RESEARCH CENTER

FIELD
Digital Health, Biology and Earth

Activity Report 2015

Section Partnerships and Cooperations

Edition: 2016-03-21

ABS Project-Team

7. Partnerships and Cooperations

7.1. National Initiatives

7.1.1. Projets Exploratoires Pluridisciplinaires from CNRS/Inria/INSERM

Title: Novel approaches to characterizing flexible macromolecular systems in biology

Modeling Large Protein Assemblies with Toleranced Models

Type: Projet Exploratoire Pluri-disciplinaire (PEPS) CNRS / Inria / INSERM

Duration: one year

Coordinator: C. Robert (IBPC / CNRS)

Other partner(s): F. Cazals (Inria Sophia Antipolis Méditerranée)

Abstract: A central problem in structural biology consists of modeling the dynamics and thermodynamics of macro-molecular assemblies involving a large number of atoms (thousands to hundreds of thousands). This requires understanding the structure of the potential and free energy landscapes (PEL and FEL) of the system. A number of approaches have been developed from the physical perspective, in particular to sample the PEL of the systems scrutinized (molecular dynamics, Monte Carlo based methods). The goal of this project is orthogonal, since our aim is to enhance the processing of samplings generated by the aforementioned approaches. Our methods aim at analyzing and comparing sampled PEL and FEL, using novel methods from computational geometry, computational topology, and optimization. These methods should foster our understanding of the behavior of macro-molecular assemblies, and in the long run, they should also trigger the development of more efficient sampling algorithms.

7.2. International Research Visitors

7.2.1. Visits of International Scientists

7.2.1.1. Internships

- N. Gayraud, from the MSc program *Computational biology and biomedicine* from the Univ. of Nice, completed his MSc internship under the guidance of F. Cazals, on the topic *Modeling cryo-electron microscopy maps*. Nathalie is now following-up as a PhD student in the Athena project team.
- S. Lundy (Supélec, Gif-sur-Yvette), completed a 3 months internship under the joint supervision of Dorian Mazauric and Jean-Daniel Boissonnat (Geometrica, Inria Sophia Antipolis Méditerranée) on the topic *Representation of simplicial complexes by directed graphs*.

AMIB Project-Team

7. Partnerships and Cooperations

7.1. National Initiatives

7.1.1. FRM

Y. Ponty is the Bioinformatics PI for a *Fondation de la Recherche Médicale*-funded project.

Fondation pour la Recherche Medicale – *Analyse Bio-informatique pour la recherche en Biologie* program

- Approche comparatives haut-débit pour la modelisation de l'architecture 3D des ARN à partir de données experimentales
- 2015–2018
- Y. Ponty, A. Denise, M. Regnier, A. Saaidi (PhD funded by FRM)
- B. Sargueil (Paris V – Experimental partner), J. Waldispuhl (Univ. McGill)

7.2. European Initiatives

Y. Ponty is the French PI for the French/Austrian RNALANDS project, jointly funded by the French ANR and the Austrian FWF, in partnership with the Theoretical Biochemistry Institute (University of Vienna, Austria), LRI (Univ. Paris-Sud) and EPI BONSAI (Inria Lille-Nord Europe).

ANR International Program

- Fast and efficient sampling of structures in RNA folding landscapes
- RNALANDS (ANR-14-CE34-0011)
- 01/10/2014–30/09/2018
- Y. Ponty (PI), M. Régnier
- EPI BONSAI/INRIA Lille - Nord Europe, Vienna University (Austria)
- LRI, Université Paris-Sud (France)

7.3. International Initiatives

7.3.1. Inria International Partners

7.3.1.1. Declared Inria International Partners

AMAVI

Title: Combinatorics and Algorithms for the Genomic sequences

International Partners (Institution - Laboratory - Researcher):

Vavilov Institute of General Genetics (Russia (Russian Federation)) - Department of Computational Biology - Vsevolod Makeev

Start year: 2013

See also: https://team.inria.fr/amib/carnage/

VIGG and AMIB teams has a more than 12 years long collaboration on sequence analysis. The two groups aim at identifying DNA motifs for a functional annotation, with a special focus on conserved regulatory regions. In the current 3-years project CARNAGE, our collaboration, that includes Inrai-team MAGNOME, is oriented towards new trends that arise from Next Generation Sequencing data. Combinatorial issues in genome assembly are addressed. RNA structure and interactions are also studied.

The toolkit is pattern matching algorithms and analytic combinatorics, leading to common software.

7.3.1.2. Informal International Partners

A long-term cooperation exists with Teheran University (Iran).

7.3.2. Participation In other International Programs

CONSEIL FRANCO-QUÉBÉCOIS DE COOPÉRATION UNIVERSITAIRE EXCHANGE PROGRAM

- Title: Réseau franco-québecois de recherche sur l'ARN
- International Partners (Institution - Laboratory - Researcher):
  Univ. McGill (Canada) - CS Dept - J. Waldispühl, M. Blanchette
  Univ. Montréal (Canada) - Biology Dept & IRIC - E. Lecuyer, F. Major
- Start year: 2012
- The partners have developped complementary expertise on RNA : bioinformatics, combinatorics and algorithms. machine learning, physics and genomics. Methodologies will be developed that combine theoretical simulations and new (high throughput) experimental data. A common high level training at Master and PhD level is organized.

PHC GERMAINE DE STAEL EXCHANGE PROGRAM

- Title: Random constrained permutations
- International Partners (Institution - Laboratory - Researcher):
  Univ. Zürich (Swiss) - Institut für Mathematik - M. Bouvel, V. Féray
- Start year: 2015
- The partners wish to develop new technique for the enumeration, analysis and random generation of constrained permutations.

CNRS UMI PIMS-VANCOUVER EXCHANGE PROGRAM

- Title: Extended research stay of Y. Ponty at the Simon Fraser University
  Simon Fraser University - Maths Dept - C. Chauve, M. Mishna, L. Stacho
  Univ. British Columbia - CS Dept - J. Manuch
- Start year: 2013
- Extended research stay in Vancouver to foster new collaborations between EPI Amib and colleagues at SFU on comparative genomics, RNA structures, and enumerative combinatorics.

7.4. International Research Visitors

7.4.1. Visits of International Scientists

Mark Ward
Date: 23/11/2015- 05/12/2015
Institution: Purdue University (USA)

Can Alkan
Date: 24/11/2015- 30/11/2015
Institution: Bilkent University (Turkey)

Evgenia Furletova
Date: 22/11/2015- 28/11/2015
Institution: IMPB (Russia)

7.4.1.1. Internships

Indrajit Saha
Date: 20/02/2015- 28/02/2015
Institution:ERCIM fellowship (Wroclaw)
Supervisor: M. Régnier

Doris Taining

Date: 01/05/2015- 07/08/2015

Institution:Singapore University (Singapore)

Supervisor: M. Régnier

7.4.2. Visits to International Teams

7.4.2.1. Sabbatical programme

Bernauer Julie

Date: Feb 2014 - Jan 2015

Institution: Stanford (United States)

7.4.2.2. Research stays abroad

Yann Ponty

Date: Sept 2013 - Sept 2015

Institution: Simon Fraser (Canada)

Amelie Héliou

Date:June 2015 -Aug 2015

Institution: HKUST (Hong Kong)

Antoine Soulé

Date: Jan 2015 - Sept 2015

Institution: McGill (Canada)

Pauline Pommeret

Date: May 2015 - Aug 2015

Institution: Vancouver (Canada)

BEAGLE Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

- Intracell X Evo, projet LABEX ECOFECT. Leaders: Thomas Henry, CIRI, Lyon, and Eric Tannier, Beagle. Other partner : Dominique Schneider, laboratoire Adaptation et pathogénie des Microorganismes, Grenoble. Duration: 3 years The objective of the project is to understand the host-pathogen interactions in the cytosol by an experimental evolution approach. Funding: 120 000 Euros.

8.2. National Initiatives

8.2.1. ANR

- Ancestrome: phylogenetic reconstruction of ancestral "-omes", a five-year project (2012-2017), call "Bioinformatics" of the "Investissements d'avenir". Supervisor: V Daubin (CNRS, LBBE, Lyon) ; with Institut Pasteur, ENS Paris, ISEM (Univ Montpellier 2) Participant: E Tannier.
- Aucomsi (2013-2016) (Models of the vocal tract to study auditory circuits): a 4-year project (2013-2016) funded by a grant from the ANR-NSF-NIH Call for French-US Projects in Computational Neuroscience. With F. Theunissen, UC Berkeley, CA, USA. Supervisor: H. Soula (for France) and F. Theunissen (for US). Participants: H. Soula, M. Fernandez.
- Dopaciumcity: Dopamine modulation of calcium influx underlying synaptic plasticity, a 4-year project (2014-2017) funded by a grant from the ANR-NSF-NIH Call for French-US Projects in Computational Neuroscience. With L. Venance, College de France, CIRB, CNRS/UMR 7241 - INSERM U1050, Paris, France and K Blackwell, Krasnow Institute of Advanced Studies, George Mason University, Fairfax, VA, USA. Supervisor: L Venance (for France) and K.L. Blackwell (for US). Participants: H Berry, I Prokin, A Foncelle

8.3. European Initiatives

8.3.1. FP7 & H2020 Projects

8.3.1.1. EvoEvo

Title: Evolution of Evolution

Programm: FP7

Duration: November 2013 - October 2016

Coordinator: Inria

Partners:

Agencia Estatal Consejo Superior de Investigaciones Cientificas (Spain)

Institut National des Sciences Appliquees de Lyon (France)

Universite Lyon 1 Claude Bernard (France)

Universite Joseph Fourier Grenoble 1 (France)

Universiteit Utrecht (Netherlands)

University of York (United Kingdom)

Inria contact: Guillaume Beslon

Evolution is the major source of complexity on Earth, at the origin of all the species we can observe, interact with or breed. On a smaller scale, evolution is at the heart of the adaptation process for many species, in particular micro-organisms (e.g. bacteria, viruses...). Microbial evolution results in the emergence of the species itself, and it also contributes to the organisms' adaptation to perturbations or environmental changes. These organisms are not only organised by evolution, they are also organised to evolve. The EvoEvo project will develop new evolutionary approaches in information science and will produce algorithms based on the latest understanding of molecular and evolutionary biology. Our ultimate goal is to address open-ended problems, where the specifications are either unknown or too complicated to express, and to produce software able to operate in unpredictable, varying conditions. We will start from experimental observations of micro-organism evolution, and abstract this to reproduce EvoEvo, in biological models, in computational models, and in application software. Our aim is to observe EvoEvo in action, to model EvoEvo, to understand EvoEvo and, ultimately, to implement and exploit EvoEvo in software and computational systems. The EvoEvo project will have impact in ICT, through the development of new technologies. It will also have impact in biology and public health, by providing a better understanding of micro-organism adaptation (such as the emergence of new pathogens or the development of antibiotic resistances).

8.3.1.2. Neuron-Astro-Nets

Title: Neuron-Astro-Nets

Programm: Marie-Curie International Outgoing Fellowship (IOF) grant FP7

Duration: 2013 - October 2017

Coordinator: Inria

Partners:

Inria (France)

Dept Statistics and Neurobiology, University of Chicago (USA)

Inria contact: Hugues Berry

This project aims at developing a new model of synaptic plasticity that takes into account astrocyte signaling, its extension to astrocytes-synapse biochemical interactions in ensembles of synapses enwrapped by the same astrocyte and, eventually, to the firing of a single neuron or networks. The project funds Maurizio De Pitta' s postdoc for 4 years (June 2013- May 2017). M. De Pitta has first spent one year in Beagle, Lyon funded by an EU ERCIM grant (06/2013-05/2014) then two years in N. Brunel's Lab in Chicago (06/2014-05/2016) and one year back in Beagle in Lyon (06/2016-05/2017). The IOF grant funds the last three years.

8.4. International Initiatives

8.4.1. Inria International Partners

8.4.1.1. Informal International Partners

Beagle collaborates with two american laboratories: the Theunissen Lab (UC Berkeley, CA, http://theunissen.berkeley.edu/publications.html) and the Blackwell lab (George Mason Univ., VA, http://krasnow1.gmu.edu/CENlab/index.html). Those labs are the partners of the two ANR-NSF-NIH grants we were awarded (cf "ANR" section above).

8.4.2. Participation In other International Programs

The Beagle team is part of the LIA (Laboratoire International Associé) EvoAct (Evolution in action with living and artificial organisms). EvoAct is a joint laboratory gathering researchers from Dominique Schneider team (UJF, LAPM, UMR CNRS 5163, France), Rich Lenski team (Michigan State University, Beacon center, US) and the Beagle team.

8.5. International Research Visitors

8.5.1. Visits of International Scientists

8.5.1.1. Internships

- Priscila Biller did a one year doctoral internship in Beagle, ending in April 2015
- Jaap Rutten started his internship in the Beagle team in December 2015. Jaap Rutten is a M2 student from the Utrecht University (NL).

8.5.2. Visits to International Teams

8.5.2.1. Research stays abroad

Eric Tannier has spent one month in July 2015 at Simon Fraser University in Vancouver, Canada.

BIGS Project-Team

9. Partnerships and Cooperations

9.1. National Initiatives

- *PhotoBrain* (2015-17), AGuIX® theranostic nanoparticles for vascular-targeted interstitial photodynamic therapy of brain tumors, Funding organism: EuroNanoMed II, Leader: M. Barberi-Heyob (CRAN), Thierry Bastogne
- (2014-16), A library of Near-InfraRed absorbing photosensitizers: tailoring and assessing photophysical and synergetic photodynamic properties, Funding organism: PHC Bosphore - Campus France, Leader: M. Barberi-Heyob (CRAN), Thierry Bastogne
- GDR 3475 Analyse Multifractale, Funding organism: CNRS, Leader: S. Jaffard (Université Paris-Est), Céline Lacaux
- GDR 3477 Géométrie stochastic, Funding organism: CNRS, Leader: P. Calka (Université Rouen), Céline Lacaux
- FHU CARTAGE (Fédération Hospitalo Universitaire Cardial and ARTerial AGEing ; leader : Pr Athanase BENETOS), Jean-Marie Monnez
- RHU Fight HF (Fighting Heart Failure ; leader : Pr Patrick ROSSIGNOL), located at the University Hospital of Nancy, Jean-Marie Monnez
- Project "Handle your heart", team responsible for the creation of a drug prescription support software for the treatment of heart failure, head: Jean-Marie Monnez

9.2. International Research Visitors

9.2.1. Visits of International Scientists

S. Roelly, University of Postdam visited P. Vallois in 2015 September.

9.2.1.1. Internships

A. Gégout-Petit and P. Vallois supervised an internship of a master IMOI student at the startup SD-Innovation, http://www.sd-innovation.fr/. The subject was the parametrization of curves issued from the aggregation of cells.

9.2.2. Visits to International Teams

9.2.2.1. Research stays abroad

- P. Vallois visited S. Roelly in Postdam (Germany), March 2015
- P. Vallois visited P. Salminien in Turku (Turkey), March 2015
- P. Vallois visited the Finance department in New York, April 2015

BONSAI Project-Team

9. Partnerships and Cooperations

9.1. National Initiatives

9.1.1. ANR

- PIA France Génomique: National funding from "Investissements d'Avenir" (call *Infrastructures en Biologie-Santé*). France Génomique is a shared infrastructure, whose goal is to support sequencing, genotyping and associated computational analysis, and increase French capacities in genome and bioinformatics data analysis. It gathers 9 sequencing and 8 bioinformatics platforms. Within this consortium, we are responsible for the workpackage devoted to the computational analysis of sRNA-seq data, in coordination with the bioinformatics platform of Génopole Toulouse-Midi-Pyrénées

9.1.2. ADT

- ADT Vidjil (2015–2017): The purpose of this ADT is to strengthen Vidjil development and to ensure a better diffusion of the software by easing the installation, administration and usability. This will make the software well suited for a daily clinical use. The software is already used in test on our own web server (more than 1,000 samples processed by now). Our goal is that several labs use Vidjil on a daily basis by the end of the ADT, and that they all have their own Vidjil server.

9.1.3. Others

- PEPS Gen-CoV: *Global bioinformatics analysis of coronavirus strain 229E in hospital outbreak.* The goal of this PEPS is to provide with a better characterization of coronavirus infections and to understand underlying mecanisms that lead to the high diversity of coronaviruses. To achieve this goal, we will sequence and analyze a number of coronavirus 229E genomes in order to characterize their diversity, identify features that influence pathogenicity and propose a model of evolution. All those results will be correlated with epidemiologic data thanks to a partnership with Lille hospital.
- PEPS JCJC: *Frugal algorithms for third-generation DNA sequencing*. The goal of this PEPS is to develop lightweight algorithms and data structures for the analysis of third-generation sequencing data. Among third-generation technologies, the MinION sequencer is a new, portable USB device that can perform DNA sequencing using only common lab equipment and a laptop computer. However, analysis of the data produced by the MinION can only be carried by uploading data to a cloud server. Indeed, all algorithms and data structures that are currently known require large computational resources to process such data. This is unfortunate for at least two reasons: analysis of the data now takes more time than its production, and confidential data needs to be processed on potentially insecure cloud servers. We seek to design methods that would enable analysis of sequenced data on the same machine as the one that performed sequencing.

9.2. European Initiatives

9.2.1. Collaborations in European Programs, except FP7 & H2020

International ANR RNAlands (2014-2017): National funding from the French Agency Research (call *International call*). The subject is fast and efficient sampling of structures in RNA Folding Landscapes. The project gathers three partners: Amib from Inria Saclay, the Theoretical Biochemistry Group from Universität Wien and Bonsai.

9.3. International Initiatives

9.3.1. Inria Associate Teams not involved in an Inria International Labs

9.3.1.1. CG-ALCODE

Title: Comparative Genomics for the analysis of gene structure evolution: ALternative CODing in Eukaryote genes through alternative splicing, transcription, and translation.
International Partner (Institution - Laboratory - Researcher):

Université du Québec À Montréal (Canada) - Laboratoire de combinatoire, informatique et mathématique (LaCIM) - Anne Bergeron

Start year: 2014
See also: http://thales.math.uqam.ca/~cgalcode/
The aim of this Associated Team is the development of comparative genomics models and methods for the analysis of eukaryotes gene structure evolution. The goal of the project is to answer very important questions arising from recent discoveries on the major role played by alternative transcription, splicing, and translation, in the functional diversification of eukaryote genes.
Two working meetings of CG-ALCODE researchers took place in 2015. First, Samuel Blanquart, Anne Bergeron and Krister Swenson met each other in Montpellier, from 27th to 30th of April. Second, Samuel Blanquart, Jean Stéphane Varré spent two weeks in Montréal, from 1st to 11th November, to work with Anne Bergeron.

9.3.1.2. Informal International Partners

- *Astrid Lindgrens Hospital, Stockholm University:* Collaboration with Anna Nilsson and Shanie Saghafian-Hedengren on RNA sequencing of stromal cells.
- *CWI Amsterdam:* Collaboration with Alexander Schoenhuth and Jasmijn Baaijens on succinct data structures and algorithms for the assembly of viral quasispecies.
- *Department of Statitics, North Carolina State University:* Collaboration with Donald E. K. Martin on spaced seeds coverage.
- *Gembloux Agro-Bio Tech, Université de Liège:* Collaboration with Philippe Jacques on nonribosomal peptides.
- *Institut für Biophysik und physikalische Biochemie, University of Regensburg:* Collaboration with Rainer Merkl on ancestral sequence inference and synthesis.
- *Makova lab, The Pennsylvania State University:* Collaboration with Kateryna Makova and Samarth Rangavittal on the assembly of the gorilla Y chromosome, and visualisation of assembly graphs.
- *Medvedev lab, The Pennsylvania State University:* Collaboration with Paul Medvedev on algorithms for constructing de Bruijn graphs.
- *Novo Nordisk Foundation Center for Biosustainability, Technical University of Denmark:* Collaboration with Tilmann Weber on nonribosomal peptides.
- *Proteome Informatics Group, Swiss Institute of Bioinformatics:* Collaboration with Frédérique Lisacek and Markus Mueller on nonribosomal peptides.
- *School of Social and Community Medicine, University of Bristol:* Collaboration with John Moppett on leukemia follow-up.
- *Science for Life Laboratory, Stockholm University:* Collaboration with Lars Arvestad and Kristoffer Sahlin on genome scaffolding of contaminated libraries.
- *Theoretical Biochemistry Group, Universität Wien:* Collaboration with Andrea Tanzer and Ronny Lorenz on RNA folding and RNA kinetics.

9.4. International Research Visitors

9.4.1. Visits of International Scientists

- Kristina Heyn, PhD student, Institut für Biophysik und physikalische Biochemie, University of Regensburg (from 6th to 11th of July)
- Burkhard Morgenstern, professeur, Universität Gottingen (from 20th to 23th of April)
- Samarth Rangavittal, PhD student, The Pennsylvania State University (from October 18th to December 6th)
- Gabriele Valiente, professeur, Universitat Politècnica de Catalunya (from 25th to 29th of May)
- Tilmann Weber, senior researcher, Novo Nordisk Foundation Center for Biosustainability, Technical University of Denmark (from 18th of October to 31st of October)

CAPSID Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

8.1.1. PEPS

Participants: Marie-Dominique Devignes [contact person], Bernard Maigret, David Ritchie.

The team is involved in the inter-disciplinary "MODEL-ICE" project led by Nicolas Soler (DynAMic lab, UMR 1128, INRA / Univ. Lorraine). The aim is to investigate protein-protein interactions required for initiating the transfer of an ICE (Integrated Conjugative Element) from one bacterial cell to another one.

8.2. National Initiatives

8.2.1. FEDER

Participants: Marie-Dominique Devignes [contact person], Jérémie Bourseau.

The project "LBS" (Le Bois Santé) is a consortium funded by the European Regional Development Fund (FEDER) and the French "Fonds Unique Interministériel" (FUI). The project is coordinated by Harmonic Pharma SAS. The aim of LBS is to exploit wood products in the pharmaceutical and nutrition domains. Our contribution has been in data management and knowledge discovery for new therapeutic applications.

8.2.2. ANR

8.2.2.1. IFB

Participant: Marie-Dominique Devignes [contact person].

The Capsid team is a research node of the IFB (Institut Français de Bioinformatique), the French national network of bioinformatics platforms (http://www.france-bioinformatique.fr). The principal aim is to make bioinformatics skills and resources more accessible to French biology laboratories.

8.2.2.2. PEPSI

Participants: David Ritchie [contact person], Marie-Dominique Devignes.

The PEPSI ("Polynomial Expansions of Protein Structures and Interactions") project is a collaboration with Sergei Grudinin at Inria Grenoble – Rône Alpes (project Nano-D) and Valentin Gordeliy at the Institut de Biologie Structurale (IBS) in Grenoble. This project funded by the ANR "Modèles Numériques" program involves developing computational protein modeling and docking techniques and using them to help solve the structures of large molecular systems experimentally.

8.3. International Initiatives

8.3.1. Participation in other International Programs

Participant: Bernard Maigret; Project: *Characterization, expression and molecular modeling of TRR1 and ALS3 proteins of Candida spp., as a strategy to obtain new drugs with action on yeasts involved in nosocomial infections;* Partner: State University of Maringá, Brasil; Funding: CNPq.

Participant: Bernard Maigret; Project: *Fusarium graminearum target selection;* Partner: Embrapa Recursos Geneticos e Biotecnologia, Brasil; Funding: CNPq.

Participant: Bernard Maigret; Project: *The thermal choc HSP90 protein as a target for new drugs against paracoccidioidomicose;* Partner: Brasília University, Brasil; Funding: CNPq.

Participant: Bernard Maigret; Project: *Protein-protein interactions for the development of new drugs;* Partner: Federal University of Goias, Brasil. Funding: Chamada MCTI/CNPq/FNDCT.

8.4. International Research Visitors

8.4.1. Visits of International Scientists

8.4.1.1. Doctoral Students

In the frame of a collaboration with the University of Brasilia, Dr. A. Abadio and three doctoral students (A. Souza, J. Ribeiro, P. Alves) visited in July 2015.

DYLISS Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

8.1.1. Regional partnership with computer science laboratories in Nantes

Participants: Anne Siegel, Jérémie Bourdon, Damien Eveillard, François Coste, Jacques Nicolas, Vincent Picard.

Methodologies are developed in close collaboration with university of Nantes (LINA) and Ecole centrale Nantes (IRCCyN). This is acted through the Biotempo and Idealg ANR projects and co-development of common software toolboxes within the Renabi-GO platform process. The Ph-D students V. Picard and J. Laniau are also co-supervised with members of the LINA laboratory.

8.1.2. Regional partnership in Marine Biology

Participants: Catherine Belleannée, Jérémie Bourdon, Guillaume Collet, Jean Coquet, François Coste, Damien Eveillard, Olivier Dameron, Clémence Frioux, Clovis Galiez, Jeanne Got, Yann Guitton, Julie Laniau, Jacques Nicolas, Vincent Picard, Camille Trottier, Anne Siegel.

A strong application domain of the Dyliss project is marine Biology. This application domain is co-developed with the station biologique de Roscoff and their three UMR and involves several contracts. The IDEALG consortium is a long term project (10 years, ANR Investissement avenir) aiming at the development of macro-algae biotechnology. Among the research activities, we are particularly interested in the analysis and reconstruction of metabolism and the characterization of key enzymes. Other research contracts concern the modeling of the initiation of sea-urchin translation (former PEPS program Quantoursin, Ligue contre le cancer and ANR Biotempo), the analysis of extremophile archebacteria genomes and their PPI networks (former ANR MODULOME and PhD thesis of P.-F. Pluchon) and the identification of key actors implied in competition for light in the ocean (PELICAN ANR project). In addition, the team participates to a collaboration program with the Biocore and Ange teams, together with Ifremer-Nantes, focused on the understanding on micro-algae (thesis of Julie Laniau).

8.1.3. Regional partnership in agriculture and bio-medical domains

Participants: Aymeric Antoine-Lorquin, Catherine Belleannée, Charles Bettembourg, François Coste, Jean Coquet, Olivier Dameron, Victorien Delannée, Jacques Nicolas, Anne Siegel, Nathalie Théret, Aurélie Evrard.

We have a strong and long term collaboration with biologists of INRA in Rennes : PEGASE and IGEEP units. This partnership is acted by the co-supervision of one post-doctoral student and the co-supervision of several PhD students. The Ph-D thesis of V. Wucher was supported by collaborations with the IGEPP laboratory. The post-doc of Charles Bettembourg strengthens these collaborations. This collaboration is also reinforced by collaboration within ANR contracts (MirNadapt, FatInteger). Lately, Aurélie Evrard joined the team at mid-part of her time in collaboration with Agrocampus Ouest and INRA to apply the semantic web to technologies developed within the mirnAdapt framework to new agriculture applications (Brassicae).

We also have a strong and long term collaboration in the bio-medical domain, namely with the IRSET laboratory at Univ. Rennes 1/Irset, acted by the co-supervised Ph-D theses of V. Delannée (Metagenotox project, funded by Anses) and J. Coquet. This partnership was reinforced in the former years by the ANR contract Biotempo ended at the end of 2014. In 2015, the project of combining semantic web technologies and bi-clustering classification based on formal concept analysis was applied to systems biology within the PEPS CONFOCAL project. This scientific project will be pushed forward in the recent TGFSYSBio project funded by Plan Cancer on the modelling of the microenvironment of TGFbeta signaling network.

8.2. National Initiatives

8.2.1. Long-term contracts

8.2.1.1. "Omics"-Line of the Chilean CIRIC-Inria Center

Participants: Anne Siegel, Jérémie Bourdon, François Coste, Marie Chevallier, Meziane Aite, Clémence Frioux, Damien Eveillard, Jacques Nicolas.

Cooperation with Univ. of Chile (MATHomics, A. Maass) on methods for the identification of biomarkers and software for biochip design. It aims at combining automatic reasoning on biological sequences and networks with probabilistic approaches to manage, explore and integrate large sets of heterogeneous omics data into networks of interactions allowing to produce biomarkers, with a main application to biomining bacteria. The program is co-funded by Inria and CORFO-chile from 2012 to 2022. In this context, IntegrativeBioChile is an Associate Team between Dyliss and the Laboratory of Bioinformatics and Mathematics of the Genome hosted at Univ. of Chile funded from 2011 to 2016.

8.2.1.2. ANR Idealg

Participants: Jérémie Bourdon, Marie Chevallier, Guillaume Collet, François Coste, Damien Eveillard, Clémence Frioux, Clovis Galiez, Jeanne Got, Yann Guitton, Jacques Nicolas, Anne Siegel.

IDEALG is one of the five laureates from the national call 2010 for Biotechnology and Bioresource and will run until 2020. It gathers 18 different partners from the academic field (CNRS, IFREMER, UEB, UBO, UBS, ENSCR, University of Nantes, INRA, AgroCampus), the industrial field (C-WEED, Bezhin Rosko, Aleor, France Haliotis, DuPont) as well as a technical center specialized in seaweeds (CEVA) in order to foster biotechnology applications within the seaweed field. It is organized in ten workpackages. We are participating to workpackages 1 (establishment of a virtual platform for integrating omics studies on seaweed) and 4 (Integrative analysis of seaweed metabolism) in cooperation with SBR Roscoff. Major objectives are the building of brown algae metabolic maps, flux analysis and the selection extraction of important parameters for the production of targeted compounds. We will also contribute to the prediction of specific enzymes (sulfatases) within workpackage 5 [More details].

8.2.2. Proof-of-concept on dedicated applications

8.2.2.1. ANR Fatinteger

Participants: Aymeric Antoine-Lorquin, Catherine Belleannée, Jacques Nicolas, Anne Siegel.

This project (ANR Blanc SVE7 "biodiversité, évolution, écologie et agronomie" from 2012 to 2015) is leaded by INRA UMR1348 PEGASE (F. Gondret). Its goal is the identification of key regulators of fatty acid plasticity in two lines of pigs and chickens. To reach these objectives, this project has for ambition to test some combination of statistics, bioinformatics and phylogenetics approaches to better analyze transcriptional data of high dimension. Data and methods integration is a key issue in this context. We work on the recognition of specific common cis-regulatory elements in a set of differentially expressed genes and on the regulation network associated to fatty acid metabolism with the aim of extracting some key regulators.

8.2.2.2. ANR Mirnadapt

Participants: Jacques Nicolas, Anne Siegel, Olivier Dameron, Charles Bettembourg.

This ANR project is coordinated by UMR IGEPP, INRA Le Rheu (D. Tagu) and funded by ANR SVSE 6 "Génomique, génétique, bioinformatique, biologie systémique" from 2012 to 2014. This cooperation was strengthened by a co-tutored PhD thesis (V. Wucher) defended in Nov. 2014 [92]. It proposes an integrative study between bioinformatics, genomics and mathematical modeling focused on the transcriptional basis of the plasticity of the aphid reproduction mode in response to the modification of environment. An important set of differentially expressed mRNAs and microRNAs are available for the two modes, asexual parthenogenesis and sexual reproduction. Our work is to combine prediction methods for the detection of putative microRNA/mRNA interactions as well as transcription factor binding sites from the knowledge of genomic sequences and annotations available on this and other insects. The results will be integrated within a coherent putative interaction network and serve as a filter for the design of new targeted experiments with the hope to improve functional annotations of implied genes.

8.2.2.3. ANR Samosa

Participants: Anne Siegel, Jeanne Got, Damien Eveillard.

Oceans are particularly affected by global change, which can cause e.g. increases in average sea temperature and in UV radiation fluxes onto ocean surface or a shrinkage of nutrient-rich areas. This raises the question of the capacity of marine photosynthetic microorganisms to cope with these environmental changes both at short term (physiological plasticity) and long term (e.g. gene alterations or acquisitions causing changes in fitness in a specific niche). Synechococcus cyanobacteria are among the most pertinent biological models to tackle this question, because of their ubiquity and wide abundance in the field, which allows them to be studied at all levels of organization from genes to the global ocean.

The SAMOSA project is funded by ANR from 2014 to 2018, coordinated by F. Gaczarek at the Station Biologique de Roscoff/UPMC/CNRS. The goal of the project is to develop a systems biology approach to characterize and model the main acclimation (i.e., physiological) and adaptation (i.e. evolutionary) mechanisms involved in the differential responses of Synechococcus clades/ecotypes to environmental fluctuations, with the goal to better predict their respective adaptability, and hence dynamics and distribution, in the context of global change. For this purpose, following intensive omics experimental protocol driven by our colleagues from « Station Biologique de Roscoff », we aim at constructing a gene network model sufficiently flexible to allow the integration of transcriptomic and physiological data.

8.2.3. Programs funded by research institutions

8.2.3.1. INSERM TGFSYSBIO

Participants: Nathalie Théret, Jacques Nicolas, Olivier Dameron, Anne Siegel, Jean Coquet.

TGFSYSBIO project aims to develop the first model of extracellular and intracellular TGF-β system that might permit to analyze the behaviors of TGF-β activity during the course of liver tumor progression and to identify new biomarkers and potential therapeutic targets. Based on collaboration with Jerome Feret from ENS, Paris,we will combine a rule-based model (Kappa language) to describe extracellular TGF-beta activation and large-scale state-transition based (Cadbiom formalism) model for TGF-β-dependent intracellular signaling pathways. The multi-scale integrated model will be enriched with a large-scale analysis of liver tissues using shotgun proteomics to characterize protein networks from tumor microenvironment whose remodeling is responsible for extracellular activation of TGF-β. The trajectories and upstream regulators of the final model will be analyzed with symbolic model checking techniques and abstract interpretation combined with causality analysis. Candidates will be classified with semantic-based approaches and symbolic bi-clustering technics. The project is funded by the national program "Plan Cancer - Systems biology" from 2015 to 2018.

8.2.3.2. ADT Complex-biomarkers and ADT Proof of concept

Participants: Jeanne Got, Guillaume Collet, Marie Chevallier, Meziane Aite, Anne Siegel.

This project started in Oct. 2014 and aims at designing a working environment based on workflows to assist molecular biologists to integrate large-scale omics data on non-classical species. The main goal of the workflows will be to facilitate the identification of set of regulators involved in the response of a species when challenged by an environmental stress. Applications target extremophile biotechnologies (biomining) and marine biology (micro-algae).

8.2.3.3. ANSES Mecagenotox

Participants: Victorien Delannée, Anne Siegel, Nathalie Théret.

The objective of Mecagenotox project is to characterize and model the human liver ability to bioactivate environmental contaminants during liver chronic diseases in order to assess individual susceptibility. Indeed, liver pathologies which result in the development of fibrosis are associated with a severe dysfunction of liver functions that may lead to increased susceptibility against contaminants. In this project funded by ANSES and coordinated by S. Langouet at IRSET/inserm (Univ. Rennes 1), we will combine cell biology approaches, biochemistry, biophysics, analytical chemistry and bioinformatics to 1) understand how the tension forces induced by the development of liver fibrosis alter the susceptibility of hepatocytes to certain genotoxic

chemicals (especially Heterocyclic Aromatic Amines) and 2) model the behavior of xenobiotic metabolism during the liver fibrosis. Our main goal is to identify "sensitive" biomolecules in the network and to understand more comprehensively bioactivation of environmental contaminants involved in the onset of hepatocellular carcinoma.

8.2.3.4. PEPS VAG

Participants: François Coste, Clovis Galiez, Jacques Nicolas.

PEPS VAG started a collaboration between IMPMC UMR 7590, Institut de biologie de l'Ecole Normale Supérieure (IBENS) UMR8197, Atelier de Bioinformatique UPMC and Dyliss. It aims at defining the needs and means for a larger project about viruses in marine ecosystems. More specifically,we develop new methods based on both sequential and structural information of proteins to improve the detection of viral sequences in marine metagenomes. This will make possible to identify new viruses and to compare the viral populations specifically associated with different environment parameters (temperature, acidity, nutriments...) and ultimately to connect them with the potential hosts identified by population sequencing.

8.2.3.5. PEPS CONFOCAL

Participants: Olivier Dameron, Jean Coquet, Nathalie Théret, Jacques Nicolas, Anne Siegel.

PEPS CONFOCAL aims at developing new bioinformatics methods for analyzing heterogeneous *omics data and for filtering them according to domain knowledge. The current approaches are facing four main limitations: (1) classic biclustering methods do not support partial overlap of clusters, which is too restrictive considering some genes' pleiotropic nature, (2) they assume that the items to analyze (the genes, the molecules, the signaling pathways...) are independent, (3) they tend to generate numerous clusters leaving to the experts the task of identifying the relevant ones, and (4) they are sensitive to noisy or incomplete data. We investigate the extension of Formal Concept Analysis (FCA) with symbolic knowledge from ontologies in order to process large and complex sets of associations between genes, signaling pathways and the molecules involved in these pathways. Future applications cover the discrete model analysis in molecular biology. CONFOCAL initiated a collaboration with Amedeo Napoli (LORIA Nancy) and Elisabeth Rémy (Mathematics Institute Luminy, "Mathematical Methods for Genomics" team).

8.3. European Initiatives

8.3.1. Collaborations with Major European Organizations

Partner: EBI (Great-Britain)

Title: Modeling the logical response of a signalling network with constraints-programming.

Partner: Potsdam university (Germany)

Title: Constraint-based programming for the modeling and study of biological networks.

8.4. International Initiatives

8.4.1. Inria International Labs

The Dyliss team is strongly involved in the Inria CIRIC center, and the research line "Omics integrative center". The associated team "IntegrativeBioChile", the post-doc of S. Thiele (2012) and the co-supervision of A. Aravena (2010-2013) contributed to reinforce the complementarity of both Chilean and French teams. In 2013, a workshop was organized in Chile to develop new French-Chilean collaborations within the framework of the CIRIC center. In 2014, Marie Chevallier joined the team as an engineer to improve softwares resulting from collaborations.

Inria Chile

Associate Team involved in the International Lab:

8.4.1.1. BIOINTEGRATIVECHILE

Title: Integrative Biology in Extreme Environments

International Partner (Institution - Laboratory - Researcher):

Universidad de Chile (Chile) - Center for Mathematical Modeling (CMM) - Alejandro Maass

Start year: 2014

See also: http://www.irisa.fr/dyliss/public/EA/index.html

The project is in the area of bioinformatics, with a special focus on bacteria living in extreme environments, more precisely on microorganisms involved in bio-remediation or bio-production processes. We are particularly interested in bioprocesses such as copper extraction, salmon lethality, metal-resistance, all having an economical interest in Chile. Since the last decade, huge databases of microbial genomic sequences, together with multi-scale and large-scale cellular observations (genomics, transcriptomics, proteomics, metabolomics) have been produced. Each one can be considered as a different scale of a biological process, either in time or space. But ultimately they are related through networks of biological interactions that control the behavior of the system. The reconstruction, analysis and modeling of such networks using all levels of information are biologically, mathematically and computationally challenging. Applied on microorganisms living in extreme environments, this question is even more challenging since relatively few knowledge is publicly available on the species, requiring to develop methods which are robust to uncertainty. We are developing methods to integrate and manage heterogeneous omics and uncertain data, this in the purpose of extracting suitable biomarkers from this multi-scale information. This question will be addressed by coupling probabilistic and static dynamical systems methods with recent and efficient paradigms of constraint programming (Answer Set Programming).

8.4.2. Inria Associate Teams

8.4.2.1. INTEGRATIVEBIOCHILE

Title: Bioinformatics and mathematical methods for heterogeneous omics data

Inria principal investigator: Anne Siegel

International Partner (Institution - Laboratory - Researcher):

University of Chile (Chile) - Center for Mathematical Modeling - Alejandro Maass

Duration: 2011 - 2016

See also: http://www.irisa.fr/dyliss/public/EA/index.html

IntegrativeBioChile is an Associate Team between Inria project-team "Dyliss" and the "Laboratory of Bioinformatics and Mathematics of the Genome" hosted at CMM at University of Chile. The Associated team is funded from 2011 to 2016. The project aims at developing bioinformatics and mathematical methods for heterogeneous omics data. Within this program, we funded long and short stay visitings in France.

8.5. International Research Visitors

8.5.1. Visits of International Scientists

- **Chile**. Centro de Modelimiento Matematico, Santiago [A. Maass, N. Loirà, M. Latorre]
- **Germany**. Frei Universitat Berlin [A. Bockmayr, H. Siebert]
- **Niger**. University of Maradi [O. Abdou-Arbi]
- **Turkey**. University of Istambul [A. Aravena]

8.5.2. Visits to International Teams

8.5.2.1. Explorer program

Galiez Clovis

Date: Mar 2015 - May 2015

Institution: University of California, Irvine (United States)

8.5.2.2. Short visits

- **Chile**. Centro de Modelimiento Matematico, Santiago de Chile [J. Bourdon, M. Chevallier, C. Frioux, A. Siegel]
- **Chile**. Centro de Modelimiento Matematico, Santiago de Chile [M. Chevallier]
- **Germany**. Frei Berlin University [A. Siegel]

ERABLE Project-Team

8. Partnerships and Cooperations

8.1. National Initiatives

8.1.1. ANR

8.1.1.1. ABS4NGS

- Title: Solutions Algorithmiques, Bioinformatiques et Logicielles pour le Séquençage Haut Débit
- Coordinator: E. Barillot
- ERABLE participant(s): V. Lacroix
- Type: ANR (2012-2016)
- Web page: https://sites.google.com/site/abs4ngs/

8.1.1.2. Colib'read

- Title: Methods for efficient detection and visualization of biological information from non assembled NGS data
- Coordinator: P. Peterlongo
- ERABLE participant(s): V. Lacroix, L. I. S. de Lima, A. Julien-Lafferière, H. Lopez-Maestre, C. Marchet, G. Sacomoto, M.-F. Sagot, B. Sinaimeri
- Type: ANR (2013-2016)
- Web page: http://colibread.inria.fr/

8.1.1.3. ExHyb

- Title: Exploring genomic stability in hybrids
- Coordinator: C. Vieira
- ERABLE participant(s): C. Vieira
- Type: ANR (2014-2018)
- Web page: Not available

8.1.1.4. IMetSym

- Title: Immune and Metabolic Control in Intracellular Symbiosis of Insects
- Coordinator: A Heddi
- ERABLE participant(s): H. Charles, S. Colella
- Type: ANR Blanc (2014-2017)
- Web page: Not available

8.1.2. Others

Notice that were included here regional projects of our members from Italy when these have no other partners than researchers from the same country.

8.1.2.1. Exomic

- Title: Functional annotation of the transcriptome at the exon level
- Coordinator: D. Auboeuf (Inserm, Lyon)
- ERABLE participant(s): V. Lacroix, M.-F. Sagot
- Type: INSERM Systems Biology Call (2012-2015)
- Web page: Not available

8.1.2.2. Amanda

- Title: Algorithmics for MAssive and Networked DAta
- Coordinator: G. Di Battista (University of Roma 3)
- ERABLE participant(s): R. Grossi, N. Pisanti
- Type: MIUR PRIN, Italian Ministery of Research National Projects (2014-2017)
- Web page: http://www.dia.uniroma3.it/~amanda/research-units.php

8.1.2.3. Effets de l'environnement sur la stabilité des éléments transposables

- Title: Effets de l'environnement sur la stabilité des éléments transposables
- Coordinator: C. Vieira
- ERABLE participant(s): C. Vieira
- Type: Fondation pour la Recherche Médicale (FRM) (2014-2016)
- Web page: Not available

8.2. European Initiatives

8.2.1. FP7 & H2020 Projects

8.2.1.1. BacHBerry

- Title: BACterial Hosts for production of Bioactive phenolics from bERRY fruits
- Duration: November 2013 - October 2016
- Coordinator: Jochen Förster, DTU Danemark
- ERABLE participant(s): R. Andrade, L. Bulteau, A. Julien-Laferriére, V. Lacroix, A. Marchetti-Spaccamela, A. Mary, D. Parrot, M.-F. Sagot, L. Stougie, A. Viari, M. Wannagat
- Type: FP7 - KBBE
- Web page: http://www.bachberry.eu/

8.2.1.2. MicroWine

- Title: Microbial metagenomics and the modern wine industry
- Duration: January 2015 - January 2019
- Coordinator: Lars Hestbjerg Hansen, University of Copenhagen
- ERABLE participant(s): A. Marchetti-Spaccamela, A. Mary, H. T. Pusa, M.-F. Sagot, L. Stougie
- Type: H2020-MSCA-ETN-2014
- Web page: http://www.microwine.eu/

8.2.1.3. SWIPE

- Title: Predicting whitefly population outbreaks in changing environments
- Duration: 2012 - 2015
- Coordinator: E. Zchori-Fein
- ERABLE participant(s): F. Vavre
- Web page: Not available

8.2.1.4. SISYPHE

- Title: Species Identity and SYmbiosis Formally and Experimentally explored
- Duration: 2010-2015 (ended March 31st)
- Coordinator: M.-F. Sagot
- BAMBOO participant(s): Whole BAMBOO team
- Type: ERC Advanced Grant
- Web page: http://team.inria.fr/erable/en/older-projects/erc-sisyphe/

8.2.2. Collaborations with Major European Organisations

By itself, ERABLE is built from what initially were collaborations with some major European Organisations (CWI, Sapienza University of Rome, Universities of Florence and Pisa, Free University of Amsterdam) and now has become a European Inria Team.

8.3. International Initiatives

8.3.1. Inria International Labs

ERABLE participates in a project within the Inria-Chile CIRIC (Communication and Information Research and Innovation Center) titled "Omics Integrative Sciences". The main objectives of the project are the development and implementation of mathematical and computational methods and the associated computational platforms for the exploration and integration of large sets of heterogeneous omics data and their application to the production of biomarkers and bioidentification systems for important Chilean productive sectors. The project started in 2011 and is coordinated in Chile by Alejandro Maass, Mathomics, University of Chile, Santiago. It is in the context of this project that we are currently hosting the presence of Alex di Genova in ERABLE as a PhD sandwich student (for 18 to 24 months). Alex is co-supervised by Alejandro Maass and by Eric Goles from the University Adolfo Ibañez, Santiago, Chile.

8.3.2. Inria Associate Teams not involved in an Inria International Labs

ALEGRIA

- Title: ALgorithms for ExplorinG the inteRactions Involving Apicomplexa and kinetoplastida
- Duration: 2015 - 2017
- Coordinator: On the Brazilian side, Andréa Rodrigues Ávila; on the French side, Marie-France Sagot
- ERABLE participant(s): M. Ferrarini, L. Ishi Soares de Lima, A. Mary, H. T. Pusa, M.-F. Sagot, M. Wannagat
- Web page: http://team.inria.fr/erable/en/alegria/

8.3.3. Participation in other International Programs

ERABLE is coordinator of a CNRS-UCBL-Inria Laboratoire International Associé (LIA) with the Laboratório Nacional de Computação Científica (LNCC), Petrópolis, Brazil. The LIA has for acronym LIRIO ("Laboratoire International de Recherche en bIOinformatique") and is coordinated by Ana Tereza Vasconcelos from the LNCC and Marie-France Sagot from BAMBOO. The LIA was created in January 2012 for 4 years, renewable once. A web page for the LIA LIRIO is available at this address: http://team.inria.fr/bamboo/en/cnrs-lia-laboratoire-international-associe-lirio/.

ERABLE coordinates another project with Brazil. This is a CAPES-COFECUB project titled: "Multidisciplinary Approach to the Study of the Biodiversity, Interactions and Metabolism of the Microbial Ecosystem of Swines". The coordinators are M.-F. Sagot (France) and A. T. Vasconcelos (LNCC, Brazil) with also the participation of Arnaldo Zaha (Federal University of Rio Grande do Sul. The project started in 2013 for 2 years, and then was renewed for 2 more years starting from 2015. The main objective of this project is to experimentally and mathematically explore the biodiversity of the bacterial organisms living in the respiratory tract of swines, many of which are pathogenic. This project is strongly linked to the LIA LIRIO. More information on it may be found at this address: http://team.inria.fr/erable/en/cnrs-lia-laboratoire-international-associe-lirio/associated-projects/#CAPES-COFECUB_Microbial_Ecosystem_of_Swines.

ERABLE had a Stic AmSud project accepted in 2015 that will start in 2016 for 2 years. The title of the project is "Methodological Approaches Investigated as Accurately as possible for applications to biology", and its acronym MAIA. This project involves the following partners: (France) Marie-France Sagot, ERABLE Team, Inria; (Brazil) Roberto Marcondes César Jr, Instituto de Matemática e Estatística, Universidade de São Paulo; and Paulo Vieira Milreu, TecSinapse; (Chile) Vicente Acuña, Centro de Modelamiento Matemático, Santiago; and Gonzalo Ruz, University Adolfo Ibañez, Santiago. One of them, TecSinapse, is an industrial partner. MAIA has two main goals: one methodological that aims to explore how accurately hard problems can be solved theoretically by different approaches – exact, approximate, randomised, heuristic – and combinations thereof, and a second that aims to better understand the extent and the role of interspecific interactions in all main life processes by using the methodological insights gained in the first goal and the algorithms developed as a consequence. A preliminary web page for MAIA is available at this address: http://team.inria.fr/erable/en/projects/maia/.

Finally, we would like to mention the participation of one member of ERABLE (Alain Viari) in the Breast Cancer French Working Group of the International Cancer Genome Consortium (ICGC, https://icgc.org) led by the Institut National du Cancer (INCa, http://www.e-cancer.fr/Professionnels-de-la-recherche/Innovations/Les-progres-de-la-genomique/ICGC-France). This project was initiated by Pr. Gilles Thomas who passed away in 2014. Alain took the head of the bioinformatics platform located at the Centre Léon Bérard. The project aims at the genomic characterisation of 75 HER2-amplified breast cancers by using high-throughput sequencing (whole genome of paired tumor/normal samples and RNAseq of tumor samples). One of the scientific goals is to decipher whether the HER2/ERBB2 amplification is a driver or passenger event in the course of tumor development.

8.4. International Research Visitors

8.4.1. Visits of International Scientists

In 2015, ERABLE greeted the following International scientists:

- In France: Katharina Huber (University of Warwick, UK), Giuseppe Italiano (Tor Vergata University of Rome, Italy, various visits), Ana Rute Neves and Zeidan (ChR Hansen, Oslo, Danemark), three members of the LIA LIRIO (Arnaldo Zaha from the Federal University of Rio Grande do Sul, Maria Cristina Motta from the Federal University of Rio Grande do Sul, and Ana Tereza Vasconcelos from the LNCC, all in Brazil), Susana Vinga and various members of her team (IDMEC-IST Portugal), Tiziana Calamoneri (Sapienza University of Rome).
- In Italy: David Coudert (Inria Sophia Antipolis, France, to Florence), Alberto Policriti (University of Udine, Italy, to Pisa), Fabio Vandin (University of Southern Danemark to Pisa), Solon Pissis (King's College London UK to Pisa), Costas Iliopoulos (King's College London UK to Pisa), Grzegorz Rozenberg (Leiden University, The Netherlands, and Boulder University of Colorado, USA, to Pisa).
- In The Netherlands: Kirk Pruhs (University of Pittsburgh, USA), Kevin Schewior (Technical University of Berlin, Germany), Paola Bonizzoni, Yuri Pirola and Simone Zaccharia (all from the University of Milano-Bicocca, Italy).

8.4.2. Internships

In 2015, ERABLE greeted on average the following internship students:

- In France: Bastien Sylvere, Master 1 (2 months); Audric Cologne, Master 1 (3 months); Henri Dupoy, Master 1 (2 months); Virginie Jouffret, Master 1 (2 months); Caroline Michaud, Master 2 (6 months); Hong-Phong Pham, Master 2 (5 months); Nabel Sersoub, Master 1 (2 months); Manon Villa, Master 1 (2 months).
- In Italy: Anna Tarsia, Master 2 (Pisa).
- In The Netherlands: Gunnar Klau supervised a couple of MSc and BSc theses.

8.4.3. Visits to International Teams

8.4.3.1. Visits

In 2015, members of ERABLE visited the following International teams:

- In France: Giuseppe Italiano (Tor Vergata University of Rome), visit to members of the LIA LIRIO at the LNCC in Brazil, visit to the Departement of Computer Science of the University of São Paulo and to members of the TecSinapse company in Brazil, Tiziana Calamoneri (La Sapienza University of Rome), Susana Vinga and the members of her team (IDMEC-IST Portugal).
- In Italy: visit to Pierre Fraigniaud and Michel Habib at LIAFA, Paris, visit to Solon Pissis and Costas Iliopoulos at King's College London UK.
- In The Netherlands: visit to the Technical University of Berlin, visit to Paola Bonizzoni and her group at the University of Milano-Bicocca.

8.4.3.2. Research stays abroad

Gunnar Klau will be spending 9 months starting from November 2015 at the Center for Computational Molecular Biology at Brown University, USA, visiting notably Benjamin Raphael, Director of the Center.

GENSCALE Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

9.1.1. Bioinformatics computing center of Roscoff

Participants: Sébastien Brillet, Erwan Drezen, Patrick Durand, Dominique Lavenier, Ivaylo Petrov.

Through the collaborative project KORIBLAST2 funded by Région Bretagne (June 2014-December 2015) and within the KoriScale lab, we worked: (1) to improve the KLAST software with new alignment methods developed by GenScale; (2) to extend the capabilities of KLAST toward metagenomic processing; (3) to develop a cloud version targeting huge sequence comparison processing.

9.1.2. Etablissement Français du sang (EFS)

Participant: Dominique Lavenier.

An active collaboration with EFS started in 2015 to speed up individual HLA genotyping. A first prototype has been designed (see section New Results) and should be intensively tested in 2016 on many patient data.

9.1.3. Rennes Hospital, Hematology service, Genetic service

Participants: Patrick Durand, Dominique Lavenier, Claire Lemaitre, Pierre Peterlongo, Guillaume Rizk.

The collaboration with the Hematology service and with the Genetic service of the Rennes hospital aims to set up advanced bioinformatics pipelines for cancer diagnosis.

9.1.4. Partnership with INRA in Rennes

Participants: Cervin Guyomar, Dominique Lavenier, Fabrice Legeai, Claire Lemaitre, Sébastien Letort, Pierre Peterlongo, François Moreews.

The GenScale team has a strong and long term collaboration with biologists of INRA in Rennes: IGEPP and PEGASE units. This partnership concerns both service and research activities and is acted by the hosting two INRA engineers (F. Legeai, F. Moreews) and one PhD student (C. Guyomar).

9.2. National Initiatives

9.2.1. ANR

9.2.1.1. Project FATINTEGER

Participants: Dominique Lavenier, François Moreews.

Coordinateur: F. Gondret
Duration: 36 months (Mar. 2012 - feb. 2015)
Partners: PEGASE Inra Rennes, CNRS IRISA Rennes, AgroCampus Ouest LMA-IRMAR Rennes

The FatInteger project aims to identify some of the transcriptional key players of animal lipid metabolism plasticity, combining high throughput data with statistical approaches, bioinformatics and phylogenetic. GenScale is involved in the design of the workflow for processing the genomic data.

9.2.1.2. Project ADA-SPODO: Genetic variation of Spodoptera Frugiperda

Participants: Claire Lemaitre, Fabrice Legeai, Anaïs Gouin, Dominique Lavenier, Pierre Peterlongo.

Coordinator: E. D'Alençon (Inra, Montpellier)
Duration: 45 months (Oct. 2012 – May 2016)

Partners: DGIMI Inra Montpellier, CBGP Inra Montpellier, URGI Inra Versailles, Genscale Inria/IRISA Rennes.

The ADA-SPODO project aims at identifying all sources of genetic variation between two strains of an insect pest: Lepidoptera Spodoptera Frugiperda in order to correlate them with host-plant adaptation and speciation. GenScale's task is to develop new efficient methods to compare complete genomes along with their postgenomic and regulatory data.

9.2.1.3. Project COLIB'READ: Advanced algorithms for NGS data

Participants: Pierre Peterlongo, Antoine Limasset, Camille Marchet, Claire Lemaitre, Dominique Lavenier, Fabrice Legeai, Guillaume Rizk, Chloé Riou.

Coordinator: P. Peterlongo (Inria, GenScale, Rennes)
Duration: 45 months (Mar. 2013 – Dec. 2016)
Partners: LIRMM Montpellier, Erable Inria Lyon, Genscale Inria/IRISA Rennes.

The main goal of the Colib'Read project is to design new algorithms dedicated to the extraction of biological knowledge from raw data produced by High Throughput Sequencers (HTS). The project proposes an original way of extracting information from such data. The goal is to avoid the assembly step that often leads to a significant loss of information, or generates chimerical results due to complex heuristics. Instead, the strategy proposes a set of innovative approaches that bypass the assembly phase, and that does not require the availability of a reference genome. https://colibread.inria.fr/

9.2.1.4. Project GATB: Genome Analysis Tool Box

Participants: Dominique Lavenier, Erwan Drezen, Pierre Peterlongo, Claire Lemaitre, Guillaume Rizk, Charles Deltel.

Coordinator: D. Lavenier (Inria/Irisa, GenScale, Rennes)
Duration: 24 months (Feb. 2013 – Jan. 2015)
Partners: GenScale Inria/IRISA, Rennes – DTI Inria, Rennes.

This project aims to develop algorithms and tools for genome analysis based on a compact data structure having a very low memory footprint allowing end-users to process huge volume of genomic data on a simple desktop computer. The GATB is structured around a C++ library from which many efficient NGS tools can be developed. GATB has been published and is used outside Genscale (LIRMM, Inria Erable team). http://gatb.inria.fr

9.2.1.5. Project HydroGen: Metagenomic applied to ocean life study

Participants: Dominique Lavenier, Pierre Peterlongo, Claire Lemaitre, Guillaume Rizk, Gaëtan Benoit.

Coordinator: D. Lavenier (Inria/Irisa, GenScale, Rennes)
Duration: 42 months (Nov. 2014 – Apr. 2018)
Partners: CEA (GenosScope, Evry), INRA (AgroParisTech, Paris – MIG, Jouy-en-Jossas).

The HydroGen project aims to design new statistical and computational tools to measure and analyze biodiversity through comparative metagenomic approaches. The support application is the study of ocean biodiversity based on the analysis of seawater samples available from the Tara Oceans expedition.

9.2.1.6. Project SpeCrep: speciation processes in butterflies

Participants: Dominique Lavenier, Pierre Peterlongo, Claire Lemaitre, Fabrice Legeai.

Coordinator: M. Elias (Museum National d'Histoire Naturelle, Institut de Systematique et d'Evolution de la Biodiversite, Paris)
Duration: 48 months (Jan. 2015 – Dec. 2018)
Partners: MNHN (Paris), INRA (Versailles-Grignon), Genscale Inria/IRISA Rennes.

The SpeCrep project aims at better understanding the speciation processes, in particular by comparing natural replicates from several butterfly species in a suture zone system. GenScale's task is to develop new efficient methods for the assembly of reference genomes and the evaluation of the genetic diversity in several butterflies populations.

9.2.2. PIA: Programme Investissement d'Avenir

9.2.2.1. RAPSODYN: Optimization of the rapeseed oil content under low nitrogen

Participants: Dominique Lavenier, Claire Lemaitre, Pierre Peterlongo.

Coordinator: N. Nessi (Inra, IGEPP, Rennes)
The objective of the Rapsodyn project is the optimization of the rapeseed oil content and yield under low nitrogen input. GenScale is involved in the bioinformatics work package to elaborate advanced tools dedicated to polymorphism and application to the rapeseed plant.

9.2.2.2. France Génomique: Bio-informatics and Genomic Analysis

Participants: Laurent Bouri, Dominique Lavenier.

Coordinator: J. Weissenbach (Genoscope, Evry)
France Génomique gathers resources from the main French platforms in genomic and bio-informatics. It offers to the scientific community an access to these resources, a high level of expertise and the possibilities to participate in ambitious national and international projects. The GenScale team is involved in the work package "assembly" to provide expertise and to design new assembly tools for the 3rd generation sequencing.

9.3. International Initiatives

9.3.1. Brazil

- IMECC, UNICAMP, Campinas [A. Mucherino]
- Federal University of Florianópolis, Santa Catarina: Distance geometry, optimal vertex orders [A. Mucherino]

9.3.2. Chile

- university of Utalca, genomes of aphid parasitoids [F. Legeai]

9.3.3. USA

- Los Alamos National Laboratory (LANL), Los Alamos: Graph algorithms, Parallelism, GPU [R. Andonov, D. Lavenier]
- University of Miami, member of the international Aphid genome consortium [F. Legeai]
- University of Arizona, genomes of aphid parasitoids [F. Legeai]
- University of Ohio, genomics of the soybean aphid [F. Legeai]

9.3.4. China

- SouthWest university, member of the international Spodoptera litura genome project [F. Legeai]

IBIS Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

Project name	Séminaire grenoblois des systèmes complexes
Coordinators	S. Achard, O. François, A. Maignan, E. Prados, S. Rafai, D. Ropers
IBIS participants	D. Ropers
Type	Funding by Institut des Systèmes Complexes de Lyon (IXXI)
Web page	http://www.ixxi.fr/?page_id=114&lang=fr

8.2. National Initiatives

Project name	AlgeaInSilico: Prédire et optimiser la productivité des microalgues en fonction de leur milieu de croissance
Coordinator	O. Bernard
IBIS participants	H. de Jong, N. Giordano
Type	Inria Project Lab (2015-)
Web page	https://project.inria.fr/iplalgaeinsilico/

Project name	RESET – Arrest and restart of the gene expression machinery in bacteria: from mathematical models to biotechnological applications
Coordinator	H. de Jong
IBIS participants	E. Cinquemani, J. Geiselmann, C. Gomez Balderas, H. de Jong, S. Lacour, Y. Markowicz, C. Pinel, D. Ropers
Type	Bioinformatics call, Investissements d'Avenir program (2012-2017)
Web page	https://project.inria.fr/reset/

Project name	Fonction du système de régulation post-transcriptionnel CSR dans la dynamique de l'adaptation métabolique chez la bactérie modèle Escherichia coli
Coordinators	M. Cocaign-Bousquet (Inra, LISBP), B. Enjalbert (INSA, LISBP), D. Ropers
IBIS participants	M. Morin, D. Ropers
Type	Contrat Jeune Scientifique Inra-Inria (2012-2015)
Web page	http://www.inra.fr/les_hommes_et_les_femmes/rejoignez_nous/completer_sa_formation/le_recrutement_de_doctorants/cjs__1/inra_inria

Project name	A web application for the analysis of time-series fluorescent reporter gene data
Coordinator	H. de Jong
IBIS participants	E. Cinquemani, J. Geiselmann, M. Page, D. Ropers, V. Zulkower (University of Edinburgh)
Type	IFB call for development of innovative bioinformatics services for life sciences (2016-2017)

8.3. European Initiatives

8.3.1. Collaborations with Major European Organizations

Computer Engineering & Systems Science Department of University of Pavia (Italy), Giancarlo Ferrari-Trecate

Control theory and systems identification with applications to systems biology

Automatic Control Lab at ETH Zürich (Switzerland), John Lygeros

Control theory and systems identification with applications to systems biology

Computational Microbiology research group, Institute of Food Research, Norwich (United Kingdom), Aline Métris and József Baranyi

Mathematical modelling of survival and growth of bacteria

8.4. International Research Visitors

8.4.1. Visits of International Scientists

Invited professor	Alberto Soria-Lopéz (Centro de Investigación y de Estudios Avanzados (Cinestav) of Instituto Politécnico Nacional (IPN), Mexico)
Subject	Development of an automatically-controlled system of multiplexed mini-bioreactors

Visiting scientist	Aline Métris (Institute of Food Research (IFR), Norwich, UK)
Subject	Comparative analysis of metabolic networks of Escherichia coli and Salmonella

LIFEWARE Project-Team

8. Partnerships and Cooperations

8.1. National Initiatives

8.1.1. ANR Projects

- ANR Blanc HYCLOCK (2014-2018) on "Hybrid modeling of time for Circadian Clock Biology and Chronopharmacology", coordinated by F. Delaunay (CNRS, Nice), F. Lévi (INSERM Paris-Sud), G. Bernot (CNRS I3S, Nice), O. Roux (Ecle Centrale Nantes).
- ANR Blanc STOCH-MC (2014-2018) on "Stochastic Models: Scalable Model Checking", coordinated by Blaise Genest (Inria Rennes), with Grégory Batt, Wieslaw Zielonka (LIAFA), and Hugo Gimbert (LaBRI).
- ANR Investissement Avenir ICEBERG project (2011-2016) "From population models to model populations", coordinated by Grégory Batt, with Pascal Hersen (MSC lab, Paris Diderot Univ./CNRS), Reiner Veitia (Institut Jacques Monod, Paris Diderot Univ./CNRS), Olivier Gandrillon (BM2A lab, Lyon Univ./CNRS), Cédric Lhoussaine (LIFL/CNRS), and Jean Krivine (PPS lab, Paris Diderot Univ./CNRS).
- ANR Blanc NET-WMS-2 (2011-2015) on "constraint optimization in Wharehouse Management Systems", coordinated by F. Fages, with N. Beldiceanu (Ecole des Mines de Nantes, EPI TASC), and Abder Aggoun (KLS optim).

8.1.2. GENCI Contract

- GENCI (2009-) attribution of 300000 computation hours per year on the Jade cluster of 10000 cores of GENCI at CINES, Montpellier. Used for our hardest parameter search problems in BIOCHAM-parallel.

8.2. International Initiatives

8.2.1. Inria International Partners

8.2.1.1. Collaboration with National Taiwan University

Since 2012, we develop a collaboration with Prof. Jie-Hong Jiang, National Taiwan University which culminated this year with the defence of the PhD Thesis of Katherine Chiang [1], co-supervised by Jie-Hong Jiang and François Fages with two internships in 2012 and 2013, and with several publications [5], [11], [6]. Our aim is to pursue our collaboration on the concept of biochemical programming and the development of biochemical programming tools, in particular for the design of artificial biosensors in partnership with Franck Molina (CNRS, Sys2diag, Montpellier).

8.2.2. Participation In other International Programs

- French-German PROCOPE (2015-2017) grant on "Réduction de modèle et analyse de grands réseaux biochimiques par des méthodes stoechiométriques et tropicales", coord. Prof Andreas Weber, University of Bonn, Germany, and Prof. Ovidiu Radulescu, Univ. Montpellier, France.

8.3. International Research Visitors

8.3.1. Visits of International Scientists

Our group received for short visits of a few days

- Prof. Hugo Fort, Univ. Montevideo, Uruguay
- Prof. Andreas Weber, Univ. Bonn, Germany
- Damien Woods, Caltech, USA

MORPHEME Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

8.1.1. Renal tumor classification

Participants: Alexis Zubiolo, Eric Debreuve, Xavier Descombes.

Informal collaboration with the team TIRO, CEA/UNS (Philippe Pognonec), and the histopathology department of the CHU Pasteur (Damien Ambrosetti), Nice.

8.2. National Initiatives

8.2.1. LABEX SIGNALIFE

The MORPHEME team is member of the SIGNALIFE Laboratory of Excellence.

Florence Besse and Xavier Descombes are members of the Scientific Committee.

Florence Besse and Grégoire Malandain participated in the selection committee for LabeX PhD programme students.

8.2.2. ANR MOTIMO

Participants: Laure Blanc-Féraud, Xavier Descombes, Eric Debreuve, Huei Fang Yang, Ana Rita Lopes Simoes.

In collaboration with Institut de Mathématiques de Toulouse, INRA, Institut de Mécanique des Fluides de Toulouse, Laboratoire J-A Dieudonné, et IMV Technologies (PME). Details on the (website)

8.2.3. ANR POXADRONO

Participants: Florence Besse [PI], Xavier Descombes, Laure Blanc-Féraud.

The young researcher ANR project POXADRONO is in collaboration with Caroline Medioni, Hélène Bruckert, Giovanni Marchetti, Charlène Perrois and Lucile Palin from iBV. It aims at studying ARN regulation in the control of growth and axonal guidance by using a combination of live-imaging, quantitative analysis of images, bio-informatic analysis and genetic screening.

8.2.4. ANR DIG-EM

Participants: Grégoire Malandain, Xavier Descombes.

Morphogenesis controls the proper spatial organization of the various cell types. While the comparatively simple process of patterning and cell differentiation has received considerable attention, the genetic and evolutionary drivers of morphogenesis are much less understood. In particular, we very poorly understand why some morphogenetic processes evolve very rapidly, while others show remarkable evolutionary stability.

This research program aims at developing a high-throughput computational framework to analyze and formalize high-throughput 4D imaging data, in order to quantify and formally represent with cellular resolution the average development of an organism and its variations within and between species. In addition to its biological interest, a major output of the project will thus be the development of robust general computational methods for the analysis, visualization and representation of massive high-throughput light-sheet data sets.

This 4-years project started october the 1st, 2014 and is leaded by P. Lemaire (CRBM, Montpellier). Participants are the CRBM, and two Inria project-team, Morpheme and Virtual Plants.

8.2.5. ANR PhaseQuant

Participants: Grégoire Malandain, Eric Debreuve.

The PhaseQuantHD project aims at developing a high-content imaging system using quadriwave lateral shearing interferometry as a quantitative phase imaging modality. Automated analysis methods will be developed and optimized for this modality. Finally an open biological study question will be treated with the system.

This 3-years project started october the 1st, 2014 and is leaded by B. Wattelier (Phasics, Palaiseau). Participants are Phasics, and three academic teams TIRO (UNS/CEA/CAL), Nice, Mediacoding (I3S, Sophia-Antipolis), and Morpheme.

8.2.6. Inria Large-scale initiative Morphogenetics

Participants: Grégoire Malandain, Xavier Descombes, Gaël Michelin.

This action gathers the expertise of three Inria research teams (Virtual Plants, Morpheme, and Evasion) and other groups (RDP (ENS-CNRS–INRA, Lyon), RFD (CEA-INRA-CNRS, Grenoble)) and aimed at understanding how shape and architecture in plants are controlled by genes during development. To do so, we will study the spatio-temporal relationship between genetic regulation and plant shape utilizing recently developed imaging techniques together with molecular genetics and computational modelling. Rather than concentrating on the molecular networks, the project will study plant development across scales. In this context we will focus on the Arabidopsis flower, currently one of the best-characterised plant systems.

8.2.7. Octopus Project

Participant: Eric Debreuve.

The Octopus project deals with automatic classification of images of zooplankton. It is conducted in collaboration with the Laboratoire d'Océanographie de Villefranche-sur-mer (LOV) et l'ENSTA Paris. The kickoff meeting took place in May 2015 and a 3-day *brainstorming* meeting on Deep Learning took place in December 2015. Participants are I3S (Frédéric Precioso and Mélanie Ducoffe), LOV (Marc Picheral and Jean-Olivier Irisson), and ENSTA Paris (Antoine Manzanera).

8.3. International Initiatives

8.3.1. Participation In other International Programs

ECOS-NORD PROJECT C15M01. In 2015 was the beginning of the execution of this project. The main work on this year was concentrated to understand clearly the DIC system located at UIS, its image formation model and phase recovery by simulations (joint paper accepted at ISBI 2016), and to acquire real data from it to be able to validate the simulated models.

Xavier Descombes was PI of a collaboration with the IITP in Moscow within a CNRS/RAS Grant (EDC26091) on the subject "Statistical Analysis of Images: mathematical modeling and applications".

8.4. International Research Visitors

8.4.1. Visits of International Scientists

Elena Zhizhina, Evgueny Pechersky and Serguei Komech from IITP Moscow (Russian Academy of Science) were invited one week respectively in october and in november.

Arturo Plata-Gomez, professor at the University Industrial of Santander (UIS) in Bucaramanga (Colombia) has visiting Morpheme from April 6 to April 24.

Simone Rebegoldi, Ph.D. student of the Department of Mathematics and Computer Science in University of Ferrara (Italy) spent 3 months in Morpheme group form may 1st to July 31.

8.4.2. Visits to International Teams

Laure Blanc-Feraud visited Universidad Industrial de Santander (UIS) in Colombia from December 3-11.

8.4.2.1. Research stays abroad

Laure en Colombie

PLEIADE Team

7. Partnerships and Cooperations

7.1. National Initiatives

7.1.1. CAER – Alternative Fuels for Aeronautics

CAER is a 6 M-Euro contract with the Civil Aviation Directorate (Direction Générale de l'Aviation Civile, DGAC), coordinated by the French Petroleum Institute (Institut français de pétrole-énergies nouvelles, IFPEN) on behalf of a large consortium of industrial (EADS, Dassault, Snecma, Turbomeca, Airbus, Air France, Total) and academic (CNRS, INRA, Inria) partners to explore different technologies for alternative fuels for aviation. PLEIADE's role concerns the genomics of highly-performant oleaginous microorganisms.

7.2. International Initiatives

7.2.1. Inria International Partners

7.2.1.1. Informal International Partners

PLEIADE collaborates with Rodrigo Assar of the Universidad Andrès Bello, and Nicolás Loira and Alessandro Maass of the Center for Genomic Regulation, in Santiago de Chile (Chile).

7.3. International Research Visitors

7.3.1. Visits of International Scientists

Rodrigo Assar, assistant professor in the ICBM Human Genetics Program of the School of Medicine of the University of Chile, was invited by PLEIADE in the context of an ongoing collaboration on hybrid, stochastic modeling of complex biological systems.

7.3.1.1. Internships

Leyla Mirvakhabova, student at the National research University Higher School of Economics, Moscow, was invited by PLEIADE for an internship to work on faster mathematical methods for nonlinear mapping, to be applied to very large distance matrices.

Ulysse Guyet, Masters student in Bioinformatique-Biostatistique at the University of Nantes, was invited by PLEIADE for an intership to work on software components for transferring DNA sequence annotations from reference genomes to newly sequenced strains.

SERPICO Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

ENSAI-CREST: Statistical methods and models for image registration, Vincent Briane PhD thesis is co-funded by Inria and ENSAI-CREST and co-supervised by Myriam Vimond (ENSAI-CREST).

Région Bretagne: Identification, localization and enumeration of ribosomes within a tomogram by combining state-of-the-art denoising methods and object descriptor-based recognition (CATLAS, see Section 8.2.1).

BioGenOuest: Collaboration with S. Prigent (engineer) in charge of the organization of image processing services for Biogenouest bio-imaging facilities.

9.2. National Initiatives

9.2.1. France-BioImaging project

Participants: Charles Kervrann, Patrick Bouthemy, Thierry Pécot, Emmanuel Moebel, Ancageorgiana Caranfil.

The goal of the project is to build a distributed coordinated French infrastructure for photonic and electronic cellular bioimaging dedicated to innovation, training and technology transfer. High-computing capacities are needed to exhaustively analyse image flows. We address the following problems: i/ exhaustive analysis of bioimaging data sets; ii/ deciphering of key steps of biological mechanisms at organ, tissular, cellular and molecular levels through the systematic use of time-lapse 3D microscopy and image processing methods; iii/ storage and indexing of extracted and associated data and metadata through an intelligent data management system. SERPICO is co-head of the IPDM (Image Processing and Data Management) node of the FBI network composed of 6 nodes.
Funding: Investissement d'Avenir - Infrastructures Nationales en Biologie et Santé ANR (2011-2016).
Partners: CNRS, Institut Jacques Monod, Institut Pasteur, Institut Curie, ENS Ulm, Ecole Polytechnique, INRA, INSERM.

9.3. European Initiatives

9.3.1. Collaborations with Major European Organizations

ESFRI Euro-BioImaging initiative: SERPICO participates in the ESFRI Euro-BioImaging project, one of the four new biomedical science projects in the roadmap of the European Strategic Forum on Research Infrastructures (ESFRI). The mission of Euro-BioImaging is to provide access, service and training to state-of-the-art imaging technologies and foster the cooperation and networking at the national and European level including multidisciplinary scientists, industry regional, national and European authorities. SERPICO also participates to the French counterpart, the so-called "France-BioImaging" (FBI) network which gathers several outstanding cellular imaging centers (microscopy, spectroscopy, probe engineering and signal processing) as described in Section 9.2.1 .

9.4. International Initiatives

9.4.1. Inria International Partners

9.4.1.1. Informal International Partners

Collaboration with UT Southwestern Medical Center, Dallas (TX), Prof. Gaudenz Danuser: Object tracking in video-microscopy.

Collaboration with Max-Planck Institute, Martinsried (Germany), Dr. Julio Ortiz: Detection and segmentation of macromolecules in cryo-electron tomography.

Collaboration with Aalborg University (Denmark), Prof. Jesper Møller: Modeling aggregation on the large scale and regularity on the small scale in spatial point pattern datasets (visit of Frédéric Lavancier from 26-30 January 2015).

VIRTUAL PLANTS Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

8.1.1. Agropolis computational plant seminar

Participants: Yann Guédon, Thierry Fourcaud [CIRAD, AMAP], Christine Granier [INRA, LEPSE], Soazig Guyomarc'H [Montpellier 2 University, DIADE], Laurent Laplaze [IRD, DIADE].

Funding: Agropolis foundation (Contractor for Virtual Plants: CIRAD. From 2013 to 2016)

In the context of the creation of a world-level pole on plant science in the region Languedoc-Roussillon, we created a monthly seminar on plant modeling and its applications. The seminar is organized by Yann Guédon, Thierry Fourcaud (CIRAD, AMAP), Christine Granier (INRA, LESPE), Soazig Guyomarc'h (Montpellier 2 University, DIADE) and Laurent Laplaze (IRD, DIADE) with the support of Agropolis International and Agropolis Foundation. In 2015, we organized a two-day workshop devoted to the modeling of plant development from the cellular to the organ scale.

8.1.2. MecaFruit3D

Participants: Mik Cieslak, Frédéric Boudon, Christophe Godin, Nadia Bertin [PSH, Avignon].

Funding: Labex Agro (Contractor for Virtual Plants: INRA, from 2013 to 2016)

The fruit cuticle plays a major role in fruit development and shelf-life. It is involved in water losses, cracking, and protection against stress, and thus it may have major economic impacts. Objectives of the project are to better understand the multiple roles of the fruit cuticle in the control of fleshy fruit growth and quality.

The multicellular model for fruit growth that we develop (see section 6.3.2) will be used to study qualitatively the impact of the cuticle mechanical properties.

Partners: PSH, INRA, Avignon; LCVN, IES, Université Sud de France, Montpellier.

8.1.3. Integrated model of plant organ growth

Participants: Yann Guédon, Christine Granier [INRA, LEPSE], Garance Koch [INRA, LEPSE], Nadia Bertin [INRA, PSH], Valentina Baldazzi [INRA, PSH].

Funding: Labex Agro (Contractor for Virtual Plants: CIRAD. From 2015 to 2018)

The objective of this project is to develop a generic model which will predict interactions among the main processes controlling the development of source and sink organs in tomato, i.e. cell division, cell expansion and endoreduplication in relation to carbon and water fluxes under fluctuating environment. To achieve this objective we will i) capitalize on expertise, multi-scale phenotyping tools and genetic resources already compiled on the fruit model tomato and the model plant *Arabidopsis thaliana*; ii) perform new experiments to collect phenotyping data currently missing in this field, especially concerning the early phase of fruit and leaf development in tomato and the interactions between genes and environment; iii) develop a process-based model of organ growth which will integrate knowledge collected at the different scales.

Partners: PSH, INRA, Avignon; LEPSE, INRA, Montpellier, Biologie du fruit et Pathologie INRA, Bordeaux;

8.1.4. SegmentationEvaluation

Participants: Sophie Ribes, Benjamin Gilles [LIRMM], Guillaume Baty, Alizon Konig, Guillaume Cerutti.

Funding: IBC (Contractor for Virtual Plants: UM, 2015)

The goal of this project is to develop a framework allowing a robust validation for image segmentation. Segmentation is an ill-posed problem, and conventional validation approaches are corrupted by both intra and inter observer variabilities. We plan to develop: efficient tools allowing a creation of gold standard segmentation data (Alizon Konig, master internship under the supervision of Sophie Ribes); robust metrics to quantify differences between ground truth and algorithmic results.

Partners: ICAR, LIRMM, Montpellier.

8.2. National Initiatives

8.2.1. HydroRoot

Participants: Mikaël Lucas [IRD], Christophe Pradal, Christophe Godin, Yann Boursiac [BPMP], Christophe Maurel [BPMP].

Funding: ANR (Contractor for Virtual Plants: Cirad, From 2012 to 2016)

The HydroRoot project proposes a unique combination of approaches in the model plant Arabidopsis thaliana to enhance our fundamental knowledge of root water transport. Accurate biophysical measurements and mathematical modeling are used, in support of reverse and quantitative genetics approaches, to produce an integrated view of root hydraulics. The HydroRoot project will address as yet unknown facets of root water transport. It will lead to an integrated view of root hydraulics that considers both tissue hydraulics and root architecture and explains how these components are controlled at the molecular level by physiological and/or environmental cues. Because of its strong physiological and genetic background, this research may also directly impact on breeding programs, for production of crops with optimised water usage and stress responses.

8.2.2. Phenome

Participants: Christian Fournier, Christophe Pradal, Sarah Cohen-Boulakia, Simon Artzet, Jerome Chopard, Patrick Valduriez.

Funding: ANR-Investissement d'avenir (Contractor for Virtual Plants: INRA, From 2015 to 2018)

The goal of Phenome is to provide France with an up-to-date, versatile, high- throughput infrastructure and suite of methods allowing characterisation of panels of genotypes of different species under climate change scenarios. We are involved in the methodological part of the project, that aims at developping a software framework dedicated to the analysis of high throughput phenotyping data and models. It will based on the OpenAlea platform that provides methods and softwares for the modelling of plants, together with a user-friendly interface for the design and execution of scientific workflows. We also develop the InfraPhenoGrid infrastructure that allows high throughput computation and recording of provenance during the execution of Workflows.

8.2.3. DigEM

Participants: Christophe Godin, Grégoire Malandain, Patrick Lemaire.

Funding: ANR (Contractor for Virtual Plants: Inria, From 2015 to 2019)

In this project, we will use advanced ligh-sheet imaging of live embryos to quantitatively describe embryonic morphogenesis in ascidians, a class of animals that undergo very rapid genomic divergence, yet show an extraordinary stasis of embryonic morphologies, based on invariant early cell lineages shared by all studied species. The global aims of the proposal, which will bridge micro- and macroevolutionary scales of analysis, are: i) to provide a global systems-level description at cellular resolution of an animal embryonic program; ii) to use this description to characterize intra-specific and inter-specific patterns of morphogenetic variations; iii) to analyze possible molecular mechanisms explaining the unusual robustness of this program to environmental and genetic perturbations. To achieve these aims, we will combine advanced live light-sheet microscopy, computational biology, functional gene assays and evolutionary approaches.

8.2.4. Leaf Serration

Participants: Christophe Godin, Eugenio Azpeitia.

Funding: ANR (Contractor for Virtual Plants: Inria, From 2014 to 2019)

Leaf growth and development result from the coordination in time and space of cellular divisions and cellular expansion, and expansion of certain plant cells reaches up to one thousand times their size when living the meristem. Transcription factors belonging to the CUP-SHAPED COTYLEDON (CUC) genes and homeodomain genes of the KNOTTED-LIKE (KNOXI) family were shown to be essential for the control of leaf size and shape. In addition, the phytohormone auxin is a critical regulator of growth and development, involved in the regulation and coordination of cell division and cell expansion. The mechanisms of auxin signalling are based on a complex set of co-receptors exhibiting high to low affinity for auxin and an even more complex modular network of transcriptional repressors and activators tightly controlling the expression of a large set of genes.

The SERRATIONS project is based on recent data relative to key transcription factors regulating leaf morphogenesis and advanced knowledge on the generic signalling mechanisms of the phytohormone auxin that plays a critical role in the control and coordination of cellular responses sustaining leaf size and shape. The goal of the project is to identify auxin signalling modules involved in leaf morphogenesis and to integrate these data in mathematical modelling to provide new insights into complex regulatory networks acting on leaf morphogenesis and to further test model-derived hypotheses.

8.2.5. Other national grants

8.2.5.1. MARS-ALT 2.0

Participants: Guillaume Baty, Christophe Pradal, Christophe Godin.

Funding: Inria ADT (Contractors for Virtual Plants: Inria from 2013 to 2015)

The goal of this project is to integrate in a single software platform all the software tools and algorithms that have been developed in various projects about meristem modeling in our teams. More precisely, we aim at building 3D models of meristem development at cellular resolution based on images obtained with confocal or multiphoton microscopy. This set of components will be used by biologists and modelers making it possible to build such meristem structures, to explore and to program them. This platform is embedded in the OpenAlea framework and is based on the imaging components of the platform MedInria. Asclepios, RDP ENS-Lyon/INRA, PHIV CIRAD

8.2.5.2. SCOOP

Participants: Pierre Fernique, Yann Guédon, Christophe Pradal, Christophe Godin, Frédéric Boudon, Jean-Baptiste Durand.

Funding: Inria ADT (Contractors for Virtual Plants: Inria from 2014 to 2016)

The goal of this project is to improve the software quality and the dissemination of Vplants components for plant phenotyping. Virtual Plants team has played a pioneering role in the development of methods for analyzing plant development that take account of the complexity of plant architecture. Numerous software components has been developed for more than 20 years and a profound re- engineering is now necessary to facilitate the collaborations with biologist and agronomists of CIRAD, INRA and IRD and to help the dissemination of ours methods in the scientific community.

8.2.5.3. Echap

Participants: Christophe Pradal, Christian Fournier, Corinne Robert [INRA, EGC].

Funding: ONEMA (Contractor for Virtual Plants: INRA, From 2012 to 2014)

The objective of the ECHAP project is to reduce the frequency of treatments and the doses of pesticides applied on crops by taking advantage of natural mechanisms of disease escape related to crop architecture and by optimizing interception of pesticides by plant canopies. It focuses on the development of an integrative, yet modular, modeling tool on the OpenAlea plateform that couples wheat architectural development, the interception and fate of fungicides and the dynamics of a pathogen. Various scenarios combining climate x architecture x fungicide treatment will be simulated to identify and propose efficient strategies of pesticide applications. Partners: UMR EGC (Paris-Grignon), UMR LEPSE (Montpellier), ARVALIS (Institut du végétal, France), ALTERRA (Research Institute for the Green World, The Nederlands) , ADAS Intitute (UK), CNRS, and IRSTEA .

8.2.5.4. Morphogenetics

Participants: Christophe Godin, Frédéric Boudon, Christophe Pradal, Grégoire Malandain, François Faure, Jan Traas, François Parcy, Arezki Boudaoud, Teva Vernoux.

Funding: Inria Project Lab (From 2013 to 2016)

Morphogenetics is an Inria transversal project gathering 3 Inria teams and two Inra teams. It aimed at understanding how flower shape and architecture are controlled by genes during development. Using quantitative live-imaging analysis at cellular resolution we will determine how specific gene functions affect both growth patterns and the expression of other key regulators. The results generated from these experiments will be integrated in a specially designed database (3D Atlas) and used as direct input to new predictive computational models for morphogenesis and gene regulation. Model predictions will then be further tested through subsequent rounds of experimental perturbation and analysis. A particular emphasis will be put on the modeling of mechanics in tissues for which different approaches will be developed.

Partners: RDP ENS-Lyon; Imagine Inria Team (Grenoble); Morpheme Inria Team (Sophia-Antipolis), UMR PCV (Grenoble).

8.2.5.5. Rose

Participants: Christophe Godin, Frédéric Boudon, Christophe Pradal.

Funding: INRA - Projet de Pari Scientifique (From 2012 to 2015)

In this project we want to quantify and understand how sugars interfere with hormonal signals (auxin, cytokinins) to regulate lateral bud outgrowth of aerial stems of roses. Experiments will be made on Rose stems to test different levels of sugar conditions and hormonal concentrations on bud outgrowth. An extension of the recently published hormonal model of apical dominance will be made to take into account the role of carbon as a signaling molecule.

Partners: UMR SAGAH, Angers

8.3. International Initiatives

8.3.1. ANR-DFG

8.3.1.1. AlternApp

Participants: Yann Guédon, Maryam Aliee.

Funding: ANR-DFG (Contractor for Virtual Plants: INRA, From 2015 to 2019)

The aim of the AlternApp project is to investigate functional hypotheses on the genetic and environmental control of floral induction in apple tree progenies. Two segregating populations will be studied in two different environmental conditions for floral induction and bearing behavior, in order to identify genomic regions associated with regular phenotypes. The specific contribution of the team will be to develop statistical methods to quantify phenotype and genotype, as well as years and climatic effects on alternation. Transcriptome of varieties contrasted in their bearing behavior and artificially set into high or low cropping conditions will be explored by New Generation Sequencing Technology (NGS) to identify new candidate genes and allelic variations of interest. By this project, new results are expected on floral induction in apple tree in relation to their alternate bearing behavior and more applied results linked to the discovery of allelic variation in key genes that could be used in breeding programs.

Partners: AFEF INRA team (Montpellier), PIAF INRA team (Clermont-Ferrand), JKI (Dresden, Germany), UHOH (Hohenheim, Germany), Foundation E. Mach (San Michele all'Adige, Italy)

8.3.2. Inria International Partners

8.3.2.1. Informal International Partners

An important collaboration with the CIRAD research unit HortSys at the Reunion island and in particular Frédéric Normand has been established for several years. The topic of the collaboration is the study of the phenology of mango tree. Three members of the team have been visiting our collaborators during the year. This is a tripartite collaboration that also involves Pierre-Eric Lauri of the AGAP/AFEF team.

We have for several years a strong partnership with Ted de Jong group at UC Davis concerning the influence of various agronomic practices (water stress, pruning) on fruit tree branching and production [21]. This is a tripartite collaboration that also involves Evelyne Costes of the AGAP/AFEF team.

A collaboration in plant phenotyping with the CSIRO and the INRA/Lepse team has been established for several years. The topic of the collaboration is to develop a full pipeline using OpenAlea 2.0 on plant phenotyping platforms. This is a joint collaboration with UMR LEPSE in Montpellier (François Tardieu).

A collaboration started in the last two years with the group of Henrik Jönsson of the Sainsbury Lab, Cambridge, UK. The collaboration is related to several modeling projects in the context of shoot apical and flower meristems development, with a particular focus on the use of quantitative 3D reconstructions of meristem structures. Yassin Refahi from the Sainsbury Lab is regularly paying visits to Montpellier. The Virtual Plants team is also regularly invited to Cambridge.

8.3.2.2. BioSensors

Participants: Guillaume Cerutti, Sophie Ribes, Frédéric Boudon, Christophe Godin, Teva Vernoux [ENS-Lyon], Géraldine Brunoud [ENS-Lyon], Carlos Galvan-Ampudia [ENS-Lyon].

Funding: Human Frontiers - HFSP (From 2014 to 2017)

We propose to elucidate the basis for positional information by hormones during plant morphogenesis. While it is known that cell fate decisions require simultaneous input from multiple hormones, to-date a precise understanding of how these signals are coordinated and act together to drive morphogenesis does not exist. Our limited mechanistic understanding is largely due to the difficulty to quantify the distribution of these small molecules in space and time. To explore this fundamental question, we will exploit recent advances in synthetic biology to engineer an RNA-based biosensor platform applicable to a broad range of small molecules and in particular to hormones. Using live-imaging technologies, we will use the sensors to obtain quantitative dynamic 3D maps of hormone distributions and relate these maps to the spatio-temporal distribution of cell identities, both during normal morphogenesis and upon perturbations of hormone levels. This analysis will be done on the shoot apical meristem, one of the bestcharacterized developmental systems in higher plants. In this context, mathematical approaches will be essential to analyze and establish a predictive model for how multiple hormones influence cell fate in a spatio-temporal manner.

8.4. International Research Visitors

8.4.1. Visits of International Scientists

The team received several visitors from foreign research groups in 2015:

- Farah Ben Naoum, from Sidi Bel Abbes University, Algeria, visited the team last summer for 1 month.
- Yoan Coudert, from University of Cambridge, UK, visited the team for 3 months.
- David Ford, from University of Washington, USA, visited the team for 1 week.
- Winfried Kurth of the University of Goettingen, Germany, visited the team for 1 week in June.
- Dennis Shasha, from Courant Institute of Mathematics, New York University, in the context of an Inria international chair, visited the team during its stay.
- Julia Pulwicki, PhD student if the University of Calgary visited the team 2 weeks in May-June.

8.4.2. Visits to International Teams

8.4.2.1. Research stays abroad

- Frédéric Boudon visited Frédéric Normand of the UR Hortsys at the CIRAD La Réunion two weeks in April.
- Christophe Pradal visited Frédéric Normand of the UR Hortsys and Ian Bally and Paula Ibell of the University of Queensland at the CIRAD La Réunion two weeks in May.
- Christophe Pradal visited Professor Kurth of the University of Goettingen, Germany one week in November.

ARAMIS Project-Team

9. Partnerships and Cooperations

9.1. National Initiatives

9.1.1. ANR

9.1.1.1. ANR PREV-DEMALS

Participants: Olivier Colliot [Correspondant], Marie Chupin, Stanley Durrleman, Anne Bertrand.

Project acronym: PREV-DEMALS

Project title: Predict to prevent frontotemporal lobar degeneration (FTLD) and amyotrophic lateral sclerosis (ALS)

Duration: Avr 2015 - Avr 2019

Amount: 487k€

Coordinator: Isabelle Le Ber

Other partners: ICM, AP-HP, CHR de Lille, CHU Limoges, CHU Rouen, Laboratory of Biomedical Imaging

Abstract: The project focuses on C9ORF72, the most frequent genetic form of frontotemporal lobar degeneration (FTLD) and amyotrophic lateral sclerosis (ALS). Since 2006, major discoveries have helped elucidate the pathological bases and linked FTLD and ALS: 1) TDP-43 aggregates in neurons and 2) C9ORF72 mutations in both disorders. Two major pathological subtypes are now defined in FTLD, FTLD-TDP and FTLD-TAU. C9ORF72 mutations (associated to FTLD-TDP) are the most frequent genetic causes of FTLD (15%), FTLD-ALS (65%) and ALS (40%). No curative treatment actually exists, but therapeutics emerged against tau aggregation. The objectives of the project are to develop appropriate cognitive, brain imaging markers and peripheral biomarkers of the early phase of FTLD, to follow disease progression and to guide future targeted therapeutic trials. To address this questions, we will conduct a multimodal study (cognition, brain structural MRI, brain metabolism - FDG-PET) in C9ORF72 families. The cohort will be followed at 3-time points (M0, M18, M36). Longitudinal analyses will aim at characterizing the trajectory of decline across time. Brain structural changes will be evaluated by 1) morphometric analysis to assess global brain atrophy, cortical thickness and study of the cortical sulci; 2) functional connectivity analysis of resting-state MR data; 3) structural connectivity analysis of diffusion-weighted MRI. Brain metabolism will be evaluated with FDG-PET. We will use the most recent RNA sequencing technology to detect gene expression and RNA splicing alterations in lymphocytes of patients and presymptomatic carriers. The discovery of new markers involved in FTLD will have practical consequences for early and accurate diagnosis of FLD and ALS disease.

9.1.2. IHU

9.1.2.1. General program

Participants: Olivier Colliot, Mario Chavez, Stanley Durrleman, Marie Chupin, Didier Dormont, Dominique Hasboun, Damien Galanaud, Fabrizio de Vico Fallani.

Project acronym: IHU-A-ICM

Project title: Institute of Translational Neuroscience

Founded in 2011

General Director: Bertrand Fontaine

The IHU-A-ICM program was selected, in 2011, in a highly competitive national call for projects. A 10-year, 55M€ program, has been implemented by a recently created foundation for scientific cooperation. Based on the clinical and scientific strenghts of the ICM and the hospital Department of Nervous System Diseases, it mainly supports neuroscience research, but is also invested in improving care and teaching. ARAMIS is strongly involved in the IHU-A-ICM project, in particular in WP6 (neuroimaging and electrophysiology), WP7 (biostatistics), WP2 (Alzheimer) and WP5 (epilepsy). We have started collaborations with the new bioinformatics/biostatistics platform (IHU WP7, head: Ivan Moszer), in particular through a joint project on the integration of imaging and genomics data.

9.1.2.2. ICM-Internal Research projects

Participants: Mario Chavez [Correspondant], Fabrizio de Vico Fallani [Correspondant].

Project title: Non-invasive manipulation of brain synchrony to enhance brain function and rehabilitate faulty cognition in humans: A proof of concept

Founded in 2014

Coordinator: Antoni Valero Cabre (ICM-team "Dynamiques Cérébrales, Plasticité et Rééducation")

Other partners: Service des Urgences Cérébro-Vasculaires de l'Hôpital Pitié-Salpêtrière, Paris.

The long-term goal of this project is to develop the use of non-invasive manipulation of abnormal cerebral oscillations underlying cognitive activity to restore brain function in neurological patients. Cognitive functions emerge from large distributed networks organized in space and time. The short-term goal of this application is to study the causal role played by oscillatory activity in visual awareness and test whether their manipulation by non-invasive brain stimulation has the potential to restore its function in stroke patients.

9.1.2.3. IFR49-Internal Research projects

Participants: Mario Chavez [Correspondant], Fabrizio de Vico Fallani [Correspondant].

Project title: Exploring the impact and time frequency signature of rhythmic patterns of Transcranial Magnetic Stimulation (TMS) on network activity by Magneto-Encephalography (MEG)

Founded in 2014

Coordinator: Antoni Valero Cabre (ICM-team "Dynamiques Cérébrales, Plasticité et Rééducation")

Other partners: TMS, EEG and MEG technical platforms of the ICM at the Hopital Pitié-Salptrière; and Service des Urgences Cérébro-Vasculaires de l'Hôpital Pitié-Salpêtrière, Paris.

The long-term goal of this project is to better understand the ability of non invasive neurostimulation to induce lasting local and distributed reorganization effects in the human brain to better plan and document therapies for patients. The short-term goal of this application is to develop a new mapping procedure to be able to capture and characterize in terms of oscillatory activity the lasting impact of repetitive Transcranial Magnetic Stimulation (TMS) on specific brain regions and associated networks.

9.1.3. CATI (Alzheimer Plan)

Participants: Olivier Colliot [Correspondant], Marie Chupin [Correspondant], Stanley Durrleman, Didier Dormont, Chabha Azouani, Ali Bouyahia, Johanne Germain, Kelly Martineau, Sonia Djobeir, Hugo Dary, Ludovic Fillon, Takoua Kaaouana, Alexandre Routier, Mathieu Dubois.

Project acronym: CATI

Project title: Centre d'Acquisition et de Traitement des Images

Founded in 2011

Amount: 9M€

Coordinator: Jean-François Mangin

Other partners: Neurospin, CENIR, Inserm U678, IM2A

Abstract: The CATI project (funded by the National Alzheimer Plan for 9M€, 2.1M€ for ARAMIS) aims at creating a national platform for multicenter neuroimaging studies. CATI aims to be a national resource for the scientific, medical and industrial research community and will provide a wide range of services: access to a national acquisition network, standardization of acquisitions, image quality control, image analysis, databasing/archiving, meta-analyses. Through CATI, our team coordinates a large network composed of over 30 image acquisition centers. CATI already supports over 15 multicenter projects including the national cohort MEMENTO (2300 subjects). CATI is integrated with France Life Imaging (PI: F. Lethimonnier) and the Neugrid for you (N4U, PI: G. Frisoni) network.

9.1.4. National Networks

- GdR Statistics and Medicine - http://gdr.statsante.fr/Accueil.html

9.1.5. Other National Programs

9.1.5.1. Programme Hospitalier de Recherche Clinique (PHRC)

Participants: Olivier Colliot, Marie Chupin, Stanley Durrleman, Didier Dormont, Damien Galanaud.

- PHRC PredictPGRN, co-funding by Alzheimer Plan, *Caractérisation multimodale prospective de la démence frontotemporale dûe à des mutations du gène PGRN à un stade symptomatique et présymptomatique*. (Coordinator : A. Brice)
- PHRC ImaBio3, co-funding by Roche (pharmaceutical industry), *Rôle des réactions cellulaires sanguines, inflammatoires et immunitaires anti-amyloïde centrales et périphériques dans la maladie d'Alzheimer débutante*. (Coordinator : M. Sarazin)
- PHRC CAPP, *Caractérisation linguistique, anatomique/métabolique et biologique des différentes formes d'aphasie primaire progressive : vers le rationnel pour des essais pharmacologiques et des rééducations du langage ciblées*. (Coordinator: M. Teichmann)

9.1.5.2. Institut Universitaire d'Ingénierie pour la Santé (IUIS)

Participants: Mario Chavez, Xavier Navarro.

Project acronym: DYSPEV

Project title: Dépistage de la dyspnée par potentiels évoqués visuels

Founded in 2014

Amount: 38K€

Coordinator: Thomas Similowski

Other partners: UPMC, Inserm UMR 1158

Abstract: Steady state visual evoked potentials (SSVEP) have been widely utilized in brain computer interfacing (BCI) in last years. In this project, we explore the possibilities of SSVEP to manage the communication between patients suffering from respiratory disorders and health care providers. By imposing different breathing constraints, we use a SSVEP-based brain computer interface to help those subjects to communicate their breathing sensations (breathing well/breathing bad).

9.2. European Initiatives

9.2.1. FP7 & H2020 Projects

Participants: Stefan Thurner, Vito Latora, Albert Diaz-Guilera, Maxi San Miguel, Cecilia Mascolo, Mirco Musolesi, Mario Chavez [Correspondant].

Project acronym: LASAGNE

Project title: multi-LAyer SpAtiotemporal Generalized NEtworks

Dates: 2012-2015

Amount: 1.6M€

Coordinator: Stefan Thurner

Other partners: Medical University of Vienna, Queen Mary University of London, Universitat de Barcelona, Universitat de les Illes Balears,University of Cambridge, University of Birmingham.

Abstract: The aim of the LASAGNE project is to provide a novel and coherent theoretical framework for analyzing and modelling dynamic and multi-layer networks in terms of multi-graphs embedded in space and time. To do this, we will treat time, space and the nature of interactions not as additional dimensions of the problem, but as natural, inherent components of the very same generalized network description. The theory will be validated on real-world applications involving large and heterogeneous data sets of brain networks, on- and off-line social systems, healthcare systems, and transportation flows in cities. The LASAGNE project will provide new quantitative opportunities in different fields, ranging from the prediction of pathologies to the diffusion of ideas and trends in societies, and for the management of socio-technological systems.

9.3. International Initiatives

9.3.1. Inria International Partners

9.3.1.1. Informal International Partners

S. Durrleman has an enduring collaboration with the Scientific Computing and Imaging (SCI) Institute at the University of Utah (USA). He is consultant for NIH Grant "4D shape analysis for modeling spatiotemporal change trajectories in Huntington's Disease "predict-HD". He is part of the PhD committees of J. Fishbaugh and A. Sharma supervised by professor Guido Gerig.

M. Chupin and O. Colliot have an enduring collaboration with the Center for Magnetic Resonance Research, University of Minnesota, USA (P-F Van de Moortele, T. Henry, M. Marjanska, K. Ugurbil) a leading center in 7T MRI.

S. Durrleman and O. Colliot have a collaboration with the Center for Medical Image Computing (CMIC) at University College London (UCL), London, UK (S. Ourselin, D. Alexander, M. Modat).

D. Galanaud has an enduring collaboration with the Massachusetts General Hospital, Harvard University, USA (R. Gupta).

M. Chavez has different collaborations with the Mathematics Departement of the Queen Mary University of London, UK (Prof. V. Latora); and the Physics Department of the Universitat de Barcelona, Spain (Prof. Albert Diaz-Guilera)

F. De Vico Fallani has a collaboration with the University Sapienza, Rome, Italy (Profs. Fabio and Claudio Babiloni) and with the IRCCS Fondazione Santa Lucia, Rome, Italy (M. Molinari and D. Mattia).

ASCLEPIOS Project-Team

8. Partnerships and Cooperations

8.1. National Initiatives

8.1.1. Consulting for Industry

Nicholas Ayache is a scientific consultant for the company Mauna Kea Technologies (Paris).

8.1.2. Collaboration with national hospitals

The Asclepios-project team collaborates with the following 3 French IHU (University Hospital Institute): the IHU-Strasbourg (Pr J. Marescaux and L. Soler) on image-guided surgery (N. Ayache serves as Chief Scientific Officer), the IHU-Bordeaux (Pr M. Haïssaguere and Pr P. Jaïs) on cardiac imaging and modeling and the IHU-Pitié Salpétrière (Dr. O. Colliot and S. Durrleman) on neuroimaging.

We also have long term collaborations with the CHU Nice and Centre Antoine Lacassagne in Nice.

The Asclepios-project team is part of the EQUIPEX MUSIC consortium with Bordeaux University Hospital, which aim is to build an XMR interventional room equipped with a medInria workstation.

8.2. European Initiatives

8.2.1. FP7 & H2020 Projects

8.2.1.1. MD PAEDIGREE

Title: Model-Driven European Paediatric Digital Repository

Programme: FP7

Period: March 2013 - February 2017

Coordinator: Ospedale Pediatrico Bambini Gesù, Rome.

Partners:

Athena Research and Innovation Center in Information Communication & Knowledge Technologies (Greece)

Biomolecular Research Genomics (Italy)

Deutsches Herzzentrum Berlin (Germany)

Empirica Gesellschaft für Kommunikations- und Technologie Forschung Mbh (Germany)

Fraunhofer-Gesellschaft Zur Foerderung Der Angewandten Forschung E.V (Germany)

Haute Ecole Specialisée de Suisse Occidentale (Switzerland)

Istituto Giannina Gaslini (Italy)

Katholieke Universiteit Leuven (Belgium)

Lynkeus (Italy)

Motek Medical B.V. (Netherlands)

Ospedale Pediatrico Bambino Gesu (Italy)

Siemens Aktiengesellschaft (Germany)

Siemens Corporation (United States)

Technische Universiteit Delft (Netherlands)

University College London (United Kingdom)

Universitair Medisch Centrum Utrecht (Netherlands)

Universita Degli Studi di Roma Lapienza (Italy)

The University of Sheffield (United Kingdom)

Universitatea Transilvania Din Brasov (Romania)

Stichting Vu-Vumc (Netherlands)

Maat Francerl (France)

Inria contact: Xavier Pennec

MD-Paedigree is a clinically-led VPH project that addresses both the first and the second actions of part B of Objective ICT-2011.5.2:

1. it enhances existing disease models stemming from former EC-funded research projects (Health-e-Child and Sim-e-Child) and from industry and academia, by developing robust and reusable multi-scale models for more predictive, individualised, effective and safer healthcare in several disease areas;
2. it builds on the eHealth platform already developed for Health-e-Child and Sim-e-Child to establish a worldwide advanced paediatric digital repository.

Integrating the point of care through state-of-the-art and fast response interfaces, MD-Paedigree services a broad range of off-the-shelf models and simulations to support physicians and clinical researchers in their daily work. MD-Paedigree vertically integrates data, information and knowledge of incoming patients, in participating hospitals from across Europe and the USA, and provides innovative tools to define new workflows of models towards personalised predictive medicine. Conceived as a part of the 'VPH Infostructure' described in the ARGOS, MD-Paedigree encompasses a set of services for storage, sharing, similarity search, outcome analysis, risk stratification, and personalised decision support in paediatrics within its innovative model-driven data and workflow-based digital repository. As a specific implementation of the VPH-Share project, MD-Paedigree fully interoperates with it. It has the ambition to be the dominant tool within its purview. MD-Paedigree integrates methodological approaches from the targeted specialties and consequently analyzes biomedical data derived from a multitude of heterogeneous sources (from clinical, genetic and metagenomic analysis, to MRI and US image analytics, to haemodynamics, to real-time processing of musculoskeletal parameters and fibres biomechanical data, etc.), as well as specialised biomechanical and imaging VPH simulation models.

8.2.1.2. VP2HF

Title: Computer model derived indices for optimal patient-specific treatment selection and planning in Heart Failure

Programme: FP7

Period: October 2013 - September 2016

Coordinator: King's College, London.

Partners:

Centron Diagnostics Ltd (United Kingdom)

CHU Côte de Nacre, Caen (France)

King's College London (United Kingdom)

Philips Technologie (Germany)

Philips France (France)

Simula Research Laboratory As (Norway)

Université Catholique de Louvain (Belgium)

Universitat Pompeu Fabra (Spain)

Inria contact: Dominique Chapelle / Maxime Sermesant

Heart failure (HF) is one of the major health issues in Europe affecting 6 million patients and growing substantially because of the ageing population and improving survival following myocardial infarction. The poor short to medium term prognosis of these patients means that treatments, such as cardiac re-synchronisation therapy and mitral valve repair, can have substantial impact. However, these therapies, are ineffective in up to 50% of treated patients and involve significant morbidity and substantial cost. The primary aim of VP2HF is to bring together image and data processing tools with statistical and integrated biophysical models mainly developed in previous VPH projects, into a single clinical workflow to improve therapy selection and treatment optimisation in HF. The tools will be tested and validated on 200 patients (including 50 historical datasets) across 3 clinical sites, including a prospective clinical study on 50 patients in the last year of the project. The key innovations in VP2HF, which make it likely that the project results will be commercially exploited and have major clinical impact, are:

1. all tools to process images and signals, and to obtain the statistical and biophysical models will be integrated into one clinical software platform that can be easily and intuitively used by clinicians and tried out in the prospective clinical study;
2. to select only the appropriate parts of the tool chain, we use a decision tree stratification approach, which will add maximum value to the predictions that will be used in individual patients, so that the more resource intensive parts will be used when they will add real value.

We expect that the study will result in substantially improved efficacy of the decision making process compared with current guidelines, and that an integrated package that is used as part of clinical workflow will ensure the industrial project partners, in particular Philips, will develop project outputs into dedicated products that will have significant clinical impact.

8.2.1.3. MedYMA

Title: Biophysical Modeling and Analysis of Dynamic Medical Images

Programme: FP7

Type: ERC

Period: April 2012 - March 2017

Coordinator: Inria

Inria contact: Nicholas Ayache

During the past decades, exceptional progress was made with in vivo medical imaging technologies to capture the anatomical, structural and physiological properties of tissues and organs in patients, with an ever increasing spatial and temporal resolution. Physicians are now faced with a formidable overflow of information, especially when a time dimension is added to the already hard to integrate 3-D spatial, multimodal and multiscale dimensions of modern medical images. This increasingly hampers the early detection and understanding of subtle image modifications, which can have a vital impact on the patient's health. To change this situation, a new generation of computational models for the simulation and analysis of dynamic medical images is introduced. Thanks to their generative nature, they will allow the construction of databases of synthetic and realistic medical image sequences simulating various evolving diseases, producing an invaluable new resource for training and benchmarking. Leveraging on their principled biophysical and statistical foundations, these new models will bring an added clinical value once they have been personalized with innovative methods to fit the medical images of any specific patient. By explicitly revealing the underlying evolving biophysical processes observable in the images, this approach will yield new groundbreaking image processing tools to correctly interpret the patient's condition (computer aided diagnosis), to accurately predict the future evolution (computer aided prognosis), and to precisely simulate and monitor an optimal and personalized therapeutic strategy (computer aided therapy). First applications concern high impact diseases including brain tumors, Alzheimer's disease, heart failure and cardiac arrhythmia and will open new horizons in computational medical imaging.

8.3. International Initiatives

8.3.1. Inria International Labs

Inria@SiliconValley

Associate Team involved in the International Lab:

8.3.1.1. GeomStats

Title: Geometric Statistics in Computational Anatomy: Non-linear Subspace Learning Beyond the Riemannian Structure

International Partner (Institution - Laboratory - Researcher):

Stanford (United States) - Department of Statistics - Susan Holmes

Starting year: 2015

See also: http://www-sop.inria.fr/asclepios/projects/GeomStats/

The scientific goal of this associated team is to develop the field of geometric statistics that have key applications in computational anatomy. Computational anatomy is an emerging discipline at the interface of geometry, statistics, image analysis and medicine, which aim is to analyze and model the biological variability of the organs shapes at the population level. An important application in neuroimaging is the spatial normalization of subjects, which is necessary to compare anatomies and functions through images in populations with different clinical conditions.

Research directions have been broken into three axes, the first two being methodologically driven and the last one being application driven. The first axis aims at generalizing the statistical framework from Riemannian to more general geometric structures and even non-manifold spaces (e.g. stratified spaces). The goal is to understand what is gained or lost using each geometric structure. The second axis aims at developing subspace learning methods in non-linear manifolds. This objective contrasts with most manifold learning methods, which assume that subspaces are embedded in a large enough Euclidean space. The third scientific direction is application driven with cross-sectional and longitudinal brain neuroimaging studies. The goal will be to extract reduced models of the brain anatomy that best describe and discriminate the populations under study. This will, for example, help determine the impact location of a treatment for traumatic brain injuries.

8.3.2. Inria International Partners

8.3.2.1. Informal International Partners

8.3.2.1.1. St Thomas' Hospital, King's College London, United Kingdom

Maxime Sermesant is a visiting lecturer in the Division of Imaging Sciences and Biomedical Engineering, St Thomas' Hospital, King's College London lead by Pr Reza Razavi. The XMR facility within this hospital is a unique opportunity to validate and exploit the cardiovascular modelling work.

8.3.2.1.2. Massachusetts General Hospital, Boston

A collaboration with Dr Jan Unklebach, Assistant Professor of Radiation Oncology and Dr Jayashree Kalpathy-Cramer, radiology instructor was initiated in 2013 around the topics of tumor growth modeling, radiotherapy planning and edema characterization from MRI.

8.3.2.1.3. Other International Hospitals

Collaborations with several other European hospitals have been established through the European projects VP2HF and MD PAEDIGREE.

8.4. International Research Visitors

8.4.1. Research visits abroad

In the context of the Associated team GeomStats, part of the Inria International Lab Inria@SiliconValley, there were two research visits in 2015 at the Stanford Statistics Department:

- Xavier Pennec: 3 months (April to June 2015)
- Nina Miolane: 8 months (April to June and August to December 2015)

ATHENA Project-Team

8. Partnerships and Cooperations

8.1. National Initiatives

8.1.1. ANR

8.1.1.1. ANR MRSEI LEMONS

Participants: Maureen Clerc, Théodore Papadopoulo.

Duration:*October 2015 to April 2017* The ANR MRSEI LEMONS aims to consolidate a European Network by organizing meetings and visits, in order to submit a proposal for a MSCA-ITN. The European consortium is led by Inria (coordinator Maureen Clerc).

8.1.1.2. ANR MOSIFAH

Participants: Rachid Deriche, Rutger Fick, Demian Wassermann, Maureen Clerc, Théodore Papadopoulo.

Duration: *October 2013 to September 2017*

This ANR project is about multimodal and multiscale modelling and simulation of the fiber architecture of the human heart. It started on October 2013 and involves three partners: Creatis Team, INSA, Lyon (I. Magnin, Y. Zhu); TIMC-IMAG, CNRS, Grenoble (Y. Uson) and the ATHENA project team.

It consists in modelling and simulating the ex vivo and in vivo 3D fiber architectures at various scales using multiphysical data from different imaging modalities working at different spatial resolutions. To this end, the myocardium of the human heart will be imaged using respectively Polarized Light Imaging (PLI) and dMRI.

Appropriate diffusion models will be explored including second and fourth order DTI models as well as HARDI models such as the single shell Q-Ball Imaging (QBI). These various types of images will be processed within the right Riemannian mathematical framework to provide tensor as well as Ensemble Average Propagator (EAP) and Orientation Distribution Function (ODF) fields. Virtual cardiac fiber structure (VCFS) will then be modelled using myocardial fiber information derived from each of these imaging modalities. Finally, diffusion behavior of water molecules in these VCFSs will be simulated by means of quantum spin theory, which allows computing ex vivo and in vivo virtual diffusion magnetic resonance (MR) images at various scales ranging from a few microns to a few millimeters. From the obtained virtual diffusion MR images, multiscale and probabilistic atlas describing the 3D fiber architecture of the heart ex vivo and in vivo will be constructed. Meanwhile, the simulation involving a large number of water molecules, grid computing will be used to cope with huge computation resource requirement.

We expect to construct a complete database containing a very wide range of simulated (noise and artifact-free) diffusion images that can be used as benchmarks or ground-truth for evaluating or validating diffusion image processing algorithms and create new virtual fiber models allowing mimicking and better understanding the heart muscle structures. Ultimately, the proposed research can open a completely novel way to approach the whole field of heart diseases including the fundamental understanding of heart physiology and pathology, and new diagnosis, monitoring and treatment of patients.

8.1.1.3. ANR VIBRATIONS

Participants: Théodore Papadopoulo, Maureen Clerc, Rachid Deriche, Demian Wassermann.

Duration: *February 2014 to January 2018*

Computational modeling, under the form of a “virtual brain” is a powerful tool to investigate the impact of different configurations of the sources on the measures, in a well-controlled environment.

The VIBRATIONS project proposes to simulate in a biologically realistic way MEG and EEG fields produced by different configurations of brain sources, which will differ in terms of spatial and dynamic characteristics. The research hypothesis is that computational and biophysical models can bring crucial information to clinically interpret the signals measured by MEG and EEG. In particular, they can help to efficiently address some complementary questions faced by epileptologists when analyzing electrophysiological data.

The project follows a three-fold strategy:

- construct virtual brain models with both dynamic aspects (reproducing both hyperexcitability and hypersynchronisation alterations observed in the epileptic brain) and a realistic geometry based on actual tractography measures performed in patients
- explore the parameter space though large-scale simulations of source configurations, using parallel computing implemented on a computer cluster.
- confront the results of these simulations to simultaneous recordings of EEG, MEG and intracerebral EEG (stereotactic EEG, SEEG). The models will be tuned on SEEG signals, and tested versus the surface signals in order to validate the ability of the models to represent real MEG and EEG signals.

The project constitutes a translational effort from theoretical neuroscience and mathematics towards clinical investigation. A first output of the project will be a database of simulations, which will permit in a given situation to assess the number of configurations that could have given rise to the observed signals in EEG, MEG and SEEG. A second – and major - output of the project will be to give the clinician access to a software platform which will allow for testing possible configurations of hyperexcitable regions in a user-friendly way. Moreover, representative examples will be made available to the community through a website, which will permit its use in future studies aimed at confronting the results of different signal processing methods on the same 'ground truth' data.

8.1.2. ADT

8.1.2.1. ADT BOLIS

Participants: Nicolas Schnitzler, Théodore Papadopoulo, Juliette Leblond [APICS], Jean-Paul Marmorat [CMA Ecole des Mines Paritech].

Duration: *December 2014 to December 2016*

ADT BOLIS aims to:

- build a sofware platform dedicated to inverse source localisation, building upon the elements of software found in FindSources3D. The platform will be modular, ergonomic, accessible and interactive. It will offer a detailed visualisation of the processing steps and the results. The goal is to provide a convenient graphical interface and a tool that can be easily distributed and used by professionals (target audience: clinicians and researchers).
- Upgrade medInria to use the latest libraries versions involved (this most notably encompasses VTK 6, Qt 5, and DTK 1.0). Then, these new versions will be used to implement a composer (a graphical tool to chain various actions in medInria) and to develop python scripting (for chaining actions and for adding non-regression testing).

8.1.2.2. ADT OpenViBE-X

Participants: Théodore Papadopoulo, Maureen Clerc, Nathanaël Foy.

Duration: *October 2014 to October 2016*

The OpenViBE-X ADT addresses the OpenViBE Brain Computer Interfaces (BCI) platform, in order to:

1. make BCI easier to apprehend by end-users
2. enrich the interaction with multimodal biosignals (eye gaze, heart-rate)
3. implement methods for auto-calibration and online adaptation of the classification
4. provide support, maintenance and dissemination for this software.

The OpenViBE platform is a central element to BCI research at Inria, and in the international community.

8.2. European Initiatives

8.2.1. FP7 & H2020 Projects

8.2.1.1. ChildBrain ETN

ATHENA is an Associated Partner in this European Training Network: the team will participate in training workshops and receive PhD students in secondments.

Program: European Training Network

Project acronym: ChildBrain

Project title: Advancing brain research in children's developmental neurocognitive disorders

Duration: March 2015 to March 2019

Coordinator: Prof. Paavo Leppänen, University of Jyváskylä, Finland

Other partners: University of Leuven (Belgium), University of Münster (Germany), Rabboud University (The Netherlands), Aston University (United Kingdom), IcoMetrix (Belgium), Elekta (Finland), BESA (Germany)

Abstract: The purpose of the ChildBrain ETN is to train young scientists, i.e. Early Stage Researchers (ESRs), to utilise evidence-based neuroscientific knowledge for helping children, especially those at high risk for dropout due to neurocognitive disorders, to meet future educational and societal demands.

8.3. International Initiatives

8.3.1. Inria International Partners

8.3.1.1. Informal International Partners

- SCIL Laboratory, Sherbrooke University, CA (Maxime Descoteaux)
- CMRR, University of Minnesota, USA (Christophe Lenglet)
- Verona University, It (Gloria Menegaz)
- Department of CISE, the University of Florida, Gainesville, USA (Baba C. Vemuri)
- Centre for Medical Image Computing (CMIC), Dept. Computer Science, UCL, UK (D. Alexander)
- SBIA, University of Pennsylvania Medical School, USA (R. Verma).
- University Houari Boumedienne (USTHB, Algiers) (L. Boumghar) and University of Boumerdes, (D. Cherifi), Algeria.
- BESA company on EEG/MEG source localisation.
- CRM, Centre de Recherche Mathématiques, Montréal, Canada.

8.4. International Research Visitors

8.4.1. Visits of International Scientists

- Maxime Descoteaux (Sherbrooke University, CA) visited ATHENA from March 13 to April 3, 2015
- Gabriel Girard (Sherbrooke University, CA) visited ATHENA from March 13 to April 3, 2015
- Mauro Zuccheli (Verona University, It) visited ATHENA from March 23 to 27, 2015
- Dalila Cherifi (Boumerdes University, Algers) visited ATHENA from April 24 to 27, 2015
- Mouloud Kachouane (USTHB, Algiers) visited ATHENA from November 2015 to October 2016.

8.4.1.1. Internships

Guillermo Alejandro Gallardo Diez

Date: June 2015 - August 2015

Institution: Universidad de Buenos Aires (Argentina)

Etienne Guerlais

Date: October 2015 - February 2016

Institution: Ecole d'ingénieurs informatique CESI, eXia

Jelena Mladenovic

Date: April 2015 - September 2015

Institution: Université de Nice-Sophia Antipolis

Siobhan Powell

Date: May 2015 - Jul 2015

Institution: Queens Univeristy, Ontario (Canada)

DEMAR Project-Team

6. Partnerships and Cooperations

6.1. Regional Initiatives

AOI PARKDEMAR Participants: Christine Azevedo Coste, Benoît Sijobert. Appel d'offre Interne (AOI) CGS Merri (CHU Montpellier). Development and evaluation of Freezing detection system in parkinson disease.
Program Région Languedoc-Roussillon "Manifestations scientifiques 2016" - 11000 euros for the organization of IFESS conference in 2016. http://ifess2016.inria.fr/
LABEX NUMEV Participants: Christine Azevedo Coste, Christian Geny, Benjamin Gilles. A M2 internship will be funded by the NUMEV Labex on the dynamic cartography of tremor using muscular echography.

6.2. National Initiatives

6.2.1. ADT SENSAS - SENSBIO

Participants: Christine Azevedo Coste, David Andreu, Benoît Sijobert.

SENSAS is an Inria ADT (Actions de Développement Technologique), implying several Inria project teams on the "SENSor network ApplicationS" theme. SENSAS aims to propose applications based on wireless sensor and actuator network nodes provided from the work done around senslab and senstools preliminary projects. SENSAS is organized around the following work packages :

- SensRob : Robotics applications
- SensBio : Bio-Logging applications
- SensMGT : Wireless sensor/actuator network management/configuration applications
- SensBox : Wireless sensor/actuator network simulation applications and tools

Our team is mainly implied in the SensBio work package, in particular for the following applications: Spinal Cord Injured Patients FES-Assisted Sit to Stand, Post-Stroke Hemiplegic Patient FES-correction of drop foot, Gait analysis of parkinson freezing and Motion analysis of longterm race data.

6.2.2. INTENSE project

Participants: David Guiraud, Olivier Rossel, Melissa Dali, Christine Azevedo Coste, David Andreu, Jérémie Salles, Guy Cathébras, Fabien Soulier, Baptiste Colombani, Guillaume Souquet, Milan Demarcq.

INTENSE (Initiative Nationale Technologique d'Envergure pour une NeuroStimulation Evoluée) is a PIA-PSPC Project (Programme Investissement d'Avenir, Projets RD Structurants des Pôles de Compétitivité) [2012-2018]. The aim of this project is to develop new implantable devices, based on neurostimulation, for heart failure.

Partners of this project are: DEMAR, SORIN CRM, MXM-Obélia, 3D plus, CEA-Leti, INRA Rennes, INSERM Rennes, HEGP, CHU Rennes.

6.2.3. BCI-LIFT: an Inria Project-Lab

Participants: Mitsuhiro Hayashibe, Saugat Bhattacharyya.

BCI-LIFT is a large-scale 4-year research initiative (2015-2018) which aim is to reach a next generation of non-invasive Brain-Computer Interfaces (BCI), more specifically BCI that are easier to appropriate, more efficient, and suit a larger number of people. We work on BCI-FES study for promoting motor learning.

6.3. European Initiatives

6.3.1. FP7 & H2020 Projects

Program: FP7

Project acronym: EPIONE

Project title: Natural sensory feedback for phantom limb pain modulation and therapy

Duration: 2013-2017

Coordinator: AAU (Aalborg, Denmark)

Other partners: Ecole polytechnique fédérale de Lausanne (EPFL), IUPUI (Indianapolis, USA), Lund University (LUNDS UNIVERSITET), MXM (Vallauris, France), Novosense AB (NS), IMTEK (Freiburg, Germany), UAB (Barcelona, Spain), Aalborg Hospital, Universita Cattolica del Sacro Cuore (UCSC), Centre hospitalier Universitaire Vaudois (CHUV)

Abstract: http://project-epione.eu/

6.4. International Initiatives

6.4.1. Inria Associate Teams not involved in an Inria International Labs

6.4.1.1. NEUROPHYS4NEUROREHAB

Title: Development of neurophysiological test setup for customizing and monitoring patient-specific non-invasive electrical stimulation-facilitated neurorehabilitation.

International Partners (Institution - Laboratory - Researcher):

IITH (India) - Centre for VLSI and Embedded Systems Technology - Shubhajit Roy Chowdhury

IIT Gandhinagar (India) - ___Centre for Cognitive Science ___ - Uttama Lahiri

Start year: 2014

See also: https://team.inria.fr/nphys4nrehab/

Stroke presents with heterogeneous patient-specific impairments in motor, sensory, tone, visual, perceptual, cognition, aphasia, apraxia, coordination, and equilibrium where the functional limitations following stroke are varied, including gait dysfunction, fall risk, limited activities of daily living, difficulties in swallowing, reduced upper extremity function, altered communication, besides others. These heterogeneous patient-specific impairments make planning of the neurorehabilitation therapy challenging. Here, it may be important to stratify the stroke survivors for restorative neurorehabilitation based on the prognosis and the ability of the stroke survivor to undergo therapy depending on their cardiovascular and neuromuscular capacity besides psychological factors such as motivation where the therapy needs to be tailored to individual health condition. The WHO International Classification of Functioning (ICF) model recommends intervention at multiple levels (e.g., impairment, activity, participation) where environment and personal factors can play an important role in resource-limited India. In fact, deconditioned chronic stroke survivor will need to recondition their cardiovascular endurance, metabolic fitness, and muscle conditions with a gradual increase in the intensity (number of hours per day) and frequency (number of days per week) of therapy, providing a higher level as they improve their function. Towards that overarching goal in a low-resource setting, we propose development of neurophysiological screening and monitoring tools using low-cost sensors.

6.4.2. Inria International Partners

6.4.2.1. Declared Inria International Partners

Technology artificial and natural control assisted by electrical stimulation in functional transfers for subjects with disabilities after spinal cord injury Inria principal investigator: Christine Azevedo Coste International partner: Faculty of Ceilandia/ University of Brasilia - Emerson Fachin Martins, leader of the NTAAI-team. Nucleus of Assistive Technology, Accessibility and Innovation. CAPES, Scholarship: BEX 3160/13-0 (Montpellier/France - December 2013 - February 2015) CAPES, Appel: 88881.068134/2014-01 (2015 - 2017) Around 90 million people acquired disabilities from Spinal Cord Injury (SCI) worldwide. The options available to stand up individuals with SCI without orthotics devices do not provide a functional upright position. The wheelchairs and seats to verticalize do not ensure an active participation based in a technology-human interaction. Moreover, the Verticalization devices are rarely used outside. The present international collaboration initiates a series of collaborations between the DEMAR- team and the NTAAI-team based on academic mobility of students and researchers. The general aim of this project is investigated technologies based in the functional electrical stimulation to promote functional transfers of the individuals with disabilities after SCI.

6.4.3. Participation In other International Programs

France-Stanford GRANT :

DEMAR and the Department of Orthopaedic Surgery of Stanford University awarded with a collaborative research grant from the France-Stanford Center for Interdisciplinary Studies. on the topic of "Inertial Sensors Based Analysis of Gait on Children with Spastic Cerebral Palsy". https://project.inria.fr/siliconvalley/2015/11/23/interview-chrisitine-azevedo-coste/

6.5. International Research Visitors

6.5.1. Visits of International Scientists

6.5.1.1. Internships

Mitsuhiro Hayashibe supervised Saugat Bhattacharyya on "Study on Probabilistic nature of Motor Imagery Electroencephalography signals for control", PhD internship, Svaagata.eu: experience Europe as an Indian Erasmus Mundus, Jadavpur University, Kolkata, India, from Oct. 2014 to Jun. 2015.

Mitsuhiro Hayashibe supervised Roberto Baptista on "Framework for Automatic Assessment of Human Motion for Rehabilitation", PhD internship, bourse d'etudes du Gouvernement Bresilien, Fondation Capes, Universidade de Brasilia (UnB), Brasil, from May 2014 to Apr. 2015.

6.5.2. Visits to International Teams

Mitsuhiro Hayashibe visited Dr. Uttama Lahiri - Centre for Cognitive Science, IIT Gandhinagar, India and Dr. Abhijit Das, MD, Director of Neurorehabilitation, AMRI Institute of Neurosciences, Kolkata, India together with Dr. Anirban Dutta under Inria-DST project. (15-24 Jan. 2015).

Mitsuhiro Hayashibe was Visiting Researcher at RIKEN BSI-TOYOYA research institute and worked on "Tacit Synergetic Motor Learning for rehabilitation" (Jul.-Aug. 2015).

6.5.2.1. Research stays abroad

Christine Azevedo Coste is spending 2,5 months (November 2015-February 2016) at Brasilia University as an invited researcher. She is working in collaboration within Emerson FACHIN-MARTINS responsible of the NTAAI (Nucléo de Tecnologia Assistiva, Acessibilidade e Inovacão) initiative. Brazilian program: Science without borders (Ciencías sem fronteiras) CAPES.

GALEN Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

8.1.1. Excellence Clusters

- Program: DIGITEO (Chair)

  Project acronym: SubSample

  Project title: Identification and prediction of Salient brain States through probabilistic structure learning towards fusion of imaging and genomic date

  Duration: 01/2012-12/2015

  Coordinator: ECP - FR
- Program: DIGITEO
  - Project acronym: SOPRANO
  - Project title: Structured Output Prediction on Large Scale Neuroscience Data
  - Duration: 3/2013-3/2016
  - Coordinator: Ecole Centrale Paris - FR
- Program: MEDICEN

  Project acronym: ADOC

  Project title: ADOC – Diagnostic peropératoire numérique en chirurgie du cancer

  Duration: 11/2011-09/2015

  Coordinator: LLTECH - FR

8.2. National Initiatives

8.2.1. ANR

- Program: ANR Blanc International

  Project acronym: ADAMANTIUS

  Project title: Automatic Detection And characterization of residual Masses in pAtients with lymphomas through fusioN of whole-body diffusion-weighTed mrI on 3T and 18F-flUorodeoxyglucoSe pet/ct

  Duration: 9/2012-8/2015

  Coordinator: CHU Henri Mondor - FR
- Program: ANR JCJC

  Project acronym: HICORE

  Project title: HIerarchical COmpositional REpresentations for Computer Vision

  Duration: 10/2010-9/2014

  Coordinator: ECP - FR
- Program: ANR JCJC

  Project acronym: LearnCost

  Project title: Learning Model Constraints for Structured Prediction

  Duration: 2014-2018

Coordinator: Inria Saclay - FR

- Program: ITMOs Cancer & Technologies pour la santé d'Aviesan / INCa

  Project acronym: CURATOR

  Project title: Slice-to-Image Deformable Registration towards Image-based Surgery Navigation & Guidance

  Duration: 12/2013-11/2015

  Coordinator: ECP - FR

8.3. European Initiatives

8.3.1. FP7 & H2020 Projects

8.3.1.1. DIOCLES

Title: Discrete bIOimaging perCeption for Longitudinal Organ modElling and computEr-aided diagnosiS

Type: FP7

Instrument: European Research Council

Duration: September 2011 - August 2016

Coordinator: Nikos Paragios

Partner: Ecole Centrale de Paris (FR)

Inria contact: Nikos Paragios

Recent hardware developments from the medical device manufacturers have made possible non-invasive/in-vivo acquisition of anatomical and physiological measurements. Despite enormous progress made on the field of biomedical image analysis still a huge gap exists between clinical research and clinical use. The aim of this proposal is three-fold. First we would like to introduce a novel biomedical image perception framework for clinical use towards disease screening and drug evaluation. Such a framework is expected to be modular (can be used in various clinical settings), computationally efficient (would not require specialized hardware), and can provide a quantitative and qualitative anatomo-pathological indices. Second, leverage progress made on the field of machine learning along with novel, efficient, compact representation of clinical bio-markers toward computer aided diagnosis. Last, using these emerging multi-dimensional signals, we would like to perform longitudinal modelling and understanding the effects of aging to a number of organs and diseases that do not present pre-disease indicators such as brain neurological diseases, muscular diseases, certain forms of cancer, etc.

8.3.1.2. I-SUPPORT

Title: ICT-Supported Bath Robots

Programm: FP7

Duration: March 2015 - March 2018

Coordinator: Robotnik Automation S.L.L.

Partners:

Bethanien Krankenhaus - Geriatrisches Zentrum - Gemeinnutzige GMBH (Germany)

Fondazione Santa Lucia (Italy)

Institute of Communication and Computer Systems (Greece)

Karlsruher Institut für Technologie (Germany)

Theofanis Alexandridis Kai Sia Ee (OMEGATECH) (Greece)

Robotnik Automation Sll (Spain)

Scuola Superiore di Studi Universitari E di Perfezionamento Sant'Anna (Italy)

Frankfurt University of Applied Sciences (Germany)

Inria contact: Iasonas Kokkinos

The I-SUPPORT project envisions the development and integration of an innovative, modular, ICT-supported service robotics system that supports and enhances older adults' motion and force abilities and assists them in successfully, safely and independently completing the entire sequence of bathing tasks, such as properly washing their back, their upper parts, their lower limbs, their buttocks and groin, and to effectively use the towel for drying purposes. Advanced modules of cognition, sensing, context awareness and actuation will be developed and seamlessly integrated into the service robotics system to enable the robotic bathing system to adapt to the frail elderly population' capabilities and the frail elderly to interact in a master-slave mode, thus, performing bathing activities in an intuitive and safe way. Adaptation and integration of state-of-the-art, cost-effective, soft-robotic manipulators will provide the hardware constituents, which, together with advanced human-robot force/compliance control that will be developed within the proposed project, will form the basis for a safe physical human-robot interaction that complies with the most up-to-date safety standards. Human behavioural, sociological, safety, ethical and acceptability aspects, as well as financial factors related to the proposed service robotic infrastructure will be thoroughly investigated and evaluated so that the I-SUPPORT end result is a close-to-market prototype, applicable to realistic living settings.

8.3.1.3. MOBOT

Title: Intelligent Active MObility Aid RoBOT integrating Multimodal Communication

Programm: FP7

Duration: February 2013 - January 2016

Coordinator: Technische Universität München

Partners:

Bartlomiej Marcin Stanczyk (Poland)

Athena Research and Innovation Center in Information Communication & Knowledge Technologies (Greece)

Bethanien Krankenhaus - Geriatrisches Zentrum - Gemeinnutzige (Germany)

Diaplasis Rehabilitation Center (Greece)

Ecole Centrale des Arts et Manufactures (France)

Technische Universitaet Muenchen (Germany)

Ruprecht-Karls-Universitaet Heidelberg (Germany)

Inria contact: Iasonas Kokkinos

Mobility disabilities are prevalent in our ageing society and impede activities important for the independent living of elderly people and their quality of life. The MOBOT project aims at supporting mobility and thus enforcing fitness and vitality by developing intelligent active mobility assistance robots for indoor environments that provide user-centred, context-adaptive and natural support. Our driving concept envisions cognitive robotic assistants that act (a) proactively by realizing an autonomous and context-specific monitoring of human activities and by subsequently reasoning on meaningful user behavioural patterns, as well as (b) adaptively and interactively, by analysing multi-sensory and physiological signals related to gait and postural stability, and by performing adaptive compliance control for optimal physical support and active fall prevention. Towards these targets, a multimodal action recognition system will be developed to monitor, analyse and predict user actions with a high level of accuracy and detail. The main thrust of our approach will be the enhancement of computer vision techniques with modalities such as range sensor images, haptic information as well as command-level speech and gesture recognition. Data-driven multimodal human behaviour analysis will be conducted and behavioural patterns will be extracted. Findings

will be imported into a multimodal human-robot communication system, involving both verbal and nonverbal communication and will be conceptually and systemically synthesised into mobility assistance models taking into consideration safety critical requirements. All these modules will be incorporated in a behaviour-based and context-aware robot control framework. Direct involvement of end-user groups will ensure that actual user needs are addressed. Finally, user trials will be conducted to evaluate and benchmark the overall system and to demonstrate the vital role of MOBOT technologies for Europe's service robotics.

8.3.1.4. RECONFIG

Type: FP7

Defi: Cognitive Systems and Robotics

Instrument: Specific Targeted Research Project

Objectif: Cognitive Systems and Robotics

Duration: February 2013 - January 2016

Coordinator: Dimos Dimarogonas

Partner: KTH (SE)

Inria contact: Iasonas Kokkinos

The RECONFIG project aims at exploiting recent developments in vision, robotics, and control to tackle coordination in heterogeneous multi-robot systems. Such systems hold promise for achieving robustness by leveraging upon the complementary capabilities of different agents and efficiency by allowing sub-tasks to be completed by the most suitable agent. A key challenge is that agent composition in current multi-robot systems needs to be constant and pre-defined. Moreover, the coordination of heterogeneous multi-agent systems has not been considered in manipulative scenarios. We propose a reconfigurable and adaptive decentralized coordination framework for heterogeneous multiple & multi-DOF robot systems. Agent coordination is held via two types of information exchange: (i) at an implicit level, e.g., when robots are in contact with each other and can sense the contact, and (ii) at an explicit level, using symbols grounded to each embodiment, e.g, when one robot notifies one other about the existence of an object of interest in its vicinity.

8.3.1.5. Strategie

Title: Statistically Efficient Structured Prediction for Computer Vision and Medical Imaging

Programm: FP7

Duration: January 2014 - December 2017

Coordinator: Inria

Inria contact: Matthew Blaschko

'Inference in medical imaging is an important step for disease diagnosis, tissue segmentation, alignment with an anatomical atlas, and a wide range of other applications. However, imperfections in imaging sensors, physical limitations of imaging technologies, and variation in the human population mean that statistical methods are essential for high performance. Statistical learning makes use of human provided ground truth to enable computers to automatically make predictions on future examples without human intervention. At the heart of statistical learning methods is risk minimization - the minimization of the expected loss on a previously unseen image. Textbook methods in statistical learning are not generally designed to minimize the expected loss for loss functions appropriate to medical imaging, which may be asymmetric and non-modular. Furthermore, these methods often do not have the capacity to model interdependencies in the prediction space, such as those arising from spatial priors, and constraints arising from the volumetric layout of human anatomy. We aim to develop new statistical learning methods that have these capabilities, to develop efficient learning algorithms, to apply them to a key task in medical imaging (tumor segmentation), and to prove their convergence to optimal predictors. To achieve this, we will leverage the structured prediction framework, which has shown impressive empirical results on a wide range

of learning tasks. While theoretical results giving learning rates are available for some algorithms, necessary and sufficient conditions for consistency are not known for structured prediction. We will consequently address this issue, which is of key importance for algorithms that will be applied to life critical applications, e.g. segmentation of brain tumors that will subsequently be targeted by radiation therapy or removed by surgery. Project components will address both theoretical and practical issues.'

8.4. International Initiatives

8.4.1. Inria International Partners

8.4.1.1. Informal International Partners

- University of Oxford – Collaborative research with Andrea Vedaldi. Collaboration Topic: Deep Learning for Texture Recognition.
- Google Research – Collaborative research with George Papandreou. Collaboration Topic: Deep Learning for Semantic Segmentation.
- Universitad Polytecnical de Catalunia – Collaborative research with Francesc Moreno. Collaboration Topic: Deep Learning for Image Descriptors.
- Ecole Polytechnique Federale de Lausanne (EPFL) – Collaborative research with Eduard Trulls. Collaboration Topic: Deep Learning for Image Descriptors.
- University of California at Los Angeles – Collaborative research with Alan Yuille. Collaboration Topic: Deep Learning for Semantic Segmentation.
- University of Massachusetts at Amherst – Collaborative research with Subhransu Maji. Collaboration Topic: Deep Learning for Texture Recognition.
- Ryerson University – Collaborative research with Kostas Derpanis. Collaboration Topic: Deep Learning for Learning Segmentation.
- Ecole Polytechnique de Montreal - Collaborative research with Samuel Kadoury. Collaboration Topic: Multi-atlas co-segmentation, co-registration.
- University of Pennsylvania - Collaborative research with Aristeidis Sotiras. Collaboration Topic: Higher Order Graphs in biomedical image analysis.

8.5. International Research Visitors

8.5.1. Visits of International Scientists

- Angst, Roland. Max Planck Center for Visual Computing and Communication, GE (April 2015)
- Professor Maragos, Petros: Technical University of Athens, GR (13-20 November 2015)

MIMESIS Team

8. Partnerships and Cooperations

8.1. National projects

8.1.1. ADT (Aide au Développement Technologique, Inria) - DynMesh

The objectives of this ADT are the coupling of SOFA, the physical simulation platform supported by Inria, and CGoGN, the mesh management library developed within the ICube lab at Strasbourg. It aims at extending the physical engine SOFA with the topological kernel of CGoGN that supports a wide variety of mesh and many local remeshing operations. The coupling of both software libraries will provide users of physical engines with new tools for the development of simulations involving topological changes like cutting, fracturing, adaptation of the resolution or improving contact management or collision detection. The impacts are numerous and will be operated directly within the MIMESIS Team, with our partners or through the establishment of new collaborations.

8.1.2. ADT - Sofa

SOFA Large Scale Development Initiative (ADT) : the SOFA project is an international, multi-institution, collaborative initiative, aimed at developing a flexible and open source framework for interactive simulations. This will eventually establish new grounds for a widely usable standard system for long-term research and product prototyping, ultimately shared by academic and industrial sites. The SOFA project involves 4 Inria teams: ASCLEPIOS, DEFROST, IMAGINE and MIMESIS. The development program of the ADT started in 2007. This ADT ended in September 2015 and the associated contract of our SOFA engineer Marc Legendre ended at the same time.

8.1.3. ADT - SofaOR

In December 2014, a new ADT national initiative started. The objective of this ADT is twofold: first, we aim at achieving a level of quality and robustness compatible with IEC 62304 for the core of SOFA and a reduced set of components. This does not include the certification of the code itself, but rather the implementation of a comprehensive development process that will enable the certification by companies wishing to integrate this code into their systems. The second objective is to add new features specific to the needs of using intra-operative guiding tools: interoperability with equipment from the operating room, acquisition and real-time processing of full HD video streams, data assimilation and predictive filters, path planning, visualization for augmented reality, or user interfaces dedicated to the operating room.

8.1.4. ANR - IDEFI

In the IDEFI ANR, the MIMESIS team is involved in the EVEREST project which aims to develop a new generation on-line training platforms, dedicated to the theory and practice of image-guided minimally invasive surgery. A central objective is to develop a framework for the integration and the rapid spread of numerical interactive simulation systems, associated with online assessment methodologies. The IHU Strasbourg is the ANR project leader and we collaborate on the topic of virtual simulations.

8.1.5. ANR - RESET

At the end of 2014, the team has been awarded a new ANR project: RESET. This project started in March 2015. Its objective is to develop a high-fidelity training system for retinal surgery. Retina surgery is an increasingly performed procedure for the treatment of a wide spectrum of retinal pathologies. Yet, as most micro-surgical techniques, it requires long training periods before being mastered. This simulator is built upon our scientific expertise in the field of real-time simulation, and our success story for technology transfer in the field of cataract surgery simulation (MSICS simulation developed for the HelpMeSee foundation).

8.1.6. IDEX - CNRS

The aim of the project CONECT (Couplage de la rObotique et de la simulatioN mEdicale pour des proCédures auTomatisées) is to develop a robotic system for needle insertion in deformable tissues which is entirely controlled and driven by a numerical simulation. The results of this work could be extremely beneficial for medical applications, such as brachytherapy or biopsy, given the accuracy and the precision required in this kind of procedures. A first demonstration is currently under development where the needle will be inserted in a silicone gel samples. Given a non-straight predefined trajectory, our goal is to control a Mitsubishi MRV1 robot that will automatically insert a needle along the predefined path, taking into account the deformation of both the environment and the needle. The deformation of the gel is tracked with camera using the Optitrack system. The simulation is based on real time finite element models. Based on inverse simulations, we are developing a control model that provides the kinematics of the robot such that the needle remains on the trajectory during the insertion. The activities carried out already allowed a first publication at IROS (2015) "Haptic Rendering of Hyperelastic Models with Friction" and the presentation of a poster at the conference DD23 in South Korea in july 2015 "Domain Decomposition for FE Simulation for Needle Insertion".

8.1.7. REBOAsim, Department of Defense USA

REBOA stands for Resuscitative Endovascular Balloon Occlusion of the Aorta. The objective of the REBOAsim project is to develop a low-cost miniaturized tracking and haptic interface for catheters and guidewires, meeting requirements for training and intraoperative guidance of Resuscitative Endovascular Balloon Occlusion of the Aorta (and other catheterization procedures). The second aspect of the project is the development of a computer-based simulation of REBOA procedures, allowing the training of medical personnel. This project was accepted in late 2015. In this context, we collaborate with the American Department of Defense.

8.1.8. IHU, Strasbourg

Our team has been selected to be part of the IHU of Strasbourg. This institute, for which funding (67M€) has just been announced, is a very strong innovative project of research dedicated to future surgery of the abdomen. It will be dedicated to minimally invasive therapies, guided by image and simulation. Based on interdisciplinary expertise of academic partners and strong industry partnerships, the IHU aims at involving several specialized groups for doing research and developments towards hybrid surgery (gesture of the surgeon and simulation-based guidance). Our group and SOFA have a important place in the project. Since September 2011 a part of our team is located within the IHU, to develop a number of activities in close collaboration with clinicians.

8.2. National collaborations

At the national level, the MIMESIS team collaborates with:

ICube AVR team: we are currently working with the medical robotics team on percutaneous procedures, in particular robotized needle insertion (with Prof. Bernard Bayle), and needle tracking in medical images (with Elodie Breton). We are also collaborating with Jonathan Vappou on elastography.

ICube IGG team: we have two active collaborations, one with Dr. Caroline Essert on trajectory planning (in the context of Deep Brain Stimulation) and the group involved in research on dynamic topologies. These collaborations are supported by two IHU projects: BILIKIMO and HAYSTACK.

IHU Strasbourg: as mentionned in 8.1.8 , our team is one of the principal partners of the IHU Strasbourg. We developed a number of projects in close collaboration with clinicians and members of IHU.

LML Lille: is a French research laboratory (UMR CNRS 8107) part of the Carnot institute ARTS. With more than two hundreds researchers, LML focuses on the following research area : mechanical reliability and Tribology, fluid mechanics, civil engineering and soil mechanics. In 2105, Mathias Brieu from LML visited our team.

Nouvel Hopital Civil, Strasbourg: since 2014 we have been working with Prof. David Gaucher, an ophthalmologist surgeon, expert in retina surgery. This led to the submission of the ANR project RESET with started in March 2015. We also collaborate with Prof. Patrick Pessaux, a surgeon who helps us in the context of the SOFA-OR project.

R&D team at IRCAD: the computer science group at IRCAD has been involved in segmentation, 3D reconstruction and augmented reality for abdominal surgery since the 2000. An important activity on simulation also took place and led to the creation of a start-up company, Digital Trainers. Currently, the main activities are centered around augmented reality, registration, and medical imaging.

TIMC, Grenoble: this large research group has a strong background in computer-aided surgery, medical imaging, registration, statistical and bio-mechanical modeling. We have regular interactions with this various members of this group. We are collaborating with Yohan Payan (DR CNRS) on the modeling and simulation of the brain shift. A common PhD thesis started on that topic in late 2014. Other areas of interest are in the field of advanced soft tissue modeling and computer aided surgery,

8.3. Inria collaborations

Within Inria, the MIMESIS team collaborates with:

ASCLEPIOS: although the core activities of team are in the field of medical image analysis, it also has a strong expertise in physics-based simulation of the heart. We collaborated on the development of an electro-mechanical model of the heart, and on some core components of SOFA. We collaborate with the ASCLEPIOS team on the development of the SOFA framework and on the development of a simulation system for radio-frequency ablation in the case of cardiac arrhythmia,

DEFROST: the team imagines future robots which don't need to be "rigid" but made of complex deformable structures, composed of stiff and soft regions, close to organic materials that can be found in nature. Soft robotics opens very attractive perspectives in terms of new applications, reduction of manufacturing costs, robustness, efficiency and security. It could constitute a great jump in robotics in the following years. We continue to interact with the team in Lille given our common research background. A joint article of constraint-based haptic modeling has already been submitted.

IMAGINe: the team has a general focus on animation and simulation of natural objects. We essentially collaborate with Prof. François Faure on real-time finite element techniques, collision detection and contact response (which led to a SIGGRAPH paper) and the development of SOFA,

MAGRIT: their research field is computer vision, with a focus on augmented reality applications. The team is also fairly involved in computer-based solutions for the planning or the simulation of interventional radiology procedures, with a strong collaboration with the CHU in Nancy. We collaborate with the MAGRIT team in the area of interventional radiology and augmented reality. A common PhD thesis, whose subject was to develop implicit representations of anatomical structures such as blood vessels or aneurysms, was defended in 2013. Another joint PhD thesis was defended in January 2015 on the topic of non-rigid augmented reality and combined the computer vision expertise of MAGRIT with our expertise on real-time simulation and biomechanical modeling.

8.4. European Initiatives

8.4.1. RASimAs

2015 was the second year of the RASimAs project (STREP project funded under FP7) during which we developed new models of the biomechanics of the leg and arm, as well as the simulation of the insertion of the anaesthesiology needle. Regional anaesthesia has been used increasingly during the past four decades. This is due to the perceived advantages of reduced postoperative pain, earlier mobility, shorter hospital stay, and significantly lower costs. Current training methods for teaching regional anaesthesia include cadavers, video teaching, ultrasound guidance, and simple virtual patient modeling. These techniques have limited capabilities

and do not consider individual anatomy. The goal of this project is to increase the application, the effectiveness and the success rates of RA and furthermore the diffusion of the method through the development VPH models for anaesthesia. The goal of the MIMESIS team is to provide the computational infrastructure for the physics-based simulation and to propose new methods for patient-specific modeling and simulation of soft tissues and their interaction with the needle, including its effect on nerve physiology.

See http://rasimas.imib.rwth-aachen.de for more details.

In the context of the RASimAS project, we collaborate with the company:

- **SenseGraphics**: develops next generation medical simulator software for a wide range of surgical procedures. It is used in simulators for training surgeons in various fields such as robotic surgery, eye surgery, dentistry, ultrasound interpretation and anesthesia. The simulators combine the latest technologies in real-time graphics rendering as well as advanced force feedback to allow the surgeons to have an experience that is as close to reality as possible.

With the RASimAS project, we also collaborate with: the University Hospital Aachen, RWTH Aachen University, Bangor University, University College Cork, Universidad Rey Juan Carlos, Foundation for Research and Technology Hellas, Zilinska univerzita v Ziline, Katholieke Universiteit Leuven and the Stiftelsen Sintef.

8.5. International Initiatives

8.5.1. Inria International Partners

At the international scale, the MIMESIS team collaborates with:

CIMIT, Boston: we are restarting our interactions on interventional radiology simulation, in particular the design and development of a hardware interface for tracking catheters and guidewires. A joint proposal to the DoD has been submitted to this end.

Harvard Biorobotics lab, Cambridge: this group focuses on the role of sensing and mechanical design in motor control, in both robots and humans. This work draws upon diverse disciplines, including biomechanics, systems analysis, and physiology. We started a collaboration on inverse problems for identifying optimal areas of cardiac ablation using our work on electro-mechanical modeling of the heart. Other areas of collaboration are planned, such as cardiac valve interactions with blood flow.

Humanoid and Intelligence Systems Lab, Karlsruhe Institute of Technology: we started a collaboration with Dr Stefanie Speidel and Dr. Stefan Suwelack on the topics of real-time soft tissue modeling and laparoscopic augmented reality.

Institute of Computer Science, Masaryk University, Czech Republic: we have an extensive collaboration with Igor Peterlik at the ICS, leading to 7 publications over that past 18 months. This collaboration covers the fields of non-rigid registration, augmented reality and haptics.

Interactive Graphics and Simulation, Innsbruck: the IGS group in Innsbruck is a continuation of a group led at ETH by Matthias Harders. Its scientific focus is on physically-based simulation, computer haptics, and to a limited extent, augmented reality. The main application area is the medical domain.

Surgical Planning Lab, Boston: this research laboratory at Brigham and Women's Hospital has a large expertise in the analysis of diagnostic data using computational image analysis. We know this group very well, in particular in the field of Deep Brain Stimulation and through their work on Open Source solutions for computer aided surgery. We are regularly interacting with them on the development of a version of SOFA dedicated to the operating room.

SINTEF, Norway: we are currently collaborating with SINTEF in the context of the european project RASimAs, and also on other aspects, such as the creation of anatomically correct and accurate datasets from patient-specific data. We are also discussing future collaborations in the context of hepatic surgery simulation and augmented reality (we have jointly written a H2020 proposal on this topic).

Team Legato, University of Luxembourg: since last year we have active discussions with Prof. Stéphane Bordas on real-time soft tissue cutting simulation. This has already led to a journal article in Media [33] and a co-supervision of a post-doctoral fellow.

8.6. International Research Visitors

8.6.1. Visitors

In 2015, MIMESIS invited several visitors:

- Jim Ueltschi (founder of the HelpMeSee non-profit organization)
- Karol Miller (Winthrop Professor, School of Mechanical and Chemical Engineering, The University of Western Australia)
- Stéphane Bordas (LEGATO team, Luxembourg)
- Karel van Gelder (Product manager, MOOG, Amsterdam)
- Alexandre Krupa (Inria, Rennes)
- Mathias Brieu (Laboratoire de Mécanique, Ecole Centrale Lille)

8.6.2. Internships

In 2015, the MIMESIS welcomed two international interns (for 6 months):

Santiago Camacho, Universidad de Buenos Aires, worked on "Improvement of Visualization Tools for Augmented Reality Applications"

Sabrina Izcovich, Universidad de Buenos Aires, worked on "Quadratic Tetrahedron Element for FEM simulations".

8.6.3. Visits to International Teams

8.6.3.1. Explorer programme

This year, Hugo Talbot obtained an Inria Explorer grant in the context of a partnership with the Harvard BioRobotics Laboratory from Harvard, Cambridge. The Explorer programme covered the one-month visit (June 2015). This visit allowed to discuss about our respective work around simulation, especially concerning simulation in the field of cardiology. This was also the opportunity to establish several academic and industrial contacts in the United States. Hugo Talbot namely visited:

- **Thermedical**: is a company developing a new generation of radio-frequency catheters.
- **Center of Medical Simulation**: is a simulation center focusing on training based on mannequins.
- **SimQuest**: is a company developing simulation technologies for medicine, very close to the research topic of our team.
- **Surgical Planning Laboratory** (Brigham and Womens' Hospital) is a research center very close to the clinics and working mainly on medical imaging, but also interested in the medical simulation.
- **CIMIT**: is a research center developing mannequins for training.

MNEMOSYNE Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

9.1.1. PsyPhINe: Cogito Ergo Es

Participant: Nicolas Rougier.

PEPS site Mirabelle (CNRS & University of Lorraine) gathering researchers from the following institutes: MSH Lorraine (USR3261), InterPsy (EA 4432), APEMAC, EPSaM (EA4360), Archives Henri-Poincaré (UMR7117), Loria (UMR7503).

PsyPhiNe is an interdisciplinary and exploratory project between philosophers, psychologists and computer scientists. The goal of the project is related to cognition and behavior. Cognition is a set of processes that are difficult to unite in a general definition. The project aims to explore the idea of assignments of intelligence or intentionality, assuming that our intersubjectivity and our natural tendency to anthropomorphize play a central role: we project onto others parts of our own cognition. To test these hypotheses, our aim is to design a "non-verbal" Turing Test, which satisfies the definitions of our various fields (psychology, philosophy, neuroscience and computer science), using a robotic prototype. Some of the questions that we aim to answer are: is it possible to give the illusion of cognition and of intelligence through such a technical device? How elaborate must be the control algorithms or ”behaviors” of such a device to fool test subjects? How many degrees of freedom must it have?

9.1.2. Project PEPS of the Idex: Dopamine control of a novel basal ganglia cell-type

Participants: André Garenne, Nicolas Rougier.

The neurotransmitter dopamine (DA) plays a key role in basal ganglia (BG) circuits. However, despite the fundamental importance of DA in those circuits, the electrophysiological effects of dopamine on target neurons are largely unknown. Furthermore, contrary to classical models that only view the globus pallidus (GP) as a relay station of the indirect pathway, our neuroscientist colleagues at IMN have discovered a novel GP cell-type called the Arkypallidal (Arky-GP) neurons that only project to striatum in a very dense way. We thus have been modeling the structure of the striatum ($\approx$ 3 millions neurons) and the globus pallidus ($\approx$ 50,000 neurons) in the mouse using down-scaled models. Two models have been made, the first one utilized the neural field theory while the other one utilized integrate-and-fire neurons. The goal was to study the activity around the electrode contact point in order to give account on recorded activity in vivo. Unfortunately, electrophysiological recording were not precise enough to conclude on these models.

9.1.3. Project of the Aquitaine Regional Council: Decision making, from motor primitives to action

Participants: Nicolas Rougier, Meropi Topalidou.

The aim of this project (partly funding the PhD of Meropi Topalidou) is to investigate decision making at intermediate level in order to establish the link between motor primitives and higher level actions. The question is to understand how continuous complex motor sequences can be dynamically represented as actions such that they can be manipulated to resolve conflict when several actions are possible. In tight collaboration with Thomas Boraud from the Institute of Neurodegenerative Diseases, we have been modeling the basal ganglia such as to explain the formation of habits in the monkey. This fruitful collaboration lead to the joint publication of several articles [4], [43], [42], [5] and the model enabled us to make very precise prediction on the behavior of the monkeys (dissociation of goal-directed and habitual behavior). Early experiments on two female macaques tend to confirm the prediction.

9.1.4. Collaboration with the Neurocentre Magendie on parameter optimization: Neurobees

Participant: André Garenne.

The development of computational models of neurons and networks typically involves tuning the numerical parameters to fit experimental results. Parameter tuning can sometimes be manually completed, it is more convenient to use automated optimization algorithms at least for two reasons: (i) to apply an homogeneous processing to all the calculation and parameter space exploration which alleviates operator influence and (ii) to avoid a tedious and uncertain result from human operators when the dimensionality increases. A multi-agent algorithm in line with ABC (Artificial Bee Colony) paradigm has been applied to new benchmark tests in order to ensure its robustness and better performances, especially when compared to evolutionary and swarm algorithms and this has recently been confirmed, thanks to the local Plafrim computation facilities. A draft paper is then currently modified before submission to take into account these last results.

9.1.5. Thematic Transverse Action of the University of Bordeaux: Project MISTERE

Participant: André Garenne.

The MISTERE (Etude du Mécanisme d'Interaction des Signaux de Téléphonie mobile sur des Réseaux de neurones in vitro) project has been recently accepted and we have obtained financial support and 1 year of post-doctoral contract by the Science and Technology department of the University of Bordeaux. The main topic of this project lies in the elucidation of the cellular mechanisms of the effects of the GSM radio frequencies (GSM-RF) on the neuronal activity. The approach will consist both in computational modeling studies and in pharmacological tests of neuronal cultures activity when submitted to GSM-RF.

9.2. National Initiatives

9.2.1. GDR3672 - BioComp - Material Implementation of natural computation

Participant: Nicolas Rougier [member of the steering commitee].

The GDR BIOCOMP has been officially created on January 2015 and gathers the INP, INSIS, INS2I, INSB, INC institutes of the CNRS. The goal of this GDR is to facilitate interdisciplinary exchanges in France around a common goal: the realization of bio-inspired hardware systems. More precisely, this GDR seeks to understand the mechanisms at work in biological systems to create chips based on natural computation, but also vice versa, building hardware architectures as test systems to better understand biology. In France there is a wealth of expertise in all disciplines concerned with hardware implementations of natural computation: biology, computational neuroscience, mathematics, computer architecture and computer systems, microelectronics, nanotechnology and physics. Making bio-inspired chips is extremely complex and requires advanced skills in all these disciplines. By organizing interdisciplinary meetings and conferences, the goal is hence to bring together different communities so that they can understand each other and work together.

9.2.2. Project Motus of the ANSES

Participant: André Garenne.

The MOTUS project (MOdulaTion dU Signal RF et effets sur le cerveau : approche in vivo et in vitro) has been recently accepted and will be financed by the ANSES (the french national agency for health security). This 3 years project includes substantial financial support as well as 2 years of post-doctoral contracts with our partner IMS regarding the effects of GSM-RF on living matter and especially neuronal activity and development. It is designed to be synergistic with the MISTERE project previously obtained (cf section 9.1.5). Our main involvement will concern electrophysiological data and spike trains analysis as well as the development of pharmacological protocols to test GSM-RF effects hypotheses.

9.2.3. Project Mimacore of the CNRS Challenge Imag'In

Participants: Frédéric Alexandre, Nicolas Rougier.

Better understanding the resting states (regional interactions and corresponding functional networks in the brain when the subject is at rest) is of central interest for a systemic approach of brain understanding. As we think that this domain is not mature enough for a direct functional modeling approach, we try to get familiar with it, through this imaging study. In this exploratory study funded by the CNRS, we are associated with three teams in neuroscience developing three imaging techniques (MRS, MRI, Clarity), to explore resting states in rodents and learn more about their genesis.

9.3. International Initiatives

9.3.1. Inria Associate Teams not involved in an Inria International Labs

9.3.1.1. Braincraft

Title: Braincraft

International Partner (Institution - Laboratory - Researcher):

University of Colorado, Boulder (United States) - Computational Cognitive Neuroscience - Randall O'Reilly

Start year: 2015

We develop with this team a computationally-based understanding of the neural circuits involved in decision making, namely basal ganglia and prefrontal cortex. More precisely, we want to understand what are the processes by which animals and humans select their actions based on their motivations and on the consequences of past actions. This is a fundamental question in neurosciences, with implications to ethology, psychology, economics, sociology and computer science. Through a unique combination of expertise in cognitive psychology, neurosciences and computer science, this associate team will foster a collaboration for developing a computationally-based understanding of the neural circuits involved in decision making, namely basal ganglia and prefrontal cortex. One of the key question is to know the overall contribution of these structures and their function in the decision process.

9.3.2. Project BGaL with India

In the 3-years project "Basal Ganglia at Large (BGaL)", funded by the CNRS and the CEFIPRA, we collaborate with the computer science department of IIIT Hyderabad and the biomedical department of IIT Madras, for the design of models of basal ganglia and for their implementation at large scale (*cf.* § 7.4) as well as for their relation with other brain structures (*cf.* § 7.2).

9.3.3. Project ECOS-Sud with Chile

In the 3-years project "A network for computational neuroscience, from vision to robotics", funded by ECOS-Sud and Conicyt, we collaborate with University Santa Maria and University of Valparaiso in Chile, and also with another Inria EPI, NeuroMathComp. The goal of the project is to rely on our experience of previous collaborations with these teams, to develop original tools and experimental frameworks to open our scientific domains of investigation to new fields of valorization, including medical (neurodegeneration) and technological aspects (robotics).

9.4. International Research Visitors

9.4.1. Visits of International Scientists

9.4.1.1. Internships

Nallapu Bhargav Teja

Date: June 2015 - Dec 2015

Institution: University of Hyderabad (India)

NEUROMATHCOMP Project-Team

7. Partnerships and Cooperations

7.1. Regional Initiatives

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

7.2. National Initiatives

7.2.1. ANR

7.2.1.1. KEOPS

See section "International Initiatives" below.

7.3. European Initiatives

7.3.1. FP7 & H2020 Projects

7.3.1.1. MATHEMACS

Title: MATHEmatics of Multi-level Anticipatory Complex Systems

Programm: FP7

Duration: October 2012 - September 2015

Coordinator: Max Planck Institute for Mathematics in the Sciences

Partners:
see the webpage of the project.

Inria contact: Olivier Faugeras

The MATHEMACS project aims to develop a mathematical theory of complex multi-level systems and their dynamics. In addition to considering systems with respect to a given level structure, as is natural in certain applications or dictated by available data, the project has the unique goal of identifying additional meaningful levels for understanding multi-level systems. This is done through a general formulation based on the mathematical tools of information and dynamical systems theories.
To ensure that the theoretical framework is at the same time practically applicable, three key application areas are represented within the project, namely neurobiology, human communication, and economics. These areas not only provide us with some of the best-known epitomes of complex multi-level systems, but also constitute a challenging test bed for validating the generality of the theory since they span a vast range of spatial and temporal scales.
Furthermore, they have an important common aspect; namely, their complexity and self-organizational character is partly due to the anticipatory and predictive actions of their constituent units. The MATHEMACS project contends that the concepts of anticipation and prediction are particularly relevant for multi-level systems since they often involve different levels. Thus, as a further unique feature, the project includes the mathematical representation and modeling of anticipation in its agenda for understanding complex multi-level systems.
For validating the theory on large heterogeneous data sets, the project has a specific component with exclusive access to a wide range of data from human movement patterns to complex urban environments.
In this way, MATHEMACS provides a complete and well-rounded approach to lay the foundations of a mathematical theory of the dynamics of complex multi-level systems.

7.3.1.2. RENVISION

Title: Retina-inspired ENcoding for advanced VISION tasks

Programm: FP7

Duration: March 2013 - February 2016

Coordinator: Instituto Italiano di Tecnologia (Pattern Analysis and Computer vision) Vittorio Murino

Partners:

PAVIS, NET3 Fondazione Istituto Italiano di Tecnologia (Italy)

Institute for Adaptive and Neural Computation, The University of Edinburgh (United Kingdom)

Institute of Neuroscience, University of Newcastle Upon Tyne (United Kingdom)

Inria contact: Bruno Cessac

The retina is a sophisticated distributed processing unit of the central nervous system encoding visual stimuli in a highly parallel, adaptive and computationally efficient way. Recent studies show that rather than being a simple spatiotemporal filter that encodes visual information, the retina performs sophisticated non-linear computations extracting specific spatio-temporal stimulus features in a highly selective manner (e.g. motion selectivity). Understanding the neurobiological principles beyond retinal functionality is essential to develop successful artificial computer vision architectures. RENVISION's goal is, therefore, twofold: i) to achieve a comprehensive understanding of how the retina encodes visual information through the different cellular layers; ii) to use such insights to develop a retina-inspired computational approach to high-level computer vision tasks. To this aim, exploiting the recent advances in high-resolution light microscopy 3D imaging and high-density multielectrode array technologies, RENVISION will be in an unprecedented position to investigate pan-retinal signal processing at high spatio-temporal resolution, integrating these two technologies in a novel experimental setup. This will allow for simultaneous recording from the entire population of ganglion cells and functional imaging of inner retinal layers at near-cellular resolution, combined with 3D structural imaging of the whole inner retina. The combined analysis of these complex datasets will require the development of novel multimodal analysis methods. Resting on these neuroscientific and computational grounds, RENVISION will generate new knowledge on retinal processing. It will provide advanced pattern recognition and machine learning technologies to ICTs by shedding a new light on how the output of retinal processing (natural or modelled) allows solving complex vision tasks such as automated scene categorization and human action recognition.

7.3.1.3. HBP

Title: The Human Brain Project

Programm: FP7

Duration: October 2013 - March 2016

Coordinator: EPFL

Partners:
see the webpage of the project.

Inria contact: Olivier Faugeras

Understanding the human brain is one of the greatest challenges facing 21st century science. If we can rise to the challenge, we can gain profound insights into what makes us human, develop new treatments for brain diseases and build revolutionary new computing technologies. Today, for the first time, modern ICT has brought these goals within sight. The goal of the Human Brain Project, part of the FET Flagship Programme, is to translate this vision into reality, using ICT as a catalyst for a global collaborative effort to understand the human brain and its diseases and ultimately to

emulate its computational capabilities. The Human Brain Project will last ten years and will consist of a ramp-up phase (from month 1 to month 36) and subsequent operational phases.
This Grant Agreement covers the ramp-up phase. During this phase the strategic goals of the project will be to design, develop and deploy the first versions of six ICT platforms dedicated to Neuroinformatics, Brain Simulation, High Performance Computing, Medical Informatics, Neuromorphic Computing and Neurorobotics, and create a user community of research groups from within and outside the HBP, set up a European Institute for Theoretical Neuroscience, complete a set of pilot projects providing a first demonstration of the scientific value of the platforms and the Institute, develop the scientific and technological capabilities required by future versions of the platforms, implement a policy of Responsible Innovation, and a programme of transdisciplinary education, and develop a framework for collaboration that links the partners under strong scientific leadership and professional project management, providing a coherent European approach and ensuring effective alignment of regional, national and European research and programmes. The project work plan is organized in the form of thirteen subprojects, each dedicated to a specific area of activity.
A significant part of the budget will be used for competitive calls to complement the collective skills of the Consortium with additional expertise.

7.4. International Research Visitors

7.4.1. Visits of International Scientists

- Paul Bressloff, a Professor of Applied Mathematics at the University of Utah visited the team in June-July as part of his Inria International chair.
- Ruben Herzog, Master student in Valparaiso, with A. Palacios, Centro Interdisciplinario de Neurociencia de Valparaíso, Univ de Valparaíso, Valparaíso. From May 4 th 2015 until May 29 th 2015.

7.4.1.1. Internships

Roberta Evangelista

During her internship (May 2015-September 2015, funded by *Action Transverse*) supervised by E. Tanré (Tosca) and R. Veltz (Neuromathcomp), Roberta Evangelista worked on “A stochastic model of gamma phase modulated orientation selectivity”.

Neurons in primary visual cortex (V1) are known to be highly selective for stimulus orientation. Recent experimental evidence has shown that, in awake monkeys, the orientation selectivity of V1 neurons is modulated by gamma oscillations. In particular, neurons’ firing rate in response to the preferred orientation changes as a function of the gamma phase of spiking. The effect is drastically reduced for non-preferred orientations. We have introduced a stochastic model of a network of orientation-dependent excitatory and inhibitory spiking neurons. We have found conditions on the parameters such that the solutions of the mathematical model reproduce the experimental behavior.

Quentin Cormier

Quentin is co-supervised by E. Tanré (Tosca) and R. Veltz (Neuromathcomp). He is a Master 1 student from ENS Lyon.

We study numerically and theoretically a model of spiking neuron in interaction with plasticity. The synaptic weights evolve according to biological law of plasticity. We study the existence of separable time scales. We are also interested in the characterization of invariant distribution for the activity of the network and the distribution of the synaptic weights. During his internship, Quentin Cormier also develop a numerical code to simulate large networks of neurons evolving according to this dynamics.

NEUROSYS Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

In the *Contrat de Plan État Région (CPER) IT2MP* 2015-2020 on *Technological innovations, modeling and Personalized Medicine*, we are contributing on platform SCIARAT (*cognitive stimulation, Ambient Intelligence, Robotic assistance and Telemedicine*). Contact in Neurosys is Laurent Bougrain.

9.2. National Initiatives

- Inria Technological development action (ADT): OpenViBE-NT
  This is a three-year multi-site project (2012–2015) to develop OpenViBE further on several fronts such as usability, new algorithms and scope of applicability. Teams of the ADT are Hybrid(Rennes), Athena (Sophia), Potioc (Bordeaux) and Neurosys. Coordinator is Laurent Bougrain.
- Multidisciplinary Exploratory Project (PEPS 2014) Bio-Maths-Info (BMI): *Characterising the laminar profile of motor cortical oscillatory synchronization during visuomotor behavior with new analysis tools.*
  Oscillations are omnipresent in the brain, but their function is still disputed. In motor cortex, beta and gamma oscillations are often observed, but their proposed roles in sensorimotor behavior are largely overlapping. While much is known on the laminar distribution of oscillations in sensory areas, the very sparse data on the laminar profile of motor cortical oscillations largely limits their functional interpretations. The 2-years project studies the layer specificity of monkey motor cortical oscillations and oscillatory interactions between the primary motor cortex (M1) and the dorsal premotor cortex (PMd) during visuomotor behavior. Extending conventional tools, such as coherency analysis, Neurosys develops a new method to quantify short-lasting partial amplitude and phase synchronization in single-trial data, based on wavelets, exploiting the predefined vicinity of contacts on the laminar probes. The application of this new method to the data recorded in Marseille will reveal instantaneous amplitude and phase synchronization between cortical layers and between the brain areas *M*1 and *P*Md, providing novel insights into the functional roles of beta and gamma oscillations in visuomotor behavior. The experimental partner at the *Institut de Neurosciences de la Timone* in Marseille is Bjork Kilavik. The contact in Neurosys is Axel Hutt.

9.3. European Initiatives

9.3.1. FP7 & H2020 Projects

The *ITN*-project *Neural Engineering Transformative Technologies (NETT)*[0] (2012-2016) is a Europe-wide consortium of 18 universities, research institutes and private companies which together hosts 17 PhD students and 3 postdoctoral researchers over the next 4 years. Neural Engineering brings together engineering, physics, neuroscience and mathematics to design and develop brain-computer interface systems, cognitive computers and neural prosthetics. Neurosys organized a NETTworkshop about *Neural Engineering in Medicine and related fields* in Nancy, 2-3 July 2015. Neurosys hosted a PhD-student, Maciej Jedynak, from Pompeu Fabra university (Spain) for one month in fall 2015. Contact is Axel Hutt.

[0] http://www.neural-engineering.eu/

9.3.2. Collaborations in European Programs, except FP7 & H2020

Program: ERC Starting Grant
Project acronym: MATHANA
Project title: Mathematical Modeling of Anaesthesia
Duration: January 2011 – October 2015
Coordinator: Axel Hutt
Abstract: MATHANA aims to study mathematically spatially extended neural systems and reveal their spatio-temporal dynamics during general anaesthesia.

9.3.3. Collaborations with Major European Organizations

Lifestyle Research Association (LIRA): Philips (Netherlands), Fraunhofer (Germany), Inria
Sleep is an essential part of a healthy life, but many people have trouble getting enough uninterrupted sleep. Special sensors installed in a mobile phone or bed can analyze activities, stress patterns and sleep sequences and provide ideas for new strategies and, eventually, products that support a healthier night's sleep. NEUROSYS has a Post-doc project running merging all sensor signals in a single data analysis technique to improve existing sleep monitors.

9.4. International Initiatives

9.4.1. Inria International Partners

9.4.1.1. Informal International Partners

- We collaborate with Jamie Sleigh (University of Auckland, New Zealand), who provides us with experimental EEG-data obtained in humans during anaesthesia (A. Hutt).
- In the collaboration with Flavio Frohlich (University of North Carolina - Chapel Hill), we receive experimental data measured intracranially in ferrets and analyse them on spectral properties (A. Hutt).
- In the collaboration with Jérémy Lefebvre (University of Lausanne), we have been working out together a stochastic delayed neural field analysis leading to new insights into the effects of additive noise (A. Hutt).
- The collaboration with Peter beim Graben (Humboldt University Berlin) on recurrence data analysis has led to analysis techniques to detect meta-stable states in EEG-signals (A. Hutt).
- We have an ongoing collaboration with Pr. Motoharu Yoshida at the Ruhr University Bochum, Germany, aiming to study the role of persistent firing neurons in memory and more specifically in neural network synchronization. M. Yoshida provides us with biological data that we combine with simulations to test hypotheses on memory formation (L. Buhry).
- We also collaborate with Pr. LieJune Shiau (University of Houston, Texas, USA) on more theoretical approaches concerning the role of intrinsic neuronal dynamics in network synchronization and brain oscillations (L. Buhry).

9.5. International Research Visitors

9.5.1. Visits of International Scientists

- We have hosted Peter beim Graben (Humboldt University Berlin) in April and May on recurrence data analysis has led to analysis techniques to detect meta-stable states in EEG-signals.
- Jérémie Lefebvre, 10 days, Scientist at Toronto Western Research Institute, University Health Network, and Assistant Professor at Department of Mathematics, University of Toronto: *Shaping oscillations in the damaged brain*.
- Fatiha Hendel, three weeks, Assistant professor at Université des Sciences et de la Technologie d'Oran :

9.5.1.1. Internships

- Kanishka Basnayake, first year master student (July 5th 2015-September 6th 2015): EPFL summer Internship. *Modelling of gamma oscillation in networks of adaptive exponential integrate-and-fire neurons*.

PARIETAL Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

9.1.1. iConnectom project

Participants: Bertrand Thirion [Correspondant], Gaël Varoquaux, Elvis Dohmatob.

This is a Digiteo project (2014-2017).

Mapping brain functional connectivity from functional Magnetic Resonance Imaging (MRI) data has become a very active field of research. However, analysis tools are limited and many important tasks, such as the empirical definition of brain networks, remain difficult due to the lack of a good framework for the statistical modeling of these networks. We propose to develop population models of anatomical and functional connectivity data to improve the alignment of subjects brain structures of interest while inferring an average template of these structures. Based on this essential contribution, we will design new statistical inference procedures to compare the functional connections between conditions or populations and improve the sensitivity of connectivity analysis performed on noisy data. Finally, we will test and validate the methods on multiple datasets and distribute them to the brain imaging community.

9.1.2. SUBSAMPLE Digiteo chair

Participants: Bertrand Thirion [Correspondant], Gaël Varoquaux, Alexandre Abraham.

Parietal is associated with this Digiteo Chair by Dimitris Samaras, in which we will address the probabilistic structure learning of salient brain states (PhD of Alexandre Abraham, 2012-2015).

Cognitive tasks systematically involve several brain regions, and exploratory approaches are generally necessary given the lack of knowledge of the complex mechanisms that are observed. The goal of the project is to understand the neurobiological mechanisms that are involved in complex neuro-psychological disorders. A crucial and poorly understood component in this regard refers to the interaction patterns between different regions in the brain. In this project we will develop machine learning methods to capture and study complex functional network characteristics. We hypothesize that these characteristics not only offer insights into brain function but also can be used as concise features that can be used instead of the full dataset for tasks like classification of healthy versus diseased populations or for clustering subjects that might exhibit similarities in brain function. In general, the amount of correlation between distant brain regions may be a more reliable feature than the region-based signals to discriminate between two populations e.g. in schizophrenia. For such exploratory methods to be successful, close interaction with neuroscientists is necessary, as the salience of the features depends on the population and the observed effects of psychopathology. For this aim we propose to develop a number of important methodological advances in the context of prediction of treatment outcomes for drug addicted populations, e.g. for relapse prediction.

9.1.3. Medilearn/braincodes Inria-MSR project

Participants: Bertrand Thirion [Correspondant], Gaël Varoquaux, Andrés Hoyos Idrobo.

Neuroimaging is accumulating large functional MRI datasets that display –among artefacts and noise– brain activation patterns giving access to a meaningful representation of brain spatial organization. This ongoing accumulation is intensified via new large-scale international initiatives such as the *Human Connectome Project* (www.humanconnectomeproject.org). but also to existing open repositories of functional neuroimaging datasets (https://openfmri.org/) or http://www.fmridc.org/. These datasets represent a very significant resource for the community, but require new analytic approaches in order to be fully exploited. The MediLearn/BrainCodes project strives to provide a synthetic picture of the brain substrate of human cognition and its pathologies. In practice, this can be achieved by learning from large-scale datasets a brain atlas that summarizes adequately these functional activation maps drawing from a large number of protocols and subjects. Once learned, such an atlas is extremely useful to understand the large-scale functional organization of the brain: it is a tool for understanding *brain segregation*, the different encoding of many cognitive parameters into different brain regions, as well as *brain integration*, *i.e.* how remote brain regions co-activate across subjects and experiments.

9.2. National Initiatives

9.2.1. ANR

9.2.1.1. BrainPedia project

Participants: Bertrand Thirion [Correspondant], Gaël Varoquaux, Yannick Schwartz.

BrainPedia is an ANR JCJC (2011-2015) which addresses the following question: Neuroimaging produces huge amounts of complex data that are used to better understand the relations between brain structure and function. While the acquisition and analysis of this data is getting standardized in some aspects, the neuroimaging community is still largely missing appropriate tools to store and organize the knowledge related to the data. Taking advantage of common coordinate systems to represent the results of group studies, coordinate-based meta-analysis approaches associated with repositories of neuroimaging publications provide a crude solution to this problem, that does not yield reliable outputs and looses most of the data-related information. In this project, we propose to tackle the problem in a statistically rigorous framework, thus providing usable information to drive neuroscientific knowledge and questions.

9.2.1.2. Niconnect project

Participants: Bertrand Thirion, Gaël Varoquaux [Correspondant], Alexandre Abraham.

- **Context:** The NiConnect project (2012-2016) arises from an increasing need of medical imaging tools to diagnose efficiently brain pathologies, such as neuro-degenerative and psychiatric diseases or lesions related to stroke. Brain imaging provides a non-invasive and widespread probe of various features of brain organization, that are then used to make an accurate diagnosis, assess brain rehabilitation, or make a prognostic on the chance of recovery of a patient. Among different measures extracted from brain imaging, functional connectivity is particularly attractive, as it readily probes the integrity of brain networks, considered as providing the most complete view on brain functional organization.
- **Challenges:** To turn methods research into popular tool widely usable by non specialists, the NiConnect project puts specific emphasis on producing high-quality open-source software. NiConnect addresses the many data analysis tasks that extract relevant information from resting-state fMRI datasets. Specifically, the scientific difficulties are *i)* conducting proper validation of the models and tools, and *ii)* providing statistically controlled information to neuroscientists or medical doctors. More importantly, these procedures should be robust enough to perform analysis on limited quality data, as acquiring data on diseased populations is challenging and artifacts can hardly be controlled in clinical settings.
- **Outcome of the project:** In the scope of computer science and statistics, NiConnect pushes forward algorithms and statistical models for brain functional connectivity. In particular, we are investigating structured and multi-task graphical models to learn high-dimensional multi-subject brain connectivity models, as well as spatially-informed sparse decompositions for segmenting structures from

brain imaging. With regards to neuroimaging methods development, NiConnect provides systematic comparisons and evaluations of connectivity biomarkers and a software library embedding best-performing state-of-the-art approaches. Finally, with regards to medical applications, the NiConnect project also plays a support role in on going medical studies and clinical trials on neurodegenerative diseases.

- **Consortium**
  - Parietal Inria research team: applied mathematics and computer science to model the brain from MRI
  - LIF INSERM research team: medical image data analysis and modeling for clinical applications
  - CATI center: medical image processing center for large scale brain imaging studies
  - Henri-Mondor hospital neurosurgery and neuroradiology: clinical teams conducting research on treatments for neurodegenerative diseases, in particular Huntington and Parkinson diseases
  - Logilab: consulting in scientific computing

9.3. European Initiatives

9.3.1. FP7 & H2020 Projects

9.3.1.1. HBP

Title: The Human Brain Project
Programm: FP7
Duration: October 2013 - April 2016
Coordinator: EPFL
Partners: See https://www.humanbrainproject.eu/fr/discover/the-community/partners
Inria contact: Olivier Faugeras
Understanding the human brain is one of the greatest challenges facing 21st century science. If we can rise to the challenge, we can gain profound insights into what makes us human, develop new treatments for brain diseases and build revolutionary new computing technologies. Today, for the first time, modern ICT has brought these goals within sight. The goal of the Human Brain Project, part of the FET Flagship Programme, is to translate this vision into reality, using ICT as a catalyst for a global collaborative effort to understand the human brain and its diseases and ultimately to emulate its computational capabilities. The Human Brain Project will last ten years and will consist of a ramp-up phase (from month 1 to month 36) and subsequent operational phases.

This Grant Agreement covers the ramp-up phase. During this phase the strategic goals of the project will be to design, develop and deploy the first versions of six ICT platforms dedicated to Neuroinformatics, Brain Simulation, High Performance Computing, Medical Informatics, Neuromorphic Computing and Neurorobotics, and create a user community of research groups from within and outside the HBP, set up a European Institute for Theoretical Neuroscience, complete a set of pilot projects providing a first demonstration of the scientific value of the platforms and the Institute, develop the scientific and technological capabilities required by future versions of the platforms, implement a policy of Responsible Innovation, and a programme of transdisciplinary education, and develop a framework for collaboration that links the partners under strong scientific leadership and professional project management, providing a coherent European approach and ensuring effective alignment of regional, national and European research and programmes. The project work plan is organized in the form of thirteen subprojects, each dedicated to a specific area of activity. A significant part of the budget will be used for competitive calls to complement the collective skills of the Consortium with additional expertise.

9.4. International Initiatives

9.4.1. Inria International Labs

Inria@SiliconValley

Associate Team involved in the International Lab:

9.4.1.1. MetaMRI

Title: Machine learning for meta-analysis of functional neuroimaging data

International Partner (Institution - Laboratory - Researcher):

Stanford (United States) - Department of Psychology - Russ Poldrack

Start year: 2015

See also: https://team.inria.fr/metamri

Neuroimaging produces huge amounts of complex data that are used to better understand the relations between brain structure and function. Observing that the neuroimaging community is still largely missing appropriate tools to store and organize the knowledge related to the data, Parietal team and Poldrack's lab, have decided to join forces to set up a framework for functional brain image meta-analysis, i.e. a framework in which several datasets can be jointly analyzed in order to accumulate information on the functional specialization of brain regions. MetaMRI will build upon Poldrack's lab expertise in handling, sharing and analyzing multi-protocol data and Parietal's recent developments of machine learning libraries to develop a new generation of meta-analytic tools.

9.5. International Research Visitors

9.5.1. Visits of International Scientists

Danilo Bzdok (Forschungszentrum Jülich and University of Aachen) visited Parietal several months in 2015 (January- December), to develop collaborations on the use of machine learning techniques to model behavioral variables and find data-driven characterization of brain diseases.

9.5.1.1. Internships

- Jacob Schreiber (Univ. Washington), went for an internship (June-September) to develop fas methods for three-based regression with Scikit-Learn.
- Giorgio Patrini (Australian National University) developed some tools for online learning during his internship (July-November) in Scikit-Learn.
- Daniel Alcala Lopez (Univ. Aachen) joined us for a three month internship to discover the use of machine learning for neuroimaging in psychiatry (June-September 2015).

POPIX Team

9. Partnerships and Cooperations

9.1. European Initiatives

9.1.1. FP7 & H2020 Projects

The Drug Disease Model Resources (DDMoRe) consortium will build and maintain a universally applicable, open source, model-based framework, intended as the gold standard for future collaborative drug and disease modeling and simulation.

The DDMoRe project is supported by the Innovative Medicines Initiative (IMI), a large-scale public-private partnership between the European Union and the pharmaceutical industry association EFPIA.

Marc Lavielle is leader of WP6: "New tools for Model Based Drug Development".

DDMoRe website: http://www.ddmore.eu

Duration: 2010 - 2016

Project members: Uppsala Universitet, Sweden; University of Navarra, Spain; Universiteit Leiden, Netherlands; Université Paris Diderot, France; Universita degli Studi di Pavia, Italy; UCB Pharma , Belgium; Simcyp, UK; Pfizer, UK; Optimata , Israel; Novo Nordisk , Denmark; Novartis, Switzerland; Merck Serono, Switzerland; Takeda, Switzerland; Mango Business Solutions , UK; Lixoft, France; Interface Europe, Belgium; Institut de Recherches Internationales Servier, France; Inria, France; GlaxoSmithKline Research and Development, UK; Freie Universitat Berlin, Germany; F. Hoffmann - La Roche , Switzerland; EMBL - European Bioinformatics Institute, UK; Eli Lilly , UK; Cyprotex Discovery, UK; Consiglio Nazionale delle Ricerche, Italy; AstraZeneca, Sweden.

9.2. International Initiatives

9.2.1. Inria International Partners

9.2.1.1. Informal International Partners

POPIX has a collaboration with the Faculty of Pharmacy of Manchester University (UK).

POPIX is Adjunct Professor at the Faculty of Pharmacy of Florida University (USA).

POPIX is Adjunct Professor at the Faculty of Pharmacy of Buffalo University (USA).

9.2.2. Participation In other International Programs

Indo French Centre for the promotion of advanced research (CEFIPRA): Marc Lavielle was invited to participate to the the IFCAM Workshop in Statistics in Bangalore (July 2015).

SISTM Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

The team have strong links with Bordeaux CHU ("Centre Hospitalier Universitaire").

8.2. National Initiatives

8.2.1. Labex Vaccine Research Institute (VRI)

There are strong collaborations with immunologists involved in the Labex Vaccine Research Institute (VRI) as RT is leading the Biostatistics/Bioinformatics division.

8.2.2. Expert Appraisals

Expertise of a project for Institut de Recherche en Santé Publique IRESP (MA)

RT is a member of the scientific advisory board of the Ebola VSV ring trial (published in New England Journal of Medicine in August 2015) and of the Pierre Louis Institute of Epidemiology and Public Health (Paris)

RT is a member of the Systems biology and cancer comity (Plan Cancer)

8.2.3. Partnership with the french swimming federation

Convention between the "Fédération francaise de natation" and Inria (18950 euros) for the R&D project "Quels schémas de périodisation pour la préparation des Jeux Olympiques à Rio ?"

8.2.4. Partnership with ANSM

DRUGS-SAFE platform funded by ANSM.

8.3. European Initiatives

8.3.1. Collaborations in European Programs, except FP7 & H2020

Program: The EBOVAC2 project is one of 8 projects funded under IMI Ebola+ programme that was launched in response to the Ebola virus disease outbreak. The project aims to assess the safety and efficacy of a novel prime boost preventive vaccine regimen against Ebola Virus Disease (EVD).

Project acronym: EBOVAC2

Project title: EBOVAC2

Coordinator: Rdolphe Thiébaut

Other partners: Inserm (France), Labex VRI (France), Janssen Pharmaceutical Companies of Johnson & Johnson, London School of Hygiene & Tropical Medicine (United Kingdom), The Chancellor, Masters and Scholars of the University of Oxford (United Kingdom), Le Centre Muraz (Burknia Faso), Inserm Transfert (France)

Abstract: Given the urgent need for an preventive Ebola vaccine strategy in the context of the current epidemic, the clinical development plan follows an expedited scheme, aiming at starting a Phase 2B large scale safety and immunogenicity study as soon as possible while assuring the safety of the trial participants.

Phase 1 trials to assess the safety and immunogenicity data of the candidate prime-boost regimen in healthy volunteers are ongoing in the UK, the US and Kenya and Uganda. A further study site has been approved to start in Tanzania. Both prime-boost combinations (Ad26.ZEBOV prime + MVA-BN-Filo boost; and MVA-BN-Filo prime + Ad26.ZEBOV boost) administered at different intervals are being tested in these trials.

Phase 2 trials (this project) are planned to start as soon as the post-prime safety and immunogenicity data from the UK Phase I are available. Phase 2 trials will be conducted in healthy volunteers in Europe (France and UK) and non-epidemic African countries (to be determined). HIV positive adults will also be vaccinated in African countries. The rationale for inclusion of European volunteers in Phase 2, in addition to the trials in Africa, is to allow for higher sensitivity in safety signal detection in populations with low incidence of febrile illnesses, to generate negative control specimens for assay development, to allow for inclusion of health care workers or military personnel that may be deployed to Ebola-endemic regions.

8.4. International Initiatives

8.4.1. Participation In International Programs

RT is participating to the EUROCOORD network on HIV cohort collaborations as :

a member of the scientific committee of IWHOD International Workshop on HIV Observational Databases from 2013,

a project leader on defining references for the CD4 count response to antiretrovirals.

8.5. International Research Visitors

8.5.1. Visits of International Scientists

David Conesa (Associate Professor of Biostatistics, "Spatial and Temporal Statistics in Epidemiology and Environment" Research Group, Universitat de Val encia, Spain) visited the team through the Erasmus+ program.

Following the RHOMEO project (ANR-BBSRC Systems biology 2007 call, 2007-2011) steered by RT, a strong collaboration has been established with Pr Robin Callard (UCL Immunology) who is visiting the team in Bordeaux one month each year, Andy Yates (Physicists, Glasgow Univ) and Ben Seddon (NIMR, UCL Immunology).

Also, several other international collaboration have been initiated through the Labex:

Raphael Gottardo, Zoe Moodie, Steve Self in Seattle (HVTN HIV vaccine Trial Network, Fred Hutchinson cancer centre)

Marcus Altfeld (Immunologists, Hambourg & Harvard).

8.5.2. Visits to International Teams

8.5.2.1. Sabbatical programme

BL was on sabbatical in Queensland University, Australia until Sep 2015.

8.5.2.2. Research stays abroad

Chloé Pasin visited (from 11/10/14 to 10/04/15) Steve Self at HVTN, Seattle.

Chariff Alkhassim (from 07/04/15 to 10/04/15) visited François Caron at Oxford University, United-Kingdom.

MA (from 24/02/15 to 10/03/15) and Perrine Soret (from 26/12/15 to 28/01/16) visited Cristian Meza and Karine Bertin (Inria Chili) at CIMFAV (Centre for Research and Modeling of Random Phenomena – Valparaíso), Univ Valparaiso, Chili, concerning the project "New challenges in mixed-effects models".

VISAGES Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

9.1.1. Biogenouest

The VisAGeS team and the Neurinfo platform integrated the Biogenouest "Groupement d'Intérêt Scientifique (GIS)" in 2012.

Biogenouest is a Western France life science and environment core facility network. Research programmes are undertaken in the fields of Marine biology, Agriculture/Food-processing, Human health, and Bioinformatics. Set up in keeping with the inter-regional principle of complementarity, Biogenouest coordinates over twenty technological core facilities in both the Brittany and Pays de la Loire regions.

9.1.2. Projet Fondation de France: PERINE

Participants: Elise Bannier, Isabelle Corouge, Olivier Commowick, Jean-Christophe Ferré, Christian Barillot.

This study evaluates the effect of prenatal exposure to neurotoxicants on the developing brain. Following previous studies in the PELAGIE cohort this MRI study involves ASL, Diffusion and working memory as well as motor inhibition BOLD fMRI together with neuropsychological tests in children. Inclusions have started in November 2014 and will continue over 2 years.

9.1.3. Fondation de l'Avenir - Depression, suicide and fMRI

Participants: Elise Bannier, Isabelle Corouge, Jean-Christophe Ferré, Christian Barillot.

initial duration: 12 months from November 2012. Project extended in 2015.

In collaboration with EA 4712 "Comportement et Noyaux Gris Centraux" of the University of Rennes I, a complementary funding (20 000€) was obtained to support an ongoing fMRI research project on emotions, impulsivity and suicide. The study protocol and the fMRI task was finalized. Inclusions started in early 2013. The project was extended in 2014 to recruit more patients.

9.1.4. Fondation de l'Avenir - Stroke, rehabilitation and fMRI

Participants: Elise Bannier, Isabelle Bonan, Isabelle Corouge, Jean-Christophe Ferré, Christian Barillot, Jean-Yves Gauvrit.

duration: 12 months from November 2012. Project extended in 2015.

A complementary funding (20 000€) was obtained to support a new research project on rehabilitation of stroke patients. The fMRI protocol was setup, the task developed and validation on volunteers is ongoing. Patient inclusions started in spring 2013. This project was also extended to 2014 to recruit more patients. Group analysis on the control group was performed and a paper will be submitted soon.

9.1.5. Projet Fondation de France: EPMR-MA

Participants: Pierre-Yves Jonin, Elise Bannier, Christian Barillot, Isabelle Corouge, Quentin Duché, Jean-Christophe Ferré.

duration: 2 years from July 2015

This project evaluates memory effects in healthy adults and in patients presenting cognitive impairments using BOLD fMRI and diffusion MRI. A pilot study has been completed in 2015 in order to optimize the experimental design. The inclusions of patients wil start early 2016.

9.2. National Initiatives

9.2.1. ANR

9.2.1.1. ANR "TRANSLATE-MS-REPAIR", RPIB 2012 program

Participants: Laurence Catanese, Olivier Commowick, Isabelle Corouge, Jean-Christophe Ferré, Elise Bannier, Gilles Edan, Christian Barillot.

It is now commonly admitted that MS is not only an inflammatory disease but a neurodegenerative disease as well. This project is devoted to show that the olesoxime molecule is not only neuroprotective, but it has the ability to promote the maturation of oligodendrocyte progenitor cells (OPCs) into myelinating oligodendrocytes. However, before considering a large-scale clinical trial to assess efficacy. An important aspect is that to date, no treatment for neuroprotection / remyelination has reached the stage of clinical proof of concept that aims Trophos company who is leading this project. It appears that the best criteria for assessing neuroprotective/remyelinating effect of the drug candidate, are MRI criteria. However, these imaging criteria have not yet been validated for use in multicentre trials - so we will also check the feasibility of such measures under this condition. In addition to Trophos company, the partners of this project are AP-HM/CNRSCEMEREM-CRMBM, CHU Rennes, CHU Reims, and Inria-VISAGES.

9.2.1.2. ANR "MAIA", 2015 generic projects program

Participants: Maia Proisy, Pierre Maurel, Olivier Commowick, Jean-Christophe Ferré, Christian Barillot.

Each year in France, 55 000 children are born prematurely, i.e., before the 37th week of gestation. Long-term studies of the outcome of prematurely born infants have clearly documented that the majority of such infants may have significant motor, cognitive, and behavioral deficits.

However, there is a limited understanding of the nature of the cerebral abnormality underlying these adverse neurologic outcomes. In this context, the emergence of new modalities of 3D functional MRI, e.g., Arterial Spin Labeling (ASL), or optical imaging technologies, e.g., Near InfraRed Spectroscopy (NIRS), brings new perspectives for extracting cognitive information, via metabolic activity measures. Other classical technics devoted to cerebral signal measurement, such as ElectroEncephaloGraphy (EEG), provide cognitive information at the cortical level. Each of these various non-invasive imaging technologies brings substantial and specific information for the understanding of newborn brain development.

This project aims at developing innovative approaches for multi-image / multi-signal analysis, in order to improve neurodevelopment understanding methods. From a fundamental point of view, mathematics and computer science have to be considered in association with imaging physics and medicine, to deal with open issues of signal and image analysis from heterogeneous data (image, signal), considered in the multiphysics contexts related to data acquisition (magnetic, optic, electric signals) and biophysics modeling of the newborn brain. A sustained synergy between all these scientific domains is then necessary.

Finally, the sine qua non condition to reach a better understanding of the coupled morphological- cognitive development of premature newborns, is the development of effective software tools, and their distribution to the whole medical community. The very target of this project will be the design of such software tools for medical image / signal analysis, actually operational in clinical routine, and freely available. Academic researchers and industrial partners will work in close collaboration to reach that ambitious goal.

9.2.2. Competitivity Clusters

9.2.2.1. The HEMISFER Project

Participants: Elise Bannier, Isabelle Bonan, Isabelle Corouge, Jean-Christophe Ferré, Jean-Yves Gauvrit, Pierre Maurel, Lorraine Perronnet, Christian Barillot.

The HEMISFER project ("Hybrid Eeg-MrI and Simultaneous neuro-FEedback for brain Rehabilitation") will be conducted at Inria Rennes with the support of the Cluster of Excellence "CominLabs" [0]. The goal of HEMISFER is to make full use of the neurofeedback paradigm in the context of rehabilitation and psychiatric disorders. The major breakthrough will come from the use of a coupling model associating functional and metabolic information from Magnetic Resonance Imaging (fMRI) to Electro-encephalography (EEG) to "enhance" the neurofeedback protocol. We propose to combine advanced instrumental devices (Hybrid EEG and MRI platforms), with new man-machine interface paradigms (Brain computer interface and serious gaming) and new computational models (source separation, sparse representations and machine learning) to provide novel therapeutic and neuro-rehabilitation paradigms in some of the major neurological and psychiatric disorders of the developmental and the aging brain (stroke, attention-deficit disorder, language disorders, treatment-resistant mood disorders, ...). This project will be conducted with the HYBRID and PANAMA Teams from Inria Rennes, the EA 4712 team from University of Rennes I and the ATHENA team from Inria Sophia-Antipolis. This work will benefit from the research 3T MRI and MRI-compatible EEG systems provided by the NeurInfo in-vivo neuroimaging platform on which these new research protocols will be set up. A budget of 500keuros will be provided by the CominLabs cluster in the next 3 years to support this project (through experimental designs, PhDs, Post-docs and Expert Engineers).

9.2.2.2. France Life Imaging (FLI)

Participants: Christian Barillot, Olivier Commowick, Florent Leray, Michael Kain, Yao Yao.

France Life Imaging (FLI) is a proposed large-scale research infrastructure project aimed at establishing a coordinated and harmonized network of biomedical imaging in France. This project was recently selected by the call “Investissements d’Avenir - Infrastructure en Biologie et Santé”. One node of this project is the node Information Analysis and Management (IAM), a transversal node build by a consortium of teams that will contribute to the construction of a network for data storage and information processing. Instead of building yet other dedicated facilities, the IAM node will use already existing data storage and information processing facilities (LaTIM Brest; CREATIS Lyon; CIC-IT Nancy; Visages U746 Inria Rennes; CATI CEA Saclay; LSIIT/ICube Strasbourg) that will increase their capacities for the FLI infrastructure. Inter-connections and access to services will be achieved through a dedicated software platform that will be developed based on the expertise gained through successful existing developments. The IAM node has several goals. It aims first at building a versatile facility for data management that will inter-connect the data production sites and data processing for which state-of-the-art solutions, hardware and software, will be available to infrastructure users. Modular solutions are preferred to accommodate the large variety of modalities acquisitions, scientific problems, data size, and adapted for future challenges. Second, it aims at offering the latest development that will be made available to image processing research teams. The team VISAGES fulfills multiple roles in this nation-wide project. Christian Barillot is the chair of the node IAM, Olivier Commowick is participating in the working group workflow and image processing and Michael Kain the technical manager. Apart from the team members, software solutions like medInria and Shanoir will be part of the final software platform.

9.2.2.3. OFSEP

Participants: Justine Guillaumont, Elise Bannier, Christian Barillot, Olivier Commowick, Gilles Edan, Isabelle Corouge, Jean-Christophe Ferré, Michael Kain, Inès Fakhfakh.

The French Observatory of Multiple Sclerosis (OFSEP) is one of 10 projects selected in January 2011 in response to the call for proposal in the “Investissements d’Avenir - Cohorts 2010” program launched by the French Government. It allows support from the National Agency for Research (ANR) of approximately € 10 million for 10 years. It is coordinated by the Department of Neurology at the Neurological Hospital Pierre Wertheimer in Lyon (Professor Christian Confavreux), and it is supported by the EDMUS Foundation against multiple sclerosis, the University Claude Bernard Lyon 1 and the Hospices Civils de Lyon. OFSEP is based on a network of neurologists and radiologists distributed throughout the French territory and linked to 61 centers. OFSEP national cohort includes more than 50,000 people with Multiple Sclerosis, approximately half of the patients residing in France. The generalization of longitudinal monitoring and systematic association

[0] https://iww.inria.fr/cominlabs-newsletter/april-2013-four-projects-selected/#hemisfer

of clinical data and neuroimaging data is one of the objectives of OFSEP in order to improve the quality, efficiency and safety of care and promote clinical, basic and translational research in MS. For the concern of data management, the Shanoir platform of Inria has been retained to manage the imaging data of the National OFSEP cohort in multiple sclerosis.

9.2.3. Collaboration with the CEA (Commissariat à l'Energie Atomique): Standardization of Arterial Spin Labeling acquisitions and imaging data quality assessment in the context of dementia related studies

Participants: Elise Bannier, Christian Barillot, Isabelle Corouge, Jean-Christophe Ferré, Cédric Meurée.

duration: from August 2014 to December 2015

Around 900,000 people are affected by various forms of dementia in France. As an early and reliable diagnosis remains difficult to provide, neuroimaging is crucial as a diagnosis assistance by analyzing structural and functional brain abnormalities related to these diseases. The CATI (Centre pour l'Acquisition et le Traitement des Images) is a multicenter neuroimaging network dedicated to the management of dementia related imaging protocols. As VisAGeS and the Neurinfo platform are recognized for their expertise in Arterial Spin Labeling (ASL) acquisition and post-processing, a collaboration contract was signed between Inria and CEA, the coordinator of the CATI initiative, in order to host an engineer in the VisAGeS team for one year. The collaboration resulted in the standardization of the ASL acquisition parameters of the CATI protocols, the setup of these parameters on the scanneres participating in the CATI studies, as well as the development and the integration of post-processing and quality assessment tools into qualiCATI, the quality control software of the CATI.

9.2.4. PEPS JCJC CNRS INS2I: FastMicroDiff: Fast acquisition for microstructure-enabled diffusion MRI

Participants: Elise Bannier, Emmanuel Caruyer.

duration: from January 2015 to December 2015 Diffusion MRI is a unique tool for the observation of brain white matter structure in vivo. Several studies have shown that it is possible to estimate intrinsic tissue parameters from diffusion, such as axonal diameter, axonal density, orientation dispersion, compartment-specific diffusion coefficients, etc. However, the reconstruction of these parameters requires specific acquisition protocols, which are to date very long and therefore poorly compatible with in vivo applications. Besides, recent development have shown that a higher sensitivity to some microstructural paramters could be obtained using non-conventional diffusion gradient sequences, such as oscillating gradient waveforms. This project aims at developping faster acquisition methods, using sparse representation for microstructure-enabled diffusion signal and time-varying diffusion sensitizing gradients.

In cooperation with the Neurinfo imaging platform and Siemens, a modification of the protocol to enable the use of non-rectangular gradient pulses has been developped and is being tested on phantom. A group of 6 healthy subjects will be scanned using this novel protocol, and acquisition will be repeated 3 times for each subject so that we can evaluate the reproducibility of the technique.

9.2.5. PHRC EMISEP: Evaluation of early spinal cord injury and late physical disability in Relapsing Remitting Multiple Sclerosis

Participants: Elise Bannier, Christian Barillot, Emmanuel Caruyer, Olivier Commowick, Gilles Edan, Jean-Christophe Ferré, Anne Kerbrat.

duration: from January 2014 to December 2017 Multiple Sclerosis (MS) is the most frequent acquired neurological disease affecting young adults (1/1000 inhabitants in France) and leading to impairment. Early and well adapted treatment is essential in patients presenting aggressive forms of MS. This PHRC project focuses on physical impairment and especially on the ability to walk. Several studies, whether epidemiolgic or based on brain MRI, have shown that several factors were likely to announce aggressive development of the disease, such as age, number of focal lesions on baseline MRI, clinical activity. However, this factors only

partially explain physical impairment progression, preventing their use at the individual level. Spinal cord is often affected in MS, as demonstrated in postmortem or imaging studies. Yet, early radiological depiction of spinal cord lesions is not always correlated with clinical symptoms. Preliminary data on a reduced number of patients, and only investigating the cervical spinal cord, have shown that diffuse spinal cord injury, observed via diffusion or magnetisation transfer imaging, would be correlated with physical impairment as evaluated by the EDSS score. Besides, the role of early spinal cord affection (first two years) in the evolution of physical impairment remains unknown.

In this project, we propose to address these different issues and to perfom a longitudinal study on Relapsing Remitting Multiple Sclerosis (RRMS) patients, recruited in the first year of the disease. Our goal is to show that diffuse and focal lesions detected on the spinal cord MRI in the first 2 years can be used to predict disease evolution and physical impairment at 5 years. Twelve centers are involved in the study to include 80 patients.

To date, 40 of the 80 subjects have been included. A PhD student started in November 2015 to work on diffusion imaging in the spinal cord.

9.3. European Initiatives

9.3.1. FP7 & H2020 Projects

9.3.1.1. EuroBioimaging

Type: CAPACITIES

Defi: Provide access and training in imaging technologies, and share the best practice and image data in order to make Euro-BioImaging an engine that will drive European innovation in imaging research and technologies

Instrument: Combination of COLLABORATIVE PROJECTS and COORDINATION and SUPPORT ACTIONS

Objective: Euro-BioImaging is a large-scale pan-European research infrastructure project on the European Strategy Forum on Research Infrastructures (ESFRI) Roadmap.

Duration: December 2010 - 2016

Coordinators: Jan Ellenberg (EMBL) and Oliver Speck (University of Magdeburg)

Partner: EMBL (Germany); Erasmus Medical Center (Netherlands) for WG11

Inria contact: C. Kervrann, C. Barillot

Abstract: Euro-BioImaging is a pan-European infrastructure project whose mission is to build a distributed imaging infrastructure across Europe that will provide open access to innovative biological and medical imaging technologies for European researchers. The project is funded by the EU and currently the consortium is finalizing the basic principles for the operation of future Euro-BioImaging organisation.

Euro-BioImaging will be governed by representatives of the European countries that will join Euro-BioImaging (Euro-BioImaging member states).

The infrastructure established by Euro-BioImaging will consist of a set of geographically distributed but strongly interlinked imaging facilities (Euro-BioImaging Nodes), which will be selected among the leading European imaging facilities based on an independent evaluation process.

Inria and the Visages team is involved through the FLI national infrastructure and contributes to the WG11 Working Group on Data Storage and Analysis. This WG performs a series of tasks to define a European Biomedical Imaging Data Storage and Analysis infrastructure plan for the construction phase.

9.3.2. Collaborations in European Programs, except FP7 & H2020

9.3.2.1. COST-AID

Program: COST

Project acronym: AID (oc-2010-2-8615)

Project title: Arterial spin labeling Initiative in Dementia

Acceptation date: 18/05/2011

Coordinator: X. Golay, UCL, London, UK

Other partners: Ghent University (BE), Liege University (BE), Hospital Cantonal de Geneve (CH), Fraunhofer MEVIS (D), Freiburg University (D), Max Planck Institute for Human Cognitive & Brain Sciences (D), Glostrup Hospital (DK), Hospital Santa Creu I Sant Pau (ES), Universidad Rey Juan Carlos (ES), University of Narvarra (ES), INSERM U836 Grenoble (FR), University of Rennes I (FR), Centro San Giovanni di Dio - Fatebenefratelli (IT), Fondazione Instituto Neurologico Besta (IT), Leiden University Medical Center (NL), UMC Utrecht (NL), VU University Medical Centre (NL), Instituto Superior Técnico (PT), University of Porto (PT), Lund University Hospital (SE), Uppsala University Hospital (SE), Skane University Hospital (SE), Bogazici University (TR), King's College London (UK), University College London (UK), University of Nottingham (UK), University of Oxford (UK)

Abstract: Dementia is a major clinical challenge with care costs approaching 1% of global GDP. Recent estimates suggest that delaying disease onset by 5 years would halve its prevalence. As new disease-modifying treatments will be specific to causative diseases, expensive and bear significant side effects, early diagnosis of dementia will be essential. Current diagnostic criteria include the use of image-based biomarkers using radiotracers. The AID Action aims at coordinating the development of an alternative and cost-effective tool based on an MRI technique, Arterial Spin Labeling (ASL), to obtain reproducible brain perfusion measurements in dementia patients by bringing together scientists and clinicians from across Europe through the flexibility of the COST mechanism. The scientific program is centered around four work packages and three workgroups aiming at developing standards, improving the reliability of the technique and as establishing it as a possible clinical trial outcome measure. Development of MRI methods, post-processing tools, protocols of cross-validation, statistical analyses and launch of clinical and comparative studies will be undertaken. The main benefit of this Action will be to provide a cost-effective alternative to radiotracer-based biomarkers, and help care providers throughout Europe balancing the need for early diagnosis of dementia with the necessary healthcare cost containment. The Visages team is involved in the workgroups ASL data acquisition (E. Bannier), ASL data analysis (C. Barillot, I. Corouge, P. Maurel, C. Meurée) and clinical validation of ASL in cognitive impairment (J.-C. Ferré).

9.3.2.2. Kic-EIT-eHealth

Program: KIC-EIT: European Institute of Innovation and Technology

Project acronym: e-Health

Project title: Innovation for healthy living and active ageing

Acceptation date: 01/12/2014

website: http://eithealth.eu/about-us/

EIT Health aims to promote entrepreneurship and develop innovations in healthy living and active ageing, providing Europe with new opportunities and resources. EIT Health will enable citizens to lead healthier and more productive lives by delivering products, services and concepts that will improve quality of life and contribute to the sustainability of healthcare across Europe. EIT Health is a strong, diverse and balanced partnership of best-in-class organisations in education, research, technology, business creation and corporate and social innovation. EIT Health intends to foster cooperation and unlock Europe's innovation and growth potential – developing and retaining the best talents, creating high-quality jobs and boosting the global competitiveness of European industry.

Visages is involved in this project through the Inserm and Inria institutions. C. Barillot is representing Inria as one expert in the dedicated WG "Healthy Brain". Visages is also concerned by the WG "big data".

9.4. International Initiatives

9.4.1. Inria Associate Teams not involved in an Inria International Labs

9.4.1.1. BARBANT

Title: Boston and Rennes, a Brain image Analysis Team

International Partner (Institution - Laboratory - Researcher):

Harvard University (United States) - Mathematics Department - Simon K. Warfield

Start year: 2012 (renewed 2015)

See also: https://team.inria.fr/barbant/

BARBANT is an Inria associate team shared between Inria VisAGeS research team and the Computational Radiology Laboratory at the Boston Children's hospital (Harvard Medical School). This associate team aims at better understanding the behavior of normal and pathological Central Nervous System (CNS) organs and systems. Pathologies of particular interest to us are multiple sclerosis, psychiatric, and pediatric diseases such as pediatric multiple sclerosis or tuberous sclerosis. A major challenge is to characterize the future course of the pathological processes in each patient as early as possible in order to predict the progression of the disease and/or adverse neurological outcomes, and to develop better techniques for both monitoring response to therapy and for altering therapy (duration, dose and nature) in response to patient-specific changes in imaging characteristics. At term, this project will allow to introduce objective figures to correlate qualitative and quantitative phenotypic markers coming from the clinic and image analysis, mostly at the early stage of the pathologies. This will allow for the selection or adaptation of the treatment for patients at an early stage of the disease.

In 2015, Renaud Hedouin had a 3 month visit in Boston in the context of the BARBANT associated team

9.4.1.2. Informal International Partners

- Collaboration with Duke University, NC : From November 2014 to February 2015, Hrishikesh Deshpande visits Duke University (in Durham, North Carolina, United States) to collaborate with Professor Guillermo Sapiro on classification using Dictionary Learning. This visit was partially founded by a mobility grant from the doctoral school MATISSE.
- Collaboration with the MS Center, Dpt. of Neurology and Center for Clinical Neuroscience, Charles University in Prague on Brain atrophy in Multiple Sclerosis. O. Commowick, C. Barillot, A. Kerbray and G. Edan had a two-days visit in April 2015.

9.5. International Research Visitors

9.5.1. Visits of International Scientists

- Within the BARBANT associate team, P. Simon K. Warfield, Dr. Benoit Scherrer and Dr. Maxime Taquet (Computational Radiology Laboratory, Harvard Medical School) visited us for a workshop on multiple sclerosis and diffusion image processing.

9.5.2. Visits to International Teams

- Several members of the Visages team (Christian Barillot, Olivier Commowick, Renaud Hédouin, Yogesh Karpate) visited the Computational Radiology Laboratory (Harvard Medical School) for an associate team (BARBANT) meeting to discuss new research topics.

9.5.2.1. Explorer programme

Hédouin Renaud

Date: Sep 2015 - Dec 2015

Institution: Boston Children's Hospital (United States)

Renaud Hédouin visited the Computational Radiology Laboratory at Boston Children's Hospital, United States, for a 3 month exchange within the BARBANT associate team working on distortion correction topic.

9.5.2.2. Research stays abroad

- From November 2014 to February 2015, Hrishikesh Deshpande visits Duke University (in Durham, North Carolina, United States) to collaborate with Professor Guillermo Sapiro on classification using Dictionary Learning. This visit was partially founded by a mobility grant from the doctoral school MATISSE.

AIRSEA Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

- Clémentine Prieur is a member of the project "Soutien à l'Excellence et à l'Innovation Grenoble INP MEPIERA (MEthodologies innovantes Pour l'Ingénierie de l'Eau et des Risques Associés) leaded by A.- C. Favre (LTHE).
- N. Feyeux PhD is sponsored by the action ARC3 Environment of the Region Rhone-Alpes.

9.2. National Initiatives

9.2.1. ANR

- A 3.5 year ANR contract: ANR CITiES (numerical models project selected in 2012). https://team.inria.fr/steep/projects/
- A 4-year ANR contract: ANR TOMMI (Transport Optimal et Modèles Multiphysiques de l'Image), see paragraphs 7.4.2 ,7.4 .
- A 5 year ANR contract (2011-2016): ANR COMODO (Communauté de Modélisation Océanographique) on the thematic "Numerical Methods in Ocean Modelling". (coordinator L. Debreu) 7.1.2

9.2.2. Other Initiatives

- A. Vidard leads a group of projects gathering multiple partners in France and UK on the topic "Variational Data Assimilation for the NEMO/OPA9 Ocean Model", see 6.3 .
- C. Prieur chairs GdR MASCOT NUM, in which are also involved M. Nodet, E. Blayo, C. Helbert, E. Arnaud, L. Viry, S. Nanty, L. Gilquin. http://www.gdr-mascotnum.fr/doku.php
- C. Prieur is the leader of the LEFE/MANU project MULTIRISK (2014-2016) on multivariate risk analysis, which gathers experts from Lyon 1 University, CNAM, LSCE and Grenoble University mainly.
- E.Kazantsev, E.Blayo, F. Lemarié participate in the project "PACO - Vers une meilleure paramétrisation de la côte et des conditions limites dans les modèles d'océan" supported by LEFE-GMMC and LEFE-MANU .

9.3. European Initiatives

9.3.1. FP7 & H2020 Projects

9.3.1.1. ERA-CLIM2

Type: COOPERATION

Instrument: Specific Targeted Research Project

Program: Collaborative project FP7-SPACE-2013-1

Project acronym: ERA-CLIM2

Project title: European Reanalysis of the Global Climate System

Duration: 01/2014 - 12/2016

Coordinator: Dick Dee (ECMWF, Europe)

Other partners: Met Office (UK), EUMETSAT (Europe), Univ Bern (CH), Univ. Vienne (AT), FFCUL (PT), RIHMI-WDC (RU), Mercator-Océan (FR), Météo-France (FR), DWD (DE), CERFACS (FR), CMCC (IT), FMI (FI), Univ. Pacifico (CL), Univ. Reading (UK), Univ. Versailles St Quentin en Yvelines (FR)

Inria contact: Arthur Vidard

9.3.2. Collaborations with Major European Organizations

Partner: European Centre for Medium Range Weather Forecast. Reading (UK)

World leading Numerical Weather Center, that include an ocean analysis section in order to provide ocean initial condition for the coupled ocean atmosphere forecast. They play a significant role in the NEMOVAR project in which we are also partner.

Partner: Met Office (U.K) National British Numerical Weather and Oceanographic service. Exceter (UK).

We do have a strong collaboration with their ocean initialization team through both our NEMO, NEMO-ASSIM and NEMOVAR activities. They also are our partner in the NEMOVAR consortium.

Partner: University of Reading, Department of Meteorology, Department of Mathematics

Subject: Data assimilation for geophysical systems.

9.4. International Initiatives

C. Prieur collaborates with Jose R. Leon (UCV, Central University of Caracas).

C. Prieur is leader of a project ECOS Nord with Venezuela (2012-2015).

9.5. International Research Visitors

9.5.1. Visits of International Scientists

Jose-Raphael Leon-Ramos, Caracas University, has been granted by the Inria international chair.

Victor Shutyaev, Russian Academy of Sciences, 2 weeks.

Pierre Ngnepieba, Florida Agricultural & Mechanical University, 2 weeks.

9.5.2. Visits to International Teams

F.-X Le Dimet has been invited two times by the Department of Mathematics at Florida State University (one week in April and 2 weeks in october). In USA he was also invited at NASA Stennis Space center (Mississipi) by NRL (Navy Resarch lab) He delivered seminars in this place.

F.-X Le Dimet has been invited by Nanjing University (Department of Meteoroly) , one week in May 2015 to give a 6 -hours tutorial on Variational Data Assimilation.

F.-X. Le Dimet and E.Kazantsev were invited by the Institute of Numerical Mathematics of the Russian Academy of Sciences to present a communication at the G.Marchuk's memorial jubilee [34].

F.-X. Le Dimet has presented a communication at the SIAM meetng on Scientific Computing held in Salt Lake city in April 2015

ANGE Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

9.1.1. Instabilities in Hydrodynamics (2011-2015)

Participant: Nicolas Seguin.

The Emergence project (Ville de Paris and FSMP) "Instabilities in Hydrodynamics" is related to theoretical, applied, and numerical mathematics for the study of hydrodynamical turbulence phenomena.

9.1.2. Plasticity of geophysical flows and seismic emissions (2013-2016)

Participant: Anne Mangeney.

This project is funded by Sorbonne Paris Cité (80.000 euros) and is a collaboration between IPGP and Univ. Paris 13.

9.1.3. LRC Manon (2014-2018)

Participants: Edwige Godlewski, Yohan Penel, Nicolas Seguin.

CEA and Laboratory Jacques-Louis Lions launched a collaboration in order to carry out studies about complex fluids (modelling, numerical simulations and optimisation), in particular about compressible two-phase flows. This includes the derivation of strategies for model coupling, for instance in the case of an asymptotic hierarchy of models.

9.2. National Initiatives

9.2.1. ANR SEDIFLO (2015-2019)

Participants: Emmanuel Audusse, Martin Parisot.

Program: ANR Défi 1 "Gestion sobre des ressources et adaptation au changement climatique" (JCJC)

Project acronym: SEDIFLO

Project title: Modelling and simulation of solid transport in rivers

Coordinator: Sébastien Boyaval (LHSV/ENPC)

Based on recent theoretical and experimental results, this project is aimed at modelling transport of sediments within rivers. It will rely on innovations from the point of view of rheology as well as advanced mathematical tools (asymptotic model reduction, PDE discretisation).

9.2.2. ANR Hyflo-Eflu (2016-2020)

Participants: Martin Parisot, Jacques Sainte-Marie, Julien Salomon.

Appel à projets ANR : Energies marines renouvelables

Project acronym: Hyflo-Eflu

Project title: Hydroliennes flottantes et énergie fluviale

Coordinator: Julien Salomon

The objective of the project HyFlo-EFlu is to deliver a numerical software able to simulate the dynamic of a floating water turbine in real context. Thanks to the collaboration between a team of mathematician specialist of free surface flow and optimization and the industrial developers of the turbine. For the academic partner, the main challenge is in the simulation of the floating structure at the scale of the river, and the modelling of the vertical and horizontal axis turbine. For the industrial partner, the objective is the validation of the stability of the structure and the performance in term of energy production.

9.2.3. ANR MIMOSA (2014–2017)

Participants: Nora Aïssiouene, Marie-Odile Bristeau, Anne Mangeney, Bernard Di Martino, Jacques Sainte-Marie.

Program: ANR Défi 1 "Gestion sobre des ressources et adaptation au changement climatique"

Project acronym: MIMOSA

Project title: MIcroseism MOdeling and Seismic Applications

Coordinator: Eleonore Stutzmann (IPGP)

Seismic noise is recorded by broadband seismometers in the absence of earthquakes. It is generated by the atmosphere-ocean system with different mechanisms in the different frequency bands. Even though some mechanisms have been known for decades, an integrated understanding of the noise in the broadband period band 1-300sec is still missing. Using novel theoretical, numerical and signal processing methods, this project will provide a unified understanding of the noise sources and quantitative models for broadband noise. Conversely, we will be able to interpret seismic noise in terms of ocean wave properties. This first analysis step will lead to the identification and characterization of source events, which we will use to improve noise tomography, and seismic monitoring.

9.2.4. ANR LANDQUAKES (2012–2016)

Program: ANR Blanc "Mathématiques et interactions"

Project acronym: LANDQUAKES

Project title: Modélisation des glissements de terrain et des ondes sismiques générées pour détecter et comprendre les instabilités gravitaires

Coordinator: Anne Mangeney

Within the ANR domain "Mathematics and Interfaces", this ANR project (between Univ. Paris-Est – LAMA, Univ. Denis Diderot Paris 7 – IPGP, Univ. Nantes – LPGN, Univ. Strasbourg EOST, 180.000 euros) deals with the mathematical and numerical modelling of landslides and generated seismic waves.

A. Mangeney is also involved in the CARIB ANR program (2014–2017) entitled "Comprendre les processus de construction et de destruction des volcans de l'Arc des Petites Antilles".

9.2.5. GdR EGRIN (2013–2017)

Participants: Emmanuel Audusse, Bernard Di Martino, Nicole Goutal, Cindy Guichard, Anne Mangeney, Martin Parisot, Jacques Sainte-Marie.

EGRIN stands for Gravity-driven flows and natural hazards. J. Sainte-Marie is the head of the scientific committee of this CNRS research group and A. Mangeney is a member of the committee. Other members of the team involved in the project are local correspondents. The scientific goals of this project are the modelling, analysis and simulation of complex fluids by means of reduced-complexity models in the framework of geophysical flows.

9.2.6. Inria Project Lab "Algae in Silico" (2015-2018)

Participants: Nora Aïssiouene, Marie-Odile Bristeau, David Froger, Raouf Hamouda, Jacques Sainte-Marie.

In the framework of the ADT Inlgae (2013–2015), we developed in collaboration with the BIOCORE Inria project-team a simulation tool for microalgae culture. An Inria Project Lab "Algae in Silico" has started in collaboration with several Inria teams, many BIOCORE and DYLISS. It concerns microalgae culture for biofuel production and the aim is to provide an integrated platform for numerical simulation "from genes to industrial processes".

9.2.7. ANR project HJnet (2013–2015)

Participant: Edwige Godlewski.

This research project consists in studying Hamilton-Jacobi equations on networks, and more generally on heterogeneous structures. This theoretical problem has several potential applications, in particular to traffic flow theory.

9.2.8. Hydraulics for environment and sustainable development (HED^2)

The scienfitic group (GIS in French), which includes Inria and the ANGE team, brings together scientists and engineers involved in hydraulics, risk management and sustainable development. It results in a continuum between fundamental research, applied research and engineering. On the one hand, the ANGE team can be provided with experimental measurements (erosion, long waves, fluid structure interactions,...) thanks to this collaboration; on the other hand, the GIS can favor the transfer of numerical tools and scientific results.

9.3. European Initiatives

9.3.1. ERC Consolidator Grant (2013-2018)

Participant: Anne Mangeney.

The project SLIDEQUAKES is about detection and understanding of landslides by observing and modelling gravitational flows and generated earthquakes and is funded by the European Research Council (2 million euros). More precisely, it deals with the mathematical, numerical and experimental modelling of gravitational flows and generated seismic waves coupled with field measurements to better understand and predict these natural hazards and their link with volcanic, seismic and climatic activities.

9.4. International Research Visitors

9.4.1. Visits of International Scientists

Spanish collaborators – Enrique Fernández-Nieto (Univ. Sevilla) and Tomás Morales de Luna (Univ. Córdoba) – spent one week in Paris (UPMC and Inria) in September.

CASTOR Project-Team

6. Partnerships and Cooperations

6.1. National Initiatives

6.1.1. ANR

- ANEMOS : ANR-11-MONU-002

  ANEMOS : Advanced Numeric for Elms : Models and Optimized Strategies associates JAD Laboratory/Inria (Nice, Manager), IRFM-CEA (Cadarache), Maison de la Simulation (Saclay) and Inria EPI Bacchus (Bordeaux). Elms are disruptive instabilities occurring in the edge region (SOL) of a tokamak plasma. The development of Elms poses a major challenge in magnetic fusion research with tokamaks, as these instabilities can damage plasma-facing components, particularly divertor plates. The mitigation or suppression of large Elms is a critical issue for successful operation of ITER. Goal for ANEMOS is to develop and improve numerical tools in order to simulate physical mechanisms of Elms and to qualify some strategies for their control. We then need to design efficient numerical strategies on the most advanced computers available to contribute to the science base underlying of proposed burning plasma tokamak experiments such as ITER.
- LIVE-CAMS: Till September 30 th 2015, R. Pasquetti was involved in the ANR project LIVE-CAMS.
- MEDIMAX: In 2015 R. Pasquetti and F. Rappeti were involved in in the ANR project MEDIMAX.

6.1.2. Inria Project Lab: FRATRES (Fusion Reactors Research and Simulation)

- Participants : Inria project-teams : CASTOR, IPSO, TONUS,
- Partners : IRFM-CEA, Max Planck Institute-IPP Garching, LJLL-Jussieu, IMT-Toulouse

The current rate of fossil fuel usage and its serious adverse environmental impacts (pollution, greenhouse gas emissions, ...) leads to an energy crisis accompanied by potentially disastrous global climate changes. The research of alternative energy sources is thus of crucial importance. Controlled fusion is one of the most promising alternatives to the use of fossil resources, potentially with a unlimited source of fuel. Controlled nuclear fusion can be considered as an example of grand challenge in many fields of computational sciences from physical modeling, mathematical and numerical analysis to algorithmics and software development and several Inria teams and their partners are developing mathematical and numerical tools in these areas.
Since january 2015, H. Guillard is coordinating the Inria Project Lab FRATRES (https://team.inria.fr/ipl-fratres/) to organize these developments on a collaborative basis in order to overcome the current limitations of today numerical methodologies. The ambition is to prepare the next generation of numerical modeling methodologies able to use in an optimal way the processing capabilities of modern massively parallel architectures. This objective requires close collaboration between a) applied mathematicians and physicists that develop and study mathematical models of PDE; b) numerical analysts developing approximation schemes; c) specialists of algorithmic proposing solvers and libraries using the many levels of parallelism offered by the modern architecture and d) computer scientists. This Inria Project Lab will contribute in close connection with National and European initiatives devoted to nuclear Fusion to the improvement and design of numerical simulation technologies applied to plasma physics and in particular to the ITER project for magnetic confinement fusion.

Contact : Hervé Guillard

6.2. European Initiatives

6.2.1. FP7 & H2020 Projects

- EUROfusion Grant agreement number 633053. Enabling Research program.
  - CfP-WP14-ER-01/CEA-01; JOREK, BOUT++ non-linear MHD modelling of MHD instabilities and their control in existing tokamaks and ITER (PI: Matthias Hoelzl, IPP)
  - CfP-WP14-ER-01; Synergetic numerical-experimental approach to fundamental aspects of turbulent transport in the tokamak edge (PI: Paolo Ricci, École Polytechnique Fédérale de Lausanne).
- EUROfusion WPCD (Working Package Code Development)
  - ACT1: Extended equilibrium and stability chain (participation)
  - ACT2: Free boundary equilibrium and control (participation and coordination)
- The team also participates in the EoCoE European project. Grant Agreement number: 676629 — EoCoE — H2020-EINFRA-2014-2015/H2020-EINFRA-2015-1.

6.3. International Initiatives

6.3.1. Inria Associate Teams not involved in an Inria International Labs

6.3.1.1. AMOSS

Title: Advanced Modeling on Shear Shallow Flows for Curved Topography : water and granular flows.

International Partner (Institution - Laboratory - Researcher):

NCKU (Taiwan)- Yih-Chin Tai

Start year: 2014

Our objective here is to generalize the promising modeling strategy proposed by S. Gavrilyuk (2012-2013) to genuinely 3D shear flows and also take into account the curvature effects related to topography. Special care will be exercised to ensure that the numerical methodology can take full advantage of massively parallel computational platforms and serve as a practical engineering tool. Cross validations will be achieved by experiments and numerical simulations with applications to landslides.

6.3.1.2. Informal International Partners

The team collaborates with TUC technical University of Crete (Prof. Argyris Delis) on the subject of shallow water models. Part of this collaboration is common with the works done in the framework of the AMOSS associate team.

6.4. International Research Visitors

6.4.1. Visits of International Scientists

- D. Balsara of the Notre Dame University (USA), as invited professor for one month at the university of Nice (June/July 2015).
- Key-Ming Shyue of the National Taiwan University, as invited professor for one month at the university of Marseille (September 2015)
- Chih-Yu Kuo, Associate Research Fellow, Research Center for Applied Sciences, Academia Sinica, Taipei, Taiwan, and Yih-Chin Tai, Professor, National Cheng Kung University, Tainan, Taiwan. Visit at Inria Sophia in July 2015.

6.4.1.1. Internships

- J. Llobell, March-June 2015, T. Goudon, S. Minjeaud, M. Ribot.
- L. Drescher, TU Berlin, September-October 2015, H. Heumann
- P. Wang, June-September 2015, J. Blum, C.Boulbe

CLIME Project-Team

8. Partnerships and Cooperations

8.1. National Initiatives

- The ANR project Estimair aims at quantifying the uncertainties of air quality simulations at urban scale. The propagation of uncertainties requires the use of model reduction and emulation. A key uncertainty source lies in the traffic emissions, which will be generated using a dynamic traffic assignment model. Ensembles of traffic assignments will be calibrated and used in the uncertainty quantification. Estimair is led by Clime.
- The IPSL project "AVES" (Ensemble Variational Assimilation applied to a shallow-water model) aims at estimating the quality of an ensemble produced by a variational ensemble algorithm applied on a shallow-water numerical model. A focus is made on the bayesian properties of the ensemble, i.e. its capacity to sample the a-posteriori probability law of the model state.

8.2. European Initiatives

8.2.1. FP7 & H2020 Projects

Program: e-Infrastructures

Project acronym: EoCoE

Project title: Energy oriented Centre of Excellence for computer applications

Duration: 3 years

Coordinator: CEA (Commissariat à l'énergie atomique et aux énergies alternatives)

Other partners: Forschungzentrum Jülich GMBH and 11 other partners. Inria is third-linked party of CEA.

Abstract: the aim of the project is to establish an Energy Oriented Centre of Excellence for computing applications, (EoCoE). EoCoE (pronounce "Echo") will use the prodigious potential offered by the ever-growing computing infrastructure to foster and accelerate the European transition to a reliable and low carbon energy supply. To achieve this goal, we believe that the present revolution in hardware technology calls for a similar paradigm change in the way application codes are designed. EoCoE will assist the energy transition via targeted support to four renewable energy pillars: Meteo, Materials, Water and Fusion, each with a heavy reliance on numerical modelling. These four pillars will be anchored within a strong transversal multidisciplinary basis providing high-end expertise in applied mathematics and HPC.

8.2.2. Collaborations with Major European Organizations

Partner: ERCIM working group "Environmental Modeling".

The working group gathers laboratories of ERCIM working on developing models, processing environmental data or data assimilation.

8.3. International Initiatives

8.3.1. Inria International Partners

8.3.1.1. Informal International Partners

Partner: Marine Hydrophysical Institute, Sevastopol.

The collaboration concerns the study of the Black Sea surface circulation and the issue of image assimilation in forecasting models.

Partner: IBM Research, Dublin, Ireland

The collaboration addresses the assimilation of classical observations as well as images, with application to geophysics. New assimilation methods are developed, mainly based on minimax filtering.

COFFEE Project-Team

7. Partnerships and Cooperations

7.1. National Initiatives

7.1.1. ANR

The ANR-project Monumentalg, led by M. Ribot, is devoted to the modeling and simulation of biological damage on monuments and algae proliferation.

7.1.2. National and European networks

- GdR MoMas.

  The research group MoMaS (Mathematical Modeling and Numerical Simulation for Nuclear Waste Management Problems) has activities centered around scientific computing, design of new numerical schemes and mathematical modelling (upscaling, homogenization, sensitivity studies, inverse problems,...). Its goal is to coordinate research in this area, as well as to promote the emergence of focused groups around specific projects
- S. Junca is involved in the GdR-e "Wave Propagation in Complex Media for Quantitative and non Destructive Evaluation".

7.2. Regional Initiatives

The team is involved in the recently granted project UCA-JEDI.

7.3. International Initiatives

7.3.1. Inria International Partners

7.3.1.1. Declared Inria International Partners

Team COKLYCO

Title: Modeling, analysis and simulation of kinetic and fluid models for MEMS

International Partner (Institution - Laboratory - Researcher):

Kyoto (Japan) - Department of Mechanical Engineering and Science (ME) - Aoki Kazuo

Start year: 2014 End year: 2016.

See also: https://team.inria.fr/coffee/?page_id=323

We wish to elaborate and analyse new models of microscopic and macroscopic type for Micro-Electro-Mechanical Systems (MEMS). The tiny scales of such technical devices induce new and challenging difficulties. A specific attention will be paid to the treatment of coupling conditions from moving boundaries, and to the multi-scale character of the problem. The project is based on a strong interplay between mathematical analysis, experiments and numerical simulations, made possible by the composition of the team.

7.3.1.2. Informal International Partners

Quite recently, S. Junca has started a collaboration with Mathias Legrand, from the Mechanical Engineering department at Mc Gill, Montréal with the supervision of the internship of a master student (S. Heng, 6 months, June-Nov. 2013). Furthermore, S. Junca is an active member of the European network "Wave propagation in complex media for quantitative and non destructive evaluation" [0]

[0] http://www.gdre-us.cnrs-mrs.fr/spip.php?rubrique8

S. Krell has a collaboration with Martin Gander (University of Geneva, Switzerland) on domain decomposition methods, adapted to DDFV discretizations.

M. Ribot started a collaboration with Roberto Natalini a couple of years ago. Connections with experts in Firenze was the starting point of the research on biofilm formation and algae proliferation. M. Ribot and R. Natalini have also worked on new well-balanced strategy — the so-called AHO schemes — in order to preserve equilibria and to capture correctly large time solutions for complex PDEs system, without knowing explicitly the equilibrium solution. They have co-advised 2 PhD thesis.

Finally, we have many international collaborations, with variable peaks of activity, in our research networks: A. Vasseur (U. T. Austin), P.E. Jabin (Univ. Maryland), J.-A. Carrillo (Imperial College London), S. Jin (U. W. Madison and Jiao Tong Univ.), R. Aavatsmark (Univ. of Bergen), etc.

M. Ribot spent a semester, funded by CNRS at ICL, UK.

7.4. International Research Visitors

7.4.1. Visits of International Scientists

Kazuo Aoki, Satushi Taguchi, Takeru Yano, Shingo Kosuge from Kyoto and Osaka University.

7.4.1.1. Internships

Luis Urrutia from Granada

FLUMINANCE Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

8.1.1. Comins'lab: SEACS

Participant: Etienne Mémin.

duration 48 months. The SEACS project whose acronym stands for: "Stochastic modEl-dAta-Coupled representationS for the analysis, simulation and reconstruction of upper ocean dynamics" is a Joint Research Initiative between the three Britanny clusters of excellence of the "Laboratoires d'Excellence" program: Cominlabs, Lebesgue and LabexMer centered on numerical sciences, mathemathics and oceanography respectively. Within this project we aim at studying the potential of large-scale oceanic dynamics modeling under uncertainty for ensemble forecasting and satellite image data assimilation.

8.2. National Initiatives

8.2.1. ANR JCJC GERONIMO : Advanced GEophysical Reduced-Order Model construction from IMage Observations

Participant: Cédric Herzet.

duration 48 months. The GERONIMO project which starts in March 2014 aims at devising new efficient and effective techniques for the design of geophysical reduced-order models from image data. The project both arises from the crucial need of accurate low-order descriptions of highly-complex geophysical phenomena and the recent numerical revolution which has supplied the geophysical scientists with an unprecedented volume of image data. The project is placed at the intersection of several fields of expertise (Bayesian inference, matrix factorization, sparse representations, etc.) which will be combined to handle the uncertainties associated to image measurements and to characterize the accurate reduced dynamical systems.

8.2.2. INSU-LEFE: Toward new methods for the estimation of sub-meso scale oceanic streams

Participant: Cédric Herzet.

duration 36 months. This project tackles the problem of deriving a precise submesoscale characterization of ocean currents from satellite data. The targeted methodologies should in particular enable the exploitation of data of different nature (for example sea surface temperature or height) and/or resolutions. This 36-month project benefits from a collaboration with the Laboratoire de Météorologie Dynamique, Ecole Normale Supérieure, Paris.

8.2.3. INSU-LEFE: MODELER

Participant: Etienne Mémin.

duration 24 months. This project with MeteoFrance aims at exploring error modeling and stochastic parameterization in geophysical flow dynamics. The theory explored in this context should enable the construction of unified image data assimilation strategies.

8.3. International Initiatives

8.3.1. Informal International Partners

Universidad de Buenos Aires (ARGENTINA) We have maintained academic exchanges with the group of Guillermo Artana.

Chico California State University (USA), We have pursue our collaboration with the group of Shane Mayor on the GPU implementation of wavelet based motion estimator for Lidar data. This code is developped in coproperty between Inria and Chico.

8.3.2. Participation In other International Programs

SticAMSUD project Voiceproduction leaded by Denisse Sciamarella (CNRS, LIMSI)

LEMON Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

- **Cart'Eaux** project (funded by Languedoc Roussillon region): in partnership with colleagues of LIRMM and HSM (Montpellier) Carole DELENNE will develop a new method to gather various types of data in order to produce a regular and complete mapping of urban assainissement, in order to allow sharp and complete hydrodynamical modeling of urban pipes.
- The GeRIMU project (Gestion du Risque d'Inondation en Milieu Urbain) counts 3 partners: Cerec Ingénierie, HSM and Predict Services. In this porject, the upscaled shallow water model with porosity SW2D developed at HSM is embedded in a software chain that will allow fast uran flood computations from forecasted precisiptation fields. The project is funded under the Feder scheme. It has earned a distinction from the local Scientific Advisory Committee ("Coup de coeur du COSTI").

9.2. National Initiatives

9.2.1. ANR

Fabien MARCHE is member of the ANR project BonD (PI Sylvie Benzoni), 2013-2017
Fabien MARCHE is member of the ANR project ACHYLLES (PI Rodolphe Turpault), 2014-2017
Fabien CAMPILLO is member of the ANR project Slofadybio, 2015-2016

9.3. International Initiatives

9.3.1. Inria International Labs

9.3.1.1. Nuwat / LIRIMA

With Moshen Chebbi (Phd student, ENIT, Tunis) we continue to explore the stochastic modeling for biotechnological problems. We proposed a framework that allows for both analysis and simulation of the models. This framework slightly generalized standard jump Markov processes on grids popularized by Tom Kurtz and co-workers. With Oussama Hadj-Abdelkader (Univ. Tlemcen) we continue to explore the nonlinear filtering techniques for the chemostat including unscented Kalman filtering and particle filtering.

9.3.1.2. Inria Chile

Antoine ROUSSEAU visited Inria Chile in January, 2015 (2 weeks) in order to prepare a long stay in Chile in 2016.

9.3.2. Inria International Partners

9.3.2.1. Declared Inria International Partners

In 2015, the *Marine Energies Research International Center* (MERIC) was launched in Chile by CORFO. Antoine ROUSSEAU will be the scientific coordinator for Inria, and several members of LEMON, CARDAMOM and TOSCA research teams will be involved in this 8 years project driven by DCNS. Antoine ROUSSEAU and Fabien MARCHE are involved in the research line *resource assessment & site characterization*.

9.3.2.2. Informal International Partners

Vincent GUINOT collaborates with B.F. Sanders (Irvine University, Californie, USA)
Vincent GUINOT collaborates with S. Soares-Frazao (Unité de Génie Civil, Université catholique de Louvain, Belgium)
Antoine ROUSSEAU and Fabien MARCHE collaborate with Rodrigo Cienfuegos and Cristián Escauriaza (CIGIDEN and PUC Chile, Santiago)

9.4. International Research Visitors

9.4.1. Visits of International Scientists

Carine Lucas (Université of Orléans, France) spent several months in LEMON to collaborate with Antoine ROUSSEAU on nontraditional models in oceanography.

MAGIQUE-3D Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

8.1.1. Partnership with I2M in Bordeaux supported by Conseil Régional d'Aquitaine

title: Imaging complex materials.

Coordinator: Hélène Barucq

Other partners: I2M CNRS Université Bordeaux I

The detection, localization and monitoring of the defect evolution in composite materials, concrete and more generally heterogeneous materials is a challenging problem for Aeronautics and energy production. It is already possible to localize defects in homogeneous materials by using methods based on ultrasonic inspection and sometimes, they are usable in particular heterogeneous materials, most of the time in 2D. Classical methods rely on the correspondence between the distance and the propagation time of the wave traveling between the defect and the receivers. In complex media, such a correspondence may be lapsed, for instance when the velocity depends on the frequency (dispersion) or of the propagation direction (anisotropy). The defect signature can also be embedded in the acoustic field sent by the structure (multiple reflections). The complexity of the propagation in heterogeneous materials makes then difficult the accurate localization of the defect, in particular in 3D.

Topological imaging techniques can be applied to heterogeneous media. They can find the positions of defects from two simulations performed in a safe experimental medium. They have been developed at I2M laboratory to carry on 2D single/multi mode inspection in isotropic and anisotropic waveguides. They have also been applied to a highly reflecting medium observed with a single sensor. The objective of this work is to extend the technique to 3D problems. In particular, we are going to handle detection in composite plates and in highly heterogeneous media including a collection of small scatterers.

This project is supported by the Conseil Régional d'Aquitaine, for a duration of 2 years.

8.2. National Initiatives

8.2.1. Depth Imaging Partnership

Magique-3D maintains active collaborations with Total. In the context of Depth Imaging, Magique-3D coordinates research activities dealing with the development of high-performance numerical methods for solving wave equations in complex media. This project involves 2 other Inria Team-Projects (Hiepacs and Nachos) which have complementary skills in mathematics, computing and in geophysics. DIP is fully funded by Total by the way of an outline agreement wit Inria .

Since its beginning (2009), eight PhD students have been funded and Magique 3D has hired six of them, one being shared with the project team Nachos (http://www-sop.inria.fr/nachos/). Moreover, several internships have been realized. In 2014 the second phase of DIP has begun. Lionel Boillot has been hired as engineer to work on the DIP platform.

8.2.2. Micro-local analysis of wave equations

The numerical solution of wave equations most often requires to truncate the propagation domain to define a computational domain limited by an artificial boundary. Magique-3D is very involved in the construction and mathematical validation of boundary conditions which are set on the artificial boundary. Different techniques can be used for the design of such conditions and Magique-3D maintains a collaboration with Prof. Olivier Lafitte from the University of Paris 13 on the mathematical analysis of the Dirichlet-to-Neumann (DtN) operator for acoustic waves. This issue is addressed by applying micro-local analysis which enables us to consider the full DtN operator in the whole space of frequencies.

8.2.3. Partnership with the department DMAE of ONERA

title: Modeling of multiperforated plates

Coordinator: Sébastien Tordeux

Other partners: Department DMAE of ONERA

Abstract: In the aeronautic industry, there is a need of numerical models for the design of turboreactors of new generation. Magique-3D is cooperating with the department DMAE of ONERA to develop acoustic models of multiperforated plates which is an important component of the turboreactors.

This project is interdisciplinary, since it involves the experimental expertise of Estelle Piot (acoustician engineer of ONERA working on acoustic bench), the competences in mathematical modeling of Magique 3D. In parallel to the obtention of new theoretical results we are jointly developing a new numerical library based on the discontinuous Galerkin approximation which aims in interpreting experimental data.

This cooperation is formalized thanks to the common supervision of the PhD of Vincent Popie funded by ONERA and DGA and is a follow-up of the ANR APAM (2008-2011).

8.3. European Initiatives

8.3.1. FP7 & H2020 Projects

8.3.1.1. GEAGAM

Title: Geophysical Exploration using Advanced GAlerkin Methods

Programm: H2020

Duration: January 2015 - January 2018

Coordinator: Universidad Del Pais Vasco (EHU UPV)

Partners:

Bcam - Basque Center for Applied Mathematics Asociacion (Spain)

Barcelona Supercomputing Center - Centro Nacional de Supercomputacion (Spain)

Total S.A. (France)

Universidad Del Pais Vasco/ Euskal Herriko Unibertsitatea (Spain)

Inria contact: Hélène BARUCQ

The main objective of this Marie Curie RISE action is to improve and exchange interdisciplinary knowledge on applied mathematics, high performance computing, and geophysics to be able to better simulate and understand the materials composing the Earth's subsurface. This is essential for a variety of applications such as CO2 storage, hydrocarbon extraction, mining, and geothermal energy production, among others. All these problems have in common the need to obtain an accurate characterization of the Earth's subsurface, and to achieve this goal, several complementary areas will be studied, including the mathematical foundations of various high-order Galerkin multiphysics simulation methods, the efficient computer implementation of these methods in large parallel machines and GPUs, and some crucial geophysical aspects such as the design of measurement acquisition systems in different scenarios. Results will be widely disseminated through publications, workshops, post-graduate courses to train new researchers, a dedicated webpage, and visits to companies working in the area. In that way, we will perform an important role in technology transfer between the most advanced numerical methods and mathematics of the moment and the area of applied geophysics.

8.3.1.2. HPC4E

Title: HPC for Energy

Programm: H2020

Duration: December 2015 - December 2017

Coordinator: Barcelona Supercomputing Center

Inria contact: Stephane Lanteri

During the last years, High Performance Computing (HPC) resources have undergone a dramatic transformation, with an explosion on the available parallelism and the use of special purpose processors. There are international initiatives focusing on redesigning hardware and software in order to achieve the Exaflop (10^{18} flops) capability. This project aims at applying the new exascale HPC techniques to energy industry simulations, customizing them if necessary, and going beyond the state-of-the-art in the required HPC exascale simulations for different energy sources that are the present and the future of energy: wind energy production and design, efficient combustion systems for biomass-derived fuels (biogas), and exploration geophysics for hydrocarbon reservoirs.

8.4. International Initiatives

8.4.1. Inria International Partners

8.4.1.1. Declared Inria International Partners

8.4.1.1.1. MAGIC2

Title: Advance Modeling in Geophysics

International Partner (Institution - Laboratory - Researcher):

California State University at Northridge (United States) - Department of Mathematics - Djellouli Rabia

The Associated Team MAGIC was created in January 2006 and renewed in January 2009. At the end of the program in December 2011, the two partners, MAGIQUE-3D and the California State University at Northridge (CSUN) decided to continue their collaboration and obtained the “Inria International Partner” label in 2013.

See also: https://project.inria.fr/magic/

The ultimate objective of this research collaboration is to develop efficient solution methodologies for solving inverse problems arising in various applications such as geophysical exploration, underwater acoustics, and electromagnetics. To this end, the research program will be based upon the following three pillars that are the key ingredients for successfully solving inverse obstacle problems. 1) The design of efficient methods for solving high-frequency wave problems. 2) The sensitivity analysis of the scattered field to the shape and parameters of heterogeneities/scatterers. 3) The construction of higher-order Absorbing Boundary Conditions.

8.5. International Research Visitors

8.5.1. Visits of International Scientists

8.5.1.1. Internships

Andrew Wang, graduate student from the Massachusetts Institute of Technology, visited MAGIQUE-3Dfor a two months internship in June and July 2015.

SAGE Project-Team

9. Partnerships and Cooperations

9.1. National Initiatives

9.1.1. ANR-MN: H2MNO4 project

Participants: Yvan Crenner, Benjamin Delfino, Jean-Raynald de Dreuzy, Jocelyne Erhel, Lionel Lenôtre, Géraldine Pichot.

Contract with ANR, program Modèles Numériques
Duration: four years from November 2012.
Title: Original Optimized Object Oriented Numerical Model for Heterogeneous Hydrogeology.
Coordination: Jocelyne Erhel and Géraldine Pichot, with Fabienne Cuyollaa.
Partners: Geosciences Rennes, University of Poitiers, University of Lyon 1, Andra, Itasca.
International collaborations: University of San Diego (USA), UPC, Barcelona (Spain)
Web page: http://h2mno4.inria.fr/
Abstract: The project H2MNO4 develops numerical models for reactive transport in heterogeneous media. It defines six mathematical and computational challenges and three applications for environmental problems with societal impact. We organized a project meeting in February.

9.1.2. Inria Project Lab: C2S@EXA project

Participants: Édouard Canot, Yvan Crenner, Jocelyne Erhel, Géraldine Pichot.

Title: C2S@EXA - Computer and Computational Scienecs at Exascale
Duration: from January 2012.
Coordination: S. Lanteri, Nachos team.
Partners: Inria teams working on HPC; external partners: ANDRA and CEA.
Webpage: http://www-sop.inria.fr/c2s_at_exa/
Abstract: The C2S@Exa Inria Project Lab is concerned with the development of numerical modeling methodologies that fully exploit the processing capabilities of modern massively parallel architectures in the context of a number of selected applications related to important scientific and technological challenges for the quality and the security of life in our society. The team participated in several workshops.

9.1.3. GENCI: project on advanced linear solvers

Participants: Yvan Crenner, Jocelyne Erhel, David Imberti, Lionel Lenôtre, Géraldine Pichot.

Title: Numerical models for hydrogeology
Duration: 2015
Coordination: J. Erhel and G. Pichot.
Webpage: http://www.genci.fr/
Abstract: To run large scale simulations, we defined a project, based on the platform H2OLab and on a new GMRES solver. We obtained and used computing time on machines located at GENCI supercomputing centers.

9.1.4. GDR MOMAS: projects on multiphase flow and reactive transport

Participants: Benjamin Delfino, Jocelyne Erhel.

Title: Workshops on multiphase flow and reactive transport
Duration: 2015
Coordination: J. Erhel
Partner: IFPEN

Webpage: http://www.irisa.fr/sage/RTworkshop and https://www.ljll.math.upmc.fr/cances/gdrmomas/
Abstract: The working group MOMAS includes many partners from CNRS, Inria, universities, CEA, ANDRA, EDF and BRGM. It covers many subjects related to mathematical modeling and numerical simulations for nuclear waste disposal problems. The team participated in a workshop on multiphase flow and organized an international workshop on reactive transport, in Paris, with IFPEN.

9.2. European Initiatives

9.2.1. FP7 & H2020 Projects: EXA2CT project

Participants: Jocelyne Erhel, David Imberti.

Title: EXascale Algorithms and Advanced Computational Techniques

Programm: FP7

Duration: September 2013 - August 2016

Coordinator: S. Ashby, IMEC, Belgium

Partners:

Fraunhofer-Gesellschaft Zur Foerderung Der Angewandten Forschung E.V (Germany)

Interuniversitair Micro-Electronica Centrum Vzw (Belgium)

Intel Corporations (France)

Numerical Algorithms Group Ltd (United Kingdom)

Systems Solutions for Research (Germany)

Universiteit Antwerpen (Belgium)

Universita della Svizzera italiana (Switzerland)

Universite de Versailles Saint-Quentin-En-Yvelines. (France)

Vysoka Skola Banska - Technicka Univerzita Ostrava (Czech Republic)

Inria contact: Luc Giraud

Abstract: Numerical simulation is a crucial part of science and industry in Europe. The advancement of simulation as a discipline relies on increasingly compute intensive models that require more computational resources to run. This is the driver for the evolution to exascale. Due to limits in the increase in single processor performance, exascale machines will rely on massive parallelism on and off chip, with a complex hierarchy of resources. The large number of components and the machine complexity introduce severe problems for reliability and programmability. The former of these will require novel fault-aware algorithms and support software. In addition, the scale of the numerical models exacerbates the difficulties by making the use of more complex simulation algorithms necessary, for numerical stability reasons. A key example of this is increased reliance on solvers. Such solvers require global communication, which impacts scalability, and are often used with preconditioners, increasing complexity again. Unless there is a major rethink of the design of solver algorithms, their components and software structure, a large class of important numerical simulations will not scale beyond petascale. This in turn will hold back the development of European science and industry which will fail to reap the benefits from exascale. The EXA2CT project brings together experts at the cutting edge of the development of solvers, related algorithmic techniques, and HPC software architects for programming models and communication. It will take a revolutionary approach to exascale solvers and programming models, rather than the incremental approach of other projects. We will produce modular open source proto-applications that demonstrate the algorithms and programming techniques developed in the project, to help boot-strap the creation of genuine exascale codes.

9.2.2. FP7 & H2020 Projects: EOCOE project

Participant: Jocelyne Erhel.

Program: EINFRA-5-2015

Project acronym: EoCoE

Project title: Energy oriented Center of Excellence for computer applications

Duration: 36 months

Coordinator: CEA

Other partners: organisme, labo (pays) : 12 other partners

Abstract: the EoCoE objectives aims at firstly, to design, test and spread new methodological and organisational paradigms (Objectives 1, 3, and 4) driven by the users communities and, secondly, to contribute to mathematical and computer sciences challenges on the whole HPC tool chain (Objective 2).

9.3. International Initiatives

9.3.1. Inria International Labs: LIRIMA Afrique, EPIC team (Tunisia)

Participants: Édouard Canot, Jocelyne Erhel.

Program: Laboratoire International de Recherche en Informatique et Mathématiques Appliquées

Title: Problèmes Inverses et Contrôle

Inria principal investigator: Houssem Haddar, Defi team

International Partner (Institution - Laboratory - Researcher): ENIT, University of Tunis, Tunisia - LAMSIN - Amel ben Abda

Duration: 2011-2015

See also: http://www.lirima.uninet.cm/index.php/recherche/equipes-de-recherche/epic

Abstract: The team deals with nonlinear and inverse problems.

9.3.2. International Program ECOS Sud (Chili): ARPHYMAT project

Participant: Édouard Canot.

Program: CONICYT

Title: Processus de formation et transformation de structures de combustion archéologique : un regard interdisciplinaire

Inria principal investigator: Édouard CANOT

International Partner (Institution - Laboratory - Researcher): Universidad de Tarapaca (Chili)

Duration: Jan 2014 - Dec 2016

Abstract: Multidisciplinary study of prehistoric fire traces in South America, by means of different approaches: taphonomy of the soil, physical processes involved during the heat transfer, modeling and numerical simulations.

9.3.3. Inria Euromediterranean: HYDRINV project

Participants: Édouard Canot, Jocelyne Erhel.

Program: Euromediterranean 3+3

Title: Direct and inverse problems in subsurface flow and transport

Coordination: H. ben Ameur, ENIT, Tunisia and J. Jaffré, Inria, Paris

Inria-Rennes principal investigator: Jocelyne Erhel

Duration: Jan 2012 - Dec 2015

International Partners (Institution - Laboratory - Researcher):

Université Ibn Tofail - Faculté des Sciences de Kénitra (Morocco) - Laboratoire Interdisciplinaire en Ressources Naturelles et en Environnement - Zoubida Mghazli

Ecole Nationale d'Ingénieurs de Tunis (Tunisia) - Laboratoire de Modélisation en Hydraulique et Environnement - Rachida Bouhlila

Universidad de Sevilla (Spain) - Department Ecuaciones Diferenciales y Anålisis Numérico - Tomas Chacon Rebollo

Universitat Politècnica de Catalunya (Spain) - Department of Geotechnical Engineering and Geo-Sciences - Xavier Sànchez Vila

University Centre of KHEMIS MILIANA (Algeria) - Laboratoire de l'Energie et des Systèmes Intelligents - Mohammed Hachama

Ecole Mohammadia d'Ingénieurs (Morocco) - LERMA - Rajae Aboulaich

Ecole Nationale d'Ingénieurs de Tunis (Tunisia) - Laboratoire de Modélisation Mathématique et Numérique dans les Sciences de l'Ingénieur - Hend Ben Ameur

The management of water resources is a problem of great importance in all countries, and is particularly acute around the Mediterranean sea. The goal is to find a reasonable balance between these resources and demand while preserving the quality of water. Towards this goal it is essential to understand and simulate flow and transport in the subsurface. The science corresponding to this topic is hydrogeology. Since models become more and more complicated and quantitative answers must be given, numerical modeling become more and more sophisticated and mathematicians must also be involved. This project brings together hydrogeologists and mathematicians from France, Spain, Algeria, Morocco and Tunisia in order to develop, analyze, and validate numerical methods for several problems arising from modeling flow and transport in the subsurface. The emphasis is put on direct nonlinear problems (air-water flow, density driven flow related to salinization, transport with chemistry) and on inverse problems.

9.4. International Research Visitors

9.4.1. Visits of International Scientists

- Nabil Nassif, American University of Beirut, Lebanon, April, 1 week
- Lamia Guellouz, ENIT, Tunisia, May, 1 week

9.4.2. Internships (Joint supervision of Ph-D students)

- Marwen ben Refifa, University of Tunis, 5 months, April-July 2015
- Salwa Mansour, Lebanese University, 8 months, Feb-Sep 2015

9.4.3. Visits to International Teams

- Lionel Lenôtre visited Pr. Dr. Sylvie Roelly and her students at Potsdam University, Potsdam, Germany, one week, December 2015.

SERENA Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

GT Elfic (Labex DigiCosme, 2014–2016): "Programmes d'éléments finis formellement vérifiés", with TOCCATA (Inria Saclay - Île-de-France), CEA LIST, LIPN (Université de Paris 13), and LMAC (Université de Technologie de Compiègne).

The research on a posteriori error estimates, unified frameworks, robustness, adaptivity, and stopping criteria of M. Vohralík was carried out with Alexandre ERN from CERMICS, Ecole Nationale des Ponts et Chaussées, see [14], [24].

A posteriori error estimates for eigenvalue problems were derived in collaboration with Geneviève DUSSON, Yvon MADAY, and Benjamin STAMM from the Laboratoire Jacques-Louis Lions and Eric CANCÈS, CERMICS, see [21] and [22].

A posteriori error estimates for problems with sign-changing coefficients describing electromagnetism for interfaces between dielectrics and negative metamaterials have been derived in collaboration with P. Ciarlet from the project-team POEMS, see [23].

9.2. National Initiatives

9.2.1. ANR

ANR GEOPOR: "Geometrical approach for porous media flows: theory and numerics", with Laboratoire Jacques-Louis Lions (University Paris VI).

ANR MANIF: "Mathematical and numerical issues in first-principle molecular simulation", with CERMICS (Ecole Nationale des Ponts et Chaussées), and Laboratoire Jacques-Louis Lions (University Paris VI).

ANR DEDALES; "Algebraic and Geometric Domain Decomposition for Subsurface Flow". The project aims at developing high performance software for the simulation of two phase flow in porous media. The project will specifically target parallel computers where each node is itself composed of a large number of processing cores, such as are found in new generation many-core architectures.

The partners are HIEPACS, Laboratoire Analyse, Géométrie et Application, Maison de la Simulation, and ANDRA. The coordiinator of the project is M. Kern.

C2S@Exa (Computer and Computational Sciences at Exascale) is an Inria Project Lab (IPL). This national initiative aims at the development of numerical modeling methodologies that fully exploit the processing capabilities of modern massively parallel architectures in the context of a number of selected applications related to important scientific and technological challenges for the quality and the security of life in our society. This project supports in particular the Ph.D. of N. Birgle (supervised by. J. Jaffré) which is part of an Inria-Andra collaboration.

9.2.2. FUI

Projet P (2011–2015) is funded by the French FUI (*Fonds Unique Interministériel*). Project P aims at supporting the model-driven engineering of high-integrity embedded real-time systems by providing an open code generation framework. The contribution of team Serena is in the domain of language translation and block-schema modelization semantics. This project supports the work of C. Franchini, under the supervision of P. Weis.

9.3. European Initiatives

9.3.1. Collaborations in European Programs, except FP7 & H2020

Program: Research, Development and Innovation Council of the Czech Republic

Project acronym: MORE

Project title: Implicitly constituted material models: from theory through model reduction to efficient numerical methods

Duration: September 2012 – September 2017

Coordinator: Josef MÁLEK, Charles University in Prague

Other partners: Institute of Mathematics, Academy of Sciences of the Czech Republic; Oxford Centre for Nonlinear Partial Differential Equations, Great Britain.

Abstract: A multidisciplinary project on nonlinear Navier–Stokes flows with implicit constitutive laws. It focuses on development of accurate, efficient, and robust numerical methods for simulations of the new class of implicit models, see http://more.karlin.mff.cuni.cz/.

9.4. International Initiatives

9.4.1. Participation In International Programs

Serena is part of the EuroMediterranean 3+3 program with the project HYDRINV (2012–2015): Direct and inverse problems in subsurface flow and transport. Besides Inria, institutions participating in this project are: Universitat Politècnica de Catalunya (Barcelona, Spain), Universidad de Sevilla (Spain), École Mohamedia d'Ingénieurs (Rabat, Morocco), Université Ibn Tofaïl (Kenitra, Morocco), University Centre of Khemis Miliana (Algeria), and École Nationale d'Ingénieurs de Tunis (Tunisia).

9.5. International Research Visitors

9.5.1. Visits of International Scientists

Josef Málek, professor, Mathematical Institute, Charles University in Prague. February 2–6, 2015.

Iuliu Sorin Pop, professor, Department of Mathematics and Computer Science, Eindhoven University of Technology. March 2–6, 2015.

H. Ben Ameur, professor at IPEST and member of ENIT-Lamsin, Tunis, Tunisia. November 9–20, 2015.

Carol Woodward, computational mathematician in the Center for Applied Scientific Computing (CASC) at Lawrence Livermore National Laboratory, USA, December 4, 2015.

STEEP Project-Team

8. Partnerships and Cooperations

8.1. National Initiatives

8.1.1. ANR

CITiES (*Calibrage et valIdation de modèles Transport - usagE des Sols*)
Program: "*Modèles Numériques*" 2012, ANR
Duration: 2013 – 2016
Coordinator: Emmanuel Prados (STEEP)
Other partners: LET, IDDRI, IRTES-SET ("Systemes and Transports" lab of Univ. of Tech. of Belfort-Montbéliard), IFSTTAR-DEST Paris (formerly INRETS), LVMT ("*Laboratoire Ville Mobilité Transport*", Marne la Vallée), VINCI (Pirandello Ingenierie, Paris), IAU Île-De-France (Urban Agency of Paris), AURG (Urban Agency of Grenoble), MOISE (Inria project-team)
Abstract: Calibration and validation of transport and land use models.

8.1.2. FRB (Fondation pour la Recherche sur la Biodiversité)

ESNET (Futures of ecosystem services networks for the Grenoble region)
Program: "Modeling and Scenarios of Biodiversity" flagship program, Fondation pour la Recherche sur la Biodiversité (FRB). This project is funded by ONEMA (*Office National de l'Eau et des Milieux Aquatiques*).
Duration: 2013 – 2016
Coordinator: Sandra Lavorel (LECA)
Other partners: EDDEN (UPMF/CNRS), IRSTEA Grenoble (formerly CEMAGREF), PACTE (UJF/CNRS), ERIC (Lyon 2/CNRS)
Abstract: This project explores alternative futures of ecosystem services under combined scenarios of land-use and climate change for the Grenoble urban area in the French Alps. In this project, STEEP works in particular on the modeling of the land use and land cover changes, and to a smaller extent on the interaction of these changes with some specific services.

TONUS Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

The thesis of Pierre Gerhard devoted to numerical simulation of room acoustics is supported by the Alsace region. It is a joint project with CEREMA (Centre d'études et d'expertise sur les risques, l'environnement, la mobilité et l'aménagement) in Strasbourg.

9.2. National Initiatives

9.2.1. ANR

- ANR project GYPSI (2010-2015), https://sites.google.com/site/anrgypsi/: coordinator Philippe Ghendrih (CEA Cadarache), other participants, University of Marseille, Universities of Strasbourg and Nancy (CALVI and then TONUS project-team). The aim is to understand the physics of turbulence in magnetically confined plasma using numerical simulation
  Participants: Philippe Helluy [local coordinator], Michel Mehrenberger.
- ANR project "PEPPSI" in Programme Blanc SIMI 9 – Sciences de l'ingénierie (Edition 2012) started in 2013.
  Participants: Giovanni Manfredi [coordinator], Sever Adrian Hirstoaga.

9.2.2. IPL FRATRES

The TONUS project belongs to the IPL FRATRES and there was an annual meeting, on 15-16 October 2015, with talks of Emmanuel Franck, Philippe Helluy, Sever Adrian Hirstoaga, Michel Mehrenberger.

9.2.3. IPL C2S@exa

The TONUS and HIEPACS project have obtained the financial support of the PhD thesis of Nicolas Bouzat thanks to the IPL C2S@exa. Nicolas Bouzat works at CEA Cadarache and is supervised locally by Guillaume Latu; the PhD advisors are Michel Mehrenberger and Jean Roman.

9.2.4. Competitivity clusters

- GENCI projet : t2015067387 "Simulation numérique des plasmas par des méthodes semi-lagrangiennes et eulériennes adaptées" 800 000 scalar computing hours on CURIE_standard (January 2015-February 2016); use: 300 000 heures.
  Participants: Sever Adrian Hirstoaga, Guillaume Latu, Michel Mehrenberger [coordinator], Thi Nhung Pham, Christophe Steiner.
- GENCI projet : t2016067580 "Simulation numérique des plasmas par des méthodes semi-lagrangiennes et PIC adaptées" 450 000 scalar computing hours on CURIE_standard (January 2016-January 2017); coordinator: Michel Mehrenberger

9.3. European Initiatives

9.3.1. FP7 & H2020 Projects

9.3.1.1. EUROfusion 2015-2017

- Eurofusion Enabling Research Project ER15-IPP01 (1/2015-12/2017) "Verification and development of new algorithms for gyrokinetic codes" (Principal Investigator: Eric Sonnendrücker, Max-Planck Institute for Plasma Physics, Garching).
  Participants: Philippe Helluy, Sever Adrian Hirstoaga, Michel Mehrenberger.

- Eurofusion Enabling Research Project ER15-IPP05 (1/2015-12/2017) "Global non-linear MHD modeling in toroidal geometry of disruptions, edge localized modes, and techniques for their mitigation and suppression" (Principal Investigator: Matthias Hoelzl, Max-Planck Institute for Plasma Physics, Garching).
  Participant: Emmanuel Franck.

9.4. International Initiatives

9.4.1. Inria International Partners

9.4.1.1. Informal International Partners

Michel Mehrenberger has a collaboration with Bedros Afeyan (Pleasanton, USA) to work on KEEN wave simulations.

9.4.2. Participation In other International Programs

Participants: Emmanuel Franck, Philippe Helluy [local coordinator].

ANR/SPPEXA "EXAMAG" is a joint French-German-Japanese project. Its goal is to develop efficient parallel MHD solvers for future exascale architectures. With our partners we plan to apply highly paralelized and hybrid solvers for plasma physics. One of our objective is to develop Lattice-Boltzmann MHD solvers based on high-order implicit Discontinous Galerkin methods using SCHNAPS and runtime systems such as StarPU.

BIOCORE Project-Team

9. Partnerships and Cooperations

9.1. National Initiatives

9.1.1. National programmes

- **ANR-Purple Sun:** The objective of this project (ANR-13-BIME-004) is to study and optimize a new concept consisting in coupling the production of microalgae with photovoltaic panels. The main idea is to derive the excess of light energy to PV electricity production, in order to reduce the phenomena of photoinhibition and overwarming both reducing microalgal productivity.
- **ANR-Facteur 4:** The objective of this project to produce non OGM strain of microalgae with enhanced performance. BIOCORE is involved in the directed selection of microalgae with interesting properties from an industrial point of view. The theory of competition is used to give a competitive advantage to some species. This competitive advantage can be provided by an online closed loop controller.
- **ANR-Phycover:** The overall objective of the PHYCOVER project is to identify a modular wastewater treatment process for the production of biogas. The method combines three modules. First, a high-rate algal pond is dedicated to the treatment of municipal wastewater. Then, an anaerobic digester capable of co- digesting biomass products (and others organic matter resources) to significantly reduce biological and chemical contaminants while producing a sustainable energy as biogas is analysed. A final module transforms the residual carbon, nitrogen and phosphorus into high-value microalgae dedicated to aquaculture and green chemistry.
- **ANR-FunFit:** The objective of this project (2013-2017) is to develop a trait-based approach linking individual fitness of fungal plant pathogens to ecological strategies. The idea is to derive eco-epidemiological strategies from fitness optimization in colonized environments and during colonization, as well as understanding the coexistence of sibling species. This project is co-coordinated by F. Grognard.
- **ANR-TripTic:** The objective of this project (2014-2018) is to document the biological diversity in the genus of the minute wasps *Trichogramma*, and to study the behavioral and populational traits relevant to their use in biological control programs.
- **ANR-GESTER:** "Management of crop resistances to diseases in agricultural landscapes as a response to new constraints on pesticide use", ANR Agrobiosphère, 2011–2016. This project aims at producing allocation scenarios of resistant varieties at the scale of cultivated landscapes, that will allow to limit disease development while ensuring sustainable efficiency of genetic resistances. BIOCORE participates in this project via MaIAGE, INRA Jouy-en-Josas.
- **ANR-MIHMES:** "Multi-scale modelling, from animal Intra-Host to Metapopulation, of mechanisms of pathogen spread to Evaluate control Strategies", ANR – Investissement d'avenir, action Bioinformatique (ANR-10-BINF-07) & Fond Européen de Développement Régional des Pays-de-la-Loire (FEDER), 2012–2017. This project aims at producing scientific knowledge and methods for the management of endemic infectious animal diseases and veterinary public health risks. BIOCORE participates in this project via MaIAGE, INRA Jouy-en-Josas.
- **RESET:** The objective of this project is to control the growth of *E. coli* cells in a precise way, by arresting and restarting the gene expression machinery of the bacteria in an efficient manner directed at improving product yield and productivity. RESET is an "Investissements d'Avenir" project in Bioinformatics (managed by ANR) and it is coordinated by H. de Jong (Ibis, Inria)

- **SIGNALIFE:** Biocore is part of this Labex (scientific cluster of excellence) whose objective is to build a network for innovation on Signal Transduction Pathways in life Sciences, and is hosted by the Université Nice Sophia Antipolis.
- **OPTIBIO:** This project is devoted to the analysis of optimal control problems related to bioprocesses. The project is funded by Programme Gaspard Monge pour L'Optimisation et la Recherche Opérationnelle and coordinated by T. Bayen (U. Montpellier 2).
- **UMT FIORIMED:** FioriMed is a Mixed Technology Unit created in January 2015 to strengthen the production and dissemination of innovation to the benefit of ornamental horticulture. Horticultural greenhouses are seen as a "laboratory" for the actual implementation of agroecology concepts with the possibility of generic outcomes being transfered to other production systems. The main partners of UMT FioriMed are ASTREDHOR (National Institute of Horticulture) and the ISA Joint Research Unit of INRA-CNRS-Univ. Nice.

9.1.2. Inria funding

- **Inria Project Lab-Algae** *in silico***:** The Algae in silico Inria Project Lab, funded by Inria and coordinated by O. Bernard, focuses on the expertise and knowledge of biologists, applied mathematician and computer scientists to propose an innovative numerical model of microalgal culturing devices. The latest developments in metabolic modelling, hydrodynamic modelling and process control are joined to propose a new generation of advanced simulators in a realistic outdoor environment. The project gathers 5 Inria project teams and 3 external teams.

9.1.3. INRA funding

- **Take Control:** This project, "Deployment strategies of plant quantitative resistance to take control of plant pathogen evolution," is funded by the PRESUME call of the SMAcH INRA metaprogram (Sustainable Management of Crop Health). BIOCORE is a partner together with INRA PACA (Sophia Antipolis and Avignon) and INRA Toulouse (2013-2016). This project provides the major part of the funding for the experiments held for Elsa Rousseau's thesis.
- **K-Masstec:** "Knowledge-driven design of management strategies for stem canker specific resistance genes", INRA Metaprogramme SMaCH, PRESUME action, 2013–2016. The project aims at developing efficient strategies for the deployment of genetic resistance in the field, based on knowledge issued from the understanding of the molecular interaction between distinct avirulence genes, and mainly the discovery of non-conventional gene-for-gene interactions.

9.1.4. Networks

- **GDR Invasions Biologiques:** The objectives of this GDR are to encourage multidisciplinary research approaches on invasion biology. It has five different thematic axes: 1) invasion biology scenarios, 2) biological invasions and ecosystem functioning, 3) environmental impact of invasive species, 4) modeling biological invasions, 5) socio-economics of invasion biology. L. Mailleret is a member of the scientific comittee of the GDR .
- **ModStatSAP:** The objective of this INRA network is to federate researchers in applied mathematics and statistics and to promote mathematical and statistical modelling studies in crop and animal health. S. Touzeau is a member of the scientific committee.
- **Seminar:** BIOCORE organizes a regular seminar "Modeling and control of ecosystems" at the station zoologique of Villefranche-sur-Mer, at INRA-ISA or at Inria.

9.2. European Initiatives

9.2.1. FP7 & H2020 Projects

SysBioDRez: Marie Curie International Incoming Fellowship FP7 (EC-PEOPLE) is a multidisciplinary CNRS-Inria project for the collaboration of Jeremie Roux (researcher) with both Paul Hofman (scientist in charge) and Jean-Luc Gouzé (partner lab), with the objective of linking in vitro quantitative dynamics to primary tumor samples profiling in order to determine the resistance probability of a specific combination of anti-cancer drugs in lung cancer, using computational methods (see [66]).

9.2.2. Collaborations with Major European Organizations

Imperial college, Department of Chemical engineering (UK),

Modelling and optimization of microalgal based processes.

Imperial College, Centre for Synthetic Biology and Innovation, Dept. of Bioengineering (UK):

Study of metabolic/genetic models

University of Stuttgart, Institute for Systems Theory and Automatic Control (D):

Identification of gene networks

9.3. International Initiatives

9.3.1. Inria International Labs

Inria Chile

Associate Team involved in the International Lab:

9.3.1.1. GREENCORE

Title: Modelling and control for energy producing bioprocesses

International Partners (Institution - Laboratory - Researcher):

CIRIC (Chile) - Mélaine Gautier

PUCV (Chile) - Escuela de Ingenieria Bioquimica (EIB) - Gonzalo Ruiz Filippi

UTFSM (Chile) - Departamento de Matematica - Eduardo Cerpa

UFRO (Chile) - Chemical Engineering Department - David Jeison

Start year: 2014

See also: https://team.inria.fr/eagreencore/

The worldwide increasing energy needs together with the ongoing demand for CO2 neutral fuels represent a renewed strong driving force for the production of energy derived from biological resources. In this scenario, the culture of oleaginous microalgae for biofuel and the anaerobic digestion to turn wastes into methane may offer an appealing solution. The main objective of our proposal is to join our expertise and tools, regarding these bioprocesses, in order to implement models and control strategies aiming to manage and finally optimize these key bioprocesses of industrial importance. By joining our expertises and experimental set-up, we want to demonstrate that closed loop control laws can significantly increase the productivity, ensure the bioprocess stability and decrease the environmental footprint of these systems. This project gathers experts in control theory and optimization (BIOCORE, UTFSM) together with experts in bioprocesses (PUCV and UFRO) and software development (CIRIC).

9.3.1.2. Other IIL projects

BIOCORE is involved in the Bionature project from Inria Chile – CIRIC (the Communication and Information Research and Innovation Center), in collaboration with four Chilean universities (Universidad de Chile, Universidad Tecnica Federico Santa Maria, Pontificia Universidad Catolica de Valparaiso, and Universidad de la Frontera). The Bionature project is devoted to natural resources management and the modeling and control of bioprocesses.

9.3.2. Inria International Partners

9.3.2.1. Informal International Partners

GRIMCAPE, Université de Douala, Cameroon. Epidemiology.

National Institute of Technology Meghalaya, India. Modelling of augmentative biological control.

Univ. Ben Gurion : Microalgal Biotechnology Lab (IL), Member of the ESSEM COST Action ES1408 European network for algal-bioproducts (EUALGAE). Modelling of photosynthesis.

Universidad de la Frontera (CL), Modelling of CO_2 transfer in a microalgal absorption column.

9.4. International Research Visitors

9.4.1. Visits of International Scientists

- Samuel Bowong (Université de Douala, Cameroon), 1 week;
- Daniel Figueriedo (University of Aveiro, Portugal), 3 weeks;
- Benoît Chachuat (Imperial College, Department of chemical engineering, UK), 1 week
- Claude Aflalo (Ben Gurion University of the Neguev, Israel), 1 week;
- Andrei Akhmetzhanov (Université Montpellier II), 2 weeks.

9.5. Project-team seminar

BIOCORE organized a 4-day seminar in November in Peyresq. On this occasion, every member of the project-team presented his/her recent results and brainstorming sessions were organised. Claude Lobry (Univ. Nice and Modemic) was invited as a guest speaker.

CARMEN Team

8. Partnerships and Cooperations

8.1. National Initiatives

8.1.1. IHU LIRYC

Our work is partially funded by the LIRYC project (ANR 10-IAHU 04).

- For 2015: the salary of M. Potse, member of Carmen, is paid by LIRYC..
- For 2012-2015: 1/2 PhD thesis associated to the project *Modélisation pour les données multimodales* (see section Regional Initiaves).

8.1.2. ANR HR-CEM

In 2014, we are supported for the project "High Resolution Cardiac Electrophysiology Models: HR-CEM" within the call for project « Modèles Numériques » of the ANR.

The scientific start of the project was on November 4th, 2013.

It is an international project that involves three partners: Inria (coordinator), IHU LIRYC, and UMI-CRM at Montréal (Canada). The project has some external collaborators in Univ. Bordeaux and Univ. Pau.

Based on these collaborations and new developments in structural and functional imaging of the heart available at LIRYC, we plan to reconsider the concepts behind the models in order to improve the accuracy and efficiency of simulations. Cardiac simulation software and high-resolution numerical models will be derived from experimental data from animal models. Validation will be performed by comparing of simulation output with experimentally recorded functional data. The validated numerical models will be made available to the community of researchers who take advantage of in-silico cardiac simulation and, hopefully, become references. In particular we shall provide the first exhaustive model of an animal heart including the four chambers coupled through the special conduction network, with highly detailed microstructure of both the atria and the ventricles. Such a model embedded in high-performance computational software will provide stronger medical foundations for in-silico experimentation, and elucidate mechanisms of cardiac arrhythmias.

8.1.3. AMIES – Medic Activ

We were granted by the Agency AMIES a financial support to complete the one obtained from the Région Aquitaine for the Medic Activ project (see above). The objective of this support is to developp reduced order models of cardiac electrophysiology that might enter the MedicActiv framework. The difficulty is to define qualitatively realistic but fast numerical simulations of the ECG and cardiac function, for educational purpose.

8.1.4. ANR Labcom CardioXcomp

We are participant in the ANR Labcom project between Inria and the society Notocord (www.notocord.com). At Inria, the proejct is leaded by J.-F. Gerbeau from the Reo team and we participate to the study and developpment of cardiac electrophysiology models suited to the context of the proejct.

The aim of CarioXcomp is to code human induced pluripotent cardiomyocyte cells and drug/hiPS-CMs interaction. N. Zemzemi works on this project with E. Abbate (PhD thesis until october 2015) for th coupling between human induced pluripotent cardiomyocyte cells and the measurement tool multi-electrode array (MEA). In this project, some different tests on drug models and selection of the most suitable for the hiPS-CMs. In the same time, N. Zemzemi with collaborators N. Fikal, R. Aboulaich and EL.M. El Guarmah worked on the quantification of the effect of uncertainty in the conductivity values on the Electrocardiography imaging (ECGI) inverse solution. N. Zemzemi and J. Lassoued C. Corrado and M. Mahjoub worked on the stability analyssis of the reduced order model for the bidomain equation using proper orthogonal decomposition and on the estimation of the location of cardiac isquemia in a 3D geometry with inverse problem tools with C. Chavez F. Alonso-Atienz, D. Alvarez and Y. Coudière.

8.1.5. REO

The CARMEN team is a partner with the REO team at Inria Paris Rocquencourt and the NOTOCORD company in the CardioXcomp project.

8.1.6. MedicActiv

The CARMEN team cooperates in interaction with the MedicActiV project.

8.1.7. GENCI

GENCI – grand équipement national de calcul intensif – is the agency that grants access to national high-performance resources for scientific purposes in France. GENCI projects have to be renewed yearly. Our project renewal *Interaction between tissue structure and ion-channel function in cardiac arrhythmia*, submitted in October 2015, has been granted 9.4 million core-hours on the three major systems Curie, Occigen, and Turing. This compute time, to be used in the calendar year 2016, is primarily destined for our research into the interaction between ionic and structural heart disease in atrial fibrillation, Brugada syndrome, and early repolarisation syndrome [37].

8.2. International Initiatives

8.2.1. Inria International Labs

LIRIMA: Associate Team involved in the International Lab:

8.2.1.1. EPICARD (https://team.inria.fr/carmen/epicard)

Title: inversE Problems In CARDiac electrophysiology

International Partner (Institution - Laboratory - Researcher):

ENIT (Tunisia) Department of Intelligence Science and Technology - Nabil Gmati

- Start year: 2015
- See also: https://team.inria.fr/carmen/epicard/
- Improving the information that we can extract from electrical signals measured on patients with heart diseases is a major priority for the IHU LIRYC in Bordeaux headed by Professor Michel Haissaguerre. We would like to non-invasively construct the electrical potential on the heart surface only from measurements of the electrical potential on the the chest of the patient. This helps the medical doctor to visualise an image of the electrical potential of the heart of the patient. It is known that have been used in the literature for solving this electrocardiography imaging (ECGI) problem, including those used in commercial medical devices have several limitations. This problem could be mathematically seen as a boundary data completion problem for elliptic equations. Many works in the literature have been carried * out in order to solve this Cauchy problem, but have never been used for solving the ECGI problem. Our goal from the associate team is to develop an experimental platform allowing to test various methods and compare their performance on real life experimental data.

8.2.2. Inria International Partners

8.2.2.1. Informal International Partners

Applied work on atrial fibrillation is performed in collaboration with the experimental and clinical groups of professors U. Schotten and H. Crijns at Maastricht University [36].

M. Potse collaborates on several projects with the Institute of Computational Science at the *Università della Svizzera italiana* in Lugano, Switzerland, and the Department of electronics, informatics, and bioengineering of the *Politecnico di Milano*, Milan, Italy.

8.3. International Research Visitors

8.3.1. Visits of International Scientists

8.3.1.1. Internships

- B. Mostafa
  - The Faculty of Mathematics and Natural Sciences, University of Oslo, Norway
  - Johann Radon Institute for Computational and Applied Mathematics (RICAM) Austrian Academy of Sciences, Linz, Austria.
  - CI^2MA y Departamento de Ingenieria Matemática, Universidad de Concepcion, Concepcion, Chile.
  - Departamento de Matemática Aplicada e Estatistica, Instituto de Ciências Matemáticas e de Computação – USP, São Carlos, Brazil

DRACULA Project-Team

8. Partnerships and Cooperations

8.1. National Initiatives

8.1.1. ANR

Projects coordination by a member of Dracula

- ANR STOCHAGENE "Role of the chromatin dynamics on the stochasticity in gene expression in higher eukaryotic cells", 2011-2015.
  Participant: Olivier Gandrillon [Coordinator].

Collaboration in other projects

- ANR RPIB PrediVac "Innovative modeling tools for the prediction of CD8 T cell based vaccine efficacy", 2013-2016. Partners: U1111 Inserm (J. Marvel, coordinator), Dracula, Altrabio (small company), CoSMo (small company). For Dracula, the budget from 2013 to 2016 is 198 keuros, including three one-year post-doc positions (one post-doc has been recruited in April 2014 (Xuefeng Gao)), and the members are Fabien Crauste and Olivier Gandrillon.
- Thomas Lepoutre participates in the ANR (jeunes chercheurs) MODPOL (head Vincent Calvez (ENS Lyon)) "Cell polarization modeling", 2011-2015.
- Thomas Lepoutre is a member of the ANR KIBORD (head L. Desvillettes) dedicated to "kinetic and related models in biology". 2012-2016.
- Thomas Lepoutre is a member of the ERC MESOPROBIO (head V. Calvez) dedicated to "Mesoscopic models for propagation in biology". 2015-2020.
- Olivier Gandrillon participates in the ANR (Investissement d'Avenir) Iceberg (head Gregory Batt (Inria)) "From population models to model populations: single cell observation, modeling, and control of gene expression".

8.1.2. Other projects

- Inria ADT : SiMuScale "Simulations Multi-Échelles de Populations Cellulaires", 2014-2016.
  Participants: Samuel Bernard [Coordinator], Fabien Crauste, David Parsons.
- Association France Alzheimer Sciences Médicales 2014-2015 : PAMELA "Prion et Alzheimer : Modélisation et Expérimentation d'une Liaison Agressive", 2014-2015. Partners: UR0892 VIM (Virologie et Immunologie Moléculaires), INRA Domaine de Vilvert, Jouy-en-Josas.
  Participants: Mostafa Adimy, Samuel Bernard, Thomas Lepoutre, Laurent Pujo-Menjouet [Coordinator], Léon Tine.

8.2. European Initiatives

8.2.1. Collaborations in European Programs, except FP7 & H2020

- Research program PHC POLONIUM (2014-2015) "Applications of reaction-diffusion equations in biology and medicine". Partners: Warsaw, Poland (Slawomir Bialecki, Jolanta Ciesielska, Bogdan Kazmierczak (coordinator), Marek Kochanczyk, Tomasz Lipniacki).
  Participants: Mostafa Adimy, Abdennasser Chekroun, Laurent Pujo-Menjouet [Coordinator], Alen Tosenberger, Vitaly Volpert.

8.2.2. Collaborations with Major European Organizations

- University of Valladolid (Spain). Collaboration with Oscar Angulo, Juan Carlos Lopez-Marcos and Miguel Ange Lopez-Marcos, on the analysis of an age-structured model describing erythropoiesis, and its numerical resolution.
- Karolinska University Hospital of Stockholm (Sweden). Collaboration with Peter Arner, Mats Eriksson, Erik Arner, Mikael Rydén and Kirsty L. Spalding, on the study of dynamics of human adipose lipid turnover in health and metabolic disease.

8.3. International Initiatives

8.3.1. Inria Associate Teams not involved in an Inria International Labs

8.3.1.1. Modelling leukemia

Title: Modeling quiescence and drug resistance in Chronic Myeloid Leukemia

International Partner (Institution - Laboratory - Researcher):

Center for Scientific Computation And Mathematical Modelling, University of Maryland (United States).

Duration: 2013 - 2015.

See also: http://dracula.univ-lyon1.fr/modelling_leukemia.php

Leukemia is the most famous disease of the blood cell formation process (hematopoiesis). Chronic myeloid leukemia results in a uncontrolled proliferation of abnormal blood cells. As the hematopoiesis involves stem cells (not accessible to observations), mathematical modeling is here a great tool to test hypothesis. We will join the expertise of Inria team DRACULA specialized on the modeling of blood cell formation and the Center for Scientific Computation and Applied Mathematical Modeling (CSCAMM, University of Maryland, College Park). The theoretical and modeling experience of team DRACULA and the numerical expertise combined with the links with experimentalists of members of CSCAMM will allow us to study deeply evolution of leukemia. We will especially focus on the behavior of leukemic stem cells and their possibility of becoming quiescent (dormant). Then we will study (using the knowledge obtained on leukemic stem cells) the phenomenon of drug resistance and its propagation over time and finally the mechanisms of multidrug resistance.

8.3.2. Participation In other International Programs

8.3.2.1. M3CD

Program: Euromediterranean 3+3

Title: Mathematical Models and Methods in Cell Dynamics

Inria principal investigator: Mostafa Adimy

International Partners (Institution - Laboratory - Researcher):

Institut Pasteur de Tunis (Tunisia) - Slimane Ben Miled

Consiglio Nazionale delle Ricerche- Istituto per le Applicazioni del Calcolo Mauro Picone (Italy) - Istituto per le Applicazioni del Calcolo Mauro Picone - Roberto Natalini

Cadi Ayyad University (Morocco) - Populations Dynamics Laboratory - Moulay Lhassan Hbid

Duration: Jan 2012 - Dec 2015

The aim of this project is to establish a network working on mathematical and computational models in cell dynamics. This network consists of five groups which have already established close bilateral relations. Those are the Inria teams Bang and Dracula in Paris and Lyon, France, the team IAC-CNR in Rome, Italy, the laboratory of Mathematical Population Dynamics (LMDP) from the university of Marrakech in Morocco, and the team of Mathematical Modelling and Computing in Biology (MoMinBi) from the Pasteur Institute in Tunis. Modelling cell dynamics and related processes is one of the main subjects of interest for the partners for many years. The issues addressed in the present project can be divided into five parts:

1) Analysis of structured models in cell population dynamics ;

2) Dynamics of normal and pathological haematopoiesis ;

3) Dynamics of Darwinian adaptation, in particular by drug resistance in competing cell or parasite populations, healthy and pathological / pathogenic (cancer, bacteria, parasites) ;

4) Dynamics of chemical and physical determinants of filament formation and intracellular spatial organisation of the cytoskeleton conformation ;

5) Coupling of the molecular mechanisms of control of the cell division cycle and cell proliferation.

The first part has been developed for many years by all the partners in this project. It tackles issues related to cell dynamics and biological mechanisms, physiological and chemical properties of cells and cell populations. The other four aspects of the project have been studied in the past by the Inria teams "Bang" and "Dracula" (**2**, **4**, **5**) and the IAC-CNR team (Rome), or are a rapidly emergent theme in Bang (**3**, cell Darwinism) with possible and natural connections with the other teams, in particular IAC-CNR and MoMinBi in Tunisia. Themes (**2**, **4**, **5**) have also been initiated (for their fundamental part) in a recent collaboration between Dracula and the teams from Morocco and Tunisia. The objectives of the present project are to pursue and deepen the study of cell proliferation dynamics and cellular mechanisms using structured models that take into account some new structure variables. The development of computer models will also be investigated in this project. Training and research activities related to these topics are currently underway between the Inria teams and the teams from Marrakech and Tunis, and between the Italian team and Bang. Two co-supervised theses are currently in progress, a Spring school on this subject will be organised by the partners in 2012. This program comes at the right time to give a new impetus to this collaboration. It will lead to the establishment of a multi-site laboratory expertise in population dynamics modelling, especially in cellular dynamics. This project will also allow the teams from Morocco and Tunisia to use their knowledge on mathematics applied to cell dynamics.

8.3.2.2. FCRF

Program: Fonds France Canada pour la recherche (FFCR)- France Canada research fund (FCRF) "New research collaboration" 2014-2015.

Title: Mathematical modelling of megakaryopoiesis and applications to platelet related diseases

Participants: Mostafa Adimy, Fabien Crauste, Laurent Pujo-Menjouet [Coordinator].

International Partners : Canada (Jiguo Cao, Nemanja Kosovalic, Jianhong Wu).

M3DISIM Team

9. Partnerships and Cooperations

9.1. European Initiatives

9.1.1. FP7 & H2020 Projects

9.1.1.1. VPH-Share

Title: Virtual Physiological Human: Sharing for Healthcare – A Research Environment

Programm: FP7

Duration: March 2011 - May 2015

Coordinator: Univ. Sheffield (UK)

Other partners: Cyfronet (Cracow), University College London, Istituto Ortopedico Rizzoli (Bologna), NHS, IBM Israel, Univ. Auckland, Agència d'Informació, Avaluació i Qualitat en Salut (Barcelona), Biocomputing Competence Centre (Milano), Universitat Pompeu Fabra (Barcelona), Philips Research, TUE (Eindhoven), Sheffield Teaching Hospitals, Atos Origin (Madrid), the Open University (UK), Univ. Vienna, King's College London, Empirica (Bonn), Fundació Clínic (Barcelona), Univ. Amsterdam

See also: http://vph-share.org/

Inria contact: Dominique Chapelle

Abstract: VPH-Share (concluded in May 2015) aimed at developing the organisational fabric (the infostructure) and integrating the optimised services to expose and share data and knowledge, to jointly develop multiscale models for the composition of new VPH workflows, and to facilitate collaborations within the VPH community. Within this project, the M3DISIM team was in charge of developing some high-performance data assimilation software tools.

9.1.1.2. VP2HF

Title: Computer model derived indices for optimal patient-specific treatment selection and planning in Heart Failure

Programm: FP7

Duration: October 2013 - September 2016

Coordinator: King's College London (UK)

See also: http://vp2hf.eu/

Inria contact: Dominique Chapelle

Abstract: Heart failure (HF) is one of the major health issues in Europe affecting 6 million patients and growing substantially because of the ageing population and improving survival following myocardial infarction. The poor short to medium term prognosis of these patients means that treatments such as cardiac re-synchronisation therapy and mitral valve repair can have substantial impact. However, these therapies are ineffective in up to 50% of the treated patients and involve significant morbidity and substantial cost. The primary aim of VP2HF is to bring together image and data processing tools with statistical and integrated biophysical models mainly developed in previous VPH projects, into a single clinical workflow to improve therapy selection and treatment optimisation in HF.

9.2. International Initiatives

9.2.1. Participation In other International Programs

M3DISIM is the leading representative of Inria within the "Living Heart Project", a research network coordinated by Dassault-Systèmes to foster collaborations on cardiac modeling between various academic and industrial partners.

9.3. International Research Visitors

9.3.1. Visits of International Scientists

9.3.1.1. Internships

Alexandre Laurin [Simon Fraser Univ., Canada] Sébastien Imperiale [correspondant] Philippe Moireau Dominique Chapelle Gabriel Valdes Alonzo [Pontificia Univ. Católica de Chile] Radomir Chabiniok [correspondant] Dominique Chapelle

A. Laurin's doctoral internship (2 months) has taken place in the context of an ongoing collaboration between the Aerospace Physiology lab (Simon Fraser University, Vancouver, Canada) and Inria (M3DISIM and Reo teams), with the objective of initiating the modelling of seismocardiography (SCG) measurements. SCG consists in measuring displacements of the sternum and ribs generated by a heart beat using accelerometers placed on the thorax. In this context, linear elastodynamics equations are applicable to account for the transient propagation of motion from the heart to the sternum via the highly heterogeneous underlying materials (cartilage and bone). Specific care has been taken to solve the aforementioned equation in a realistic 3D geometry including the complete thoracic cage. Fully coupled simulations (beating heart with thorax deformation) are planned at the final stage of this modelling work. Following the completion of his PhD, A. Laurin has joined the team for a post-doc, which provides the setting for continuing and extending this work.

G. Valdes (Master's student at Pontificia Univ. Católica de Chile) has been awarded a Conicyt funding for a 3 months internship within our team. He has worked on a simplified dynamical model of venous return, allowing to account for the evolution of the preload – the pressure that induces the filling of the heart – under the effect of variations of cardiac output. This is crucial for simulating sequences of heartbeats in transient regimes, and one major motivation for this was to initiate the modeling of the dynamics of heart failure.

MAMBA Project-Team

8. Partnerships and Cooperations

8.1. National Initiatives

8.1.1. ANR

8.1.1.1. ANR 2011-2014 Bimod

It has been prolonged until March 2015, time at which an international workshop on "Multi-scale and hybrid modelling in cell and cell population biology" has been held at UPMC, Paris (J. Clairambault and V. Volpert organisers), with 25-30 speakers on invitations. Its proceedings under the form of extended abstracts are available on a dedicated website: http://www.itm-conferences.org/articles/itmconf/abs/2015/02/contents/contents.html

8.1.1.2. ANR Blanc 2014-2018 "Kibord"

This recently accepted project gathers several members of the Mamba team together with the ENS Cachan and Université Paris-Dauphine on the mathematical study of PDE models with application to biology.

8.1.1.3. ANR 2014-2017 IFLOW

Eric Vibert, Hopital Paul Brousse (coordinator). Partners: Inria REO, Hopital Toulouse, Dirk Drasdo. Objectives are simulation of liver perfusion after partial hepatectomy (PHx) with and without therapeutic manipulations to improve patients survival after PHx.

8.1.1.4. INSERM 2014 - 2016, INVADE.

Emmanuel Barillot, Institut Curie (coordinateur). Partners: Groups from Institut Curie, Dirk Drasdo. Objective is a model for a better understanding of breast cancer invasion.

8.2. European Initiatives

8.2.1. FP7 & H2020 Projects

8.2.1.1. ERC Starting Grant SKIPPER^{AD}, 2012-2017, Principal Investigator: M. Doumic.

This grant allowed to fund Sarah Eugène's Ph.D and M. Tournus's post-doc, as well as to develop the new collaborations with W-F. Xue in Canterbury and T. Teixeira in IBCP.

8.2.2. Collaborations in European Programs, except FP7 & H2020

8.2.2.1. NOTOX

Type: COOPERATION

Instrument: Integrated Project

Objectif: NC

Duration: January 2011 - December 2015

Inria contact: Dirk Drasdo

NOTOX developed and established a spectrum of systems biological tools including experimental and computational methods for (i) organotypic human cell cultures suitable for long term toxicity testing and (ii) the identification and analysis of pathways of toxicological relevance. NOTOX initially used available human HepaRG and primary liver cells as well as mouse small intestine cultures in 3D systems to generate own experimental data to develop and validate predictive mathematical and bioinformatic models characterizing long term toxicity responses. Cellular activities were monitored continuously by comprehensive analysis of released metabolites, peptides and proteins and by estimation of metabolic fluxes using 13C labelling techniques (fluxomics). At selected time points a part of the cells was removed for in-depth structural (3D-optical and electron microscopy tomography), transcriptomic, epigenomic, metabolomic, proteomic and fluxomic characterisations. Together with curated literature and genomic data the toxicological data was organised in a toxicological database (cooperation with DETECTIVE, COSMOS and TOXBANK). Physiological data including metabolism of test compounds have been incorporated into large-scale computer models that are based on material balancing and kinetics. Various "-omics" data and 3D structural information from organotypic cultures will be integrated using correlative bioinformatic tools. These data also served as a basis for large scale mathematical models. The overall objectives are to identify cellular and molecular signatures allowing prediction of long term toxicity, to design experimental systems for the identification of predictive endpoints and to integrate these into causal computer models.
Inria contributions were multilevel and multiscale models of drug toxicity and its consequences on ammonia detoxification and are detailed in the result section on liver modeling. Webpage: http://notox-sb.eu/fp7-cosmetics-europe/

8.2.3. Collaborations with Major European Organisations

U. Klingmüller: DKFZ (German Cancer Research Centre), Department for Systems Biology (Germany)

Role of HGF in liver regeneration. Lung cancer.

K. Breuhahn: University Hospital of Heidelberg, Pathology (Germany)

Lung cancer invasion. Role of HGF in liver regeneration.

JG Hengstler: Leibniz Center, IfADo (Germany)

Liver research, toxicology, regeneration.

University of Leipzig, Interdisciplinary center for bioinformatics (Germany)

Projects on tissue regeneration, software

8.3. International Initiatives

8.3.1. Inria International Partners

8.3.1.1. Declared Inria International Partners

1. German Research Ministry (BMBF) funded project on the systems biology of lung cancer. The major aim is to better understand the early metastasis formation and invasion of lung cancer, including therapeutical options. Data on all levels ranging from intracellular up to organ level will be used to establish successively an integrated multiscale model of cellular and migration decisions in lung cancer. A particular focus will be on dissecting how cellular organisation and communication in spheroid cultures and co-cultures of lung cancer cell lines with selected endothelial cells affects information processing and the proliferation and migration decisions downstream. To reveal the inhomogeneous spatio-temporal organisation in these tumour growth models, specific probes for medical imaging, quantify extracellular cytokine concentrations will be used, and the effects of pharmacological inhibitors be monitored. By data and model integration, parameters should be identified that critically determine early spread and facilitate to predict possibilities for improved therapeutic options. The project coordinator is Ursula Klingmueller, German Cancer Research Centre (DKFZ), Heidelberg (http://www.lungsys.de/)

2. German Research Ministry (BMBF) funded project on the systems biology of liver (Virtual Liver Network). The aim of the VLN project is to set up multiscale models of liver. The Virtual Liver will be a dynamic model that represents, rather than fully replicates, human liver physiology morphology and function, integrating quantitive data from all levels of organisation. Our part ranges from the intracellular up to the level of groups of liver lobules. A liver lobule is the basic repetitive functional unit of liver. Applications are explained in the text. The networks has 69 Principle Investigators organised in about 10 work packages, each of which have a number of sub-projects (http://www.virtual-liver.de).

8.3.2. Participation In other International Programs

8.3.2.1. EuroMed3+3 programme

The M3CD network (https://www.rocq.inria.fr/bang/M3CD_website/), coordinated by J. Clairambault, has led in 2015 as usual to bilateral visits (M. Adimy, J. Clairambault, to Marrakesh and to Tlemcen, T. Touaoula to Lyon, visits of students to Paris and Lyon). It has terminated its activities in 2015 by a meeting in September in Rabat (Morocco) together with other EuroMed3+3 networks. The future of EuroMed3+3 (http://www.inria.fr/en/europe-international/international-relations/international-calls-for-projects/euromediterranean-3-3) will be discussed in June 2016 in a meeting at the Sophia-Antipolis Inria research centre.

8.3.2.2. CAPES-COFECUB project

"Modeling innovative control methods for dengue fever", in collaboration with Fondation Oswaldo Cruz (FioCruz), Rio de Janeiro, Brazil.

8.3.2.3. Convergence SU/FAPERJ programme

"Control and identification for mathematical models of dengue epidemics" in collaboration with IMPA, Rio de Janeiro, Brazil.

8.4. International Research Visitors

8.4.1. Visits of International Scientists

Juan Calvo came for a one month visit in January and February, 2015, to work on a new model for long-term protein polymerisation (work in progress).

8.4.2. Internships

Andreas Buttenschön (Team of Thomas Hillen, University of Alberta, Canada) visits the team from December 2015 to May 2016 for be trained on agent-based modeling and the software tool TiSim.

Geert Peeters (Team Patrick Segers, University of Gent, Belgium) visited the German subgroup of the team in January 2015 for one week to be trained on the software tool TiQuant.

8.4.2.1. Research stays abroad

Nicolas Vauchelet stayed two months at IMPA, Rio de Janeiro, Brazil, in the framework of a teaching agreement between UPMC and IMPA.

MODEMIC Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

8.1.1. Labex Numev

Within the Labex Numev (Solutions Numériques, Matérielles et Modélisation pour L'Environnement et le Vivant [0]), the team has obtained several funding for internships and invitation of international visitors, for the coming year:

- six months of MsC internships on optimal control for bioprocesses (jointly with the LBE unit, Inra Narbonne),
- the venue of Prof. Chris Klausmeir from Michigan State Univ. about micro-algae modeling (jointly withe the UMR EcoSols, Montpellier).

8.1.2. Inter-teams seminar

J. Harmand is the coordinator of the inter-teams seminar about the modeling of bioprocesses [0], involving the labs INRA-LBE (Narbonne), UMR LISPB (Toulouse) and the two Inria project teams BIOCORE and MODEMIC.

C. Lobry has been invited to participate to the "Séminaire au vert" of BIOCORE team in November 2015.

8.2. National Initiatives

8.2.1. ANR Soil$\mu 3D$

The team is partner of the ANR project SoilMicro-3D: *Emergent properties of soil microbial functions: Upscaling from 3D modeling and spatial descriptors of pore scale heterogeneity*, conducted by the UMR EGC for 4 years (2015-19). The other partners are UMR iEES, UMI UMMISCO, SIMBIOS (Scotland), UMR Géosciences Rennes, UMR JJL and UR Inra Science du Sol Orléans). The main goal of the project are

- develop new descriptors of the pore scale 3D soil heterogeneity that explain the fluxes measured at the core scale,
- improve the performance of 3D pore scale models to simulate processes from pores to cores with a reduction of the computational time,
- develop new simple models describing the soil micro-heterogeneity and integrating these micro-features into field-scale models.

The kick-off meeting is held in Jan 2016.

8.2.2. PGMO "OPTIBIO"

OPTIBIO (New challenges in the optimal control of bioprocesses [0]) is a new project funded by the french Fundation FMJH (Fondation Mathématique Jacques Hadamard) in 2014 for three years, within the program PGMO (Gaspard Monge Program for Optimization and operations research).

The project is coordinated by T. Bayen (ACSIOM, Univ. Montpellier II) and the other partners are: MODEMIC, Univ. Limoges, EPI COMMANDS (Saclay) and EPI BIOCORE (Sophia Antipolis).

[0] http://www.lirmm.fr/numev
[0] https://sites.google.com/site/journeesthematiquesdulbe/
[0] http://www.math.univ-montp2.fr/~bayen/articles/posterPGMO.pdf

The overall objective of this project is to address the optimization of bioprocesses over an *infinite horizon*. Infinite horizon optimal control is well suited for every problem where the time horizon is uncertain and can be expected to be large: e.g. economics models related to optimal growth and sustainable development, biological models such as the optimal control of interacting species and pest control, stabilization of controlled mechanical systems...The recent expectations of sustainable development raise new optimization problems that take into account auxiliary outputs, such as bio-gas production, that were neglected in the past. It appears that mathematical problems that come from the modeling of these processes are often difficult to solve, and one objective of the proposal is to develop new mathematical methods in order to address these issues. More precisely, the objective of the project is to study the following issues:

- Optimization of bioprocess over an infinite horizon.
- Development of accurate methods in order to deal with uncertainties that affects the chemostat model (uncertainties come from unknown parameters or noise from the measurements).
- Stabilization of the chemostat model including delay in the system.

8.2.3. INRA-MIA methodological networks

The team is involved in two new networks of the MIA (Applied Mathematics and Informatics) Department of INRA:

- MEDIA [0] (Modèles d'Équations DIfférentielles et Autres systèmes dynamiques pour l'écologie),
- REM [0] (RÉduction de Modèles),

that have been launched last year.

8.3. International Initiatives

8.3.1. Inria International Labs

Inria Chile
Associate Team involved in the International Lab:

8.3.1.1. DYMECOS2

Title: Modeling of microbial ecosystems, bioprocesses control and numerical simulations

International Partner (Institution - Laboratory - Researcher):

Universidad de Chile (Chile) - Center for Mathematical Modeling (CMM) - Hector Ramirez

Start year: 2014

See also: https://sites.google.com/site/eadymecos/

The objective is to develop, from expert knowledge and experimental observations, models of microbial ecosystems that are simple enough to carry out the determination of explicit "control laws", and realistic enough to represent real bio-processes. One of the difficulties is to identify the limits of the validity of these models, in terms of spatial heterogeneity and microbial population size. We aim also to obtain outcomes of the modeling for the optimal design of waste-water treatment plants.

8.3.2. Inria International Partners

8.3.2.1. Informal International Partners

CESAME, Univ. Louvain, Belgium : D. Dochain

3BIO, Univ. Mons, Belgium : A. Vande Wouver

Univ. Neuchâtel, Switzerland : M. Benaim

Univ. Newcastle, U.K. : M. Wade

[0] http://www.netvibes.com/reseaumiamedia
[0] https://sites.google.com/site/reseaurem2/

MOMAT, Univ. Madrid, Spain : B. Ivorra

Univ. Sevilla, Spain : T. Caraballo

8.3.3. Participation In other International Programs

8.3.3.1. CIB (Centre Interfacultaire Bernoulli)

Program: Bernoulli workshops

Title: The role of mathematics and computer science in ecological theory

Inria principal investigator: MODEMIC (C. Lobry),

Partners: EPFL, Lausanne (Switzerland).

Duration: July 2014 to Feb 2015

Abstract: A former collaboration of Inria with ecologists (the COREV network presently animated by R. Arditi) initiated (at the beginning of the 90s) by J-L. Gouzé and C. Lobry within the framework of the Inria project team COMORE, pursued then by MERE and COMORE raised an important event: the half-year *Mathematics and computer sciences in theoretical ecology* which we co-organize with R. Arditi (associated with D. de Angelis and L. Ginzburg) at the Federal Polytechnical School of Lausanne (Centre Interfacultaire Bernoulli).

The program lasted from July 1 to December 31, 2014 (see the 2014 activity report), but a follow-up workshop has been organized in February 2015 on the Persistence of population models in temporally fluctuating environments. This workshop has led to the writing of a review paper [31] in common.

Web-site: http://mathcompecol.epfl.ch/

8.3.3.2. TREASURE

Program: Euromediterranean 3+3

Title: Treatment and Sustainable Reuse of Effluents in semiarid climates

Inria principal investigator: MODEMIC (J. Harmand),

Partners: Centre de Biotechnology de Sfax, Department of environmental engineering (Tunisia), Ecole Nationale des Ingénieurs de Tunis, Dept. de Mathématiques (Tunisia), Institut National de la Recherche Agronomique, Dept. EA, MICA et MIA (France), National Research Center, Water Pollution Control (Egypt), University of Patras, Process Control Laboratory (Greece), University of Tlemcen, Automatic control (Algeria), University of santiago de compostella, Environmental engineering (Spain) Université Cadi Ayyad de Marrakech, Faculté des Sciences de Semlalia, Dépt. de Mathématiques (Morocco), Centre National de Recherche sur l'Eau et l'Energie, Université Française d'Egypte (Egypt)

Duration: Jan 2012 - Dec 2015

Abstract: The TREASURE network aims at integrating knowledge on the modeling, the control and the optimization of biological systems for the treatment and reuse of waste-waters in countries submitted to semi-arid climates under both socio-economical and agronomic constraints within the actual context of global changes. A special focus of the actual project concerns the integration of technical skills together with socio-economical and agronomic studies for the integrated solutions developed within the network to be evaluated and tested in practice in the partner's countries and, as possible as it may be within the context of the actual research network, valorizing these proposed technologies with the help of industrial on site in partners from South.

Web-site: https://project.inria.fr/treasure

8.3.3.3. TASSILI

Program: Hubert Curien Program

Title: Procédés membranaires pour le traitement anaérobie des eaux usées - Modélisation, commande et optimisation

Inria principal investigator: MODEMIC (J. Harmand),

Partners: LBE-INRA (Narbonne), Univ. Tlemcen (Algeria)

Duration: 3 years since 2014

Abstract: This project aims at promoting collaborations with our historical Algerian partners of the department of automatic control of the University of Tlemcen. The objectives of the project are to develop research on the modeling and the control of anaerobic systems through the co-advisoring of Zeyneb Khedim (PhD 'co-tutelle' between UM2 and Univ. Tlemcen).

8.3.3.4. MOSTICAW

Program: STIC AmSud

Title: MOdeling the Spread and (opTImal) Control of Arboviroses by Wolbachia

Inria principal investigator: P.A. Bliman (Inria Rocquencourt and Fundção Vargas, Rio de Janeiro, Brazil)

Partners: Inria (Rocquencourt and Metz), UPMC, CIRAD, MISTEA, Fundção Vargas (Brazil), Univ. Fed. Fluminense (Brazil), Fiocruz (Brazil), Univ. Buenos Aires (Argentina), UTFSM (Chile), Univ. de Chile, Univ. de Quindio (Colombia), Univ. Aut. de Occidente (Colombia), Nat. Univ. Nac. Mayor de San Marcos (Peru), Univ. of Asuncion (Paraguay).

Duration: 2016-2017

Abstract: The present project is concerned with new method of control of dengue fever, and potentially other severe diseases transmitted by mosquitoes Aedes (chikungunya, yellow fever). The goal of the project is to elaborate and analyze related models, along with control strategies, with the aim of testing concepts and estimating feasibility. The team is mainly involved in the modeling of interactions of bacteria Wolbachia with mosquitoes, and control systems tools (observers and optimal control).

8.4. International Research Visitors

8.4.1. Visits of International Scientists

Matthieu Sebbah

Subject: Optimal control for lagoon management

Date: from June 2015 until Sept 2105

Institution: Univ. Tecnico Federico Santa Maria, Valparaiso, Chile.

8.4.1.1. Internships

Maria Crespo (PhD)

Subject: Consideration of inhomogeneity in activated sludge bioreactors for the bioremediation of water resources

Date: Feb 2015

Institution: Univ. Complutense, Madrid (Spain)

Pascale Cuevas (MsC)

Subject: Numerical simulation of the heterogeneity in transport diffusion with nutrients

Date: from Sep 2015 until Nov 2015

Institution: Univ. Santiago (Chile)

Yessmine Daoud (PhD)

Subject: Mathematical analysis of anaerobic digestion models

Date: from Mar 2015 until Jul 2015

Institution: LAMSIN, Tunis (Tunisia)

Alejandro Rojas-Palma (PhD)

Subject: Study of some problems related to modeling and optimization of bioprocesses

Date: from May 2015 until Oct 2015

Institution: Univ. of Chile

Victor Riquelme (PhD)

Subject: Optimal control for the preservation of exploited water resources

Date: from April 2015 until Nov 2015

Institution: Univ. of Chile

Camila Romero (MsC)

Subject: Minimal time crisis problem for Lotka-Volterra prey-predator model.

Date: from Jan 2015 until Mar 2015

Institution: Univ. of Chile

8.4.2. Visits to International Teams

8.4.2.1. Research stays abroad

B. Cloez has spent one month in Switzerland at Univ. Neuchâtel and at CIB-EPFL, Lausanne.

Monc Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

8.1.1. BIS-Japan Idex Université de Bordeaux

- Project acronym - BIS-Japan Idex
- Duration - 2015
- Coordinator - C. Poignard
- Abstract - The project proposes to gather the skills of the Japanese partner on cell migration modeling, molecular pathways in cancer and theoretical aspects of partial differential equations with the experience of the Bordeaux team MONC (Modeling in ONCology), which involves researchers from University of Bordeaux, IPB, CNRS and Inria, in cancer modeling. More particularly, the team MONC is invoved in the derivation of tumor growth models and of accurate finite volume numerical schemes to solve the partial differential equations in order to provide a deep multiscale knowledge of the tumor development at the cell scale. The overall aim of this project is to propose a comprehensive study of the metastatic processes at the cell scale, by highlithing the molecular pathways and the main chemical processes involved in cancer cell migration and division.

8.2. National Initiatives

8.2.1. Plan cancer DYNAMO

- Project acronym - Plan Cancer DYNAMO
- Partners - Lab Ampère-Lyon, Lab. Vectorologie et thérapies anticancéreuses- Villejuif and Equipe Inria MONC-Talence
- Duration - from sep. 2015 to sep 2018
- Coordinator - R. Scorretti, Lab. Ampère / Local coordinator - C. Poignard
- Team participants - C. Poignard
- Abstract - Electroporation (EPN) is a method which allows either killing the cells in a target region (tumors) by a nonthermal mechanism (irreversible EPN, or IRE) or allowing non permeant molecules (drugs, DNA) to penetrate the cells. EPN opens new perspectives for cancer treatment (electrochemotherapy, or ECT) and for gene therapy. In spite of its advantages, applications of EPN are still limited because of the scarcity of quantitative data concerning the reaction of tissues following electric pulses. Moreover, due to the lack of reliable tools for treatment planning, most clinical applications deal with superficial tumors in patients treated in more than 130 EU cancer centers using validated standard operating procedures. However the more difficult treatment of deep-seated tumors is still at the stage of academic research and a crucial challenge for forthcoming cancer therapies. This project aims at investigating how EPN can be effectively modeled, from the scale of cell up to the scale of tissue, and how molecular uptake holds and is enhanced by electric field delivery. To develop a dynamic model of tissue EPN, two approaches will be followed: one derived from the macroscopic scale (ad hoc tissue model) and the other from the microscopic scale using homogenization techniques. In order to enable accurate elaboration of the models, experiments will be carried out on raw potato tubers, HEK-293 (Human Embryonic Kidney) cell aggregates and on mice liver and muscle. The transport of molecules through the tissue, which is also a bottleneck, will be overcome thanks to a porous medium approach, which will provide qualitative and quantitative behaviour of the transport in the tissue.

8.2.2. Plan Cancer METASIS

- Project acronym - Plan Cancer METASIS
- Partner - Laboratory of Biology, Bordeaux University
- Duration - from 2013 to 2015
- Coordinator - A. Bikfalvi
- Team participants - S. Benzekry, Th. Colin, C. Poignard, O. Saut
- Title - Modeling the Interaction of the (Metastasis) Vascular/Tumor Niche Using a Systems Biology Approach

8.2.3. Plan Cancer MIMOSA

- Project acronym - Plan Cancer MIMOSA (Physique, Mathématiques et Sciences de l'ingénieur appliqués au Cancer)
- Partner - Laboratory of Biology, Bordeaux University
- Duration - from 2014 to 2017
- Coordinator - Th. Colin
- Team participants - S. Benzekry, Th. Colin, C. Poignard, O. Saut
- Title - Mathematical modeling for exploration of the impact of mechanical constraints on tumor growth

*8.2.4. A*Midex MARS*

- Project acronym - A*Midex MARS
- Partner - Service d'Oncologie Multidisciplinaire & Innovations Thérapeutiques, Hopitaux de Marseille
- Duration - from 2014 to 2016
- Coordinator - F. Barlesi
- Team participant - S. Benzekry
- Title - Modeling Anticancer Research & Simulation

8.2.5. PEPS CNRS

- Project acronym - PEPS Electroporation
- Partners - Lab Ampère-Lyon and Equipe Inria MONC-Talence
- Duration - June-Dec 2015
- Leader - D. Voyer, Lab. Ampère / Local leader - C. Poignard

8.3. International Initiatives

8.3.1. Inria International Partners

8.3.1.1. Informal International Partners

LIA EBAM

- Title - LIA EBAM
- Partners - University of Ljubljana, IPBS, Institut Gustave Roussy, XLim, Institute of Oncologie, Ljubljana and Equipe Inria MONC-Talence
- Duration - 2015-2019 (renewal)
- Leader - L.M. Mir / Local leader - C. Poignard

- The main aim of the LIA EBAM is to use an interdisciplinary approach, integrating biology, chemistry, physics, biophysics, mathematics, computational modelling and engineering, through the expertise of its members in order to 1- Enhance our understanding on the mechanisms of classical electropermeabilization and of the new nanopermeabilization (electropermea-bilization using nanosecond electric pulses), as well as on the mechanisms of transmembrane transport of molecules into electroporated cells and tissues on a microscopic and macroscopic scale. 2- Contribute to a better and safer implementation of the electropermeabilization-based applications, and to the development of new applications. 3- Develop new devices and new equipment for the nanopermeabilisation at cell and tissue levels. 4- Develop new approaches like treatment planning in existing applications, such as antitumor electrochemotherapy and in vivo gene transfer for therapeutic purposes. 5- Disseminate the knowledge and the applications in the scientific community and in the society, through publications, a one-week course (already implemented) co-directed by the LEA directors, internal and external training, and through other means that the LEA will develop and/or will apply for (to the EC programs for example). Partners participating in the project possess complementary knowledge and skills, which only if brought together will allow for successful accomplishments of the above objectives.

JSPS Core-to-Core Program on Establishing International Research Network of Mathematical Oncology

- Title - JSPS Core-to-Core Program on Establishing International Research Network of Mathematical Oncology
- Partners - Osaka University, Vanderbilt University, Dundee university and Equipe Inria MONC-Talence
- Duration - 2015-2019 (renewal)
- Leader - T. Suzuki, Osaka University / Local leader - C. Poignard
- Establishing International Research Network of Mathematical Oncology

Collaboration with John Ebos, Roswell Park Cancer Institute, Buffalo, NY, USA. Quantification of metastatic potential and differential effect of anti-angiogenenic therapies on primary tumor and metastasis, in a preclinical setting.

8.4. International Research Visitors

8.4.1. Visits of International Scientists

- Tadeja Forjanic (PhD Student Ljubljana), 2 weeks in jan. 2015. *Tumor growth modeling after electroporation* (Local supervisor: C. Poignard)
- Ariff Admon (PhD Student Osaka University), 1month June 2015. *Free boundary problem for invadopodia*. (Local supervisor: C. Poignard)

MYCENAE Project-Team

7. Partnerships and Cooperations

7.1. National Initiatives

7.1.1. ANR

Jonathan Touboul is member of the Kibord (KInetic models in Biology Or Related Domains) project obtained in 2014.

Mathieu Desroches is the coordinator of the SloFaDyBio (SLOw-FAst Dynamics applied to the BIOsciences) network mounted in 2014.

7.1.2. National Networks

- GdR REPRO (member of the direction board, F. Clément)
- MIA REM network: Réduction de modèles (PI Béatrice Laroche, INRA Jouy)

7.1.3. National Collaborations

- UMR Physiologie de la Reproduction et des Comportements, INRA Tours (Bios and Bingo teams)
- Jacques-Louis Lions Laboratory, Pierre & Marie Curie University (Jean-Pierre Françoise, Marie Postel)
- Developmental Biology Laboratory, Pierre & Marie Curie University (Alice Karam, Sylvie Schneider Maunoury), in the framework of the NeuroMathMod, Sorbonne-Universités Émergence call
- Center for Interdisciplinary Research in Biology, Collège de France (Alain Prochiantz)
- Centre de Recherche en Mathématiques de la Décision, Paris Dauphine University (Stéphane Mischler)
- Computational Biology and Biomathematics, Jacques Monod Institute, Paris Diderot University (Khashayar Pakdaman)
- Département d'Informatique de l'ENS, équipe DATA, Paris-Nord University (Gilles Wainrib)
- Unité de Neurosciences, Information & Complexité (UNIC), CNRS Gif-sur-Yvette (Alain Destexhe)

7.2. International Initiatives

7.2.1. Informal International Partners

- **USA**: Florida State University (Richard Bertram, Patrick Fletcher, Joël Tabak), University of Pittsburgh (Bard Ermentrout, Jonathan Rubin), Princeton University (William Bialek, Thibault Taillefumier, Simon Levi)
- **Spain**: University of the Balearic Islands (Antonio .E. Teruel, Rafel Prohens), Polytechnic University of Catalunya (Toni Guillamon), University of Sevilla (Enrique Ponce)

NUMED Project-Team

6. Partnerships and Cooperations

6.1. Regional Initiatives

- Paul Vigneaux: collaborative project of the Fédération Mathématique Rhone-Alpes-Auvergne, on the growth of biological tissue.
- Emmanuel Grenier and Paul Vigneaux: Member of a collaborative project of the Fédération Mathématique Rhone-Alpes-Auvergne headed by Adeline Samson, on PDE and Statistics.

6.2. National Initiatives

6.2.1. ANR.

Thibault Bourgeron is part of "Keyboard" (head: Laurent Desvillettes)

6.3. European Initiatives

6.3.1. FP7 & H2020 Projects

Vincent Calvez: ERC starting grant Mesoprobio "Mesoscopic models for propagation in biology". 2015-2020

6.3.1.1. DDMoRE

Title: DDMORE

Programm: FP7

Duration: February 2011 - January 2016

Coordinator: Pfizer

Inria contact: Marc Lavielle

6.4. International Research Visitors

6.4.1. Visits to International Teams

6.4.1.1. Explorer programme

Bouin Emeric

Date: Jan 2015 - Apr 2015

Institution: Stanford (United States)

6.4.1.2. Research stays abroad

Thibault Bourgeron visited Granada University in october 2015.

REO Project-Team

9. Partnerships and Cooperations

9.1. National Initiatives

9.1.1. ANR

9.1.1.1. ANR Project "EXIFSI"

Participants: Benoit Fabrèges, Miguel Ángel Fernández Varela [Principal Investigator], Mikel Landajuela Larma, Marina Vidrascu.

Period: 2012-2016
The aim of this project, coordinated by Miguel Ángel Fernández Varela, is to study mathematically and numerically new numerical methods for incompressible fluid-sructure interaction.

9.1.1.2. ANR LabCom "CARDIOXCOMP"

Participants: Muriel Boulakia, Damiano Lombardi, Jean-Frédéric Gerbeau [Principal Investigator], Fabien Raphel, Eliott Tixier.

Period: 2013-2016.
This project, coordinated by Jean-Frédéric Gerbeau, is carried out in the framework of a joint laboratory ("LabCom" call of ANR) with the software company NOTOCORD. The focus is the mathematical modeling of a device measuring the electrical activity of cardiomyocytes. The overall objective of CardioXcomp is to enrich NOTOCORD's software with modelling and simulation solutions and provide to pharmacology research a completely new set incorporating state of the art signal processing and numerical simulation.

9.1.1.3. ANR Project "iFLOW"

Participants: Chloé Audebert, Jean-Frédéric Gerbeau, Irène Vignon-Clementel [co-Principal Investigator].

Period: 2013-2017.
This ANR-TecSan, co-managed by Eric Vibert (Paul Brousse Hospital) and Irène Vignon-Clementel, aims at developing an Intraoperative Fluorescent Liver Optimization Workflow to better understand the relationship between architecture, perfusion and function in hepatectomy.

Other partners: DHU Hepatinov - Hôpital Paul Brousse, Inria Mamba, Fluoptics, IfADo, MID.

9.1.1.4. ANR Project "IFSMACS"

Participants: Muriel Boulakia, Céline Grandmont [local coordinator].

Period: 2015-2019.
The objective of this project, coordinated by Takéo Takahashi (Inria Nancy Grand-Est), is the mathematical analysis of systems involving structures immersed in a fluid. This includes the asymptotic analysis, the study of the controllability and stabilization of fluid-structure interaction systems, the understanding of the motion of self-propelled structures and the analysis and development of numerical methods to simulate fluid-structure systems.

9.1.1.5. Participation to other ANR projects

- Laurent Boudin is a member of the ANR Blanc project Kibord on kinetic models in biology and related domains
- Laurent Boudin is a member of the ANR TecSan Oxhelease
- Céline Grandmont is a member of the ANR TecSan Oxhelease
- Marina Vidrascu is a member of the ANR ARAMIS

9.1.2. Inria initiatives

9.1.2.1. ADT Project "MENAMES "

Participants: Miguel Ángel Fernández Varela [Principal Investigator], Axel Fourmont, Marina Vidrascu.

Period: 2014-2016
The aim of this project, coordinated by Miguel Ángel Fernández Varela, is to implement in the FELiScE library several algorithms included in the shelddon and Modulef library, in particular shell elements and domain decomposition methods.

9.2. European Initiatives

9.2.1. FP7 & H2020 Projects

9.2.1.1. REVAMMAD

Title: "Retinal Vascular Modeling, Measurement and Diagnosis"

Programm: FP7

Duration: April 2013 - March 2017

Coordinator: University of Lincoln

Partners: See the web site http://revammad.blogs.lincoln.ac.uk/partners/

Inria contact: J.-F. Gerbeau

REVAMMAD is a European Union project aimed at combatting some of the EU's most prevalent chronic medical conditions using retinal imaging. The project aims to train a new generation of interdisciplinary scientists for the academic, clinical and industrial sectors, and to trigger a new wave of biomedical interventions. The role of REO team within this consortium is to propose a mathematical model and a simulation tool for the retina hemodynamics. See http://revammad.blogs.lincoln.ac.uk for more details.

9.3. International Initiatives

9.3.1. Inria International Labs

Participants: Céline Grandmont, Jessica Oakes, Irène Vignon-Clementel [correspondant].

Period: 2014-2015

Jessica Oakes was awarded an Inria@SiliconValley Grant for a post-doc at UC Berkeley to work on aerosol deposition in the lung.

9.3.2. Trans-Atlantic Network of Excellence for Cardiovascular Research

Participants: Jean-Frédéric Gerbeau, Sanjay Pant, Irène Vignon-Clementel [correspondant].

Period: 2010-2015

This network, funded by the Leducq fondation, is working on the multi-scale modeling of single ventricle hearts for clinical decision support.

Other partners: see http://modelingventricle.clemson.edu/home.

9.3.3. German BMBF national project Lungsys II

Participant: Irène Vignon-Clementel.

Period: 2012-2015

"Systems Biology of Lung Cancer: Dynamic Properties of Early Spread and Therapeutic Options". In collaboration with Dirk Drasdo (EPI Mamba).

Other partners: see http://www.lungsys.de.

9.3.4. Participation In other International Programs

- Laurent Boudin
  - Member of the French-Italian Galileo PHC on the kinetic modelling and numerical simulation of gaseous mixtures and plasmas, supervised by F. Charles (UPMC) for France.
  - Member of a French-Serbian CNRS PICS on the kinetic modelling of gaseous mixtures, supervised by B. Grec (Université Paris-Descartes) for France.

9.4. International Research Visitors

9.4.1. Visits of International Scientists

9.4.1.1. Internships

Visiting PhD student: Stephanie Lindsey, Cornell University (May 4th - May 20th)