RESEARCH CENTER

FIELD
Digital Health, Biology and Earth

Activity Report 2017

Section Partnerships and Cooperations

Edition: 2018-02-19

MODELING AND CONTROL FOR LIFE SCIENCES

ABS Project-Team (section vide)

AMIBIO Team

6. Partnerships and Cooperations

6.1. National Initiatives

6.1.1. FRM

AMIBio is in charge of Bioinformatics developments in this project on structural prediction from RNA probing data (SHAPE). It involves Biochemists at Université Paris Descartes (France, PI B. Sargueil) and is funded by a "Fondation pour la Recherche Medicale" grant. It also involves partners in Paris-Sud (France) and McGill University (Canada).

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.

6.3. International Initiatives

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

6.3.1.1. ALARNA

Title: Associated Laboratory for the Analysis of RiboNucleic Acids

International Partner (Institution - Laboratory - Researcher):

McGill University (Canada) - REUSSI Program - Jerome Waldispuhl

Start year: 2017

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

RiboNucleic Acids (RNAs) are ubiquitous biomolecules whose structure, adopted as the outcome of a complex folding process, often plays a crucial part in cellular processes. The ALARNA Associate Team (Laboratory for the Analysis of RiboNucleic Acids), which consist of the AMIBio project-team (Inria Saclay/Ecole Polytechnique, France) and the CSB (Computer Science and Biology) group at university McGill (Montreal, Canada), addresses key questions in RNA bioinformatics. More specifically, it dedicates much of its effort to the production and interpretation of chemical probing data generated by SHAPE, an experimental technology which allows to accurately predict, in a high-throughput, one or several secondary structure(s) adopted by an RNA. To that end, the teams contribute their unique combinations of expertise, ranging from combinatorial optimization to sequence algorithmics through structural bioinformatics.

6.3.1.2. Informal International Partners

AMIBio enjoys regular interactions with the following institutions:

- TBI, University of Vienna (Austria). Within the RNALands project funded by the Austrian FWF and the french ANR, we frequently interact with our partners at the TBI, on projects associated with the kinetics of RNAs. Over the course of 2017, we have visited our partners twice, once in Vienna and once in Bled (Slovenia) over the course of the 2017 Winter retreat of the TBI. Additionally, Andrea Tanzer has visited AMIBio for a month in Oct 2018, funded by a visiting scholar program of Ecole Polytechnique;
- 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) has visited Inria Saclay in January 2017 to push an ongoing 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 AMIBio members, we have increased our interactions on SHAPE data analysis through the ALARNA associate team;
- King's college (London, UK). Our collaboration with L. Mouchard (AMIBio associate) and S. Pissis on string processing and data structures was at the core of Alice Héliou's PhD, defended in July 2017.

6.3.2. Participation in Other International Programs

Title: PHC GRO-algo – Combination of time-course GRO-seq assay, algorithmics and software development for measuring genome-wide transcription elongation rates

International Partner (Institution - Laboratory - Researcher):

Wuhan University (China), College of Life Science – Pr Yu Zhou

Start year: 2017

Participant in a French-Chinese Hubert Curien Partnerships (PHC), supported by CampusFrance and funding bilateral exploratory research exchanges in Bioinformatics. The program involves research scientists from Wuhan University, Ecole Polytechnique and Univ. Paris-Sud.

Title: Computational methods and databases to identify small RNA-binding molecules regulating gene expression

International Partner (Institution - Laboratory - Researcher):

University McGill (Canada), Computer Science & Biochemistry – J. Waldispühl, N. Moitessier; Univ. Strasbourg, IBMC - E. Westhof.

Start year: 2017

The project, headed by N. Moitessier and J. Waldispühl (McGill University, Canada) strives to develop tools to derive a mechanical understanding of riboswitches at the 2D and 3D levels, including chemoinformatics aspects.

6.4. International Research Visitors

6.4.1. Visits of International Scientists

Andrea Tanzer

Date: Oct 2017 - Nov 2017

Institution: TBI Vienna, Austria

Mathieu Blanchette

Date: June 2017

Institution: Univ. McGill, Canada

6.4.1.1. Internships

Paul Arijit

Institution: IISc Bangalore (India)

Supervisor: Mireille Régnier

Chinmay Singhal

Date: May 2017 - July 2017

Institution: IIT Guwahati, India (India)

Supervisor: Yann Ponty

BEAGLE Project-Team

7. Partnerships and Cooperations

7.1. Regional Initiatives

IntraCellXevo (2016-2018). 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. It has been funded by the Labex Ecofect up to 120keuros.

Lipuscale (2017-2019). Participants: C. Knibbe, in collaboration with S. Bernard (Inria Dracula) and M.-C. Michalski (CarMeN laboratory, INSERM U1060/ INRA U1397/ Université Lyon1/ INSA de Lyon). This project aims at reaching a quantitative understanding of the lipolysis and adsorption of dietary triglycerides, by using and adapting SimuScale (a multi-scale simulator developed by the Inria Dracula team) to model and simulate the processes, and by using wet experiments on in vitro systems and cellular cultures to calibrate the models parameters. It is funded by the Rhône-Alpes Institute for Complex Systems (IXXI, 5k€ for two years).

PMSISEE (2017-2019): The goal of the PMSISEE (Performance, Maintainability and Scalability of In-Silico Experimental Evolution Simulation) project is to improve the collaboration between the Inria Avalon team of the LIP laboratory and the Inria Beagle team of the LIRIS laboratory through research activities on programming model and tools for High Performance Computing applied to in-silico experimental evolution. One of the outcome is to improve the scalability and performance of the Aevol software. Moreover, we are formalizing a mini-application (mini-Aevol) representative of the resources usage of Aevol. The goal of this mini-application is to propose a simplify version of Aevol that could be used by the parallel computing community as use case to test new improvements. It is founded by the Lyon Computer Science Federation (FIL FR2000).

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

Although the EvoEvo project was officially closed in December 2016, we let it in the 2017 report because (*i*) the scientific actions and the cooperations started in the project were still very active in 2017, (*ii*) the remaining of the project grant has served to fund many actions of the team in 2017 (including of course the continuation of the EvoEvo researches themselves).

Title: Evolution of Evolution
Programm: FP7
Duration: November 2013 - October 2016
Coordinator: Inria
Partners:

Agencia Estatal Consejo Superior de Investigaciones Cientificas (Spain)
Institut National des Sciences Appliquees de Lyon (France)
Universite Lyon 1 Claude Bernard (France)
Universite Joseph Fourier Grenoble 1 (France)
Universiteit Utrecht (Netherlands)
University of York (United Kingdom)

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

7.4. International Initiatives

7.4.1. Participation in International Programs

Beagle is a member of the CNRS "Laboratoire International Associé" (LIA) EvoAct together with Dominique Schneider's team at TIMC-IMAG (Université Grenoble Alpes) and the Beacon center at Michigan State University (Richard Lenski and Charles Ofria). EvoAct aims at studying "Evolution in Action" by *in vivo*, *in vitro* and *in silico* experiments. More specifically the Beagle team is in charge of the *in silico* experiments.

BIGS Project-Team

8. Partnerships and Cooperations

8.1. National Initiatives

- *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.
- 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
- "ITMO Physics, mathematics applied to Cancer" (2017-2019): "Modeling ctDNA dynamics for detecting targeted therapy", Funding organisms: ITMO Cancer, ITMO Technologies pour la santé de l'alliance nationale pour les sciences de la vie et de la santé (AVIESAN), INCa, Leader: N. Champagnat (Inria TOSCA), Participants: A. Gégout-Petit, A. Muller-Gueudin, P. Vallois
- Modular, multivalent and multiplexed tools for dual molecular imaging (2017-2020), Funding organism: ANR, Leader: B Kuhnast (CEA). Participant: T. Bastogne.

8.2. European Initiatives

8.2.1. 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

8. Partnerships and Cooperations

8.1. National Initiatives

8.1.1. 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.

8.1.2. ADT

- ADT Vidjil (2015–2017): The purpose of this ADT was to strengthen Vidjil development and to ensure a better diffusion of the software by easing its installation, administration and usability. This enabled the software to be well suited for a daily clinical use. Vidjil is now used in routine practice by seven European hospitals (France, Germany, Italy and Czech Republic). Hospitals from the United Kingdom and the Japan are currently assessing Vidjil and may do their clinical routine practice with the software in a near future.
- ADT SeedLib (2017–2019): The SeedLib ADT aims to consolidate existing software developments in Bonsai, into an existing and well-engineered framework. Bonsai has published several new results on spaced seeds and developed several tools that integrate custom implementations of spaced seeds. In parallel, the GATB project is a C++ software library that facilitates the development of next-generation sequencing analysis tools. It is currently maintained by a collaboration between the GenScale team at Inria Rennes and the Bonsai team. Many users from other institutions (including the Erable team at Inria Rhones-Alpes) actively develop tools using GATB. The core object in GATB is k-mers, which can be seen as the predecessor of spaced seeds. The goal of this ADT is to integrate existing space seeds formalisms into GATB, therefore further expanding the features offered by the library, and at the same time provide visibility for tools and results in the Bonsai team.

8.2. European Initiatives

8.2.1. Collaborations in European Programs, Except FP7 & H2020

- International ANR RNAlands (2014-2018): 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.

8.3. International Initiatives

8.3.1. Inria International Partners

8.3.1.1. Informal International Partners

- *Astrid Lindgrens Hospital, Stockholm University:* Collaboration with Anna Nilsson and Shanie Saghafian-Hedengren on RNA sequencing of stromal cells (pilot study done in 2017).
- *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 on data structures for genomic data.
- *Department of Statitics, North Carolina State University:* Collaboration with Donald E. K. Martin on spaced seeds coverage [21].
- *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.
- *Institute of Biosciences and Bioresources, Bari:* Collaboration with Nunzia Scotti on the assembly of plant mitochondrial genomes.
- *Medvedev lab, The Pennsylvania State University:* Collaboration with Paul Medvedev on algorithms and data structures for genomic data, e.g. the Allsome Sequence Bloom Trees.
- *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 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.

8.3.2. 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). Withing this consortium, we participated to a lead opinion paper on immunohematology [20].

CAPSID Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

8.1.1. CPER – IT2MP

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

Project title: *Innovations Technologiques, Modélisation et Médecine Personnalisée*; PI: Faiez Zannad, Univ Lorraine (Inserm-CHU-UL). Value: 14.4 M€ ("SMEC" platform – Simulation, Modélisation, Extraction de Connaissances – coordinated by Capsid and Orpailleur teams for Inria Nancy – Grand Est, with IECL and CHRU Nancy: 860 k€, approx); Duration: 2015–2020. Description: The IT2MP project emcompasses four interdisciplinary platforms that support several scientific pôles of the university whose research involves human health. The SMEC platform supports research projects ranging from molecular modeling and dynamical simulation to biological data mining and patient cohort studies.

8.1.2. LUE – CITRAM

Participants: Marie-Dominique Devignes [contact person], Isaure Chauvot de Beauchêne, Bernard Maigret, Philippe Noël, David Ritchie.

Project title: *Conception d'Inhibiteurs du Transfert de Résistances aux agents Anti-Microbiens: bio-ingénierie assistée par des approches virtuelles et numériques, et appliquée à une relaxase d'élément conjugatif intégratif*; PI: N. Leblond, Univ Lorraine (DynAMic, UMR 1128); Other partners: Chris Chipot, CNRS (SRSMSC, UMR 7565); Value: 200 k€ (Capsid: 80 k€); Duration: 2017–2018. Description: This project follows on from the 2016 PEPS project "MODEL-ICE". 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, and to develop small-molecule inhibitors of these interactions.

8.1.3. PEPS – DynaCriGalT

Participants: Isaure Chauvot de Beauchêne [contact person], Bernard Maigret, David Ritchie.

Project title: *Criblage virtuel et dynamique moléculaire pour la recherche de bio-actifs ciblant la β4GalT7, une enzyme de biosynthèse des glycosaminoglycanes*; PI: I. Chauvot de Beauchêne, Capsid (Inria Nancy – Grand Est); Partners: Sylvie Fournel-Gigleux, INSERM (IMoPA, UMR 7365); Value: 15 k€; Duration: 2017–2018. Description: The β4GalT7 glycosyltransferase initiates the biosynthesis of glycosaminoglycans (GAGs), and is a therapeutical target for small molecules which might correct a defect in the synthesis and degradation of GAGs in rare genetic diseases. Classical approaches to propose active molecules have failed for this target. The DynaCriGalT project combines molecular dynamics modelling of the GAG active site with virtual screening in order to propose a diverse set of small molecules for *in vitro* compound testing.

8.1.4. PEPS – InterANRIL

Participant: Isaure Chauvot de Beauchêne [contact person].

Project title: *Identification et modélisation des interactions nécessaires à l'activité du long ARN non-codant ANRIL dans la régulation épigénétique des gènes*; PI: Sylvain Maenner, Univ Lorraine (IMoPA, UMR 7365); Value: 20 k€; Duration: 2017–2018. Description: ANRIL is a long non-coding RNA (lncRNA) which has been identified as an important factor in the susceptibility cardiovascular diseases. ANRIL is involved in the epigenetic regulation of the expression of a network of genes via mechanisms that are still largely unknown. This project aims to identify and model the protein-RNA and/or DNA-RNA interactions that ANRIL establishes within the eukaryotic genome.

8.2. National Initiatives

8.2.1. FEDER – SB-Server

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

Project title: *Structural bioinformatics server*; PI: David Ritchie, Capsid (Inria Nancy – Grand Est); Value: 24 k€; Duration: 2015–2020. Description: This funding provides a small high performance computing server for structural bioinformatics research at the Inria Nancy – Grand Est centre.

8.2.2. ANR

8.2.2.1. Fight-HF

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

Project title: *Combattre l'insuffisance cardiaque*; PI: Patrick Rossignol, Univ Lorraine (FHU-Cartage); Partners: multiple; Value: 9 m€ (Capsid and Orpailleur: 450 k€, approx); Duration: 2015–2019. Description: This "Investissements d'Avenir" 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.

Project title: *Institut Français de Bioinformatique*; PI: Jean-François Gibrat (CNRS UMS 3601); Partners: multiple; Value: 20 M€ (Capsid: 126 k€); Duration: 2014–2021. Description: 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.

8.3. International Initiatives

8.3.1. Informal International Partners

Participant: David Ritchie; Project: *Integrative Modeling of 3D Protein Structures and Interactions;* Partner: Rocasolano Institute of Physical Chemistry, Spain. Funding: Inria Nancy – Grand Est ("Nancy Emerging Associate Team").

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.

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

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

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

8.4. International Research Visitors

8.4.1. Visits of International Scientists

8.4.1.1. Internships

Isis Grenier Capoci from the State University of Maringá, Brasil visited the team (through the programme "Doutorado Sanduiche no Exterior") to develop new inhibitors of *Candida albicans* TRR1 under the supervision of Bernard Maigret.

DYLISS Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

9.1.1. 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 & Pays de la Loire) aiming at the emergence of Systems Ecology at the level of western France 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.

9.1.2. Regional partnership with computer science laboratories in Nantes

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

Methodologies are developed in close collaboration with the LS2N (fusion of LINA and IRCCyN) located at University of Nantes and École centrale de Nantes. 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 ongoing Ph-D student J. Laniau is co-supervised with a member of the LS2N laboratory. Finally, M. Folschette is a PostDoc working on on a project aiming at analyzing TGF-beta-related pathways evolutions after epithelial-mesenchymal transition in liver cancer, which is a recognized biological process leading to metastasis. This project is based on a topic shared with the LS2N: the use of graph coloring and reconstruction to witness expression changes, and is funded by the Université Bretagne Loire.

9.1.3. Regional partnership in Marine Biology

Participants: Meziane Aite, Arnaud Belcour, 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. Our approach based on parcimonious modelling allowed an in silico characterization of processes required within sea urchin translation [83], [95]. We are also strongly involved in the the IDEALG consortium, 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. Our methods based on combinatorial optimization for the reconstruction of genome-scale metabolic networks and on classification of enzyme families based on local and partial alignments allowed the *E. Siliculosus***seaweed metabolism** to be deciphered [97], [67]. As a further study, we reconstructed the metabolic network of a symbiot bacterium *Ca. P. ectocarpi* [69] and used this reconstructed network to decipher interactions within the **algal-bacteria holobiont** [21].

9.1.4. Regional partnership in agriculture and environmental sciences

Participants: Catherine Belleannée, François Coste, Olivier Dameron, Xavier Garnier, François Moreews, Jacques Nicolas, Anne Siegel, Denis Tagu.

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/IGEPP who spends 20% of his time in the team to develop collaborative projects. This partnership has been supported by the co-supervision of phDs, post-docs and engineers. This collaboration was also reinforced by collaboration within ANR contracts (MirNadapt, FatInteger).

In collaboration with researchers from the PEGASE center (INRA) focused on breeding animals, we have contributed to several studies aiming at better integrating and investigating data in order to facilitate animal selection and alimentation. The *NutritionAnalyzer* prototype was developed to understand better the impact of several diaries or treatments for lactary cows over the composition of milk [37]. Our work on the identification of upstream regulators within large-scale knowledge databases (prototype *KeyRegulatorFinder*) [59] and on semantic-based analysis of metabolic networks [54] was also very valuable for interpreting differences of gene expression in pork meat [79] and figure out the main gene-regulators of the response of porks to several diets (see [74], [76] and [18]).

In addition, constraints-based programming also allows us to decipher regulators of reproduction for the pea aphid, an insect that is a pest on plants in the framework of the *MirnAdapt* project. In terms of biological output of the network studies on the pea aphid microRNAs, we have identified one new microRNA (apmir-3019, not present in any known species other than the pea aphid) who has more than 900 putative mRNA targets. All these targets, as well as apmir3019, are differentially expressed between sexual and asexual embryos [85], [119].

9.1.5. Regional partnership in health

Participants: Jean Coquet, Olivier Dameron, Victorien Delannée, Marine Louarn, Anne Siegel, Nathalie Théret, Pierre Vignet.

We also have a strong and long term collaboration in health, namely with the IRSET laboratory at Univ. Rennes 1. 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 [14], M. Conan (Metagenotox project, funded by Anses) and J. Coquet [12]. This partnership was reinforced 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).

A new application was initiated in 2017 through a collaboration with Rennes hospital, supported by a Inria-INSERM Ph-D thesis (M. Louarn).

9.2. National Initiatives

9.2.1. ANR Idealg

Participants: Meziane Aite, Arnaud Belcour, Jérémie Bourdon, Marie Chevallier, François Coste, Damien Eveillard, Clémence Frioux, Jeanne Got, Julie Laniau, 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. We are participating to the tasks related to the establishment of a virtual platform for integrating omics studies on seaweeds 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 of symbiotic bacteria to brown algae. We will also contribute to the prediction of specific enzymes (sulfatases) [More details].

9.2.2. Programs funded by research institutions

9.2.2.1. 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, several teams at Inria Rennes develop generic methods supporting efficient and semantically-rich queries for pharmaco-epidemiology studies on medico-administrative databases. The leader is Thomas Guyet (Inria 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 [45], [99], [98]. 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).

9.2.2.2. Cancer Plan: TGFSysBio

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

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 Jérôme 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.

9.2.2.3. ANR Samosa

Participants: Mael Conan, 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.

9.2.2.4. ANSES Mecagenotox

Participants: Victorien Delannée, Mael Conan, 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 to xenobiotics. 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.

9.2.3. Programs funded by Inria

9.2.3.1. ADT Complex-biomarkers and ADT Proof of concept

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

These projects 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).

9.2.3.2. IPL Algae in silico

Participants: Meziane Aite, Jeanne Got, Julie Laniau, Anne Siegel.

Microalgae are recognized for the extraordinary diversity of molecules they can contain: proteins, lipids (for biofuel or long chain polyunsaturated fatty acids for human health), vitamins, antioxidants, pigments. The project aims at predicting and optimizing the productivity of microalgae. It involves mainly the inria teams BIOCORE (PI), ANGE and DYLISS. Dyliss is in charge of the identification of physiological functions for microalgae based on their proteomes, which is undergone through the reconstruction of the metabolic network of the *T. lutea* microalgae.

9.2.3.3. IPL Neuromarkers

Participants: Olivier Dameron, Anne Siegel.

The project aims at identifying the main markers of pathologies through the production and the integration of imaging and bioinformatics data. It involves mainly the inria teams Aramis (PI) Dyliss, Genscale and Bonsai. Dyliss is in charge of facilitating the interoperability of imaging and bioinformatics data.

9.2.3.4. FederatedQueryScaler (Exploratory Research Action)

Participants: Olivier Dameron, Xavier Garnier, Vijay Ingalalli.

This project aims at developing automatic generation of abstractions for biological data and knowledge in order to scale federated queries in the context of semantic web technologies. It is a common project with the WIMMICS Inria team.

9.3. European Initiatives

9.3.1. Collaborations with Major European Organizations

Partner: Aachen university (Germany)

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

9.4. International Initiatives

9.4.1. Inria International Labs

9.4.1.1. Other IIL projects

We have a cooperation with Univ. of Chile (MATHomics, A. Maass) on methods for the identification of biomarkers and software for biochip design. It aims at combining automatic reasoning on biological sequences and networks with probabilistic approaches to manage, explore and integrate large sets of heterogeneous omics data into networks of interactions allowing to produce biomarkers, with a main application to biomining bacteria. The program is co-funded by Inria and CORFO-chile from 2012 to 2016. In this context, Integrative-BioChile was 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. The collaboration is now supported by Chilean programs.

9.5. International Research Visitors

9.5.1. Visits of International Scientists

- **Niger**. University of Maradi [O. Abdou-Arbi]
- **Poland**. Politechnika Wroclawska [W. Dyrka]
- **India**. VIT University, Vellore [K. Lakshmanan]

9.5.2. Visits to International Labs

- **Chile**. University of Chile [A. Siegel, C. Frioux]

9.5.2.1. Research Stays Abroad

- **Germany**. University of Potsdam [L. Bourneuf, 3 months (nov 2017 - jan 2018)]

ERABLE Project-Team

8. Partnerships and Cooperations

8.1. National Initiatives

8.1.1. ANR

8.1.1.1. Aster

- Title: Algorithms and Software for Third gEneration Rna sequencing
- Coordinator: Hélène Touzet, University of Lille and Inria EPI Bonsai.
- ERABLE participants: Vincent Lacroix (ERABLE coordinator), Clara Benoît-Pilven, Audric Cologne, Alex di Genova, Leandro I. S. de Lima, Arnaud Mary, Marie-France Sagot, Camille Sessegolo, Blerina Sinaimeri.
- Type: ANR (2016-2020).
- Web page: http://bioinfo.cristal.univ-lille.fr/aster/.

8.1.1.2. ExHyb

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

8.1.1.3. 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/

8.1.1.4. Green

- Title: Deciphering host immune gene regulation and function to target symbiosis disturbance and endosymbiont control in insect pests
- Coordinator: A. Heddi
- ERABLE participant(s): M.-F. Sagot, C. Vieira
- Type: ANR (2018-2021)
- Web page: Not yet available

8.1.1.5. Hmicmac

- Title: Host-microbiota co-adaptations: mechanisms and consequences
- Coordinator: F. Vavre
- ERABLE participant(s): F. Vavre
- Type: ANR PRC (2017-2020)
- Web page: Not available

8.1.1.6. IMetSym

- Title: Immune and Metabolic Control in Intracellular Symbiosis of Insects

- Coordinator: A. Heddi
- ERABLE participant(s): H. Charles, S. Colella
- Type: ANR Blanc (2014-2017)
- Web page: Not available

8.1.1.7. Resist

- Title: Rapid Evolution of Symbiotic Interactions in response to STress: processes and mechanisms
- Coordinator: N. Kremer
- ERABLE participant(s): F. Vavre
- Type: ANR JCJC (2017-2020)
- Web page: Not available

8.1.1.8. Suzukill

- Title: Managing cold tolerance and quality of mass-produced *Drosophila suzukii* flies to facilitate the application of biocontrol through incompatible and sterile insect techniques
- Coordinator: H. Colinet
- ERABLE participant(s): F. Vavre
- Type: ANR PCRI (2015-2018)
- Web page: Not available

8.1.1.9. Swing

- Title: Worldwide invasion of the Spotted WING Drosophila: Genetics, plasticity and evolutionary potential
- Coordinator: P. Gibert
- ERABLE participant(s): C. Vieira
- Type: ANR PCR (2016-2020)
- Web page: Not available

8.1.2. ADT Inria

8.1.2.1. ADT Inria Kirikomics

- Main objective: Development of a portal to increase the visibility of the tools and resources elaborated by Erable around the analysis – using omics data – of metabolic networks modelled by hypergraphs, and enable to visualise the results. (the web page is for now private, it will be made public later in the project).
- Duration: 2016-2017, renewable one more year.
- Person responsible for ADT: Arnaud Mary with David Parsons (Inria).
- Beneficiary of ADT: Martin Wannagat.
- Funds received: Salary for engineer.

8.1.3. Others

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

8.1.3.1. Advanced computational methodologies for the analysis of biomedical data

- Title: Advanced computational methodologies for the analysis of biomedical data
- Coordinator: P. Milazzo
- ERABLE participant(s): R. Grossi, N. Pisanti
- Type: PRA, MIUR PRIN, Italian Ministery of Research National Projects (2017-2018)
- Web page: Not available

8.1.3.2. Advanced Tools and Techniques for the analysis of criminal networks

- Title: Advanced Tools and Techniques for the analysis of criminal networks
- Coordinator: G. Italiano
- ERABLE participant(s): G. Italiano
- Type: LEONARDO SpA (2015-2018)
- Web page: Not available

8.1.3.3. Amanda

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

8.1.3.4. CMACBioSeq

- Title: Combinatorial Methods for analysis and compression of biological sequences
- Coordinator: G. Rosone
- ERABLE participant(s): N. Pisanti
- Type: SIR, MIUR PRIN, Italian Ministery of Research National Projects (2015-2019)
- Web page: http://pages.di.unipi.it/rosone/CMACBioSeq.html

8.1.3.5. Statistical Models for Structural Genetic Variants in the Genome of the Netherlands

- Title: Statistical Models for Structural Genetic Variants in the Genome of the Netherlands
- Coordinator: A. Schönhuth
- ERABLE participant(s): A. Schönhuth
- Type: Nederlandse Wetenschappelijke Organisatie (NWO) (2013-2018)
- Web page: Not available

8.1.3.6. TALS and splicing

- Title: Development of bioinformatic methods for the analysis of splicing events in patients with the Taybi-Linder Syndrome (TALS)
- Coordinator: P. Edery
- ERABLE participant(s): C. Benoît-Pilven, Audric Cologne, V. Lacroix
- Type: INSERM
- Web page: Not available

8.2. European Initiatives

8.2.1. FP7 & H2020 Projects

8.2.1.1. 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: https://team.inria.fr/erable/en/microwine/ and http://www.microwine.eu/

8.2.2. Collaborations in European Programs, Except FP7 & H2020

8.2.2.1. Combinatorics of co-evolution

- Title: The combinatorics of co-evolution
- Duration: 2015 - 2018
- Coordinator: Katharina Huber, University of Warwick, UK
- ERABLE participant(s): M.-F. Sagot, B. Sinaimeri
- Type: The Royal Society
- Web page: not available

8.2.3. 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.

8.3. International Initiatives

8.3.1. Inria International Labs

ERABLE participates in a project within the Inria-Chile CIRIC (Communication and Information Research and Innovation Center) titled "Omics Integrative Sciences". The main objectives of the project are the development and implementation of mathematical and computational methods and the associated computational platforms for the exploration and integration of large sets of heterogeneous omics data and their application to the production of biomarkers and bioidentification systems for important Chilean productive sectors. The project started in 2011 and is coordinated in Chile by Alejandro Maass, Mathomics, University of Chile, Santiago. It is in the context of this project that we hosted Alex di Genova in ERABLE as a PhD sandwich student (for 18 months in 2015-2017). Alex has now defended his PhD. He was co-supervised by Gonzalo Ruz from the University Adolfo Ibañez, Santiago, Chile. He now, since Dec 2017, joined again ERABLE as postdoc.

8.3.2. Inria Associate Teams Not Involved in an Inria International Lab

ALEGRIA

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

8.3.3. Participation in Other International Programs

ERABLE is coordinator of a CNRS-UCBL-Inria Laboratoire International Associé (LIA) with the Laboratório Nacional de Computação Científica (LNCC), Petrópolis, Brazil. The LIA has for acronym LIRIO ("Laboratoire International de Recherche en bIOinformatique") and is coordinated by Ana Tereza Vasconcelos from the LNCC and Marie-France Sagot from 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 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 succint web page for MAIA is available at this address: http://team.inria.fr/erable/en/projects/maia/.

ERABLE also participated to the BASIS project. This was funded by the European Community Seventh Framework Programme (Grant 242006 - 2010-2015). It was led by Dr. Mike Stratton and involved six European countries. It was primarily focused on ER+/HER2- breast cancers, but during the course of the project, was merged with the HER2+ French-ICGC and triple negative UK-ICGC projects, resulting in the analysis of the whole spectrum of breast cancers. The French group was initiated by Dr. Gilles Thomas and was pursued by Alain Viari after the loss of Dr. Thomas in 2014. The project resulted in the sequencing and thorough analysis of 560 breast cancer whole genomes (Nik-Zainai *et al.*, *Nature*, 534:47-54, 2016), including 75 HER2+ performed by the French working group (Ferrari *et al.*, *Nature Communications*, 7, 2016) and funded by the Institut National du Cancer and by Inserm.

Finally, Marie-France Sagot participates in a Portuguese FCT project, Perseids for "Personalizing cancer therapy through integrated modeling and decision" (2016-2019), with Susana Vinga and a number of other Portuguese researchers. The budget of Perseids is managed exclusively by the other Portuguese partner.

8.4. International Research Visitors

8.4.1. Visits of International Scientists

In 2017, ERABLE greeted the following International scientists:

- In France: Katharina Huber and Vincent Moulton (University of Warwick, UK), Ifigeneia Kyrkou (Aarhus University, Danemark), three members of the LIA LIRIO (Arnaldo Zaha from the Federal University of Rio Grande do Sul, Maria Cristina Motta from the Federal University of Rio de Janeiro, and Ana Tereza Vasconcelos from the LNCC, both in Brazil), two members of the Inria Associated Team Alegria (Andréa Ávila and Helisson Faoro), Ariel Silber (University of São Paulo, Brazil), Susana Vinga and various members of her team (IST Portugal).
- In Italy: May Alzamel, Lorraine A. K. Ayad, Panagiotis Charalampopoulos, Costas Iliopoulos, and Solon Pissis (King's College, London, UK) visited the University of Pisa as did Luca Cardelli (Microsoft Research), Giulia Bernardini (University of Milano Bicocca), Anthony Cox (Illumina) and Raffaele Giancarlo (University of Palermo); Loukas Georgiadis (University of Ioannina, Greece), Shahbaz Khan (University of Vienna, Austria), and Adam Karczmarcz, (University of Warsaw, Poland) visited the University of Rome Tor Vergata.
- In the Netherlands: Martin Dyer (Leeds University, England), Frans Schalekamp(Cornell University, Ithaca, New York, USA), and Anke van Zuylen (College of William and Mary, Virginia, USA) visited the FU & CWI.

8.4.2. Internships

In 2017, ERABLE greeted the following internship students:

- In France: Irene Ziska, Master Free University Berlin (6 months).

8.4.3. Visits to International Teams

In 2017, members of ERABLE visited the following International teams:

- From France: Visit to members of the LIA LIRIO at the LNCC in Brazil, the Department of Computer Science of the University of São Paulo and to members of the TecSinapse company in Brazil, Susana Vinga and members of her team (IST Portugal).

GENSCALE Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

9.1.1. Rennes Hospital, Hematology service

Participants: Dominique Lavenier, Patrick Durand.

The collaboration with the Hematology service of the Rennes hospital aims to set up advanced bioinformatics pipelines for cancer diagnosis. More precisely, we evaluated a new method of predictions of small cancer-related mutations (such as SNPs and small insertions/deletions) from raw DNA sequencing data.

9.1.2. Partnership with INRA in Rennes

Participants: Susete Alves Carvalho, Cervin Guyomar, Dominique Lavenier, Fabrice Legeai, Claire Lemaitre, Sebastien 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 two INRA engineer (F. Legeai, S. Alves Carvalho) and one PhD student (C. Guyomar).

9.2. National Initiatives

9.2.1. ANR

9.2.1.1. Project HydroGen: Metagenomic applied to ocean life study

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

9.2.1.2. Project SpeCrep: speciation processes in butterflies

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

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)
Duration:7.5 year (2012-2019)

Partners: 5 companies, 9 academic research labs.

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. (http://www.rapsodyn.fr)

9.2.2.2. Institut Français de Bioinformatique: Plant node

Participant: Fabrice Legeai.

Coordinator: Hadi Quesneville (INRA, Versailles)

The aim of the Institut Francais de Bioinformatique (IFB) offers resources for a large community of French biologist. With INRA and CIRAD, we were part of the plant node of IFB, and focused on delivering efficient tools for sharing agronomical data, such as Askomics.

9.2.3. Programs from research institutions

9.2.3.1. Inria ADT DiagCancer

Participants: Dominique Lavenier, Patrick Durand.

Since October 1st, 2016, Genscale 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.

9.2.3.2. CNRS Mastodons program: C3G

Participants: Dominique Lavenier, Pierre Peterlongo, Claire Lemaitre, Camille Marchet, Lolita Lecompte.

High-throughput sequencing applications now cover all life sciences: from medicine to agronomy. The 3rd generation sequencing produces very long reads, but the reads are extremely noisy, which has a strong impact on the quality of bioinformatics analyses. The challenge of the C3G project is to bring this type of data to a high level of quality through the development of new correction strategies.

9.2.3.3. Inria Project Lab: Neuromarkers

Participants: Dominique Lavenier, Pierre Peterlongo, Claire Lemaitre.

The IPL Neuromarkers aims to design imaging biomarkers of neurodegenerative diseases for clinical trials and study of their genetic associations. In this project, GenScale bring its expertise in the genomic field.

9.3. International Initiatives

9.3.1. Inria Associate Team: HipcoGen

- Title: High-Performance Combinatorial Optimization for Computational Genomics
- International Partner (Institution - Laboratory - Researcher):
  - Los Alamos National Laboratory (LANL)-NM, United States, CCS-3, Hristo Djidjev
- Start year: 2017
- Teams' web site: https://team.inria.fr/genscale/presentation/associated-team/

Genome sequencing and assembly, the determination of the DNA sequences of a genome, is a core experiment in computational biology. During the last decade, the cost of sequencing has decreased dramatically and a huge amount of new genomes have been sequenced. Nevertheless, most of recent genome projects stay unfinished and nowadays the databases contain much more incompletely assembled genomes than whole stable reference genomes. The main reason is that producing a complete genome, or an as-complete-as-possible-genome, is an extremely difficult computational task (an NP-hard problem) and, in spite of the efforts and the progress done by the bioinformatics community, no satisfactory solution is available today. New sequencing technologies (such as PacBio or Oxford Nanopore) are being developed that tend to produce longer DNA sequences and offer new opportunities, but also bring significant new challenges. The goal of this joint project–a cooperation between Los Alamos National Laboratory, US and Inria, is to develop a new methodology and tools based on novel optimization techniques and massive parallelism suited to these emerging technologies and able to tackle the complete assembly of large genomes.

9.3.2. Informal International Partners

- Free University of Brussels, Belgium: Genome assembly [P. Perterlongo, A. Limasset]

9.4. International Research Visitors

9.4.1. Visits of International Scientists

- Visit of Hristo Djidjev from Los Alamos National Laboratory, June 5 to July 4, 2017

9.4.2. Visits to International Teams

- Visit of R. Andonov at LANL from May 4th to May 30th. Work on Task 2 from HipcoGen project.
- Visit of S. Francois at LANL from May 4th to May 30th and from August 2 to August 23. Work on Task 2 from HipcoGen project.
- Visit of Pierre Peterlongo at LANL, May 2017 (one week). Talk to SFAF conference: "Assembly of heterozygous genomes".

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 (2016-2019)

8.2. National Initiatives

Project name	COSY: real-time COntrol of SYnthetic microbial communities
Coordinator	E. Cinquemani
IBIS participants	E. Cinquemani, H. de Jong, J. Geiselmann, M. Mauri, T. Muszbek, C. Pinel, D. Ropers
Type	Inria Project Lab (2017-2021)
Web page	https://project.inria.fr/iplcosy/

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	MAXIMIC – Optimal control of microbial cells by natural and synthetic strategies
Coordinator	H. de Jong
IBIS participants	C. Boyat, E. Cinquemani, J. Geiselmann, H. de Jong, C. Pinel, D. Ropers
Type	ANR project (2017-2021)

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)

Project name	CoSoft – Control software for a system of mini-bioreactors
Coordinator	E. Cinquemani
IBIS participants	E. Cinquemani, H. de Jong, J. Geiselmann, T. Muszbek
Type	Inria Hub (2017-2018)

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

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 (2011-2017) "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. Inria Project Lab

- IPL COSY (2017-2021) "real-time control of synthetic microbial communities", coordinated by Eugenio Cinquemani (Ibis, Inria), with Jean-Luc Gouzé (Biocore, Inria), Gregory Batt, Frédéric Bonnans (Commands, Inria), Efimov Denis (Non-A, Inria), and Hans Geiselmann (BIOP, Université Grenoble-Alpes), Beatrice Laroche (Maiage, Inra Jouy-en-Josas), and Hyun Youk (Youk lab, TU Delft).

8.2. European Initiatives

8.2.1. FP7 & H2020 Projects

- H2020 FET-OPEN COSY-BIO (2017-2020), "Control Engineering of Biological Systems for Reliable Synthetic Biology Applications", coordinated by Diego di Bernardo (Tigem), with Filippo Menolascina (Edinburgh U), Mario di Bernardo (Naples U), Pascal Hersen (Paris7 U), Mustafa Khammash (ETHZ), Gregory Batt, Guy-Bart Stan (Imperial College), and Lucia Marucci (Bristol U).

8.3. International Initiatives

8.3.1. Participation in 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.

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.

7.1.2. Idex UCA Jedi

Four projects leading by team members were funded.

7.2. National Initiatives

7.2.1. ANR RNAGRIMP

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

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, Christelle Requena.

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. International Initiatives

7.3.1. Participation in Other International Programs

ECOS-Nord France - Colombie 2015-2017: visit of the Pr Arturo Plata from the University Industrial of Santnder, Bucaramanga, Columbia, in June 2017.

7.4. International Research Visitors

7.4.1. Visits of International Scientists

7.4.1.1. Internships

Nilgoon Zarei:University of British Columbia, Vancouver, Canada, Jul 2017 - Dec 2017

A Novel approach for Renal Cell Carcinoma Classification Using Vascular, Morphological and Spatial Information

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

Combinaison adaptative des informations texture et couleur pour la segmentation d'images médicales

Vanna Lisa Coli: PhD, University of Modena and Reggio Emilia, Bologna Italy., from January to April 2017.

TV regularization for the reconstruction of microwave tomographic imagery, with application to the detection of cerebrovascular accidents.

PLEIADE Team

7. Partnerships and Cooperations

7.1. Regional Initiatives

7.1.1. COTE – Continental to Coastal Ecosystems

The Labex cluster of excellence COTE (Continental To coastal Ecosystems: evolution, adaptability and governance) develops tools to understand and predict ecosystem responses to human-induced changes as well as methods of adaptative management and governance to ensure their sustainability. The LabEx includes nine laboratories of the University of Bordeaux and major national research institutes involved in research on terrestrial and aquatic ecosystems (INRA, CNRS, IFREMER and IRSTEA). PLEIADE is a partner in one project funded by COTE:

- *Aerobarcoding: détection de pollens allergenisants*. 2017-18.

7.2. National Initiatives

7.2.1. 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.

This working group continues work started in CAER – Alternative Fuels for Aeronautics, 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.

7.2.2. Agence Française pour la Biodiversité

The AFB is a public law agency of the French Ministry of Ecology that supports public policy in the domains of knowledge, preservation, management, and restoration of biodiversity in terrestrial, aquatic, and marine environments. PLEIADE is a partner in two AFB projects developed with the former ONEMA:

- *Methods for metabarcoding*. 2017-18.
- *Molecular diagnosis of freshwater quality*. 2014-present.

7.2.3. Inria Projet Lab in silico Algae

In 2017 PLEIADE joined the IPL "In silico Algae" coordinated by Olivier Bernard. The IPL addresses challenges in modeling and optimizing microalgae growth for industrial applications. PLEIADE worked this year on comparative genomic analysis of genes implicated in lipid production by the picoalgae *Ostreococcus tauri*, in collaboration with Florence Corellou of the CNRS UMR 5200 (Laboratoire de Biogénèse Membranaire). The goal of this work is the production of long-chain polyunsaturated fatty acids, developed as nutritional additives. Mercia Ngoma Komb's two-month internship in PLEIADE contributed to this work.

7.3. European Initiatives

7.3.1. Collaborations in European Programs, Except FP7 & H2020

Alain Franc has been appointed co-chair of Working Group 4 (Data Analysis and Storage) of COST DNAqua.net [0], at the Sarajevo meeting in Fall 2017, with the main task of developing contact with HPC and metabarcoding for serving the whole community. The goal of DNAqua-Net is to nucleate a group of researchers across disciplines with the task to identify gold-standard genomic tools and novel eco-genomic indices and metrics for routine application for biodiversity assessments and biomonitoring of European water bodies.

7.4. International Initiatives

7.4.1. CEBA – Center for the study of biodiversity in Amazonia

The Laboratoire of excellence CEBA promotes innovation in research on tropical biodiversity. It brings together a network of internationally-recognized French research teams, contributes to university education, and encourages scientific collaboration with South American countries. PLEIADE participates in three current international projects funded by CEBA:

- *MicroBIOMES: Microbial Biodiversities*. 2017-19.
- *Neutrophyl: Inferring the drivers of Neotropical diversification*. 2017-19.
- *Phyloguianas: Biogeography and pace of diversification in the Guiana Shield*. 2015-present

[0] http://dnaqua.net/

SERPICO Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

ENSAI-CREST: Statistical methods and models for image registration, PhD thesis of Vincent Briane 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) (PhD thesis of Emmnuel Moebel); motion saliency in video sequences (PhD thesis of Léo Maczyta).

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 PhD thesis of A. Caranfil).

9.2. National Initiatives

9.2.1. France-BioImaging project

Participants: Charles Kervrann, Patrick Bouthemy.

The goal of the France-BioImaging project (http://france-bioimaging.org/) 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. Serpico is co-head of the IPDM (Image Processing and Data Management) node of the FBI network composed of 6 nodes. In this context, we address the following scientific 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 recruited R&D engineers (2011-2016) to disseminate image processing software, to build the Mobyle@Serpico web portal and to manage the IGRIDA-Serpico cluster (200 nodes; batch scheduler: OAR; File management: Puppet/Git/Capistrano; OS: Linux Debian 7; User connexion: public ssh key) opened for end-users and dedicated to large scale computing and data sets processing (storage: 200 TeraBytes).

- **Coordinator:**CNRS (Jean Salamero, UMR 144 CNRS-Institut Curie).
- **Partners:**University of Paris-Diderot-Paris 7, Aix-Marseille University, University of Bordeaux, University of Montpellier, Institut Pasteur, Institut Curie, Inria, ENS Ulm, University of Paris Descartes, UPMC, Ecole Polytechnique, Inserm.
- **Funding:**Investissement d'Avenir Infrastructures Nationales en Biologie et Santé, ANR INBS-PIA 2011.
- **Total amount:**26 000 Keuros (Inria Serpico: 606 Keuros).

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, Vincent Briane, Ancageorgiana Caranfil, Antoine Salomon.

Cutting-edge LLS microscopy represents 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 biological condition can result into up to one terabyte of data.The goal of the project is to develop new paradigms and computational strategies for image reconstruction and 3D molecule tracking/motion estimation. Furthermore, establishing correspondences between image-based measurements and features, stochastic motion models, and underlying biological and biophysical information remains a challenging task. In a larger perspective, the quantitative description of image data corresponding to protein transport will be a prerequisite for understanding the functioning of a cell in normal and pathological situations including cancer, viral infection and neurodegenerative diseases.

- **Coordinator:**Inria (Charles Kervrann)
- **Partners:**Inria (Serpico, Beagle, Fluminance teams), INRA MaIAGE Unit Jouy-en-Josas, Institut Curie (UMR 144 CNRS & U1143 Inserm UMR 3666) Paris
- **Funding:**ANR (Agence Nationale de la Recherche) PRC (Collaborative Research Project)
- **Total amount:**440 Keuros (Inria Serpico: 170 Keuros).

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 .

- **Coordinator:** EMBL (Jan Ellenberg, Heideldberg, Germany)
- **Partners:** 15 european countries in 2017
- **Funding:** Member states of the European Union

9.4. International Initiatives

9.4.1. Informal International Partners

Collaboration with Max-Planck Institute, Martinsried (Germany), Dr. Julio Ortiz and Antonio Martinez: 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 with Frédéric Lavancier).

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

9.4.2.1. 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

Participants: Sandeep Manandhar, Patrick Bouthemy, Charles Kervrann.

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 second meeting of the AT CytoDI took place in Rennes in July 2017 (visit of P. Roudot and K. Dean), to discuss and update current research direction and discuss scientific progress. Several meetings were organized with students (S. Manandhar, V. Briane, E. Moebel, T. Dubois, Q. Delannoy) to synchronize development in optical flow, co-orientation and visualization. The Danuser team focused on presenting recent imaging and analysis capacities as well as the current solution in development for the systematic analysis, contextualization and interpretation of 3D dynamics for quantitative biology.

9.5. International Research Visitors

9.5.1. Visits to International Teams

Emmanuel Moebel attended a summer school (one week): Signal Processing Meets Deep Learning (Capri, Italy, 4-8 september 2017).
Sandeep Manandhar attended a summer school (one week): VISion Understanding and Machine intelligence (Porto, Portugal, 7-14 July 2017).

TAPDANCE Team

6. Partnerships and Cooperations

6.1. European Initiatives

6.1.1. FP7 & H2020 Projects

Woods applied for an ERC Consolidator award. The application was successful and begins in 2018.

6.2. International Research Visitors

6.2.1. Visits of International Scientists

David Doty (UC Davis) visited the team several times in 2017.

VIRTUAL PLANTS Project-Team

7. Partnerships and Cooperations

7.1. Regional Initiatives

7.1.1. 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.

7.1.2. 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;

7.2. National Initiatives

7.2.1. 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.

7.2.2. Phenome

Participants: Christian Fournier, Christophe Pradal, Yann Guédon, Sarah Cohen-Boulakia, Christophe Pradal, Pierre Fernique, 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.

7.2.3. 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.

7.2.4. 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.

7.2.5. Other national grants

7.2.5.1. Morphogenetics

Participants: Christophe Godin, Olivier Ali, Frédéric Boudon, 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).

7.2.5.2. 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

7.2.5.3. 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

7.3. European Initiatives

7.3.1. Collaborations in European Programs, Except FP7 & H2020

Program: H2020

Project acronym: ROMI

Project title: RObotics for MIcrofarms

Duration: November 2017 - October 2021

Coordinator: Sony

Other partners: Iaac, (Spain), FEI (France), Inria (France), CNRS (France), UBER (Germany), Chatelain (France)

Abstract: All over Europe, young farmers are starting small market farms and direct sales businesses. These farms can be found both in rural, peri-urban and urban areas. They grow a large variety of crops (up to 100 different varieties of vegetables per year) on small surfaces (0.01 to 5 ha) using organic farming practices. These farms have proven to be highly productive, sustainable and economically viable. However, a lot of work is done manually, resulting in physically challenging work conditions. ROMI will develop an open and lightweight robotics platform for these microfarms. We will assist these farms in weed reduction and crop monitoring. This will reduce manual labour and increase the productivity through advanced planning tools. Thanks to ROMI's weeding robot,

farmers will save 25 percents of their time. This land robot will also acquire detailed information on sample plants and will be coupled with a drone that acquires more global information at crop level. Together, they will produce an integrated, multi-scale picture of the crop development that will help the farmer monitor the crops to increase efficient harvesting. For this, ROMI will have to adapt and extend state-of-the-art land-based and air-borne monitoring tools to handle small fields with complex layouts and mixed crops. To achieve this, we will: (i) develop and bring to the market an affordable, multi-purpose, land-based robot, (ii) develop a weeding app for this robot that is adapted for organic microfarms, (iii) apply advanced 3D plant analysis and modelling techniques to in-field data acquisition, (iv) integrate these analysis techniques in the robot for detailed plant monitoring, (iv) integrate these techniques also in the aerial drone N-E-R-O for multi-scale crop monitoring, (v) extend the robot with novel, adaptive learning techniques to improve sensorimotor control of the plant monitoring app, and (vii) test the effectiveness of our solution in real-world field conditions.

This project was accepted in July 2017 and started Nov. 2017.

7.4. International Initiatives

7.4.1. Inria International Partners

7.4.1.1. Informal International Partners

An important collaboration with the CIRAD research unit HortSys at the Reunion island and in particular Frédéric Normand and Isabelle Grechi 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).

7.5. International Research Visitors

7.5.1. Research Stays Abroad

In the context of the project on mango modelling and the PhD of S. Persello, F. Boudon was positioned in the Reunion island in the Hortsys unit for one year until August. He developed 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-NSF NETBCI

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, UPenn, USA

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-NIH-NSF HIPLAY7

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

Project acronym: HIPLAY7

Project title: Hippocampal layers: advanced computational anatomy using very high resolution MRI at 7 Tesla in humans

Duration: Jan 2017 - Jan 2020

Amount: 770k€

Coordinator: Olivier Colliot and Pierre-François Van de Moortele

Other partners: University of Minnesota, Neurospin

Abstract: The overall goal of this proposal is to develop a coherent mathematical framework for computational anatomy of the internal structures of the hippocampus based on cutting edge MRI acquisition techniques at 7 Tesla. These mathematical and computational approaches are expected to significantly advance the field of computational anatomy of the human brain, breaking down the millimeter barrier of conventional brain morphometry and providing a coherent analysis framework for anatomical data at ultra-high spatial resolution.

9.1.1.3. 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.

9.1.1.4. 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. Inria Project Labs

9.1.2.1. IPL Neuromarkers

Participants: Stanley Durrleman [Correspondant], Olivier Colliot [Correspondant], Fabrizio de Vico Fallani, Anne Bertrand, Stéphane Epelbaum.

Project acronym: Neuromarkers

Project title: Design of imaging biomarkers of neurodegenerative diseases for clinical trials and study of their genetic associations

Duration: 2017-2021

Amount: 633k€

Coordinators: Stanley Durrleman and Olivier Colliot

Other partners: Inria GENSCALE, Inria BONSAI, Inria DYLISS, Inria XPOP, ICM, IHU/ICM iConics

Abstract: The Inria Project Lab Neuromarkers to develop new statistical and computational approaches to integrate multimodal imaging and omics data and to demonstrate their potential to identify early alterations and predict progression of neurodegenerative diseases. To tackle this challenge, the project brings together multidisciplinary expertise from Inria and ICM (Brain and Spine Institute) in the fields of statistical learning, brain imaging, bioinformatics, knowledge modeling, genomics and neurodegenerative diseases.

9.1.3. IHU

9.1.3.1. 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.

9.1.3.2. 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

Started 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.

9.1.3.3. 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

Started 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.

9.1.3.4. 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.

9.1.3.5. 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.

9.1.4. National Networks

- GdR Statistics and Medicine - http://gdr-stat-sante.math.cnrs.fr/spip/
- 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

Participants: Stanley Durrleman, Raphael Couronné.

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. Inria International Partners

9.3.1.1. Informal International Partners

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

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).

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".

O. Colliot has 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).

S. Durrleman has a collaboration with the department of Computer Science at New York University (NYU) (G. Gerig and J. Fishbaugh)

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

- Professor Tom Fletcher from the University of Utah visited ARAMIS from January 23 to January 27.

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.

9.4.2. Visits to International Teams

9.4.2.1. Research Stays Abroad

Junhao Wen, PhD candidate, did a 3-month internship in the team of Hui Zhang, UCL, to develop pipelines of analysis for advanced diffusion MRI acquisitions (Neurite Orientation Dispersion and Density Imaging). This internship was funded by the ICM Carnot Program.

ASCLEPIOS Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

- Marco Lorenzi is principal investigator of the project Big Data for Brain Research, funded in 2017 by the Department des Alpes Maritimes (AAP Santé 2017). The project aims at creating a computing platform within the facility of Inria Sophia Antipolis dedicated to the analysis of large biomedical datasets. The realization of the data management system and computational platform will be achieved through the collaboration with the Maison de la Modélisation, de la Simulation et des Interactions (MSI) of the Université Côte d'Azur.
- N. Ayache and P. Robert are principal invesgators of the project MNC3 (Médecine Numérique, Cerveau, Cognition, Comportement) financé par l'Idex Jedi du UCA (2017-2021, 450k€). M. Lorenzi (Inria) actively participates to the supervision of this project with the help of V. Manera (ICP).

8.2. National Initiatives

8.2.1. Consulting for Industry

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

8.2.2. 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.

8.3. European Initiatives

8.3.1. FP7 & H2020 Projects

8.3.1.1. ECSTATIC

Title: Electrostructural Tomography – Towards Multiparametric Imaging of Cardiac Electrical Disorders

Programm: H2020

Type: ERC

Duration: 2017 - 2022

Coordinator: U. Bordeaux

Inria contact: Maxime Sermesant

Cardiac electrical diseases are directly responsible for sudden cardiac death, heart failure and stroke. They result from a complex interplay between myocardial electrical activation and structural heterogeneity. Current diagnostic strategy based on separate electrocardiographic and imaging assessment is unable to grasp both these aspects. Improvements in personalised diagnostics are urgently needed as existing curative or preventive therapies (catheter ablation, multisite pacing, and implantable defibrillators) cannot be offered until patients are correctly recognised.

ECSTATIC aims at achieving a major advance in the way cardiac electrical diseases are characterised and thus diagnosed and treated, through the development of a novel non-invasive modality (Electrostructural Tomography), combining magnetic resonance imaging (MRI) and non-invasive cardiac mapping (NIM) technologies.

The approach will consist of: (1) hybridising NIM and MRI technologies to enable the joint acquisition of magnetic resonance images of the heart and torso and of a large array of body surface potentials within a single environment; (2) personalising the inverse problem of electrocardiography based on MRI characteristics within the heart and torso, to enable accurate reconstruction of cardiac electrophysiological maps from body surface potentials within the 3D cardiac tissue; and (3) developing a novel disease characterisation framework based on registered non-invasive imaging and electrophysiological data, and propose novel diagnostic and prognostic markers.

This project will dramatically impact the tailored management of cardiac electrical disorders, with applications for diagnosis, risk stratification/patient selection and guidance of pacing and catheter ablation therapies. It will bridge two medical fields (cardiac electrophysiology and imaging), thereby creating a new research area and a novel semiology with the potential to modify the existing classification of cardiac electrical diseases.

8.3.1.2. MD PAEDIGREE

Title: Model-Driven European Paediatric Digital Repository

Programm: FP7

Duration: 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 (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 health-care 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 of 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 multiplicity 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, and others), as well as specialised biomechanical and imaging VPH simulation models.

8.3.1.3. 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.

8.4. International Initiatives

8.4.1. Inria International Labs

8.4.1.1. Inria Associate Team GeomStats (part of Inria@SiliconValley)

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.

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

8.4.2.1. PERSOCARDIOLEARN

Title: Personalization of Cardiac Models using Experimental Data and Machine Learning

International Partner (Institution - Laboratory - Researcher):

University of Toronto (Canada) - Sunnybrook Research Institute - Mihaela Pop

Start year: 2017

See also: https://team.inria.fr/asclepios/research/associated-team-persocardiolearn/

Multi-scale computer modelling is a powerful tool that could be used to simulate in silico cardiac electrical activity and biomechanical function of individual heart. Imaging and 3D heart models built from images can help us understand the basis of structurally-diseased hearts at organ level and to predict in silico the changes in electro-mechanical function as a consequence of muscle remodelling in pathologic state (e.g. chronic infarction, a major cause of death). We hypothesize that MRI-based predictive models can help us identify new opportunities to intervene or to predict the outcome of ablation therapy, which currently has low clinical success. However, these predictive models need to be validated and thoroughly tested in preclinical experiments prior to their integration into the clinical stage. Hence, the next logical step for our joint Inria-SB efforts is to expand our experimental-theoretical framework and to personalize fast 3D heart models from in vivo MR-EP data. This translational step involves numerous challenging tasks from the modelling perspective since the in vivo imaging and physiological signals are rather noisy and obtained at a poor spatial resolution, potentially leading to erroneous customization of mathematical model parameters. However, this collaboration employs a rare combination of experiments and modelling specialists. Moreover, the originality of the proposed approach is to build upon machine-learning techniques rather than on data assimilation methods that are more explored in the literature but have inherent limitations (robustness to noise, local minima...).

8.4.3. Inria International Partners

8.4.3.1. Informal International Partners

8.4.3.1.1. 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.

8.4.3.1.2. 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.

8.4.3.1.3. University College London (UCL), London, UK

Marco Lorenzi is collaborator of 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.

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

Marco Lorenzi is currently collaborator with the IGC for the investigation of the 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.

8.4.3.1.5. Other International Hospitals

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

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 [95]. Another strategy [80] 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 project-team GALAAD/AROMATH and leverage the methods they developed [85], [86], [84] to have a better insight in this problem of rotational invariants of ternary quartics.

In collaboration with GALAAD/AROMATH, we developped a complete set of rational invariants for ternary quartics [44]. Being rational, they are very close to the polynomial invariants developed in [80] but they constitute a complete set of invariants. They also are good tools to understand better the algebraic invariants of [95] and some others based on spherical harmonics decomposition [61].

9.1.2. Inria SAM Action Transverse

Participants: Yann Thanwerdas [Asclepios Project-Team], Xavier Pennec [Asclepios Project-Team], Maureen Clerc, Nathalie Gayraud.

The goal of the proposed internship will be to study and implement the barycentric subspace analysis procedure on SPD matrices endowed with the affine invariant metric and to test it with BCI datasets. In the context of BCI, the problem is not trivial. The cross-session and cross-subject variability must be taken into account during the process of selecting the optimal lower dimensional subspace. In a first step, algorithms will be developed to project points into a barycentric subspace, and then to optimize the location of the reference points themselves. In order to avoid an intensive optimization, one will usefully restrict reference points to belong to the original data points. In a second step, the barycentric coordinates will be used to describe the data in the hierarchy of embedded barycentric subspaces and one will study the power of this signature to classify / predict the correct brain state

9.1.3. 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. The goal 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. 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*
Call: *ANR MRSEI Montage de réseaux scientifiques européens ou internationaux 2015*

LEMONS (Learning, Monitoring, Operating Neural Interface) aims to consolidate a European Network by organizing meetings and visits, in order to submit a proposal for a MSCA-ITN Training Network. The European consortium was led by ATHENA (coordinator Maureen Clerc). The European consortium was composed of 8 beneficiaries from 6 countries (Inria, EPFL, TU Graz, Fondazione Santa Lucia, Albert-Ludwigs Universität Freiburg, Universiteit Leiden, Université Lyon 1, eemagine GmbH) and 8 additional Partner Organizations from clinical and industrial sectors. The LEMONS project was submitted twice but was eventually not selected for EU funding.

9.2.2.2. ANR NeuroRef

Participants: Demian Wassermann, Antonia Machlouziredes, Guillermo Gallardo, Rachid Deriche.

Duration: *October 2016 to September 2019*
Call: *NSF-ANR Program Collaborative Research in Computational Neuroscience 2015*

This project is a collaboration with Pr.S.Bouix and his team at the Psychiatry NeuroImaging Lab, Dept of Radiology, Brigham and Women's Hospital, Harvard Medical School (USA) to build MRI reference atlases to analyze brain trauma and post-traumatic stress. The goal 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.

9.2.2.3. ANR MOSIFAH

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

Duration: *October 2013 to September 2017*
Call: *ANR Numerical Models 2013*

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.

9.2.2.4. ANR VIBRATIONS

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

Duration: *February 2014 to January 2018*
Call:ANR Programme de Recherche Translationnelle en Santé (PRTS) 2013

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.

9.2.3. ADT

9.2.3.1. AMDT BCI-Browser

Participants: Théodore Papadopoulo, Maureen Clerc.

Duration: 1 year

Most often, BCI techniques are demonstrated in simple toy applications made. The only "few" real BCI applications are specific developments and are not used much as they lack of functionality, maintenance, ... The goal of this development contract is to demonstrate a new approach to BCI, in which BCI interactions are integrated in existing applications. Ideally, the original software is not modified and not even recompiled. It is modified by providing either modified GUI libraries or providing extensions as plugins. As a proof of concept, we aim at modifying C++/Qt applications with a focus on web browsing, by redefining some of its basic interactions (mouse clicks, keyboard, ...) using some BCI components. In this manner, it might be possible to drive standard and state-of-the-art application using BCI and at a limited maintenance cost.

This contract is part of the AMDT initiative.

9.2.3.2. ADT BOLIS 2

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

Duration: *6 months.*

This contract is a follow-up of ADT BOLIS which aimed at building a sofware platform dedicated to inverse source localisation, building upon the elements of software found in FindSources3D. The platform is modular, ergonomic, accessible and interactive and offers a detailed visualisation of the processing steps and the results. Its 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). BOLIS 2 aims at simplifying some maintenance aspects of the software.

This contract is part of the AMDT initiative.

9.2.4. Other Funding Programs

9.2.4.1. Big Brain Theory ICM Program: 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 clinical value** will open new perspectives in neuroimaging.

9.3.1.2. ERC StG NeuroLang

Program: H2020-EU.1.1. (ERC-StG-2016 - ERC Starting Grant)

Project acronym: NEUROLANG

Project title: Accelerating Neuroscience Research by Unifying Knowledge Representation and Analysis Through a Domain Specific Language

Start date: March 2018, End date: Fe. 2023

P.I : D. Wassermann

Partners: ATHENA project-team (Till Oct. 2017). PARIETAL project-team (Since Nov. 2017)

Abstract: The grand challenge of NeuroLang is to unify neuroanatomical descriptions into a formal language embodied by a Domain Specific Language (DSL) which can be used to perform neuroimaging data analysis. NeuroLang will formalise neuroanatomical knowledge into a DSL, providing an individualized as well as a population-based methodology to represent the anatomy and function of the brain and facilitating the analysis of large neuroimaging datasets and ontologies. Besides formalizing and unifying neuroanatomy, there are four major challenges in NeuroLang: (i) Developing a Neuroanatomical DSL,(ii) Representation of Neuroanatomical Data, (iii) Enabling Large-Scale Inference in a Neuroanatomical DSL and (iv) Reproducible Research and Applicability in Clinical and Cognitive Research.

9.3.1.3. ChildBrain ETN

ATHENA is an Associated Partner in the ChildBrain European Training Network: the team participates 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 Jyväskylä, 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

Duration :Jan. 2016 – Dec. 2018

Partners: ATHENA project-team,

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

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. Declared Inria International Partners

- Sherbrooke University, CA (M. Descoteaux)
- Harvard Medical School, USA (S. Bouix)
- 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).
- BESA company on EEG/MEG modeling.

9.4.3. Participation in Other International Programs

- University Houari Boumedienne (USTHB, Algiers) (L. Boumghar) and University of Boumerdes, (D. Cherifi), Algeria.

9.5. International Research Visitors

9.5.1. Visits of International Scientists

- Dr. Lang Chen, Research Fellow, Stanford Medical School, USA (October 2017)

9.5.1.1. Internships

- Gaston Zanitti, Computer Science Department, School of Sciences, University of Buenos Aires, Argentina (Mars-June 2017)

BIOVISION Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

9.1.1. VREAD: Making reading enjoyable again

Participants: Marco Benzi, Pierre Kornprobst, Stéphanie Baillif [Centre hospitalier Pasteur 2 (service d'ophtalmologie, Nice, France)], Annick Martin ["27Delvalle" (Centre d'Innovation Santé de la ville de Nice, France)], Eric Castet [Aix-Marseille Université (CNRS, Laboratoire de Psychologie Cognitive, Marseille, France)], Fabio Solari [University of Genoa (DIBRIS, Genoa, Italy)], Manuela Chessa [University of Genoa (DIBRIS, Genoa, Italy)]

Coordinator: Pierre Kornprobst

Duration: August 2017 to January 2019

Our goal is to develop a new platform to bring reading experience to a higher level of immersivity, making reading enjoyable again for low-vision people. This project received funding from Université Côte d'Azur (France), in the "Pré-maturation" call which finances actions that transform existing proof of concept into an operational laboratory prototype allowing either the realization of "robust" demonstrators or the complete experimental validation of concept. The perspective is industrialisation, through transfer or start-up creation.

9.1.2. Modélisation Théorique et Computationnelle en Neurosciences et Sciences Cognitives

The Biovision team is a member of this "Axe Interdisciplinaire de Recherche de l'Université de Nice – Sophia Antipolis". It has participated to the Rencontre C@UCA 2017 in Fréjus (April 2017). This axe is partly funding our work on retinal waves.

9.2. National Initiatives

9.2.1. ANR

9.2.1.1. Trajectory

Title: Encoding and predicting motion trajectories in early visual networks

Programme: ANR

Duration: October 2015 - September 2020

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

Partners:

Institut de Neurosciences de la Timone (CNRS and Aix-Marseille Université, France)

Institut de la Vision (Paris, France)

Universidad Tecnico Federico Santa María (Electronics Engineering Department, Valparaíso, Chile)

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.

9.3. European Initiatives

9.3.1. Collaborations in European Programs, Except FP7 & H2020

- Program: Leverhulme Trust
- Project acronym:
- Project title: A novel approach to functional classification of retinal ganglion cells
- Duration: 2017-2020
- Coordinator: Evelyne Sernagor, Institute of Neuroscience (ION, Newcastle, UK)

- Other partners:

  Melissa Bateson Institute of Neuroscience (ION, Newcastle, UK)

  Matthias Hennig Institute for Adaptive and Neural Computation (ANC, School of Informatics University of Edinburgh, UK)

- Abstract: Vision begins with photoreceptors converting light from different parts of the visual scene into electrical signals, compressing our visual world into a parsimonious code of impulses at the retinal output level, the retinal ganglion cells (RGCs). This information is sent to the brain via only ≈1m RGCs (45,000 in mouse). Amazingly, the brain can recreate images from interpreting these "barcodes" or trains of impulses. This ability is partly due to the astonishing functional diversity of RGCs, each interpreting a different feature of the visual scene. It is all these parallel streams of information that impart the complexity of visual scenes to our brain visual areas. At present, at least 30 RGC subtypes have been identified. Classification is typically based on common anatomical features, or on basic functions (e.g. whether cells respond to the onset or offset of the light, or whether they are sensitive to motion direction) and it has recently progressed to include molecular markers. Recent studies have successfully characterised common physiological properties between RGCs sharing gene expression, suggesting that their molecular signature may indeed be a good indicator of function. However, according to mouse genetics repositories (e.g., the Allen Brain Project) many genes are expressed in subpopulations of RGCs for which we have no phenotype yet. Genes that are expressed in most RGCs probably do not reflect specific functional populations, but some other genes are expressed only in sparse RGC groups. Each gene-specific class exhibits a distinct spatial mosaic pattern across the retina, suggesting that the cells belong to a common group. Many classes, even sparse, exhibit asymmetric distributions across the retina, e.g., with larger numbers on the ventral or dorsal side, suggesting specific roles in ecological vision, e.g., specialised in detecting moving objects in the sky (ventral) or on the ground (dorsal).

9.4. International Initiatives

9.4.1. International Research Network to Study Predictive Coding in the Retina

Program: CHILEAN SUPPORT OF INTERNATIONAL NETWORKING BETWEEN RESEARCH CENTRES

Project title: International Research Network to Study Predictive Coding in the Retina

Duration: 2018-2020

Coordinator: Maria-José Escobar, Advanced Center for Electrical and Electronic Engineering, Universidad Técnica Federico Santa María, Chile

Other partners:

Advanced Center for Electrical and Electronic Engineering (Valparaiso, Chili)

Centro Interdisciplinario de Neurociencia de Valparaíso (CINV, Valparaíso, Chile)

Abstract: The retina, a well-structured multilayer neural system, encodes the visual information of the environment from an input of photon flux to a series of electrical pulses that are ultimately readout by the brain to create perception and program motor actions. The retina, from an engineering point of view, can be seen as a series of circuits computing visual features from the visual world in parallel encoding only informative inputs that are then sent to the brain. Regarding all the visual features that can be detected from the outer world, motion processing represents a fundamental visual computation ruling many visuomotor behaviours. Motion sensitive neurons have been early reported in the retina, but recently additional features have been added to the pool of capabilities present in this organ: especially motion direction selectivity and predictive coding. Motion processing presents predictive coding characteristics, in the sense that there is an anticipatory response of the visual system when an object in motion follows a trajectory in the visual field. Motion anticipation is fundamental for survival. Interestingly, this mechanism, observed in the visual cortex, has been also

reported in the retina. Understanding how the visual system accumulates information along a certain trajectory raises fundamental questions about neural computation, its dynamics, and implementation. This understanding could be also extended to new algorithms to image/video processing, and also, autonomous navigation of robots.

In this project, we propose the formal establishment of a collaborative network between the AC3E Biomedical System group (AC3E-UTFSM), Centro Interdisciplinario de Neurociencia de Valparaíso (CINV -UV) and Biovision team (Inria Sophia-Antipolis Mediterranée), gathering together skills related with physiological recording in the retina, data analysis and theoretical tools to implement functional and biophysical models. This network aims to study the anticipatory response observed in the mammalian retina, characterizing its underlying mechanisms and the predictive coding capabilities present in this part of the nervous system.

9.4.2. Inria International Partners

Institute of Neuroscience (ION, Newcastle, UK)

Institute for Adaptive and Neural Computation (ANC, School of Informatics University of Edinburgh, UK)

Universidad Tecnico Federico Santa María (Electronics Engineering Department, Valparaíso, Chile)

Centro Interdisciplinario de Neurociencia de Valparaíso (CINV, Valparaíso, Chile)

University of Genoa (DIBRIS, Genoa, Italy)

9.5. International Research Visitors

9.5.1. Visits of International Scientists

- Harold E. Bedell (University of Houston College of Optometry, USA)
- Fabio Anselmi (University of Genoa, Italy)
- Jennifer Sarah Goldman (McGill University, Montreal Neurological Institute and Hospital, Canada)

9.5.1.1. Internships

- Jenny Kartsaki, Greek Msc student, March-August 2017. Now a PhD student supervised by Bruno Cessac.

CAMIN Team

8. Partnerships and Cooperations

8.1. 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)".

8.2. European Initiatives

8.2.1. 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.

8.3. International Initiatives

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

8.3.1.1. CACAO

Lower limb electrical stimulation for function restoration University of Brasilia, UNB (Brazil)
Núcleo de Tecnologia Assistiva, Acessibilidade e Inovação (NTAAI)
https://team.inria.fr/cacao/
Start year: 2016

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 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.

8.3.2. Participation in Other International Programs

Programme Ciensia Sem Fronteiras CAPES, avec l'Univeristé Brasilia (chercheur invité).

8.4. International Research Visitors

8.4.1. Visits of International Scientists

Antonio Lanari Padilha Bo spent one month in CAMIN in July 2017 as invited reseracher (LIRMM funding).
Adriana Mendes, M2 Univ Lisboa spent 9 months (funded by Erasmus) from october 2016 to june 2017
Lucas Fonseca, PhD student in Brasilia University, spent 9 months in CAMIN.

8.4.2. Visits to International Teams

Thomas Guiho, Aurora program with Norway, short stays to initiate collaborations

8.4.2.1. Research Stays Abroad

Christine Azevedo spent 1 month in Brasilia University between october and december in the context of CACAO associate team with a grant from CAPES for invited researchers.

GALEN Project-Team

9. Partnerships and Cooperations

9.1. National Initiatives

9.1.1. 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: ANR JCJC

Project acronym: MajIC

Project title: Majorization-Minimization Algorithms for Image Computing

Duration: 2017-2021

Coordinator: E. Chouzenoux

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

9.1.2. Others

Program: CNRS MASTODONS
Projet acronym: TABASCO
Project title: Traitement du bruit non Gaussien en spectroscopie
Duration: 2016-2018
Coordinator: E. Chouzenoux

Program: CNRS-CEFIPRA
Project acronym: NextGenBP
Project title: Looking Beyond Backpropagation in Deep Learning
Duration : 2017-2019
Coordinator: E. Chouzenoux

9.2. European Initiatives

9.2.1. FP7 & H2020 Projects

9.2.1.1. 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)

Institute of Communication and Computer Systems (Greece)

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.

9.2.1.2. 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.'

9.2.2. I-SUPPORT

Title: ICT-Supported Bath Robots

Project-Team GALEN 17

Program: 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, ICTsupported 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.

9.3. International Initiatives

9.3.1. Inria International Partners

9.3.1.1. Informal International Partners

Sup'Com Tunis - Collaborative research with Amel Benazza-Benhayia. Collaboration Topic: Multi-spectral imaging.

Universidad Tecnica Federico Santa Maria - Collaborative research with Luis M. Briceno Arias. Collaboration Topics: Variational approaches for monotone inclusions.

University of Patras, Greece - Collaborative research with V. Megalooikonomou. Collaboration Topic: Biosignal analysis.

University of Pennsylvania - Collaborative research with Aristeidis Sotiras. Collaboration Topic: Higher Order Graphs in biomedical image analysis.

9.4. International Research Visitors

9.4.1. Visits of International Scientists

9.4.1.1. Internships

The following international students did an internship at CVN in the past year:
Huidong Liu, Stony Brook University, NY (may 2017)
Zhixin Shu, Stony Brook University, NY (may 2017)
Vu Nguyen, Stony Brook University, NY (jul. 2017)
Han Anh Vu Le, Houston University (jul. 2017)
Anisia Florescu, University of Galati Romania (feb. 2017)
Vyacheslav Dudar, Taras Sheuchenko National University of Kyiv (nov. 2017)
Carla Bertolocchi, Universita degli studi di Modena e Reggio Emilia (dec. 2017)
Yana Vedel, Taras Sheuchenko National University of Kyiv (dec. 2017)

MATHNEURO Team

5. Partnerships and Cooperations

5.1. European Initiatives

5.1.1. FP7 & H2020 Projects

5.1.1.1. 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.

5.2. International Research Visitors

5.2.1. Visits of International Scientists

Invitation of Antoni Guillamon (as part of a sabbatical semester), Polytechnic University of Catalonia (Spain), March-April 2017

Invitation of Vivien Kirk, University of Auckland (New Zealand), April 2017

Invitation of Jeff Moehlis, University of California Santa Barbara (USA), April 2017

Invitation of Martin Wechselberger, University of Sydney (Australia), August 2017

Invitation of Cian O'Donnell, University of Bristol (UK), September 2017

invitation of Moritz Helias and Tobias Kuehn, University of Aachen and Juelich Research Center (Germany), September 2017

Invitation of David Terman (as part of a sabbatical semester), Ohio State University (USA), October 2017

Invitation of Zack Kilpatrick, University of Colorado Boulder (USA), November 2017

5.2.1.1. Internships

Leila Bekri, co-supervised by Romain Veltz and Hélène Marie (IPMC), Feb.-Apr. 2017

Raphael Forquet, co-supervised by Romain Veltz and Hélène Marie (IPMC), until Jan. 2017

Anna Song, supervised by Olivier Faugeras, Feb.-June 2017

5.2.2. Visits to International Teams

Visit of Mathieu Desroches to Mirela Domijan (University of Liverpool, UK) in March 2017

Visit of Mathieu Desroches to Daniele Avitabile (University of Nottingham, UK) in August 2017

Visit of Fabien Campillo & Mathieu Desroches to Serafim Rodrigues (BCAM, Bilbao, Spain) in September 2017

Visit of Mathieu Desroches to Serafim Rodrigues (Basque Center for Applied Mathematics, Bilbao, Spain) in December 2017

5.2.2.1. Research Stays Abroad

One-month research stay of Mathieu Desroches at BCAM (Bilbao, Spain) on an invited professor scholarship to work with Serafim Rodrigues, June 2017

MIMESIS Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

9.1.1. Institute of Image-Guided Surgery (IHU) Strasbourg

The Institute of Image-Guided Surgery of Strasbourg develops innovative surgery to deliver personalized patient care, combining the most advanced minimally invasive techniques and the latest medical imaging methods.

Project *CIOS Alpha Fusion* funded by IHU Strasbourg has started at the beginning of 2017. The goal of the project is to develop a solution for real-time, accurate, image fusion between 3D anatomical data and 2D X-ray images. This requires to spatially align these two imaging datasets with each other, knowing that a deformation has occurred between the 2 acquisitions. We consider two different cases, of increasing scientific complexity: static image fusion using 2 fluoroscopic images taken at 2 different angles, and dynamic image fusion using a single fluoroscopic image. We also consider two additional scenarios: in the first one, a 3D image or a 3D model has been obtained from a preoperative CTA or MRA while in the second scenario it has been acquired using an intra-operative contrast-enhanced CBCT. In the second case, tissue deformation between the 2D and 3D data is significantly reduced.

The project team involves scientists from the MIMESIS team at Inria, engineers from Siemens as industrial partner, and clinicians from the NHC hospital and IHU.

9.1.2. Research and Clinical Partners

At the regional level, the MIMESIS team collaborates with

ICube Automatique Vision et Robotique (AVR): We have been collaborating 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): MIMESIS 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 Hôpital Civil, Strasbourg: since 2014 we have been working with Prof. David Gaucher, an ophthalmologist and 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.

9.2. National Initiatives

9.2.1. ADT (Action de Développement Technologique)

Team MIMESIS received a support for the development of the SOFA framework through two ADTs:

DynMesh (Sep 2015 – Aug 2017): The objectives of the 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.

ASNAP (*Accélération des Simulations Numériques pour l'Assistance Peropératoire*, Jan 2017 – Dec 2018). We are partners of ADT ASNAP with principal investigator being Inria team CAMUS. The goal of the project is a significant acceleration of physics-based simulations developed by MIMESIS. The technologies such as Apollo, XFOR, ORWL, developed by team CAMUS are used to optimize the execution of different components of framework SOFA, taking into account the possibilities provided by modern CPUs and GPGPUs. Since team CAMUS is also located in Strasbourg, the project benefits from the geographical location: an engineer Maxim Mogé was recruited, starting from 01/01/2017 and he shares his time between the two teams.

9.2.2. ANR (Agence Nationale de la Recherche)

MIMESIS participates in the following ANR projects:

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. Retinal 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.

EVEREST: The overall objective of the EVEREST project is thus to bring a leap forward in factorization of large sparse tensors in order to improve the accessibility, completeness and reliability of real-world KBs. This line of research could have a huge impact in industry (Semantic Web, biomedical applications, etc.). For that reason, Xerox Research Center Europe is supporting this project and will supply data, provide expertise and ease industrial transfer. This proposal is also consistent with the long-term research direction of its principal partner, Heudiasyc, since it contributes in several aspects of the 10 years LabEx program on *Technological Systems of Systems* started in 2011.

Coordinator: IHU Strasbourg

Partners: Inria, IRCAD, University of Strasbourg, Siemens Healthcare, Karl Storz GmbH., University of Twente

9.2.3. Inria Collaborations

MIMESIS is closely connected to the SOFA Consortium, created by Inria in November 2015 with the objective to support the SOFA community and encourage contributions from new SOFA users. The Consortium should also be a way to better answer to the needs of academic or industrial partners. MIMESIS actively participates at the development of SOFA and contributed to the evolution of the framework. Moreover, MIMESIS also participates in an initiative aiming at verification and validation of codes and algorithms of SOFA.

Further, MIMESIS actively collaborates with the following Inria teams:

MAGRIT: The team at Inria Grand Est focuses on research in computer vision and is also actively involved in computer-based solutions for the planning or the simulation of interventional radiology procedures, with a strong collaboration with the CHU in Nancy. We collaborate with MAGRIT in the area of interventional radiology and augmented reality. Currently, two PhD thesis are co-supervised by researcher from Magrit: the PhD thesis of Jaime Garcia Guevara and Raffaella Trivisonne.

CAMUS: The team focuses on developing, adapting and extending automatic parallelizing and optimizing techniques, as well as proof and certification methods, for the efficient use of current and future multi-core processors. Currently, we collaborate with team CAMUS on parallelization of framework SOFA in ADT project ASNAP.

DEFROST: The team conducts research in soft robotics. We continue mutual interaction with DEFROST mainly in the context of contact modeling.

9.2.4. National Collaborations

At the national level, the MIMESIS team collaborates with:

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.

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.

Hôpital Paul-Brousse: a hospital in South Paris. We collaborate with *Centre Hépato-Biliaire* via the co-supervision of the Ph.D. thesis of Nicolas Golse, MD, who is a surgeon at the center.

9.3. European Initiatives

9.3.1. FP7 & H2020 Projects

Program: H2020, Innovative Training Network, MSCA

Project acronym: HiPerNav

Project title: High performance soft tissue navigation

Coordinator: Oslo University Hospital

Other partners: SINTEF Trondheim, University of Bern

Abstract: HiPerNav is an Innovative Training Network (ITN) funded through a Marie Skłodowska-Curie grant. There will be 14 fully funded and 2 partially funded PhD's working on the project. The project aims to improve soft tissue navigation through research and development, to improve several bottleneck areas:

- Creating effective pre-operative model(s) and planning
- Faster and more accurate intra-operative model updates
- Faster and more accurate model-to-patient registration
- More intuitive user-interaction and effective work flow
- Usage of high performance computing (e.g. GPU)

9.3.2. Informal Collaborations

University of Twente: Thanks to our clinical partner IHU, we collaborate with Prof. Stefano Stramigioli, head of a group at Robotics and Mechatronics laboratory.

Faculty of Informatics, Masaryk University, Czech Republic: We collaborate on simulation of living cells in fluorescent microscopy. The collaboration resulted in a presentation at an international conference [29] and a journal paper [18].

Team Legato, University of Luxembourg: we have an active collaboration with Prof. Stéphane Bordas on error estimation in real-time simulations of deformable objects. The collaboration resulted in a common publication [16].

9.4. International Initiatives

The MIMESIS team actively collaborates with following international partners:

CIMIT & Harvard Medical School, Boston, USA: We collaborate on a project REBOASim in the contect of interventional radiology, , in particular the design and development of a hardware interface for tracking catheters and guidewires. The common DoD project REBOASim focuses on development of the physics-based models for catheter and guidewire motion, blood flow and graphical rendering towards a novel simulator for REBOA that will include physical vascular access, simulated passage of the IR instruments into the aorta with accompanying training/educational content, device withdrawal and closure: Duration of the project: Feb 2017 – Feb 2019.

9.5. International Research Visitors

9.5.1. Visits of International Scientists

From Feb 2017 to July 2017, **Prof. Adam Wittek** joined team MIMESIS as a visiting scientist. Prof. Wittek is with Intelligent Systems for Medicine Laboratory, School of Mechanical and Chemical Engineering at the University of Western Australia, Perth. His research focuses on patient-specific biomechanical modeling and he has published an important number of high-quality publications on this topic with more than 2,000 citations.

During his stay, Prof. Wittek provided his highly valuable expertise in various domains of patient-specific simulations and advanced techniques of modeling of deformations in soft tissues such as meshless methods. He was also involved in projects related to insertions of flexible needles into soft tissues.

9.5.1.1. Internships

From Jul 2017 to Dec 2017, Vincent Magnoux, a Canadian PhD student from École polytechnique de Montréal, joined MIMESIS as an international intern. During his stay, he has worked on implementing and validating a meshless method for computing organ deformation. This work also involved exploring methods to accelerate these computations on multi-core systems for an interactive simulation.

MNEMOSYNE Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

9.1.1. PsyPhINe

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 at exploring 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. We've organized our third national conference in Nancy gathering speakers from philosophy, robotics, art and psychology and closed a three years cycle. The group now aims at publishing a book gathering text from all the invited speakers.

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 SOMA (PRCI)

Participant: Nicolas Rougier.

This new project is a convergence point between past research approaches toward new computational paradigms: adaptive reconfigurable architecture, cellular computing, computational neuroscience, and neuromorphic hardware:

1. SOMA is an adaptive reconfigurable architecture to the extent that it will dynamically re-organize both its computation and its communication by adapting itself to the data to process.
2. SOMA is based on cellular computing since it targets a massively parallel, distributed and decentralized neuromorphic architecture.
3. SOMA is based on computational neuroscience since its self-organization capabilities are inspired from neural mechanisms.
4. SOMA is a neuromorphic hardware system since its organization emerges from the interactions between neural maps transposed into hardware from brain observation.

This project represents a significant step toward the definition of a true fine-grained distributed, adaptive and decentralized neural computation framework. Using self-organized neural populations onto a cellular machine where local routing resources are not separated from computational resources, it will ensure natural scalability and adaptability as well as a better performance/power consumption tradeoff compared to other conventional embedded solutions.

9.2.3. 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.

9.2.4. 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.

This year, we have designed and realised new experiments in order to better caracterize the effect of 1800 Mz RF field of GSM on the spontaneous activity of in-vitro cortical cell cultures. In the current study, our aim was to highlight a dose-response relationship for this effect. To do this, we have recorded the spontaneous bursting activity of cortical neurons cultures on multi-electrodes arrays. We have thus shown that at SAR (Specific Absorption Rate) ranging from 0.01 to 9.2 W/kg the signal elicited a clear decrease in bursting rate during the RF exposure phase that lasted even after the end of the exposure. Moreover, the effect grew larger with increasing SAR, and the amplitude of the change was greater with a GSM signal than with a continuous wave RF field of the same energy level. These experimental findings provide evidence for clear effects of RF signals on the bursting rate of neuronal cultures.

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

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 worked on a model of a dopaminergic region, VTA, central for reinforcement learning in the basal ganglia.

9.4. International Research Visitors

9.4.1. Visits of International Scientists

Prof. Chakravarthy Srinivasa

Date: Nov-Dec 2017

Institution: IIT Madras, Chennai (India)

Johannes Twiefel

Date: 10 days, Sep 2017; 1 week, Nov 2017.

Institution: University of Hamburg, Germany.

Luiza Mici

Date: 10 days, Sep 2017.

Institution: University of Hamburg, Germany.

9.4.1.1. Internships

Remya Sankar

Date: June 2017 - Dec 2017

Institution: IIIT Hyderabad (India)

NEUROSYS Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

Within 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*) observing electroencephalographic activity of humans during motor tasks. Contact in Neurosys is Laurent Bougrain.

8.2. National Initiatives

Inria project-Lab BCI-LIFT, Brain-Computer Interfaces: Learning, Interaction, Feedback, Training, Maureen Clerc, 2015-2018, 7 Inria project-teams (Aramis, Athena, Demar, Hybrid, Mjolnir, Neurosys, Potioc), university of Rouen, Dycog team at Centre de Recherche en Neurosciences de Lyon.

BCI-LIFT is a research initiative 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. With this concern of usability as our driving objective, we build non-invasive systems that benefit from advanced signal processing and machine learning methods, from smart interface design, and where the user immediately receives supportive feedback. What drives this project is the concern that a substantial proportion of human participants is currently categorized “BCI-illiterate” because of their apparent inability to communicate through BCI. Through this project we aim at making it easier for people to learn to use BCI, by implementing appropriate machine learning methods and developing user training scenarios.

8.3. International Initiatives

8.3.1. Inria International Partners

8.3.1.1. Informal International Partners

- We have an ongoing collaboration with Prof. Motoharu Yoshida at 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).
- We also collaborate with Anton Popov (Kiev Polytechnic Institute, Ukraine) on feature extraction of brain signal and deep learning (L. Bougrain).

8.4. International Research Visitors

8.4.1. Visits of International Scientists

- Anton Popov, Ass. Prof, Kiev Polytechnic Institute, Ukraine, 5 weeks (May 2017)
- Yevgeniy Karplyuk, Ass. Prof, Kiev Polytechnic Institute, Ukraine, 3 weeks (May 2017)
- Widodo Budiharto, Full Prof, university of Binus, Indonesia, 1 week (Jan 2017)

8.4.1.1. Internships

- Oleksii Avilov, Erasmus+, Kiev Polytechnic Institute, Ukraine, Jan-Jul 2017
- Ivan Kotiuchi, Erasmus+, Kiev Polytechnic Institute, Ukraine, Jan-Jul 2017

PARIETAL Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

9.1.1. CoSmic project

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

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

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 (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-telescopes, the goal consists in extracting high temporal resolution information in order to study fast transient events.

9.1.2. BrainAMP project

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

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

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.

9.1.3. 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.

9.1.4. 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 activation. 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.

9.1.5. HighDimStat project

Participants: Bertrand Thirion [Correspondant], Jérome-Alexis Chevalier, Joseph Salmon.

This is a Digicosme project (2017-2020) and a collaboration with Joseph Salmon (Telecom Paritech).

The HiDimStat project aims at handling uncertainty in the challenging context of high dimensional regression problem. Though sparse models have been popularized in the last twenty years in contexts where many features can explain a phenomenon, it remains a burning issue to attribute confidence to the predictive models that they produce. Such a question is hard both from the statistical modeling point of view, and from a computation perspective. Indeed, in practical settings, the amount of features at stake (possibly up to several millions in high resolution brain imaging) limit the application of current methods and require new algorithms to achieve computational efficiency. We plan to leverage recent developments in sparse convex solvers as well as more efficient reformulations of testing and confidence interval estimates to provide several communities with practical software handling uncertainty quantification. Specific validation experiments will be performed in the field of brain imaging.

9.1.6. AMPHI project

Participants: Bertrand Thirion [Correspondant], Joseph Salmon, Antonio Andre Monteiro Manoel.

This is a Digicosme project (2017-2020) and a collaboration with Joseph Salmon (Telecom Paritech) and Lenka Zdeborova (CEA, IPhT).

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 neuroimaging 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 (AMP) 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. AMPHI 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.

9.1.7. CDS2

Participants: Bertrand Thirion [Correspondant], Gaël Varoquaux, Guillaume Lemaitre, Joris Van Den Bossche.

CDS2 is an "Strategic research initiative" 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 Guillaume Lemaitre and an engineer position for Joris van den Bossche.

9.2. National Initiatives

9.2.1. ANR

9.2.1.1. 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.

9.2.1.2. Niconnect project

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

- **Context:** The NiConnect project (2012-2017) arises from an increasing need of medical imaging tools to diagnose efficiently brain pathologies, such as neuro-degenerative and psychiatric diseases or lesions related to stroke. Brain imaging provides a non-invasive and widespread probe of various features of brain organization, that are then used to make an accurate diagnosis, assess brain rehabilitation, or make a prognostic on the chance of recovery of a patient. Among different measures extracted from brain imaging, functional connectivity is particularly attractive, as it readily probes the integrity of brain networks, considered as providing the most complete view on brain functional organization.
- **Challenges:** To turn methods research into popular tool widely usable by non specialists, the NiConnect project puts specific emphasis on producing high-quality open-source software. NiConnect addresses the many data analysis tasks that extract relevant information from resting-state fMRI datasets. Specifically, the scientific difficulties are *i)* conducting proper validation of the models and tools, and *ii)* providing statistically controlled information to neuroscientists or medical doctors. More importantly, these procedures should be robust enough to perform analysis on limited quality data, as acquiring data on diseased populations is challenging and artifacts can hardly be controlled in clinical settings.
- **Outcome of the project:** In the scope of computer science and statistics, NiConnect pushes forward algorithms and statistical models for brain functional connectivity. In particular, we are investigating structured and multi-task graphical models to learn high-dimensional multi-subject brain connectivity models, as well as spatially-informed sparse decompositions for segmenting structures from brain imaging. With regards to neuroimaging methods development, NiConnect provides systematic comparisons and evaluations of connectivity biomarkers and a software library embedding best-performing state-of-the-art approaches. Finally, with regards to medical applications, the NiConnect project also plays a support role in on going medical studies and clinical trials on neurodegenerative diseases.
- **Consortium**
  - Parietal Inria research team: applied mathematics and computer science to model the brain from MRI
  - LIF INSERM research team: medical image data analysis and modeling for clinical applications

- CATI center: medical image processing center for large scale brain imaging studies
- Henri-Mondor hospital neurosurgery and neuroradiology: clinical teams conducting research on treatments for neurodegenerative diseases, in particular Huntington and Parkinson diseases
- Logilab: consulting in scientific computing

9.3. European Initiatives

9.3.1. FP7 & H2020 Projects

9.3.1.1. HBP

Title: The Human Brain Project

Programm: FP7

Duration: October 2013 - September 2016

Coordinator: EPFL

Partners:

- Inria contact: Olivier Faugeras
- Understanding the human brain is one of the greatest challenges facing 21st century science. If we can rise to the challenge, we can gain profound insights into what makes us human, develop new treatments for brain diseases and build revolutionary new computing technologies. Today, for the first time, modern ICT has brought these goals within sight. The goal of the Human Brain Project, part of the FET Flagship Programme, is to translate this vision into reality, using ICT as a catalyst for a global collaborative effort to understand the human brain and its diseases and ultimately to emulate its computational capabilities. The Human Brain Project will last ten years and will consist of a ramp-up phase (from month 1 to month 36) and subsequent operational phases. This Grant Agreement covers the ramp-up phase. During this phase the strategic goals of the project will be to design, develop and deploy the first versions of six ICT platforms dedicated to Neuroinformatics, Brain Simulation, High Performance Computing, Medical Informatics, Neuromorphic Computing and Neurorobotics, and create a user community of research groups from within and outside the HBP, set up a European Institute for Theoretical Neuroscience, complete a set of pilot projects providing a first demonstration of the scientific value of the platforms and the Institute, develop the scientific and technological capabilities required by future versions of the platforms, implement a policy of Responsible Innovation, and a programme of transdisciplinary education, and develop a framework for collaboration that links the partners under strong scientific leadership and professional project management, providing a coherent European approach and ensuring effective alignment of regional, national and European research and programmes. The project work plan is organized in the form of thirteen subprojects, each dedicated to a specific area of activity. A significant part of the budget will be used for competitive calls to complement the collective skills of the Consortium with additional expertise.

9.4. International Initiatives

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

9.4.1.1. MetaMRI

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

International Partner (Institution - Laboratory - Researcher):

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

Start year: 2015

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

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

9.4.1.2. 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: 2016

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.

9.5. International Research Visitors

9.5.1. Visits of International Scientists

Parietal has welcome François Meyer, Univ Colorado at Boulder, for a six months visit (Jan-June 2017), funded by a D'Alembert fellowship of Paris Saclay University. The project of François is to assess novel statistical models of functional connectivity based on the generalized resistivity model he has developed within a graph theoretical framework.

9.5.2. Visits to International Teams

9.5.2.1. Research Stays Abroad

9.5.2.1.1. Denis Engemann

has spent two months in Boston (April-May) with the MEG Core lab, Athinoula A. Martinos Center (MGH/Harvard-MIT) working on functional connectivity methods and population analysis for MEG.

9.5.2.1.2. Arthur Mensch

has spent 3 months in Japan (Sept-Dec) with NTT, working on dynamic time warping problems with Mathieu Blondel.

9.5.2.1.3. Jérome Dockès

has spent two months with Poldracklab at Stanford, as part of the MetaMRI associated team. He has worked on the statistical relationships between neuroscientific concepts (whether anatomical or cognitive) and brain activation loci.

VISAGES Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

9.1.1. 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 representations, in order to reconstruct the diffusion signal from fewer measurements, using results from the compressive sensing theory.

9.2. National Initiatives

9.2.1. Projet Fondation de France: PERINE

Participants: Élise Bannier, Isabelle Corouge, Julie Coloigner, Maia Proisy, 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 PhD started in January 2017 to process the functional MRI data of this project and Julie Coloigner was hired as a post doc to work on the Diffusion and ASL data.

9.2.2. Projet Fondation de France: EPMR-MA

Participants: Pierre-Yves Jonin, Élise Bannier, Christian Barillot, Quentin Duché.

This project evaluates memory effects in healthy adults and in patients presenting cognitive impairments using BOLD fMRI and diffusion MRI. The inclusions of patients started in 2016 and all inclusions will be over by the end of 2017. Quentin Duché was hired to process the functional MRI and diffusion data end of 2016 and his contract was extended until May 2018.

9.2.3. 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 techniques 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 goa.

9.2.4. Fondation pour la recherche médicale (FRM) - Project "Hybrid EEG/IRM Neurofeedback for rehabilitation of brain pathologies

Participants: Élise Bannier, Jean-Marie Batail, Isabelle Bonan, Isabelle Corouge, Jean-Christophe Ferré, Jean-Yves Gauvrit, Pierre Maurel, Mathis Fleury, Giulia Lioi, Christian Barillot.

The goal of this project is to make full use of neurofeedback (NF) paradigm in the context of brain rehabilitation. The major breakthrough will come from the coupling associating functional and metabolic information from Magnetic Resonance Imaging (fMRI) to Electro-encephalography (EEG) to “optimize” the neurofeedback protocol. We propose to combine advanced instrumental devices (Hybrid EEG and MRI platforms), with new hybrid Brain computer interface (BCI) paradigms and new computational models to provide novel therapeutic and neuro-rehabilitation paradigms in some of the major mental and neurological disorders of the developmental and the aging brain (stroke, language disorders, Mood Depressive Disorder (MDD), ...). Though the concept of using neurofeedback paradigms for brain therapy has somehow been experimented recently (mostly through case studies), performing neurofeedback through simultaneous fMRI and EEG has almost never been done before so far (two teams in the world including us within the HEMISFER CominLabs project). This project will be conducted through a very complementary set of competences over the different involved teams: VISAGES U1228, HYBRID and PANAMA Teams from Inria/Irisa Rennes and EA 4712 team from U. of Rennes I.

9.2.5. 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 epidemiologic 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, all subjects have been included. H. Snoussi is working in the scope of his PhD thesis on diffusion imaging in the spinal cord starting with distortion correction. The results of this study were presented at the ESMRMB 2017 conference [38].

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. Preliminary results were presented at the ESMRMB and ECTRIMS 2017 conferences [33] [43].

9.2.6. Competitivity Clusters

9.2.6.1. The HEMISFER Project

Participants: Élise Bannier, Jean-Marie Batail, Isabelle Bonan, Isabelle Corouge, Claire Cury, Jean-Christophe Ferré, Jean-Yves Gauvrit, Marsel Mano, Pierre Maurel, Saman Norzade, Lorraine Perronnet, Christian Barillot.

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

9.2.6.2. 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 U1228 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

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

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.

9.2.6.3. OFSEP

Participants: 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.

9.3. European Initiatives

9.3.1. Collaborations in European Programs, Except FP7 & H2020

- **OpenAire-Connect**
  The OpenAire-Connect H2020 project 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.
  - Participants: Christian Barillot; Michael Kain; Camille Maumet
  - Partners: PI: CNR, Italy; Athena Research And Innovation Center In Information Communication & Knowledge Technologies, Greece; Uniwersytet Warszawski, Poland; JISC LBG, UK; Universitaet Bremen, Germany; Universidade Do Minho, Portugal; CNRS (Visages, Creatis), France; Universita Di Firenze, Italy; Institut De Recherche Pour Le Developpement (IRD), France; European Organization For Nuclear Research (CERN), Switzerland; International Center For Research On The Environment And The Economy, Greece

  - Budget: 2M € (120k€ for CNRS)

- **Health**
  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".
  - Participants: Christian Barillot, Michael Kain
  - Partners: see https://www.eithealth.eu/partners

9.4. International Initiatives

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

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.

9.4.2. Inria International Partners

9.4.2.1. Informal International Partners

- Collaboration with the Department of Computer Science, University of Verona: Emmanuel Caruyer visited the group of Gloria Menegaz and Alessandro Daducci in the context of the 2017 School on Brain Connectomics (http://brainconnectomics.org/).
- Collaboration with Neuropoly, Polytechnique Montreal: Haykel Snoussi is visiting the group of Julien Cohen-Adad and received an Inria-MITACS fellowship for a 3 months period (Nov. 2017-Jan. 2018). He will be working on the processing of diffusion-weighted images of multiple sclerosis patients' spinal cord in the context of the EMISEP project.

- Collaboration with Department of Mathematics and Statistcis at the Politechnico di Milano, Italy (Simone Vantini, Aymeric Stamm): Lorenzo Rota did visit the team between Oct. 2016 to March 2017 for his Tesi (Master degree) on "Application of shape analysis and functional data analysis tools on fiber bundles analysis".

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. 2017.

9.5.2. Visits to International Teams

- Sudhanya Chatterjee visited the Computational Radiology Lab, the Boston Children's Hospital, at Harvard University in Nov. 2017. This stay was funded by the international program of University of Rennes 1. Christian Barillot and Olivier Commowick visited the same lab for a 3 days workshop in the context of the Associate Team.
- Haykel Snoussi visited the NeuroPoly Lab for 3 months from Nov. 2017. This stay was funded by the international program of University of Rennes 1.

AIRSEA Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

STAREX - Clémentine Prieur obtained a 8kE two-years funding for a local project on risk by the Labex Persyval. Philippe Naveau (from LSCE, Paris) visited the team during one month in spring 2017 in this context.

C. Prieur is co-leader of work-package 3 of the cross-disciplinary-project Trajectories from Idex Grenoble.

9.2. National Initiatives

9.2.1. ANR

COCOA: COmprehensive Coupling approach for the Ocean and the Atmosphere. PI: E. Blayo. Duration: 4 years (Jan. 2017 - Dec. 2020). Other partners: Laboratoire des Sciences du Climat et de l'Environnement (UMR8212, Gif-sur-Yvette), Laboratoire de Météorologie Dynamique (UMR8539, Paris), Laboratoire d'Océanographie Physique et Spatiale (UMR6523, Brest), Centre National de Recherche Météorologique (UMR3589, Toulouse), Cerfacs (Toulouse). This project aims at revisiting the overall representation of air-sea interactions in coupled ocean-atmosphere models, and particularly in climate models, by coherently considering physical, mathematical, numerical and algorithmic aspects.

C. Prieur and E. Arnaud are involved as experts in project High-Tune http://www.agence-nationale-recherche.fr/Projet-ANR-16-CE01-0010 funded by ANR.

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 6.6 .

C. Prieur chaired GdR MASCOT NUM 2010-2017, 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.

LEFE/GMMC CASIS, Coupled Assimilation Strategies for the Initialisation of an ocean- atmospheric boundary layer System, A. Vidard. en collaboration avec Mercator océan

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 6.6 .

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 Center 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

F. Lemarié is involved in the Inria associate team NEMOLOCO with Santiago University (Chile)

9.4.1. Inria International Partners

9.4.1.1. Informal International Partners

C. Prieur collaborates with Jose R. Leon (UCV, Central University of Caracas), who was funded by the international Inria chair program. He moved in June 2017 to Montevideo, Uruguay, and the collaboration goes on.

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.

F. Lemarié and L. Debreu collaborate with Hans Burchard from the Leibniz-Institut für Ostseeforschung in Warnemünde (Germany).

F. Lemarié and L. Debreu collaborate with Knut Klingbeil from the Dept. of Mathematics of the University of Hamburg (Germany).

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:

Universidad de Valparaiso (Chile) - CIMFAV - Facultad de Ingeniería - Karine Bertin

Universidad Central de Venezuela (Venezuela) - Departamento de Matemáticas - Jose León

Duration: 2016 - 2017

Start year: 2016

See also: http://sidre.cimfav.cl/

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 of International Scientists

Werner Bauer (Imperial College, London) spent one week in the AIRSEA team from October 9th to October 13th to work on mimetic schemes for atmospheric models.

9.5.1.1. Internships

Gino Rivano from the university of Valparaiso (Chile) : « High-resolution numerical modeling of the oceanic circulation in central Chile: application to larvae dispersal » (advisor: F. Lemarié), 3 months in the framework of the Inria MERIC center of excellence.

9.5.2. Visits to International Teams

9.5.2.1. Research Stays Abroad

C. Prieur visited during two weeks Karine Bertin in Chile. CIMFAV – Facultad de Ingeniería Universidad de Valparaíso.

F.-X. Le Dimet visited Florida State University, Dpt of Mathematics during two weeks in May 2017

F.-X. Le Dimet visited Harbin Institute of Technology, Dpt of Mathematics during 10 days in July 2017

ANGE Project-Team

9. Partnerships and Cooperations

9.1. National Initiatives

9.1.1. 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).

9.1.2. 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 optimisation, 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 horisontal 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.

9.1.3. ANR MIMOSA (2014–2017)

Participants: 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 modelling 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 characterisation of source events, which we will use to improve noise tomography, and seismic monitoring.

9.1.4. ANR CHARMS (2016-2020)

Participant: Cindy Guichard.

ANR project call: Transformations et inter-conversions énergétiques

Project acronym: CHARMS

Project title: Modèles de réservoirs quantitatifs pour les systèmes hydrothermaux complexes

Coordinator: Simon Lopez (BRGM)

Funding: 73k euros for LJLL (in 767k euros for the whole project)

CHARMS ANR project is focused on the mathematical methods and software tools dedicated to the simulation of the physical models issued from geothermal engineering. The final objective is the achievement of a highly parallel code, validated on realistic cases.

9.1.5. 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.

9.1.6. CNRS Simulations of free-surface flows (2017)

Participants: Cindy Guichard, Martin Parisot, Yohan Penel, Jacques Sainte-Marie.

CNRS project call: PEPS JC

Project title: modélisation avancée et simulation d'écoulements à surface libre

Coordinator: Yohan Penel

Funding: 2.5k euros

In collaboration with E. Fernaández-Nieto.

Free-surface flows are extensively studied in the literature by means of simplified models (like the Shallow Water equations) due to the theoretical and numerical issues related to the Euler system. Intermediate models have then been derived to improve the accuracy and the physical relevance (e.g. taking into account hydrodynamic pressure or multilayer approaches). This collaboration aims at designing a hierarchy of multilayer models with a non-hydrostatic pressure as a discretisation along the vertical axis of the Euler equations. The hierarchy relies on the degree of approximation of the variables discretised with a Discontinuous Galerkin method for the vertical direction. These innovative models will imply a theoretical study and the development of numerical tools in dimensions 1 and 2 before the modelling of other physical phenomena (viscosity effects, ...).

9.1.7. CNRS Mocha (2017-2018)

Participant: Martin Parisot.

CNRS project call: LEFE

Project acronym: MOCHA

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

Coordinator: Martin Parisot

Funding: 14k euros

In collaboration with S. Barthélémy, N. Goutal, S. Ricci, M. Hoang Le.

Multi-dimensionnal coupling in river hydrodynamics offers a conveninent solution to properly model complex flow while limiting the computational cost and making the most of pre-exsiting models. The project aims to adapt the lateral interface coupling proposed in [39] to the implicit version and test it on real data for the Garonne River.

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

Participants: Marie-Odile Bristeau, Yohan Penel, Jacques Sainte-Marie, Fabien Souillé.

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".

9.1.9. Inria Project Lab "CityLab" (2015-2018)

Participants: Vivien Mallet, Raphaël Ventura.

CityLab@Inria studies ICT solutions toward smart cities that promote both social and environmental sustainability.

9.1.10. 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.

9.1.11. ANR ESTIMAIR (2013-2017)

Participant: Vivien Mallet.

ANR project call: Modèles numériques

Project acronym: ESTIMAIR

Project title: Estimation d'incertitudes en simulation de la qualité de l'air à l'échelle urbaine

Coordinator: Vivien Mallet

Funding: 415k euros

The project aims to propagate uncertainties in a complete air quality modelling chain at urban scale, from road traffic assignment to air pollutant dispersion.

9.1.12. ANR FireCaster (2017-2020)

Participants: Frédéric Allaire, Vivien Mallet.

ANR project call: DS0104

Project acronym: FireCaster

Project title: Plateforme de prévision incendie et de réponse d'urgence

Coordinator: Jean-Baptiste Filippi (Univ. Corse)

Funding: 442k euros

The goal of the FireCaster project is to prototype a fire decision support system at the national scale to estimate upcoming fire risk (H+24 to H+48) and in case of crisis, to predict fire front position and local pollution (H+1 to H+12).

9.1.13. ANR CENSE (2017-2020)

Participants: Antoine Lesieur, Vivien Mallet.

ANR project call: DS0601

Project acronym: CENSE

Project title: Caractérisation des environnements sonores urbains : vers une approche globale associant données libres, mesures et modélisations

Coordinator: Judicaël Picaut (IFSTTAR)

Funding: 856k euros

The CENSE project aims at proposing a new methodology for the production of more realistic noise maps, based on an assimilation of simulated and measured data through a dense network of low-cost sensors.

9.1.14. ANR RAVEX (2017-2020)

Participant: Anne Mangeney.

ANR project call: DS0106

Project acronym: RAVEX

Project title: Développement d'une approche intégrée pour la réduction des Risques Associés au Volcanisme EXplosif, de la recherche sur l'aléa aux outils de gestion de crise : le cas de la Martinique

Coordinator: Olivier Roche (IRD)

Funding: 619k euros

9.1.15. ANR CARIB (2014-2017)

Participant: Anne Mangeney.

ANR project call: Simi6

Project acronym: CARIB

Project title: Fréquence et processus de mise en place des avalanches de débris tsunamigènes de l'arc des Petites Antilles : apport des forages de l'Expédition IODP 340 et impact en termes de risque

Coordinator: Anne Le Friant (IPGP)

Funding: 274k euros

9.1.16. ANR CINE-PARA (2015-2019)

Participant: Julien Salomon.

ANR project call: DS0708

Project acronym: CINE-PARA

Project title: Méthodes de parallélisation pour cinétiques complexes

Coordinator: Yvon Maday (LJLL)

9.2. European Initiatives

9.2.1. FP7 & H2020 Projects

9.2.1.1. 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.

9.2.1.2. EoCoE (2015-2018)

Title: Energy oriented Centre of Excellence for computer applications

Program: H2020

Duration: October 2015 - October 2018

Coordinator: Édouard Audit (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), Université Libre de Bruxelles (Belgium), BSC (Centro Nacional de Supercomputacion, Spain)

Inria contact: Michel Kern (Serena team)

Participants: Vivien Mallet

Abstract: 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.

9.2.1.3. Env&You (2017)

Title: Env&You

Program: EIT Digital

Duration: January 2016 - December 2016

Coordinator: Inria (MiMove)

Partners: NUMTECH, Ambiciti, ForumVirium, TheCivicEngine

Inria contact: Valérie Issarny (Mimove project-team)

Participants: Vivien Mallet, Raphaël Ventura

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 citisens and governments, informing their decisions for healthy urban living.

9.2.2. Collaborations with Major European Organisations

9.2.2.1. CNRS PICS NHML (2017-2019)

Program: CNRS PICS (projet international de collaboration scientifique)

Project acronym: NHML

Project title: non-hydrostatic multilayer models

Duration: 01/17-12/19

Coordinator: Yohan Penel (CEREMA)

Other partners: IMUS (Sevilla, Spain)

Participants: Martin Parisot (Inria), Jacques Sainte-Marie (CEREMA), Enrique Fernández-Nieto (Sevilla), Tomas Morales de Luna (Cordoba)

Funding: 12k euros

Abstract: This collaboration aims at designing a hierarchy of multilayer models with a non-hydrostatic pressure as a discretisation along the vertical axis of the Euler equations. The hierarchy relies on the degree of approximation of the variables discretised with a Discontinuous Galerkin method for the vertical direction. These innovative models will imply a theoretical study and the development of numerical tools in dimensions 1 and 2 before the modelling of other physical phenomena (viscosity effects, ...).

9.3. International Initiatives

9.3.1. Inria International Partners

9.3.1.1. Informal International Partners

Two collaborations with foreign colleagues are to be mentioned:

- A collaboration with spanish researchers has been initiated in 2016 to derive accurate models and effecient algorithms for free surface flows including non-hydrostatic effects.
- A joint work with R. LeVeque (Univ. Seattle) and M. Berger (New York Univ.) consists in modelling the impact of asteroids on the generation of tsunamis.

9.3.2. Participation in Other International Programs

9.3.2.1. PROCORE Hong-Kong (2016-2017)

Program: Hubert Curien PROCORE

Project title: time-parallelisation methods for control

Duration: 01/16-12/17

Coordinator: Felix Kwok (Univ. Hong-Kong)

Other partners: HKBU (Hong-Kong)

Funding: 5k euros

9.4. International Research Visitors

9.4.1. Visits to International Teams

9.4.1.1. Research Stays Abroad

- Y. Penel spent one month and a half (Mar.-Apr.) at the university of Sevilla (Spain) to collaborate with E. Fernández-Nieto.
- M. Parisot spent a week to Sevilla in April.

We also mention that M. Parisot spent four separate weeks at the university of Toulouse (CERFACS).

CASTOR Project-Team

8. Partnerships and Cooperations

8.1. National Initiatives

8.1.1. 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

8.2. European Initiatives

8.2.1. FP7 & H2020 Projects

8.2.1.1. 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”
- Enabling research contract 2014-2018. (B. Nkonga, H. Guillard, A. Sangam) CfP-WP15-ENR-01/IPP-05, Grant agreement No 633053. «Global non-linear MHD modeling in toroidal X-point geometry of disruptions, edge localized modes, and techniques for their mitigation and suppression »
- EUROfusion WPCD (Working Package Code Development)
  - ACT1: Extended equilibrium and stability chain (participation)
  - ACT2: Free boundary equilibrium and control (participation and coordination)

8.2.1.2. EoCoE

Title: Energy oriented Centre of Excellence for computer applications

Programm: H2020

Duration: October 2015 - October 2018

Coordinator: CEA

Inria contact: Michel Kern

The aim of the present proposal 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.

8.3. International Initiatives

8.3.1. Inria International Partners

The team collaborates with TUC (Technical University of Crete, Prof. Argyris Delis) on extension of the shallow water model to turbulent flows. These common works overlap with the collaboration with Taiwan in the framework of the former AMOSS associate team. [27]

8.3.2. Participation in Other International Programs

ITER Contracts (B. Nkonga):

- ITER IO/17/CT/4300001505 : 2017-2019, "Non-linear MHD simulations for ITER QH-mode plasma with & without 3D magnetic field perturbations from in-vessel ELM control coils". (150KE)
- ITER IO/15/PR/11410/MCI: 2015-2017, "Modeling of plasma instabilities in ITER" (120KE)

COFFEE Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

The team is involved in the IDEX project UCA-JEDI.

- PhD of Laurence Beaude (october 2015 - december 2018) co-funded by BRGM and Region PACA and dealing with the simulation of geothermal systems, supervised by Roland Masson, Konstantin Brenner from LJAD-Inria and by Simon Lopez, Farid Smai from BRGM.

8.2. National Initiatives

8.2.1. ANR

- ANR CHARMS (Quantitative Reservoir Models for Complex Hydrothermal Systems): december 2016 - december 2020, partners BRGM (leader), LJAD-Inria, Storengy, MdS, LJLL.

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 GdR 3437 DYNOLIN “Dynamique non linéaire” and GdR MecaWave.
- LJAD-Inria and BRGM are the French partners of the Norvergian, German French project InSPiRE "International Open Source Simulation Software Partnership in Research and Education” which has just been accepted by the Research Council of Norway with the code ComPASS as one of the softwares of this project together with Dune, Dumux and OPM.

8.3. International Research Visitors

8.3.1. Visits of International Scientists

- Felix Kwok, one month in may 2017: nonlinear domain decomposition methods for the Richards equation with Roland Masson and Victorita Dolean.

8.3.1.1. Internships

- Internship of Willy Bonneuil (March 2017-August 2017) funded by EDF Chatou on nonlinear solvers based on variable switches for the Richards equation, supervision Konstantin Brenner and Roland Masson from LJAD-Inria and Jerome Bonnelle and Raphael Lamouroux from EDF.

FLUMINANCE Project-Team

9. Partnerships and Cooperations

9.1. National Initiatives

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

Participants: Pierre Derian, Cédric Herzet, 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, mathematics 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.

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

Participants: Mamadou Diallo, 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.

9.1.3. 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.

9.1.4. 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 until April 2017.
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.

9.1.5. GDR MANU

Participants: Yvan Crenner, Jocelyne Erhel, Bastien Hamlat.

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 organizes a workshop on reactive transport, Paris, February 2018.

9.2. International Initiatives

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

9.2.1.1. 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

9.2.1.2. Informal International Partners

Imperial College, London (UK), Collaboration with Dan Crisan and Darryl Holm on Stochastic transport for the upper ocean dynamics

Chico California State University (USA), We have pursued 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.

9.2.2. Participation in Other International Programs

Royal Society funding, collaboration between Dominique Heitz, Etienne Mémin and Sylvain Laizet (Imperial College) on Stochastic large-eddies simulation and data assimilation for the reconstruction of 3D turbulent flows.

China Scholarship Council funding, Collaboration between Etienne Memin, Shengze Cai and Chao Xu (Zhejiang University, College of Control Science & Engineering), on turbulent motion estimation and modeling under uncertainty.

9.3. International Research Visitors

- 3 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 12 month of Shengze Cai PhD student in the College of Control Science & Engineering, Zhejiang University to work with Etienne Mémin

LEMON Team

7. Partnerships and Cooperations

7.1. 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) will be based on the SW2D computational code. The purpose is to optimize and implement the commercial version of the code into a complete software chain for the forecasting and scenario appraisal for rainfall-generated urban floods on the scale of the urban area. The test and application site is the entire urban area of Montpellier.

7.2. National Initiatives

7.2.1. ANR

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

7.2.2. LEFE-INSU

Gwladys TOULEMONDE is head of a project (2016-2018) funded by INSU via the action MANU (MAthematical and NUmerical methods) of the LEFE program. This project, called Cerise, aims to propose methods for simulating scenarii integrating spatio-temporal extremes fields with eventual asymptotic independence for impact studies in environmental sciences.

7.3. International Initiatives

7.3.1. Inria International Labs

Antoine ROUSSEAU collaborates with Inria Chile through the partnership with MERIC in Chile. Two visits every year.

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

7.3.2.1. NEMOLOCO

Title: NEw MOdeLing tOols for Coastal Oceanography

International Partner (Institution - Laboratory - Researcher):

Pontificia Universidad Católica de Chile (Chile) - CIGIDEN - Rodrigo Cienfuegos

Start year: 2017

See also: https://team.inria.fr/lemon/en/

The NEMOLOCO project targets the improvement of models in the coastal zone. Expected contributions concern: - design and implementation of domain decomposition and coupling techniques for coastal modeling - high resolution ocean simulation (including nesting) thanks to the software ROMS-CROCO, applied to biological tracers tracking.

7.3.3. Inria International Partners

7.3.3.1. Declared Inria International Partners

In 2015, the *Marine Energies Research International Center* (MERIC) was launched in Chile by CORFO. Antoine ROUSSEAU is 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*.

7.3.3.2. 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)

7.3.4. Participation in Other International Programs

Antoine ROUSSEAU was member of a successfull application to the REDES (Conicyt, Chile) program with H. Ramirez (CMM, Santiago) and P. Gajardo (UTFSM, Valparaiso).

7.4. International Research Visitors

7.4.1. Visits of International Scientists

Andres Sepulveda (Univ Concepcion, Chile) visited the team in the framework of the CROCO summer school organized in Toulouse by the AIRSEA project-team.

José Galaz (PUC Santiago, Chile) visited Montpellier for one week.

7.4.1.1. Internships

Joao CALDAS (Ecole des Ponts, Ecole Polytechnique de Sao Paulo) was intern at Inria Chile / MERIC, advised by A. Rousseau.

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. Six PhD students have defended their PhD since 2014 and they are now post-doctoral researchers or engineers 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 2016 in Strasbourg and a second one in Paris in July 2017. Thanks to this support, we have submitted a ETPHPC proposal in September 2017 The project is funded for 18 months starting from August 2016. The funding amounts 30000€.

8.2.3. ANR NonLocalDD

Magique 3-D is a partner of the ANR project entitled "Non Local Domain Decomposition Methods in Electromagnetics" that begins in october 2015. The aim of this project is to develop domain decomposition methods for the efficient solution of acoustics and Maxwell's equation either with boundary integral equations or finite element volume method. To obtain an exponential convergence of the iterative solution, non-local operators are studied and optimized to achieve a faster convergence. A post-doctoral student Marcella Bonazzoli has been hired by Magique 3-D in 2017 to study multi-domain integral equations for wave propagation. This student is supervised by Xavier Claeys, a partner of the NonLocalDD ANR project.

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, Izar Azpiroz visited CSUN in May 2017 and Rabia Djellouli (CSUN) visited Magique 3D in December 2017

8.5. International Research Visitors

8.5.1. Visits of International Scientists

- Rabia Djellouli (CSUN) visited Magique 3D in December 2017.
- Damien Fournier (MPS) visited Magique 3D in October 2017.
- Morgane Bergot (Univ Lyon) visited Magique 3D in November 2017.

8.5.2. Visits to International Teams

8.5.2.1. Research Stays Abroad

- In the framework of the European project Geagam, Izar Azpiroz and Justine Labat visited Ignacio Muga, PUCV, Chile, in April 2017.
- In the framework of the International Partnership Magic2, Izar Azpiroz visited Rabia Djellouli, CSUN (California State University at Northridge), USA, in May 2017.

SERENA Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

GiS: scientific collaboration network between ten public institutions from the Paris (Ile-de-France) region, focused on natural resources and environment. The project-team SERENA is a member.

9.2. National Initiatives

9.2.1. 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.

9.3. European Initiatives

9.3.1. 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 Simulation and 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.

9.3.2. Collaborations in European Programs, Except FP7 & H2020

OPENCPS

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.

MoRe

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.

9.4. International Initiatives

9.4.1. Inria International Partners

9.4.1.1. Informal International Partners

Erik Burman, Professor at University College London, UK, unfitted methods.

Jean-Luc Guermond, Professor at Texas A&M University, USA, finite element methods.

Ulrich Rüde, Professor at Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, multigrid methods.

Mary Wheeler, professor, University of Texas at Austin, USA, porous medial applications.

Barbara Wohlmuth, Professor at Technical University of München, Germany, mixed finite element methods.

9.5. International Research Visitors

9.5.1. Visits of International Scientists

Lars Diening, Professor at University of Bielefeld, Germany, February 17–23, 2017.

Christian Kreuzer, Professor at University of Dortmund, Germany, February 19–25, 2017.

Joscha Gedicke, post-doc at University Vienna, Austria, May 29–June 2, 2017.

Martin Eigel, post-doc at Weierstrass Institute Berlin, Germany, May 29–June 2, 2017.

Carsten Carstensen, Professor at Humboldt University Berlin, Germany, August 15–September 15, 2017.

Peter Minev, Professor at the University of Alberta, Canada, September 15–October 15, 2017.

Hend Ben Ameur, Professor at IPEST and member of ENIT-Lamsin, Tunis, Tunisia, October 23–November 3, 2017.

9.5.1.1. Internships

K. Talali, université de Fez, Morocco, April 1–August 31 (Master degree).

9.5.2. Visits to International Teams

9.5.2.1. Research Stays Abroad

Alexandre Ern participated as Invited Professor to the HIM Program on Multiscale Problems: Algorithms, Numerical Analysis and Computation, in Bonn, Germany, January 2017.

Martin Vohralík was invited for two weeks stay to Charles University in Prague collaboration with J. Málek, April 2017.

STEEP Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

8.1.1. QAMECS : ATMOSPHERIC POLLUTION: Characterization of novel exposure markers, of biological, health, economic and societal impacts and evaluation of public policies

Project funded by ADEME and Grenoble metropolis
Duration: 2016 – 2019
Project coordinator : Remy Slama - INSERM. Inria Coordinator: Emmanuel Prados
Other partners: Air Rhône-Alpes, CNRS, Sciences Po Grenoble, Inserm, IAB, Université Grenoble-Alpes
Abstract: Urban atmospheric pollution is one of the main threats to human health that can be to some extent controlled by public action. In Europe, many cities have implemented various types of low emission zones (LEZ, focused on traffic and heating emissions), France being a notable exception. Although fine particulate matter (PM2.5) is usually assessed through its mass concentration, other metrics, such as PM chemical speciation as well as the so far little considered oxidative potential (OP) of PM, are worth considering, both in terms of associations with human health and in the context of monitoring of the efficiency of LEZ. QAMECS covers all dimensions from atmospheric emissions, impact of meteorological conditions on air pollution human behaviours related to transportation, environmental levels, health, associated economic costs and societal awareness. The project relies on environmental measurements, modelling, repeated observational (representative) population studies, an existing mother-child cohort, a controlled human experiment, health impact and related economic assessment. It is conducted by a consortium of specialists of chemistry and physics of air pollution, economics, sociology, epidemiology, geography, in relation with local authorities. It will bring results important for urban planning, public health, and more fundamental research on the measurement of PM and assessment of their biological and health impact.

8.2. National Initiatives

8.2.1. AF Filières : Analyse des Flux des Filières biomasse pour des stratégies régionales de bioéconomie

Project funded by ADEME
Duration: 2017-2019
Coordinator: Jean-Yves COURTONNE (Equipe STEEP, Inria) [Emmanuel Prados (STEEP/Inria) for Inria partner]
Other partners: Equipe STEEP, Inria, Grenoble Rhônalpénergie-Environnement (RAEE), Lyon Laboratoire d'Economie Forestière (LEF), INRA / AgroParisTech Nancy.
Keywords: Environmental assessment, Ecological accounting, Material Flow Analysis, Sustainable supply chains, Multicriteria analysis.
Abstract: Flow analyses of biomass supply chains for regional bioeconomy policies. The goals of the project are the following:

- Improve knowledge on the material flows of the forest-wood and agri-food supply chains in France at national and regional levels,
- Provide a holistic vision of the situation by associating environmental and socio-economic indicators to material flows,
- Provide a more precise assessments (quantitatively and qualitatively) in the case of the Auvergne-Rhône-Alpes region.

8.2.2. ESNET : Futures of ecosystem services networks for the Grenoble region

Project funded by FRB (Fondation pour la Recherche sur la Biodiversité)
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 – 2017
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.

8.2.3. CITiES: Calibrage et valIdation de modèles Transport - usagE des Sols

Project funded by ANR
Program: "*Modèles Numériques*" 2012, ANR
Duration: 2013 – 2017
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.

TONUS Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

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

9.2. National Initiatives

9.2.1. Contracts with Industry

We are involved in a common project with the company AxesSim in Strasbourg. The objective is to help to the development of a commercial software for the numerical simulation of electromagnetic phenomena. The applications are directed towards antenna design and electromagnetic compatibility. This project was partly supported by DGA through "RAPID" (régime d'appui à l'innovation duale) funds. A CIFRE PhD has started in AxesSim on the same kinds of subjects in March 2015 (Bruno Weber). The new project is devoted to the use of runtime system in order to optimize DG solvers applied to electromagnetism [10]. The resulting software will be applied to the numerical simulation of connected devices for clothes or medicine. The project is supported by the "Banque Publique d'Investissement" (BPI) and coordinated by the Thales company.

9.2.2. ANR

ANR project PEPPSI (models for edge plasma physic in Tokamak) in *Programme Blanc* SIMI 9, started in 2013, ended this year.
Participants: David Coulette, Giovanni Manfredi [coordinator], Sever Hirstoaga.

9.2.3. IPL FRATRES

The TONUS project belongs to the IPL FRATRES (models and numerical methods for Tokamak).
Funded by the IPL, Xiaofei Zhao was a post-doctoral fellow until September 2017, under the joint supervision of Nicolas Crouseilles (team IPSO, Inria Rennes) and Sever Hirstoaga.

9.2.4. 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.

9.2.5. HPC resources

- GENCI project *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 Hirstoaga, Guillaume Latu, Michel Mehrenberger, Thi Nhung Pham, Christophe Steiner, Yann Barsamian.
- GENCI project *Simulations 3D de plasmas deux espèces avec des méthodes particulaires et semi-lagrangiennes*: 400 000 scalar computing hours accepted in October 2017 on supercomputer OCCIGEN. Coordinator: Sever Hirstoaga
  Participants: Yann Barsamian, Sever Hirstoaga, Michel Mehrenberger.

- PRACE project *SME HPC Adoption Programme in Europe: full simulation of an electromagnetic wave inside and ouside a fully modeled human body*: 40 000 GPU computing hours accepted in October 2017 on supercomputer Piz Daint. Coordinator: Bruno Weber
  Participants: Philippe Helluy, Bruno Weber.

9.3. European Initiatives

9.3.1. FP7 & H2020 Projects

9.3.1.1. EUROfusion 2015-2017

- Eurofusion Enabling Research Project ER15-IPP01 (1/2015-12/2017) "Verification and development of new algorithms for gyrokinetic codes" (Principal Investigator: Eric Sonnendrücker, Max-Planck Institute for Plasma Physics, Garching).
  Participants: Philippe Helluy, Sever Hirstoaga, Michel Mehrenberger.
- Eurofusion Enabling Research Project ER15-IPP05 (1/2015-12/2017) "Global non-linear MHD modelling in toroidal geometry of disruptions, edge localized modes, and techniques for their mitigation and suppression" (Principal Investigator: Matthias Hoelzl, Max-Planck Institute for Plasma Physics, Garching).
  Participant: Emmanuel Franck.

9.4. International Initiatives

9.4.1. Participation in Other International Programs

Participants: David Coulette, Conrad Hillairet, 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.

9.5. International Research Visitors

9.5.1. Visits of International Scientists

Christian Klingenberg from Würzburg university was invited several times in 2017, by Philippe Helluy.

Roberto Ferretti was invited one month in 2017 at IRMA, by Michel Mehrenberger, for working on the stability of semi-Lagrangian schemes.

9.5.2. Visits to International Teams

9.5.2.1. Research Stays Abroad

Philippe Helluy, Emmanuel Franck and David Coulette visited Christian Klingenberg at Würzburg university.

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, 2013-2017) 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 (2012-2017) is 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 (2014-2018) 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 (2016-2019) 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 (2013-2018) is to develop a trait-based approach linking individual fitness of fungal plant pathogens to ecological strategies. The idea is to derive eco-epidemiological strategies from fitness optimization in colonized environments and during colonization, as well as understanding the coexistence of sibling species. This project is co-coordinated by F. Grognard.
- **ANR-TripTic:** The objective of this project (2014-2018) is to document the biological diversity in the genus of the minute wasps *Trichogramma*, and to study the behavioral and populational traits relevant to their use in biological control programs.
- **ANR-MIHMES:** "Multi-scale modeling, 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 aimed at producing scientific knowledge and methods for the management of endemic infectious animal diseases and veterinary public health risks. BIOCORE participated in this project via MaIAGE, INRA Jouy-en-Josas. This project supported 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.

- **ANR - Maximic:** The goal of the project (accepted in July 2017) is to design and implement control strategies in a bacterium from producing at maximal rate a high value product. It is coordinated by H. de Jong (IBIS Grenoble), and involves members of Biocore and McTao.
- **RESET:** The objective of this project (2012-2017) 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.
- **AMIES-PEPS Exactcure:** The goal of the project is to study pharmacokinetic models, in collaboration with the start-up Exactcure (Nice). This funded the M2 internship of L. Dragoni.

9.1.2. Inria funding

- **Inria Project Lab, Algae** ***in silico*****:** (2014-2018) The Algae in silico Inria Project Lab, funded by Inria and coordinated by O. Bernard, focuses on the expertise and knowledge of biologists, applied mathematicians and computer scientists to propose an innovative numerical model of microalgal culturing devices. The latest developments in metabolic modeling, hydrodynamic modeling 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.
- **Inria Project Lab, Cosy:** (2017-...) This proposal aims at exploiting the potential of state-of-art biological modeling, control techniques, synthetic biology and experimental equipment to achieve a paradigm shift in control of microbial communities. We will investigate, design, build and apply an automated computer-driven feedback system for control of synthetic microbial communities, not just accounting for but rather leveraging population heterogeneity in the optimal accomplishment of a population-level task. The development of methodologies of general applicability will be driven by and applied to two different applications closely connected with real-world problems in the biomedical and biotechnological industry. The consortium is composed of the four Inria project-teams IBIS, BIOCORE, COMMANDS, NON-A, the Inria Action Exploratoire INBIO, as well as the external partners BIOP (Université Grenoble Alpes, including members of IBIS), MaIAge (INRA), and YoukLAB (TU Delft). The project began in November.

9.1.3. INRA funding

- **MoGeR:** "From knowledge to modeling: towards a user-friendly simulation tool to test crop resistance management scenarios in the Phoma-oilseed rape case study", INRA Metaprogramme SMaCH, 2017–2019. This is a follow-up of the K-Masstec project, which focused on sustainable strategies for the deployment of genetic resistance in the field, based on molecular knowledge on avirulence genes.
- **ABCD:** INRA SPE is funding the project ABCD "Augmentative Biological Control; optimizing natural ennemies Deployment" (2017-2019) in which Biocore is a partner with INRA Sophia Antipolis.

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 modeling 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. Collaborations with Major European Organizations

Imperial college, Department of Chemical engineering (UK),
Modeling and optimization of microalgal based processes; with B. Chachuat.
Imperial College, Centre for Synthetic Biology and Innovation, Dept. of Bioengineering (UK):
Study of metabolic/genetic models; with D.A. Oyarzún.
University of Padova (Italy):
Modelling and control of microalgal production at industrial scale; with F. Bezzo.
University of Aveiro, Dept. of Mathematics (Portugal):
Hybrid models and boolean networks; with M.A. Martins.

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: Modeling and control for energy producing bioprocesses
International Partners (Institution - Laboratory - Researcher):

CIRIC (Chile) - Mélaine Gautier
PUCV (Chile) - Escuela de Ingenieria Bioquimica (EIB) - David Jeison
UTFSM (Chile) - Departamento de Matematica - Pedro Gajardo
Univ. Chile (Chile) - Centro de modelacion matematica - Hector Ramirez

Inria coordinator: O. Bernard
Start year: 2017
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 CMM) and software development (CIRIC).

LIRIMA

Associate Team involved in the International Lab:

9.3.1.2. EPITAG

Title: Epidemiological Modeling and Control for Tropical Agriculture

International Partner (Institution - Laboratory - Researcher):

Université de Douala (Cameroon) - Mathematics Department - Samuel Bowong

Inria coordinator: S. Touzeau

Start year: 2017

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

EPITAG gathers French and Cameroonian researchers, with a background in dynamical systems and control and with an interest in crop diseases. Crop pests and pathogens are responsible for considerable yield losses. Their control is hence a major issue, especially in Cameroon, where agriculture is an important sector in terms of revenues and employment. To help design efficient strategies for integrated pest management, mathematical models are particularly relevant. Our main objective is to study the epidemiology and management of tropical crop diseases, with a focus on Cameroon and Sub-Saharan Africa. Our approach consists in developing and analysing dynamical models describing plant-parasite interactions, in order to better understand, predict and control the evolution of damages in crops. To ensure the relevance of our models, “end users” will be closely associated. We will focus on three pathosystems: cocoa plant mirids, coffee berry borers and plantain plant-parasitic nematodes.

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). Modeling of photosynthesis.

9.3.3. Participation in Other International Programs

Biocore is involved in the IFCAM project, with India, PULSPOP "PULses in Spatial POPulation dynamics" (2016-2017) whose partners are Institut Sophia Agrobiotech and National Institute of Technology, Meghalya (India). This project financed the visit of Bapan Ghosh to ISA and BIOCORE, and the visit of Nicolas Bajeux to India.

9.4. International Research Visitors

9.4.1. Visits of International Scientists

- Claude Aflalo (Ben Gurion University of the Neguev, Israel), 6 months.
- Samuel Bowong (University of Douala, Cameroon), 5 days.
- Myriam Djoukwe Tapi (University of Douala, Cameroon), 1 week.
- Bapan Ghosh (National Institute of Technology Meghalaya, India), 1 month.
- Yves Fotso Fotso (University of Dschang, Cameroon), 4 months.
- Israël Tankam Chedjou (University of Yaoundé 1, Cameroon), 4 months.

9.5. Project-team seminar

BIOCORE organized a 4-day seminar in September in Porquerolles. On this occasion, every member of the project-team presented his/her recent results and brainstorming sessions were organized.

CARMEN Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

8.1.1. CALM

The project "Cardiac Arrhythmia Localization Methods" has been granted by the Région Nouvelle-Aquitaine, with matching from funds held by our clinical collaboraters Dr. Hubert Cochet and Dr. Pierre Jaïs, and from Inria. The purpose of this project is to develop a tool that can predict the exit site of an arrhythmia with moderate accuracy (1 cm) in an absolute sense, with respect to the anatomy of the heart in situ, and with a resolution of about 2 mm in a relative sense, with respect to a nearby pacing site. This tool must fulfill the following criteria:

- it uses only data that are already recorded in the cathlab by other systems: ECG data and electroanatomical mapping data;
- it must work in nearly real-time; catheter displacement advice must be available within 5 seconds after a paced beat;
- it must work automatically, requiring the operator only to indicate which ECG data correspond to the target arrhythmia; and
- it must be safe and easy to operate.

We will in the first place test a number of proposed methods using synthetic data, produced with our realistic models of cardiac electrophysiology and accurate geometric models of different patients. This in-silico testing phase will answer a number of important practical questions. Subsequently we will use offline clinical data, and within 2 years we aim to build a clinical prototype that can be tested (without interfering in the procedure) in the cathlab. In order to work real-time we will initially use very simple methods. However, the clinical prototype and the collectoin of synthetic data that we created will later serve also as a platform to test also more sophisticated inverse methods.

8.1.2. EXACARD

We started a collaboration with the STORM team at Inria Bordeaux Sud-Ouest to work on further scaling of the Propag code, to push the limit from about 10^4 to 10^6 parallel processors. A pre-proposal has been submitted to the ANR, and we are doing preparatory work.

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 lasted until November 2017.

This international project involved 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 MITOCARD

The MITOCARD project (Electrophysiology of Cardiac Mitochondria), coordinated by S. Arbault (Université de Bordeaux, ISM), was granted by the ANR in July 2017. The objective of MITOCARD is to improve understanding of cardiac physiology by integrating the mitochondrial properties of cell signaling in the comprehensive view of cardiac energetics and rhythm pathologies. It was recently demonstrated that in the heart, in striking contrast with skeletal muscle, a parallel activation by calcium of mitochondria and myofibrils occurs during contraction, which indicates that mitochondria actively participate in Ca2+ signaling in the cardiomyocyte. We hypothesize that the mitochondrial permeability transition pore (mPTP), by rhythmically depolarizing inner mitochondrial membrane, plays a crucial role in mitochondrial Ca2+ regulation and, as a result, of cardiomyocyte Ca2+ homeostasis. Moreover, mitochondrial reactive oxygen species (ROS) may play a key role in the regulation of the mPTP by sensing mitochondrial energetics balance. Consequently, a deeper understanding of mitochondrial electrophysiology is mandatory to decipher their exact role in the heart's excitation-contraction coupling processes. However, this is currently prevented by the absence of adequate methodological tools (lack of sensitivity or selectivity, time resolution, averaged responses of numerous biological entities). The MITOCARD project will solve that issue by developing analytical tools and biophysical approaches to monitor kinetically and quantitatively the Ca2+ handling by isolated mitochondria in the cardiomyocyte.

MITOCARD is a multi-disciplinary project involving 4 partners of different scientific fields: the CARMEN team as well as

ISM, the largest chemistry laboratory of the Université de Bordeaux, where the necessary measurement methods will be developed;

Liryc, where mitochondria are studied at all levels of integration from the isolated mitochondrion to the intact heart; and

LAAS, the MiCrosystèmes d'Analyse (MICA) group at the Laboratory of Analysis and Architecture of Systems, which develops the biological microsensors for this project.

The project will

- develop chips integrating 4 different electrochemical microsensors to monitor in real-time key mitochondrial signaling parameters: Ca2+, membrane potential, quinone reduction status, O2 consumption, and ROS production;
- develop microwell arrays integrating ring nanoelectrodes to trap single mitochondria within micrometric chambers and measure locally by combined fluorescence microscopy and electrochemical techniques intra- (by fluorescence) and extra-mitochondrial (electrochemistry) metabolites; and
- develop a mathematical model of mitochondrial Ca2+ and ROS handling built on existing knowledge, new hypotheses, and the measured data.

The model may serve both to assess biological assumptions on the role of mitochondria in Ca2+ signaling and to integrate pathological data and provide clues for their global understanding.

8.2.3. 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 September 2017, has been granted 9 million core-hours on the three major systems Curie, Occigen, and Turing. This compute time is primarily destined for our research into the interaction between ionic and structural heart disease in atrial fibrillation, Brugada syndrome, and early repolarisation syndrome [7] [61].

8.3. European Initiatives

8.3.1. FP7 & H2020 Projects

We participated in two H2020 Research and Innovation Action proposals.

8.3.2. Collaborations in European Programs, Except FP7 & H2020

We coordinated a proposal with 5 European partners. The proposal could not be submitted due to administrative problems related to one of the partners, but we will benefit from the existing consortium to submit a new proposal in April 2018.

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 in Bordeaux headed by Professor Michel Haïssaguerre. We would like to non-invasively construct the electrical potential on the heart surface only from measurements of the electrical potential on the the chest of the patient.

This helps the medical doctor to visualise an image of the electrical potential of the heart of the patient. It is known that have been used in the literature for solving this electrocardiography imaging (ECGI) problem, including those used in commercial medical devices have several limitations. This problem could be mathematically seen as a boundary data completion problem for elliptic equations.

Many works in the literature have been carried out in order to solve this Cauchy problem, but have never been used for solving the ECGI problem. Our goal from the associate team is to develop an experimental platform allowing to test various methods and compare their performance on real life experimental data.

8.4.2. Inria International Partners

8.4.2.1. Informal International Partners

Y. Coudière works with the group of Prof. Y. Bourgault from the Department of Mathematics and Statistics of the University of Ottawa (Canada). Some results on the numerical analysis of time-stepping methods from C. Douanla's PhD were carried out together, as well as some theoretical results on parameter identification in the PhD of A. Gérard.

M. Potse and O. Bernus (Liryc) work with the group of Prof. A. Panfilov in Ghent, Belgium, on simulation and analysis of complex reentrant arrhythmia.

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 [51]. The Maastricht group was partially funded by the FP7 project EUTRAF and our simulations were supported by GENCI (section 8.2.3).

M. Potse set up a project and recruited a PhD student to co-direct with Dr. Esther Pueyo of the University of Zaragoza, within the context of the H2020 International Training Network "Personalised In-silico Cardiology" (PIC), coordinated by Dr. Pablo Lamata of King's College London.

N. Zemzemi works with Cesare Corrado at King's College London on the development of new eikonal models allowing conduction velocity adaptation [14].

N. Zemzemi collaborated with Jesús Requena-Carrión from the Queen Mary University of London to study the effects of the spatial resolution of electrode systems on the spectrum of cardiac signals in cardiac electrocardiography [12].

N. Zemzemi worked with R. Aboulaich group from Mohamed V university in Morocco on sensitivity of the electrocardiographic problem to multiple independent sources of uncertainty including noise in the measurements and the heterogenity in the torso [34].

DRACULA Project-Team

7. Partnerships and Cooperations

7.1. 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”.

7.2. National Initiatives

7.2.1. ANR

- 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". 2012-2017 (https://contraintes.inria.fr/~batt/iceberg/home.html).
- 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/.
- Céline 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.

7.2.2. Other projects

- Inria ADT : SiMuScale "Simulations Multi-Échelles de Populations Cellulaires", 2014-2017.
  Participants: Samuel Bernard [Coordinator], Fabien Crauste, Olivier Gandrillon, David Parsons.
- Association France Alzheimer Sciences Médicales: PAMELA “Prion et Alzheimer : Modélisation et Expérimentation d’une Liaison Agressive”, 2014-2017 (https://www.youtube.com/watch?v=X0mLf8IJhV4).
  Participants: Mostafa Adimy, Samuel Bernard, Thomas Lepoutre, Laurent Pujo-Menjouet [Coordinator], Léon Tine.
- Thomas Lepoutre is a member of the ERC MESOPROBIO (head V. Calvez) dedicated to "Mesoscopic models for propagation in biology". 2015-2020: http://cordis.europa.eu/project/rcn/193664_en.html.

7.3. International Initiatives

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

- Associate Teams Inria project, "Modelling Leukemia", 2014-2017.
  - Participants (Dracula): Mostafa Adimy, Samuel Bernard, Apollos Besse, Abdenasser Chekroun, Raouf El-Cheikh, Thomas Lepoutre [Coordinator], Laurent Pujo-Menjouet, Léon Tine, Céline Vial.
  - Partners: This is joint with Center for Scientific Computing and Applied Mathematical Modeling (Doron Levy) at University of Maryland (USA) (http://dracula.univ-lyon1.fr/modelling_leukemia.php).

– The project Modelling Leukemia is devoted to the modeling of several aspects of Chronic Myeloid Leukemia. 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 want to add up 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).

7.4. International Research Visitors

7.4.1. Visits of International Scientists

- Claudia Pio Ferreira holded an Invited Professor position in the dracula team for two months (Octobre 14th - December 14th), she is affiliated to the Sao Paulo State University (UNESP), Institute of Biosciences, Department of Biostatistics, Botucatu, Brazil.

M3DISIM Project-Team

9. Partnerships and Cooperations

9.1. National Initiatives

9.1.1. ANR

ANR METIS(ANR-13-BS09-0004-02). Title: "Mechanics of Tissues: multiscale structural approach of Ehlers-Danlos Syndrome". Involved research groups: LMS (Ecole Polytechnique, CNRS, Mines ParisTech, PI: Jean-Marc ALLAIN), LOB - Optics and Biosciences Laboratory (Ecole Polytechnique, CNRS, INSERM), IGFL - Institut de Génétique Fonctionelle de Lyon (ENS Lyon, Université Lyon 1, CNRS, INRA). Total amount of the grant: 200k€ for the team. The METIS project is dedicated to the study of the biomechanics of connective tissues. Soft connective tissues such as skin, tendon or cornea are made of more than 90% of extracellular matrix proteins, fibrillar collagens being by far the predominant component. The rationale of this project is to understand the link between the microstructure of connective tissues and their macroscopic mechanical properties. To achieve this, observations of the fibrilar collagen will be done at different levels of stretch, while recording the mechanical properties. The consequences of change in the microstructure will also be explored through mutants mimicking the Ehler-Danlos syndrome, but also aging or wound-healing experiments. The project was completed on September 30th 2017 (4 years project).

9.1.2. Other funding

IPM-MS project (for Imagerie Polarimétrique de Mueller pour la réalisation d'un système original de caractérisation des propriétés mécaniques des Matériaux Structurés). 50k€ funded by the LABEX Lasips. This project, which involves the LPICM laboratory (Ecole Polytechnique, CNRS), the LMS (Ecole Polytechnique, CNRS, Mines ParisTech) and the Centre des Matériaux (Mines ParisTech), aims at developing an optical tool to study the link between the mechanical properties of a material and its hierarchical organization. Despite the development of new methods to observe the microstructure, one of the limitations is the number of observations that can be obtained on a given sample in a realistic experimental time. To overcome this difficulty, we are planning to use the Mueller polarimetry to obtain at a fast rate (a few frames per second, compared to a few frames per half-hour) relevant information on the local anisotropy of biological (heart, skin) and composite (short fibers composite) samples.

G. Bureau, software engineer in the team, is funded by an Inria Reo industrial contract with Kephalios, a startup working on innovative artificial valves devices.

9.2. European Initiatives

9.2.1. FP7 & H2020 Projects

9.2.1.1. 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)

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 aging population and improving survival following myocardial infarction. The poor short to medium term prognosis of these patients means that treatments such as cardiac re-synchronisation therapy and mitral valve repair can have substantial impact. However, these therapies are ineffective in up to 50% of the treated patients and involve significant morbidity and substantial cost. The primary aim of VP2HF is to bring together image and data processing tools with statistical and integrated biophysical models mainly developed in previous VPH projects, into a single clinical workflow to improve therapy selection and treatment optimisation in HF.

9.3. International Initiatives

9.3.1. Inria International Partners

9.3.1.1. Informal International Partners

We have started a collaboration with the University of Texas Southwestern Medical Center in Dallas. A joint PhD student based at Inria and funded by UTSW is starting in October 2017. An associated team proposal has been submitted in October 2017.

9.4. International Research Visitors

9.4.1. Visits of International Scientists

9.4.1.1. PhD exchange program

J. Albella, PhD student at University of Santiago de Compostela, has spent 3 months in M3DISIM, working with S. Imperiale on numerical methods for elastodynamics wave propagation.

E. Bertoberoglu, PhD Student at ETH Zurich, has spent multiple weeks in M3DISIM to work with M. Genet on computational models of growth and remodeling of the heart, validated on MRI data acquired at ETH Zurich.

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 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 artificial liver intended for liver replacement.

8.1.1.4. ANR InTelo 2017-2020

Telomere dynamics, headed by Teresa Teixeira (IBPC, Paris).

8.1.2. ITMO Cancer 2016 - 2020, HTE call (heterogeneity of tumours in their ecosystems)

8.1.2.1. ITMO Cancer EcoAML

Early leukaemogenesis in Acute Myelogenous Leukaemia (AML), 8 teams headed by François Delhommeau (CDR St Antoine, Paris).

8.1.2.2. ITMO Cancer MoGlImaging

Treatment-induced treatment resistance and heterogeneity in glioblastoma, 8 teams headed by Elizabeth Moyal (INSERM, Toulouse).

8.2. European Initiatives

8.2.1. FP7 & H2020 Projects

Research axis 1 (population dynamics): The ERC Starting Grant SKIPPER^{AD} (Marie Doumic, 2014-2018) supported and was the guideline for the study of nucleation, growth and fragmentation equations.

Benoît Perthame has obtained in April 2017 the ERC Advanced Grant ADORA (Asymptotic approach to spatial and dynamical organisations)

8.2.2. Collaborations with Major European Organisdations

German BMBF: LiverSimulator (Dirk Drasdo, 2014 - 2017)

8.3. International Initiatives

8.3.1. Participation in International Programs

CAPES/COFECUB project "Modelling innovative control methods for dengue fever" (Bliman)

STIC AmSud project “MOSTICAW- MOdelling the Spread and (opTImal) Control of Arboviroses by Wolbachia" (2016-2017) (Bliman)..

ECOS-Nord project “New methods for controlling epidemics of dengue fever and arboviroses" (2017-2019) (Bliman)

(See below)

8.3.1.1. International Initiatives

MOSTICAW

Title: 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

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 compartmental models; and to specific focus on the spatial aspects, achieved through more elaborate models (PDE, models on interaction graphs, stochastic models). We further propose to elaborate on the risks involved in the spreading of Wolbachia, implementing in mathematical models critical analysis, complex systems (R. García) and a complexity aware epistemology (E. Morin) in contrast with the instrumental reason (Horkheimer).

8.3.1.2. International Initiatives

C17M01

Title: New methods for the control of epidemics of dengue and arboviroses

International Partner (Institution - Laboratory - Researcher):

Universidad del Valle (Colombia) - Olga Vasilieva

Duration: 2017 - 2019

Start year: 2017

8.4. International Research Visitors

8.4.1. Internships

September 2016-January 2017: Julie Favre, M1 student at EPFL (Zürich), research internship report [39]

8.4.2. Visits to International Teams

8.4.2.1. Sabbatical programme

Doumic Marie

Date: Sep 2016 - Jul 2018

Institution: Wolfgang Pauli Institute, Vienna (Austria)

8.4.2.2. Research Stays Abroad

P.-A. Bliman is still a professor at Funadação Getulio Vargas, Rio de Janeiro, Brazil, and makes frequent stays there.

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 - ITAV, Toulouse
- Duration - from 2014 to 2017
- Coordinator - Th. Colin
- Team participants - Th. Colin, C. Poignard, O. Saut
- Title - Mathematical modeling for exploration of the impact of mechanical constraints on tumor growth

8.1.2. Systems Biology of Renal Carcinoma using a Mouse RCC model

- Title: Plan Cancer Systems Biology of Renal Carcinoma using a Mouse RCC model
- Partners : LAMC, INSERM-Univ. Bordeaux.
- Team participants: O. Saut, S. Benzekry (co-PI)
- 116.64k€

8.1.3. Transnation call: INCA/ARC

- Title: Minimally and non-invasive methods for early detection and/or progression of cancer
- Acronym: TRANSCAN
- Team participants: A. Collin, C. Poignard, O. Saut (local PI)
- Total funds: 1M150, Monc's share 275k€.

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. European Initiatives

MONC is partner of the European Lab EBAM devoted to electroporation. C.Poignard is member of the steering committee.

8.3. International Initiatives

MONC is partner of the Japanese Core-to-Core project « Establishing networks in mathematical medicine » coordinated by T. Suzuki (Osaka University) with Vanderbilt Univ, and St Andrews Univ. Local PIs are V. Quaranta (Vanderbilt), M. Chaplain (St Andrews) and C.Poignard (MONC).

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

8.3.1.1. METAMATS

Title: Modeling ExperimenTAl MetAsTasiS

International Partner (Institution - Laboratory - Researcher):

Roswell Park Cancer Institute (United States) - Department of Cancer Genetics Department of Medicine Department of Pharmacology and Therapeutics (Graduate Program) - John Ebos

Start year: 2017

See also: http://metamats.bordeaux.inria.fr/

The aim of the METAMATS associate team is to bring together a cancer biology experimental laboratory led by John ML Ebos (Roswell Park Cancer Institute) and the inria MONC team composed of applied mathematicians. The Ebos laboratory is specialized in the study of anti-cancer therapeutics (in particular, novel biologically targeted therapeutics such as anti-angiogenics and immunotherapies) on the development of metastases and produces unique, hard-to-obtain data sets on this process' dynamics. The MONC team is specialized in mathematical models in oncology, with a dedicated axis about modeling support and methodological development for analysis of data from preclinical studies. In particular, the work of S. Benzekry puts emphasis on proposing, studying and validating mathematical models of metastatic development under the action of various therapeutic modalities. Indeed, metastatic expansion remains the main challenge in the treatment of cancer and integrative studies combining experiments, mathematical models and clinical data have the potential to yield predictive computational tools of help to assist both the design of clinical trials and clinical oncologists in therapeutic decisions such as the control of the toxicity/efficacy balance or the optimal combination of treatment modalities.

8.3.1.2. Num4SEP

Title: Numerics for Spherical Electroporation

International Partner (Institution - Laboratory - Researcher):

University of California, Santa Barbara (United States) - ___Mechanical Engineering___ - Frederic Gibou

Start year: 2017

See also: http://num4sep.bordeaux.inria.fr/

Electroporation-based therapies (EPTs) consist in applying high voltage short pulses to cells in order to create defects in the plasma membrane. They provide interesting alternatives to standard ablative techniques, for instance for deep seated badly located tumors. However their use is still limited due to a lack of knowledge of tissue electroporation. The goal of the associate team is to focus on the multiscale numerical modeling of spheroid electroporation, in order to provide new insights in electroporation at the mesoscopic scales (spheroids provide interesting tumor-like biological models). Benefiting from the expertise of F. Gibou's team in HPC for multiphysics, and the expertise of the team MONC in tumor growth and cell electroporation modeling, the goal of the associate team Num4SEP is to obtain accurate and efficient numerical tools for the quantitative evaluation of the EPTs at the mesoscopic scale.

MYCENAE Project-Team

8. Partnerships and Cooperations

8.1. European Initiatives

Together with our BIOS INRA partner, we have participated in a synergistic way in the proposal EVE (*In-Silico Safety and Efficacy Assessment of Reproductive Endocrinology Treatments*) submitted to the H2020-SC1-2016-2017 call (Personalised Medicine), whose PI was Enrico Tronci (Sapienza, Roma).

8.2. National Initiatives

8.2.1. 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.

8.2.2. National Networks

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

8.2.3. National Collaborations

- 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
- Center for Interdisciplinary Research in Biology (CIRB), Collège de France (Alain Prochiantz, Marie Manceau, Laurent Venance)

NUMED Project-Team

5. Partnerships and Cooperations

5.1. National Initiatives

5.1.1. ANR

CNRS InFIniti, 2017-2018 (P. Vigneaux): 12ke in 2017 (pending for 2018)

REO Project-Team

9. Partnerships and Cooperations

9.1. National Initiatives

9.1.1. ANR

9.1.1.1. ANR Project "iFLOW"

Participants: Chloé Audebert, Jean-Frédéric Gerbeau, Florian Joly, 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.

9.1.1.2. 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.

9.1.1.3. 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 "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 Research Visitors

9.3.1. Internships

- Gonzalo Castineira Veiga, Visiting PhD student, Universidade da Coruña, Apr 2017–Jun 2017

SISTM Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

The team have strong links with :

- 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), "Computer research applied to health" (ERIAS) emerging research team.
- Bordeaux and Limoges CHU ("Centre Hospitalier Universitaire").
- Institut Bergonié, Univ Bordeaux through the Euclid platform
- Inria Project-team MONC and CQFD

The project team members are involved in:

- EUCLID/F-CRIN clinical trials platform (Laura Richert)
- The research project “Self-management of injury risk and decision support systems based on predictive computer modelling. Development, implementation and evaluation in the MAVIE cohort study” funded by the Nouvelle-Aquitaine regional council (Marta Avalos).
- Phenotyping from Electronic Health Records pilot project in cooperation with with the ERIAS Inserm emerging team in Bordeaux and the Rheumatology service from the Bordeaux Hospital (Boris Hejblum)

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 http://vaccine-research-institute.fr.

Collaboration with Inserm PRC (pôle Recherche clinique).

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).
- Rodolphe Thiébaut is a member of the CNU 46.04 (Biostatistiques, informatique médicale et technologies de communication).
- Rodolphe Thiébaut is a member of the Scientific Council of INSERM.
- 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).
- Laura Richert is an expert for the PHRC (Programme hospitalier de recherche Clinique).
- Marta Avalos is an expert for L’ANSM (Agence nationale de sécurité du médicament et des produits de santé)

9.2.3. Various Partnership

The project team members are involved in:

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

- F-CRIN (French clinical research infrastructure network) was initiated in 2012 by ANR under two sources of founding "INBS/Infrastructures nationales en biologie et en santé" and "Programme des Investissements d'avenir". (Laura Richert)
- 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)
- INCA (Institut National du Cancer) funded the project « Evaluation de l'efficacité d'un traitement sur l'évolution de la taille tumorale et autres critères de survie : développement de modèles conjoints. » (Principal PI Virginie Rondeau Inserm U1219, Mélanie Prague is responsible of Work package 4 mechanistic modeling of cancer: 5800 euros).
- Contrat Initiation ANRS MoDeL-CI: Modeling the HIV epidemic in Ivory Coast (Principal PI Eric Ouattara Inserm U1219 in collaboration with University College London, Mélanie Prague is listed as a collaborator).

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

9.4.1. Inria International Labs

Fred Hutchinson Cancer center, Seattle;

Baylor Institute for Immunology (Dallas);

Duke University;

Collaborations through clinical trials: NIH for the Prevac trial, NGO Alima for the Prevac trial, Several African clinical sites for Ebovac2 and Prevac trials;

NIH program project grant "Revealing Reservoirs During Rebound", Harvard School of Public Health (HSPH) and the University of California, San Diego (P01AI131385, total budget $1.5M/yr for 5 years starting Oct 2017, both university manage the funding. Mélanie Prague is part of modelling unit of the "Quantitative Methods" research project (budget $220,000/yr). The principal investigator for this core is Victor de Grutolla (HSPH) The overall goal of this grant is to characterize viral rebound following antiretroviral therapy cessation in cohorts of patients who have started therapy early in infection, as well as in a cohort of terminally-ill patients who will interrupt therapy before death and subsequently donate their bodies to research.

Project submitted by the Inria DYNMO-HIVE team with the laboratory "Program for evolutionary Dynamics" at Harvard (head Martin Nowak).

Denis Agniel from the RAND Corporation on developing statistical methods for the analysis of RNA-seq data (Boris Hejblum).

Tianxi Cai from Harvard University on developing methods for the linkage and analysis of Electronic Health Records data (Boris Hejblum).

Katherine Liao from Harvard University on the analysis of Electronic Health Records data in the context of Rheumatoid Arthritis (Boris Hejblum).

Machine learning team Data61 at CSIRO, Australia

9.5. International Research Visitors

9.5.1. Visits of International Scientists

Alison Hill from "Program for evolutionary Dynamics" at Harvard visited the SISTM team twice (each time for 5 days) in May 2017 and July 2017. Main topic discussed was mechanistic modelling of new agents in HIV cure.

Linda Valeri from "Harvard medical school" visited the SISTM team 3 days. Main topic discussed was mediation analysis in high dimension.

Denis Agniel (RAND Corporation) visited B. Hejblum in Bordeaux for a week in May for a research collaboration

Visiting PhD student from Marcus Altfeld's team: Annika Niehrs (2 week stay with SISTM).

9.5.2. Visits to International Teams

Marta Avalos visited David Conesa 1 week in October through the Erasmus+ program Universidad de Valencia (Espagne).

Mélanie Prague got invited in University of Pennsylvania (Philadelphia) for a 2-days research trip in the Biostatistics department on April 2-3 2017.

Mélanie Prague spend 10 days in Boston as an invited researcher in Harvard School of Public Health, Biostatistics department on April 10-15 2017.

Boris Hejblum visited Harvard University for a week in November 2017 for a research collaboration with Katherine Liao & Tianxi Cai.

9.5.2.1. Research Stays Abroad

Marta Avalos was 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/

Perrine Soret was a research student visitor at CSIRO's Data61 in Canberra (Australia) from Feb. 2017 to April 2017. Collaboration with Cheng Soon Ong. Funding: The University of Bordeaux Initiative of Excellence and Zellidja travel grants for a research visit of 3 months.

XPOP Project-Team

9. Partnerships and Cooperations

9.1. National Initiatives

9.1.1. ANR

Mixed-Effects Models of Intracellular Processes: Methods, Tools and Applications (MEMIP)

Coordinator: Gregory Batt (InBio Inria team)

Other partners: InBio and IBIS Inria teams, Laboratoire Matière et Systèmes Complexes (UMR 7057; CNRS and Paris Diderot Univ.)

9.1.2. Institut National du Cancer (INCa)

Targeting Rac-dependent actin polymerization in cutaneous melanoma - Institut National du Cancer

Coordinator: Alexis Gautreau (Ecole Polytechnique)

Other partners: Laboratoire de Biochimie (Polytechnique), Institut Curie, INSERM.

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.

Geneviève Robin was recipient of a *Visiting Student Researcher Fellowship* from the France Stanford Centre for a research fellowship in the Department of Statistics at Stanford University. She worked on imputation of missing data to medical databases in a distributed framework.

9.3. International Research Visitors

9.3.1. Visits of International Scientists

Ricardo Rios, Universidad Central de Venezuela, Caracas: September 2017.