INSTITUT NATIONAL DE RECHERCHE EN INFORMATIQUE ET EN AUTOMATIQUE

Team Sosso2

Applications and tools for automatic control

Rocquencourt

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Activity Report

2005

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2. Overall Objectives

2.1. Overall Objectives

Keywords: *bioenergetics*, *biology*, *cardiovcascular system*, *combustion engine*, *control*, *energetics*, *fuel cell*, *health*, *modelling*, *multi-scale systems*, *observation*, *ovulation control*, *process engineering*.

The SOSSO2 team is involved in modelling, observation and control of natural or engineered feedback-controlled systems. A particular emphasis is on applications to some controlled multi-scale systems in physiology or engineering. Two such multi-scale systems concern energy conversion: the Human Heart, a naturally controlled pump, and the controlled combustion in some new engines for automobiles. A third multi-scale system is considered for modelling the development of ovarian follicles. In the case of physiological systems some applications to diagnosis and therapy are also considered.
The main part of the research on the cardiovascular system is done in the framework of the Inria Large-scale Initiative Action, Cardiosense3D. See http://www-sop.inria.fr/CardioSense3D. The present topics of the team are:

- Multi-scale modelling of the controlled chemomechanical conversion in the heart (cell, tissue and organ scales) ;
- Model-based non-invasive assessment of the function of the cardiac pump on the cardiovascular system scale ;
- Multi-scale modelling of the selection of ovulatory follicles.

Control of energy conversion is also considered in low-emission vehicles:

- Multi-scale reduced-order modelling and control of auto-ignition in internal combustion engines ;
- Multi-scale modelling, monitoring and control of fuel-cell systems.

3. Software

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

Participant: Claire Médigue.

LARY_CR is a software package dedicated to the study of cardiovascular and respiratory rhythms, developed in the SCILAB_SCICOS scientific environment [70]. 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.

3.2. The System Identification ToolBox (SITB)

Participant: Qinghua Zhang.

Contract with The Mathworks, from July 2005 to July 2010.

The System Identification ToolBox (SITB) is one of the main Matlab toolboxes commercialized by The Mathworks. The current version of the toolbox is limited to the identification of linear systems. In collaboration with Lennart Ljung (Sweden), the author of the current version of the SITB, and also with Anatoli Juditsky (Grenoble University) and Peter Lindskog (Sweden), an extension of the SITB for nonlinear system identification is under development. Future versions of the toolbox will include algorithms for black box and grey box identification of nonlinear dynamic systems. INRIA is mainly responsible for the development of black box identification.

4. New Results

4.1. System control and observation

Keywords: *ECG, LMI, diagnosis, heart, hybrid systems, identification, observation, ovulation control, pressure, robust control, stability, systems of agents.*

4.1.1. Linear Parameter Varying Systems

Participant: Pierre-Alexandre Bliman.

One provided this year some refinements of methods previously developed. We developed with P. Tsiotras and X. Zhang an LMI criterion to analyze the robust stability of linear systems with a real parameter intervening polynomially in the state matrix. The criterion is exact and low-dimensional, in the sense that the size of the matrices in the LMIs involved take explicitly into account the range of the perturbation to the nominal matrix.

4.1.2. Stability Analysis of Multi-Agent Systems

Participants: Pierre-Alexandre Bliman, Giancarlo Ferrari-Trecate.

We first established tight stability conditions for an average consensus algorithm for some multi-agent systems with delay on the communications. In the framework adopted here, the models are continuous-time linear models, and the communication graphs are undirected and may vary with time. The accent is put on the determination of the maximal delay preserving stability.

We also began with D. Angeli (Università degli Studi di Firenze) a work on stability of discrete-time multi-agent systems in a general framework. Here, the communication graphs are directed, and bounded delays are also allowed. Both the communication topology and the delays may vary. We proposed an extension of a result proved by L. Moreau, relating stability to the connectedness properties of the graph.

4.1.3. Robust control of some fractional delay systems of neutral type

Participants: Catherine Bonnet, Jonathan Partington.

We have been interested this year in the robust control of some fractional delay systems of neutral type for which we had obtained in [8] only sufficient conditions ensuring H_∞-stability.
For systems with transfer function

$$G(s) = \frac{r(s)}{p(s) + q(s)e^{-sh}} \tag{1}$$

with $h > 0$, p, q, r real polynomials in the variable s^μ $(0 < \mu < 1)$ and such that $\deg p = \deg q \geq \deg r$, we have considered first an extension of the Walton and Marshall method for the stability testing of delay systems (we recall that this method essentially determines the values of h for which G has all its poles in the left half-plane).

Second, we classified the location of poles of G according to the value of $\alpha = \lim\limits_{\substack{s \in \mathbb{C} \setminus R_- \\ |s| \to \infty}} p(s)/q(s)$ as was done for standard neutral systems in [71] and analyzed the H_∞-stability of G, obtaining necessary and sufficient conditions in terms of $\deg r$, which is a more general result than the one obtained in the standard case.

Both results were in use in order to get a particular controller of G and then a parametrization of all H_∞-stabilizing controllers of G.

4.1.4. Observability analysis and state observers for hybrid systems: theory and automotive applications

Participants: Giancarlo Ferrari Trecate, Mehdi Gati.

We considered the problem of computing sets of observable states for discrete-time, piecewise affine systems. When the maximal set of observable states is full-dimensional, we derived an algorithm for reconstructing it up to a zero measure set. The core of the method is a quantifier elimination procedure that, in view of basic results on piecewise linear algebra, can be performed via the projection of polytopes on subspaces. We also provided a necessary condition on the minimal length of the observability horizon in order to expect a full-dimensional set of observable states. Numerical experiments highlight that the new procedure is considerably faster than the one proposed in [16].

We applied the above mentioned algorithm for analyzing the observability properties of automotive powertrains with backlash. We modeled the powertrain as a hybrid system in the piecewise affine form and used measurements of the torque and the angular speed of the engine for computing the maximal set of observable states. This set, that is usually non convex and disconnected, captures in a precise way how the main variables and parameters of the driveline influence the possibility of estimating the shaft twist. Then, we showed how to exploit the knowledge of observable states in order to build computationally efficient deadbeat observers for the reconstruction of the powertrain states. An advantage of the new observer is that it allows one to detect if the state to be reconstructed is observable or not. This enable the switching to the open-loop simulation of the system when unobservable regions are crossed.

4.1.5. Nonlinear system fault diagnosis based on particle filters

Participants: Qinghua Zhang, Fabien Campillo, Frédéric Cérou, François LeGland.

Because of the difficulties in studying nonlinear dynamic systems, few results are available for the detection and isolation of faults in such systems. The known results on this topic have been mainly based on deterministic nonlinear system theory, with strong restrictions on system structure or strong requirements on sensor instrumentation. In this work, fault detection and isolation in nonlinear systems has been studied in a stochastic framework. The advantage of the developed method is its generality: it is applicable to quite general stochastic nonlinear dynamic systems in discrete time. The main result consists of a new particle filter algorithm, derived from the basic bootstrap particle filter, and capable of rejecting a subset of the faults possibly affecting the considered system. When a system is subject to faults, it is impossible to apply basic particle filters, because some of the state equations used for particle propagation would be corrupted by unknown faults. Our solution to this problem is to compensate the corrupted state equations by part of the output equations. For the purpose of fault isolation, different hypotheses on the occurrence of the possible faults are made and a particle filter is designed under each of these hypotheses. Fault isolation is then achieved by the evaluation of the estimated likelihoods related to the designed filters, since the correct hypothesis should lead to the highest likelihood value. One should note that the generality of this method is at the price of intensive numerical computation, like in most particle filter applications.

This work will be presented at *CDC-ECC*, Seville, December 2005.

4.1.6. Sensor fault diagnosis based on adaptive observers

Participant: Qinghua Zhang.

Studies on the application of adaptive observers to fault diagnosis have been made in the former SIGMA2 project for several years. However, these studies have been focused on actuator and system internal faults, while assuming fault-free sensors. It turns out that existing methods based on adaptive observers almost always require fault-free sensors, because of a difficulty in the design of adaptive observers when sensors are corrupted by faults.

In collaboration with Gildas Besançon of Laboratoire d'Automatique de Grenoble (LAG), Université de Grenoble, the design of adaptive observers capable of estimating sensor faults has been studied, both for linear and nonlinear systems. The key work has been the understanding of the effect of sensors faults in the feedback term of an observer. It then becomes possible to compensate this effect with appropriate additional terms. An algorithm has been first successfully designed for linear time varying systems, then extended to nonlinear systems in combination with high gain observers.

This work has been presented at *IFAC World Congress*, Prague, July 2005.

4.1.7. Control of Real-Time Feedback Rate-Monotonic Schedulers

Participant: Giancarlo Ferrari Trecate.

An optimal control scheme for a real-time feedback control rate-monotonic scheduling (FC-RMS) system has been proposed. We consider two-version tasks composed of a mandatory and an optional part to be scheduled according to the FC-RMS. In FC-RMS, the controller provides a feedback strategy for deciding about the execution or rejection of the optional sub-tasks. By modeling the task execution times as random variables, we first have derived a statistical model of FC-RMS and then designed a pure optimal controller and an optimal controller with feedforward integral compensation. The comparison of these two schemes with common Proportional-Integral-Derivative (PID) controllers highlights the benefits of the optimal scheme with integral compensation. The results have been also demonstrated through the real implementation of FC-RMS on RT-Linux.

4.2. Modelling, observation and control in biosciences: the controlled cardiovascular system

Keywords: *bioenergetics*, *biology*, *cardiovcascular system*, *health*, *heart*, *modelling*.

4.2.1. The cardiovascular system: a multi-scale controlled system

From the cardiovascular system scale to the cell scale, the function of the circulation is to supply cells with oxygen, nutrients and to remove carbon dioxide and other catabolits. On each of these scales, variables involved in cardiovascular regulation, such as blood flow, blood pressure, oxygen blood concentration, ATP concentration, are kept around their reference points by different feedback control mechanisms having different dynamics depending upon the considered scale.

We are interested in the mechano-energetics of the heart with its short term (some few minutes) intrinsic control mechanisms, from the cell scale to the cardiovascular system scale:

- On the cell and tissue scales, models of the mechano-energetics of the heart provide us with constitutive laws for the cardiac tissue, used in $3D$ models for computing stress, strain and action potential fields in the heart from three-dimensional image processing, as in our CardioSense3D project where, the chemically-controlled constitutive law of cardiac myofibre that we have obtained [5] is currently used [2]. This law ensues from the modelling of the collective behaviour of actin-myosin molecular motors converting chemical energy into mechanical energy. It is thermodynamically consistent and the resulting dynamics of sarcomeres is consistent with the “sliding filament hypothesis” of A. F. Huxley.

Intrinsic heart control mechanisms we consider, range from the Starling and Treppe effects on the cell scale to the excitability of the cardiac tissue. They all contribute to the function of the heart in a coordinated manner that we want to analyse and assess.

This year we have continued the mathematical analysis of the models used in CardioSense3D, see 4.2.2 and studied a reduced order model of the intracellular calcium dynamics that will be useful to represent the rate-dependent inotropic effects like Treppe effect (also called positive staircase effect). See 4.2.3.

- On the cardiovascular system and heart scales, we use $0D$ models of the electro-mechanical activity of the cardiac muscle for control analysis and signal processing applications. Here the heart is seen as a small number of “averaged cells” representing the walls of the atrial and ventricular chambers. The short term control of blood flow and pressure on the cardiovascular system scale (the heart and the vascular compartments) is performed by the autonomic nervous system through baroreceptor control loops. We don’t consider longer horizons where slower control mechanisms operate such as hormonal regulation. A good autonomic function is of crucial importance for life and is of great prognostic value in many diseases.

Our objective here, is to relate discrete-time cardiovascular signal analysis to models of the cardiovascular and control systems taking into account its multiple feedback loop organisation. This will lead to a model-based signal processing approach for the estimation of the classical arterial-pressure/heart-rate baroreflex sensitivity and of several other discrete-time feedback loop sensitivities of pratical interest.

This year we have studied control effects during a standard cardiac test, the “tilt test”, see 4.2.4 and we have continued our researches on arterial pressure analysis, see 4.2.5 and ECG analysis, see 4.2.6.

4.2.2. *Multi-scale modelling of the controlled contraction of cardiac muscle*

Participant: Michel Sorine.

This work takes place in the framework of CardioSense3D.

We have used ideas originating from the kinetic equation theory to model, on the molecular scale, the controlled collective behaviour of actin-myosin nanomotors at the root of muscle contraction. The classical Huxley’s model is recovered on the sarcomere scale by using moment equations. A controlled constitutive law on the tissue scale is obtained using the same type of scaling techniques. This multi-scale description of controlled muscle contraction may be useful in studying modelling and control problems associated to the heart considered as a multi-scaled system. The control viewpoint is useful in accounting for macroscopic properties (such as the Starling law or the Hill force-velocity relation) on lower scales and defining performance indexes of the electro-mechanical coupling on each scale.

This year, in a joint work with Pavel Krejčí (Weierstrass Institute for Applied Analysis and Stochastics, Berlin), J. Sainte-Marie (MACS project) and J.M. Urquiza (CRM, Montreal), we have considered the mathematical analysis of the fibre model used in CardioSense3D in the more simple case of a one dimensional geometry ($1D$ problem). We have proved the well-posedness of that model and some asymptotic behaviour results [36] and we begin to study a more complete system with valves and vascular compartments [66].

4.2.3. *Differential model of excitation - contraction coupling in a cardiac cell for multi-cycles simulations*

Participants: Karima Djabella, Michel Sorine.

We have presented [45] a differential model of excitation - contraction coupling in a cardiac cell intended to be used in simulations of one or many heart cycles on the cell or the heart scales. It takes into account the dynamics of the main ionic currents flowing through the membrane channels (fast sodium, L-type calcium and outward potassium) and Na+/Ca2+ exchangers and Na+/K+ pumps. The model includes also a description of the dynamics of the main calcium buffers in the bulk cytosol and in the sarcoplasmic reticulum. With thirteen state variables, its complexity is between that of FitzHugh-Nagumo type models of the action potential (two state variables) and that of the more complex ionic channels models (up to sixty state variables for some of them). It allows realistic modelling of action potential, total ionic current, current gating, intracellular calcium transients, in particular for calcium bound on troponin C, and multicycle effects, like restitution curves for the action potential duration, CICR dependence on intracellular calcium concentration, positive staircase effect for the heart rate. Due to its sound asymptotic behavior without drifts of the state and its medium complexity, this model can be used in multi-beat simulations from the cell to the heart scales.

4.2.4. *The cardiovascular system and its short-term control: the “tilt-test” analysis*

Participants: Karima Djabella, Claire Médigue, Michel Sorine.

We have presented [44] a differential model of the cardiovascular system and its baroreflex control. This simplified model of the circulation includes the left heart, arterial and venous compartments, the afferent baroreceptor pathway, the sympathetic and vagal efferent activities and excitation-contraction coupling on the heart scale. The model is used to simulate the interactions among the baroreflex control loop, the pulsating heart and the effector during a graded orthostatic tilt. There is a satisfactory agreement between the model and experimental results illustrated through heart rate variability analysis. Experimental data on heart rate control can then be explained fairly well by a rather simple action of the sympathetic-parasympathetic system on the heart rate. The output of the proposed model are usually measured cardiovascular signals. An objective is to use it in model-based signal processing in order to assess the short-term control of cardiovascular system.

4.2.5. Reduced model of pulsatile flow in an arterial compartment and application to pressure estimation

Participants: Emmanuelle Crépeau-Jaisson, Taous-Meriem Laleg, Claire Médigue, Yves Papelier, Michel Sorine.

We have proposed [42] a reduced model of the input-output behaviour of an arterial compartment, including the short systolic phase where wave phenomena are predominant. The objective is to provide basis for model-based signal processing methods for the estimation from non-invasive measurements and the interpretation of the characteristics of these waves. Standard space discretizations of distributed models of the flow lead to high order models for the pressure wave transfer function, and low order rational transfer functions approximations give poor results. The main idea developed here to circumvent these problems is to explicitly use a propagation delay in the reduced model. Due to phenomena such that peaking and steepening, the considered pressure pulse waves behave more like solitons generated by a Korteweg de Vries (KdV) equation than like linear waves. So we start with a quasi-1D Navier-Stokes equation that takes into account a radial acceleration of the wall, in order to be able to recover, during the reduction process, the dispersive term of KdV equation which, combined with the nonlinear transport term gives rise to solitons. The radial and axial acceleration terms being supposed small, a multiscale singular perturbation technique is used to separate the fast wave propagation phenomena taking place in a boundary layer in time and space described by a KdV equation from the slow phenomena represented by a parabolic equation leading to two-elements windkessel models. Some particular solutions of the KdV equation, the 2 soliton solutions, seem to be good candidates to match the observed pressure pulse waves. They are given by close form formulae involving propagation delays that are proposed to represent input and output wave shapes. Some very promising preliminary comparisons of numerical results obtained along this line with real pressure data are shown.
This work will be continued within the preparation of the PhD of M. Laleg and it will lead to clinical studies.

4.2.6. ECG analysis: T-wave end location

Participants: Alfredo Illanes Manriquez, Claire Médigue, Yves Papelier, Michel Sorine, Qinghua Zhang.

For the purpose of developping methods associating mathematical modeling of the cardio-vascular system and the processing of non invasive measurements, studies on new methods for electrocardiogram (ECG) processing have been carried out [58]. The results of these studies can also have direct applications to computer-aided cardiac disease diagnosis. One important result of these studies is a new algorithm for ECG T-wave end location. It mainly consists of the computation of an indicator related to the area covered by the T-wave curve and delimited in a special manner. Based on simple assumptions, essentially on the concavity of the T-wave form, it is formally proved that the maximum of the computed indicator inside each cardiac cycle coincides with the T-wave end. The resulting algorithm is computationally very simple: the main computation can be implemented as a simple finite impulse response (FIR) filter. The most remarkable property of the algorithm is its robustness to measurement noise, to wave form morphological variations and to baseline wander. This robustness has been demonstrated in the processing of ECG signals recorded during handgrip exercise and also in the processing of the PhysioNet QT database. This new algorithm is playing an important role in our current studies on cardio-vascular modeling related to the restitution curve.

4.3. Clinical and physiological applications

Keywords: *Heart rate variability, cardiovcascular system, health*.

Participants: François Cottin, Claire Médigue, Yves Papelier, Michel Sorine.

4.3.1. Effect of exercise intensity and repetition on heart rate variability during training in elite trotting horse.

Collaboration with the LIGE (Laboratoire Interaction Génétique Entraînement, Université d'Evry).

RR intervals of ten elite trotting horses were recorded during an interval training session performed on track. This study examined two hypothesis. Firstly, like in humans, the hyperpnea combined with a decrease in cardiac autonomic control on heart rate during heavy exercise could result in a prevalence of high frequency heart rate variability. Secondly, this prevalence could increase with the heavy exercise repetition. Two exercise intensities were compared: moderate (ME) and heavy (HE). Furthermore, heavy exercise repetitions were compared between the beginning and the end of the interval training session. When comparing ME and HE periods: heart rate was significantly lower (155 $\pm$ 12 vs. 210$\pm$9 ms, P<0.001), LF spectral energy (0.04-0.2 Hz) was significantly higher (ME: 6.94$\pm$4.80 and HE: 0.24$\pm$0.14 $ms^2 Hz^{-1}$, P<0.001) whereas HF (0.2-2 Hz) was significantly lower (ME: 7.09$\pm$2.24 and HE: 10.60$\pm$3.64 $ms^2 Hz^{-1}$, P<0.05). In relative terms, ME showed similar results in both LFn (LF/LF+HF) and HFn (HF/LF+HF) whereas HE showed a large prevalence of HFn energy compared to LFn (P<0.001). The difference in LF/HF ratio between the two exercise conditions was significant (1.14 $\pm$0.92 vs. 0.09 $\pm$ 0.12, P<0.001). Exercise repetition induced a significant increase in heart rate between the beginning and the end of the interval training session (207$\pm$10 beats.min-1 vs. 212$\pm$9 beats.min-1, P<0.001) whereas LF energy decreases (1.54$\pm$1.65 vs. 0.32$\pm$0.24 $ms^2 Hz^{-1}$, P<0.01) and HF energy remained constant (10.79$\pm$4.10 vs. 10.40$\pm$3.35 $ms^2 Hz^{-1}$, NS). This study confirmed the results observed in humans during heavy exercise conditions with a large prevalence of HF in contrast to LF, this prevalence increasing with exercise repetitions. The observed decrease in LF/HF ratio could provide an index of hyperpnea in horses during interval training.

4.3.2. Assessment of the ventilatory thresholds from heart rate variability in well-trained subjects during cycling.

Collaboration with the LIGE.

The purpose of this study was to implement a new method for assessing the ventilatory thresholds from heart rate variability (HRV) analysis. ECG, VO2, VCO2, and VE were collected from eleven well-trained subjects during an incremental exhaustive test performed on a cycle ergometer. The "Short- Term Fourier Transform" analysis was applied to RR time series to compute the high frequency HRV energy (HF, frequency range: 0.15-2 Hz) and HF frequency peak (fHF) vs. power stages. For all subjects, visual examination of ventilatory equivalents, fHF and instantaneous HF energy multiplied by fHF (HF.fHF) showed two non linear increases. The first non linear increase corresponded to the first ventilatory threshold (VT1) and was associated with the first HF threshold (TRSA1 from fHF and HFT1 from HF.fHF detection). The second non linear increase represented the second ventilatory threshold (VT2) and was associated with the second HF threshold (TRSA2 from fHF and HFT2 from HF.fHF detection). HFT1, TRSA1, HFT2 and TRSA2 were, respectively, not significantly different from VT1 (VT1 = 219 $\pm$ 45 vs. HFT1 = 220 $\pm$ 48 W, p=0.975; VT1 vs. TRSA1 = 213 $\pm$ 56 W, p=0.662) and VT2 (VT2 = 293 $\pm$ 45 vs. HFT2 = 294 $\pm$-48 W, p=0.956; vs. TRSA2 = 300 $\pm$ 58 W, p=0.445). In addition, when expressed as a function of power, HFT1, TRSA1, HFT2 and TRSA2 were respectively correlated with VT1 (with HFT1 R^2 = 0.94, p<0.001; with TRSA1 R^2 = 0.48, p<0.05) and VT2 (with HFT2 R^2 = 0.97, p<0.001; with TRSA2 R^2 = 0.79, p<0.001). This study confirms that ventilatory thresholds can be determined from RR time series using HRV time- frequency analysis in healthy well-trained subjects. In addition it shows that HF.fHF provides a more reliable and accurate index than fHF alone for this assessment.

4.4. Modelling, observation and control in biosciences: ovulation control

Keywords: *conservation laws*, *coupled oscillators*, *dynamical systems*, *neuro-endocrinology*, *physiology*.

4.4.1. Multi-scale modelling of the selection of ovulatory follicles

Participants: Frédérique Clément, Nki Echenim, Michel Sorine.

This work is the matter of a PhD thesis (University Paris 11, Sciences and Technologies for Information, Telecommunications and Systems).

Biological background. Ovarian follicles are spheroidal structures sheltering the maturating oocytes. Follicular development is the process of growth and functional maturation undergone by ovarian follicles, from the time they leave the pool of primordial follicles until ovulation, at which point they release a fertilizable oocyte.

Actually, very few terminally developing follicles reach ovulatory size; most of them undergo a degeneration process, known as atresia. The species-specific ovulation rate (number of ovulatory follicles) results from an FSH-dependent follicle selection process. FSH acts on the somatic cells surrounding the oocyte, making-up the granulosa cell layer, and controls their commitment toward either proliferation, differentiation or apoptosis. The cellular composition of the granulosa ultimately determines the follicular fate: a shift from a proliferative state to a differentiated one characterizes an ovulatory trajectory, while a trend toward apoptosis leads to atresia. FSH release by the pituitary gland is in turn modulated by granulosa cell products such as estradiol and inhibin. This feedback is responsible for reducing FSH release, leading to the degeneration of all but those follicles selected for ovulation.

Modelling approach. Up to now, the mathematical models interested in follicular development could be cast into two approaches. One focuses on the mechanims underlying follicular development, on the molecular and cellular scales, and considers separately either ovulatory or atretic (degenerating) paths. The other focuses on the selection process by itself which is investigated in the sense of population dynamics. We aim at merging the molecular and cellular mechanistic description introduced by the former approach with the competition process dealt with in the latter, using both multi-scale modelling and control theory concepts [34]. Each ovarian follicle is described through a 2D density function, $\varphi_f\,(a,\gamma,t)$, giving an age and maturity-structured description of its cell population. The conservation law for φ_f reads :

$$\frac{\partial\varphi_f}{\partial t}+\frac{\partial(h_f\varphi_f)}{\partial\gamma}+\frac{\partial(g_f\varphi_f)}{\partial a}=G-L \qquad (2)$$

where a represents the cytological age and γ the cellular maturity. A control term representing FSH signal intervenes in the aging (g_f) and maturation (h_f) velocities, gain (G) and loss (L) terms of this conservation law. The multi-scale feature of the model operates through the zero and first-order moments of the density, corresponding respectively to the total number of cells and global maturity in a follicle. Summing those moments on the whole population of follicles gives further information on the ovarian scale. The model accounts for the changes in the total cell number, growth fraction (proportion of proliferating cells in the whole population) and global maturity of both ovulatory and degenerating follicles for various intensities of the selection rate. The different selection process outputs (mono- or poly-ovulation, anovulation) predicted by the model are consistent with physiological knowledge regarding vascularisation, pituitary sensitivity to ovarian feedback and treatment with exogenous FSH.

The model is associated with two nested accessibility problems, respectively on the ovarian scale (reachability of the conditions for ovulatory surge triggering) and on the follicular scale (reachability of the conditions for ovulation). Due to the complexity of the model formulation (hybrid features, feedback in the velocity and loss terms), such problems cannot be tackled head-on. Defining similar accessibility problems from a characteristics-like formulation of the conservation law is the subject of current research.

4.4.2. Modelling of the GnRH pulse and surge generator

Participants: Frédérique Clément, Jean-Pierre Françoise.

Biological background. The reproductive axis is under the control of the GnRH (Gonadotropin Releasing Hormone), which is secreted from specific hypothalamic areas in a pulsatile manner. This pulsatility (between 1 pulse per hour and 1 pulse every 6 hours) has a fundamental role in the differential control of the secretion of both gonadotropins: LH (Luteinizing Hormone)–enhanced by higher frequency– and FSH (Follicle Stimulating Hormone) –enhanced by lower frequency–. The pulsatile pattern is tremendously altered once per ovarian cycle into a surge which triggers ovulation in response to increasing levels of estradiol. The estradiol signal is conveyed to GnRH neurons through a network of interneurons. The balance between stimulatory and inhibitory signals emanating from interneurons controls the behaviour of the GnRH network.

Modelling approach. We propose a mathematical model allowing for the alternating pulse and surge pattern of GnRH (Gonadotropin Releasing Hormone) secretion. The model is based on the coupling between two FitzHugh-Nagumo 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. Specifications on the model parameter values are derived from physiological knowledge in terms of amplitude, frequency and plateau length of oscillations. The behavior of the model is finally illustrated by numerical simulations.

4.4.3. Signal processing of GnRH neuron-derived data

Participants: Frédérique Clément, Claire Médigue, Anne Duittoz.

Biological background. The pulsatility pattern of GnRH secretion ensues from the synchronisation of the secretory activity of several GnRH neurons. Such secretory rhythms result from calcium rhythms which in turn are determined by electrical rhythms. The direct investigation of the synchronisation mechanims is difficult, since GnRH neurons are both scarce (at most 3000 in the sheep) and scattered in different areas of the hypothalamus. We can yet dispose of data collected separately on the neuron network scale: time series of GnRH concentration measured within the hypothalamo-hypophyseal portal blood in the sheep, or on the individual neuron scale: calcium dynamics in primary cultures of sheep olfactory placode explants (GnRH neurons originate from the olfactory bulb from where they migrate into the hypothalamus in the course of embryonic life).

Signal processing. In both cases, we apply signal processing methods (mainly Fast Fourier Transform and Smoothed Pseudo-Wigner-Ville Distribution) to extract dynamical features from the data. From GnRH secretion pattern, we aim at detecting subtle changes occuring at the transition between the pulse and surge secretion pattern. The main question is whether an underlying pulsatile pattern may remain during the surge. From the calcium data, we aim at studying the maturation of calcium oscillations in embryonic neurons and characterising the effect of pharmacological drugs on calcium dynamics. This will help to identify the ionic channels involved in calcium signalling within GnRH neurons, and ultimately to understand the coupling between calcium dynamics and secretory events.

4.5. Modelling and control of Homogeneous Charge Compression Ignition (HCCI) engines

4.5.1. Modelling of HCCI combustion using reduced chemical kinetics of n-Heptane with multidimensional code

Keywords: *combustion engine, control, energetics, modelling, process engineering.*

Participants: Ludovic Noël, Fadila Maroteaux.

This work corresponds to the PhD thesis of Ludovic Noel which has been defended in March 2005. In order to reduce significantly diesel engine emissions for the future regulations, research is heading towards alternative combustion modes, which allow a drastic reduction of engine-out emissions. One way to achieve these objectives can be to use homogeneous charge compression ignition (HCCI) combustion. HCCI operation is based on burning a homogeneous mixture of air fuel and burned gas (internal or external EGR) with reduced combustion temperatures. Furthermore, theoretically the HCCI process eludes locally lean high temperature regions and rich low temperature regions compared to the combustion process for conventional diesel engines, thereby reducing NOx and particulate matter (PM) formation. Many studies have confirmed that during this mode the combustion process is mainly controlled by chemical kinetics. On another hand, the heat release during the HCCI combustion for most fuels occurs in two stages; the first stage is associated with low temperature kinetic reactions (or cool flame) and the time delay between the first stage and the main heat release (or second stage) is due to the negative temperature coefficient regime (NTC). The main issue is then to control the start of ignition and the rate of heat release over a wide range of engine operating conditions. Therefore, there is no direct control method as in spark ignition or conventional diesel engines.

In order to implement this combustion process in production engines, it is thus necessary to achieve more accurate analysis of homogeneous combustion by multidimensional simulation. The simulation of the homogeneous combustion mode as described above requires an accurate description of chemical reaction kinetics, especially for the description of low temperature reactions. However, a coupled CFD and detailed chemistry simulation requires substantial memory and CPU time which may be very difficult with current computer capabilities. Thus a reduced mechanism is required to simulate the engine cycle during this operating mode.

In this study three reduced mechanisms for n-heptane were developed using Chemkin code based on detailed mechanisms developed by Lawrence Livermore National Laboratory with 2446 reactions and 544 species, and by Chalmers University with 250 reactions and 57 species. The sensitivity analysis approach and the steady state approximation (QSS) were used to derive the reduced mechanisms for different engine applications, the three mechanisms are:

- 61 step mechanism (with 61 reactions and 37 species)
- 26 step mechanism (with 26 reactions and 26 species).
- Two steps mechanism (with 7 reactions and 14 species) with temperature criterion.

The two first mechanisms above have been implemented in a CFD code (Star-CD/Kinetics) in order to understand the effects of the main engine control parameters for homogeneous charge combustion. The main conclusions from this first part of our investigations on HCCI mode were:

- the rate of heat release is very steep for all the EGR rates investigated in this study;
- for very high charge dilution (EGR rate higher than 50 % and inlet temperature lower than 350K), a slow oxidation process occurs, with a very slow heat release, not adapted to engine operation;
- a high boost pressure enables HCCI combustion with high EGR rates;
- the HCCI combustion process is not efficient for equivalence ratios lower than 0.3 for air/fuel mixture when the inlet temperature slower than 350K.

5. Contracts and Grants with Industry

5.1. Reduced order models of HCCI engines (Renault contract)

Participants: Mehdi Gati, Fadila Maroteaux, Jean-Baptiste Millet, Eric Rodrigues, Michel Sorine.

Renault contract 1 02 D0667 00 21102 01 2. J.B. Millet is preparing his PhD in the framework of this CIFRE contract.
The HCCI engine tuning requires a large number of engine tests which are time-consuming and very expensive. To reduce the number of tests, a model with a very short computational time to simulate the engines in the whole operating range is needed. Therefore, the objective of this study is to present a new type of zero-dimensional thermodynamic model without chemical kinetics to analyze the HCCI combustion process. A model based on mathematical bifurcation is proposed, where stabilities of the system describe the cool flame and the main ignition. The system of equations governing the model is reduced to three state variables: the temperature and two mass fractions. The model has been compared to the detailed mechanism developed by Lawrence Livermore National laboratory (LLNL) and to Renault engine experimental data. This comparison shows that the model gives reasonable accuracy.

5.2. Modelling of HCCI combustion: effects of chemical kinetics and turbulent mixing (Renault contract)

Participants: Ludovic Noël, Fadila Maroteaux, Pierre-Lin Pommier, Michel Sorine.

Renault contract 104 D1151 00 21102. P.-L. Pommier is preparing his PhD in the framework of this contract.

The numerical modelling of complex turbulent flow is an important issue in engines applications. In order to investigate the effects of both the chemical kinetics and turbulent mixing, a stochastic model is used. At first a simple partially stirred plug flow (PaSPFR) is considered, where spatial homogeneity is assumed and were only two physical processes remain: chemical reaction and mixing. In the combustion chamber, local quantities are chemical species mass fractions and temperature and are assumed to be random variables (with their joint random vector). The time evolution of the mass density function (MDF) transport equation takes into account the terms representing the mixing properties and the reaction mechanism of the system. The two terms are approached by a stochastic process, the 26 reactions mechanism developed above is used to model the reaction term. This work is under progress with the PhD of Pierre-Lin Pommier, where the first step was centred on the general modelling of reacting system.

5.3. Mathematical modelling monitoring and control of a fuel cell system with a fuel processor

Keywords: *control*, *energetics*, *fuel cell*, *fuel processor*, *modelling*, *monitoring*, *process engineering*.

Participants: Fehd Benaïcha, Damiano Di Penta, Karim Bencherif, Masoud Najafi, Stefano Perabò, Michel Sorine, Qinghua Zhang.

During the last 4 years we have considered modelling and control of polymer electrolyte fuel cells (PEMFC) [4]. PEMFC have a high energy conversion efficiency and zero pollutant emission when fueled with hydrogen. They are one of the most promising candidates for fuel cell powered vehicles. Hydrogen can be stored or produced onboard the vehicle by reforming methanol or hydrocarbon fuels in a so called “fuel processor” (or reformer). In our present researches, we consider modelling, monitoring and control problems for a complete system with four stacks of 100 PEMFC each and a gasoline processor. The framework for this work is the cooperative research project RESPIRE, which is partly supported by a public agency, ADEME, and two CIFRE contracts with Renault for Fehd Benaïcha and Damiano Di Penta.

5.3.1. RESPIRE project (ADEME contract)

For the purpose of developing new generation automotive vehicles with reduced exhaust emission, a research project on fuel cells and fuel reformer system, entitled RESPIRE (“Réduction des Emissions par Système PIle et Reformeur Essence” or Emission reduction with onboard gasoline reformer fuel cell system), has been started since September 2004 with industrial partners, Renault (prime contractor), Snecma, Total ; academic partners, Armine, Supelec, INRIA, and some Renault suppliers, 3M and Nuvera.

The technology of fuel cells is used to generate electric power for electric engines. When hydrogen is used as fuel, this technology allows to design vehicles with almost total absence of pollution at exhaust emission. However, in addition to the difficulty of on board hydrogen storage, it is not realistic to quickly develop a large number of hydrogen service stations when the first cars equipped with fuel cells are available on the market. The particularity of the RESPIRE project is a combination of fuel cells with a fuel reformer. Conventional gasoline stored on board is used by the reformer to produce hydrogen fuel which is then fed to the fuel cells. This solution has the advantage of using normal petrol stations. Though gasoline is still used as energy source, with this new technology, the pollution emission can be considerably reduced, and the energy efficiency is better than with the classical thermal engines.

As the fuel reformer is not perfect, its product is a mixture of hydrogen and some other gas components, in particular the carbon monoxide (CO) which can poison the fuel cells. We are developping methods for monitoring the problems related to the presence of CO. More generally, the SOSSO2 team takes in charge of the control and fault diagnosis of the fuel cells and fuel reformer system in the RESPIRE project.

5.3.2. Modelling and monitoring of a single PEMFC (Renault contract)

In this CIFRE contract with Renault, Damiano Di Penta will study modelling and monitoring of a single PEMFC or of a stack of PEMFC (a series of 100 PEMFC), considered as an averaged PEMFC. This year, the problem of CO poisoning has been studied and a reduced fuel cell stack model for control and fault diagnosis has been proposed [43].

5.3.3. Modelling and control of a single PEMFC (Renault contract)

In this CIFRE contract with Renault, Fehd Benaïcha will study control strategies optimising the system efficiency. This work is done in cooperation with Jean-Claude Vivalda (CONGE team-project).

5.4. Modelling and compensation of backlash in power transmission systems (Renault contract)

Participants: Giancarlo Ferrari Trecate, Mehdi Gati, Michel Sorine.

Renault contrat 1 04 D0004 00 21102 012. M. Gati is preparing his PhD in the framework of this CIFRE contract.
Gear trains are used to convert the high speed - low torque output of the engine into a lower speed - higher torque input to the wheels. These transmissions systems have two main disadvantages: 1) contact between rotating parts may be lost somewhere along the kinematic chain during some transients, this is the backlash effect; 2) some undesired compliance is introduced into the system. Our objective is the suppression of the transient vibrations induced by the combined effect of backlash and compliance. The existence of contact and non-contact phases leads us to adopt an hybrid-system point of view for modelling and backlash compensation. See [16] for some first results in this direction.

5.5. Nonlinear system identification (The Mathworks contract)

Participant: Qinghua Zhang.

Contract with The Mathworks, from July 2005 to July 2010. See the software section 3.2.

6. Other Grants and Activities

6.1. National grants

6.1.1. CardioSense3D (Inria Large Initiative Action)

Participants: Karima Djabella, Nki Echenim, Alfredo Illanes Manriquez, Taous-Meriem Laleg, Yves Papelier, Michel Sorine, Qinghua Zhang.

CardioSense3D is a 4-year Large Initiative Action launched in 2005 and funded by INRIA, which focuses on the electro-mechanical modeling of the heart. This action follows the 4-year ICEMA project and is described in great details in http://www-sop.inria.fr/CardioSense3D.

6.1.2. REGLO (Inria Cooperative Research Initiative)

Participants: Frédérique Clément, Nki Echenim, Jean-Pierre Françoise, Claire Médigue, Michel Sorine.

http://www-rocq.inria.fr/who/Frederique.Clement/reglo.html
This project deals with the multi-scale modelling and imaging of the ovarian function and gathers experts in the fields of mathematical modelling and control, Physiology and image processing. 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 well as to manage ovulation rate and ovarian cycle chronology in domestic species. From a more fundamental viewpoint, the regulation of ovulation raises scientific issues that go beyond the strict scope of reproductive physiology, especially in cellular biology and neuro-endocrinology.

6.2. European grants

6.2.1. NoE HYCON

Participants: Giancarlo Ferrari Trecate, Michel Sorine.

G. Ferrari Trecate has been the coordinator of the INRIA team participating to the Network of Excellence HYCON ("Taming Heterogeneity and Complexity of Networked Embedded Systems") started on 15/09/04 in the context of the Sixth Framework Programme.

6.2.2. STREP HYGEIA

Participant: Giancarlo Ferrari Trecate.

G. Ferrari Trecate has been the coordinator of the INRIA team participating to the Specific Targeted Research or Innovation Project HYGEIA ("Hybrid Systems for Biochemical Network modelling and Analysis") started on 01/01/05 in the context of the Sixth Framework Programme.

6.3. Invitations

In March 2005, G. Ferrari Trecate was awarded a fellowship from the Italian Ministry of University and Research within the program "Rientro dei cervelli" for joining the Dipartimento di Elettronica Informazione of the Politecnico di Milano where he stayed until 31/10/2005.

Since 01/11/05, he is on leave at the Universit degli Studi di Pavia, where he works as "Professore Associato".

7. Dissemination

7.1. Scientific activity and coordination

7.1.1. Coordination activity

P.A. Bliman:
- Member of International Program Committee of IFAC TDS'06, L'Aquila, Italy.
- Responsible for INRIA, Rocquencourt Research center, of the activities of the Multi-partner Marie Curie Training Site entitled Control Training Site (beginning in 2002).
- Member of the panel for the PhD thesis defence of V.J.S. Leite (Unicamp, Campinas, Brazil and INSA-Toulouse).

C. Bonnet:
- Member of the IFAC technical committee on Robust Control (2005-2008).
- Member of the International Program Committees of JDMACS 2005, IFAC TDS'06.
- Member of the board of directors of the GDR MACS (Research group on modelisation analysis and tracking of systems of the CNRS).
- Member of CCRRESTI (Conseil Consultatif Regional de la Recherche, de l'Enseignement Superieur, de la Technologie et de l'Innovation).
- Member of the board of the association *Femmes et mathématiques* (Women and Mathematics).
- Member of the french piloting committee of the Helsinki group on Women and Science of the European Commission.
- Member of the piloting committee of the convention 'INRIA-Académie de Versailles.

F. Clément:
- Coordination of the REGLO Cooperative Research Initiative.
- Organisation of the conference cycle "Modelling in the life sciences", in the framework of the "Thematiques INRIA" (cf http://thematiques.inria.fr/cyclemodeliser.htm), April-May 2005.
- Member of evaluation boards.

G. Ferrari Trecate:
- Member of the International Program Committee for the conference HSCC05 - Hybrid Systems: Computation and Control, Swiss Federal Institute of Technology (ETH) Zurich, Switzerland March 9-11, 2005.
- Member of the International Program Committee for the 2nd IFAC Conference on Analysis and Design of Hybrid Systems (ADHS'06), Alghero, Sardinia, Italy - June 7-9, 2006.
- Member of the IFAC Technical Committee on Power Plants and Power Systems (up to November 2005).
- Vice-chair of the IFAC Technical Committee on Control Design (from November 2005).
- Organisation (together with A. Juloski) of the following workshop:
Identification of Hybrid Systems, December 11, 2005, CDC-ECC 2005, Sevilla, Spain.

M. Sorine:
- Member of the International Program Committees for the JDMACS 2005, CIFA 2006 and IFAC MCBMS'06 conferences.
- Member of the program committee of the Cnrs-Inria-Inserm program “Health: information and technology”.
- Member of the program committe of the 13th INRIA-Industry Meeting on Information and Communication Science and Technology for Medicine.
- Member of the scientific board of the “Pôle mécatronique du Mantois”.
- Member of four PhD committees.

Q. Zhang:
- Member of IFAC Technical Committee on Fault Detection, Supervision and Safety of Technical Processes (SAFEPROCESS).
- Associate editor of the joint IEEE Conference on Decision and Control and European Control Conference (CDC-ECC) 2005.
- IPC member of the International Conference on Machine Intelligence (ICMI) 2005.
- Coordinator of the national working group “Sûreté-Supervision-Surveillance”, till September 2005.
- Participation in the activities of the European Research Network on System Identification.
- Participation in the activities of the European Network of Excellence on Embedded Systems Design (ARTIST2).

7.2. Teaching activity

- P.A. Bliman: “Linear Matrix Inequalities and Control Theory” for 3rd year students at ENSTA (21h)
- F. Clément: “Modelling and control of biological systems” course, part of the "Master's Degree in BioInformatics and BioStatistics" (Paris 11 University).
- G. Ferrari Trecate: Course “Automatica”, Facolta di Ingegeneria Industriale, Politecnico di Milano, Italy ; Lecture “Identification Algorithms for Hybrid Systems” within the “1st HYCON PhD school on Hybrid Systems”, July 19-22, Siena, Italy ; Lecture “Controllo Predittivo per Sistemi Ibridi” within the PhD school on Model Predictive Control, October 19, Politecnico di Milano, Italy.

7.3. Seminars

- P.A. Bliman, 1 lecture in Brasil at State University of Campinas, August 2005
- G. Ferrari Trecate, “Analysis of coordination in multi-agent systems through partial difference equations”, September 13, Universit degli Studi del Sannio, Benevento, Italy.
- M. Sorine: "Le cœur : un système multi-échelles contrôlé", Université technologique de Compiègne, February 2005.
“Clean, Secure Vehicles: Onboard Energy and Information Management”. Prospective seminar of the Scientific and Technological Orientation Council of Inria. September, 2005.

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