHAM. In order to find and fine-tune the structure of the network and the values of the kinetic parameters, model-checking techniques will permit a systematic comparison between the model behavior and the results of experiments. In the end, the cell-level model should be abstracted to a much simpler model that can be embedded into a multiscale one without losing its main characteristics.

Bifurcations in coupled neuronal oscillators.

We have proposed a mathematical model allowing for the alternating pulse and surge pattern of GnRH (Gonadotropin Releasing Hormone) secretion [5]. The model is based on the coupling between two systems running on different time scales. The faster system corresponds to the average activity of GnRH neurons, while the slower one corresponds to the average activity of regulatory neurons. The analysis of the slow/fast dynamics exhibited within and between both systems allows to explain the different patterns (slow oscillations, fast oscillations and periodical surge) of GnRH secretion.
This model will be used as a basis to understand the control exerted by ovarian steroids on GnRH secretion, in terms of amplitude, frequency and plateau length of oscillations and to discriminate a direct action (on the GnrH network) from an indirect action (on the regulatory network) of steroids. From a mathematical viewpoint, we have to fully understand the sequences of bifurcations corresponding to the different phases of GnRH secretion. This study will be derived from a 3D reduction of the original model.

4. Software

4.1. The Matlab System Identification ToolBox (SITB)

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.

4.2. Inverse Scattering for Transmission Lines (ISTL)

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. This software is mainly for the purpose of demonstrating a numerical solution to the inverse problem of non uniform transmission lines. Its current version is limited to the case of lossless transmission lines. It is registered at Agence pour la Protection des Programmes (APP) under the number IDDN.FR.001.120003.000.S.P.2010.000.30705.

4.3. CGAO: Contrôle Glycémique Assisté par Ordinateur

Participants: Alexandre Guerrini, Michel Sorine.

This development is made in collaboration with Pierre Kalfon (Chartres Hospital) and Gaëtan Roudillon (LK2).

This software developed with LK2 and 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. It is used in a large clinical study, CGAO-REA. Commercialization will be done by LK2.

The software is designed to assist physicians to deal with a variant of the classical Stability/Precision dilemma of control theory met during blood-glucose control. It has been tested in the ICU of Chartres and, since November 2009, it is used in a large scale study launched by the SFAR (French Society of Anesthesia and Intensive Care) involving 62 ICUs and including 6422 patients.

More than 3500 patients have been included in CGAO-REA.

4.4. LARY_CR: Software package for the Analysis of Cardio Vascular and Respiratory Rhythms

Participants: Claire Médigue, Serge Steer.

LARY_CR is a software package dedicated to the study of cardiovascular and respiratory rhythms [77]. It presents signal processing methods, from events detection on raw signals to the variability analysis of the resulting time series. The events detection concerns the heart beat recognition on the electrocardiogram, defining the RR time series, the maxima and minima on the arterial blood pressure defining the systolic and diastolic time series. These detections are followed by the resampling of the time series then their analyse. This analyse uses temporal and time frequency methods: Fourier Transform, spectral gain between the cardiac and blood pressure series, Smooth Pseudo Wigner_Ville Distribution, Complex DeModulation, temporal method of the cardiovascular Sequences. The objective of this software is to provide some tools for studying the autonomic nervous system, acting in particular in the baroreflex loop; its functionning is reflected by the cardiovascular variabilities and their relationships with the other physiological signals, especially the respiratory activity. Today LARY_CR is used only internally, in the framework of our clinical collaborations.

5. New Results

5.1. Modeling, observation and control: systems modeled by ordinary differential equations

5.1.1. Nonlinear system identification

Participants: Pierre-Alexandre Bliman, Michel Sorine, Qinghua Zhang.

Our current researches on nonlinear system identification are mainly in the framework of the joint Franco-Chinese ANR-NSFC EBONSI project (See Section 6.5), started in March 2011 for three years, in collaboration with the Laboratory of Industrial Process Monitoring and Optimization of Peking University and with Centre de Recherche en Automatique de Nancy (CRAN). Three topics have been studied this year: system identification with a continuous time autoregressive model, system identification with quantized data, and Hammerstein-Wiener system identification.

Though discrete time models are widely used in system identification, some advantages of continuous time models are also of practical importance, in particular, the ability of fully benefiting from fast sampling devices. Our studies on this topic have resulted in a continuous time black-box model structure for nonlinear system identification, together with an efficient model estimation method. This model structure belongs to the class of continuous time nonlinear ARX (AutoRegressive with eXogenous input) models, with the particularity of being integrable. By applying techniques of adaptive observer, models of the proposed structure can be efficiently estimated from input-output data. This result has been presented at the last Journées Identification et Modélisation Expérimentale [49].

System identification is usually based on sampled and quantized data, because of the important role of digital computers. When quantized data are coded with a sufficiently large number of bits, the effect of quantization is often ignored in the design of system identification methods. However, when data are quantized with few bits, sometimes to a single bit leading to binary data, then the effect of quantization must be explicitly taken into account. Data quantization can be modeled as a non differentiable hard nonlinearity, hence the well known gradient-based optimization methods cannot be used for the identification of such nonlinear systems. We have developed a quadratic programming-based method for system identification from quantized data, which, in contrast to most existing methods, can be applied to systems with general input excitations. This result has been presented at the last IFAC World Congress [46].

A Hammerstein-Wiener system is composed of a dynamic linear subsystem preceded and followed by two static nonlinearities. Typically, the nonlinearities of such a system is caused by actuator and sensor distortions. The identification of such systems with a continuous time model had been studied by colleagues of CRAN with the refined instrumental variable (RIV) method. Stable low-pass filters were used to overcome the difficulties related to the continuous time nature of the model. Our study of this year is about the application of the Kalman filter at the place of the previously used low-pass filters. The advantages of this new method include the stability of the numerical algorithm and the fact that the Kalman filter does not color white noises.

5.1.2. Model-based fault diagnosis

Participants: Abdouramane Moussa Ali, Qinghua Zhang.

The increasing requirements for higher performance, efficiency, reliability and safety of modern engineering systems call for continuous research investigations in the field of fault detection and isolation. In the framework of the MODIPRO project funded by Paris Region ASTech, we are currently studying model-based fault diagnosis for nonlinear systems. Motivated by an application in the MODIPRO project, the considered system is modeled by nonlinear algebro-differential equations, with the particularity that the differential part of the model is linear in state variables. Instead of using general numerical solvers of algebro-differential equations, we are developing a method based on ordinary differential equation solvers, by taking advantage of the particular algebro-differential structure of the considered system.

5.2. Observation, control and traveling waves in systems modeled by partial differential equations

5.2.1. Inverse scattering for soft fault diagnosis in electric transmission lines

Participants: Michel Sorine, Huaibin Tang, Qinghua Zhang.

The inverse scattering theory is helpful for efficient use of the reflectometry technology in the field of electric transmission line fault diagnosis. Our recent studies on this topic have been published in [35], [33], [32]. The main progress of this year in our study has been the experimental validation of the inverse scattering-based method for soft fault diagnosis. In collaboration with Florent Loete of LGEP (Laboratoire de Génie Electrique de Paris), we have tested the inverse scattering-based method on cables used in Trucks. By slightly separating the two wires of a twisted pair following a predefined spatial profile, a soft fault in the cable is physically simulated. The spatially smoothly varying characteristic impedance of the cable is computed from the physical and geometrical parameters of the cable, and also computed from the reflection coefficient measured with a network analyzer at one end of the cable. The two results are close enough to clearly detect and to locate the physically simulated soft fault from the measured reflection coefficient. A demonstration software has been developed and registered at Agence pour la Protection des Programmes (APP). See Section 4.2.

5.2.2. Modeling of electric transmission networks

Participants: Mohamed Oumri, Michel Sorine, Filippo Visco Comandini, Qinghua Zhang.

The increasing number and complexity of wired electric networks in modern engineering systems is amplifying the importance of the reliability of electric connections. In the framework of the ANR 0-DEFECT project, we have studied mathematical models of complex electric networks with the aim of designing an algorithm for fault diagnosis (see [34], [20] for some theoretical results). A generalization of the Baum-Liu-Tesche (BLT) equation to the case of inhomogeneous transmission lines has been developed this year. Efforts have been made in particular to elaborate a fully automatized method for numerical simulation of complex networks with inhomogeneous transmission lines. An efficient method has been designed for the computation of the propagation matrix of each inhomogeneous transmission line and also for the computation of the scattering matrix at each network node. The implemented numerical simulator is based on these propagation and scattering matrices associated to the BLT equation, and on a numerical solution of this equation.

5.2.3. Diagnosis of insulator degradation in long electric cables

Participants: Leila Djaziri, Michel Sorine, Huaibin Tang, Qinghua Zhang.

For the diagnosis of insulator degradation in long electric cables, the estimation of the shunt conductance of such cables have been studied, in the framework of the ANR INSCAN project. The shunt conductance of a healthy electric cable is usually very weak. Even when the insulator in the cable is significantly degraded, the shunt conductance can still remain at a quite low level. The main difficulty in this study is due to the fact that the measurements made at the ends of a cable are hardly sensitive to the variations of the shunt conductance. To overcome this difficulty, two methods have been studied. The first one is based on the processing of long time data records. It is designed for the estimation of distributed shunt conductance, in order to detect and to locate inhomogeneous degradation of the insulator. The main idea of this method is to compensate the weak sensitivity of the measurement by long time data records. Numerical simulations have confirmed its feasibility. The second method aims at assessing the average shunt conductance along a cable. It is based on the analysis of the sensitivity of the wave propagation velocity to the shunt conductance. This method is currently tested through experiments made on cables of SNCF (Société Nationale des Chemins de Fer français).

5.3. System theory approach of some quantum systems

5.3.1. Design of strict control-Lyapunov functions for quantum systems with QND measurements

Participants: Hadis Amini, Mazyar Mirrahimi, Pierre Rouchon.

We have proposed a feedback scheme for quantum systems undergoing discrete-in-time non-destructive measurements. Under some observability assumptions, the proposed feedback law ensures the stabilization of any desired equilibrium state of the measurement process. This theoretical contribution has given rise to a primary conference paper [40] and we are currently working on a more complete journal paper that proves the convergence in presence of various measurement noises and uncertainties. The proposed feedback scheme has been applied in a recent experiment realized by Serge Haroche and Jean-Michel Raimond's group at Ecole Normale Supérieure and has given rise to a journal paper [29].

5.3.2. Approximate stabilization of an infinite dimensional quantum stochastic system

Participants: Ram Somaraju, Mazyar Mirrahimi, Pierre Rouchon.

Extending our previous feedback schemes dealing only with finite dimensional quantum systems, we have proven the approximate stabilization of any desired Fock state in the microwave cavity setup of Ecole Normale Supérieure. By appropriately choosing the Lyapunov function, we avoid the mass-loss phenomena through high energy levels and ensure the pre-compactness (in probability) of the trajectories. This work has given rise to a conference paper [48] and a submitted journal paper [56].

5.3.3. On stability of continuous-time quantum filters

Participants: Hadis Amini, Mazyar Mirrahimi, Pierre Rouchon.

We have studied the stability of quantum filters for continuous-in-time measurement processes. Indeed, we have proven that the filter between the quantum state governed by a continuous time stochastic master equation driven by a Wiener process and its associated quantum-filter state is a sub-martingale. This result has given rise to a conference paper [41].

5.4. Modeling, observation and control in biosciences - Reproductive system

5.4.1. Numerical simulation of the selection process of the ovarian follicles

Participants: Benjamin Aymard, Frédérique Clément.

Collaboration with Frédéric Coquel and Marie Postel.

We have designed and implemented a numerical method to simulate a multiscale model describing the selection process in ovarian follicles [9], [8]. The PDE model consists in a quasi-linear hyperbolic system of large size, namely $N_f \times N_f$, ruling the time evolution of the cell density functions of N_f follicles (in practice N_f is of the order of a few to twenty). These equations are weakly coupled through the sum of the first order moments of the density functions. The time-dependent equations make use of two structuring variables, age and maturity, which play the roles of space variables. The problem is naturally set over a compact domain of $\mathbf{R}^2$. The formulation of the time-dependent controlled transport coefficients accounts for available biological knowledge on follicular cell kinetics. We introduce a dedicated numerical scheme that is amenable to parallelization, by taking advantage of the weak coupling. Numerical illustrations assess the relevance of the proposed method both in term of accuracy and HPC achievements [50], [51].

5.4.2. *Multiscale modeling of follicular ovulation as a mass and maturity dynamical system*

Participants: Frédérique Clément, Philippe Michel, Danielle Monniaux.

We have analyzed the dynamics of the solutions using bifurcation tools on a reduced, ODE model [73]. In a first stage, the 2D PDE model is reduced to a 1D PDE model, where the only remaining variable is the age. This reduction is based on a result of exponential convergence in maturity ; we have proved that the granulosa cell density of each follicle converges to a “dirac mass in maturity”, which can be understood as: “the follicle becomes uniform in maturity”. The proof is based on the crucial decay property of the maturity speed rate with respect to the maturity variable, so that the support of the cell density of each follicle concentrates its mass around a curve given by a characteristic equation. In a second stage, the mitosis rate is averaged in age, reducing the 1D PDE to a simpler system of two coupled nonlinear ODE, where each follicle is characterized by its cell number (the follicle mass) and global maturity. These variables correspond respectively to the zero-order moment and first-order moment in maturity of the cell density in the original model. The dynamics of one given follicle can then be studied with respect to the pressure exerted collectively by all other growing follicles, in the framework of dynamical games. In some sense, the pressure can be considered as an exogenous parameter, so that we can detect dynamical bifurcations according to the pressure value. Each follicle plays against the others for its survival. In the course of its terminal development, a follicle first remains in the proliferative zone of the mass-maturity plane and then enters the differentiated zone. At the transition from proliferation to differentiation, the follicle is highly sensitive to the pressure. In the worst (doomed) case, the follicle becomes atretic, due to prolongated cell loss. In the best (saved) case, it manages to go through the vulnerability zone and becomes insensitive to the pressure of other follicles.

5.4.3. *Optimal control for a conservation law modeling the development of ovulation*

Participants: Frédérique Clément, Peipei Shang.

Collaboration with Jean-Michel Coron
We are now investigating control problems associated to the multiscale model of follicle selection. The conditions for the triggering of the ovulatory surge, coupled with the sorting of the ovulatory follicles, define a complex, nested reachability problem. We have considered a more tractable version of that problem, which is centered on defining the optimal local control corresponding to a single ovulatory trajectory. Under some simplifying assumptions (no loss term and constant aging velocity), we have obtained analytical and numerical results in the case when the density is idealized by one or several Dirac mass. We are extending our results to the PDE original model.

5.4.4. *Multiscale analysis of mixed-mode oscillations in a phantom bursting model*

Participants: Frédérique Clément, Mathieu Desroches, Maciej Krupa, Alexandre Vidal.

We have carried on the study of our fast-slow model of the GnRH (gonadotropin-releasing hormone) pulse and surge generator [5], [4]. If we relax a little the constraints imposed by the biological specifications on the parameters, very rich and complex behaviours can be further exhibited by the model. More precisely, both a delay to the surge and a post-surge pause (before pulsatility resumption) may occur. A detailed examination of the pause has revealed that it is shaped by mixed-mode oscillations (MMO). We are currently investigating how the precise sequence of MMO is determined by the global return map from the surge to the pulse regime.

5.4.5. Transient synchronization of calcium oscillations in cultures of GnRH neurons.

Participants: Frédérique Clément, Maciej Krupa, Alexandre Vidal.

We have started to study the individual dynamics of GnRH neurons and the conditions under which they may synchronize. We are more specifically tacking the issue of synchronization of calcium oscillations in cultures obtained from the olfactory placodes of rhesus monkey embryos [81]. We have introduced a class of models explaining the synchronization events; their main idea was to introduce a global variable controlling the onset of synchronization that was subsequently reset by the subsequent high firing rate caused by the activation of an adaptation current.

5.5. Clinical and physiological applications

5.5.1. DynPeak: An algorithm for pulse detection and frequency analysis in hormonal time series

Participants: Frédérique Clément, Claire Médigue, Alexandre Vidal, Qinghua Zhang.

Collaboration with Stéphane Fabre (UMR CNRS-INRA 6175).
The endocrine control of the reproductive function is often studied from the analysis of luteinizing hormone (LH) pulsatile secretion by the pituitary gland. Whereas measurements in the cavernous sinus cumulate anatomical and technical difficulties, LH levels can be easily assessed from jugular blood. However, plasma levels result from a convolution process due to clearance effects when LH enters the general circulation. Simultaneous measurements comparing LH levels in the cavernous sinus and jugular blood have revealed clear differences in the pulse shape, the amplitude and the baseline. Besides, experimental sampling occurs at a relatively low frequency (typically every 10 min) with respect to LH highest frequency release (one pulse per hour) and the resulting LH measurements are noised by both experimental and assay errors. As a result, the pattern of plasma LH may be not so clearly pulsatile. Yet, reliable information on the InterPulse Intervals (IPI) is a prerequisite to study precisely the steroid feedback exerted on the pituitary level. Hence, there is a real need for robust IPI detection algorithms. We have designed an algorithm for the monitoring of LH pulse frequency, basing ourselves both on the available endocrinological knowledge on LH pulse (shape and duration with respect to the frequency regime) and synthetic LH data generated by a simple model [57]. We make use of synthetic data to make clear some basic notions underlying our algorithmic choices. We focus on explaining how the process of sampling affects drastically the original pattern of secretion, and especially the amplitude of the detectable pulses. We then describe the algorithm in details and perform it on different sets of both synthetic and experimental LH time series. We further comment on how to diagnose possible outliers from the series of IPIs which is the main output of the algorithm.

6. Contracts and Grants with Industry

6.1. LK2 contract: TIght glycemic control for Intensive Care Units

Participants: Alexandre Guerrini, Michel Sorine.

Collaboration with the Intensive Care Unit (ICU) of Chartres Hospital headed by Dr Pierre Kalfon.

This work on tight glycaemic control (TGC) for ICU started in Septembrer 2008. It is done in the framework of the CIFRE contract of Alexandre Guerrini with the small medtech company LK2 (Tours, France). For the medical context of this study, see [69]. Blood glucose has become a key biological parameter in critical care since publication of the study conducted by van den Berghe and colleagues [85], who demonstrated decreased mortality in surgical intensive care patients in association with TGC, based on intensive insulin therapy. However, two negative studies were recently reported, which were interrupted early because of high rates of severe hypoglycaemia, namely the VISEP study [65] and the Glucontrol trial.

After having studied a possible origin of the failure of the recent study NICE-SUGAR, we have worked on more robust control algorithms based on a database of representative “virtual patients” [66].

In this study, we have developed efficient monitoring and control tools, now marketed by LK2 that will help clinicians and nursing staff to control blood glucose levels in ICU patients, in particular to avoid hyperglycaemia superior to 10 mmol/l and hypoglycaemia episodes. Our first controller has been assessed in the study CGAO-REA (see 4.3) with more than 3500 included patients. The controller determines the insulin infusion rate on the basis of the standard available glycaemia measurements despite their irregular sampling rate.

6.2. CARMAT SAS contract: Modeling and control of a Total Artificial Heart

Participants: Julien Bernard, Michel Sorine.

This is a cooperation with CARMAT SAS (Suresnes, France) on the development of a Total Artificial Heart.

This fully implantable artificial heart is designed to replace the two ventricles, possibly as an alternative to heart transplant from donors. In a first time, it will be used as a end-of-life treatment for patients waiting for a transplant. The first patients may receive this artificial organ in less than three years.

Compared with the mechanical hearts used up today, that are mainly LVAD (left ventricular assist devices) or with its main concurrent, the Abiocor implantable replacement heart system (Abiomed), the present artificial heart is designed to be highly reliable and with a low thromboembolism rate. It will allow longer waiting periods for heart transplants and even, in a next future, may be an alternative to these transplants.

The prosthesis uses two controlled pumps that are not in direct contact with the blood, eliminating hemolysis risk and is equipped with miniature sensors in order to have a full control of the heart rate and arterial blood pressure. Our objective is to improve the control strategies by mimicking the physiological feedback loops (Starling effect, baroreflex loop, ...) to allowing patients to live as normally as possible. In a first step, this year we have modeled the prosthesis with its present controller and its testbed, a “mock circulation system” (MCS). This year we have tried some control algorithms with the MCS.

6.3. ANR project DMASC: Scaling Invariance of Cardiac Signals, Dynamical Systems and Multifractal Analysis

Participants: Julien Barral, Patrick Loiseau, Claire Médigue, Michel Sorine.

Collaboration with Denis Chemla (Kremlin-Bicêtre Hospital), Paulo Gonçalves (INRIA Rhônes-Alpes) and Stéphane Seuret (Paris 12 University).

The ANR project DMASC (Program SYSCOMM 2008) started in January 2009 under the coordination of J. Barral.

Numerical studies using ideas from statistical physics, large deviations theory and functions analysis have exhibited striking scaling invariance properties for human long-term R-R interval signals extracted from ECG (intervals between two consecutive heartbeats). These numerical studies reveal that the scaling invariance may have different forms depending upon the states of the patients in particular for certain cardiac diseases. These observations suggest that a good understanding of multifractal properties of cardiac signals might lead to new pertinent tools for diagnosis and surveillance. However, until now, neither satisfactory physiological interpretations of these properties nor mathematical models have been proposed for these signals. For medical applications we need to go beyond the previously mentioned works and achieve a deepened study of the scaling invariance structure of cardiac signals. This is the aim of DMASC.

New robust algorithms for the multifractal signals processing are required ; specifically, it seems relevant to complete the usual statistical approach with a geometric study of the scaling invariance. In addition, it is necessary to apply these tools to a number of data arising from distinct pathologies, in order to start a classification of the different features of the observed scaling invariance, and to relate them to physiology. This should contribute to develop a new flexible multifractal mathematical model whose parameters could be adjusted according to the observed pathology. This multifractal analysis can be applied to another fundamental signal, the arterial blood pressure, as well as to the couple (R-R, Blood Pressure). An article has been submitted [54].

6.4. Modeling for diagnosis and prognosis (Paris Region ASTech project)

Participants: Abdouramane Moussa Ali, Qinghua Zhang.

In order to improve the safety and reliability of airplanes, the MODIPRO project (Modélisation pour le Diagnostic et le Pronostic) funded by the Pôle de Compétitivité Aérospatial ASTech of Paris Region aims at developing a software for deriving airplane functional models for the purpose of fault diagnosis and prognosis, by analyzing the flight data of a fleet of airplanes. The involved partners are Dassault Aviation (project leader), Snecma, IT4Control, Bayesia, KBS, UPMC, Supelec and INRIA.

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

Participants: Pierre-Alexandre Bliman, Michel Sorine, Qinghua Zhang.

The main idea of block-oriented nonlinear system identification is to model a complex system with interconnected simple blocks. Such models can cover a large number of industrial applications, and are yet simple enough for theoretic studies. The objectives of the EBONSI project are to extend block-oriented nonlinear models with hysteresis blocks and bilinear blocks, and to relax some traditional restrictions on nonlinearity structures and on experimental conditions. The two extensions with hysteresis blocks and bilinear blocks have been motivated by their importance in process control. Through these extensions, it is expected to considerably increase the applicability of block-oriented nonlinear system identification to industrial systems. This is an international project jointly funded by the French Agence Nationale de la Recherche (ANR) and the Chinese National Natural Science Foundation (NSFC). Its duration is 3 years starting from March 2011. The project partners are the SISYPHE project-team of INRIA (project leader), the Centre de Recherche en Automatique de Nancy (CRAN), and the Laboratory of Industrial Process Monitoring and Optimization of Peking University.

6.6. ANR project 0-DEFECT: On-board fault diagnosis for wired networks in automotive systems

Participants: Mohamed Oumri, Michel Sorine, Qinghua Zhang.

The number of electric and electronic equipments is increasing rapidly in automotive vehicles. Consequently, the reliability of electric connections is becoming more and more important. The project entitled “Outil de diagnostic embarqué de faisseaux automobiles” (0-DEFECT) aims at developping tools for on-bord diagnosis of failures in electric wire connections in automotive systems. This project is funded by Agence Nationale de la Recherche (ANR) for three years from 2009. The involved partners are CEA LIST (project leader), Renault Trucks, Freescale, PSA, Delphi, Supelec LGEP and INRIA. A prototype of a reflectometry-based diagnosis tool is under development in this project.

6.7. ANR project INSCAN: Fault diagnosis for security critical long distance electric transmission lines

Participants: Leila Djaziri, Michel Sorine, Huaibin Tang, Qinghua Zhang.

The wired electric networks of the French railway system cover more than 50000 km. The electric insulation of the signaling lines along the railways is monitored by regular inspections. Today these inspections are based on an expensive procedure realized by human operators located at both ends of each transmission line. The service of signaling devices has to be interrupted during this procedure, and so does the railway traffic. The in situ monitoring of the transmission lines, without interruption of service, is thus an important economic issue. For this purpose, the project entitled “Diagnostic de câbles électriques sécuritaires pour grandes infrastructures" is funded by ANR for three years in order to study the feasibility of in situ monitoring tools for these transmission lines. The involved partners are SNCF (project leader), CEA LIST and INRIA.

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

Participants: Hadis Amini, Zaki Leghtas, Ram Somaraju, Mazyar Mirrahimi, Pierre Rouchon, Michel Sorine, Filippo Visco Comandini.

The project EPOQ2 is an ANR "Young researcher" project led by Mazyar Mirrahimi (Sisyphe). It has for goal to address a class of inverse problems rising 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. The partners of INRIA are Emmanuelle Crépeau-Jaisson (University of Versailles - Saint Quentin), Hideo Mabuchi (Stanford University), Herschel Rabitz and Ramon Van Handel (Princeton University), Pierre Rouchon (Mines de Paris). See EPOQ2.

6.9. Renault contract: Modeling, Control, Monitoring and Diagnosis of Depollution Systems

Participants: Pierre-Alexandre Bliman, David Marie-Luce, Michel Sorine.

This work is done in cooperation with Renault in the framework of a CIFRE contract. The issue of depollution has become a central preoccupation for the automotive industry, and the increased severity of the emission norms necessitates tight modeling and control solutions. We have worked on simple models for two devices, namely the NOx-trap and the SCR (Selective catalytic reduction). Observers have been obtained and tested against real-world data. See [25].

7. Partnerships and Cooperations

7.1. Regional Initiatives

Participation to the MODIPRO project funded by Paris Region and Pôle de Compétitivité ASTech.
Partners: Bayesia, Dassault Aviation, INRIA (EPI I4S and Sisyphe), IT4 Control, KBS, Snecma, Supélec, UPMC.
The objective is to improve some algorithms for use in Dassault Aviation aircraft monitoring procedures.

7.2. National Initiatives

REGATE (REgulation of the GonAdoTropE axis) is 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 INRIA participants to this action are researchers of 2 INRIA research teams, Contraintes and Sisyphe. There are also participants from INRA, Université Libre de Bruxelles (Unité de Chronobiologie théorique) and Université Paris 6 (Laboratoire Jacques-Louis Lions).

7.3. European Initiatives

7.3.1. Collaborations in European Programs, except FP7

The SISYPHE team is involved in the activities of the European Research Network on System Identification (ERNSI) federating major European research teams on system identification.

Program: Funded as a SCIENCE project (1992 - 1995), HCM Project (1993-1996), TMR Project (1998 - 2003).

Project acronym: ERNSI

Project title: European Research Network System Identification

Duration: 1992 - –

Coordinator: The network ERNSI is currently coordinated by Bo Wahlberg, Automatic Control, KTH SE 100 44 Stockholm, SWEDEN.

Other 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).

Abstract: Modeling of dynamical systems is fundamental in almost all disciplines of science and engineering, ranging from life science to plant-wide process control. Engineering uses models for the design and analysis of complex technical systems. System identification concerns the construction, estimation and validation of mathematical models of dynamical physical or engineering phenomena from experimental data.

7.4. International Initiatives

7.4.1. INRIA International Partners

Mazyar Mirrahimi has a close collaboration with the QLab group at Yale (Michel Devoret) and the Quantum-Mechanical Electronics Group at ENS Paris (Benjamin Huard). He is on a sabbatical leave at Yale since february 2011.

7.4.2. Visits of International Scientists

Martin Krupa (Nijmegen, Department of Mathematics) has been visiting the project-team for 12 months to set up a collaboration in the field of Mathematical Neuroendocrinology.

8. Dissemination

8.1. Animation of the scientific community

P.A. Bliman:
- Scientist in charge of latin America at Department of International Affairs, INRIA.
- Member of the Scientific Committee of the collaboration program STIC AmSud.
- Associate Editor of Systems & Control Letters.
- Member of the Board for recruitment of Chargés de recherche (Centre de recherche INRIA, Bordeaux, 2011) and Directeurs de recherche.

F. Clément:
Responsibilities:
- Scientific head of the Large Scale Initiative Action REGATE (REgulation of the GonAdoTropE axis).
- Appointed member of the scientific board of the PHASE (Animal Physiology and Breeding Systems) department of INRA http://www.inra.fr/internet/Departements/phase/.
- Appointed member of the scientific board of the INRA Research Centre of Jouy-en-Josas http://www.jouy.inra.fr/.
- 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.
Participations in examination boards:
- INRA Experienced Research Scientist open competitions for non-assigned positions (admissibility phase).
- INRA Research Director open competitions (admissibility and admission phases).
- Inria Research Director open competitions (admission).
Conference organizations: Member of the organizing committee of the second annual symposium of ITMO BCDE, “Cell dynamics and cellular interactions in reproductive biology”, 7 September 2011, Paris.

M. Mirrahimi:

- Associate Editor of Systems & Control Letters.
- Organizer of the CEA-EDF-INRIA school on “Quantum Information, Measurement and Control”, INRIA Rocquencourt, 29/11/2011 - 2/12/2011.

M. Sorine:
- Member of IFAC Technical Committee on the Biological and Medical Systems (IFAC TC 8.2).
- Member of the Program Committee of FHIES 2012, the “Second International Symposium on Foundations of Health Information Engineering and Systems”.
- Member of the Program Committee and local organizer of the conference SFIMAR 2011 (workshop of the Société Francophone d’Informatique et de Monitorage en Anesthésie - Réanimation), INRIA Rocquencourt, May 5 - 6, 2011.
- Organizer of the Aviesan “ITMO CMN - Inria Biological-systems modelling day”, Paris, March, 3, 2011.
- 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).
- Member of the steering committee of the clinical study CGAO-REA.
- Member of several PhD committees.

Q. Zhang:
- Member of IFAC Technical Committee on Fault Detection, Supervision and Safety of Technical Processes (SafeProcess).
- Member of the Program Committee of the 3èmes Journées Identification et Modélisation Expérimentale.
- Member of the International Program Committee of the 16th IFAC Symposium on System Identification.

8.2. Participation in conferences, seminars

- Vidal A, Desroches M, Krupa M, Clément F. Model-based study of the back-and-forth transitions between the pulsatile and surge phase in GnRH secretion (invited presentation to the minisymposium “Mathematical Neuroendocrinoly”). *SIAM Conference on Applications of Dynamical Systems*. Snowbird, Utah, US, 22-26 May 2011.
- Clément F. [Steroid control of the hypothalamic GnRH generator.] Journée ITMO CMN-INRIA, Modélisation des systèmes biologiques, Paris, 3 March 2011.

8.3. Teaching

Master: F. Clément, “Modelling and control of biological systems” course, 2,5 ECTS, part of the “Master’s Degree in BioInformatics and BioStatistics” (Paris-Sud 11 University, in collaboration with Béatrice Laroche) http://www.bibs.u-psud.fr/

Master: M. Sorine, “The cardiovascular system and its short-term control - Modelling and signal analysis”, 3 ECTS. BioMedical Engineering - Master?s Degree Program, Paris-Descartes University and the Paris Institute of Technology (ParisTech).

PhD & HdR

HdR : Mazyar Mirrahimi, “Estimation et contrôle non-linéaire : application à quelques systèmes quantiques et classiques, UPMC (Université Pierre et Marie Curie), january 27, 2011.

PhD : Filippo Visco Comandini, “Some inverse scattering problems on star-shaped graphs: application to fault detection on electrical transmission line networks”, “University of Versailles Saint-Quentin-en-Yvelines”, December 5, 2011, Advisors: M. Sorine, M. Mirrahimi.

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