Activity Report 2016

Section Highlights of the Team

MODELING AND CONTROL FOR LIFE SCIENCES

ABS Project-Team

4. Highlights of the Year

4.1. Highlights of the Year

In 2016, several achievements are worth noticing in three realms, namely in computer science, computational structural biology, and software.

4.1.1. *Computer Science*

▶ **Optimal transportation problems with connectivity constraints**
Reference: [21]

In a nutshell: Optimal transportation theory provides a rich framework to compare *measures*, both in the continuous and discrete settings. In this work, we study generalization of discrete transportation problems, when the supply and demand nodes are endowed with a graph structure; due to these constraints, our study focuses on transport plans respecting selected connectivity constrains. Our contributions encompass a formalization of these problems, as well as hardness results and heuristic algorithms.

Assessment: To the best of our knowledge, this work is the first one focusing on transport plans with connectivity constraints. One of the key applications targeted is the comparison of potential energy landscapes (PEL) in biophysics. Our algorithms provide a novel way to compare PEL, a topic overlooked so far.

▶ **Clustering stability revealed by matchings between clusters of clusters**
Reference: [22]

In a nutshell: Clustering is a fundamental problem in data science, yet, the variety of clustering methods and their sensitivity to parameters make clustering hard. This work provides a new tier of methods to compare two clusterings, by computing meta-clusters within each clustering– a meta-cluster is a group of clusters, together with a matching between these.

Assessment: Our methods will help assess the coherence between two clusterings, in two respects: by stressing the (lack of) stability of clustering while varying the parameters of a given algorithm, and by allowing a detailed comparisons of various algorithms.

4.1.2. *Computational Structural Biology*

▶ **Novel structural parameters of Ig-Ag complexes yield a quantitative description of interaction specificity and binding affinity**
Reference: [23]

In a nutshell: Understanding the specificity of antibodies for the targeted antigens, and predicting the affinity an antibody - antigen complexes is a central question in structural immunology. Using novel parameters acting as proxys for important biophysical quantities, we obtained affinity predictions of unprecedented accuracy, and were able to provide a quantitative explanation for the specific role of so-called *complementarity determining regions* – in particular CDR3 of heavy chains. See details in section 6.1.2 .

Assessment: Our affinity predictions are the most accurate known to date, and show that for certain classes of IG - Ag complexes, the affinity prediction problem may be solved from databases of high resolution crystal structures.

▶ **Energy landscapes and persistent minima**
Reference: [15]

In a nutshell: Potential energy landscapes (PEL) of molecular systems are complex high-dimensional height functions. In this work, we introduced several tools from graph theory, optimization, and computational topology, so as to identify prominent features of PEL – prosaically distinguishing the signal from the noise. See details in section 6.3.1 .

Assessment: Our work calls for important developments in two directions. The first one is concerned with the *calibration / learning* of features of PEL. The second one is the systematic comparison of force fields used in biophysics, as from current knowledge, deciding which force field is best for a given task or system is an open issue.

▶ **Hybridizing rapidly growing random trees and basin hopping yields an improved exploration of energy landscapes**
Reference: [18]

In a nutshell: We developed a novel exploration algorithm for high-dimensional non convex (potential) energy functions used in biophysics. Our algorithm exploits the ability of *basin hopping* to locate low-lying local minima, and that of *rapidly exploring random tree* to foster the exploration of yet unexplored regions. See details in section 6.3.2 .

Assessment: Our exploration algorithm outperform the two classical algorithms it is derived from. To strike a major impact, though, our exploration strategy needs to be complemented by enhanced thermodynamic sampling algorithms, able to bridge the gap between structures on the one hand, and thermodynamics / dynamics on the other hand.

4.1.3. *Software*

▶ **The Structural Bioinformatics Library**
Reference: [20]

In a nutshell: The SBL was released in 2015. In 2016, two important milestones were achieved, with the addition of several important packages, notably geared towards the generation and the analysis of conformational ensembles, and the publication of [20]–to appear in Bioinformatics.

Assessment: As outlined by the reviewers of [20], the SBL is to the best of our knowledge the first library proposing a coherent framework, in terms of algorithms, data structures and biophysical models, to tackle the most important problems in structural bioinformatics. Our paper presenting the SBL being in press as of December 2016, statistics on users and downloads will be reported in the 2017 activity report.

AMIB Project-Team (section vide)

BEAGLE Project-Team

4. Highlights of the Year

4.1. Highlights of the Year

EvoMove

We completed the implementation of the EvoMove system, an evolving music generation system based on performer moves. The moves are not predefined, they are identified by an evolutionary subspace clustering algorithm that builds on-the-fly move categories. Such a category is created when similar moves are repeated, but it remains flexible in the sense that it can adapt to gradual changes of the moves. A category can also be forgotten when the corresponding moves do not occur any longer. We run working sessions with dancers and record parts of these performances on videos. The first prototype of EvoMove has been tested with the Anou Skan company (https://www.youtube.com/channel/UCoyfXJx_izpQZi6hD8w5M3A). The system immediately convinced the dancers of its interest and we are now working on the creation of a short play with Claire Lurin, an INSA-Lyon student who is also a semi-professional dancer.

ECAL

The Beagle team was chosen by the board of the ISAL (International Society For Artificial Life) to organize ECAL 2017, the 14th European Conference on Artificial Life. ECAL is the offical conference of the ISAL on odd years. Organizing ECAL 2017 will confirm the Beagle team as a major player in the international artificial life community and as the domain leader in France.

5. Highlights of the Year

5.1. Highlights of the Year

BIGS team has organised a two-days workshop "Rencontres des équipes Inria travaillant sur le cancer" that took place Paris in March. 10 inria teams were present. The program is available on https://team.inria.fr/bigs/workshopcancer/.

<p style="text-align:center"><strong style="color:red">BONSAI Project-Team</p>

5. Highlights of the Year

5.1. Highlights of the Year

The software SortMeRNA, developed by the team, has reached the number of 100 labs worldwide that have been using it to analyze their sequencing data. SortMeRNA is able to deal with large metagenomics projects with multiple applications in health (gut microbiome,...), environment (sea, lakes, soil,...), biotechnologies (bio-films,...). The first version was released at the end of 2012, and it is still under active maintenance.

CAPSID Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

5.1.1. Awards

A figure from our article in the *Journal of Applied Crystallography* [19] was used to illustrate the front cover of the February issue of the journal.

DYLISS Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

The first main novelty in 2016 is the release of our first methods and tools based on semantic web technologies. These methods enable the pre-processing of heterogeneous data prior to their integration in the toolboxes developped by the team. Methods for the transparent integration and querying of heterogeneous data (AskOmics) as well as the user-friendly tracable reconstruction of metabolic networks (PADmet package) have been developped in collaboration with our main partners (INRA Rennes, University of Chile, Station biologique de Roscoff) to facilitate the comparison of phenotypes accross several species or several strains.

ERABLE Project-Team (section vide)

<p style="text-align:center; color:red">**GENSCALE Project-Team**</p>

5. Highlights of the Year

5.1. Highlights of the Year

- **Colib'read Workshop, Nov 7-8 th, Institut Curie, Paris.** GenScale organized a two-day workshop to present the main results of the Colib'read ANR (2013-2016, Coordinator P. Peterlongo) to the scientific community.
- **GATB Programming days.** In 2016, GenScale organized two Genome Analysis Toolbox (GATB) trainings days in Rennes (June 15 th) and Paris (Nov. 9 th). Each event gathered 15 persons who learned how to use the GATB library to design efficient NGS tools.

<center>IBIS Project-Team</center>

4. Highlights of the Year

4.1. Highlights of the Year

A paper based on the PhD thesis of Manon Morin was published in *Molecular Microbiology* this year [14]. Furthermore, two papers appeared in *PLoS Computational Biology*, one by Eugenio Cinquemani and colleagues from the LIFEWARE project-team and the University of Pavia [13], and one describing results from the PhD thesis of Nils Giordano, in collaboration with colleagues from the BIOCORE project-team [12]. Eugenio Cinquemani co-organized the Fifth International Conference on Hybrid Systems Biology (HSB 2016) (http://hsb2016.imag.fr/) in Grenoble.

<p align="center" style="color:red">**LIFEWARE Project-Team**</p>

5. Highlights of the Year

5.1. Highlights of the Year

Creation of the Exploratory Action *InBio* with Pasteur Institute in Paris

The InBio project has been selected in the context of a call for new research groups organized by the Center for Bioinformatics, Biostatistics and Integrative Biology (C3BI) of Institut Pasteur.

The main scientific question investigated in InBio is how one can exploit cell-to-cell differences to better learn and control the functioning of biological systems. That is, instead of seeing phenotypic variability as undesired noise that beclouds the processes of interest, we will try to harness cellular heterogeneity. In particular for control problems, because one interacts with the system, it is important to be able to predict the dynamical evolution of phenotypic heterogeneity.

A second important scientific objective of InBio is to develop more rational and systematic interactions between experimental and computational work. The virtuous loop in which experiments nurture models, that in turn, orient further experiments is universally acclaimed and installing such a loop is a central objective of many research projects. In interdisciplinary research, it is expected that this exchange of information will emerge from the interactions between the two disciplinary groups. For both practical and theoretical reasons, this is actually often not the case. In InBio, we will adopt a multidisciplinary research approach and develop an integrated environment around the design-and-test loop. This will notably involve the rational design of cell stains and of experimental plans, so that experiments are maximally-informative, and of efficient model calibration and discrimination methods. This specific focus explains the full name given to the InBio group: "Experimental and Computational Methods for Modeling Cellular Processes" (InBio simply abridges integrative biology).

InBio will be hosted at Institut Pasteur and will host experimental and theoretical research. It is a mixed structure between Inria (action exploratoire attached to Lifeware) and Institut Pasteur (research unit attached to the C3BI), and is headed by Grégory Batt.

The Dogma of the Control of the Cell Cycle by the Circadian Clock Revisited

Our long-standing and tight collaboration with Franck Delaunay's lab in Nice culminated this year with a revisiting of the dogma of the control of the cell cycle by the circadian clock. In [9] we showed, using a coupled reaction model of the cell cycle and the circadian clock and BIOCHAM analysers [4], that a selective upregulation of Reverb-α (or an inhibition of Bmal1) during mitosis is necessary to explain the period and phase data observed in NIH3T3 fibroblasts in different serum concentrations. This mechanism constitutes a reverse control of the circadian clock by the cell divisions which was previously outlooked but is overriding in some spontaneously dividing cell types such as non-confluent NIH3T3 fibroblasts.
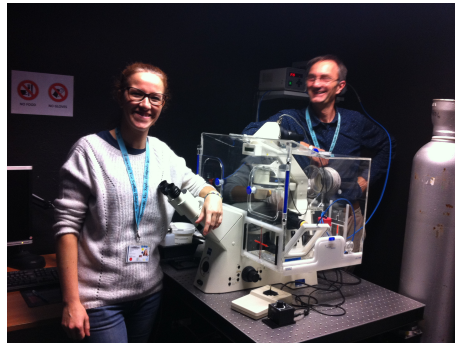
Figure 1.

Céline Feillet and Franck Delaunay, CNRS Nice,

with the large-scale time-lapse video microscope which produced the unicellular 72h data studied in [9].

MORPHEME Project-Team (section vide)

<div align="center">

PLEIADE Team

</div>

5. Highlights of the Year

5.1. Highlights of the Year

5.1.1. Biotechnology

In collaboration with MIAT INRA and UMR 5234 CNRS/Université de Bordeaux, PLEIADE assembled and analyzed *Clavispora lusitaniae*, an ubiquist environmental ascomycetous yeast that can be pathogenic and is responsible for invasive candidiases in pediatric and onco-haematology patients [24].

In collaboration with UMR 5200 CNRS/Université de Bordeaux, PLEIADE assembled and analyzed transcriptomes from three tissues of the oil palm tree *Elaeis guineensis* Jacq., whose mesocarp contains oil up to 90% of its dry weight. Our goal is to increase, by synthetic biology approaches, the yield in oil for crops grown in Europe. The yield and the composition of oil measured from wild-type palm tree specimens varies dramatically, indicating a high level of bio-diversity.

5.1.2. Biodiversity

PLEIADE and the HIEPACS team developed connections between random projection methods and multi-dimensional scaling, in order to compute eigenvectors and eigenvelaues in space of reasonable dimension. The method for MDS developed by Pierre Blanchard has proved to be surprisingly efficient and precise. It was presented at PASC 2016 Lausanne. This work improves the analysis of microbial communities, where the shape of the point cloud built from pairwise distances between a large set of NGS reads is used to describe the diversity of the community.

SERPICO Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

5.1.1. New projects

The 4 year-ANR-DALLISH proposal (PRC / Challenge 7 / Topic 5), coordinated by the Serpico Team-Project, has been accepted in September 2016.

The CytoDI Associated Team, in collaboration with University of Texas, SouthWestern Medical Center, Dallas (TX, USA) started in January 2016.

TAPDANCE Team

4. Highlights of the Year

4.1. Highlights of the Year

TAPDANCE Team created in June 2016.

A Starting Research Fellow, Pierre-Étiene Meunier, was hired by Inria to begin work with TAPDANCE in January 2017.

VIRTUAL PLANTS Project-Team

4. Highlights of the Year

4.1. Highlights of the Year

- *Stochastic model of Phyllotaxis*: Exploration of developmental mechanisms classically relies on analysis of pattern regularities. Whether disorders induced by biological noise may carry information on building principles of developmental systems is an important debated question. In this work, we addressed theoretically this question using phyllotaxis, the geometric arrangement of plant aerial organs, as a model system. Phyllotaxis arises from reiterative organogenesis driven by lateral inhibitions at the shoot apex. Motivated by recurrent observations of disorders in phyllotaxis patterns, we revisited in depth the classical deterministic view of phyllotaxis. We developed a stochastic model of primordia initiation at the shoot apex, integrating locality and stochasticity in the patterning system. This stochastic model recapitulates phyllotactic patterns, both regular and irregular, and makes quantitative predictions on the nature of disorders arising from noise. Altogether, we show that disorders in phyllotaxis instruct us on the parameters governing phyllotaxis dynamics, and thus that disorders can reveal biological watermarks of developmental systems [27].

- *Statistical methods*: One of our main activities consists of identifying and characterizing developmental patterns in plant phenotyping data. Phenotyping data are very diverse ranging from the tissular to the whole plant scale but are often highly structured in space, time and scale. We intend to analyse such data using state-of-the-art methods at the crossroad between statistical modelling, machine learning and pattern recognition. This generates regularly new methodological results as illustrated this year by [18] and [25].

ARAMIS Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

- Stanley Durrleman's ERC Starting Grant "LEASP" has started.
- H2020 project EuroPOND, under societal challenge "Personalizing Health and Care" has started.
- ANR-NIH project NETBCI, under the "Collaborative Research in Computational Neuroscience" program (CRCNS) has started.
- The team has been awarded the ANR-NIH project HIPLAY7, under the "Collaborative Research in Computational Neuroscience" program (CRCNS)
- The team has been awarded the ANR project BRANDY, under the generic call programme "Vie, Sante et Bien-etre", Project duration: 2017-2020
- ARAMIS participates to the Human Brain Project (European Flagship).
- Anne Bertrand was awarded a one year Inria-APHP interface contract (i.e., "poste d'accueil"), allowing her to work half-time in the ARAMIS project team, from november 2016 to november 2017.
- Pietro Gori and Barbara Gris successfully defended their PhD.
- S. Durrleman has been appointed associate editor of IEEE Transactions on Medical Imaging (TMI).

<p style="text-align: center; color: red;">**ASCLEPIOS Project-Team**</p>

4. Highlights of the Year

4.1. Highlights of the Year

Marco Lorenzi has been recruited as Chargé de Recherche in the Asclepios team from December 2016.

4.1.1. Awards

- Nina Miolane received the l'Oréal-UNESCO Fellowship for Women In Science. She counts among the 30 awardees who have been selected by an independent jury to stress the excellence and originality of their scientific research and their dedication to share their knowledge in the broader society.

- Shuman Jia received the Best Challenge Paper Award during the 7th international workshop on Statistical Atlases and Computational Modeling of the Heart (STACOM), held in Conjunction with MICCAI 2016 in Athens, Greece.

BEST PAPERS AWARDS :

[39] **7th International Statistical Atlases and Computational Modeling of the Heart (STACOM) Workshop, Held in Conjunction with MICCAI 2016**. S. JIA, L. CADOUR, H. COCHET, M. SERMESANT.

ATHENA Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

5.1.1. Awards

R. Deriche and the ATHENA team has been awarded by an ERC Advanced Grant from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation program (ERC AdG agreement No 694665 "Computational Brain Connectivity Mapping" started on Sept. 1st, 2016.)

Guillermo Guallardo, PhD has been awarded by a Merit Abstract Award by the 2016 OHBM Annual Meeting in Geneva, Switzerland for his work entitled *Efficient Population-Representative Whole-Cortex Parcellation Based on Tractography* [34].

5.1.2. Press coverage

Brain-Computer Interfaces developped in Athena attracted attention of the media, at regional and national levels: Nice Matin, Le Dauphiné Libéré and Le Figaro Santé have published articles about our translational research on the P300 speller. This system enables severely disabled patients, who are deprived of voluntary motor control, to communicate by using only their visual attention.

BIOVISION Team (section vide)

CAMIN Team

5. Highlights of the Year

5.1. Highlights of the Year

International Functional Electrical Stimulation Society Conference organization

In 2016, CAMIN organized the 20th International Functional Electrical Stimulation Society Conference. 135 participants attended the event. Papers are referenced in Pubmed and published in European Journal of Translationnal Myology. A special issue with a selection of best articles will be published in 2017 in Artificial Organs Journal. http://ifess2016.inria.fr/

Figure 3. Flyer of IFESS 2016 conference

Participation into Cybathlon competition

We have participated in the first international competition Cybathlon held in Kloten, Switzerland in October 2016. After more than one year of physical and technical preparation, our team, Freewheels, was present with one complete paraplegic pilot in the FES cycling discipline. http://freewheels.inria.fr/

Figure 4. Freewheels team at Cybathlon 2016

GALEN Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

5.1.1. Awards

- Wacha Bounliphone and Eugène Belilovsky received the Université Paris-Saclay STIC Doctoral School Best Scientific Contribution Award

- Eugène Belilovsky received the MITACS-Inria Globalink Award

- Prof. Iasonas Kokkinos was invited as keynote speaker in Astronomical Data Analysis Summer School, Chania, Greece, May 2016

- Prof. Iasonas Kokkinos was invited as keynote speaker in Local features workshop, held in conjunction with ECCV, October 2016

- Dr. Evangelia Zacharaki was appointed as guest associate editor for the Medical Physics journal

- 2nd place at the 2016 IEEE GRSS Data Fusion Contest for the paper: Simultaneous Registration, Segmentation and Change Detection from Multisensor, Multitemporal Satellite Image Pairs [30].

- Finalists (not-awarded) of the Best Papers award at the IEEE conference ICIP'16 for the paper: A Block Parallel Majorize-Minimize Memory Gradient Algorithm [16].

- Oral presentation in the Neural Information Processing Systems (NIPS), 2016 conference of the paper: Testing for Differences in Gaussian Graphical Models: Applications to Brain Connectivity [15] (oral presentations: only 1% of more than 2000 submitted papers).

- Oral presentation in the British Machine Vision Conference (BMVC), 2016, of the paper: Efficient Learning for Discriminative Segmentation with Supermodular Losses [33] (oral presentations: 7% of submitted papers).

- Oral presentation in the International Conference on Artificial Intelligence and Statistics (AISTATS), 2016, of the paper: A Convex Surrogate Operator for General Non-Modular Loss Functions [32] (oral presentations: 11% of submitted papers).

5.1.2. Other

- Acceptance of the project entitled «Predicteurs performants de l'efficacite des agents anticancereux par apprentissage profond (deep learning) de donnees radiomiques et genomiques» as part of the program *Imagerie Médicale Computationnelle*. PI: Dr. Charles Ferte, Gustave Roussy, 94805 Villejuif.

MATHNEURO Team (section vide)

MIMESIS Team (section vide)

MNEMOSYNE Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

5.1.1. First PhDs defended

2016 is a very special year for our young team Mnemosyne, since our first three PhDs have been defended in October and November [1], [2], [3].

NEUROSYS Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

- Laurent Bougrain has co-supervised and co-written a two-volume book for anyone who uses Brain-Computer Interfaces, in English [17], [18] and for the first time in French [19], [20]. The multidisciplinary work has involved around fifty authors from various backgrounds, who write about their particular area of expertise in a way that makes it accessible to a wider audience. That includes healthcare professionals, video game developers, researchers and students, as well as a much wider audience, curious to explore the philosophical and ethical aspects of this subject. The book also has a practical side, with tutorials illustrating the use of BCI and the OpenViBE software platform (see 6.6 and http://openvibe.inria.fr). Laurent Bougrain contributed to several chapters about the state of the art, medical applications and OpenViBE [15], [10], [12], [13] (French version: [16], [9], [11], [14]).

- We stepped up our collaboration with the *department of neurology of the university hospital in Nancy* (Louise Tyvaert, Louis Maillard, Laurent Koessler) leading to i) a **project PEPS JCJC** on modeling and simulation of the oscillatory activity of the memory system during sleep and under general anesthesia (see section 9.2) a **PhD thesis** started in October 2016 (Amélie Aussel), funded by UL and co-supervised by Laure Buhry (Loria-Neurosys) and Radu Ranta (CRAN). This thesis will make use of SEEG recordings made in epileptic patients and will use preliminary results on hippocampal modelling obtained thanks to the project PEPS JCJC.

PARIETAL Project-Team (section vide)

SISTM Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

Modeling clinical trials of IL7

We have published the results of two clinical trials [17] that are showing the feasability of repeating IL-7 cycles and confirmed the predictions performed with our dynamical model published in [49]. This mecanistic modeling allow to propose protocol which decrease the number of injection within each IL-7 cycle while keeping the same efficacy [35].

Awards Mélanie Prague published an invited paper on her PhD works (which was supervized by Daniel Commenges and co-suppervized by Rodolphe Thiébaut) as a perks for the attribution of the "Marie-Jeanne Laurent-Duhamel PhD award (2015) by the SFdS (Société Francaise de statistiques). [15]

<p style="text-align:center">**VISAGES Project-Team**</p>

5. Highlights of the Year

5.1. Highlights of the Year

5.1.1. Awards

- In 2015, the Neurinfo platform obtained an "Emergence" label from the IBISA agency, this label has been upgraded in 2016 as a "platform of Excellence" and sustained by IBISA in 2016 and onward. The IBISA label is a national label for technological platforms awarded by the GIS IBISA on an annual basis.

5. Highlights of the Year

5.1. Highlights of the Year

R Foundation

Julie Josse has been elected member of the R Foundation for Statistical Computing.

mlxR 3.1

mlxR 3.1 available on CRAN

AIRSEA Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

In collaboration with M. Asch and M. Bocquet, M. Nodet published a book about Data Assimilation [30].

5.1.1. Awards

Jose R. Leon was granted by an International Inria Chair.

E. Arnaud was granted by a CRCT (Congé pour recherches ou conversions thématiques) by the CNU.

L. Debreu was awarded IMarEST Deny Medal for the best paper in journal of operational oceanography for year 2014.

ANGE Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

While the theory and the numerics related to the nonlinear shallow water equations are extensively studied, the understanding of more complex models including dispersive ones is not achieved. Two PhD theses about these issues were defended in 2016 within the team (N. Aïssiouene and D. Kazerani). To go further, a collaboration with spanish collaborators from the university of Sevilla was launched with multiple trips in Spain and France resulting in a preprint [25]. The collaboration is expected to be made more formal in 2017.

Moreover, the team has been reinforced by two young engineers: J. Ledoux in the framework of the ANR project Hyflo-Eflu and F. Souillé. The latter recruitment has been allowed by the Inria ADT grant F2O ("Freshkiss to Others") and is aimed at easing the transfer of the Freshkiss code in cooperation with SciWorks Technologies.

CASTOR Project-Team (section vide)

CLIME Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

5.1.1. Awards

Inria and Paris City were awarded a Décibel d'Argent 2016 in research category for the mobile application Ambiciti. The award was attributed by the Conseil National du Bruit, which depends on the Ministry of Ecology, Sustainable Development and Energy, and is a national organization in charge of noise. The selection committee pointed out the Ambiciti articulation between research, citizen involvement, city or government actions and the operational development of a rich and perennial mobile application.

COFFEE Project-Team (section vide)

FLUMINANCE Project-Team (section vide)

LEMON Team

5. Highlights of the Year

5.1. Highlights of the Year

- Antoine ROUSSEAU spent 9 months in the office of Inria Chile (Santiago, Chile) from February to October 2016 to collaborate on the new project on *Marine Energies Research International Center* (MERIC) in Chile. Antoine is the scientific coordinator of the research line "Advanced modeling for marine energy", and several members of LEMON, CARDAMOM and TOSCA research teams will be involved in this 8 years project in partnership with DCNS and Enel.

MAGIQUE-3D Project-Team (section vide)

SERENA Team (section vide)

STEEP Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

This year represents an important landmark in the life of the team, who witnessed the first PhD defense since it has been formed.

The thesis of Jean-Yves Courtonne beared on ecological accounting, with the inception and implementation of a new downscaling method allowing us to track material flow through supply chains at various nested geographical scales; the method also provides an assessment of the associated environmental pressures and an analysis of the errors of the process. This thesis has been recognized by the two referees as a major step forward in France in this field. Four articles have come out of this work; they are published or considered for publication in the leading journals in the field.

A second PhD defense took place this year, by Laurent Gilquin who did most of his PhD studies in STEEP before he followed his supervisor (E. Arnaud) to the AIRSEA project-team.

TONUS Team (section vide)

BIOCORE Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

- The question of how many and how frequently natural enemies should be introduced into crops to most efficiently fight a pest species is an important issue of integrated pest management, which depends on the pest-natural enemies interaction. Since some natural enemies may exhibit positive predator density dependence in the predation interaction, we studied its impact on the optimal biological control introduction strategies [15].

- Optimal allocation of resources in a bacterium. We studied by techniques of optimal control the optimal allocation between metabolism and gene expression during growth of bacteria, in collaboration with Inria IBIS project-team. We showed that a good suboptimal control solution could be implemented in the cell by ppGpp (a small molecule involved in the regulation of ribosomes) [23].

<p style="text-align: center; color: red;">**CARMEN Project-Team**</p>

5. Highlights of the Year

5.1. Highlights of the Year

5.1.1. Events

On 4 November 2016 the new building of the IHU Liryc was officially opened in the presence of representatives from the municipal, departmental, regional, and national authorities.

On 9 December 2016 A. Davidović defended her thesis Multiscale Mathematical Modeling of Structural Heterogeneities in Cardiac Electrophysiology.

5.1.2. Recruitments

M. Potse, whose work had been funded by IHU Liryc since 2013, has become a full-time member of the Carmen team and has won an Inria Advanced Research Position in June 2016. He will continue his numerical studies on cardiac sudden-death syndromes and atrial fibrillation and is developing a new project on the application of electrocardiographic inverse methods in the catheterization laboratory.

We recruited the engineer P. Migerditichan; she started working in November 2016 on a project named EPICARDial electrical signals VIZualisation (EPICARD-VIZ). The aim of this project is to build a software solution for the electrocardiographic inverse problem, coded in the MUSIC platform. The goal of the project is twofold: First, we aim at building a semi-automatic functionality that allows to obtain meshes of the epicardium, torso, lungs, liver, and skeletal muscle with minimal human interaction. Second, our aim is to include a dense linear algebra library and to construct a computational framework in which we will be able to compare different methods of solving the inverse problem.

After the completion of her PhD thesis A. Davidović was hired as an Engineer, granted by the ANR HR-CEM project. She continues her work on multiscale modelling of heterogeneities in cardiac tissue. She is going to use the experimental high-resolution MRI data on animal and human hearts that are provided by the imaging team of IHU Liryc. By means of image analysis and numerical simulations she is going to study the effects of fibrotic, fatty, and other kinds of tissue on AP propagation.

DRACULA Project-Team (section vide)

5. Highlights of the Year

5.1. Highlights of the Year

- Official launch of M3DISIM as an Inria project-team (joint with Ecole Polytechnique / LMS) on June 1st
- Habilitation (HDR) of Philippe Moireau on November 28th

MAMBA Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

5.1.1. Personnel

Marie Doumic has moved in September 2015 for a 1-year sabbatical to the Wolfgang Pauli Institute in Vienna. Stefan Hoehme left in July 2015 to start a prestigious "Emmy Noether" junior research group at University of Leipzig, faculty for computer sciences. Of note, this is the first Emmy Noether research group in Leipzig, and he was the only one accepted this year (out of 20 presented).

Nicolas Vauchelet left the team in September 2015, becoming a full professor at University Paris XIII.

5.1.2. THE ITMO Cancer national call.

The team has been successful in simultaneously participating in 2 different funded projects of the ITMO Cancer THE ("Tumour Heterogeneity in its Ecosystem", a programme managed by INSERM) national call for 2016: one, EcoAML (4 teams), on early leukaemogenesis in Acute Myelogenous Leukaemia (AML), headed by François Delhommeau (CDR St Antoine, Paris), with whom we have a long-lasting collaboration, and the other, MoGlImaging (8 teams), on treatment-induced treatment resistance and heterogeneity in glioblastoma, headed by Elizabeth Moyal (INSERM, Toulouse), a project inside which we have recently developed a work collaboration with the team of François Vallette (INSERM, Nantes) on the in-vitro resistance of glioblastoma to temozolomide. In both these collaborative projects, begun in November 2016 and to be integrated in 2017 in the future THE consortium (gathering the 6 projects laureates to the national call), we propose to develop our phenotype-structured models for both the cancer and the supporting stromal cell populations, with representation of mutualistic interactions between them.

MONC Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

Last year saw a net increase in the diffusion of our work outside our own academic circle. Perrine Berment has clinched a seat in the national final of *Ma thèse en 180 secondes* after winning regional competition. Research achieved in the team was mentioned in popular radio shows like https://www.franceinter.fr/emissions/futur-proche/futur-proche-28-octobre-2016?xtmc=kurde_medecin&xtnp=1&xtcr=14. This opens new collaboration opportunities locally and nationaly for the team.

On a scientific point of view, the team has significantly increased its work on modeling tumor heterogeneity and texture analysis with very promising results so far, particularly in the thesis of Thibaut Kritter, Agathe Peretti, Cynthia Perier. We have developed a model for texture evolution over time which may offer a much better insight than approaches using statistical methods on texture features (*e.g.* radiomics).

5.1.1. *Awards*

Julien Jouganous has won *Prix Le Monde de la Recherche Universitaire*, http://www.lemonde.fr/sciences/article/2016/11/23/prix-le-monde-de-la-recherche-2016-l-evolution-du-cancer-en-equations_5036804_1650684.html.

<p style="text-align:center; color:red;">**MYCENAE Project-Team**</p>

5. Highlights of the Year

5.1. Highlights of the Year

- PhD defense of Lucile Megret. Explosion of limit cycles : qualitative analysis, numerical simulations and models. Université Pierre & Marie Curie – Sorbonne Universités, November 25th 2016.

- PhD defense of Elif Köksal Ersöz. A mathematical study on coupled multiple timescale systems, synchronization of populations of endocrine neurons. Université Pierre & Marie Curie – Sorbonne Universités, December 13th 2016.

- PhD defense of Tanguy Cabana. Limits of randomly connected networks and their dynamics. Université Pierre & Marie Curie – Sorbonne Universités, December 14th 2016.

- Invited plenary conference at ICAR2016 http://www.icar2016.org 18th International Congress on Animal Reproduction. Multiscale mathematical modeling of the hypothalamo-pituitary-gonadal axis. Tours (France), June 26-30th 2016.

NUMED Project-Team

4. Highlights of the Year

4.1. Highlights of the Year

In the context of a long standing collaboration with Sanofi group, E. Grenier develops a software for the study of the stability of vaccines. This software has been used in a formal presentation of a new vaccine to the FDA (Food and Drug Administration).

4.1.1. Awards

Vincent Calvez has been award the prize of the European Mathematical Society (2016).

REO Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

An important industrial partnership has been signed with the start-up companies Kephalios and Epygon, for the mathematical modeling of implantable cardiac devices.