RESEARCH CENTER

FIELD
Digital Health, Biology and Earth

Activity Report 2016

Section Partnerships and Cooperations

Edition: 2017-08-25

ABS Project-Team (section vide)

AMIB Project-Team

6. Partnerships and Cooperations

6.1. National Initiatives

6.1.1. FRM

Yann 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
- Yann Ponty, A. Denise, M. Regnier, A. Saaidi (PhD funded by FRM)
- B. Sargueil (Paris V – Experimental partner), J. Waldispuhl (Univ. McGill)

6.2. European Initiatives

6.2.1. Collaborations in European Programs, Except FP7 & H2020

Yann 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).

French/Austrian International Program

RNALANDS (ANR-14-CE34-0011)

Fast and efficient sampling of structures in RNA folding landscapes

01/10/2014–30/09/2018

Coordinated by AMIB (Inria Saclay) and TBI Vienna (University of Vienna)

EPI BONSAI/INRIA Lille - Nord Europe, Vienna University (Austria), LRI, Université Paris-Sud (France)

The main goal of the RNALands project is to provide efficient tools for studying the kinetics of RiboNucleic Acids, based on efficient sampling strategies.

Partenariat Henri Curien (CampusFrance, programme Staël)

Random constrained permutations: Algorithms and Analysis

01/01/2015–31/12/2016

Coordinated by CMAP (Ecole Polytechnique) and Maths Dept (Univ. Zürich, Switzerland)

LIX (Ecole Polytechnique), LIPN (Univ Paris XIII), LIGM (Univ Marne-la-Vallée)

The goals of this collaborative network is to initiate or push several collaborations related to the structure of random constrained permutations. AMIB bring their strength in random generation and discrete algorithms, and benefit from the considerable expertise accumulated at University of Zürich on permutation patterns.

6.3. International Initiatives

6.3.1. Inria International Labs

6.3.1.1. Declared Inria International Partners

Title: AMAVI - Combinatorics and Algorithms for the Genomic sequences

International Partner (Institution - Laboratory - Researcher):

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

Duration: 2013 - 2017

Start year: 2013

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 Inria-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.

6.3.1.2. Regular International Partners

AMIB enjoys regular interactions with the following institutions:

- Simon Fraser University (Vancouver, Canada). The Mathematics department at SFU has ongoing projects on RNA design, comparative genomics and RNA structure comparison with our team. M. Mishna (SFU) will also visit Inria Saclay in January 2017 to push an oingoing collaboration on 2D walks;
- McGill University (Montréal, Canada). Following our productive collaboration with J. Waldispühl (Computer Science Dept, McGill), and the recent defense of V. Reinharz's PhD, whose thesis was co-supervised by AMIB members, we plan to increase our interactions on SHAPE data analysis by applying for an Inria associate team;
- King's college (London, UK). Our collaboration with L. Mouchard (AMIB associate) and S. Pissis on string processing and data structures is at the core of Alice Héliou's PhD. To finalize the implementation of her algorithms and apply them on real data, Alice has spent a two month period during the summer of 2016 at the EBI.

6.3.2. Participation in Other International Programs

France-Stanford exchange program

Duration: 2014 - 2016

Start year: 2014

See also: http://francestanford.stanford.edu/collaborative_projects

Amélie Héliou is co-supervised by H. Van Den Bedem in Stanford. Her tow-months visit to Stanford during the Fall of 2016 was funded by France-Stanford.

6.4. International Research Visitors

6.4.1. Visits of International Scientists

6.4.1.1. Internships

Frédéric Lavner

Date: 01/07/2016- 31/08/2016

Institution: ENSEA (France)

Supervisor: Mireille Régnier

Maria Waldl

Date: 01/08/2016 - 31/09/2016

Institution: TBI, University of Vienna (Austria)

Supervisor: Yann Ponty

6.4.2. Visits to International Teams

- Yann Ponty has visited M. Mishna and C. Chauve at the Simon Fraser University for two weeks in July 2016;
- Juraj Michalik has visited A. Tanzer and I. Hofacker at the university of Vienna (Austria) for one week in November 2016;
- Mireille Régnier has visited MIPT (Moscow) and Novossibirsk University to enhance student exchanges between these universities and Ecole polytechnique.

6.4.2.1. Research Stays Abroad

- Alice Héliou has visited the EBI (UK) for two months during the Fall of 2016;
- Amélie Héliou has visited Stanford University (USA) for two months during the Summer of 2016;

BEAGLE Project-Team

7. Partnerships and Cooperations

7.1. Regional Initiatives

- Labex Ecofect IntraCellXevo. Participants: E Tannier, in collaboration with T Henry, Insem Lyon. This projects mixes an experimental evolution of *Franscicella tumarensis* in the cytosol and a bioinformatics analysis of the adaptive mutations. There is one publication associated with this project [19]. It has been funded by ANR and Investissements d'Avenir up to 120keuros.

7.2. National Initiatives

7.2.1. ANR

- Ancestrome (2012-2017): phylogenetic reconstruction of ancestral "-omes", a five-year project, 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 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 (2014-2017): Dopamine modulation of calcium influx underlying synaptic plasticity, a 4-year project 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
- Dallish (2016-2020): Data Assimilation and Lattice LIght SHeet imaging for endocytosis/exocytosis pathway modeling in the whole cell, Call AAPG ANR 2016. With C. Kervrann (Inria Rennes), J. Salamero (Institute Curie, Paris), B. Laroche (INRA, Jouy-en-Josas). Participants: H. Berry.

7.2.2. Inria

- ADT Phylophile. Participants: E Tannier, in collaboration with D Parsons, Inria, V Daubin, B Boussau, CNRS, Université de Lyon 1. This project aims at producing an easy to use software integrating modern algorithmic methods to build gene trees. It has been funded by Inria by a 24 month software engineer.
- ADT Aevol. Participants: C Kinbbe, G Beslon, V Liard, J Rouzaud-Cornabas, D Parsons. This project aims at speeding and scaling and maintaining the code for our most complex software, aevol. It has been funded by Inria by a 24 month software engineer.

7.3. European Initiatives

7.3.1. FP7 & H2020 Projects

7.3.1.1. EvoEvo

Title: Evolution of Evolution

Programm: FP7

Duration: November 2013 - October 2016

Coordinator: Inria

Partners:

Instituto de Biología Molecular y Celular de Plantas, Agencia Estatal Consejo Superior de Investigaciones Cientificas (Spain)

LIRIS, Institut National des Sciences Appliquees de Lyon (France)

LIRIS, Universite Lyon 1 Claude Bernard (France)

LAPM, Universite Joseph Fourier Grenoble 1 (France)

Bioinformatics and Theoretical Biology, Universiteit Utrecht (Netherlands)

Computer science department, 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).

7.3.1.2. Neuron-Astro-Nets

Title: Neuron-Astro-Nets

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

Duration: 2013-2017

Partners: Inria Grenoble-Rhone-Alpes; Dept Statistics and Neurobiology, University of Chicago, USA (N. Brunel)

Inria contact: H. 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 Pittá's postdoc for 4 years (June 2013- May 2017). M. De Pittá´ spent two years in N. Brunel's group in Chicago (06/2014-05/2016) then one year back in Beagle in Lyon (06/2016-05/2017).

7.4. International Initiatives

- 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's team (UJF, LAPM, UMR CNRS 5163, France), Richard Lenski's team (Michigan State University, Beacon center, US) and the Beagle team.

BIGS Project-Team

9. Partnerships and Cooperations

9.1. National Initiatives

- *PEPS AMIES* (2016), Apprentissage supervisé pour l'aide au diagnostic, Collaboration Institut Elie Cartan avec la StartUp SD Innovation Frouard. Participants: A. Gégout-Petit, P. Vallois
- *Popart (2016-2017)* In the framework of collaboration with A. Deveau of Inra Nancy, A. Gégout-Petit and A. Muller-Gueudin are included in the Inra "Microbial Ecosystems & Metaomics, Call 2016" Project "Popart"for "Regulation of the Poplar microbiome by its host: is the immune system involved ? ". The aim is to develop methodology for the inference of regulation network betwen micro-organisms around Poplar. The specificity of the data is the inflation of zeros that has to be taken into account.
- *Intérêt des antiangiogènes dans la potentialisation des thérapies par rayonnement dans le cas des glioblastomes* (2016). Funding organism: Ligue contre le Cancer (CCIR-GE). Leader: N. Thomas (CRAN, U. Lorraine). Participants : C. Lacaux and A. Muller-Gueudin
- (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. European Initiatives

9.2.1. Collaborations in European Programs, Except FP7 & H2020

- Photobrain project. AGuIX theranostic nanoparticles for vascular-targeted interstitial photodynamic therapy of brain tumors, project **EuroNanoMed II**, resp.: M. Barberi-Heyob, (2015-2017), participant: T. Bastogne.
- NanoBit Project. Nanoscintillator-Porphyrin Complexes for Bimodal RadioPhotoDynamic Therapy, project **EuroNanoMed II**, resp.: P. Juzenas, (2016-2018), participant: T. Bastogne.

BONSAI Project-Team

9. Partnerships and Cooperations

9.1. National Initiatives

9.1.1. ANR

- ANR ASTER: ASTER is a national project that aims at developing algorithms and software for analyzing third-generation sequencing data, and more specifically RNA sequencing. BONSAI is the principal investigator in this ANR. Other partners are Erable (LBBE in Lyon) and two sequencing and analysis platforms that have been very active in the MinION Access Program (Genoscope and Institut Pasteur de Lille).
- 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 increases 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 its installation, administration and usability. This will enable the software to be well suited for a daily clinical use. The software is already used in test on our own web server (more than 5,000 samples processed by now). Vidjil is now used in a routine practice by three French hospitals and one German hospital. By the end of the ADT, we expect this number to increase and the software to be directly installed inside some hospitals.

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*). Our objective is the 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.

Interreg Va (France-Wallonie-Vlaanderen) : Portfolio "SmartBioControl", including 5 constitutive projects and 25 partners working together towards sustainable agriculture.

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 et d'informatique mathématique (LaCIM) - Anne Bergeron

From 2014 to 2017

The aim of this Associated Team is the development of comparative genomics models and methods for the analysis of eukaryote genes structure evolution. Our goal 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 meeting took place in 2016. S. Blanquart and J.-S. Varré met A. Bergeron and K. Swenson in Montpellier, from 13th to 15th of April. J.-S. Varré and K. Swenson met A. Bergeron in Montréal, from 8th to 19th of November.

9.3.2. Inria International Partners

9.3.2.1. Informal International Partners

- *Astrid Lindgrens Hospital, Stockholm University:* Collaboration with Anna Nilsson and Shanie Saghafian-Hedengren on RNA sequencing of stromal cells.
- *Childhood Leukaemia Investigation Prague (CLIP), Department of Pediatric Hematology/Oncology, 2nd Faculty of Medicine, Charles University, Prague, Czech Republic:* Collaboration with Michaela Kotrová and Eva Fronkova on leukemia diagnosis and follow-up.
- *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.
- *Département des Sciences de la Vie, Faculté des Sciences de Liège:* Collaboration with Denis Beaurain on nonribosomal peptides.
- *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.
- *Institute of Biosciences and Bioresources, Bari:* Collaboration with Nunzia Scotti on the assembly of plant mitochondrial genomes.
- *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 on nonribosomal peptides.
- *School of Social and Community Medicine, University of Bristol:* Collaboration with Marc Duez, John Moppett and Stephanie Wakeman on leukemia diagnosis follow-up.
- *Theoretical Biochemistry Group, Universität Wien:* Collaboration with Andrea Tanzer and Ronny Lorenz on RNA folding and RNA kinetics.

9.3.3. Participation in Other International Programs

- Participation in the EuroClonality-NGS consortium. This consortium aims at standardizing the study of immune repertoire, clonality and minimal residual disease in leukemia at the european level. We are part of the bioinformatics workgroup led by Nikos Darzentas (CEITEC, Brno, Czech Republic).

9.4. International Research Visitors

9.4.1. Visits of International Scientists

- Dr. Alexander Schoenhuth (group leader, *CWI Amsterdam*) and Jasmijn Baaijens (PhD student, *CWI Amsterdam*).

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

8.2.1.1. LBS

Participant: Marie-Dominique Devignes [contact person].

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. Fight-HF

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

This "Investissements d'Avenirs" project aims to discover novel mechanisms for heart failure and to propose decision support for precision medicine. The project has been granted € 9M, and involves many participants from Nancy University Hospital's Federation "CARTAGE" (http://www.fhu-cartage.com/). In collaboration with the Orpailleur Team, Marie-Dominique Devignes is coordinating a work-package on network-based science and drug discovery for this project.

8.2.2.2. IFB

Participants: Marie-Dominique Devignes [contact person], Sabeur Aridhi, Isaure Chauvot de Beauchêne, David Ritchie.

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.

8.2.2.3. 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 shock 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 to International Teams

8.4.1.1. Research Stays Abroad

Gabin Personeni visited the Biomedical Informatics Research Laboratory of Prof. Michel Dumontier at Stanford University for 3 months (Nov 2015 – Feb 2016).
Seyed Ziaeddin Alborzi visited the UniProt development team of Maria Martin at the European Bioinformatics Institute (EBI), Hinxton UK, for 3 months (Oct – Dec 2016) in partial fulfilment of the requirements for a European PhD.

DYLISS Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

8.1.1. Regional initiative: the Ecosyst project

Participants: Damien Eveillard, Marie Chevallier, Clémence Frioux, Anne Siegel, Camille Trottier.

EcoSyst is a Biogenouest inter-regional federating project (Brittany â Pays de la Loire) aiming at the emergence of Systems Ecology at the level of western regions. Drawing on the strengths and skills involved, EcoSyst targets the incubation of new ideas and new projects at disciplinary interfaces. Thanks to this community project, we want to develop the skills of Ecology, Environment, Modeling, Bioinformatics and Systems Biology and their application to organisms and ecosystems of interest in agronomy, sea and health. EcoSyst includes also the identification of the major issues and concerns, the fundamental and essential methods and the very real needs of the community (training, tools, ...); this in order to consider the construction of a community platform (or an offer of service within an existing platform) on complex systems modeling, meeting expectations of the community as fully as possible.

8.1.2. Regional partnership with computer science laboratories in Nantes

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

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 support. C. Trottier is a co-supervised bioianalysis and software development engineer within the Idealg project. M. Chevallier is a co-supervised development and animation engineer within the regional initiative "Ecosyst". In addition, the former Ph-D student V. Picard and the ongoing Ph-D student J. Laniau are also co-supervised with members of the LINA laboratory.

8.1.3. Regional partnership in Marine Biology

Participants: Catherine Belleannée, Jérémie Bourdon, Jean Coquet, François Coste, Damien Eveillard, Olivier Dameron, Clémence Frioux, Jeanne Got, Julie Laniau, Jacques Nicolas, 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 (Inria Project Lab) with the Biocore and Ange teams, together with Ifremer-Nantes, focused on the understanding on micro-algae (Ph-D thesis of J. Laniau).

8.1.4. Regional partnership in agriculture and bio-medical domains

Participants: Aymeric Antoine-Lorquin, Catherine Belleannée, François Coste, Jean Coquet, Olivier Dameron, Victorien Delannée, Aurélie Evrard, François Moreews, Jacques Nicolas, Anne Siegel, Nathalie Théret, Denis Tagu, Pierre Vignet.

We have a strong and long term collaboration with biologists of INRA in Rennes : PEGASE and IGEPP units. F. Morrews is a permanent engineer from PEGASE center hosted in the team to develop methods for integrative biology applied to species of interest in agriculture. D. Tagu is a research director at INRA who spends 20% of his time in the team to develop collaborative projects. This partnership is supported 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 former post-doc of Ch. Bettembourg strengthened these collaborations. This collaboration was also reinforced by collaboration within ANR contracts (MirNadapt, FatInteger). Lately, A. 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. N. Théret, research director at INSERM, is hosted in the team to strenghen our collaborative projects. Our collaborations are 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 has been recently pushed forward in the recent TGFSYSBio project funded by Plan Cancer on the modelling of the microenvironment of TGFbeta signaling network (P. Vignet has been recruited on this contract at the end of 2016).

8.2. National Initiatives

8.2.1. Long-term contracts

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

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

We have a cooperation with Univ. of Chile (MATHomics, A. Maass) on methods for the identification of biomarkers and software for biochip design, supported by a national Inria initiative. 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, François Coste, Damien Eveillard, Clémence Frioux, Jeanne Got, 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 in the tasks related to the establishment of a virtual platform for integrating omics studies on seaweed) and the 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) [More details].

8.2.2. Programs funded by research institutions

8.2.2.1. PEPS PEPS: a platform for supporting studies in pharmaco-epidemiology using medico-administrative databases

Participants: Olivier Dameron, Yann Rivault.

As a partner of the PEPS platform, IRISA develops generic methods supporting efficient and semantically-rich queries for pharmaco-epidemiology studies on medico-administrative databases. The leader is Thomas Guyet (IRISA team Lacodam). We showed that Semantic Web technologies are technically suited for representing patients' data from medico-administrative databases as RDF and querying them using SPARQL. We also demonstrated that this approach is relevant as it supports the combination of patients' data with hierarchical knowledge in order to address the problem of reconciling precise patients data with more general query criteria [33], [31], [30]. This work is mostly conducted by Yann Rivault, whose PhD thesis is supervized by Olivier Dameron and Nolwenn LeMeur (Ecole des Hautes Etudes en Santé Publique).

8.2.2.2. Cancer Plan: TGFSYSBIO

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

The TGFSYSBIO project aims to develop the first model of extracellular and intracellular TGF-beta system that might permit to analyze the behaviors of TGF-beta 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-beta-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-beta. 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.

8.2.2.3. ANR Samosa

Participants: Damien Eveillard, Jeanne Got, Anne Siegel.

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.

8.2.2.4. ADT Complex-biomarkers and ADT Proof of concept

Participants: Jeanne Got, 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).

8.2.2.5. 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.

8.2.2.6. PEPS CONFOCAL

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

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 Remy (Mathematics Institute Luminy, "Mathematical Methods for Genomics" team).

8.3. European Initiatives

8.3.1. Collaborations with Major European Organizations

Partner: Aachen university (Germany)

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 and Meziane Aite joined the team as engineers to improve softwares resulting from collaborations. Maria-Paz Cortes visited the team during 6 monthes in the framework of her ph-D thesis.

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) - Maass Alejandro

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 viewed as a different scale of a biological process, either in time or space, but ultimately 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-level 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).

8.5. International Research Visitors

8.5.1. Visits of International Scientists

- **Argentina**. Fundation Leloir, Buenos Aeres [S. Videla]
- **Chile**. Centro de Modelimiento Matematico, Santiago [A. Maass, N. Loiraâ , M. Latorre, M.-P. Cortes]
- **Niger**. University of Maradi [O. Abdou-Arbi]
- **Germany**. Max Planck Institute for Biophysical Chemistry [C. Galiez]

8.5.2. Research stays abroad

- **Germany**. University of Kaiserslautern [A. Antoine-Lorquin, 2 months]
- **Germany**. University of Potsdam [C. Frioux, 2 months]
- **Japan**. National Institute of Informatics in Tokyo [J.Coquet, 3 months]

8.5.3. Visits to International Teams

- **Chile**. Centro de Modelimiento Matematico, Santiago de Chile [J. Bourdon, M. Aite, F. Coste, A. Siegel]
- **Germany**. Frei Berlin University [A. Siegel]
- **Poland**. Wroclaw University of Science and Technology [F. Coste]
- **Netherland**. Utrecht University [F. Coste]

ERABLE Project-Team

7. Partnerships and Cooperations

7.1. Regional Initiatives

7.1.1. ICEbErg

- Title: Integrating Co-phylogeny in the analysis of Ecological nEtworks
- Coordinator: B. Sinaimeri and S. Dray
- ERABLE participant(s): B. Sinaimeri
- Type: Inter-departmental project funded by the LBBE (Sept 2016 - Sept 2017)
- Web page: Not available

7.2. National Initiatives

7.2.1. ANR

7.2.1.1. 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/

7.2.1.2. 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-Laferrière, H. Lopez-Maestre, C. Marchet, G. Sacomoto, M.-F. Sagot, B. Sinaimeri
- Type: ANR (2013-2016)
- Web page: http://colibread.inria.fr/

7.2.1.3. ExHyb

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

7.2.1.4. GraphEn

- Title: Enumération dans les graphes et les hypergraphes : algorithmes et complexité
- Coordinator: D. Kratsch
- ERABLE participant(s): A. Mary
- Type: ANR (2015-2019)
- Web page: http://graphen.isima.fr/

7.2.1.5. 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

7.2.2. Others

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

7.2.2.1. 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/

7.2.2.2. 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

7.2.2.3. QualiBioConsensus

- Title: Qualité des classements consensuels de données biologiques massives
- Coordinator: S. Cohen-Boulakia
- ERABLE participant(s): L. Bulteau (external collaborator of ERABLE)
- Type: Défi Mastodons (2016)
- Web page: Not available

7.3. European Initiatives

7.3.1. FP7 & H2020 Projects

7.3.1.1. 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-Laferrière, 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/

7.3.1.2. 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/

7.3.2. Collaborations in European Programs, Except FP7 & H2020

7.3.2.1. Combinatorics of co-evolution

- Title: The combinatorics of co-evolution
- Duration: 2015 - 2017
- Coordinator: Katharina Huber, University of Warwick, UK
- ERABLE participant(s): M.-F. Sagot, B. Sinaimeri
- Type: The Royal Society
- Web page: not available

7.3.3. 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.

7.4. International Initiatives

7.4.1. 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 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.

7.4.2. 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/

7.4.3. 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 BAOBAB-ERABLE. 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/erable/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", and its acronym MICO. 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, Brazil). The project started in 2013 for 2 years, and 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 has a Stic AmSud project that started 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 tumour/normal samples and RNAseq of tumour samples). One of the scientific goals is to decipher whether the HER2/ERBB2 amplification is a driver or a passenger event in the course of tumour development.

7.5. International Research Visitors

7.5.1. Visits of International Scientists

In 2016, ERABLE greeted the following International scientists:

- In France: Katharina Huber and Vincent Moulton (University of Warwick, UK), Giuseppe Italiano (Tor Vergata University of Rome, Italy, various visits), Ana Rute Neves and Thomas Janzen (ChR Hansen, Oslo, Danemark), two members of the LIA LIRIO (Arnaldo Zaha from the Federal University of Rio Grande do Sul, and Ana Tereza Vasconcelos from the LNCC, both in Brazil), Susana Vinga and various members of her team (IDMEC-IST Portugal), Tiziana Calamoneri (Sapienza University of Rome).
- In Italy: Costas Iliopoulos and Solon Pissis (King's College, London, UK).

7.5.2. Internships

In 2016, ERABLE greeted the following internship students:

- In France: Audric Cologne, Master 2 (6 months); Irene Ziska, Master Free University Berlin (2 months), Louis Duchemin Master 1 (5 months).

7.5.3. Visits to International Teams

7.5.3.1. Visits

In 2016, 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 Department 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 members of her team (IDMEC-IST Portugal), Rafaelle Giancarlo (Palermo University, Italy).
- In Italy: Costas Iliopoulos (King's College, London, UK), Luís Russo (INESC-IST, Lisbon, Portugal), Paola Bonizzoni (Milan-Bicocca, Italy), Rafaelle Giancarlo (Palermo University, Italy).

7.5.3.2. Research stays abroad

Gunnar Klau spent 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. 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. More precisely, we are in the process of setting up and evaluating a new method of predictions of small cancer-related mutations (such as SNPs and small insertions/deletions) from raw DNA sequencing data. The method relies on the use of k-mers and clustering of reads to call for mutations. Current prototype relies on Python programming language just for the purpose of evaluating the prediction quality of the software. However, final software is expected to use GATB library to highly increase the performance of the new tool.

9.1.2. Partnership with INRA in Rennes

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

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 of one INRA engineer (F. Legeai) and one PhD student (C. Guyomar).

9.2. National Initiatives

9.2.1. ANR

9.2.1.1. 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.

9.2.1.2. 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 do not require the availability of a reference genome. https://colibread.inria.fr/

9.2.1.3. Project HydroGen: Metagenomic applied to ocean life study

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

Coordinator: P. Peterlongo (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.

9.2.1.4. 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 butterfly 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, Sebastien Letort, Pierre Peterlongo.

Coordinator: N. Nesi (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.

9.2.3. Programs from research institutions

9.2.3.1. Inria ADT DiagCancer

Participants: Dominique Lavenier, Patrick Durand.

Since October 1st, 2016, Genscale has started a one-year Inria ADT called DiagCancer. It aims at: (1) including the DiscoSnp++ tool within the current data production pipeline at Pontchaillou Hospital (Rennes), (2) providing a new prediction tool applied to the calling of cancer related mutations from DNA sequencing data and (3) creating new analysis tools to facilitate the interpretation of results by end-users (biologists, doctors). The project is done in close collaboration with Haematology Service, CHU Pontchaillou, Rennes.

9.3. International Initiatives

9.3.1. Informal International Partners

- Free University of Brussels, Belgium: Genome assembly [P. Perterlongo, R. Andonov]
- IMECC, UNICAMP, Campinas, Brazil: Distance geometry problem [A. Mucherino]
- Los Alamos National Laboratory (LANL), Los Alamos: Graph structure, Parallelism, GPU [R. Andonov, D. Lavenier, G. Rizk]

9.4. International Research Visitors

9.4.1. Visits of International Scientists

- Visit of prof. Tomi Klein from Bar Ilan University (Israel). One week, december 2016. Collaboration for the application of approximate hash function to the TGS data analysis [P. Peterlongo]
- Visit of Hristo Djidjev from Los Alamos National Laboratory, June 2016. Graph algorithms for scaffolding problem, professeur invité, University of Rennnes 1, [R. Andonov]
- Visit of Guillaume Chapuis from Los Alamos National Laboratory, June 2016. Parallelism, GPU. [R. Andonov, D. Lavenier]

9.4.2. Internships

- Samyadeep Basu, BITS Pilani, India, May - July 2016. Development of a web server for assembling bacteria genomes [D. Lavenier, P. Durand, C. Deltel]

9.4.3. Visits to International Teams

9.4.3.1. Research Stays Abroad

- Visit of Guillaume Rizk to Los Alamos National Laboratory, USA, August - September 2016 (2 months). Efficient combinatorial optimization using quantum computing.

IBIS Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

Project name	RNAfluo: Quantification d'ARN régulateurs in vivo
Coordinators	S. Lacour
IBIS participants	S. Lacour
Type	AGIR program, Université Grenoble Alpes

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 (2015-2019)
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	C. Boyat, E. Cinquemani, J. Geiselmann, H. de Jong, S. Lacour, L. Lancelot, Y. Markowicz, C. Pinel, D. Ropers
Type	Bioinformatics call, Investissements d'Avenir program (2012-2017)
Web page	https://project.inria.fr/reset/

Project name	MEMIP – Modèles à effets mixtes de processus intracellulaires : méthodes, outils et applications
Coordinator	G. Batt
IBIS participants	E. Cinquemani, D. Ropers
Type	ANR project (2016-2020)

Project name	ENZINVIVO – Détermination in vivo des paramètres enzymatiques dans une voie métabolique synthétique
Coordinator	G. Truan
IBIS participants	J. Geiselmann, H. de Jong
Type	ANR project (2016-2020)

Project name	Analyse intégrative de la coordination entre stabilité des ARNm et physiologie cellulaire chez Escherichia coli
Coordinators	D. Ropers, M. Cocaign-Bousquet (Inra, LISBP)
IBIS participants	T. Etienne, D. Ropers
Type	Contrat Jeune Scientifique Inra-Inria (2016-2019)

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, Y. Martin, M. Page, D. Ropers, V. Zulkower (University of Edinburgh)
Type	IFB call for development of innovative bioinformatics services for life sciences (2016-2017)

Project name	FluoBacTracker – Adaptation et valorisation scientifique du logiciel FluoBacTracker
Coordinator	H. de Jong, H. Berry
IBIS participants	C. Dutrieux, H. de Jong, J. Geiselmann
Type	Inria Hub (2016-2017)

8.3. European Initiatives

8.3.1. Collaborations with Major European Organizations

Laboratoire d'Automatique at Ecole Polytechnique Fédérale de Lausanne (Switzerland), 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 researcher	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

Invited researcher	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-MOST BIOPSY (2016-2020) on "Biochemical Programming System", coordinated by F. Molina (CNRS, Sys2diag, Montpellier) and J.H. Jiang (National Taiwan University), with F. Fages.
- ANR MEMIP (2016-2020) on "Mixed-Effects Models of Intracellular Processes", coordinated by G. Batt, with P. Hersen, (CNRS/Paris7), E. Cinquemani (Inria EPI IBIS) and M. Lavielle (Inria/CNRS/Polytechnique, EPI XPOP).
- ANR COGEX (2016-2019) on "Computer Aided Control of Gene Expression" coordinated by P. Hersen (MSC lab, CNRS/Paris7), with G. Batt and G. Truan (LISBP, CNRS/INSA).
- ANR Blanc HYCLOCK (2014-2018) on "Hybrid modeling of time for Circadian Clock Biology and Chronopharmacology", coordinated by F. Delaunay (CNRS, Nice), with F. Lévi (INSERM Paris-Sud), G. Bernot (CNRS I3S, Nice), O. Roux (Ecole Centrale Nantes), F. Fages and S. Soliman.
- 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).

8.1.2. GENCI Contract

- GENCI (2009-2016) 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. Informal International Partners

In the context of the PhD thesis of Virgile Andréani, we initiated a collaboration with the lab of Lingchong You in the Biomedical Engineering department of Duke University (NC, USA).

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 a sabbatical stay of six months

- Prof. David Rosenblueth, University of Mexico, Mexico.

We also received for short visits:

- Prof. Mark Chaplain, University of St-Andrews, UK,
- Prof. Attila Attila Csikász-Nagy, King's College London,
- Dr. Jakob Ruess, IST Austria,
- Dr. Amaury Pouly, Univ. Oxford, UK,
- Dr. Christoph Zechner, ETH Zurich,
- Prof. Natalio Krasnogor, Newcastle University, UK,

8.3.1.1. Research Stays Abroad

Virgile Andréani visited Lingchong You's lab (Duke U.) for two weeks in March 2016.

MORPHEME Project-Team

7. Partnerships and Cooperations

7.1. Regional Initiatives

7.1.1. 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 Xavier Descombes participated in the selection committee for LabeX PhD program students.

7.2. National Initiatives

7.2.1. ANR RNAGRIMP

Participants: Florence Besse [PI], Xavier Descombes, Eric Debreuve, Djampa Kozlowski, Nicolas Cedilnik.

Here, we propose to study the molecular bases underlying the assembly and regulation of RNA granules, using the highly conserved IMP-containing granules as a paradigm. Specifically, we propose to perform an unbiased genome-wide RNAi screen on Drosophila cultured cells to identify mutant conditions in which the organization and/or distribution of IMP-containing granules is altered. To quantitatively and statistically analyze mutant conditions, and to define precise and coherent classes of mutants, we will combine high throughput microscopy with the development of a computational pipeline optimized for automatic analysis and classification of images. The function of positive hits isolated in the screen will then be validated in vivo in Drosophila neurons using fly genetics and imaging techniques, and characterized at the molecular and cellular levels using biochemical assays, in vitro phase transition experiments and live-imaging. Finally, the functional conservation of identified regulators will be tested in zebrafish embryos combining gene inactivation and live-imaging techniques. This integrative study will provide the first comprehensive analysis of the functional network that regulates the properties of the conserved IMP RNA granules. Our characterization of the identified regulators in vivo in neuronal cells will be of particular significance in the light of recent evidence linking the progression of several degenerative human diseases to the accumulation of non-functional RNA/protein aggregates.

This 4-years project started january, 2016 and is leaded by F. Besse (iBV, Nice). Participants are iBV, institut de biologie Paris Seine (IBPS, Paris), and Morpheme.

7.2.2. ANR HMOVE

Participants: Xavier Descombes, Eric Debreuve.

Among the signaling molecules involved in animal morphogenesis are the Hedgehog (Hh) family proteins which act at distance to direct cell fate decisions in invertebrate and vertebrate tissues. To study the underlying process we will develop accurate tracking algorithm to compare trajectories of different Hh pools transportation in live animals. This will allow us to analyze the contribution of the different carriers in the establishment of the Hh gradient. Moreover, we will develop new methods to modify the spatio-temporal and dynamical properties of the extra-cellular Hh gradient and separate the contribution of the apical versus basal Hh pools. We will complete this study with a genome-wide screen to identify genes and related cellular processes responsible for Hh release. The particular interest of this collaboration lies in the combination of development of tracking algorithm to analyze Hh distribution and trajectories with extremely powerful genetics, ease of in vivo manipulation and lack of genetic redundancy of Drosophila.

This 4-years project started january, 2016 and is leaded by P. Thérond (iBV, Nice). Participants are iBV and Morpheme.

7.2.3. ANR DIG-EM

Participants: Grégoire Malandain, Xavier Descombes, Gaël Michelin.

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.

7.2.4. 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.

7.2.5. 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 modeling. 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-characterized plant systems.

7.2.6. 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).

7.3. European Initiatives

7.3.1. Collaborations in European Programs, Except FP7 & H2020

- COST Action (The COST Program is supported by the EU Framework Program H2020). We are part of a consortium of teams which submitted in December a COST Action proposal on machine learning and intelligent systems for the marine and aquatic sciences.

7.4. International Research Visitors

7.4.1. Visits of International Scientists

7.4.1.1. Internships

Mohammed Lamine Benomar, PhD, Université Abou Bekr Belkaid Tlemcen, Algérie, from October 2016 until April 2017.

Hibetallah Ouazaa, PhD, National Engineering School of Tunis, from May 2016 until Jun 2016

PLEIADE Team

8. Partnerships and Cooperations

8.1. National Initiatives

8.1.1. ANTICOR – Biocontamination in aircraft reservoirs

ANTICOR is an industrial-academic research and development working group coordinated by Dassault Aviation, investigating the causes of microbial contamination in aircraft reservoirs and aimed at developing mitigating procedures and equipment. Previous results have shown that this contamination forms biofilms at the fuel-water interface and is comprised of complex communities of hundreds of bacterial and fungal species. PLEIADE is particularly interested in measuring and modeling these communities, especially as concerns understanding how they change based on environmental conditions and on reservoir geometry.

8.1.2. 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.

8.2. International Initiatives

8.2.1. Supervised clustering

One way to build an inventory in a community on a molecular basis is to map unknown reads onto a taxonomically annotated reference database. We (AF, PC, JMF, FS) have developed a cooperation with UMR Carrtel (A. Bouchez, F. Rimet) and SLU at Uppsala (Sweden, M. Kahlert) for industrializing molecular based inventories from data production (NGS facilities, PGTB, Pierroton) to data analysis. Molecular based inventories of about 200 samples have been done, for diatoms Mayotte rivers, and the same number for diatoms in Fennoscandian rivers. The method has been published in [13]. As far as those tools and metagenomics are concerned, a complementary partnership has been established with UMR BioGER (V. Laval) on metabarcoding of fungal communities.

8.2.2. Metagenomics for zoonoses

In the framework of CEBA Cluster of Excellence (Centre d'Etude de la Biodiversité Amazonienne), Pleiade team has been successful in an application for being part of a so called long term strategic project (2017-2019) called microbiome, chaired by Institut Pasteur in Cayenne and UMR MIVEGEC (CNRS-IRD) at Montpellier. The role of the team is twofold: (i) develop methods for metabarcoding of viral and bacterial communities in some hosts (bats, birds, ...) and (ii) run some data analysis for scaling up from microbiomes to landscape ecology, having in mind the dilution effect, i.e. pristine forest offer a better protection against disease spread than disturbed ones. The project starts on January 1, 2017.

8.2.3. Historical biogeography of plant families

In the framework of CEBA too, AF and David Sherman have worked in providing some tools for mapping paleoclimatic conditions on the Earth over geological times, elaborating on datasets of paleoclimates produced by running General Circulation Models (work done by UMR LSCE, Orsay, in a previous ANR project lead by AF). These maps will be part of a collaboration established with The Royal Botanical Gardens at Kew (UK) and several Brasilian Universities in a join project on historical biogeography of Myrtaceae, a large family of trees and shrubs, well developed in the Neotropoics. A. Franc has been visiting E. Lucas, at Kew Botanical gardens, in March 2016 for setting up a cooperation. A first workshop has been organized by F. Salgeiro and AF at Rio in May 2016. The next one will be held in August 2017, organized by E. Lucas and coll. An an open access paper on historical biogeography of the genus Quercus, in collaboration with University of Padova and Museum of Natural History of Stockholm, is [11].

8.2.4. 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). Our focus is inference of metabolic and regulatory models by comparative genomics, and their description using stochastic transition systems.

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.

IGDR: Collaboration with J. Pecreaux, Y. Le Cunff (co-supervision of A.G. Caranfil's PhD thesis).

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.

9.2.2. ANR DALLISH project (2016-2020): Data Assimilation and Lattice LIght SHeet imaging for endocytosis/exocytosis pathway modeling in the whole cell

Participants: Charles Kervrann, Patrick Bouthemy, Vincent Briane, Ancageorgiana Caranfil.

The Lattice Light Sheet Microscopy (LLS-M) represents at present the novel generation of 3D fluorescence microscopes dedicated to single cell analysis, generating extraordinarily high resolved and sharp, but huge 3D images and videos: one single live cell experiment in one single condition, imaging two molecular markers of the endocytosis pathway and using cutting-edge LLS-M can result into up to one Terabyte of data, at the spatial resolution of 100-200 nanometers in 3D. In such a situation, it is found the usual conventional image reconstruction algorithms and image analysis methods developed for 3D fluorescence microscopy are likely to fail to process a deluge of voxels generated by LLS-M instruments. The goal of the project is then to develop new paradigms and computational strategies for image reconstruction and 3D molecule tracking/motion estimation. Furthermore, establishing correspondences between the image-based measurements and features (e.g., motion vectors, trajectories), stochastic motion models and the underlying biological and biophysical information remains a challenging task.

The impact of the project will be three-fold. First, our new image processing paradigms and improved algorithms (allowing faster, more resolved and more accurate results) will have direct benefits in modern bioimaging. Second, the methods and algorithms will apply to decipher molecular mechanisms of protein transports, here focused on endocytosis/exocytosis. Finally, in a larger perspective, the quantitative description of protein transport will be a prerequisite for understanding the functioning of a cell in normal and pathological situations, as default in protein transport appeared over the years, as a major contributory factor to a number of diseases, including cancer, viral infection and neurodegenerative diseases.
Funding: ANR - Agence Nationale de la Recherche
Partners: Inria (SERPICO, BEAGLE, Fluminance), INRA MaIAGE Unit Jouy-en-Josas, Institut Curie (UMR CNRS 144 & U1143 Inserm UMR 3666) Paris

9.3. European Initiatives

9.3.1. Major European Organizations with which the Team have followed Collaborations

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. Informal International Partners

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

Collaboration with Aalborg University (Denmark), Prof. Rasmus Waagepetersen : Estimating equations for inhomogeneous determinantal point processes (project in progress with Frédéric Lavancier).

Collaboration with EPFL (M. Unser's Team, Switzerland). D. Fortun: optical flow computing (project in progress with Charles Kervrann).

9.4.2. CytoDI Inria Associated-Team

Title: Quantitative Imaging of Cytoskeleton Dynamics in 3D
International Partner:

University of Texas, SouthWestern Medical Center, Dallas (United States) - Gaudenz Danuser

Start year: 2016
See also: http://serpico.rennes.inria.fr/doku.php?id=research:cytodi
The main scientific goal of the Associated-Team is the spatiotemporal characterization and comparison of cytoskeleton networks involved in cell migration and observed through live cell imaging in three dimensions (3D). Those networks include the cytoskeleton, i.e., microtubules (MT), intermediate filaments (IF), dynamically resolvable by Bessel Beam Light Sheet fluorescent microscopy. The goal will be achieved through the design of local and global descriptors of the spatial conformation and deformation of the cytoskeleton. Subsequently, general metrics to compare and classify the MT and IF networks will be investigated. This study will be carried out on oncogenically transformed lung cancer epithelial cells.

The first meeting took place in Dallas in May 2016 as originally scheduled, to discuss and update current research direction and discuss scientific progress.

9.5. International Research Visitors

9.5.1. Visits to International Teams

Visit of 3 months of Juan Manuel Perez Rua in the Philip Torr's team (University of Oxford, UK).
Visit of 1 one week of Vincent Briane to the ESGI (European Study Group in Industry) in Dublin (Ireland, July 2016).

Visit of 1 one week of Vincent Briane to the University of Limerick (K. Burke's team) (Ireland, November 2016).

TAPDANCE Team

5. Partnerships and Cooperations

5.1. International Research Visitors

5.1.1. Visits of International Scientists

Prof. David Doty from UC Davis, California, was hosted for 1 week in 2016.

5.1.2. Visits to International Teams

Woods visited Caltech for several weeks in 2016.
Woods visited Dagstuhl 3-8 July 2016 for Caltech for several weeks in 2016. Dagstuhl Seminar 16271 Algorithmic Foundations of Programmable Matter. Collaborative work with workshop attendees. Invited talk.

VIRTUAL PLANTS Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

8.1.1. New pearl

Participants: Sixtine Passot, Yann Guédon, Soazig Guyomarc'h [Montpellier University, DIADE], Laurent Laplaze [IRD, DIADE].

Funding: Labex Agro (Contractor for Virtual Plants: CIRAD, from 2014 to 2017)

Pearl millet is an orphan crop regarding research effort despite its key role for food safety in Sub-Saharan Africa. The objective of the New Pearl project is to develop basic biological knowledges concerning Pearl millet development and genetic diversity. We are more specifically involved in the study of the root system development and the genetic diversity on the basis of root phenotypic traits.

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;

8.2. 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, Yann Guédon, 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. 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.

8.2.5.2. Morphogenetics

Participants: Christophe Godin, Frédéric Boudon, Olivier Ali, Jean Phillipe Bernard, Hadrien Oliveri, Christophe Pradal, Guillaume Cerutti, Grégoire Malandain, François Faure, Jan Traas, François Parcy, Arezki Boudaoud, Teva Vernoux.

Funding: Inria Project Lab (From 2013 to 2017)
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).

8.2.5.3. Rose

Participants: Christophe Godin, Frédéric Boudon.

Funding: INRA - PhD project (From 2016 to 2019)
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

8.2.5.4. ReProVirtuFlow

Participants: Christophe Pradal, Sarah Cohen-Boulakia, Jerome Chopard.

In the life science domain, scientists are facing the deluge and the size of available data, the composition of a myriad of existing tools, and the complexity of computational experiment. In this context, reproducing an experiment is particularly difficult, as evidenced by numerous recent studies. The aim of this GDR CNRS project is to make a complete review of existing approaches in this field, considering in priority as elements of solution: (i) scientific worklfows, (ii) data provenance, and (iii) virtual machines. This project brings together experts in data bases, algorithms and virtual environments, working in the domain of life science.

Funding: GDR - CNRS

8.3. European Initiatives

8.3.1. Collaborations with Major European Organizations

8.3.1.1. Hook

Participants: Christophe Godin, Olivier Ali.

A new collaboration started with the University of Umeä (Sweden) on the modeling of the apical hook in the hypocotyl of *Arabidopsis thaliana*. The question we want to answer is what regulates the opening dynamics of the apical hook at the tip of the hypocotyl and how. For this, a multidisciplinary approach, combining 3D laser imaging, molecular biology, genetics and modeling will be developed by the partners.

Partners: University of Umeä, RDP ENS-Lyon.

8.4. International Initiatives

8.4.1. ANR-DFG

8.4.1.1. 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)

8.4.2. Inria International Partners

8.4.2.1. 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.

8.4.2.2. Informal International Partners

An important collaboration with the CIRAD research unit HortSys at the Reunion island and in particular Frédéric Normand, Yann Guédon, Pierre Fernique and Christophe Pradal has been established for several years. The topic of the collaboration is the study of the phenology of mango tree. This is a tripartite collaboration that also involves Pierre-Eric Lauri of the System research unit (INRA, Montpellier).

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. 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.

8.5. International Research Visitors

8.5.1. Visits of International Scientists

Julia Pulwicki from the University of Calgary, Canada, spent 10 days at our lab in May to study the opportunity to define a post-doctoral project for her and to set up the basis of a joint scientific project. This project has lead us to submit to the Inria post-doctoral programme a project on that was accepted. Julia arrived for a 12 month post-doctoral project in November.

In this study, we want to formalize the analogy between the development of shapes in biology and the feedback between mass and space curvature in general relativity. Our aim is to propose a quantitative approach of such a vision by developing a mathematical and computational framework combining formalisms from non-euclidean geometry developed in general relativity and models of signal propagation and gene regulation in plant tissues.

8.5.1.1. Research Stays Abroad

In the context of the project on mango modelling and the PhD of S. Persello, F. Boudon is currently positioned in the Reunion island in the Hortsys unit for one year. He develops there a project on Mango modelling in collaboration with F. Normand.

ARAMIS Project-Team

9. Partnerships and Cooperations

9.1. National Initiatives

9.1.1. ANR

9.1.1.1. ANR-NIH CRCNS

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

Project acronym: NETBCI

Project title: Modeling and predicting brain-computer interface learning from dynamic networks

Duration: Avr 2016 - Avr 2020

Amount: 322k€

Coordinator: Fabrizio De Vico Fallani

Other partners: Complex system group, Université Penn, Etats-units

Abstract: This project will bring together expertise in computational and experimental neuroscience, signal processing and network science, statistics, modeling and simulation, to establish innovative methods to model and analyze temporally dynamic brain networks, and to apply these tools to develop predictive models of brain-computer interface (BCI) skill acquisition that can be used to improve performance. Leveraging experimental data and interdisciplinary theoretical techniques, this project will characterize brain networks at multiple temporal and spatial scales, and will develop models to predict the ability to control the BCI as well as methods to engineer BCI frameworks for adapting to neural plasticity. This project will enable a comprehensive understanding of the neural mechanisms of BCI learning, and will foster the design of viable BCI frameworks that improve usability and performance.

9.1.1.2. 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.

9.1.1.3. ANR IVMRS

Participants: Anne Bertrand [Correspondant], Alexandra Petiet, Mathieu Santin, Francesca Branzoli, Benoit Delatour, Marc Sanson.

Project acronym: IVMRS

Project title: Implantable miniaturized probe for In-vivo Magnetic Resonance Spectroscopy: Application to Murine models of Alzheimer's disease and Gliomas.

Duration: Oct 2016 - Oct 2020

Amount: 633k€

Coordinator: Luc Hebrard

Other partners: ICube - Unistra, Strasbourg; ISA Laboratory, Lyon; NYU School of Medicine, NY, USA.

Abstract: During the development of new therapeutics against brain diseases, the pre-clinical phase, i.e. the validation of treatment delivery, safety and efficacy in animal models of the disease, represents a crucial step. Magnetic Resonance Imaging (MRI) is a method of particular interest at this stage, as it provides non-invasive surrogate endpoints that can help selecting appropriate candidates during the process of drug development. Single Voxel Magnetic Resonance Spectroscopy (SVS) provides non-invasive, in-vivo quantitative measurements of brain metabolites, which reflects functional changes at the cellular and subcellular levels, and can be repeated longitudinally. As high-field MRI has become the benchmark in preclinical research on animal models, it appears possible to investigate the cerebral metabolomics changes in animals, and to use it as a surrogate marker in preclinical therapeutic trials. However, the number of relevant metabolites is much higher than the low number of measurable metabolites with conventional in-vivo high-field SVS. Moreover, considering also the subtle changes of these metabolites at the early stage of the disease, the use of conventional high-field SVS in preclinical studies remains strongly limited. The high volume of the Voxel-of-Interest (VOI), ranging from 10 to 30mm3, which is required to have a usable signal in conventional SVS, and the inherent variability of longitudinal SVS measurement due to the variable position of the VOI in the successive experiments, remain the two major issues when looking during time for small changes in metabolic concentrations and metabolites ratios in a specific small region of the animal brain. The IvMRS project aims at filling this gap by developing the first chronic implantable MRS micro-probe (μ- probe), minimally invasive, exhibiting very high signal sensitivity, and sharp spectral peaks, from sub-millimetric VOI. Such a probe will allow detecting a much higher number of metabolites than conventional in-vivo SVS. The μ-probe will work at frequencies ranging from 300MHz to 500MHz in ultra-high field Magnetic Resonance Imaging scanners, 7T and 11.7T. It will embed a specific micro-coil antenna, a low-noise signal conditioning circuit designed in CMOS microelectronics technology, as well as an accurate on-chip positioning sensor. It will be dedicated to the study of changes in brain metabolite markers of two major diseases, Alzheimer's disease and cerebral gliomas, and to the assessment of effective therapeutic strategies.

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: Anne Bertrand [Correspondant], Takoua Kaaouana, Benoit Delatour, Alexandra Petiet.

Project title: The Histo-MRI project: targeting MR signature of tauopathy from micro- to macroscopy

Founded in 2014

Coordinator: Anne Bertrand

Identifying morphological MR signatures of brain diseases usually follows a top-down process, which starts by describing a pattern of MR signal changes in patients, hypothesizes an underlying pathological mechanism, and confirms this mechanism by correlating the observed MR signal changes with histological lesions on post-mortem examination. This top-down process, relevant for large, centimetric brain lesions, becomes inappropriate when targeting the MR signal intensity changes associated with microscopic lesions. Our project aims at developing an MR biomarker of NFT using a new bottom-up approach. We will start by identifying the MR signal changes associated with the presence of NFT at the level of the histological slice, and utilize these findings to develop a method of NFT quantification on clinical, millimetric 3D MR images. To achieve this goal, we will develop and implement a 11.7T histological coil dedicated to the scanning of histological slices, which allows both ultra-high resolution MR imaging (up to 33 microns in-plane) and perfect co-registration with histological staining, performed subsequently on the same slice. This method has the potential to provide a novel biomarker of tauopathy that could not have been identified using the usual top-down approach. It also envisions the possibility to describe and understand new MRI contrasts in other neurodegenerative diseases associated with microscopic deposition of various proteins.

9.1.2.3. 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.

9.1.2.4. ICM Big Brain Theory Program

Participants: Stanley Durrleman [Correspondant], Harald Hampel [Correspondant], Sabrina Fontanella, Simone Lista, Olivier Colliot, Stephanie Allassonniere, Jean-Baptiste Schiratti, Bruno Dubois, Hovagim Bakardjian, Remi Genthon, Enrica Cavedo, Katrine Rojkowa.

Project title: Dynamic models of disease progression across Alzheimer's disease stages informed by multimodal neuroimaging and biological data

Founded in 2016-2017

Coordinator: Stanley Durrleman and Harald Hampel

Other partners: Institut de la Mémoire et de la maladie d'Alzheimer

The estimation of data-driven models of disease progression for neurodegenerative diseases, including Alzheimer's disease (AD), is crucial to confirm, refine and extend the current hypothetical models. The estimation of such quantitative models from longitudinal data sets is notably difficult because of the lack of principled methodological frameworks for the analysis of spatiotemporal data.

The project builds on an innovative mathematical, statistical, and computational framework to automatically align the dynamics and the direction of individual trajectories of the evolving pathology, and then to infer a normative scenario of disease progression across different disease stages. The estimated scenario will combine spatiotemporal maps of lesion propagation, such as maps of amyloid deposition or cortical atrophy, and global measurements such as levels of CSF biomarkers. It will be possible to estimate not only a normative scenario but also the inter-individual variability in the values, dynamics and direction of both topographical and pathophysiological biomarkers changes during the course of the disease.

The application of this technology to publicly available and in-house longitudinal data sets of individuals from the asymptomatic at risk to the prodromal and dementia stages will yield new insights into the pathophysiology of AD from the preclinical to the AD dementia stages. This quantitative data-driven approach will be exploited to assess and refine the current qualitative hypothetical models of AD progression. Notably, it will complement these models with typical pathways of lesion propagation in the brain during disease progression. It will also highlight the effect of the known risk factors of AD such as apolipoprotein E genotype on the disease progression profile.

The project will open up the concrete possibility to derive a computer-aided diagnosis, staging, and prognosis tool for a better recruitment of patients in clinical studies and to assist clinicians in the diagnosis and the monitoring of both disease progression and treatment efficacy.

9.1.2.5. 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

Funded 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
- GdR (MaDICS) Masses de Données, Informations et Connaissances en Sciences Big Data - Data ScienceStatistics and Medicine - http://www.madics.fr/reseaux/

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

Funded 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

9.2.1.1. H2020 - Project EuroPOND

Participants: Olivier Colliot, Stanley Durrleman, Manon Ansart, Igor Koval, Alexandre Bône.

Project acronym: EuroPOND

Project title: Data-driven models for Progression Of Neurological Disease

Duration: Jan 2016 - Dec 2019

Amount: 6M€

Coordinator: Daniel Alexander

Other partners: University College London (UK), EMC Rotterdam (The Netherlands), VUMC (The Netherlands), Fate Bene Fratelli (Italy), Carol Besta Institute (Italy), Université de Genève (Switzerland), Icometrix (Belgium)

Abstract: EuroPOND will develop a data-driven statistical and computational modeling framework for neurological disease progression. This will enable major advances in differential and personalized diagnosis, prognosis, monitoring, and treatment and care decisions, positioning Europe as world leaders in one of the biggest societal challenges of 21st century healthcare. The inherent complexity of neurological disease, the overlap of symptoms and pathologies, and the high comorbidity rate suggests a systems medicine approach, which matches the specific challenge of this call. We take a uniquely holistic approach that, in the spirit of systems medicine, integrates a variety of clinical and biomedical research data including risk factors, biomarkers, and interactions. Our consortium has a multidisciplinary balance of essential expertise in mathematical/statistical/computational modelling; clinical, biomedical and epidemiological expertise; and access to a diverse range of datasets for sporadic and well-phenotyped disease types.The project will devise and implement, as open-source software tools, advanced statistical and computational techniques for reconstructing long-term temporal evolution of disease markers from cross-sectional or short-term longitudinal data. We will apply the techniques to generate new and uniquely detailed pictures of a range of important diseases. This will support the development of new evidence-based treatments in Europe through deeper disease understanding, better patient stratification for clinical trials, and improved accuracy of diagnosis and prognosis. For example, Alzheimer's disease alone costs European citizens around €200B every year in care and loss of productivity. No disease modifying treatments are yet available. Clinical trials repeatedly fail because disease heterogeneity prevents bulk response. Our models enable fine stratification into phenotypes enabling more focussed analysis to identify subgroups that respond to putative treatments.

9.2.1.2. FET Flagship - Human Brain Project

Participants: Olivier Colliot, Stanley Durrleman.

Project acronym: HBP

Project title: Human Brain Project

Sub-project: SP8 - Medical Informatics Platform

Duration (for this phase): 2016-2018

Abstract: The Human Brain Project (HBP) is a European Commission Future and Emerging Technologies Flagship. The HBP aims to put in place a cutting-edge, ICT-based scientific Research Infrastructure for brain research, cognitive neuroscience and brain-inspired computing. The Project promotes collaboration across the globe, and is committed to driving forward European industry. Our team is involved in the Subproject SP8 (Medical Informatics Platform). The Medical Informatics Platform (MIP) is an innovative data management system that gives researchers the means to access and analyse large amounts of anonymized clinical neuroscience data. Within that framework, we will develop and implement a method to construct disease progression models from longitudinal biomarkers. The method will use statistical learning techniques to infer a long-term disease progression model from multiple short term data from a series of individuals. The model will account for variability in age at disease onset, pace of disease progression and trajectories of biomarkers changes across individuals in the observed population.

9.2.1.3. ERC - LEASP

Participant: Stanley Durrleman.

Project acronym: LEASP

Project title: Learning Spatiotemporal Patterns in Longitudinal Image Data Sets of the Aging Brain

Duration: 2016-2021

Abstract: Time-series of multimodal medical images offer a unique opportunity to track anatomical and functional alterations of the brain in aging individuals. A collection of such time series for several individuals forms a longitudinal data set, each data being a rich iconic-geometric representation of the brain anatomy and function. These data are already extraordinary complex and variable across individuals. Taking the temporal component into account further adds difficulty, in that each individual follows a different trajectory of changes, and at a different pace. Furthermore, a disease is here a progressive departure from an otherwise normal scenario of aging, so that one could not think of normal and pathologic brain aging as distinct categories, as in the standard case-control paradigm.

Bio-statisticians lack a suitable methodological framework to exhibit from these data the typical trajectories and dynamics of brain alterations, and the effects of a disease on these trajectories, thus limiting the investigation of essential clinical questions. To change this situation, we propose to construct virtual dynamical models of brain aging by learning typical spatiotemporal patterns of alterations propagation from longitudinal iconic-geometric data sets.

By including concepts of the Riemannian geometry into Bayesian mixed effect models, the project will introduce general principles to average complex individual trajectories of iconic-geometric changes and align the pace at which these trajectories are followed. It will estimate a set of elementary spatiotemporal patterns, which combine to yield a personal aging scenario for each individual. Disease-specific patterns will be detected with an increasing likelihood.

This new generation of statistical and computational tools will unveil clusters of patients sharing similar lesion propagation profiles, paving the way to design more specific treatments, and care patients when treatments have the highest chance of success.

9.3. International Initiatives

9.3.1. Informal International Partners

F. De Vico Fallani has a collaboration with the University Penn, Philadelphia, US (Prof. Danielle Bassett).

S. Durrleman has an enduring collaboration with professor Guido Gerig, Tandon School of Engineering, NYU. He is consultant for NIH Grant "4D shape analysis for modeling spatiotemporal change trajectories in Huntington's Disease "predict-HD".

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 an enduring 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).

A. Bertrand has an enduring collaboration with professor Youssef Z. Wadghiri, head of the Preclinical Imaging Core, Center for Biomedical Imaging, NYU School of Medicine, New York, NY, USA.

9.4. International Research Visitors

9.4.1. Visits of International Scientists

9.4.1.1. Internships

Kuldeep Kumar (Ecole de Technologie Supérieure, Montréal, Canada) is visiting ARAMIS from October 2016 to March 2017 under the MITACS programme.

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, 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 exploit an XMR interventional room equipped with a MUSIC 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 Associate Teams Not Involved in an Inria International Labs

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

Start year: 2015

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

The scientific goal of the associated team is to develop the field of geometric statistics with key applications in computational anatomy.

Computational anatomy is an emerging discipline at the interface of geometry, statistics, image analysis and medicine that aims at analyzing and modeling 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.

The 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 assumes 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. One intend for instance to show where is impact 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. University College London (UCL), London, UK

Marco Lorenzi holds an honorary position with the Translational Imaging Group of UCL, led by Prof. Sebastien Ourselin. His collaboration is around the topic of spatio-temporal analysis of medical images, with special focus on brain imaging analysis and biomarker development in Alzheim disease. He is also collaborating with the "Progression Over Neurodegenerative Disorders" (POND) group (Prof. Daniel Alexander) for developing new computational models and techniques for learning characteristic patterns of disease progression using large longitudinal clinical data sets, with special focus on dementias.

8.3.2.1.4. Imaging Genetics Center (IGC), University of Southern California (USC), CA, USA

Marco Lorenzi is currently collaborator with the IGC for the investigation of the very complex relationship between brain atrophy and genetics in Alzheimer's disease, in particular for demonstrating the effectiveness of multivariate statistical models in providing a meaningful description of the relationship between genotype and brain phenotype.

8.3.2.1.5. 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. Visits of International Scientists

8.4.1.1. Research Stays Abroad

In the context of the Associated team GeomStats, part of the Inria International Lab Inria@SiliconValley, Nina Miolane spent 3 months (April to June 2016) at the Stanford Statistics Department:

ATHENA Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

9.1.1. Inria SAM Action Transverse

Participants: Paul Görlach, Evelyne Hubert [Aromath project team], Théodore Papadopoulo, Rachid Deriche.

Finding biomarkers of abnormalities of the white matter is one important problem in dMRI processing. As these biomarkers need to be independent of the orientation of the head, they are functions of the rotational invariants of the shapes that characterize the diffusion probabilities in the white matter. While the situation is well understood for second order tensors, these are not powerful enough to represent crossings in the white matter. Acquisitions made with the HARDI scheme allow for a richer description of probabilities, which have been modelled in the literature team as (positive) ternary quartics (tensors of order 4). But invariants of these quartics are not well known. For a long period, only six (out of 12 in theory) were known. Previous work in the ATHENA team developed some new strategies to compute more invariants. But these were ever non-polynomial and had some stability problems [99]. Another strategy [85] was leading to polynomial and stable invariants, but the approach was generating a number of invariants (more than 12) for which it was impossible to extract an irreducible family. The goal of this "Transverse action" was to join forces with the team AROMATH and leverage the methods they developed [87], [88], [86] to have a better insight in this problem of rotational invariants of ternary quartics.

9.1.2. Inria SAM Action Marquante

Participants: Demian Wassermann, Maureen Clerc, Théodore Papadopoulo, Amandine Audino.

Duration: *october 2016 to January 2018*

Elucidating the structure-function relationship of the brain is one of the main open question in neuroscience. The capabilities of diffusion MRI-based techniques to quantify the connectivity strength between brain areas, namely structural connectivity (SC), in combination with modalities such as electro encephalography (EEG) to quantify brain function have enabled advances in this field. However, the actual relationship between these SC measures and measures of information transport between neuronal patches is still far from being determined.

In this project, we will address this problem by establishing a relationship between diffusion MRI (dMRI) SC measures and electrical conductivity on the human brain cortex. We will exploit the Athena's competences in dMRI (Deriche-Wassermann) and EEG (Clerc-Papadopoulo) and our collaboration with the neurosurgical service at CHU Nice (Fontaine-Almairac). In successfully addressing this problem, we will set the bases to solve the current open problem of non-invasively measuring cortico-cortical (CC) connectivity in the human brain. This will boost the understanding of cognitive function as well as neurosurgical planning for the treatment of pathologies such as drug-resistant epilepsy and resection of glioblastomas.

9.2. National Initiatives

9.2.1. Inria Project Lab

9.2.1.1. IPL BCI-LIFT

Participants: Maureen Clerc, Théodore Papadopoulo, Nathanaël Foy, Nathalie Gayraud, Federica Turi.

Duration: *January 2015 to December 2018*

The Inria Project-Lab BCI-LIFT is an Inria-funded reasearch consortium to foster collaborative research on Brain-Computer Interfaces on the topic of Learning, Interaction, Feedback and Training. It is coordinated by Maureen Clerc. Its members are from 6 Inria teams: Athena, Camin, Hybrid, Mjolnir, Neurosys, Potioc, and from Dycog team from CRNL Lyon, and University of Rouen. For more information, refer to the BCI-LIFT website.

9.2.2. ANR

9.2.2.1. 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).

9.2.2.2. 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.

9.2.2.3. 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.

9.2.3. ADT

9.2.3.1. ADT BOLIS

Participants: Nicolas Schnitzler, Théodore Papadopoulo, Juliette Leblond [APICS project-team], 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).

9.2.3.2. 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.

9.2.4. Other Funding Programs

9.2.4.1. Big Brain Theory: MAXIM'S

Participants: Demian Wassermann, Alexandra Petiet [ICM, CENIR, Paris], Stéphane Lehericy [ICM, CENIR, Paris], Julien Valette [Institut d'Imagerie Biomédicale, CEA, France], Virginie Callot [Center for Magnetic Resonance in Biology and Medicine - UMR 7339,Center for Magnetic Resonance in Biology and Medicine - UMR 7339].

Shedding light on the specificity of microstructural MRI biomarkers of axonal and myelin integrity using multi-modal imaging in rodents and quantitative histological correlations.

Magnetic Resonance Imaging (MRI) biomarkers (BMs) of axonal and myelin integrity suffer from lack of specificity at the microstructural level, which hinders our understanding of disease mechanisms. A better knowledge of the role of the white matter (WM) microstructure in normal and abnormal function relies on the development of MRI metrics that can provide (i) increased specificity to distinct attributes of WM such as local fiber architecture, axon morphology, myelin content, and (ii) specific markers of axonal vs. myelin pathologies. Advanced diffusion-weighted (DW) imaging techniques based on biophysical models of cerebral tissues and cellular compartments can extract for example mean axonal diameters or cellular geometry. In addition, diffusion-weighted spectroscopy (DWS) offers new insights into the diffusion properties of intracellular metabolites. More specifically, probing metabolite diffusion at different time scales allows assessing fiber diameter and length, and the specific compartmentalization of different metabolites in different cell types allows differentiating between astrocytic and neuronal microstructural parameters. Although very promising, these novel techniques still need extensive histological validation.

We propose to develop these two cutting-edge MRI techniques – DW-MRI and DWS, at 11.7T to investigate axonopathy and myelinopathy in well-established mouse models with a single lesion type, and to validate these new microstructural BMs with multivariate quantitative histological analyses.

Duration: *March 2016 to March 2019*

9.3. European Initiatives

9.3.1. FP7 & H2020 Projects

9.3.1.1. ERC AdG CoBCoM

Program: H2020-EU.1.1. (ERC-ADG-2015 - ERC Advanced Grant)

Project acronym: CoBCoM - **ID:** 694665

Project title: *Computational Brain Connectivity Mapping*

Start date: 2016-09-01, End date: 2021-08-31

P.I : R. Deriche

Partners: ATHENA project-team

Abstract:

One third of the burden of all the diseases in Europe is due to problems caused by diseases affecting brain. Although exceptional progress has been obtained for exploring it during the past decades, **the brain is still terra-incognita** and calls for specific research efforts to better understand its architecture and functioning.

CoBCoM is our response to this great challenge of modern science with the overall goal to **develop a joint Dynamical Structural-Functional Brain Connectivity Network (**DSF-BCN**)** solidly grounded on advanced and integrated methods for diffusion Magnetic Resonance Imaging (dMRI) and Electro & Magneto-Encephalography (EEG & MEG).

To take up this grand challenge and achieve new frontiers for brain connectivity mapping, we will develop a new generation of computational models and methods for identifying and characterizing the structural and functional connectivities that will be at the heart of the DSF-BCN. Our strategy is to break with the tradition to incrementally and separately contributing to structure or function and develop **a global approach involving strong interactions between structural and functional connectivities.** To solve the limited view of the brain provided just by one imaging modality, our models will be developed under a rigorous computational framework integrating complementary non invasive imaging modalities: dMRI, EEG and MEG.

CoBCoM will push far forward the state-of-the-art in these modalities, developing **innovative models and ground-breaking processing tools** to provide in-fine a joint DSF-BCN solidly grounded on a detailed mapping of the brain connectivity, both in space and time.

Capitalizing on the strengths of dMRI, MEG & EEG methodologies and building on the **bio-physical and mathematical foundations** of our new generation of computational models, CoBCoM will be applied to high-impact diseases, and its **ground-breaking comput ational nature and added clini cal value** will open new perspectives in neuroimaging.

9.3.1.2. 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.

9.4. International Initiatives

9.4.1. Inria Associate Teams Not Involved in an Inria International Labs

9.4.1.1. LargeBrainNets

Title: Characterizing Large-scale Brain Networks Using Novel Computational Methods for dMRI and fMRI-based Connectivity

International Partner (Institution - Laboratory - Researcher):

Stanford (United States) - Stanford Cognitive and Systems Neuroscience Laboratory - Vinod Menon

Start year: Jan. 2016

Partners: ATHENA project-team,

See also: http://www-sop.inria.fr/members/Demian.Wassermann/large-brain-nets.html

In the past two decades, brain imaging of neurotypical individuals and clinical populations has primarily focused on localization of function and structures in the brain, revealing activation in specific brain regions during performance of cognitive tasks through modalities such as functional MRI. In parallel, technologies to identify white matter structures have been developed using diffusion MRI. More recently, interest has shifted towards developing a deeper understanding of the brain's intrinsic architecture and its influence on cognitive and affective information processing. Using for this resting state fMRI and diffusion MRI to build the functional and structural networks of the human brain.

The human brain is a complex patchwork of interconnected regions, and graph-theoretical approaches have become increasingly useful for understanding how functionally connected systems engender, and constrain, cognitive functions. The functional nodes of the human brain and their

structural inter-connectivity, collectively the "connectome", are, however, poorly understood. Critically, there is a dearth of computational methods for reliably identifying functional nodes of the brain and their structural inter-connectivity in vivo, despite an abundance of high-quality data from the Human Connectome Project (HCP). Devising and validating methods for investigating the human connectome has therefore taken added significance.

The first major goal of this project is to develop and validate appropriate sophisticated computational and mathematical tools for identifying functional nodes at the whole-brain level and measuring structural and functional connectivity between them, using state-of-the-art human brain imaging techniques and open-source HCP data. To this end, we will first develop and validate novel computational tools for (1) identifying stable functional nodes of the human brain using resting-state functional MRI and (2) measuring structural connectivity between functional nodes of the brain using multi-shell high-angular diffusion MRI. Due to the complementarity of the two imaging techniques fMRI and dMRI, our novel computational methods methods, the synergy between the two laboratories of this associate team will allow us to reveal in unprecedented detail the structural and functional connectivity of the human brain.

The second major goal of this project is to use our newly developed computational tools to characterize normal structural and functional brain networks in neurotypical adults.

9.4.2. Inria International Partners

9.4.2.1. 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 modeling.
- CRM, Centre de Recherche Mathématiques, Montréal, Canada.

9.4.3. Participation in Other International Programs

9.4.3.1. Program: Collaborative Research in Computational Neuroscience (NSF – ANR)

Project acronym: NEUROREF

Project title: *Building MRI Reference Atlases to Analyze Brain Trauma and Post- Traumatic Stress*

Start date: 2016-10-01, End date: 2019-12-31

P.I : D. Wassermann (Athena) – S. Bouix (Harvard Medcical School)

Partners: ATHENA project-team,

International Partner (Institution - Laboratory - Researcher):

Harvard Medical School (United States) - Psychiatry and Neuroimaging Lab - Sylvain Bouix

Abstract:

While mild traumatic brain injury (mTBI) has become the focus of many neuroimaging studies, the understanding of mTBI, particularly in patients who evince no radiological evidence of injury and yet experience clinical and cognitive symptoms, has remained a complex challenge. Sophisticated imaging tools are needed to delineate the kind of subtle brain injury that is extant in these patients, as existing tools are often ill-suited for the diagnosis of mTBI. For example, conventional magnetic resonance imaging (MRI) studies have focused on seeking a spatially consistent pattern of abnormal signal using statistical analyses that compare average differences between groups, i.e., separating mTBI from healthy controls. While these methods are successful in many diseases, they are not as useful in mTBI, where brain injuries are spatially heterogeneous. The goal of this proposal is to develop a robust framework to perform subject-specific neuroimaging analyses of Diffusion MRI (dMRI), as this modality has shown excellent sensitivity to brain injuries and can locate subtle brain abnormalities that are not detected using routine clinical neuroradiological readings. New algorithms will be developed to create Individualized Brain Abnormality (IBA) maps that will have a number of clinical and research applications. In this proposal, this technology will be used to analyze a previously acquired dataset from the INTRuST Clinical Consortium, a multi-center effort to study subjects with Post- Traumatic Stress Disorder (PTSD) and mTBI. Neuroimaging abnormality measures will be linked to clinical and neuropsychological assessments. This technique will allow us to tease apart neuroimaging differences between PTSD and mTBI and to establish baseline relationships between neuroimaging markers, and clinical and cognitive measures. Upon completion of this project, a set of tools, which have the potential to establish radiological evidence of brain injury in mTBI, will have been designed and evaluated, thereby enhancing both the diagnosis and monitoring of progression/recovery of injury, as well assessing the efficacy of therapies on the injured brain.

9.5. International Research Visitors

9.5.1. Visits of International Scientists

- Sadegh Masjoodi (PhD Student, Tehran University of Medical Sciences, Iran) visited ATHENA from April 2nd, 2016 to Sept, 10, 2016
- Lorenza Brusini (PhD Student, Univ. of Verona, Italy), visited ATHENA from Jan. 2016 until Apr 2016.
- Maria Carla Piastra (PhD Student, Univ. Clinic of Münster, Germany), visited ATHENA from Jul 2016 until Aug 2016.
- Mouloud Kachouane (PhD Student, Univ. USTHB, Alger) visited ATHENA from Nov. 2015 until Aug 2016.
- Thinhinane Megherbi (PhD Student, Univ. USTHB, Alger) visited ATHENA from Jan. 2016 until Feb. 2016.
- Vinod Menon (Stanford Medical School) visited ATHENA during June 2016
- John Kolchaka (Stanford Medical School) visited ATHENA during June 2016

9.5.1.1. Internships

Graeme Baker

Date: May 2016 – Sept 2016

Queen's University,

Supervisor: Rachid Deriche

Nahuel Lascano

Date: Jun 2016 – Sept 2016

University of Buenos Aires,

Supervisor: Demian Wassermann

Leonel Exequiel Gomez

Date: Jun 2016 – Sept 2016

University of Buenos Aires,

Supervisor: Demian Wassermann

Paul Gorlach

Date: Jul 2016 – Dec. 2016

University of Buenos Aires,

Supervisor: Theo Papadopoulo and Evelyne Hubert

BIOVISION Team

7. Partnerships and Cooperations

7.1. National Initiatives

7.1.1. ANR

7.1.1.1. Trajectory

Title: Encoding and predicting motion trajectories in early visual networks

Programm: ANR

Duration: October 2015 - September 2020

Coordinator: Invibe Team, Institut des Neurosciences de la Timone, Frédéric Chavane,

Partners:

AMU INT Aix-Marseille, Université Institut de Neurosciences de la Timone

INSERM IDV INSERM Institut de la Vision

USM UV U Santa Maria & U Valparaiso

Inria contact: Bruno Cessac

Global motion processing is a major computational task of biological visual systems. When an object moves across the visual field, the sequence of visited positions is strongly correlated in space and time, forming a trajectory. These correlated images generate a sequence of local activation of the feed-forward stream. Local properties such as position, direction and orientation can be extracted at each time step by a feed-forward cascade of linear filters and static non-linearities. However such local, piecewise, analysis ignores the recent history of motion and faces several difficulties, such as systematic delays, ambiguous information processing (e.g., aperture and correspondence problems) high sensitivity to noise and segmentation problems when several objects are present. Indeed, two main aspects of visual processing have been largely ignored by the dominant, classical feed-forward scheme. First, natural inputs are often ambiguous, dynamic and non-stationary as, e.g., objects moving along complex trajectories. To process them, the visual system must segment them from the scene, estimate their position and direction over time and predict their future location and velocity. Second, each of these processing steps, from the retina to the highest cortical areas, is implemented by an intricate interplay of feed-forward, feedback and horizontal interactions. Thus, at each stage, a moving object will not only be processed locally, but also generate a lateral propagation of information. Despite decades of motion processing research, it is still unclear how the early visual system processes motion trajectories. We, among others, have proposed that anisotropic diffusion of motion information in retinotopic maps can contribute resolving many of these difficulties. Under this perspective, motion integration, anticipation and prediction would be jointly achieved through the interactions between feed-forward, lateral and feedback propagations within a common spatial reference frame, the retinotopic maps. Addressing this question is particularly challenging, as it requires to probe these sequences of events at multiple scales (from individual cells to large networks) and multiple stages (retina, primary visual cortex (V1)). “TRAJECTORY” proposes such an integrated approach. Using state-of-the-art micro- and mesoscopic recording techniques combined with modeling approaches, we aim at dissecting, for the first time, the population responses at two key stages of visual motion encoding: the retina and V1. Preliminary experiments and previous computational studies demonstrate the feasibility of our work. We plan three coordinated physiology and modeling work-packages aimed to explore two crucial early visual stages in order to answer the following questions: How is a translating bar represented and encoded within a hierarchy of visual networks and for which condition does it elicit

anticipatory responses? How is visual processing shaped by the recent history of motion along a more or less predictable trajectory? How much processing happens in V1 as opposed to simply reflecting transformations occurring already in the retina? The project is timely because partners master new tools such as multi-electrode arrays and voltage-sensitive dye imaging for investigating the dynamics of neuronal populations covering a large segment of the motion trajectory, both in retina and V1. Second, it is strategic: motion trajectories are a fundamental aspect of visual processing that is also a technological obstacle in computer vision and neuroprostheses design. Third, this project is unique by proposing to jointly investigate retinal and V1 levels within a single experimental and theoretical framework. Lastly, it is mature being grounded on (i) preliminary data paving the way of the three different aims and (ii) a history of strong interactions between the different groups that have decided to join their efforts.

7.2. European Initiatives

7.2.1. FP7 & H2020 Projects

7.2.1.1. 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 (UK)

Institute of Neuroscience, University of Newcastle Upon Tyne (UK)

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. International Initiatives

7.3.1. Informal International Partners

- Maria-Jose Escobar, University Santa-Maria, Valparaiso;
- Adrian Palacios, Centro de Neurociencia, Valparaiso

7.4. International Research Visitors

7.4.1. Visits of International Scientists

7.4.1.1. Internships

- Marco Benzi (grant: Stage Master Transverse Biovision–GraphDeco), Retina-inspired tone mapping. Supervisors: Pierre Kornprobst and Adrien Rousseau (GraphDeco), in collaboration with Maria-Jose Escobar (Universidad Técnica Federico Santa María, Valparaíso, Chile)
- Alberto Patino (grant: CONACYT), Studying image transforms at neuronal level and in Virtual Reality. Supervisors: Pierre Kornprobst (Biovision) and Fabio Solari (University of Genoa, Italy)

CAMIN Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

- LABEX NUMEV (postdoc):

  Participants: Mitsuhiro Hayashibe, Denis Mottet (EUROMOV).

  A 1-year postdoc was funded by the NUMEV Labex on "Control of Arm Synergies After a Stroke (CASAS)".
- LABEX NUMEV (PhD grants co-fundings): Participants: Christine Azevedo, David Andreu, Benoit Sijobert.
  Participants: Sofiane Ramdani, François Bonnetblanc, Anthony Boyer.

9.2. National Initiatives

- 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.
- ADT PersoBalance2

  Participants : Mitsuhiro Hayashibe, Philippe Fraisse.

  A half-year engineer was funded by Inria ADT on "Personalized Balance Assessment in Home Rehabilitation, version2 (PersoBalance2)".

9.2.1. Excellence intitiative, PSPC

- Project INTENSE 2012-2018
- Leader: LIVANOVA
- Partners: LTSI, INRA Rennes, CEA LETI, HEGP, CHU Rennes, MXM-Axonic, 3D+
- the aim of the project is to treat severe obesity and cardiac failure through Vagus Nerve Stimulation (VNS). Our contirubution concerned the development of innovative hardware and software architecture to allow for selective stimulation. We developped the models that were used to optimize the settings of the stimulators taking into account the geometry of the 12-pole neural electrode. The selectivity and the efficacy of the stimulation were also improved through the study of original stiumulus waveforms. As a whole the idea was to further enhance the therapy while limiting the side effects that VNS my induce.
- the cardiac application stops end of august due to internal decisions at LIVANOVA but the obesity application continues to be investigated.

9.3. European Initiatives

9.3.1. 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/. The aim of the project is to treat phantom limb pain. CAMIN is only involved in the invasive approach using intrafascicular electrodes. We developed certified software with EPFL and AAU, co-supervised animal tests and data processing with UAB, provide support to clinical trials with IMTEK and UCSC and developped a new stimulator with MXM.

9.4. International Initiatives

9.4.1. Inria Associate Teams Not Involved in an Inria International Labs

9.4.1.1. 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) - Department of Electrical Engineering- 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.

9.4.1.2. CACAO

Title: Lower limb electrical stimulation for function restoration

International Partner (Institution - Laboratory - Researcher):

UNB (Brazil) - NTAAI - FACHIN-MARTINS Emerson

UNB (Brazil) - LARA - Padilha-Bo Antonio

Start year: 2016

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

Electrical stimulation (ES) can activate paralyzed muscles to support rehabilitation. ES applied to fully or partially paralyzed muscles artificially induces muscle contraction substituting or completing the normal volitional control. In CACAO team we will join our efforts and specific expertise to develop approaches of lower limb function restoration in spinal cord injured individuals. Two main applications will be addressed: 1) Functional Electrical Stimulation (FES) to assist SCI individuals to perform pivot transfers and 2) FES-assisted cycling (we already jointly prepared and participated to CYBATHLON'16). We aim at proposing solutions that can have an effect on patients' quality of life, thus our choices intend to be realistic form a practical point of view. We will take care in evaluating both functional and psychological effects of our solutions and to constrain technical choices to be acceptable by final user. CACAO project will be a good opportunity to combine "bioengineer" (DEMAR) and "physiology/rehabilitation" (NTAAI) visions and knowledges towards solutions for clinical applications.

9.5. International Research Visitors

9.5.1. Visits to International Teams

9.5.1.1. France-Stanford program

The Executive Committee of the France-Stanford Center for Interdisciplinary Studies supported our collaboration (§7.1.1) with Prof. Jessica Rose (Department of Orthopaedic Surgery, Stanford University). As part of the collaboration, Professor Rose presented a keynote lecture on Artificial Walking Technologies for Neuromuscular stimulation-assisted Gait for children with cerebral palsy at the International Functional Electrical Stimulation Society (IFESS) conference hosted by CAMIN. In July, a Benoît Sijobert spent 2 weeks in July 2016 to setup the experiment and Christine Azevedo Coste 1 week to run experiments.

9.5.1.2. Asgard program

From may 5 to may 13, François Bonnetblanc visited The Endestad Brain Imaging Group, the Institute of Basic Medical Sciences, Akershus universitetssykehus HF, Sunnaas Sykehus HF, UiO Department of Psychology, and the Norwegian School of Sport Sciences in Norway thanks to the Asgard programme. (http://www.france.no/if/oslo/cooperation/sciences/programmes-sciences/asgard/)

A shared project about the closed-loop stimulation of urinal control of pigs has been proposed with the Institute of Basic Medical Sciences in the framework of Aurora (followup of Adgard).

9.5.1.3. Research Stays Abroad

Christine Azevedo Coste spent 2,5 months (November 2015-February 2016) at Brasilia University as an invited researcher 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. She spent 10 days in May 2016 together with Charles FATTAL to perform experiments.

Mitsuhiro Hayashibe was invited to participate to JSPS Program: Program for Advancing Strategic International Networks to Accelerate the Circulation of Talented Researchers. (PI Prof. Hitoshi Hirata, Dep. of Med. Nagoya Univ.)(Feb. 2016)

Mitsuhiro Hayashibe was visiting Researcher at EPFL, BIOROB supported by Swiss National Science Foundation (Sep.-Oct. 2016)

GALEN Project-Team

8. Partnerships and Cooperations

8.1. National Initiatives

8.1.1. 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

8.2. European Initiatives

8.2.1. FP7 & H2020 Projects

8.2.1.1. 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.

8.2.1.2. 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.

8.2.1.3. 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.

8.2.1.4. 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.'

8.2.2. Collaborations with Major European Organizations

8.2.2.1. CT dose and IQ optimization

Title: Development of a system helping in optimizing and tailoring computed tomography protocols

Program: Collaboration et encadrement de these CIFRE

Partners: GE Medical Systems, Université Paris-Est Créteil Val de Marne

Duration: December 2014 - November 2017

The purpose of the PhD is to create a method of CT dose and IQ optimization taking into account clinical indication, patient's characteristics and previous exams. The method will consist (i) in linking a clinical indication to IQ defined by quantitative physical metrics and (ii) in quantifying the patient's morphology from the analysis of local scans.

8.2.2.2. Imaging biomarkers in ILD

Title: Développement d' outils de Quantification en Imagerie dans les maladies respiratoires chroniques fibrosantes et obstructives

Program: Fondation de Coopération Scientifique

Partners: GE Medical Systems SCS

Duration: April 2016 - March 2019

We aim to test two different approaches for the development of new imaging biomarkers in interstitial lung disease (scleroderma): assessment of the regional lung elasticity through deformable registration and tissue characterization by textural analysis. We will also study structural changes in obstructive lung disease (cystic fibrosis) in order to develop new imaging biomarkers based on elastic registration, histogram and textural analysis.

8.2.2.3. SuBSAmPLE

Title: Identification and prediction of salient brain states through probabilistic structure learning towards fusion of imaging and genomic date

Partners: Fondation de Coopération Scientifique Digiteo

Duration: January 2012 - December 2016 (extended by 1 year)

8.3. International Initiatives

8.3.1. Inria International Partners

8.3.1.1. Informal International Partners

- UCL – Collaboration with Professor Arthur Gretton. Topic: non-parametric hypothesis testing
- University of Toronto – Collaboration with Professors Raquel Urtasun and Richard Zemel. Topic: Representation of Scene Graphs for Image Retrieval and Visual Question Answering
- MILA, Universite de Montreal - Collaboration with Kyle Kastner from the lab of Professor Yoshua Bengio. Topic: Efficient Inference of Graph Structures using Deep Learning

- Sup'Com Tunis – Collaborative research with Amel Benazza-Benhayia. Collaboration Topic: Multispectral imaging
- University of Patras, Greece – Collaborative research with V. Megalooikonomou. Collaboration Topic: Biosignal analysis.
- 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.
- University of Pennsylvania - Collaborative research with Aristeidis Sotiras. Collaboration Topic: Higher Order Graphs in biomedical image analysis.

MATHNEURO Team

6. Partnerships and Cooperations

6.1. 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".

6.2. National Initiatives

6.2.1. ANR

6.2.1.1. SloFaDyBio

Title: a network for Slow-Fast Dynamics in the Biosciences

Programm: ANR "amorçage"

Duration: January 2015 - January 2017 (extension up to January 2018)

Coordinator: Inria

PI: Mathieu Desroches

Partners:
see the webpage of the project.

The SloFaDyBio project targets to gather European researchers from about 10 cost countries in order to build up a network project on "Multi-Scale Dynamics in Neuroscience" and to submit within two years a large-scale proposal to a European funding agency such as COST. The initial fund provided by the ANR is used to meet regularly over this period and write a complete proposal. We now have an operational team and we are in the process of writing a full proposal which will be submitted at the next COST call, that is, at the end of September 2017.

6.3. European Initiatives

6.3.1. FP7 & H2020 Projects

6.3.1.1. HBP

Title: The Human Brain Project

Programm: FP7

Duration: October 2013 - March 2016 (first part) and then : April 2016 - March 2018 (second part)

Coordinator: EPFL

Partners:
see the webpage of the project.

Inria contact: Olivier Faugeras (first part) and then : Romain Veltz (second part)

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.

6.4. International Research Visitors

6.4.1. Visits of International Scientists

Invitation of Martin Wechselberger, University of Sydney (Australia), June 2016

Invitation of Daniele Avitabile, University of Nottingham (UK), June 2016

Invitation of James MacLaurin, University of Sydney (Australia), December 2016

Invitation of Tim O'Leary, University of Cambridge (UK), December 2016

Invitation of Antonio Teruel, University of the Balearic Islands (Spain), December 2016

6.4.1.1. Internships

Cantin Baron (collaboration with H. Marie at IPMC, Feb-June 2016)

Raphaël Fourquet (collaboration with H. Marie at IPMC, Feb-June 2016)

6.4.2. Visits to International Teams

Visit of Mathieu Desroches to Daniele Avitabile (University of Nottingham, UK) in April 2016

Visit of Romain Veltz to Cian O'Donnell (University of Bristol, UK) in April 2016

Visit of Mathieu Desroches to Martin Wechselberger (University of Sydney, Australia) in August 2016

Visit of Mathieu Desroches to Vivien Kirk (University of Auckland, New Zealand) in September 2016

Visit of Mathieu Desroches to Daniele Avitabile (University of Nottingham, UK) in April 2016

Visit of Mathieu Desroches to Serafim Rodrigues (Plymouth University, UK) in October 2016

MIMESIS Team

7. Partnerships and Cooperations

7.1. Regional Initiatives

7.1.1. Institut Hospitalo-Universitaire de Strasbourg

Our team has been selected to be part of the IHU of Strasbourg. This institute is a very strong innovative project of research dedicated to future surgery of the abdomen. It is dedicated to minimally invasive surgery, 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). The MIMESIS team is an important part of the project. Since September 2011, we develop numerous experimental activities in close collaboration with clinicians.

7.1.2. Other research teams

At the regional level, the MIMESIS team also collaborates with:

Inria Magrit team: we closely collaborate with the Magrit team on the use of augmented reality in surgical procedures, through the PhD thesis of Jaime Garcia Guevara and the postdoctoral position of Nazim Haouchine. This collaboratin leads to many publications [14].

ICube *Automatique Vision et Robotique* (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 *Informatique Géométrique et Graphqiue* (IGG) team: the Mimesis team joined the IGG team and develops collaboration in the domain of dynamic topologies, mainly through the use of the CGoGN framework. CGoGN is a C++ library for the manipulation of meshes. It implements combinatorial maps and their multiresolution extensions and has been used in various high level application like the simulation of crowds of autonomous agents and the simulation of cuts, tears and fractures in the context of surgical simulations.

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 which started in March 2015. We also collaborate with Prof. Patrick Pessaux, a surgeon who helps us in the context of the SOFA-OR project.

7.1.3. ADT: Aide au Développement Technologique

The MIMESIS receives support for the development of the SOFA framework through two ADT:

SofaOR (Jan 2015-Dec 2016): The objective of this ADT was twofold: first, we aimed 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 was 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.

DynMesh (Sep 2015-Aug 2017): The objectives of this ADT was the coupling of SOFA, the physical simulation platform supported by Inria, and CGoGN, the mesh management library developed within the ICube lab at Strasbourg. The goal is to extend 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.

7.2. National Initiatives

7.2.1. ANR

MIMESIS participates to the following ANR project:

RESET: This project started in March 2015 and will end in May 2017. 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).

Coordinator: MIMESIS

Partners: the InSimo company, the AVR team of the ICube lab.

7.2.2. National Collaborations

At the national level, the MIMESIS team collaborates with:

The LML laboratory *(Laboratoire de Mécanique de Lille)*: a French research laboratory (UMR CNRS 8107) part of the Carnot institute ARTS. With more than two hundred researchers, LML focuses on the following research areas: mechanical reliability and Tribology, fluid mechanics, civil engineering and soil mechanics.

The TIMC laboratory *(Techniques de l'Ingénierie Médicale et de la Complexité)* in 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 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,

7.3. European Initiatives

7.3.1. FP7 & H2020 Projects

MIMESIS participates to the following European project:

Program: FP7

Project acronym: **RASimAs**

Project title: Regional Anaesthesia Simulator and Assistant

Duration: Nov 2013 - Nov 2016

Coordinator: Department of Medical Informatics, Uniklinik RWTH Aachen (Germany)

Other partners: we collaborate, among others, with: the University Hospital Aachen, RWTH Aachen, 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.

Abstract: The goal of this project was to increase the application, the effectiveness and the success rates of regional anaesthesia and furthermore the diffusion of the method into a broader clinical use through the development of clinical tools to train new anaesthesiologists and assist them during the operation. The project combine two independent but complementary systems: one system is for training and the other one is for operational guidance. The training system consists in one medical simulator recreating RA operation for the anaesthesiologist in a virtual reality environment. The trainee is able to practise virtually the operation on various patient anatomies. The guidance system consists in assisting anaesthesiologists during the practise of RA by providing enhanced feedback on image interpretation and patient-specific anatomy. These two prototypes have been evaluated through a multi-centre clinical trial in Germany, Belgium and Ireland.

7.4. International Initiatives

The MIMESIS team has collaboration with the following international partners:

- **Team Legato, University of Luxembourg**: since last year we have active collaborations with Prof. Stéphane Bordas on real-time soft tissue cutting simulation. This has already led to a journal article [19] and the co-supervision of a post-doctoral fellow ;
- **Humanoid and Intelligence Systems Lab, Karlsruhe Institute of Technology**: we started a collaboration with Stefanie Speidel and Stefan Suwelack on the topics of real-time soft tissue modeling and laparoscopic augmented reality.
- **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).
- **Faculty of Informatics, Masaryk University, Czech Republic**: We began collaborations with Professor Ludek Matyska on biomedical simulations. The PhD thesis of Lukas Rucka on the Validation and verification of soft tissue models; takes place in this context.

MNEMOSYNE Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

9.1.1. PsyPhINe: Cogito Ergo Es

Participant: Nicolas Rougier.

Project gathering researchers from: MSH Lorraine (USR3261), InterPsy (EA 4432), APEMAC, EPSaM (EA4360), Archives Henri-Poincaré (UMR7117), Loria (UMR7503) & Mnemosyne.

PsyPhiNe is a pluridisciplinary and exploratory project between philosophers, psychologists, neuroscientists and computer scientists. The goal of the project is to explore cognition and behavior from different perspectives. 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, we ran a series of experiments with human subject confronted to a motorized lamp that can or cannot interact with them while they're doing a specific task. Early results (analysis not yet finished) tend to show that people have a tendency to over-interpret any kind of behavior as intentional and meaningful. We also organized our second national conference in Nancy gathering speakers from philosophy, robotics, art and psychology and hired a new post-doc to work on the new experimental setup (http://poincare.univ-lorraine.fr/fr/manifestations/psyphine-2016)

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

Participants: Nicolas Rougier, Meropi Topalidou.

This project has ended with the PhD defense of Meropi Topalidou on October 10th, 2016. Using a computational model, we investigated the classic hypothesis of habits formation and expression in the basal ganglia and proposed a new hypothesis concerning the respective role for both the basal ganglia and the cortex. Inspired by previous theoretical and experimental works [47], we designed a computational model of the basal ganglia- thalamus-cortex system that uses segregated loops (motor, cognitive and associative) and makes the hypothesis that basal ganglia are only necessary for the acquisition of habits while the expression of such habits can be mediated through the cortex. This work leads to several publications including an important article in "Movement disorders" [7] explaining some counter-intuitive clinical observations. Furthermore, the early work during the first year of the PhD led N.Rougier to create the ReScience journal.

9.1.3. 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.

9.2. National Initiatives

9.2.1. FUI Sumatra

Participants: Frédéric Alexandre, Thalita Firmo Drumond, Xavier Hinaut, Randa Kassab, Nicolas Rougier, Thierry Viéville.

This FUI project, supported by the Aerospace Valley Innovation Pole, gathers two industrial groups (Safran Helicopter and SPIE), three research labs and four SME. Its goal is to provide contextualized information to maintenance operators by the online analysis of the operating scene. We are concerned in this project with the analysis of visual scenes, in industrial contexts, and the extraction of visual primitives, categories and pertinent features, best decribing the scenes, with biologically inspired neuronal models.

Firstly, this is an opportunity for us to revisit the principles of deep network architectures by adapting principles that we will elaborate from the context of the hierarchical architecture of the temporal visual cortex. Secondly, we intend to exploit and adapt our model of hippocampus to extract more heterogenous features. This project is an excellent opportunity to associate and combine our models and also to evaluate the robustness of our models in real-world applications.

9.2.2. ANR MACAQUE40

Participant: Nicolas Rougier.

Most of the theoretical models in economics proposed so far to describe money emergence are based on three intangible assumptions: the omniscience of economic agents, an infinite time and an extremely large number of agents (not bounded). The goal of this interdisciplinary study is to investigate the condition of apparition of a monetary economy in a more ecological framework provided with the assumption that the market is made up of a finite number of agents having a bounded rationality and facing a time constraint.

In this study, we propose a generic model and environment of monetary prospecting. Our first objective is to artificially identify structural (trading organisation, agents specialisation) and cognitive conditions (learning skills, memory and strategic anticipation abilities, tradeoff exploration/exploitation) that allowed money emergence. This will provide relevant environmental constraints that we will use during our manipulations in the laboratory. The agents that will be involved in these manipulations will be of two types: non-human primates (rhesus macaques) and humans.

9.2.3. 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) is financed by the ANSES (the french national agency for health security). This 3 years project is studying the effects of GSM-RF on living matter and especially neuronal activity and development. Our main involvement concerns electrophysiological data and spike trains analysis as well as the development of pharmacological protocols to test GSM-RF effects hypotheses.

9.2.4. 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. Participation in Other International Programs

9.3.2.1. Project LingoRob with Germany

LingoRob - Learning Language in Developmental Robots - is a project of the Programme Hubert Curien PHC Procope with Germany (University of Hamburg). The scientific objective of the collaboration is to better understand the mechanisms underlying language acquisition and enable more natural interaction between humans and robots in different languages, while modelling how the brain processes sentences and integrates semantic information of scenes. Models developed in both labs involve artificial neural networks, and in particular Echo State Networks (ESN), also known as pertaining to the Reservoir Computing framework. These neural models allow insights on high-level processes of the human brain, and at the same time are well suited as robot control platform, because they can be trained and executed online with low computational resources. The collaborators will also combine Deep Learning networks to the reservoir models already used in order to benefit from their very good feature extraction abilities.

9.3.2.2. 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 as well as for their relation with other brain structures. This year we have developed a model of a dopaminergic region, VTA, central for reinforcement learning in the basal ganglia.

9.3.2.3. 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). This year, in addition to the visits of a Professor and a PhD student, we have written a chapter book that will be published next year and have prepared together a summer school to be held in Chile in january 2017 (http://www.laconeu.cl/).

9.4. International Research Visitors

9.4.1. Visits of International Scientists

Prof. Palacios Adrian

Date: Sep 2016

Institution: Univ. Valparaiso (Chile)

Ravello Cesar (PhD student)

Date: Nov 2016

Institution: Univ. Valparaiso (Chile)

Prof O'Reilly Randall

Date: June 2016

Institution: U. Colorado Boulder (USA)

Mollick Jessica (PhD student)

Date: Jul 2016 - Aug 2016

Institution: U. Colorado Boulder (USA)

9.4.1.1. Internships

Kaushik Pramod

Date: June 2016 - Dec 2016

Institution: IIIT Hyderabad (India)

Sabyasachi Shivkumar

Date: June 2016 - July 2016

Institution: IIIT Madras (India)

NEUROSYS Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

In the *Contrat de Projet 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

PEPS JCJC INS2I 2016 Modeling and simulation of the oscillatory activity of the memory system during sleep and under general anesthesia (L. Buhry, L. Bougrain).

In order to better understand the mechanisms of amnesia under anesthesia, we propose, on the one hand, to carry out a comparative study, to model and simulate the hippocampal oscillatory activity under general anesthesia and during sleep (tasks 1 and 2). Deep SEEG recordings in epileptic patients during seizures will serve as a reference for modeling and simulation. On the other hand, on the basis of data recorded during sleep, we wish (tasks 3 and 4) to analyze and model the interactions between two structures involved in memory, the hippocampus and the prefrontal cortex, and (tasks 5) propose an automated method to reveal markers of the hippocampal activity characteristics of the sleep stages making use of sole surface recordings. *As it is widely acknowledged that the consolidation of memory occurs mostly during the deep sleep stages, this should make it possible to distinguish the parts of the signal corresponding to periods of consolidation and to propose, through mathematical modeling and simulation, mechanisms explaining the effects of amnesia, or even the absence of memory formation under general anesthesia.

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 past 4 years. Neural Engineering brings together engineering, physics, neuroscience and mathematics to design and develop brain-computer interface systems, cognitive computers and neural prosthetics. Contact is L. Bougrain.

9.4. International Initiatives

9.4.1. Inria International Partners

9.4.1.1. Informal International Partners

+ We have an ongoing collaboration with Prof. 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 Prof. 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

Prof. LieJune Shiau, University of Houston, June 2016. (collab. with L. Buhry)

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

PARIETAL Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

8.1.1. CoSmic project

Participants: Philippe Ciuciu [Correspondant], Carole Lazarus, Loubna El Gueddari.

This is a collaborative project with Jean-Luc Stark, (CEA) funded by the CEA program drf-impulsion.

Compressed Sensing is a recent theory in maths that allows the perfect recovery of signals or images from compressive acquisition scenarios. This approach has been popularized in MRI over the last decade as well as in astrophysics (noticeably in radio-astronomy). So far, both of these fields have developed skills in CS separately. The aim of the COSMIC project is to foster collaborations between CEA experts in MRI (Inria-CEA Parietal team within NeuroSpin) and in astrophysics (CosmoStat lab within the Astrophysics Department). These interactions will allow us to share different expertise in order to improve image quality, either in MRI or in radio-astronomy (thanks to the interferometry principle). In this field, given the data delivered by radio-telescopet he goal will consist of extracting high temporal resolution information in order to study fast transient events.

8.1.2. BrainAMP project

Participants: Bertrand Thirion [Correspondant], Gaël Varoquaux, Andre Monteiro Manoel.

This is a collaborative project with Lenka Zdeborová, Theoretical Physics Institute (CEA) funded by the CEA program drf-impulsion.

In many scientific fields, the data acquisition devices have benefited of hardware improvement to increase the resolution of the observed phenomena, leading to ever larger datasets. While the dimensionality has increased, the number of samples available is often limited, due to physical or financial limits. This is a problem when these data are processed with estimators that have a large sample complexity, such as multivariate statistical models. In that case it is very useful to rely on structured priors, so that the results reflect the state of knowledge on the phenomena of interest. The study of the human brain activity through high-field MRI belongs among these problems, with up to 10^6 features, yet a set of observations limited by cost and participant comfort.

We are missing fast estimators for multivariate models with structured priors, that furthermore provide statistical control on the solution. Approximate message passing methods are designed to work optimally with low-sample-complexity, they accommodate rather generic class of priors and come with an estimation of statistical significance. They are therefore well suited for our purposes.

We want to join forces to design a new generation of inverse problem solvers that can take into account the complex structure of brain images and provide guarantees in the low-sample-complexity regime. To this end, we will first adapt AMP to the brain mapping setting, using first standard sparsity priors (e.g. Gauss-Bernoulli) on the model. We will then consider more complex structured priors that control the variation of the learned image patterns in space. Crucial gains are expected from the use of the EM algorithm for parameter setting, that comes naturally with AMP. We will also examine the estimators provided by AMP for statistical significance. BrainAMP will design a reference inference toolbox released as a generic open source library. We expect a 3- to 10-fold improvement in CPU time, that will benefit to large-scale brain mapping investigations.

8.1.3. 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.

8.1.4. MetaCog project

Participants: Bertrand Thirion [Correspondant], Gaël Varoquaux, Jérome Dockès.

This is a Digicosme project (2016-2019) and a collaboration with Fabian Suchanek (Telecom Paritech).

Understanding how cognition emerges from the billions of neurons that constitute the human brain is a major open problem in science that could bridge natural science –biology– to humanities –psychology. Psychology studies performed on humans with functional Magnetic Resonance Imaging (fMRI) can be used to probe the full repertoire of high-level cognitive functions. While analyzing the resulting image data for a given experiment is a relatively well-mastered process, the challenges in comparing data across multiple datasets poses serious limitation to the field. Indeed, such comparisons require to pool together brain images acquired under different settings and assess the effect of different *experimental conditions* that correspond to psychological effects studied by neuroscientists.

Such meta-analyses are now becoming possible thanks to the development of public data resources –OpenfMRI http://openfmri.org and NeuroVault http://neurovault.org. As many others, researchers of the Parietal team understand these data sources well and contribute to them. However, in such open-ended context, the description of experiments in terms of cognitive concepts is very difficult: there is no universal definition of cognitive terms that could be employed consistently by neuroscientists. Hence meta-analytic studies loose power and specificity. On the other hand, http://brainspell.org provide a set of curated annotation, albeit on much less data, that can serve as a seed or a ground truth to define a consensual ontology of cognitive concepts. Relating these terms to brain activity poses another challenge, of statistical nature, as brain patterns form high-dimensional data in perspective with the scarcity and the noise of the data.

The purpose of this project is to learn a semantic structure in cognitive terms from their occurrence in brain activations. This structure will simplify massive multi-label statistical-learning problems that arise in brain mapping by providing compact representations of cognitive concepts while capturing the imprecision on the definition these concepts.

8.1.5. CDS2

Participants: Bertrand Thirion [Correspondant], Gaël Varoquaux, Guillaume Lemaitre.

CDS2 is an "Strategic research initiatice” of the Paris Saclay University Idex http://datascience-paris-saclay.fr. Although it groups together many partners of the Paris Saclay ecosystem, Parietal has been deeply involved in the project. It currently funds a post-doc for Guillume Lemaitre.

8.2. National Initiatives

8.2.1. ANR

8.2.1.1. MultiFracs project

Participants: Philippe Ciuciu [Correspondant], Daria La Rocca.

The scale-free concept formalizes the intuition that, in many systems, the analysis of temporal dynamics cannot be grounded on specific and characteristic time scales. The scale-free paradigm has permitted the relevant analysis of numerous applications, very different in nature, ranging from natural phenomena (hydrodynamic turbulence, geophysics, body rhythms, brain activity,...) to human activities (Internet traffic, population, finance, art,...).

Yet, most successes of scale-free analysis were obtained in contexts where data are univariate, homogeneous along time (a single stationary time series), and well-characterized by simple-shape local singularities. For such situations, scale-free dynamics translate into global or local power laws, which significantly eases practical analyses. Numerous recent real-world applications (macroscopic spontaneous brain dynamics, the central application in this project, being one paradigm example), however, naturally entail large multivariate data (many signals), whose properties vary along time (non-stationarity) and across components (non-homogeneity), with potentially complex temporal dynamics, thus intricate local singular behaviors.

These three issues call into question the intuitive and founding identification of scale-free to power laws, and thus make uneasy multivariate scale-free and multifractal analyses, precluding the use of univariate methodologies. This explains why the concept of scale-free dynamics is barely used and with limited successes in such settings and highlights the overriding need for a systematic methodological study of multivariate scale-free and multifractal dynamics. The Core Theme of MULTIFRACS consists in laying the theoretical foundations of a practical robust statistical signal processing framework for multivariate non homogeneous scale-free and multifractal analyses, suited to varied types of rich singularities, as well as in performing accurate analyses of scale-free dynamics in spontaneous and task-related macroscopic brain activity, to assess their natures, functional roles and relevance, and their relations to behavioral performance in a timing estimation task using multimodal functional imaging techniques.

This overarching objective is organized into 4 Challenges:

1. Multivariate scale-free and multifractal analysis,
2. Second generation of local singularity indices,
3. Scale-free dynamics, non-stationarity and non-homogeneity,
4. Multivariate scale-free temporal dynamics analysis in macroscopic brain activity.

8.2.1.2. BrainPedia project

Participants: Bertrand Thirion [Correspondant], Gaël Varoquaux.

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.

8.2.1.3. Niconnect project

Participants: Bertrand Thirion, Gaël Varoquaux [Correspondant], Alexandre Abraham, Kamalaker Reddy Dadi, Darya Chyzhyk, Mehdi Rahim.

- **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

8.3. European Initiatives

8.3.1. FP7 & H2020 Projects

8.3.1.1. HBP

Title: The Human Brain Project

Programm: FP7

Duration: October 2013 - September 2016

Coordinator: EPFL

Partners: 100 across Europe

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.

8.3.2. Collaborations in European Programs, Except FP7 & H2020

Program: Marie Curie

Project acronym: Neuroimaging Power

Project title: Effect size and power for neuroimaging.

Duration: mois année début - mois année fin

Coordinator: Inria

Other partners: Univ. Stanford, USA

Abstract: There is an increasing concern about statistical power in neuroscience research. Critically, an underpowered study has poor predictive power. Findings from a low-power study are unlikely to be reproducible, and thus a power analysis is a critical component of any paper. This project aims to promote and facilitate the use of power analyses.A key component of a power analysis is the specification of an effect size. However, in neuroimaging, there is no standardised way to communicate effect sizes, which makes the choice of an appropriate effect size a formidable task. The best way today to perform a power analysis is by collecting a pilot data set, a very expensive practice. To eliminate the need for pilot data, we will develop a standardised measure of effect size taking into account the spatial variance and the uncertainty of the measurements. Communicating effect sizes in new publications will facilitate the use of power analyses.To further alleviate the need for pilot data, we will provide a library of effect sizes for different tasks and contrasts, using open data projects in neuroimaging. We will integrate our effect size estimator in open repositories NeuroVault and OpenfMRI. Consequently, these effect sizes can then serve as a proxy for a pilot study, and as such, a huge cost in the design of an experiment is eliminated.A new experiment will not be identical to the open data and as such the hypothesised parameters might not be fully accurate. To address this issue, we present a flexible framework to analyse data mid-way without harming the control of the type I error rate. Such a procedure will allow re-evaluating halfway an experiment whether it is useful to continue a study, and how many more subjects are needed for statistically sound inferences.To make our methods maximally available, we will write a software suite including all these methods in different programming platforms and we will provide a GUI to further increase the use of power analyses.

8.4. International Initiatives

8.4.1. 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.

SISTM Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

The team have strong links with :

Université de Bordeaux

ISPED (Institut de Santé Publique et du Développement)

Bordeaux CHU ("Centre Hospitalier Universitaire").

Limoges CHU ("Centre Hospitalier Universitaire").

Research teams of the research center INSERM U1219 : "Injury Epidemiology, Transport, Occupation" (IETO), Biostatistics, "Pharmacoepidemiology and population impact of drugs", "Multimorbidity and public health in patients with HIV or Hepatitis" (MORPH3Eus) and "Maladies infectieuses dans les pays à ressources limitées" (IDLIC).

Institut Bergonié, Univ Bordeaux through the EUCLID platform

Inria Project-team MONC and CQFD

9.2. National Initiatives

9.2.1. Labex Vaccine Research Institute (VRI)

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

9.2.2. Expert Appraisals

Rodolphe Thiébaut is an expert for INCA (Institut National du Cancer) for the PHRC (Programme hospitalier de recherche Clinique en cancérologie) and for the PRME (Programme de recherche médico-économique en cancérologie).

Mélanie Prague is an expert for ANRS (France Recherche Nord&Sud Sida-HIV Hépatites) in the CSS 3 (Recherches cliniques et physiopathologiques dans l'infection à VIH).

Rodolphe Thiébaut is a member of the Membre du CNU 46.04 (Biostatistiques, informatique médicale et technologies de communication).

Laura Richert is an expert for the PHRC (Programme hospitalier de recherche Clinique).

Laura Richert is a member of F-CRIN Steering Committee.

Marta Avalos is an expert for L'ASNM (Agence nationale de sécurité du médicament et des produits de santé)

9.2.3. Various Partnership

The project team members are involved in:

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 ?" (Marta Avalos).

DRUGS-SAFE platform funded by ANSM (Marta Avalos).

F-CRIN (French clinical research infrastructure network) was initiated in 2012 by ANR under a PIA founding (Programme des Investissements d'avenir) named "INBS/Infrastructures nationales en biologie et en santé". (Laura Richert)

The project team members also collaborate with:

I-REIVAC is the French vaccine research network. This network is part of the Consortium de Recherche en Vaccinologie (CoReVac) created by the Institut de Microbiologie et des Maladies Infectieuses (IMMI). (Laura Richert)

9.3. European Initiatives

9.3.1. FP7 & H2020 Projects

The member of SISTM Team are involved in EHVA (European HIV Vaccine Alliance):

Program: Most information about this program can be found at http://www.ehv-a.eu/.

Coordinator: Rodolphe Thiébaut is Work Package leader of the WP10 "Data Integration".

Other partners: The EHVA encompasses 39 partners, each with the expertise to promote a comprehensive approach to the development of an effective HIV vaccine. The international alliance, which includes academic and industrial research partners from all over Europe, as well as sub-Saharan Africa and North America, will work to discover and progress novel vaccine candidates through the clinic.

Abstract: With 37 million people living with HIV worldwide, and over 2 million new infections diagnosed each year, an effective vaccine is regarded as the most potent public health strategy for addressing the pandemic. Despite the many advances in the understanding, treatment and prevention of HIV made over the past 30 years, the development of broadly-effective HIV vaccine has remained unachievable. EHVA plans to develop and implement:

- Discovery Platform with the goal of generating novel vaccine candidates inducing potent neutralizing and non-neutralizing antibody responses and T-cell responses
- Immune Profiling Platform with the goal of ranking novel and existing (benchmark) vaccine candidates on the basis of the immune profile
- Data Management/Integration/Down-Selection Platform, with the goal of providing statistical tools for the analysis and interpretation of complex data and algorithms for the efficient selection of vaccines
- Clinical Trials Platform with the goal of accelerating the clinical development of novel vaccines and the early prediction of vaccine failure.

The member of SISTM Team and particularly Laura Richert are also involved in other H2020 projects such as SenseCog, Medit'aging and Orthunion.

9.3.2. 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: Rodolphe 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.

9.3.3. Collaborations with Major European Organizations

University of Oxford;

London School of Hygiene and Tropical Medicine;

University Hospital Hamburg;

Heinrich Pette Institute for Experimental Virology, Hambourg;

MRC, University College London

9.4. International Initiatives

Scharp, Seattle;

Fred Hutchinson Cancer center, Seattle;

Baylor Institute;

NIH for the Prevac trial;

NGO Alima for the Prevac trial;

Several African clinical sites for Ebovac2 and Prevac trials.

9.5. International Research Visitors

9.5.1. Visits of International Scientists

Cristian Meza, Associate Professor of the Universidad de Valparaiso (Chili), member of the research center CIMFAV : http://cmeza.cimfav.cl/ collaborates on the project entitled "Longitudinal high-dimensional data" (septembre)

David Conesa, Associate Professor of the Universidad de Valencia (Espagne), member of the research group GEEITEMA : http://www.geeitema.org/conesa/ collaborates on the project entitled "Bayesian predictive methods with application to the home and leisure injuries in France study MAVIE" (septembre)

Sam Doerken, PhD student of the University of Freiburg (Allemagne), member of the Institute for Medical Biometry and Statistics : http://portal.uni-freiburg.de/imbi/employees/persons/doerken collaborates on the project entitled "Penalization regression methods for sparse exposures with application to pharmacoepidemiology" (septembre - octobre)

Jessica Gronsbell, PhD student of the Harvard T.H. Chan School of Public Health, came as a visiting scholar on a subject of "analysis of high dimensional genetic data" (May).

9.5.2. Visits to International Teams

Marta Avalos will be a research visitor at CSIRO's Data61 in Canberra, Australia from Dec. 2016 until June 2017. Collaboration with Cheng Soon Ong http://www.ong-home.my/

Marta Avalos (in April and october) visited David Conesa through the Erasmus+ program Universidad de Valencia (Espagne).

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".

Laura Richtert spent 6 months as visiting researcher at Heinrich Pette Institut for experimental virology, department virus immunology (Pr M. Altfeld), Hamburg Germany in 2016

Boris Hejblum is a Visiting Scientist appointment at Harvard University (not paid), Department of Biostatistics

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: Élise 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 lasted for 2 years. The MRI acquisitions of the PERINE projects have all been performed and 101 children included. A post-doc will start in April 2017 to process the diffusion MRI and ASL data of this project.

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

Participants: Élise 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 tasks were setup and validated on healthy controls (paper ready for submission). The project was extended in 2014 to recruit more patients.

9.1.4. Projet Fondation de France: EPMR-MA

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

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 started in 2016 and are ongoing. A Post Doc was recruited to work on fMRI and DTI processing.

9.1.5. Allocation d'Installation Scientifique – Rennes Métropole

Participant: Emmanuel Caruyer.

Diffusion MRI has been a tremendous tool for the diagnosis of a number of brain pathologies such as abnormal development, neuro-degenerative or inflammatory disorders or brain tumors. Typical resolution in diffusion MRI is about 2mm – this suggests that in white matter, any volume element may contain millions of axons. Although currently we can characterize molecular diffusion, recent developments in diffusion MRI have shown the possibility to quantify more specifically some physical tissue parameters in white matter, such as axonal density and diameter: this means that we can retrieve information from a much smaller scale than the typical imaging resolution.

Acquisition time for this kind of measurements remains long and largely incompatible with in vivo application in humans. This projects aims at developing novel signal processing and acquisition methods for the reconstruction of microstructural informations in a reasonable acquisition time. We will study how sparse representations can be applied to the diffusion signal, in order to enable microstructure information reconstruction. In conjunction with this, we will develop acquisition sequences adapted to these sparse represnetations, in order to reconstruct the diffusion signal from fewer measurements, using results from the compressive sensing theory.

9.2. National Initiatives

9.2.1. ANR

9.2.1.1. ANR "MAIA", 2015 generic projects program

Participants: Maia Proisy, Pierre Maurel, Antoine Legouhy, Olivier Commowick, Isabelle Corouge, 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: Élise Bannier, Jean-Marie Batail, 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

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

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, Michael Kain, Florent Leray, Julien Louis, Aneta Morawin, Mathieu Simon, Yao Chi.

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, Élise Bannier, Christian Barillot, Olivier Commowick, Gilles Edan, 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 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.

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

Participants: Élise Bannier, Christian Barillot, Emmanuel Caruyer, Benoit Combès, Olivier Commowick, Gilles Edan, Jean-Christophe Ferré, Anne Kerbrat, Haykel Snoussi.

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 focusses 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, these 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 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 perform 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 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, 65 of the 80 subjects have been included. H. Snoussi is working in the scope of his PhD thesis on diffusion imaging in the spinal cord and has dedicated his first year to literature review and definition of methodological aspects to tackle starting with distortion correction. B. Combès started as a post doc in November 2016 to process the EMISEP imaging data, starting with morphological data processing (registration, segmentation) and magnetization transfer data processing.

9.3. European Initiatives

9.3.1. FP7 & H2020 Projects

9.3.1.1. EuroBioimaging

Type: CAPACITIES

Challenge: 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, Christian 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.

9.3.1.2. H2020 OpenAire-Connect

Program: E-INFRA

Topic: EINFRA-22-2016

Type of Action: RIA

Project acronym: OpenAIRE-Connect

Project title: OpenAIRE - CONNECTing scientific results in support of Open Science

Acceptation date: 01/09/2016

Open Science is around the corner. Scientists and organizations see it as a way to speed up, improve quality and reward, while policy makers see it as a means to optimize cost of science and leverage innovation. Open Science is an emerging vision, a way of thinking, whose challenges always gaze beyond its actual achievements. De facto, today's scientific communication ecosystem lacks tools and practices to allow researchers to fully embrace Open Science. OpenAIREConnect aims to provide technological and social bridges, and deliver services enabling uniform exchange of research artefacts (literature, data, and methods), with semantic links between them, across research communities and content providers in scientific communication. It will introduce and implement the concept of Open Science as a Service (OSaaS) on top of the existing OpenAIRE infrastructure, delivering out-of-the-box, on-demand deployable tools. OpenAIRE-Connect will adopt an end-user driven approach (via the involvement of 5 prominent research communities), and enrich the portfolio of OpenAIRE infrastructure production services with a Research Community Dashboard Service and a Catch-All Notification Broker Service. The first will offer publishing, interlinking, packaging functionalities to enable them to share and re-use their research artifacts (introducing methods, e.g. data,software, protocols). This effort, supported by the harvesting and mining "intelligence" of the OpenAIRE infrastructure, will provide communities with the content and tools they need to effectively evaluate and reproduce science. OpenAIRE-Connect will combine dissemination and training with OpenAIRE's powerful NOAD network engaging research communities and content providers in adopting such services. These combined actions will bring immediate and long-term benefits to scholarly communication stakeholders by affecting the way research results are disseminated, exchanged, evaluated, and re-used.

In this project VisAGeS is acting, through CNRS, as the French coordinator to develop the link with the Neuroimaging research community. This will be performed in the context of the FLI-IAM national infrastructure

9.3.2. Collaborations in European Programs, Except FP7 & H2020

9.3.2.1. 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. Christian 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: 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.

9.4.1.2. Informal International Partners

- Collaboration with Sherbrooke University (Sherbrooke, Canada): From Jun to Aug 2016, Michael Paquette, PhD student from Sherbrooke supervised by Maxime Descoteaux, visited the VisAGeS team to collaborate with Emmanuel Caruyer on the development on new analysis techniques for the structural brain connectome. This visit was funded by a MITACS/Inria scholarship.
- Collaboration with LTS5, EPFL (Lausanne, Switzerland) and Computer Science department, University of Verona (Verona, Italy): Alessandro Daducci, Gabriel Girard and Jean-Philippe Thiran visited the VisAGeS team for a 2 days workshop on the development of novel validation methods for the human brain connectome using software generated phantoms.
- Collaboration with the Mathematics department, Politecnico di Milano (Italy): Olivier Commowick and Christian Barillot visited the department for the annual meeting of the Italian statistical society and collaborated with Aymeric Stamm and Simone Vantini.
- Collaboration with the Microstructure Imaging Group, UCL (London, UK): Christian Barillot, Emmanuel Caruyer, Olivier Commowick and Sudhanya Chatterjee visited the group of Daniel Alexander for a workshop on "MRI based Virtual Histology: Meeting Tomorrow's Healthcare Challenges Today"
- visit of Tobias Kober and Bénédicte Maréchal from the ACIT Siemens research group in Lausanne [0] to discuss potential collaborations on the MP2Rage sequence and other brain MR imaging topics

[0] http://w1.siemens.ch/home/ch/de/healthcare/produkte/ACIT/Pages/ACIT.aspx

9.5. International Research Visitors

9.5.1. Visits of International Scientists

- Simon Warfield and Benoit Scherrer, Harvard University, visited the VisAGeS team for the annual seminar on Jun 9-10 2016.
- From Jun to Aug 2016, Michael Paquette, PhD student from Sherbrooke supervised by Maxime Descoteaux, visited the VisAGeS team to collaborate with Emmanuel Caruyer on the development on new analysis techniques for the structural brain connectome. This visit was funded by a MITACS/Inria scholarship.
- Alessandro Daducci, Gabriel Girard and Jean-Philippe Thiran visited the VisAGeS team for a 2 days workshop on the development of novel validation methods for the human brain connectome using software generated phantoms.

9.5.2. Visits to International Teams

- Sudhanya Chatterjee visited the Computational Radiology Lab, Boston Children's Hospital, Harvard University for 3 weeks in Oct-Nov 2016. This stay was funded by the international program of University of Rennes 1. Christian Barillot, Emmanuel Caruyer and Olivier Commowick visited the same lab for a 3 days workshop in the context of the Associate Team.
- Christian Barillot, Emmanuel Caruyer, Olivier Commowick and Sudhanya Chatterjee visited the Microstructure Imaging Group, UCL (London, UK) of Daniel Alexander for a workshop on "MRI based Virtual Histology: Meeting Tomorrow's Healthcare Challenges Today"
- Olivier Commowick and Christian Barillot visited the Mathematics department, Politecnico di Milano (Italy) for the annual meeting of the Italian statistical society and collaborated with Aymeric Stamm and Simone Vantini.

XPOP 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 was 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. Informal International Partners

Marc Lavielle is Adjunct Professor at the Faculty of Pharmacy of Florida University.

Marc Lavielle is Adjunct Professor at the Faculty of Pharmacy of Buffalo University.

Julie Josse collaborates with Susan Holmes, Stanford University.

Eric Moulines regularly collaborates with Sean P. Meyn, University of Florida.

9.3. International Research Visitors

9.3.1. Visits of International Scientists

Ricardo Rios, Universidad Central de Venezuela, Caracas: September 2016.

AIRSEA Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

N. Feyeux PhD is sponsored by the action ARC3 Environment of the Region Rhone-Alpes.

Clémentine Prieur obtained a 8kE two-years funding for a local project on risk by the Labex Persyval. Philippe Naveau (from LSCE, Paris) will visit the team during one month in this context.

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), see 7.1.1 .

A 4-year contract : ANR HEAT (Highly Efficient ATmospheric modelling) http://www.agence-nationale-recherche.fr/?Project=ANR-14-CE23-0010.

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 6.5 .

C. Prieur chaired GdR MASCOT NUM 2010-2015, in which are also involved M. Nodet, E. Blayo, C. Helbert, E. Arnaud, L. Viry, S. Nanty, L. Gilquin. She is still strong involved in thie group (co-chair) 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.

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

9.4.1. Inria International Partners

9.4.1.1. Informal International Partners

F. Lemarié and L. Debreu collaborate with Hans Burchard and Knut Klingbeil from the Leibniz-Institut für Ostseeforschung in Warnemünde.

C. Prieur collaborates with Jose R. Leon (UCV, Central University of Caracas), who is funded by the international Inria chair program.

C. Prieur is collaborating with AC Favre (LTHE, Grenoble) in the framework of a two-years canadian funding from CFQCU (Conseil franco-québécois de coopération universitaire) 2015-2016.

9.4.2. Participation in Other International Programs

9.4.2.1. International Initiatives

SIDRE

Title: Statistical inference for dependent stochastic processes and application in renewable energy

International Partners (Institution - Laboratory - Researcher):

Universidad de Valparaiso (Chile) - Karine Bertin

Universidad Central de Venezuela (Venezuela) - Jose León

Duration: 2016 - 2017

Start year: 2016

C. Prieur is one of the two french coordinators of the MATH AmSud project SIDRE. We want to develop, apply and study the properties of statistical tools in several non-parametric models, segmentation models, time series and random fields models, and to study some classes of long-range dependent processes, for their possible application in renewable energies and other domains. In particular non-parametric statistical procedure in Markov switching non-linear autoregressive models, finite mixture, non-parametric functional test and non-parametric estimators in stochastic damping Hamiltonian systems will be considered. Statistical tools for segmenting dependent multiples series, censoring processes in time series models and a new model interpolation scheme will be studied.

9.5. International Research Visitors

9.5.1. Visits to International Teams

F.-X. Le Dimet has been invited for 2 weeks in October 2016 at Florida State University. He has delivered a seminar.

F.-X. Le Dimet has been invited for 3 weeks at the Harbin Institute of Technology in June 2016 to work with Ma Jianwei and Long Li. He delivered 2 seminars and 2 courses on data assimilation.

F.-X. Le Dimet has been invited for a week at Universidad Complutense in Maddrid in November 2016 to lecture (8 hours) on Variational Data Assimilation. A collaboration has been started on oil pollution on the ocean. The project will include the developments of Assimilation of Images and data assimilation for pollution carried out at the Institute of Mechanics in Hanoi.

ANGE Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

9.1.1. 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.

9.1.2. 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: Jérémy Ledoux, Martin Parisot, Jacques Sainte-Marie, Julien Salomon.

ANR project call: Energies marines renouvelables

Project acronym: Hyflo-Eflu

Project title: Hydroliennes flottantes et énergie fluviale

Coordinator: Julien Salomon

The project is a collaboration between the Inria-team ANGE, specialist of free surface flow and optimization, and the industrial developers of the turbine, HYDROTUBE ENERGIE. 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. 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. CNRS CORSURF (2016)

Participants: Bernard Di Martino, Cindy Guichard, Anne Mangeney, Jacques Sainte-Marie.

CNRS project call: INSU-INSMI

Project acronym: CORSURF

Project title: COmplex Rheology SURface Flows

Coordinator: Cindy Guichard

In collaboration with E. Fernández-Nieto (Sevilla, Spain).

Geophysical flows like avalanches (mud, snow) or landslides involve surface flows with non-Newtonian fluids. The goal is to develop numerical models, both accurate with respect to the material behavior and industrially efficient.

9.2.4. CNRS MOCHA (2016)

Participant: Martin Parisot.

CNRS project call: PEPS

Project acronym: MOCHA

Project title: Multi-dimensiOnal Coupling in Hydraulics and data Assimilation

Coordinator: Martin Parisot

Multi-dimensionnal coupling in river hydrodynamics offers a convenient solution to properly model complex flow while limiting the computational cost and making the most of pre-existing models. The project aims to adapt the lateral interface coupling proposed in [37] to the implicit version and test it on real data for the Garonne River.

9.2.5. CNRS Moset (2016-2017)

Participants: Emmanuel Audusse, Martin Parisot.

CNRS project call: INSU Tellus

Project acronym: Moset

Project title: Modélisation des suspensions concentrées naturelles

Coordinator: Emmanuel Audusse

In collaboration with G. Antoine (EDF), S. Boyaval (LHSV), C. Le Bouteiller (Irstea), M. Jodeau (EDF).

Gathering mathematicians (numerical analysis) and geophysicists, this project focuses on the quantitative prediction of solid transport. This issue raises several questions about rheology when the sediment concentration is high enough. It is crucial for modelling the dynamics of suspension. The collaboration aims at assessing models by means of experimental data and at providing preliminary numerical results to evaluate the order of magnitude of constraints.

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

Participants: Nora Aïssiouene, Marie-Odile Bristeau, David Froger, Yohan Penel, Jacques Sainte-Marie, Fabien Souille.

In the aftermath of the ADT In@lgae (2013–2015), we developed a simulation tool for microalgae culture. An Inria Project Lab "Algae in Silico" has started in collaboration with Inria teams 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 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.

9.2.8. ANR LANDQUAKES (2012–2016)

Participant: Anne Mangeney.

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".

9.2.9. 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.

9.3. European Initiatives

9.3.1. ERC Consolidator Grant (2013-2018)

Participants: Anne Mangeney, Hugo Martin.

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 Initiatives

9.4.1. Inria International Partners

9.4.1.1. Informal International Partners

The collaboration with IMUS (Institute of Mathematics of the university of Sevilla, Spain) was informaly launched in 2016 through several visits in Spain of members of ANGE and the writing of a paper. To go further, a submission was made to create an Inria Associate Team.

9.5. International Research Visitors

9.5.1. Visits of International Scientists

In the framework of the collaboration with researchers at the university of Sevilla (Spain), Enrique Fernández-Nieto spent two weeks (weeks n. 13 and 41) at Inria. IPGP hosted several researchers who work with A. Mangeney: Pere Roig (PhD, Departamento de Geodinámica i Geofísica, University of Barcelona, Spain), Giulia Bossi (postdoc, ETH, Zürich), Andrea Wolter and Margherita Spreafico (permanent positions, ETH, Zürich).

9.5.2. Visits to International Teams

9.5.2.1. Research Stays Abroad

- Y. Penel spent three months (Jan.-Mar.) at the university of Sevilla (Spain) to collaborate with E. Fernández-Nieto.
- N. Aissiouene went to the university of Málaga for one month (Apr.) and was involved in the project EDANYA.
- C. Guichard, Y. Penel and J. Sainte-Marie were invited to the university of Sevilla for one week (week n. 42) to set up a forthcoming project.
- A. Mangeney went to Sevilla in November (week n. 47).

We also mention that M. Parisot spent one week (week n. 48) at the university of Toulouse (CERFACS).

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). Final report, oral talk and poster to the "Journées des Rencontres Numériques de l'ANR" (16-17 nov. 2016), http://www.rencontres-numerique-anr.fr/.

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

Controlled nuclear fusion can be considered as an example of grand challenge in many fields of computational sciences from physical modelling, 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 modelling 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

6.2.1.1. EuroFusion Consortium

CASTOR participates to the following EuroFusion consortium projects :

- CfP-WP14-ER-01/Swiss Confederation-01. École Polytechnique Fédérale de Lausanne (PI: Paolo Ricci) "Synergetic numerical-experimental approach to fundamental aspects of turbulent transport in the tokamak edge"
- CfP-WP14-ER-01/CEA-01. CEA (PI: Matthias Hoelzl IPP) "JOREK, BOUT++ non-linear MHD modelling of MHD instabilities and their control in existing tokamaks and ITER"
- EUROfusion WPCD (Working Package Code Development)
  - ACT1: Extended equilibrium and stability chain (participation)
  - ACT2: Free boundary equilibrium and control (participation and coordination)

6.2.1.2. EoCoE

The team also participates in the EoCoE European project. Grant Agreement number: 676629 — EoCoE — H2020-EINFRA-2014-2015/H2020-EINFRA-2015-1.

Title: Energy oriented Centre of Excellence for computer applications

Programm: H2020

Duration: October 2015 - October 2018

Coordinator: CEA

Partners:

Barcelona Supercomputing Center - Centro Nacional de Supercomputacion (Spain)

Commissariat à l'Energie Atomique et Aux Energies Alternatives (France)

Centre Europeen de Recherche et de Formation Avancee en Calcul Scientifique (France)

Consiglio Nazionale Delle Ricerche (Italy)

The Cyprus Institute (Cyprus)

Agenzia Nazionale Per le Nuove Tecnologie, l'energia E Lo Sviluppo Economico Sostenibile (Italy)

Fraunhofer Gesellschaft Zur Forderung Der Angewandten Forschung Ev (Germany)

Instytut Chemii Bioorganicznej Polskiej Akademii Nauk (Poland)

Forschungszentrum Julich (Germany)

Max Planck Gesellschaft Zur Foerderung Der Wissenschaften E.V. (Germany)

University of Bath (United Kingdom)

Universite Libre de Bruxelles (Belgium)

Universita Degli Studi di Trento (Italy)

Inria contact: Michel Kern

The aim of the present proposal is to establish an Energy Oriented Centre of Excellence for computing applications. 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. EoCoE is structured around a central Franco-German hub coordinating a pan-European network, gathering a total of 8 countries and 23 teams. Its partners are strongly engaged in both the HPC and energy fields; a prerequisite for the long-term sustainability of EoCoE and also ensuring that it is deeply integrated in the overall European strategy for HPC. The primary goal of EoCoE is to create a new, long lasting and sustainable community around computational energy science. At the same time, EoCoE is committed to deliver high-impact results within the first three years. It will resolve current bottlenecks in application codes, leading to new modelling capabilities and scientific advances among the four user communities; it will develop cutting-edge mathematical and numerical methods, and tools to foster the usage of Exascale computing. Dedicated services for laboratories and industries will be established to leverage this expertise and to foster an ecosystem around HPC for energy. EoCoE will give birth to new collaborations and working methods and will encourage widely spread best practices.

6.3. International Initiatives

6.3.1. Inria Associate Teams Not Involved in an Inria International Labs

6.3.1.1. AMOSS

Title: Advanced modelling 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 modelling 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.

Closing workshop of the associated team, 7-10 nov. 2016 - Tainan (Taïwan)

6.3.2. Inria International Partners

6.3.2.1. 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.

CLIME Project-Team

9. Partnerships and Cooperations

9.1. 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 are generated using a dynamic traffic assignment model. Ensembles of traffic assignments are 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.
- Two new ANR projects have been accepted in 2016 and will begin in January 2017.
  FireCaster aims at fire forecasting and risk mitigation.
  Cense aims at the estimation of urban noise, using numerical simulation and a dense monitoring network.

9.2. European Initiatives

9.2.1. FP7 & H2020 Projects

9.2.1.1. EoCoE

Title: Energy oriented Centre of Excellence for computer applications

Program: H2020

Duration: October 2015 - October 2018

Coordinator: CEA

Partners:

CEA, Commissariat à l'Énergie Atomique et aux Énergies Alternatives (France)

Forschungszentrum Julich (Germany)

Max Planck Gesellschaft (Germany)

ENEA, Agenzia Nazionale Per le Nuove Tecnologie, l'energia E Lo Sviluppo Economico Sostenibile (Italy)

CERFACS, European Centre for Research and Advanced Training in Scientific Computing (France)

Instytut Chemii Bioorganicznej Polskiej Akademii Nauk (Poland)

Universita Degli Studi di Trento (Italy)

Fraunhofer Gesellschaft (Germany)

University of Bath (United Kingdom)

CYL, The Cyprus Institute (Cyprus)

CNR, National Research Council of Italy (Italy)

Université Libre de Bruxelles (Belgium)

BSC, Barcelona Supercomputing Center - Centro Nacional de Supercomputacion (Spain)

Inria contact: Michel Kern (Serena team)

The aim of the projevt 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. EoCoE is structured around a central Franco-German hub coordinating a pan-European network, gathering a total of 8 countries and 23 teams. Its partners are strongly engaged in both the HPC and energy fields; a prerequisite for the long-term sustainability of EoCoE and also ensuring that it is deeply integrated in the overall European strategy for HPC. The primary goal of EoCoE is to create a new, long lasting and sustainable community around computational energy science. At the same time, EoCoE is committed to deliver high-impact results within the first three years. It will resolve current bottlenecks in application codes, leading to new modelling capabilities and scientific advances among the four user communities; it will develop cutting-edge mathematical and numerical methods, and tools to foster the usage of Exascale computing. Dedicated services for laboratories and industries will be established to leverage this expertise and to foster an ecosystem around HPC for energy. EoCoE will give birth to new collaborations and working methods and will encourage widely spread best practices.

9.2.1.2. Env&You 2016

Title: Env&You

Program: EIT Digital

Duration: January 2016 - December 2016

Coordinator: Inria (MiMove)

Partners and subgrantees:

Inria

NUMTECH

Cap Digital

Forum Virium (Finland)

TheCivicEngine (United States)

Ambientic

Inria contact: Valérie Issarny (Mimove project-team)

Env&You aims at delivering the whole picture of urban pollution, from the individual exposure to neighborhood-by-neighborhood and day-to-day variation, to citizens and governments, informing their decisions for healthy urban living. There is a clear, and probably increasing, desire from the citizens to better know their individual exposure to pollution. Partial solutions exist to the exposure data problem but each focuses on one or another domain of information—crowdsourcing exposure, translating governmental open data to usable consumer information, harnessing social media information, harnessing biometrics—what is unique about Env&You is that it will assimilate a multi-dimensional picture of exposure and provide the integrated information to citizen, government, and business use.

9.3. International Initiatives

9.3.1. Inria International Partners

9.3.1.1. Informal International Partners

Partner: Marine Hydrophysical Institute, Ukraine.

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

8. Partnerships and Cooperations

8.1. Regional Initiatives

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

8.2. National Initiatives

8.2.1. ANR

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

Coffee is among the partners of the project CHARMS, with a funding starting in 2016; the project is devoted to the modeling of reservoirs in complex hydrothermal networks.

8.2.2. National and European networks

- GdR MANU.

  The research group MANU 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".

8.3. International Initiatives

8.3.1. 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.

8.3.2. 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.

8.4. International Research Visitors

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

FLUMINANCE Project-Team

8. Partnerships and Cooperations

8.1. National Initiatives

8.1.1. Comins'lab: SEACS : Stochastic modEl-dAta-Coupled representationS for the analysis, simulation and reconstruction of upper ocean dynamics

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.

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

Participant: Cédric Herzet.

duration 48 months. The GERONIMO project which started 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.

8.1.3. ANR BECOSE : Beyond Compressive Sensing: Sparse approximation algorithms for ill-conditioned inverse problems.

Participants: Dominique Heitz, Cédric Herzet.

duration 48 months. The BECOSE project aims to extend the scope of sparsity techniques much beyond the academic setting of random and well-conditioned dictionaries. In particular, one goal of the project is to step back from the popular L1-convexification of the sparse representation problem and consider more involved nonconvex formulations, both from a methodological and theoretical point of view. The algorithms will be assessed in the context of tomographic Particle Image Velocimetry (PIV), a rapidly growing imaging technique in fluid mechanics that will have strong impact in several industrial sectors including environment, automotive and aeronautical industries. The consortium gathers the Fluminance and Panama Inria research teams, the Research Center for Automatic Control of Nancy (CRAN), The Research Institute of Communication and Cybernetics of Nantes (IRCCyN), and ONERA, the French Aerospace Lab.

8.1.4. ANR-MN: H2MNO4 project

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

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 presented a poster at the ANR-day (rencontre du numérique, Parius, Nov. 2016)

8.1.5. 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.

8.1.6. 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.

8.1.7. Inria Project Lab: C2S@EXA project

Participants: Yvan Crenner, Jocelyne Erhel.

Title: C2S@EXA - Computer and Computational Scienecs at Exascale
Duration: from January 2012 until April 2017
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.

8.1.8. GENCI: project on advanced linear solvers

Participants: Yvan Crenner, Jocelyne Erhel, David Imberti.

Title: Numerical models for hydrogeology
Duration: 2016
Coordination: J. Erhel
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.

8.1.9. GDR MANU

Participants: Benjamin Delfino, Jocelyne Erhel.

Title: Mathematics for Nuclear industry
Duration: From 2016 to 2019
Coordination: C. Cancès
Webpage: http://gdr-manu.math.cnrs.fr/
Abstract: The working group MANU is a follow-up to the group MOMAS. It covers many subjects related to mathematical modeling and numerical simulations for problems arising from nuclear industry and nuclear waste disposal. The team participated in the conference JEMP2016.

8.2. European Initiatives

8.2.1. EXA2CT

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. 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.

8.2.2. 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).

8.3. International Initiatives

8.3.1. Inria Associate Teams Not Involved in an Inria International Labs

8.3.1.1. LFD-FLU

Title: Large-scale Fluid Dynamics analysis from FLow Uncertainty

International Partner (Institution - Laboratory - Researcher):

Universidad de Buenos Aires (Argentina) - Department of Computer Science and Electrical Engineering - Guillermo Artana

Start year: 2016

See also: http://www.irisa.fr/prive/memin/LFD-FLU/

The first objective of this associate team is primarily concerned with the establishment of efficient fluid flow image data analysis procedures. This concerns for instance data assimilation issues to reconstruct meaningful numerical representation of experimental fluid flows for analysis purpose. The second objective focuses on the incorporation of uncertainties in the flow dynamical evolution models

8.3.2. Inria International Partners

8.3.2.1. Informal International Partners

Imperial College (London, UK) We have initiated a collaboration with the Department of Aeronautics within the PhD thesis of Pranav Chandramoulli

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.

College of Control Science & Engineering of Zhejiang University We have initiated a collaboration with Prof. Chao Xu on the study of fluid motion estimator.

8.4. International Research Visitors

8.4.1. Visits of International Scientists

- 2 month sojourn of Gisela Charo (PhD student University of Buenos Aires) to work with Etienne Mémin and Valentin Resseguier within the associate team LFD
- 2 weeks visit of Alejandro Gronskis (Researcher Conicet Argentina) to work with Dominique Heitz, Etienne Mémin and Pranav Chandramouli within the associate team LFD
- Sojourn of 9 month of Shengze Cai PhD student in the College of Control Science & Engineering, Zhejiang University to work with Etienne Mémin
- 2 weeks visit of Prof. Luigi Berselli (U. Pisa) to work with Roger Lewandowski.

LEMON Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

- **Cart'Eaux** project (European Regional Development Fund (ERDF)): in partnership with colleagues of LIRMM and HSM (Montpellier) and with Berger-Levrault company, Carole DELENNE and Benjamin COMMANDRE are developing a methodology that will collect and merge multi-sources data in the aim of mapping urban drainage networks for hydraulic modeling purpose. This chain of treatment includes: i) detection of manhole covers from remote sensing data (aerial images, numerical elevation models...), 2) development of an algorithm to retrieve the network from the detected points and other information such as roads or topography, 3) data manning to extract useful characteristics for the hydraulic model, from various databases available or from documents automatically gathered from the web. A confidence index will be given to each characteristic assessed and a sensitivity analysis will enable the software to propose a hydraulic model together with an associated uncertainty.
- 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

Antoine ROUSSEAU is member of the ANR project ANSWER (PI Céline Casenave), 2016-2019

9.3. European Initiatives

9.3.1. FP7 & H2020 Projects

Vincent GUINOT was the main investigator of an International Training Network (ITN) proposal in 2016. The proposal was not accepted and will be submitted again in 2017, accounting for the remarks made by the reviewers.

9.4. International Initiatives

9.4.1. Inria International Labs

9.4.1.1. Inria Chile

Antoine ROUSSEAU spent 9 months at Inria Chile from January to October 2016.

9.4.2. Inria International Partners

9.4.2.1. 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 *advanced modeling for marine energy*.

9.4.2.2. Informal International Partners

Vincent GUINOT collaborates with B.F. Sanders (Irvine University, Californie, USA)

Carole DELENNE and Vincent GUINOT collaborates with S. Soares-Frazao (Unité de Génie Civil, Université catholique de Louvain, Belgium)

Antoine ROUSSEAU continues to collaborate with H. Ramirez (CMM, Santiago) and P. Gajardo (UTFSM, Valparaiso) after the end of the Inria associated team Dymecos (2015).

9.5. International Research Visitors

9.5.1. Research Stays Abroad

Antoine ROUSSEAU spent 9 months at Inria Chile from January to October 2016. He co-advised 2 master students and 1 research engineer in the framework of the MERIC project in Chile. Antoine ROUSSEAU also participated to the Tsunamilab project between Inria Chile and CIGIDEN.

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 has involved 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 with Inria .

In 2014, the second phase of DIP has begun. Lionel Boillot has been hired as engineer to work on the DIP platform. 4 PhD students have defended their PhD in 2015 and they have now post-doctoral researchers in Europe. DIP is currently employing 2 PhD students and one post-doctoral researcher.

8.2.2. ANR Num4Sun

The ANR has launched a specific program for supporting and promoting applications to European or more generally International projects. Magique-3D has been selected in 2016 after proposing a project to be applied as a FET project on the occasion of a call that will open in 2017 April. This project will gather researchers of the MPS (https://www.mps.mpg.de/en), of the BSC (https://www.bsc.es/), of the BCAM (http://www.bcamath.org/en/), of Heriot-Watt University (https://www.hw.ac.uk/) and Inria teams.
A kick-off meeting has been held in November in Strasbourg. The second one will be held in Paris in March 2017. The project is funded for 18 months starting from August 2016. The funding amounts 30000€.

8.3. European Initiatives

8.3.1. FP7 & H2020 Projects

8.3.1.1. GEAGAM

Title: Geophysical Exploration using Advanced GAlerkin Methods

Program: H2020

Duration: January 2015 - December 2017

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 Ehu Upv (Spain)

Pontificia Universidad Catolica de Valparaiso (Chile)

Universidad de Chile (Chile)

Universidad Tecnica Federico Santa Maria (Chile)

University of Texas at Austin (USA)

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

Program: H2020

Duration: December 2015 - November 2017

Coordinator: Barcelona Supercomputing Center

Partners:

Centro de Investigaciones Energeticas, Medioambientales Y Tecnologicas-Ciemat (Spain)

Iberdrola Renovables Energia (Spain)

Repsol (Spain)

Lancaster University (United Kingdom)

Total S.A. (France)

Fundação Coordenação de Projetos, Pesquisas e Estudos Tecnològicos, (Brazil)

National Laboratory for Scientific Computation, (Brazil)

Instituto Tecnològico de Aeronàutica, (Brazil)

Petrobras, (Brazil)

Universidade Federal do Rio Grande do Sul, (Brazil)

Universidade Federal de Pernambuco, (Brazil)

Inria contact: Stéphane Lanteri

This project aims to apply the new exascale HPC techniques to energy industry simulations, customizing them, and going beyond the state-of-the-art in the required HPC exascale simulations for different energy sources: wind energy production and design, efficient combustion systems for biomass-derived fuels (biogas), and exploration geophysics for hydrocarbon reservoirs. For wind energy industry HPC is a must. The competitiveness of wind farms can be guaranteed only with accurate wind resource assessment, farm design and short-term micro-scale wind simulations to forecast the daily power production. The use of CFD LES models to analyse atmospheric flow in a wind farm capturing turbine wakes and array effects requires exascale HPC systems. Biogas, i.e. biomass-derived fuels by anaerobic digestion of organic wastes, is attractive because of its wide availability, renewability and reduction of CO2 emissions, contribution to diversification of energy supply, rural development, and it does not compete with feed and food feedstock. However, its use in practical systems is still limited since the complex fuel composition might lead to unpredictable combustion performance and instabilities in industrial combustors. The next generation of exascale HPC systems will be able to run combustion simulations in parameter regimes relevant to industrial applications using alternative fuels, which is required to design efficient furnaces, engines, clean burning vehicles and power plants. One of the main HPC consumers is the oil & gas (O&G) industry. The computational requirements arising from full wave-form modelling and inversion of seismic and electromagnetic data is ensuring that the O&G industry will be an early adopter of exascale computing technologies. By taking into account the complete physics of waves in the subsurface, imaging tools are able to reveal information about the Earth's interior with unprecedented quality.

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.

In the framework of Magic2, Rabia Djellouli (CSUN) visited Magique 3D in December 2016

8.5. International Research Visitors

8.5.1. Visits of International Scientists

- Antoine Chaigne (University of Music and Performing Arts Vienna) visited Magique 3D in November 2016.
- Rabia Djellouli (CSUN) visited Magique 3D in December 2016.

8.5.2. Visits to International Teams

8.5.2.1. Research Stays Abroad

- In the framework of the European project Geagam, Aralar Erdozain and Victor Péron visited Ignacio Muga, PUCV, Chile, in January and November 2016.
- In the framework of the European project Geagam, Florian Faucher and Ha Pham visited Henri Calandra, Total Houston, USA, in October 2016.

SERENA Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

GT Elfic (Labex DigiCosme, 2014–2016): "Formal proof for finite element programs", with TOCCATA (Inria Saclay - Île-de-France), CEA LIST, LIPN (Université de Paris 13), and LMAC (Université de Technologie de Compiègne).

8.2. National Initiatives

8.2.1. ANR

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. It specifically targets 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 project had its intermediate review in December 2016, and received excellent marks from the expert panel.

The partners are HIEPACS, Laboratoire Analyse, Géométrie et Application, University Paris 13, Maison de la Simulation, and ANDRA. SERENA representants are M. Kern (grant leader) and M. Vohralík, period 2014–2017.

ANR GEOPOR: "Geometrical approach for porous media flows: theory and numerics". A new approach to numerical methods for multiphase simulations based on the concept of gradient flows is investigated. With Laboratoire Jacques-Louis Lions, University Pierre and Marie Curie. SERENA representant is M. Vohralík, period 2013–2017.

ANR H2MNO4: "Original optimized object-oriented numerical model for heterogeneous hydrogeology". The project H2MNO4 develops numerical models for reactive transport in heterogeneous media. The objective is to design both Eulerian and Lagrangian models. Three applications are concerned: freshwater supply, remediation of mine drainage, and waste geological disposal. The project relies on a consortium of six partners, involving four public research laboratories (Inria, Geosciences Rennes, University of Lyon 1, University of Poitiers, Pprime Institute), one public institution (ANDRA), and one enterprise (ITASCA). International collaborations are pursued with University of San Diego (USA) and UPC (Spain). SERENA representant is G. Pichot, period 2012–2016.

ANR HHOMM: "Hybrid high-order methods on polyhedral meshes", Theoretical foundations and applications (up to software development) for the recently-devised Hybrid high-order methods. Coordinated by D. Di Pietro, University of Montpellier. SERENA representant is A. Ern, period 2015–2019.

C2S@Exa: "Computer and Computational Sciences at Exascale". This 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 supported in particular the Ph.D. of N. Birgle in the framework of the Inria–ANDRA collaboration.

8.3. European Initiatives

8.3.1. FP7 & H2020 Projects

ERC GATIPOR: "Guaranteed fully adaptive algorithms with tailored inexact solvers for complex porous media flows". The subject of this project are new approaches to porous media multiphase flows: inexact Newton-multigrid solvers, local stopping criteria, adaptivity, and a posteriori error control. The goal is to guarantee the overall simulation error and to speed-up importantly the present-day simulations. SERENA representant is M. Vohralík (grant leader), period 2015–2020.

EoCoE: "Energy Oriented Center of Excellence" This project is coordinated by Maison de la Simulationand gathers 23 partners from 13 countries to use the tremendous potential offered by the ever-growing computing infrastructure to foster and accelerate the European transition to a reliable low carbon energy supply using HPC (High Performance Computing). SERENA representant M. Kern, period 2015–2018.

8.3.2. Collaborations in European Programs, Except FP7 & H2020

8.3.2.1. ITEA 3

Program: ITEA 3

Project acronym: OPENCPS

Project title: Open cyber-physical system model-driven certified development

Duration: Dec 2015–Dec 2018

Coordinator: Magnus Eek

Other partners: AB SKF, CEA, ELTE-Soft Kft., ESI Group, EDF, Wqua Simulation AB, Ericsson, IncQuery Labs Kft., KTH, Linköping University, RTE, SICS, SIREHNA, Saab AB, Sherpa Engineering, Siemens Industrial Torbumachinery AB, VTT Technical Research Center of Finland Ltd.

Abstract: Cyber-physical systems put increasing demands on reliability, usability, and flexibility while, at the same time, lead time and cost efficiency are essential for industry competitiveness. Tools and environments for model-based development of cyber-physical systems are becoming increasingly complex and critical for the industry: tool interoperability, vendor lock-ins, and tool life-cycle support are some of the challenges. The project focuses on interoperability between the standards Modelica/UML/FMI, improved execution speed of (co-)simulation, and certified code generation.

8.3.2.2. ERC CZ

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. SERENA representant is M. Vohralík.

Other partners: Institute of Mathematics, Czech Academy of Sciences; University of Oxford

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.

8.4. International Research Visitors

8.4.1. Visits of International Scientists

H. Ben Ameur, Professor at IPEST and member of ENIT-Lamsin, Tunis, Tunisia, November 1–15, 2016.

G. Hammond, Applied Systems Analysis and Research Sandia National Laboratories, USA, April 18, 2016.

M. Köppel, Ph.D. student, University of Stuttgart, Germany, October 1–December 31, 2016.

Z. Strakoš, Professor at the Charles University in Prague, April, 17–21, 2016.

STEEP Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

The design of our LUTI model of Grenoble based on TRANUS platform takes place in the framework of a tight collaboration with the AURG, the Urban Planning Agency of the Grenoble area.

9.2. National Initiatives

9.2.1. 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.

9.2.2. 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.

9.3. International Research Visitors

9.3.1. Visits of International Scientists

9.3.1.1. Internships

- Songyou Peng (summer internship, MSc student in the ViBOT Erasmus Mundus program).

TONUS Team

8. Partnerships and Cooperations

8.1. 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.

8.2. National Initiatives

8.2.1. ANR

ANR project PEPPSI (models for edge plasma physic in Tokamak) in *Programme Blanc* SIMI 9, started in 2013. Participants, G. Manfredi (coordinator), S. Hirstoaga, D. Coulette.
Participants: Giovanni Manfredi [coordinator], Sever Adrian Hirstoaga.

8.2.2. IPL FRATRES

The TONUS project belongs to the IPL FRATRES (models and numerical methods for Tokamak). The annual meeting has been organized in Strasbourg by Emmanuel Franck and Philippe Helluy.

8.2.3. IPL C2S@exa

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

8.2.4. Competitivity clusters

GENCI projet : "*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
Participants: Sever Adrian Hirstoaga, Guillaume Latu, Michel Mehrenberger, Thi Nhung Pham, Christophe Steiner, Yann Barzamian.

8.3. European Initiatives

8.3.1. FP7 & H2020 Projects

8.3.1.1. 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.

8.4. International Initiatives

8.4.1. Inria International Partners

8.4.1.1. Informal International Partners

Michel Mehrenberger collaborates with Bedros Afeyan (Pleasanton, USA) on KEEN wave simulations.

Emmanuel Franck collaborates with E. Sonnendruecker (IPP Garching) and S. Serra Capizzano (University of Como, Italy) on preconditioning for IGA methods.

8.4.2. Participation In other International Programs

Participants: Conrad Hillairet, David Coulette, 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 parallelized and hybrid solvers for plasma physics. One of our objectives 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.
- **ITE-OPALE:** The goal of the Institut de la Transition Énergétique - OPALE project is to increase the lipid content of microalgae by specific selection pressure. The project relies on the strain already selected during the facteur 4 project, whose productivity was 4 times higher than the wild type. We expect to still increase strain performances up to 10 times the productivity of the wild type.
- **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 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. This project supports Natacha Go's postdoctoral position.

- **ANR-ICycle:** This project (2016-2020) aims at understanding the communication pathways between the cell division cycle and the circadian clock, using mathematical modeling and control theory to construct and implement two coupled synthetic biological oscillators. Project coordinated by M. Chaves.
- **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 University of Nice Sophia Antipolis.
- **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 [91]).

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 Aveiro, Portugal
Interconnected boolean networks
Roslin Institute, Edinburgh, UK
Epidemiology
University of Padova, Italy.
Modelling and control of microalgal production at industrial scale.

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 expertise 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

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.

GRIMCAPE, Université de Douala, Cameroon. Epidemiology.

9.4. International Research Visitors

9.4.1. Visits of International Scientists

- Claude Aflalo (Ben Gurion University of the Neguev, Israel), 1 week;
- Eduardo Sontag (Rutgers University);
- Laurent Tournier (Inra Jouy-en-Josas), 1 week;
- Bapan Ghosh (National Institute of Technology Meghalaya, India), 1 month.

9.5. Project-team seminar

BIOCORE organized a 4-day seminar in September in La Colle-sur-Loup. On this occasion, every member of the project-team presented his/her recent results and brainstorming sessions were organized. Jacques-Alexandre Sepulchre (INLN, Univ. Nice) was invited as a guest speaker.

CARMEN Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

8.1.1. IHU LIRYC

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

- Until November 2016 the salary of M. Potse was funded by LIRYC.

8.2. National Initiatives

8.2.1. ANR HR-CEM

The project "High Resolution Cardiac Electrophysiology Models: HR-CEM" within the ANR call *Modèles Numériques* started in November 2013 and will last until November 2017.

It is an international project that involves three partners: Inria (coordinator), IHU LIRYC, and UMI-CRM in Montréal (Canada). The project has 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.

8.2.2. ANR Labcom CardioXcomp

We are participant in the ANR Labcom project between Inria and the company Notocord (www.notocord.com). In this project, we propose a mathematical approach for the analysis of drug effects on the electrical activity of human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs) based on multi-electrode array (MEA) experiments. Our goal is to produce an *in-silico* tool able to simulate drug actions in MEA/hiPSC-CM assays. The mathematical model takes into account the geometry of the MEA and the electrode properties. The electrical activity of the stem cells at the ion-channel level is governed by a system of ordinary differential equations (ODEs). The ODEs are coupled to the bidomain equations, describing the propagation of the electrical wave in the stem cells preparation. The field potential (FP) measured by the MEA is modeled by the extra-cellular potential of the bidomain equations. First, we propose a strategy allowing us to generate a field potential in good agreement with the experimental data. We show that we are able to reproduce realistic field potentials by introducing different scenarios of heterogeneity in the action potential. This heterogeneity reflects the differentiation atria/ventricles and the age of the cells. Second, we introduce a drug/ion channels interaction based on a pore block model. We conduct different simulations for five drugs (mexiletine, dofetilide, bepridil, ivabradine and BayK). We compare the simulation results with the field potential collected from experimental measurements. Different biomarkers computed on the FP are considered, including depolarization amplitude, repolarization delay, repolarization amplitude and depolarization-repolarization segment. The simulation results show that the model reflect properly the main effects of these drugs on the FP.

8.2.3. REO

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

8.2.4. MedicActiv

The CARMEN team cooperates in interaction with the MedicActiV project.

8.2.5. GENCI

GENCI (*grand équipement national de calcul intensif*) is the agency that grants access to all 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 [51]. A renewal request has been submitted in October 2016 and was granted with 9.8 million core-hours.

8.3. European Initiatives

8.3.1. FP7 & H2020 Projects

The Carmen team is a core member of two H2020 proposals that are to be submitted in March 2017.

8.4. International Initiatives

8.4.1. Inria International Labs

8.4.1.1. 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. We would like to non-invasively construct the electrical potential on the heart surface only from measurements of the potential on the the chest of the patient. It is known that algorithms 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 studies have been carried out in order to solve this Cauchy problem, but have never been used for solving the ECGI problem. The goal of this Inria International Lab (IIL) is to develop an experimental platform allowing to test various methods and compare their performance on real life experimental data.

We describe here two projects that have been performed in the context of this IIL.

8.4.1.1.1. Mathematical analysis of the parameter estimation problem

N. Zemzemi, J. Lassoued, and M. Mahjoub worked on the mathematical analysis of a parameter identification problem in cardiac electrophysiology modeling. The work was based on a monodomain reaction-diffusion model of the heart. The purpose was to prove the stability of the identification of the parameter τ_{in}, which is the parameter that multiplies the cubic term in the reaction term. The proof of the result is based on a new Carleman-type estimate for both the PDE and ODE problems. As a consequence of the stability result they proved the uniqueness of the parameter τ_{in} giving some observations of both state variables at a given time t_0 in the whole domain and the PDE variable in a non empty open subset w_0 of the domain.

8.4.1.1.2. Uncertainty quantification in the electrocardiography problem

N. Zemzemi worked with N. Fikal, R. Aboulaich and EL.M. El Guarmah on uncertainty quantification in electrocardiography imaging. The purpose of this work was to study the influence of errors and uncertainties of the imput data, like the conductivity, on the electrocardiographic imaging (ECGI) solution. They propose a new stochastic optimal control formulation to calculate the distribution of the electric potentiel on the heart from the measurement on the body surface. The discretization was done using a stochastic Galerkin method allowing to separate random and deterministic variables. The problem was discretized, in spatial part, using the finite element method and the polynomial chaos expansion in the stochastic part of the problem. The problem was solved using a conjugate gradient method where the gradient of the cost function was computed with an adjoint technique. The efficiency of this approach to solve the inverse problem and the usability to quantify the effect of conductivity uncertainties in the torso were demonstrated through numerical simulations on a 2D analytical geometry and on a 2D cross section of a real torso.

8.4.1.2. Informal International Partners

M. Potse works with the group of Prof. U. Schotten at Maastricht University (The Netherlands) and the Center for Computational Medicine in Cardiology at the *Università della Svizzera italiana* (Lugano, Switzerland) on simulation studies of atrial fibrillation [20]. The Maastricht group was partially funded by the FP7 project EUTRAF and our simulations were supported by GENCI (section 8.2.5).

8.5. International Research Visitors

8.5.1. Visits of International Scientists

Professor Y. Bourgault (University of Ottawa) visited the team from 12 to 26 March.

Professor A. Fraguela Collar, from the *Benemerita Universidad Autonoma de Puebla-Mexico* visited us in July 2016.

8.5.2. Visits to International Teams

8.5.2.1. Other international activities

N. Zemzemi gave a course in the CIMPA research school: “Modelling and simulating the electrical activity of the heart Direct and Inverse problems.”

N. Zemzemi organized a mini-symposium intitled “Imaging and inverse modeling” in PICOF 2016: https://picof.sciencesconf.org/resource/page/id/4#. From 01/06/2016 to 03/06/2016. Autrans, France.

DRACULA Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

In the context of the chair of applied mathematics “OQUAIDO”, driven by Olivier Roustand (Mines de St Etienne), Celine Vial is the scientific responsible of a contract with the BRGM (Orléans) 2016-2018: “Study of a submergence problem: identify the critical offshore conditions for coastal flooding”.

8.2. National Initiatives

8.2.1. ANR

Collaboration in other projects

- ANR RPIB PrediVac "Innovative modeling tools for the prediction of CD8 T cell based vaccine efficacy", 2013-2016 (jeune): http://www.agence-nationale-recherche.fr/?Projet=ANR-12-RPIB-0011. Partners: U1111 Inserm (J. Marvel, coordinator), Dracula, Altrabio (small company), The Cosmo Company (small company). Members are Fabien Crauste and Olivier Gandrillon.
- Thomas Lepoutre is a member of the ANR KIBORD (head L. Desvillettes) dedicated to “kinetic and related models in biology". 2014-2017: https://www.ljll.math.upmc.fr/kibord/.
- Thomas Lepoutre is a member of the ERC MESOPROBIO (head V. Calvez) dedicated to "Mesoscopic models for propagation in biology". 2015-2020: https://erc.europa.eu/projects-and-results/erc-funded-projects/mesoprobio.
- 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". 2011-2017: https://contraintes.inria.fr/~batt/iceberg/home.html.
- Celine Vial participates in the ANR PEPITO (head M. Henner) dedicated to “Design of Experiment for the Industry of transportation and Optimization”. 2014-2018: http://www.agence-nationale-recherche.fr/?Project=ANR-14-CE23-0011.

8.2.2. Other projects

- Inria ADT : SiMuScale "Simulations Multi-Échelles de Populations Cellulaires", 2014-2016.
  Participants: Samuel Bernard [Coordinator], Fabien Crauste, Olivier Gandrillon, 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.

8.3. 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):

University of Maryland (United States) - Center for Scientific Computation and Mathematical Modeling (CSCAMM) - Levy Doron

Start year: 2013

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.

8.4. International Research Visitors

8.4.1. Visits to International Teams

8.4.1.1. Research Stays Abroad

Mostafa Adimy has been invited for three months (September-December) to “Fundação Getulio Vargas (FGV)” of Rio de Janeiro. He gave a course of 45 hours to students of Master of the School of Applied Mathematics (EMAp): “Reaction-diffusion and age-structured equations with application to biological populations”. A collaboration has been started with FGV on mathematical modeling of human transmissible diseases.

M3DISIM Project-Team

8. Partnerships and Cooperations

8.1. European Initiatives

8.1.1. FP7 & H2020 Projects

8.1.1.1. VP2HF

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

Programm: FP7

Duration: October 2013 - March 2017

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.

MAMBA Project-Team

8. Partnerships and Cooperations

8.1. National Initiatives

8.1.1. ANR

8.1.1.1. ANR Blanc 2014-2018 "Kibord"

This 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.

8.1.1.2. 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.

8.1.1.3. ANR iLITE 2016 - 2020

Jean-Charles Duclos-Vallée, Paul Brousse Hospital, Villejuif. Partners are several departments in Paul Brousse Hospital, ENS Cachan, University of Compiègne and several companies all over France, and REO team, Inria Paris. The pursued objective is the bioengineering design of an artifical liver intended for liver replacement.

8.1.2. ITMO Cancer

8.1.2.1. ITMO Cancer 2014 - 2016, INVADE.

Emmanuel Barillot, Institut Curie (coordinator). Partners: Groups from Institut Curie, Dirk Drasdo. Objective is a model for a better understanding of breast cancer invasion.

8.1.2.2. ITMO Cancer 2016 THE call

See above "Highlights of the year"

8.2. European Initiatives

8.2.1. FP7 & H2020 Projects

8.2.1.1. ERC Starting Grant SKIPPER^{AD}, 2012-2017, Principal Investigator: Marie Doumic.

This grant allowed to fund Sarah Eugène's and Mathieu Mézache's Ph.Ds, as well as to develop new collaborations as with Wei-Feng Xue in Canterbury, Piotr Gwiazda in Poland, Teresa Teixeira and Zhou Xu in IBCP.

8.3. International Initiatives

8.3.1. Participation in Other International Programs

8.3.1.1. International Initiatives

CAPES-COFECUB Modelling innovative control methods for dengue fever

- Brazilian part headed by Claudio Struchiner
- French part headed by Benoît Perthame

MOSTICAW MOdelling the Spread and (opTImal) Control of Arboviroses by Wolbachia
International Partners (Institution - Laboratory - Researcher):

- Universidad de Buenos Aires (Argentina) - Hernán G. Solari
- Universidad de Chile (Chile) - Carlos Conca

- Universidade Federal Fluminense (Brazil) - Max Souza
- Universidad Tecnica Federico Santa Maria (Chile) - Pablo Aguirre
- EMAp (Brazil) - Pierre-Alexandre Bliman
- CIRAD (France) - Yves Dumont
- Duration: 2016 - 2017
- Start year: 2016
- The spread of certain strains of the intracellular parasitic bacterium Wolbachia in populations of mosquitoes Aedes aegypti drastically reduces their competence as vector of dengue and other severe mosquito-borne viral diseases known as arboviral infections. In absence of vaccine, or of preventive or curative treatment, the release of mosquitoes infected by the bacterium has been recently considered a promising tool to control these diseases, and experimental introductions in wild populations are currently under way in Brazil and Colombia. A key question about this method concerns the effective strategies of release of the infected mosquitoes in the field that can be applied with limited cost to reach the desired state of complete exclusion of Wolbachia-free mosquitoes. The mathematical study of central topics is the core of this project. The scientific questions to be addressed during this project are related to the study of the dynamic and control of the key invasion mechanism on finite-dimensional compartments.
- Pierre-Alexandre Bliman is International and Brazilian coordinator of the STIC AmSud project *MOdeling the Spread and (opTImal) Control of Arboviroses by Wolbachia* (MOSTICAW), 2016-2017. Partners: UBA (Argentina); FGV, Fiocruz, UFF (Brazil); UC, UTFSM (Chile), Universidad de Quindio, Universidad Autónoma de Occidente (Colombia), EPI MAMBA, INRA-Montpellier, CIRAD-Montpellier(France); UNA (Paraguay); Universidad Nacional Mayor de San Marcos (Peru).
- Pierre-Alexandre Bliman is also French coordinator of the ECOS-NORD project *New methods for the control of epidemics of dengue and arboviroses*, 2017-2019. Partner: Universidad del Valle, Cali, Colombia.

LiSym Liver Systems Medicine, BMBF funded project.

- Duration: 2016 - 2020
- Start year: 2016
- LiSym addresses liver diseases and regeneration, namely, steatosis, fibrosis and cirrhoses, and acutisation of chronic liver disease. It is composed of three subprojects and three junior research groups. Dirk Drasdo is co-coordinator of one of these three projects and participates in one of the others. He is also member of the leadership board.

8.4. International Research Visitors

8.4.1. Internships

- Andreas Buttenschoen (PhD student of Thomas Hillen, Univ. Edmonton, Alberta, Canada) has been welcomed in the MAMBA team, under Dirk Drasdo's supervision, for a 6-month internship within the framework of the Inria-MITACS programme. Program of the stay: Training on agent-based modeling of growth and cell migration; training on the software tool TiSim.
- Shalla Hanson (Duke University, Durham, NC) has been welcomed in the MAMBA team for a 6-month internship within the framework of the Chateaubriand programme. She is since October 2015 in a PhD thesis in co-tutela under the supervision of Michael Reed (Duke) and Jean Clairambault (MAMBA & UPMC).

8.4.2. Visits to International Teams

8.4.2.1. Sabbatical programme

BLIMAN Pierre-Alexandre

Date: Jun 2014 - Jul 2016

Escola de Matemática Aplicada

Institution: Fundação Getulio Vargas, Rio de Janeiro, Brazil

Chargé de mission at Direction des Partenariats Européens et Internationaux (DPEI), Inria

DOUMIC-JAUFFRET Marie

Date: Jun 2016 - Jul 2017

Institution: Wolfgang Pauli Institute, University of Vienna (Austria)

Sabbatical

8.4.2.2. Research Stays Abroad

STRUGAREK Martin

Date: Oct 2016

Institution: Fundação Oswaldo Cruz, Rio de Janeiro

Programme CAPES-COFECUB “Modelling innovative control methods for dengue fever”

VAUCHELET Nicolas

Date: Jan-Feb 2016

Institution: IMPA, Rio de Janeiro

Teaching collaboration between IMPA, Rio and UPMC, Paris

MONC Project-Team

8. Partnerships and Cooperations

8.1. National Initiatives

8.1.1. Plan Cancer

8.1.1.1. NUMEP

Plan Cancer NUMEP: 2016–2019. Numerics for Clinical Electroporation Funding: 460 kE Partners: Inria Team MONC, Institut de Pharmacologie de Toulouse, CHU J. Verdier de Bondy Duration: Octobre 2016—Septembre 2019 Project leader: C. Poignard Co-PI: M-P. Rols (IPBS), O. Séror (CHU J. Verdier)

8.1.1.2. Dynamo

Plan Cancer DYNAMO: 2015–2018. Dynamical Models for Tissue Electroporation Funding: 370 kE Partners: Laboratoire Ampère, Lab. Vectorology and Anticancerous Therapies (IGR), Inria Team MONC Duration: Octobre 2015—Septembre 2018 Project leader: R. Scorretti (Laboratoire Ampère) Co-PI: L.M. Mir (IGR), C. Poignard (Inria Team MONC)

8.1.1.3. Moglimaging

- Project acronym - Moglimaging: Modeling of Glioblastoma treatment-induced resistance and heterogeneity by multi-modal imaging.
- Partners -
- Duration - from Nov. 2016 to Nov 2019.
- Coordinator - E. Cohen-Jonathan Moyal, Institut Universitaire du Cancer Toulouse / Local coordinator - O. Saut.
- Team participants - S. Benzekry, A. Collin, C. Poignard, O. Saut.

8.1.1.4. 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

*8.1.2. 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

8.1.3. PEPS CNRS

- PEPS CNRS "Jeune chercheur" Acronym: Metamat Partners: J. Ebos, Roswell Park Cancer Institute, Buffalo, USA Duration: October - November 2016 PI: S. Benzekry

8.1.4. Competitivity Clusters

- Labex TRAIL (http://trail.labex.u-bordeaux.fr): MOD Project Consolidation. 1 2-years post-doc position (100k€), led by A. Collin, 1 PhD funding (100k€) led by O. Saut.

8.2. International Initiatives

8.2.1. Inria International Partners

8.2.1.1. Informal International Partners

- LEA EBAM on electroporation http://lea-ebam.cnrs.fr,
- JSPS Core-to-Core "Establishing Network in Mathematical Medicine" granted by Japan, led by T. Suzuki, Osaka University, (local PI: C. Poignard).

8.3. International Research Visitors

8.3.1. Visits of International Scientists

Clair Poignard and the team had visits from the following scientists:

- T. Suzuki, Osaka University, Japan,
- R. Natalini, IAC, Rome (PhD co-supervision of M. Deville)
- F. Gibou, UCSB, Santa Barbara (Numerical methods for cell aggregate electroporation).
- Rouzimaimati Makemuti (Associate professor at Xingiang University, China);

Thierry Colin and Olivier Saut had the pleasure to welcome Hassan Fathallah-Shaykh (neuro-oncologist, Univ. Alabama at Birmingham) for two weeks to work on ours models for glioblastoma.

MYCENAE Project-Team

8. Partnerships and Cooperations

8.1. National Initiatives

8.1.1. ANR

Jonathan Touboul is member of the Kibord (KInetic models in Biology Or Related Domains) project obtained in 2014.

He is also PI of the projects "Mathematical modeling of synaptic plasticity" (with Laurent Venance, CIRB) funded as an interdisciplinary structuring project of INSB (Institut des Sciences Biologiques in CNRS) and "Altering Fear Memory" (with Sidney Wiener, CIRB and Karim Benchenane, ESPCI) funded by the PSL Labex MemoLife.

8.1.2. National Networks

- GdR REPRO (F. Clément is member of the direction board)
- MIA REM network: Réduction de modèles (PI Béatrice Laroche, INRA Jouy)

8.1.3. National Collaborations

- Center for Interdisciplinary Research in Biology (CIRB), Collège de France (Alain Prochiantz, Marie Manceau, Laurent Venance)
- UMR Physiologie de la Reproduction et des Comportements, INRA Centre- Val de Loire (Bios and Bingo teams)
- Université Pierre & Marie Curie (UPMC)
  - Jacques-Louis Lions Laboratory, Pierre & Marie Curie University (Jean-Pierre Françoise, Marie Postel)
  - Developmental Biology Laboratory, Institut de Biologie Paris Seine (IBPS), Pierre & Marie Curie University (Alice Karam, Sylvie Schneider Maunoury), in the framework of the NeuroMathMod, Sorbonne-Universités Émergence call
- Jacques Monod Institute (IJM)
  - Computational Biology and Biomathematics (Khashayar Pakdaman)
  - Génétique et développement du cortex cérébral (Alessandra Pierani)
- Centre de Recherche en Mathématiques de la Décision (CEREMADE), Paris Dauphine University (Stéphane Mischler)
- Unité de Neurosciences, Information & Complexité (UNIC), CNRS Gif-sur-Yvette (Alain Destexhe)

8.2. International Research Visitors

8.2.1. Visits to International Teams

Jonathan Touboul has visited Simon Levin in Princeton University (December 15-26)

NUMED Project-Team

7. Partnerships and Cooperations

7.1. European Initiatives

Vincent Calvez is the main investigator of an ERC.

7.1.1. FP7 & H2020 Projects

7.1.1.1. DDMoRE

Programm: FP7

Duration: February 2011 - January 2016

Coordinator: Pfizer

Inria contact: Marc Lavielle

7.2. International Research Visitors

7.2.1. Visits of International Scientists

Toan Nguyen (Penn State University) has visited Numed in june 2016.

REO Project-Team

9. Partnerships and Cooperations

9.1. National Initiatives

9.1.1. ANR

9.1.1.1. ANR Project "EXIFSI"

Participants: Faisal Amlani, Miguel Ángel Fernández Varela [Principal Investigator], Axel Fourmont, 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-structure 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 modeling and simulation solutions and provide to safety 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, Irene Vignon-Clementel [co-Principal Investigator].

Period: 2013-2017.
This ANR-TecSan, co-managed by Eric Vibert (Paul Brousse Hospital) and Irene 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
- Irene Vignon-Clementel is a member of the project iLite (09/16-), RHU-santé grant, a large French hospital-medical research consortium that aims at developing innovations for liver and tissue engineering (Inria PI: Dirk Drasdo).

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 the shell elements included in the shelddon and Modulef libraries.

9.1.2.2. ADT Project "PARASOL"

Participants: Miguel Ángel Fernández Varela [Principal Investigator], Axel Fourmont, Marina Vidrascu.

Period: 2016-2017
The aim of this project, coordinated by Miguel Ángel Fernández Varela, is to implement in the FELiScE library several balancing domain decomposition methods (BDD) for solid-mechanics.

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.

9.2.2. Collaborations in European Programs, Except FP7 & H2020

9.2.2.1. SimInhale COST

Participant: Irene Vignon-Clementel.

Action MP1404, a pan-European network of experts in the field of inhaled medicine

9.3. International Initiatives

9.3.1. Trans-Atlantic Network of Excellence for Cardiovascular Research

Participants: Jean-Frédéric Gerbeau, Sanjay Pant, Irene Vignon-Clementel [correspondant].

Period: 2010-2016

This network, funded by the Leducq foundation, is working on the multi-scale modeling of single ventricle hearts for clinical decision support.

Other partners: see http://modelingventricle.clemson.edu/home.

9.4. International Research Visitors

9.4.1. Visits of International Scientists

- Visiting Professor: Rodolfo Araya, University of Concepcion (Chile), from Apr 2016 to Jul 2016
- Visiting PhD student: Michele Annese, Universita degli Studi di Brescia (Italy), from Mar to Jul 2016
- Visiting PhD student: Stefano Zonca, Politecnico di Milano (Italy), from Oct to Sep 2016